Exploring the biodegradability and biocompatibility of candidate metallic intravascular stent materials using microCT and CECT.

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INTRODUCTION: During the last two decades, biodegradable metals have been studied in an effort to replace permanent intravascular stents. The material with ideal degradation rate and behavior, mechanical properties, and biocompatibility has not yet been found. We evaluated the *in vitro* degradation and surface properties and the *in vivo* behavior of different biodegradable metals using microfocus X-ray computed tomography (microCT) and contrast-enhanced microCT (CECT). Wires were used to mimic a single stent strut.

METHODS: For all experiments, Co-Cr alloy (biostable reference), Fe, Zn, and Zn-Ag-Cu-Mn-Zr alloy (Zn alloy) [1] wires (diameter - 250 µm) were used. *In vitro immersion* – Wires were immersed in Hanks' solution for 1, 4, or 7 days. Wires were imaged with microCT prior to and after immersion. Based on the 3D images, degradation rate (based on volume loss), degradation mode, and surface roughness (using surface profile evaluation [2]) were determined. *In vivo implantation* – Wires were imaged with microCT prior to implantation. Then, they were implanted in the rat aorta. Rats were euthanized after 7, 24, or 84 days and the aorta implanted with the wire was harvested [3]. The samples were fixed in 4% formaldehyde. They were first imaged with microCT to visualize the wire. They were then stained with isotonic Lugol's iodine solution (1:1 dilution in Sorenson's buffer) for 17 hours and imaged with CECT. Degradation rate and degradation mode were evaluated.

RESULTS: The microCT images of the wires from the *in vitro* and *in vivo* experiments show consistent results. Fe shows only surface corrosion and low variation in roughness. Zn exhibits heterogeneous pitting corrosion and a large increase in roughness. The Zn alloy corrodes more homogeneously with less pitting compared to pure Zn. However, the formation of internal dendrites is observed (Fig. 1). The Zn alloy shows the lowest increase in roughness across all time points. In terms of corrosion rate, the pure Zn degrades faster than pure Fe. The newly developed Zn alloy has a degradation rate that is close to that of the pure Zn, which is considered a good compromise between Fe and Mg, which degrades too fast. In a next step, the CECT-based images from the *in vivo* implantations will be used to identify the formation of neointima to determine biocompatibility of the materials by evaluating the neointimal activation (Fig. 2).

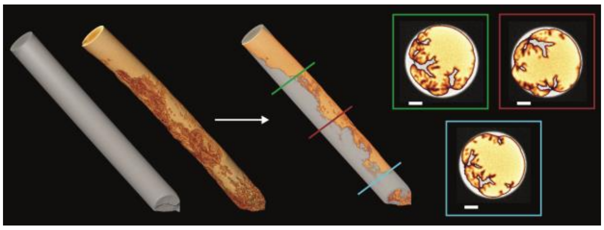

Fig. 1: MicroCT-based images of degradation behavior of Zn alloy. Grey at time point 0 and orange after 7d of immersion. Scalebar = 50 µm.

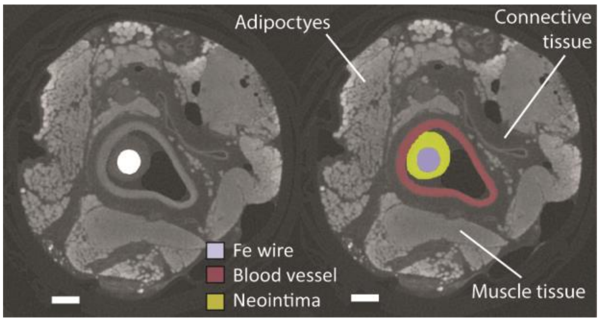

Fig. 2: CECT-based image of Fe wire implanted in the rat aorta and identification of the neointima at 24d - time point. Scalebar = 300 µm.

DISCUSSION & CONCLUSIONS: This study proposes a novel microCT- and CECT-based technique for evaluating alloys for intravascular stent applications. This technique provides new insights into the *in vitro* and *in vivo* behavior of biodegradable alloys. The results could potentially inform the development of more effective biodegradable materials for medical devices.

REFERENCES: [1] A.A. Oliver (2020) *Bio Mater*. **3**:6779-6789, [2] G. Kerckhofs (2013) *Adv. Eng. Mater.* **15**:153-158 [3] R.J. Guillory II (2019), **11**:19884-19893

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