

IN VIVO RESULTS FROM A NEW PERMANENT REDIRECTION DEVICE FOR EMBOLIC STROKE PREVENTION

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ABSTRACT

Based on in vitro hemodynamic optimization study, 16 Diverters composed of fine wire meshes, were successfully implanted, by percutaneous approach into the swine ilio-femoral bifurcation. The bifurcations were harvested for evaluation at 3, 10 and 17 weeks post implantation. The patency of the filtered ostium was calculated using microscopy and computerized image processing morphometry. Anti-BrdU monoclonal antibody was used to measure tissue proliferation rate in another subgroup (n=10) of Diverters up to 6 months.

Flow patency of the Diverter was confirmed prior to animal sacrifice by angiography and Duplex ultrasound, and no stenosis was noted. Morphometry and microscopy showed that most of the filtered area (92% in average) of the 16 specimens remained patent. The Diverters were fully covered with endothelium at the non-filtering portion area after 3 weeks.

Permanent arterial filtration by percutaneous implantation of the Diverter is feasible and efficacious. Our preliminary findings give hope for a new and promising strategy for preventing embolic stroke.

Keywords: arterial blood filter, carotid flow, implant, emboli diversion, stroke prevention

INTRODUCTION

Stroke is the third leading cause of death and the major cause of disability. In the US alone there are more than 730,000 stroke victims and 4.4 million stroke survivors annually. Stroke is a syndrome of multiple etiologies. Emboli emerging from the heart, aortic arch and the large arteries, mainly carotids, account for about 60% of all stroke cases [1-10]. A new permanent arterial filtering device (*the Diverter*) was designed for implantation at the carotid bifurcation (CCA to ECA, thus filtering the ICA ostium, Fig. 1). The filter prevents thrombi originating proximal to it from reaching the intracranial circulation and inducing an embolic stroke.

Our aim in this study was to test the patency of the permanent arterial filter in the ilio-femoral bifurcations of swine.

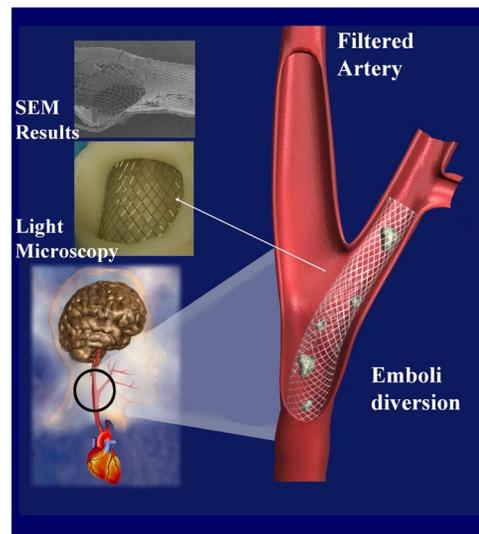


Fig. 1. The Diverter implanted from the CCA to the ECA in the carotid bifurcation. The filtered ICA ostium prevents emboli from reaching the brain (bottom left)

METHODS

Fine meshed Diverters (n=16), designed to divert emboli >0.5mm, were percutaneously implanted into the swine ilio-femoral bifurcation. Bifurcations were harvested at 3, 10 and 17 weeks post implantation. The patency of the “guarded” ostium was calculated using computerized morphometry. For additional 10 implanted Diverters, the animals were sacrificed within up-to 6 months, and were injected with bromodeoxyuridine (BrdU; 40mg/kg) 24h and 1h prior to sacrifice. Immunohistolabeling at the guarding parts was performed using an anti-BrdU monoclonal antibody. Tissue

proliferation rate was measured as the percent of BrdU stained vs. the total number of cells at the guarded area.

RESULTS

Angiography and ultrasound Duplex scanning prior to animal sacrifice found the Diverter open to flow without occlusion or discernable stenosis up to 24 weeks post implantation in all devices. On average, the Diverter mesh covered a lumen at the bifurcation twice larger than average cross sectional area of the filtered artery one diameter distal to the bifurcation.

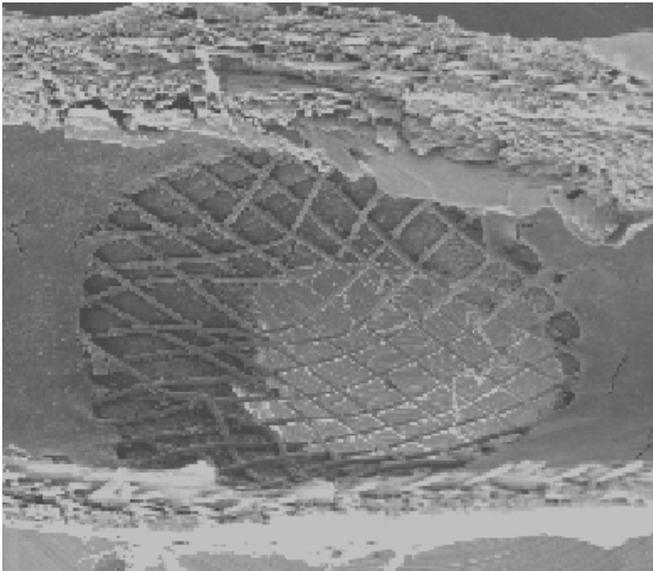
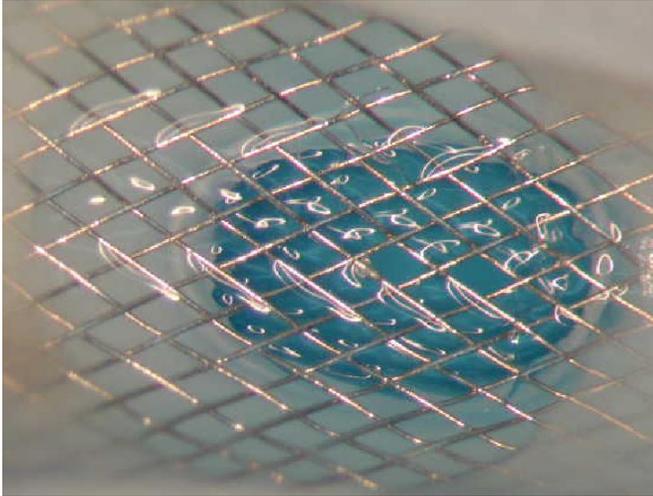


Fig. 2, Light microscopy (top) and Scanning electron microscopy (SEM) at bottom of a specimen (4 months) exhibits a fully open filtering area, and neointimal covering at the non-filtering part of the Diverter.

No Diverter occlusion or discernable stenosis were noted prior sacrifice by angiography and ultrasound flowmetry. Morphometry and microscopy showed that the guarded area remained patent (99.0%±1.0, 91.8%±10.6 and 93.3±8.8 at 3,10 and 17 weeks respectively) as shown in Table 1. Light microscopy and SEM (Fig. 2) revealed a monolayer of endothelial cells covering portions of the guarding mesh, mostly at the rim. The percent of BrdU stained cells at the guarding portion, which corresponds to the proliferation

rate, was 18.7±7.3% (1 week), 12.8±4.6 (3 weeks), but only 0.7±0.6% after 6 months.

Harvested specimens	Follow-up	Patent area percentage (Std.)
3	3 weeks	99.0 (1)
9	10 weeks	91.8 (10.6)
4	17 weeks	93.3 (8.8)

Table 1, Filtered area average patency results

CONCLUSIONS

Implantation of a permanent arterial diversion device in a swine model is feasible and such a device remains patent. The proliferation rate indicated that neointimal growth reaches steady state within 6 month. This novel device could serve as a useful endovascular approach for embolic stroke prevention in high-risk patients with proximal sources of embolism and contraindications to anticoagulation.

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