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ORIGINAL ARTICLE

Differences in tissue proliferation and maturation between Matrix2 and bare platinum coil embolization in experimental swine aneurysms

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Summary
Background and purpose: Recanalization of post-embolization cerebral aneurysms remains a serious problem that influences treatment outcomes. Matrix2 is a bioactive, bio-absorbable, detachable coil that was developed to reduce the risk of recanalization. We examined the short-term efficacy of the Matrix2 coil system, and evaluated the temporal profile of tissue proliferation in a swine experimental aneurysm model compared with the bare platinum (BP) coil.
Materials and methods: Thirty-six experimental aneurysms were created in 18 swine. All aneurysms were tightly packed with Matrix2 or BP coils. Comparative histologic and morphologic analyses were undertaken 1, 2 and 4 weeks post-embolization.
Results: Endothelial-like cells were observed partially lining the aneurysmal opening one week post-embolization with both coil types. At two and four weeks post-embolization, the aneurysms treated with Matrix2 coils had more extensive areas of organized thrombus than those packed with BP coils, but the numbers of functional proliferating endothelial cells identified by immunohistochemistry in the tissue were broadly comparable between the groups. Moreover, morphological analysis suggested there were more mature endothelial cells in aneurysms treated with bare platinum rather than Matrix2 coils.

Abbreviations: BP, bare platinum; GDC, Guglielmi detachable coil.

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Conclusions: Our results indicate that aneurysms embolized with Matrix2 coils build thicker scaffolds for endothelialization, but this is not necessarily evidence of earlier tissue proliferation and maturation than those embolized with BP coils. Matrix2 coils may not be superior to BP coils for preventing aneurysmal recanalization after endovascular treatment of cerebral aneurysms.

Introduction

Endovascular therapy has become a popular and effective alternative to surgical clipping for ruptured and unruptured intracranial aneurysms since the advent of platinum Guglielmi detachable coils (GDCs) in the 1990s. The International Subarachnoid Aneurysm Trial demonstrated better clinical outcomes with endovascular treatments, with relative and absolute risk reductions in dependency or death one year after allocation to the endovascular treatment of group of 22.6% compared with microsurgical clipping [1]. However, an important limitation of coil embolization with bare platinum (BP) or other techniques is the potential for coil compaction and aneurysmal recanalization, especially with giant and wide-necked aneurysms [2].

Bare platinum coils are biologically inert, so the inflammatory response that they provoke may be limited and delayed [3]. To overcome this limitation the Matrix2 bioactive, bio-absorbable coil system (Boston Scientific, Fremont, CA) was developed. The Matrix2 coil is composed of a central platinum core encased in bio-absorbable polyglycolic/poly-L-lactic acid copolymer. This system reportedly accelerates clot maturation, promoting the development of mature connective tissue and formation of the neointima [4].

It is not clear whether these apparent biological advantages translate into improved long-term functional outcomes for patients. There is, however, evidence of improved mechanical performance and anatomic outcome in the short-, medium- and long-terms with Matrix2 coils [2,4], although there have been several conflicting reports that superior anatomic outcomes can be achieved with BP coils [5—7].

We used histochemical and morphological techniques to assess the characteristics of proliferating tissue covering the aneurysmal orifices in a swine model of sidewall-type aneurysms to ascertain whether embolization with Matrix2 coils is superior to treatment with BP coils.

Materials and methods

Sidewall-type aneurysm model

All animal procedures described in this report were approved by the Animal Care Committee of Juntendo University. Adult male and female Landrace — Yorkshire — Duroc swine weighing 35—40 kg were obtained from the National Livestock Breeding Center Ibaraki Station (Ibaraki, Japan) and maintained on a 12-hour light/dark cycle with free access to food and water. As described previously [8], 36 experimental sidewall-type aneurysms were created surgically in both carotid arteries in 18 swine, which were subsequently embolized with either BP or Matrix2 coils. Briefly, the left external jugular vein was exposed and isolated via a midline neck incision using a sterile technique under general anesthesia. Two 6-mm lengths of venous pouch were harvested and each was used to create a single end-to-side anastomosis in each of the carotid arteries (vein to artery), with 2.8-mm necks and 6-mm domes. Cineangiography was undertaken to ensure that there was no major bleeding or leakage from the anastomosis before blood flow was re-established [9]. The stump of the venous pouch was clipped to allow thrombectomy to be performed if the aneurysm had spontaneously thrombosed during the procedure.

Embolization procedure

Coil embolization was performed via the right femoral artery within 12 hours to avoid spontaneous thrombosis [10]. Briefly, a 4 Fr guiding catheter (JNS Type I, Medikit, Tokyo, Japan) was placed over an angled guide wire (Radifocus Guidewire, Terumo, Tokyo, Japan) and advanced into the proximal right carotid artery. A microcatheter (Excelsior™ SL-10 Microcatheter, Boston Scientific/Target Therapeutics, Fremont, CA) was then inserted coaxially through the guiding catheter (Transend™ Guidewires, Boston Scientific/Target Therapeutics) into the aneurysmal cavity. Cineangiography was performed after injection of 5 mL iodinated contrast medium (Iopamiron Inj. 300, Bayer Healthcare, Leverkusen, Germany). The aneurysms were packed as densely as possible with BP (Guglielmi Detachable Coil [GDC], Stryker, Tokyo, Japan) or Matrix2 coils (Matrix2™ Detachable Coil, Boston Scientific/Target Therapeutics). A packing density was assessed using a classification of angiographic results described in detail previously: class 1, complete obliteration (CO); class 2, residual neck (RN); and class 3, residual aneurysm (RA) [11].

Harvesting procedures

Swine were terminally anesthetized with an intravenous injection of pentobarbital (Kyoritsu Seiyaku Corporation, Tokyo, Japan) 1, 2 or 4 weeks after the procedure ($n = 3$ for each group) after cineangiographic assessment. The aneurysms, parent arteries and normal arterial tissue (as control specimens) were immediately removed *en bloc* and fixed for 48 hours in either 4% paraformaldehyde or 2.5% glutaraldehyde in phosphate-buffered saline (PBS) at 4 °C.