ExoSeal®: A Novel Bioabsorbable Vascular Closure Device

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Statement of Purpose: Currently available access site closure devices have demonstrated reduced time to hemostasis (TTH) and time to ambulation (TTA) with similar complication rates compared to manual compression (MC). ExoSeal®, an investigational product, is a novel extra-vascular closure device with a unique visually guided deployment mechanism that delivers a polyglycolic acid (PGA) plug atop the femoral artery anchored by the neuro-vascular bundle sheath. The PGA plug is hydrolyzed within 60 to 90 days.

Methods: The porous vascular closure device or plug was prepared from a bioabsorbable material such as PGA. A typical process to prepare the plug was to melt extrude PGA in to multi-filaments which were then crimped, cut, carded and needle punched to prepare a non-woven mat with the desired density and integrity. The mat was then cut in to cylindrical plugs. Molecular weight of the plugs was measured by using a tetradetection gel permeation chromatography (GPC-T, Model 302) by Viscotek using hexafluroisopropanol (HFIP) as the mobile phase. Inherent viscosity (IV) of the plugs was determined by using Ubbelohde viscometer in HFIP. Thermal properties of the plug were measured by Perkin Elmer Differential Scanning Calorimeter (DSC-7) at 15°C/min under nitrogen. The evaluation of the tissue reaction and absorption of the plug was determined in a rat gluteal flap model and porcine vessels. The ECLIPSE clinical trial has been conducted in the U.S. at multiple centers comparing the safety and efficacy of the plug and MC in femoral access site closure with 2:1 randomization in patients following 6 Fr diagnostic and interventional coronary and peripheral procedures.

Results:

Material Characterization: IV of pre-sterile PGA plugs ranged from about 0.8 to 1.0 dL/g and the weight average molecular weight (M_w) was determined to be 24,000 to 27,000 g/mole. The melting point of the plug was about 235°C with the heat of fusion value of about 86 J/g. The percent crystallinity of PGA was determined to be about 62% based on heat of fusion value of 139 J/g for pure PGA (1). An optical and a scanning electron micrograph of a typical PGA plug are shown in Figures 1 and 2. The plug structure can have different porosity and absorbent capacity based on the density of the non-woven structure. The porosity was optimized in order to provide rapid hemostasis. When the plugs were soaked in heparinized porcine blood for 2 minutes, the weight of the plug including blood increased by almost 230% in an *in vitro* test.

Pre-Clinical Studies: Several studies were conducted to understand the biocompatibility and absorption of the plugs in different animal models. Figures 3 (a) and (b) show the cross-sections of the plug after 3 days and 90 days, respectively, in a rat gluteal flap model. It shows significant mass loss at 90-day time point with minimum tissue reactions. Figures 4 (a) and (b) represents the cross-sections of the plug deployed in the porcine vessel, and sectioned within 1 h of deployment. Figure 4 (a) shows that the plug is secured beneath the femoral sheath fascia layer after device deployment. The fascia layer provides support to the plug for secured positioning and holds the plug in place. Figure 4 (b) shows that the plug is positioned above arteriotomy at the outer margin of the vessel wall. It should be noted that the plug absorbs blood in a very short time and a perfect anatomical fit of the plug is obtained to seal the puncture site.

Clinical Studies: Several clinical studies have been conducted outside and the U.S. (2). Both TTH and TTA time were significantly reduced in ExoSeal® patients compared with MC. ExoSeal® deployment was achieved in about 1 minute on average following procedure. Remarkably, there were no 30-day access site complications reported in either treatment cohort.

Conclusions: A novel biobabsorbable vascular closure device has been developed from PGA. Preclinical and clinical studies have shown that the device is safe and efficacious, and provides significant improvement in TTH and TTA compared to MC.

References:

1. Barrows TH. Clin Mater. 1986; 1:233.
2. Wong SC. American College of Cardiology Abstracts, March 2008.

Figure 1: OM of Plug

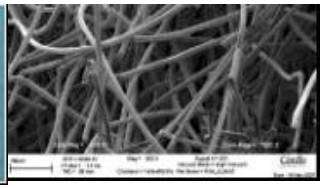

Figure 2: SEM of Plug

Figure 3 (a): 3 Days

Figure 3 (b): 90 Days

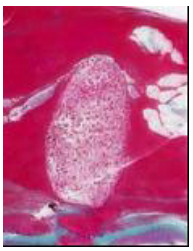

Figure 4 (a)

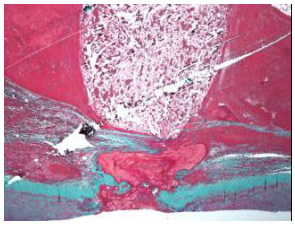

Figure 4 (b)