

Translational Research in Expansile Devices for Aneurysm Embolization

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Statement of Purpose: Research and development pathways of synthetic, non-resorbable hydrogel embolization devices are presented that resulted in several commercially available products for the treatment of intra-cranial aneurysms. Based on what was learned thus far, the present pathways are being evaluated for future development of expansile embolic devices.

Methods: Device Designs. Five versions of embolic devices were evaluated. *Version A* was based on a high surface area, super-expansile foam, polymerized from a solution of acrylamide, acrylic acid, an emulsifier and a gas forming agent.¹ Pieces of this hydrogel and platinum spacer balls were placed over a nitinol wire. The hydrogel of *Version B* was similar in composition, but not foamed, and was prepared in a cylindrical mold, into which a platinum coil was inserted through the long axis. Resulting assemblies were also incubated in low pH solutions to further control the rate of expansion. The hydrogel of *Version C* is identical to that of *Version B*, however, a stretched platinum coil was placed over the dried hydrogel-coated coil. *Version C* is commercially available as the HydroCoil[®] line of products. *Version D* consists of a poly(poly(ethylene glycol)-co-acrylic acid) hydrogel inside a stretched platinum coil. *Version D* is commercially available as the HydroSoft[®] product. *Version E* is currently under development and is simply a radiopaque hydrogel filament free of metals.

Device Analysis. The device versions were first bench tested by buckling force evaluation, followed by preclinical testing. The buckling force was determined by advancing the devices down a tube (0.078 in ID) using an Instron 5543 tensile tester (1N load cell and Bluehill2 software) until the first buckle was observed. Preclinical testing of the device versions was conducted in experimental aneurysms in rabbits and dogs.² The devices were inserted into carotid bifurcation aneurysms through a microcatheter under fluoroscopic guidance. Aneurysm occlusion was evaluated angiographically and histologically from 2 wk to 52 wk post-embolization.

Results: Bench and preclinical testing identified deficiencies in the *Version A* design. The super-expansile hydrogel foam expanded rapidly, and the microcatheter had to be filled with a non-aqueous solvent to permit delivery into the aneurysm. The large expansion resulted in a weak, easily deformable hydrogel that was readily compacted into the dome in experimental aneurysms. *Version B*, with a buckling force equivalent to conventional platinum coils (Figure 1), addressed both of the *Version A* deficiencies: Removal of the foaming process made the hydrogel less expansile, and incubation in low pH solution protonated carboxylic acid in the hydrogel backbone, delaying the expansion. This permitted the delivery and repositioning of *Version B* devices through a saline-filled microcatheter, although consistency was not achieved. *Version B*-hydrogel (HG) coils proved to be

more resistant to compaction in preclinical aneurysms (Figure 2). The addition of the stretched coil over the dried hydrogel permitted consistent delivery of *Version C* devices, the overcoil also restricting in-vivo hydrogel (HG) expansion (Figure 2). Although stiffer than a platinum coil, this device is successfully used clinically.³

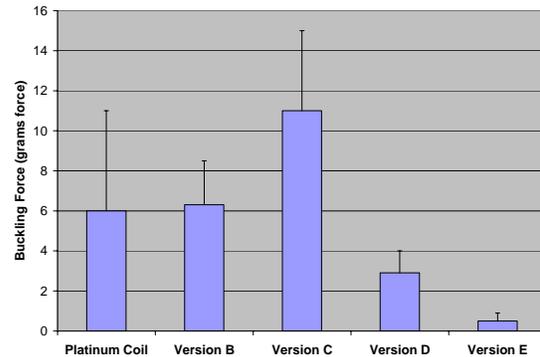


Figure 1. Buckling Force Results

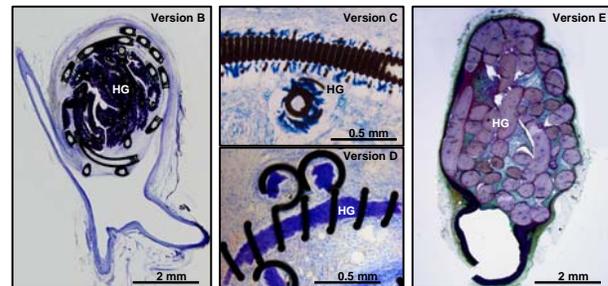


Figure 2. Histological Results

Version D addressed the stiffness problems of *Versions B and C* by using only a stretched platinum coil over a different hydrogel which is flexible in the dry state, imparting lower buckling forces (Figure 1). However, *Version D*-hydrogel (HG) does not expand as much as *Versions B or C* (Figure 2). *Version E* is currently under development. Having a low buckling force (Figure 1), and the expansion of *Versions B and C*, this hydrogel (HG) allows nearly complete filling of the experimental aneurysm (Figure 2) without metal. It is noteworthy that all tested non-resorbable hydrogels exhibited less foreign body response than the conventional platinum coils.

Conclusions: Translational research into expansile embolic devices has progressed from bench to successful testing in preclinical models, and has resulted in clinical products for aneurysm occlusion.

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References:

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- 2 Cruise GM, J Mater Chem. 2007; 17: 3965-3973.
- 3 White PM, Am J Neuroradiol. 2008; 29: 217-223.