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Organic and inorganic nanofilms on Nitinol and Phynox: from fundamental towards applications in biomaterials

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By Sébastien Devillers

Abstract:

This thesis is devoted to the improvement of biomaterials and more specifically of two increasingly used ones: Nitinol and Phynox. Nitinol is a very complex yet promising material especially in the field of biomedical applications because of its remarkable mechanical properties (shape memory alloy). Phynox is another alloy very commonly used for the design of biomedical devices such as stents and coils specifically because of its important corrosion resistance.

In the first part of this thesis, the characterization of the Nitinol and Phynox surface states are reported as well as several surface modification methods applied to these materials. The goal of these surface modifications is not to obtain a perfect “ready to use” biomaterial but rather to provide interesting functionalization methods with two targets: to protect the underlying substrate against corrosion (and avoid ions leaching) and to form functional platforms for the post-grafting of a broad range of molecules in order to improve the material-biological environment interactions.

Regarding Nitinol, the impact of typical shape-setting heat treatment and chemical etching on the surface composition and the resulting resistance to corrosion of Nitinol wires identical to the ones used for the fabrication of braided Nitinol stents is studied. The modification of Nitinol by the electrografting of 1,4-carboxybenzene diazonium and the formation of a 11-phosphoundecanoic acid monolayer is carried out with the prospect of using these coatings as platform for post-grafting chemical reactions. The electrografting method is proved to have negative impact on the corrosion resistance of Nitinol and the resulting electrografted carboxybenzene coating leads to a poor efficiency for these post-grafting chemical reactions. On the other hand, 11-phosphoundecanoic acid monolayers exhibit a much better efficiency to act as a platform for post-grafting chemical reactions and no negative impact on the corrosion resistance of the underlying substrate. A brief study of the impact of the solvent and temperature on the grafting of phosphonic acids on the surface of mechanically polished Nitinol is also carried out. On the one hand, it turns out that water is a very suitable solvent for this surface modification method. On the other hand, increasing the temperature does not lead to an increase of the quantity of grafted phosphonic acids but to an improvement of the organization of the resulting monolayer and therefore of its efficiency as corrosion inhibitor. Finally, induction heating of Nitinol in pure water appears to be an original and promising alternative to conventional hydrothermal treatment usually applied in order to decrease the surface nickel concentration and reinforce the resistance of the oxide layer to corrosion. Both induction and conventional heating treatments lead to similar results. However, on the whole,

induction heating leads to slightly better results than conventional heating does (i.e. a higher hydroxylation of the surface, a more important decrease of the nickel surface concentration and a similar corrosion resistance improvement).

Regarding Phynox, a systematic corrosion resistance evaluation of Phynox stents provided by Cardiatis is carried out after several different surface treatments. It appears that Phynox have a remarkable resistance to corrosion and especially to localized corrosion phenomena. However, despite this very good corrosion resistance, there is a strong interest in modifying its surface with the prospect of improving the material-biological environment interactions. Therefore, similarly to Nitinol, the Phynox surface functionalization with bifunctional phosphonic acid molecules toward a versatile platform for post-grafting chemical reactions is carried out. The effect of induction heating on the grafting of such bifunctional phosphonic acids is also studied. It turns out that induction heating can lead to a much more selective adsorption of bifunctional phosphonic-carboxylic molecules via the phosphonic acid function, leaving a higher amount of free carboxylic acid functions to react during the second modification step. Finally, it is shown that such phosphonic acid monolayers perfectly resist the typical ethylene oxide sterilization process applied to biomaterials before their conditioning and utilization.

In the second part of this thesis, we present a research carried out at the University Hospital of Geneva (HUG) in the frame of the FIRST-DEI VISMAT convention (RW – n°516114) in collaboration with Cardiatis and the HUG. This work is dedicated to a study of the impact of different surface treatments and of the imaging parameters and conditions on the MRI visibility of Nitinol and Phynox wires and stents. Two main types of artifacts are investigated: susceptibility and RF artifacts.

By means of an algorithm developed for this purpose, it is shown that the surface state of the observed material can have a significant influence on the produced susceptibility artifact. Heat treatment of Nitinol appears to have a negative impact on its apparent magnetic susceptibility while the removal of the oxide layer by chemical etching is favorable to a low apparent magnetic susceptibility. Phynox is a much less suitable material for MRI examinations given its apparent magnetic susceptibility about 10-fold higher than the one of Nitinol. In the case of Phynox, however, the heat treatment of Phynox induces a slight decrease of this apparent magnetic susceptibility while its chemical etching does not appear to have any significant impact.

The impact of several parameters on the MRI visibility of braided stents i.e. on the importance of the produced susceptibility and RF artifacts is also studied. SE sequences are less sensitive to susceptibility artifacts and lead to the acquisition of better images than the GRE sequences do. The stent orientation with respect to the main magnetic field is also crucial. Interestingly, it is shown that the RF artifacts could be beneficial as they could lead to a signal enhancement in the stent lumen at low flip angles.

Finally, antiferromagnetic NiO and CoO layers are formed on Nitinol and Phynox wires, respectively, by electrodeposition and thermal oxidation. The impact of such oxide layers on the MRI behavior of Nitinol and Phynox appears to be dramatically negative.

God made solids, but surfaces were the work of the devil - Wolfgang Pauli

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General Introduction

Chapter 1. General introduction

The research presented in this manuscript deals with two increasingly used biomaterials i.e. Nitinol and Phynox. This manuscript is divided into two main parts: a first one (including chapters 2 and 3) gathering several studies about the characterization and the application of various surface treatments on Nitinol and Phynox and a second one consisting in a study of the MRI visibility of these materials (chapter 4).

Among the surface treatments presented in the first part, some have already been largely studied in the literature. This manuscript aims to bring supplementary data on these topics in order to clarify some controversial results presented in the literature. Other treatments presented in this work are innovative and could constitute an effective basis for the further improvement of the surface properties of these biomaterials. The goal of these surface modifications is thus not to obtain a perfect “ready to use” biomaterial but rather to provide interesting functionalization methods with two targets: to protect the underlying substrate against corrosion (and avoid ions leaching) and to form functional platforms for the post-grafting of a broad range of molecules in order to improve the material-biological environment interactions.

This manuscript is divided into four chapters. The first one is an introductory chapter dedicated to a review of the literature concerning the considered topics. General considerations about stents and biomaterials and about the molecular surface modification of oxidizable metals with self-assembled monolayers are first presented. Then the reader is introduced to the Nitinol discovery, its remarkable mechanical properties and its various application fields. Nitinol biocompatibility and resistance to corrosion is discussed as well as various reported methods aiming to improve these properties. This first chapter ends with a few words about Phynox and more generally about Co-Cr alloys, their properties and surface modification.

The second chapter is dedicated to Nitinol. In a first part, we report on the impact of typical shape-setting heat treatment and chemical etching on the surface composition and the resulting resistance to corrosion of Nitinol wires identical to the ones used for the fabrication of braided Nitinol stents. In a second part, we report on studies carried out on plane Nitinol substrates. These Nitinol substrates were analyzed in their “as received”, heat treated and mechanically polished states. The rest of the second part of this chapter is dedicated to the surface modification of mechanically polished plane Nitinol substrates toward a versatile platform for post-grafting chemical reactions, the study of parameters influencing the grafting of phosphonic acids SAMs on these surfaces and on an original and promising alternative to conventional hydrothermal treatment usually applied in order to reinforce the resistance of the oxide layer to corrosion.

The third chapter focuses on the case of Phynox. In the first part, we present the results of a systematic corrosion resistance evaluation of Phynox stents provided by Cardiatis after

several different surface treatments. The second part of this chapter is dedicated to the study of Phynox surface functionalization with bifunctional phosphonic-carboxylic acid molecules toward a versatile platform for post-grafting chemical reactions. In this context, the impact of induction heating on the grafting of these bifunctional molecules has been assessed as well as the resistance of the obtained coating to the ethylene oxide sterilization treatment.

In the fourth chapter of this manuscript, we present a research carried out at the University Hospital of Geneva (HUG) in the frame of the FIRST-DEI VISMAT convention (RW – n°516114) in collaboration with Cardiatis and the HUG. This work is dedicated to a systematic study of the impact of different surface treatments and of the imaging parameters and conditions on the MRI visibility of Nitinol and Phynox wires and stents. Two main types of artifacts are presented and investigated: susceptibility and RF artifacts. In the first part of this chapter, we report on the influence of the Nitinol and Phynox surface state on their apparent magnetic susceptibility assessed by means of an algorithm developed in the frame of this work. The second part is dedicated to the study of the impact of several parameters on the MRI visibility of braided stents. In the last part of this chapter, we report on the creation, the characterization and the impact of NiO and CoO layers on the MRI behavior of Nitinol and Phynox.

1.1. Stents and biomaterials: general considerations

1.1.1. Biocompatibility

The consensus conference of the European Society for Biomaterials defined the biomaterial as “a nonviable material used in a medical device, intended to interact with biological systems” (Chester, UK, 1986). During the second Biomaterials Consensus Conference, this definition has been updated as “a material intended to interface with biological systems to evaluate, treat, augment, or replace any tissue, organ, or function of the body” (Chester, UK, 1992). This definition extends the use of the “biocompatibility” term to any kind of device intended to interface with biological systems and not only prostheses.

When a synthetic material interacts with a biological system, one should consider two types of effects: the effects of the biological system on the biomaterial (i.e. wear, fatigue, degradation or corrosion, *etc.*) and the effects of the biomaterial on the biological system (i.e. its aimed effect but also all the possible side effects such as possible inflammatory responses, ions releases that could lead to allergenic/carcinogenic effects, ...). Thus a biomaterial has to be inert toward the biological system i.e. to not lead to negative responses of the body but also to resist degradation in the biological system.

In this context, the choice of the material is obviously crucial in order to obtain a biomedical device with the desired bulk properties and able to play its role. However, the surface of the biomaterial is the only part of the device which is in direct contact with the biological environment. Therefore, the surface properties of a biomedical device are one of the key factors to control in order to improve the biomaterial-biological system interactions.

1.1.2. Stents

In medicine, a stent is a tubular device inserted into the lumen of an anatomical vessel to prevent or counteract a localized flow constriction. Most of the time, stents are made of metal alloys such as SS316L, Co-Cr alloys or Ti-alloys. Although stents can basically be used to maintain any tubular structure opened (e.g. laryngeal and tracheal stents, urethral stents, etc.), one of the most common use of such implants is the treatment of cardiovascular diseases by angioplasty with vascular stenting. Angioplasty is a minimally invasive procedure performed to improve blood flow in the body's arteries and veins. This procedure is commonly used to treat conditions that involve a narrowing or blockage of arteries or veins including narrowing of large arteries due to atherosclerosis, peripheral artery disease, renal vascular hypertension, carotid or coronary artery diseases just to name a few of them. In an angioplasty procedure, imaging techniques are used to guide a balloon-tipped catheter into an artery or vein and advance it to where the vessel is narrow or blocked. The balloon is then inflated to open the vessel, deflated and removed. During this procedure, a stent may be permanently placed in the newly opened artery or vein to help it remain open ¹. Even if the use of stents contributes to decrease the restenosis phenomenon (reobstruction of the vessel after the angioplasty), in-stent restenosis remains a great concern ². Restenosis can be due to an exaggerated deployment of the stent ³, an inappropriate design ^{4,5} or the leaching of potentially toxic metallic elements ^{6,7}. The combination of these factors results in the formation of a thrombus, inflammation reactions, an exaggerated cellular proliferation and the formation of a new extracellular matrix inside the vessel ⁴. The restenosis and stent corrosion (thus metallic ion leaching) issues strongly depend on the surface properties of the implant. It is thus clear that the control of these surface properties is essential in order to decrease at most the risk of restenosis.

1.2. Molecular surface modification of oxidizable metals

Since R. G. Nuzzo and D. L. Allara first reported on the self-assembling of disulfide on gold in 1983 ⁸, self-assembled monolayers (SAMs) have attracted immense attention for both fundamental and applied research. By definition, SAMs are ordered molecular assemblies that are formed spontaneously by the adsorption of a surfactant with a specific affinity of its head group to a substrate ⁹. A SAM is composed of a large number of molecules with a head group that chemisorbs onto a substrate, an end group that interacts with the outer surface of the film, and a spacer (backbone) chain group that connects the head and end groups resulting in a coating. Interactions between spacer groups of different molecules, such as Van der Waals forces and/or electrostatic interactions (e.g. hydrogen bonding), hasten SAM film formation, contribute to its stability and lead to the organization and close packing of the SAM. At their best, self-assembled monolayers provide a dense, nearly crystalline organic skin on an underlying solid surface (Figure 1.1).

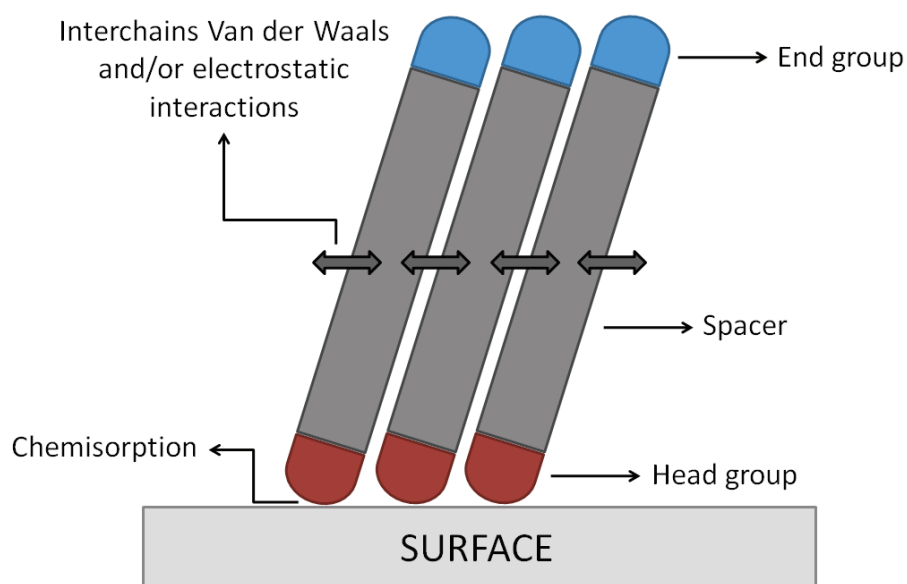


Figure 1.1. Schematic representation of a surfactant molecule in interaction with a surface and the rest of the monolayer.

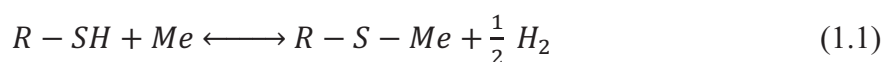
Nowadays, numerous publications report on the use of surface modification with SAMs for various purposes such as adherence, lubrication, the study of electrochemical processes and of biological interfaces, catalysis, corrosion inhibition, *etc.* Actually, one can impart the desired surface properties or activity to a substrate by choosing properly the end group of the grafted molecules.

The choice of the head group is obviously also crucial in order to form a strongly attached SAM to the desired surface. Several chemical functions can be used as head group for the formation of SAMs. Among them, the most studied ones are the organothiols, organosilanes, carboxylic acids and organophosphonic acids. In the following sections, we will provide an overview of the scientific literature content regarding the formation of SAMs with these head groups.

1.2.1. Organothiol monolayers

Due to their ease of preparation and well-defined order and also the relative inertness of the substrate, which makes it comparatively easy to clean, thiols on gold have become a model system for SAMs⁹⁻¹¹. However, there are also practical interests in modifying oxidizable metal surfaces (e.g. silver, copper, nickel, iron, zinc, *etc.*) with such SAMs.

It is usually assumed that stable SAMs involve the oxidative addition of the S-H bond to the metal surface, followed by a reductive elimination of the hydrogen as described in the reaction (1.1).



where Me is the metal surface¹⁰.

The formation of an alkanethiol monolayer can be schematized as the succession of two distinct steps ¹²:

- The first and quick one consists in the chemisorption of most of the molecules constitutive of the monolayer. For example, the adsorption of *n*-alkanethiols from a dilute solution at room temperature leads to the formation of a relatively dense monolayer in a few minutes. At the end of this step, the hydrocarbonated chains (spacers) are close enough to each other to allow Van der Waals interactions to appear but the monolayer is still poorly organized.
- The second step is much longer (from several hours to a few days) and consists in an optimization of the interchain interactions and a densification of the monolayer. Supplementary thiols adsorb on the surface and the grafted molecules organize themselves in order to obtain a stable and organized configuration.

The structure of the SAM strongly depends on the underlying surface. Probably the most popular system is that of *n*-alkanethiols on Au(111). In the full coverage phase (that corresponds to the highest possible packing of molecules by definition), *n*-alkanethiols on Au(111) adopt a $(\sqrt{3}\times\sqrt{3})R30^\circ$ structure relative to the underlying Au(111) substrate corresponding to a molecule-molecule spacing of ~ 5 Å. This structure implies that hydrocarbon chains of the grafted alkanethiols are tilted away from the normal by about 32° with the structure consisting of an all-*trans* zig-zag chain ⁹. The tilt of the hydrocarbonated chains maximizes the attractive interactions (Van der Waals type interactions of about 5.8-7.5 kJ.mol⁻¹) between them ¹².

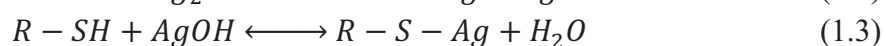
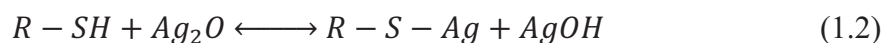
Ethanol is the solvent that is most widely used for preparing SAMs even if the limiting mass coverage and wettability of SAMs formed with other solvents (e.g. tetrahydrofuran, dimethylformamide, acetonitrile, cyclooctane or toluene) do not vary significantly from those formed from ethanolic solutions. The widespread use of ethanol is due to the fact that it solvates a variety of alkanethiols with varying degrees of polar character and chain length, it is inexpensive, available in high purity and has a low toxicity. The effect of the solvent on the kinetics of formation and the mechanism of assembly are complex and poorly understood. However, some studies on this topic have led to a qualitative understanding of how solvent can affect the assembly process: solvent-substrate and solvent-adsorbate interactions complicate the thermodynamics and kinetics of the assembly. For example, solvent-substrate interactions can decrease the rate of adsorption of thiols from solution because the solvent molecules must be displaced from the surface prior to the adsorption of thiols, which are less prevalent in solution than the solvating molecules ¹¹. The use of long hydrocarbons, such as dodecane and hexadecane, as solvents may improve the kinetics of formation in some cases, but the strong solvent-adsorbate interactions impede the organization of the resulting alkanethiol SAMs.

As already said, gold is a model substrate for the study of organothiol SAMs because of its inertness (it does not oxidize at temperatures below its melting point, it does not react with atmospheric O₂, it does not react with most chemicals), the commercial availability of gold single crystals and its ability to bind thiols with high affinity ¹¹. However, there is a

significant interest in modifying more complex metals such as Ag, Cu, Ni, Zn, Fe or even alloys such as steel ¹³⁻¹⁵. These metals and alloys are oxidizable i.e. unlike gold, an oxide layer spontaneously forms at their surface.

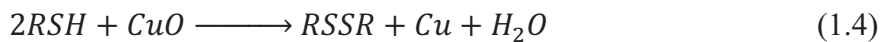
When grafted on silver surface, organothiol monolayers adopt a different structure than on gold i.e. the hydrocarbon chains are canted 12° relative to the surface normal (vs. 32° for SAMs on gold) ^{16,17}. The packing density of alkyl thiolates is thus greater on silver than on gold ^{16,18}. Note that it is actually thought that the alkyl chains tilt to acquire a closer packing of the molecules without changing the 2D periodicity of the anchoring groups ¹⁷. The nature of the Ag-S bond is described as covalent ¹⁹ with a small ionic contribution ²⁰. Such monolayers have been shown to be able to effectively block the oxidation of the underlying substrate as well as the electrochemical reactions at the surface ²¹⁻²³.

Even more interestingly, authors pointed out the ability of organothiols to remove the oxides as well as the physisorbed atmospheric carbon contaminants present at the silver surface ^{16,24}. Himmelhaus *et al.* investigated this phenomenon and stated that the self-assembling of organothiols on silver occurs following an island growth model i.e. that well-packed island of molecules appears on the surface before reaching a high coverage ²⁵. Initial adsorption occurs into a physisorbed state on the oxidized silver surface, which is contaminated by adsorbed hydrocarbons or solvent and molecular contaminants from the alkanethiol solution. In the physisorbed phase, reduction of the surface oxide by the alkanethiols creates active surface sites for silver-thiolate formation. According to their results, they proposed the following equations for the grafting of organothiols on oxidized silver surface

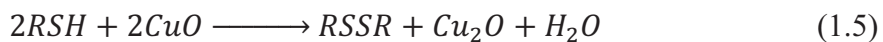


However, the initial oxide layer is often removed before the self-assembling process in order to decrease the amount of oxides to be reduced by the thiols ²³.

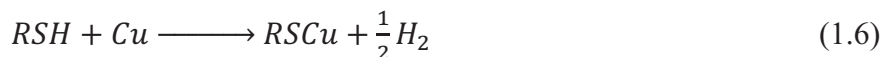
Organothiol self-assembled monolayers have also been shown to form protective monolayers on both electroreduced ²⁶ and oxidized copper surface ^{27,28}. The alkanethiol monolayers formed on copper are structurally similar to those formed on silver (i.e. the hydrocarbon chain is oriented more perpendicularly with respect to the surface than on gold) ²⁹. However, the alkanethiol monolayers formed on copper and silver exhibit similar wetting properties than the ones formed on gold, although they differ significantly in structure ³⁰. Folkers *et al.* showed that the oxidation of an organothiol SAM on copper proceeds with a transformation of the adsorbed thiolates into sulfonates which are then quickly displaced when the surface is exposed to fresh organothiols ³¹. Note that it has also been shown that such oxidized sulfur species can appear during the self-assembling process and not be replaced by fresh thiols if the steric hindrance of the grafted molecules is too important ³². As is the case of silver, the cleaning and reducing properties of organothiols have been largely reported and discussed ³³⁻³⁶. It has been showed ³⁷ that the alkanethiols are not adsorbed directly on the CuO surface but reduce the oxide layer with disulfide formation:



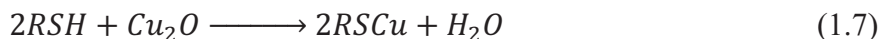
or



This reaction continues to reduce all the CuO layer and the monolayer is formed on the reduced surface by the following equations:



or



Note also that a better efficiency in reducing the copper oxide layer is obtained when the organothiol concentration is increased ³⁸.

Zinc is a material of interest for many applications including the replacement of chromate conversion coatings. In this context, it has been shown that freshly electrodeposited Zn layers can be successfully modified with organothiols used as a junction between zinc and polymer coatings ^{39,40}. More fundamentally, Nogues and Lang studied the modification of metallic zinc with pure organothiols of different chain length and showed that zinc behaves similarly to Ag and Cu. They deduced from their analysis that the alkyl chains tilt angle is 14° for *n*-decanethiol and 18° for *n*-dodecanethiol (and thus depends on the chain length) ⁴¹. Note that good quality organothiol SAMs can also be obtained on oxidized zinc surfaces ^{42,43}. However, the modification of oxidized zinc surfaces leads to the oxidation of anchored thiolate species to sulfinates and sulfonates. Therefore, the modification is of much better quality when carried out on oxide-free zinc surface (e.g. electroreduced) ⁴⁴. As the organothiols act as reductive agents on oxidized zinc like in the case of Cu and Ag ⁴⁵, the immersion solution concentration has also a critical influence on the quality of the resulting SAM ⁴⁴.

The case nickel surface is somewhat different from the cases of silver, zinc and copper in the sense that organothiols have been shown to be inefficient in reducing nickel oxides present at the surface of the substrate during the immersion step ⁴⁶. As a result, the oxides present at the surface cause the thiolate species to transform into sulfinates and sulfonates which are known to be responsible for poor organization and stability of the monolayer. It is thus necessary to get rid of this oxide layer prior to the exposure of the surface to thiols. This can be made by an electrochemical reduction before ⁴⁶ or during ⁴⁷ the exposure of the surface to organothiols. The choice of the solvent is also critical for obtaining a good monolayer on nickel. Ethanol molecules can adsorb on nickel surface and therefore compete the adsorption of organothiols. Exposing the oxide free nickel surface to pure organothiol liquids has been shown to lead to the formation of organized and chemically stable SAMs with only thiolates as anchoring groups (with a small amount of disulfide species) ^{46,48}. Note that good quality monolayers can nevertheless be obtained from organothiol solutions in polar solvents (for example ethanol or acetonitrile) provided using sufficiently high concentrations and long immersion times while apolar solvents do not lead to the formation of SAMs on Ni ^{49,50}. Iron is somewhat similar to

nickel in the sense that one has to get rid of the oxides present at the surface prior to the SAM formation because of the inability of organothiols to reduce iron oxides present at the surface of the substrate during the immersion step ⁵¹. Nevertheless, provided having an oxide-free surface, fairly packed self-assembled monolayers comparable to the ones obtained on copper can be formed on iron and efficiently protect its surface from corrosion ^{52,53}.

1.2.2. Organosilanes monolayers

Like organothiols, the formation of SAMs from organosilicon compounds is one of the oldest and most studied methods for forming organic monolayers particularly often applied on glass and on the native surface oxide layer of silicon ⁵⁴. Aswal *et al.* wrote a review gathering the typical conditions used for the formation of organosilicon SAMs and the formation mechanism of these SAMs during the silanization process ⁵⁵.

Typically, the chemisorption of silane molecules is achieved by immersion of freshly prepared hydroxylated surfaces into a reaction bath which is usually a 10^{-3} M solution of silane (RSiX_3 where $\text{X}=\text{H}$, Cl , OCH_3 or OC_2H_5) in alkane solvent such as dicyclohexyl or *n*-hexane (the addition of a fraction of CCl_4 favoring the solubility of polar end group $-\text{SiX}_3$ of the silane molecule). As they are extremely water sensitive, trichlorosilanes or trialkoxysilanes are incorporated at the last moment under inert atmosphere to avoid their polymerization in the medium. Monolayers prepared with trichlorosilane molecules typically form in about 1 h, while for trimethoxysilane or triethoxysilane molecules the monolayer formation takes about 2 days. Note that, like for alkanethiols, the choice of the solvent is critical for the formation of organosilicon monolayers. For instance, while hexane or heptanes solvent results in the formation of compact high-quality octadecyltrichlorosilane monolayers, dodecane causes the formation of multilayered films.

The mechanism of SAM formation during silanization process takes place in four steps schematized in Figure 1.2. The first step consists in the physisorption of the silane molecules at the hydrated oxide surface. In the second step the silane head groups arriving close to the substrate undergo a hydrolysis (in the presence of the adsorbed water layer on the surface) into highly polar trihydroxysilane $-\text{Si}(\text{OH})_3$. These polar $-\text{Si}(\text{OH})_3$ groups form covalent bounds with the hydroxyl groups on the oxide surface and finally, the condensation reaction goes on between silanol functions of neighbor molecules leading to the formation of a siloxane network at the surface.

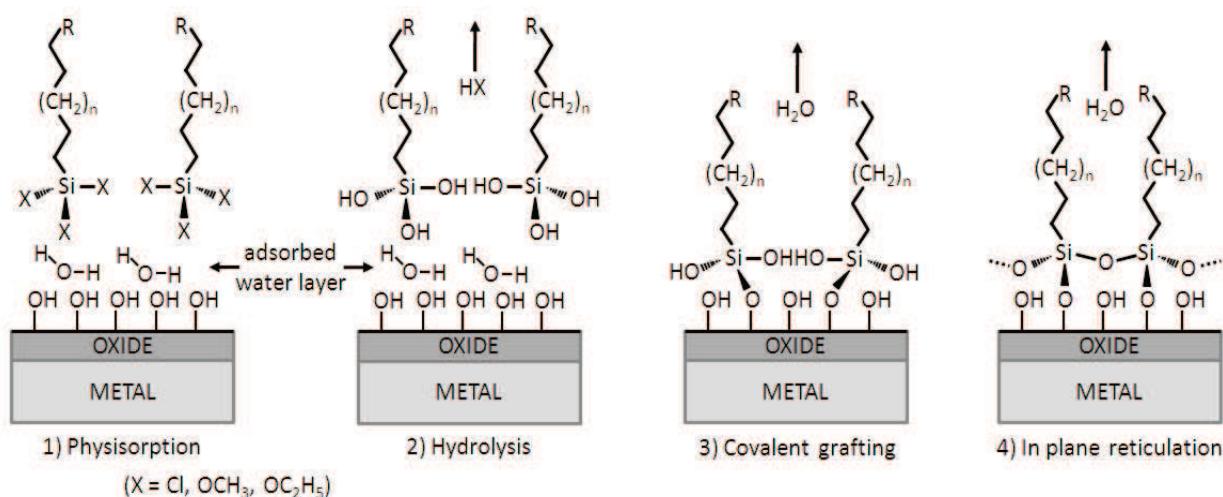


Figure 1.2. Schematic representation of different steps involved in the mechanism of organosilanes SAM formation on a hydrated oxide surface⁵⁵.

It has been shown⁵⁶ that the lateral condensation reaction (formation of the siloxane network) dominates the anchorage at the surface. As a consequence, organosilicon monolayers most likely grow via island nucleation (islands of well-ordered and reticulated molecules) followed by the coalescence of these islands^{55,57}.

Note also that the reactivity of the organosilanes depends on the anchoring group nature. Fadeev established the following reactivity ranking among three commonly used anchoring groups: $R-SiCl_3 > R-Si(OCH_3)_3 > R-SiH_3$ ⁵⁶. However, alkyltrichlorosilanes have a major drawback i.e. hydrochloric acid is produced at the surface during their hydrolysis. This acid can induce the corrosion of the substrate and therefore alters the modified material but also decreases the uniformity of the formed monolayer⁵⁷.

Similarly to gold for organothiols, silicon is the typical model substrate for the study of organosilicon compounds SAMs. However, unlike organothiols, organosilicon compounds form SAMs on hydrated oxide layers. Therefore, this method appears to be *a priori* more suitable for the formation of SAMs on oxidizable substrates. As a result, numerous publications report on the surface modification of oxidizable metals such as Ag^{58,59}, Al and its alloys⁶⁰⁻⁶⁴, Cu⁶⁵⁻⁶⁷, Fe⁶⁸⁻⁷⁰, Ta^{71,72}, Ti⁷³⁻⁹⁰, Zn⁹¹, Zr and Hf⁵⁶ and alloys such as steel^{92,93} but also glasses such as ITO⁹⁴⁻¹⁰¹.

1.2.3. Organocarboxylic acid monolayers

Among the different possible head groups, carboxylic acid function has received considerable attention for the formation of SAMs¹⁰². Alkanecarboxylic acids have been shown to form compact SAMs on oxidizable metals such as Ag¹⁰³⁻¹⁰⁶, Al¹⁰⁷⁻¹⁰⁹, Cu¹¹⁰, Fe¹¹¹⁻¹¹³, Ti¹¹⁴⁻¹¹⁶, Zn¹¹⁷⁻¹¹⁹, on alloys such as steel¹²⁰⁻¹²³ and Mg alloys¹²⁴ or on glasses such as ITO¹²⁵.

It is known that carboxylate ion CO_2^- can coordinate to a metal M ion three mode as described in Figure 1.3.¹²⁶

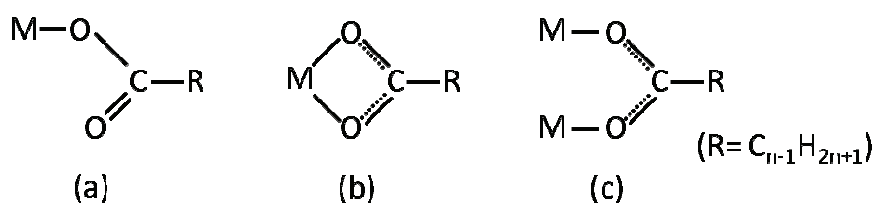


Figure 1.3. Schematic representation of the three modes of metal coordination by CO_2^- function: monodentate complex (a), bidentate chelate (b) and bridging complex (c) ¹²⁶.

The binding mode of alkanecarboxylates depends on the nature of the modified surface. For examples, carboxylates exhibits bidentate bonding on silver ¹²⁷ or iron ¹²⁸ oxide surfaces and monodentate bonding on copper ¹¹⁰, aluminum ¹²⁹, titanium ¹³⁰ and magnesium alloys ¹²⁴.

1.2.4. Organophosphonic acid monolayers

Organophosphonic acids constitute another class of compounds that can form SAMs. Like organosilicons and carboxylic acids, phosphonic acids are able to graft the oxide layer present at the surface of oxidizable metals alloys such as steel ¹³¹⁻¹³⁴, Ta ¹³⁵⁻¹³⁹, Ti ^{57,140-142}, Zr ^{142,143}, Al ¹⁴⁴⁻¹⁵¹, Si ¹⁵²⁻¹⁵⁶, Cu ^{157,158} or Zn ¹⁵⁹⁻¹⁶¹.

In the literature, the grafting of phosphonic acids on oxide surfaces is described as an acid-base reaction between the phosphonic acid functions and the hydroxide groups present at the surface of the oxide layer, resulting in covalent P-O-M bounds. The number of formed P-O-M bonds depends on the substrate. Organophosphonic acids can bind a surface is a mono- ^{135,143}, bi- ^{131,135,143,162} or tridentate way ^{143,153,155,158,163} (Figure 1.4). Note that the binding mode of phosphonic acids can change over time. Indeed, Pellerite *et al.* ¹⁶⁴ showed that at low degree of modification, all phosphonic acid are bound to the Al surface in a tridentate way while, as the modification time increases, bidentate and even monodentate binding mode appear on the surface along with a decrease of the tilt angle of the spacer groups with respect to the normal surface.

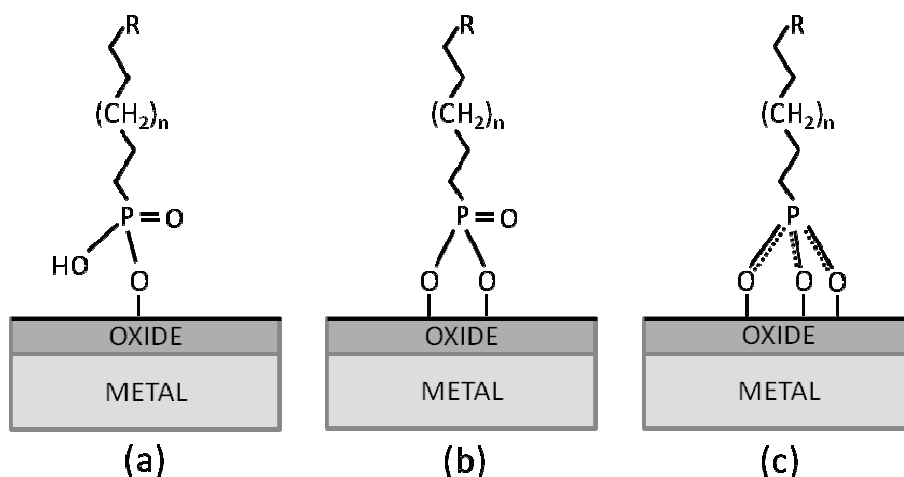


Figure 1.4. Schematic representation of the three binding modes of an organophosphonic acid molecule on the oxide layer present at the surface of the metallic substrate: mono- (a), bi- (b) or tridentate (c).

Phosphonic acids have two main advantages compared to organosilicon compounds. First, they are resistant to homocondensation (creation of P-O-P bonds) while organosilicons form siloxane networks¹⁶⁵. As a consequence, the formation of organophosphonic acid monolayers is more similar to the formation of organothiol monolayers than to the formation of organosilicons ones: while organosilicons SAMs have an islandlike growth (due to the rapid formation of Si-O-Si bounds between the molecules), organophosphonic acids bind uniformly and randomly on the surface, leading to the formation of loose-packed and weakly organized SAMs at low coverage⁵⁷. The second advantage of organophosphonic acids is their important resistance to hydrolysis^{142,163,165}. This makes phosphonic acid compounds particularly interesting candidates for the formation of SAMs designed to be applied in aqueous medium.

1.3. Nitinol

1.3.1. History, mechanical properties and applications

1.3.1.1. History¹⁶⁶

This Ni-Ti alloy was discovered by W. J. Buehler in 1959 at the Naval Ordnance Laboratory and named it Nitinol as an acronym for **N**ickel **T**itanium **N**aval **O**rdnance **L**aboratory. He demonstrated the material's unique fatigue-resistant and shape memory properties. In 1962, F. E. Wang joined Buehler's group at the NOL. His expertise in crystal physics allowed him to discover how the shape-memory of Nitinol works.

However, progress in getting Nitinol into consumer applications came slowly because of early problems with its manufacture and because of its cost. The first successful Nitinol product was the Raychem Corporation's CryofitTM "shrink-to-fit" pipe coupler, introduced in 1969 which solved the problem of coupling hydraulic-fluid lines in the F-14 jet fighter built by the

Grumman Aerospace Corporation. Another early use of Nitinol was in orthodontic bridge wires by the Dr. G. Andreasen. With improved manufacturing techniques the commercial use of Nitinol increased during the 1970s and 1980s.

1.3.1.2. Mechanical properties ¹⁶⁷

Nitinol is known to be a shape memory alloy (SMA). These materials are characterized by a solid-solid (austenite-martensite) transformation through a critical temperature range or in special situations with applied stress and strain. Thus Nitinol is said to undergo a martensite transformation. In the austenite (high temperature) form, the Nitinol crystal structure is that of an “ordered” cubic structure. As the alloy cools through the transformation temperature range, its atoms “shear”, forming the new martensite phase. In the Nitinol-type alloys, this transformation temperature range can be varied over a realistic temperature range from 100°C to well below the liquid nitrogen temperature (-195.8°C) by varying the nickel-titanium ratio or ternary alloying with small amounts of other metallic elements, e.g. Co, Fe, V, *etc.* ¹⁶⁶ The two external variables inducing the martensite transformation are the temperature and the stress. It is thus possible to draw the stability domains of these two crystalline phases with respect to these two variables (Figure 1.5).

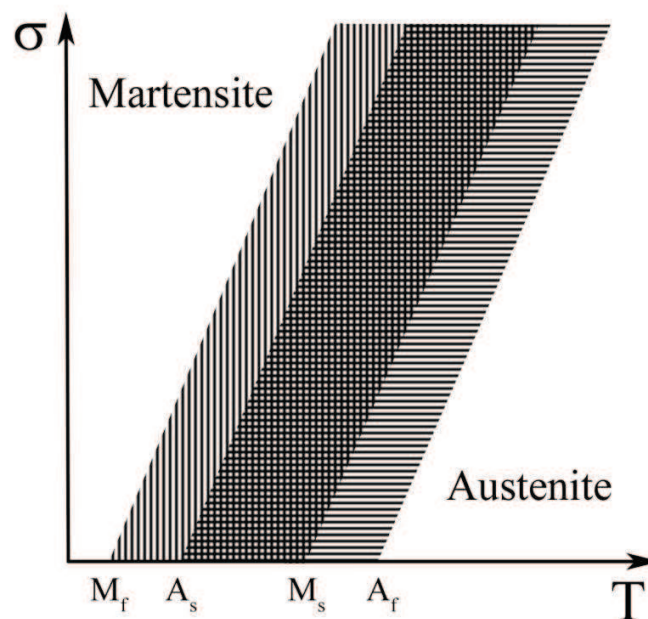


Figure 1.5. Martensite and austenite stability domains as a function of the stress and the temperature ¹⁶⁷.

On this phase diagram, four points can be defined:

- M_s (martensite start): the temperature or the stress value at which the martensite phase starts to form in an austenite SMA
- M_f (martensite finish): the temperature or the stress value at which the austenite phase has completely disappeared (the SMA being in the martensite phase at 100%)

- A_s (austenite start): the temperature or the stress value at which the austenite phase starts to form in a martensite SMA
- A_f (austenite finish): the temperature or the stress value at which the martensite phase has completely disappeared (the SMA being in the austenite phase at 100%)

The origin of the special mechanical properties of Nitinol lies in the reversibility of the martensite transformation. This transformation is characterized by a hysteresis as shown in Figure 1.6.

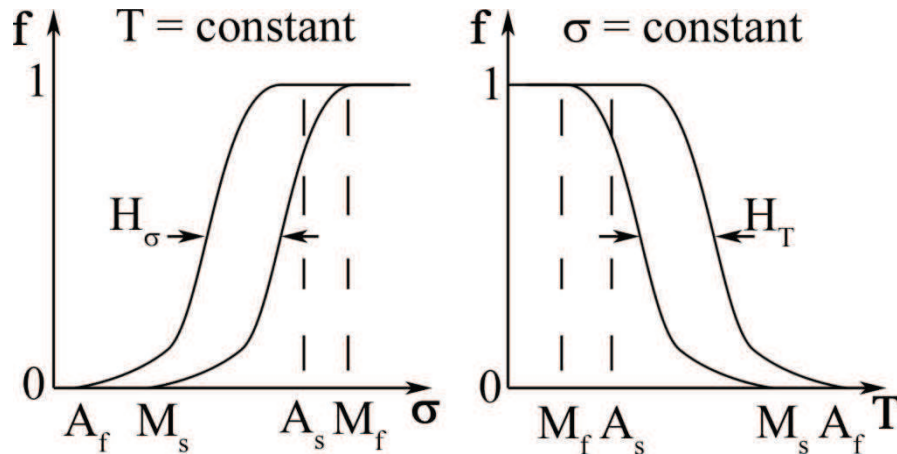


Figure 1.6. Representation of the phase transformation hysteresis: volume fraction of austenite vs. stress (left part) and volume fraction of austenite vs. temperature (right part) ¹⁶⁷.

Two very interesting properties ensue from this reversible phase transformation: the simple shape memory effect and the superelasticity.

1.3.1.2.1. Simple shape memory effect

If one applies a sufficient stress (σ) to an “ordinary” alloy, it undergoes a permanent strain (ϵ_p) which remains after the removal of the stress (see Figure 1.7). This plastic strain does not evolve if the alloy is then submitted to temperature variations. The pure elastic strain (corresponding to the elastic limit σ_E) does not exceed a few per thousands (‰) while the plastic strain varies from a few per cents (%) to a few dozen of per cents (%).

On the other hand, a SMA in a complete martensite state ($T_0 < M_f$) can undergo an apparent plastic deformation of a few per cents (up to 6%) and completely recovers its initial shape by a simple heating up to T_1 ($T_1 > A_f$). This effect is called the simple shape memory effect.

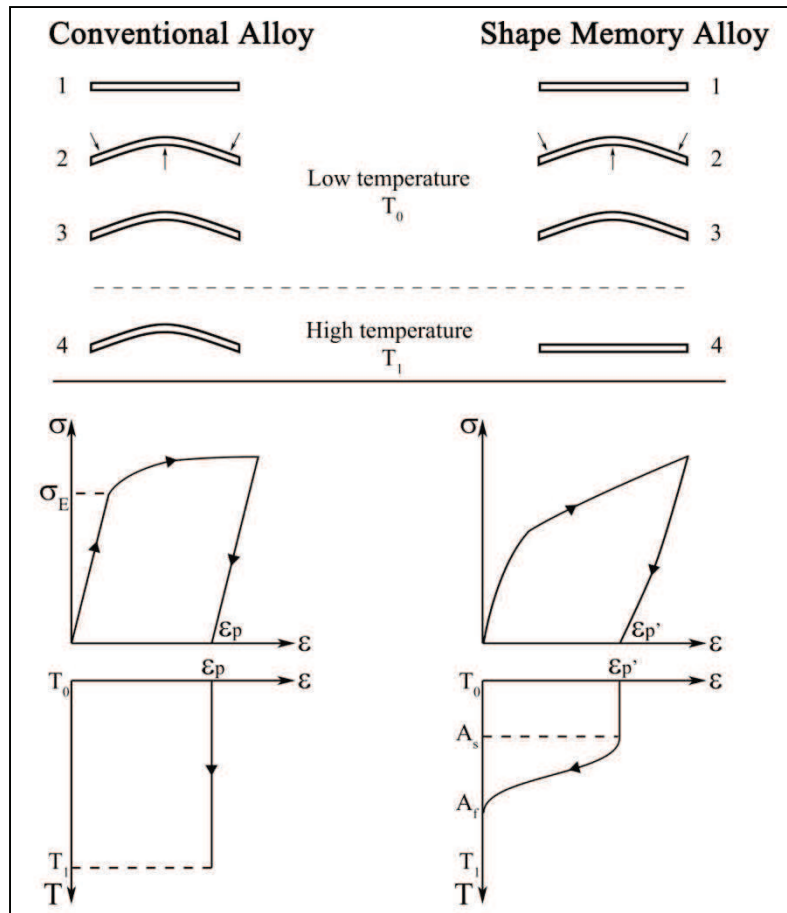


Figure 1.7. Illustration of the simple shape memory effect of SMA's ¹⁶⁷.

The low temperature phase of a SMA is constituted of martensite small plates randomly oriented. The application of an external strain at T_0 induces mainly a motion of the interfaces between these small martensite plates (which orient themselves) associated to the shape change. During heating, the material undergoes a martensite-austenite phase transformation between the A_s and A_f temperatures. The oriented martensite variants (associated with the shape change) disappear and the alloy returns to its original shape.

1.3.1.2.2. Superelasticity

There are two main types of superelasticity effects: the superelasticity by transformation and the superelasticity by reorientation.

- Superelasticity by transformation

In the range of temperatures in which the SMA is in the austenitic phase ($T > A_f$), the martensite transformation is induced by the application of a stress inducing a deformation. The stress-strain curve (Figure 1.8) presents a normal elastic strain up to a critical stress value (point B in Figure 1.8). From this critical stress value, martensite plates start to form and the strain continues as for a plastic strain (BC segment in Figure 1.8). When the stress in

removed, the formed martensite phase disappears (as $T > A_f$) and the alloy returns to the austenite phase recovering its original shape.

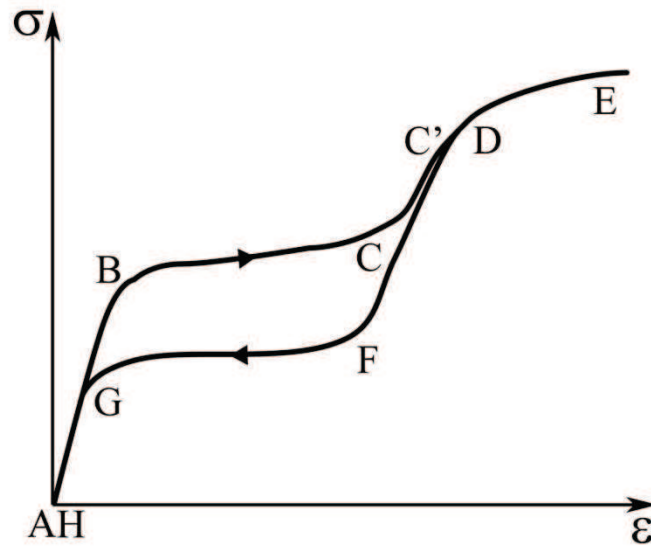


Figure 1.8. Illustration of the superelasticity by transformation of SMA's¹⁶⁷.

- Superelasticity by reorientation

For this superelasticity phenomenon, the alloy is initially in the martensite phase and its stress-strain curve is analogous to the one presented in Figure 1.8. In this situation, the deformation is essentially associated with a motion of the interfaces between the martensite plates and to the growth of the most favorably orientated martensite variants. This microstructural motion can lead to the formation of a martensite monocrystal.

The two deformation processes (by transformation and by reorientation) can be combined to obtain the stress-strain curve presented in Figure 1.9.

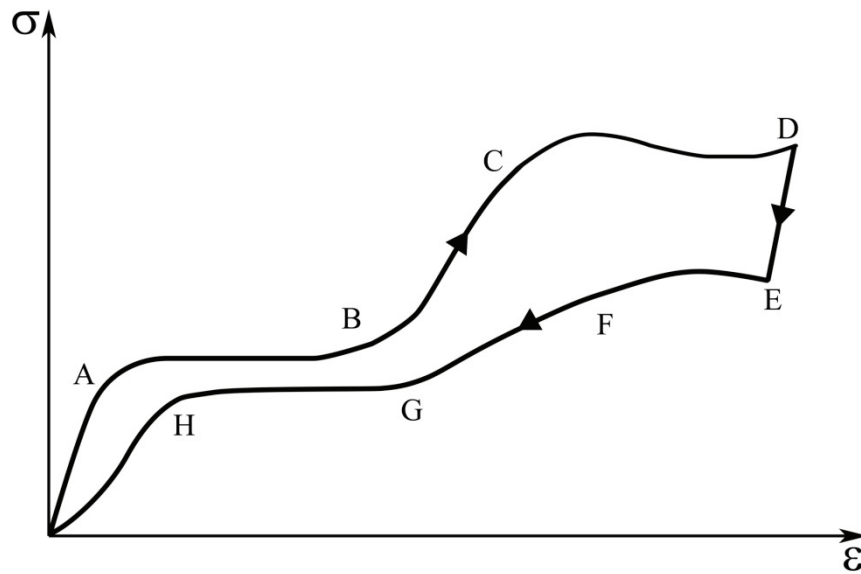


Figure 1.9. Illustration of the superelasticity effect of SMA's (superelasticity by transformation and reorientation) ¹⁶⁷.

On the strain-stress diagram presented in Figure 1.9, the formation of the martensite phase starts at point A and continues to point B. The BC section represents the elastic deformation of the martensite phase while the BC section represents the martensite phase reorientation process responsible of the superelasticity by reorientation.

1.3.1.3. Applications of SMA's

1.3.1.3.1. *Non-medical applications* ¹⁶⁸

Nowadays, the diversity of potential applications using SMA's has become quite large. Besides the interest of such materials in medical technology, they can also be used in several other fields.

A first application area could be described as "fashion, decoration and gadgets" including eye glass frames, antennas for portable cellular telephones, headbands of headphones, supporting frames for clothes (e.g. wedding dresses), etc. It is interesting to notice that also artists see SMA as an original tool in dynamic sculptures. A reference example is "The Skier", designed for the Winter Olympic Games of Albertville in 1990. SMA's are also used for couplings and fasteners design by making use of the force created by a deformed SMA element during constrained recovery. Actuators and microactuators, adaptive materials and hybrid composites constitute other examples of application area of SMA's.

1.3.1.3.2. *Medical applications*

Nitinol is now a common and well-known engineering material in the medical industry ¹⁶⁹⁻¹⁷² even if its application took a long time to start. There appear to be three primary reasons for the sudden success of Nitinol for biomedical applications. Perhaps most importantly, the medical industry itself has been driven towards less and less invasive medical procedures.

This, in turn has created a demand for new medical devices that could not be made with conventional materials. Other factors were the availability of microtubing and the ability to laser cut tubing with very high precision. Finally, the “release” of the technology from material science technologists and companies to product designers and doctors is not to be neglected ¹⁷⁰. Nowadays, there are numerous examples of medical application of Nitinol and SMA’s in general. We will here present a few of them.

One of the first medical applications of Nitinol are orthodontic archwires as a superelastic wire can deliver a constant stress when deformed between 1.5% and 7%. Here the archwire is constrained while being installed into brackets mounted on mal-aligned teeth. During the treatment, the arch struggles to restore the teeth to their proper location, but always applies forces according to the unloading plateau of the arch’s stress-strain curve. This maintains a therapeutically ideal force while eliminating adjustments, causing the patient less discomfort and accelerating treatment ¹⁶⁹.

SMA’s have a large number of orthopedic applications ¹⁷¹. For example, several types of shape memory orthopedic staples are used to accelerate the healing process of bone fractures. With respect to the healing of fractured bones, one can also point out shape memory plates for the recovery of bones. These plates are primarily used in situations where a cast cannot be applied to the injured area i.e. nose, jaw or eye socket. They are placed on the fracture and fixed with screws, maintaining the original alignment of the bone and allowing cellular regeneration. Another example of orthopedic applications of SMA’s is the spinal vertebra spacer. The insertion of this spacer between two vertebrae assures the local reinforcement of the spinal vertebrae, preventing any traumatic motion during the healing process. The use of a shape memory spacer permits the application of a constant load regardless of the position of the patient, who preserves some degree of motion. This device is used in the treatment of scoliosis.

As the medical industry has been driven towards less and less invasive medical procedures, shape memory surgical instruments have been developed. Among the advantages of these tools, one can emphasize their flexibility as well as their possibility to recover their former shape when heated. Laparoscopy (which involves performing operations through very small ports into the body called trocars and cannulae) is one of the procedures where SMA’s have been employed ^{169,171}. This field requires highly specialized and complex instruments in order to pass through a narrow cannula yet be able to perform tasks such as gripping, cutting, retracting, viewing, etc. ¹⁶⁹

Another medical application field of Nitinol (and maybe the most well-known) is the treatment of cardiovascular diseases. In 1975, Simon proposed to use Nitinol for a *vena cava* filter to break-up blood clots (thrombus) in the *vena cava* which can lead to life threatening pulmonary embolism ¹⁶⁹. Persons who cannot take anticoagulant medicines are the major users of the Simon filter. The purpose of this device is to filter clots that travel inside the bloodstream. The Simon filter traps these clots that in time are dissolved by the bloodstream. The insertion of the filter inside the human body is done by exploiting the shape memory

effect. From its original shape in the martensitic state the filter is deformed and placed on a catheter tip. Saline solution flowing through the catheter is used to keep a low temperature, while the filter is placed inside the body. When the catheter releases the filter, the flow of the saline solution is stopped. As a result, the bloodstream promotes the heating of the filter that returns to its former shape ¹⁷¹.

Another example of the use of Nitinol for the treatment of cardiovascular diseases (and the one that interests us particularly in the frame of this research) is the self-expanding stent. As we already explained earlier, stents are small tubular devices used to scaffold or brace the inside circumference of tubular passages or lumens, such as the esophagus, biliary duct, or blood vessels including coronary, carotid, iliac, aorta and femoral arteries. Stenting in the cardiovascular system is most often used as a follow-up to balloon angioplasty, a procedure in which a balloon is placed in the diseased vessel and expanded in order to reopen a closed lumen. These balloons are introduced percutaneously (non-surgically), most often through the femoral artery. Ballooning provides immediate improvement in blood flow, but 30% of the patients have restenosed within a year and need further treatment. The placement of a stent immediately after angioplasty has been shown to significantly decrease the propensity for restenosis ¹⁷⁰. Stents are also used to support grafts or to canalize the blood flow in the treatment of aneurysms. An aneurysm is caused by the weakening of an arterial wall that balloons out and presents a risk of rupture. Most stents today are 316L stainless steel, and are expanded against the vessel wall by plastic deformation caused by the inflation of a balloon placed inside the stent. Nitinol stents, on the other hand, are self-expanding i.e. they are shape-set to the open configuration, compressed into a catheter, then pushed out of the catheter and allowed to expand against the vessel wall by recovering their original shape due to the body temperature ^{170,171}. Stents made of conventional alloys such as 316L stainless steel have to be balloon expanded to a diameter much bigger than the target artery one in order to ensure the stent anchors firmly in place. However, this stent over-expansion may cause injuries to the artery wall and therefore induce a faster restenosis. One of the main advantages of self-expanding stents is that they can be manufactured so that their open diameter is greater than the vessel lumen (typically, about 10% greater ¹⁷⁰) to ensure a firm anchoring of the device without causing injuries to the vessel wall. Another very interesting feature of self-expanding Nitinol stents is their superelasticity properties. The stent flexibility induced by these superelasticity properties plays a role in some superficial stent applications such as the carotid and femoral arteries, where the vessels may be subject to outside pressures that would cause conventional stents to crush. Such deformations have been observed in stainless steel stents, and can lead to serious consequences ¹⁷⁰.

1.3.2. Nitinol biocompatibility and resistance to corrosion

As we have seen, Nitinol is a very innovative and interesting alloy in the field of metallic biomaterials. However, this alloy contains a high amount of nickel which is proven to have cytotoxic effects and therefore to be a non biocompatible material ¹⁷³. Therefore, the question of the Nitinol biocompatibility remains controversial. On the one hand, numerous studies show negative results ¹⁷⁴ such as possible cytotoxic effects ¹⁷⁵ or a risk of promoting inflammatory response in soft tissues by activating monocytes ¹⁷⁶. Shih *et al.* also showed that

the precipitated corrosive products of Nitinol stent wires were potentially toxic to vascular smooth muscle cells, especially when the released nickel concentration was higher than 9 ppm¹⁷⁷. On the other hand, many other authors claim that Nitinol has a good biocompatibility¹⁷⁸ i.e. no or very low cytotoxic¹⁷⁹⁻¹⁸⁵, allergic or genotoxic activity^{186,187} related to a low release of nickel ions¹⁸⁸⁻¹⁹², with concentrations below the normal human daily intake^{193,194} (i.e. between 300 and 500 µg/day/person, depending on the environmental pollution of water with nickel and on the dietary preference¹⁹⁵), a low adsorption of fibrinogen¹⁹⁶ and a low platelet adhesion¹⁹⁷ or a high fibroblast proliferation rate compared to other biologically applied materials such as pure titanium or Ti6Al4V¹⁹⁸.

Obviously, the biocompatibility of a material strongly depends on its resistance to corrosion. Therefore, an overview of the literature reveals the same kind of controversy regarding the corrosion resistance of Nitinol than the one that can be found regarding its biocompatibility. Some studies report on a very good resistance to corrosion^{199,200} while some other are more nuanced stating that Nitinol presents a good corrosion resistance but is very sensitive to localized corrosion^{201,202} or that even if Nitinol exhibits small passive currents and large passive potential ranges, strong anodic dissolution of the passive film occurs during potentiodynamic and potentiostatic polarizations in Ringer's solution resulting in a thinning of the passive film²⁰³. However, a large number of corrosion studies carried out on bare Nitinol substrates concludes on a poor resistance of this alloy²⁰⁴ i.e. a passivity current density higher than other materials commonly used as implants²⁰⁵ and a high susceptibility to localized corrosion²⁰⁶⁻²¹³ that could be related to surface defects due to fabrication processes²¹⁴ or inhomogeneities in the passive oxide layer²¹⁵. This is confirmed by *in vivo* studies. For example, Eliades *et al.* reported on the identification of delamination, pitting and crevice corrosion defects in Nitinol orthodontic archwires retrieved after 1-6 months use²¹⁶.

Therefore, it clearly appears that the use of Nitinol with original oxides for long-term implantation is not necessarily safe. This is especially true for Ni-enriched surfaces such as heat treated Nitinol²¹⁷ but also if the external surface layers are adjusted to relatively low Ni concentrations because of the possible presence of Ni-rich buried surface sublayers serving as permanent Ni reservoir²¹⁸.

Note that heat treatment is nearly systematically applied during the processing of Nitinol in order to set the desired final shape and to optimize the mechanical properties of the SMA. Usually, this treatment involves temperatures in the range of approximately 350 to 550°C. Heat treatment of Nitinol in atmospheric conditions at these temperatures is reported to induce a strong increase of the oxide layer thickness^{219,220} and a diffusion of nickel to the surface resulting in an increased nickel surface concentration^{220,221}. After typical heat treatment, the oxide layer consists in a mechanical mixture of TiO₂ (dominant oxide) and nickel oxides (mainly NiO)^{222,223}. Note that the oxidation of Ti is a much more favorable process than the oxidation of Ni as the free energy of formation ΔG (298 K) of NiO, TiO and TiO₂ is -50.6, -118.3 and -212.6 kcal mol⁻¹, respectively²²². This leads to the appearance of a Ni-enriched sublayer between the oxide layer and the bulk material^{220,223}. Heat treatment induces a decrease of the Nitinol corrosion resistance^{219,224}. Therefore, a surface treatment of the material is reported as necessary in order to reduce the surface nickel levels^{217,221}. Furthermore, it has been showed that thick oxide layers can crack when strained in the superelastic regime and do not repair after unloading, exposing Ni-enriched regions^{225,226}.

Chemical etching is one of the most commonly applied methods to get rid of this original oxide layer. This treatment is carried out by immersion of the alloy in a HF/HNO₃ aqueous solution and commonly followed by a hydrothermal treatment^{218,221,223,227}.

The hydrothermal treatment also called boiling procedure (immersion of Nitinol in boiling water) was introduced for Nitinol many years ago²²⁸, induces an increase of the oxide layer thickness²²⁹ and proved to be very effective in blocking Ni release^{229,230}. Shabalovskaya *et al.* also showed that boiling in water of chemically etched samples results in a slight extension of the passivity region and a reduction of the current density by one order of magnitude at the potentials above the corrosion potential, indicating a significant drop in the anodic dissolution of material²²⁵.

1.3.3. Inorganic coatings

Since Nitinol is considered as a promising biomaterial, an important number of researches have been undertaken in order to improve its biocompatibility and its corrosion resistance. Among those, numerous publications report on the creation of an inorganic layer using various physical or (electro)chemical methods.

One of the most common physical surface modification methods applied to Nitinol implies ions implantation and/or deposition^{231,232}. In this context, nitrogen is very widely used. It has been shown during the 90's that nitrogen ions implantation can significantly improve the corrosion²³³ and wear²³⁴ resistance as well as an increase of the surface hardness and a decrease of the surface friction coefficient²³⁵. Plasma immersion ion implantation (PIII) of nitrogen has been shown as an efficient method to obtain a titanium nitride (TiN) surface layer (i.e. a Ni depleted layer and a Ni enriched sublayer²³⁶) which is effective in impeding the out-diffusion of Ni ions²³⁷ and allows a better proliferation of cells such as osteoblasts²³⁸, leads to a significant improvement of the corrosion and localized corrosion resistance²³⁹ but also improves the mechanical properties of the surface²⁴⁰ such as the wear resistance^{241,242} or the surface hardness²⁴³. Several other methods such as plasma immersion ion implantation and deposition (PIII&D)²⁴⁴⁻²⁴⁸, pulse-biased arc ion plating²⁴⁹, PIRAC (Powder Immersion Reaction-Assisted Coating) nitriding²⁵⁰⁻²⁵², laser gas nitriding²⁵³⁻²⁵⁵ or DC magnetron sputtering²⁵⁶ has been used to form a TiN layer at the Nitinol surface and lead to similar results.

Carbon is another widely used atom for the formation of a protective inorganic layer. Plasma ion implantation can be used to form titanium carbide (TiC) at the surface of Nitinol leading to an increase of its corrosion resistance²⁵⁷⁻²⁵⁹ and a decrease of the Ni release²⁵⁸, an improvement of its mechanical properties (such as hardness^{258,260} and wear resistance²⁵⁹) as well as its cytocompatibility^{257,259}. More commonly, PIII&D is used to form a diamond like carbon (DLC) film which can also considerably enhance the corrosion resistance²⁶¹⁻²⁶⁴, improve the mechanical properties^{262,263}, decrease the Ni release²⁶⁴ and increase the biocompatibility²⁶¹ of Nitinol. Similar DLC films can also be obtained by arc discharge ion plating²⁶⁵ or by arc enhanced magnetic sputtering (AEMS)²⁶⁶.

Obviously, PIII is also widely used to implant oxygen into the Nitinol surface. This method has been shown to lead to the formation of a TiO₂ (rutile) layer and a Ni enriched (Ni₃Ti) sublayer²⁶⁷⁻²⁷⁰. The PIII of oxygen can improve the resistance to corrosion²⁷¹, to localized and to wear corrosion²⁷², increase the wear resistance²⁷³ and the biocompatibility²⁷⁴ of Nitinol and reduce the Ni release^{275,276}. Note that comparative studies have shown that PIII of nitrogen, carbon and oxygen leads to similar results^{258,277} but that better biological effects are obtained with nitrogen²⁵⁸. Note also that nitrogen, carbon and oxygen are not the only elements that have been considered for implantation on the surface of Nitinol. For examples, high dose ion implantation of Cu and Ti has been shown to have a protective effect against crack formation and to reduce the Ni amount at the surface²⁷⁸, high energy argon implantation may be beneficial for the wear and fatigue resistance of Nitinol due to the formation of an amorphous surface layer²⁷⁹ or plasma based ion implantation of phosphorus leads to an increase of the open-circuit potential and a decrease of the corrosion current density²⁸⁰. Tantalum has also been used for PIII^{281,282} and zirconium for PIII&D^{283,284} in order to increase the corrosion resistance of Nitinol. Such ZrO₂ and Ta₂O₅ layers can also be created by electrodeposition^{285,286}. Note that tantalum has the important advantage to considerably increase the X-ray visibility of the material which is an essential requirement to help surgeons or cardiologists to determine the location and orientation of the implanted device more accurately²⁸⁷.

An alumina (Al₂O₃) layer can also be formed on the surface on Nitinol by micro-arc oxidation deposition in order to increase its resistance to corrosion²⁸⁸⁻²⁹¹ and surface mechanical properties^{292,293}. Obviously, as the TiO₂ present at the surface of Nitinol is considered as responsible of its inherent relative biocompatibility, many studies have been led in order to form a pure TiO₂ layer by various ways such as sol-gel²⁹⁴⁻²⁹⁶, soaking into a Ti⁴⁺ solution^{297,298}, cathodic deposition²⁹⁹ or plasma deposition³⁰⁰.

1.3.4. Organic coatings

With the prospect of improving the corrosion resistance and the biocompatibility of Nitinol, many works have been published on the modification of its surface with organic coatings. Most of these studies report on the Nitinol coating with a polymeric layer such as polyurethane³⁰¹⁻³⁰³, poly(*p*-xylene) derivatives^{304,305}, hyaluronan³⁰⁶ or polytetrafluoroethylene³⁰⁷⁻³⁰⁹ derivatives, *N*-isopropylacrylamide and *N*-*tert*-butylacrylamide copolymers³¹⁰ or thermoplastic polyamides³¹¹, polypyrrole³¹², phosphorylcholine³¹³, or polyethylene glycol derivatives³¹⁴⁻³¹⁶. These polymer layers are often used as reservoir for drugs elution³¹³ or as platform for the immobilization of an antithrombogenic agent such as heparin^{317,318}. Polyethylene glycol (PEG) is one of the most commonly used polymers in this context as it has been widely reported that it has very interesting anti-biofouling properties³¹⁹⁻³²¹ and it can decrease platelet adhesion³²² as well as cell-attachment^{320,321} but phosphorylcholine (PC) derivatives are also widely used.

In a recent paper, Chen *et al.* review the role of protein-surface interactions for such biocompatible polymer materials as well as the interest of using an anticoagulant such as heparin in the coating³²³.

Regarding PEG, it is believed that its protein resistance is associated with two main mechanisms including steric repulsion and a hydration layer formation. However, those models present an incomplete description of a more complex reality since the adsorption mechanism can be influenced by many parameters such as the size of the adsorbing protein, the distance between the grafted chains (density), chain length, chain-protein interactions, protein-surface interactions and so on.

Regarding the zwitterionic PC anti-fouling properties, the mechanism describing how PC-containing polymers and proteins interplay with each other to prevent protein adsorption has also not yet been completely elucidated. However, several comparatively reasonable explanations have been brought forward. One explanation considers that on a material surface there are abundant free water molecules around the PC group, and it is this large hydration layer that permits the protein to remain in a stable conformation when the protein contacts the material surface while other more conventional hydrophobic material surfaces result in significant change in protein confirmation. Therefore, the PC-containing hydration layer is believed to be responsible for the repelling property of PC-containing polymers.

Heparin is a sulfated polysaccharide which is not only used as an anticoagulant drug based on its ability to interfere in the coagulation cascade, but also mediates various physiological and pathophysiological processes based on its interaction with heparin-binding proteins. It is well-established that the reduced thrombogenicity of a heparin-coated surface can be attributed to the catalytic effects of heparin on antithrombin III. Additionally, some studies have also suggested that heparin-modified surfaces lead to reduced or selective adsorption of other plasma proteins as well as the maintenance of the proteins in their native state.

Since the last few years, several publications report also on the formation of layer-by-layer assembly of polyanions and polycations into multilayers on Nitinol. Biomedical purposed polyelectrolyte coatings are often composed of polysaccharides combinations such as hyaluronan and chitosan³²⁴, alginate and heparin (using a photosensitive cross-linker)³²⁵, chitosan and heparin^{326,327}, heparin and dextran sulfate³²⁸ but also synthetic polymers such as polyacrylic acid (PAA) and polyallylamine hydrochloride (PAH)³²⁹ or polyethyleneimine (PEI) used with heparin³³⁰. Note however that PEI which is commonly used as precursor base layer in polyelectrolyte multilayer films can be potentially cytotoxic and may not be biocompatible enough for clinical applications³³¹.

Another common way used to create a protective organic coating on oxides surfaces such as Nitinol is the formation of a self-assembled monolayer. Several publications report on the modification of the Nitinol oxide layer with organosilanes³³², organophosphonic acids³³³⁻³³⁶ and the use of such covalently grafted organic monolayers as adhesion promoters or polymerization initiators for the formation of a polymeric layer^{337,338}. Note that the important resistance of organophosphonic acids to homocondensation and hydrolysis make them particularly interesting candidates for Nitinol surface functionalizations when aiming applications in aqueous medium.

1.4. Phynox

1.4.1. History, properties and applications

Phynox, Conichrome and Elgiloy are all trademark names for the cobalt-chromium-nickel-molybdenum-iron alloy specified by ASTM F1058 and ISO 5832-7³³⁹. Elgiloy was developed at the Elgin Watch Company (Elgin, IL, USA). At the end of World War II, returning servicemen complained that their Elgin watches could not withstand the punishment of corrosive environmental situations encountered during active service. The Elgin team took those complaints to heart and after four years of research, “Elgiloy” (a non-corroding watch spring material) was born³⁴⁰.

Phynox is an austenitic alloy capable of additional hardening by aging at a moderate temperature (around 500°C). Its elastic modulus in the fully hardened condition is of the order of 210 000 MPa. In addition to its very high yield strength, Phynox has a wide range of physical and chemical properties such as an important resistance to corrosion, a good fatigue strength, the ability to be used over a wide range of temperatures (from liquid helium to about 500°C), *etc.*³⁴¹.

Besides springs for watch motors, Phynox is used in numerous applications fields such as electrical and electronic apparatus, equipment for the chemicals and oil and gas industries, weaponry (e.g. special collars for missiles), aeronautical and aerospace equipment, automotive industry (ABS and injection systems), *etc.*³⁴¹. Phynox finds also numerous applications in the biomedical field e.g. for the conception of stents^{342,343}, aneurysm clips³⁴⁴, vena cava filters³⁴⁵ or septal occluders (for atrial septal defects treatment)³⁴⁶.

1.4.2. Surface modification

Despite the fact that cobalt-based alloys are known for their generally superior mechanical properties and corrosion resistance compared to stainless steels, failures have been reported. For example, Es-Souni *et al.*³⁴⁷ point out that Elgiloy is characterized by lower corrosion resistance and biocompatibility (high Ni and Co ions release, poor repassivation ability, *etc.*) than other commonly used alloys for biomedical applications. They attribute this to the lower surface finish quality, the in-process strain hardening and the presence of numerous inclusions and precipitates. It thus appears that surface modification treatments are required in order to obtain reproducible and biocompatible Phynox surface. However, only a few studies have been published recently on the surface modification of CoCr alloys with SAMs of organosilanes³⁴⁸ or organophosphonic acids^{349,350}.

Part I

Characterization and application of surface
treatments on Nitinol and Phynox

Chapter 2. Study and modification of the Nitinol surface state

As described in the general introduction, Nitinol is a very complex yet promising material especially in the field of biomedical applications.

In the first part of this chapter, we report on the impact of typical shape-setting heat treatment and chemical etching on the surface composition and the resulting resistance to corrosion of Nitinol wires identical to the ones used for the fabrication of braided Nitinol stents.

In the second part, we report on studies carried out on plane Nitinol substrates. The choice of plane Nitinol substrates instead of wires is justified by the convenience of plane substrates for many surface characterization techniques. These Nitinol substrates were analyzed in their “as received”, heat treated and mechanically polished states. The rest of the second part of this chapter is dedicated to the surface modification of mechanically polished plane Nitinol substrates toward a versatile platform for post-grafting chemical reactions, the study of parameters influencing the grafting of phosphonic acids SAMs on these surfaces and on an original and promising alternative to conventional hydrothermal treatment usually applied in order to reinforce the resistance of the oxide layer to corrosion.

2.1. Nitinol wires

2.1.1. Heat treatment

2.1.1.1. Introduction

During the processing of Nitinol, a heat treatment is applied after the last cold work step to impart a “memory” of the desired final shape (shape setting treatment) and to optimize the shape memory, superelastic and mechanical properties of the material. Usually, shape setting involves annealing the material while constrained in a final shape at a temperature in the range of approximately 350 to 550°C^{217,351}. Therefore, despite the consequent literature already published on this topic²¹⁷⁻²²⁶, we carried out an examination of the typical shape setting heat treatment impacts on the surface composition and on the corrosion resistance of commercially available Nitinol wires i.e. 240 µm diameter wires supplied by SAES Memry and 50 µm diameter wires supplied by Fort Wayne Metals. The choice of using wires as substrates is justified by the fact that Nitinol stents are often composed of several Nitinol wires braided together. Thus working with wires allows us to characterize Nitinol in a situation really close to the one corresponding to its application.

2.1.1.2. Samples preparation

The Nitinol wires were cut in small segments, cleaned by sonication 15 minutes in ethanol and dried overnight at room temperature in a closed box in order to avoid recontaminations. These segments were then submitted to heat treatment at air in a resistance furnace according

to the usual shape setting procedure which depends on the wire diameter. The different tested heat treatments parameters for each type of Nitinol wire are summarized in Table 2.1.

Table 2.1. Heat treatments applied to Nitinol wires according to their diameter

	Ø 240 µm			Ø 50 µm		
Temperature (°C)	480	480	550	430	430	500
Time (min)	15	60	15	15	60	15

After the heat treatment, the wires were allowed to cool down for several hours at room temperature, cleaned again by sonication 15 minutes in ethanol and dried overnight at room temperature in a closed box.

2.1.1.3. XPS analysis

In order to collect a sufficient XPS signal from these wires, the analysis area had to be significantly increased. This was done by sticking several wire segments side by side (at least 10 wire segments for the 240 µm wire and at least 50 wire segments for the 50 µm wire).

The XPS survey spectra obtained for 240 µm wires and 50 µm wires are presented in Figures 2.1 and 2.2, respectively.

First of all, the peaks characteristic of the main elements present in Nitinol i.e. the titanium (Ti3p, Ti2p and Ti2s around 38 eV, 455 eV and 565 eV, respectively) and the nickel (Ni3p, Ni3s and Ni2p around 68 eV, 110 eV and 855 eV, respectively) are clearly visible. Beside those elements, an intense O1s core level photoelectron peak (centered around 530 eV) attributed to the oxygen present in the oxide layer as well as a C1s core level photoelectron peak (centered around 285 eV) can be pointed out for each analyzed sample. The presence of the C1s peak is attributed to the presence of adsorbed atmospheric contaminations remaining on the surface of the analyzed wires. Note also the presence of relatively intense silicon peaks on the survey spectra of the 50 µm wires. This silicon signal is attributed to the electrically conductive tape used to immobilize the wires to the sample holder (the XPS survey spectrum of this tape being presented in Figure 2.3).

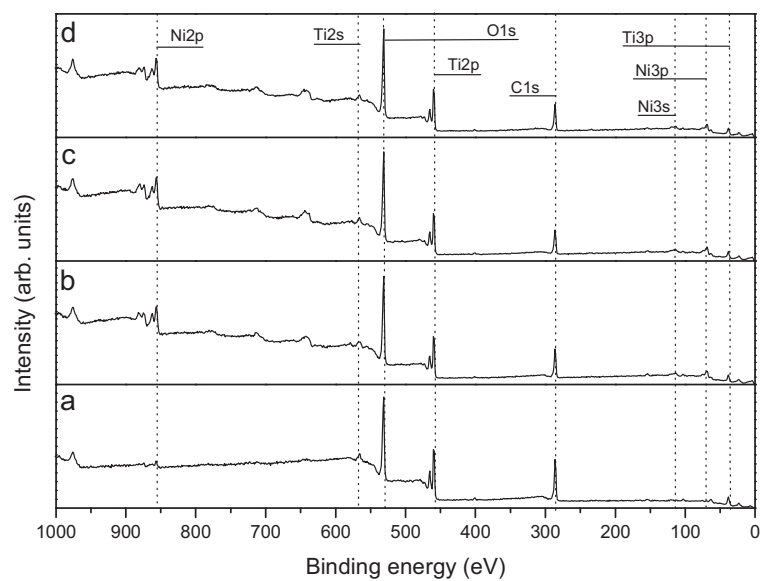


Figure 2.1. XPS survey spectra of 240 μm Nitinol wires untreated (a) and after a heat treatment of 15 min at 480°C (b), 60 min at 480°C (c) and 15 min at 550°C (d).

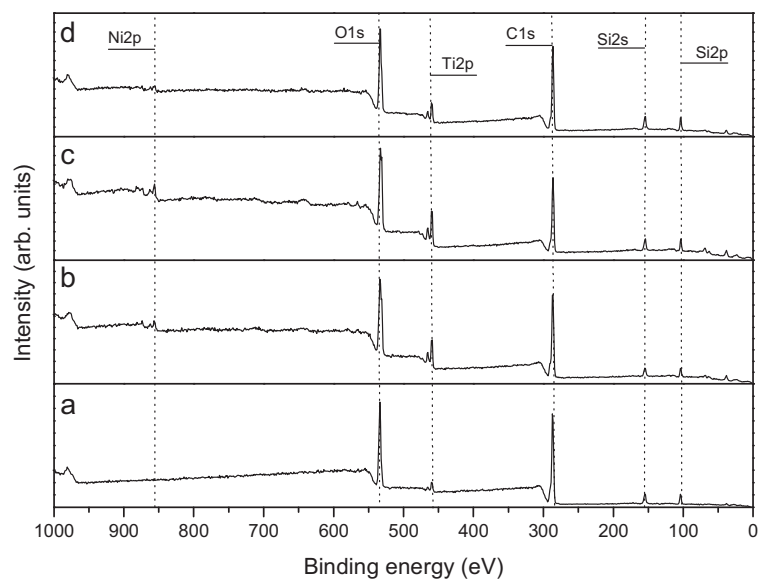


Figure 2.2. XPS survey spectra of 50 μm Nitinol wires untreated (a) and after a heat treatment of 15 min at 430°C (b), 60 min at 430°C (c) and 15 min at 500°C (d).

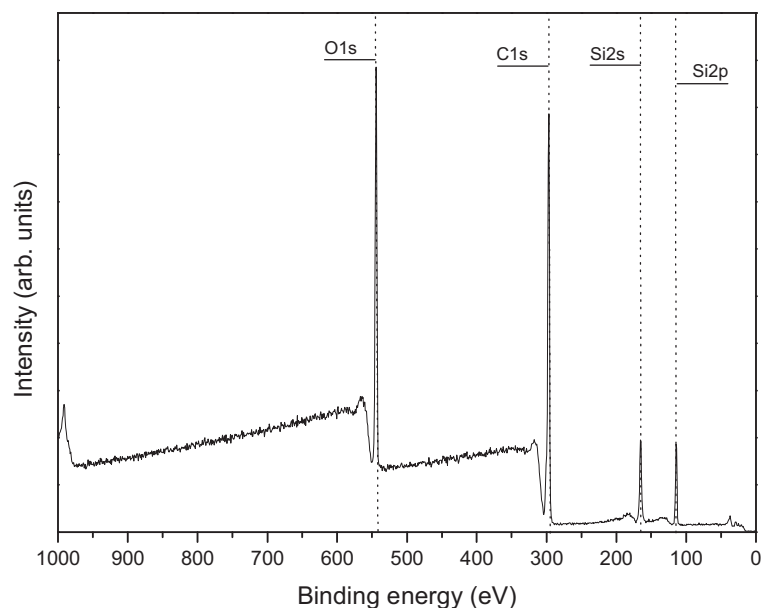


Figure 2.3. XPS survey spectrum of the electrically conductive tape used to immobilize the Nitinol wires to the XPS sample holder.

For both 240 μm and 50 μm Nitinol wires, it can be pointed out that the heat treatment induces an important increase of the nickel signal intensity. The Ni/Ti ratio calculation (i.e. the ratio of the corresponding XPS peak areas normalized with the corresponding Scofield factors) allows us to assess the proportion of nickel at the surface of the oxide layer (Table 2.2).

Table 2.2. Ni/Ti ratios calculated on the basis of XPS analysis of 240 μm and 50 μm Nitinol wires untreated and heat treated with different times and temperatures.

	Ø 240 μm	Ø 50 μm	
Untreated	0.16	0.00	Untreated
480°C / 15 min	0.66	0.38	430°C / 15 min
480°C / 60 min	0.82	0.54	430°C / 60 min
550°C / 60 min	0.72	0.58	500°C / 60 min

It clearly appears that heat treatment of Nitinol induces an important increase of the nickel proportion in the oxide layer i.e. a diffusion of the nickel toward the surface. An increase of the time and temperature of the heat treatment reinforces this diffusion phenomenon and induces a further increase of the nickel proportion in the oxide layer. For 240 μm wires, it seems that the nickel proportion increases more with the time than with the temperature while the opposite is observed for 50 μm wires. In any case, an increase of the temperature and time of the heat treatment induces a further diffusion of nickel toward the surface of the Nitinol oxide layer.

The high resolution XPS analysis of the Ti2p and Ni2p core level photoelectron peaks has also been carried out systematically for all these wires. Representative spectra are presented in Figures 2.4 and 2.5 for 240 μm and 50 μm wires, respectively.

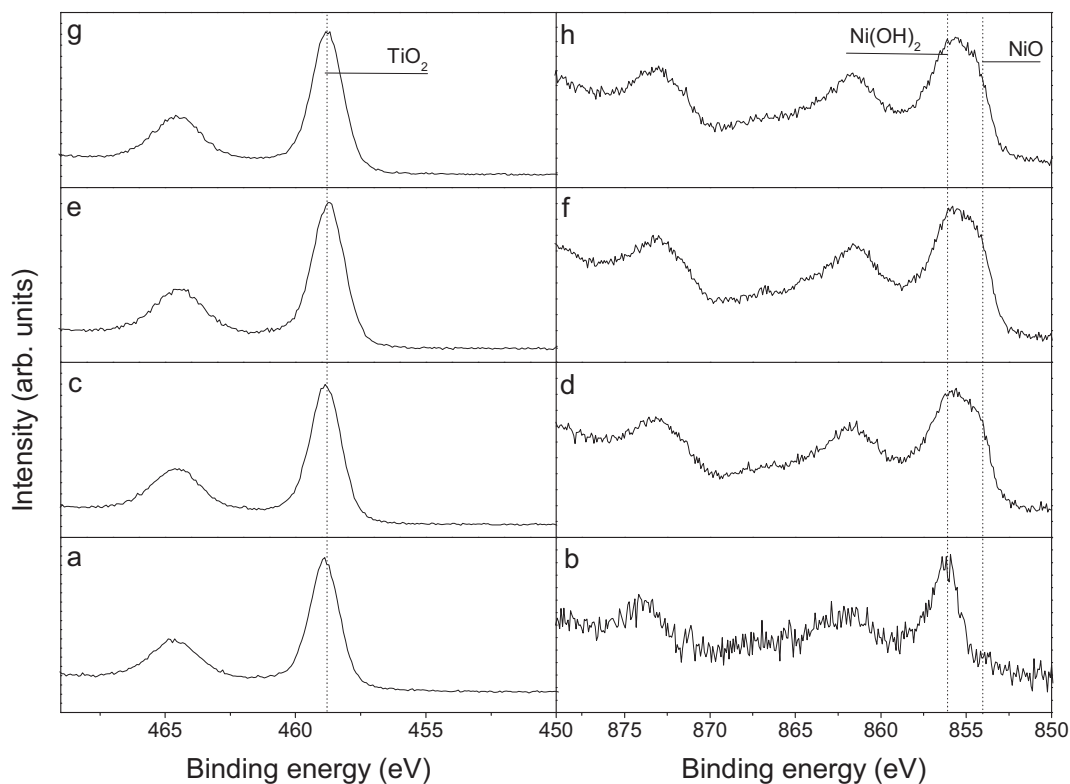


Figure 2.4. High resolution XPS spectra of the Ti2p (a, c, e and g) and Ni2p (b, d, f and h) core level photoelectron peaks of 240 μm Nitinol wires untreated (a and b), and after a heat treatment of 15 min at 480°C (c and d), 60 min at 480°C (e and f) and 15 min at 550°C (g and h).

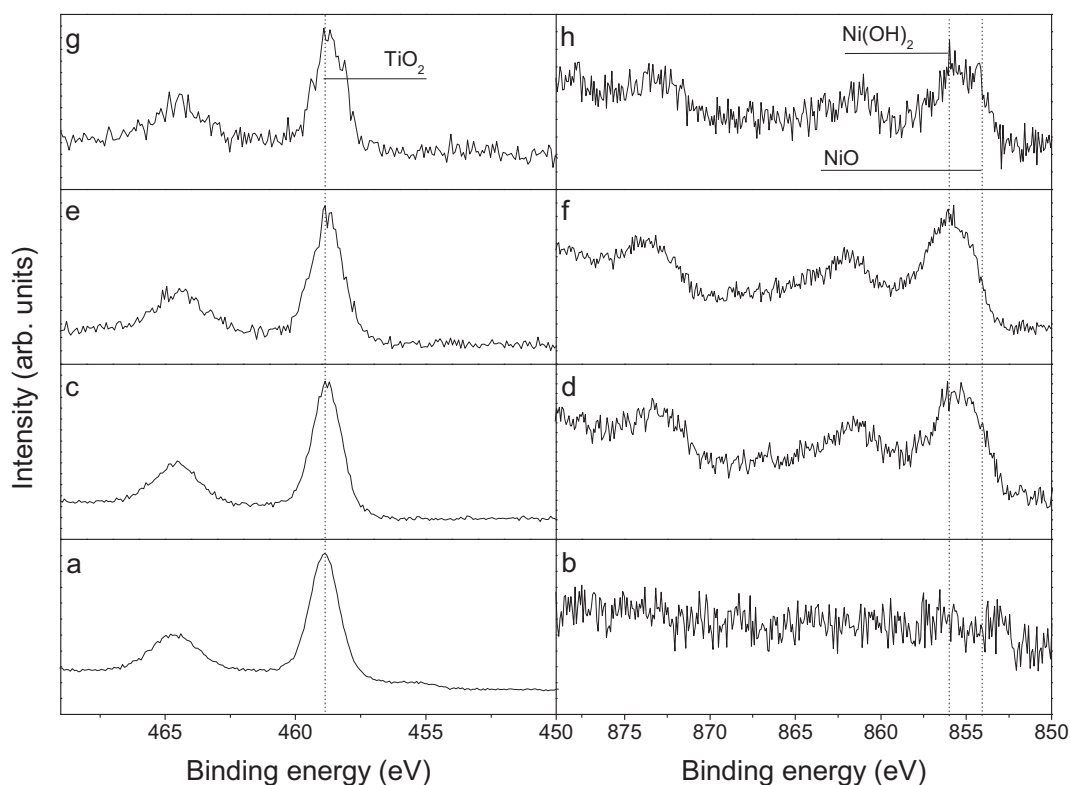


Figure 2.5. High resolution XPS spectra of the Ti2p (a, c, e and g) and Ni2p (b, d, f and h) core level photoelectron peaks of 50 μm Nitinol wires untreated (a and b), and after a heat treatment of 15 min at 430°C (c and d), 60 min at 430°C (e and f) and 15 min at 500°C (g and h).

For each analyzed Nitinol sample, the Ti2p_{3/2} peak is centered at 458.9 eV. This binding energy is characteristic of titanium in TiO₂. Therefore, titanium in the outermost part of the oxide layer is fully oxidized, even before thermal oxidation treatment. Quite obviously, it remains in the TiO₂ state after thermal oxidation treatment.

Regarding nickel, the Ni2p peak is almost completely absent in the spectra obtained from the 50 μm untreated wires while the 240 μm untreated wires Ni2p spectra show only one Ni2p_{3/2} component centered around 856.2 eV. This binding energy is characteristic of nickel in nickel hydroxide (Ni(OH)₂). First, this is a clear evidence that the surface composition of Nitinol wires (and therefore their properties) strongly depends on the manufacturer as it has already been described in the literature^{194,208,221,352-354} and justifies the application of a surface treatment of this material before any biomedical application in order to achieve a control of its surface state. The hydroxylated nature of the nickel in the untreated 240 μm wires oxide layer suggests that Ni is mainly located in the outermost part of the oxide layer and therefore exposed to the atmospheric humidity.

After heat treatment, each sample shows an important increase of the nickel signal (as described before). For both 240 μm and 50 μm wires and all the applied heat treatments, the Ni2p_{3/2} core level photoelectron peak has the same shape i.e. much broader than the Ni2p_{3/2}

peak of the untreated 240 μm Nitinol wire: a second component clearly appears at 854.2 eV characteristic of nickel in nickel oxide (NiO). The appearance of NiO in the outermost part of the oxide layer can be attributed to the nickel diffusion phenomenon toward the surface and its thermal oxidation as well as to some nickel hydroxide dehydration. No further distinction could be made between the surfaces resulting from the different studied heat treatments.

2.1.1.4. ToF-SIMS analysis

In order to have more information on the effects of the heat treatment on the Nitinol oxide layer, ToF-SIMS analysis of the 50 μm Nitinol wires set have been carried out (Table 2.1). The main goal of these depth profile experiments was to obtain complementary information on the evolution of the oxide layer thickness under thermal oxidation. These analyses were carried out with a Xe^+ beam for sputtering and a Ga^+ beam for secondary ions ejection. As the main elements present in Nitinol (Ni and Ti) are rather electropositive, positive ions spectra were acquired.

Note that the acquired profiles had to be reconstructed by selecting a very small surface of the sample i.e. by taking only the data from the center of the wire into account. ToF-SIMS being very sensitive to the surface roughness and morphology, when a cylindrical sample is sputtered and analyzed, the obtained signal obviously always contains a certain proportion of the signal from the extreme surface (this proportion being different at each step of the sputtering) as schematized in Figure 2.6. The reconstruction aims to minimize at most this geometrical effect.

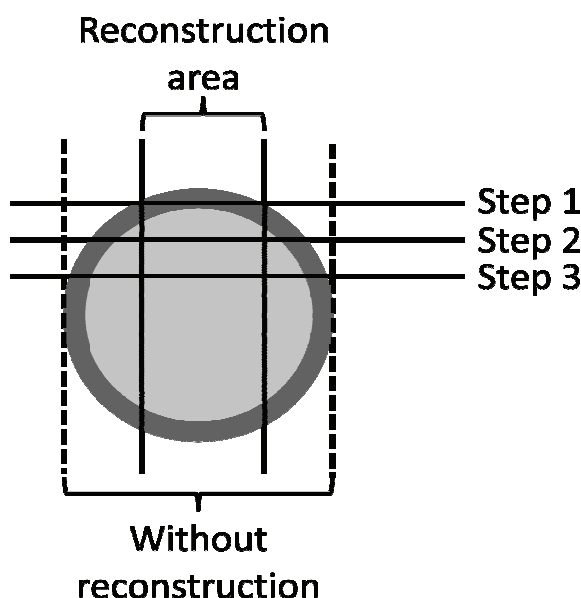


Figure 2.6. Schematic representation of the slice of a 50 μm Nitinol wire analyzed with ToF-SIMS: horizontal lines (Step 1, 2 and 3) represent the surfaces from which the signal is collected at different analysis times; dark grey area represents the oxide layer and light grey area represents the bulk material.

The thickness of the different oxide layers have been compared taking benefit of the well-known “matrix” effect i.e. that the presence of oxygen in the analyzed material induces a strong increase of the positive ions emission yield. The attenuation of this matrix effect can be assessed by measuring the profiling time needed to reach a certain percentage of a positive ion maximum value. Therefore, this profiling time is proportional to the oxygen abundance and thus to the oxide layer thickness. The obtained profiles for 50 μm Nitinol wires untreated, heat treated for 15 min at 430°C, for 60 min at 430°C and for 15 min at 500°C are presented in Figure 2.7.

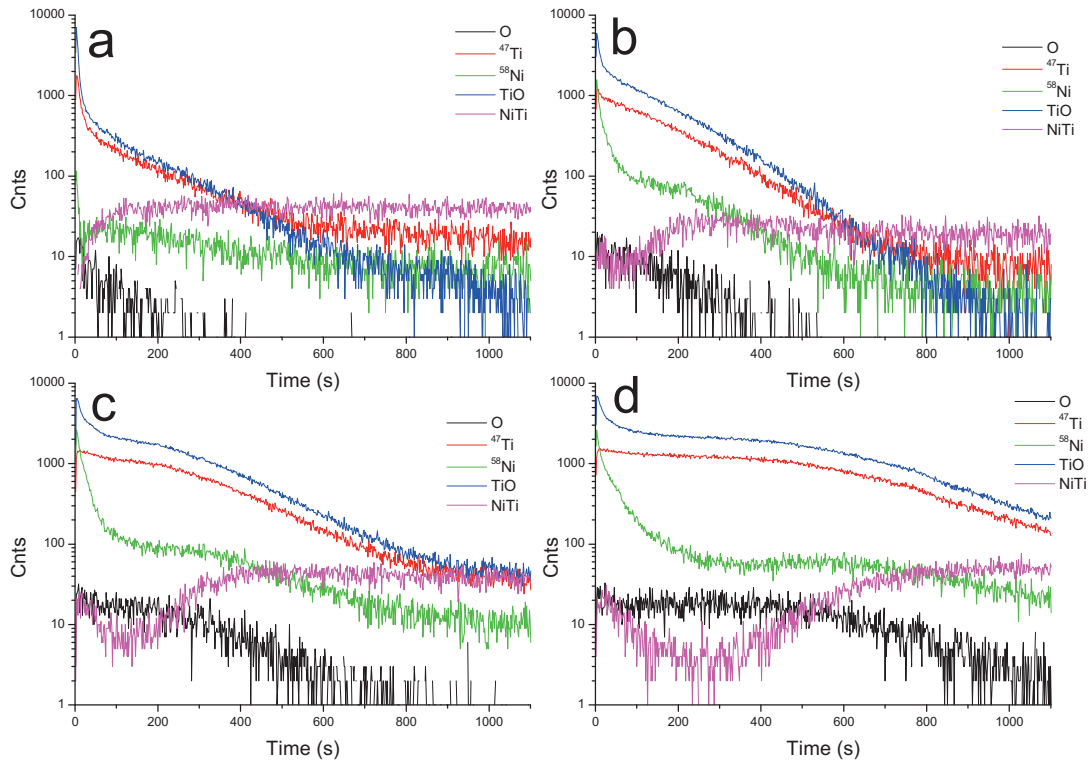


Figure 2.7. ToF-SIMS positive ions profiles obtained for an untreated 50 μm Nitinol wire (a) and for a 50 μm Nitinol wire heat treated for 15 min at 430°C (b), heat treated for 60 min at 430°C (c) and heat treated for 15 min at 500°C (d).

TiO^+ ions signal has been selected to trace this attenuation of the matrix effect: the profiling times needed to induce a decrease of this signal down to 10% and 1% of its maximum value (called TiO10% and TiO1%, respectively) have been measured. In order to ensure the reliability of the obtained results, the profiling time at which the TiO^+ signal (characteristic of the oxide layer) crosses the NiTi^+ signal (characteristic of the bulk material) has also been measured. This profiling time is noted TiOxNiTi. The results of these measurements are presented in Figure 2.8.

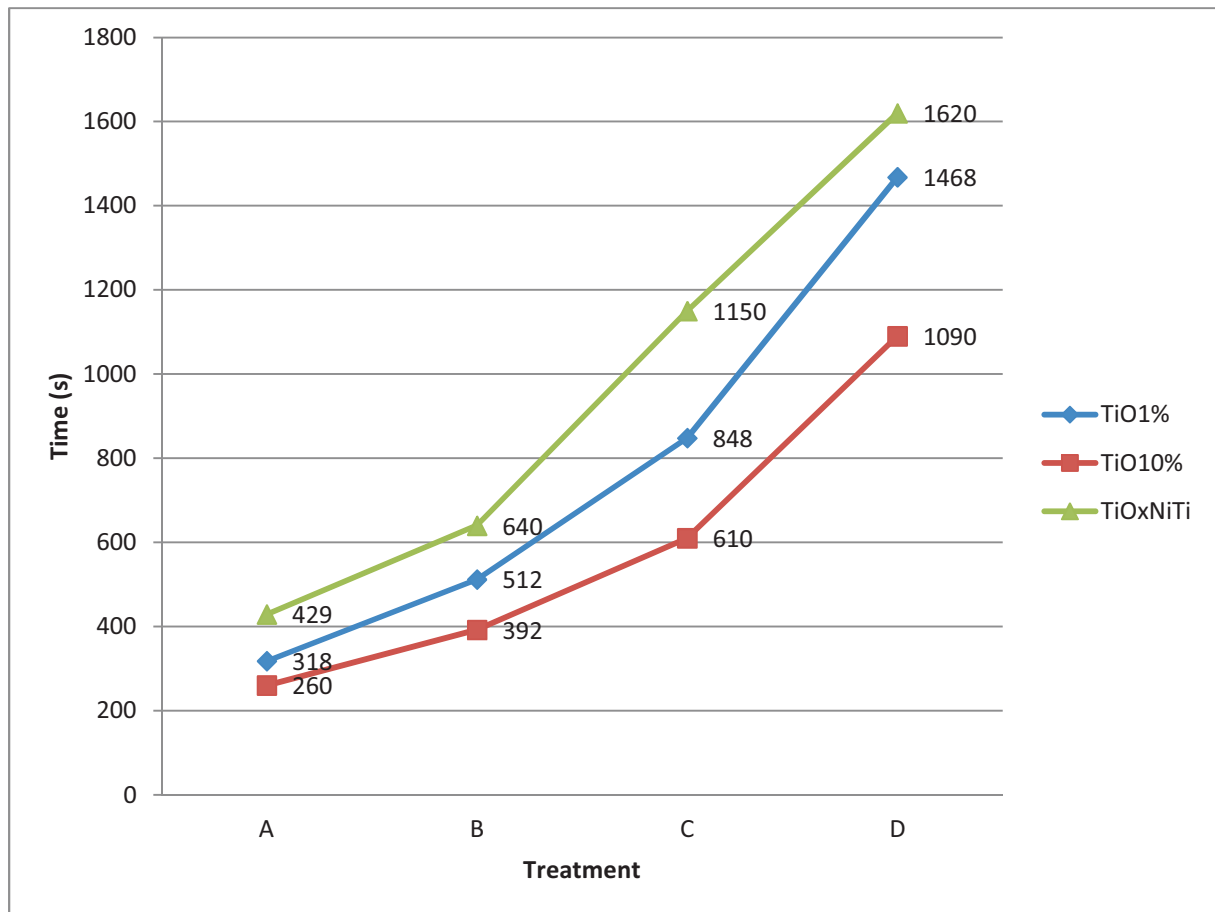


Figure 2.8. Profiling time needed to induce a decrease of the TiO^+ signal down to 1% (TiO1%) and 10% (TiO10%) of its maximum value of the profiling time at which the TiO^+ signal cross the NiTi^+ signal (TiOxNiTi) for 50 μm Nitinol wires untreated (A), heat treated for 15 min at 430°C (B), for 60 min at 430°C (C) and for 15 min at 500°C (D).

First, it can be pointed out that a heat treatment of 15 min at 430°C induces an important increase of the oxide layer thickness (the oxide layer being about 1.5-fold thicker after the heat treatment). An increase of the heat treatment time induces a further increase of the oxide layer thickness (the oxide layer being about 2.5-fold thicker after the heat treatment). However, the most important thickness increase is recorded with a higher heat treatment temperature. Indeed, while a heat treatment of 15 min at 430°C leads to an oxide layer about 1.5-fold thicker than the native one, a heat treatment of the same time at 500°C leads to an oxide layer about 4.2-fold thicker than the native one. Note also that after each studied heat treatment, the nickel signal is much higher than for the untreated wires and much more subject to matrix effect. These observations support the results obtained by XPS i.e. that heat treatment of Nitinol induces an important nickel diffusion toward the surface of the material and, therefore, an increase of the nickel proportion in the oxide layer.

2.1.1.5. Polarization curves measurements

The impact of heat treatments on the corrosion resistance of Nitinol has been assessed by polarization curves measurements. These polarization curves measurement have been carried

out in a Hank's solution (composition provided in Table 2.3) thermostated at $37\pm1^{\circ}\text{C}$ with the pH adjusted to 7.40 ± 0.05 (by addition of HCl or NaOH 1M aqueous solution). The electrochemical setup used is a conventional three electrodes electrochemical cell with a Pt foil as counter electrode, a saturated calomel electrode (SCE) connected with a salt bridge junction as reference electrode and a ~ 4 cm segment of Nitinol wire as working electrode. Note that knowing the precise length and diameter of the tested wire segments, it was always possible to calculate the area exposed to the electrolyte and therefore to normalize the measured current densities. It also important to note that, in order to characterize exclusively the oxide layer behavior, we covered the immersed extremity of the tested wire segments with a drop of varnish. According to ASTM F2129-04 (Electrochemical Corrosion Testing of Surgical Implants), the Hank's solution was deaerated for 30 min with a nitrogen flow prior the wire immersion. The wire segment is then immersed and its open circuit potential (OCP) curve measured for one hour. The polarization experiment itself is then started at a potential 100 mV more cathodic than the measured final OCP. The wire segment is polarized up to 1 V vs. SCE at a sweeping rate of 10 mV/s.

Table 2.3. Composition of the Hank's solution used for the polarization curves experiments

NaCl	CaCl₂.2H₂O	KCl	MgCl₂.6H₂O	MgSO₄.7H₂O
8.0 g	0.163 g	0.4 g	0.10 g	0.10 g
NaHCO₃	Na₂HPO₃	KH₂PO₄	Phenol Red	Glucose
0.337 g	0.12 g	0.06 g	0.02 g	1.00 g

Using this method, the corrosion resistance of 240 μm Nitinol wires has been assessed before and after the three heat treatments described in Table 2.1 have been assessed. As the results were quite different from one test to another, the experiment has been reproduced nine times for each studied surface state. The mean open circuit potentials (OCP), corrosion potentials (E_{cor}), corrosion current densities (i_{cor}), breakdown potentials (E_{br}) and passivity potential ranges (E_{pass}) as well as the corresponding standard deviations are summarized in Table 2.4. Representative OCP and polarization curves are presented in Figures 2.9 and 2.10, respectively.

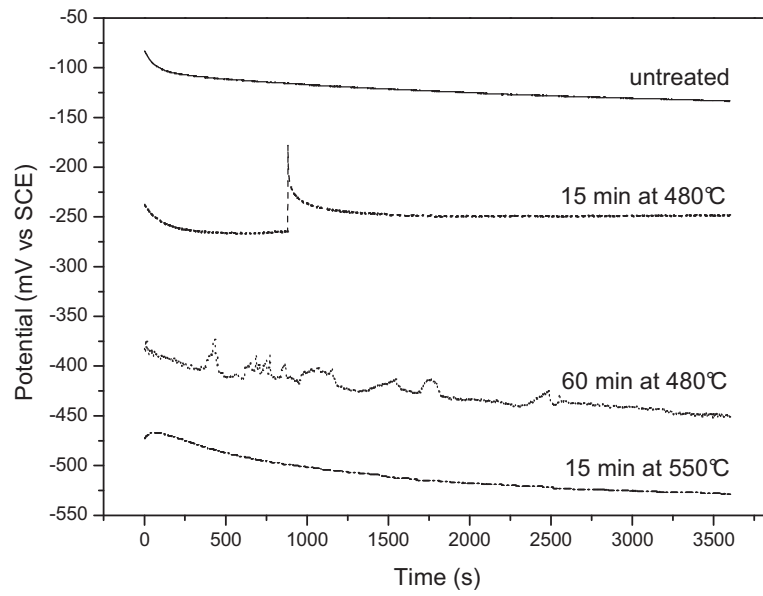


Figure 2.9. Open circuit potential curves of 240 μm Nitinol wires untreated (plain line) and submitted to a heat treatment for 15 min at 480°C (dashed line), 60 min at 480°C (dotted line) and 15 min at 550°C (dash-dotted line).

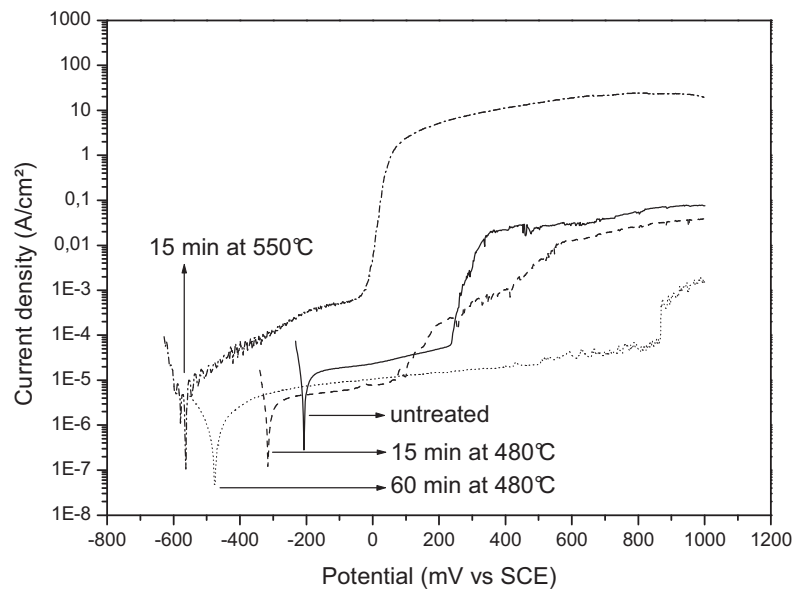


Figure 2.10. Polarization curves of 240 μm Nitinol wires untreated (plain line) and submitted to a heat treatment for 15 min at 480°C (dashed line), 60 min at 480°C (dotted line) and 15 min at 550°C (dash-dotted line).

Table 2.4. Numerical results of the polarization curves experiments carried out on 240 μm Nitinol wires untreated, submitted to heat treatment for 15 min at 480°C, for 60 min at 480°C and for 15 min at 550°C.

	OCP (mV vs SCE)	E_{cor} (mV vs. SCE)	i_{cor} (A/cm ²)	E_{br} (mV vs. SCE)	E_{pass} (mV)
Untreated	-153 $\pm$ 27	-201 $\pm$ 39	$4.0 \times 10^{-6} \pm 2.3 \times 10^{-6}$	238 $\pm$ 190	439 $\pm$ 195
480°C / 15 min	-228 $\pm$ 54	-302 $\pm$ 52	$1.4 \times 10^{-6} \pm 4.3 \times 10^{-7}$	147 $\pm$ 90	449 $\pm$ 94
480°C / 60 min	-454 $\pm$ 52	-505 $\pm$ 57	$1.8 \times 10^{-6} \pm 7.5 \times 10^{-7}$	294 $\pm$ 355	799 $\pm$ 380
550°C / 60 min	-489 $\pm$ 44	-523 $\pm$ 48	$6.6 \times 10^{-6} \pm 2.0 \times 10^{-6}$	-5 $\pm$ 22	518 $\pm$ 27

First of all, it can be pointed out that the heat treatment of the Nitinol for 15 min at 480°C leads to a significant shift of the corrosion potential toward more cathodic values as well as to a slight decrease of the corrosion current density. This is characteristic of a mainly cathodic corrosion inhibition which is in good accordance with the results presented previously i.e. as the heat treatment induces an increase of the oxide layer thickness, the transfer of electrons from the metal to the solution is inhibited and therefore, the cathodic reaction rate (reduction of the protons into molecular hydrogen) is decreased. Both untreated and heat treated Nitinol wires show susceptibility to pitting corrosion. The passivity potential range of untreated and heat treated wires is similar. However, the results obtained with heat treated wires are slightly more reproducible as shown by the decreased standard deviation.

An increase of the heat treatment time induces a further shift of the corrosion potential toward more cathodic values. However, the corrosion current density does not change significantly with an increase of the heat treatment time from 15 to 60 minutes. Regarding pitting corrosion resistance, the Nitinol wires treated for 60 min at 480°C show a much higher mean breakdown potential. However, it is important to point out the evident lack of reproducibility of these results as shown by the huge corresponding standard deviation.

Interestingly, with an increase of the heat treatment temperature, the corrosion current density slightly increases while the corrosion potential is further shifted toward more cathodic values. Thus, even if an increase of the heat treatment temperature leads to the thickest oxide layer (explaining the more cathodic corrosion potential), this oxide layer does not seem to provide an efficient corrosion resistance to the material ²¹⁷.

2.1.1.6. Conclusions

As shown in this section, the typical shape-setting heat treatment of Nitinol has a significant effect on its surface composition and resistance to corrosion.

First, we have seen that the heat treatment induces an important diffusion of nickel toward the surface of the material leading to a more important amount of nickel in the oxide layer. Furthermore, while the oxide layer of untreated Nitinol wires is mainly composed of TiO₂ and nickel hydroxide, the heat treatment leads to a significant increase of the NiO proportion among the nickel oxide species present at the surface of Nitinol.

ToF-SIMS analysis allowed us to characterize the relative thicknesses of the obtained oxide layers. It appeared that the heat treatment induces a significant increase of the oxide layer thickness. It was also shown that an increase of the heat treatment temperature leads to a

much more important increase of the resulting oxide layer than an increase of the heat treatment time does.

Finally, polarization curves experiments were carried out to study the impact of the heat treatment on the resistance to corrosion of Nitinol. It is found that the typical shape-setting heat treatment induces a very slight decrease of the corrosion current density and a significant cathodic shift of the corrosion potential. An increase of the time or the temperature of the heat treatment induces a further cathodic shift of the corrosion potential but no reduction of the corrosion current density. Note that all the tested Nitinol wires were sensitive to pitting corrosion. The largest passive ranges were measured for longer heat treatment times but the corresponding results were highly irreproducible.

Therefore, the oxide layer obtained after the heat treatment should be considered as bad regarding the Nitinol biocompatibility as it induces the presence of a higher amount of nickel at the surface of the material (which could *a priori* lead to a higher toxic nickel ions leaching) without improving significantly its resistance to corrosion. This confirms the necessity of further surface treatments of the alloy in order to improve its biocompatibility.

2.1.2. Chemical etching

2.1.2.1. Introduction

As we have just seen, the presence of a thick oxide layer on the surface of Nitinol is not necessary beneficial regarding the nickel abundance at the surface (and therefore the material biocompatibility) as well as the material resistance to corrosion. Chemical etching is a common way to remove the formed oxide layer^{218,221,223,227}. In line with the heat treatment study presented here above, we studied the impact of a chemical etching treatment on Nitinol surface composition, morphology and resistance to corrosion.

2.1.2.2. Samples preparation

The Nitinol 50 μm and 240 μm diameter wires were cut in small segments, cleaned by sonication 15 minutes in ethanol and dried overnight at room temperature in a closed box in order to avoid recontaminations.

Half of these segments were then submitted to heat treatment at air in a resistance furnace for 15 min at 480°C for the 240 μm diameter wires and 430°C for the 50 μm diameter wires. After the heat treatment, the wires were allowed to cool down for several hours at room temperature, cleaned again by sonication 15 minutes in ethanol and dried overnight at room temperature in a closed box.

Untreated and heat treated wires were then submitted to a chemical etching treatment by immersion 5 min in a 5% vol. HF/12% vol. HNO₃ aqueous solution. The sample were then copiously rinsed several times with milli-Q water, cleaned by sonication 15 minutes in ethanol and dried overnight at room temperature in a closed box.

2.1.2.3. XPS analysis

As described previously, the analysis area has been increased by sticking several wire segments side by side (at least 10 wire segments for the 240 μm wire and at least 50 wire segments for the 50 μm wire) in order to collect a sufficient XPS signal from these wires. The XPS survey spectra for 240 μm wires and 50 μm wires are presented in Figures 2.11 and 2.12, respectively.

First of all, as previously, the peaks characteristic of the main elements present in Nitinol i.e. the titanium (Ti3p, Ti2p and Ti2s around 38 eV, 455 eV and 565 eV, respectively) and the nickel (Ni3p, Ni3s and Ni2p around 68 eV, 110 eV and 855 eV, respectively) are visible on each spectrum. Beside those elements, the presence of an intense O1s core level photoelectron peak (centered around 530 eV) attributed to the oxygen present in the oxide layer as well as a C1s core level photoelectron peak (centered around 285 eV) is noticed on each analyzed sample (attributed to the presence of adsorbed atmospheric contaminations). Note that for the chemically etched samples, no nitrogen or fluorine peak can be observed indicating that no chemical from the etching bath remain on the treated surfaces.

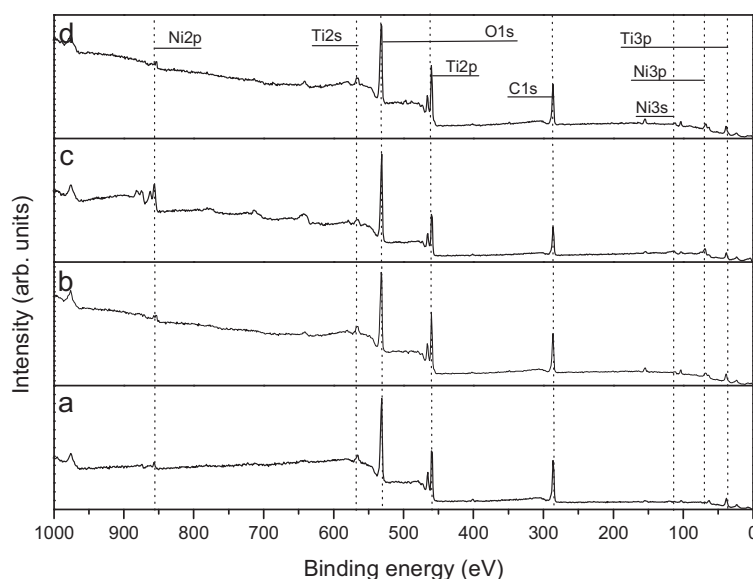


Figure 2.11. XPS survey spectra of 240 μm Nitinol wires untreated (a), after a chemical etching of 5 min (b), after a heat treatment of 15 min at 480°C (c) and after a heat treatment of 15 min at 480°C followed by a chemical etching of 5 min (d).

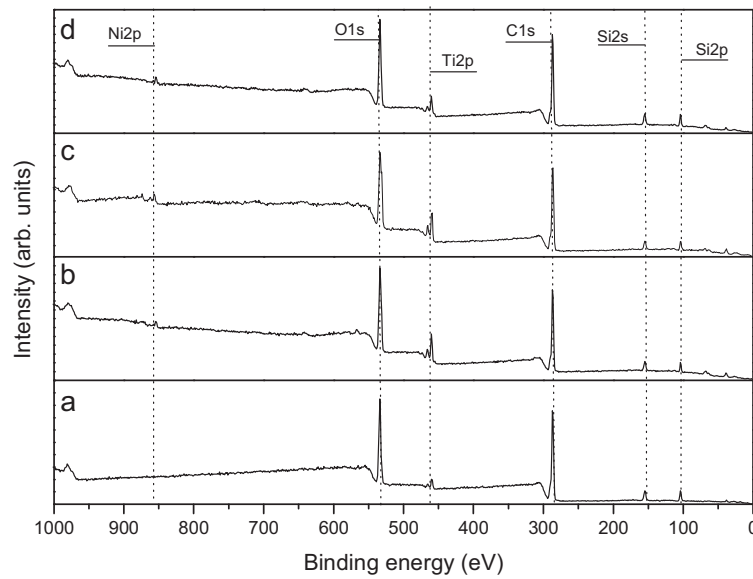


Figure 2.12. XPS survey spectra of 50 μm Nitinol wires untreated (a), after a chemical etching of 5 min (b), after a heat treatment of 15 min at 430°C (c) and after a heat treatment of 15 min at 430°C followed by a chemical etching of 5 min (d).

On the basis of these XPS analysis, the Ni/Ti ratios have been calculated in order to assess the proportion of nickel at the surface of the wires. These ratios are presented in Table 2.5.

Table 2.5. Ni/Ti ratios calculated on the basis of XPS analysis of 240 μm and 50 μm Nitinol wires untreated, etched, heat treated and etched after a heat treatment.

	Ø 240 μm	Ø 50 μm
Untreated	0.16	0.00
Etched	0.13	0.30
Heat treated	0.66	0.38
Heat treated and etched	0.14	0.31

When applied to 240 μm untreated wires, a chemical etching does not change significantly the Ni/Ti ratio. On the opposite, when applied after a heat treatment, the chemical etching treatment induces an important decrease of this ratio. Regarding the 50 μm diameter wires, a chemical etching of the surface leads to the appearance of nickel at the surface of the material while the oxide layer of the untreated wires was only composed of titanium oxide (TiO_2). When applied on heat treated 50 μm wires, the chemical etching induces an important decrease of the Ni/Ti ratio as observed for 240 μm wires.

In order to explain these results, the high resolution XPS analysis of the Ti2p and Ni2p core level photoelectron peaks has been carried out systematically for all these wires. Representative spectra are presented in Figures 2.13 and 2.14 for 240 μm and 50 μm wires, respectively.

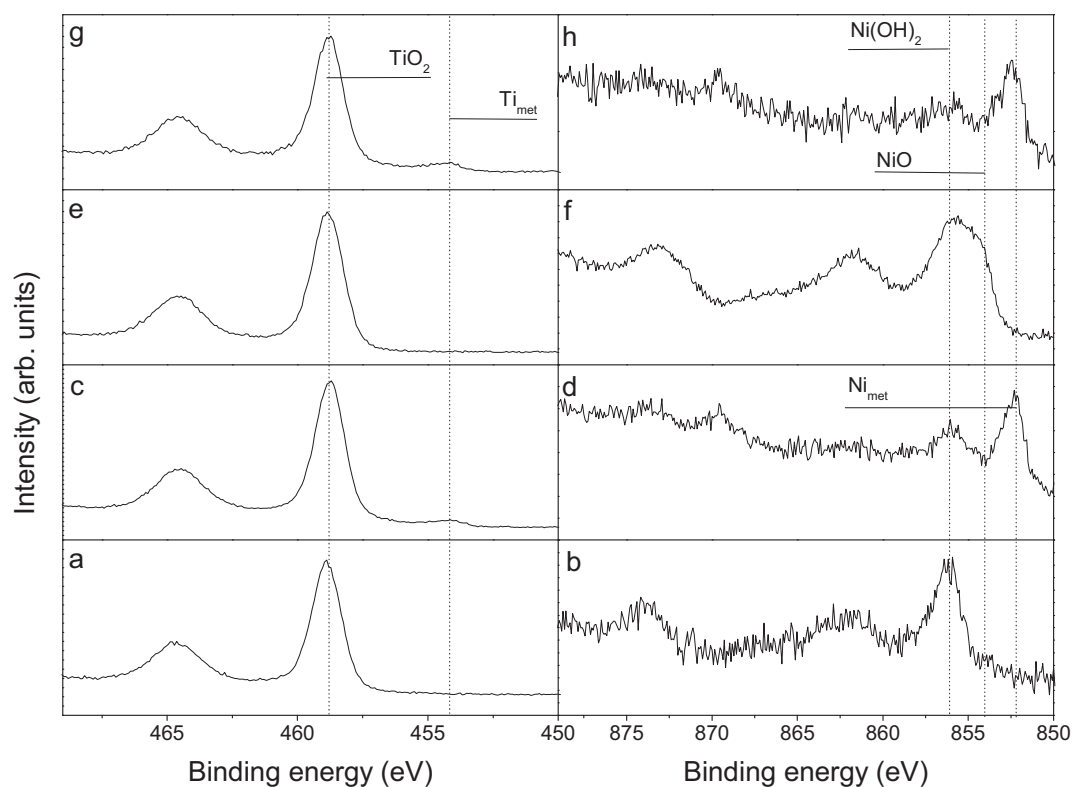


Figure 2.13. High resolution XPS spectra of the Ti2p (a, c, e and g) and Ni2p (b, d, f and h) core level photoelectron peaks of 240 μm Nitinol wires untreated (a and b), after a chemical etching of 5 min (c and d), after a heat treatment of 15 min at 480°C (e and f) and after a heat treatment of 15 min at 480°C followed by a chemical etching of 5 min (g and h).

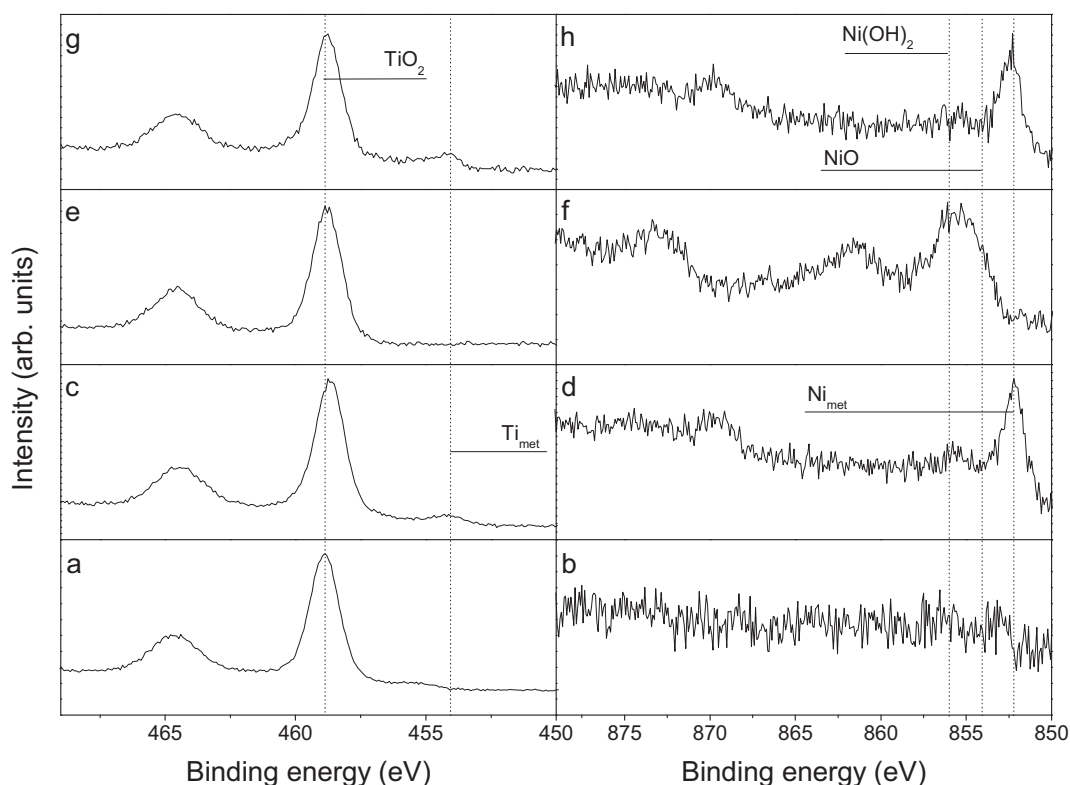


Figure 2.14. High resolution XPS spectra of the Ti2p (a, c, e and g) and Ni2p (b, d, f and h) core level photoelectron peaks of 50 μm Nitinol wires untreated (a and b), after a chemical etching of 5 min (c and d), after a heat treatment of 15 min at 430°C (e and f) and after a heat treatment of 15 min at 430°C followed by a chemical etching of 5 min (g and h).

For all the analyzed Nitinol samples, the main Ti2p_{3/2} peak is centered at 458.9 eV (characteristic of titanium in TiO₂). However, for each chemically etched set of wires, a titanium Ti2p_{3/2} peak centered at 454.2 eV (characteristic of titanium in the metallic state) appears. As the origin of this metallic titanium signal is the bulk material, it can reasonably assumed that the oxide layer resulting from a chemical etching treatment is thinner than the analysis depth of the spectrometer i.e. about 10 nm.

Regarding the Ni2p regions from 240 μm wires, it clearly appears that the chemical etching induces a significant decrease of the nickel oxides signal and the appearance of an important component centered at 852.2 eV, characteristic of nickel in the metallic state. This behavior can be observed on both untreated and heat treated samples. Regarding the 50 μm diameter wires, a nickel signal appears on chemically etched samples while no signal could be detected on the untreated ones. Again, the main component of this nickel signal, centered at 852.2 eV, is characteristic of metallic nickel while a second component centered around 856.2 eV (characteristic of nickel in nickel hydroxide (Ni(OH)₂)) can be pointed out. When applied to the heat treated 50 μm wires, the chemical etching treatment induces a significant decrease of the nickel oxides signal and the appearance of an important metallic nickel component.

These XPS results suggest that the chemical etching treatment completely remove the existing oxide layer from the surface of the Nitinol wires. The resulting “naked” surface being exposed to an aqueous solution containing oxidative nitrate ions, a new native oxide layer is directly formed.

2.1.2.4. SEM analysis

In order to confirm the hypothesis built on the basis of XPS results, a SEM analysis of 240 μm Nitinol wires have been carried out just after the chemical etching treatment. Note that in order to characterize to the best the chemical etching process, we observed heat treated wires (whose oxide layer is much more important as described before) gently removed from the etching bath and not rinsed and compared these results with heat treated wires before the chemical etching treatment. Representative pictures are presented in Figure 2.15 and 2.16.

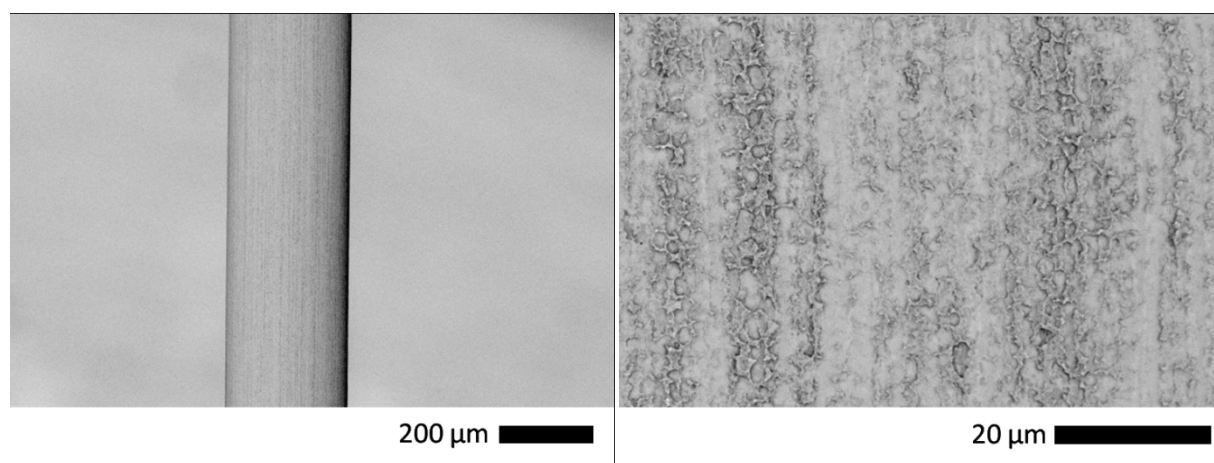


Figure 2.15. Representative SEM images of 240 μm Nitinol wires heat treated for 15 min at 480°C.

Pictures from the heat treated Nitinol wires surface show a relatively rough oxide layer with longitudinal strips resulting from the drawing process. A closer look at the surface morphology reveals several cracks and pits in the oxide layer. These structures are weak points and most probably, at least to some extent, responsible of the pitting corrosion susceptibility of the Nitinol wires that we described earlier^{214,215}.

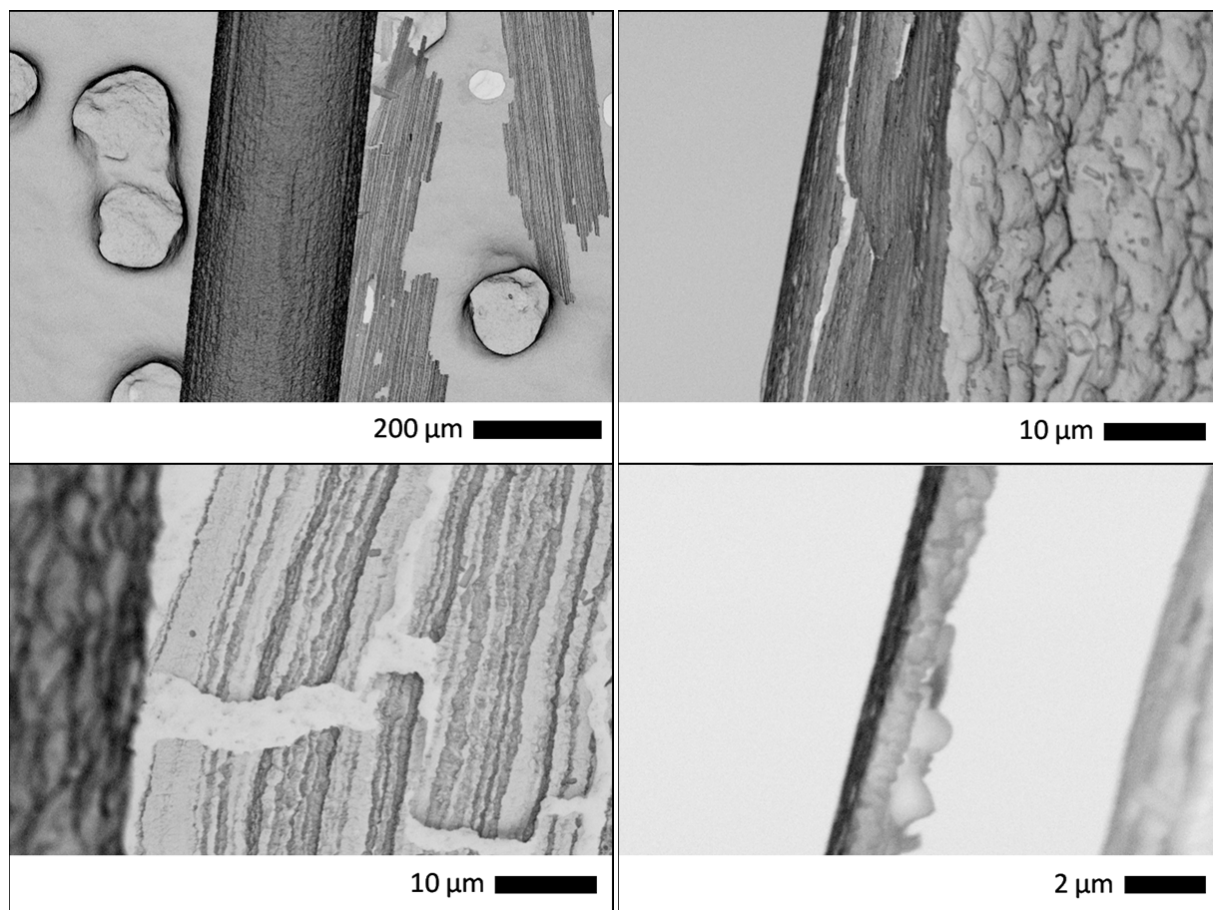


Figure 2.16. Representative SEM images of heat treated (480°C / 15 min) 240 μm Nitinol wires after a 5 min chemical etching without rinsing.

From the pictures of the chemically etched samples, it clearly appears that the etching process results in a complete removal of the original oxide layer. This confirms our hypothesis built on the basis of XPS results. The resulting surface morphology appears much rougher than the original oxide layer but also much more homogeneous and without clearly apparent defects that could enhance pitting corrosion phenomenon.

2.1.2.5. ToF-SIMS analysis

In order to further characterize the oxide layer formed on Nitinol after the chemical etching treatment, ToF-SIMS analysis of 50 μm Nitinol wires have been carried out following the experimental method described in section 2.1.1.4. The Nitinol wires were analyzed in four different surface states: untreated, chemically etched, heat treated (15min at 430°C) and chemically etched after a heat treatment. The obtained profiles and the corresponding etching time measurements ($\text{TiO}10\%$, $\text{TiO}1\%$ and TiO_xNiTi) are presented in Figures 2.17 and 2.18, respectively.

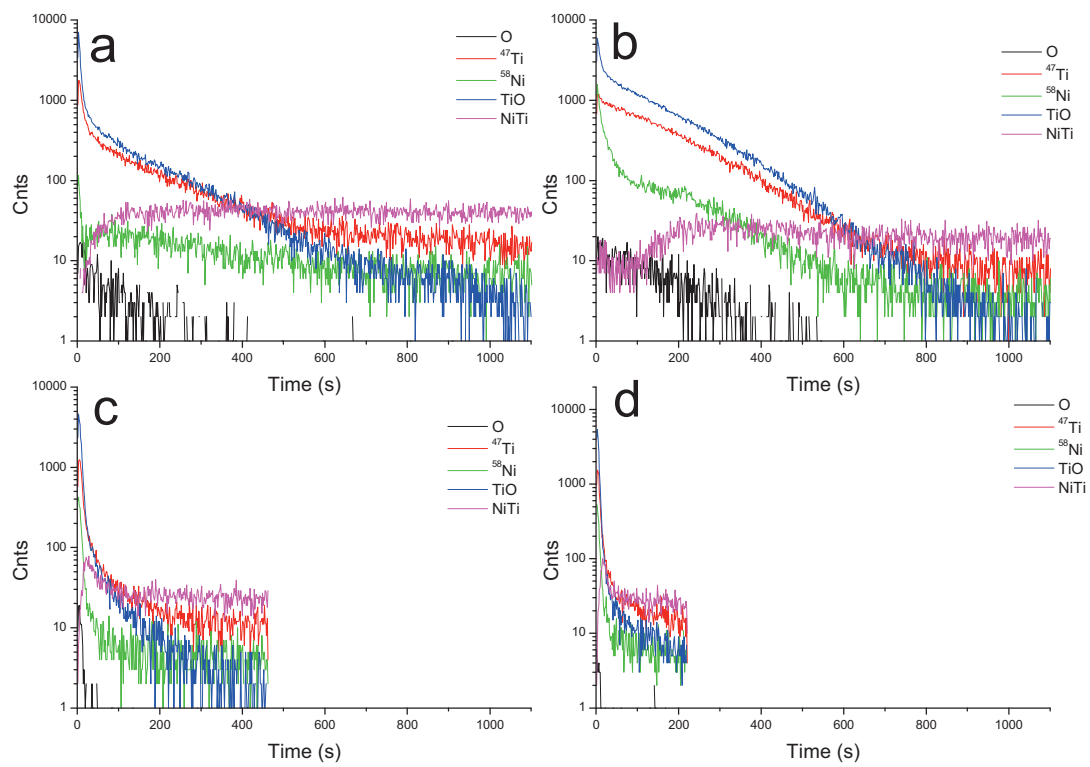


Figure 2.17. ToF-SIMS positive ions profile obtained for a 50 μm Nitinol wire untreated (a), heat treated for 15 min at 430°C (b), chemically etched for 5 min in a HF5%vol./HNO₃12%vol. aqueous solution (c) and chemically etched after a heat treatment (d).

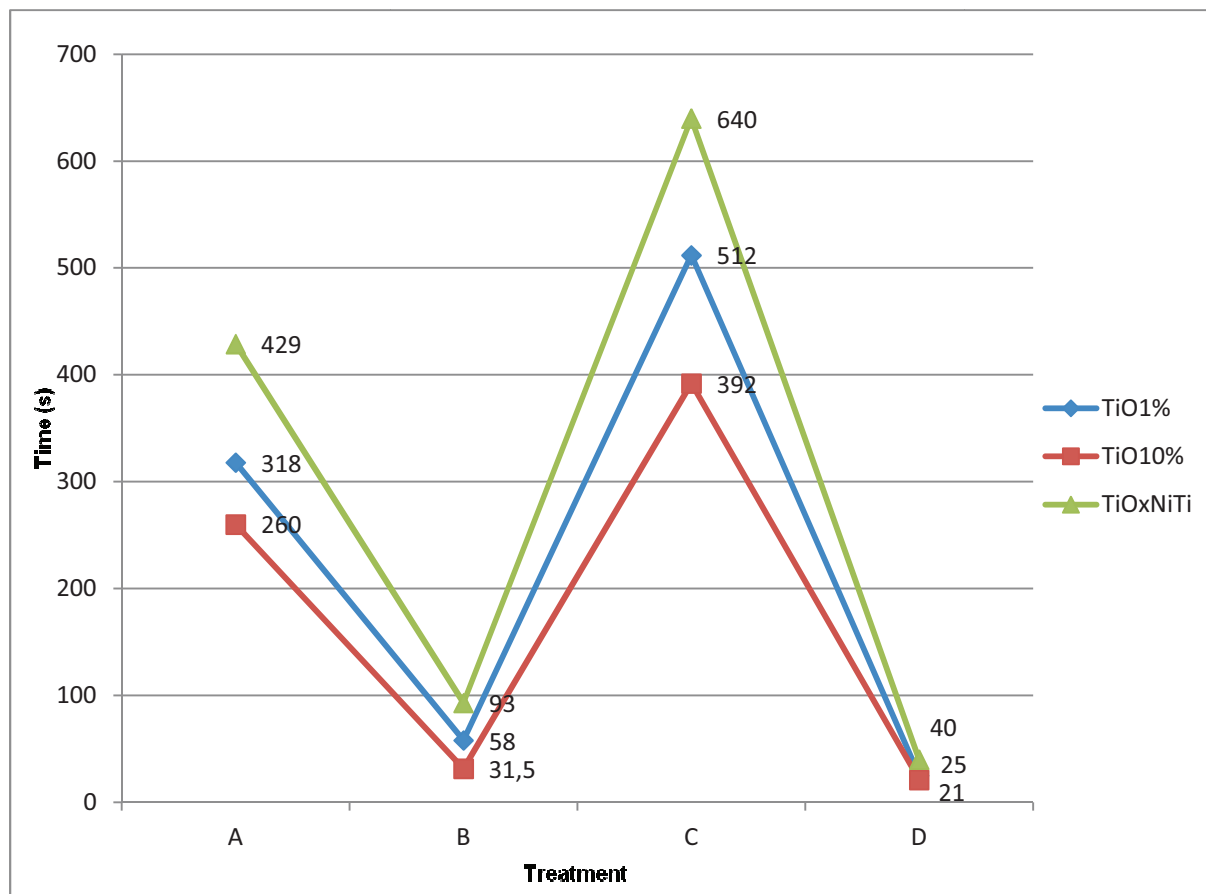


Figure 2.18. Profiling time needed to induce a decrease of the TiO^+ signal down to 1% (TiO1%) and 10% (TiO10%) of its maximum value of the profiling time at which the TiO^+ signal cross the NiTi^+ signal (TiOxNiTi) for 50 μm Nitinol wires untreated (A), chemically etched for 5 min in a $\text{HF}5\%\text{vol.}/\text{HNO}_312\%\text{vol.}$ aqueous solution (B), heat treated for 15 min at 430°C (C) and chemically etched after a heat treatment (D).

These measurements confirm our previous results i.e. that the chemical etching treatment leads to the formation of a much thinner oxide layer. This newly formed oxide layer is about 6-fold thinner than the native one (present on untreated wires) and about 18-fold thinner than the oxide layer present on the surface of heat treated Nitinol wires. Note that there is no significant thickness difference between the oxide layers resulting from the chemical etching of a heat treated wire and of an untreated wire. This method seems therefore suitable for a complete removal of the oxide layer resulting from the manufacturing process (untreated) or from the shape setting heat treatment.

2.1.2.6. Polarization curves measurements

The corrosion resistance of chemically etched 240 μm Nitinol wires has been assessed by polarization curves measurements. The experimental method has been described in section 2.1.1.5. Again, the experiment has been reproduced nine times for each studied surface state. Representative OCP and polarization curves are presented in Figures 2.19 and 2.20, respectively.

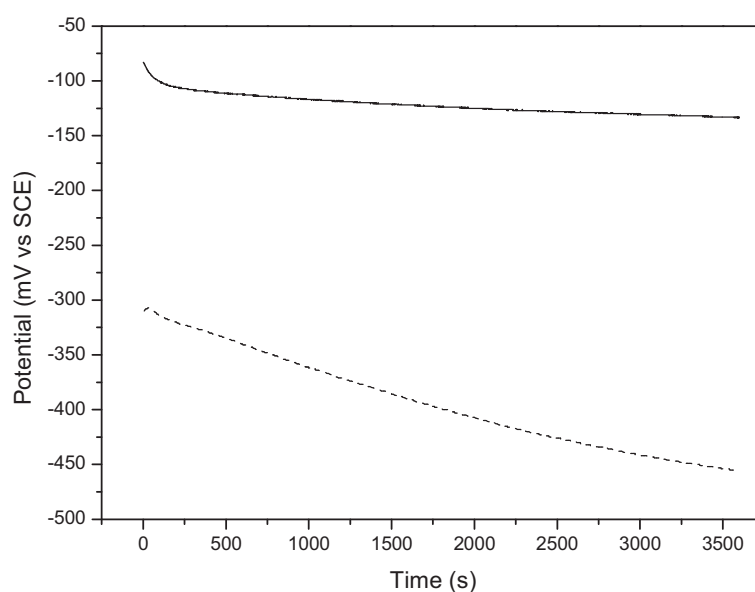


Figure 2.19. Open circuit potential curves of 240 μm Nitinol wires untreated (plain line) and submitted to a chemical etching treatment (dashed line).

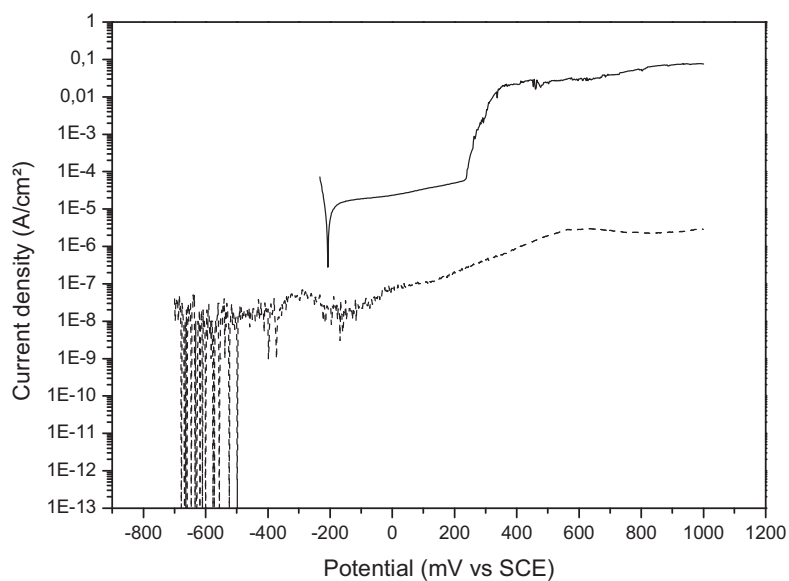


Figure 2.20. Polarization curves of 240 μm Nitinol wires untreated (plain line) and submitted to a chemical etching treatment (dashed line).

From these analyses, it appears that the chemical etching of Nitinol wires induces a significant shift of the corrosion potential toward more cathodic values. Furthermore on Figure 2.20, it can clearly be pointed out that both cathodic and anodic branches are lower after the chemical etching treatment. This is indicative of a mixed corrosion inhibition with a more pronounced inhibition of the cathodic reaction i.e. the formation of molecular hydrogen by reduction of

the protons in solution. This observation is surprising as we showed that the oxide layer resulting from a chemical etching treatment is much thinner than the native oxide layer of untreated Nitinol wires. Therefore, we could have expected the opposite behavior i.e. that a thinner oxide layer would have allowed an easier electron transfer from the metal to the electroactive species in solution. However, previous results showed that the chemical etching treatment also results in a much more elementally and morphologically homogeneous oxide layer. Indeed, the proportion of oxidized nickel is much less important after chemical etching and the newly formed oxide layer appeared to be exempt of structural weaknesses such as cracks and pits. These important factors could explain the much better resistance to corrosion of chemically etched Nitinol wires.

Note that the obtained polarization curves are very noisy. Therefore, it was impossible to measure precisely the corrosion potential and corrosion current density values for chemically etched wires. However, it clearly appears that the corrosion current density value of these wires is around 1×10^{-8} A/cm² i.e. about 100-fold lower than the one obtained for untreated wires ($4 \times 10^{-6} \pm 2.3 \times 10^{-6}$). Furthermore, all the chemically etched wires analyzed showed a very good resistance to pitting corrosion.

2.1.2.7. Conclusions

In this section, the impact of a chemical etching treatment on the surface of Nitinol wires has been studied. We showed that the chemical etching of Nitinol wires in a HF/HNO₃ solution results in a complete removal of the pre-existing oxide layer and the formation of a new native oxide layer.

This new oxide layer is very thin (<10 nm) and mainly composed of TiO₂ with a small amount of nickel oxides. Morphologically, the Nitinol surface appears to have a more important roughness after chemical etching but also to be much more homogeneous than the pre-existing oxide layer. Regarding the polarization curves experiments, the chemical etching treatment induces an important cathodic shift of the corrosion potential and a decrease of about two decades of the corrosion current density. Even more interestingly, the chemically etched Nitinol wires show a very good resistance to pitting corrosion.

Thus the chemical etching treatment appears to be a valuable solution to remove the oxide layer obtained after the shape-setting heat treatment and therefore obtain a Nitinol surface which contains much less nickel and provides a better resistance to corrosion (and therefore resulting *a priori* in a better biocompatibility of the alloy).

2.2. Nitinol plates

As a proper characterization of Nitinol wires is tricky for geometrical reasons (as we have seen in the frame of XPS and ToF-SIMS analyses), the choice has been made to work on planar Nitinol substrates for the rest of this study.

2.2.1. Analysis and heat treatment of “as received” Nitinol plates

2.2.1.1. Introduction

The Nitinol (2x1x0.2 cm³) plates (SE-508, lot # 82199, A_f 15°C max.) were provided by AMF France. Their bulk composition is presented in Table 2.6.

Table 2.6. Bulk composition of the LM81 Nitinol plates provided by AMF France

Ti %	Ni %	O %	H %	Co %	Fe %	Cu %	C %
Bal.	56.2	0.0257	0.0009	0.005	0.005	0.005	0.002

2.2.1.2. Samples preparation

First of all, the native oxide layer present on these substrates as well as the impact of a typical heat treatment on the composition of this oxide layer have been characterized. The Nitinol plates were cleaned by sonication 15 minutes in ethanol and flushed dry with a nitrogen steam. These substrates were then submitted to heat treatment at air in a resistance furnace for different times and temperatures: 20 minutes at 490°C, 60 minutes at 490°C and 20 minutes at 550°C. After the heat treatment, the substrates were allowed to cool down for several hours at room temperature, cleaned again by sonication 15 minutes in ethanol and flushed dry with a nitrogen steam.

2.2.1.3. XPS analysis

These substrates were systematically analyzed with XPS. The characteristic survey spectra are presented in Figure 2.21. First of all, as it was observed for Nitinol wires, the peaks characteristic of the main elements present in Nitinol i.e. the titanium (Ti3p, Ti2p and Ti2s around 38 eV, 455 eV and 565 eV, respectively) and the nickel (Ni3p, Ni3s and Ni2p around 68 eV, 110 eV and 855 eV, respectively) are well visible on these spectra. Furthermore, the presence of an important O1s core level photoelectron peak (centered around 530 eV) attributed to the oxygen present in the oxide layer as well as a C1s core level photoelectron peak (centered around 285 eV) can be observed on each analyzed sample. This C1s peak is attributed to the presence of adsorbed atmospheric contaminations remaining on the surface of the analyzed substrates.

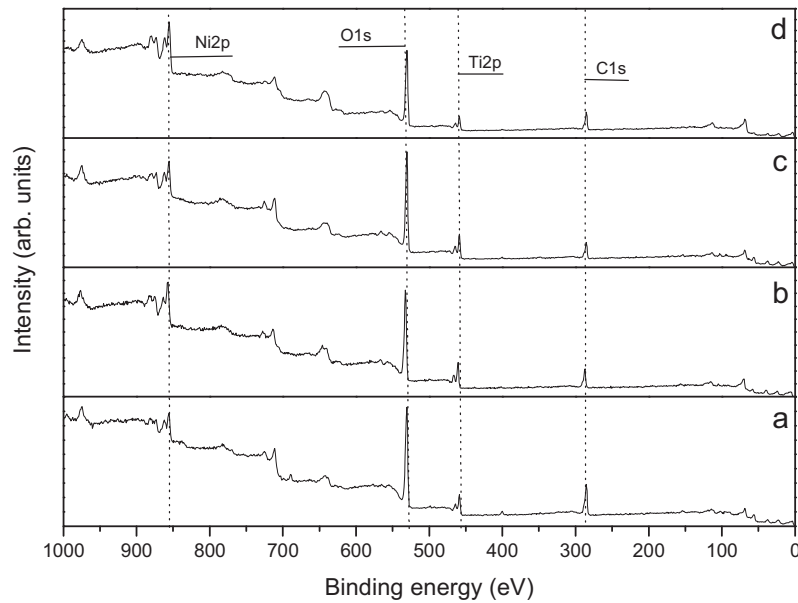


Figure 2.21. XPS survey spectra of Nitinol plates untreated (a) and after a heat treatment of 20 min at 490°C (b), 60 min at 490°C (c) and 20 min at 550°C (d).

Compared to the results obtained for Nitinol wires, it clearly appears that the nickel content of the untreated is much more important in the case of Nitinol plates. This is another clear evidence of the fact that the surface composition of Nitinol strongly depends on the provider and the manufacturing process as it was already suggested in the literature^{194,208,221,352-354}. This implies again the necessity of applying a surface modification to Nitinol prior any biomedical application. As noticed for Nitinol wires, the heat treatment of Nitinol induces an increase of the nickel proportion in the oxide layer i.e. a diffusion of the nickel to the surface. In order to further characterize this nickel proportion increase as well as the homogeneity of the Nitinol substrates, three different points of the surface were analyzed and the Ni/Ti ratios have been calculated on the basis of these analyses. These ratios are presented in Table 2.7.

Table 2.7. Ni/Ti ratios calculated on the basis of XPS analysis of 3 different points on Nitinol plates untreated and heat treated with different times and temperatures.

	Untreated	490°C / 20 min	490°C / 60 min	550°C / 20 min
Point #1	1.9	2.6	1.8	5.4
Point #2	1.8	3.7	2.3	4.7
Point #3	1.6	2.1	3.4	2.7
Mean	1.8	2.8	2.5	4.2

From these analyses, it clearly appears that the oxide layer on the surface of these samples is not homogeneous. This inhomogeneity is much more evident on heat treated surfaces suggesting that the outward nickel diffusion depends on the pre-existing oxide layer and can vary significantly at different places of the same substrate. Note that in the case of plane

Nitinol substrates, the increase of the heat treatment temperature seems to enhance the outward diffusion of nickel while the increase of the heat treatment time does not seem to change significantly the proportion of nickel in the resulting oxide layer.

The high resolution XPS analysis of the Ti2p and Ni2p core level photoelectron peaks has also been carried out systematically for all these substrates. Representative spectra are presented in Figure 2.22.

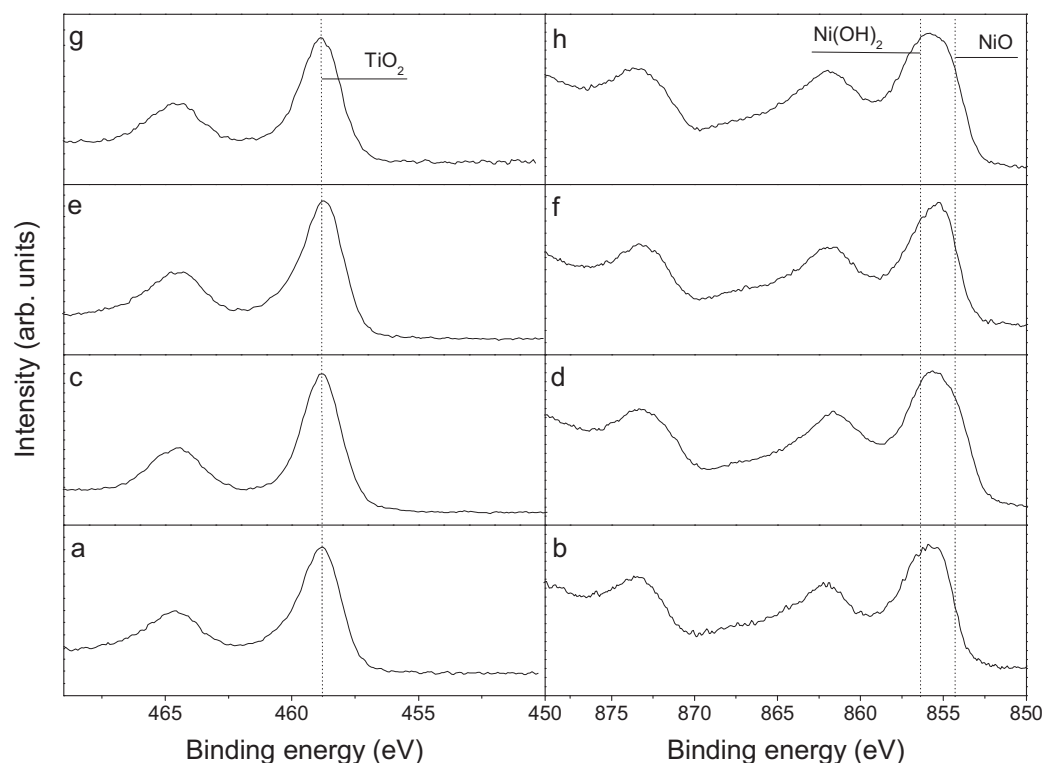


Figure 2.22. High resolution XPS spectra of the Ti2p (a, c, e and g) and Ni2p (b, d, f and h) core level photoelectron peaks of Nitinol plates untreated (a and b), and after a heat treatment of 20 min at 490°C (c and d), 60 min at 490°C (e and f) and 20 min at 550°C (g and h).

Like in the case of Nitinol wires, the Ti2p_{3/2} peak is systematically centered at 458.9 eV (characteristic of titanium in TiO₂). Therefore, titanium in the oxide layer is fully oxidized, even before thermal oxidation treatment.

Unlike Nitinol wires, beside a strong proportion of Ni(OH)₂ (Ni2p_{3/2} peak centered at 856.2 eV), the nickel present in the oxide layer of untreated Nitinol plates already shows a significant component relative to NiO (centered at 854.2 eV). After the heat treatment, the Ni2p spectrum of each sample shows a significant broadening of the nickel peak toward lower binding energies indicating an increase of the NiO proportion among the nickel oxides present at the surface of Nitinol. This latter observation is consistent with the observations carried out on Nitinol wires i.e. that the typical shape setting heat treatment of Nitinol induces a

significant increase of the proportion of NiO in the oxide layer beside the already mentioned increase of the Ni/Ti ratio.

2.2.1.4. Conclusions

As shown in this section, the oxide layer present on “as received” Nitinol plates is spatially inhomogeneous and significantly different from the one present on the surface of Nitinol wires. Obviously, the study and development of any further surface treatment and/or coating requires the control of the initial surface. Therefore, for the sequel of the studies carried out on Nitinol plates, an initial mechanical polishing step will be applied in order to remove completely the initial oxide layer. Note that mechanical polishing is not always considered as the most appropriate pretreatment in the literature^{207,209,220,355} but has the advantages of being quick, convenient and to lead to a homogeneous and reproducible surface state.

2.2.2. Analysis and modification of mechanically polished Nitinol plates

2.2.2.1. Introduction

In this chapter, we will expose three different studies carried out on polished Nitinol plates. The first one consists in a comparison study of the Nitinol surface modification by electrografting of a diazonium salt and by the formation of an organophosphonic acid monolayer. The ability of these two coatings to act as a convenient platform for post-grafting chemical reactions has been assessed with the prospect of grafting biocompatible molecules such as PEG.

The second part is a more fundamental examination of the solvent and temperature impact on the grafting of the *n*-dodecylphosphonic acid on Nitinol surface and of the resulting corrosion inhibition.

The last part of this chapter consists in a comparison of a conventional boiling water treatment of heat treated Nitinol plates with a similar oxidation treatment implying an original heat treatment i.e. induction heating.

2.2.2.2. Surface state of the Nitinol plates after mechanical polishing

The Nitinol substrates were mechanically polished down to 1 μm on a Buehler Phoenix 4000 instrument using various grit silicon carbide papers and diamond pastes. At the end of the polishing steps, the metal coupons were cleaned by sonication 15 min in ethanol, blown dry under a nitrogen flow and stored until their characterization.

The mean roughness of these substrates has been measured with a DEKTAK profilometer. It turns out that the mechanical polishing method applied to the Nitinol substrates induces a strong decrease of their mean roughness from 460 nm to 85 nm.

The high resolution XPS spectra of the Ti2p and Ni2p core level photoelectron regions have also been acquired. These spectra are presented in Figure 2.23.

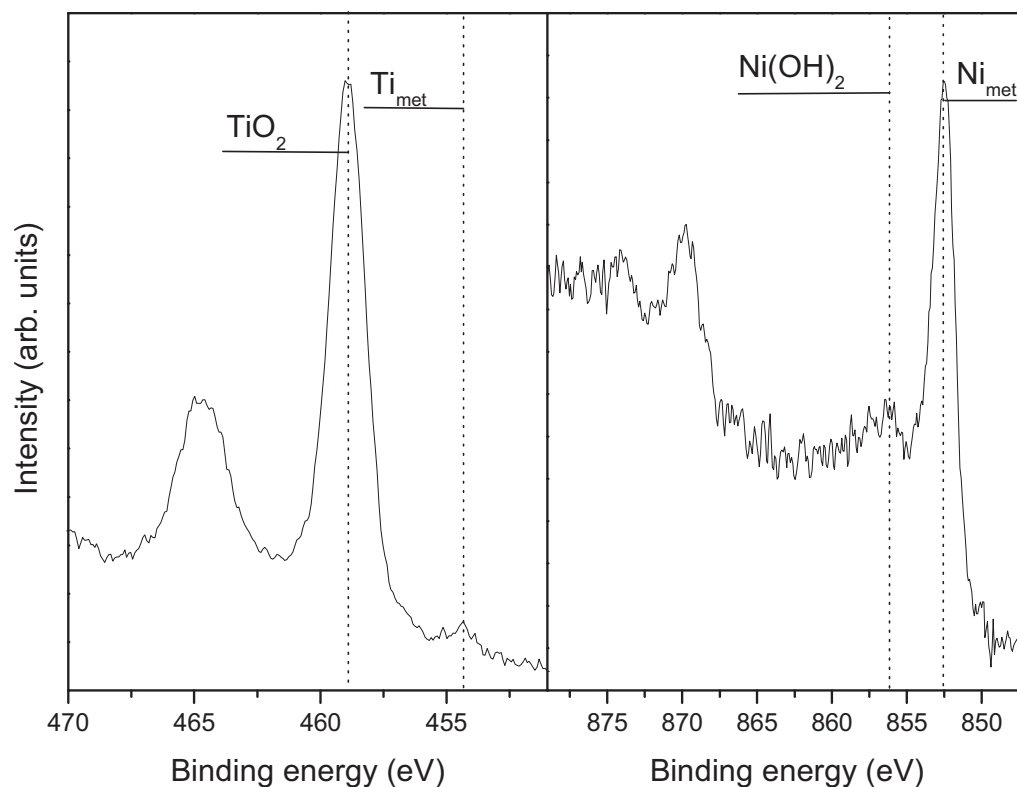


Figure 2.23. High resolution XPS spectra of the Ti2p (left) and Ni2p (right) core level photoelectron peaks of Nitinol plates after a mechanical polishing treatment.

On the Ti2p core level photoelectron spectrum, two main Ti2p_{3/2} components can be pointed out. The first one, centered at 458.9 eV, is characteristic of oxidized titanium in TiO₂ while the second one, centered at 424.2 eV, is characteristic of titanium in the metallic state. As the origin of this metallic titanium signal is the bulk material, we can reasonably conclude that the oxide layer formed on Nitinol substrates after mechanical polishing is thinner than the analysis depth of the spectrometer i.e. about 10 nm.

The Ni2p_{3/2} component centered at 852.7 eV clearly dominates the Ni2p region spectrum. This peak being characteristic of metallic nickel from the bulk material, this observation allows us to confirm the previous conclusion i.e. that the obtained oxide layer is thinner than 10 nm. Another low intensity component can be pointed out at 856.2 eV, characteristic of the nickel oxidized (Ni(OH)₂).

From the comparison of these two spectra and the calculation of the Ni/Ti ratio (about 0.27), it can be reasonably stated that the native oxide layer formed on the mechanically polished Nitinol substrates is mainly composed of TiO₂ and a very small amount of oxidized nickel. This confirms the widely reported preferential oxidation of titanium over nickel^{222,225,356}.

Note that unlike unpolished Nitinol plates, the surface composition of mechanically polished Nitinol plates is spatially homogeneous. This provides us a convenient reference surface for further functionalizations.

2.2.2.3. Functionalization of Nitinol surface toward a versatile platform for post-grafting chemical reactions

2.2.2.3.1. *Introduction*

Since the covalent modification of carbon surfaces by electrochemical reduction of diazonium salts has been first described by M. Delamar *et al.*³⁵⁷, this surface modification method has been largely reported in the literature³⁵⁸⁻³⁶³ and applied to several other materials such as gold³⁶⁴⁻³⁷², platinum³⁷³, nickel³⁷⁴, ZnNi³⁷⁵ or carbon nanotubes³⁷⁶.

With the prospect of improving the Nitinol-biological environment interactions, biocompatibility and hemocompatibility in particular, the aim of the present study is to compare the Nitinol surface modification by electrochemical reduction of the 1,4-carboxybenzene diazonium and its modification by formation of a 11-phosphonoundecanoic acid monolayer. The resulting surface is meant to constitute a reference platform for a large variety of post-grafting chemical reactions, e.g. with alcohols, amines, etc., to modify and control the surface properties of Nitinol. To assess this potential, we carried out the post-grafting with a fluorinated alcohol (the 1H,1H-perfluoro-1-decanol) by the Steglich esterification reaction between the carboxylic acid function of the grafted carboxybenzene or 11-phosphonoundecanoic acid molecules and the alcohol function. Note that this molecule is not grafted for biocompatibility purposes but used as a model. Indeed, the interest of working with such a fluorinated alcohol is the possibility to assess the “yield” of post-grafting with XPS analysis because of the absence of any fluorine atom in the initial system. Therefore, this study should be considered as a proof of concept work as the choice of a fluorinated molecule is clearly not the most suitable one for the improvement of the biocompatibility of the modified material.

2.2.2.3.2. *Samples preparation*

The Nitinol substrates were mechanically polished as described previously (see section 2.2.2.2) and stored until their modification.

Just before the electrografting of the 1,4-carboxybenzene diazonium, the Nitinol substrates were cleaned again by sonication 15 min in ethanol and blown dry under a nitrogen flow. The electrografting of the 1,4-carboxybenzene diazonium was carried out in a 0.1 M tetrabutylammonium tetrafluoroborate and 2 mM 1,4-carboxybenzene diazonium tetrafluoroborate solution in acetonitrile with a three electrodes electrochemical setup using a Pt foil as counter electrode, a saturated calomel electrode (SCE) connected with a salt bridge junction as reference and a controlled area of the Nitinol substrate (1 cm²) as working electrode. A schematic representation of this reaction is presented in Figure 2.24.

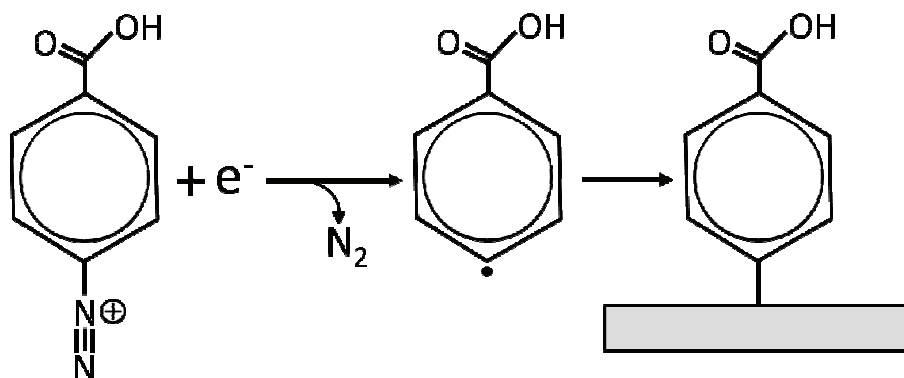


Figure 2.24. Schematic representation of the electrografting of the 1,4-carboxybenzene diazonium on a surface.

The 1,4-carboxybenzene diazonium was electroreduced on Nitinol surface by sweeping a range of potentials from 0.4 V to -1.4 V vs. SCE with a scan rate of 10 mV/s. The corresponding electroreduction curve is presented in Figure 2.25. After this step, the substrates were copiously rinsed with water and acetone, blown dry under a nitrogen flow and characterized directly or submitted to the post-grafting Steglich esterification reaction.

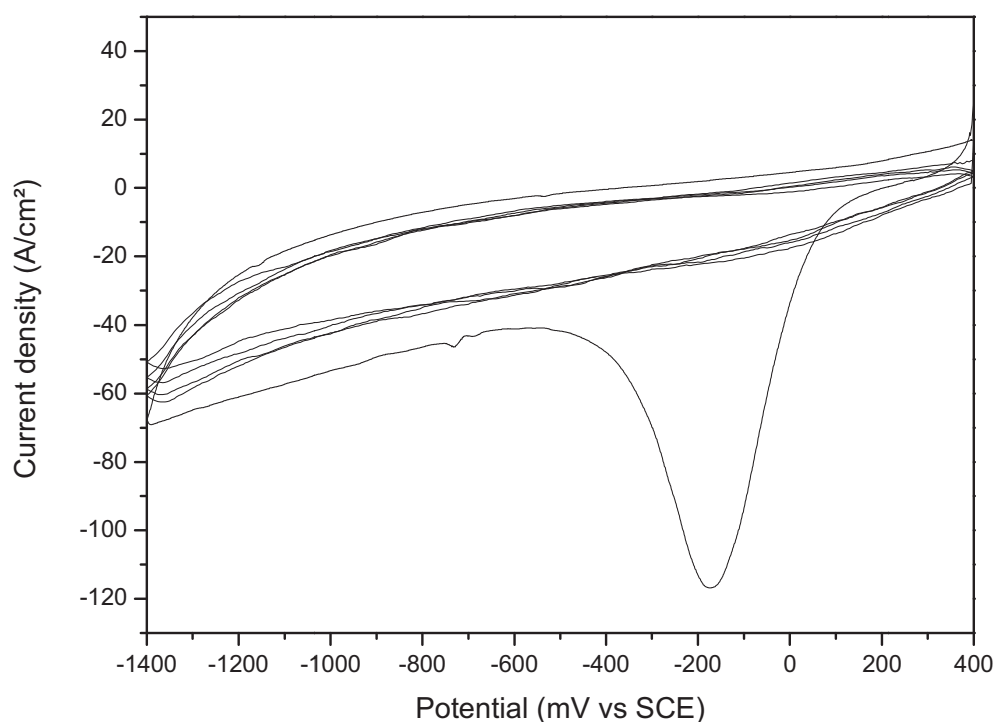
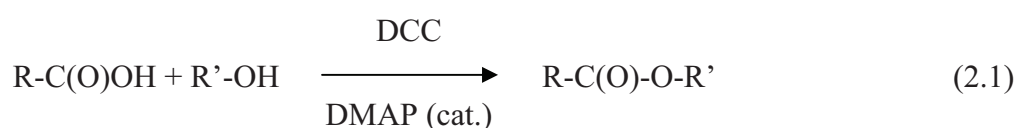


Figure 2.25. Characteristic cyclic voltammogram of the 1,4-carboxybenzene diazonium electrografting on polished Nitinol substrate (in a 0.1 M tetrabutylammonium tetrafluoroborate and 2 mM 1,4-carboxybenzene diazonium tetrafluoroborate solution in acetonitrile / scan rate : 10 mV/s).

Before the grafting of the 11-phosphonoundecanoic acid, the Nitinol substrates were cleaned again by sonication 15 min in ethanol, blown dry under a nitrogen flow and submitted to a UV/O₃ treatment for 30 min. The substrates were then directly immersed in a 1 mM ethanolic solution of 11-phosphonoundecanoic acid for 24 h at 50°C. The substrates were then copiously rinsed with ethanol, cleaned by sonication 15 min in ethanol, blown dry under a nitrogen flow and characterized directly or submitted to the post-grafting Steglich esterification reaction.

The last step of this study is the assessment of the efficiency of the modified Nitinol substrates as a platform for post-grafting chemical reactions. This has been done by studying the grafting of the 1H,1H-perfluoro-1-decanol (called CF) on the carboxylic functions available on modified Nitinol substrates via a Steglich esterification reaction. The general reaction is described in equation (2.1).



This reaction is carried out in anhydrous environment under nitrogen atmosphere. The modified Nitinol substrates were immersed in a solution of 20 ml anhydrous CH₂Cl₂, 1 mmol 1,3-dicyclohexylcarbodiimide (DCC), 1mmol 4-N,N-dimethylaminopyridin (DMAP) and 1 mmol CF. This system was cooled at 0°C and maintained under continuous stirring. After 24 hours of reaction, the substrates were removed from the solution, copiously rinsed with anhydrous CH₂Cl₂, cleaned by two successive sonication steps of 15 min in CH₂Cl₂ and ultrapure water and finally blown dry with a nitrogen flow.

2.2.2.3.3. *Electrografting of the 1,4-carboxybenzene diazonium*

After the electrografting step, as described in the experimental section, Nitinol substrates were first characterized by XPS. The corresponding survey spectra are presented in Figure 2.26. On the bare NiTi spectra, the characteristic peaks of the different elements present at Nitinol surface, namely titanium, nickel and oxygen, can be pointed out. Note also the presence of a relatively important Cls peak attributed to the presence of some physisorbed atmospheric contaminations. Beside these elements, we can also point out the presence of a significant N1s core level photoelectron peak on the spectrum of the electrografted sample.

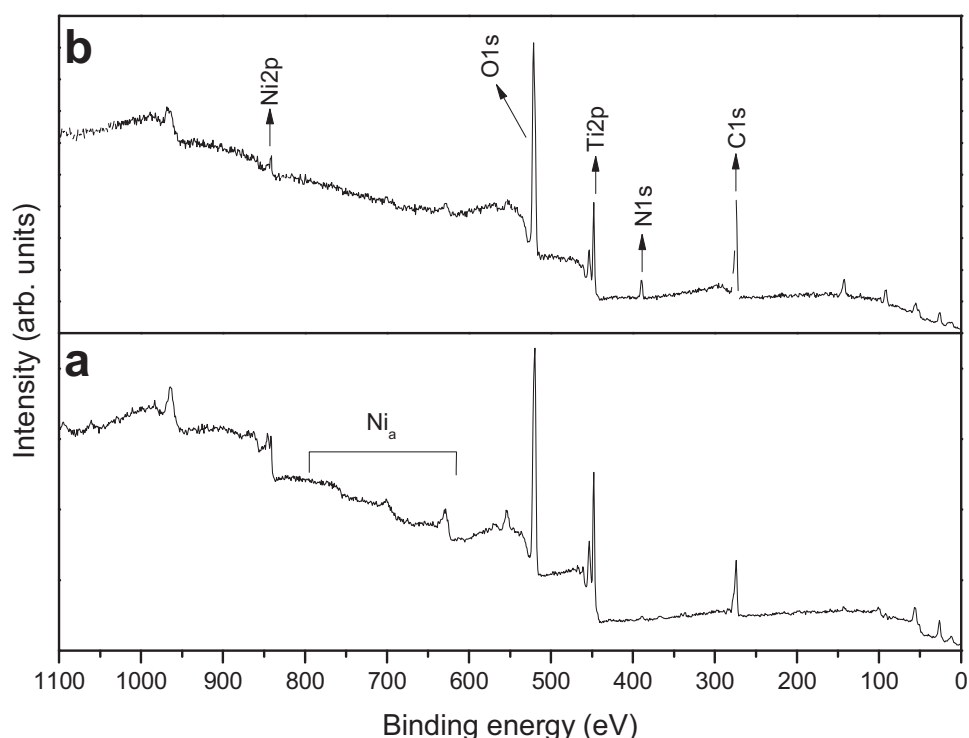


Figure 2.26. XPS survey spectra of a bare polished Nitinol substrate (a) and a Nitinol substrate modified by electrografting the 1,4-carboxybenzene diazonium (b).

In order to determine the origin of this significant amount of nitrogen on the electrografted Nitinol substrates, the high resolution spectra of the N1s and C1s regions have been acquired (Figure 2.27). The C1s photoelectron peak has been analyzed with four peaks centered at 284.4, 285.0, 286.3 and 288.4 eV attributed to aromatic (“sp²”), aliphatic (“sp³”), slightly oxidized (“SO”) and highly oxidized (“HO”) carbon atoms, respectively. The peak characteristic of aromatic carbon allows us to confirm the presence of carboxybenzene on the electrografted Nitinol surfaces as well as the HO peak centered at 288.4 eV corresponding to the carboxylic function of the grafted molecule. However, the ratio of areas sp²/HO is around 2.6 which is far lower than the theoretical value (sp²/HO = 6 according to the molecule stoichiometry). A significant part of the HO peak is thus attributed to physisorbed atmospheric contaminations as well as the SO and sp³ peaks corresponding to slightly oxidized carbon and aliphatic carbon atoms both absent in the grafted molecule. The N1s photoelectron peak has been analyzed with two components. The first one, centered at 400.0 eV, can be assigned to the nitrogen atom of the acetonitrile used as solvent for the electrografting. Considering the composition of acetonitrile, this is consistent with the analysis of the C1s spectrum; the CH₃ group corresponds to the sp³ peak and the photoelectrons from the carbon atom of the nitrile function have a binding energy corresponding to the SO peak. Note that this peak could also be attributed to some N₂ adsorbed contaminations (from the atmosphere or from the drying step). The second component, centered at 401.7 eV, can either be assigned to the nitrogen atom of the

tetrabutylammonium cation or to some unreduced diazonium functions. However, the complete absence of any reduction peak on the electroreduction voltammogram after the first cathodic sweep suggests the fact that the electrografted layer has reached a sufficient thickness to become insulating enough to prevent any further diazonium ion addition (see Figure 2.25). As a consequence, the N1s photoelectron peak component centered at 401.7 eV can only be assigned to tetrabutylammonium. Again this is consistent with our analysis of the C1s spectrum as the carbon atoms of the tetrabutylammonium are aliphatic and therefore included in the sp^3 peak. It thus appears that some solvent molecules as well as some tetrabutylammonium cations are entrapped in the formed layer. As it is a well-known fact that the electroreduction of diazonium salts can lead to the formation of a reticulated multilayer instead of a monolayer ^{362,366,373,375}, we can reasonably make the hypothesis that the electroreduction of the 1,4-carboxybenzene diazonium in the conditions used in the frame of this work leads to the formation of such a reticulated multilayer comforting the hypothesis on the entrapment of solvent molecules and tetrabutylammonium cations. It is also interesting to notice that several publications reporting on the electrografting of diazonium salts mention the possibility of the formation of azo bridges in the electrografted layer ³⁷⁷⁻³⁸². In these studies, the binding energy of the N1s photoelectrons in these azo bridges is reported to be 400.0 eV with all spectra corrected according to the C1s peak at 284.5 eV ³⁸¹ i.e at 400.5 eV with all spectra corrected according to the C1s peak at 285.0 eV for the present study. As a consequence, the azo bridges N1s photoelectron peak should be located between the two peaks of the Figure 2.27. Therefore it is difficult to confirm or infirm the presence of such azo bridges in the grafted multilayer.

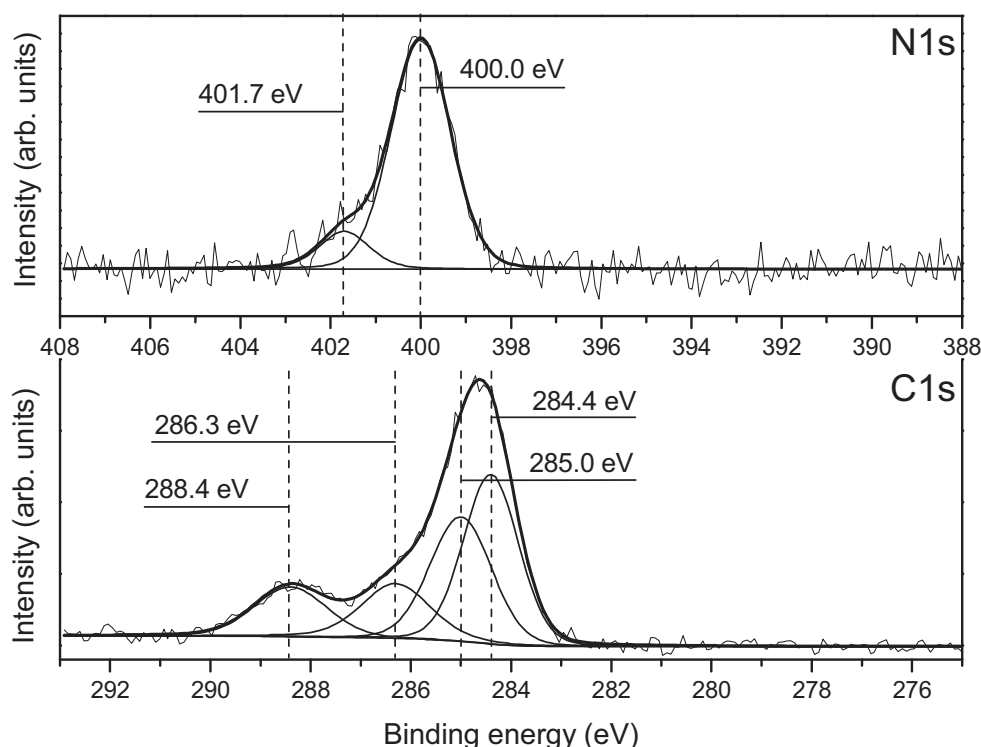


Figure 2.27. XPS high resolution spectra of the N1s and C1s core level photoelectron peaks of Nitinol substrates modified by electrografting the 1,4-carboxybenzene diazonium.

The electrografting of 1,4-carboxybenzene diazonium is associated with an important increase of the surface hydrophilicity as the contact angle decreases from 64° for a bare Nitinol substrate to 48° for a modified Nitinol substrate. This behavior is in good correlation with the nature of the electrografted molecule itself i.e. each 1,4-carboxybenzene diazonium brings one hydrophilic carboxyl group on the NiTi surface and with the XPS data i.e. that the formed layer is a non-compact reticulated multilayer (which obviously leads to the presence of more hydrophilic carboxyl groups per unit area than a monolayer).

In order to characterize the impact of the electrografted layer on the corrosion resistance of Nitinol, polarization curves analysis of bare and modified Nitinol substrates have been carried out. These polarization curves experiments have been carried out in a 0.5 M NaCl aqueous solution by sweeping a range of potentials from -1 to 1 V vs. SCE at 1 mV/s (see Figure 2.28). First of all, it can be seen that the corrosion current density of the modified sample is higher than for the bare Nitinol sample. It also clearly appears that the increase of the cathodic part of the curve is more important than the anodic one, leading to a shift of the corrosion potential from -377 to -224 mV vs. SCE. Furthermore, the passivity domain (potential range between the corrosion potential and the pitting corrosion potential) of Nitinol is drastically reduced when its surface is modified with an electrografted carboxybenzene layer (from 460 mV for a bare Nitinol substrate to 235 mV for a modified one). All these observations can be explained by the nature of the grafted layer and the process used to graft this layer. First, the electrografting is a reductive process which obviously leads to an alteration of the passivating

native oxide layer present at the surface of bare polished Nitinol substrate. Furthermore, the resulting electrografted layer is a non-compact hydrophilic multilayer which does not prevent accessibility of electroactive species to the NiTi surface.

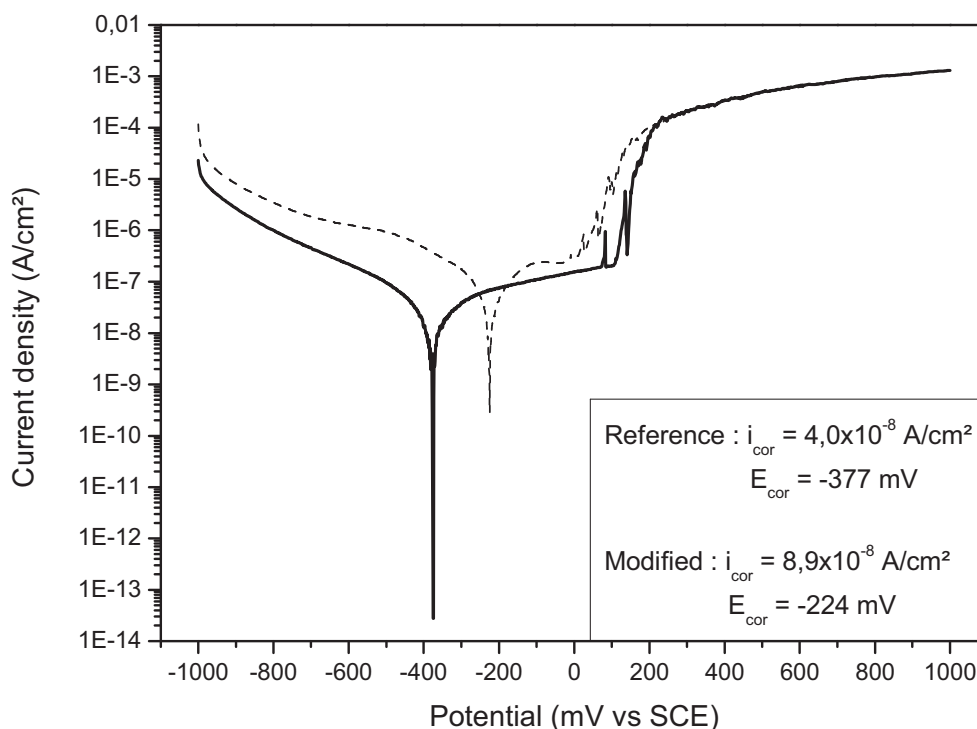


Figure 2.28. Polarization curves of a bare polished Nitinol substrate (thick plain line) and a Nitinol substrate modified by electrografting the 1,4-carboxybenzene diazonium (dashed line) acquired by sweeping a range of potentials from -1 to 1 V vs. SCE at 1 mV/s in a 0.5 M sodium chloride solution.

2.2.2.3.4. Grafting of the 11-phosphonoundecanoic acid

The grafting of the 11-phosphonoundecanoic acid has been carried out on Nitinol as described previously. The modified Nitinol substrates were first characterized by XPS. By comparison of the survey spectra of a bare Nitinol substrate with a modified one, an increase of the C1s signal as well as the appearance of a P2p core level photoelectrons peak accompanying the grafting of the 11-phosphonoundecanoic acid monolayer can be pointed out (see Figure 2.29). The presence of a small N1s peak on the survey spectrum of the modified Nitinol substrate can also be noticed. As no nitrogen is present in the grafted molecule, this peak is attributed to adsorbed N₂ contaminations.

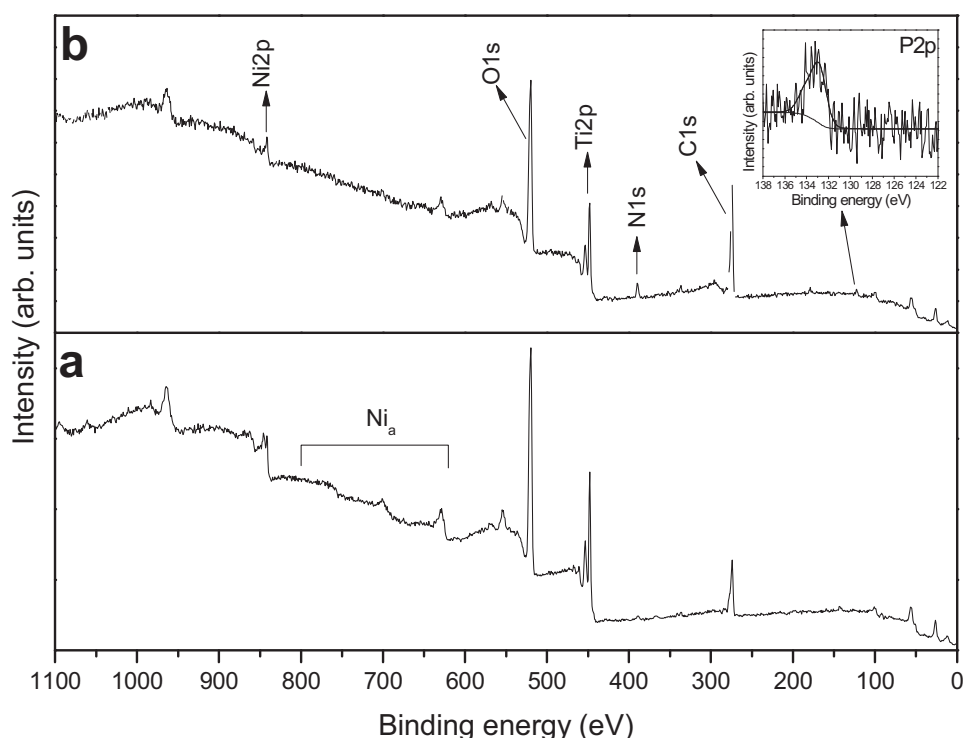


Figure 2.29. XPS survey spectra of a bare polished Nitinol substrate (a) and a Nitinol substrate modified by immersion 24h in a 1 mM 11-phosphonoundecanoic acid solution in ethanol at 50°C (b).

Beside the presence of photoelectron peaks characteristic of phosphorus atoms, the high resolution C1s core level XPS spectrum can be analyzed with three peaks that can be related to the grafted molecule: the first one centered at 285.0 eV is attributed to the alkyl chain between the phosphonic and the carboxylic acid functions, the second one centered at 286.5 is attributed to the carbon atom directly linked to the phosphorus atom and the last one centered at 288.7 eV is characteristic of strongly oxidized carbon atoms and attributed to the carboxylic acid function of the grafted molecule (see Figure 2.30). This confirms the presence of a 11-phosphonoundecanoic acid monolayer on the Nitinol surface. However, each of these peaks can also be related to carbonated atmospheric contaminations as explained previously. Therefore, the C/P intensities ratio has been calculated and appears to be around 29. This value is far higher than the one expected from the molecule stoichiometry ($C/P = 12$) confirming that a significant proportion of the C1s signal of the modified substrates have to be attributed to strongly physisorbed contaminations.

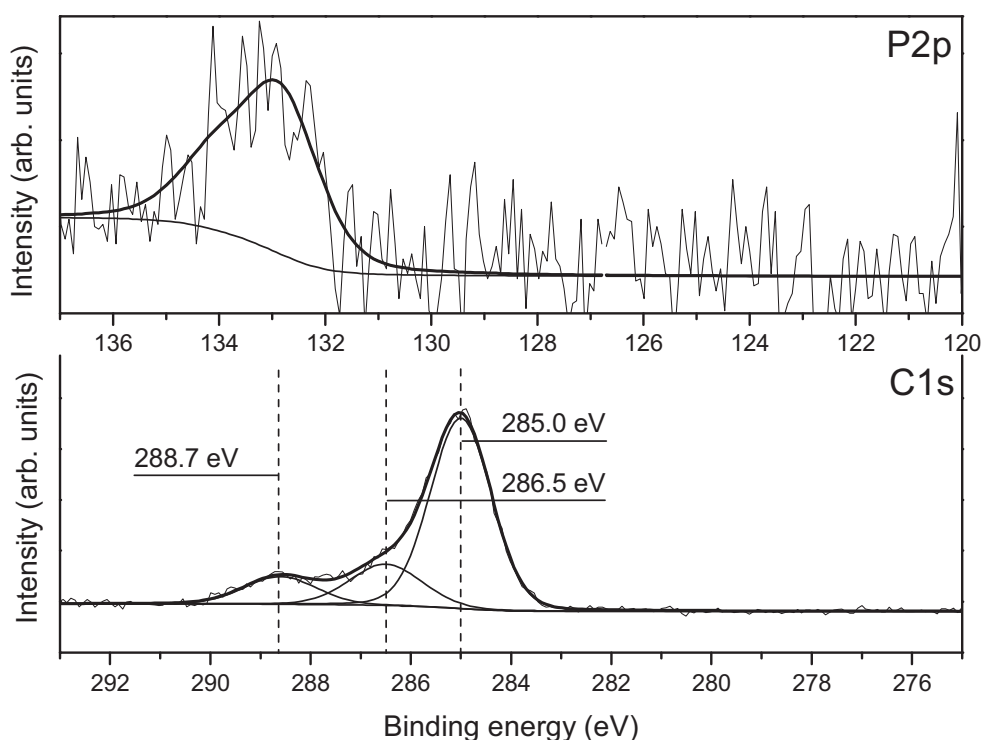


Figure 2.30. XPS high resolution spectra of the P2p and C1s core level photoelectron peaks of Nitinol substrates modified by immersion in a 11-phosphonoundecanoic acid 1 mM solution in ethanol for 24 h at 50°C.

The grafting of this layer induces a significant increase of the surface hydrophobicity as the contact angle increases from 49° (measured on a UV/O₃ treated bare Nitinol substrate) to 67° for a modified Nitinol substrate while we could have expected an increase of the hydrophilicity as the grafted molecules have a hydrophilic (carboxylic acid) terminal group. This can be explained by the ability of the carboxylic acid function to bind the oxide surface as described in the introduction (section 1.2.3). Therefore, the formed monolayer is a complex system in which a certain proportion of the molecules are grafted via the phosphonic acid moiety, another via the carboxylic acid moiety and other molecules can be bound to the surface via both functions (as a bridge or laying on the surface). Thus the formed monolayer exposes carboxylic and phosphonic acid moieties but also methylene groups (in the case of bridge-grafted molecules) at its extreme surface. This explains the relative hydrophobic property of the obtained surface compared to the UV/O₃ treated bare Nitinol one.

Polarization curves characterization of these surfaces has also been systematically carried out. Representative curves are presented in Figure 2.31. It appears that the grafting of a 11-phosphonoundecanoic acid monolayer on Nitinol induces a slight increase of the cathodic current while the anodic part of the polarization curve is a little lower than the reference one. This results in a slight increase of the corrosion current density and shift of the corrosion current potential toward more anodic values. These observations are consistent with the hydrophilic nature of the end function of 11-phosphonoundecanoic acid and the method used to form a monolayer of this molecule. Regarding the small increase of the cathodic current

density, one should consider that the obtained monolayer is a complex system of simply/doubly bound molecules and therefore not close-packed. As the grafted molecules have a hydrophilic nature, the aqueous electrolyte and thus the electroactive species in it are free to reach the surface for being reduced. The small decrease of the anodic part of the polarization curves can be explained by the fact that the grafted 11-phosphonoundecanoic acid molecules induce a decrease of the number of active sites at Nitinol surface (preventing its oxidation) and by the absence of alteration of the oxide layer during the grafting process (contrary to the electrografting process). Regarding the passivity domain, it seems mostly unchanged since the pitting corrosion potential is also shifted toward more anodic values (from 82 mV vs. SCE for the reference to 219 mV vs. SCE for the modified samples).

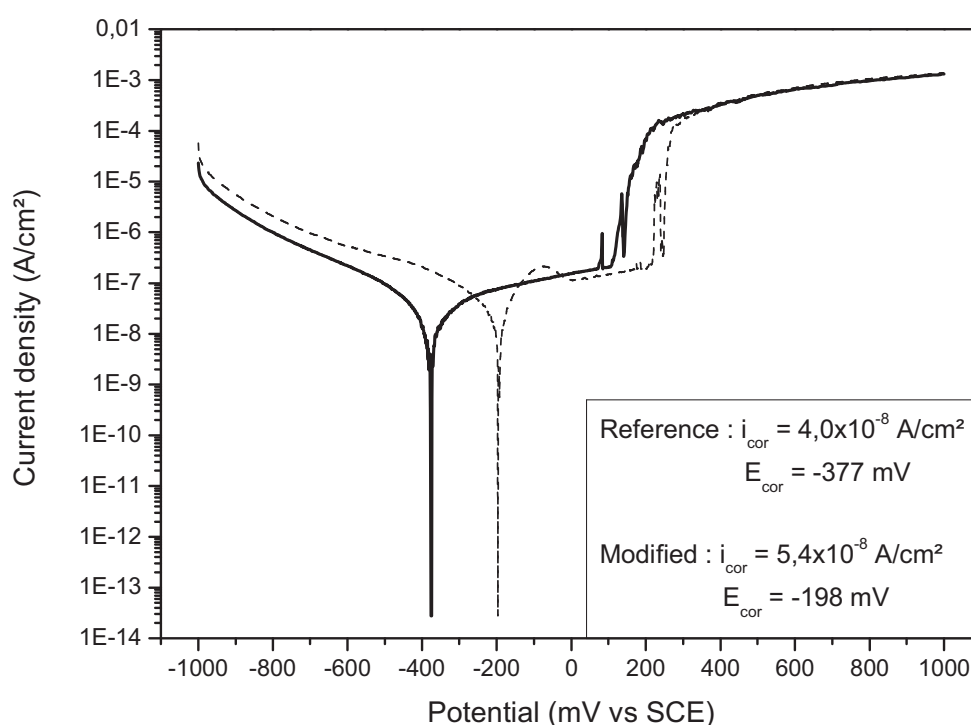


Figure 2.31. Polarization curves of a bare polished Nitinol substrate (thick plain line) and a Nitinol substrate modified by immersion in a 11-phosphonoundecanoic acid 1 mM solution in ethanol for 24 h at 50°C (dashed line) acquired by sweeping a range of potentials from -1 to 1 V vs. SCE at 1 mV/s in a 0.5 M sodium chloride solution.

2.2.2.3.5. Grafting of the CF alcohol on the modified Nitinol substrates

As mentioned previously, this last step aims to assess the efficiency of modified Nitinol substrates to act as a platform for post-grafting chemical reactions with the prospect of grafting biocompatible molecules such as PEG. The particular case of the 1H,1H-perfluoro-1-decanol (called CF) grafting via a Steglich esterification reaction has been studied. It is important to remind that this molecule is not grafted for biocompatibility purposes but used as a model to assess the “yield” of grafting with XPS analysis.

ATR characterization has been carried out systematically before and after the CF grafting on Nitinol substrates pre-modified either by electrografting of the 1,4-carboxybenzene or by grafting of a 11-phosphonoundecanoic acid monolayer. The corresponding spectra are presented in Figure 2.32 and 2.33. In both cases, the appearance of three strong absorption bands around 1110, 1260 and 1730 cm^{-1} can be pointed out after the Steglich esterification. The bands at 1110 and 1260 cm^{-1} are attributed to the symmetric and asymmetric stretching modes of the formed ester function and the band around 1730 cm^{-1} is attributed to the C=O stretching mode. The presence of these absorption bands on the ATR spectra of Nitinol substrates confirms that the CF alcohol molecules are covalently bound to the first grafted layer and thus that the Steglich esterification reaction involving the carboxyl groups present on the surface works for both pre-layers.

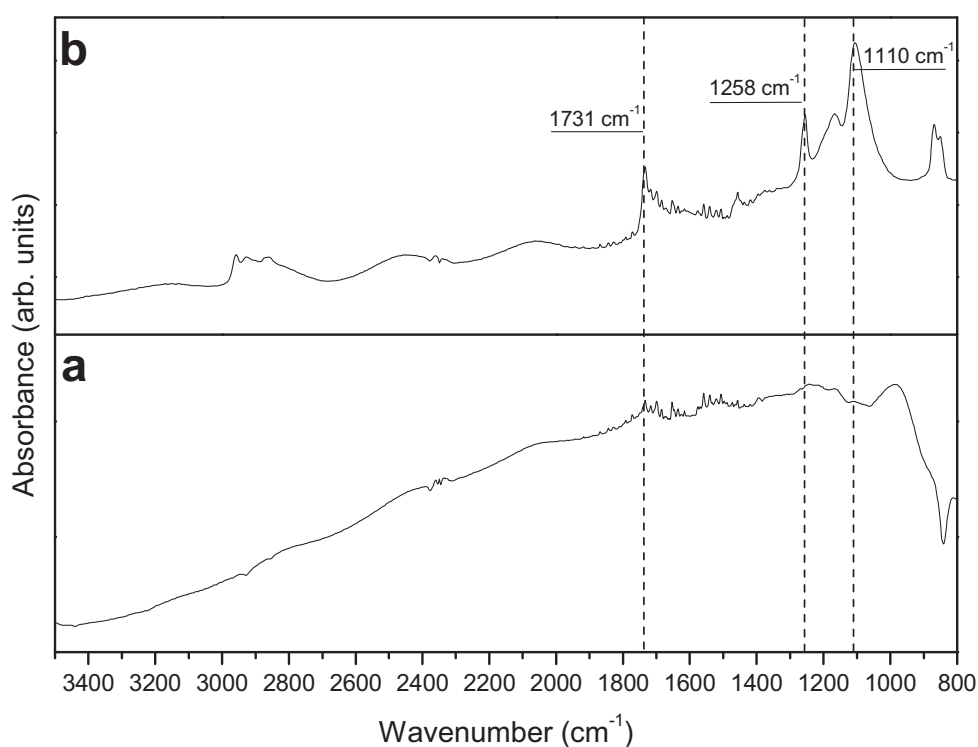


Figure 2.32. ATR spectra of a Nitinol substrate modified by electrografting the 1,4-carboxybenzene diazonium before (a) and after the grafting of the CF alcohol via a Steglich esterification reaction (b).

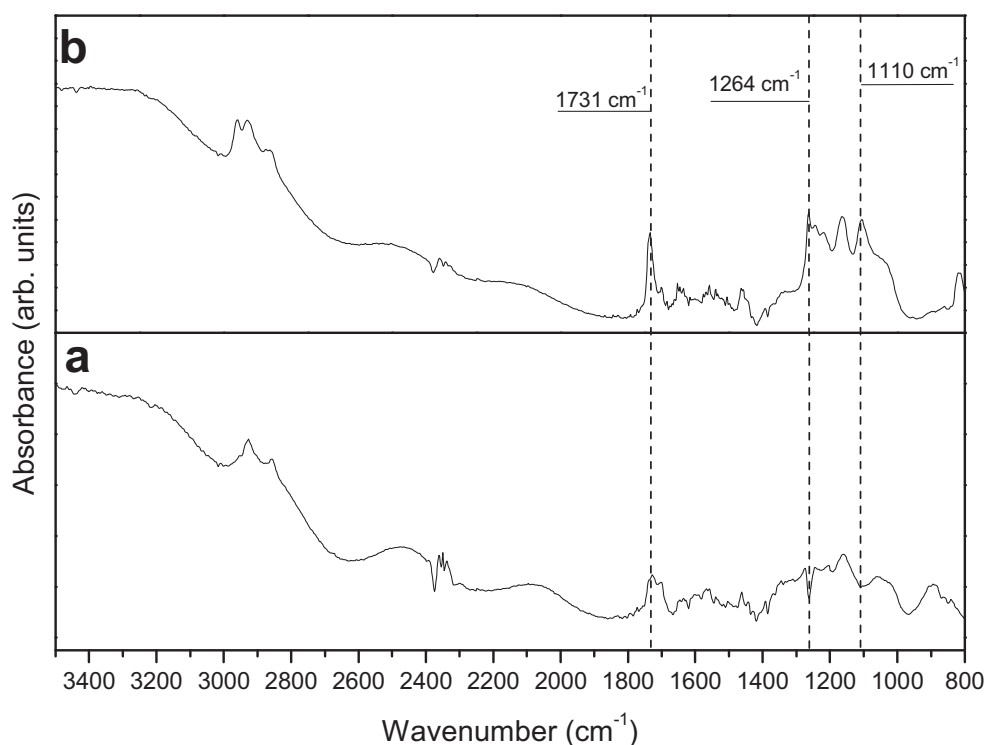


Figure 2.33. ATR spectra of a Nitinol substrate modified by electrografting the 1,4-carboxybenzene diazonium before (a) and after the grafting of the CF alcohol via a Steglich esterification reaction (b).

Systematic XPS characterization of these substrates has also been carried out. Representative survey spectra are presented at Figure 2.34 and 2.35. In each case, the F1s core level photoelectron peak appears confirming the presence of the CF alcohol on Nitinol surface. In order to compare the amount of grafted CF and thus the efficiency of the two tested coatings to act as a platform for post-grafting chemical reactions, we calculated and compared the F/substrate ratios where “F” is the normalized area of the F1s peak and “substrate” is the sum of the normalized areas of the Ti2p and Ni2p peaks. It turns out that the F/substrate ratio is almost twice higher when the CF grafting is carried out on the 11-phosphonoundecanoic acid monolayer than on the 1,4-carboxybenzene electrografted layer (F/substrate ratios of 0.53 and 0.21, respectively).

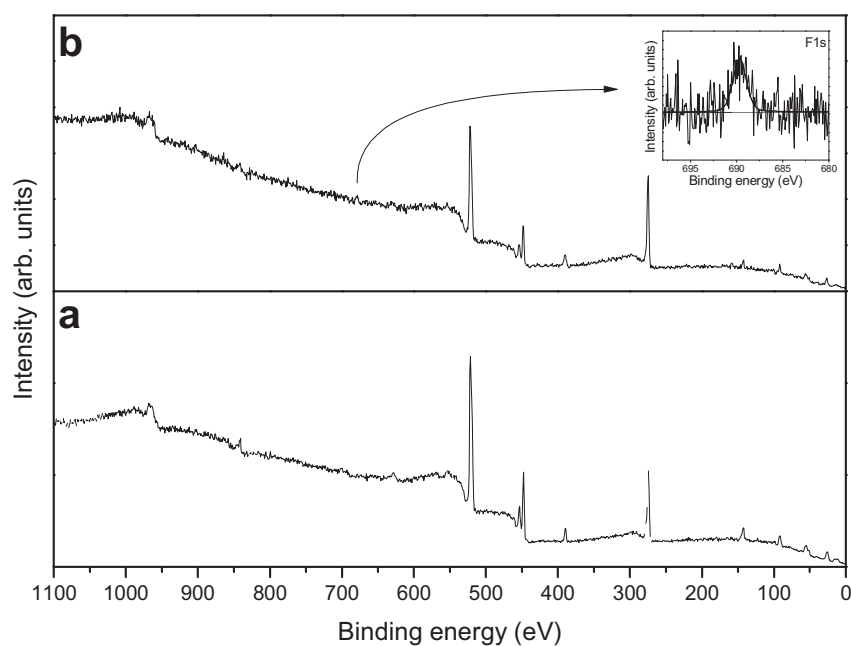


Figure 2.34. XPS survey spectra of a Nitinol substrate modified by electrografting the 1,4-carboxybenzene diazonium before (a) and after the grafting of the CF alcohol via a Steglich esterification reaction (b).

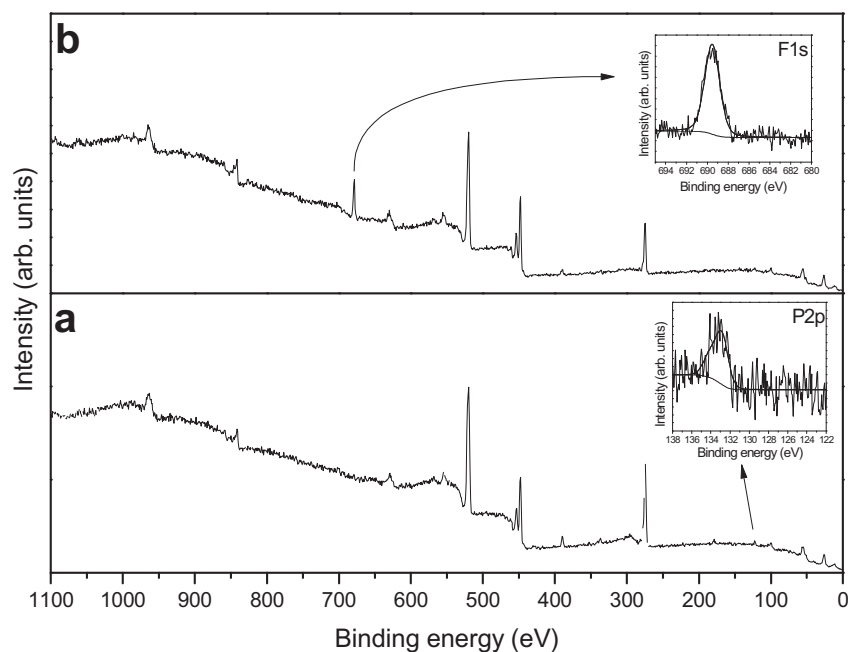


Figure 2.35. XPS survey spectra of a Nitinol substrate modified by immersion 24h in a 1 mM 11-phosphonoundecanoic acid solution in ethanol at 50°C before (a) and after the grafting of the CF alcohol via a Steglich esterification reaction (b).

As expected, the grafting of the CF alcohol on the initial layers induces an important increase of the surface hydrophobicity in both cases (see Figure 2.36). However, the water contact angle appears to be slightly higher when CF is grafted on the 11-phosphonoundecanoic acid monolayer than on the 1,4-carboxybenzene electrografted layer (77° and 73°, respectively). This confirms the trend revealed by the XPS analysis results i.e. that the 11-phosphonoundecanoic acid monolayer seems to be a better platform than the 1,4-carboxybenzene layer for carrying out the grafting of an alcohol via a Steglich esterification reaction.

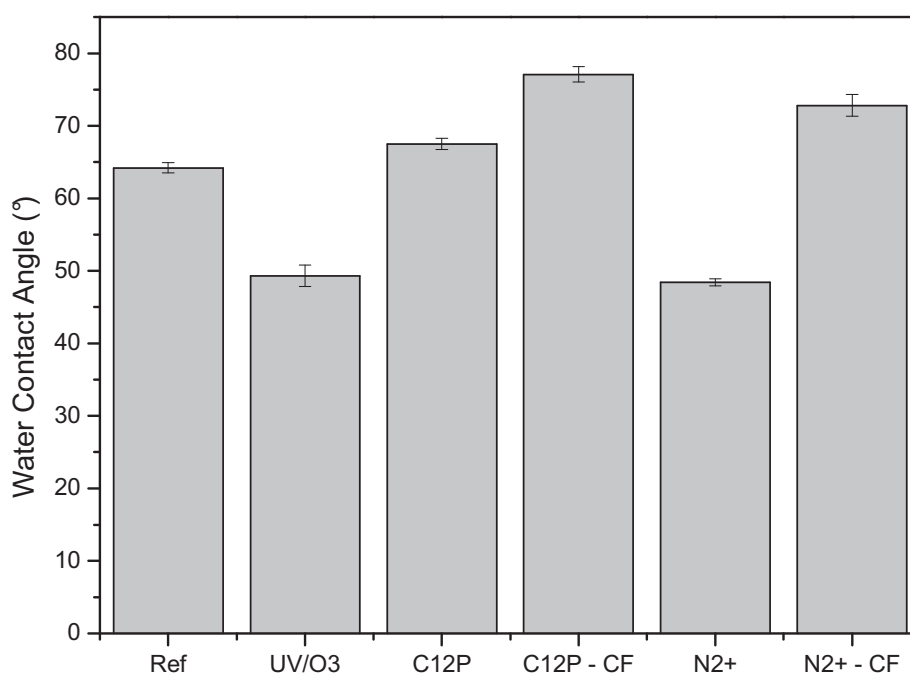


Figure 2.36. Water contact angle measured on a bare polished Nitinol substrate (Ref), a bare Nitinol substrate submitted to a UV/O₃ treatment for 30 min (UV/O₃), a Nitinol substrate modified with a 11-phosphonoundecanoic acid monolayer (C12P), a CF grafted 11-phosphonoundecanoic acid monolayer (C12p - CF), a Nitinol substrate modified with an electrografted 1,4-carboxybenzene layer (N2+) and a CF grafted 1,4-carboxybenzene layer (N2+ - CF).

The polarization curves analysis of the obtained Nitinol surfaces reveals that the CF grafting induces a significant decrease of the corrosion current density with respect to the results obtained for both initial layers (see Figure 2.37). No matter the initial layer, it appears that the grafting of the CF alcohol leads to a decreased anodic current density and thus a shift of the corrosion potential toward higher potentials. It is also interesting to point out the complete absence of any pitting corrosion for both CF grafted Nitinol surfaces. The hydrophobicity conferred to the Nitinol surface by the presence of the CF alcohol has thus a very beneficial effect on the corrosion resistance of modified Nitinol. Note also that this effect is slightly

more pronounced when the CF grafting is carried out on the 11-phosphonoundecanoic acid monolayer than when it is carried out on the carboxybenzene electrografted layer which is in good correlation with the results presented here above.

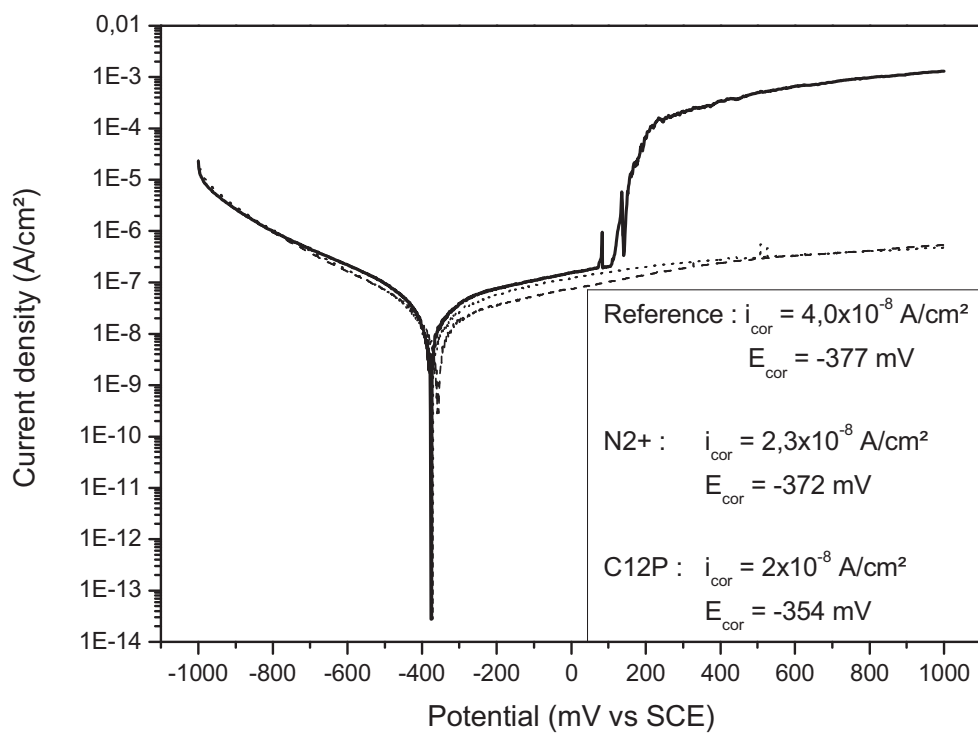


Figure 2.37. Polarization curves of a bare polished Nitinol substrate (thick plain line/Reference), a Nitinol substrate modified with a CF grafted carboxybenzene layer (dotted line/N2+) and a Nitinol substrate modified by a CF grafted 11-phosphonoundecanoic acid monolayer (dashed line/C12P) acquired by sweeping a range of potentials from -1 to 1 V vs. SCE at 1 mV/s in a 0.5 M sodium chloride solution.

2.2.2.3.6. Conclusions

This work aimed to study the modification of Nitinol by the electrografting of the 1,4-carboxybenzene diazonium and the formation of a 11-phosphonoundecanoic acid monolayer as well as to assess the efficiency of these coatings to act as a platform for post-grafting chemical reactions. This has been done by studying the grafting of the 1H,1H-perfluoro-1-decanol (called CF) on the carboxylic functions available on modified Nitinol substrates via a Steglich esterification reaction.

The electrografting of the 1,4-carboxybenzene diazonium has been carried out successfully. The obtained layer appeared to be a non-compact hydrophilic multilayer with some acetonitrile (solvent) and tetrabutylammonium cations entrapped in it. This layer has a negative impact on the Nitinol corrosion resistance properties (increased corrosion current density and decreased passivity domain) that can be explained by the reductive nature of the electrografting process (altering the Nitinol passivating native oxide layer) and by the non-

compact and hydrophilic nature of the resulting layer which do not leads to a decreased accessibility of electroactive species to the Nitinol surface.

The grafting of 11-phosphonoundecanoic acid on Nitinol has also been studied. The resulting monolayer showed less pronounced hydrophilic properties than the electrografted carboxybenzene layer did. This has been explained by the ability of the 11-phosphonoundecanoic acid to bind the surface via both extremities leading to a complex monolayer structure with simply and doubly bond molecules. However, the corrosion resistance behavior of the Nitinol substrates is slightly better when their surface is modified with an 11-phosphonoundecanoic acid monolayer than with an electrografted carboxybenzene layer but still not better than in the case of a bare Nitinol substrate. Note that from the study of this first modification step, it appears that even if hydrophilicity is desirable for the antithrombogenic surface properties, it has a negative impact on the corrosion resistance of Nitinol.

The grafting of the CF alcohol via a Steglich esterification reaction with available carboxylic groups on the modified Nitinol surfaces has been carried out for both coatings. In each studied situation, it has been shown that this esterification reaction has been successfully achieved. The consequences of this CF grafting are an important increase of the surface hydrophobicity and a significant improvement of the corrosion resistance of modified Nitinol. However, it clearly appeared that the CF grafting is more efficient when carried out on an 11-phosphonoundecanoic acid monolayer than on the carboxybenzene electrografted layer.

2.2.2.4. Assessment of the solvent and temperature impact on the grafting of phosphonic acid molecules on Nitinol surface

2.2.2.4.1. Introduction

This study aims to overview the solvent and temperature impact on the grafting of the *n*-dodecylphosphonic acid on Nitinol surface and of the resulting corrosion inhibition. In a first time, XPS characterizations were used to determine the more suitable solvents among the three tested ones (THF, absolute ethanol or water). In a second time, XPS, contact angle measurements and polarization curves analysis were applied in order to determine the impact of a heating of the immersion solution on the obtained monolayer and its ability to improve the corrosion resistance of Nitinol.

2.2.2.4.2. Samples preparation

The Nitinol substrates were mechanically polished as described previously (see section 2.2.2.2) and stored until their modification. Before the grafting of the *n*-dodecylphosphonic acid, the Nitinol substrates were cleaned again by sonication 15 min in ethanol, blown dry under a nitrogen flow and submitted to a UV/O₃ treatment for 30 min.

For the solvent effect study, the substrates were immersed in a 1 mM solution of *n*-dodecylphosphonic acid in THF, absolute ethanol or water for 24 h at room temperature. The substrates were then copiously rinsed with the solvent used for the modification, cleaned by sonication 15 min in the same solvent, blown dry under a nitrogen flow and characterized

directly. For the temperature effect study, the Nitinol samples were immersed in a 1 mM solution of *n*-dodecylphosphonic acid in the most suitable solvent for 24 h at room temperature or 50°C. The substrates were then copiously rinsed with the solvent used for the modification, cleaned by sonication 15 min in the same solvent, blown dry under a nitrogen flow and characterized directly.

2.2.2.4.3. Solvent effect

Directly after their modification in the three tested solvents, the Nitinol substrates were characterized by XPS. The corresponding representative spectra are presented in Figure 2.38. By comparison of the survey spectra of a bare polished Nitinol substrate and of the Nitinol substrates modified in the three different tested solvents, the appearance of a P2p photoelectron peak accompanying the grafting of the *n*-dodecylphosphonic acid can be pointed out in each situation.

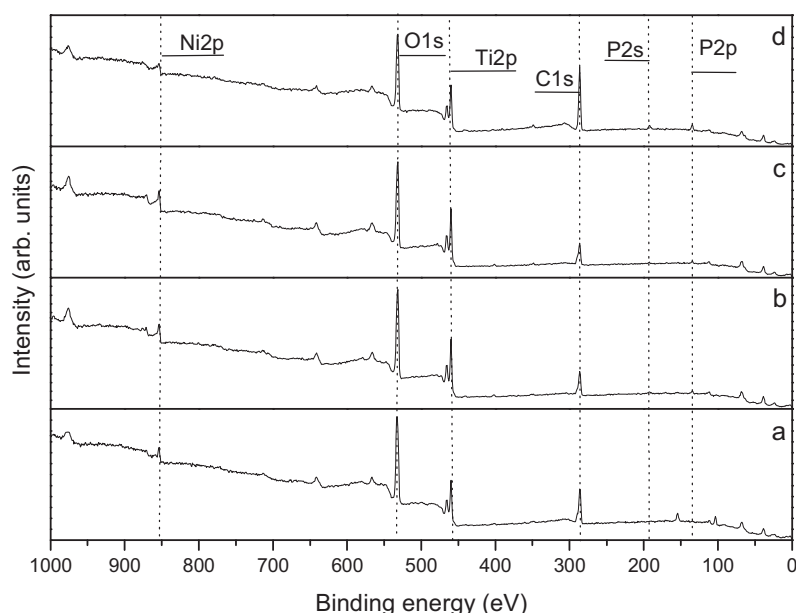


Figure 2.38. XPS survey spectra of a bare polished Nitinol substrate (a) and of a Nitinol substrate modified by immersion 24h at room temperature in a 1 mM *n*-dodecylphosphonic acid solution in THF (b), absolute ethanol (c) and ultra pure water (d).

C1s and P2p core level photoelectrons high resolution spectra of these modified Nitinol substrates have also been systematically acquired (Figure 2.39). Beside the presence of a P2p photoelectron peak centered around 133.3 eV on each modified substrate, the high resolution C1s core level XPS spectrum can be analyzed with four peaks in each case. The first one centered at 285.0 eV, characteristic of aliphatic carbon atoms, can be attributed to the alkyl chain of the grafted molecule and to some physisorbed carbonated contaminations. The second and last ones, centered at 285.7 and 288.7 eV are characteristic of weakly and strongly

oxidized carbon atoms, respectively, and attributed to physisorbed carbonated contaminations. The second component, centered at 286.5 eV can be attributed to the carbon atom directly linked to the phosphorus atom of the grafted molecule.

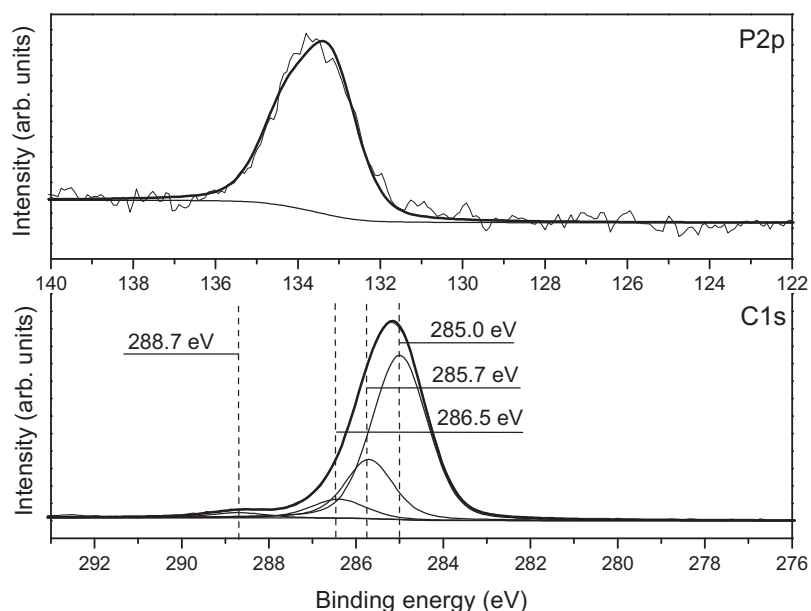


Figure 2.39. XPS high resolution spectra of the P2p and C1s core level photoelectron peaks of Nitinol substrates modified by immersion in 1 mM *n*-dodecylphosphonic acid solution in ultra pure water for 24 h at room temperature.

These results confirm the presence of a *n*-dodecylphosphonic acid layer on each modified Nitinol substrate. However, atmospheric contaminations are systematically present no matter the modification conditions. In order to assess the amount of contaminations, the C/P ratio has been calculated for each formed monolayer (a complete absence of any carbonated contaminations being characterized by a C/P ratio close to 12 according to the grafted molecule stoichiometry). The ratio of the normalized area of the P2p peak on the sum of the normalized areas of the Ni2p and Ti2p peaks i.e. P/(Ni+Ti) has also been systematically calculated in order to assess the quantity of grafted *n*-dodecanethiol molecules in function of the solvent used for the modification. These ratios are presented in Table 2.8.

Table 2.8. C/P and P/(Ni+Ti) ratios calculated on the basis of XPS analysis of Nitinol substrates modified by immersion 24h at room temperature in a 1 mM *n*-dodecylphosphonic acid solution in absolute ethanol (EtOH), in THF (THF) and ultra pure water (H₂O).

	EtOH	THF	H ₂ O
C/P	25.4	17.1	15.7
P/(Ni+Ti)	0.06	0.11	0.33

From the calculation of these ratios, it clearly appears that the solvent used for the modification has a significant impact on the formed monolayer. Regarding the C/P ratio, the modification in absolute ethanol seems to lead to the highest amount of carbonated contaminations while the use of ultra pure water as solvent for this modification lead to a ratio of 15.7 close to the theoretical one (12). The amount of *n*-dodecylphosphonic acid molecules grafted on Nitinol surface is also much higher when water is used as solvent for the modification while absolute ethanol again appears as the worse choice. Regarding both ratios, THF leads to intermediate results.

Despite the common use of THF or ethanol in the literature^{333,336,338}, ultra pure water thus appears to be the best choice of solvent among the three tested ones for the grafting of *n*-dodecylphosphonic acid on mechanically polished Nitinol substrates and therefore has been selected to study the impact of the temperature on the formed monolayer.

2.2.2.4.4. Temperature effect

As described in the sample preparation section, the temperature effect study was carried out by comparison of the monolayers obtained by immersion of Nitinol substrates in a 1 mM solution of *n*-dodecylphosphonic acid in the most suitable solvent (i.e. ultra pure water) for 24 hours at room temperature and at 50°C.

The Nitinol substrates modified this way were systematically analyzed by XPS. The obtained spectra are similar to the ones presented in Figures 2.38 and 2.39 (not shown here). The C/P and P/(Ni+Ti) ratios have been calculated on the basis of these analysis and presented in Table 2.9.

Table 2.9. C/P and P/(Ni+Ti) ratios calculated on the basis of XPS analysis of Nitinol substrates modified by immersion 24h in a 1 mM *n*-dodecylphosphonic acid solution in ultra pure water at room temperature and at 50°C.

	Room temperature	50°C
C/P	15.7	16.1
P/(Ni+Ti)	0.33	0.29

From these ratios, it appears that an increase of the immersion temperature does not induce any significant change of the amount of physisorbed contaminations and of the quantity of grafted molecules.

However, the measurement of water contact angles on these modified surfaces shows a significant increase of the surface hydrophobicity along with an increase of the immersion temperature. Indeed, the contact angle increases from 64° for a bare polished Nitinol substrate to 94° and 102° for Nitinol substrates modified at room temperature and at 50°C, respectively. This suggests that increasing the immersion temperature does not lead to an increase of the quantity of adsorbed molecules but rather to an improvement of the resulting monolayer organization.

The protective nature of the formed monolayers against corrosion of Nitinol has been assessed by polarization curves measurements. These measurements have been carried out in a NaCl

0.5 M aqueous solution by sweeping a range of potentials from -0.5 to 1 V vs. SCE at 1 mV/s. The representative curves are presented in Figure 2.40.

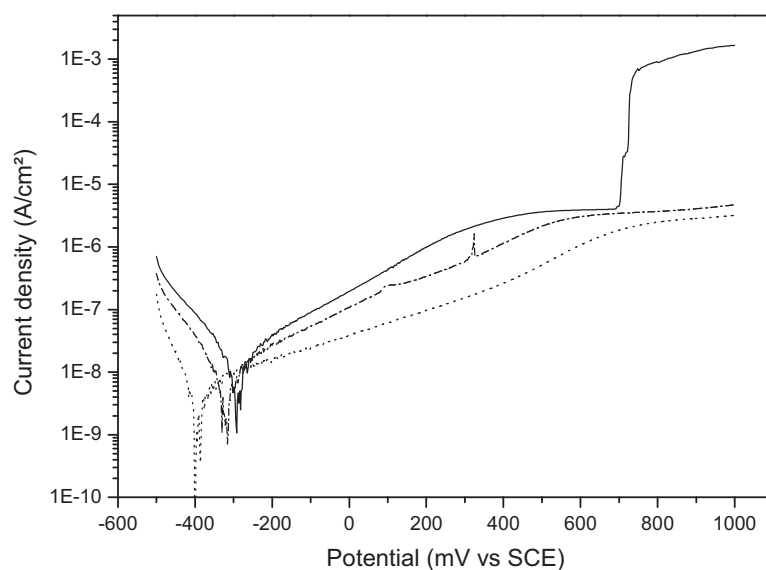


Figure 2.40. Polarization curves of a bare polished Nitinol substrate (plain line) and of a Nitinol substrate modified by immersion 24h in a 1 mM *n*-dodecylphosphonic acid solution in ultra pure water at room temperature (dashed line) and at 50°C (dotted line) acquired by sweeping a range of potentials from -0.5 to 1 V vs. SCE at 1 mV/s in a 0.5 M sodium chloride solution.

As noticed previously, bare polished Nitinol substrate are susceptible to pitting corrosion as proved by the important current density increase around 710 mV vs. SCE. On the contrary, Nitinol substrates modified with a *n*-dodecylphosphonic acid monolayer show a very good resistance to pitting corrosion up to 1 V vs. SCE. Regarding corrosion current densities and potentials (presented in Table 2.10), it clearly appears that the modification of Nitinol with a *n*-dodecylphosphonic acid monolayer has a beneficial effect on the resistance of this alloy to corrosion. After a modification at room temperature, the corrosion current density is about twice lower than the one measured for a bare Nitinol substrate while the corrosion potential is slightly shifted toward more cathodic values indicating a mixed corrosion inhibition with a slightly preferential inhibition of the cathodic reaction. An increase of the modification solution temperature from ~21°C to 50°C allows an enhancement of this behavior i.e. a more important decrease of the corrosion current density and a further shift of the corrosion potential toward more cathodic values.

Table 2.10. Numerical results of the polarization curves experiments carried out on bare polished Nitinol substrates and Nitinol substrates modified by immersion 24h in a 1 mM *n*-dodecylphosphonic acid solution in ultra pure water at room temperature and at 50°C.

	Corrosion potential (mV vs. SCE)	Corrosion current density (A/cm ²)
Reference	-297	1.8x10 ⁻⁸
Room temperature	-326	1.1x10 ⁻⁸
50°C	-400	6.0x10 ⁻⁹

2.2.2.4.5. Conclusions

From this set of analysis, it clearly appears that the formation of a *n*-dodecylphosphonic acid monolayer can be highly beneficial for the Nitinol corrosion resistance. It has been shown that the quality of the formed monolayer strongly depends on the solvent used for the preparation of the modification solution (ultra pure water leading to the best results for the three solvents tested in the frame of this study) and on the temperature of this modification solution. The choice of the solvent appeared to be critical regarding the amount of grafted *n*-dodecylphosphonic acid molecules. While an increase of the temperature does not seem to increase significantly the amount of grafted phosphonic acid molecules, the hydrophobic and corrosion resistance properties obtained with a higher modification temperature clearly indicate a better organization of the resulting monolayer and is therefore beneficial.

2.2.2.5. Induction heating of Nitinol in water: study of the impact on the oxide layer

2.2.2.5.1. Introduction

The boiling procedure (immersion of Nitinol in boiling water) was introduced for Nitinol many years ago ²²⁸ and it proved to be very effective in blocking the Ni release ^{229,230}. Shabalovskaya *et al.* also showed that boiling in water of chemically etched samples results in a slight extension of the passivity region and a reduction of the current density by one order of magnitude at the potentials above the corrosion potential, indicating a significant drop in the anodic dissolution of material ²²⁵.

The aim of the present work is to study the induction heating behavior of Nitinol and compare the impact of the heating method (induction heating vs. conventional heating) on the boiling procedure result. In order to compare the impact of these treatments on the nickel amount present at the surface of Nitinol, this study has been carried out on nickel enriched surfaces i.e. heat treated Nitinol substrates.

Induction heating is a heating method based on Faraday's law of induction and Joule's law which allows heating of a piece of metal directly and contactless (see Annex 2). In practice, the piece of metal is placed in a solenoid in which a high frequency alternating current flows. The piece of metal is thus exposed to rapid magnetic field changes that induce eddy currents in it and therefore a temperature increase according the Joule's law. In addition to being

contactless and localized, this heating method has the main advantages to be more rapid and energetically economic than other conventional heating methods.

2.2.2.5.2. Samples preparation

The Nitinol substrates were mechanically polished as described previously (see section 2.2.2.2) before being submitted to a thermal treatment for 15 minutes at 500°C (similar to the shape setting treatment). The substrates are then either immersed in boiling milli-Q water for 1 hour (named “CH” for “conventional heating”) or immersed in 10 ml room temperature milli-Q water and submitted to the selected induction heating profile (named “IH” for “induction heating”). After this treatment, the substrates are rinsed copiously with ethanol, cleaned by sonication 15 minutes in the same solvent and blown dry under a nitrogen flow and characterized directly.

2.2.2.5.3. Temperature measurements

The first step of this study is obviously to characterize the efficiency of the induction heating (IH) of Nitinol substrates. Induction heating was performed with an Ambrell EasyHeat induction heating system with a power output of 725 W and a frequency of 198 kHz. The used solenoid is composed of 7 loops with an internal diameter of 9 cm. Temperature measurements were made with K-type thermocouples soldered on the substrate surface. Note that with this method, it is impossible to measure the temperature of the substrate during the induction phase because of the creation of eddy currents in the thermocouple wires themselves. The heating experiments were thus realized by applying sequences of induction heating followed by cooling periods allowing temperature measurements. The substrates were immersed into a controlled volume of milli-Q water (10 ml) and centered into the solenoid with their plane perpendicular to the solenoid axis. Several heating sequences were tested (not shown here) and we selected one of them for the rest of this study. This sequence consists in an alternation of a 120 s IH pulse and a 180 s cooling period. This 5 minutes sequence is repeated during 1 hour (thus 12 times). The temperature curve of this profile is presented in Figure 2.41. Note that after the third 120 s IH pulse, the water starts to boil at the surface of the Nitinol substrate. After this point, boiling is observed at the surface during each induction heating pulse and stops during each cooling period.

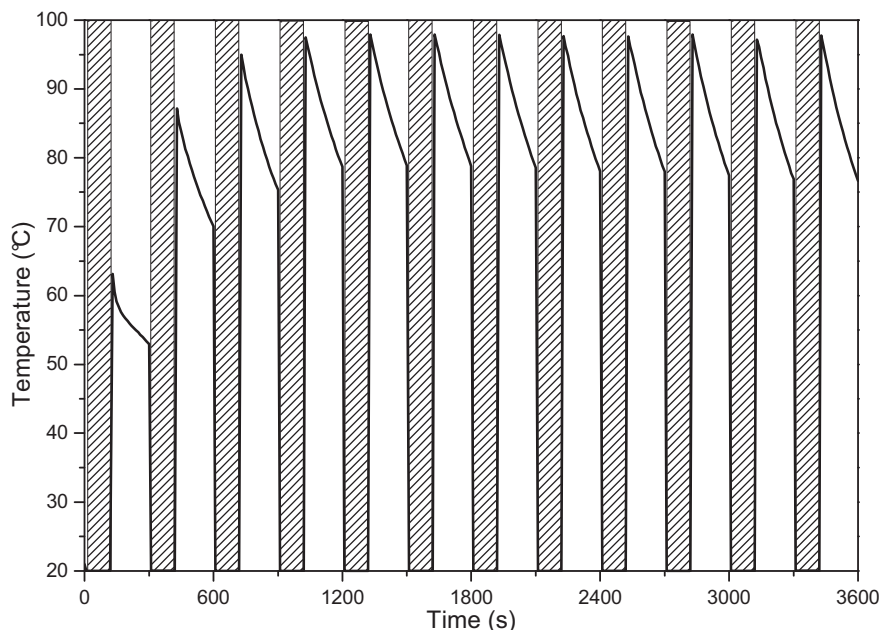


Figure 2.41. Evolution of the temperature at the surface of a heat treated (15 min at 500°C) NiTi substrate immersed into 10 ml milli-Q water during the induction heating sequence.

2.2.2.5.4. XPS characterizations

First of all, the surface state and nickel content of untreated and heat treated polished Nitinol plates were compared (see Figure 2.42). As described earlier, before heat treatment the titanium Ti2p signal is dominated by the Ti2p_{3/2} component centered at 458.9 eV characteristic of titanium in TiO₂ but a second Ti2p_{3/2} component centered at 424.2 eV and characteristic of metallic titanium is clearly visible. After heat treatment, this metallic titanium component completely disappears from the Ti2p spectrum indicating that the titanium is completely oxidized in TiO₂. Regarding the Ni2p spectra, it clearly appears that the heat treatment induces an important decrease of the metallic nickel component centered at 852.7 eV (attributed to metallic nickel) which is the main component of the Ni2p spectra of the untreated Nitinol surface. At the same time, an important peak appears around 854.2 eV with a small shoulder around 856.2 eV characteristic of nickel oxide and hydroxide (NiO and Ni(OH)₂), respectively. Furthermore, the heat treatment induces a significant increase of the Ni/Ti ratio from 0.27 for an untreated mechanically polished Nitinol substrate to 0.51 for the same substrate after a heat treatment at 500°C for 15 min.

These observations are consistent with the results obtained from the study of the impact of the heat treatment on Nitinol wires i.e. that the typical shape setting heat treatment of Nitinol induces an obvious further oxidation of the surface, an outward diffusion of the nickel and therefore a significant increase of the proportion of NiO in the oxide layer.

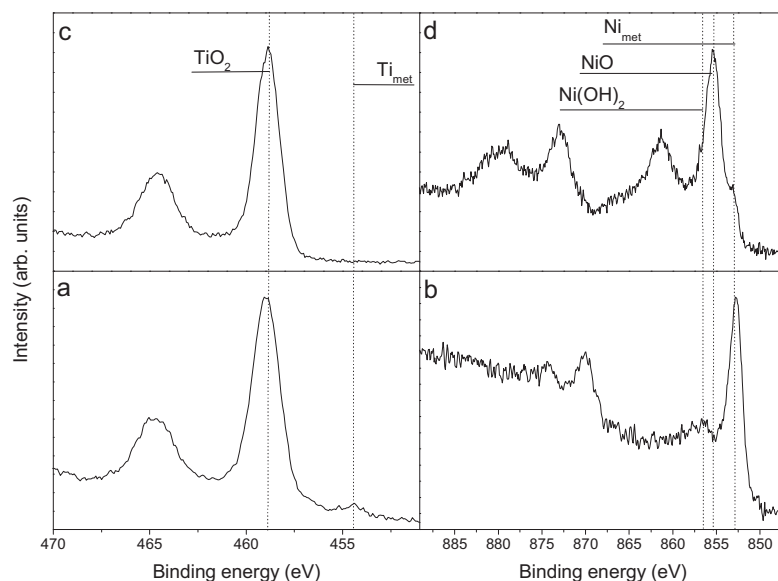


Figure 2.42. High resolution XPS spectra of the Ti2p (a and c) and Ni2p (b and d) core level photoelectron peaks of mechanically polished Nitinol plates untreated (a and b), and after a heat treatment of 15 min at 500°C (c and d).

Systematic XPS characterizations of Nitinol substrates treated in boiling milli-Q water for one hour with a conventional heating (CH treated) and submitted to induction heating in 10 ml milli-Q water (IH treated) have also been carried out.

The experimental O1s core level photoelectrons XPS spectra of these samples can be analyzed with three to four different peaks. The first one, centered at 530.0 eV, is attributed to the photoelectrons coming from the metal oxides (mainly TiO₂ and NiO) and is noted “O²⁻”. The second peak, centered at 531.5 eV, corresponds to the different metal hydroxides present at the surface (mainly Ti(OH)₄ and Ni(OH)₂) and is noted “OH⁻”. The third peak, centered at 532.8 eV is related to oxygen atoms from atmospheric carbonated contaminations. In the case of IH treated samples, a fourth peak centered at 533.7 eV can be pointed out and attributed to adsorbed water molecules on the surface. All these spectra are presented in Figure 2.43. From this analysis, the OH⁻/O²⁻ ratio (representative of the hydroxylation level of the outer part of the oxide layer) can be calculated (see Figure 2.44). The OH⁻/O²⁻ ratio obtained for the reference sample is around 0.25 while it is drastically increased after the CH treatment (one hour immersion in boiling water) to 0.38 and even more after the IH treatment (induction heating for one hour in 10 ml milli-Q water) that leads to a OH⁻/O²⁻ ratio of 0.56. In the case of the IH treated sample, the presence of strongly adsorbed water on the Nitinol surface has been pointed out. This is indicative of a reaction between the metal oxides at the outer surface of Nitinol and the water leading to hydroxylation of these oxides. This increase of the OH⁻/O²⁻ ratio maybe beneficial for at least two reasons: it is expected on the one hand to increase the hydrophilicity of the surface (the measured water contact angle being 68°, 59° and 55° for reference, CH treated and IH treated samples, respectively; see Figure 2.45) and thus the hemocompatibility of Nitinol devices^{343,383,384} and, on the other hand to improve the grafting

of phosphonic acids on the oxide layer as these molecules bind the substrates via a reaction between the phosphonic acid function and the hydroxyl groups on the surface^{163,333,338}.

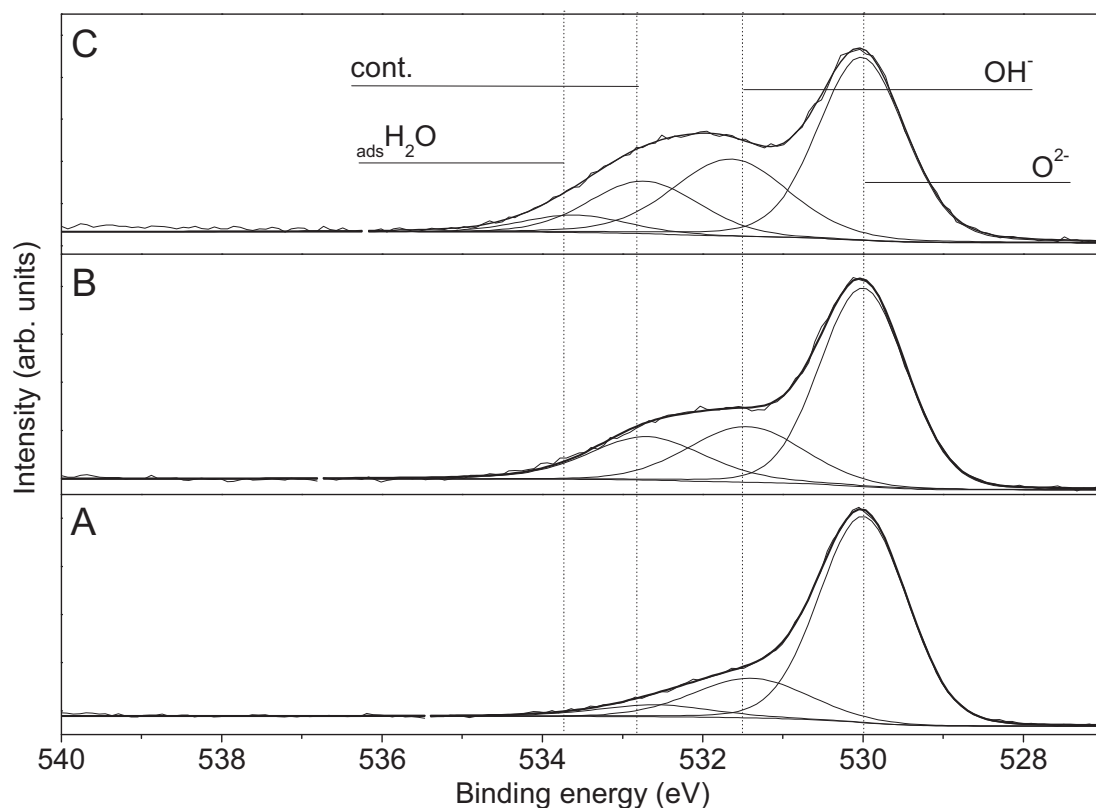


Figure 2.43. O1s core level photoelectrons high resolution XPS spectra of heat treated Nitinol samples without any further treatment (A), immersed in boiling water for one hour (B) and submitted to induction heating in milli-Q water (C).

As said before, another essential consideration when aiming to use Nitinol for biological applications is the nickel quantity in the oxide layer. Roughly speaking, as nickel ions may have toxic and carcinogenic effects, the lowest quantity of nickel at the surface leads to the more biologically compatible Nitinol device. To assess this parameter, the Ni/Ti ratio has been calculated from XPS spectra for each of the studied samples (see Figure 2.44). This ratio is much more important for reference samples (0.51) than for the CH and IH treated samples (0.37 and 0.31, respectively).

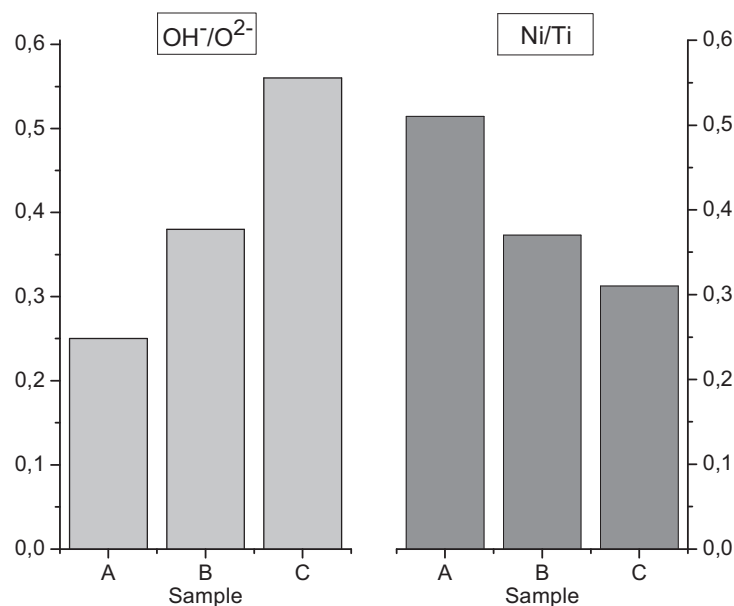


Figure 2.44. Left part: $\text{OH}^-/\text{O}^{2-}$ ratio; Right part: Ni/Ti ratio of heat treated Nitinol samples without any further treatment (A), immersed in boiling water for one hour (B) and submitted to induction heating in milli-Q water (C) calculated on the basis of the relative XPS analysis.

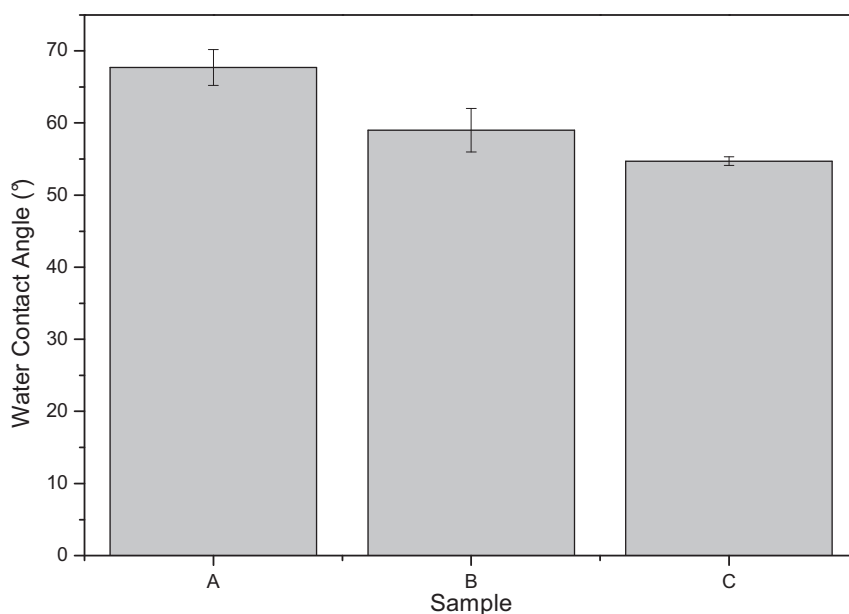


Figure 2.45. Contact angle of a 2.0 μl milli-Q water droplet on heat treated Nitinol sample without any further treatment (A), immersed in boiling water for one hour (B) and submitted to induction heating in milli-Q water (C).

These first results indicate that the IH treatment leads to similar results than a classical boiling treatment with conventional heating i.e. a hydroxylated Nitinol surface with a lower amount of nickel in the outer part of the oxide layer (and thus a bigger proportion of TiO_2). Nevertheless, it appears that the surface hydroxylation and the Ni/Ti ratio decrease are more important when IH is used instead of CH.

2.2.2.5.5. Electrochemical characterizations

Polarization curves experiments were used to assess the impact of the two studied treatments on the corrosion resistance of Nitinol. These experiments have thus been systematically carried out on our Nitinol samples using a three-electrode electrochemical setup with SCE as reference electrode and a platinum foil as counter electrode in a 0.5 M sodium chloride solution by sweeping a range of potential from -1 to 1 V vs. SCE at 1 mV/s. The resulting curves and corresponding numerical values are presented in Figure 2.46 and Table 2.10, respectively. For each of the treated samples, an important decrease of the corrosion current density and a shift of the corrosion potential towards more cathodic values are observed. Note that the corrosion current density measured for CH treated samples is slightly lower than the one measured for IH treated samples (7.5×10^{-9} and 2.2×10^{-8} A.cm⁻², respectively). However, corrosion current densities measured for treated samples are always at least 10-fold lower than for the reference samples indicating an improvement of the general corrosion resistance of Nitinol. The observed cathodic shift of the corrosion potentials is indicative of a mixed but slightly more cathodic corrosion inhibition. This can be related to the XPS analysis i.e. that CH treatment as well as IH treatment leads on the one hand to a bigger proportion of TiO₂ in the outer part of the oxide layer (which is more stable than nickel oxides) and on the other hand, to a hydroxylation of the surface and thus a reaction of the oxides with water leading most probably to a slight restructuration/growing of the oxide layer. This can explain either the decrease of the cathodic current density and the observed flat anodic part of the curves for treated samples indicative of a good passivity of the oxide layer.

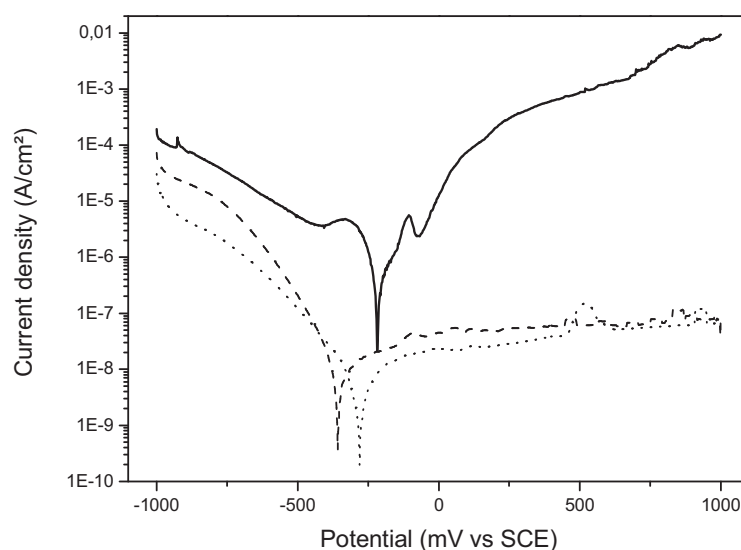


Figure 2.46. Polarization curves of a mechanically polished and heat treated (500°C 15 min) Nitinol sample without any further treatment (thick plain line); after the CH treatment (immersion of 1 hour in boiling water) (dotted line) and after the IH treatment (induction heating in 10 ml milli-Q water) (dashed line).

Table 2.10. Corrosion potentials and corrosion current densities measured for a mechanically polished and heat treated (500°C 15 min) Nitinol without any further treatment (Reference), after a 1 h immersion in boiling water (CH treated) and after being submitted to induction heating in 10 ml milli-Q water (IH treated).

	E_{cor} (mV vs. SCE)	i_{cor} (A.cm ⁻²)
Reference	-220	7.8×10^{-7}
CH treated	-275	7.5×10^{-9}
IH treated	-355	2.2×10^{-8}

2.2.2.5.6. Conclusions

The impact of an induction heating treatment in pure water (IH treatment) on heat treated (15 min at 500°C) Nitinol surface composition and corrosion resistance has been investigated for the first time and compared with a conventional boiling water treatment (CH treatment). Both IH and CH treatments leads to similar results. It has been shown that the amount of hydroxyl groups on Nitinol surface is much more important after the CH treatment than for the untreated samples and even more important after the IH treatment. At the same time, the Ni/Ti ratio is drastically decreased with both CH and IH treatments. The measured corrosion current densities for IH and CH treated Nitinol substrates are about 10-fold lower than the one measured for untreated Nitinol substrates indicating an important increase of the corrosion resistance.

It thus appears that induction heating can be considered as a very promising alternative to other conventional heating methods for surface treatments that require thermal activation. Beyond these results one should also consider the potential advantages of the induction heating method such as its high versatility resulting from its nature (heating of the surface itself) and the possibility post- and/or pre-treatment of the surface combined with the one studied in the frame of this work.

Chapter 3. Study and modification of the Phynox surface state

Phynox being another alloy very commonly used for the design of biomedical devices such as stents and coils, several studies of corrosion resistance and modification of its surface have been carried out with the prospect of improving the alloy-biological environment interactions. In the first part of this chapter, we will present the results of a systematic corrosion resistance evaluation of Phynox stents provided by Cardiatis after several different surface treatments. In the second part of this chapter, the study of the Phynox surface functionalization with bifunctional phosphonic acid molecules toward a versatile platform for post-grafting chemical reactions will be presented.

3.1. Corrosion study of Phynox braided stents

3.1.1. Introduction

Nine groups of Phynox braided stents provided by Cardiatis were tested in accordance to the ASTM F2129 standard: "Standard Test Method for Conducting Cyclic Potentiodynamic Polarization Measurements to Determine the Corrosion Susceptibility of Small Implant Devices". The surface treatments applied to each group, as well as the acronyms used throughout this chapter to designate these treatments are given in Table 3.1 hereunder.

Table 3.1. Treatments applied to each group of tested stents and corresponding acronyms

Group	Stent diameter	5mm	6-7mm	8-9mm
	Wire diameter	Phynox 75 μm	Phynox 80 μm	Phynox 90 μm
1	Rough braid		B	
2	Treated stent		TT	
3	Treated, pickled, passivated stent		TDP	
4	Treated, sterilized stent		TT St	
5	Treated, pickled, sterilized stent		TD St	
6	Treated, passivated, sterilized stent		TP St	
7	Treated, pickled, passivated, sterilized stent	TDP St $\varnothing$ 5mm	TDP St $\varnothing$ 7mm	TDP St $\varnothing$ 9mm

The stents were fabricated according to Cardiatis manufacturing process. Rough braid stents did not undergo any post-treatment after their fabrication except for a cleaning by sonication 15 minutes in ethanol. This surface state is the starting point for any subsequent treatment. Treated stents were submitted to a heat treatment at 550°C in air for 3 hours. The pickling treatment (chemical etching) has been carried out by immersion of the stents for 5 minutes in an HF 5% vol./HNO₃ 12% vol. aqueous solution. The passivation treatment consists in an immersion of the stent for 30 minutes in a HNO₃ 20% vol. aqueous solution. Sterilization was achieved in compliance with the validated cycle for Cardiatis i.e. by a controlled exposition to

ethylene oxide in a humid atmosphere. Group no.7 samples were included beforehand in their release system (catheter) before being sterilized in compliance with the sterilization cycle validated for Cardiatiss.

The corrosion tests by polarization curves measurements were carried out with a three electrode electrochemical setup using saturated calomel electrode (SCE) as the reference electrode and a platinum sheet was used as the counter-electrode. A salt bridge was inserted between the reference electrode and the working electrode. Tests were carried out in Hank's solution with 7.40 ± 0.05 pH in a thermostated electrochemical cell at $37 \pm 1^\circ\text{C}$.

As a first step, the electrolytical solution was de-oxygenated for 30 minutes, using a stream of nitrogen. The stent was then immersed, and its equilibrium potential (E_r) was measured for 1h. Next, cyclic polarization was started 100 mV below final equilibrium potential, scanning to anodic potentials up to 1V at 1mV/s. This step was immediately followed by a reverse scan. The resistance of the tested stents to corrosion was characterized in terms of corrosion potential (E_{corr}), corrosion current density (i_{corr}) and breakdown corrosion potential (E_{br}).

3.1.2. Results

The values of these various corrosion parameters are presented in Table 3.2.

Interestingly, none of the tested stents showed a sudden increase in current density during the anodic scan up to 1V, which would have indicated pitting corrosion. This shows that Phynox is inherently an excellent material to resist this type of corrosion.

Table 3.2. Representative averaged results of corrosion tests performed on the various groups of Phynox stents

	E_{corr} (mV vs. SCE)	i_{corr} (A/cm ²)	Standard Deviation (A/cm ²)	E_{br} (mV vs. SCE)
Rough	-180	3.40×10^{-9}	1.32×10^{-9}	-
TT	-415	6.10×10^{-8}	2.25×10^{-8}	-
TT St	-435	4.00×10^{-8}	9.49×10^{-9}	-
TD St	-240	7.30×10^{-9}	2.06×10^{-9}	-
TP St	-225	1.50×10^{-8}	6.12×10^{-9}	-
TDP	-240	1.00×10^{-8}	4.83×10^{-9}	-
TDP St Ø7mm	-280	1.70×10^{-8}	1.14×10^{-8}	-
TDP St Ø5mm	-260	1.70×10^{-8}	5.18×10^{-9}	-
TDP St Ø9mm	-280	9.00×10^{-9}	2.50×10^{-9}	-

As far as surface corrosion is concerned, the thermal treatment causes a significant increase of the corrosion current density (from 3.4×10^{-9} A/cm² on average for rough braids to 6.1×10^{-8} A/cm² on average for TT stents), while the corrosion potential is significantly shifted towards

more cathodic values (from -180 mV on average for rough braids to -415 mV on average for TT stents). The sterilization of TT stents seems to slightly decrease the corrosion current density (4×10^{-8} A/cm² on average after sterilization), while the average corrosion potential remains practically unchanged.

The pickling treatment of TT stents, followed by sterilization, results in stents having an average corrosion current density significantly lower than TT and TT St stents (7.3×10^{-9} A/cm²), and a mean corrosion potential shifted towards anodic values (-240 mV for TD St stents vs. -435 mV for TT St stents), which means a significant decrease of material-oxidation speed in a TD St state vs. TT and TT St states.

Thermally-treated, passivated and sterilized stents (TP St) show an average corrosion potential quite similar to that of pickled stents (TD St), but a slightly higher mean corrosion current density (1.5×10^{-8} A/cm² for the TP St vs. 7.3×10^{-9} A/cm² for the TD St stents). Thus, passivation of thermally-treated Phynox stents improves their resistance to corrosion, but slightly less than with a pickling treatment.

Thermally-treated, pickled, and passivated stents (TDP) give intermediary results vs. TD St and TP St stents. Their mean corrosion potential is the same as that of TD St stents, while their mean corrosion current density is 1×10^{-8} A/cm².

After a sterilization treatment with ethylene oxide, these stents exhibit a slightly more cathodic average corrosion potential (-280 mV for TDP St vs. -240 mV for TDP stents) while their mean corrosion current density seems to be slightly higher (1.7×10^{-8} A/cm² for TDP St vs. 1×10^{-8} A/cm² for TDP stents). Nevertheless, the small differences noticed between mean corrosion current densities and mean corrosion potentials cannot be considered as really significant, given the variations observed between various samples in a same group.

Regarding the 5mm- and 9mm-diameter stents, we did not notice significant differences when compared to 7mm-diameter stents. In particular, 5mm- and 7mm-diameter stents have almost identical mean corrosion current density values and mean corrosion potential values. However, the stents with a larger diameter showed a lower mean corrosion current density (9×10^{-9} A/cm² vs. 1.7×10^{-8} A/cm² for stents with a shorter diameter) and much more reproducible results.

3.1.3. Conclusions

This systematic analysis shows that all braided Phynox stents are resistant to corrosion, and in particular to the pitting-corrosion phenomenon which is especially harmful. The thermal treatment needed to achieve the desired mechanical properties of the material, induces a steady increased corrosion rate. Nevertheless, the treatments applied by Cardiatis after thermal treatment results in a very good resistance to corrosion (comparable to the resistance of the rough material).

3.2. Surface modification of Phynox substrates

As mentioned earlier, this part of the chapter focuses on the modification of Phynox surface toward a versatile platform for post-grafting chemical reactions. Indeed, even if Phynox has a

very good corrosion resistance as shown in the previous section, there is a strong interest in modifying its surface with the prospect of improving the material-biological environment interactions. In order to be able to carry out surface characterization easily, plane Phynox substrates were used instead of Phynox wires.

3.2.1. XPS analysis of bare Phynox substrates

The surface state of the Phynox substrates was characterized before any modification. Those substrates (foils of about 0.1 mm thickness) were purchased from Arcelor Mittal Imphy Service (Clichy, France). Phynox is mainly composed of Co (39-41%), Cr (19-21%), Ni (15-16%), Mo (6.5-7.5%), Mn (1.5-2.0%) and Fe (balance) with small percentages of other elements such as Si ($\leq 1.2\%$), C ($\leq 0.15\%$), P ($\leq 0.015\%$), S ($\leq 0.015\%$) and Be ($\leq 0.001\%$). The substrates were mechanically polished down to 1 μm on a Buehler Phoenix 4000 instrument using various grit silicon carbide papers and diamond pastes. At the end of the polishing steps, the metal coupons are cleaned by sonication 15 min in ethanol and blown dry under a nitrogen flow. Phynox substrates were thus characterized in two different states: as received (after a cleaning step by sonication 15 minutes in ethanol) and after being mechanically polished. Representative XPS survey spectra are presented in Figure 3.1.

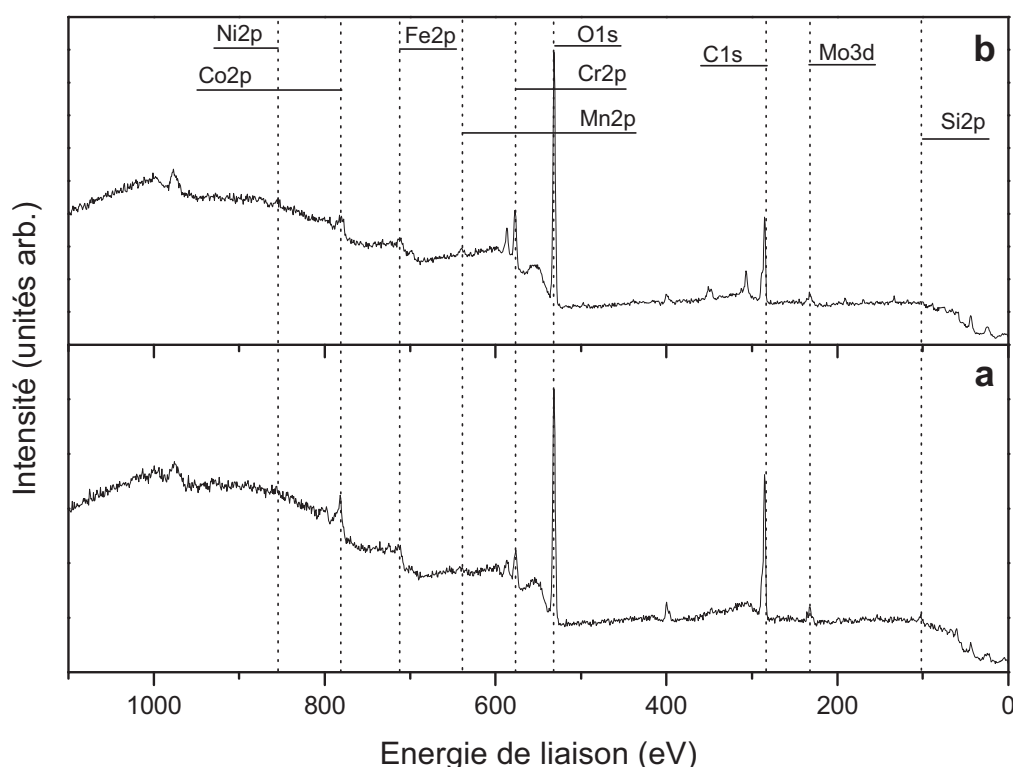


Figure 3.1. XPS survey spectra of Phynox substrates as received (a) and after a mechanical polishing step (b).

On both spectra, the presence of the peaks of the main elements present in Phynox is noticed i.e. Si, Mo, Cr, Mn, Fe, Co and Ni but also a very intense O1s peak attributed to the oxygen of the oxide layer as well as a C1s peak attributed to physisorbed atmospheric carbonated contaminations.

Table 3.3. Percentages of the main metallic elements present at the surface of Phynox substrates as received and after a mechanical polishing step

	Si	Mn	Ni	Cr	Mo	Fe	Co
As received	17	5	5	22	6	18	27
Mechanically polished	14	5	7	35	6	13	20

The surface composition of Phynox substrates is somewhat different from the bulk composition: the main metallic elements constitutive of the protective oxide layer present on as received Phynox substrates are Co (27%), Cr (22%), Si (17%), Fe (18%), Mn (5%), Mo (6%) and Ni (5%). The mechanical polishing of these surfaces induces a change in the surface composition. The same main metallic elements are present but their abundance varies significantly: the percentages of Si, Co and Fe decrease from 17 to 14%, 27 to 20 % and 18 to 13%, respectively while the percentage of Cr increases from 22 to 35%.

3.2.2. Grafting PEG Fragments on Phynox substrates modified with 11-phosphonoundecanoic acid

3.2.2.1. Introduction

The aim of the present work was to functionalize the Phynox surfaces with 11-phosphonoundecanoic acid monolayers. The resulting surface is meant to constitute a reference platform for a large variety of post-grafting chemical reactions, e.g. with alcohols, amines, etc., to modify and control the surface properties of Phynox. To illustrate this potential, we report on the post-grafting of small PEG fragments by the Steglich esterification reaction between the carboxylic end function of the grafted 11-phosphonoundecanoic acid molecules and the alcohol function of PEG fragments. Three different PEG fragments were used in this work: HO-(CH₂)₂-O-CH₃, HO-(CH₂)₂-O-(CH₂)₂-O-CH₃ and HO-(CH₂)₂-O-(CH₂)₂-O-(CH₂)₂-O-CH₃ called PEG1, PEG2 and PEG3, respectively.

First, the interaction between the phosphonic acid anchoring group of *n*-dodecanephosphonic acid and the Phynox oxide layer was studied. Then the grafting of *n*-dodecanoic acid was studied using in the same conditions in order to assess the competition of the carboxylic function with the phosphonic group to bind the surface. Grafting of the 11-phosphonoundecanoic acid was then achieved, followed by the binding of different alcohols by a Steglich esterification reaction. The different steps of the work are schematically summarized in Figure 3.2.

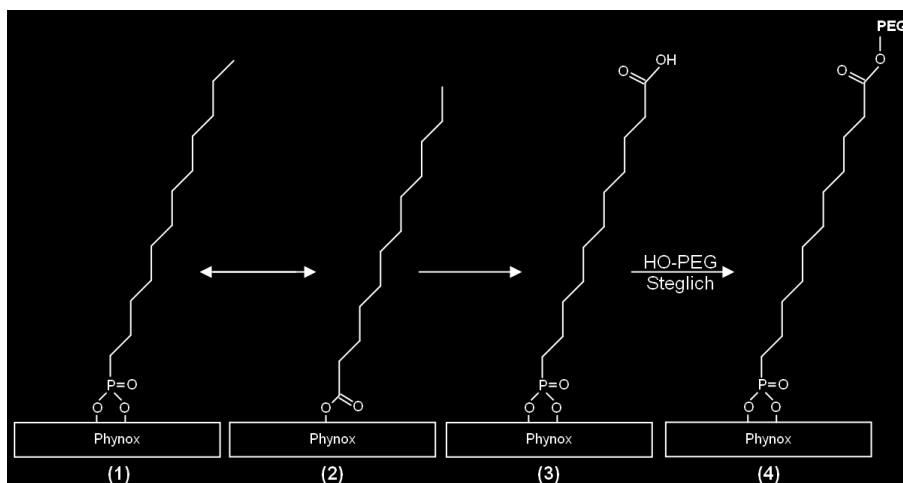


Figure 3.2. Schematic of the Phynox surface modification methodology used in this work.

3.2.2.2. Samples preparation

The Phynox substrates were mechanically polished as described previously (see section 3.2.1) and stored until their modification. Just before modification, the substrates were cleaned again by sonication 15 minutes in ethanol and undergo a UV/O₃ treatment of 30 minutes. The monolayers were then formed by immersing the samples in 1 mM aqueous solutions of the molecule to graft during 5 hours. They were then rinsed copiously with ethanol, cleaned by sonication 15 min in the same solvent, blown dry under a nitrogen flow and characterized directly.

3.2.2.3. Grafting of the *n*-dodecylphosphonic acid

After the *n*-dodecylphosphonic acid grafting, as described in the experimental section, Phynox substrates were first characterized by XPS. Survey spectra of the bare and modified Phynox are shown in Figure 3.3. The appearance of the P2p photoelectrons peaks in the modified substrate spectrum indicates the presence of the molecule at the surface. These substrates were also characterized by PM-IRRAS (see Figure 3.4). The spectra of the unmodified Phynox substrates contained no peaks attributable to organic deposition (figure not shown). In the spectra of the modified substrates, the presence of an important bands overlapping in the 1000-1500 cm⁻¹ region corresponding to the different vibration modes of the phosphonic moiety is clearly visible, confirming the grafting of the *n*-dodecylphosphonic acid on the Phynox surface. However, this spectrum does not provide information about the grafting mode of the molecule (mono-, bi- or tridentate). In the 2850-3000 cm⁻¹ region of the spectra, very weak C-H asymmetric and symmetric stretching vibrations bands are observed at 2920 and 2854 cm⁻¹ (ν_{CH2asym} and ν_{CH2sym} , respectively) and at 2966 and 2877 cm⁻¹ (ν_{CH3asym} and ν_{CH3sym} , respectively). These values are indicative of a weakly organized monolayer.

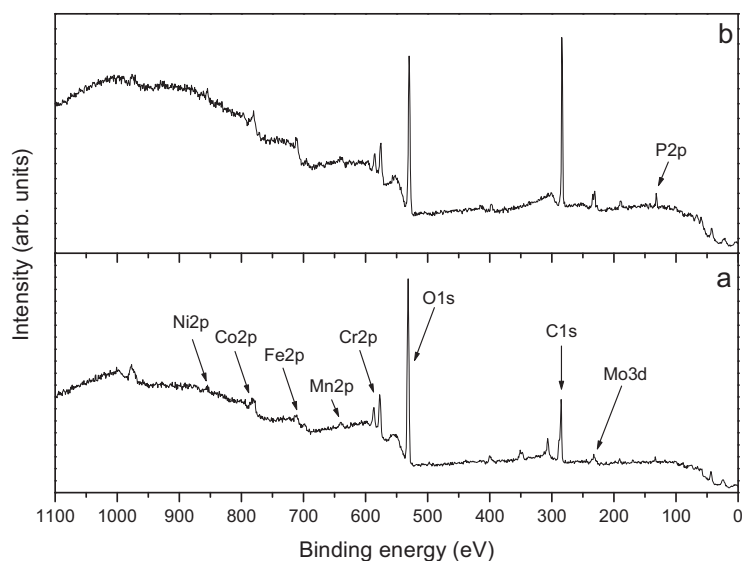


Figure 3.3. XPS survey spectra of bare mechanically polished Phynox (a) and mechanically polished Phynox modified by immersion 5 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at 100°C (b).

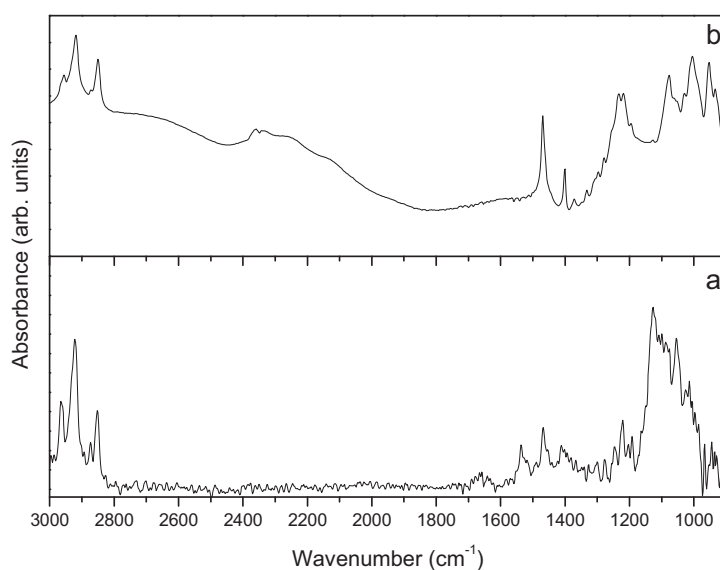


Figure 3.4. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 5 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at 100°C (a) and IR spectra of the *n*-dodecylphosphonic acid dispersed in a KBr pellet (b).

The characterization of the layer by cyclic voltammetry reveals a blocking factor of 98%. The obtained voltammogram is presented in Figure 3.5. It indicates that grafting of

organophosphonic acids on Phynox oxide layer leads to a high coverage ratio and thus a high degree of functionalization of the surface.

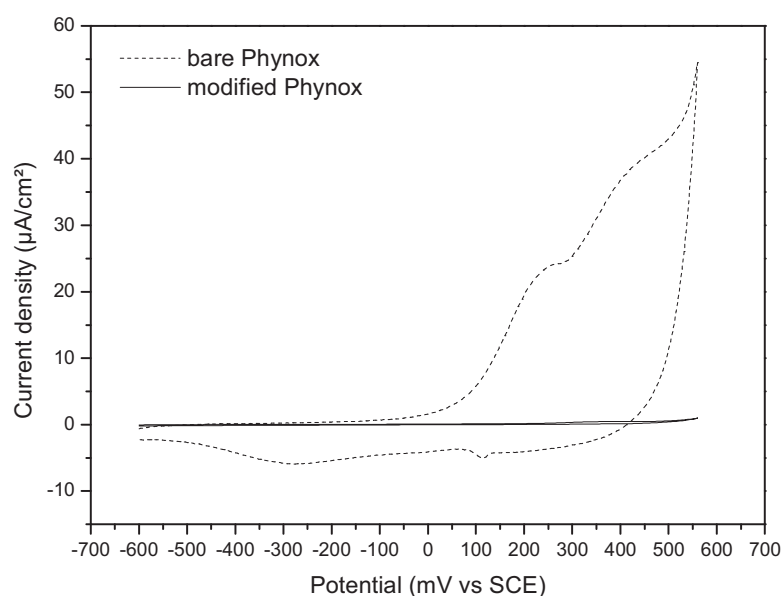


Figure 3.5. Voltammograms of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at 100°C (plain line).

Polarization curves technique reveals that the modification of Phynox with *n*-dodecylphosphonic acid does not change significantly its corrosion potential (Figure 3.6). However, the corrosion current density of the modified Phynox is about 10-fold lower than the bare one (6.5×10^{-8} A/cm² and 1.5×10^{-6} A/cm², respectively), indicating a mixed corrosion inhibition. The planned surface modification is thus expected to be beneficial in terms of corrosion resistance of Phynox.

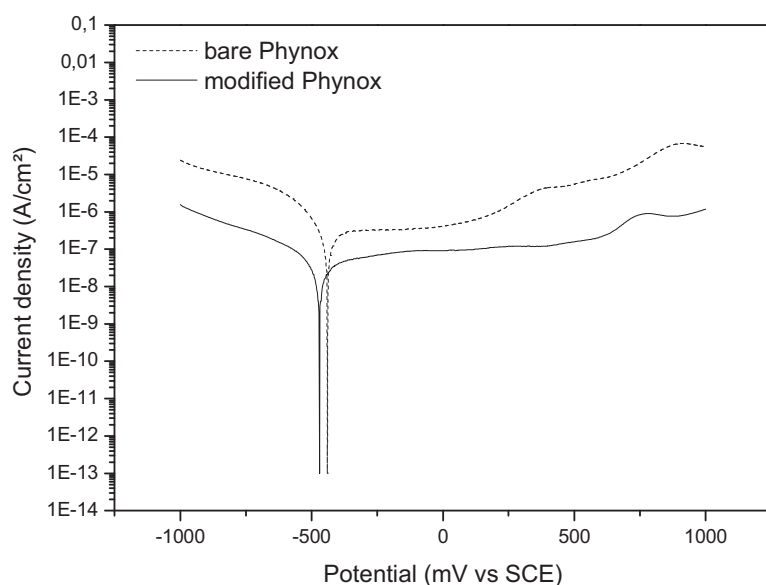


Figure 3.6. Polarization curves of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at 100°C (plain line).

3.2.2.4. Grafting of the *n*-dodecanoic acid

In order to assess the ability of the carboxylic function to bind the Phynox surface and thus compete with the phosphonic function, the grafting of *n*-dodecanoic acid has been studied in the same conditions. In this case, XPS analysis does not provide information on its presence on the surface since no specific atom is present in this molecule (like phosphorus in *n*-dodecylphosphonic acid). However, PM-IRRAS analysis of the treated samples reveals the presence of absorption bands attributable to organic deposition (Figure 3.7): the different angular deformation absorption bands of the CH₂ and CH₃ moieties in the region between 1000 and 1800 cm⁻¹ of the spectra as well as the $\nu_{\text{CH}_2\text{asym}}$ and $\nu_{\text{CH}_2\text{sym}}$ bands (at 2925 and 2854 cm⁻¹, respectively) and the $\nu_{\text{CH}_3\text{asym}}$ and $\nu_{\text{CH}_3\text{sym}}$ bands (at 2965 and 2877 cm⁻¹, respectively) are well visible. These latter bands are again characteristics of a weakly organized layer. Note that the $\nu_{\text{C=O}}$ band at 1700 cm⁻¹ which is expected to be very strong is not present in the PM-IRRAS of the treated Phynox substrates. This could be explained either by the involvement of this moiety in the binding of the molecule to the surface (implying a shift of the band towards lower frequencies) or, as the molecule is bound to the surface, by the orientation of the C=O bond parallel to the surface. In this case, the dipolar moment variations would be cancelled by the creation of an image dipolar moment in the metallic substrate.

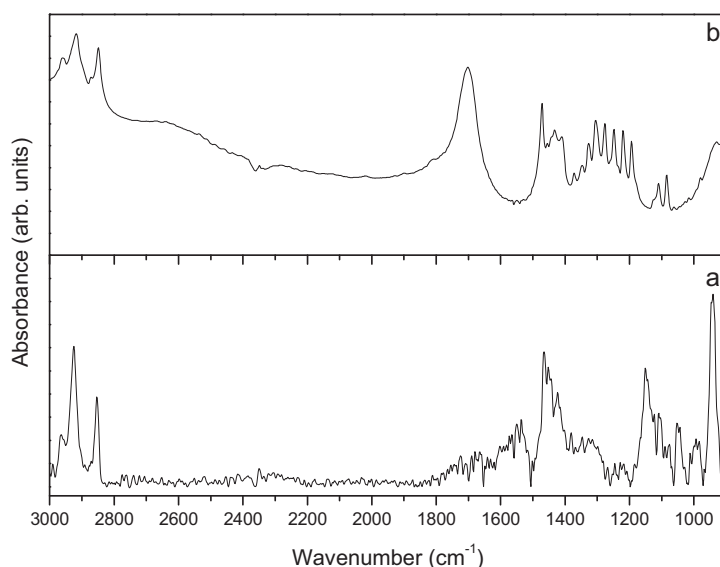


Figure 3.7. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 5 h in a 1 mM aqueous solution of *n*-dodecanoic acid at 100°C (a) and IR spectra of the *n*-dodecanoic acid dispersed in a KBr pellet (b).

Cyclic voltammetry analysis of the treated samples reveals that the presence of *n*-dodecanoic acid molecules at the surface induces a blocking factor of 86%, significantly lower than in the case of *n*-dodecylphosphonic acid grafting (Figure 3.8). As the grafting conditions used are the same in both cases, it can be concluded that carboxylic functions are able to bind the Phynox substrate but have a lower affinity to it than the phosphonic acid functions. Moreover, in the case of substrates treated with *n*-dodecanoic acid, we can observe a high increase of the current density at potentials higher than 300 mV vs. SCE which was not observed in the case of substrates treated with *n*-dodecylphosphonic acid. This could be explained by an oxidation and a degradation of the grafted molecules at the surface of the electrode. The degradation of the layer at high potential is confirmed by the appearance of the reduction peak on the reverse scan of the modified substrates. This confirms the lower stability and affinity for the substrate of the *n*-dodecanoic acid in comparison with the *n*-dodecylphosphonic acid.

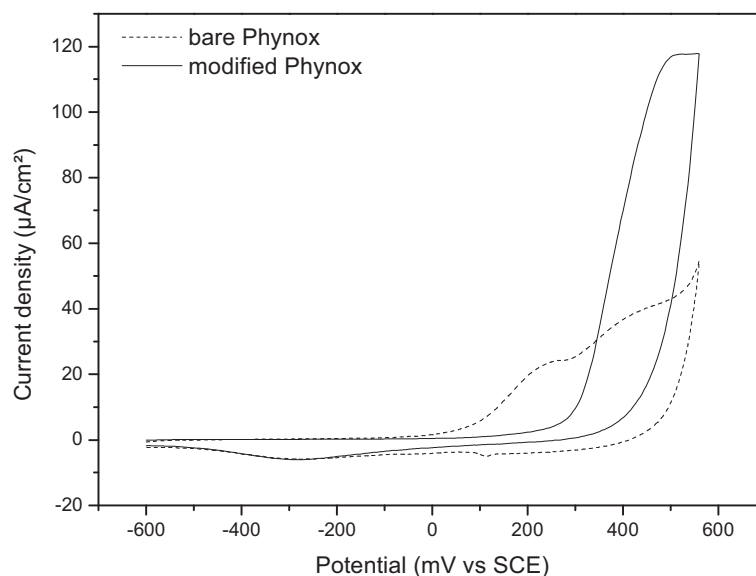


Figure 3.8. Voltammograms of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of *n*-dodecanoic acid at 100°C (plain line).

Polarization curves analysis reveals that the modification of Phynox with *n*-dodecanoic acid does not change significantly its corrosion potential (Figure 3.9). However, the corrosion current density of the modified Phynox is lower than the bare one (2.6×10^{-7} A/cm² and 1.5×10^{-6} A/cm², respectively), indicating a mixed corrosion inhibition like in the case of Phynox substrates modified with *n*-dodecylphosphonic acid. However, the lower decrease of the current density confirms that the *n*-dodecanoic acid, and thus the carboxylic acid function, has a lower affinity for the Phynox surface and leads to a monolayer of lower quality than the phosphonic acid function does. Bifunctional molecules such as the 11-phosphonoundecanoic acid are thus expected to bind the substrate mainly via the phosphonic acid moiety.

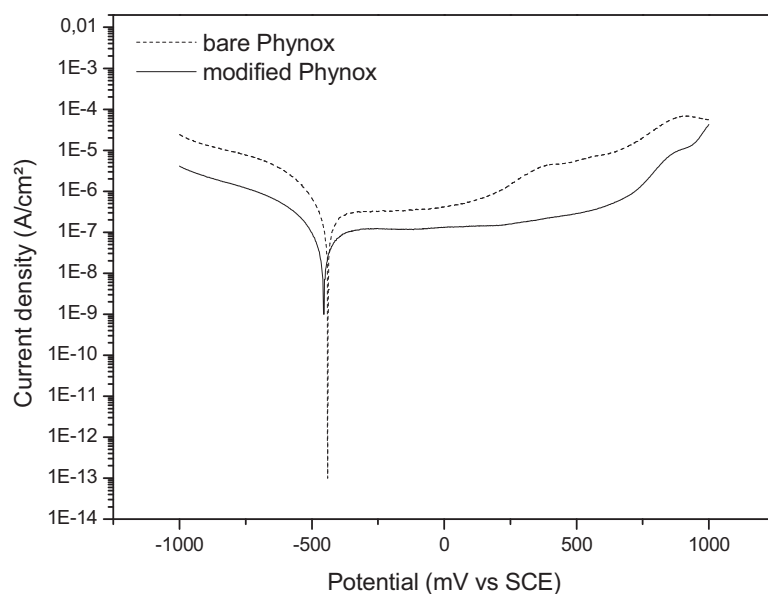


Figure 3.9. Polarization curves of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of *n*-dodecanoic acid at 100°C (plain line).

3.2.2.5. Grafting of the 11-phosphonoundecanoic acid

After the individual characterization of the carboxylic acid and phosphonic acid grafting on Phynox, the grafting of the 11-phosphonoundecanoic acid (in which both functions are present) has been studied.

XPS characterizations of the 11-phosphonoundecanoic acid modified Phynox substrates reveal the presence of the P2p photoelectrons peaks, indicative of the presence of the molecule on the surface (Figure 3.10).

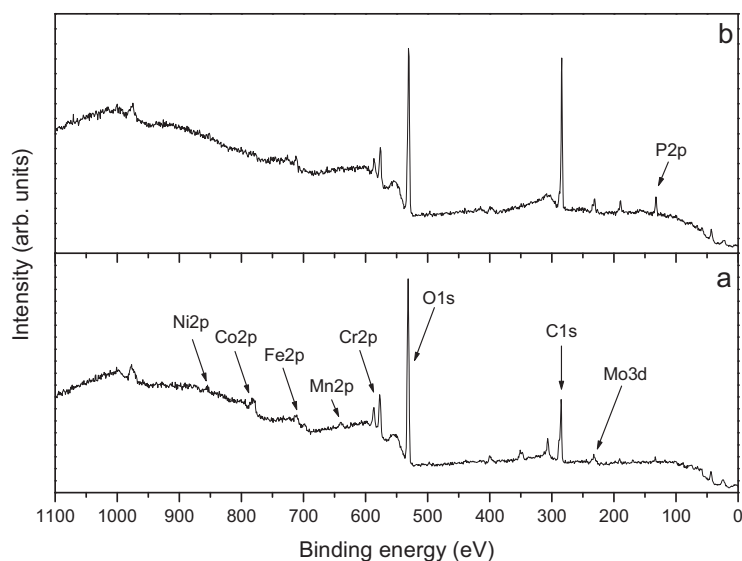


Figure 3.10. XPS survey spectra of bare mechanically polished Phynox (a) and mechanically polished Phynox modified by immersion 5 h in a 1 mM aqueous solution of 11-phosphonoundecanoic acid at 100°C (b).

The PM-IRRAS spectrum of the modified substrate is presented in the Figure 3.11. The ν_{CH2asym} and ν_{CH2sym} bands can be observed at 2925 and 2850 cm^{-1} , respectively. This indicates no improvement of the organization of the monolayer. Note that contrary to the case of the *n*-dodecanoic acid grafting, the absorption band of the C=O stretching (around 1700 cm^{-1}) is now visible on the PM-IRRAS spectrum. As it was not when the carboxylic function was bound to the substrate, this indicates that at least a certain proportion of the bifunctionnal molecules are bound to the substrate via the phosphonic acid function, confirming our previous hypothesis.

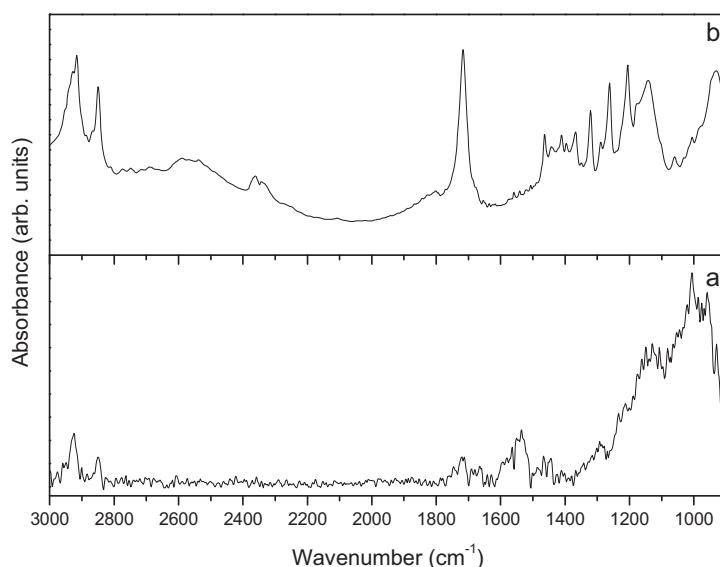


Figure 3.11. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 5 h in a 1 mM aqueous solution of 11-phosphonoundecanoic acid at 100°C (a) and IR spectra of the 11-phosphonoundecanoic acid dispersed in a KBr pellet (b).

Cyclic voltammetry analysis of the treated samples reveals a blocking factor of 74%, significantly lower than in both previous cases (Figure 3.12). This could be explained on the one hand by the hydrophilicity of the monolayer ($-\text{COOH}$ and/or $-\text{PO}(\text{OH})_2$ termination) allowing the aqueous electrolytic solution to reach the substrate more easily than in the case of methyl terminated molecules and, on the other hand, by the most probably more important interchain distance in the bifunctional molecules monolayer induced by the steric hindrance of the terminal groups. Moreover, we notice a high increase of the current density at potentials over 400 mV vs. SCE like in the case of a *n*-dodecanoic acid monolayer. This indicates clearly that a certain amount of the bifunctional molecules are grafted via the carboxylic function.

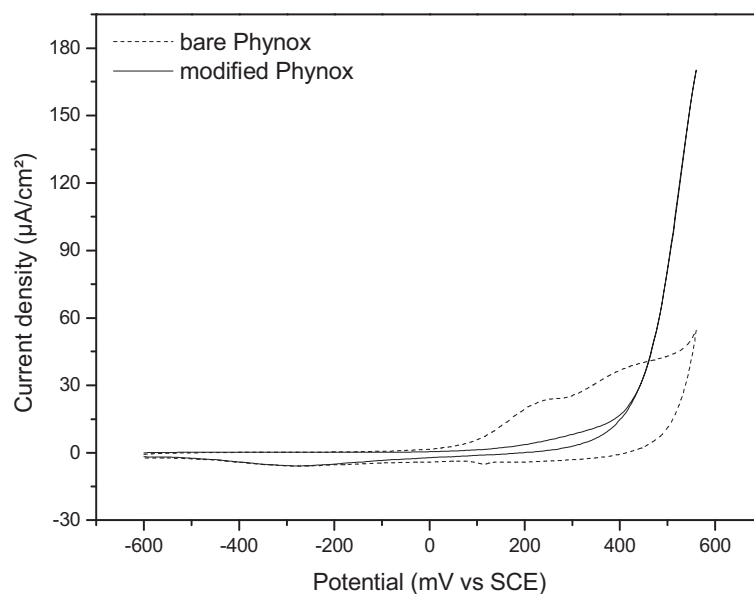


Figure 3.12. Voltammograms of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of 11-phosphonoundecanoic acid at 100°C (plain line).

Polarization curves of the treated samples are presented in Figure 3.13. The electrochemical behavior of the modified Phynox is radically different than in both previous cases: an important shift of the corrosion potential towards cathodic values (from -438 to -814 mV vs. SCE for unmodified and modified substrates, respectively) can be observed. On the other hand, the corrosion current density does not seem to vary significantly.

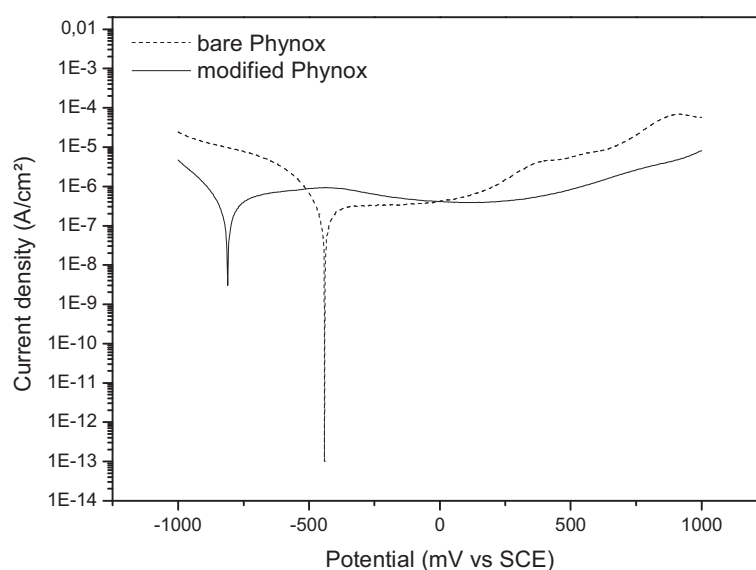


Figure 3.13. Polarization curves of a bare mechanically polished Phynox (dotted line) and a modified Phynox substrate by immersion 5 h in a 1 mM aqueous solution of 11-phosphonoundecanoic acid at 100°C (plain line).

3.2.2.6. Grafting of PEG oligomers on 11-phosphonoundecanoic acid modified surface

The last step of this surface modification is the grafting of alcohol terminated PEG oligomers on the carboxylic functions of the formed monolayer via a Steglich esterification reaction. This grafting step is carried out in anhydrous environment under nitrogen atmosphere. The 11-phosphonoundecanoic acid grafted substrates are immersed in a solution of 20 ml anhydrous CH_2Cl_2 , 1 mmol DCC (dicyclohexylcarbodiimide), 1 mmol DMAP (4-N,N-dimethylaminopyridin) and 1 mmol of the alcohol to be grafted on the external carboxylic functions of the monolayer. This system is cooled at 0°C and maintained under continuous stirring. After 24 hours of reaction, the substrates are removed from the solution, copiously rinsed with anhydrous CH_2Cl_2 , cleaned by sonication 15 min in ultrapure water and blown dry with a nitrogen flow.

Four different alcohols have been grafted this way: three PEG oligomers ($\text{HO}-(\text{CH}_2)_2-\text{O}-\text{CH}_3$, $\text{HO}-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{O}-\text{CH}_3$ and $\text{HO}-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{O}-(\text{CH}_2)_2-\text{O}-\text{CH}_3$ called PEG1, PEG2 and PEG3, respectively) and one fluorinated alcohol ($\text{HO}-\text{CH}_2-(\text{CF}_2)_8-\text{CF}_3$ called CF) for comparison. As described in section 2.2.2.3, the interest of working with such fluorinated alcohol is the possibility to assess the “yield” of grafting with XPS analysis i.e. the quantity of grafted alcohol vs. the quantity of grafted phosphonic acid because of the presence of specific functions for each of the two steps of the grafting process (phosphorus for the phosphonic acid and fluorinated carbon atoms for the alcohol).

XPS analyses have thus been systematically carried out. The high resolution C1s core level photoelectrons spectra of these four types of samples and their developed formulae are presented in Figures 3.14-3.17. As the only difference between PEG1, PEG2 and PEG3 molecules is the number of (CH₂-CH₂-O) monomeric units, a parallel analysis of their XPS spectra can be carried out. The experimental C1s core level spectra of these layers can be analyzed with five different peaks. The first one, centered at 286.4 eV is related to the carbon atom directly bound to the phosphorus atom of the phosphonic acid moiety (C1 in Figures 3.14-3.16). The peak of the photoelectrons from the aliphatic carbon atoms, noted C2 in Figures 3.14-3.16, is centered at 285.0 eV. Note that, in each studied case, the experimental ratio of the peaks area C2/C1 is higher than the theoretical ratio of 8. This means that a certain quantity of atmospheric contaminations is still present at the surface after the cleaning step of the substrates. The third peak, centered at 285.7 eV, is related to the carbon atom bound to the carbonyl function of the phosphonic acid as well as to the carbon atom bound to the oxygen in the ethylene glycol units (C3 in Figures 3.14-3.16). This peak can also be related to the slightly oxidized carbon atoms of some atmospheric contaminations. The peak centered at 287 eV is attributed to the carbon atoms bound to the oxygen atom of the formed ester function as well as to the terminal methyl function of the grafted alcohols (C4 in Figures 3.14-3.16). As this peak is only attributed to carbon atoms presents in the grafted alcohols, its presence on the C1s core level spectra confirms the achievement of the esterification reaction. Finally, the peak of the most oxidized carbon atoms (C5 in Figures 3.14-3.16) is centered at 289 eV. This peak is attributed to the carbon atom of the carbonyl function but a certain proportion of its area can also be attributable to highly oxidized carbon atoms of the atmospheric contaminations presents at the surface.

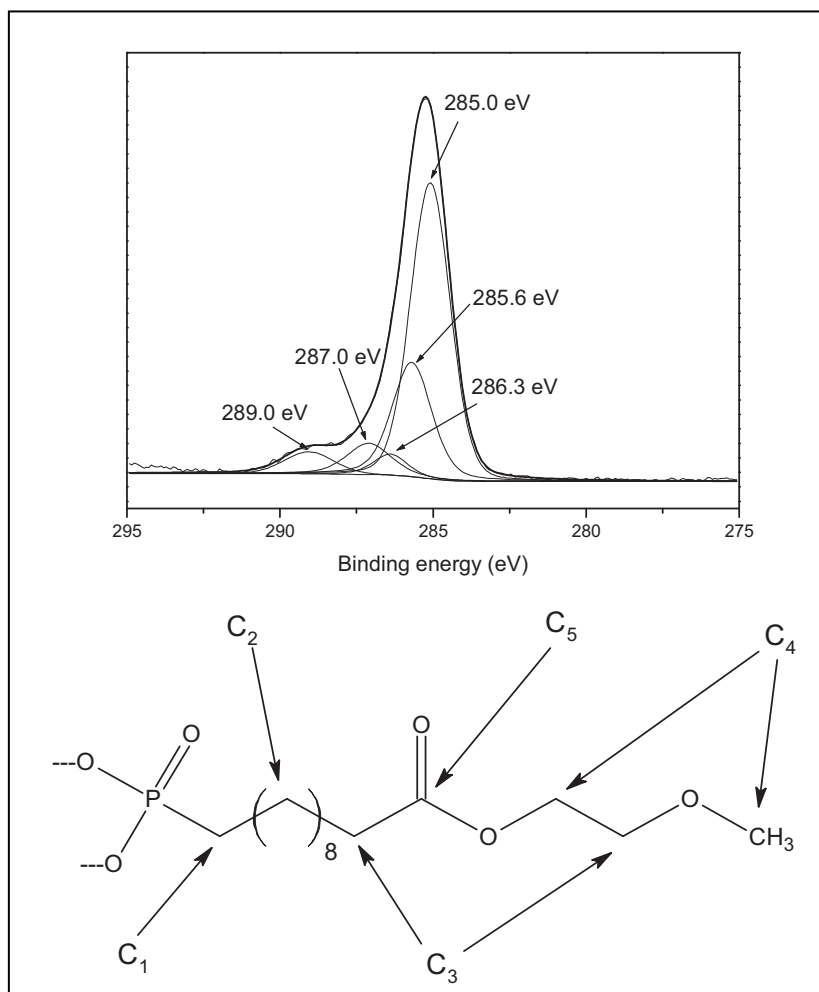


Figure 3.14. XPS C1s core level spectrum of the PEG1 grafted 11-phosphonoundecanoic acid monolayer and the corresponding developed formula.

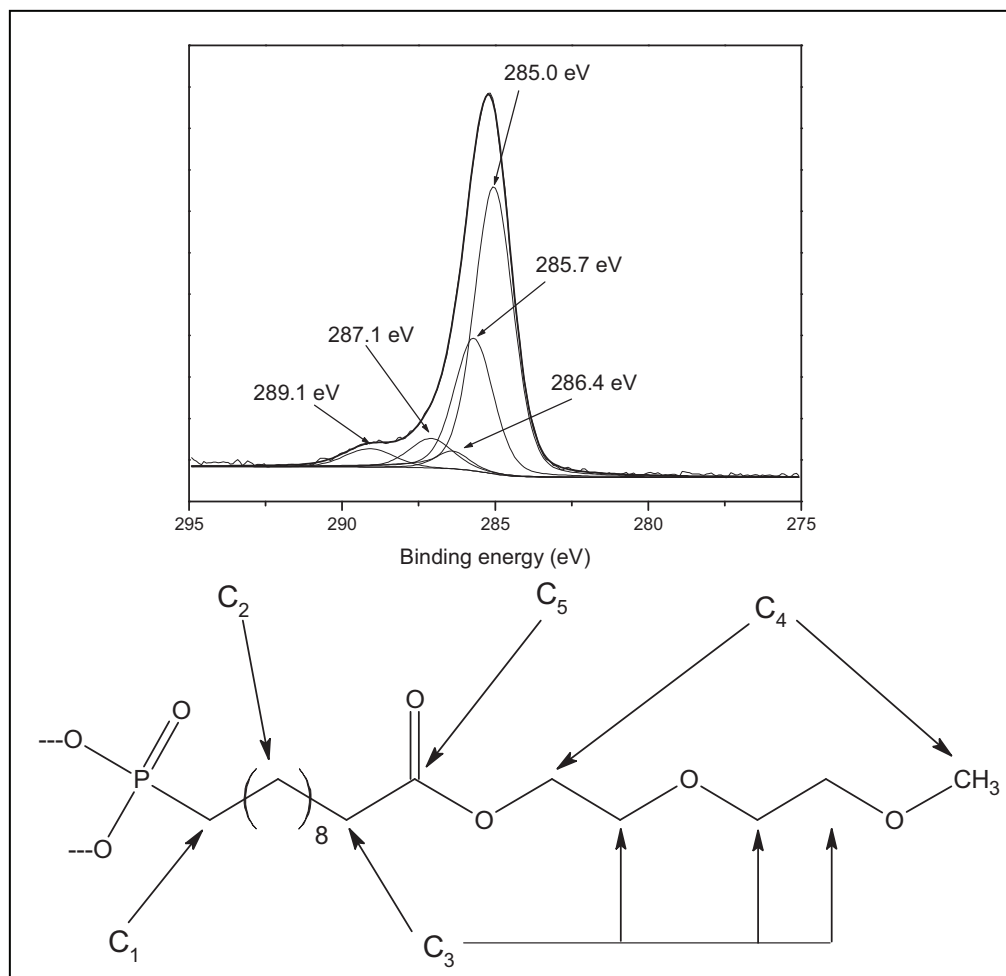


Figure 3.15. XPS C1s core level spectrum of the PEG2 grafted 11-phosphonoundecanoic acid monolayer and the corresponding developed formula.

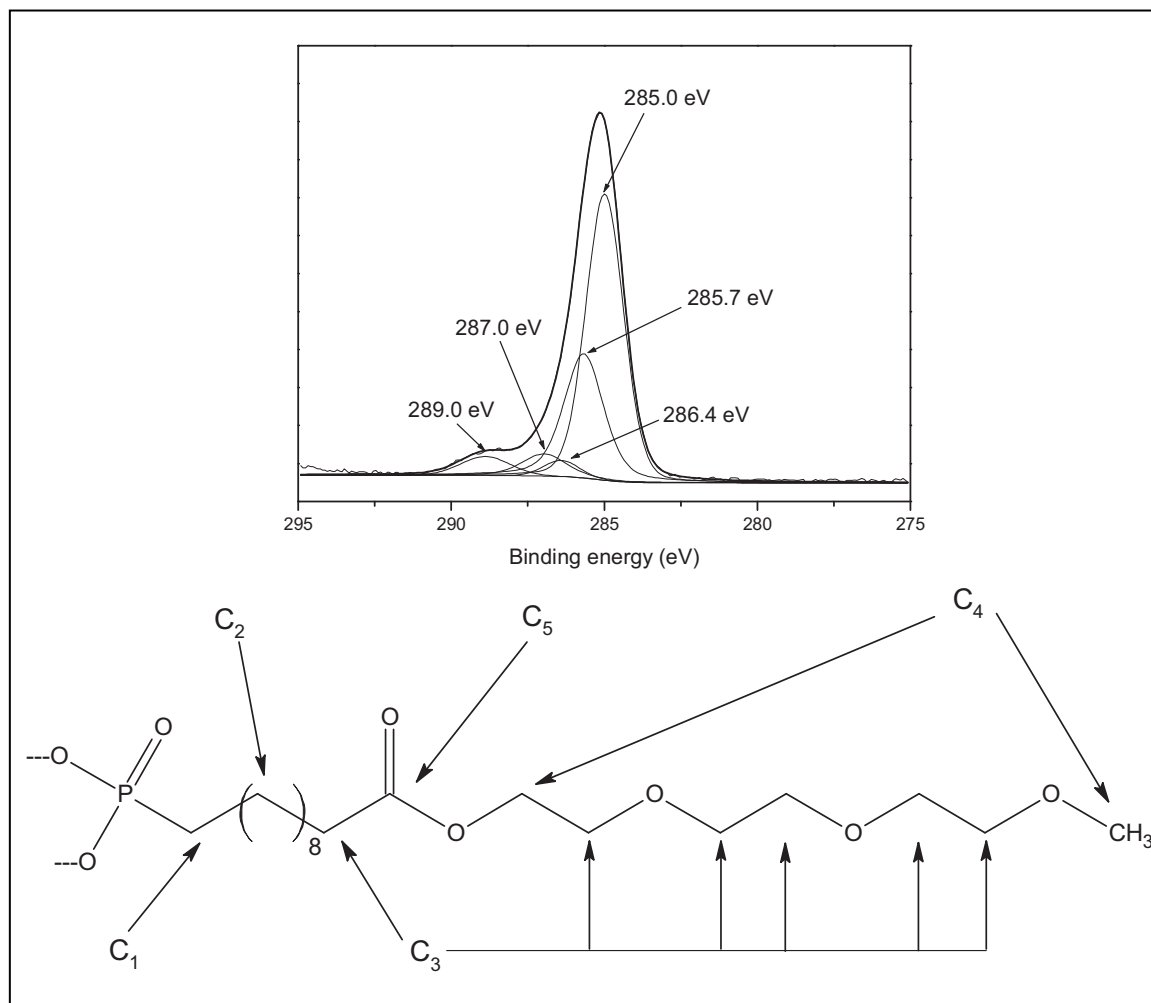


Figure 3.16. XPS C1s core level spectrum of the PEG3 grafted 11-phosphonoundecanoic acid monolayer and the corresponding developed formula.

The C1s core level spectra of the CF grafted monolayer is obviously radically different from the PEG grafted monolayers (Figure 3.17) and has been analyzed with height peaks. C1, C2, C3 and C5 carbon atoms peaks (centered at 286.5, 285.0, 285.8 and 289.2 eV, respectively) are the same as in the PEG grafted monolayers, being attributed to carbon atoms presents in the 11-phosphonoundecanoic acid monolayer and/or in atmospheric contaminations (C2, C3 and C5). The peak centered at 287.7 eV is attributed to the only hydrogenated carbon atom of the CF alcohol (C4 in Figure 3.17). The peak of the first carbon atom of the fluorinated moiety (C6 in Figure 3.17) is centered at 291.8 eV while the highest binding energy peak (294.6 eV) is attributed to the terminal CF₃ (C8 in Figure 3.17). Finally, the C1s core level photoelectrons peak of the carbon atoms in the middle of the fluorinated moiety of the molecule (C7 in Figure 3.17) is centered at 292.5 eV. As the C6 and C8 atoms are only related to the grafted alcohol and C1 to the 11-phosphonoundecanoic acid, the ratio of the area of their C1s peaks can be used to assess the “yield” of the esterification reaction. The value of these calculated ratios C8/C1 and C6/C1 is 0.4, indicating that more or less half of the 11-phosphonoundecanoic acid molecules has been involved into the esterification reaction.

Several hypotheses are proposed to explain this result. First, we have shown that the carboxylic acid function is able to bind the Phynox surface. It is thus reasonable to think that a certain proportion of the grafted 11-phosphonoundecanoic acid molecules are bound to the substrate via the carboxylic acid function, making it inaccessible to the esterification reaction. Secondly, we have to consider the possibility of dimerisation reactions between neighbouring carboxylic functions, making them much less prone to be involved in the esterification reaction. Moreover, after the very first steps of the esterification reaction, the steric hindrance induced by the presence of the grafted alcohols makes difficult the access of other free carboxylic functions present on the surface. It thus appears that the alcohols are probably not grafted in a dense configuration but rather spaced. This observation, based on the results of the fluorinated alcohol grafting, can be logically generalized to the grafting of PEG1, PEG2 and PEG3 molecules.

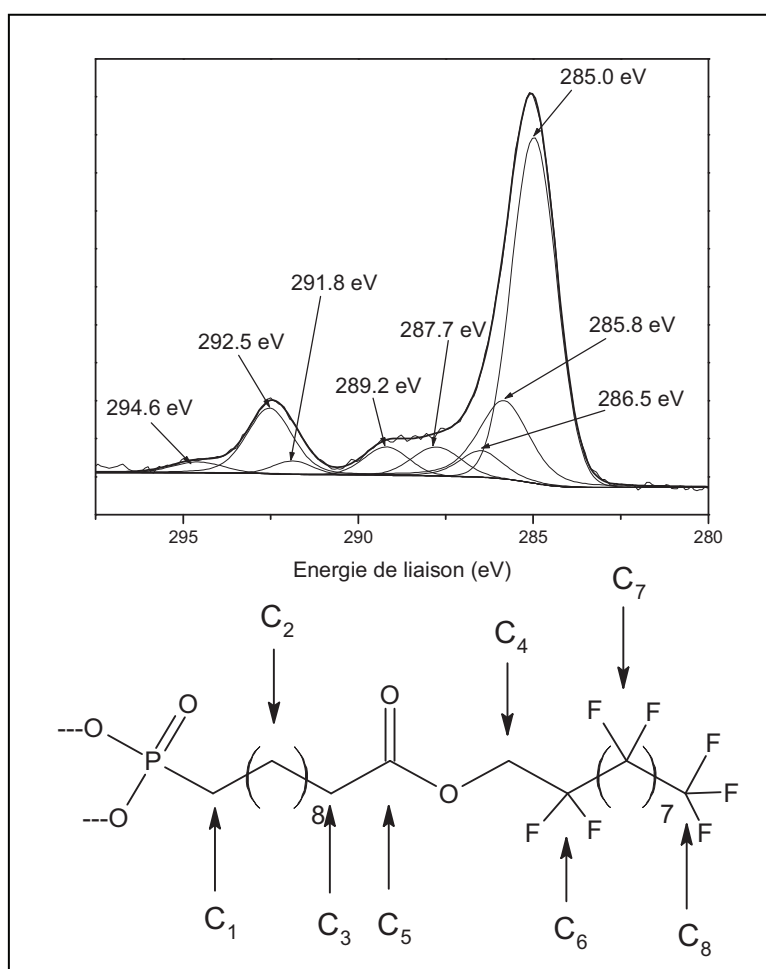


Figure 3.17. XPS C1s core level spectrum of the CF grafted 11-phosphonoundecanoic acid monolayer and the corresponding developed formula.

PM-IRRAS analysis of the formed layers has also been systematically carried out. On the spectra of all esterified monolayers (Figure 3.18), we can clearly see the appearance of a strong absorption band at 1264 cm^{-1} and a weaker one at 1110 cm^{-1} attributed to the

asymmetric and symmetric stretching of the formed ester function, respectively. This confirms that the alcohols are not simply physisorbed on the 11-phosphonoundecanoic acid monolayer but covalently bound to the terminal carboxylic functions of this monolayer.

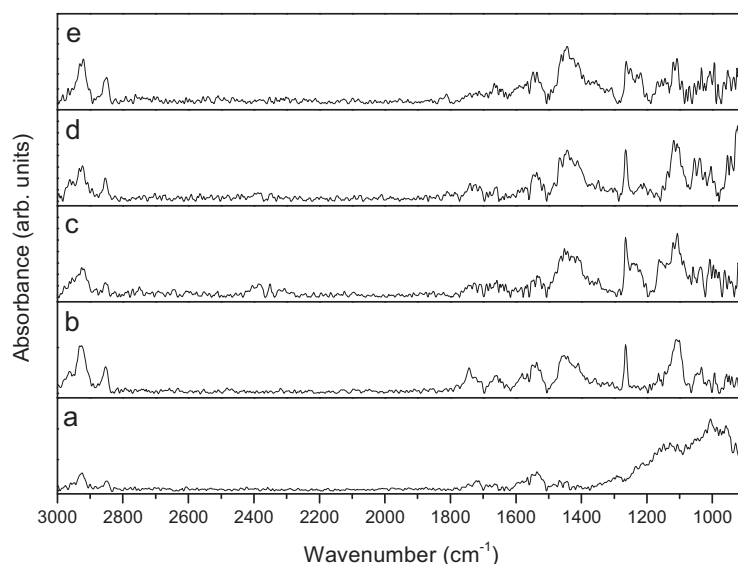


Figure 3.18. PM-IRRAS spectra of a 11-phosphonoundecanoic acid monolayer (a), PEG1 grafted 11-phosphonoundecanoic acid monolayer (b), PEG2 grafted 11-phosphonoundecanoic acid monolayer (c), PEG3 grafted 11-phosphonoundecanoic acid monolayer (d) and CF grafted 11-phosphonoundecanoic acid monolayer (e).

Blocking factors calculated on the basis of cyclic voltammetry experiments are presented in Table 3.4. It appears that the grafting of the different alcohols used in this work do not seem to change significantly the initial blocking factor of the 11-phosphonoundecanoic acid monolayer (despite a very small increase of this factor when a longer PEG fragment is grafted). This could be explained by the important spacing of the grafted alcohols suggested by the XPS analyses results.

Table 3.4. Blocking factors of a 11-phosphonoundecanoic acid monolayer, PEG1 grafted 11-phosphonoundecanoic acid monolayer, PEG2 grafted 11-phosphonoundecanoic acid monolayer, PEG3 grafted 11-phosphonoundecanoic acid monolayer and CF grafted 11-phosphonoundecanoic acid monolayer.

Surface Coating	Blocking Factor (%)
11-phosphonoundecanoic monolayer	74
PEG1	78
PEG2	79
PEG3	82
CF	75

Polarization curves experiments have been systematically carried out. Related numerical values are presented in Table 3.5. The grafting of PEG fragments and CF alcohols induces a small shift of the corrosion potential towards more anodic values relatively to the 11-phosphonoundecanoic acid monolayer. Even if this monolayer alone does not lead to any significant decrease of the corrosion current density of the Phynox, the esterified samples exhibit corrosion current densities 10-fold lower than the bare Phynox substrate. The final state of the created layer is thus expected to improve the biological response of the body to the implant but also to improve the resistance of the alloy to corrosion.

Table 3.5. Corrosion potentials and corrosion current densities of polished Phynox substrate untreated, treated with a 11-phosphonoundecanoic acid monolayer, PEG1 grafted, PEG2 grafted, PEG3 grafted and CF grafted.

Surface Coating	Corrosion Potential (mV vs. SCE)	Corrosion Current Density (A.cm ⁻²)
Untreated Phynox	-438	1.5x10 ⁻⁶
11-phosphonoundecanoic acid monolayer	-814	1.2x10 ⁻⁶
PEG1	-783	1.9x10 ⁻⁷
PEG2	-689	1.2x10 ⁻⁷
PEG3	-752	1.7x10 ⁻⁷
CF	-691	8.1x10 ⁻⁸

3.2.2.7. Conclusions

11-Phosphonoundecanoic acid monolayers on Phynox surfaces have been used as platforms to graft PEG segments of increasing length. This was achieved through a Steglich esterification reaction. The modifications on the surfaces have been characterized by XPS and PM-IRRAS and the properties of the films have been assessed by electrochemical characterizations.

Functionalizations of Phynox with *n*-dodecanephosphonic acid and *n*-dodecanoic acid indicate that the carboxylic function competes to a certain extent with the grafting of the phosphonic group on the Phynox surfaces.

In order to understand the possible competition between the two different end functions of the 11-phosphonoundecanoic acid (phosphonic acid and carboxylic acid functions) with the Phynox surfaces, the grafting of the *n*-dodecylphosphonic acid and *n*-dodecanoic acid on this substrate has been studied separately. The conclusion of this preliminary study is that, even if carboxylic acid function is able to bind the substrate, phosphonic acid function has a greater affinity for the Phynox substrate as *n*-dodecylphosphonic acid grafting leads to a more stable monolayer and a higher coverage than the *n*-dodecanoic acid grafting.

The 11-phosphonoundecanoic acid mainly binds the substrate via the phosphonic acid function, leaving a sufficient number of carboxylic functions available for the second step of the functionalization. Even if it was possible to graft different alcohol molecules to these carboxylic functions via an esterification reaction, about half of the grafted 11-phosphonoundecanoic acid molecules were involved in this reaction. Small PEG oligomers are thus dispersed over the 11-phosphonoundecanoic acid monolayer. The final functionalized

surfaces exhibit corrosion current densities about ten times lower than the bare Phynox substrates.

3.2.3. Grafting of bifunctional phosphonic and carboxylic acids on Phynox : impact of induction heating

3.2.3.1. Introduction

The aim of the present work was to study the influence of induction heating vs. conventional heating method on the functionalization of Phynox surfaces with bifunctional organophosphonic acid monolayers. Again, the resulting surface is meant to constitute a reference platform for a large variety of post-grafting chemical reactions, e.g. with alcohols, amines, etc., to modify and control the surface properties of Phynox. To assess this potential, we report on the post-grafting of a fluorinated alcohol (the 1H,1H-perfluoro-1-decanol) by the Steglich esterification reaction between the carboxylic end of the grafted 6-phosphonohexanoic acid molecules and the alcohol function.

First, the interaction between the phosphonic acid anchoring group of *n*-dodecanephosphonic acid and the Phynox oxide layer and the influence of the heating method on the resulting monolayer has been investigated. Then the grafting of *n*-dodecanoic acid has been studied using the same conditions in order to assess the competition of the carboxylic function with the phosphonic group to bind the surface. The influence of induction heating on the grafting of 6-phosphonohexanoic acid and 11-phosphonoundecanoic acid has then been investigated and followed by the reaction with the 1H,1H-perfluoro-1-decanol by Steglich esterification process.

3.2.3.2. Samples preparation

The Phynox substrates were mechanically polished as described previously (see section 3.2.1) and stored until their modification. Just before modification, the substrates were cleaned again by sonication 15 minutes in ethanol and undergo a UV/O₃ treatment of 30 minutes. The monolayers were then formed by immersing the samples in 1 mM aqueous solutions of the molecule to graft during 1 hour for the different heating parameters under study. They were then rinsed copiously with ethanol, cleaned by sonication 15 min in the same solvent, blown dry under a nitrogen flow and characterized directly.

3.2.3.3. Temperature measurements

Efficiency of the induction heating of polished Phynox coupons has been assessed. Induction heating was performed with an Ambrell EasyHeat induction heating system with a power output of 725 W and a frequency of 198 kHz. Like previously, the heating experiments were realized by applying sequences of induction heating followed by cooling periods allowing temperature measurements. The substrates were immersed into milli-Q water and centered

into the solenoid with their plane perpendicular to the solenoid axis. Two different heating profiles were assessed. Profile A begins with a very long heating pulse (480 s) followed by a 180 s cooling period. The rest of the profile is an alternation of 120 s heating pulses and 180 s cooling periods. Profile B begins with shorter pulses (120 s) followed by cooling periods of 60 s. This sequence is repeated three times. Then, like in profile A, the rest of the profile is an alternation of 120 s heating pulses and 180 s cooling periods. The temperature curves of these two profiles are shown in Figures 3.19 and 3.20.

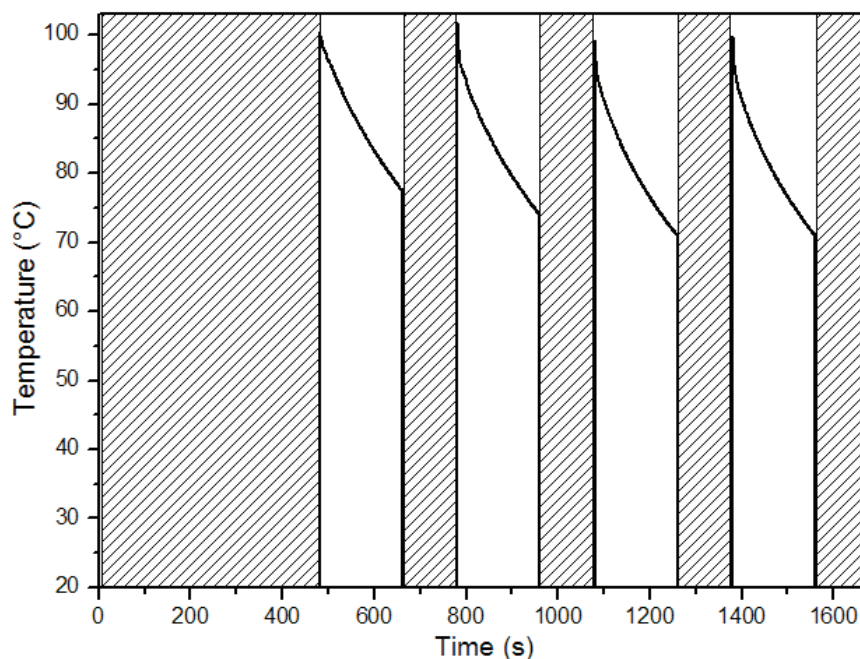


Figure 3.19. Evolution of the temperature at the surface of a Phynox coupon immersed into 10 ml milli-Q water during the induction heating sequences (profile A).

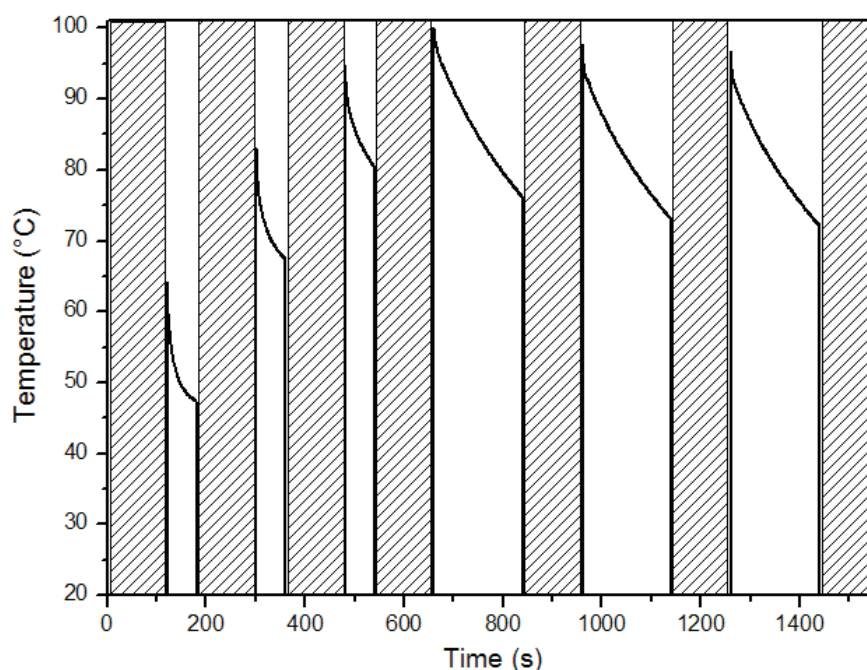


Figure 3.20. Evolution of the temperature at the surface of a Phynox coupon immersed into 10 ml milli-Q water during the induction heating sequences (profile B).

In the case of profile A, it appears that after 480 s of induction heating, the temperature at the surface of the Phynox coupon has reached its highest value (100°C) as all measurements are made in water. During the 180 s after the end of the first induction pulse, the surface temperature decreases from 100°C to 77°C. The aim of the rest of the profile is to maintain the temperature in the same range (between 100 and 70°C) for longer times (e.g. 1 hour). In the case of profile B, it appears that a 120 s induction pulse increases the temperature from 21°C to 65°C. After 60 s of cooling and again 120 s of induction, the final surface temperature is higher (83°C). A third 120 s induction pulse allows the Phynox surface to reach the highest temperature possible in water (100°C). Like in the case of profile A, the aim of the rest of the profile is to maintain the temperature in the same range for longer times as it is not possible to maintain a stable and constant surface temperature with this heating method. As the presented induction heating profiles keeps the temperature between 100 and 70°C, an intermediate temperature of 85°C has been selected for the conventional heating experiments.

3.2.3.4. Grafting of the *n*-dodecylphosphonic acid

After the *n*-dodecylphosphonic acid grafting, as described in the experimental section, Phynox substrates were first characterized by cyclic voltammetry. For the induction heated samples, the A and B profiles were prolonged to maintain the temperature between 100 and 70°C, as described in the previous section. The resulting representative voltammograms are presented in Figure 3.21. It appears that the sample modification at room temperature leads to unreproducible coverage values (from 50 to 82 %). The coverage obtained for a modification under induction heating with profile A is a little bit better (90 %) but the best results are obtained for Phynox samples modified in a conventionally heated solution and under induction heating with profile B (99 and 98 %, respectively). Hence, induction heating allows obtaining similar results than the ones obtained with a conventional heating method, as soon as proper induction heating parameters are used. Indeed, it seems that starting the modification with short pulses (profile B) leads to better results than starting with a long pulse (profile A), even if the highest temperature is reached earlier with profile A.

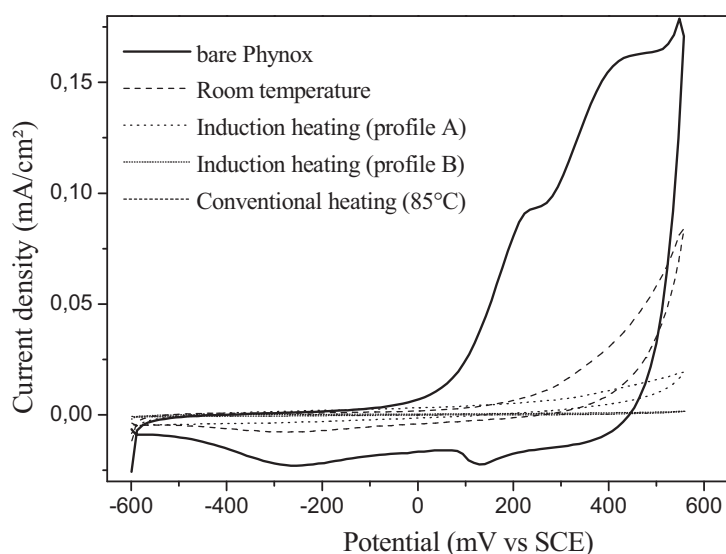


Figure 3.21. Voltammograms of a bare mechanically polished Phynox (thick plain line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at room temperature (dashed line), 85°C (short dashed line), with induction heating profile A (dotted line) and induction heating profile B (short dotted line).

Contact angle measurements (Table 3.6) confirm that induction heating leads to results similar to the ones obtained with a conventional heating method. Nevertheless, the two different induction heating profiles seem to lead to the same hydrophobicity (101°) while a conventional heating method leads to a little bit more hydrophobic surface (105°).

Table 3.6. Contact angles of milli-Q water droplets deposited on bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with *n*-dodecylphosphonic acid for the different studied conditions.

	Water contact angle (°)
Bare Phynox	43
Room temperature	96
Conventional heating (85°C)	105
Induction heating (profile A)	101
Induction heating (profile B)	101

These substrates were also characterized by PM-IRRAS (see Figure 3.22). The spectra of the unmodified Phynox substrates contain no peaks attributable to an organic deposition (figure not shown). In the spectra of the modified substrates, an important bands overlapping in the 1000-1500 cm⁻¹ region corresponding to the different vibration modes of the phosphonic moiety can be pointed out, confirming the grafting of the *n*-dodecylphosphonic acid on the Phynox surface. However, the spectra do not provide information about the grafting mode of the molecule (mono-, bi- or tridentate). In the 2850-3000 cm⁻¹ region of the spectra, very weak C-H asymmetric and symmetric stretching vibrations bands are observed around 2920

and 2854 cm^{-1} (ν_{CH2asym} and ν_{CH2sym} , respectively) and around 2966 and 2877 cm^{-1} (ν_{CH3asym} and ν_{CH3sym} , respectively). These values are indicative of weakly organized monolayers.

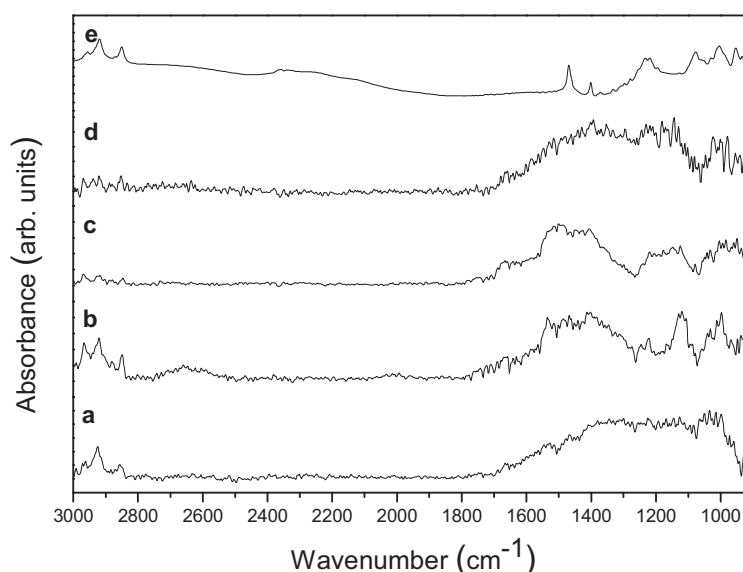


Figure 3.22. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 1 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at room temperature (a), at 85°C (b), with induction heating profile A (c), with induction heating profile B (d) and IR spectra of the *n*-dodecylphosphonic acid dispersed in a KBr pellet (e).

Polarization curves measurements reveal that the modification of Phynox with *n*-dodecylphosphonic acid does not change significantly its corrosion potential (Figure 3.23 and Table 3.7). Nevertheless, the corrosion current densities of the modified Phynox substrates are lower than for the bare Phynox and characteristic of a mixed corrosion inhibition, except in the case of the room temperature modification where not significant change in corrosion current density and corrosion potential can be pointed out. The same observation can be made in the case of a substrate modified with induction heating profile A. The lowest corrosion current density is measured for a Phynox sample modified with the *n*-dodecylphosphonic acid under induction heating (profile B). This heating method yields better results in terms of corrosion resistance than the conventional heating method.

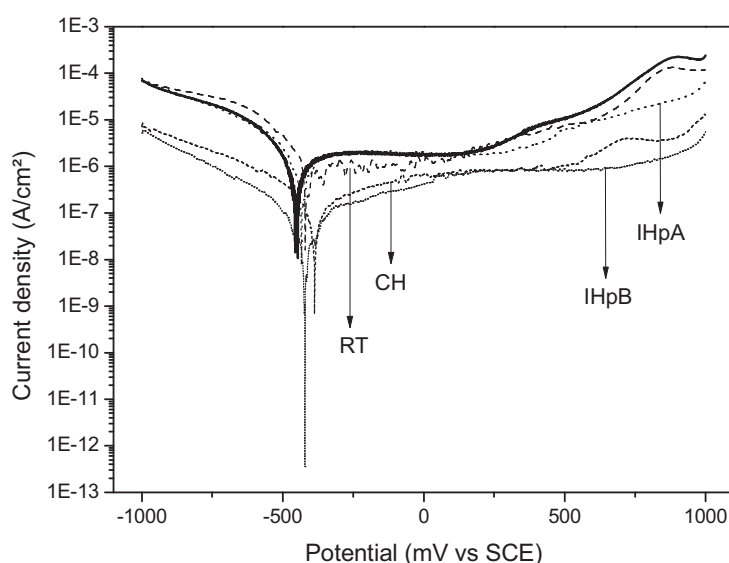


Figure 3.23. Polarization curves of a bare mechanically polished Phynox (thick plain line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at room temperature (RT in dashed line), 85°C (CH in short dashed line), with induction heating profile A (IHpA dotted line) and induction heating profile B (IHpB in short dotted line).

Table 3.7. Corrosion potentials and corrosion current densities measured for bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with *n*-dodecylphosphonic acid for the different studied conditions.

	Corrosion potential (mV vs SCE)	Corrosion current density (A.cm ⁻²)
Bare Phynox	-454	4.9×10^{-6}
Room temperature	-418	8.4×10^{-6}
Conventional heating (85°C)	-386	2.4×10^{-7}
Induction heating (profile A)	-436	3.8×10^{-6}
Induction heating (profile B)	-424	8.7×10^{-8}

XPS characterization of the obtained Phynox substrates has also been carried out systematically. The corresponding XPS survey spectra are presented in Figure 3.24. First, the presence of the P2p core level photoelectrons peak for each modified substrate confirms the presence of the grafted molecule on the Phynox surface. Calculation of the P2p/Metals ratio, in which “P2p” represents the normalized area of the P2p photoelectrons peak and “Metals” represents the sum of the normalized area of the different metallic elements of the substrate (Ni2p, Co2p, Fe2p, Mn2p, Cr2p and Mo3d), allows us to compare the different grafting conditions in terms of “quantity” of grafted molecules. Theses calculated ratios are presented in Table 3.8.

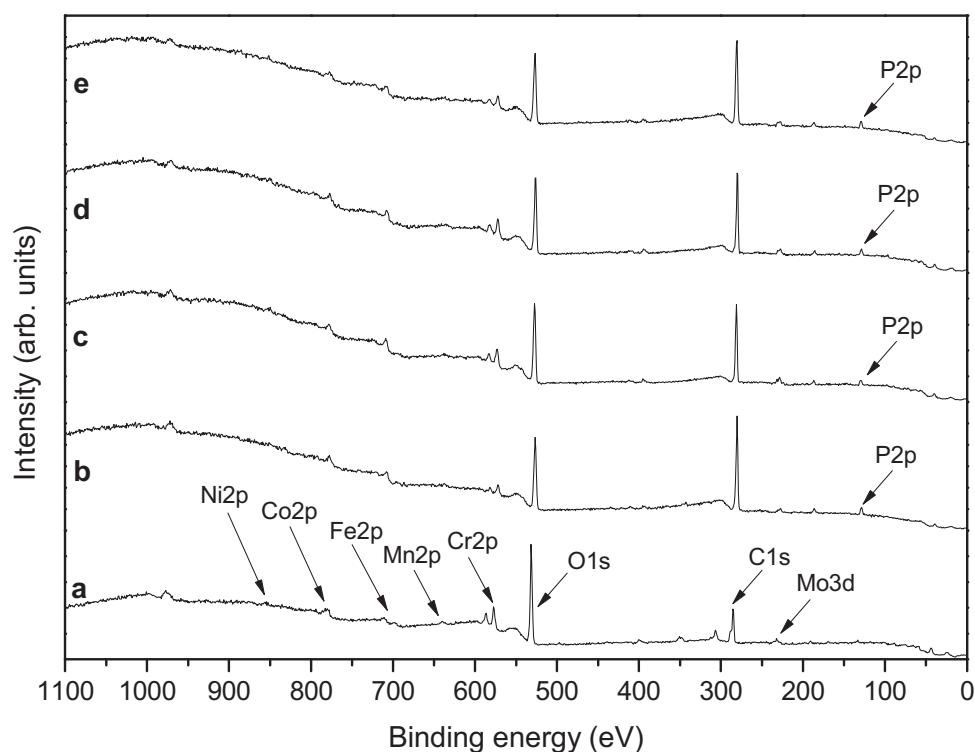


Figure 3.24. XPS survey spectra of a bare mechanically polished Phynox (a) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of *n*-dodecylphosphonic acid at room temperature (b), 85°C (c), with induction heating profile A (d) and induction heating profile B (e).

Table 3.8. P2p/Metals ratios calculated on basis of the XPS analysis of Phynox substrates modified with *n*-dodecylphosphonic acid for the different studied conditions.

	P2p/Metals ratio
Room temperature	0.15
Conventional heating (85°C)	0.22
Induction heating (profile A)	0.21
Induction heating (profile B)	0.36

It clearly appears that a Phynox modification at room temperature leads to the lowest amount of phosphorus on the surface while using induction heating profile B leads to the highest one. Both conventional heating method and induction heating profile A lead to similar values of P2p/Metals ratio. The trends pointed out from previous experiments are thus confirmed here: a room temperature modification is quite inefficient in forming a good organophosphonic acid monolayer compared to a higher temperature modification, induction heating can lead to similar or even better results than a conventional heating method and, in our specific case, induction heating parameters of the profile B seems to be the best one for obtaining a dense and protective *n*-dodecylphosphonic acid monolayer on Phynox surface.

3.2.3.5. Grafting of the *n*-dodecanoic acid

In order to assess the ability of the carboxylic function to bind the Phynox surface and thus compete with the phosphonic function, the grafting of *n*-dodecanoic acid has been studied in the three best grafting conditions for the *n*-dodecylphosphonic acid: with a conventional heating of the solution at 85°C, with the induction heating profile A and with the induction heating profile B. These modified Phynox substrates were first characterized by cyclic voltammetry (the resulting voltammograms are presented in Figure 3.25).

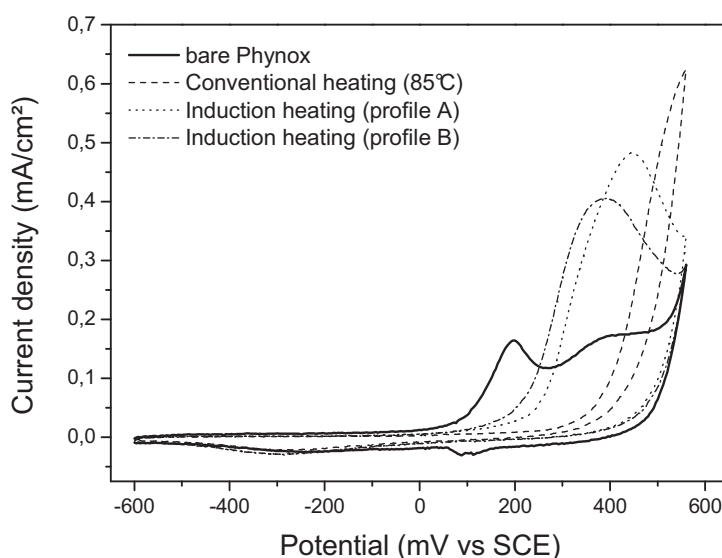


Figure 3.25. Voltammograms of a bare mechanically polished Phynox (thick plain line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of *n*-dodecanoic acid at 85°C (dashed line), with induction heating profile A (dotted line) and induction heating profile B (dash-dotted line).

It appears that the presence of *n*-dodecanoic acid molecules at the surface of the Phynox substrates modified at 85°C (conventional heating) induces a coverage of 90 %, significantly lower than in the case of *n*-dodecylphosphonic acid grafting. Carboxylic functions are thus able to bind the Phynox substrate but have a lower affinity to it than the phosphonic acid functions does. Moreover, in the case of substrates treated with *n*-dodecanoic acid with a conventional heating of the solution up to 85°C, a high increase of the current density can be observed at potentials higher than 300 mV vs. SCE (which was not observed in the case of substrates treated with *n*-dodecylphosphonic acid) that could be explained by an oxidation of the grafted molecules at the surface of the electrode and thus a degradation of the monolayer. This confirms the lower stability and affinity for the substrate of the *n*-dodecanoic acid in comparison with the *n*-dodecylphosphonic acid. On the other hand, when the *n*-dodecanoic acid grafting is carried out with induction heating, the resulting coverages are 74 % and 54 % for the induction heating profiles A and B, respectively. Thus it seems that the induction heating profile B leads to a much less efficient grafting of the carboxylic acid functions to the

Phynox surface. Furthermore, the high current density pointed out at potentials higher than 300 mV vs. SCE in the case of a *n*-dodecanoic acid monolayer formed under conventional heating takes place at lower potentials when the grafting is carried out under induction heating conditions (around 200 mV vs. SCE). This is indicative of a weaker and less stable monolayer. Induction heating is somewhat aggressive, since it increases rapidly the surface temperature and provokes cavitations phenomena when applied to a substrate immersed in an aqueous solution. Our hypothesis to explain this behavior is that this heating prevents the Van der Waals interactions between the grafting molecules to develop thereby leading to a more disorganized monolayer thus less stable than the more densely packed monolayer obtained with the conventional heating method.

This trend is confirmed by the contact angle measurements (Table 3.9) as the conventional heating of the modification solution at 85°C leads to the most hydrophobic surface after grafting (99°). Note that even if the coverage obtained with the induction heating profile A is lower than the one obtained with the conventional heating method, both methods lead to the same surface hydrophobicity. The grafting of *n*-dodecanoic acid on Phynox surface with the induction heating profile B leads to the lowest contact angle (94°) confirming that this grafting method is not favorable to the attachment and organization of alkanecarboxylic acids on this substrate.

Table 3.9. Contact angles of milli-Q water droplets deposited on bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with *n*-dodecanoic acid for the different studied conditions.

	Water contact angle (°)
Bare Phynox	43
Conventional heating (85°C)	99
Induction heating (profile A)	99
Induction heating (profile B)	94

PM-IRRAS analysis of the treated samples reveals the presence of absorption bands attributable to organic deposition (Figure 3.26). The angular deformation absorption bands of the CH₂ and CH₃ moieties in the region between 1000 and 1800 cm⁻¹ of the spectra as well as the $\nu_{\text{CH}_2\text{asym}}$ and $\nu_{\text{CH}_2\text{sym}}$ bands (at 2925 and 2854 cm⁻¹, respectively) and the $\nu_{\text{CH}_3\text{asym}}$ and $\nu_{\text{CH}_3\text{sym}}$ bands (at 2965 and 2877 cm⁻¹, respectively) can be pointed out. These latter bands are again characteristic of a weakly organized layer. Note that the $\nu_{\text{C=O}}$ band at 1700 cm⁻¹ which is expected to be very strong is not visible in the PM-IRRAS of the treated Phynox substrates. This could be explained either by the involvement of this moiety in the binding of the molecule to the surface (implying a shift of the band towards lower frequencies) or, as the molecule is bound to the surface, by the orientation of the C=O bond parallel to the surface. In this case, the dipolar moment variations would be cancelled by the creation of an image dipolar moment in the metallic substrate.

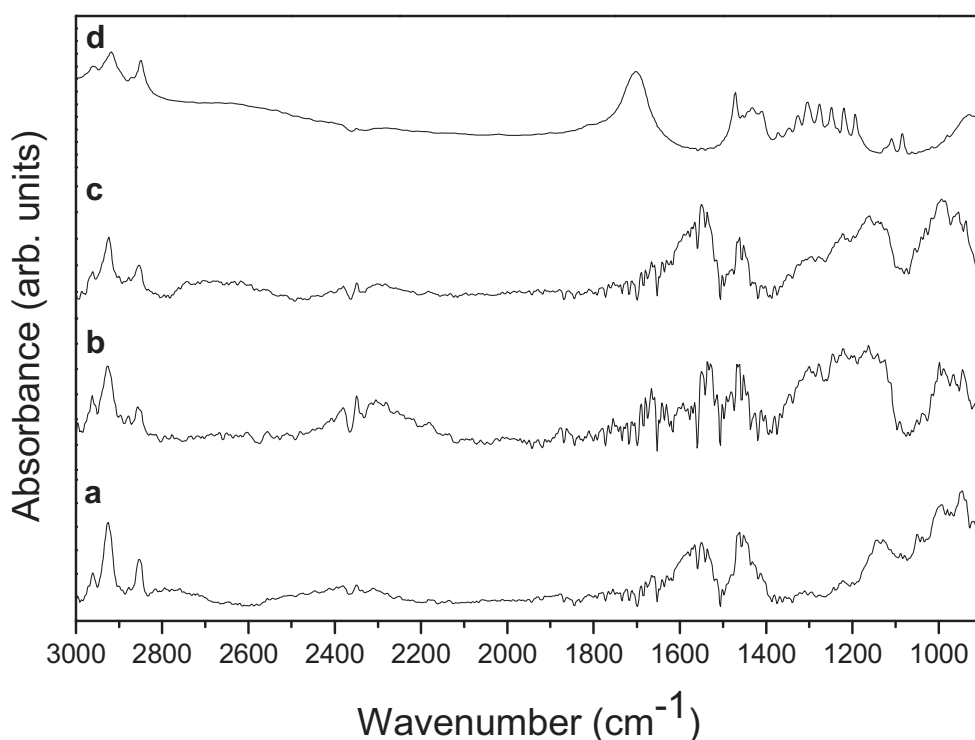


Figure 3.26. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 1h in a 1mM aqueous solution of *n*-dodecanoic acid at 85°C (a), with induction heating profile A (b), with induction heating profile B (c) and IR spectra of the *n*-dodecanoic acid dispersed in a KBr pellet (d).

The analysis of these monolayers by polarization curves has also been systematically carried out. The resulting curves and corresponding numerical values are presented in Figure 3.27 and Table 3.10, respectively. The corrosion current density does not seem to be significantly changed by the presence of the *n*-dodecanoic acid monolayer. However, the systematic repetition of the characterizations allowed us to deduce a trend from these results: corrosion current densities measured from a monolayer formed under induction heating are always higher than when the monolayer is formed under conventional heating conditions. The corrosion potential is not significantly changed by the presence of the *n*-dodecanoic acid monolayer.

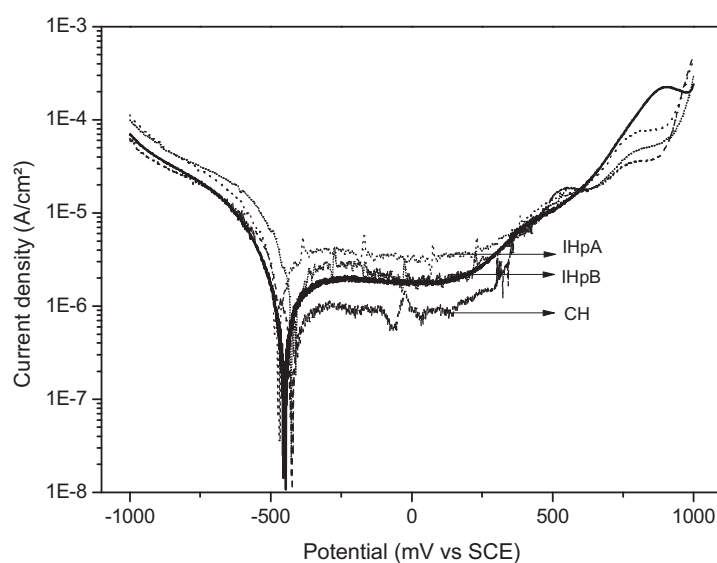


Figure 3.27. Polarization curves of a bare mechanically polished Phynox (thick plain line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of *n*-dodecanoic acid at 85°C (CH in dashed line), with induction heating profile A (IHpA in dotted line) and induction heating profile B (IHpB in short dotted line).

Table 3.10. Corrosion potentials and corrosion current densities measured for bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with *n*-dodecanoic acid for the different studied conditions.

	Corrosion potential (mV vs SCE)	Corrosion current density (A.cm ⁻²)
Bare Phynox	-454	4.9x10 ⁻⁶
Conventional heating (85°C)	-386	3.7x10 ⁻⁶
Induction heating (profile A)	-436	7.5x10 ⁻⁶
Induction heating (profile B)	-424	7.8x10 ⁻⁶

Regarding the results presented at this stage, it appears that the phosphonic acid function has a definitely greater affinity for the Phynox surface than the carboxylic acid function does, leading to a better and more stable monolayer, in line with the results presented by A. Raman *et al.*³³⁵. Moreover, it also appears that applying the induction heating profile B during de surface modification is favorable to the grafting of a phosphonic acid function while disadvantaging the grafting of a carboxylic function. Thus this induction heating profile seems adequate for the selective grafting of a more complex bifunctional molecule bearing both chemical functions via the phosphonic acid one, thereby leaving the carboxylic acid function free for future chemical reaction.

3.2.3.6. Grafting of bifunctional molecules

After studying individually the grafting of the phosphonic acid and carboxylic acid functions on Phynox surface, the grafting of two bifunctional molecules has been carried out: 11-phosphonoundecanoic acid and 6-phosphonohexanoic acid. Note that these two molecules have both a phosphonic and a carboxylic acid functions. The only difference is in the length of the alkyl chain between these two chemical functions.

The Phynox substrates were modified with these molecules considering two different temperature conditions: a conventional heating of the modification solution at 85°C and the application of the induction heating profile B during the modification.

These substrates were first characterized by cyclic voltammetry (the resulting voltammograms are presented in Figure 3.28). The modification of Phynox surface with the 6-phosphonohexanoic acid in a conventionally heated solution (85°C) leads to a coverage of 50 % while the coverage obtained in the same conditions with the 11-phosphonoundecanoic acid is around 72 %. When the surface modification is carried out with the induction heating profile B, the obtained coverages are 39 % and 72 % for the 6-phosphonohexanoic acid and the 11-phosphonoundecanoic acid, respectively.

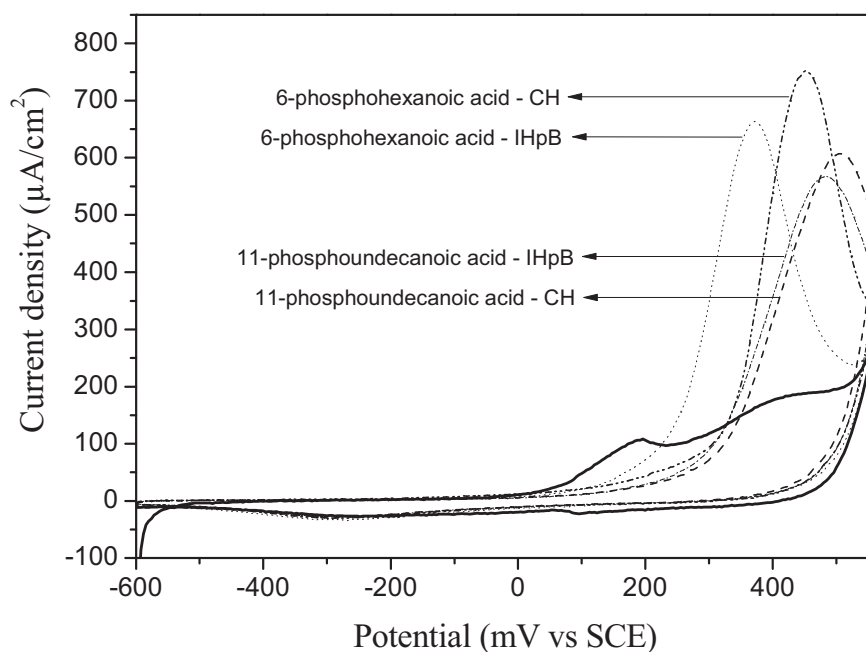


Figure 3.28. Voltammograms of a bare mechanically polished Phynox (thick plain line), modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of 11-phosphonoundecanoic acid at 85°C (11-phosphonoundecanoic acid – CH in dashed line), with induction heating profile B (11-phosphonoundecanoic acid – IHpB in dash dotted line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of 6-

phosphonohexanoic acid at 85°C (6-phosphonohexanoic acid – CH in dotted line) and with induction heating profile B (6-phosphonohexanoic acid – IHpB in dash dot dotted line).

In each case, a quick current density increase at high potentials characteristic of a degradation of the monolayer is observed like in the case of a *n*-dodecanoic acid monolayer. As this behavior was only observed in the case of a carboxylic acid function, it can reasonably be assumed that at least a certain proportion of the bifunctional molecules are bound to the Phynox surface via the -COOH function, even if the phosphonic acid function has a greater affinity for the substrate.

This degradation of the monolayer begins earlier for 6-phosphonohexanoic acid monolayers formed under induction heating profile B (around 225 mV vs. SCE) than for 6-phosphonohexanoic acid monolayers formed under conventional heating conditions (around 330 mV vs. SCE). Regarding the 11-phosphonoundecanoic acid monolayers, it appears that the heating method influences much less the degradation potential which is around 330 mV and 350 mV vs. SCE for a 11-phosphonoundecanoic acid monolayer grafted under induction heating and conventional heating conditions, respectively.

When the Phynox modification is carried out under induction heating conditions, the length of the alkyl chain of the grafted bifunctional molecules seems to have a significant impact on the stability of the resulting monolayer: the shorter the chain is the less stable is the monolayer. On the other hand, when the Phynox modification is carried out under conventional heating conditions, the length of this alkyl part seems to affect much less the stability of the resulting monolayer at high potentials.

These observations can be explained by the vigorous nature of the induction heating. Indeed, when the induction heating is applied to Phynox in aqueous solution, the water directly in contact with the surface quickly starts to boil. Moreover, even when induction heating is not applied (during the relaxation periods), temperature gradients exist in the modification bath leading to convection movements above the surface. Compared to conventional heating, induction heating leads thus to a much more energetic modification conditions disturbing the stabilization of the assembling monolayer by interchain Van der Waals interactions. On the other hand, from the results obtained with the 11-phosphonoundecanoic acid, it can be seen that when the grafted bifunctional molecule has a longer alkyl chain, the resulting monolayer is more stable at high potentials, even when induction heating is used. This confirms our hypothesis that induction heating disturbs the appearance of interchain Van der Waals interactions but also shows that this disadvantage can be thwarted by increasing the length of the hydrocarbonated part of the grafted molecule.

Contact angle measurements (Table 3.11) show that the modification of Phynox surface with these two bifunctional molecules in the different studied heating conditions lead to comparable hydrophobicities. Moreover, the modified surfaces are slightly more hydrophobic than the unmodified surface. This latter observation can be explained by the presence of a certain quantity of hydrophobic CH₂ groups at the extreme surface of the monolayer due to its weak organization while contact angle on unmodified substrates were measured just after a UV/O₃ treatment which is known to increase the amount of hydroxide groups on the surface (and thus its hydrophilicity).

Table 3.11. Contact angles of milli-Q water droplets deposited on bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with 6-phosphonohexanoic acid and 11-phosphonoundecanoic acid for the different studied heating conditions.

		Water contact angle (°)
	Bare Phynox	43
6-phosphonohexanoic acid	Conventional heating (85°C)	47
	Induction heating (profile B)	53
11-phosphonoundecanoic acid	Conventional heating (85°C)	51
	Induction heating (profile B)	54

PM-IRRAS spectra of these different monolayers are presented in Figure 3.29. In each of these spectra, the presence of an important bands overlapping in the 900-1800 cm⁻¹ region corresponding to the different vibration modes of the phosphonic and carboxylic moieties is clearly visible, confirming the grafting of the bifunctional molecules on the Phynox surface. Unfortunately, the absorption bands in this region are too poorly defined to clearly identify them and eventually determine the way the bifunctional molecules bind the surface.

The ν_{CH2asym} and ν_{CH2sym} bands can also be pointed out in the 2800-2900 cm⁻¹ region. Again, the signal/noise ratio is too low to allow any measurement of the position of these bands and thus any assessment of the monolayers organization.

Regarding the results presented at this stage about grafting of bifunctional molecules and knowing the ability of both carboxylic and phosphonic acid function to bind the Phynox surface, it can be reasonably deduced that a certain proportion of the grafted bifunctional molecules bind the Phynox surface via the carboxylic acid moiety, via the phosphonic acid moiety but also via both moieties at the same time. The 6-phosphonohexanoic acid and 11-phosphonoundecanoic acid monolayers are thus most probably complex systems in which a certain part of the grafted molecules bind the surface via the carboxylic function, another part bind the surface via the phosphonic function and even some molecules could be doubly bound. This complex configuration could explain the absence of the $\nu_{\text{C=O}}$ band at 1700 cm⁻¹ in the monolayer PM-IRRAS spectra (Figure 3.29). Indeed, because a certain proportion of the carboxylic acid functions are involved in the binding of the bifunctional molecules to the surface and also because of the very weak intensity of the spectra, the carbonyl function absorption band at 1700 cm⁻¹ is most likely present but too weak to be detectable.

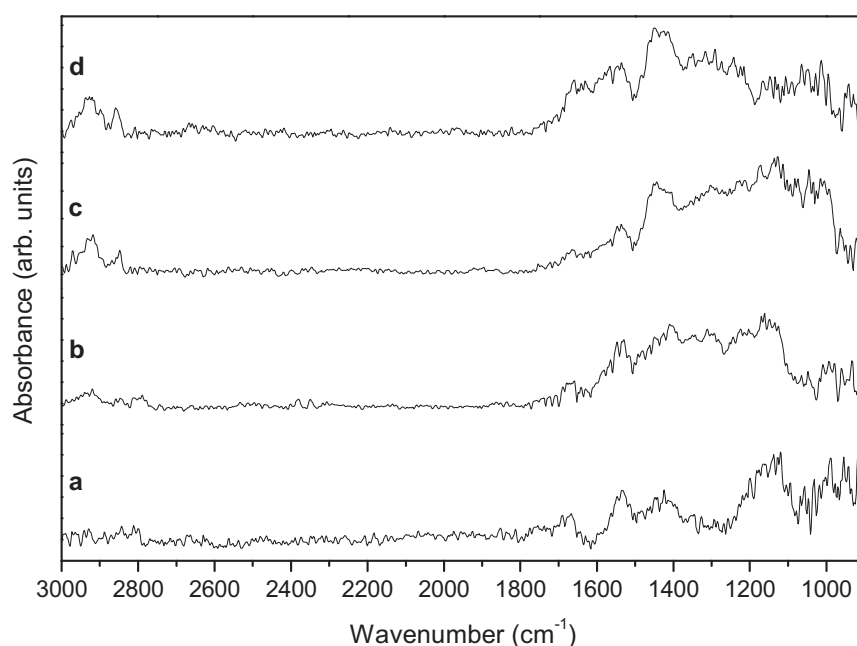


Figure 3.29. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 1 h in a 1 mM aqueous solution of 6-phosphonohexanoic acid at 85°C (a), with induction heating profile B (b) and Phynox modified by immersion 1 h in 1 mM aqueous solution of 11-phosphonoundecanoic acid at 85°C (c) and with induction heating profile B (d).

XPS characterization of these modified substrates has been carried out systematically. Again, the presence of the P2p core level photoelectrons peak can be pointed out on each modified substrate, confirming the presence of the grafted molecules on the Phynox surface (figure not shown). As previously, calculation of the P2p/Metals ratio allows us to compare the different grafting conditions in terms of “quantity” of grafted molecules. These calculated ratios are presented in Table 3.12. It clearly appears that the amount of phosphorus (and thus the amount of grafted molecules) is more important when the Phynox substrates are modified with the 11-phosphonoundecanoic acid. Furthermore, when the 6-phosphonohexanoic acid is grafted, the induction heating profile B seems to lead to a higher amount of grafted molecules than when the modification solution is conventionally heated at 85°C. This result is quite surprising, knowing that the grafting of the 6-phosphonohexanoic acid with induction heating profile B leads to the lowest coverage and the less stable monolayer (from CV results). On the contrary, the heating method does not seem to have a significant impact on the amount of grafted molecules when the 11-phosphonoundecanoic acid is used.

Table 3.12. P2p/Metals ratios calculated on basis of the XPS analysis of Phynox substrates modified with 6-phosphonohexanoic acid and 11-phosphonoundecanoic acid for the different studied conditions.

		P2p/Metals ratio
6-phosphonohexanoic acid	Conventional heating (85°C)	0.12
	Induction heating (profile B)	0.19
11-phosphonoundecanoic acid	Conventional heating (85°C)	0.32
	Induction heating (profile B)	0.31

Polarization curves experiments allow us to assess the impact of the formed monolayers on the corrosion resistance of Phynox. The resulting curves and corresponding numerical values are presented in Figure 3.30 and Table 3.13, respectively. For each of the studied monolayers, a decrease of the cathodic current density and a shift of the corrosion potential towards more cathodic values are observed. The corrosion current densities measured for modified Phynox substrates are slightly lower than for the bare Phynox substrates. Nevertheless, the difference is too low to be really significant. Grafting these bifunctional molecules on Phynox leads thus to a slight and mainly cathodic inhibition of the corrosion while the alkane phosphonic acid and alkane carboxylic acid monolayers led to a mixed inhibition of the corrosion. Furthermore, it appears clearly that the presence of these monolayers on Phynox lead to a considerable enlargement of the passivity domain (from about 650 mV before modification to about 1000 mV, after modification as shown in Figure 3.30). Even if the corrosion current density is not significantly decreased, the grafting of these bifunctional molecules increases to a certain degree the protection of Phynox against corrosion.

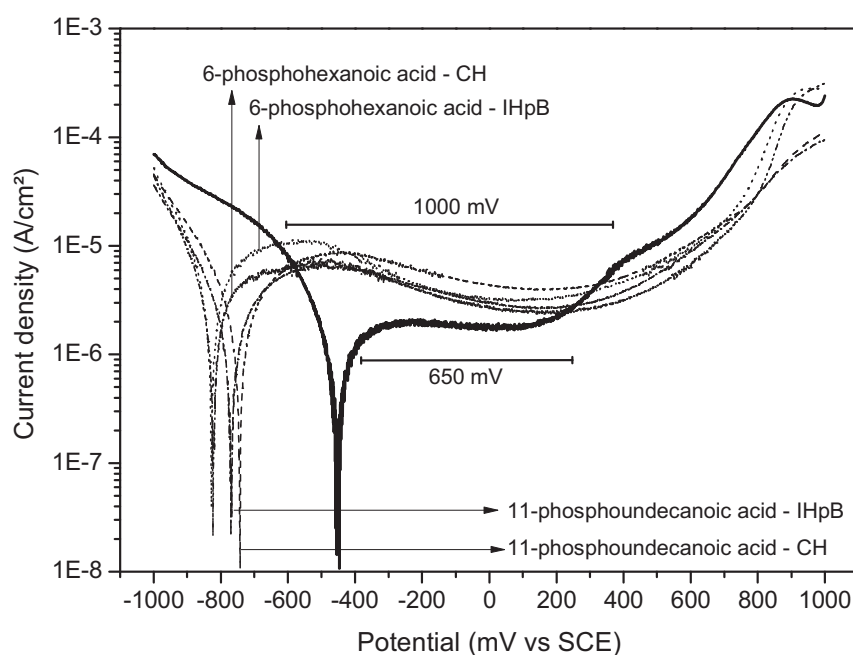


Figure 3.30. Polarization curves of a bare mechanically polished Phynox (thick plain line), modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of 11-phosphoundecanoic acid at 85°C (11-phosphoundecanoic acid – CH in dashed line), with induction heating profile B (11-phosphoundecanoic acid – IHpB in dash dotted line) and modified Phynox substrates by immersion 1 h in a 1 mM aqueous solution of 6-phosphohexanoic acid at 85°C (6-phosphohexanoic acid – CH in dotted line) and with induction heating profile B (6-phosphohexanoic acid – IHpB in dash dot dotted line).

Table 3.13. Corrosion potentials and corrosion current densities measured for bare Phynox substrates (pretreated with UV/O₃ for 30 min) and Phynox substrates modified with 6-phosphohexanoic acid and 11-phosphoundecanoic acid for the different studied conditions.

		Corrosion potential (mV vs. SCE)	Corrosion current density (A.cm ⁻²)
		- 467	5.2x10 ⁻⁶
6-phosphohexanoic acid	Bare Phynox		
	Conventional heating (85°C)	- 823	3.4x10 ⁻⁶
	Induction heating (profile B)	- 824	3.1x10 ⁻⁶
11-phosphoundecanoic acid	Conventional heating (85°C)	- 744	3.2x10 ⁻⁶
	Induction heating (profile B)	- 764	2.5x10 ⁻⁶

3.2.3.7. Grafting of alcohol on 6-phosphohexanoic acid modified Phynox susbtrates

The effect of induction heating being more pronounced when the 6-phosphohexanoic acid is used, the last step of this study has been carried out with this molecule. This last step aims

at exploiting the free carboxylic acid functions at the surface of 6-phosphonohexanoic acid modified Phynox substrates to graft alcohols via a Steglich esterification reaction. The Steglich esterification reaction has been carried out using the same experimental protocol as the one described in section 3.2.1.

This experimental protocol was used to graft a fluorinated alcohol ($\text{HO-CH}_2\text{-(CF}_2\text{)}_8\text{-CF}_3$ called CF) on two different 6-phosphonohexanoic acid monolayers: a first one formed with a conventional heating of the modification solution at 85°C and a second one formed under induction heating profile B. The obtained system is called and P-C-CF (after CF grafting). XPS analysis of this system has been systematically carried out as well as PM-IRRAS analysis aiming to confirm the ester function formation. Representative PM-IRRAS spectra are presented in Figure 3.31. After the CF grafting on both 6-phosphonohexanoic monolayers (formed under conventional or induction heating), strong absorption bands appear at 1265 and 1104 cm^{-1} characteristic of the asymmetric and symmetric stretching mode of the ester function, respectively. The presence of these absorption bands indicates that the CF alcohol molecules are successfully chemisorbed on the 6-phosphonohexanoic acid monolayer via the formation of an ester function and not only physisorbed on the surface.

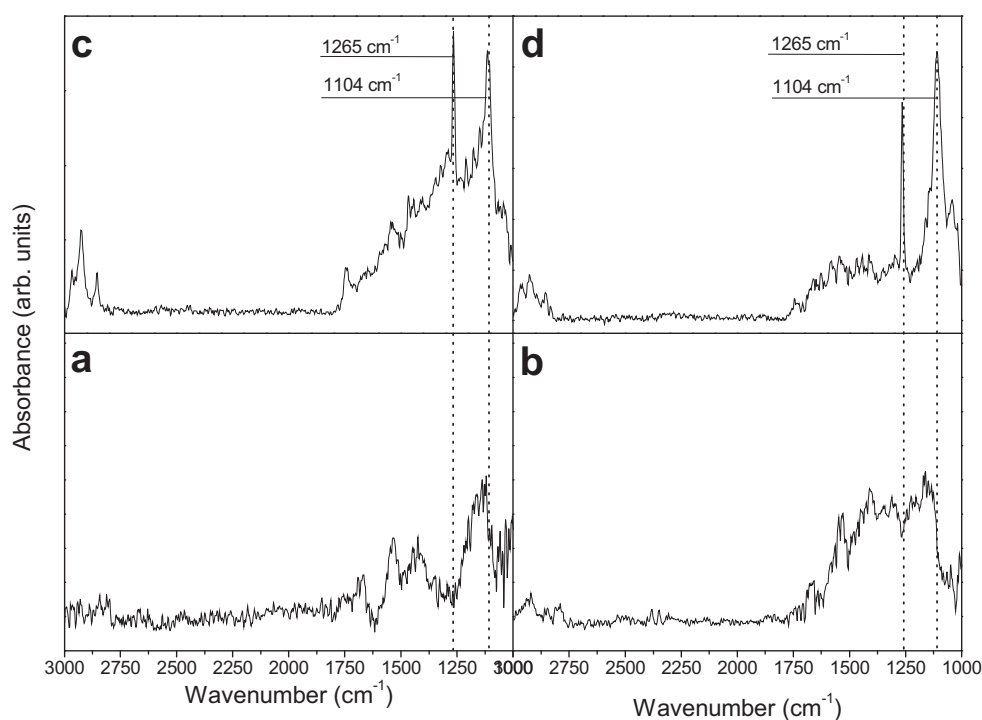


Figure 3.31. PM-IRRAS spectra of a mechanically polished Phynox modified by immersion 1 h in a 1 mM aqueous solution of 6-phosphonohexanoic acid at 85°C (a and c), with induction heating profile B (b and d) before (a and b) and after (c and d) the CF grafting via a Steglich esterification reaction.

Regarding the XPS analysis, as there are 19 fluorine atoms in each grafted alcohol and one phosphorus atom for each initially grafted bifunctional molecule, the normalized area under the F1s photoelectrons peak has been divided by 19 (the resulting value being noted “F”) and the F/P ratio has been calculated (where “P” is the normalized area under the P2p photoelectrons peaks). These ratios, indicative of the “yield” of the Steglich esterification reaction, are presented in Table 3.14. Note that if each molecule of the initial monolayer was implied in the esterification reaction with CF, the value of this ratio would be close to 1. It clearly appears that the F/P value is twice larger when the initial monolayer was formed under induction heating profile B. This result indicates a preferential grafting of the phosphonic acid moiety when the modification is carried out under induction heating profile B than with a conventional heating of the solution at 85°C. Moreover, the “yield” of esterification is quite low (at most around 36%). This can be explained not only by the ability of carboxylic acid functions to bind the substrate (rendering them useless regarding the esterification reaction) but also by the steric hindrance induced by the presence of the first grafted CF alcohols, probably preventing the alcohols to reach the surface after a few minutes of reaction. Nevertheless, it has been shown that using a suitable induction heating profile during the initial monolayer formation can lead to a much more selective adsorption of the phosphonic acid function (at least when the grafted bifunctional molecule is short enough), leaving a higher amount of free carboxylic acid functions for post-chemistry on the resulting monolayer.

Table 3.14. Normalized fluorine/phosphorus ratios after CF grafting on 6-phosphonohexanoic acid monolayers formed in the different studied conditions (theoretical F/P ratio = 1).

	F/P ratio
Conventional heating (85°C)	0.15
Induction heating (profile B)	0.36

3.2.3.8. Conclusions

The effect of induction heating on the grafting of the 6-phosphonohexanoic acid and the 11-phosphonoundecanoic acid on Phynox surface has been studied. Such bifunctional molecules can be successfully used to functionalize the surface with the perspective of post-grafting biocompatible chemical functions via a Steglich esterification reaction involving the carboxylic acid function. Therefore, it is of great interest to keep this function free at the top of the formed monolayer while functionalizations of Phynox with *n*-dodecanephosphonic acid and *n*-dodecanoic acid indicate that the carboxylic function competes to a certain extent with the grafting of the phosphonic group on the Phynox surfaces.

In order to understand the possible competition between the two different end groups of the 6-phosphonohexanoic acid and the 11-phosphonoundecanoic acid (phosphonic acid and carboxylic acid functions) with the Phynox surfaces, the grafting of the *n*-dodecylphosphonic acid and *n*-dodecanoic acid on this substrate and the influence of the heating method on the resulting monolayer has been studied separately. The conclusions of this preliminary study is that, even if carboxylic acid function is able to bind the substrate, phosphonic acid function

has a greater affinity for the Phynox substrate as *n*-dodecylphosphonic acid grafting leads to a more stable monolayer and a higher coverage than the *n*-dodecanoic acid grafting. Furthermore, it has been shown that induction heating can lead to similar results than a conventional heating method regarding the grafting of phosphonic acid functions while the same induction heating profile lead to a lower grafting of carboxylic acid functions.

The 6-phosphonohexanoic acid and the 11-phosphonoundecanoic acid mainly bind the substrate via the phosphonic acid function, leaving a sufficient number of carboxylic functions available for a second step of functionalization. It has also been shown by studying the impact of the heating method on the grafting of the two bifunctional molecules on Phynox that the differences in the resulting monolayer are much more important when the alkyl chain separating the two end functions is shorter.

Even if it was possible to graft an alcohol molecule to the free carboxylic functions via an esterification reaction, only a limited proportion of the 6-phosphonohexanoic acid on the surface of Phynox was involved in this reaction. Nevertheless, the amount of grafted alcohols is much more important when the 6-phosphonohexanoic acid monolayer was initially grafted under induction heating conditions. This confirmed the hypothesis that induction heating can lead to a much more selective adsorption of bifunctional molecules on the surface of Phynox, leaving a higher amount of free carboxylic acid functions to react during the second modification step.

3.2.4. Grafting of the 11-phosphonoundecanoic acid on Phynox: study of the impact of ethylene oxide sterilization process

3.2.4.1. Introduction

We have seen in the previous sections that the 11-phosphonoundecanoic acid can be successfully used to form a monolayer on Phynox surface. The free carboxylic acid functions exhibited at the surface of the formed monolayer were then exploited as anchoring group for the grafting of small PEG oligomers via a Steglich esterification reaction. However, regardless the surface treatment applied to the material, the very last treatment applied to any biomaterial is sterilization. Ethylene oxide sterilization process being one of the most used ones in the field of stenting, we asked ourselves two questions. The first one is quite evident: can the formed monolayer resist this sterilization treatment? The second one is based on the fact that ethylene oxide is actually the monomer of PEG. Therefore, it would be of great interest if the sterilization process could lead to the formation of a PEG layer on the sterilized surfaces. Thus the second question to answer is “does the presence of free carboxylic functions at the surface of Phynox lead to the PEG polymerization during the ethylene oxide sterilization process?”

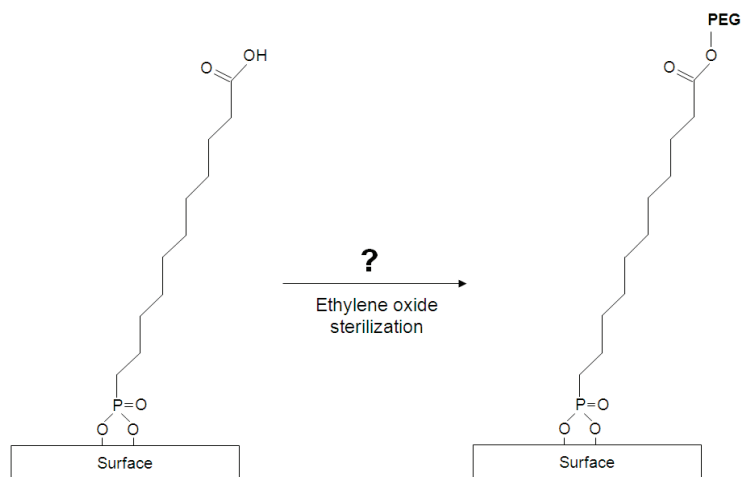


Figure 3.32. Schematic of the Phynox surface modification methodology used in this work.

3.2.4.2. Samples preparation

The Phynox substrates were mechanically polished as described previously (see section 3.2.1). These samples were then submitted to a heat treatment for 3 hours at 550°C and allowed to cool down at air. Just before modification, the substrates were cleaned again by sonication 15 minutes in ethanol and underwent a UV/O₃ treatment of 30 minutes. The monolayers were then formed by immersing the samples in 1 mM 11-phosphonoundecanoic acid aqueous solutions for 1 hour at 100°C. They were then rinsed copiously with ethanol, cleaned by sonication 15 min in the same solvent, blown dry under a nitrogen flow and conditioned for the ethylene oxide sterilization process.

3.2.4.3. Results

The ATR analysis of the modified Phynox substrates has been systematically carried out before and after their sterilization (see Figure 3.33). The presence of the absorption bands of the CH₂ groups (around 2854 and 2922 cm⁻¹) in both situations is indicative of the preservation of the initial monolayer during the sterilization process. However, there is no sign of the appearance of absorption bands at 1264 and 1110 cm⁻¹ characteristic of the ester function that would have appeared if the ethylene oxide had polymerized on the top of the monolayer. Note that the water contact angles do not change significantly with the sterilization treatment (i.e. 60° and 59° before and after the sterilization, respectively), confirming these observations.

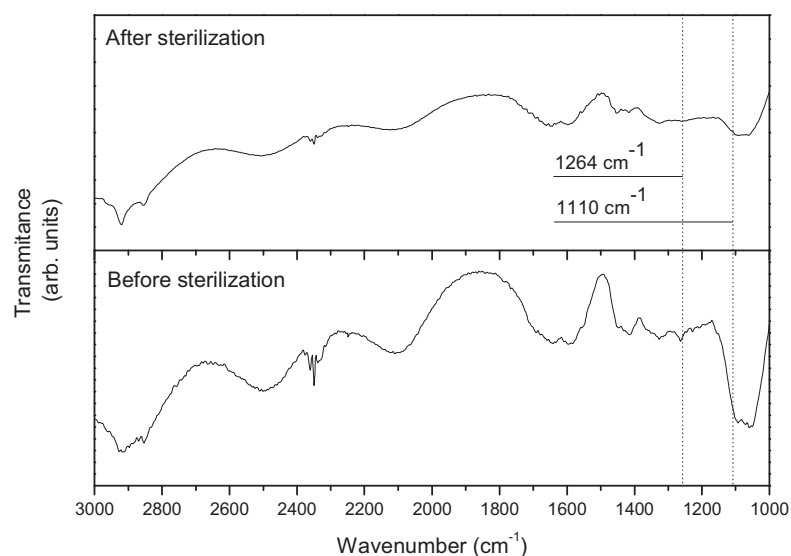


Figure 3.33. ATR spectra of a mechanically polished Phynox modified by immersion 1h in a 1mM 11-phosphonoundecanoic acid aqueous solution at 100°C before (lower part) and after (upper part) the ethylene oxide sterilization process.

XPS analysis of the samples has also been carried out systematically before and after sterilization. The detailed examination of the C1s core level photoelectron region does not reveal any difference between the two situations. This confirms that no PEG was formed during the sterilization process. The calculation of the ratio of the normalized P2p peak area on the sum of the normalized areas of the metal peaks (called P/TotMet and presented in Table 3.15) indicates that the amount of phosphorus on the surface remains the same after the sterilization treatment and therefore allows us to confirm the 11-phosphonoundecanoic acid monolayer resistance to this treatment.

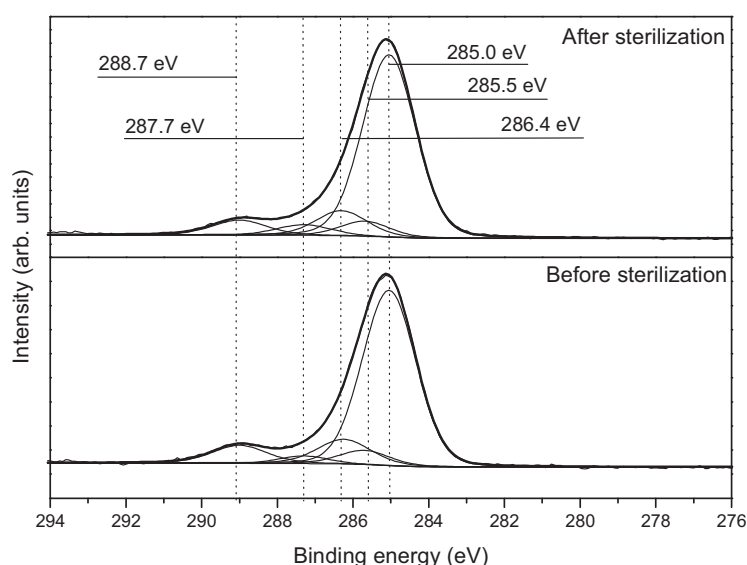


Figure 3.34. XPS C1s core level photoelectron spectra of a mechanically polished Phynox modified by immersion 1 h in a 1 mM 11-phosphonoundecanoic acid aqueous solution at 100°C before (lower part) and after (upper part) the ethylene oxide sterilization process.

Table x.15. P2p/Metals ratios calculated on basis of the XPS analysis of Phynox substrates modified by immersion 1 h in a 1 mM 11-phosphonoundecanoic acid aqueous solution at 100°C before (lower part) and after (upper part) the ethylene oxide sterilization process.

	P/Metals ratio
Reference	0
Before sterilization	0,2
After sterilization	0,2

3.2.4.4. Conclusions

In order to determine the impact of the ethylene oxide sterilization process on 11-phosphonoundecanoic acid monolayer (and more generally on phosphonic acid monolayers) grafted on Phynox surface, modified Phynox substrates were submitted to the sterilization protocol validated for Cardiatis (and actually applied to stents before implantation). From this quick study, it appeared that the phosphonic acid monolayers perfectly resist the sterilization treatment. However, no polyethylene glycol formation from the free carboxylic acid functions present on the top of the 11-phosphonoundecanoic acid monolayer could be pointed out.

Part II

Study of the MRI artifacts induced by Nitinol
and Phynox

Chapter 4. VISMAT - Influence of the surface treatment of Phynox and Nitinol on the MRI artifacts

During this thesis, several ways have been explored to improve Nitinol and Phynox stents properties in terms of corrosion resistance and biocompatibility. However, after stent deployment, surgeons need to assess the efficiency of the intervention. Biomedical imaging is used in this context to follow the evolution of the treated artery segment in order to detect in-stent restenosis or stent displacements. Nowadays, X-ray angiography is the most commonly used imaging technique for post-stenting patient monitoring. However, this technique has the main inconvenient to repetitively submit the patient to relatively high X-ray doses. There is thus an increasing interest in MRI monitoring because it allows noninvasive determination of coronary blood flow velocities after stent deployment (similar to Doppler flow measurements) and can be used to detect in-stent restenosis to some extent while being completely harmless for the patient³⁸⁵. However, it is well known that the presence of stents induces the appearance of artifacts and signal loss on the acquired MRI images³⁸⁶⁻³⁹⁰. There is thus a great interest in having a better understanding of these artifacts and in decreasing them as much as possible to improve the efficiency and the medical relevance of MRI stent imaging. In this chapter, we report on the assessment of the artifacts caused by several types of Nitinol and Phynox wires and stents after a brief introduction part describing the basic principles of MRI and the origin of the main artifacts.

4.1. Basic principles of MRI³⁹¹

Magnetic Resonance Imaging technique is based on the nuclear magnetic resonance phenomenon (NMR) and particularly on the water protons NMR. Note that the following explanation of the technique is obviously simplified as it aims to present only the principles required to understand this study.

4.1.1. Resonance phenomenon

The hydrogen atom nucleus is constituted of only one proton having a spin property that can be considered schematically as the fact that it can turn on himself. This confers to the proton an angular momentum on one hand and, given its nonzero electrical charge, a magnetic dipole moment (μ) on the other hand. These two factors are related to each other via a constant γ called the gyromagnetic ratio (different for each atomic nucleus).

When placed into a magnetic field B_0 , this nuclear magnetic dipole moment will align itself along the field direction and precess around B_0 with an angular frequency ω_0 described by the Larmor's equation (4.1) according to the equation of motion (4.2).

$$\omega_0 = \gamma B_0 \quad (4.1)$$

$$\frac{d\vec{\mu}}{dt} = \gamma \cdot \vec{\mu} \times \vec{B}_0 \quad (4.2)$$

Given a B_0 magnetic field applied along the z axis, if we place ourselves in a (x', y', z) reference frame rotating at ω_0 around B_0 (in which the spin is immobile) and apply a B_1 magnetic field along the x' direction, the magnetic dipole moment will precess around this B_1 magnetic field according to Larmor's equation. This is the resonance phenomenon: when a B_1 magnetic field rotating at the precession frequency of the spins is applied, these spins will enter into resonance. Practically, this is done with a coil (RF transmitter) in which a controlled and time-variable current flows. The spins leave then their equilibrium alignment along B_0 direction. If B_1 is applied during a very short and controlled time τ , the flip angle of the spins can be controlled as described by the equation (4.3).

$$\theta = \gamma B_1 \tau \quad (4.3)$$

As soon as B_1 is not applied anymore, the spins return to their equilibrium position along B_0 according to different relaxation phenomena that will be described here under.

If we consider a small volume of a material (V) placed into a B_0 magnetic field, the sum of all spins in precession around the B_0 direction with the same angular frequency will result in the appearance of nonzero magnetization M along B_0 according to equation (4.4).

$$\vec{M} = \frac{1}{V} \sum_{volume} \vec{\mu}_i \quad (4.4)$$

The equation of motion (4.2) can thus be expressed as follows:

$$\frac{d\vec{M}}{dt} = \gamma \cdot \vec{M} \times \vec{B}_0 \quad (4.5)$$

Given an external magnetic field B_0 along the z axis of a motionless reference frame, when all the spins are at their equilibrium position, the resulting magnetization M_0 has only one component parallel to the z axis. When these spins enter into resonance, the resulting magnetization M will be tipped away from the z axis. Therefore, M components in the two other directions of space become nonzero. The magnetization vector can thus be decomposed into a parallel (M_z) and a perpendicular ($M_{\perp} = M_x \hat{x} + M_y \hat{y}$ where $\hat{x}$ and $\hat{y}$ are unitary vectors) component.

Note that as the signal acquisition is carried out with the same RF coil used to produce the B_1 rotating magnetic field (thus in the xy plane), only the perpendicular component of the magnetization vector can be detected.

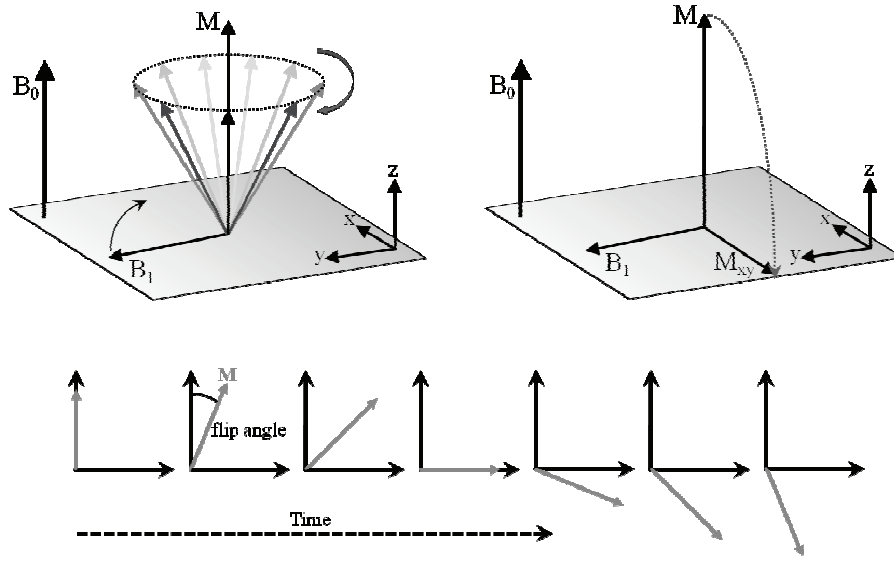


Figure 4.1. Schematic representation of the spins in precession around the external magnetic field B_0 , of the resulting magnetization vector M and of the flip of this vector due to the application of a rotating B_1 magnetic field, the flip angle being proportional to the B_1 application time.

4.1.2. Relaxation phenomena

When the rotating magnetic field B_1 is not applied anymore, the spins flipped from their equilibrium position along the B_0 direction will tend to return to this position. This phenomenon is called relaxation. They are actually two main relaxation phenomena (longitudinal and transverse relaxation), each of them being characterized by a time constant. The value of these constants is mainly related to the type of tissue which is observed.

The longitudinal relaxation, characterized by the time constant T_1 ('spin-lattice relaxation time'), is due to the thermal interactions between the spins and their atomic neighborhood and describe the regrowth of the longitudinal component of the magnetization M according to equation (4.6).

$$\frac{dM_z}{dt} = (M_0 - M_z) \frac{1}{T_1} \quad (4.6)$$

and thus

$$M_z(t) = M_z(0)e^{-t/T_1} + M_0(1 - e^{-t/T_1}) \quad (4.7)$$

where M_0 is the equilibrium magnetization.

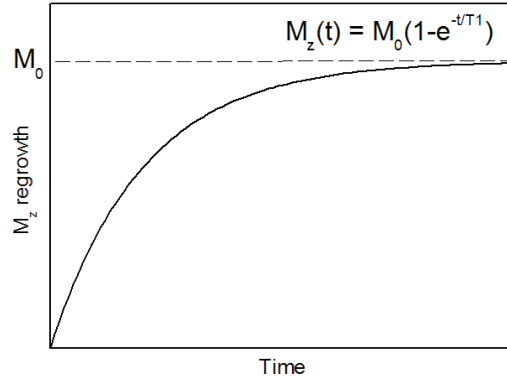


Figure 4.2. Regrowth of the longitudinal component of the magnetization vector M after a flip of 90° ($M_z(0)=0$). After a long relaxation time, the longitudinal component reaches a plateau at the equilibrium value M_0 .

The transverse relaxation, characterized by the time constant T_2 ('spin-spin relaxation time'), is due to the dephasing of the spins contained in a voxel (small volume element) due to the local precession frequencies variations and describe the disappearance of the transversal component of the magnetization M . Note that T_2 is often replaced by T_2^* (smaller than T_2) in order to consider a supplementary decrease of the transverse component of M due to the spins dephasing caused by local B_0 inhomogeneities.

The variation of the transverse component of M with time can be described according to equation (4.8) in a motionless reference frame and according to equation (4.9) in a reference frame rotating at the precession frequency of the spins.

$$\frac{d\vec{M}_\perp}{dt} = \gamma \vec{M}_\perp \times \vec{B}_0 - \frac{1}{T_2} \vec{M}_\perp \quad (4.8)$$

$$\left(\frac{d\vec{M}_\perp}{dt} \right)' = -\frac{1}{T_2} \vec{M}_\perp \quad (4.9)$$

and thus

$$\vec{M}_\perp(t) = \vec{M}_\perp(0)e^{-t/T_2} \quad (4.10)$$

Note that T_2 takes into account the effect of 'spin-spin' and the 'spin-lattice' interactions. As a consequence, the transverse relaxation rate is higher than the longitudinal one ($T_2 < T_1$).

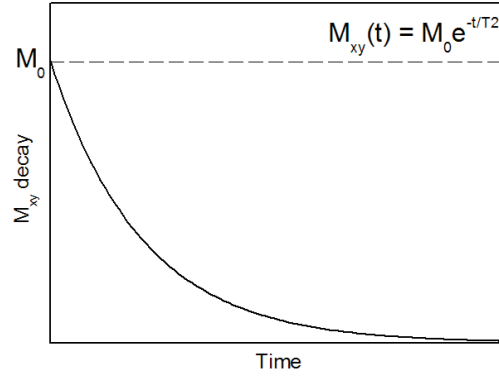


Figure 4.3. Decay of the transverse component of the magnetization vector M after a flip of 90° (the initial transverse component being equal to M_0). After a long relaxation time, the transverse component tends to zero.

The spins phase difference due to the B_0 inhomogeneities is characterized by a time constant T_2' . The actually observed T_2^* time constant is therefore a combination of T_2 and T_2' (equation (4.11)).

$$1/T_2^* = 1/T_2 + 1/T_2' \quad (4.11)$$

Note that the term $1/T_2$ takes into account the spins dephasing due to local and random variation of the magnetic field (and thus non reversible) while the term $1/T_2'$ describes the spins phase difference due to the static external magnetic field B_0 inhomogeneities. These inhomogeneities being constant, this dephasing is reversible.

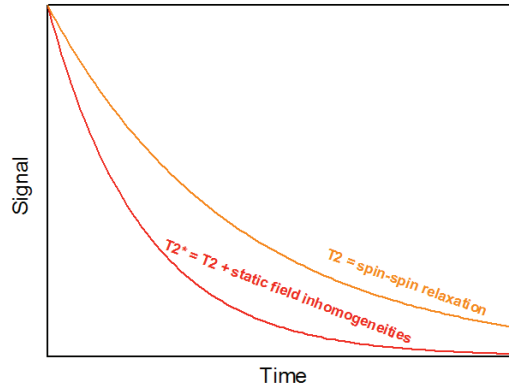


Figure 4.4. Evolution of the transverse component of the magnetization vector M in an ideal situation (upper curve) and in a realistic situation taking into account the external magnetic field B_0 inhomogeneities (lower curve).

The combination of the precession, the longitudinal and the transverse relaxation (equations (4.5), (4.6) and (4.8)) leads to the expression of the Bloch's equation:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B}_0 + \frac{1}{T_1} (M_0 - M_z) \hat{z} - \frac{1}{T_2} \vec{M}_\perp \quad (4.12)$$

Considering B_0 in the z axis direction, this equation can be decomposed as follows:

$$\frac{dM_z}{dt} = \frac{M_0 - M_z}{T1} \quad (4.13)$$

$$\frac{dM_x}{dt} = \omega_0 M_y - \frac{M_x}{T2} \quad (4.14)$$

$$\frac{dM_y}{dt} = \omega_0 M_x - \frac{M_y}{T2} \quad (4.15)$$

If we replace $M_x = m_x e^{-t/T2}$, $M_y = m_y e^{-t/T2}$ and integrate these equations, we obtain the equations describing the evolution of the three components of the magnetization vector M with time:

$$M_z(t) = M_z(0)e^{-t/T1} + M_0(1 - e^{-t/T1}) \quad (4.16)$$

$$M_x(t) = e^{-t/T2} (M_x(0)\cos(\omega_0 t) + M_y(0)\sin(\omega_0 t)) \quad (4.17)$$

$$M_y(t) = e^{-t/T2} (M_y(0)\cos(\omega_0 t) - M_x(0)\sin(\omega_0 t)) \quad (4.18)$$

It clearly appears that when t increases, the transversal components M_x and M_y tend to zero while the longitudinal component M_z tends to M_0 which is the equilibrium value.

The precessing spins phase can be described according to equation (4.19).

$$\Phi(\vec{r}, t) = -\omega(\vec{r})t + \phi_0(\vec{r}) = -\gamma B_z(\vec{r})t + \phi_0(\vec{r}) \quad (4.19)$$

where the vector $\vec{r}$ is the position vector.

Note that $\Phi_0(\vec{r})$ can be fixed to zero by choosing properly the direction of the RF field (and thus the direction of the magnetic field B_1 in the rotating referential).

4.1.3. MRI image acquisition principles

The aim of MRI is to decompose the NMR signal of water protons into signals from small volume elements (called voxels) and to relocate these signals into space. Thus the intensity of each voxel corresponds to the intensity of a pixel in the resulting image.

In a homogeneous magnetic field B_0 , all the water protons have the same resonance frequency as this frequency only depends on the intensity of the applied magnetic field (according to Larmor's equation). If we overlay a magnetic field gradient to this initial B_0 field in only one direction (the z direction for example), the protons will enter into resonance at different frequencies as a function of their position along the z axis according to equation (4.20).

$$\omega(z) = \gamma B(z) = \gamma B_0 + \gamma G_z z \quad (4.20)$$

where G_z is the intensity of the applied gradient.

In these conditions, it is possible to induce the resonance phenomenon in a “slice” of an imaged body by applying a rotating B_1 magnetic field at the proper frequency. The gradient G_z is thus called “slice selection gradient”. A slice with a thickness Δz can thus be selected by applying a rotating magnetic field B_1 such as:

$$\Delta\omega = \gamma G_z \Delta z \quad (4.21)$$

Note that slices can be selected in every desired direction by combination of different gradients in the three directions of space.

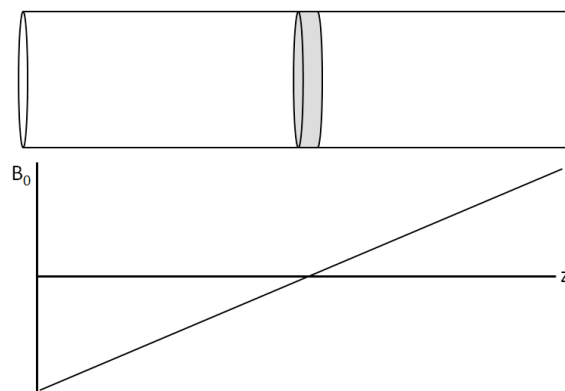


Figure 4.5. Schematic representation of the selection of a slice in a sample (upper part) and the corresponding applied slice selection gradient (lower part).

In order to obtain an MRI image, it is necessary to encode the signal from the selected slice into the two other directions (x and y in our example). This encoding is carried out by the successive application of gradients in these two directions before the spins of the selected slice return to their equilibrium position.

The first of these two gradient, called “phase encoding gradient” (which we will consider along the y axis) aims to induce a phase shift of the precessing spins along the gradient direction. This allows determining the origin of the signal along this direction according to the phase of the signal. Note that it is necessary to make as many acquisitions (with different phase encoding gradients) as the number of points along the encoded direction. The acquisition sequence has thus to be repeated several times in order to obtain an image. The repetition time of a sequence (thus the time between two excitations of the selected slice) is called TR.

The second gradient, called “readout gradient” or “frequency encoding gradient” (which is along the x axis in our example) is applied during the signal acquisition itself. As a consequence, the measured precession frequency depends on the position of the spins along the x axis. This allows determining the origin of the signal along this direction according to the frequency of the signal.

This intensity of the applied magnetic field gradients is about 10 mT/m. This intensity of these gradients is actually ruled by three imaging parameters: the field of view (FOV expressed in mm), the size of the image matrix (MS expressed in number of pixels) and the bandwidth (BW expressed in Hz/pixel) such as:

$$\text{Gradient intensity} = 2\pi \frac{BW \cdot MS}{FOV \cdot \gamma} \quad (4.22)$$

The total signal is processed by two dimensional Fourier transform.

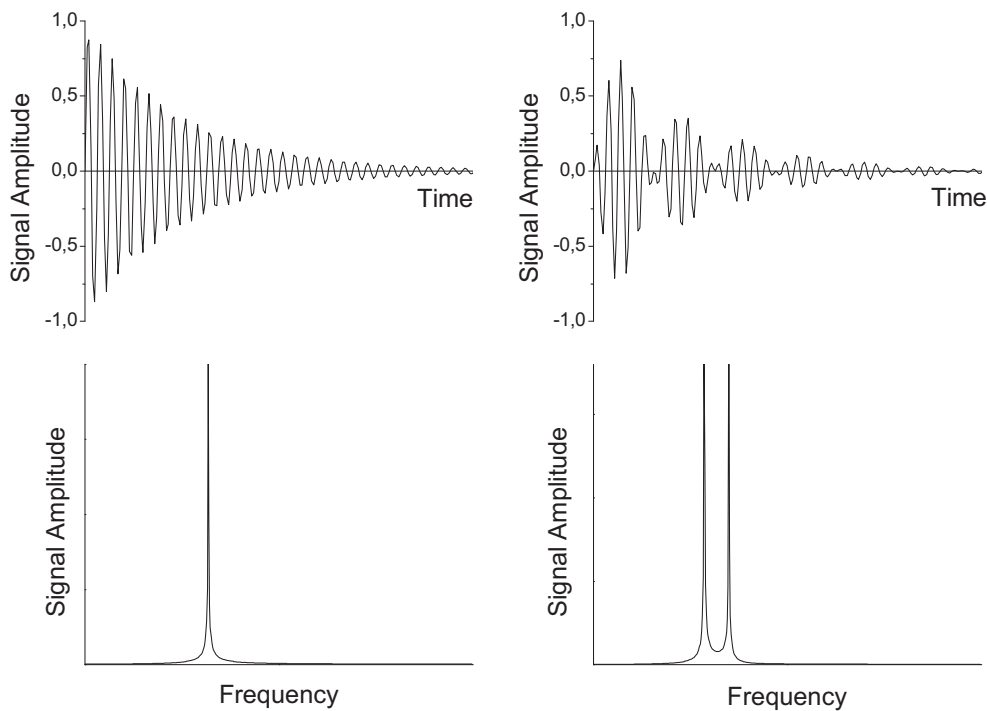


Figure 4.6. Upper part: free precession spins signal without (left) and with (right) frequency encoding allowing to relocate the origin of the signal along the encoding direction. Lower part: corresponding signal after its Fourier transform.

4.1.4. Main types of imaging sequences

The signal of water protons contained in the imaged the object or body can be acquired in many different ways. However, most of the imaging sequences are based on two basis sequences that are the spin echo sequences (SE) and the gradient echo sequences (GRE).

Spin echo sequences involve two RF pulses (thus two successive applications of a rotating magnetic field B_1). The first of these two pulses aim to bring into resonance the spins of a slice of the sample. As explained before, the flip angle of the spins is proportional to the intensity of the rotating magnetic field but also to the application time of this rotating magnetic field. Usually, the first pulse flips the spins by 90° i.e. in the plane perpendicular to

the static magnetic field B_0 . As soon as the first pulse stops, the spins are in free precession and are thus submitted to relaxation phenomena. The signal that would be measured at that moment decays proportionally to $e^{-t/T2^*}$. However, we have seen that the signal decay due to the B_0 inhomogeneities is reversible. If a second RF pulse of 180° and perpendicular to the first one is applied after a time τ , the spins which had previously accumulated extra positive phase now have the negative of that phase and vice versa. After a time 2τ called echo time (TE), all the spins will be realigned. This induces an increase of the signal intensity called spin echo. This echo is the actually measured signal in SE sequences. These sequences have the main advantage to get rid of the B_0 inhomogeneities.

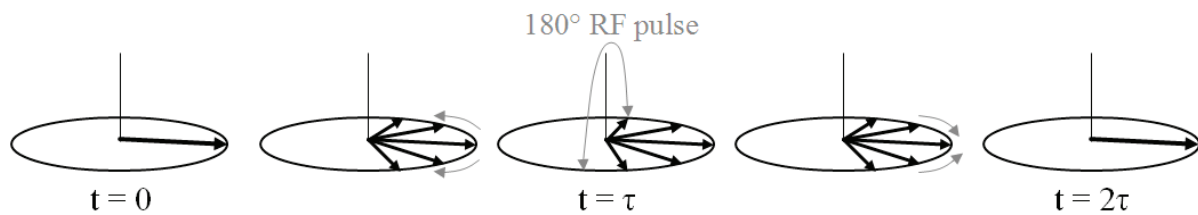


Figure 4.7. Schematic representation of the dephasing spins in free precession and of their rephasing with a 180° RF pulse.

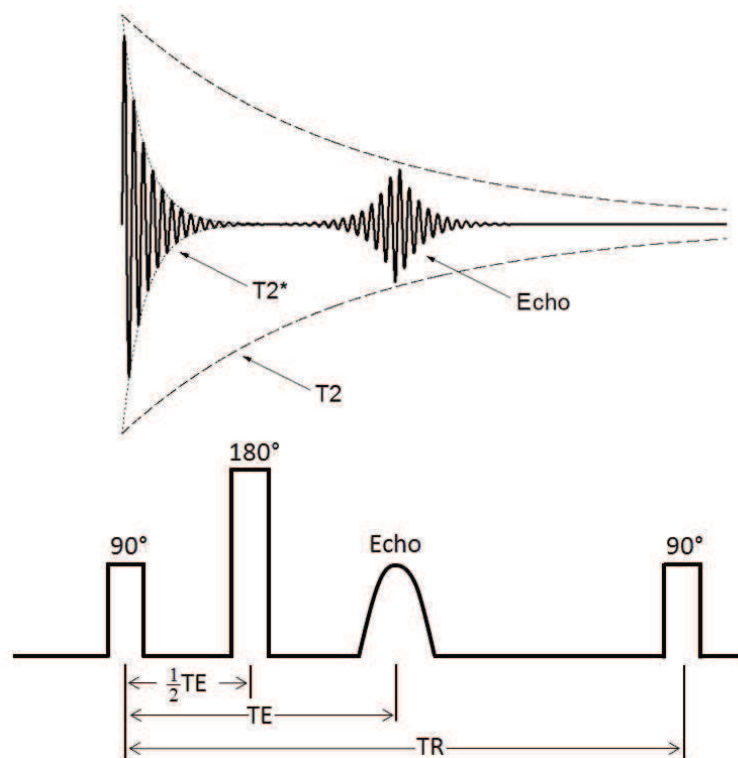


Figure 4.8. Diagram of a basic SE sequence. Upper part: schematic representation of the obtained signal. Note that the envelope of the actually measured signal is proportional to $T2^*$ but that the curve proportional to $T2$ can be recovered by measuring several echoes at different times. Lower part: Schematic representation of the different parts of the sequence i.e. an excitation RF pulse (90°), a rephasing RF pulse (180°) and the consecutive echo. The time between two repetitions of the sequence is called “repetition time” (TR).

Gradient echo sequences (GRE) involve only one RF pulse to bring into resonance the spins of a slice of the sample. Once again, the signal actually measured is an echo but in this case, the echo is produced differently than in SE sequences. After the excitation of a slice of the sample and the phase encoding of this slice in one of the two directions of the imaged plane, a magnetic field gradient is applied in the second direction of this plane during a time t inducing a dephasing of the spins in this direction. The polarity of this gradient is then inverted. This leads to the rephasing of the spins. An echo will thus appear a time t after the inversion of the gradient polarity. Contrary to SE sequences, GRE sequences do not cancel the spins dephasing due to B_0 inhomogeneities but allow obtaining images much faster than SE sequences.

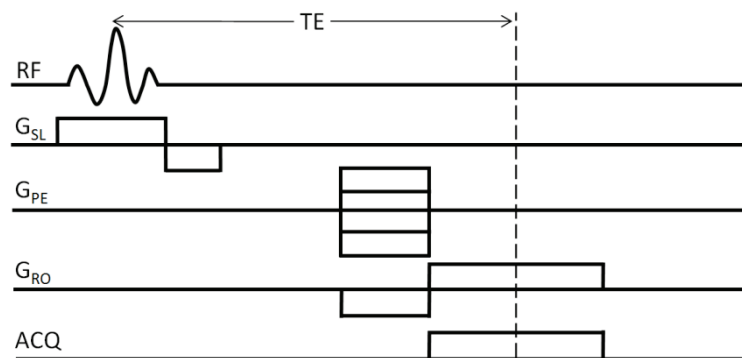


Figure 4.9. Diagram of a basic GRE sequence. The RF pulse is applied along with the slice selection gradient (G_{SL}). Note that the inversion of the G_{SL} after the slice selection aims to cancel the spins dephasing induced by this first gradient. G_{PE} is the phase encoding gradient. G_{RO} represent the readout gradient (frequency encoding gradient) which also aims to induce the echo in the frame of a GRE sequence. ACQ represent the time interval in which the signal is acquired.

4.1.5. Contrast mechanisms

According to Bloch's equation, the acquired signal intensity can be expressed as:

$$S \sim \rho (1 - e^{-t/T1}) e^{-t/T2^*} \quad (4.23)$$

where ρ is the proton density.

We have seen previously that a sequence has to be repeated several times in order to obtain an image. The time between two repetitions (and thus the time between two excitations of the imaged slice) is called repetition time (TR). We have also pointed out that the values of the time constants $T1$ and $T2$ are mainly dependent of the nature of the imaged tissue.

On Figure 4.10 we can see that for the same TR, the regrowth of the longitudinal component of the magnetization vector (M_z) is different for tissues with different $T1$. After the excitation

pulse at TR (flipping M_z into the xy plane), the component of the magnetization vector in the xy plane (plane of signal acquisition) will thus be more important for short T1 tissues than for long T1 tissues. Therefore, it is possible to differentiate tissues by choosing TR properly. On Figure 4.10 for example, using TR_1 will lead to a good T1 contrast on the resulting image i.e. the short T1 tissue will appear much brighter than the long T1 tissue while using TR_2 will lead to a poor T1 contrast, the M_z regrowth being too similar between the different imaged tissues.

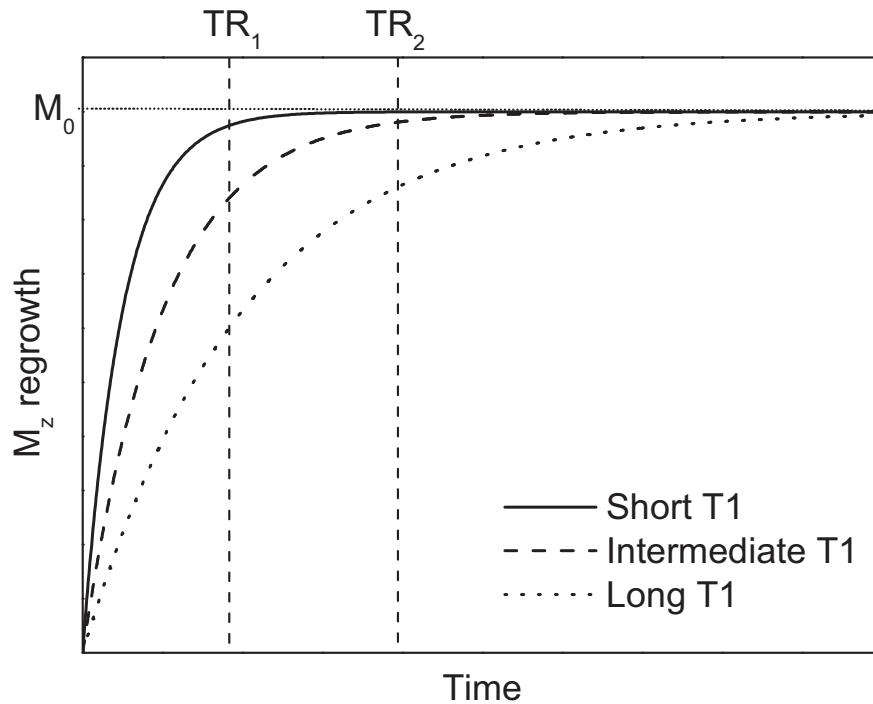


Figure 4.10. Schematic representation of the M_z regrowth for tissues having a different T1 constant.

Choosing TE properly also allows introducing contrast in the obtained image. As we can see on Figure 4.11, the signal difference between the three represented tissues will be more important for TE_1 than for TE_2 .

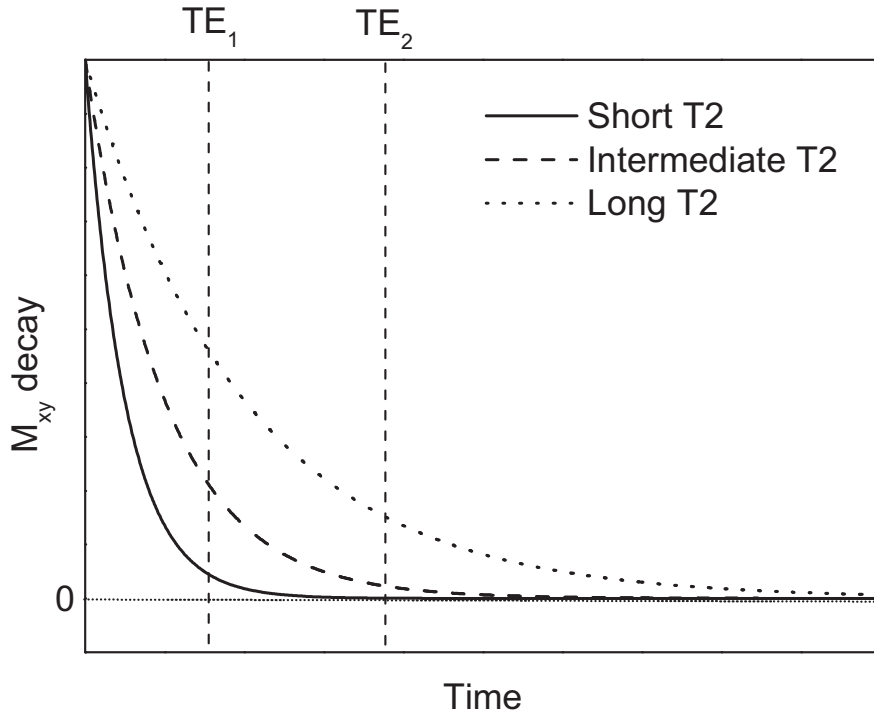


Figure 4.11. Schematic representation of the M_{xy} decay for tissues having a different T2 constant.

Therefore, for one specific sequence, the signal intensity can be expressed as follows.

$$S \sim \rho (1 - e^{-TR/T1}) e^{-TE/T2^*} \quad (4.24)$$

Let us imagine a SE sequence with an initial RF pulse of 90° . The obtained contrast between a tissue A and a tissue B is:

$$C_{AB} = S_A - S_B = \rho_A (1 - e^{-TR/T1,A}) e^{-TE/T2,A^*} - \rho_B (1 - e^{-TR/T1,B}) e^{-TE/T2,B^*} \quad (4.25)$$

Three types of contrast can be obtained: spin density weighting (related to the proton density), T1-weighting and T2*-weighting contrast.

➤ Spin density weighting

In order to get a spin density weighted image, the influence of T1 and T2* of the imaged tissues on the contrast have to be minimized. Therefore TE and TR are chosen such that

$$\begin{aligned} TE \ll T2_{A,B}^* &\longrightarrow e^{-TE/T2_{A,B}^*} \simeq 1 \\ TR \gg T1_{A,B} &\longrightarrow e^{-TR/T1_{A,B}} \simeq 0 \end{aligned}$$

In these conditions,

$$C_{A,B} \simeq \rho_A - \rho_B$$

➤ T1-weighting

As the spin density cannot be neglected, the T2* effect has to be minimized. Therefore, TE has to be chosen such that $TE \gg T2_{A,B}^*$.

In these conditions,

$$C_{A,B} \simeq (\rho_A - \rho_B) - (\rho_A e^{-TR/T1,A} - \rho_B e^{-TR/T1,B})$$

➤ T2-weighting

In order to get a T2-weighting of the image, the T1 effect has to be minimized by choosing a $TR \gg T1_{A,B}$.

In these conditions,

$$C_{A,B} \simeq \rho_A e^{-TE/T2,A^*} - \rho_B e^{-TE/T2,B^*}$$

Table 4.1. General set of rules for generating tissue contrast

Type of contrast	TR	TE
Spin density	As long as possible	As short as possible
T1-weighted	Of the order of the T1 values	As short as possible
T2-weighted	As long as possible	Of the order of the T2 values

4.1.6. Artifacts related to metallic implants imaging

4.1.6.1. Susceptibility artifacts

Susceptibility artifacts are quite easy to understand intuitively: when a metallic implant is placed into a magnetic field, this field is modified in the neighborhood of the implant. As MRI is based on the accurate control of the magnetic field in the space, the presence of a metallic implant leads to a distortion of the image in its neighborhood.

These artifacts obviously depend on the magnetic susceptibility of the metal but also on the geometry of the metallic piece, on its orientation with respect to the external magnetic field (B_0), on the intensity of B_0 , on the type of sequence applied (SE or GRE), on the intensity of the gradients, on the echo time (for GRE sequences), etc. ^{388,392-398}

To understand these artifacts, a simple geometrical model has been previously studied i.e. the model of an infinite cylinder immersed in a magnetic field ^{391-393,399}. This model is particularly consistent with our study as the geometry of the metallic wires used to design braided stents is analogous. Consider this cylinder aligned with the external magnetic field B_0 , the magnetic field stays unchanged outside the cylinder. Inside the cylinder, the magnetic field B can be expressed as follow.

$$\mathbf{B} = [1 + (\chi_i - \chi_e)] \mathbf{B}_0 \quad (4.26)$$

where χ_i and χ_e are the magnetic susceptibility of the materials inside and outside the cylinder, respectively.

On the contrary, when the cylinder main axis is not aligned with $\mathbf{B}_0$, the magnetic field is also modified outside the cylinder. As we are interested in studying metallic (Nitinol and Phynox) wires that do not contain any water and thus do not provide any MRI signal, we will focus on the magnetic field perturbation outside the cylinder. This perturbation obviously depends on the magnetic susceptibility difference between the cylinder and its surrounding but also on the angle between the cylinder main axis and $\mathbf{B}_0$ direction such that

$$\vec{B} = B_0 \cos \theta \hat{z} + B_0 \sin \theta \left[\hat{x} + \frac{\Delta\chi/2}{1+\Delta\chi/2} \left(\frac{a}{\rho}\right)^2 (\hat{x} \cos 2\Phi + \hat{y} \sin 2\Phi) \right] \quad (4.27)$$

The different variables of this equation are summarized on Figure 4.12.

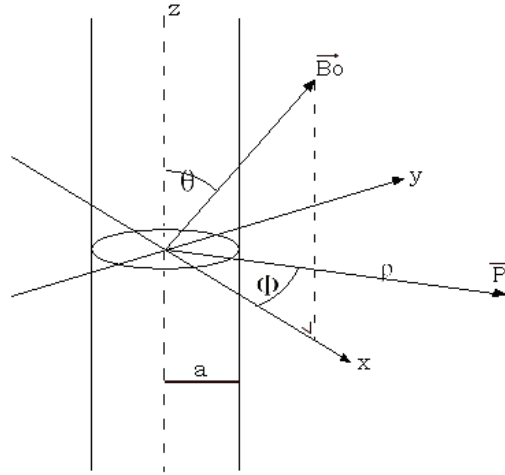


Figure 4.12. Schematic representation of a cylinder parallel to the z axis and of the different variables involved in the equation (4.27) of the magnetic field variation outside the cylinder.

Using this formula and Matlab[®] software, we could simulate the variation of the magnetic field B_0 (3T) around a cylinder of 240 μm diameter perpendicular to $\mathbf{B}_0$ with a magnetic susceptibility difference of 10^{-4} between the cylinder and the medium materials which is a situation similar to a Nitinol wire immersed into water. The algorithm is presented in Annex 3.1 and the simulated images are presented in Figure 4.13.

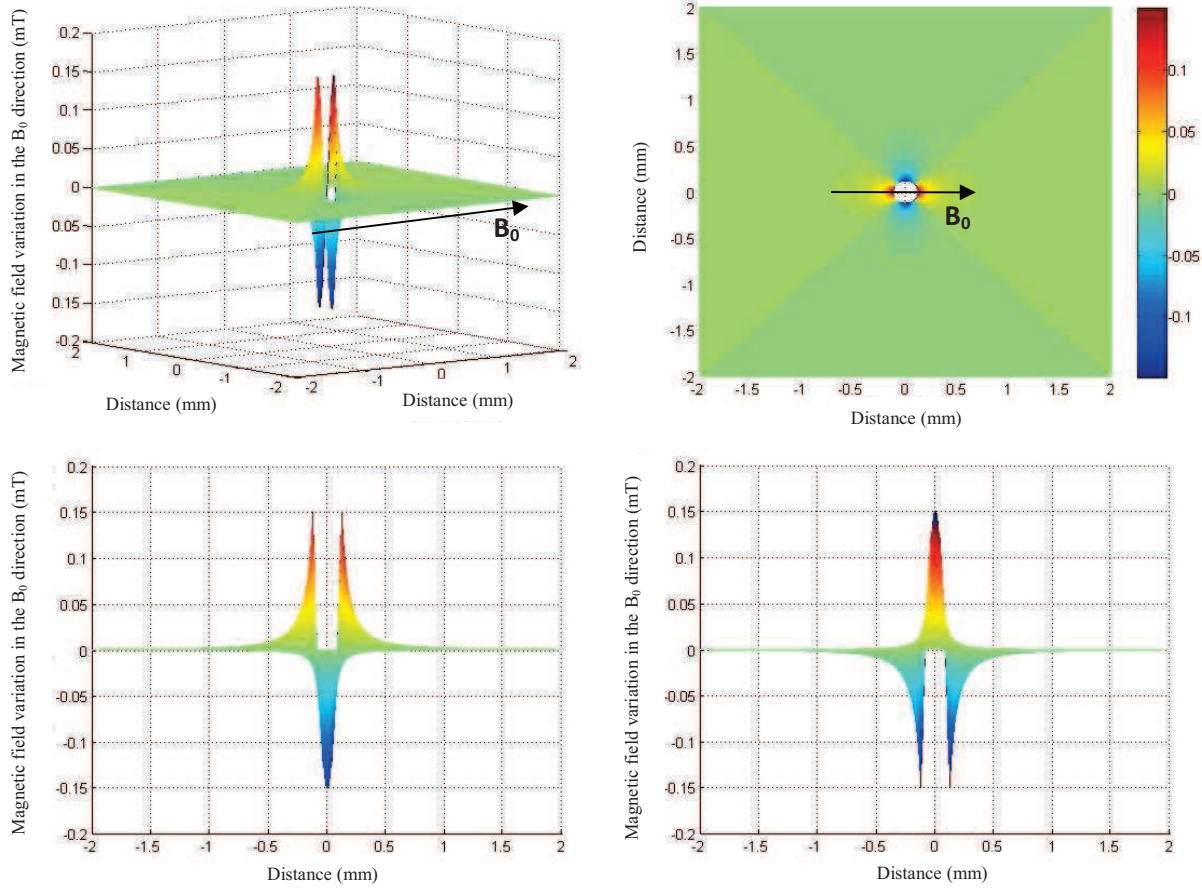


Figure 4.13. Variation of the magnetic field around a cylinder of 240 μm diameter perpendicular to B_0 (3T) with a magnetic susceptibility difference of 10^{-4} between the cylinder and the medium materials.

Consider a simple MRI experiment in which the main magnetic field B_0 and the readout gradient direction are aligned along the z axis and the selected slice is in the xy plane³⁹². Consider also a cylinder of a material whose magnetic susceptibility is χ_i oriented along the y axis (thus perpendicular to B_0) in a medium whose magnetic susceptibility is χ_e such that $\chi_i > \chi_e$. As stated by equation (4.27), the magnetic field will be perturbed in the cylinder neighborhood. The component of the resulting magnetic field in the direction of B_0 can be expressed as follow.

$$(B_e)_z = B_0 \left[1 - \frac{\mu_e - \mu_i}{\mu_e + \mu_i} R^2 \frac{z^2 - x^2}{r^4} \right] \quad (4.28)$$

with $r^2 = x^2 + z^2$

and where μ_e and μ_i are the relative magnetic permeabilities of the materials outside and inside the cylinder, respectively
 R is the cylinder radius.

For magnetic susceptibility values $\ll 1$, we can approximate that $\frac{\mu_e - \mu_i}{\mu_e + \mu_i} \cong \frac{\Delta\chi}{2}$ ³⁹².

This magnetic field perturbation will interfere with the gradients applied during the imagery experiment. This will result in the selection of a non-plane slice, a geometrical distortion of the image plane and a non-uniform pixel intensity.

4.1.6.1.1. Slice selection

In the presence of such a cylinder, a frequency $2\pi f = \gamma(B_0 + yG_y)$ applied to select a slice at y (along the y axis) results in an excited slice at $y'(x,y,z)$ defined by

$$B_z(x,y',z) + y'G_y = B_0 + yG_y \quad (4.29)$$

Using equation (4.28) together with the approximation $\frac{\mu_e - \mu_i}{\mu_e + \mu_i} \cong \frac{\Delta\chi}{2}$,

$$\Delta y = y' - y = \frac{\Delta\chi}{2} \frac{B_0}{G_y} R^2 \frac{z^2 - x^2}{r^4} \quad (4.30)$$

The selected slice has thus the typical shape presented in Figure 4.14.

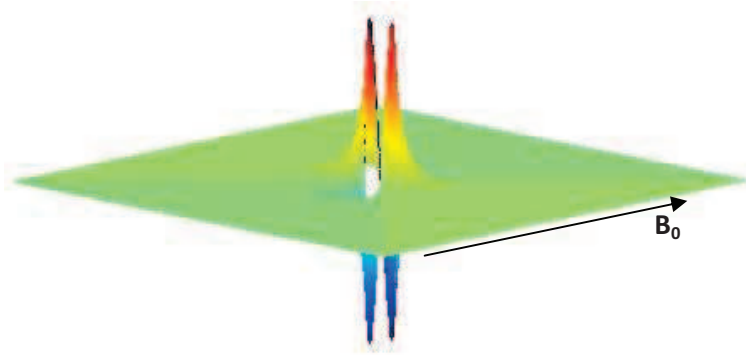


Figure 4.14. Representation of the shape of a slice selected perpendicularly to a cylinder of 240 μm diameter perpendicular to B_0 (3T) with a magnetic susceptibility difference of 10^{-4} between the cylinder and the medium materials (algorithm presented in Annex 3.1).

4.1.6.1.2. Geometrical distortion of the image plane

As a consequence of the magnetic field variations in the direction of B_0 (along the z axis), pixels of the resulting image and the original voxels (small imaged volume elements) will not match anymore. A pixel at the position (x,z) will be moved after the Fourier transform operation to the position (x,z') such that

$$z' = z + \frac{\Delta B_z(x,y',z)}{G_z} = z + \Delta z \quad (4.31)$$

Using equations (4.28) and (4.31) together with the approximation $\frac{\mu_e - \mu_i}{\mu_e + \mu_i} \cong \frac{\Delta\chi}{2}$, the displacement Δz_c in the image plane outside the cylinder can be expressed as follow.

$$\Delta z_e = -\frac{\Delta\chi}{2} \frac{B_0}{G_z} R^2 \frac{z^2 - x^2}{(x^2 + z^2)^2} \quad (4.32)$$

The image outside the cylinder will thus be deformed (typically in an arrow shape) in the readout gradient direction (Figure 4.15).

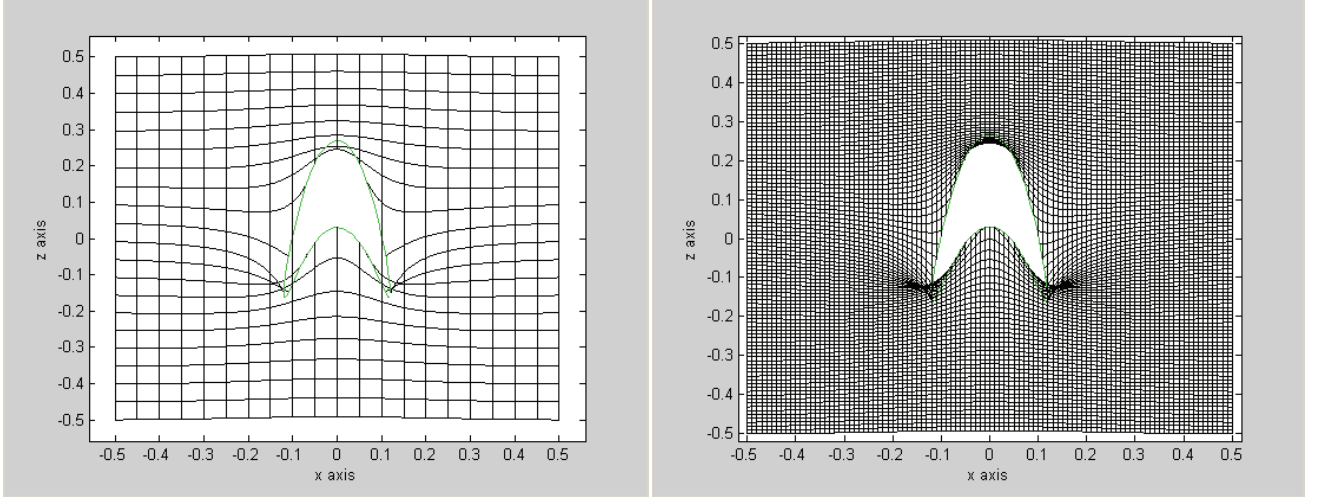


Figure 4.15. Representation of the voxels deformation in the surrounding of a cylinder of 240 μm diameter perpendicular to a 3T B_0 (in the z direction) with a magnetic susceptibility difference of 10^{-6} between the cylinder and the medium materials in a slice imaged with a readout gradient of 10 mT/m parallel to the z axis. The voxels size has been set to 0.05x0.05 mm (left) and 0.01x0.01 mm (right) (algorithm presented in Annex 3.1).

4.1.6.1.3. Distortion of the pixels intensity

In a homogeneous area of the medium in the neighborhood of the cylinder, the relative pixels intensity is related to their relative size (thus the size of the corresponding voxel) but also to the possibility for the signal of a voxel to be dispatched into several pixels (leading to a hyposignal) or conversely, the possibility for the signal of several voxels to be assigned to the same pixel (leading to a hypersignal).

The influence of the type of sequence on the susceptibility artifacts is quite obvious and largely reported in the literature^{388,393-397}: as we have seen previously, SE sequences are characterized by a RF pulse of 180° aiming to thwart the spins dephasing due to the main magnetic field inhomogeneities. On the opposite, GRE sequences do not include such refocusing RF impulsion. Therefore, magnetic field variations around a metallic implant induce a dephasing of the spins inside the voxels (the magnetic field being inhomogeneous inside the voxels) that leads to an important signal loss. This signal loss can be reduced by using an echo time as short as possible (thus by measuring the signal as soon as possible after the spins excitation to limit the intravoxel dephasing of the spins) but also by reducing the voxels size.

4.1.6.2. RF artifacts

RF artifacts are another kind of artifacts frequently observed in the context of stents MRI imaging^{388,400}. They have been theoretically studied by Camacho *et al.*⁴⁰¹.

This kind of artifacts occurs when a conductive loop is imaged. As MRI implies the application of RF pulses and therefore the application of oscillating magnetic field B_1 , an electromotive force is induced in the conductive loop according to Faraday's law:

$$Emf = - \int_S \frac{\delta \vec{B}}{\delta t} \cdot d\vec{S} \quad (4.33)$$

where Emf is the induced electromotive force in the conductive loop, $\vec{B}$ is the magnetic field vector, t is the time and $d\vec{S}$ is a vector perpendicular to the surface S formed by the loop.

Note that the negative sign of the equation (4.33) translates the Lenz law which states that when an emf is generated by a change in magnetic flux, the polarity of the induced emf is such that it produces a current whose magnetic field opposes the change which produces it (and thus opposes the oscillating magnetic field B_1). Moreover, we have seen that the flip angle of the spins is controlled and determined by the time of B_1 application and by B_1 intensity (equation (4.3)). RF artifacts are thus caused by variations of the spins flip angle.

These artifacts obviously depend on the RF pulse frequency (B_1 angular rate) and therefore on B_0 intensity as it governs the precession speed of the spins according to Larmor's equation (equation (4.1)).

Camacho *et al.* imaged a copper loop immersed into water⁴⁰¹. As copper has a magnetic susceptibility very similar to the water one, susceptibility artifacts are as limited as possible. Observed RF artifacts consist in a signal loss inside the loop and an annular hypersignal area outside the loop. Unlike susceptibility artifacts (whose shape depends on the orientation of the readout gradient and therefore on the orientation of the imaged slice), RF artifacts do not depend on the orientation of the imaged slice, the oscillating magnetic field B_1 being itself independent of this orientation. This characteristic confers to RF artifacts a fixed tridimensional nature.

RF artifacts also depend on the type of sequence and are usually more pronounced with SE sequences than with GRE sequences^{394,401}. This may be due to the fact that SE sequences require a correct adjustment of the spins flip angle, this condition being not fulfilled anymore inside stents³⁹⁴.

Actually, stents can be considered as Faraday cages as they are constituted of an important number of conductive loops. If a current is induced into the stent wires, B_1 intensity (and therefore the spins flip angle) will be decreased inside the stent lumen. This leads to a signal decrease of the tissue located inside the implant. Moreover, the signal of the spins precessing inside the implant is also diminished by the same phenomenon. Thus RF artifacts strongly depend on the implant geometry, on its orientation with respect to the RF antenna and on the electrical conductivity of the metal used for its manufacturing⁴⁰².

4.1.6.3. Study of the artifacts caused by stents

Numerous studies have been carried out in order to determine the more MRI adapted stents^{386,388-390,400,403} or the impact of the conditions and imagery parameters on the intensity of these artifacts^{386-390,400,402,404}.

It appears that stents made of stainless steel and cobalt alloys induce enormous susceptibility artifacts preventing the visibility of the stent lumen (the area inside the stent). On the contrary, Nitinol and tantalum stents usually induce less pronounced susceptibility artifacts. Nevertheless, stents made of the same material can have different behavior when imaged with MRI (regarding susceptibility as well as RF artifacts). RF artifacts differences between stents made from the same material are clearly indicative of the crucial impact of the stent geometry.

The MRI parameters influencing artifacts during stents imaging correspond to the parameters influencing susceptibility and RF artifacts (described here above).

Several authors pointed out a method allowing a reduction of RF artifacts^{400,402,404}. We have seen that these artifacts are caused by a decrease of B_1 intensity inside the stent. Therefore, it is possible to “recover” the signal from this area by using a flip angle much more important than the ideal one used for the imagery of the external areas. This is done by applying B_1 for a longer time.

4.1.6.4. Other artifacts caused by stents

Another kind of artifacts related to the induction phenomenon has been reported in the literature. This kind of artifacts is produced by the switching on and off of the different magnetic field gradients used for signal encoding (Gradient Field Switching Artifacts or GFSA)^{405,406}.

In this case, induced current appears in the implant during the switching on and off of the gradients. This intensity of these induced currents (and thus of the resulting artifacts) depends on the intensity of the applied magnetic field gradients but also on their evolution over time and therefore on different imagery parameters such as the gradient switching rate, the field of view, the resolution and the position of the implant into the magnet. Stent imaging has thus to be carried out with the stent positioned as close as possible to the center of the magnet (where the gradients intensities are the weakest)⁴⁰⁵.

Note that GFSA artifacts are maximal when the axis of the conductive loop is parallel to the main magnetic field B_0 (and thus parallel to the direction of the gradients) unlike RF artifacts that are maximal when the axis of the conductive loop is perpendicular to B_0 direction (and thus parallel to the plane in which the oscillating magnetic field B_1 is applied)⁴⁰⁵.

As the currents induced by the switching on and the switching off of a same gradient have more or less the same intensity but opposite signs, a refocusing of the spins is possible. This refocusing occurs for all the gradients switched on and off between the excitation RF pulse and the signal acquisition (such as phase encoding gradients)⁴⁰⁶.

Obviously, GFSA artifacts depend on the electrical resistivity of the material used for the manufacture of the implant (like RF artifacts). Note that GFSA artifacts are not important for small implants like Nitinol or titanium stents and clips ⁴⁰⁶.

In the frame of blood vessels imaging, artifacts related to the blood flow can appear. These flow artifacts are related to an intravoxel dephasing of the spins (and thus a signal loss) due to a flow perturbation. In the case of stents for example, turbulences can appear when the stent is not well attached to the vessel wall ³⁸⁸.

4.2. Results and discussion

The present work aims to systematically study the impact of different surface treatments and of the imaging parameters and conditions on the MRI visibility of Nitinol and Phynox wires and stents.

4.2.1. Quantitative assessment of the apparent magnetic susceptibility of wires

In order to characterize the influence of the surface treatment (and thus of the surface composition) on the apparent magnetic susceptibility of Nitinol and Phynox wires, the simple geometric model of the infinite cylinder immersed into a magnetic field has been used. Indeed, this model fits the real situation of a wire held perpendicularly to the main magnetic field B_0 . The basic idea of the apparent magnetic susceptibility estimation consists in the characterization and the quantification of the susceptibility artifact due to the magnetic susceptibility difference between the medium and the metallic wire. Knowing the magnetic susceptibility of the medium, this artifact measurement allows us to determine the apparent magnetic susceptibility of the immersed wire.

4.2.1.1. Materials and method optimization

All measurements have been carried out with a Siemens Trio MRI with a 3T main magnetic field B_0 .

The tested wires were held horizontally in a phantom i.e. a non-living object containing a material proving MRI signal. In a first time, we used a phantom made from a plastic container filled with distilled water (about 1 liter) in which the wires were drawn tight between two plastic bars as schematized in Figure 4.16.

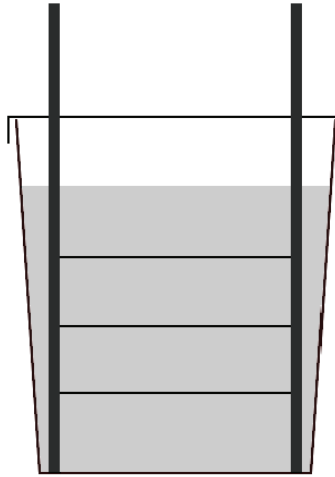


Figure 4.16. Schematic representation of the phantom used for the quantitative assessment of the apparent magnetic susceptibility of metal wires in MRI.

However, pure water has a very long transverse relaxation time constant (T_2). As a result, the signal obtained from this medium (and therefore the background of our measurements) is extremely inhomogeneous due to the motion of water molecules (see Figure 4.17). Thus we had to reduce the T_2 constant of our medium in order to reach a T_2 value low enough (compared to the echo time of the used sequence) to decrease the effects of the water molecules motion. Note that the parameters of all the sequences used in the frame of this study are detailed in Annex 3.2.

The most common method to reduce T_2 is to introduce a paramagnetic contrast agent in the medium (typically a gadolinium complex). However, this solution did not fit the goal of our study. Indeed, the introduction of a paramagnetic contrast agent in the medium would have led to an increase of its magnetic susceptibility and therefore a decrease of the susceptibility difference (and thus of the resulting artifact). The measurable effect would thus have been reduced.

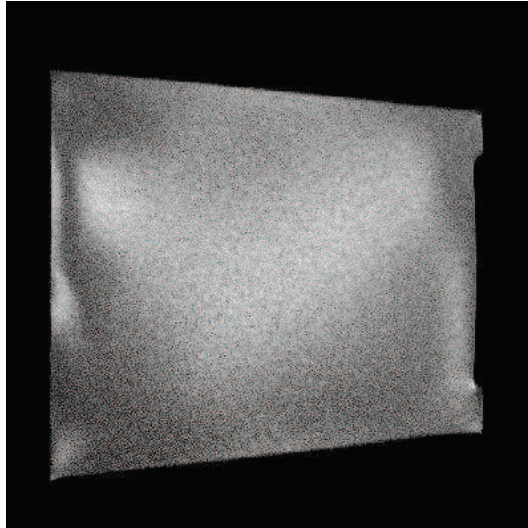


Figure 4.17. MRI image of a sagittal slice of the phantom filled with distilled water (acquired with a SE sequence identical to the one used for the apparent magnetic susceptibility measurements). Beside the evident inhomogeneity of the signal in the middle of the phantom, some image deformations and pixels intensity variations at the borders of the phantom due to the magnetic susceptibility difference between water and the surrounding air can be noticed.

Therefore, we adopted an alternative solution described in the literature by H.J. Laubach *et al.* i.e. that it is possible to decrease the transverse relaxation time of water by adding sucrose to it ⁴⁰⁷. This method does not change significantly the magnetic susceptibility of the aqueous medium i.e. -9.05×10^{-6} ³⁹⁹.

Several sucrose concentrations have been tested: 10, 20 and 30 w/w (in sucrose mass percentage per water mass). The T2 constant of these solutions has been measured by imaging several times the phantom with SE sequences keeping all the sequence parameters strictly the same except the echo time. Images were acquired with five different echo times: 15, 30, 50, 100 and 150 ms. By measuring the intensity of the signal obtained in a region of interest (ROI) in the middle of the phantom for these different echo times, intensity values of the transversal magnetization decay curve are obtained (see Figure 4.18). Therefore, it is possible to fit this curve with a function $f = y \cdot e^{-t/x}$ (similar to the transversal magnetization decay curve function) and deduce the T2 value (the x variable in the general function).

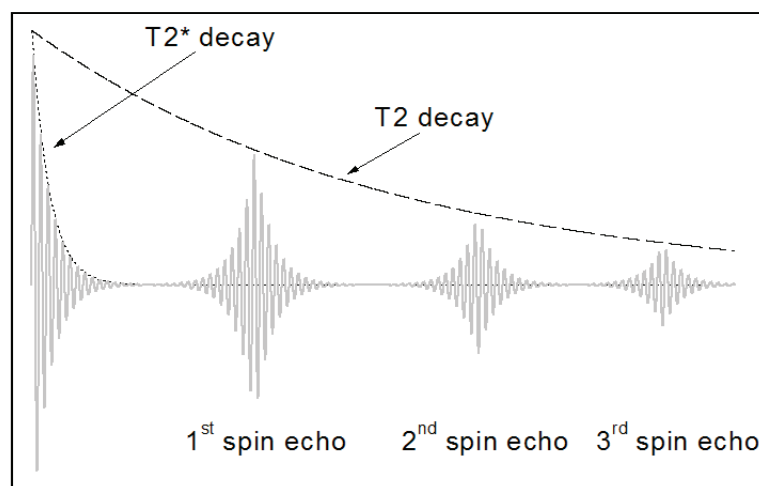


Figure 4.18. Schematic representation of the T2* and T2 signal decay curves. The signal measurement at different echo times allows finding the envelope of the T2 decay.

The measured signal intensities and the corresponding fitted curves are presented in Figure 4.19. It can be clearly seen that an increase of the sucrose concentration leads to a decrease of T2. It can also be pointed out that this T2 decrease is very fast at the beginning (a 55 ms decrease when the concentration increases from 10 to 20 w/w) and much slower at higher concentrations (a 9 ms decrease when the concentration increases from 20 to 30 w/w). This is in good accordance with results presented by H.J. Laubach *et al.* i.e. that at sucrose concentrations higher than 20 w/w, the T2 constant of the solution tends to a limit value⁴⁰⁷.

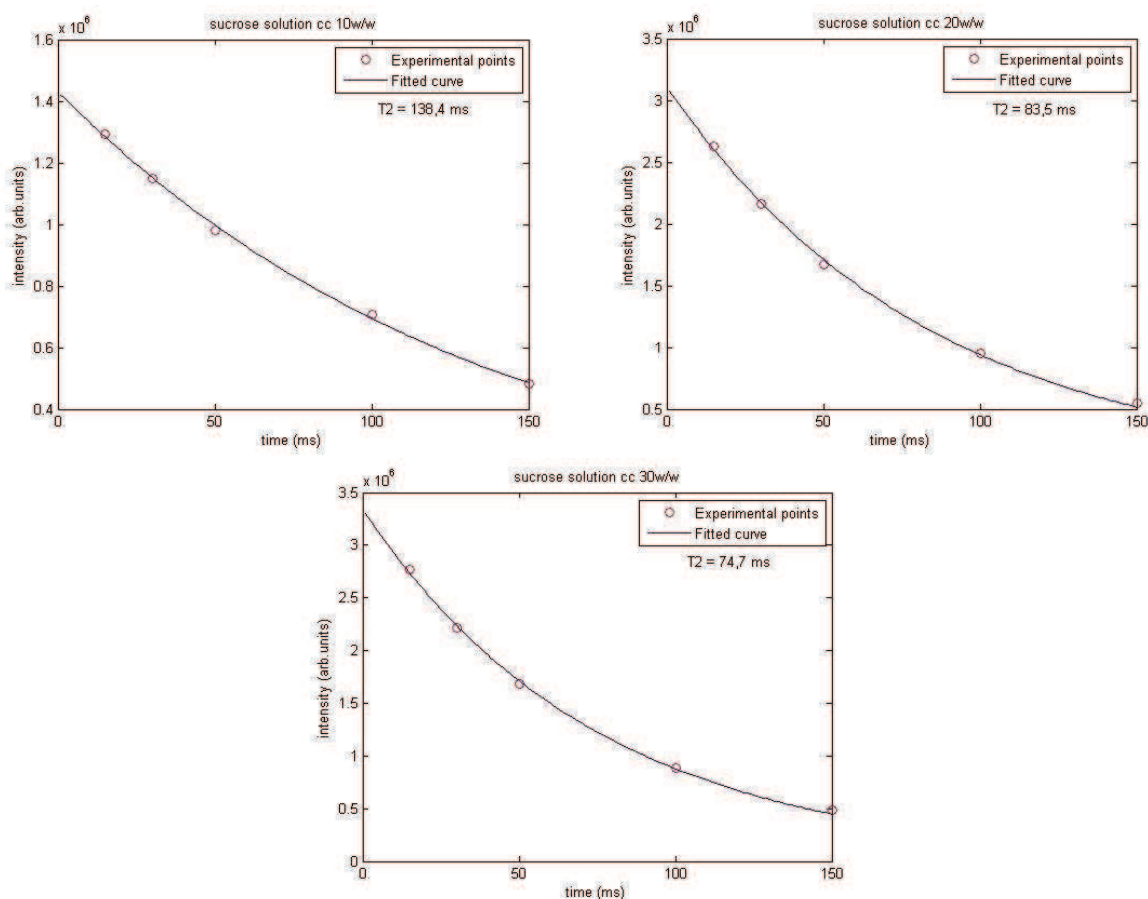


Figure 4.19. Fitted T₂ decay curves of sucrose aqueous solutions at different concentrations (10, 20 and 30 w/w).

As the T₂ constant tends to a limit value at sucrose concentrations higher than 20 w/w, we chose to work with a sucrose concentration of 25 w/w. We measured the T₂ constant of this solution more accurately by measuring the signal intensity at 7 echo times instead of five (i.e. 10, 30, 50, 75, 100, 125 and 150 ms). The resulting fitted T₂ decay curve and an image of the phantom in these conditions are presented in Figure 4.20. It clearly appears that the background signal in the middle of the phantom is much more homogeneous than the one obtained with distilled water (Figure 4.17). Note also that the T₂ constant measured for a sucrose concentration of 25 w/w is lower than the one obtained previously for a concentration of 30 w/w. The overestimation of the T₂ constant with a concentration of 30 w/w may be due to the imprecision of the measurement carried out from the acquisition of only 5 experimental points. Anyway, these results confirm that a sucrose concentration of 25 w/w leads to a sufficient T₂ decrease for our forthcoming experiments.

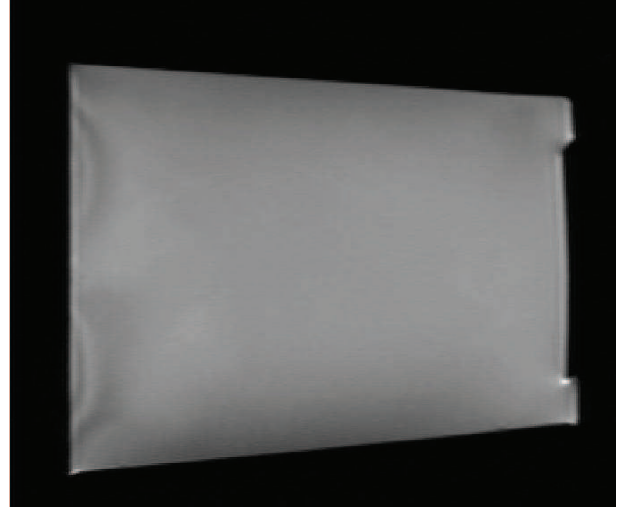
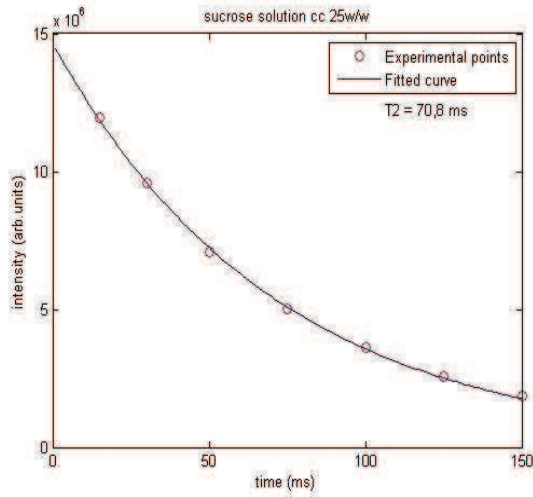


Figure 4.20. Fitted T2 decay curve of 25 w/w sucrose aqueous solutions (left) and the corresponding phantom image acquired with a SE sequence and an echo time of 15 ms (right).

4.2.1.2. Phase measurement method

The phase measurement method is described in *Magnetic Resonance Imaging – Physical Principles and Sequence Design*³⁹¹ as a way to measure the magnetic susceptibility according to the cylinder geometrical model. This method is based on the measurement of the spins phase with a GRE sequence. As shown previously, when magnetic field gradients are applied, the phase of the precessing spins can be expressed as follow.

$$\Phi(\vec{r}, t) = \phi_0 - \gamma B_z(\vec{r})t \quad (4.34)$$

In the case of a GRE sequence applied with a magnetic field deformed by the presence of a material with a magnetic susceptibility different from the imaged medium, the phase can be expressed according to equation (4.35)

$$\Phi(\vec{r}, TE) = \phi_0 - \gamma B_z(\vec{r})TE \quad (4.35)$$

where TE is the sequence echo time i.e. the time interval between the spins excitation RF pulse and the signal measurement (in the case, the measurement of the spins phase).

If two GRE sequences are applied with two different echo times (all other parameters being kept strictly identical), two phase images corresponding to the following equations are obtained.

$$\Phi(\vec{r}, TE_1) = \phi_0 - \gamma B_z(\vec{r})TE_1 \quad (4.36)$$

$$\Phi(\vec{r}, TE_2) = \phi_0 - \gamma B_z(\vec{r})TE_2 \quad (4.37)$$

Subtraction of equations (4.36) and (4.37) leads to equation (4.38).

$$\Delta B(\vec{r}) = \frac{\Phi(\vec{r}, TE_2) - \Phi(\vec{r}, TE_1)}{\gamma(TE_1 - TE_2)} \quad (4.38)$$

Therefore, this kind of measurement gives a direct access to the magnetic field variations induced by the presence of a metallic wire. Furthermore, as we know from equation (4.28) that

$$\Delta B = \frac{\Delta\chi}{2} R^2 \frac{y^2 - x^2}{(x^2 + y^2)^2} \quad (4.39)$$

the measurement of the magnetic field variations can lead to the determination of the apparent magnetic susceptibility difference between the metallic wire and the medium.

This measurement has been carried out on an untreated Nitinol wire of 170 μm diameter. The wire was held horizontally in a phantom filled with a 25 w/w sucrose aqueous solution and placed in the middle of the MRI, perpendicular to B_0 direction. Sagittal slices images (perpendicular to the wire) have been acquired with GRE sequences fully described in Annex 3.2. These two GRE sequences are strictly identical except for their echo time (3.2 and 6.2 ms). In order to minimize the signal loss due to intravoxel spins dephasing, the highest possible readout gradient was used. The obtained phase images are presented in Figure 4.21.

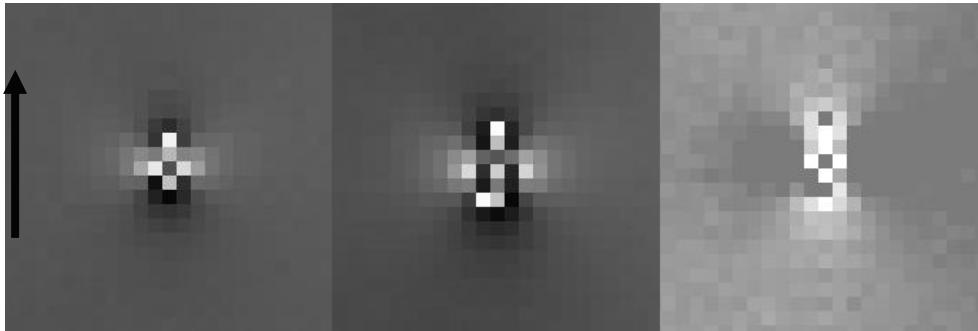


Figure 4.21. Sagittal phase images of the precessing spins in the neighborhood of an untreated Nitinol wire of 170 μm diameter acquired with an echo time of 3.2 ms (left), 6.2 ms (center) and the image resulting from the subtraction of these two phase images (right). The black arrow indicates the direction of the B_0 magnetic field and of the readout gradient.

As expected, the image resulting from the subtraction of the two phase images has the typical shape of the magnetic field deformation around a cylinder with a magnetic susceptibility different from the one of the medium (Figure 4.13). Note that the important intensity variations at very short distance of the wire are due to the aliasing phenomenon (i.e. a “phase folding”). Indeed, the measured phase values are obviously always comprised between $-\pi$ and π radians. This implies that when the “real” phase of the spins quickly increases (and is therefore more important than π like in the very close neighborhood of a metallic wire) it is encoded as a succession of switching from $-\pi$ and π radians (periodic evolution) instead of as a continuous evolution.

The magnetic field variation profile obtained in the direction of B_0 is in good accordance with the theoretically expected one as shown in Figure 4.22. However, it is not possible to obtain any accurate information from this experimental profile as the region of interest is extremely

narrow. Indeed, the main part of the magnetic field variation profile is unexploitable because of the aliasing phenomenon. This makes impossible an accurate positioning of the wire on the experimental profile and therefore the fitting of the magnetic field variation profile.

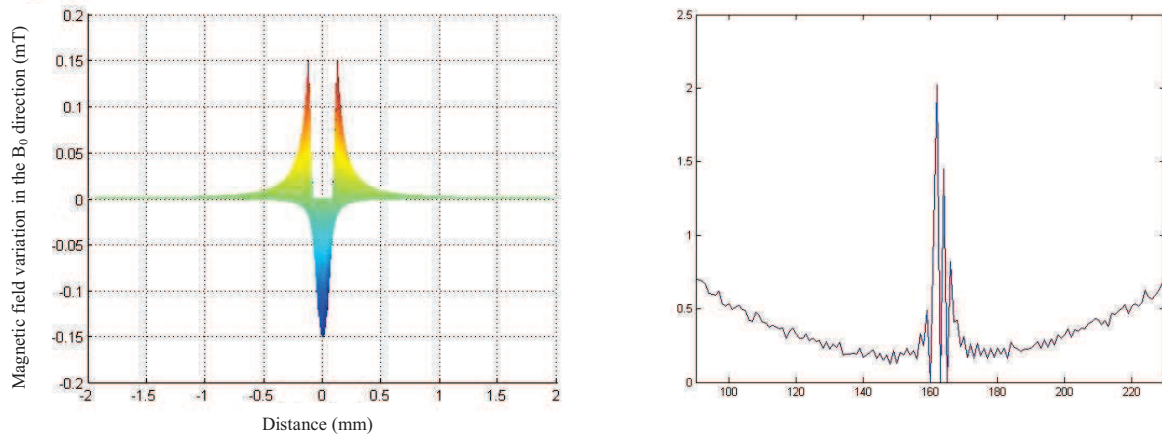


Figure 4.22. Simulated profile of the magnetic field variation in the B₀ direction (left) and the corresponding experimental profile obtained with an untreated Nitinol wire of 170 μm diameter (right).

4.2.1.3. Iterative susceptibility artifact measurement method

As the phase measurement method did not allow the determination of the apparent magnetic susceptibility of Nitinol and Phynox wires, we considered an alternative method based on the measurement of the geometric distortion of the image plane and the distortion of pixels intensity. As specified previously, the image plane is deformed in the direction of the readout gradient (now set along the y axis) and is proportional to the magnetic susceptibility difference between the metallic wire and the medium as expressed in equation (4.40).

$$\Delta y = \frac{\Delta\chi}{2} \frac{B_0}{G_y} R^2 \frac{y^2 - x^2}{(x^2 + y^2)^2} \quad (4.40)$$

Each parameter of this equation (except $\Delta\chi$) being determined by the experimental setup and the used MRI sequences, it is possible to calculate Δy (and thus to simulate the image deformation) for a given $\Delta\chi$. Thus, we created an algorithm that allows a simulation of the image plane deformation via a numerical method.

4.2.1.3.1 *Algorithm conception method*

The medium being homogeneous (25 w/w aqueous sucrose solution), the intensity of each pixel has been arbitrarily set to a value of 1. Without any image deformation, the area and the position of a pixel are the same than the area and the position of the corresponding voxel. Let us consider the middle pixel on the Figure 4.23. The corresponding voxel is submitted to a deformation in the direction of the readout gradient. The deformation of its upper (red) and lower (blue) boundaries is thus calculated according to equation (4.40). The new deformed

voxel boundaries can thus be determined (i.e. the dark red and dark blue curves on Figure 4.23). The new voxel area is calculated by integration of the area between its deformed boundaries. Finally, the voxel intensity (renormalized with respect to its new area) is dispatched among the different surrounding pixels. The complete algorithm is presented in Annex 3.1.

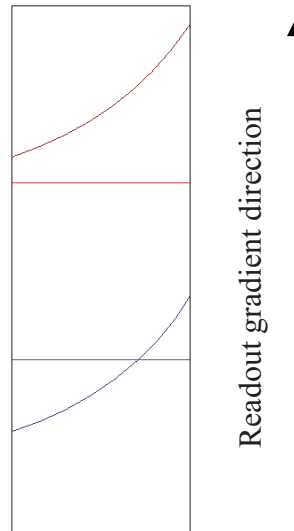


Figure 4.23. Schematic representation of three pixels of the deformed image. The corresponding voxel original boundaries are represented in red (upper one) and blue (lower one). The deformed voxel boundaries are represented in dark red (upper one) and dark blue (lower one).

This image simulation algorithm has then been used as a basis to build up another algorithm aiming at fitting experimental images in order to determine the magnetic susceptibility difference between the metallic wire and the medium ($\Delta\chi$ being the only unknown variable in equation (4.40)). Basically, this algorithm simulates a first image, compares it with the experimental one (by the method of least squares), adjusts $\Delta\chi$ and simulates a new image, etc. The process stops when the simulated image is similar enough to the experimental one. Note also that the simulation algorithm set all the pixels intensity to unity which is obviously not the case anymore for experimental images. The fitting algorithm is therefore designed to determine not only $\Delta\chi$ but also the normalization factor value. The complete algorithm is presented in Annex 3.1.

4.2.1.3.2 Results

All the Nitinol and Phynox wires tested with this method and the surface treatments applied to them are presented in Tables 4.2, 4.3 and 4.4.

The experimental setup is strictly the same as the one used for the phase measurement method. SE sequences were used in order to minimize the signal loss due to intravoxel spin dephasing (encountered with GRE sequences) thanks to the characteristic 180° RF pulse as well as to keep only the geometric distortion of the image plane. As said previously, the readout gradient has a strong impact of the size of the susceptibility artifacts. Therefore, for

each of the tested wires, the same SE sequence was repeated with two different bandwidths i.e. 100 and 150 Hz/pxl. These bandwidths values correspond to readout gradient intensities of 8.6 and 12.9 mT/m, respectively. Note that these SE sequences are fully described in Annex 3.2. Each wire has been imaged with 8 parallel slices for each sequence. 16 images per wire have thus been acquired. The apparent magnetic susceptibilities values obtained and presented in Tables 4.5, 4.6 and 4.7 are the arithmetic mean of the values obtained from these 16 images. Experimental representative images obtained with a bandwidth of 150 Hz/pxl and the corresponding simulated images are also presented in Tables 4.5, 4.6 and 4.7.

Table 4.2. List of the 240 μm diameter Nitinol wires tested with the artifact fitting algorithm

Material	Diameter	Treatments	Acronyms
Nitinol	240 μm	none	NiTi240 NT
Nitinol	240 μm	Ethylene oxide sterilization	NiTi240 NT St
Nitinol	240 μm	Thermal treatment of 20 min at 490°C	NiTi240 TT490_20
Nitinol	240 μm	Thermal treatment of 20 min at 490°C + Ethylene oxide sterilization	NiTi240 TT490_20 St
Nitinol	240 μm	Thermal treatment of 60 min at 490°C	NiTi240 TT490_60
Nitinol	240 μm	Thermal treatment of 60 min at 490°C + Ethylene oxide sterilization	NiTi240 TT490_60 St
Nitinol	240 μm	Thermal treatment of 20 min at 550°C	NiTi240 TT550_20
Nitinol	240 μm	Thermal treatment of 20 min at 550°C + Ethylene oxide sterilization	NiTi240 TT550_20 St
Nitinol	240 μm	Chemical etching by 5 min immersion in 5%vol HF/12%vol HNO ₃ solution	NiTi240 D5

Table 4.3. List of the 170 μm diameter Nitinol wires tested with the artifact fitting algorithm

Material	Diameter	Treatments	Acronyms
Nitinol	170 μm	none	NiTi170 NT
Nitinol	170 μm	Ethylene oxide sterilization	NiTi170 NT St
Nitinol	170 μm	Thermal treatment of 20 min at 490°C	NiTi170 TT490_20
Nitinol	170 μm	Thermal treatment of 20 min at 490°C + Ethylene oxide sterilization	NiTi170 TT490_20 St
Nitinol	170 μm	Thermal treatment of 60 min at 490°C	NiTi170 TT490_60
Nitinol	170 μm	Thermal treatment of 60 min at 490°C + Ethylene oxide sterilization	NiTi170 TT490_60 St
Nitinol	170 μm	Thermal treatment of 20 min at 550°C	NiTi170 TT550_20
Nitinol	170 μm	Thermal treatment of 20 min at 550°C + Ethylene oxide sterilization	NiTi170 TT550_20 St
Nitinol	170 μm	Chemical etching by 5 min immersion in 5%vol HF/12%vol HNO ₃ solution	NiTi170 D5

Table 4.4. List of the 80 μm diameter Phynox wires tested with the artifact fitting algorithm

Material	Diameter	Treatments	Acronyms
Phynox	80 μm	none	Ph80 NT
Phynox	80 μm	Ethylene oxide sterilization	Ph80 NT St
Phynox	80 μm	Thermal treatment of 3 hours at 550°C	Ph80 TT550_3h
Phynox	80 μm	Thermal treatment of 3 hours at 550°C + Ethylene oxide sterilization	Ph80 TT550_3h St
Phynox	80 μm	Thermal treatment of 5 hours at 550°C	Ph80 TT550_5h
Phynox	80 μm	Thermal treatment of 5 hours at 550°C + Ethylene oxide sterilization	Ph80 TT550_5h St
Phynox	80 μm	Thermal treatment of 3 hours at 600°C	Ph80 TT600_3h
Phynox	80 μm	Thermal treatment of 3 hours at 600°C + Ethylene oxide sterilization	Ph80 TT600_3h St
Phynox	80 μm	Chemical etching by 30 min immersion in 5%vol HF/12%vol HNO ₃ solution	Ph80 D30

Table 4.5. Apparent magnetic susceptibilities assessed for the 240 µm diameter Nitinol wires

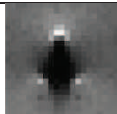
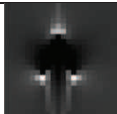
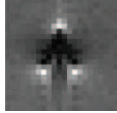
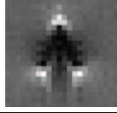
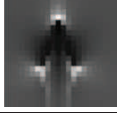
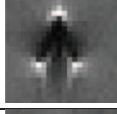
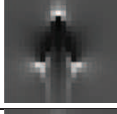
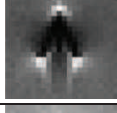
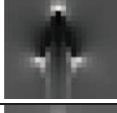
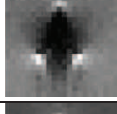
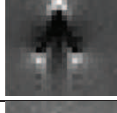
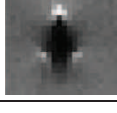
Wire	Apparent magnetic susceptibility	Experimental image	Simulated image
NiTi240 NT	3.16×10^{-4}		
NiTi240 NT St	2.53×10^{-4}		
NiTi240 TT490_20	4.46×10^{-4}		
NiTi240 TT490_20 St	4.44×10^{-4}		
NiTi240 TT490_60	4.51×10^{-4}		
NiTi240 TT490_60 St	4.95×10^{-4}		
NiTi240 TT550_20	5.04×10^{-4}		
NiTi240 TT550_20 St	4.40×10^{-4}		
NiTi240 D5	2.39×10^{-4}		

Table 4.6. Apparent magnetic susceptibilities assessed for the 170 μm diameter Nitinol wires

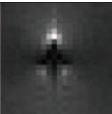
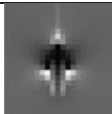
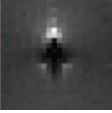
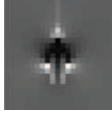
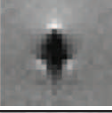
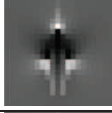
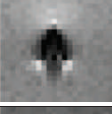
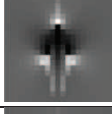
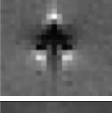
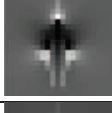
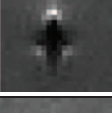
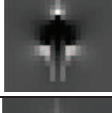
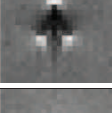
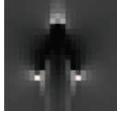
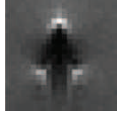
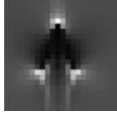
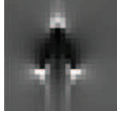
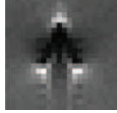
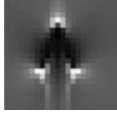
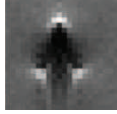
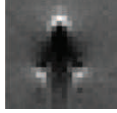
Wire	Apparent magnetic susceptibility	Experimental image	Simulated image
NiTi170 NT	2.42×10^{-4}		
NiTi170 NT St	2.08×10^{-4}		
NiTi170 TT490_20	3.38×10^{-4}		
NiTi170 TT490_20 St	3.59×10^{-4}		
NiTi170 TT490_60	3.50×10^{-4}		
NiTi170 TT490_60 St	3.37×10^{-4}		
NiTi170 TT550_20	5.50×10^{-4}		
NiTi170 TT550_20 St	4.50×10^{-4}		
NiTi170 D5	1.60×10^{-4}		

Table 4.7. Apparent magnetic susceptibilities assessed for the 80 μm diameter Phynox wires

Wire	Apparent magnetic susceptibility	Experimental image	Simulated image
Ph80 NT	5.25×10^{-3}		
Ph80 NT St	5.31×10^{-3}		
Ph80 TT550_3h	3.97×10^{-3}		
Ph80 TT550_3h St	3.59×10^{-3}		
Ph80 TT550_5h	3.82×10^{-3}		
Ph80 TT550_5h St	3.76×10^{-3}		
Ph80 TT600_3h	4.18×10^{-3}		
Ph80 TT600_3h St	4.20×10^{-3}		
Ph80 D30	5.08×10^{-3}		

First of all, it can be pointed out that the surface state of Nitinol and Phynox wires has an actual impact on the apparent magnetic susceptibility of the material. For two untreated Nitinol wires of different diameters (240 μm and 170 μm), the apparent magnetic susceptibility varies slightly but significantly. This confirms that the surface state of Nitinol strongly depends on the provider and the manufacturing process.

Heat treatment induces a clear increase of the apparent magnetic permeability and therefore of the size of the resulting susceptibility artifact. This behavior is much more enhanced when the heat treatment is carried out at a higher temperature than when the heat treatment is carried out for longer times. Several hypotheses can be formulated to explain this behavior. It has been shown in Chapter 2 that the heat treatment of Nitinol induces an important increase of the oxide layer thickness and that an increase of the temperature induces a more important further increase of the oxide layer thickness than an increase of the heat treatment time does. There may thus be a relationship between the oxide layer thickness and the apparent magnetic susceptibility of Nitinol. Indeed, even if the heat treatment induces the appearance of

antiferromagnetic NiO at the surface of Nitinol (which could *a priori* have a beneficial effect on the resulting susceptibility artifacts), it also induces an increase of the TiO₂ quantity present at the surface (TiO₂ being a paramagnetic material). Furthermore, heat treatment is an oxidative treatment and it has been shown that the paramagnetic behavior of a Ti-O system increases with the concentration of oxygen⁴⁰⁸. It has also been shown that in a thin TiO₂ layer, interfacial defects can induce an enhanced magnetism⁴⁰⁹. After the heat treatment, the resulting oxide layer is not only thicker but also more heterogeneous given the fact that the heat treatment induces a strong diffusion of nickel toward the surface and thus the formation of a mixed Ni and Ti oxides layer. Another possible explanation of this susceptibility artifact enhancement could be a change of the TiO₂ crystalline state in the Nitinol oxide layer with the heat treatment. Indeed, it has been shown that TiO₂ can start changing from anatase to rutile in the heat treatment conditions applied in this work (490°C or 550°C)^{410,411} but also that rutile has a more important magnetic susceptibility than anatase⁴¹².

The ethylene oxide sterilization of untreated Nitinol wires seems to decrease their apparent magnetic susceptibility. On the other hand, this sterilization process does not seem to have a significant impact on the apparent magnetic susceptibility of heat treated Nitinol wires except for the ones treated at higher temperature (550°C for 20 min).

Nitinol wires submitted to a chemical etching treatment induce less important susceptibility artifacts than heat treated wires: their apparent magnetic susceptibility is similar to the one of untreated sterilized Nitinol wires. This could be explained by the fact that the oxide layer resulting from a chemical etching is much thinner and homogeneous than the original oxide layer (only composed of TiO₂) and by the absence of any heat treatment of this TiO₂ layer (and therefore the absence of rutile phase in this layer).

For comparison, the measurements carried out on Phynox wires show that the apparent magnetic susceptibility of this alloy is 10-fold more important than the one of Nitinol. Nitinol is thus intrinsically a particularly well suited material for MRI examinations compared to other alloys commonly used for biomedical applications even without specific surface treatment. Contrary to what was observed for Nitinol wires, the heat treatment of Phynox seems to decrease its apparent magnetic susceptibility. Regarding the other tested treatments, neither the ethylene oxide sterilization nor the chemical etching treatment seem to have a significant impact on the Phynox apparent magnetic susceptibility.

4.2.2. Assessment of the stents behavior in MRI

4.2.2.1. Study of the imagery parameters influence

This study has been carried out with the same phantom than the one used for the quantitative assessment of the apparent magnetic susceptibility of wires (described in section 4.2.1.1) on a 7 mm diameter braided Nitinol stent. This stent is constituted of 24 braided 170 µm diameter Nitinol wires and was submitted to a heat treatment for 20 min at 490°C.

The stent has been imaged in two extreme positions with respect to the main magnetic field B₀: parallel and perpendicular. Three main imagery parameters have been studied: the

orientation of the stent with respect to the main magnetic field B_0 , the intensity of the readout gradient and the type of imaging sequence. Five sequences (fully described in Annex 3.2) were used in the frame of this study:

- a GRE sequence (noted TOF3D) typically used for MRI angiography examinations
- a second typical TOF-GRE sequence (noted TOF2D)
- a SE sequence with a bandwidth of 160 Hz/pixel (noted TSE160). This sequence is actually a Turbo Spin Echo one which means that several signal acquisitions are carried out after only one excitation pulse (using several successive 180° refocusing pulses)
- a second SE sequence identical to the previous one except for a bandwidth of 425 Hz/pixel instead of 160 Hz/pixel (noted TSE425)
- a simple SE sequence identical to the one used for the quantitative assessment of the apparent magnetic susceptibility of wires.

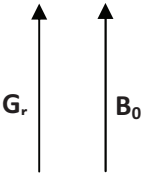
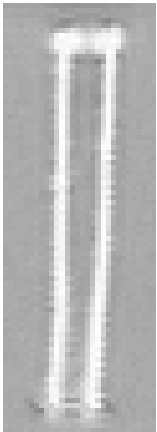
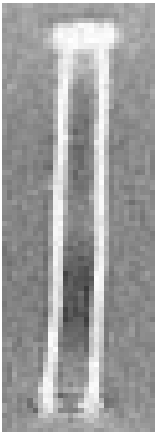
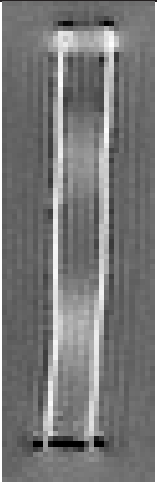
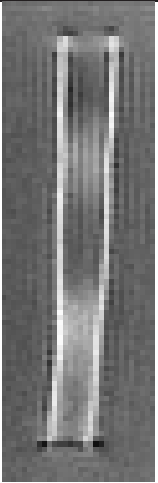
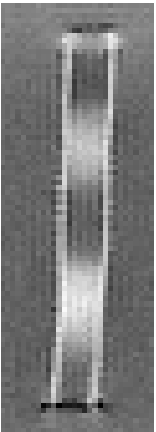
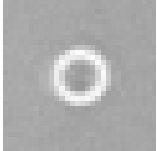
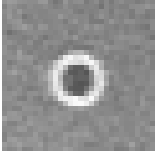
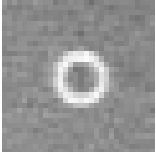
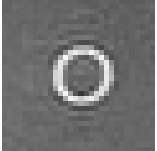
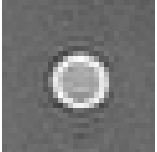
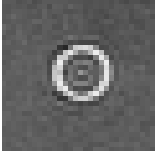
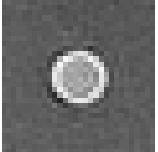
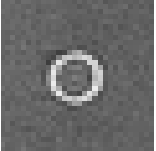
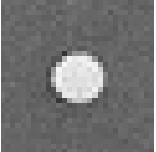
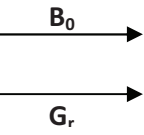
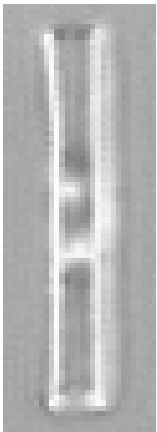
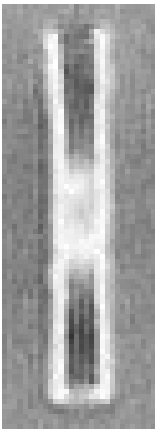
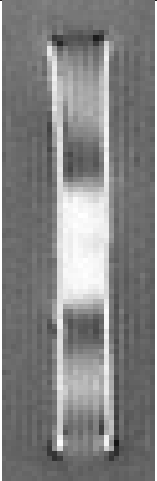
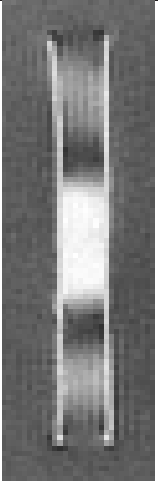
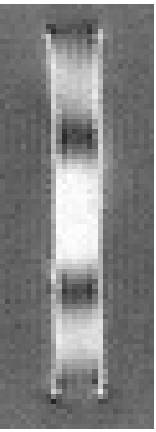
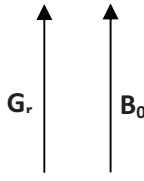
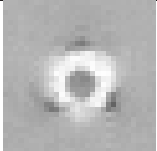
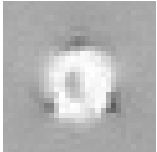
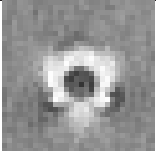
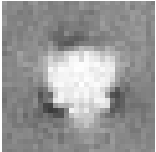
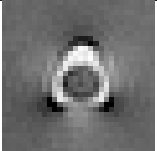
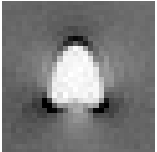
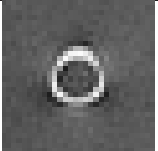
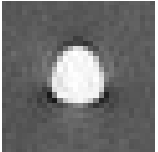
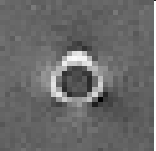
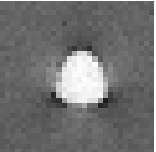
The obtained images are presented in Table 4.8.

From these images, the strong impact of the stent orientation with respect to the main magnetic field B_0 can be clearly pointed out. When the stent is oriented perpendicularly to B_0 direction, susceptibility artifacts are the more important ones: the typical arrow shape image distortion in the readout gradient direction can be observed on transverse images. This behavior is easily understandable as the stents have a cylindrical geometry. Indeed it has been shown that the main magnetic field deformation (and therefore the resulting artifact size) is maximal when the cylinder is oriented perpendicularly to this magnetic field.

When the stent is parallel to the main magnetic field, the quality of transverse images is much better (no arrow shape deformation). In this case, the arrow shape image deformation is visible on sagittal images and located at the stent extremities (more visible on SE sequence images).

The influence of the readout gradient intensity can be clearly observed on the images of the Nitinol stent oriented perpendicularly to the main magnetic field obtained with TSE160 and TSE425 sequences. On the transverse images obtained in these conditions, the arrow shape distortion is much more pronounced with a 160 Hz/pixel readout gradient than with a higher readout gradient.

Table 4.8. MRI images obtained a 7 mm diameter Nitinol stent constituted of 24 braided 170 μm diameter wires.

Parallel to B_0	TOF3D	TOF2D	TSE160	TSE425	SE
					
		 	 	 	 
Perpendicular to B_0	TOF3D	TOF2D	TSE160	TSE425	SE
					
	 	 	 	 	 

The type of used sequence has also a critical impact on the artifacts caused by the stent. The signal loss in pixels located near the stent wall is much more important with GRE sequences than with SE sequences. This is explained by the fact that with GRE sequences, the main magnetic field deformation close to the Nitinol wires induces an intravoxel dephasing of the spins which is not corrected by refocusing pulses like the ones used for SE sequences.

Finally, hypo- and hypersignal areas can be observed in the stent lumen. The non-uniformity of the lumen signal is not explained. Nevertheless, these signal intensity variations are attributed to RF artifacts and not to susceptibility artifacts for two reasons. First, susceptibility artifacts are easily recognizable (typical arrow shape) and have a small influence area (located really close to the stent walls). Second, the signal intensity variations inside the stent lumen are much more pronounced with SE sequences than with GRE sequences. This observation is in good agreement with the well known fact that SE sequences are much more sensitive to the B_1 rotating magnetic field variations than GRE sequences do.

4.2.2.2. Study of the stent composition and surface treatment influence

In the frame of this study, 15 stents have been studied. These stents are composed of braided Nitinol, NiTiDFT10% or Phynox wires. Note that DFT is an acronym that stands for Drawn Filled Tube. The DFT10% wires are composite materials composed of Nitinol around a Pt core (fill ratio 10%). The interest of using such wires for stents design is the important radioopacity of Pt compared to Nitinol alone and therefore allowing much more efficient X-ray angiography examinations. Table 4.9 summarizes the different stents used in this study, their diameter, composition and diameter of the constituting wires and the surface treatments applied to the stent i.e. heat treatment, chemical etching and ethylene oxide sterilization process.

These stents were expanded in artery silicon models (with an adapted diameter), immersed in a Plexiglas container filled with water heated at 37°C and oriented parallel to the main magnetic field B_0 . The sequences used (a GRE and a SE sequence) are fully described in Annex 3.2.

Note that only representative images are presented here. The entire set of images is presented in Annex 3.3.

Table 4.9. Characteristics of the stents used for the study of the influence of the stent composition and surface treatment on the obtained MRI images.

Stent #	Alloy	Wire diameter	Stent diameter	# wires	Heat treatment	Chemical etching	Ethylene oxide Sterilization
1	NiTi	170 μm	7 mm	24	490°C-20min	no	no
2	NiTi	170 μm	7 mm	24	490°C-20min	no	yes
3	NiTi DFT10%	80 μm	8 mm	80	500°C-15min	no	no
4	NiTi DFT10%	80 μm	8 mm	80	500°C-15min	no	yes
5	NiTi	100 μm	4mm	16	490°C-15min	no	no
6	NiTi	100 μm	4mm	16	490°C-15min	no	yes
7	NiTi	100 μm	4mm	16	490°C-15min	yes	no
8	NiTi	100 μm	4mm	16	490°C-15min	yes	yes
9	Phynox	80 μm	8mm	80	550°C-3h	no	no
10	Phynox	80 μm	8mm	80	550°C-3h	no	yes
11	Phynox	80 μm	8mm	80	550°C-3h	yes	no
12	Phynox	80 μm	8mm	80	550°C-3h	yes	yes
13	NiTi	50 μm	5 mm	64	490°C-15min	no	no
14	NiTi DFT10%	80 μm	+/- 4 mm	56	490°C-15min	no	no
15	NiTi DFT10%	80 μm	+/- 4 mm	56	500°C-30 min	no	no

As susceptibility artifacts have been previously studied with a simple geometric model which allows avoiding any other kind of artifact, we focused here on the RF artifacts induced by the presence of these different stents. The key parameter in the frame of this study is thus the spins flip angle. It is essential to remind that the spins flip angle is related to the intensity and the application time of the oscillating magnetic field B_1 (equation (4.3)) and that, when RF artifacts occur, the real spins flip angle inside the stents lumen is different than the one expected from equation (4.3). This induces a difference in the signal intensity between the area inside the lumen of the stent and the surrounding medium.

Let us first focus on Nitinol and NiTiDFT10% stents (stents # 1 to 6, see Figure 4.24). First of all, we can point out again the clearly more important sensitivity of SE sequences to RF artifacts compared to GRE sequences. On the other hand, susceptibility artifacts are much more important on GRE images than on the SE ones. The signal intensity inside the stents lumen is clearly different for GRE sequences than for SE sequences.

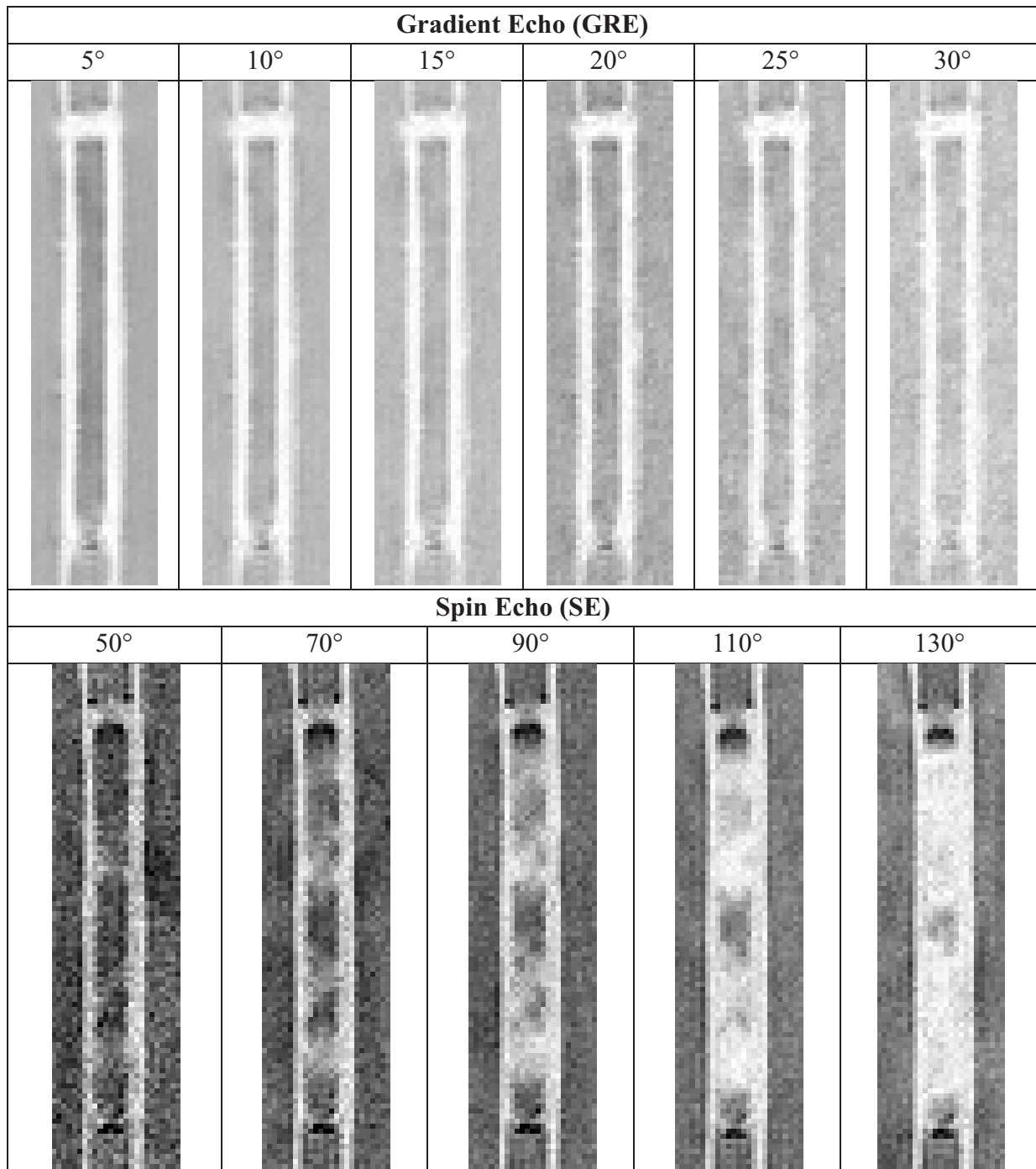


Figure 4.24. MRI images of the stent #1 obtained with various flip angles (°) with GRE and SE sequences

Regarding the GRE sequences, a slight hypersignal can be pointed out inside the stent lumen when small flip angles are used. This hypersignal is less and less pronounced as the flip angle is increased. This behavior is opposite to the one usually observed with RF artifacts and could be explained by the nature of the electrically conductive loops inducing these artifacts. Indeed, these stents being composed of braided wires covered with a relatively thick oxide layer, the nature of the electrical contacts between these wires is more capacitive than inductive. Furthermore, in capacitive electric circuits, the induced current has a 180° phase difference with the induced electromotive force (and therefore with the oscillating magnetic

field B_1). This leads to a slight increase of spins flip angle inside the lumen of the stents and thus a slight hypersignal (instead of a hyposignal) which has already been reported by Camacho *et al.*⁴⁰¹. It also clearly appears that this hypersignal is less and less pronounced as the flip angle is increased. A reasonable hypothesis to explain this behavior is that, with a low flip angle, the TR (repetition time of the sequence) is long enough to allow a complete regrowth of the longitudinal component of the spins magnetization vector both inside and outside the stent. On the contrary, when the applied flip angle is bigger, it seems that the real spins flip angle inside the stents lumen is too important to allow a complete regrowth of the longitudinal component of the spins magnetization vector between two repetitions of the sequence. This induces a decrease of the signal intensity inside the stent lumen while, outside the stent, the applied (non-altered) flip angle is still small enough to allow a complete regrowth of the longitudinal component of the spins magnetization vector between two repetitions of the sequence. By increasing the flip angle, one thus reaches a situation where the signal outside the stent keeps increasing while the signal inside the stent lumen is limited by the regrowth of the longitudinal component of the spins magnetization vector.

Regarding the images obtained with SE sequences, the origin of the signal heterogeneity inside the stents lumen is not clear. However, signal variations inside the lumen definitely depend on the flip angle. This is a clear evidence of the fact that these signal variations are related to RF artifacts.

The same observations can be made for the stents # 5 and 6 as well as for the stents # 13 to 15. This indicates that, even if the stent geometry (number of wires in the braid, wires diameter and stent diameter) and the electrical conductivity of the wires (Nitinol or Nitinol with a platinum core for DFT wires) have an evident impact on the intensity of the resulting RF artifacts, similar surface states induce RF artifacts of the same nature.

Note also that no significant difference between stents submitted or not to the ethylene oxide sterilization treatment could have been observed. Therefore, as observed for the susceptibility artifacts, the sterilization treatment does not seem to have a significant impact on the resulting RF artifacts.

Stents # 7 and 8 (chemically etched) seem to induce much less pronounced RF artifacts than the non-etched ones (see Figure 4.25). Regarding the GRE sequences results, no significant difference of the signal intensity inside and outside the stent lumen could have been pointed out even with the lowest flip angle. Regarding the images obtained with SE sequences, the signal intensity is quite homogeneous except for very high flip angle values. Again, the ethylene oxide sterilization treatment does not seem to induce any significant variation of the stent behavior in MRI. Note the poor image quality obtained for these stents with GRE sequences is not due to the presence of the stent but to an aliasing phenomenon (due to a too small sampling area).

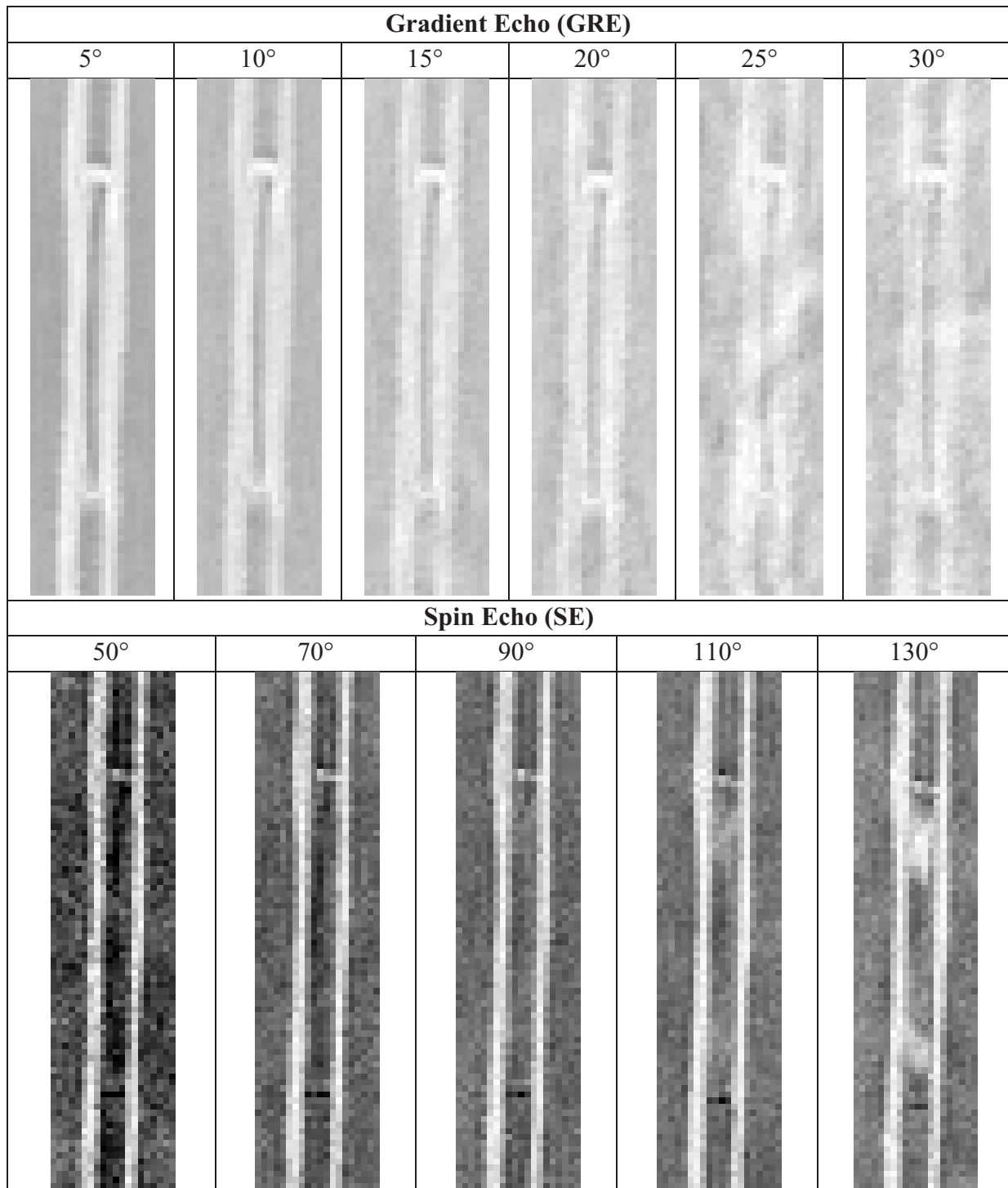


Figure 4.25. MRI images of the stent #7 obtained with various flip angles (°) with GRE and SE sequences

Four Phynox stents were assessed the same way (stents # 9 to 12). For all these stents, very important susceptibility artifacts can be pointed out (as observed in the frame of the susceptibility artifacts study). Regarding the RF artifacts, the non-etched stents (stents # 9 and 10, see Figure 4.26) have a behavior similar to the non-etched Nitinol and NiTiDFT10% stents but much less pronounced. The chemically etched Phynox stents (stents # 11 and 12, see Figure 4.27) show the classical behavior related to RF artifacts with GRE sequences i.e.

the signal (weak and homogeneous inside the stent lumen) increases when the applied flip angle is increased. The images of these stents obtained with SE sequences show a nearly complete signal loss into the stent lumen for all the tested flip angles. Thus in this case the chemical etching treatment induces the appearance of electrical contacts between the wires and these electrical contacts are important enough to result in inductive conductive loops rather than capacitive ones as it was the case when the original oxide layer is conserved. Note that, again, the ethylene oxide sterilization treatment does not seem to have a significant influence on the Phynox stent behavior in MRI.

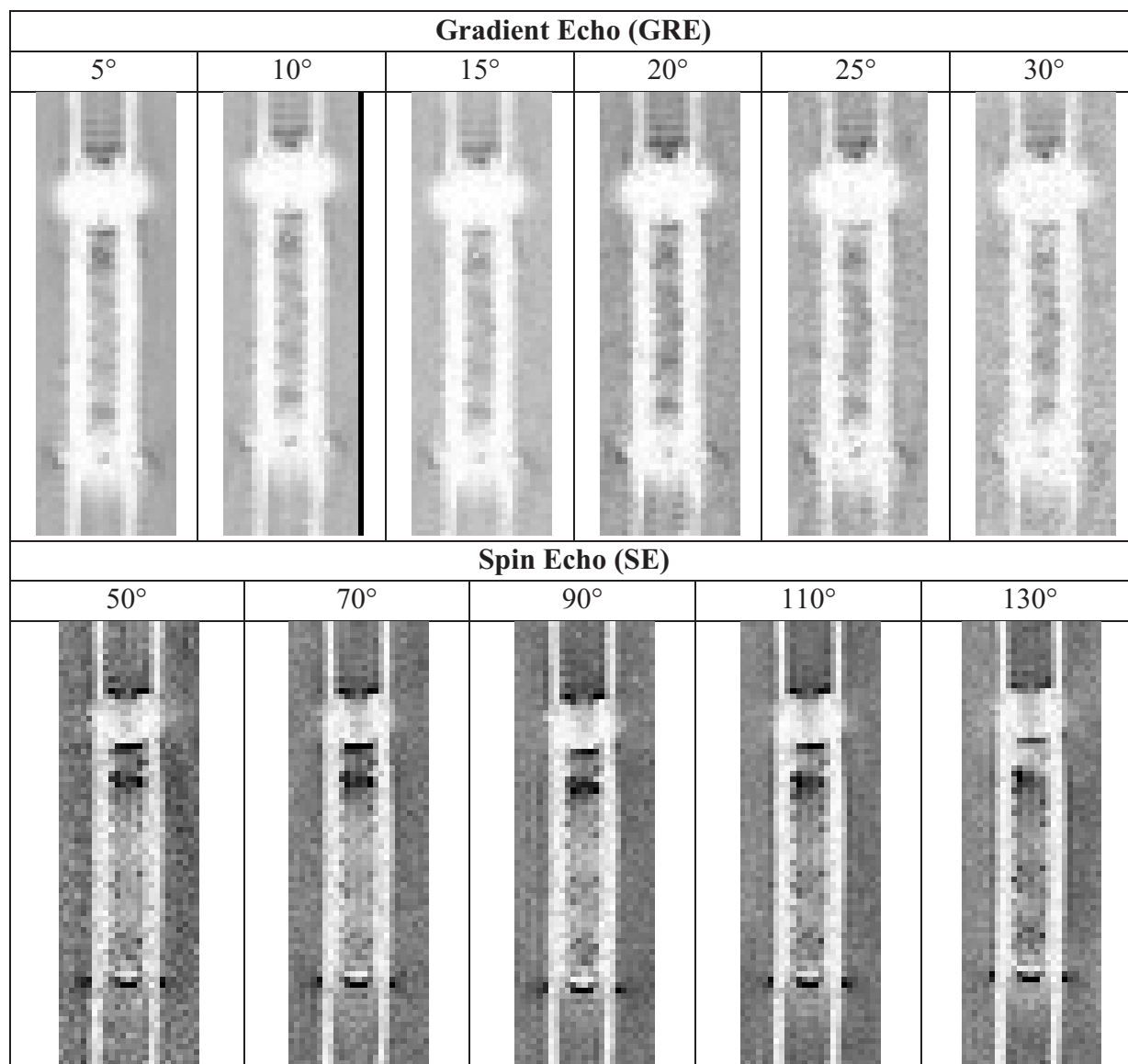


Figure 4.26. MRI images of the stent #9 obtained with various flip angles (°) with GRE and SE sequences

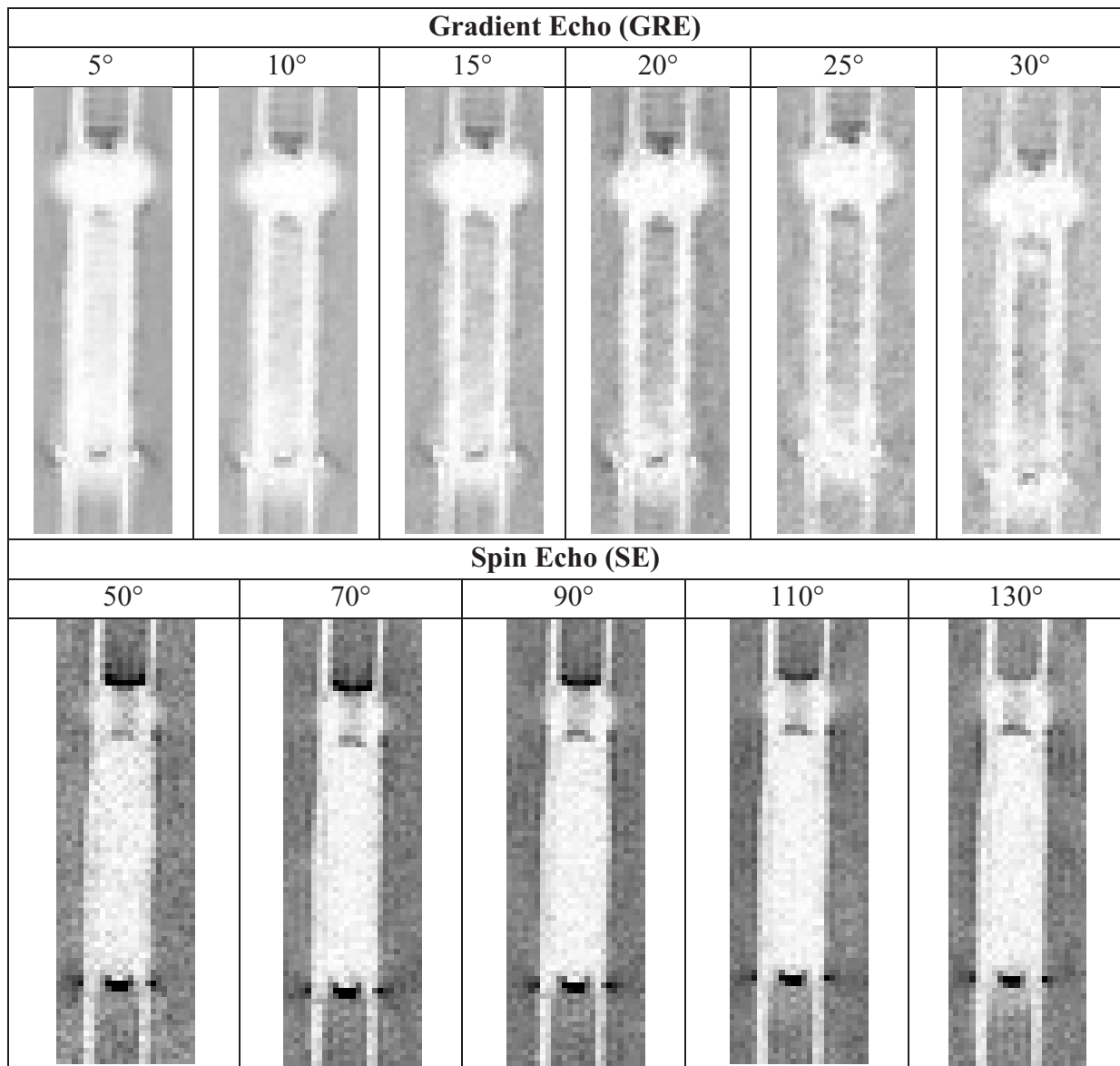


Figure 4.27. MRI images of the stent #11 obtained with various flip angles (°) with GRE and SE sequences

Finally, the imaging of a commercial Nitinol stent has been carried out: the Enterprise stent provided by Cordis Corporation (Johnson&Johnson). The Enterprise is a laser cut Nitinol stent thus there is a very good electrical connection between the different struts. Therefore, the Enterprise stent should exhibit the classical RF artifacts behavior. This behavior can be actually observed (see Figure 4.28) even if it is much less pronounced than for the Phynox etched stents (stents # 11 and 12). This could be explained by the fact that the braided stents exhibit much more current loops per unit area than the Enterprise stent does.

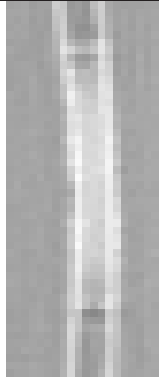
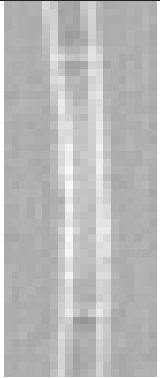
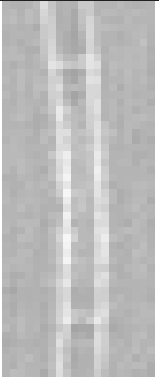
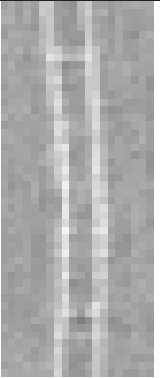
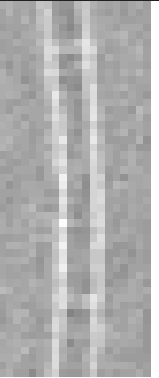
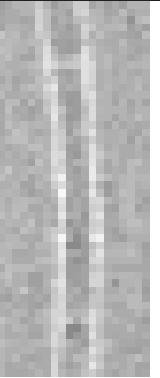
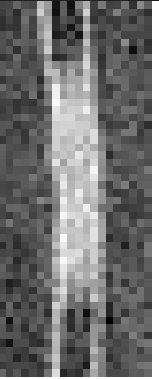
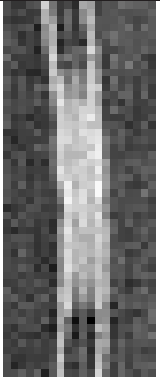
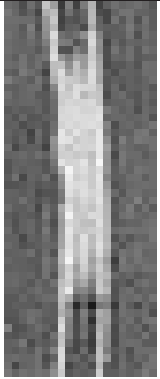
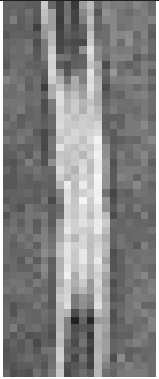
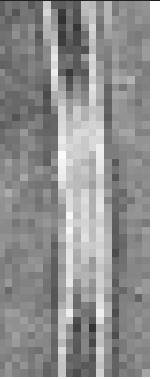
Gradient Echo (GRE)					
5°	10°	15°	20°	25°	30°
					
Spin Echo (SE)					
50°	70°	90°	110°	130°	
					

Figure 4.28. MRI images of the Cordis Enterprise Nitinol stent obtained with various flip angles (°) with GRE and SE sequences

4.2.2.3. Study of the stent composition and orientation on the RF artifacts

In the frame of this study, 3 stents have been examined: a first one composed of 40 braided NiTiDFT30% 40 μm diameter wires, a second one composed of 40 braided Nitinol 50 μm diameter wires and a last (hybrid) one composed of 8 Nitinol 50 μm diameter wires and 32 NiTiDFT30% 40 μm diameter wires braided together. All these stents were submitted to a shape setting heat treatment, a chemical etching and an ethylene oxide sterilization treatment.

They were placed in the phantom described in section 4.2.1.1 and imaged with two typical sequences (a SE sequence and a GRE sequence) and different flip angles. These sequences are fully described in Annex 3.2. Each imagery experiment has been repeated with the stent in two extreme positions: parallel and perpendicular to the main magnetic field B_0 . The obtained images are presented in Figures 4.29, 4.30 and 4.31.

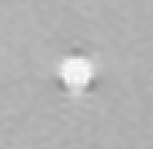
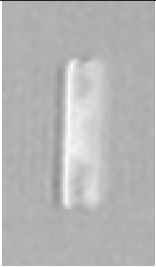
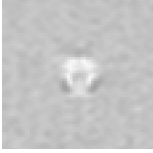
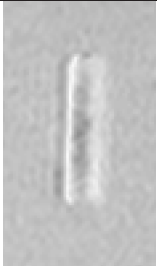
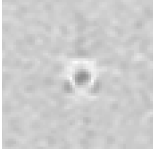
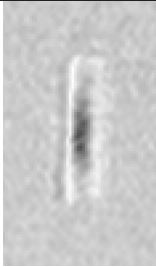
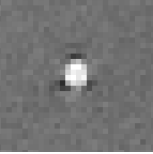
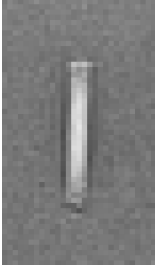
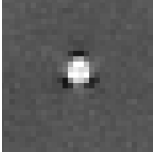
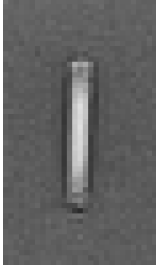
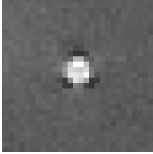
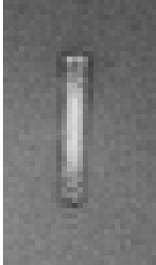
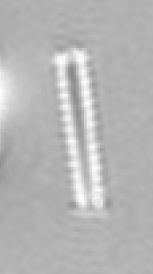
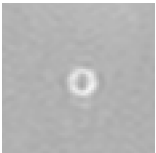
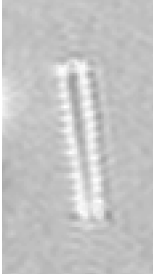
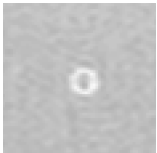
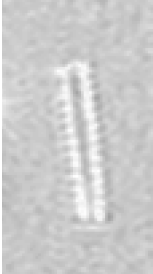
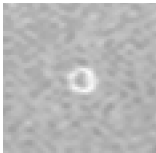
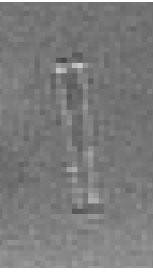
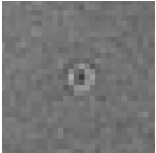
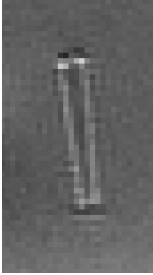
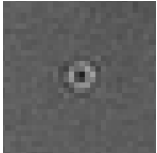
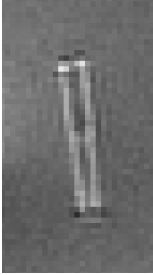
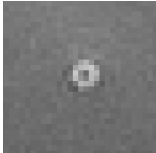
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GRE						
	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
SE						
Parallel to B_0						
	Sagittal Flip angle 10°	Transverse Flip angle 10°	Sagittal Flip angle 20°	Transverse Flip angle 20°	Sagittal Flip angle 30°	Transverse Flip angle 30°
GRE						
	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
SE						

Figure 4.29. MRI images of the stent NiTiDFT30% oriented parallel or perpendicular to the main magnetic field B_0 obtained with various flip angles ($^\circ$) with GRE and SE sequences

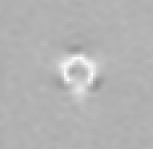
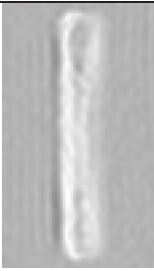
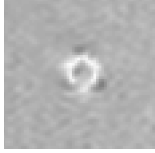
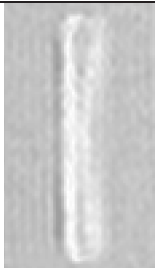
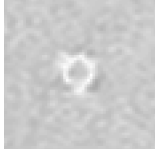
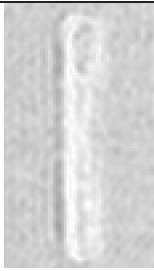
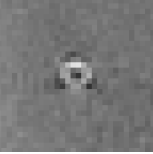
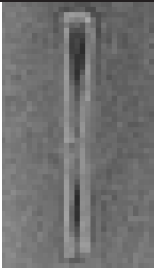
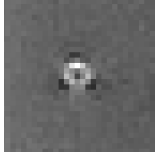
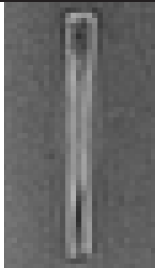
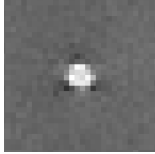
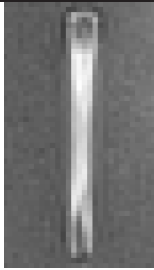
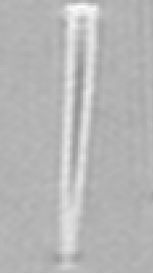
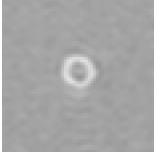
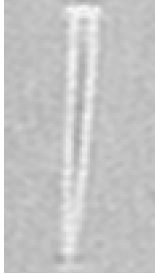
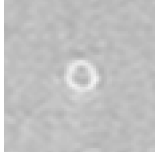
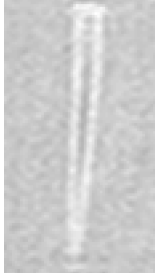
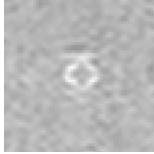
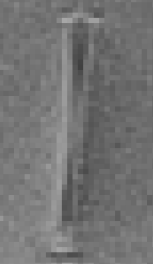
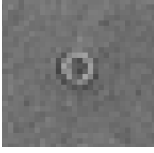
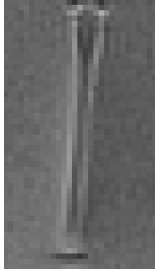
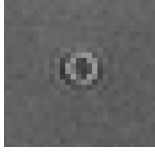
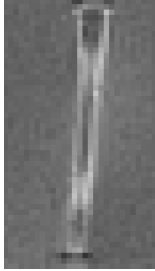
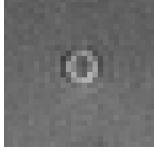
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SE	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
						
Parallel to B_0						
GRE	Sagittal Flip angle 10°	Transverse Flip angle 10°	Sagittal Flip angle 20°	Transverse Flip angle 20°	Sagittal Flip angle 30°	Transverse Flip angle 30°
						
SE	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
						

Figure 4.30. MRI images of the stent Nitinol oriented parallel or perpendicular to the main magnetic field B_0 obtained with various flip angles ($^\circ$) with GRE and SE sequences

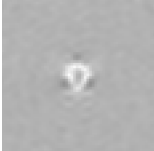
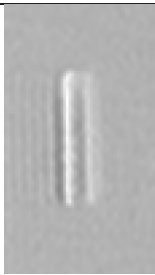
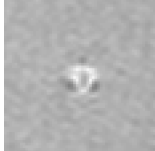
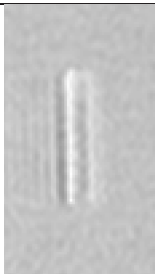
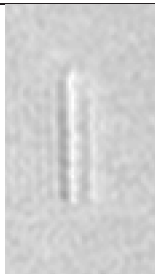
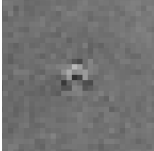
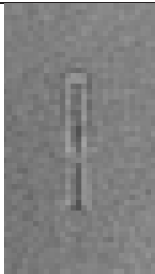
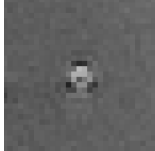
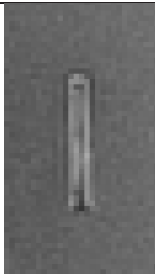
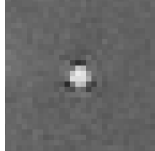
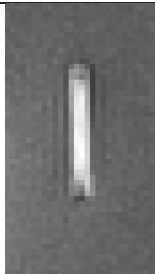
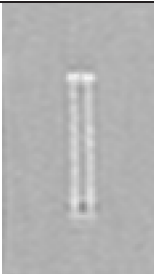
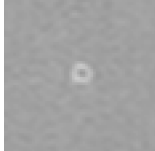
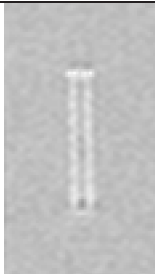
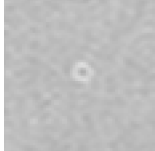
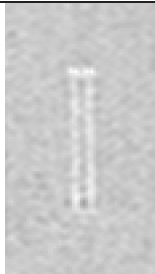
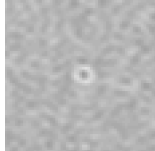
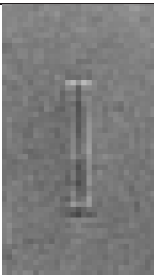
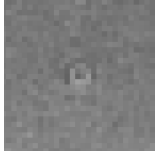
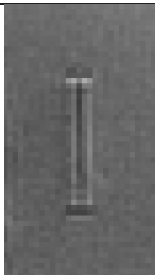
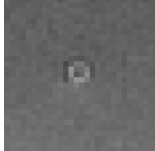
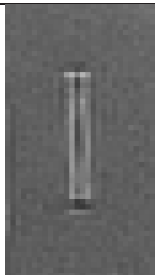
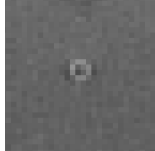
Perpendicular to B_0						
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SE	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
						
Parallel to B_0						
GRE	Sagittal Flip angle 10°	Transverse Flip angle 10°	Sagittal Flip angle 20°	Transverse Flip angle 20°	Sagittal Flip angle 30°	Transverse Flip angle 30°
						
SE	Sagittal Flip angle 50°	Transverse Flip angle 50°	Sagittal Flip angle 90°	Transverse Flip angle 90°	Sagittal Flip angle 130°	Transverse Flip angle 130°
						

Figure 4.31. MRI images of the hybrid stent Nitinol/NiTIDFT30% (8/32) oriented parallel or perpendicular to the main magnetic field B_0 obtained with various flip angles ($^\circ$) with GRE and SE sequences

All these stents induce susceptibility artifacts of a reasonable size in the readout gradient direction. When the stents are placed parallel to B_0 , these susceptibility artifacts are limited to an area really close to the stent wall.

When the implants are parallel to the main magnetic field, the induced RF artifacts are quite weak even with SE sequences (particularly sensitive to RF artifacts). On the contrary, when the stents are perpendicular to B_0 , a complete signal loss can be observed for SE sequences at high flip angles. It thus clearly appears that the stent orientation has a significant influence on the resulting RF artifacts.

To explain the orientation influence on RF artifacts, let us consider a braided stent parallel to the main magnetic field B_0 (see Figure 4.32). The rotating magnetic field B_1 is thus perpendicular to the stent (the B_1 rotation plane being perpendicular to the Figure 4.32(a) plane). In this situation, the conductive loops responsible of the appearance of RF artifacts are the meshes of the braid. These ones are very small (important variations of the magnetic flux) but each conducting loop is constituted of four small conducting segments and four contact points susceptible to block the induced currents. Let us now consider the same stent perpendicular to the main magnetic field (see Figure 4.32(b)). In this situation, the conductive loops responsible of the appearance of RF artifacts follow the entire circumference of the stent wall. These ones are much bigger than in the previous situation (smaller variations of the magnetic flux) but each conductive loop is constituted of only two long conducting segments and two contact points susceptible to block the induced currents. It clearly appears from the MRI examination that these bigger conductive loops are responsible of more important RF artifacts.

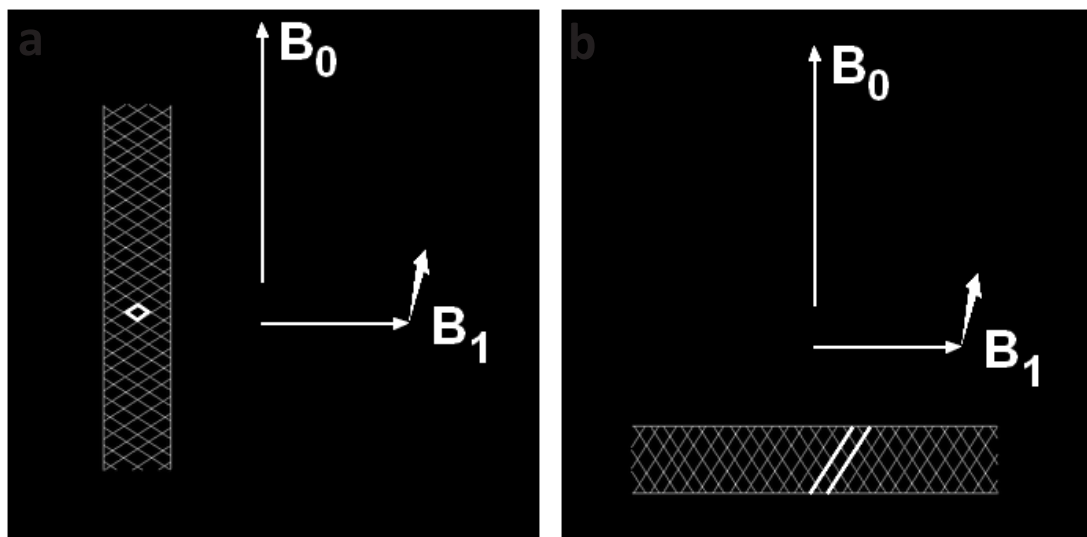


Figure 4.32. Schematic representation of a braided stent oriented parallelly (a) and perpendicularly (b) to the main magnetic field, of the different applied magnetic fields and of the corresponding conductive loops responsible of the appearance of RF artifacts.

From the comparison of the different stents composition, it can be observed that the introduction of pure Nitinol wires (less electrically conductive than the Pt core in the NiTiDFT wires) in a NiTiDFT30% braided stent clearly induces a decrease of the RF artifacts

intensity. Therefore, it can be reasonably concluded that the use of a weakly conductive material and the presence of an insulating material at the surface of the braided wires are two parameters allowing a significant limitation of the RF artifacts.

4.2.3. Electrodeposition, characterization and assessment of the impact on MRI imaging of thin nickel and cobalt oxide layers

Nickel oxide (NiO) and cobalt oxide (CoO) are known to have antiferromagnetic properties. Thus *a priori* the creation of an antiferromagnetic NiO or CoO layer on the surface of Nitinol or Phynox wires (respectively) could be beneficial for the MRI behavior of these materials. Therefore, in the frame of this chapter topic, it was interesting to assess the possible decrease of susceptibility artifacts induced by such oxide layers.

4.2.3.1. Electrodeposition of nickel and cobalt layers on Nitinol and Phynox

In order to make the surface characterization easier, the deposition parameters were optimized on plane mechanically polished Nitinol and Phynox substrates (for the substrates preparation method, see Chapters 2 and 3).

4.2.3.1.1. *Electrodeposition of nickel on Nitinol*

The nickel electrodeposition has been carried out in a nickel chloride (300g/l) and boric acid (30g/l) aqueous solution under slight and constant stirring. We used a two electrodes electrochemical setup with a pure nickel wire as the counter-electrode and the Nitinol substrate as the working electrode. Note that the Nitinol surface has been activated by immersion 1 h in a 30% vol. H₂SO₄ aqueous solution prior electrodeposition. The electrodeposition was carried out in galvanostatic conditions by applying a constant current density of -10 mA/cm² to the working electrode for 10 minutes. The Nitinol substrate was then copiously rinsed with ultra pure water and cleaned by sonication 15 minutes in ultra pure water before being submitted to an oxidizing heat treatment of 15 minutes at 480°C. The Nitinol substrate was then cleaned again by sonication 15 minutes in ultra pure water before being analyzed or sent for an ethylene oxide sterilization treatment before analysis.

First, the thickness and roughness of the obtained deposit has been characterized (before and after the heat treatment) with a DEKTAK profilometer and its morphology by SEM analysis. Representative SEM pictures are presented in Figures 4.33 and 4.34. Before the heat treatment, the nickel coating has a mean thickness of 1.7 µm and a mean roughness of 90 nm. SEM pictures of this deposit shows that the nickel layer obtained under these conditions is complete, dense and homogeneous. The highly crystalline morphology of this nickel layer is well visible on high magnification images (Figure 4.33).

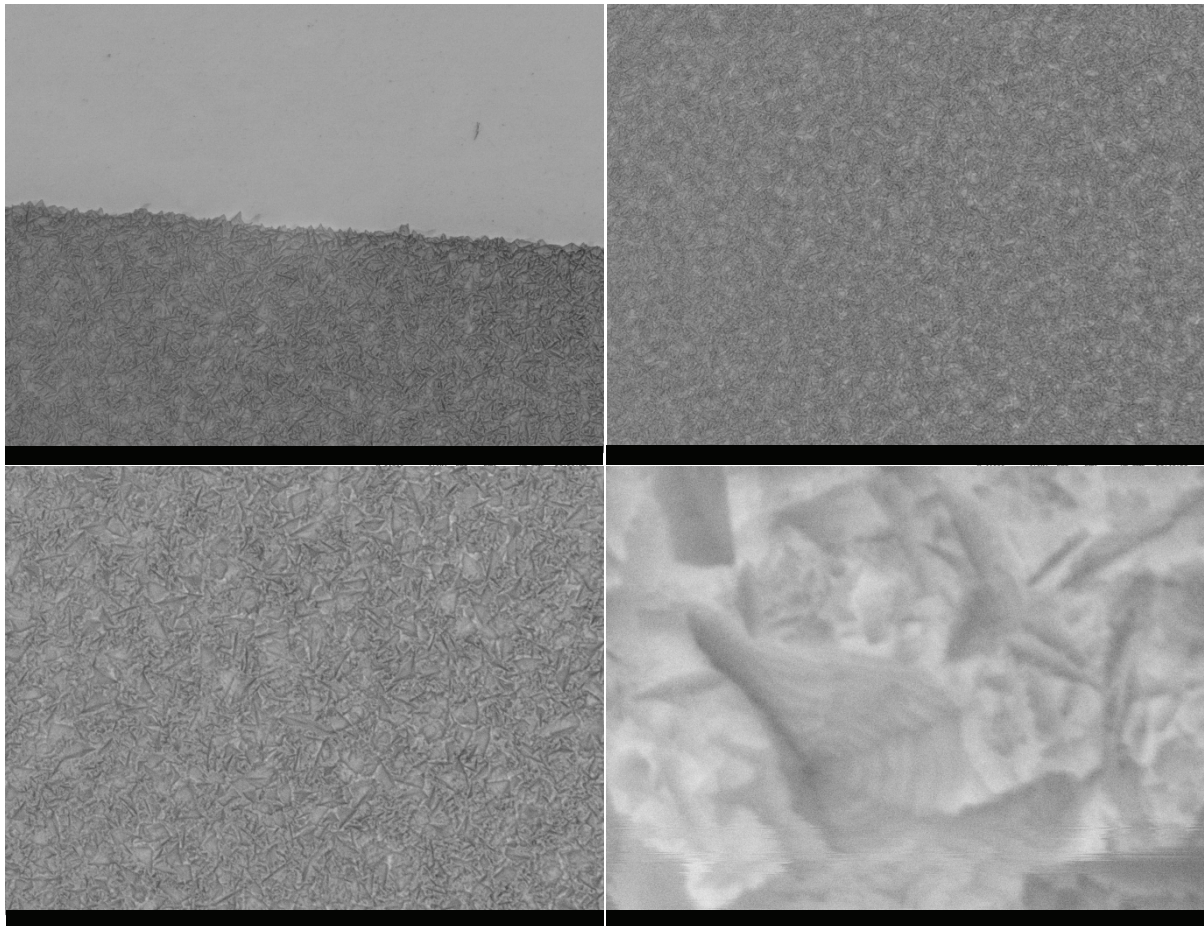


Figure 4.33. Representative SEM pictures of the nickel layer galvanostatically (-10 mA/cm^2) electrodeposited on mechanically polished Nitinol substrates in a NiCl_2 (300g/l)/ H_3BO_3 (30g/l) aqueous solution.

After the oxidative heat treatment of 15 minutes at 480°C , a slightly lower mean thickness of $1.3 \text{ }\mu\text{m}$ has been measured as well as a slightly lower mean roughness of 50 nm . SEM observation of the nickel deposit after the heat treatment shows that the nickel layer remains defect free and homogeneous. However, the microscopic structure has been altered: while a highly crystalline morphology was observed on high magnification pictures of the untreated deposit, the heat treated deposit appears to be much less crystalline (Figure 4.34).

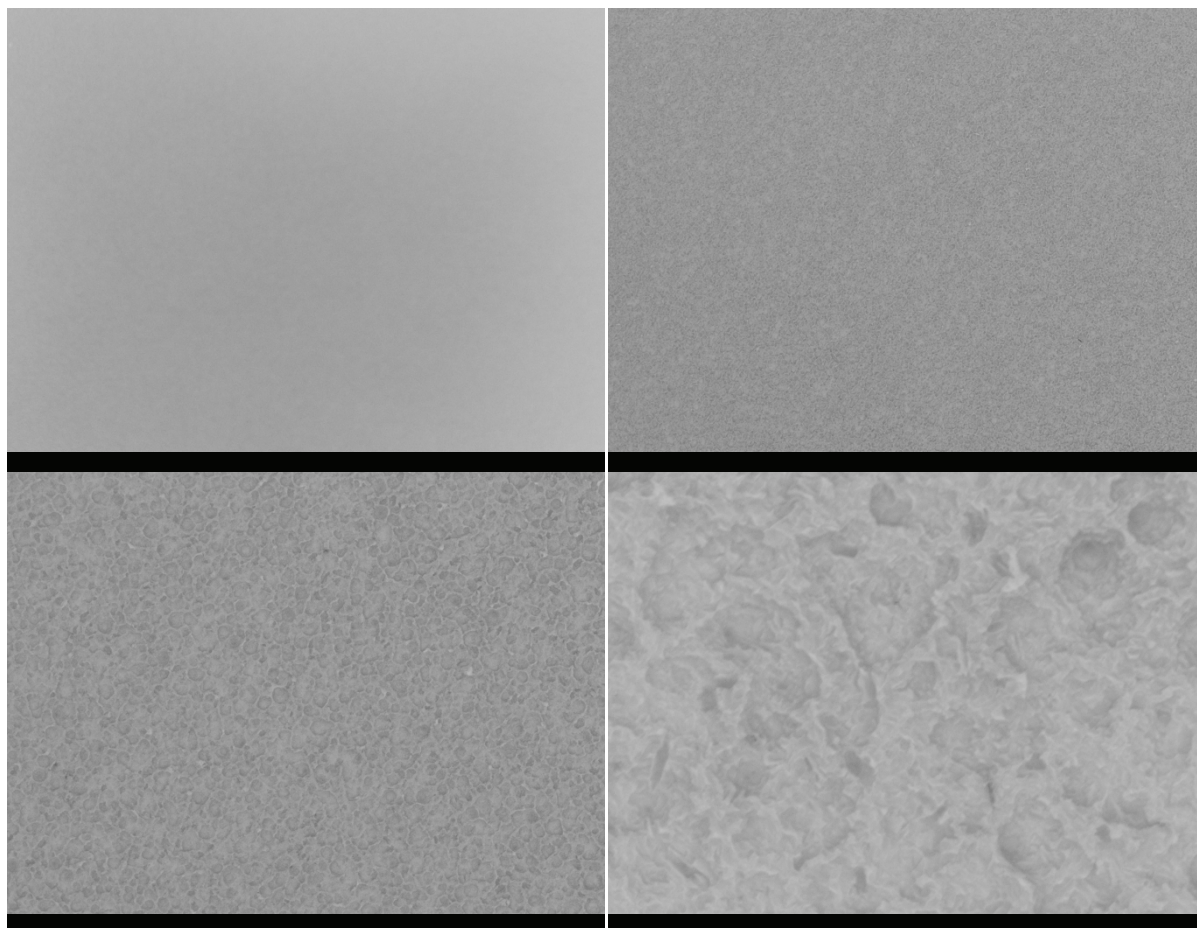


Figure 4.34. Representative SEM pictures of the nickel layer galvanostatically (-10 mA/cm^2) electrodeposited on mechanically polished Nitinol substrates in a NiCl_2 (300g/l)/ H_3BO_3 (30g/l) aqueous solution and heat treated at 480°C for 15 minutes.

The XPS analysis of this deposit has been carried out after the heat treatment before and after the ethylene oxide sterilization treatment. The corresponding high resolution Ni2p core level photoelectron peaks spectra are presented in Figure 4.35. Before the ethylene oxide sterilization treatment, the Ni2p high resolution spectrum exhibits a main Ni2p_{3/2} component centered at 854.2 eV attributed to NiO and a smaller one at 856.2 eV characteristic of the presence of nickel hydroxide ($\text{Ni}(\text{OH})_2$). No component could be observed at 852.2 eV which is the characteristic binding energy of Ni2p_{3/2} photoelectrons from nickel in the metallic state. The oxidative heat treatment allows thus to obtain a completely oxidized nickel deposit without metallic nickel at least in the first $\sim 10 \text{ nm}$ below the extreme surface (analysis depth of the spectrometer). The presence of nickel hydroxide is probably due to the hydroxylation of the NiO at the extreme surface.

After the sterilization process, the component relative to the presence of NiO (centered at 854.2 eV) is clearly less important while the main component is now centered at 856.2 eV and attributed to nickel hydroxide. This could be explained by the long time exposure of the coating to a hot and extremely humid atmosphere during the sterilization process. Again, no component could be observed at 852.2 eV which is the characteristic binding energy of Ni2p_{3/2} photoelectrons from nickel in the metallic state.

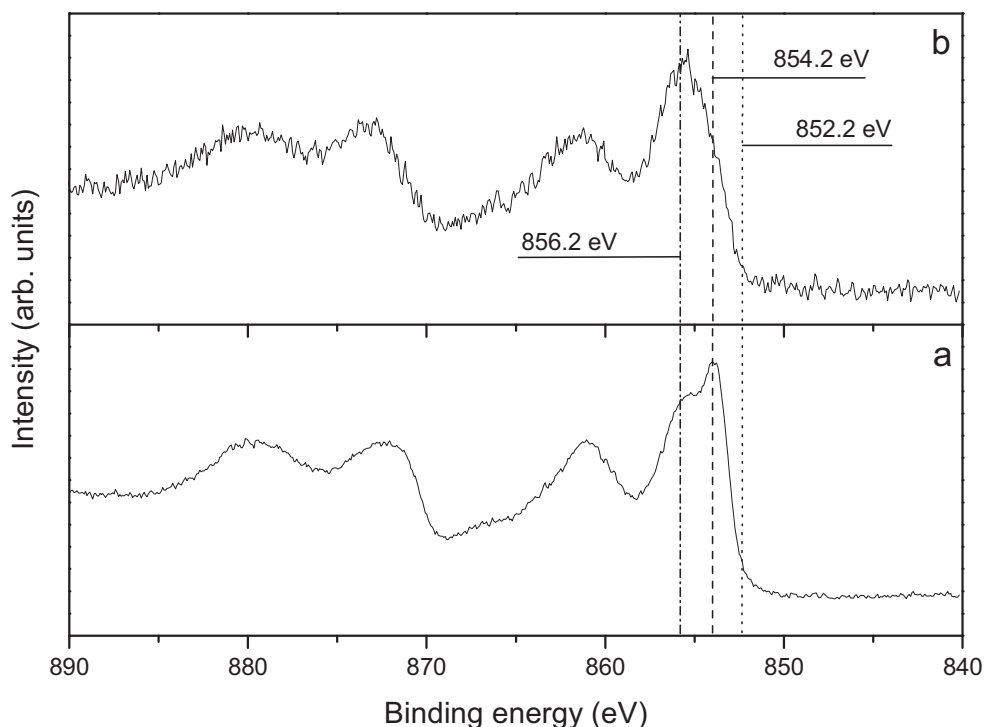


Figure 4.35. High resolution XPS spectra of the Ni2p core level photoelectron peaks of nickel layer galvanostatically (-10 mA/cm^2) electrodeposited on mechanically polished Nitinol substrates in a NiCl_2 (300g/l)/ H_3BO_3 (30g/l) aqueous solution and heat treated at 480°C for 15 minutes before (a) and after (b) being submitted to an ethylene oxide sterilization treatment.

4.2.3.1.2. Electrodeposition of cobalt on Phynox

The cobalt electrodeposition has been carried out in a cobalt chloride (550g/l) and boric acid (30g/l) aqueous solution under slight and constant stirring. Again, a two electrodes electrochemical setup has been used with a pure cobalt plate as the counter-electrode and the Phynox substrate as the working electrode. Note that the Phynox surface has been activated by immersion 10 minutes in a 30% vol. H_2SO_4 aqueous solution. The electrodeposition was carried out in galvanostatic conditions by applying a constant current density of -1 mA/cm^2 to the working electrode for 10 minutes. The Phynox substrate was then copiously rinsed with ultra pure water and cleaned by sonication 15 minutes in ultra pure water before being submitted to an oxidizing heat treatment of 3 hours at 550°C . A cleaning by sonication 15 minutes in ultra pure water has been carried out before the coated Phynox substrates have been analyzed or sent for an ethylene oxide sterilization treatment before analysis.

The morphology of the obtained cobalt deposits has been characterized (before and after the heat treatment) by SEM analysis. Representative SEM pictures are presented in Figures 4.36 and 4.37. The cobalt layer observed before the heat treatment appears to be complete, dense

and homogeneous. A quite crystalline morphology of this cobalt layer is also visible on high magnification images.

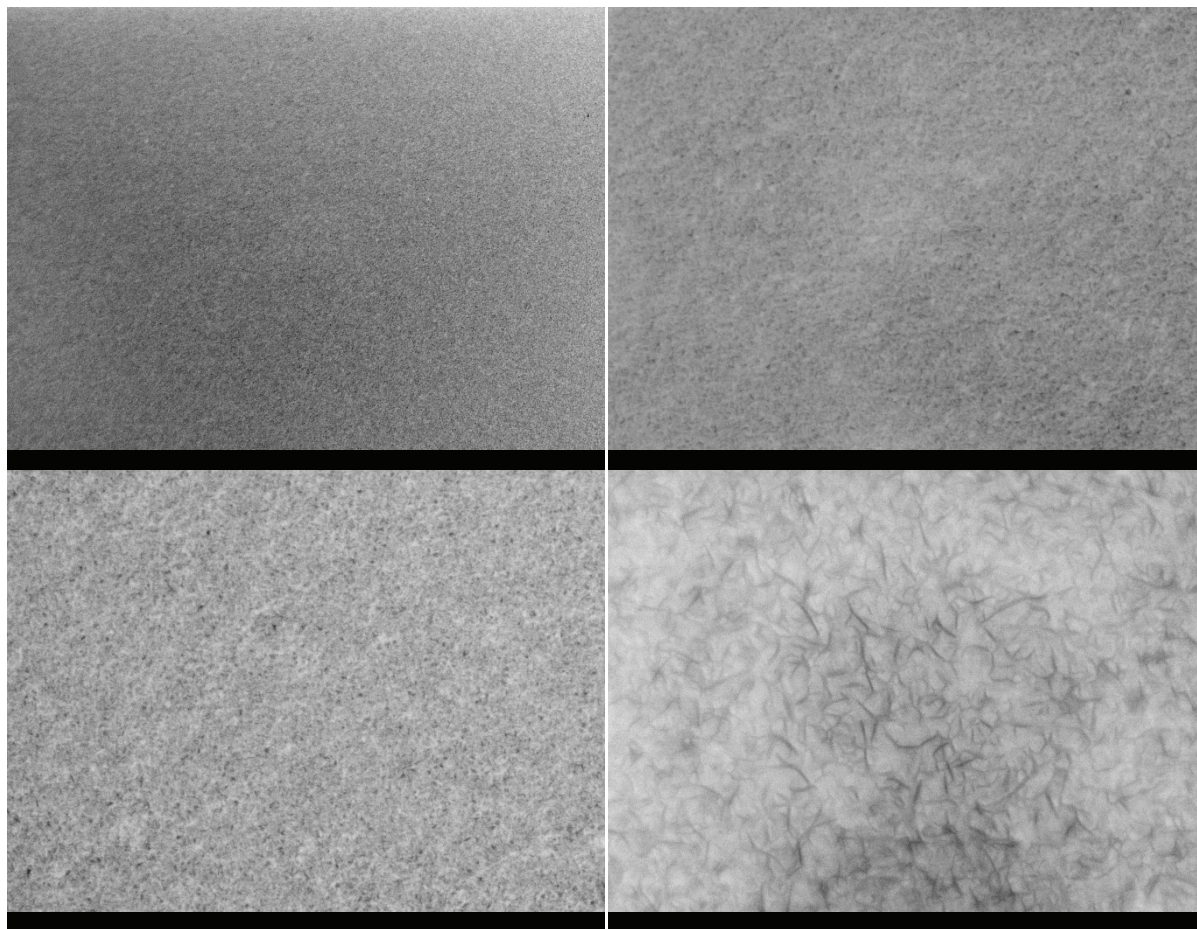


Figure 4.36. Representative SEM pictures of the cobalt layer galvanostatically (-1 mA/cm^2) electrodeposited on mechanically polished Phynox substrates in a CoCl_2 (550g/l)/ H_3BO_3 (30g/l) aqueous solution.

After the oxidative heat treatment of 3 hours at 550°C , the cobalt layer remains complete and homogeneous but the initial crystalline structure visible at high magnification before the heat treatment has changed to a granular structure. This heat treated deposit has a mean thickness of 320 nm and a mean roughness of 90 nm (vs. 15 nm for a mechanically polished bare Phynox substrate).

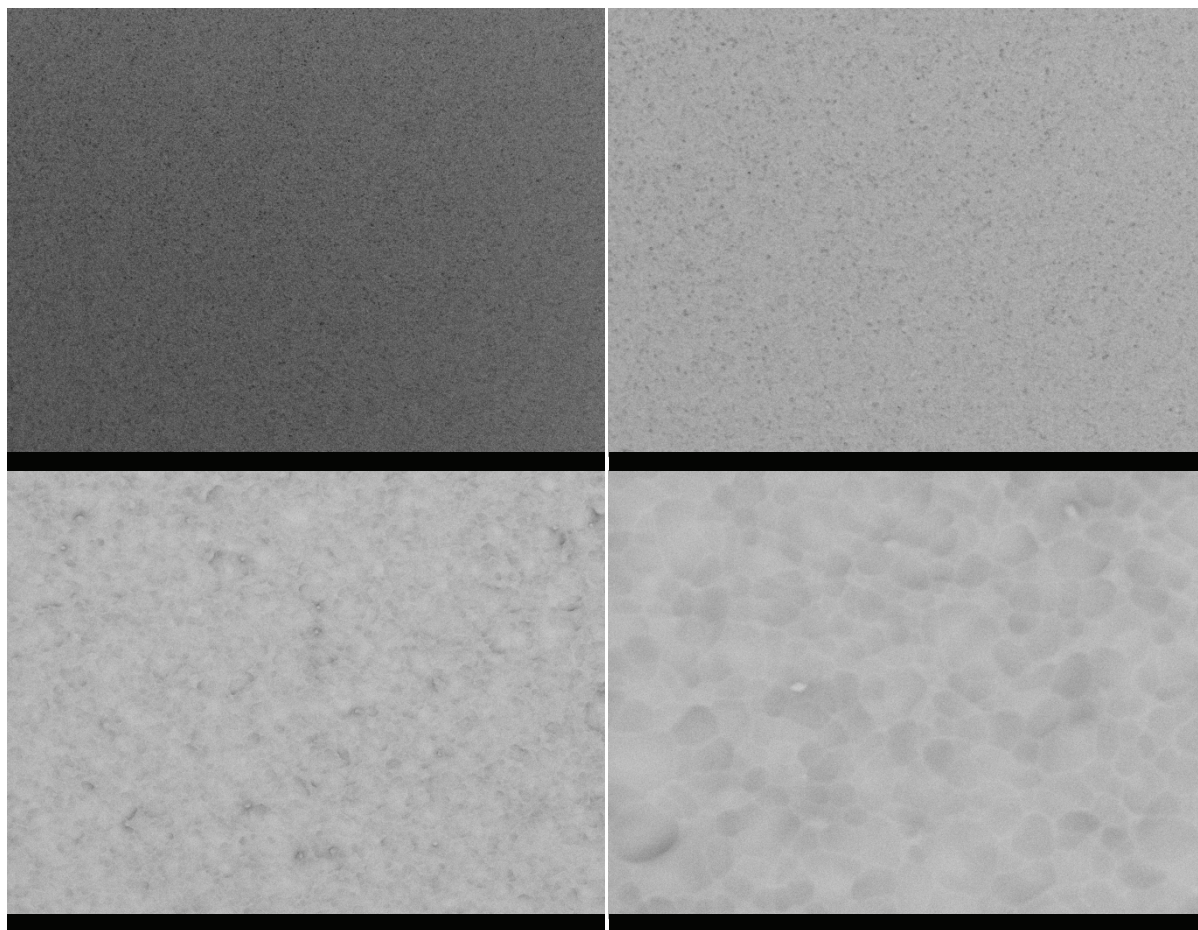


Figure 4.37. Representative SEM pictures of the cobalt layer galvanostatically (-1 mA/cm^2) electrodeposited on mechanically polished Phynox substrates in a CoCl_2 (550g/l)/ H_3BO_3 (30g/l) aqueous solution and heat treated at 550°C for 3 hours.

Again, the XPS analysis of the deposit has been carried out after the heat treatment before and after the ethylene oxide sterilization treatment. The corresponding high resolution $\text{Co}2\text{p}$ core level photoelectron peaks spectra are presented in Figure 4.38. Before the ethylene oxide sterilization treatment, only one main $\text{Co}2\text{p}_{3/2}$ component centered at 780.2 eV attributed to CoO is visible on the XPS $\text{Co}2\text{p}$ high resolution spectrum. Like in the case of nickel deposits, no component characteristic of the cobalt in the metallic state (centered at 778.2 eV) could be observed. The oxidative heat treatment allows thus to obtain a completely oxidized cobalt deposit without metallic cobalt at least in the first $\sim 10 \text{ nm}$ below the extreme surface.

After the sterilization process, no significant difference of the $\text{Co}2\text{p}$ high resolution spectrum could have been observed: only one main component is visible at 780.2 eV, characteristic of the CoO . However, $\text{Co}2\text{p}$ photoelectrons from COOH and $\text{Co}(\text{OH})_2$ species have a very similar binding energy (less than 1 eV difference). It is thus possible that the cobalt oxide at the extreme surface is hydroxylated during the sterilization process (like the nickel oxide layer did) even if the XPS spectrum remains very similar. Again, no component could be observed at 778.2 eV which is the characteristic binding energy of $\text{Co}2\text{p}_{3/2}$ photoelectrons from cobalt in the metallic state.

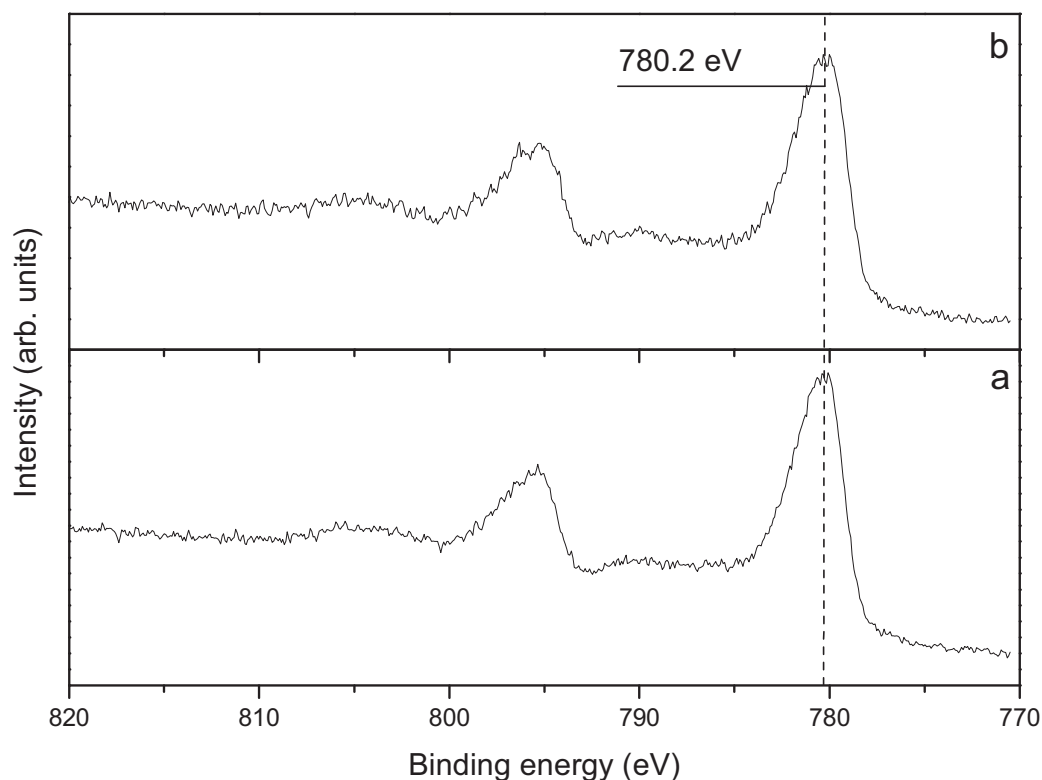


Figure 4.38. High resolution XPS spectra of the Co2p core level photoelectron peaks of cobalt layer galvanostatically (-1 mA/cm^2) electrodeposited on mechanically polished Phynox substrates in a CoCl_2 (550g/l)/ H_3BO_3 (30g/l) aqueous solution and heat treated at 550°C for 3 hours before (a) and after (b) being submitted to an ethylene oxide sterilization treatment.

4.2.3.2. Study of the impact of the nickel oxide and cobalt oxide layers on the MRI behavior of Nitinol and Phynox wires

These coating methods have been applied to Nitinol wires (50 μm , 170 μm and 240 μm diameter) and Phynox wires (80 μm diameter) in order to assess their impact on the susceptibility artifacts of these wires in MRI. The MRI analyses have been carried out with the same phantom and experimental conditions as the ones described in section 4.2.1.1 and the same sequence used for the iterative susceptibility artifact measurement method (section 4.2.1.3.2) i.e. a SE sequence with a bandwidth of 100 Hz/pixel. This sequence is fully described in Annex 3.2.

Regarding Phynox, the MRI examinations of 80 μm diameter wires in four different surface states have been carried out: untreated and sterilized (called “Ste”), heat treated for 3 hours at 550°C and sterilized (called “HT Ste”), coated with an electrodeposited cobalt layer and sterilized (called “Co Ste”) and finally, coated with an electrodeposited cobalt layer, heat

treated for 3 hours at 550°C and sterilized (called “Co HT Ste”). The corresponding transverse MRI images are presented in Figure 4.39.

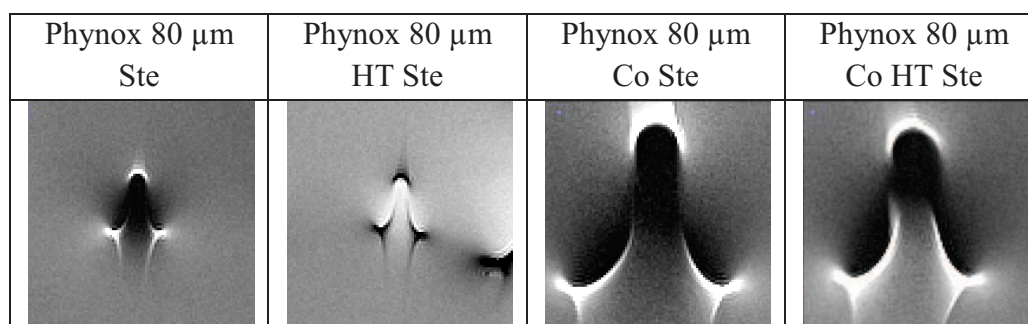


Figure 4.39. Transverse MRI images of a 80 μm diameter Phynox wire untreated and sterilized (Ste), heat treated and sterilized (HT Ste), coated with an electrodeposited cobalt layer and sterilized (Co Ste) and coated with an electrodeposited cobalt layer, heat treated and sterilized (Co HT Ste).

First of all, it clearly appears that the heat treatment of bare Phynox wires induces a slight decrease of the susceptibility artifact size. This confirms the results presented in section 4.2.1.3.2. On the contrary, the “Co Ste” Phynox wire shows a susceptibility artifact 3- to 4-fold bigger than the untreated one (“Ste”). Even if this artifact seems a little smaller when the coated wire is submitted to an oxidative heat treatment (“Co HT Ste”), it clearly appears that this coating is unfavorable to a decrease of the susceptibility artifacts induced by the presence of Phynox wires in MRI.

Similarly, the MRI examinations of 50 μm , 170 μm and 240 μm diameter Nitinol wires in height different surface states have been carried out: untreated (called “bare”), untreated and sterilized (called “Ste”), heat treated for 20 min at 480°C (called “HT”), heat treated for 20 min at 480°C and sterilized (called “HT Ste”), coated with an electrodeposited nickel layer (called “Ni”), coated with an electrodeposited nickel layer and sterilized (called “Ni Ste”), coated with an electrodeposited nickel layer and heat treated for 20 min at 480°C (called “Ni HT”) and finally, coated with an electrodeposited nickel layer, heat treated for 20 min at 480°C and sterilized (called “Ni HT Ste”). The corresponding transverse MRI images are presented in Figures 4.40, 4.41 and 4.42.

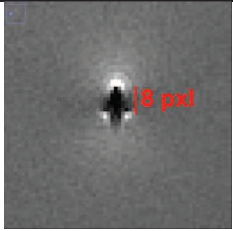
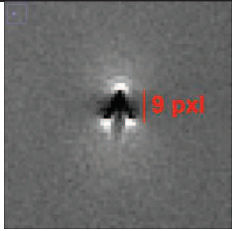
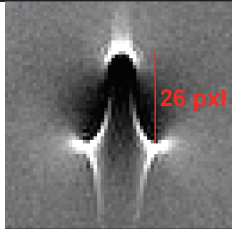
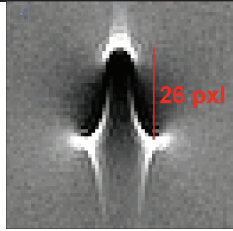
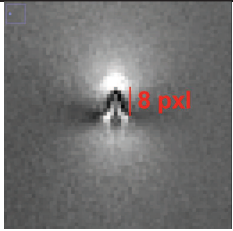
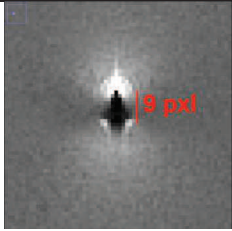
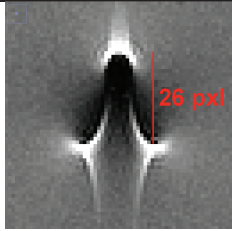
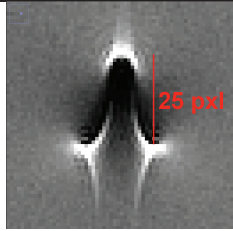
Nitinol 240 μm bare	Nitinol 240 μm HT	Nitinol 240 μm Ni	Nitinol 240 μm Ni HT
			
Nitinol 240 μm Ste	Nitinol 240 μm HT Ste	Nitinol 240 μm Ni Ste	Nitinol 240 μm Ni HT Ste
			

Figure 4.40. Transverse MRI images of a 240 μm diameter Nitinol wire untreated (bare), untreated and sterilized (Ste), heat treated (HT), heat treated and sterilized (HT Ste), coated with an electrodeposited nickel layer (Ni), coated with an electrodeposited nickel layer and sterilized (Ni Ste), coated with an electrodeposited nickel layer and heat treated (Ni HT) and coated with an electrodeposited nickel layer, heat treated and sterilized (Ni HT Ste).

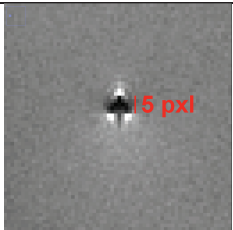
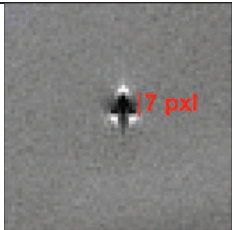
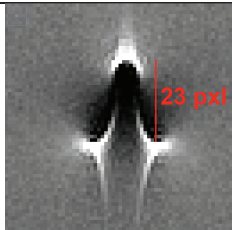
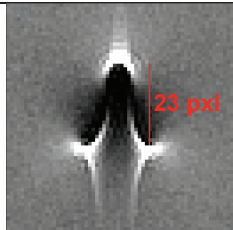
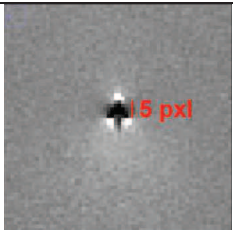
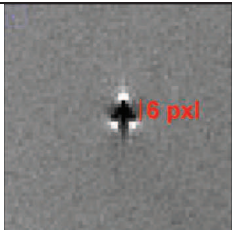
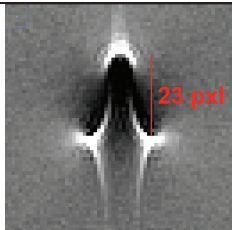
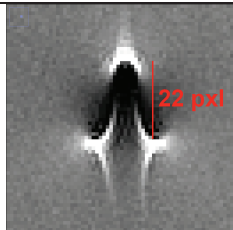
Nitinol 170 μm bare	Nitinol 170 μm HT	Nitinol 170 μm Ni	Nitinol 170 μm Ni HT
			
Nitinol 170 μm Ste	Nitinol 170 μm HT Ste	Nitinol 170 μm Ni Ste	Nitinol 170 μm Ni HT Ste
			

Figure 4.41. Transverse MRI images of a 170 μm diameter Nitinol wire untreated (bare), untreated and sterilized (Ste), heat treated (HT), heat treated and sterilized (HT Ste), coated with an electrodeposited nickel layer (Ni), coated with an electrodeposited nickel layer and sterilized (Ni Ste), coated with an electrodeposited nickel layer and heat treated (Ni HT) and coated with an electrodeposited nickel layer, heat treated and sterilized (Ni HT Ste).

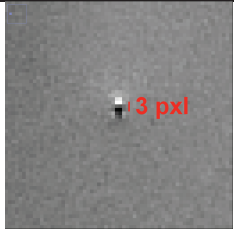
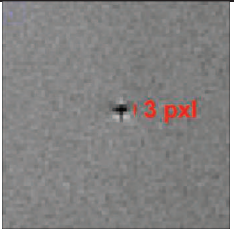
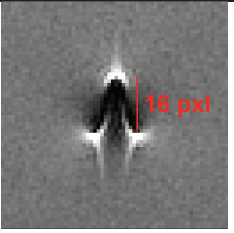
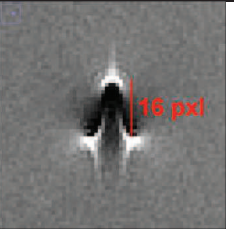
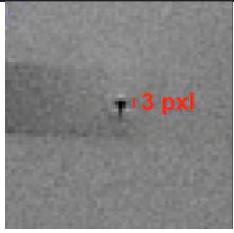
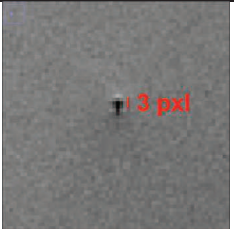
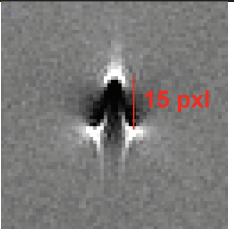
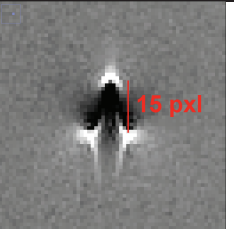
Nitinol 50 μm bare	Nitinol 50 μm HT	Nitinol 50 μm Ni	Nitinol 50 μm Ni HT
			
Nitinol 50 μm Ste	Nitinol 50 μm HT Ste	Nitinol 50 μm Ni Ste	Nitinol 50 μm Ni HT Ste
			

Figure 4.42. Transverse MRI images of a 50 μm diameter Nitinol wire untreated (bare), untreated and sterilized (Ste), heat treated (HT), heat treated and sterilized (HT Ste), coated with an electrodeposited nickel layer (Ni), coated with an electrodeposited nickel layer and sterilized (Ni Ste), coated with an electrodeposited nickel layer and heat treated (Ni HT) and coated with an electrodeposited nickel layer, heat treated and sterilized (Ni HT Ste).

Again, these analyses allow us to confirm the results presented in section 4.2.1.3.2 i.e. unlike Phynox, the heat treatment of Nitinol wires induces a small increase of their susceptibility artifact size. This can be pointed out easily by simply measuring the artifact size (in pixels). Note also that again, the sterilization treatment seems to slightly decrease the susceptibility artifact size of HT Nitinol wires (see Figure 4.41).

Nitinol wires coated with a nickel layer induce much bigger susceptibility artifacts than the uncoated ones. This behavior was expected for the wires coated with a nickel layer and not submitted to a heat treatment given the ferromagnetic nature of metallic nickel. However, no significant improvement of the susceptibility artifact is noticed with sterilization or with a heat treatment of this nickel coating (both oxidative treatments) while the XPS analysis of the heat treated nickel coating showed the presence of NiO in the coating. Therefore, it clearly appears that this coating is unfavorable to a decrease of the susceptibility artifacts induced by the presence of Nitinol wires in MRI. Note that the sterilization of the heat treated nickel coating induces a small decrease of the susceptibility artifact size.

In conclusion, even if nickel oxide (NiO) and cobalt oxide (CoO) are known to have antiferromagnetic properties, the creation of NiO or CoO layer on the surface of Nitinol or Phynox wires (respectively) has a highly negative impact on the MRI behavior of these materials.

4.3. Conclusions

This last chapter aimed to study the impact of different surface treatments and of the imaging parameters and conditions on the MRI visibility of Nitinol and Phynox wires and stents. Two main types of artifacts were investigated: susceptibility and RF artifacts.

In the first part of this study, the influence of the Nitinol and Phynox surface state on their apparent magnetic susceptibility (and therefore the importance of the resulting susceptibility artifact) has been assessed. It appeared that the surface state of the observed material can have a significant influence on the produced susceptibility artifact.

Regarding Nitinol, it has been shown that the shape-setting heat treatment induces an increase of the Nitinol apparent magnetic susceptibility. An increase of the time or the temperature of this treatment reinforces this behavior. The ethylene oxide sterilization treatment slightly increases the Nitinol apparent magnetic susceptibility when applied to untreated wires. On the contrary, it does not have any significant impact when applied on heat treated Nitinol wires except for the ones treated at higher temperatures. Finally, the chemical etching of Nitinol was favorable to a low apparent magnetic susceptibility.

Phynox appeared to be a less suitable material for MRI examinations. Indeed, its apparent magnetic susceptibility is always about 10-fold higher than the one of Nitinol. However, the heat treatment of Phynox induces a slight decrease of its apparent magnetic susceptibility while the chemical etching and the sterilization treatments do not seem to have any significant impact.

In the second part of this chapter, the impact of several parameters on the MRI visibility of braided stents i.e. on the importance of the produced susceptibility and RF artifacts has been studied.

Regarding the susceptibility artifacts, it has been shown that SE sequences are less sensitive and lead to the acquisition of better images than the GRE sequences do. The stent orientation with respect to the main magnetic field is also crucial: when the stent is placed perpendicularly to B_0 , the artifacts are much more important than when the stent is placed parallelly to B_0 . When the stent is oriented parallelly to B_0 , the produced artifacts are localized at the stent extremities. Again, we confirmed that Phynox stents produce much more important susceptibility artifacts than the Nitinol ones.

Contrary to the susceptibility artifacts, RF artifacts are much more important when SE sequences are used than with GRE sequences. Again, the stent orientation with respect to the main magnetic field B_0 and thus to the rotating magnetic field B_1 plane has a strong influence on the intensity of the produced RF artifact: in the case of braided stents such as the ones we studied in the frame of this work, the RF artifacts are more important when the stent is oriented perpendicularly to B_0 . Both for susceptibility and RF artifacts, there is thus an interest in placing the stent as parallel as possible to B_0 . Interestingly, it has been shown that the RF artifacts could be beneficial as they could lead to a signal enhancement in the stent lumen at low flip angles. This behavior has been explained by the nature of the conductive loops (capacitive rather than inductive) and therefore by the geometry of the stents (braided rather than laser cut). It has also been shown that even if the stent geometry (number of wires

in the braid, wires diameter and stent diameter) and the electrical conductivity of the wires (Nitinol or Nitinol with a platinum core for DFT wires) have an evident impact on the intensity of the resulting RF artifacts, similar surface states induce RF artifacts of the same nature. There could thus be an interest in the creation of electrically insulating contact between the wires of the stent in order to get RF artifacts leading to a hypersignal in the stent lumen. In line with this result, it appeared that the introduction of a less electrically conductive material in the braid of the stent (pure Nitinol wires in a NiTiDFT braid) leads to a decrease of the RF artifact intensity.

The last part of this chapter reports on the creation, the characterization and the impact of NiO and CoO layers on the MRI behavior of Nitinol and Phynox. Nickel oxide (NiO) and cobalt oxide (CoO) are known to have antiferromagnetic properties. Thus *a priori* the creation of an antiferromagnetic NiO or CoO layer on the surface of Nitinol or Phynox wires (respectively) could have been beneficial for the MRI behavior of these materials.

These layers were produced by electroreduction followed by an oxidative heat treatment and characterized by SEM and XPS. Both obtained nickel and cobalt deposits were complete and homogeneous. XPS analysis showed that the applied oxidative heat treatments lead to a complete oxidation of at least 10 nm of the deposits.

Unfortunately, the creation of such NiO or CoO layer on the surface of Nitinol or Phynox wires (respectively) appeared to have a highly negative impact on the MRI behavior of these materials.

General conclusions and outlooks

Chapter 5. General conclusions and outlooks

5.1. Conclusions

This work focused on the surface characterization and modification of two widely used biomaterials i.e. Nitinol and Phynox and aimed to bring supplementary data for some topics appearing as controversial in the literature as well as to introduce original surface treatments that could constitute interesting basis for the further improvement of the surface properties of these biomaterials.

Nitinol has been studied in two different shapes: wires (used for the fabrication of braided stents) and sheets (more convenient than wires for many surface characterization methods).

The typical shape-setting heat treatment of Nitinol wires has been shown to have a significant negative impact on their surface composition and resistance to corrosion. Therefore, the oxide layer obtained after the heat treatment must be considered as bad regarding the Nitinol biocompatibility as it induces the presence of a higher amount of nickel at the surface of the material (which could *a priori* lead to a higher toxic nickel ions leaching) without improving significantly its resistance to corrosion. The chemical etching of Nitinol wires in a HF/HNO₃ solution results in a complete removal of the pre-existing oxide layer and the formation of a new native oxide layer. Chemical etching appeared to be a valuable solution to remove the oxide layer obtained after the shape-setting heat treatment and therefore obtain a Nitinol surface which contains much less nickel and provides a better resistance to corrosion.

The oxide layer present on “as received” Nitinol sheets has been showed to be spatially inhomogeneous and significantly different from the one present on the surface of Nitinol wires confirming the widely reported fact that the Nitinol surface state strongly depends on the manufacturing process.

The functionalization of mechanically polished Nitinol sheets surface toward a versatile platform for post-grafting chemical reactions has been studied. In this context, the electrografting of 1,4-carboxybenzene diazonium and the grafting of a 11-phosphonoundecanoic acid monolayer have been carried out in order to exploit the covalently attached carboxylic acid functions as anchoring points for the post-grafting of alcohols via a Steglich esterification reaction. This post-grafting reaction has been shown to be more efficient when carried out on an 11-phosphonoundecanoic acid monolayer than on the carboxybenzene electrografted layer.

A systematic assessment of the solvent and temperature impact on the grafting of phosphonic acid molecules on Nitinol surface has also been carried out. Ultra pure water has been shown to lead to the best results among the three solvents tested in the frame of this study and an increase of the temperature leads to an increase of the obtained hydrophobic and corrosion resistance properties indicating a better organization of the resulting monolayer.

Finally, the impact of an induction heating treatment in pure water on heat treated Nitinol surface composition and corrosion resistance has been investigated for the first time and compared with the impact of a conventional boiling water treatment. It appeared that

induction heating led to similar (or slightly better) results than conventional heating and thus can be considered as a very promising alternative to other conventional heating methods for surface treatments that require thermal activation.

Regarding Phynox, the systematic corrosion study shows that all the tested braided Phynox stents are resistant to corrosion, and in particular to the pitting-corrosion phenomenon which is especially harmful. The thermal treatment needed to achieve the desired mechanical properties of the material induces a steady increased corrosion rate. Nevertheless, the treatments applied by Cardiatis after thermal treatment results in a very good resistance to corrosion (comparable to the resistance of the rough material).

11-phosphonoundecanoic acid monolayers have been formed on mechanically polished Phynox surfaces and used as platforms to graft PEG segments of increasing length exploiting the free carboxylic acid functions at the surface of the formed monolayers. The 11-phosphonoundecanoic acid have been shown to binds the substrate mainly via the phosphonic acid function, leaving a sufficient number of carboxylic functions available for the second step of the functionalization. However, only about half of the grafted 11-phosphonoundecanoic acid molecules were involved in this post-grafting reaction.

In order to improve the amount of free carboxylic acid functions available after the grafting of bifunctional phosphonic-carboxylic acid molecules, the effect of induction heating on the grafting of the 6-phosphonohexanoic acid and the 11-phosphonoundecanoic acid on Phynox surface has been studied. Induction heating has been shown to lead to a much more selective adsorption of short bifunctional molecules on the surface of Phynox, leaving a higher amount of free carboxylic acid functions to react during the second modification step.

Finally, the impact of ethylene oxide sterilization process on 11-phosphonoundecanoic acid monolayers grafted on mechanically polished Phynox surfaces has been assessed. These monolayers perfectly resist the sterilization treatment.

The last chapter of this work was dedicated to a study of the impact of different surface treatments and of the imaging parameters and conditions on the MRI visibility of Nitinol and Phynox wires and stents.

In this context, the influence of the Nitinol and Phynox surface state on their apparent magnetic susceptibility (and therefore the importance of the resulting susceptibility artifact) has been assessed by means of an algorithm developed for this purpose. It appeared that the surface state of the observed material can have a significant influence on the produced susceptibility artifact. Regarding Nitinol, heat treatment appeared to have a negative impact on the apparent magnetic susceptibility while the removal of the oxide layer by chemical etching is favorable to a low apparent magnetic susceptibility. Phynox appeared to be a less suitable material for MRI examinations: its apparent magnetic susceptibility is always about 10-fold higher than the one of Nitinol. In the case of Phynox, however, the heat treatment of Phynox induces a slight decrease of its apparent magnetic susceptibility while the chemical etching and the sterilization treatments do not appear to have any significant impact.

The impact of several parameters on the MRI visibility of braided stents i.e. on the importance of the produced susceptibility and RF artifacts was also studied. SE sequences are less sensitive to susceptibility artifacts and lead to the acquisition of better images than the GRE

sequences do. The stent orientation with respect to the main magnetic field is also crucial: when the stent is placed perpendicularly to B_0 , the susceptibility artifacts are much more important than when the stent is parallel to B_0 . When the stent is parallel to B_0 , the produced artifacts are localized at the stent extremities. Again, it has been confirmed that Phynox stents produce much more important susceptibility artifacts than the Nitinol ones. On the contrary of the susceptibility artifacts, RF artifacts are much more important when SE sequences are used than with GRE sequences. Furthermore, the stent orientation has a strong influence on the intensity of the produced artifacts: in the case of braided stents such as the ones we studied in the frame of this work, the RF artifacts are more important when the stent is oriented perpendicularly to B_0 . Both for susceptibility and RF artifacts, there is thus an interest in placing the stent as parallel as possible to B_0 . Interestingly, it has been shown that the RF artifacts could be beneficial as they could lead to a signal enhancement in the stent lumen at low flip angles. Even if the stent geometry and the electrical conductivity of the wires have an evident impact on the intensity of the resulting RF artifacts, similar surface states induce RF artifacts of the same nature. There could thus be an interest in the creation of electrically insulating contact between the wires of the stent in order to get RF artifacts leading to a hypersignal in the stent lumen. In line with this result, we showed that the introduction of a less electrically conductive material in the braid of the stent (pure Nitinol wires in a NiTiDFT braid) leads to a decrease of the RF artifact intensity.

Finally, antiferromagnetic NiO and CoO layers were successfully formed on Nitinol and Phynox wires, respectively, by electrodeposition and thermal oxidation. The impact of such oxide layers on the MRI behavior of Nitinol and Phynox appeared to be dramatically negative.

5.2. Outlooks

Even if this work clearly does not bring any radical solution to the biocompatibility and corrosion resistance issues linked to the use of Nitinol and Phynox as biomaterials, several interesting outlooks can be drawn.

The study of the bifunctional phosphonic-carboxylic acids molecules grafting on Nitinol and Phynox showed the existence of a competition between the two terminals functions (both able to act as anchoring group). Nevertheless, we showed that induction heating could be used to reach a more selective adsorption of short bifunctional molecules, leaving a higher amount of free carboxylic acid functions for post-grafting chemical reactions. This behavior has an important fundamental interest. Therefore, it would be interesting to study the impact of induction heating on the grafting of different other bifunctional molecules. Furthermore, the surface modification of Nitinol and Phynox with phosphonic acids monolayers could be applied for the grafting of polymerization initiator (whose terminal function cannot bind the surface) and the growth of bioactive polymer layers.

Induction heating treatment of Nitinol in pure water revealed to be slightly more efficient than a conventional hydrothermal treatment to decrease the Ni surface concentration and to

increase the amount of OH groups on the surface. This higher OH groups availability can in turn be beneficial for the grafting of phosphonic acids monolayers. More generally, induction can be considered as a very promising alternative to other conventional heating methods for surface treatments that require thermal activation and could thus be applied to a very wide range of surface treatments. Indeed, this heating method has several important advantages compared to other heating methods i.e. it is contactless, the heat is generated directly into the target material and very effectively, leading to a significantly lower energy consumption than conventional heating ways.

The systematic study of the MRI imaging parameters revealed that RF artifacts can lead to a signal enhancement in the stent lumen at low flip angles and thus be beneficial for the post implantation examinations. This behavior is observed when the conductive loops of the imaged stent are capacitive rather than inductive. Therefore, it could be highly interesting to study the impact of the presence of a highly capacitive (and biologically suitable) material such as Ta₂O₅ on the intra-lumen signal enhancement induced by RF artifacts.

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Annexes

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1. Characterization techniques

1.1. X-ray Photoelectron Spectroscopy (XPS)

1.1.1. Basic Principles

This spectroscopic technique, also known as ESCA (Electronic Spectroscopy for Chemical Analysis) is based on the photoionization phenomenon: a photon X can induce the ejection of an electron (called photoelectron) from an atom if its energy is superior to the ionization energy. The analysis of the emitted photoelectrons energy allows the study of the elemental composition as well as of the electronic state of a surface.

XPS analyses are thus carried out by irradiation of a surface with a monochromatic X-ray beam. These X-rays deeply penetrate into the material (several hundreds of nanometers) but the detection of the ejected photoelectrons is limited by their small mean free path inside this material as they quickly undergo inelastic collisions with other atoms. Therefore, the information provided by the detection of these photoelectrons concerns only the few first nanometers under the surface (typically between 4 and 10 nm). This makes XPS a particularly suitable technique for surface analyses.

The principle of photoelectrons excitation and emission is based on the energy conservation principle i.e. the energy of the photon X leads to the ejection of an electron and the energy excess is provided to the electron as kinetic energy according to the following formula:

$$h\nu = E_b + E_k + \phi$$

where h is the Planck constant (6.62×10^{-34} J.s)

ν is the frequency of the incident radiation

E_b is the binding energy of the emitted photoelectron

E_k is the kinetic energy of the emitted photoelectron

Φ is the work function of the spectrometer (i.e. the energy needed to remove an electron from a solid to a point immediately outside the solid surface)

The binding energy of a core level photoelectron is a very informative value: not only it is characteristic of the atom and the considered core level but it is characteristic of the chemical environment of this atom as well. An atom located in an electronegative environment tends to cede its valence electrons. As a result, its core electrons will tend to get closer to the nucleus resulting in a higher binding energy.

After the emission of a photoelectron, the emitting atom is in an excited state. Two relaxation phenomena can then occur: the emission of X-rays (fluorescence) or the emission of an Auger electron (Figure A1). When the emitting atom is in its ionized state, an electron located on a higher energetic level relaxes to the electronic level left unoccupied by the photoelectron. The energy lost by this electron can be emitted as photons (X-rays) or provided to another electron which is, in turn, ejected (Auger electron). Note that the X-ray emission probability is very

weak for light elements and quickly increases with the atomic number proportionally to Z^4 . After these relaxation phenomena, the atom recovers its neutral state by ground connection.

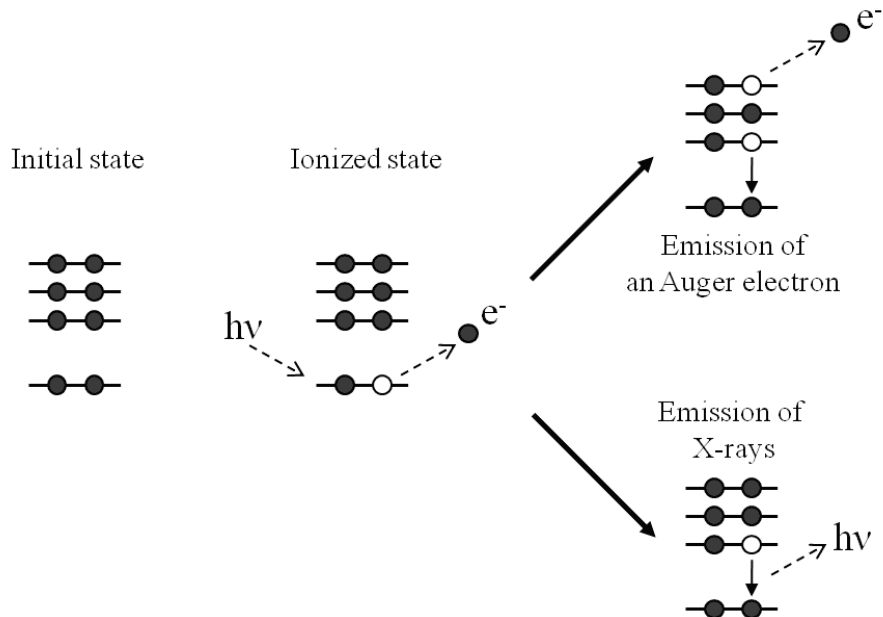


Figure A1. Schematic representation of the photoionization process and the two main relaxation phenomena that can occur: the emission of X-rays (fluorescence) or the emission of an Auger electron.

1.1.2. Quantitative Aspect

As the intensity of the photoelectron peaks is proportional to the amount of atoms, XPS also provides quantitative information about the atoms present at the surface of a sample. The intensity of a photoelectron peak can be expressed as follows:

$$I = K.N.t.\sigma.\lambda.A.T$$

where K is a constant

N is the number of atoms/cm³

t is the signal acquisition time

σ is the ionization cross-section of the considered element

λ is the mean free path of the photoelectron

A is the analyzed area of the surface

T is the transmission function of the analyzer

Each spectrometer is provided with a table of sensitivity factors for the different orbitals of each element. This factor F (also called Scofield factor) allows the normalization of the different measured intensities:

$$F = K.t.\sigma.\lambda.A.T$$

Therefore, for an element X, the number of atoms per cubic centimeter can be expressed as follows:

$$N_X = I_X/F_X$$

Thus the calculation of atomic ratios provides information on the relative abundance of two elements A and B:

$$\frac{N_A}{N_B} = \frac{I_A/F_A}{I_B/F_B}$$

1.1.3. Experimental setup

The schematic representation of the XPS used in the frame of this work (SSX-100 from Surface Science Instrument) is presented in Figure A2. The X-rays are produced from a rotating aluminum anode. A quartz monochromator allows keeping only the Al K α line (1486.6 eV). The photoelectrons emitted from the sample are collected by an analyzer (at 35° take off angle with respect to the normal surface) measuring their kinetic energy.

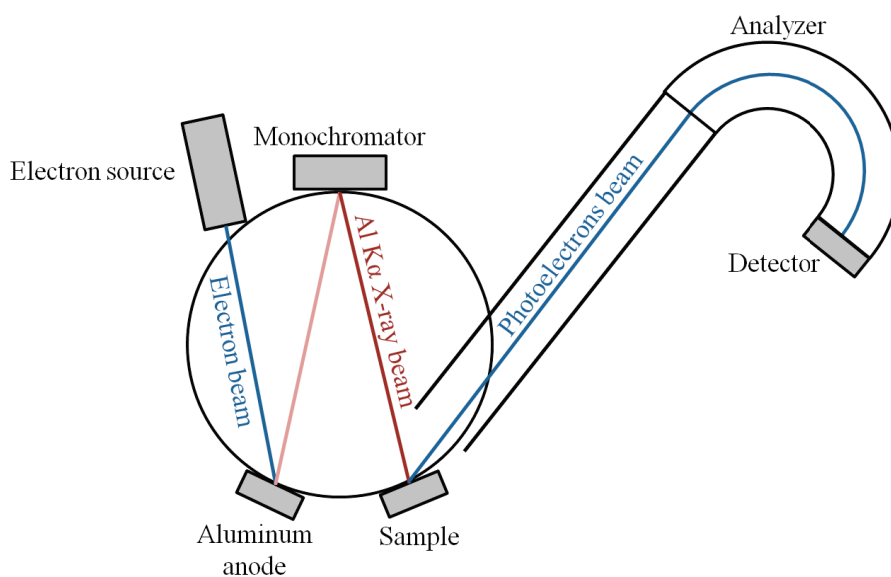


Figure A2. Schematic representation of the experimental XPS setup.

The analysis of the photoelectron peaks were carried out using the WINSPEC software developed at the LISE laboratory. The binding energy of core levels spectra was calibrated against the C1s binding energy set at 285.0 eV, an energy characteristic of alkyl moieties. The peaks were analyzed using mixed Gaussian-Lorentzian curves (80% of Gaussian character).

1.2. Infrared Techniques

Besides the conventional transmission IR characterization method, two specific techniques were used in the frame of this work: Polarization Modulation Infrared Reflection Absorption Spectroscopy (PM-IRRAS) and Attenuated Total Reflectance (ATR).

Infrared spectroscopy is a widely used method exploiting the fact that molecules absorb electromagnetic waves at specific frequencies that are characteristic of their structure. These absorptions are resonant frequencies i.e. the frequency of the absorbed radiation matches the frequency of the chemical function that vibrates. Thus this technique allows the characterization of the chemical functions present in an organic compound. Using a grazing incidence IR beam (IRRAS) makes the characterization of organic molecules on a surface possible if the surface is able to reflect this incident IR beam. However, a major problem arises from the very low quantity of organic material present at the surface for systems such as thin organic films or SAMs. Indeed, IRRAS requires a reference sample whose spectrum is used as a background. This background is subtracted from the sample spectrum in order to get rid of the signal from the contaminants present on the surface and in the device itself. Concretely, these contaminants are the water and carbon dioxide present in the atmosphere producing an intense signal preventing the correct acquisition of the surface signal.

1.2.1. Polarization Modulation – Infrared Reflection Absorption Spectroscopy

In order to resolve this issue, PM-IRRAS involves the use of a polarization modulation. This modulation consists in an alternative polarization of the IR light parallel (s) and perpendicular (p) to the surface (Figure A3).

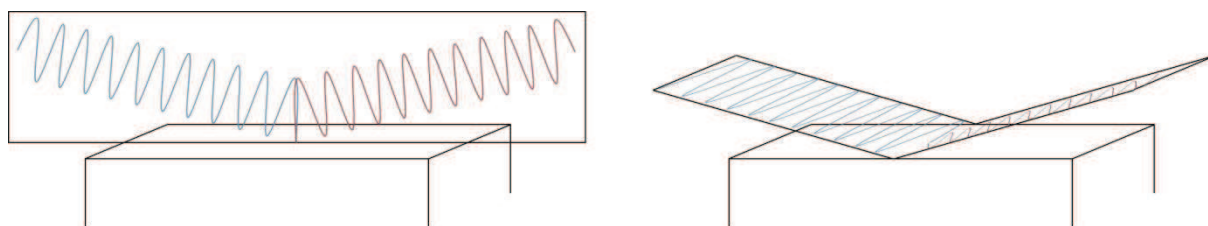


Figure A3. Schematic representation of p (left) and s (right) polarized IR light.

In PM-IRRAS, like in conventional IR spectroscopy, the electromagnetic field of the incident radiation interacts with the oscillating dipoles associated with the vibrational modes of the molecules adsorbed on the surface. However, on a metallic surface, only the perpendicular component of the vectors associated to the dipole moment variations is observed. Indeed, the electrical fields associated to the dipole moments induce the appearance of image dipoles into the metallic surface (Figure A4). If the dipole moment of an adsorbed molecule is parallel to the surface, the image dipole compensates it and the resulting electric field is zero. On the contrary, if the dipole moment of the adsorbed molecule is perpendicular to the surface, the image dipole reinforces it. Note that for dipole moments having both a parallel and perpendicular component, the only reinforced component is the perpendicular one. Therefore,

when the IR light is polarized perpendicular to the surface (p), the obtained signal corresponds to the one of the organic molecules at the surface and the environment (CO_2 and H_2O) while when it is polarized parallel to the surface (s), the obtained response does not contain the signal of the molecules at the surface but only the signal of the environment.

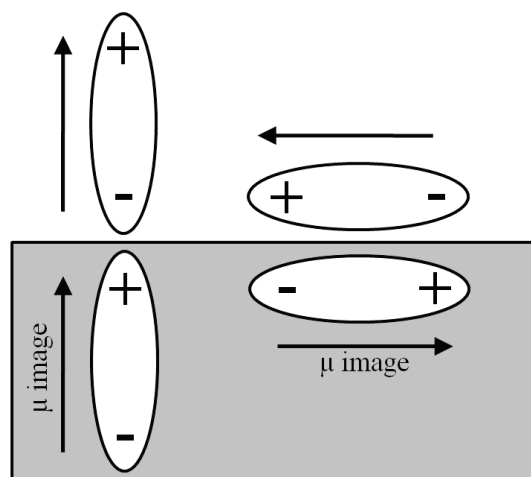


Figure A4. Schematic representation of the reinforcement of perpendicular dipoles and the cancellation of parallel dipoles by image dipoles in PM-IRRAS

Furthermore, the perpendicular component of the vector associated to the dipole moment of a vibrational mode is dependent of position of the atoms implied in this vibrational mode. Thus PM-IRRAS can also provide information on the orientation of the chemical groups with respect to the surface.

In the frame of this work, the obtained spectra were acquired on a Bruker Equinox 55-PMA37 equipped with a liquid nitrogen cooled mercury-cadmium-telluride (MCT) detector and a zinc-selenide photoelastic modulator. The infrared light was modulated between s- and p-polarization at a frequency of 50 kHz and an incident angle upon the sample surface of around 85° . Signals generated from each polarization (R_s and R_p) were detected simultaneously by a lock-in amplifier and used to calculate the differential surface reflectivity $(\Delta R/R) = (R_p - R_s)/(R_p + R_s)$. All spectra are the average of 512 scans at a spectral resolution of 2 cm^{-1} .

1.2.2. Attenuated Total Reflectance

Attenuated total reflectance (ATR) is a particular sampling method using a property of total internal reflection resulting in an evanescent wave. The IR beam is passed through ATR crystal with an appropriate angle such that it reflects at the internal surface in contact with the sample (Figure A5). This reflection leads to the formation of an evanescent wave into the sample. The number of reflections may be varied by varying the angle of incidence. The IR beam is then collected by a detector as it exits the crystal.

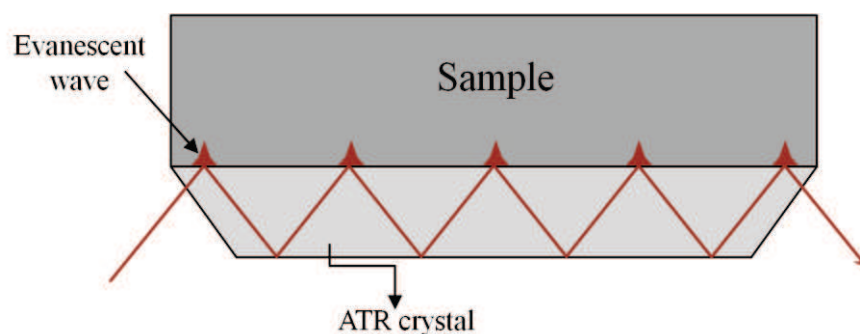


Figure A5. Schematic representation of the ATR setup

This evanescent effect only works if the ATR crystal material has a higher refractive index than the sample being studied. In the case of a solid sample (like in the frame of this work), it is pressed into direct contact with the crystal. Typical materials for ATR crystals include germanium and zinc selenide.

In the frame of this work, we used a MIRacle™ ATR device (PIKE technologies) with a Bruker Equinox 55 setup. This ATR device is equipped with a single reflection Ge crystal plate (refractive index 4 at 1000 cm^{-1} ; spectral range $5500\text{--}780\text{ cm}^{-1}$).

1.3. Time-of-Flight Secondary Ion Mass Spectrometry (ToF-SIMS)

1.3.1. Basic Principles

Secondary ion mass spectrometry is the mass spectrometry of ionized particles which are emitted when a surface is bombarded with energetic primary particles, usually ions (for example, Ar^+ , Ga^+ , Cs^+). The emitted (sputtered) “secondary” particles will be electrons; neutral species atoms or molecules; atomic and cluster ions. The vast majority of species emitted are neutral but it is the secondary ions that are detected and analyzed by a mass spectrometer. It is this process which provides a mass spectrum of a surface and enables a detailed chemical analysis of a surface or solid to be performed.

Time-of-flight SIMS (ToF-SIMS) is the dominant experimental variant of static SIMS that emerged as a technique of potential importance in surface science in the late 1960’s. Conceptually the process is very simple (Figure A6).

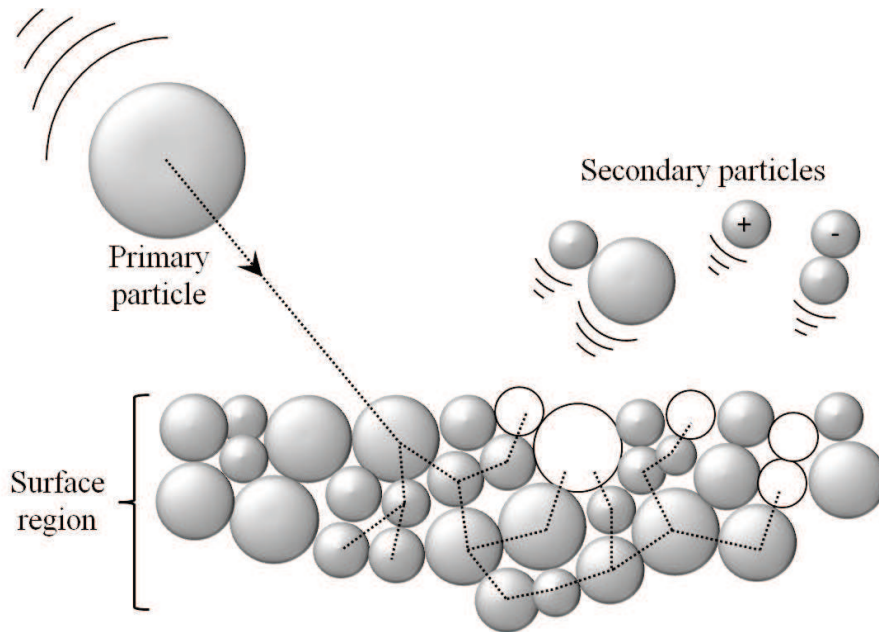


Figure A6. Schematic representation of the SIMS process.

When a high energy (between 1 and 25 keV) beam of ions or neutrals bombards a surface, the particle energy is transferred to the atoms of the solid by a billiard-ball-type collisional process. A “cascade” of collisions occurs between the atoms in the solid; some collisions return to the surface and result in the emission of atoms and atom clusters, some of which are ionized in the course of leaving the surface. While the technique is apparently destructive, the essence of the *static* mode is to use an extremely low dose of primary ions (never more than 10^{13} ions/cm²), such that within the time scale of the experiment very much less than 1% of the top surface layer of atoms or molecules receives an ion impact. Under these conditions on a random impact basis no spot on the surface should receive more than one primary ion strike. Over 95% of the secondary particles originate from the top two layers of the solid. Thus the possibility of a soft ionization mass spectrometry of the surface layers emerges.

1.3.2. Experimental Parameters

1.3.2.1. Basic Equation

Static SIMS (SSIMS) is thus concerned with the analysis of secondary *ions*. Ionization occurs at, or close to, emission of the particles from the surface with the consequence that the matrix participates in the electronic processes involved. This means that the yield of secondary ions is strongly influenced by the electronic state of the material being analyzed with consequent complications for quantitative analysis. The basic SIMS equation is

$$I_m = I_p Y_m \alpha^+ \theta_m \eta$$

where I_m is the secondary ion current of species m , I_p is the primary particle flux, Y_m is the sputter yield, α^+ is the ionization probability to positive ions, θ_m is the fractional concentration of the species m in the surface layer and η is the transmission of the analysis system.

1.3.2.2. Sputtering and Ionization

The two fundamental parameters are Y_m and α^+ . Y_m is the total yield of sputtered particles of species m , neutral and ionic, per primary particle impact. It increases linearly with primary flux. It also increases with primary particle mass, charge and energy, although not linearly. The crystallinity and topography of the bombarded material will also affect the yield. The threshold for sputtering occurs at about 20 to 40 eV primary particles energy and Y tends to maximize with energy at around between 5 and 50 keV. Beyond this energy yield drops away as the primary beam penetrates deeper into the solid and less energy returns to the surface region.

Secondary ion formation is strongly influenced by electron exchange processes between the departing species and the surface. Thus the electronic state of the surface is critical. The yields of elemental secondary ions can vary by several orders of magnitude across the periodic table and are very dependent on the chemical state of the surface (the matrix effect). Thus the ion yield for a particular element will vary dramatically, from example, from a metal as compared to its oxide. It can be seen that oxidation changes the elemental ion yields to differing extents resulting in significant complications when absolute quantitative data is required.

1.3.2.3. The ToF-SIMS Experiments

There are four main components for the static SIMS experiments: the primary particles source, the mass spectrometer and, since the secondary ions are emitted with a range of kinetic energies, an ion optical system which selects ions within a defined energy band compatible with the capability of the mass analyzer and finally a detector. An electron source will also be required for charge compensation.

Time-of-Flight mass spectrometry is conceptually the simplest means of mass separation. In ToF analysis pulses of secondary ions are accelerated to a given potential (3 to 8 keV) such that all ions possess the same kinetic energy; they are allowed to drift through a field free space before striking the detector. According to the equation of kinetic energy, heavier masses travel more slowly through the “flight tube” and so the measured flight time, t , of ions of mass to charge ratio, m/z , accelerated by a potential V down a flight path of length L provides a simple means of mass analysis.

$$t = L \left(\frac{m}{2zV} \right)^{1/2}$$

The basic experimental requirements are a precisely-pulsed primary ion source, a highly accurate computer clock, a drift tube and considerable computing power for data acquisition. The flight times of all the ions to the detector are electronically measured and related to ion mass. Thus a mass spectrum of all the ions is generated from the flight time spectrum. Mass

resolution is critically dependent on the pulse length of the generated secondary ion pulse which should be precisely defined and very short. This in turn is dependent on the pulse length of primary beam which is typically in the order of nanoseconds.

In the frame of this work, the depth profile experiments were carried out with a ToF-SIMS IV from ION-TOF GmbH using a Ga^+ gun for analysis and a Xe^+ gun for sputtering.

1.4. Scanning Electron Microscopy (SEM)

This imaging technique, based on the electrons-material interactions, is widely used for the morphological study of surfaces. In a typical SEM, an electron beam is emitted from an electron gun. The electron beam (which typically has an energy ranging from 0.5 keV to 40 keV) is focused to a spot. This beam is then deflected in the x and y axes so that it scans in a raster fashion over a rectangular area of the sample surface.

When the primary electron beam interacts with the sample, the electrons lose energy within a teardrop-shaped volume of the specimen known as the interaction volume (Figure A7). The energy exchange between the electron beam and the sample results in the reflection of high-energy electrons by elastic scattering, the emission of secondary electrons by inelastic scattering and the emission of electromagnetic radiations (X-rays). Electronic amplifiers are used to amplify the signals which are displayed as variations in brightness. The resulting image is thus a distribution map of the intensity of the signal being emitted from the scanned area of the specimen.

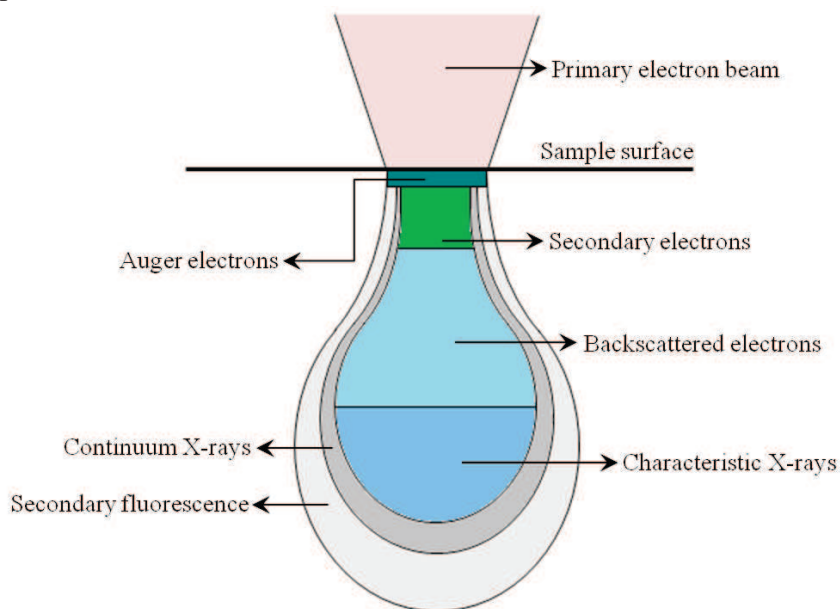


Figure A7. Schematic representation of the interaction volume of a primary electron beam with a surface.

The most common imaging mode collects low-energy secondary electrons emitted by inelastic scattering interactions with the primary electrons beam. The secondary electrons are

collected and further accelerated towards a scintillator which then emits flashes of light conducted to a photomultiplier. The amplified electrical signal output by the photomultiplier is displayed as a two-dimensional intensity distribution that can be displayed and saved as a digital image. The brightness of the signal depends on the number of secondary electrons reaching the detector. If the beam enters the sample perpendicular to the surface, the activated region is uniform and a certain number of electrons "escape" from within the sample. As the angle of incidence increases, the "escape" distance will decrease and more secondary electrons will be emitted. Thus edges tend to be brighter than flat surfaces, which results in images with a well-defined, three-dimensional appearance.

In the frame of this work, SEM characterizations have been carried out using a JEOL 7550 FEG-SEM microscope.

1.5. Contact Angle Measurements

The contact angle measurements are convenient for the determination of the affinity of a surface for a solvent. Therefore, when water is used as solvent, the contact angle measurements provide an indication of the hydrophilic or hydrophobic nature.

A drop of a liquid is deposited on a solid surface spreads until it reaches an equilibrium shape as schematized in Figure A8.

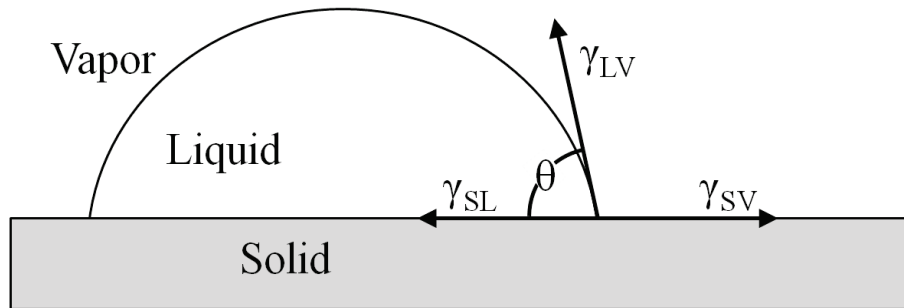


Figure A8. Schematic representation of a liquid drop deposited on a solid surface and of the solid/liquid (γ_{SL}), liquid/vapor (γ_{LV}) and solid/vapor (γ_{SV}) interfacial tensions.

The contact angle θ formed by the drop on the surface results from the equilibrium formed between three interfacial tensions: solid/liquid (γ_{SL}), liquid/vapor (γ_{LV}) and solid/vapor (γ_{SV}). These three interfacial tensions and the contact angle value are related by the Young's equation:

$$\gamma_{LV} \cdot \cos(\theta) = \gamma_{SV} - \gamma_{SL}$$

The θ angle value for a water droplet provides information on the wettability of the surface. These values can be classified as follow:

- $\theta = 0^\circ$ is the theoretical situation for a perfectly hydrophilic surface.

- $0^\circ < \theta < 90^\circ$ is the typical range of θ values for surfaces considered as hydrophilic.
- $90^\circ < \theta < 180^\circ$ is the typical range of θ values for surfaces considered as hydrophobic.
- $\theta = 180^\circ$ is the theoretical situation for a perfectly hydrophobic surface.

Four conditions are essential for a stable equilibrium of the drop at the surface and thus for a correct contact angle measurement:

- a rigid and motionless surface
- a smooth surface (an important roughness can lead to wrong interpretations)
- an homogeneous surface composition
- no reactivity between the liquid and the surface

In the frame of this work, we carried out contact angle measurements with a DIGIDROP Contact Angle Meter from GBX from milli-Q water droplets of 2 μ l. Several measurements (at least five) have been carried out on each sample. The values presented are the mean values of these measurements results.

1.6. Contact Profilometry

This technique uses a probe (a stylus) to physically measure the topography of a surface. This probe is placed in contact (with a specified contact force) and moved across the surface (for a specified distance). The height position of the stylus generates an analog signal which is converted into a digital signal recorded and displayed. In this manner, surface roughness and step heights can be measured.

In the frame of this work, we used a Dektak 8 Stylus Profilometer (Veeco Metrology Group) with a 5 μ m $\varnothing$ diamond stylus.

1.7. Electrochemical Techniques

Two electrochemical techniques were used: the cyclic voltammetry and the polarization curves measurement, also called linear sweep voltammetry (LSV). For both techniques, a classical three electrodes cell is used (Figure A9) with a Pt foil as counter electrode, a saturated calomel electrode (SCE) as reference electrode ($E=242$ mV vs. SHE) and the substrate to characterize as working electrode.

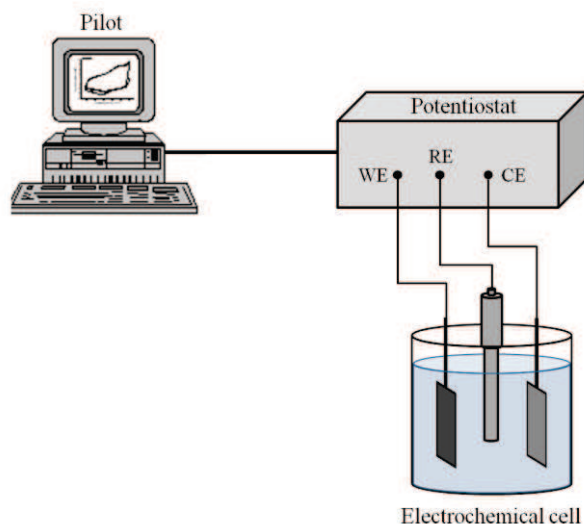


Figure A9. Schematic representation of the electrochemical setup used in the frame of this work (WE: working electrode; RE: reference electrode; CE: counter electrode).

For the analysis of a controlled area of a plane electrode, a spot cell was used (Figure A10). The analyzed electrode is placed on the spot of this cell with a fixed size o-ring (0.28 cm²).



Figure A10. Picture of an electrochemical spot cell.

1.7.1. Cyclic Voltammetry

Voltammetry describes the electrochemical techniques based on the measurement of the current response obtained when an electrode is submitted to a potential variation.

In cyclic voltammetry, a range of potential is linearly scanned forward and backward (from an initial potential E_i to a final potential E_f and *vice versa*) while the current response is measured.

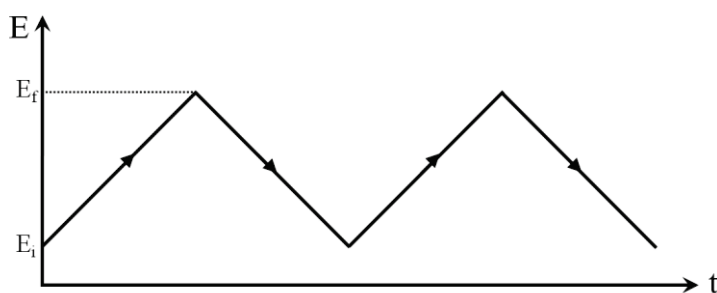


Figure A11. Representation of the linear potential scans used for cyclic voltammetry.

From the obtained current vs. potential curves, it is possible to assess the coverage of an electrode surface with a self-assembled monolayer i.e. the surface percentage electrochemically blocked by the presence of the monolayer. This coverage is calculated by measuring the area of the oxidation peak for an unmodified electrode (A_u) and for a modified one (A_m) and by applying the following formula:

$$C(\%) = 100 \times \frac{(A_u - A_m)}{A_u}$$

1.7.1. Linear Sweep Voltammetry

Linear sweep voltammetry (LSV, also called polarization curves measurements) aims to characterize the corrosion resistance of an electrode. As indicated by its name, this technique is based on the linear scanning of a range of potentials and the measurement of the current response.

The electrochemical reactions taking place at the electrode surface can be limited by charge transfer or mass transfer. Thus these two parameters play an important role in the kinetics of electrochemical reactions at the surface of an electrode. However, the mass transfer limitation can be considered as negligible in some conditions such as with a stirring of the electrolyte or with a very low potential scan rate (condition applied in the frame of LSV).

The Butler-Volmer describes the relation between the overpotential (i.e. the difference between the applied potential and the reversible potential) and the current density i for a system submitted to charge transfer limitation. The reversible potential corresponds to the potential spontaneously reached by the electrode without any external current (i.e. the open circuit potential).

$$i = i_a + i_c = i_0 e^{\frac{\alpha n F}{RT} \eta} - i_0 e^{\frac{(1-\alpha) n F}{RT} \eta}$$

where i_a is the anodic current density

i_c is the cathodic current density

i_0 is the exchange current density characterizing the charge transfer rate at the equilibrium

α is the charge transfer coefficient

η is the overpotential

n is the number of electron implied in the considered reaction

T is the temperature

R is the ideal gas constant ($8.314 \text{ J.K}^{-1}.\text{mol}^{-1}$)

F is the Faraday constant (96485 C.mol^{-1})

Anodic and cathodic Tafel coefficients are thus defined as:

$$\beta_a = \frac{RT}{\alpha nF}$$

$$\beta_c = \frac{RT}{(1 - \alpha)nF}$$

and the Butler-Volmer equation can be written as follows:

$$i = i_0 e^{\frac{\eta}{\beta_a}} - i_0 e^{-\frac{\eta}{\beta_c}}$$

When the overpotential is high enough, the kinetics of one of the two reactions becomes negligible. Therefore, a linear relationship exists between the current density logarithm and the overpotential. By neglecting successively the cathodic and anodic reactions, the expression of the anodic and cathodic Tafel lines is:

$$\eta = a_a + b_a \log(i)$$

$$\eta = a_c + b_c \log|i|$$

where a and b are the Tafel constants.

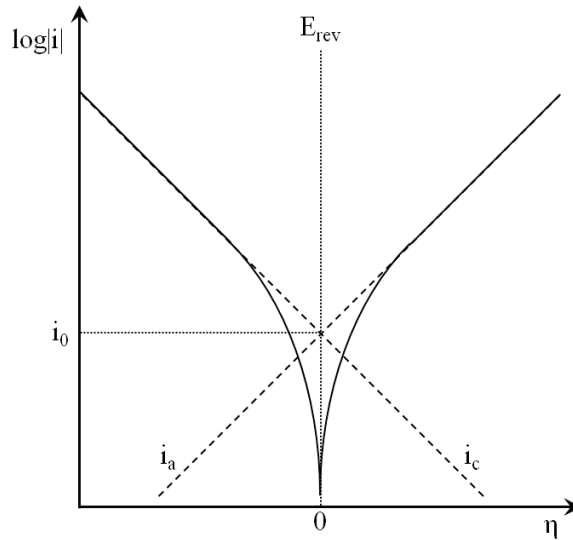


Figure A12. Representation of the current density variation as a function of the overpotential and the corresponding Tafel lines.

In the case of a mixed electrode i.e. a system in which two different reactions can occur (in the presence of the redox couple of the electrode and another one), the corrosion potential is defined as the potential spontaneously reached by the electrode without any external current. A variation of the potential with respect to the corrosion potential is called polarization (ζ). A positive polarization leads to an anodic current while a negative polarization leads to a

cathodic current. Therefore, for a corrosion reaction involving an anodic reaction ($M \rightarrow M^{n+} + ne^-$) and a cathodic reaction ($X^{n+} + ne^- \rightarrow X$), a current density corresponding to the sum of the partial current densities is observed when the electrode is polarized:

$$i = i_{a,M} + i_{c,M} + i_{a,X} + i_{c,X}$$

At potentials close to the corrosion potential, $i_{c,M}$ and $i_{a,X}$ are negligible and thus:

$$i = i_{a,M} + i_{c,X}$$

This situation is similar to the case of a simple electrode near the reversible potential (Figure A12). At the corrosion potential, the electrons produced by the anodic reaction are fully consumed by the cathodic reaction. Thus the total current density is zero. The Evans diagram represents the partial anodic and cathodic current densities of each reaction (Figure A13). On the Evans diagram schematized in Figure A13, the bold lines correspond to the ones measured in practice during an LSV experiment. The corrosion potential is located between the reversible potentials of the two considered electrochemical couples. Its exact position depends on $i_{c,X}$ and $i_{a,M}$. Similarly, the corrosion current density value depends on the partial current values.

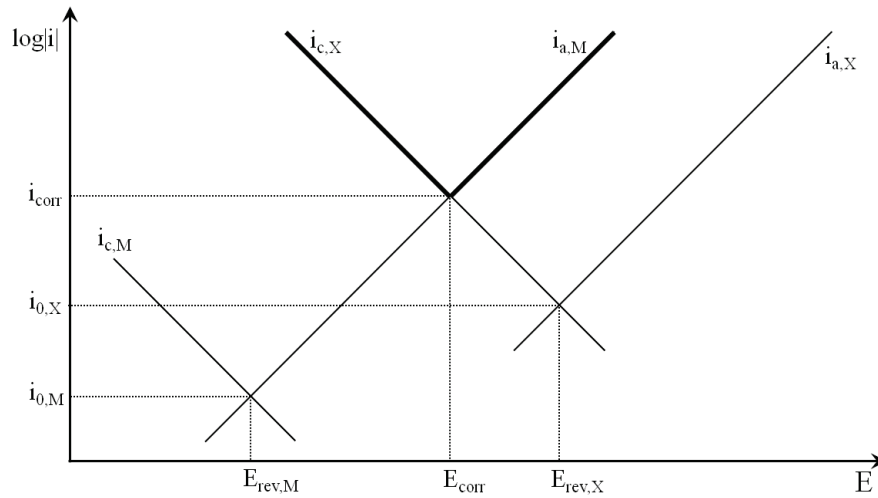


Figure A13. Evans diagram for a corrosion reaction involving an anodic reaction ($M \rightarrow M^{n+} + ne^-$) and a cathodic reaction ($X^{n+} + ne^- \rightarrow X$)

Polarization curves measurements allow thus to study the corrosion phenomenon on an electrode and to characterize the efficiency of a coating to protect the electrode against corrosion. As shown in Figure A14, an cathodic shift of the corrosion potential indicates an inhibition of the cathodic reaction while an anodic shift indicates an inhibition of the anodic reaction. Obviously, a mixed inhibition is also possible. In this situation, the shift of the corrosion potential is small while the corrosion current density decreases significantly. Therefore, LSV allows determining the kind of inhibition induced by a coating.

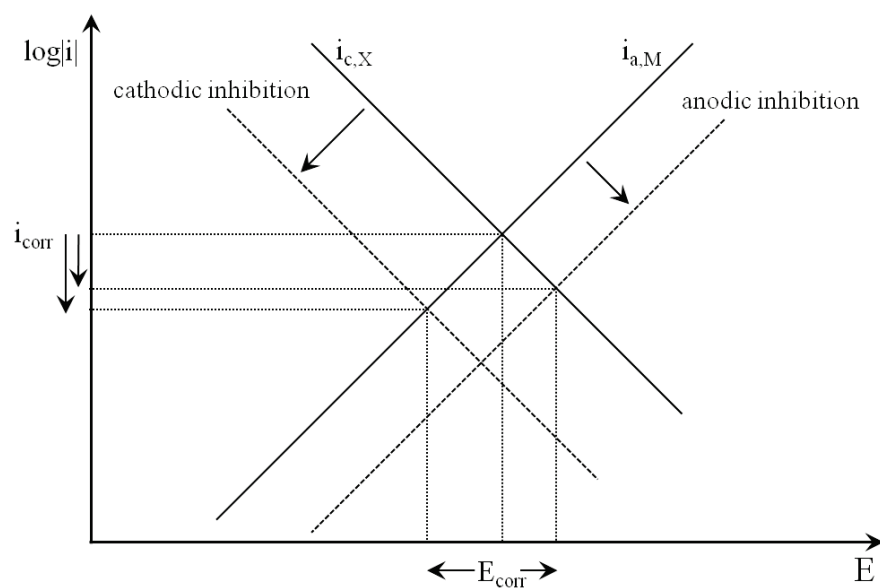


Figure A14. Schematic representation of the cathodic and anodic shift of the corrosion potential induced by a cathodic or anodic corrosion inhibition, respectively.

2. Induction Heating

Induction heating is a non-contact heating process that uses high frequency electricity to heat materials that are electrically conductive. Compared to other conventional heating methods, induction heating has the advantage to avoid material contamination as it is non-contact but also to be very efficient since the heat is actually generated inside the workpiece.

2.1. Basic Principles

2.1.1. Electromagnetic Induction

Induction heating is based on electromagnetic induction which was first discovered by Faraday in 1831. On one hand, Faraday's law of induction states that any change in the magnetic environment of a coil of wire will cause a voltage (emf) to be "induced" in the coil. On the other hand, Lenz's law states that when an emf is generated by a change in magnetic flux, the polarity of the induced emf is such that it produces a current whose magnetic field opposes the change which produces it.

$$Emf_{ind} = - \frac{d\Phi_B}{dt}$$

When a solid piece of metal is exposed to a magnetic flux change (or placed in an alternating magnetic field), induced currents that appear are called eddy currents. These eddy currents induce heating of the material via internal electrical resistance according to Joule's law that states that when a current (i) flows through a conductor with an electrical resistance R during a time t , the energy dissipated in the conductor is expressed as:

$$W = Ri^2t$$

Induction heating is based on this phenomenon. A source of high frequency electricity is used to drive a large alternating current through a work coil. The passage of current through this coil generates a rapidly changing magnetic field in the space within the work coil. The workpiece to be heated is placed within this intense alternating magnetic field. In addition to this, the high frequency used in induction heating applications gives rise to a phenomenon called skin effect.

2.1.2. Skin effect

One of the general characteristics of alternative currents is to not use the entire useful section of a conductor to flow but to concentrate in the peripheral parts of the conductor. This phenomenon is called "Skin effect" or "Kelvin effect". The current density in an infinitely thick plane conductor decreases exponentially with depth d from the surface according to the following equation:

$$i = i_s e^{-d/\delta}$$

where i is the current density

i_s is the current density at the extreme surface

d is the distance from the surface

δ is the skin depth constant

Thus this skin effect forces the alternating current to flow in a thin layer towards the surface of the workpiece. In the frame of induction heating, the eddy currents induced in the workpiece are thus more important in the outside parts than in the bulk. Heat is thus mainly generated in these parts. The skin effect increases the effective resistance of the metal to the passage of the large current. Therefore it greatly increases the heating effect caused by the current induced in the workpiece.

The skin depth constant is related to the electrical and magnetic properties of the considered material and the frequency of the alternating current according to the following equation:

$$\delta = \sqrt{\frac{\rho}{\pi \mu f}}$$

where ρ is the resistivity of the material

μ is the absolute magnetic permeability of the material

f is the frequency of the alternating current

2.1.3. Hysteresis loss

When a ferromagnetic material (like iron, nickel, some types of steel, *etc.*) are submitted to induction heating, an additional heating mechanism takes place at the same time than the eddy currents mentioned above. These materials are characterized by the existence of magnetic domains (Weiss domains). When they are exposed to the strong alternating magnetic field inside the working coil, the material is rapidly magnetized and de-magnetized. This rapid flipping of the magnetic domains causes considerable friction and heating inside the material. This heating mechanism, known as “Hysteresis loss”, is more important for materials that have a large area inside their B-H curve. This is the reason why magnetic materials are heating more easily than non-magnetic materials. The fact that copper and aluminum are both non-magnetic and very good electrical conductors can make these materials a challenge to heat efficiently.

Note that ferromagnetic materials lose their magnetic properties when heated above the Curie temperature. This Curie temperature (or Curie point) is the temperature at which a ferromagnetic material becomes paramagnetic on heating. Above the Curie point, any further heating of the material must be due to induced eddy current alone.

2.2. Experimental setup

In the frame of this work, induction heating was performed with an Ambrell EasyHeat induction heating system with a power output of 725 W and a frequency of 198 kHz. The used solenoid is composed of 7 spires with an internal diameter of 9 cm.

Temperature measurements were carried out with a K-type thermocouple soldered at the center of the sample with a Fluke 54II thermometer.

3. Informations related to the study of the influence of the surface treatment of Phynox and Nitinol on the MRI artifacts

3.1. Algorithms

3.1.1. Algorithm developed for the calculation of the main magnetic field deformation around a cylinder with a magnetic susceptibility different from the one of the surrounding medium

```
function mapfield()

Bo=input('Bo (in Tesla) ');
th=input('theta (in radians) ');
a=input('a (in mm) ');
chi=input('magnetic susceptibility difference ');
step=input('steps length ');

    m=1;
    for x=-2:step:2,
        n=1;
        for y=-2:step:2,

            [phi,rho] = cart2pol(x,y);

            dB=dfield (Bo, th, phi, chi, a, rho);

            [Bov]=af(Bo, th);

            dBpsBov=dB*(Bov'/norm(Bov));

            zf(m,n)=dBpsBov;

            if x^2+y^2 < a^2
                zf(m,n)=NaN;
            end

            n=n+1;
        end
        m=m+1;
    end

x=-2:step:2;
y=-2:step:2;

[X,Y]=meshgrid(x,y);
Zf=zf';

Zf=Zf*1000;

mesh(X,Y,Zf);
```

```

xlabel('distance (mm)');ylabel('distance (mm)');zlabel('');
axis([-2 2 -2 2 -0.2 0.2]);

end

function [dB]=dfield (Bo, th, phi, chi, a, rho)
% dfield calculates the vector dB which is the variation of the magnetic
field
% near an infinite cylindrical metallic object (the main axis of the
cylinder
% being the z-axis)

chi=chi/2;

dBx=Bo*(chi/(1+chi))*(a/rho)^2*cos(2*phi)*sin(th);
dBy=Bo*(chi/(1+chi))*(a/rho)^2*sin(2*phi)*sin(th);
dBz=0;

dB=[dBx dBy dBz];

chi=chi*2;

end

function [Bov]=af(Bo, th)
% af calculates the component in x, y and z of the Bo vector in function of
% its magnitude (variable "Bo") and the angle between this vector and the z
axis
% (variable "th").
% Note that the Bo vector stays in the 'x-z' plane

Box=Bo*sin(th);
Boy=0;
Boz=Bo*cos(th);

Bov=[Box Boy Boz];

End

```


3.1.2. Algorithm developed for the calculation of the voxels deformation in the imaged plane perpendicular to a cylinder with a magnetic susceptibility different from the one of the surrounding medium

```
function voxeldistorsion()

Bo=input('Bo in T ');
dchi=input('magnetic susceptibility difference ');
Gz=input('readout gradient in mT/m ');
Gz=Gz*0.000001;
R=input('radius of the wire in mm ');
step=input('voxel size in mm ');
limit=0.5;

% plot of the distorted horizontal lines
x=-limit:0.001:limit;
rangez=-limit:step:limit;

figure(1); clf;

graphlim=0;

    for z=rangez,

        dz=deformfunct(x,z,Bo,dchi,Gz,R);

        %test to define the axes ranges
        graphlimtotest=z+max(dz);
        if graphlimtotest>graphlim
            graphlim=graphlimtotest;
        end

        %-----
        figure(1);
        plot(x,z+dz,'black');
        hold on;

    end

%Drawing of the distorted wires shape
[xwire zwire]=drawwire(R);

endwire=length(xwire);

    for j=1:endwire,
        xfor=xwire(j);
        zfor=zwire(j);
        dzwire=-(dchi/2)*(Bo/Gz)*R^2*((zfor^2-xfor^2)/(zfor^2+xfor^2)^2);
        zdefwire(j)=zwire(j)+dzwire;
    end

figure(1);
plot(xwire,zdefwire,'g');
```

```

%-----
%Definition of two vectors determining the limits of the NaN area in the
%plot of the vertical lines

for x=0:step:R,
    if x<=R
        limix=x;
    end
end

rangewirex=-limix:step:limix;
lengthx=length(rangewirex);
zdownstop=zeros(1,lengthx);
zdownstop=zdownstop-limit;
zupstop=zeros(1,lengthx);
zupstop=zupstop+limit;
testNaNforzdownstop=0;
testNaNforzupstop=0;

for k=1:lengthx,
    x=rangewirex(k);

    bornestopdown=0;
    bornestopup=0;
    phi=acos(x/R);
    zdownnonwire=-R*sin(phi);
    zuponwire=R*sin(phi);
    dzdownnonwire=-(dchi/2)*(Bo/Gz)*R^2*((zdownnonwire^2-
x^2)/(zdownnonwire^2+x^2)^2);
    dzuponwire=-(dchi/2)*(Bo/Gz)*R^2*((zuponwire^2-x^2)/(zuponwire^2+x^2)^2);
    zdownnonwire=zdownnonwire+dzdownnonwire;
    zuponwire=zuponwire+dzuponwire;

    for z=-limit:step:limit,
        dz=deformfunct(x,z,Bo,dchi,Gz,R);
        z=z+dz;
        testNaNforzdownstop=isnan(z);

        if bornestopdown == 1
            zdownstop(k)=zdownstop(k);
        elseif testNaNforzdownstop == 1
            zdownstop(k)=zdownstop(k);
            bornestopdown=1;
        elseif z > zdownstop(k)

            if z < zdownnonwire
                zdownstop(k)=zdownnonwire;
            elseif z > zdownnonwire
                zdownstop(k)=z;
            end

        end
    end
end
end

```

```

for z=limit:-step:-limit,
dz=deformfunct(x,z,Bo,dchi,Gz,R);
z=z+dz;
testNaNforzupstop=isnan(z);

    if bornestopup == 1
        zupstop(k)=zupstop(k);
    elseif testNaNforzupstop == 1
        zupstop(k)=zupstop(k);
        bornestopup=1;
    elseif z < zupstop(k)

        if z > zuponwire
            zupstop(k)=zuponwire;
        elseif z < zuponwire
            zupstop(k)=z;
        end

    end

end

end

end

%-----
% Plot of the vertical lines

rangex=-limit:step:limit;
lengthx=length(rangex);

ind=find(rangex>=-R & rangex<=R);
minind=min(ind);
maxind=max(ind);

    for k=1:minind,
        x=rangex(k);

        z=-limit:0.001:limit;
        upz=recal(x,limit,Bo,dchi,Gz,R);
        z=z+upz;

        figure(1);
        plot(x,z,'black');
        hold on;
    end

n=1;

    for k=minind:maxind,
        x=rangex(k);
        zdownstopn=zdownstop(n);
        zupstopn=zupstop(n);

```

```

z=-limit:0.001:limit;
upz=recal(x,limit,Bo,dchi,Gz,R);
z=z+upz;

indi=find(z>zdownstopn & z<zupstopn);
z(indi)=NaN;

figure(1);
plot(x,z,'black');
hold on;

n=n+1;
end

for k=maxind:lengthx,
x=rangex(k);

z=-limit:0.001:limit;
upz=recal(x,limit,Bo,dchi,Gz,R);
z=z+upz;

figure(1);
plot(x,z,'black');
hold on;
end
%-----
graphlim=graphlim+step;
figure(1);
xlabel('x axis'); ylabel('z axis');
axis([-graphlim graphlim -graphlim graphlim]);
end

function [dz]=deformfunct(x,z,Bo,dchi,Gz,R)
dR=x.^2+z.^2;

ind=find(dR<=R^2);
x(ind)=NaN;

dz=-(dchi/2)*(Bo/Gz)*R^2*((z^2-x.^2)./(z^2+x.^2).^2);
end

function [xwire zwire]=drawwire(R)
i=1;
for th=0:0.1:2*pi
xwire(i)=R*cos(th);
zwire(i)=R*sin(th);
i=i+1;
end
end

function [upz]=recal(x,limit,Bo,dchi,Gz,R)
limit=-limit;

```

```

upz=- (dchi/2)*(Bo/Gz)*R^2*((limit^2-x^2)/(limit^2+x^2)^2);
limit=-limit;
end

```

3.1.3. Algorithm developed for the fitting of experimental susceptibility artifacts images

3.1.3.1. Main algorithm

```

function
[fitdchi,fact,resnorm]=loopfitsimulimage(dcmimg,Bo,Gz,R,limit,step)

vectresnorm=zeros(1,6);
vectfitdchi=zeros(1,6);
vectfact=zeros(1,6);
vectdchio=zeros(1,6);

n=1;
for i=3:8,
%dchio=input('dchio ');
dchio=-1/10^i;
%facto=input('facto ');
facto=250;
%chimin=input('chimin ');
dchimin=-1e-2;
%chimax=input('chimax ');
dchimax=0;
%factmin=input('factmin ');
factmin=0;
%factmax=input('factmax ');
factmax=1000;

ydata=double(dcmimg);

sizex=size(ydata);
xdata=zeros(sizex);

display(dchio);
options=optimset('lsqcurvefit');
options=optimset(options,'Display','iter');

Xo=[dchio facto];
lb=[dchimin factmin];
ub=[dchimax factmax];

save LoopFit

[X,resnorm]=lsqcurvefit(@(X,xdata)Simuli(X,xdata,Bo,Gz,R,limit,step),Xo,xdata,ydata,lb,ub,options);

dchi=X(1);
fact=X(2);

```

```

display(dchi);
display(fact);
display(resnorm);

vectresnorm(1,n)=resnorm;
vectfitdchi(1,n)=dchi;
vectfact(1,n)=fact;
vectdchio(1,n)=dchio;

n=n+1;

save LoopFit

end

ind=find(vectresnorm <= min(vectresnorm));
dchio=vectdchio(ind);
display('selected dchio= ');display(num2str(dchio));

save LoopFit

Xo=[dchio facto];

options=optimset('lsqcurvefit');
options=optimset(options,'Display','iter','DiffMinChange',1e-11,'TolX',1e-10);
[X,resnorm]=lsqcurvefit(@(X,xdata)Simuli(X,xdata,Bo,Gz,R,limit,step),Xo,xdata,ydata,lb,ub,options);

fitdchi=X(1);
fact=X(2);

end

```

3.1.3.2. Subroutine 1 (image simulation)

```

function img = Simuli(X,xdata,Bo,Gz,R,limit,step)

xdata=xdata*1;

fact=X(2); %Multiplication factor applied on calculated normalized values

dchi=X(1);
Gz=Gz*0.000001;

matriceimage=-limit:step:limit;
matriceimage=length(matriceimage);
img=zeros(matriceimage,matriceimage);

for cntx=1:matriceimage,

for cntz=1:matriceimage,

```

```

Voxeldefsansnan=0; %preparation of the variable in case of NaN segment
%aim : complete the intensity of the deformed voxel for the normalization
including
%the absence of signal from the wire

xvoxelstart=-limit-step+cntx*step;
xvoxelend=xvoxelstart+step;
x=xvoxelstart:0.001:xvoxelend;

%redefinition of z
z=-limit+cntz*step;
zdefup=zdisto(x,z,dchi,Bo,Gz,R);
maxzup=max(zdefup);
minzup=min(zdefup);
%redefinition of z
z=z-step;
zdefdown=zdisto(x,z,dchi,Bo,Gz,R);
maxzdown=max(zdefdown);
minzdown=min(zdefdown);
% -> Each subroutine is started with z=inferior limit of the voxel

% VERTICAL SEGMENTATION OF THE VOXEL

groups=zdefup-zdefdown;
signgroups=sign(groups);

lengthz=length(x);
for i=1:lengthz,
testifisnansigngroups = isnan(signgroups(i));
    if testifisnansigngroups == 1
        signgroups(i) = 2; % a value of NaN différent of -1, 0 or 1
    end
end

vertcut=0;
xvertcut=0;
for i=2:lengthz,
    if signgroups(i) ~= signgroups(i-1)
        vertcut=vertcut+1;
        xvertcut(vertcut)=i;
    %xvertcut signalize the position of the first step of different sign
    end
end
xvertcut=xvertcut-1; % !!! -1 !!!

if vertcut == 0 % MAIN IF : if the voxel is not segmented
    if signgroups(1) == 2 && signgroups(lengthz) == 2
        %display('voxel NaN')
        IPartielsup=0;
        IPartielinf=0;
        Voxeldef=0;
    elseif signgroups(1) > 0 && signgroups(lengthz) > 0

```



```

        %display('zdown below')
%
BASE ROUTINE
%
                                Part over the considered pixel
%redefinition of z !! UP
z=z+step;

%Determination of the number of cycles
cycl=abs(maxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition of z !! DOWN
z=z-step;

%Determination of the number of cycles
cycl=abs(maxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end
end

```

```

Iinf=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
    placetocut=z+i*step;
    Itocut=quadl (@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
    ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
    Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%                                     Part under the considered pixel
%Determination of the number of cycles
cycl=abs(minzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=minzdown+i*step;
    zup=z+step;
    zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z+step-i*step;
    Itocut=quadl (@(x) zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstar
t,xvoxelend);
    IPartielinef(i)=abs(Iinf-Itocut)-Itocutfromdown;
    Itocutfromdown=Itocutfromdown+IPartielinef(i);
end

%redefinition of z !! UP
z=z+step;

%Determination of the number of cycles
cycl=abs(minzup/step);

```

```

cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=minzup+i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,xvoxelend);
ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
end

for i=1:n,
    IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
end
%
%                                END OF THE BASE ROUTINE
%    elseif signgroups(1) < 0 && signgroups(lengthz) < 0
%        %display('zdown au dessus')
%
%                                INVERSE ROUTINE
%
%                                Part over the considered pixel
%redefinition of z !! UP so zdown is kept as inferior limit

%Determination of the number of cycles
cycl=abs(maxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadl(@(x)zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

IPartielsup=zeros(1,n);

```

```

Itocutfromup=0;
for i=n:-1:1,
placetocut=z+i*step;
Itocut=quadl(@(x)zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition de z !! DOWN
z=z+step;

%Determination of the number of cycles
cycl=abs(maxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadl(@(x)zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x)zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%Determination of the number of cycles
cycl=abs(minzup/step);
cycl=uint16(cycl);
cycl=double(cycl);

```

```

cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=minzup+i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstar
t,xvoxelend);
IPartielinef(i)=abs(Iinf-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+IPartielinef(i);
end

%redefinition of z !!
z=z-step;

%Determination of the number of cycles
cycl=abs(minzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=minzdown+i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z+step-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstar
t,xvoxelend);
ItocutfromPartielinef(i)=abs(Isup-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+ItocutfromPartielinef(i);
end

for i=1:n,
    IPartielinef(i)=IPartielinef(i)-ItocutfromPartielinef(i);
end

```

```

end
%
%                               FIN DU PROGRAMME INVERSE
end

elseif vertcut ~= 0 % MAIN IF : if the voxel is segmented

bornestosegmentx=zeros(1,vertcut);
for i=1:vertcut,
    bornestosegmentx(i)=xvoxelstart+xvertcut(i)*0.001;
end

segmentsign=zeros(1,vertcut+1);
segmentsign(1)=signgroups(1);
for i=1:vertcut
    n=xvertcut(i)+1;
    segmentsign(i+1)=signgroups(n);
end

numberofsegements=length(segmentsign);
cellx=cell(1,numberofsegements);
cellx{1}=xvoxelstart:0.001:(bornestosegmentx(1)-0.001);
for i=1:vertcut-1,
    segstop=bornestosegmentx(i+1)-0.001;
    cellx{i+1}=bornestosegmentx(i):0.001:segstop;
end
cellx{numberofsegements}=bornestosegmentx(vertcut):0.001:xvoxelend;

cellVoxeldef=cell(1,numberofsegements);
cellIPartielsup=cell(1,numberofsegements);
cellIPartielinef=cell(1,numberofsegements);

    for cntofseg=1:numberofsegements,
        if segmentsign(cntofseg) == 2
            %display('segment NaN')
            cellIPartielsup{cntofseg}=0;
            cellIPartielinef{cntofseg}=0;
            cellVoxeldef{cntofseg}=0;

%redefinition of x!!
segvoxelstart=min(cellx{cntofseg});
segvoxelend=max(cellx{cntofseg});
Voxeldefsansnan=abs(segvoxelend-segvoxelstart)*step;

            elseif segmentsign(cntofseg) > 0
                %display('segment where zdown is below')
%                               BASE ROUTINE FOR SEGMENT
%redefinition of x!!
x=cellx{cntofseg};
segvoxelstart=min(cellx{cntofseg});
segvoxelend=max(cellx{cntofseg});
%                               Part over the considered pixel
%redefinition of z !! UP
z=z+step;

```

```

segzdefup=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzup=max(segzdefup);
segminzup=min(segzdefup);

%Determination of the number of cycles
cycl=abs(segmaxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segmaxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition of z !! DOWN
z=z-step;
segzdefdown=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzdown=max(segzdefdown);
segminzdown=min(segzdefdown);

%Determination of the number of cycles
cycl=abs(segmaxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segmaxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

```

```

Iinf=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
    placetocut=z+i*step;
    Itocut=quadl (@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
    Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%                                     Part under the considered pixel
%Determination of the number of cycles
cycl=abs(segminzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segminzdown+i*step;
    zup=z+step;
    zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z+step-i*step;
    Itocut=quadl (@(x) zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    IPartielinef(i)=abs(Iinf-Itocut)-Itocutfromdown;
    Itocutfromdown=Itocutfromdown+IPartielinef(i);
end

%redefinition of z !!
z=z+step;

%Determination of the number of cycles
cycl=abs(segminzup/step);

```



```

cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segminzup+i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelst
art,segvoxelend);
ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
end

for i=1:n,
    IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
end

%redefinition of z !! in order to reach the next segment with z=zdown
z=z-step;
%-----
cellIPartielsup{cntofseg}=IPartielsup;
cellIPartielinf{cntofseg}=IPartielinf;
cellVoxeldef{cntofseg}=Voxeldef;
%
%                               END OF THE BASE ROUTINE FOR SEGMENT
    elseif segmentsign(cntofseg) < 0
        %display('segment where zdown is above')
%
%                               INVERSE ROUTINE FOR SEGMENT
%redefinition of x!!
x=cellx{cntofseg};
segvoxelstart=min(cellx{cntofseg});
segvoxelend=max(cellx{cntofseg});
%
%                               Part over the considered pixel
%redefinition of z !! UP so zdown is kept as upper limit

segzdefdown=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzdown=max(segzdefdown);
segminzdown=min(segzdefdown);

%Determination of the number of cycles
cycl=abs(segmaxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);

```

```

cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segmaxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z+i*step;
Itocut=quadl (@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstar
t,segvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition of z !! DOWN
z=z+step;

segzdefup=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzup=max(segzdefup);
segminzup=min(segzdefup);

%Determination of the number of cycles
cycl=abs(segmaxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segmaxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%
```

```

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x)zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%                               Part under the considered pixel
%Determination of the number of cycles
cycl=abs(segminzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segminzup+i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
IPartielinf(i)=abs(Iinf-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+IPartielinf(i);
end

%redefinition of z !!
z=z-step;

%Determination of the number of cycles
cycl=abs(segminzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segminzdown+i*step;

```

```

zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z+step-i*step;
    Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
    Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
end

for i=1:n,
    IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
end
%-----
cellIPartielsup{cntofseg}=IPartielsup;
cellIPartielinf{cntofseg}=IPartielinf;
cellVoxeldef{cntofseg}=Voxeldef;
%
%                               END OF THE INVERSE ROUTINE FOR SEGMENT
%       end %if segmentsign(cntofseg) > < ou =
%       end %for cntofseg=1:numberofsegements

% Compilation of the different segments
Voxeldef=0;
for i=1:numberofsegements,
    Voxeldef=Voxeldef+cellVoxeldef{i};
end

lengthIPartielsup=zeros(1,numberofsegements);
for i=1:numberofsegements,
    lengthIPartielsup(i)=length(cellIPartielsup{i});
end
lengthmaxIPartielsup=max(lengthIPartielsup);
for i=1:numberofsegements,
    lengthvect=length(cellIPartielsup{i});
    toadd=lengthmaxIPartielsup-lengthvect;
    matrixtoadd=zeros(1,toadd);
    cellIPartielsup{i}=[cellIPartielsup{i} matrixtoadd];
end
for i=1:lengthmaxIPartielsup,
    element=0;
    for j=1:numberofsegements,
        element=element+cellIPartielsup{j}(i);
    end
    IPartielsup(i)=element;
end

```

```

lenghtIPartielinef=zeros(1,numberofsegements);
for i=1:numberofsegements,
    lenghtIPartielinef(i)=length(cellIPartielinef{i});
end
lenghtmaxIPartielinef=max(lenghtIPartielinef);
for i=1:numberofsegements,
    lengthvect=length(cellIPartielinef{i});
    toadd=lenghtmaxIPartielinef-lengthvect;
    matrixtoadd=zeros(1,toadd);
    cellIPartielinef{i}=[cellIPartielinef{i} matrixtoadd];
end
for i=1:lenghtmaxIPartielinef,
    element=0;
    for j=1:numberofsegements,
        element=element+cellIPartielinef{j}(i);
    end
    IPartielinef(i)=element;
end
%
end % OF THE MAIN IF

%Normalization
if Voxeldef == 0
    stayin=0;
    IPartielsupnl=IPartielsup;
    Ipartielinefnl=IPartielinef;
elseif Voxeldef ~= 0
    IPartielsupnl=IPartielsup./(Voxeldef+Voxeldefsansnan);
    Ipartielinefnl=IPartielinef./(Voxeldef+Voxeldefsansnan);
    stayin=Voxeldef/(Voxeldef+Voxeldefsansnan);
end

n=length(IPartielsupnl);
for i=1:n,
    stayin=stayin-IPartielsupnl(i);
end
n=length(Ipartielinefnl);
for i=1:n,
    stayin=stayin-Ipartielinefnl(i);
end

%Fill of the considered voxel by stayin
counter=matriceimage-cntz+1;
img(counter,cntx)=img(counter,cntx)+stayin;

% Repartition of the narmalized partial integrals
n=length(IPartielsupnl);
for i=1:n,
    mobilecounter=counter-i;
    if mobilecounter < 1
        mobilecounter=1;
        IPartielsupnl(i)=0;
    end
end

```

```

%IPartielsupnl(i)
img(mobilecounter,cntx)=img(mobilecounter,cntx)+IPartielsupnl(i);
end
n=length(Ipartielinfnl);
for i=1:n,
mobilecounter=counter+i;
    if mobilecounter > matriceimage
        mobilecounter=matriceimage;
        Ipartielinfnl(i)=0;
    end
%Ipartielinfnl(i)
img(mobilecounter,cntx)=img(mobilecounter,cntx)+Ipartielinfnl(i);
end

end %for cntz=1:matriceimage,

end %for cntx=1:matriceimage,

%But : ligne inférieure de l'image doit recevoir du signal d'en-dessous
%Aim : the lowest line of the image must receive signal from below
img(:,cntx)=[]; %remove the last column
img(:,1)=[]; %remove the first column
img(cntz,:)=[]; %remove the last line
img(1,:)=[]; %remove the first line

img=fact*img;

end %of the function simulimage

```

3.1.3.3. Subroutine 2 (image simulation and result display)

```

function Simulimage(dchi,fact,Bo,Gz,R,limit,step)

Gz=Gz*0.000001;

matriceimage=-limit:step:limit;
matriceimage=length(matriceimage);
img=zeros(matriceimage,matriceimage);

for cntx=1:matriceimage,

for cntz=1:matriceimage,

Voxeldefsansnan=0; %preparation of the variable in case of NaN segment

%aim : complete the distorted voxel intensity for normalization and thus
include
%the absence of signal from the wire

xvoxelstart=-limit-step+cntx*step;
xvoxelend=xvoxelstart+step;
x=xvoxelstart:0.001:xvoxelend;

```

```

%redefinition of z !!
z=-limit+cntz*step;
zdefup=zdisto(x,z,dchi,Bo,Gz,R);
maxzup=max(zdefup);
minzup=min(zdefup);
%redéfinition de z !!
z=z-step;
zdefdown=zdisto(x,z,dchi,Bo,Gz,R);
maxzdown=max(zdefdown);
minzdown=min(zdefdown);
% -> each subroutine is started with z=inferior limit of the voxel

% VERTICAL SEGMENTATION OF THE VOXEL

groups=zdefup-zdefdown;
signgroups=sign(groups);

lengthz=length(x);
for i=1:lengthz,
testifisnaninsigngroups = isnan(signgroups(i));
    if testifisnaninsigngroups == 1
        signgroups(i) = 2; % a value for NaN différent from -1, 0 or 1
    end
end

vertcut=0;
xvertcut=0;
for i=2:lengthz,
    if signgroups(i) ~= signgroups(i-1)
        vertcut=vertcut+1;
        xvertcut(vertcut)=i; %xvertcut signalize the first step of different
sign
    end
end
xvertcut=xvertcut-1; % !!! -1 !!!

if vertcut == 0 % MAIN IF : if the voxel is not segmented
    if signgroups(1) == 2 && signgroups(lengthz) == 2
        %display('voxel NaN')
        IPartielsup=0;
        IPartielinf=0;
        Voxeldef=0;
    elseif signgroups(1) > 0 && signgroups(lengthz) > 0
        %display('zdown en dessous')
    %
% BASE ROUTINE
%
% Part over the considered pixel
%redefinition de z !! UP
z=z+step;

%Determination of the number of cycles
cycl=abs(maxzup/step);
cycl=uint16(cycl);

```

```

cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition of z !! DOWN
z=z-step;

%Determination of the number of cycles
cycl=abs(maxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,

```



```

placetocut=z+i*step;
Itocut=quadl(@(x)zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%                                Part under the considered pixel
%Determination of the number of cycles
cycl=abs(minzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=minzdown+i*step;
    zup=z+step;
    zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z+step-i*step;
    Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstar
t,xvoxelend);
IPartielinf(i)=abs(Iinf-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+IPartielinf(i);
end

%redefinition of z !! UP
z=z+step;

%Determination of the number of cycles
cycl=abs(minzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=minzup+i*step;
    zup=z;
    zdown=z-step;
    if testif <= zup && testif >= zdown

```

```

        n=i;
        end
    end

    ItocutfromPartielinf=zeros(1,n);
    Itocutfromdown=0;
    for i=n:-1:1,
        placetocut=z-i*step;
        Itocut=quadl(@(x) zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,xvoxelend);
        ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
        Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
    end

    for i=1:n,
        IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
    end
    %
    %                               END OF THE BASE ROUTINE
    elseif signgroups(1) < 0 && signgroups(lengthz) < 0
        %display('zdown au dessus')
    %
    %                               INVERSE ROUTINE
    %
    %                               Part over the considered pixel
    %redefinition of z !! UP so zdown is kept as upper limit

    %Determination of the number of cycles
    cycl=abs(maxzdown/step);
    cycl=uint16(cycl);
    cycl=double(cycl);
    cycl=cycl+matriceimage;

    n=1;
    for i=1:cycl,
        testif=maxzdown-i*step;
        zup=z+step;
        zdown=z;
        if testif <= zup && testif >= zdown
            n=i;
            end
    end

    Isup=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

    IPartielsup=zeros(1,n);
    Itocutfromup=0;
    for i=n:-1:1,
        placetocut=z+i*step;
        Itocut=quadl(@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,xvoxelend);
        IPartielsup(i)=Isup-Itocut-Itocutfromup;
        Itocutfromup=Itocutfromup+IPartielsup(i);
    end

    %redefinition of z !! DOWN

```

```

z=z+step;

%Determination of the number of cycles
cycl=abs(maxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=maxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadl(@(x) zdisto(x,z,dchi,Bo,Gz,R),xvoxelstart,xvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadl(@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,
xvoxelend);
ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%                               Part under the considered pixel
%Determination of the number of cycles
cycl=abs(minzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=minzup+i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

```

```

end

IPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,xvoxelend);
IPartielinf(i)=abs(Iinf-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+IPartielinf(i);
end

%redefinition of z !!
z=z-step;

%Determination of the number of cycles
cycl=abs(minzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=minzdown+i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
placetocut=z+step-i*step;
Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),xvoxelstart,xvoxelend);
ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
end

for i=1:n,
    IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
end
%
%                               END OF THE INVERSE ROUTINE
end

elseif vertcut ~= 0 % MAIN IF : if the voxel is segmented

bornestosegmentx=zeros(1,vertcut);
for i=1:vertcut,
    bornestosegmentx(i)=xvoxelstart+xvertcut(i)*0.001;
end

```

```

segmentsign=zeros(1,vertcut+1);
segmentsign(1)=signgroups(1);
for i=1:vertcut
n=xvertcut(i)+1;
segmentsign(i+1)=signgroups(n);
end

numberofsegements=length(segmentsign);
cellx=cell(1,numberofsegements);
cellx{1}=xvoxelstart:0.001:(bornestosegmentx(1)-0.001);
for i=1:vertcut-1,
    segstop=bornestosegmentx(i+1)-0.001;
    cellx{i+1}=bornestosegmentx(i):0.001:segstop;
end
cellx{numberofsegements}=bornestosegmentx(vertcut):0.001:xvoxelend;

cellVoxeldef=cell(1,numberofsegements);
cellIPartielsup=cell(1,numberofsegements);
cellIPartielinef=cell(1,numberofsegements);

    for cntofseg=1:numberofsegements,
        if segmentsign(cntofseg) == 2
            %display('segment NaN')
            cellIPartielsup{cntofseg}=0;
            cellIPartielinef{cntofseg}=0;
            cellVoxeldef{cntofseg}=0;

%redefinition of x!!
segvoxelstart=min(cellx{cntofseg});
segvoxelend=max(cellx{cntofseg});
Voxeldefsansnan=abs(segvoxelend-segvoxelstart)*step;

            elseif segmentsign(cntofseg) > 0
                %display('segment where zdown is below')
%
                BASE ROUTINE FOR SEGMENT
%redefinition of x!!
x=cellx{cntofseg};
segvoxelstart=min(cellx{cntofseg});
segvoxelend=max(cellx{cntofseg});
%
                Part over the considered pixel
%redefinition of z !! UP
z=z+step;
segzdefup=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzup=max(segzdefup);
segminzup=min(segzdefup);

%Determination of the number of cycles
cycl=abs(segmaxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

```

```

n=1;
for i=1:cycl,
testif=segmaxzup-i*step;
zup=z;
zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Isup=quadr(@ (x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
placetocut=z-step+i*step;
Itocut=quadr(@ (x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
IPartielsup(i)=Isup-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition of z !! DOWN
z=z-step;
segzdefdown=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzdown=max(segzdefdown);
segminzdown=min(segzdefdown);

%Determination of the number of cycles
cycl=abs(segmaxzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
testif=segmaxzdown-i*step;
zup=z+step;
zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadr(@ (x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,

```

```

placetocut=z+i*step;
Itocut=quadl(@(x)zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%                                Part under the considered pixel
%Determination of the number of cycles
cycl=abs(segminzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segminzdown+i*step;
    zup=z+step;
    zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinf=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z+step-i*step;
    Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    IPartielinf(i)=abs(Iinf-Itocut)-Itocutfromdown;
    Itocutfromdown=Itocutfromdown+IPartielinf(i);
end

%redefinition of z !!
z=z+step;

%Determination of the number of cycles
cycl=abs(segminzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segminzup+i*step;
    zup=z;
    zdown=z-step;
    if testif <= zup && testif >= zdown

```

```

        n=i;
        end
    end

    ItocutfromPartielinf=zeros(1,n);
    Itocutfromdown=0;
    for i=n:-1:1,
        placetocut=z-i*step;
        Itocut=quadl(@(x) zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
        ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
        Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
    end

    for i=1:n,
        IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
    end

    %redefinition of z !! in order to reach the next segment with z=zdown
    z=z-step;
    %-----
    cellIPartielsup{cntofseg}=IPartielsup;
    cellIPartielinf{cntofseg}=IPartielinf;
    cellVoxeldef{cntofseg}=Voxeldef;
    %
    %                               END OF THE BASE ROUTINE FOR SEGMENT
    elseif segmentsign(cntofseg) < 0
        %display('segment where zdown is above')
    %
    %                               INVERSE ROUTINE FOR SEGMENT
    %redefinition de x!!
    x=cellx{cntofseg};
    segvoxelstart=min(cellx{cntofseg});
    segvoxelend=max(cellx{cntofseg});
    %
    %                               Part over the considered pixel
    %redefinition of z !! UP thus zdown is kept as upper limit

    segzdefdown=zdisto(x,z,dchi,Bo,Gz,R);
    segmaxzdown=max(segzdefdown);
    segminzdown=min(segzdefdown);

    %Determination of the number of cycles
    cycl=abs(segmaxzdown/step);
    cycl=uint16(cycl);
    cycl=double(cycl);
    cycl=cycl+matriceimage;

    n=1;
    for i=1:cycl,
        testif=segmaxzdown-i*step;
        zup=z+step;
        zdown=z;
        if testif <= zup && testif >= zdown
            n=i;
        end
    end

```



```

end

Isup=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

IPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
    placetocut=z+i*step;
    Itocut=quadl (@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    IPartielsup(i)=Isup-Itocut-Itocutfromup;
    Itocutfromup=Itocutfromup+IPartielsup(i);
end

%redefinition de z !! DOWN
z=z+step;

segzdefup=zdisto(x,z,dchi,Bo,Gz,R);
segmaxzup=max(segzdefup);
segminzup=min(segzdefup);

%Determination of the number of cycles
cycl=abs(segmaxzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segmaxzup-i*step;
    zup=z;
    zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

Iinf=quadl (@(x) zdisto(x,z,dchi,Bo,Gz,R),segvoxelstart,segvoxelend);

%Calculation of the voxel area for normalization
Voxeldef=Isup-Iinf;
%

ItocutfromPartielsup=zeros(1,n);
Itocutfromup=0;
for i=n:-1:1,
    placetocut=z-step+i*step;
    Itocut=quadl (@(x) zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut),segvoxelstart,segvoxelend);
    ItocutfromPartielsup(i)=Iinf-Itocut-Itocutfromup;
    Itocutfromup=Itocutfromup+ItocutfromPartielsup(i);
end

```

```

for i=1:n,
    IPartielsup(i)=IPartielsup(i)-ItocutfromPartielsup(i);
end
%-----
%
%Determination of the number of cycles
cycl=abs(segminzup/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segminzup+i*step;
    zup=z;
    zdown=z-step;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

IPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,
    placetocut=z-i*step;
    Itocut=quadl(@(x)zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelst
art,segvoxelend);
    IPartielinef(i)=abs(Iinf-Itocut)-Itocutfromdown;
    Itocutfromdown=Itocutfromdown+IPartielinef(i);
end

%redefinition of z !!
z=z-step;

%Determination of the number of cycles
cycl=abs(segminzdown/step);
cycl=uint16(cycl);
cycl=double(cycl);
cycl=cycl+matriceimage;

n=1;
for i=1:cycl,
    testif=segminzdown+i*step;
    zup=z+step;
    zdown=z;
    if testif <= zup && testif >= zdown
        n=i;
    end
end

ItocutfromPartielinef=zeros(1,n);
Itocutfromdown=0;
for i=n:-1:1,

```

```

placetocut=z+step-i*step;
Itocut=quadl (@(x) zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut),segvoxelst
art,segvoxelend);
ItocutfromPartielinf(i)=abs(Isup-Itocut)-Itocutfromdown;
Itocutfromdown=Itocutfromdown+ItocutfromPartielinf(i);
end

for i=1:n,
    IPartielinf(i)=IPartielinf(i)-ItocutfromPartielinf(i);
end
%-----
cellIPartielsup{cntofseg}=IPartielsup;
cellIPartielinf{cntofseg}=IPartielinf;
cellVoxeldef{cntofseg}=Voxeldef;
%
%                               END OF THE INVERSE ROUTINE FOR SEGMENT
%       end %if segmentsign(cntofseg) > < or =
%       end %for cntofseg=1:numberofsegements

% Compilation of the different segments
Voxeldef=0;
for i=1:numberofsegements,
    Voxeldef=Voxeldef+cellVoxeldef{i};
end

lenghtIPartielsup=zeros(1,numberofsegements);
for i=1:numberofsegements,
    lenghtIPartielsup(i)=length(cellIPartielsup{i});
end
lenghtmaxIPartielsup=max(lenghtIPartielsup);
for i=1:numberofsegements,
    lengthvect=length(cellIPartielsup{i});
    toadd=lenghtmaxIPartielsup-lengthvect;
    matrixtoadd=zeros(1,toadd);
    cellIPartielsup{i}=[cellIPartielsup{i} matrixtoadd];
end
for i=1:lenghtmaxIPartielsup,
    element=0;
    for j=1:numberofsegements,
        element=element+cellIPartielsup{j}(i);
    end
    IPartielsup(i)=element;
end

lenghtIPartielinf=zeros(1,numberofsegements);
for i=1:numberofsegements,
    lenghtIPartielinf(i)=length(cellIPartielinf{i});
end
lenghtmaxIPartielinf=max(lenghtIPartielinf);
for i=1:numberofsegements,
    lengthvect=length(cellIPartielinf{i});
    toadd=lenghtmaxIPartielinf-lengthvect;
    matrixtoadd=zeros(1,toadd);
    cellIPartielinf{i}=[cellIPartielinf{i} matrixtoadd];
end

```

```

end
for i=1:lenghtmaxIPartielinef,
element=0;
    for j=1:numberofsegements,
        element=element+cellIPartielinef{j}(i);
    end
    IPartielinef(i)=element;
end
%
end % OF THE MAIN IF

%Normalization
if Voxeldef == 0
    stayin=0;
    IPartielsupnl=IPartielsup;
    Ipartielinefnl=IPartielinef;
elseif Voxeldef ~= 0
    IPartielsupnl=IPartielsup./(Voxeldef+Voxeldefsansnan);
    Ipartielinefnl=IPartielinef./(Voxeldef+Voxeldefsansnan);
    stayin=Voxeldef/(Voxeldef+Voxeldefsansnan);
end

n=length(IPartielsupnl);
for i=1:n,
    stayin=stayin-IPartielsupnl(i);
end
n=length(Ipartielinefnl);
for i=1:n,
    stayin=stayin-Ipartielinefnl(i);
end

% Fill of the considered voxel with stayin
counter=matriceimage-cntz+1;
img(counter,cntx)=img(counter,cntx)+stayin;

% Repartition of the normalized partial integrals
n=length(IPartielsupnl);
for i=1:n,
    mobilecounter=counter-i;
    if mobilecounter < 1
        mobilecounter=1;
        IPartielsupnl(i)=0;
    end
    img(mobilecounter,cntx)=img(mobilecounter,cntx)+IPartielsupnl(i);
end
n=length(Ipartielinefnl);
for i=1:n,
    mobilecounter=counter+i;
    if mobilecounter > matriceimage
        mobilecounter=matriceimage;
        Ipartielinefnl(i)=0;
    end
    img(mobilecounter,cntx)=img(mobilecounter,cntx)+Ipartielinefnl(i);
end

```

```

end

end %for cntz=1:matriceimage,

end %for cntx=1:matriceimage,

%Aim : the lowest line of the image have to receive signal from below
img(:,cntx)=[]; %removes the last column
img(:,1)=[]; %removes the first column
img(cntz,:)=[]; %removes the last line
img(1,:)=[]; % removes the first line

img=fact*img;
img=uint16(img);

imtool(img);

end %of the function simulimage

```

3.1.3.4. Subroutine 3 (distortion calculation)

```

function zdef=zdisto(x,z,dchi,Bo,Gz,R)

dR=x.^2+z.^2;

ind=find(dR<=R^2);
x(ind)=NaN;
dz=-(dchi/2)*(Bo/Gz)*R^2*((z^2-x.^2)/(z^2+x.^2).^2);
zdef=z+dz;

end

```

3.1.3.5. Subroutine 4 (calculation of the distortion for the repartition of the signal in the lowest pixels)

```

function zapl = zdistoapplatiedown(x,z,dchi,Bo,Gz,R,placetocut)

dR=x.^2+z.^2;

ind=find(dR<=R^2);
x(ind)=NaN;

dz=-(dchi/2)*(Bo/Gz)*R^2*((z^2-x.^2)/(z^2+x.^2).^2);
zapl=z+dz;

lengthx=length(x);

for i=1:lengthx,
    zapli=zapl(i);
    if zapli < placetocut
        zapl(i) = placetocut;
    end
end

```

end

end

3.1.3.6. Subroutine 5 (calculation of the distortion for the repartition of the signal in the upper pixels)

```
function zapl = zdistoapplatieup(x,z,dchi,Bo,Gz,R,placetocut)
```

```
dR=x.^2+z.^2;
```

```
ind=find(dR<=R^2);
```

```
x(ind)=NaN;
```

```
dz=-(dchi/2)*(Bo/Gz)*R^2*((z^2-x.^2)./(z^2+x.^2).^2);
```

```
zapl=z+dz;
```

```
lengthx=length(x);
```

```
for i=1:lengthx,
```

```
zapli=zapl(i);
```

```
    if zapli > placetocut
```

```
        zapl(i) = placetocut;
```

```
    end
```

```
end
```

end

3.1.3.7. Subroutine 6 (calculation of the distortion without the mathematic aberrations)

```
function zdef=zdistosansnan(x,z,dchi,Bo,Gz,R)
```

```
dz=-(dchi/2)*(Bo/Gz)*R^2*((z^2-x.^2)./(z^2+x.^2).^2);
```

```
zdef=z+dz;
```

end

3.1.3.8. Graphical interface algorithm

```
function varargout = DefFitting(varargin)
```

```
% DEFFITTING M-file for DefFitting.fig
```

```
%     DEFFITTING, by itself, creates a new DEFFITTING or raises the  
existing
```

```
%     singleton*.
```

```
%
```

```
%     H = DEFFITTING returns the handle to a new DEFFITTING or the handle  
to
```

```
%     the existing singleton*.
```

```
%
```

```
%     DEFFITTING('CALLBACK',hObject,eventData,handles,...) calls the local
```

```
%     function named CALLBACK in DEFFITTING.M with the given input
```

```
arguments.
```

```

%
%   DEFFITTING('Property','Value',...) creates a new DEFFITTING or
raises the
%   existing singleton*. Starting from the left, property value pairs
are
%   applied to the GUI before DefFitting_OpeningFunction gets called.
An
%   unrecognized property name or invalid value makes property
application
%   stop. All inputs are passed to DefFitting_OpeningFcn via varargin.
%
%   *See GUI Options on GUIDE's Tools menu. Choose "GUI allows only one
%   instance to run (singleton)".
%
% See also: GUIDE, GUIDATA, GUIHANDLES

% WEditFOV the above text to modify the response to help DefFitting

% Last Modified by GUIDE v2.5 18-Dec-2006 19:19:05

% Begin initialization code - DO NOT WEDITFOV
gui_Singleton = 1;
gui_State = struct('gui_Name',       mfilename, ...
                  'gui_Singleton',   gui_Singleton, ...
                  'gui_OpeningFcn', @DefFitting_OpeningFcn, ...
                  'gui_OutputFcn',  @DefFitting_OutputFcn, ...
                  'gui_LayoutFcn',   [] , ...
                  'gui_Callback',    []);
if nargin && ischar(varargin{1})
    gui_State.gui_Callback = str2func(varargin{1});
end

if nargout
    [varargout{1:nargout}] = gui_mainfcn(gui_State, varargin{:});
else
    gui_mainfcn(gui_State, varargin{:});
end
% End initialization code - DO NOT WEDITFOV

% --- Executes just before DefFitting is made visible.
function DefFitting_OpeningFcn(hObject, eventdata, handles, varargin)
% This function has no output args, see OutputFcn.
% hObject    handle to figure
% eventdata  reserved - to be defined in a future version of MATLAB
% handles     structure with handles and user data (see GUIDATA)
% varargin   command line arguments to DefFitting (see VARARGIN)

handles.DefBo='3';
handles.DefGro='8.6';
handles.DefR='0.12';
handles.DefFOV='140';
handles.DefMatrix='512';

```

```

handles.Bo='';
handles.Gro='';
handles.R='';
handles.FOV='';
handles.Matrix='';

% Choose default command line output for DefFitting
handles.output = hObject;

% Update handles structure
guidata(hObject, handles);

% UIWAIT makes DefFitting wait for user response (see UIRESUME)
% uiwait(handles.figure1);

% --- Outputs from this function are returned to the command line.
function varargout = DefFitting_OutputFcn(hObject, eventdata, handles)
% varargout    cell array for returning output args (see VARARGOUT);
% hObject      handle to figure
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)

% Get default command line output from handles structure
varargout{1} = handles.output;

function WEditFilename_Callback(hObject, eventdata, handles)
% hObject      handle to WEditFilename (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)

handles.filename=get(hObject,'String');
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditFilename as text
%        str2double(get(hObject,'String')) returns contents of
%        WEditFilename as a double

% --- Executes during object creation, after setting all properties.
function WEditFilename_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditFilename (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%        See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUiControlBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

```



```

% --- Executes on button press in WPushImport.
function WPushImport_Callback(hObject, eventdata, handles)
% hObject      handle to WPushImport (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.sliceimg=dicomread(handles.filename);
guidata(hObject,handles)

% --- Executes on button press in WPushVisualize.
function WPushVisualize_Callback(hObject, eventdata, handles)
% hObject      handle to WPushVisualize (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.sliceimg=dicomread(handles.filename);
guidata(hObject,handles)
imtool(handles.sliceimg);

% --- Executes on selection change in WPopInapxl.
function WPopInapxl_Callback(hObject, eventdata, handles)
% hObject      handle to WPopInapxl (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
val = get(hObject,'Value');
switch val
case 1
handles.size=0;
handles.limit=0;
guidata(hObject,handles)
case 2
handles.size=22;
guidata(hObject,handles)
case 3
handles.size=10;
guidata(hObject,handles)
case 4
handles.size=20;
guidata(hObject,handles)
case 5
handles.size=30;
guidata(hObject,handles)
case 6
handles.size=40;
guidata(hObject,handles)
case 7
handles.size=50;
guidata(hObject,handles)
case 8
handles.size=60;
guidata(hObject,handles)
end

```

```

% Hints: contents = get(hObject,'String') returns WPopInapxl contents as
cell array
%         contents{get(hObject,'Value')} returns selected item from
WPopInapxl

% --- Executes during object creation, after setting all properties.
function WPopInapxl_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WPopInapxl (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: popupmenu controls usually have a white background on Windows.
%         See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUiControlBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

% --- Executes on selection change in WPopBtwn2pxls.
function WPopBtwn2pxls_Callback(hObject, eventdata, handles)
% hObject      handle to WPopBtwn2pxls (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
val = get(hObject,'Value');
switch val
case 1
handles.size=0;
handles.limit=0;
guidata(hObject,handles)
case 2
handles.size=21;
guidata(hObject,handles)
case 3
handles.size=11;
guidata(hObject,handles)
case 4
handles.size=31;
guidata(hObject,handles)
case 5
handles.size=41;
guidata(hObject,handles)
case 6
handles.size=51;
guidata(hObject,handles)
case 7
handles.size=61;
guidata(hObject,handles)
end
% Hints: contents = get(hObject,'String') returns WPopBtwn2pxls contents as
cell array

```

```

%         contents{get(hObject,'Value')} returns selected item from
WPopBtwn2pxls

% --- Executes during object creation, after setting all properties.
function WPopBtwn2pxls_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WPopBtwn2pxls (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: popupmenu controls usually have a white background on Windows.
%         See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

% --- Executes on button press in WPushVisualizeROI.
function WPushVisualizeROI_Callback(hObject, eventdata, handles)
% hObject      handle to WPushVisualizeROI (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
imtool(handles.ROI);

function WEditCutleft_Callback(hObject, eventdata, handles)
% hObject      handle to WEditCutleft (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.cutleft=str2double(get(hObject,'String'));
if isnan(handles.cutleft)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditCutleft as text
%         str2double(get(hObject,'String')) returns contents of WEditCutleft
as a double

% --- Executes during object creation, after setting all properties.
function WEditCutleft_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditCutleft (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%         See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

```

```

function WEditCutoff_Callback(hObject, eventdata, handles)
% hObject      handle to WEditCutoff (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.cutoff=str2double(get(hObject,'String'));
if isnan(handles.cutoff)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditCutoff as text
%        str2double(get(hObject,'String')) returns contents of WEditCutoff
as a double

```

% --- Executes during object creation, after setting all properties.

```

function WEditCutoff_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditCutoff (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

```

% Hint: weditfov controls usually have a white background on Windows.

```

%        See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

```

% --- Executes on button press in WPushSelectROI.

```

function WPushSelectROI_Callback(hObject, eventdata, handles)
% hObject      handle to WPushSelectROI (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
size=handles.size-1;
i=handles.cutoff;
j=i+size;
k=handles.cutleft;
l=k+size;
handles.ROI=handles.sliceimg(i:j,k:l);
guidata(hObject,handles)

```

```

function WEditBo_Callback(hObject, eventdata, handles)

```

```

% hObject      handle to WEditBo (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.Bo=str2double(get(hObject,'String'));
if isnan(handles.Bo)
    errordlg('You must enter a numeric value','Bad Input')
end

```

```

guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditBo as text
%         str2double(get(hObject,'String')) returns contents of WEditBo as a
double

% --- Executes during object creation, after setting all properties.
function WEditBo_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditBo (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%         See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUiControlBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

function WEditGro_Callback(hObject, eventdata, handles)
% hObject      handle to WEditGro (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.Gro=str2double(get(hObject,'String'));
if isnan(handles.Gro)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditGro as text
%         str2double(get(hObject,'String')) returns contents of WEditGro as
a double

% --- Executes during object creation, after setting all properties.
function WEditGro_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditGro (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%         See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUiControlBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

function WEditR_Callback(hObject, eventdata, handles)
% hObject      handle to WEditR (see GCBO)

```

```

% eventdata reserved - to be defined in a future version of MATLAB
% handles structure with handles and user data (see GUIDATA)
handles.R=str2double(get(hObject,'String'));
if isnan(handles.R)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditR as text
% str2double(get(hObject,'String')) returns contents of WEditR as a
double

% --- Executes during object creation, after setting all properties.
function WEditR_CreateFcn(hObject, eventdata, handles)
% hObject handle to WEditR (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
% See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

% --- Executes on button press in WPushDef.
function WPushDef_Callback(hObject, eventdata, handles)
% hObject handle to WPushDef (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles structure with handles and user data (see GUIDATA)
set(handles.WEditBo,'string',handles.DefBo);
set(handles.WEditGro,'string',handles.DefGro);
set(handles.WEditR,'string',handles.DefR);
set(handles.WEditFOV,'string',handles.DefFOV);
set(handles.WEditMatrix,'string',handles.DefMatrix);
handles.Bo=str2double(handles.DefBo);
handles.Gro=str2double(handles.DefGro);
handles.R=str2double(handles.DefR);
handles.FOV=str2double(handles.DefFOV);
handles.Matrix=str2double(handles.DefMatrix);
guidata(hObject,handles)

% --- Executes on button press in WPushSaveasdef.
function WPushSaveasdef_Callback(hObject, eventdata, handles)
% hObject handle to WPushSaveasdef (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles structure with handles and user data (see GUIDATA)
handles.DefBo=handles.Bo;
handles.DefGro=handles.Gro;
handles.DefR=handles.R;
handles.DefFOV=handles.FOV;

```

```
handles.DefMatrix=handles.Matrix;
guidata(hObject,handles)
```

```
% --- Executes on button press in WPushFit.
function WPushFit_Callback(hObject, eventdata, handles)
% hObject      handle to WPushFit (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.step=handles.FOV/handles.Matrix;
handles.step=handles.step*10;
handles.step=round(handles.step);
handles.step=handles.step/10;
handles.limit=((handles.size+1)/2)*handles.step;
[handles.dchi,handles.fact,handles.resnorm]=loopfitsimulimage(handles.ROI,h
andles.Bo,handles.Gro,handles.R,handles.limit,handles.step);
set(handles.WEditdX,'string',handles.dchi);
set(handles.WEditFact,'string',handles.fact);
set(handles.WEditResnorm,'string',handles.resnorm);
guidata(hObject,handles)
```

```
function WEditdX_Callback(hObject, eventdata, handles)
% hObject      handle to WEditdX (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.dchi=str2double(get(hObject,'String'));
if isnan(handles.dchi)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditdX as text
%        str2double(get(hObject,'String')) returns contents of WEditdX as a
double
```

```
% --- Executes during object creation, after setting all properties.
function WEditdX_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditdX (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%        See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUiControlBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end
```

```
function WEditFact_Callback(hObject, eventdata, handles)
% hObject      handle to WEditFact (see GCBO)
```

```

% eventdata reserved - to be defined in a future version of MATLAB
% handles structure with handles and user data (see GUIDATA)
handles.fact=str2double(get(hObject,'String'));
if isnan(handles.fact)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditFact as text
% str2double(get(hObject,'String')) returns contents of WEditFact as
a double

% --- Executes during object creation, after setting all properties.
function WEditFact_CreateFcn(hObject, eventdata, handles)
% hObject handle to WEditFact (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
% See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

function WEditResnorm_Callback(hObject, eventdata, handles)
% hObject handle to WEditResnorm (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles structure with handles and user data (see GUIDATA)

% Hints: get(hObject,'String') returns contents of WEditResnorm as text
% str2double(get(hObject,'String')) returns contents of WEditResnorm
as a double

% --- Executes during object creation, after setting all properties.
function WEditResnorm_CreateFcn(hObject, eventdata, handles)
% hObject handle to WEditResnorm (see GCBO)
% eventdata reserved - to be defined in a future version of MATLAB
% handles empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
% See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end

% --- Executes on button press in WPushSimuli.
function WPushSimuli_Callback(hObject, eventdata, handles)

```



```
% hObject      handle to WPushSimuli (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
Simulimage(handles.dchi,handles.fact,handles.Bo,handles.Gro,handles.R,handles.limit,handles.step);
```

```
function WEditFOV_Callback(hObject, eventdata, handles)
% hObject      handle to WEditFOV (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.FOV=str2double(get(hObject,'String'));
if isnan(handles.FOV)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditFOV as text
%        str2double(get(hObject,'String')) returns contents of WEditFOV as
a double
```

```
% --- Executes during object creation, after setting all properties.
function WEditFOV_CreateFcn(hObject, eventdata, handles)
% hObject      handle to WEditFOV (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%        See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end
```

```
function WEditMatrix_Callback(hObject, eventdata, handles)
% hObject      handle to WEditMatrix (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      structure with handles and user data (see GUIDATA)
handles.Matrix=str2double(get(hObject,'String'));
if isnan(handles.Matrix)
    errordlg('You must enter a numeric value','Bad Input')
end
guidata(hObject,handles)

% Hints: get(hObject,'String') returns contents of WEditMatrix as text
%        str2double(get(hObject,'String')) returns contents of WEditMatrix
as a double
```

```
% --- Executes during object creation, after setting all properties.
function WEditMatrix_CreateFcn(hObject, eventdata, handles)
```

```
% hObject      handle to WEditMatrix (see GCBO)
% eventdata    reserved - to be defined in a future version of MATLAB
% handles      empty - handles not created until after all CreateFcns called

% Hint: weditfov controls usually have a white background on Windows.
%           See ISPC and COMPUTER.
if ispc && isequal(get(hObject,'BackgroundColor'),
get(0,'defaultUicontrolBackgroundColor'))
    set(hObject,'BackgroundColor','white');
end
```

3.2. Acquisition parameters of the MRI Sequences used

3.2.1. Optimization of the phantom medium composition

se_5mm_140_bw150

Type : Spin Echo

Orientation: sagittal

TR: 500 ms

TE: 10,15, 30, 50, 75, 100, 125 or 150 ms

Base resolution: 512

Phase resolution: 100%

FOV read: 140 mm

FOV phase: 100% (of the FOV read)

Slice thickness: 5 mm

Distance factor between slices: 100% (of the slice thickness)

Voxel size: 0.3 x 0.3 x 5.0 mm

Flip angle: 90° - 180°

Phase encoding direction: A>>P

Bandwidth: 150 Hz/px

3.2.2. Phase images acquisition

gre_5mm_140_bw520_te3.2

Type : Gradient Echo

Orientation: sagittal

TR: 400 ms

TE: 3.2 ms

Base resolution: 320

Phase resolution: 100%

FOV read: 140 mm

FOV phase: 100% (of the FOV read)

Slice thickness: 5 mm

Distance factor between slices: 100% (of the slice thickness)

Voxel size: 0.4 x 0.4 x 5.0 mm

Flip angle: 60°

Phase encoding direction: A>>P

Bandwidth: 520 Hz/px

gre_5mm_140_bw520_te6.2

Type : Gradient Echo

Orientation: sagittal

TR: 400 ms

TE: 6.2 ms

Base resolution: 320
Phase resolution: 100%
FOV read: 140 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 5 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.4 x 0.4 x 5.0 mm
Flip angle: 60°
Phase encoding direction: A>>P
Bandwidth: 520 Hz/px

3.2.3. Iterative susceptibility artifact measurement method

se_5mm_140_bw100

Type : Spin Echo
Orientation: sagittal
TR: 500 ms
TE: 15 ms
Base resolution: 512
Phase resolution: 100%
FOV read: 140 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 5 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.3 x 0.3 x 5.0 mm
Flip angle: 90° - 180°
Phase encoding direction: A>>P
Bandwidth: 100 Hz/px

se_5mm_140_bw150

Type : Spin Echo
Orientation: sagittal
TR: 500 ms
TE: 15 ms
Base resolution: 512
Phase resolution: 100%
FOV read: 140 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 5 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.3 x 0.3 x 5.0 mm
Flip angle: 90° - 180°
Phase encoding direction: A>>P
Bandwidth: 150 Hz/px

3.2.4. Study of the imagery parameters influence

TOF3D

Type : Gradient Echo
Orientation: sagittal/transversal
TR: 10 ms
TE: 3.69 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 75% (of the FOV read)
Slice thickness: 1 mm
Voxel size: 0.9 x 0.9 x 1.0 mm
Flip angle: 10°
Phase encoding direction: A>>P
Bandwidth: 188 Hz/px

TOF2D

Type : Gradient Echo
Orientation: sagittal/transversal
TR: 20 ms
TE: 4.77 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 81.3% (of the FOV read)
Slice thickness: 2 mm
Voxel size: 0.9 x 0.9 x 2.0 mm
Flip angle: 10°
Phase encoding direction: A>>P
Bandwidth: 199 Hz/px

TSE160

Type : Spin Echo
Orientation: sagittal/transversal
TR: 11295 ms
TE: 102 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 200 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 1.5 mm
Distance factor between slices: 0% (of the slice thickness)

Voxel size: 0.8 x 0.8 x 1.5 mm
Flip angle: 150 - 180°
Phase encoding direction: A>>P
Bandwidth: 160 Hz/px

TSE425

Type : Spin Echo
Orientation: sagittal/transversal
TR: 8590 ms
TE: 80 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 200 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 1.5 mm
Distance factor between slices: 0% (of the slice thickness)
Voxel size: 0.8 x 0.8 x 1.5 mm
Flip angle: 150 - 180°
Phase encoding direction: A>>P
Bandwidth: 160 Hz/px

SE

Type : Spin Echo
Orientation: sagittal/transversal
TR: 836 ms
TE: 9.8 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 1.5 mm
Voxel size: 0.9 x 0.9 x 1.5 mm
Flip angle: 90 - 180°
Phase encoding direction: A>>P
Bandwidth: 296 Hz/px

3.2.5. Study of the stent composition and surface treatment influence

TOF3D-flp***

Orientation: sagittal/transversal
TR: 10 ms
TE: 3.69 ms
Base resolution: 256
Phase resolution: 100%

FOV read: 220 mm
FOV phase: 75% (of the FOV read)
Slice thickness: 1 mm
Voxel size: 0.9 x 0.9 x 1.0 mm
Flip angle: *** ° (5 – 10 – 15 – 20 – 25 – 30)
Phase encoding direction: A>>P
Bandwidth: 188 Hz/px

SE-flp***

Orientation: sagittal/transversal
TR: 836 ms
TE: 9.8 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 1.5 mm
Voxel size: 0.9 x 0.9 x 1.5 mm
Flip angle: *** ° - 180° (50 – 70 – 90 – 110 – 130)
Phase encoding direction: A>>P
Bandwidth: 296 Hz/px

3.2.6. Study of the stent composition and orientation influence on the resulting RF artifacts

TOF3D-flp***

Type: Gradient Echo
Orientation: sagittal/transversal
TR: 10 ms
TE: 3.69 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 75% (of the FOV read)
Slice thickness: 1 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.9 x 0.9 x 1.0 mm
Flip angle: *** ° (10 – 20 - 30)
Phase encoding direction: A>>P
Bandwidth: 188 Hz/px

SE-flp***

Type: Spin Echo

Orientation: sagittal/transversal
TR: 836 ms
TE: 9.8 ms
Base resolution: 256
Phase resolution: 100%
FOV read: 220 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 1.5 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.9 x 0.9 x 1.5 mm
Flip angle: *** ° (50 – 90 - 130)
Phase encoding direction: A>>P
Bandwidth: 296 Hz/px

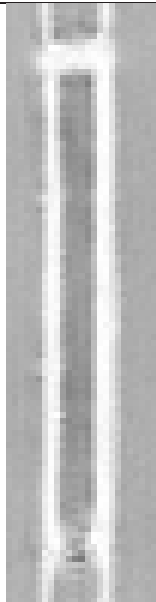
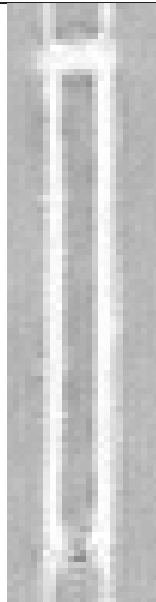
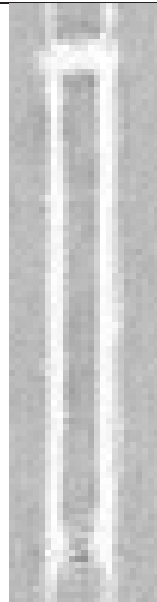
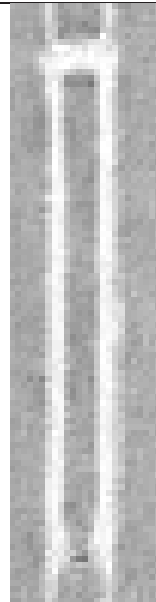
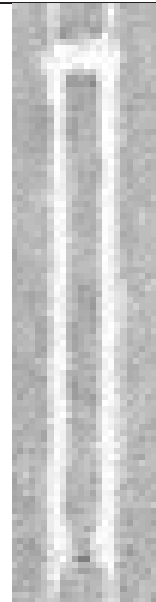
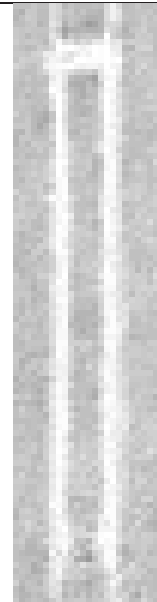
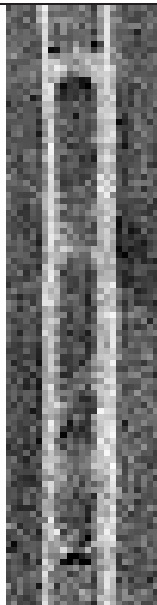
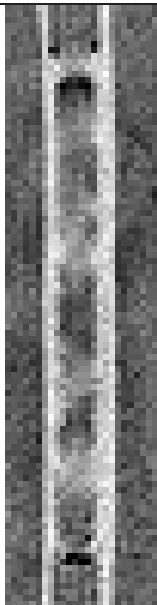
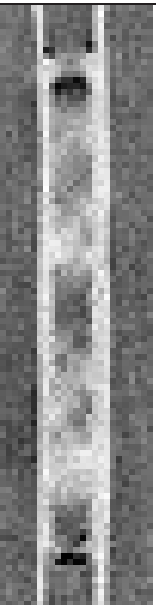
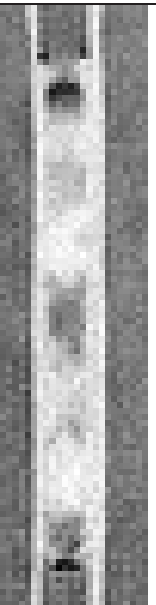
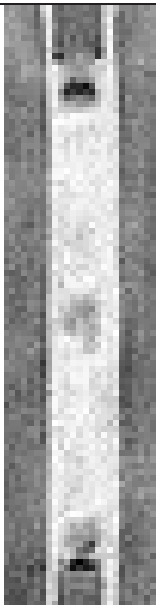
3.2.7. Study of the impact of the nickel oxide and cobalt oxide layers on the MRI behavior of Nitinol and Phynox wires

se_5mm_140_bw100

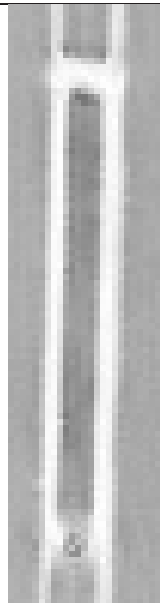
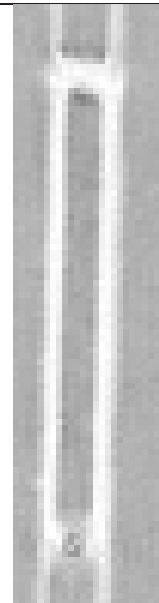
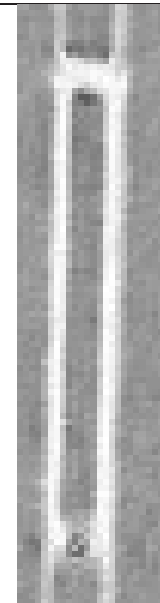
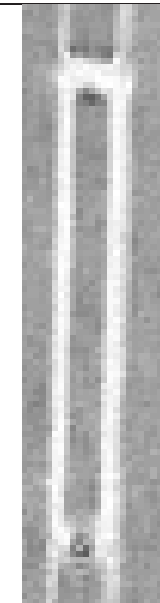
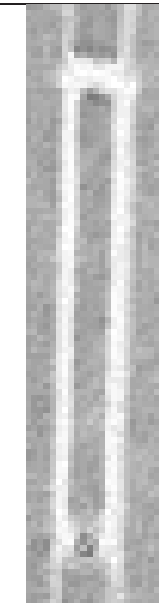
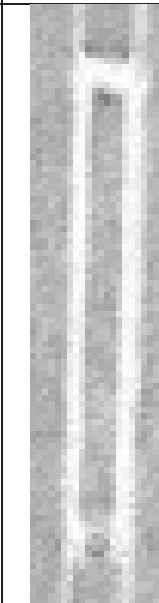
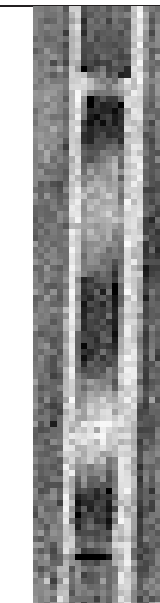
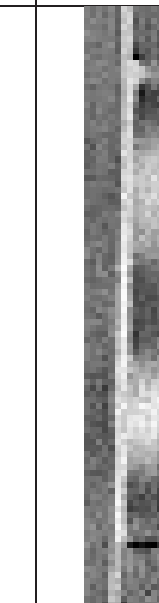
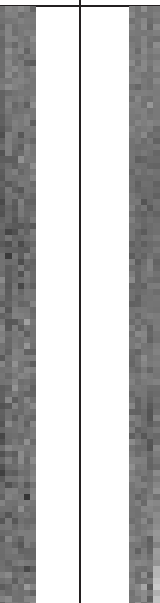
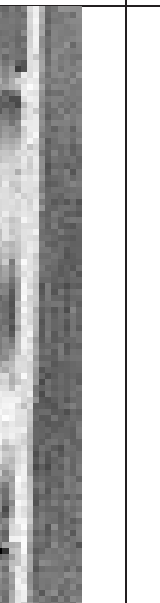
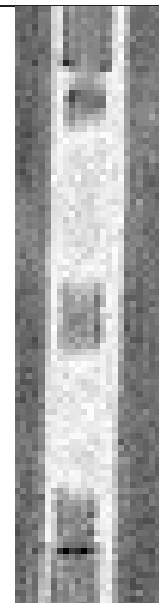
Type : Spin Echo
Orientation: sagittal
TR: 500 ms
TE: 15 ms
Base resolution: 512
Phase resolution: 100%
FOV read: 140 mm
FOV phase: 100% (of the FOV read)
Slice thickness: 5 mm
Distance factor between slices: 100% (of the slice thickness)
Voxel size: 0.3 x 0.3 x 5.0 mm
Flip angle: 90° - 180°
Phase encoding direction: A>>P
Bandwidth: 100 Hz/px

3.3. MRI images of the studied stents obtained with various flip angles (°) with Gradient Echo and Spin Echo sequences

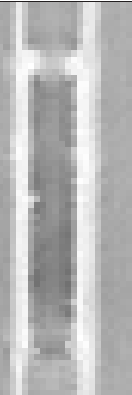
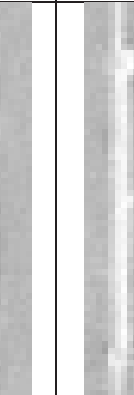
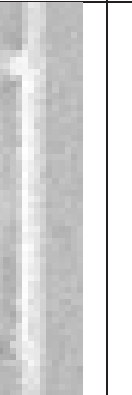
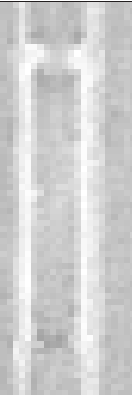
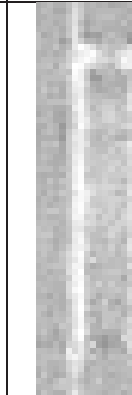
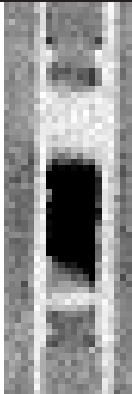
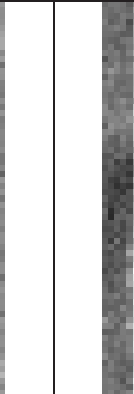
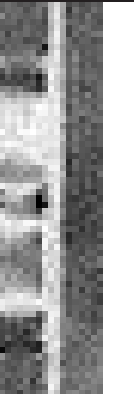
Stent #1. Nitinol stent (diameter 7 mm) composed of 24 braided wires ($\varnothing$ 170 μ m) heat treated for 20 min at 490°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

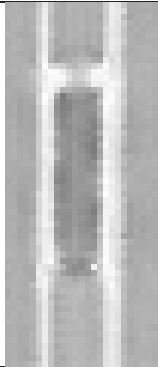
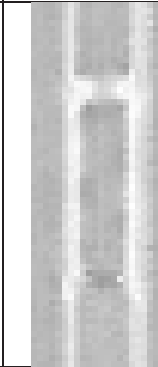
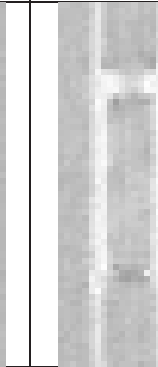
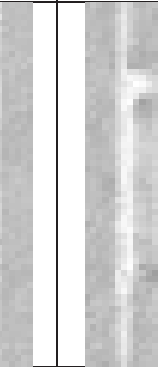
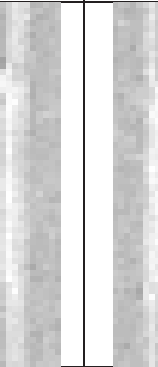
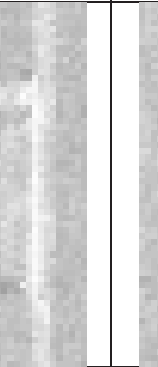
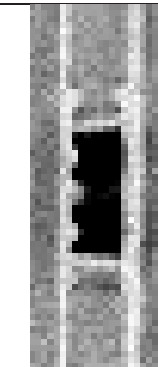
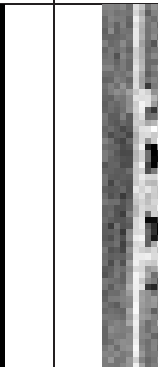
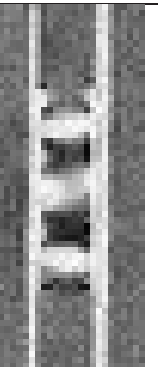
Stent #2. Nitinol stent (diameter 7 mm) composed of 24 braided wires (Ø 170 µm) heat treated for 20 min at 490°C and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

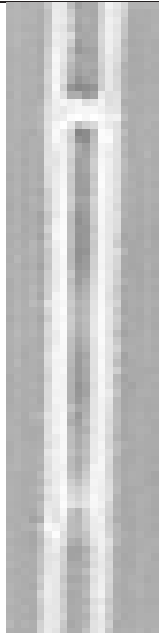
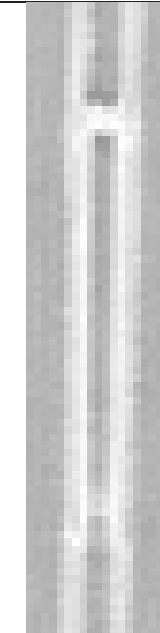
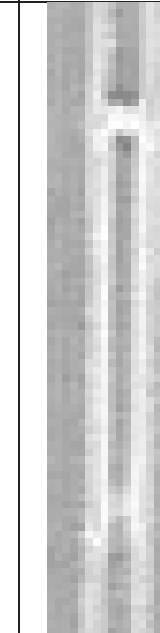
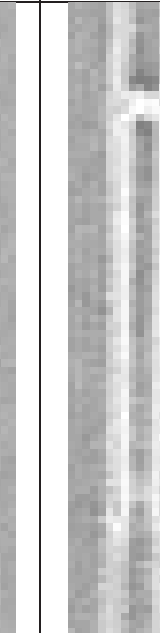
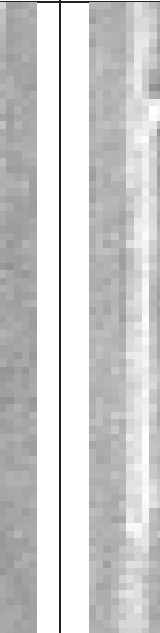
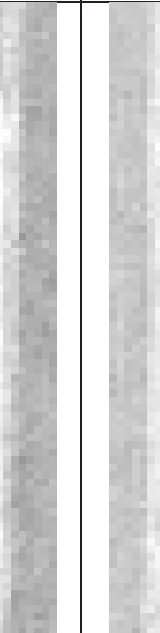
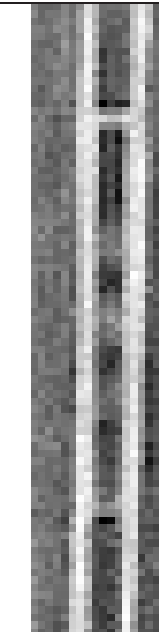
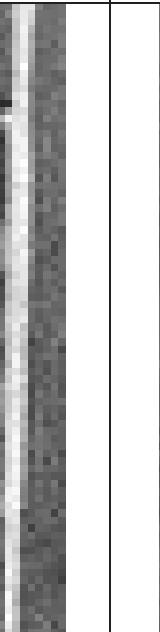
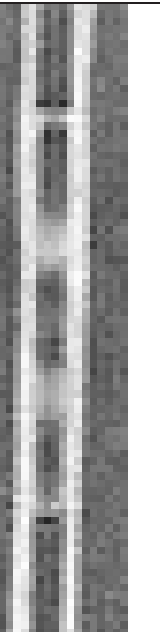
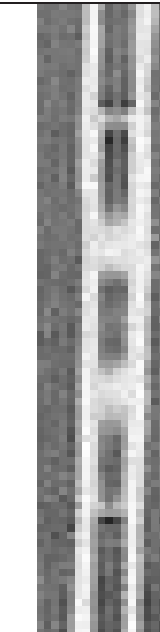
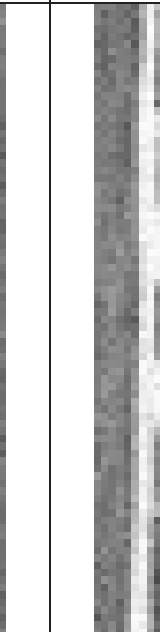
Stent #3. Nitinol DFT10% stent (diameter 8 mm) composed of 80 braided wires (Ø 80 µm) heat treated for 15 min at 500°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

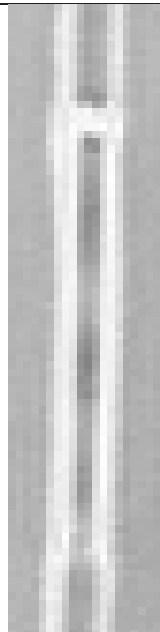
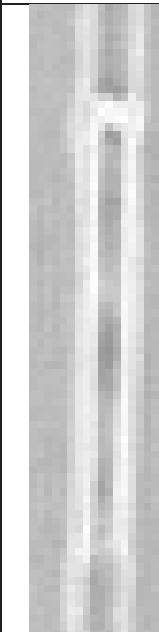
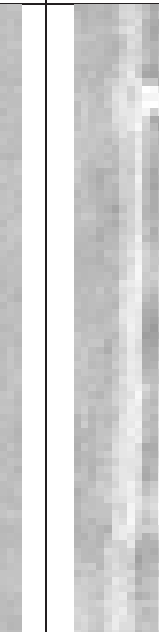
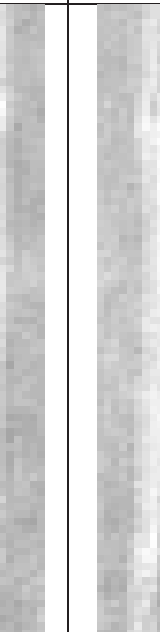
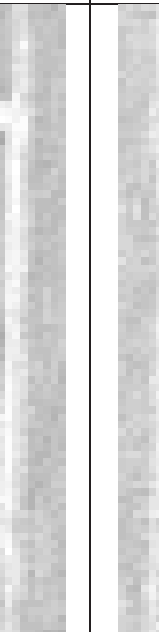
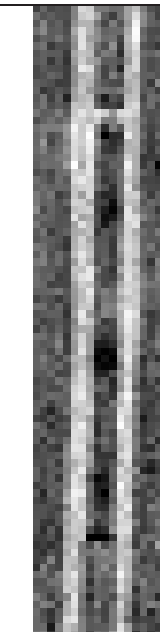
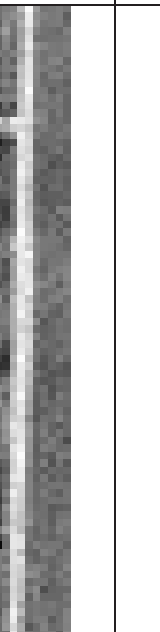
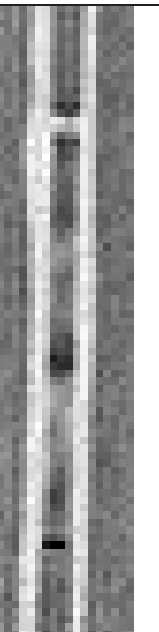
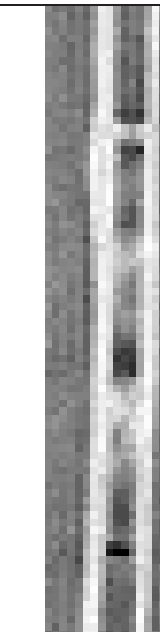
Stent #4. Nitinol DFT10% stent (diameter 8 mm) composed of 80 braided wires (Ø 80 µm) heat treated for 15 min at 500°C and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

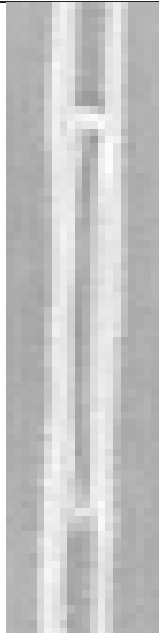
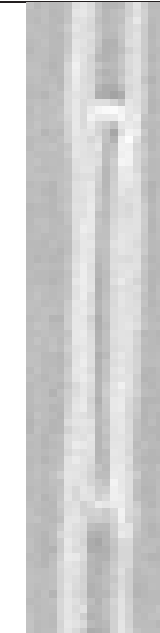
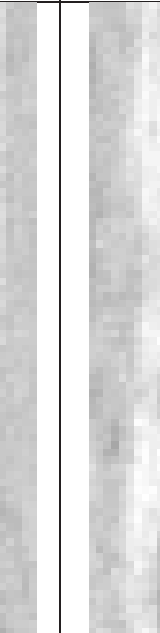
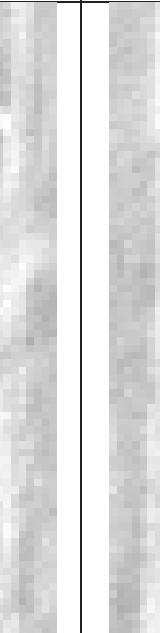
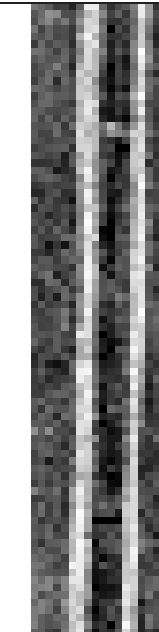
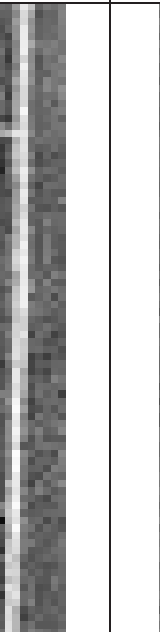
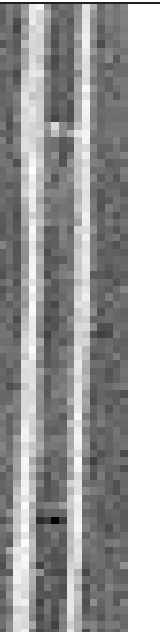
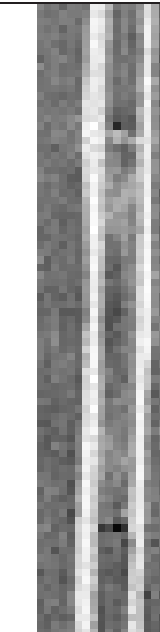
Stent #5. Nitinol stent (diameter 4 mm) composed of 16 braided wires (Ø 100 µm) heat treated for 15 min at 490°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

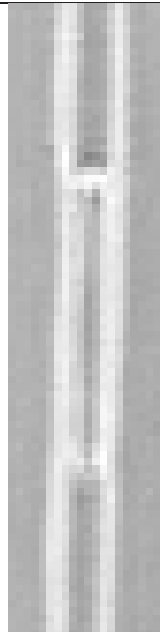
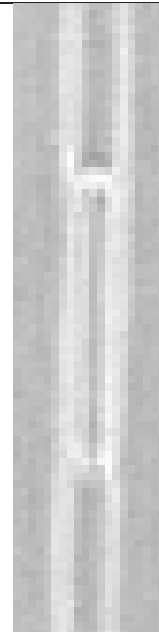
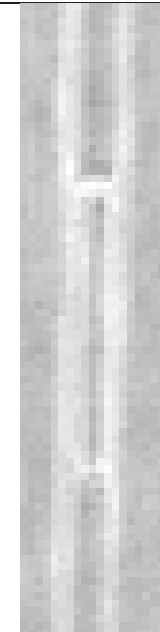
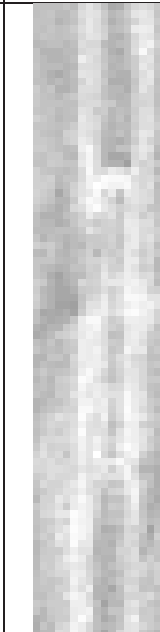
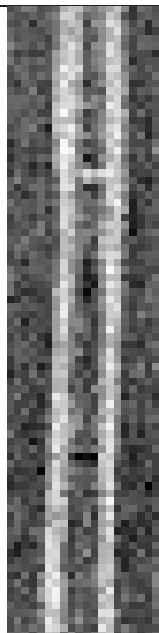
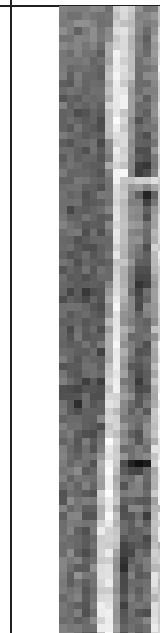
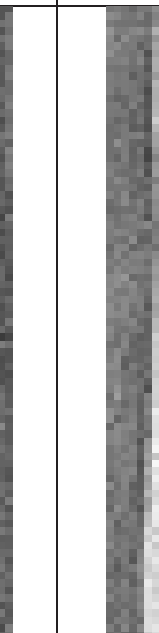
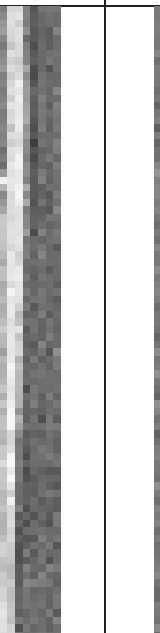
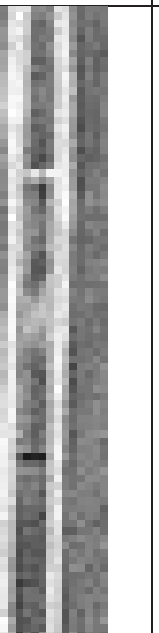
Stent #6. Nitinol stent (diameter 4 mm) composed of 16 braided wires (Ø 100 µm) heat treated for 15 min at 490°C and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

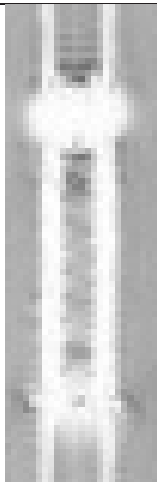
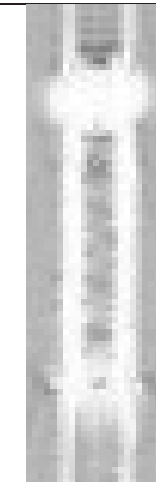
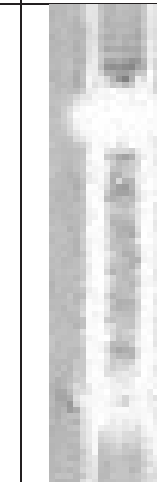
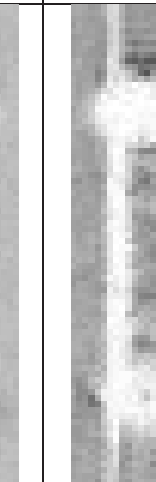
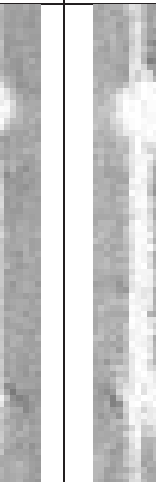
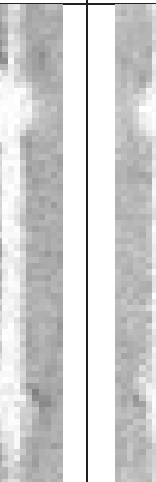
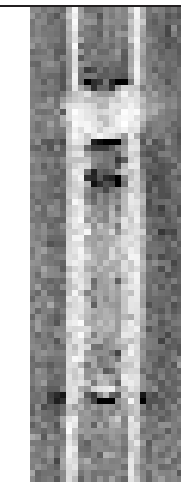
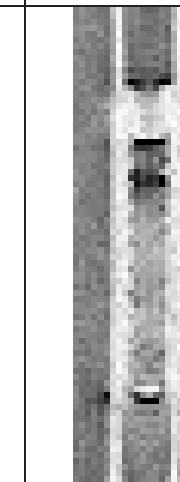
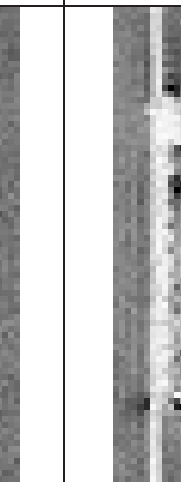
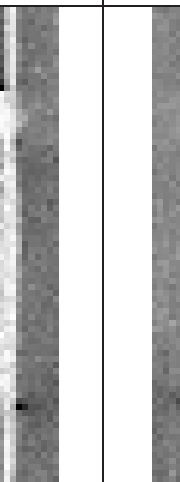
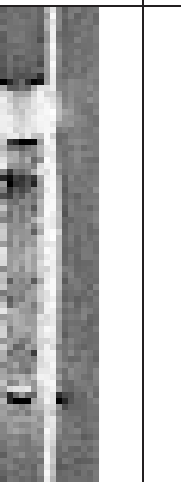
Stent #7. Nitinol stent (diameter 4 mm) composed of 16 braided wires (Ø 100 µm) heat treated for 15 min at 490°C and chemically etched.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

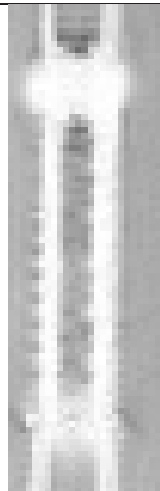
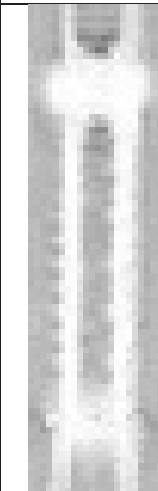
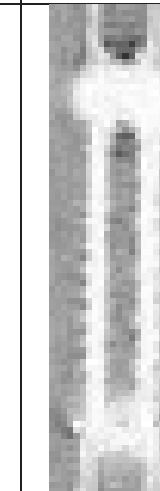
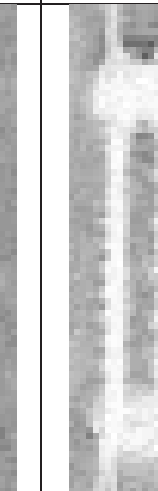
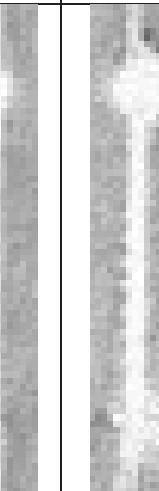
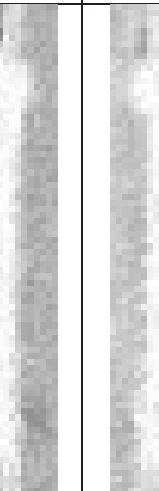
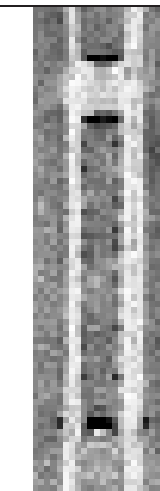
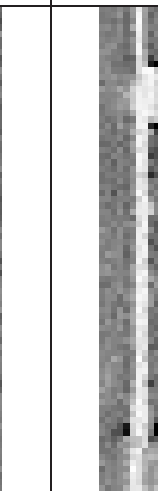
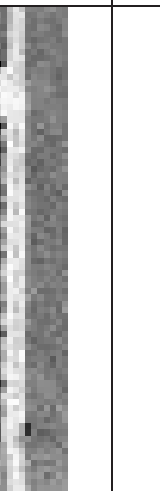
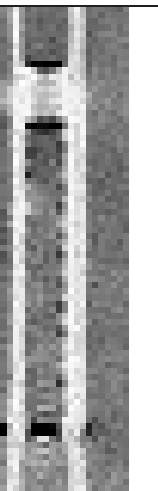
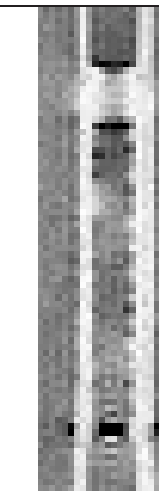
Stent #8. Nitinol stent (diameter 4 mm) composed of 16 braided wires ($\varnothing$ 100 μ m) heat treated for 15 min at 490°C, chemically etched and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

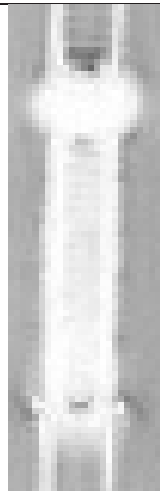
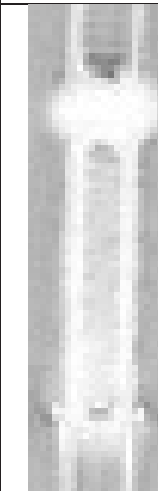
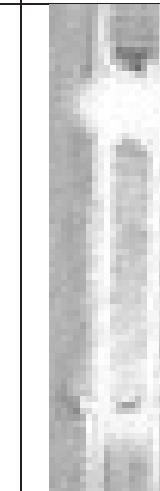
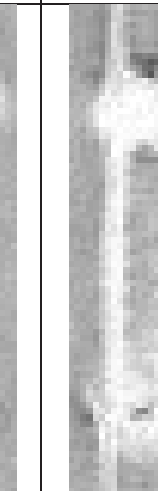
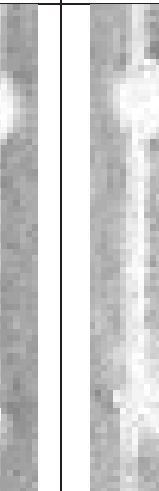
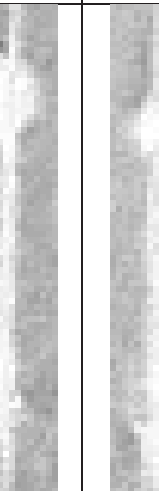
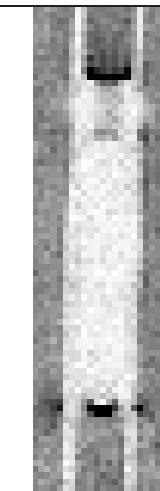
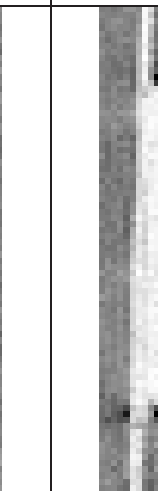
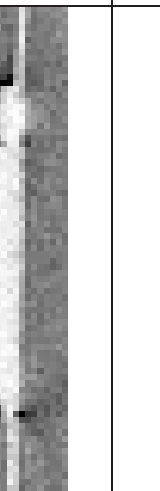
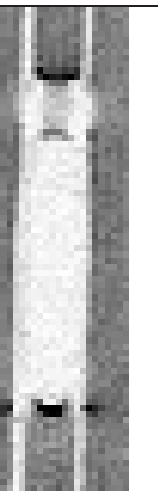
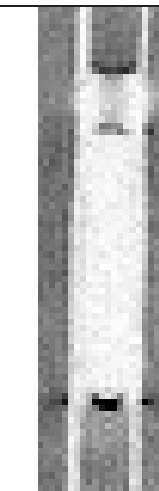
Stent #9. Phynox stent (diameter 8 mm) composed of 80 braided wires ($\varnothing$ 80 μ m) heat treated for 3 h at 550°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

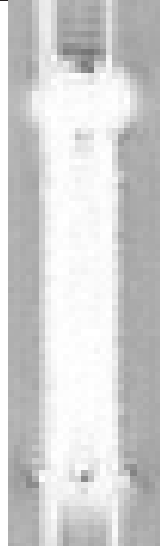
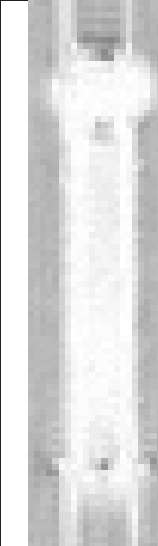
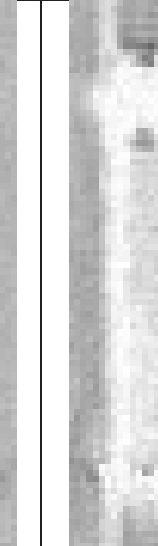
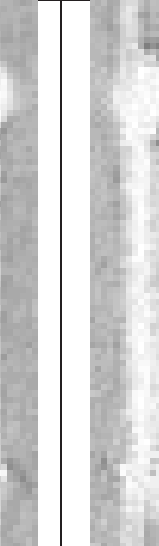
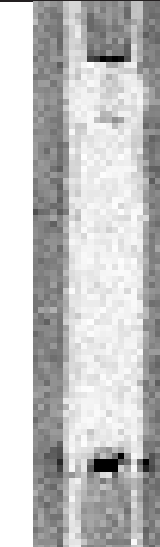
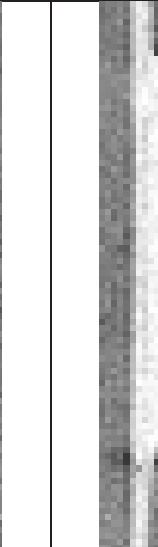
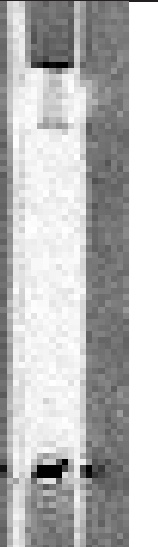
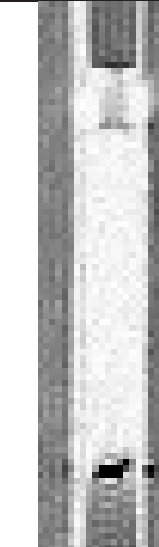
Stent #10. Phynox stent (diameter 8 mm) composed of 80 braided wires ($\varnothing$ 80 μ m) heat treated for 3 h at 550°C and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

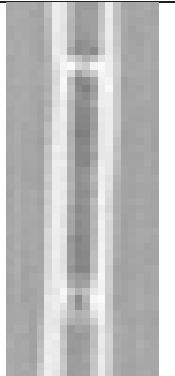
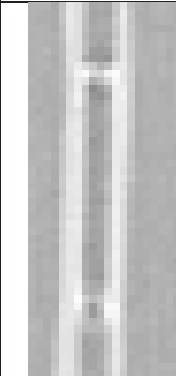
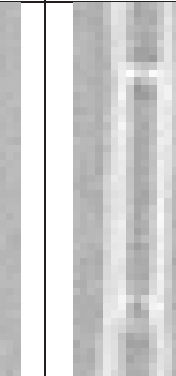
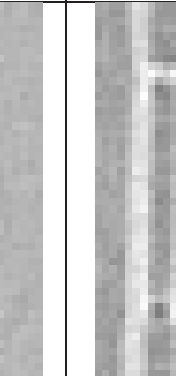
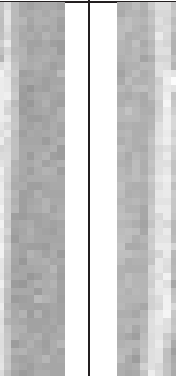
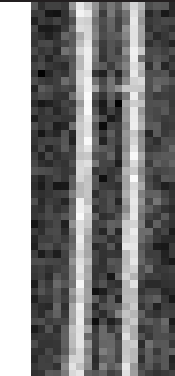
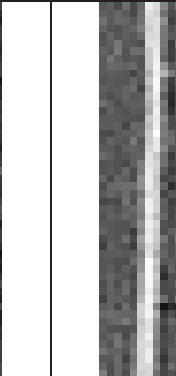
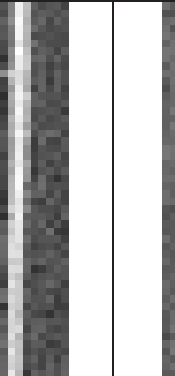
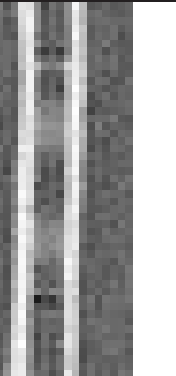
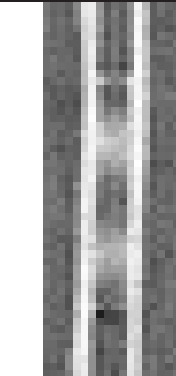
Stent #11. Phynox stent (diameter 8 mm) composed of 80 braided wires ($\varnothing$ 80 μ m) heat treated for 3 h at 550°C and chemically etched.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

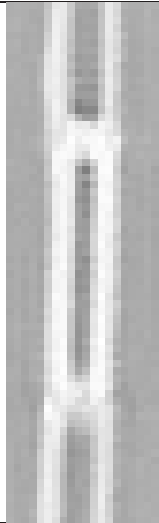
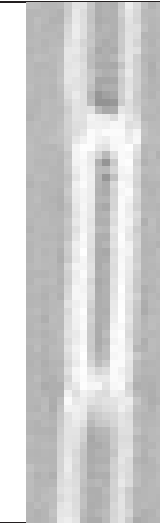
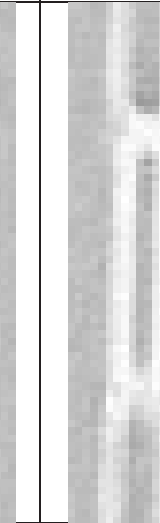
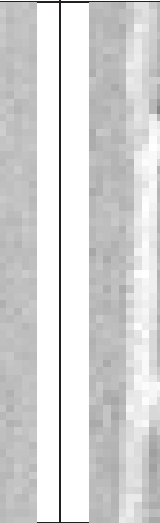
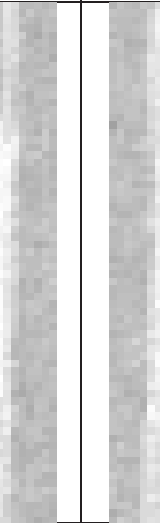
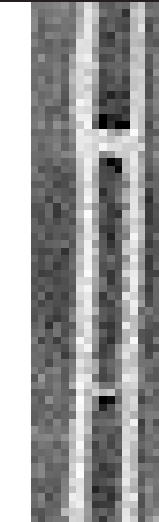
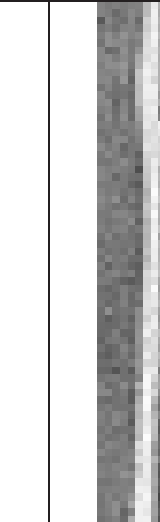
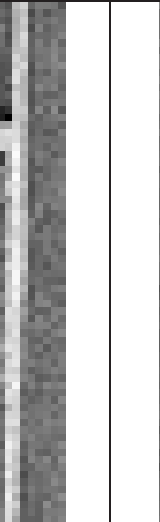
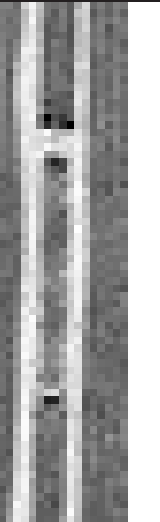
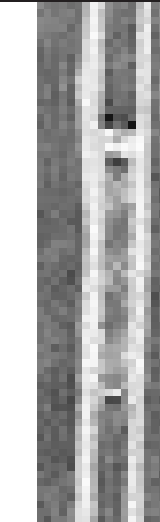
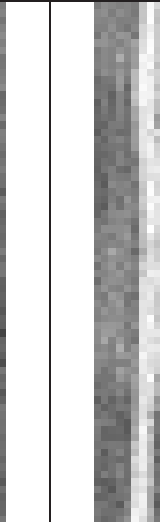
Stent #12. Phynox stent (diameter 8 mm) composed of 80 braided wires ($\varnothing$ 80 μ m) heat treated for 3 h at 550°C, chemically etched and submitted to ethylene oxide sterilization treatment.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

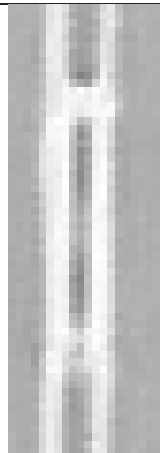
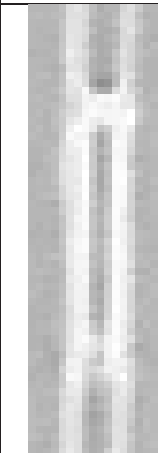
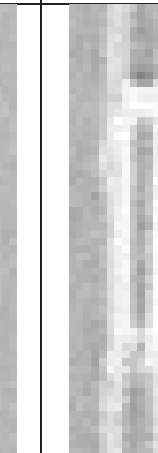
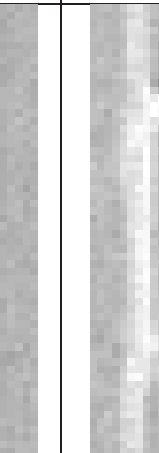
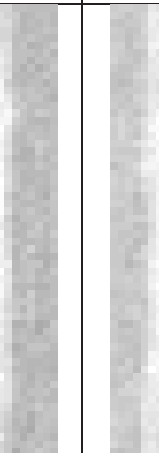
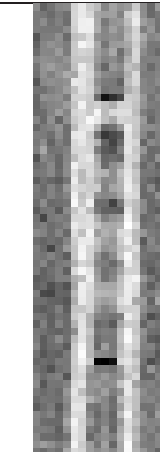
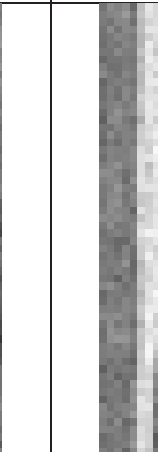
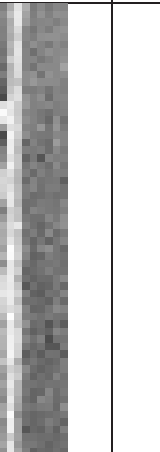
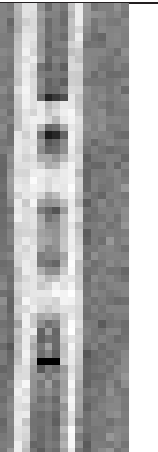
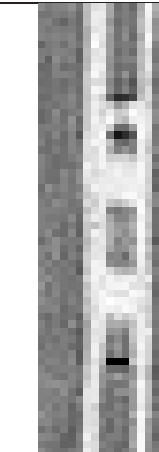
Stent #13. Nitinol stent (diameter 5 mm) composed of 64 braided wires ($\varnothing$ 50 μ m) heat treated for 15 min at 490°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

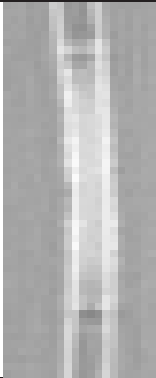
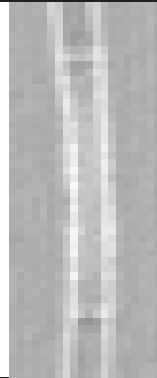
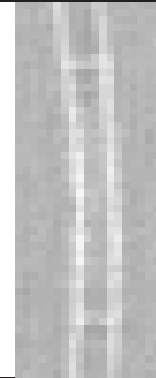
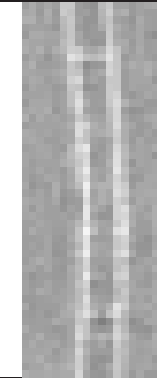
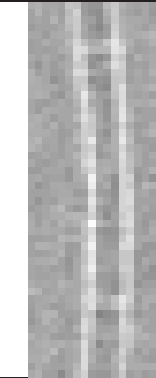
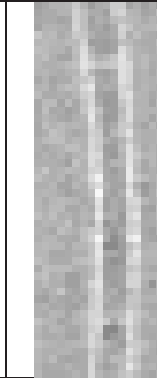
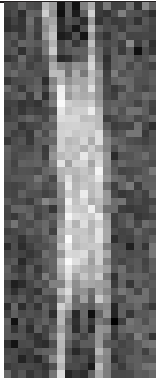
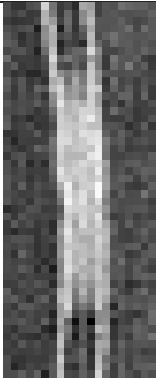
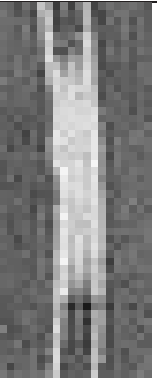
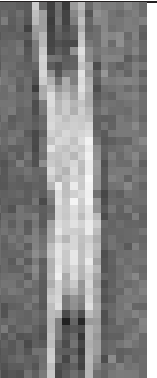
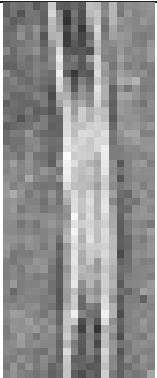
Stent #14. Nitinol DFT10% stent (diameter 4 mm) composed of 56 braided wires (Ø 80 µm) heat treated for 15 min at 490°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

Stent #15. Nitinol DFT10% stent (diameter 4 mm) composed of 56 braided wires (Ø 80 µm) heat treated for 30 min at 500°C.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

Stent #16. Cordis Enterprise Nitinol stent.

Gradient Echo					
5°	10°	15°	20°	25°	30°
					
Spin Echo					
50°	70°	90°	110°	130°	
					

4. Technical datas

4.1. Substrates

4.1.1. Nitinol

Different Nitinol substrates were used in this work i.e. wires and plates.

- 240 μm diameter wires supplied by SAES Memry
- 170 μm diameter wires supplied by SAES Memry
- 100 μm diameter wires supplied by SAES Memry
- 80 μm diameter wires (Ni 56.0 %) supplied by Fort Wayne Metals
- 50 μm diameter wires (Ni 56.0 %) supplied by Fort Wayne Metals
- 80 μm diameter DFT10% wires (Ni 56.0 %) supplied by Fort Wayne Metals
- 2x1x0.2 cm^3 Nitinol plates (Ni 56.2 %) supplied by AMF France

4.1.2. Phynox

Like Nitinol, Phynox was studied in two different forms.

- 80 μm diameter wires supplied by Fort Wayne Metals
- 2x1x0.1 cm^3 Phynox plates supplied by Arcelor Mittal Imphy Service, Clichy, France

4.2. Chemicals

n-Dodecylphosphonic acid (95% purity) was purchased from Polycarbon Industries Inc. *n*-Dodecanoic acid (98% purity), 11-phosphoundecanoic acid (96% purity), anhydrous 2-methoxyethanol (99.8% purity), diethylene glycol methyl ether (99.0% purity), triethylene glycol monoethyl ether (95% purity), 2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-nonadecafluoro-1-decanol(98% purity), 1,3-dicyclohexylcarbodiimide (DCC, 99% purity), tetrabutylammonium tetrafluoroborate, nickel chloride and boric acid were purchased from Aldrich. 4-N,N-dimethylaminopyridin(DMAP, 99% purity) was purchased from Janssen Chimica. 1,4-carboxybenzene diazonium tetrafluoroborate was purchased from Best West Laboratories (USA). Sodium hydroxide, sodium chloride, potassium chloride, magnesium chloride hexahydrate, potassium sulfate heptahydrate, sodium bicarbonate, sodium hydrogen phosphate, potassium dihydrogen phosphate, hydrofluoric acid (48-51%), nitric acid (63%), phenol red, cobalt chloride octahydrate, alpha-D(+)-glucose and D(+)-sucrose were purchased from Acros Organics. Calcium chloride dehydrate, absolute ethanol and anhydrous dichloromethane were purchased from Merck. Acetonitrile was purchased from Chem-Lab. All these chemicals were used without any further purification. Milli-Q water was used for the preparation of all aqueous solutions.

Publications

1. Publications related to this thesis

- (1) Sébastien Devillers, Nathalie Cuvelier, Joseph Delhalle and Zineb Mekhalif, Grafting PEG Fragments on Phynox Substrates Modified with 11-Phosphoundecanoic Acid, *Journal of the Electrochemical Society* **2009**, 156 (12), P177-P184.
- (2) Sébastien Devillers, Larissa Lanners, Joseph Delhalle and Zineb Mekhalif, Grafting of bifunctional phosphonic and carboxylic acids on Phynox: Impact of induction heating, *Applied Surface Science* **2011**, 257, 6152-6162.
- (3) Sébastien Devillers, Bastien Barthélémy, Isabelle Fery, Joseph Delhalle and Zineb Mekhalif, Functionalization of Nitinol surface toward a versatile platform for post-grafting chemical reactions, *Electrochimica Acta* **2011**, 56, 8129-8137.
- (4) Sébastien Devillers, Bastien Barthélémy, Joseph Delhalle and Zineb Mekhalif, Induction Heating vs Conventional Heating for the Hydrothermal Treatment of Nitinol and Its Subsequent 2-(Methacryloyloxy)ethyl 2-(trimethylammonio)ethyl Phosphate Coating by Surface-Initiated Atom Transfer Radical Polymerization, *Applied Materials and Interfaces* **2011**, 3, 4059-4066.

2. Other publications

- (5) Claire Amato, Sébastien Devillers, Patrick Calas, Joseph Delhalle and Zineb Mekhalif, New Semifluorinated Dithiols Self-Assembled Monolayers on a Copper Platform, *Langmuir* **2008**, 24, 10879-10886.
- (6) Bastien Barthélémy, Sébastien Devillers, Isabelle Minet, Joseph Delhalle and Zineb Mekhalif, Induction heating for surface triggering styrene polymerization on titanium modified with ATRP initiator, *Journal of Colloid and Interface Science* **2011**, 354, 873-879.
- (7) Sébastien Devillers, Quentin Lemineur, Joseph Delhalle and Zineb Mekhalif, Exploratory study of copper particles electrodeposition on nickel by induction heating, *Electrochimica Acta* **2011**, 56, 4953-4959.
- (8) Sébastien Devillers, Quentin Lemineur, Joseph Delhalle and Zineb Mekhalif, Induction vs. Conventional Heating: Impact on the Morphology and Crystallinity of Copper Electrodeposits on Nickel, *Journal of the Electrochemical Society* **2011**, 158 (11), E111-E118.
- (9) Sébastien Devillers, Alexandre Hennart, Joseph Delhalle and Zineb Mekhalif, 1-Dodecanethiol Self-Assembled Monolayers on Cobalt, *Langmuir* **2011**, 27 (24), 14849-14860.

- (10) Bastien Barthélémy, Sébastien Devillers, Isabelle Minet, Joseph Delhalle and Zineb Mekhalif, Surface-initiated ATRP of 2-(methacryloyloxy)ethyl 2-(trimethylammonio)ethyl phosphate on Phynox, *Applied Surface Science* **2011**, 258, 466-473.
- (11) Gregory Fonder, Isabelle Minet, Cédric Volcke, Sébastien Devillers, Joseph Delhalle and Zineb Mekhalif, Anchoring of alkylphosphonic derivatives molecules on copper oxide surfaces, *Applied Surface Science* **2011**, 257, 6300-6307.
- (12) Simon Detriche, Sébastien Devillers, Jean-François Seffer, Janos B. Nagy, Zineb Mekhalif and Joseph Delhalle, The use of water-soluble pyrene derivatives to probe the surface of carbon nanotubes, *Carbon* **2011**, 49, 2935-2943.

3. Submitted publications

- (13) Sundar Rajalingam, Sébastien Devillers, Joseph Delhalle and Zineb Mekhalif, An easy two step process to form organothiol self-assembled monolayers on nickel surfaces, in *Thin Solid Films*.

4. Publications to be submitted

- (14) Bastien Barthélémy, Marie-Laure Piedboeuf, Sébastien Devillers, Amory Jacques, Joseph Delhalle and Zineb Mekhalif, Pyrrole-dodecylphosphonic acid monolayer: nanolink between polypyrrole and Nitinol platform.
- (15) Sébastien Devillers, Jean-François Lemineur, Bastien Barthélémy, Joseph Delhalle and Zineb Mekhalif, Organophosphonic acids nanofilms and LBL films on nickel: electrochemical and spectroscopic evaluation for biomaterials applications on Nitinol

5. Contributions to other publications

- (16) A.G. Radaelli, L. Augsburger, J.R. Cebal, M. Ohta, D.A. Rüfenacht, R. Balossino, G. Benndorf, D.R. Hose, A. Marzo, R. Metcalfe, P. Mortier, F. Mut, P. Reymond, L. Socci, B. Verheghe and A.F. Frangi, Reproducibility of haemodynamical simulations in a subject-specific stented aneurysm model - A report on the Virtual Intracranial Stenting Challenge 2007, *Journal of Biomechanics* **2008**, 41, 2069-2081.