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Development of a Novel Calcified Chronic Total Occlusion In a Rabbit Femoral Artery

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Background: Percutaneous revascularization of chronic total occlusions (CTO) is limited by failure of guidewire crossing. Calcification in the CTO increases with age of occlusion and counted as one of the most important obstacles to guidewire crossing. The aim of the current study was to develop an animal model of CTO that will contain significant amount of amorphous calcified mineral as well as bone.

Methods and results: CTO (n= 15) were created in the femoral arteries of New Zealand White rabbits using the thrombin injection model. Different concentration of bone morphogenetic protein (BMP-2; 0.5,1,2, 6 µg), dipotassium phosphate and calcium chloride (0,100,200 mM) were tested and injected to the site of femoral occlusion. 3 animals received high cholesterol diet 0.5%, calcium carbonate 75mg/d and vitamin D 50,000 units/d. In 8, the calcium carbonate/vitamin D was given every other day, 4 rabbits were on 0.25% cholesterol only. Animals were sacrificed at 2, 6 and12 weeks post treatment and arterial samples were excised for micro CT imaging (µCT) and histology analysis. At the side of BMP and calcium phosphate injection-µCT imaging showed significant calcification at 6 weeks and 12 weeks. On histology-amorphous calcium crystals were found in the medial layer and throughout the occluded lumen of the CTO, these were mostly diet dependant. Active formation and resorption of cartilaginous or bone like structures by osteoblasts and osteoclasts respectively were seen in the occluded CTO lumen, the fragments size was correlated with age of occlusion and BMP-2 dose.

Conclusions: This calcified model simulates occlusions found in humans CTO and will serve as a basic model for learning the pathophysiology of CTO calcification and development of treatments modalities that will enhance guidewire crossing.

<IMAGE02>,<IMAGE04>,<IMAGE06>