This presentation will give an overview of the work that has been up to now in these areas in particular in relation to the response assessment of neoadjuvant treatments of rectum and esophageal cancers. A special focus is given to the technical challenges that go along with quantitative MRI imaging in the thoracic and abdominal domain.

SP-0111 Imaging biomarkers to predict and early assess the response to radiation therapy. Potential impact of studies in small animals

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• Predictive markers (used before treatment planning) may help in defining which patient may benefit from a specific intervention in radiation therapy
• Early markers of treatment response may help in the management of patients by predicting the outcome of a specific therapeutic intervention and potential adaptation of the therapeutic strategy
• Examples of imaging biomarkers (MRI and PET) related to hypoxia-guided intervention will be presented (1-5)
• Validation of these markers is mandatory for translation into the clinical arena

References

1. B.F. Jordan and B. Gallez. Surrogate MR markers of response to chemo- or radiotherapy in association with co-treatments: a retrospective analysis of multi-modal studies. Contrast Media Mol Imaging. 2010;5:323-32
2. L.B. Tran et al. Potential role of hypoxia imaging using ^{18}F-FAZA PET to guide hypoxia-driven interventions (carbogen breathing or dose escalation) in radiation therapy. Radiother Oncol. 2014;113:204-9
3. L.B. Tran et al. Predictive value of ^{18}F-FAZA PET imaging for guiding the association of radiotherapy with nimorazole: a preclinical study. Radiother Oncol. 2015;114:189-94
4. L.B. Tran et al. DW-MRI and ^{18}F-FLT PET for early assessment of response to radiation therapy associated with hypoxia-driven interventions. Preclinical studies using manipulation of oxygenation and/or dose escalation. Contrast Media Mol Imaging. 2016;11:115-21
5. T.T. Cao-Pham et al. Monitoring Tumor Response to Carbogen Breathing by Oxygen-Sensitive Magnetic Resonance Parameters to Predict the Outcome of Radiation Therapy: A Preclinical Study. Int J Radiat Oncol Biol Phys. 2016;96:149-60.

Symposium: Comprehensive motion management and immobilisation solutions in radiation therapy

SP-0112 Immobilising the patient to be as comfortable as possible. A general overview

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Purpose

An individual tailored radiotherapy treatment with high accuracy represents daily clinical routine in most of the high-income countries worldwide. In the last two decades, technology has been rapidly progressing from 3D / intensity modulated radiotherapy (IMRT) to volumetric modulated arc therapy (VMAT) treatment techniques. With these developments it was possible to reduce the integral dose on normal tissue, increase the single / total dose to the planning target volume (PTV) and reduce the safety margins. Therefore, the reproducibility of the daily patient positioning has become of major importance. All these high technical achievements have a natural limitation, which is the patients' compliance and cooperation in immobilization. Immobilization devices for comfortable and accurate reproducible patient positioning is indispensable in radiotherapy departments. Actual immobilisation devices have limitations regarding patients' comfort and substantial evidence in the literature shows the incidence of anxiety and distress among patients requiring immobilization during radiation therapy [1,2]. Radiation therapists (RTTs) are regularly in close personal contact with their patients and are aware of discomfort and worries, therefore playing a major role in reducing anxiety and distress. Adequate communication and training for correct use of the immobilization devices between RTTs and patients is likely to have positive impact for more precise treatment with the currently existing immobilisation devices.

Conclusion

There is still a great need to evaluate the accuracy and reproducibility of patient positioning in radiotherapy and moreover to create new immobilisation devices with greater comfort and higher tolerability for patients. This field of RTTs research will be ongoing in the next years and is supposed to show high impact on the precision and reliability of radiation therapy. Nevertheless, in order to achieve the full potential of immobilisation devices, the patients' close cooperation and compliance has to be regarded as integral part of any working process of RTTs and is based on adequate and comprehensive information and also emotional support.

References

[1] Goldsworthy S, Tuke K, Latour J.(2016) Jouranal of Radiotherapy in Practice A focus group consulatation round exploring patient experiences of comfort during radiotherapy for head and neck cancer [2] Merchant S., O'Conner M. & Halkett G. (2015) European Journal of Cancer Care Time, space and technology in radiotherapy departments: how do these factors impact on patients' experiences of radiotherapy? .

SP-0113 Added value of mechanical ventilation in the treatment of moving tumors with photon and proton therapies

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Breathing-related motion is a well-known and significant source of geometrical uncertainties in radiotherapy planning and delivery. For this reason, several respiratory-synchronized techniques have been proposed to mitigate the motion, such as 4D (robust) optimization, respiratory gating or tracking. However, all these techniques face the same issue: the motion model derived from the planning 4D-CT does not necessarily represent the actual motion at the time of treatment, because the depth and pattern of spontaneous breathing are known to vary markedly over time.

Consequently, an efficient motion management strategy should not only focus on the tumour motion itself, but also on the underlying mechanism of this motion, namely the breathing. In this regard, mechanically-assisted ventilation might offer new perspectives. Quite recently, some research groups have shown that mechanical ventilation can be easily performed on patients who are conscious and unsedated, without feedback to or participation from the patient. As a first application, it can be used to impose a completely regular pattern of breathing frequency and inflation volume on the patient for as long as required for patient positioning, image acquisition and treatment delivery. As long as the mechanical ventilation matches the metabolic rate of the patient and is tolerated well enough, a wide range of inflation frequencies and volumes could also be applied to suits the particular needs in delivering personalized RT.

On the other hand, JET ventilation may be used to fix the breathing, and thus reduce markedly the residual tumour motion.
This presentation will browse the various applications of mechanical ventilation for motion mitigation in photon and proton therapies of moving thoracic/upper abdomen tumours, and will discuss their advantages, potential drawbacks and pending issues.

SP-0114 Motion of liver tumours using Active Breathing Control: keeping the margins small and the patient comfortable

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In Stereotactic Body Radiation Therapy (SBRT) for liver metastases, treating the target volume as accurate as possible, is challenged by several factors. Movement of the liver due to breathing is the most prominent one. From literature it appeared that liver motion was largest in the cranio-caudal direction. To compensate for this movement a diversity of options is used. One of these options is performing a breath-hold technique. When using this technique the influence of respiration is strongly reduced and the Clinical Target Volume (CTV) – Planning Target Volume (PTV) margins can be decreased. Therefore, we copied our Active Breathing Control (ABC) technique for left-sided breast cancer patients to the liver SBRT, since we found that 98% of our breast cancer patients were able to undergo this technique successfully.
Liver SBRT delivery requires multiple breath-holds. The reproducibility of the diaphragm position for several consecutive breath-holds is one factor determining the CTV-PTV margin. We assessed this reproducibility of the ABC technique by making 10 consecutive CT-scans in breath-hold. Also, in order to compare with the broadly accepted Internal Target Volume (ITV) based technique to determine the PTV, we made a 4D-CTscan. For each patient individual margins were calculated for both the ABC technique and the ITV technique. The overall CTV-PTV margins are based on several uncertainties, such as patient set-up, reproducibility of the diaphragm position during breath-hold, physical inaccuracies, etc. We consistently found that the CTV-PTV margins in breath-hold were smaller compared to CTV-PTV margins based on the ITV technique.
Another advantage of the ABC technique is that the ConeBeamCT (CBCT), used in the position verification procedure, shows a sharper defined liver contour compared to the CBCT during free breathing. This enables a better volume match on the liver contour. Previous studies have shown that the entire liver contour is a representative surrogate for the liver tumour. Consequently, there was no need to use radio-opaque markers in the liver. This is another important advantage of application of ABC for liver SBRT.
We are the first radiotherapy department in the Netherlands that perform liver SBRT in combination with ABC. From January 2016 up until now we have treated 14 patients. All patients successfully used the ABC technique, and in all patients the liver contour could be used for the tumour match. All together, the use of ABC in liver SBRT is a feasible, patient friendly treatment technique as there is no need for invasive marker placement.
Liver SBRT team: L. de Boer, H. Ceha, J. van Egmond, S. van Geen, M. Florijn, Y. Kalidien, E. Kouwenhoven, I. Mudde, N. Nobel, P. Rietveld, J. Roos, L. Rovers, W. van der Togt, J. van Santvoort, S. de Vet, N. van der Voort van Zyp, F. Wenmakers, J. van Wingerden

Symposium with Proffered Papers: Novel approaches in brain matters

SP-0115 Response of adult neural stem cells to radiation-induced DNA damage

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Oncogenesis and aging often correlate with the accumulation of DNA damage and genetic mutations in long-lived adult stem and progenitor cells. Here, using the mouse brain as a model, we define the functional consequences and mechanisms by which adult neural stem cells (NSCs) and their progeny respond to radiation-induced DNA damage within the sub-ventricular zone (SVZ). Exploiting recent evidence showing regional differences within the SVZ, we spatially mapped apoptosis, DNA repair capacity and proliferation along the dorso-ventral axis of the SVZ of wild type and ataxia telangiectasia mutated mice in response to 2 Gy X-rays. We showed that progenitors and neuroblasts, in contrast to NSCs, undergo radiation-induced apoptosis. This differential response is cell type-dependent and is not the result of quiescence status, senescence induction or distinctions in DNA repair. Moreover, we showed that apoptosis together with proliferation arrest drive quiescent NSC activation allowing repopulation of the SVZ. In addition to the adult brain, we examined the DNA damage response of the neonatal SVZ at postnatal day 5, which is of importance for assessing their higher sensitivity to radiation-induced carcinogenesis. Radiation-induced apoptosis at P5 was overall higher than in the adult SVZ; however, the neonatal SVZ displays a lack of proliferation arrest such that repopulation occurs more rapidly from damaged progenitors and neuroblasts. We have demonstrated a spatially and temporally heterogeneous DNA damage response in adult NSCs and their progeny, thus providing new insight for development in radiotherapy and radiation protection.

SP-0116 The cognitive defects of neonatally irradiated mice are accompanied by changes in adult neurogenesis

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Epidemiological studies on cancer survivors provide strong evidence for multifaceted damage to brain after ionizing radiation. Decreased neurogenesis and differentiation, alteration in neural structure and synaptic plasticity as well as increased oxidative stress and inflammation are suggested to contribute to adverse effects in the brain. In addition to neural stems cells, several brain-specific mature cell types including endothelial and glial cells are negatively affected by ionizing radiation. The radiation-induced changes in hippocampus using different mouse models irradiated with low to moderate doses of either total body or cranial exposure will be discussed. Not only the dose but also the age at exposure seems to play a significant role in the outcome. A better understanding of how irradiation impairs hippocampal neurogenesis at low and moderate doses is crucial to minimize normal tissue damage of therapeutic irradiation.