Biointegrative & Biodurable Reticulated Elastomeric Matrix for Intra-cranial Aneurysm Therapy

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Introduction: In the last fifteen years, endovascular embolization using platinum coils has become an attractive approach for intra-cranial aneurysm therapy [1]. Bare metal (platinum) coils however show high aneurysm recurrence rates (~30%) at 6 months [1,2,3]. These are attributed to coil compaction and inadequate sac fibrosis, due to low packing density and sub-optimal healing, respectively. The problem of suboptimal healing has been addressed using bioactive coils incorporating degradable polymer coatings which produce sac fibrosis via the inflammatory pathway during release of acidic degradation by products [2,3]. Coil compaction has been addressed using expandable hydrogels incorporated into metallic coils [3]. However both of these approaches show suboptimal outcomes in recent clinical studies with bioactive coatings failing to prevent aneurysm recurrence [1] and hydrocoils leading to concern over increased risk of hydrocephalus and aseptic meningitis [3]. Thus, improvement in clinical outcomes remains as a goal of endovascular embolization. Biostable and biointegrative scaffold coatings in the form of 3-D polymeric matrix, that promote attachment and proliferation of cells represent a potential solution owing to superior bio-integration that can be obtained from synthesis of organized extracellular matrix within the aneurysm sac provided by the polymeric scaffold. The aim of this study was to investigate whether platinum coils covered with a biostable and biointegrative polymer matrix acting as scaffold for cell and tissue ingrowth and proliferation would provide improved outcomes in a canine vein pouch aneurysm model.

Materials and Methods: The polymeric scaffold used to cover the endovascular coils is a biodurable, crosslinked, reticulated elastomeric polycarbonate-poyurethane-urea matrix consisting of an interconnected and inter-connecting network of cells and pores [4]. The scaffold permits cellular proliferation and tissue ingrowth throughout the scaffold. It is biostable resisting hydrolytic, enzymatic and oxidative degradation. The device (NeuroString or NS) is a permanent implant containing a shape-set superelastic nitinol core wire, and a platinum coil covered with the polymer matrix. The devices have an OD of ~325 μm (Fig. 1) and are constructed in various lengths, shapes, and forms – Framing (firm), Filling (soft), and Finishing (very soft), and are attached to the distal end of a delivery system with a mechanical on-demand detachment mechanism.

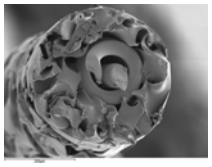

Figure 1

Bifurcated carotid artery vein pouch aneurysms (volume 150-375 mm3) were surgically created in skeletally mature dogs. Using femoral artery access, coils were delivered under fluoroscopic guidance through a microcatheter and deployed into the aneurysm. Neurostring coils (N=6 dogs) represented the treatment arm and Bioactive Matrix2® coils (Boston Scientific, Natick, MA) represented the control arm (N=2). Embolization was achieved with about 30% packing density for both arms, with complete acute occlusion confirmed using angiography for all aneurysms. Post procedure, the dogs were survived, with angiographic images taken at 8 & 26 weeks to evaluate aneurysm occlusion. The dogs were sacrificed after 26 weeks and histological assays were used to evaluate the sac morphology. The study was conducted at University of Wisconsin Hospital Radiology Research Lab at Madison, WI and analyzed at CVPath Institute, Gaithersburg, MD.

Results and Discussion: Angiographic assessment at 26 weeks demonstrated superior outcomes for NS with respect to presence of aneurysm remnant (0% NS vs. 50% Matrix). Macroscopic and microscopic images of the cross sectioned aneurysm model at 26 weeks confirmed complete and effective occlusion of the canine carotid bifurcation aneurysm treated with NS embolic devices with no device fractures or aneurysm perforations. The histopathology of the aneurysm showed advanced healing with neointimal formation and large area of endothelialization of the neck. The sac and devices show incorporation by organized fibrous tissue at both intra and inter coil regions with moderate to focally marked angiogenesis surrounding the embolic material both at sac periphery and sac center (Fig. 2). Histological analysis also showed that NS was substantially more resistant to coil compaction compared to Matrix. The NS embolic device also shows an overall mild to moderate chronic inflammation response with no acute inflammation.

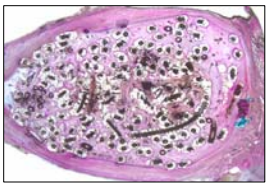

Figure 2

Conclusions: Biodurable reticulated elastomeric scaffolds appear to produce effective and improved occlusion of intracranial aneurysms by creating a mature organized fibrocollagenous tissue within the sac.

References:

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