

Development and Characterization of a Reproducible Swine Model of Peripheral Artery Disease with Medial Calcification

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Introduction

- The impact of medial calcification on the treatment of peripheral artery disease, especially using drug-coated balloons, remains unclear partly due to the lack of a relevant and reproducible preclinical model
- Hydroxyapatite nanoparticles, as a synthetic source of calcium phosphate, may be able to simulate the calcified element of atherosclerotic lesions



Methods

- Lesions were created in the external femoral arteries in three Yorkshire swine by local, extravascular injection of a suspension of hydroxyapatite nanoparticles
- Swine were anesthetized and the external femoral arteries surgically accessed, visualized and up to 2 mL of a nanoparticle suspension was injected into the media at each arterial site via a 25 gauge needle
- Animals were survived for either 7, 14, or 30 days post injection
- The injected sites were imaged using intravascular ultrasound (IVUS) prior to euthanasia
- Lesions were fixed and sectioned for histological assessment of medial calcification using hematoxylin-eosin (H&E) and von Kossa tissue stains



Results

Medial calcification was produced in porcine peripheral arteries with similarities to human medial calcification.

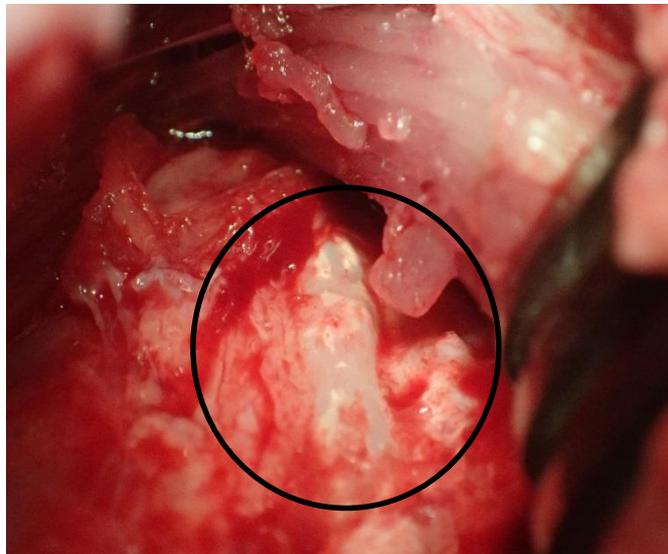


Figure 1. External view of the injection sites on day 0.

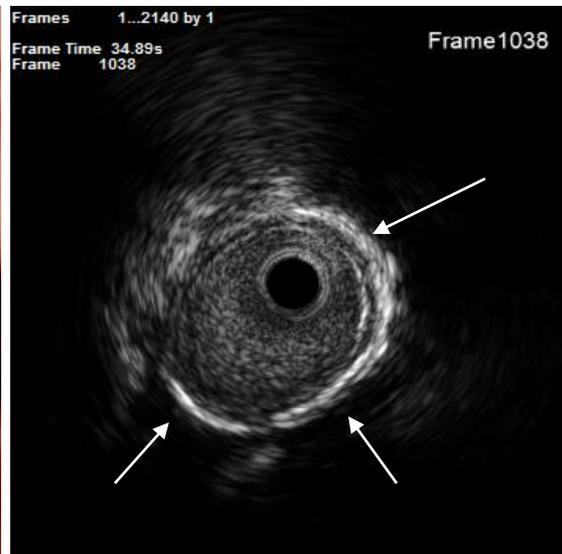


Figure 2. IVUS image of the calcified lesion on day 7 (white arrows).

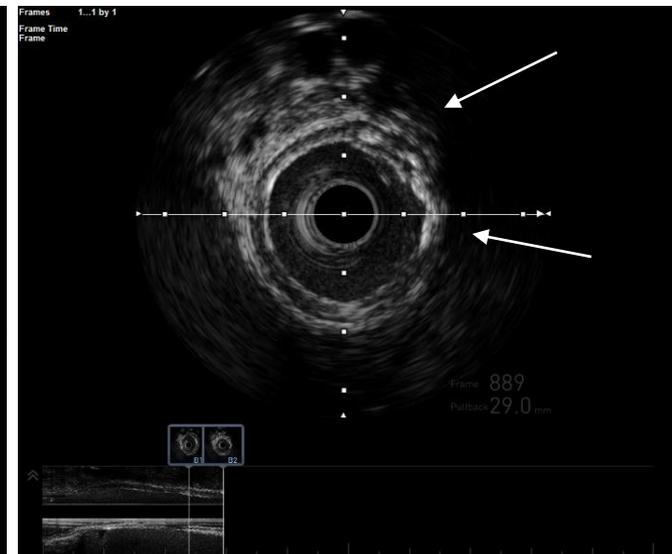


Figure 3. IVUS image of the calcified lesion on day 30 (white arrows).

Results

At all three time points, the lesions showed varying degrees of medial calcification with significant adventitial hyperplasia and fibrosis.

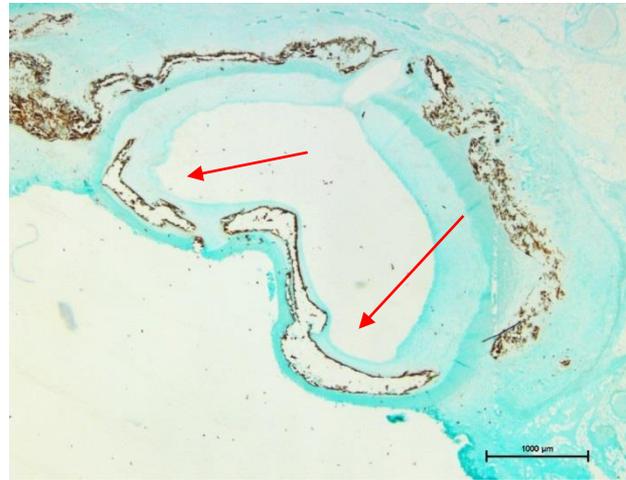
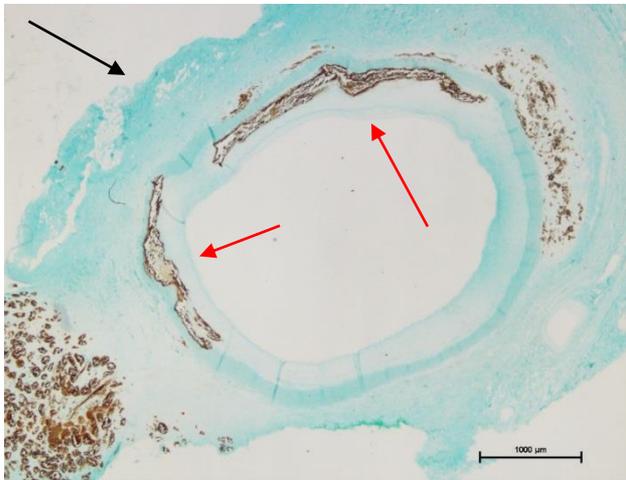


Figure 5 & 6. Von Kossa stain of External Femoral Artery at 7 days. **Red Arrows** point to regions of medial calcification. **Black arrow** shows regions of adventitial hyperplasia.

Figure 4. Von Kossa stain of External Femoral Artery at 30 days. **Red Arrows** point to regions of medial calcification.

Conclusion

- This model may provide a preclinical platform for future studies to evaluate the impact of medial calcification in the deployment and efficacy of paclitaxel coated balloons and other catheter based therapeutic technologies in peripheral arteries
- Currently, investigations are focused on the intravascular, circumferential deployment of the hydroxyapatite solution

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