Initial clinical experience with Matrix detachable coils for the treatment of intracranial aneurysms

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Object. The Matrix detachable coil is a new bioactive, bioabsorbable coil used in the endovascular embolization of intracranial aneurysms. It has a platinum core covered with a bioactive, bioabsorbable polymer (polyglycolic acid/lactide). The authors report on their initial midterm clinical experience with the first-generation Matrix detachable coil.

Methods. One hundred twelve patients harboring 118 aneurysms were treated using Matrix coils. Forty-nine aneurysms (41.5%) were associated with acute subarachnoid hemorrhage (SAH). Twenty-four lesions (49%) were harbored by patients with Hunt and Hess Grade I, 11 (23.4%) by patients with Grade II, eight (16.3%) by those with Grade III, and six (12.2%) by those with Grade IV. Four aneurysms (3.4%) were harbored by patients who had presented with nonacute SAH. Sixty-five aneurysms (55%) were unruptured. Fifty-seven lesions (49.3%) were small with a small neck, 29 (24.6%) were small with a wide neck, 30 (25.4%) were large, and two (1.7%) were giant. All patients were followed up to obtain angiography and clinical outcome data.

Technical complications occurred in six patients: two thromboembolic complications and four aneurysm perforations. Of these six patients, the status of two deteriorated because of aneurysm perforation and another two because of thrombus formation (morbidity 3.6%). There were five deaths—one due to rerupture after embolization. Angiography follow-up studies of 87 aneurysms were obtained. Seventy aneurysms demonstrated progressive occlusion or a stable neck (80.5%), and 17 had some degree of recanalization (19.5%). The aneurysms originally diagnosed as a neck remnant showed a 15% rate of recanalization.

Conclusions. Matrix coils can be delivered into aneurysms with technical complications similar to those encountered using GDCs. Midterm anatomic outcomes to date have shown moderate improvement in the recanalization rate when compared with those realized using the GDC system. Because of the increased friction associated with the first-generation Matrix coil, the packing density in most aneurysms was less than that achieved with GDCs. Prolonged angiography follow-up evaluations are needed to document long-term efficacy.

KEY WORDS • cerebral aneurysm • embolization • bioabsorbable polymer • Matrix detachable coil

Cerebral aneurysm recanalization due to coil compaction is the main technical limitation of current endovascular treatment.1,3,8,24,26 This anatomical finding is more frequently seen in small aneurysms with a wide neck (> 4 mm in diameter), large aneurysms, and giant lesions. Recanalization appears to be related to anatomical and biological factors and flow dynamics.3,8,19–21,30,31 The clot generally fills approximately 70% of the aneurysm sac and is a weak barrier to the water-hammer effect produced by blood flow. This weak mechanical barrier is particularly important in wide-necked aneurysms.

The platinum GDC is biologically inert and fosters limited, delayed clot maturation within the aneurysm.2,4,9,12,16,27 To overcome this biological limitation the Matrix bioactive, bioabsorbable coil system (Boston Scientific, Inc., Fremont, CA) was developed. This system accelerates clot maturation, promoting the development of mature connective tissue and neointimal formation. Such tissue is more elastic and resistant to the biomechanical forces of blood flow that are applied to the coils at the neck level of a wide-necked aneurysm.1,3,5,6,11 Preclinical experimental data based on an animal model have demonstrated the validity of this new concept.22 In that study we compared the histological changes that occurred in experimental aneurysms after delivering standard platinum GDCs and those that occurred after inserting Matrix coils. The Matrix coil was approved by the Food and Drug Administration in February 2002. It is the first commercially available bioactive embolic coil for the treatment of cerebral aneurysms. In the present study we report our clinical experience with the consecutive embolization of 118 aneurysms in 112 patients by using the Matrix system.
Matrix coils for aneurysm embolization

Clinical Material and Methods

The Matrix Detachable Coil

Bioabsorbable polymers have been widely used in surgical sutures and implants. More recently, they have also been used as drug delivery vehicles or as scaffolds for tissue engineering. This polymer stimulates cellular reaction during its in situ biodegradation.10,11,12,13,14,15,26,29 This cellular reaction promotes the formation of connective tissue and the development of a neointima across the aneurysm neck. The speed and extent of this histological process may be modified by varying the composition of the copolymers.16,25

The Matrix detachable coil is composed of a central platinum core covered (by heating) with a bioabsorbable polymer, PGLA copolymer (Fig. 1). The volume of the coil includes 30% platinum and 70% biopolymer. The central platinum coil provides radiopacity and memory, and its platinum content and diameter are similar to those of the GDC-10 platinum coil. The Matrix coil is 0.32 mm in diameter; the GDC-18, 0.38 mm in diameter.

There are four types of Matrix coils, differing in stiffness and memory: extra firm, firm, standard, and soft. The Matrix Firm coil is mechanically similar to the standard GDC-18, and the Matrix Standard coil is similar to the standard GDC-10. As a general principle, Extra-Firm and Firm coils are most appropriate for framing, whereas Standard and Soft coils are best utilized for filling. In vitro evaluation of the PGLA copolymer has shown that it begins to lose tensile strength after 5 weeks, and is completely absorbed within 10 to 12 weeks (unpublished data).

Patient Population

Between July 2001 and April 2004 at our institution, 112 patients (62 women and 50 men) harboring 118 aneurysms were treated using Matrix coils. Forty-nine of the aneurysms (49 [41.5%] of 118) were associated with a subarachnoid hemorrhage due to acute lesion rupture. Twenty-four of these 49 lesions (49%) were harbored in patients with Hunt and Hess Grade I, 11 (22.4%) in those with Grade II, eight (16.3%) in those with Grade III, and six (12.2%) in those with Grade IV. Four aneurysms (four [3.4%] of 118) were associated with a nonacute SAH (15 days or more before treatment). Sixty-five aneurysms (65 [55%] of 118) were unruptured. Fifty aneurysms (50 [42%] of 118) were discovered incidentally during angiography, computed tomography angiography, or magnetic resonance angiography, and 15 (15 [12.7%] of 118) caused mass effect.

Aneurysm Size and Location

Fifty-seven aneurysms (48.3%) were small (largest diameter 4–10 mm) with a small neck (neck < 4 mm), 29 (24.6%) were small with a wide neck (neck > 4 mm), 30 (25.4%) were large (11–25 mm), and two (1.7%) were giant (> 25 mm). Ninety-two aneurysms (78%) were located in the anterior circulation, and 26 (22%) in the posterior circulation. The most common location was the carotid ophthalmic/paraclinoid segment (27 [22.9%] of 118), followed by the PCoA (25 [21.2%] of 118), ACoA (20 [16.9%] of 118), and basilar tip (16 [13.6%] of 118; Table 1). The other 30 lesions had various locations.

Matrix ACTIVE Study

From among the 112 patients, the first consecutive 15, who harbored 16 aneurysms, became part of the Matrix ACTIVE clinical registry (sponsored by Boston Scientific, Inc.). This prospective, nonrandomized, multisite study was performed in accordance with the International Conference on Harmonisation guidelines for good clinical practice. Institutional review board or ethics committee approval of the protocol, informed consent, other written patient information, and advertising material were obtained before initiating the study at each center. Eleven US and European centers participated in the study, with the stated goal of evaluating the safety and midterm efficacy of the Matrix coil for the treatment of cerebral aneurysms. Patients whose condition was rated Hunt and Hess Grade I to III were eligible to participate in this study. Giant aneurysms were excluded from the study. The protocol precluded the use of a balloon-assisted technique, stent placement, and non-Matrix coils.

Angiography Studies

Immediate and follow-up angiography results were categorized as follows: complete occlusion, no contrast filling in the aneurysm; neck remnant, small amount of contrast filling at the aneurysm neck; and residual aneurysm, any contrast filling in the aneurysm dome. Long-term aneurysm anatomy findings were evaluated using 3D digital subtraction angiography in multiple projections, compared with immediate postembolization angiography data, and were classified as follows: unchanged, no increase in contrast filling in the aneurysm; further thrombosis, no or less contrast filling in the residual neck or residual aneurysm; and recanalization, any increase in contrast filling in the aneurysm or remodeling of the coil shape.

Results

Immediate Angiography Outcome

In the early phase of our clinical experience, the aneurysm packing density achieved using Matrix coils was less
than that obtained with GDCs (Fig. 2). Limiting factors responsible for these anatomical results included the relative increased friction associated with coil delivery and the unavailability of balloon-assisted technology and stent placements in the treatment of wide-necked or large aneurysms. Sixteen aneurysms were embolized using the Matrix coils in the ACTIVE protocol (ACTIVE group, 15 patients with 16 aneurysms). Immediate postembolization angiograms showed four lesions (25%) with residual aneurysm, 10 (62.5%) with a neck remnant, and two (12.5%) with complete occlusion. Anatomical results were improved when the ACTIVE protocol was discontinued and replaced with the balloon-assisted technique and GDCs. In this arm (post-ACTIVE group, 97 patients with 102 aneurysms), immediate postembolization angiograms showed complete occlusion in 29 cases (28.4%), a neck remnant in 46 (45.1%), and residual aneurysm in 27 (26.5%). Overall, 31 cases were completely occluded (31 [26.3%] of 118 aneurysms), 56 (47.5%) demonstrated a neck remnant, and 31 (26.3%) aneurysms showed residual aneurysm.

Procedural Complications

Technical complications occurred in six patients (5%). Thrombi formed during the embolization procedure in two patients, and successful thrombolysis resulted in moderate neurological deficits (hemiparesis). Four aneurysm perforations occurred during embolization. One lesion was perforated during microcatheter manipulation, two were perforated during regular GDC placement to finish embolization, and one was perforated during Matrix coil delivery. Among these four cases of perforation, two patients suffered neurological deterioration. Overall morbidity was 3.6%.

Immediate Clinical Outcome

One hundred four patients (93%) remained neurologically unchanged or were improved. Two patients suffered new neurological deficits due to perforation and two patients experienced mild neurological deterioration (hemiparesis 4/5) due to thrombus formation. There were four deaths (overall mortality 3.6%). No deaths were related to the procedure and were instead associated with pneumonia, cardiac failure, and a poor subarachnoid hemorrhage grade. There was no technical-associated morbidity or death in patients presenting with unruptured aneurysms.

Midterm Anatomical Outcome

Follow-up angiograms were obtained in 87 cases a mean of 8 months after treatment (range 2–22 months). Among these, three aneurysms demonstrated a translucent border between the coil mass and the parent artery, which represented neointima formation across the aneurysm neck. Such findings have never been seen with the use of bare platinum coils (Figs. 3 and 4).

In the ACTIVE group (15 lesions), only four aneurysms (26.7%) were completely occluded, eight (53.3%) had a stable neck remnant, and three (20%) demonstrated residual aneurysm. In this group, five aneurysms (33.3%) demonstrated recanalization due to underpacking (Fig. 5); the other 10 lesions remained unchanged or exhibited progressive thrombosis.

In the post-ACTIVE group (72 lesions), 41 aneurysms (56.9%) were completely occluded, 16 (22.2%) had a stable neck remnant, and 15 (20.8%) demonstrated residual aneurysm. In this group, five aneurysms (33.3%) demonstrated recanalization due to underpacking (Fig. 5); the other 60 (83.3%) demonstrated progressive thrombosis or were unchanged.

Overall, 45 aneurysms (51.7%) were completely occluded, 24 (27.6%) had a stable neck remnant, and 18 (20.7%) demonstrated residual aneurysm. Forty-five aneurysms (51.7%) were anatomically stable, 25 (28.7%) demonstrated progressive thrombosis, and 17 (19.5%) recanalized (Fig. 6). Recanalization of an aneurysm that had originally been diagnosed as a neck remnant was 15%, and recanalization from residual aneurysm was 38%. No recanalization was observed in aneurysms that had been completely occluded with Matrix coils (Fig. 7).
Midterm Clinical Outcome

Midterm clinical follow-up data were obtained in patients at clinic visits or by telephone interview. One hundred three patients (92%) were neurologically intact or their condition remained unchanged after hospital discharge. Two patients with aneurysm perforation remained severely disabled. Two patients who suffered a thromboembolic complication remained hemiparetic. Five patients died—four due to causes not directly related to the aneurysm or the endovascular procedure. One aneurysm reruptured. This lesion was probably a posttraumatic dissecting aneurysm of the basilar trunk. The patient continued to take aspirin and Plavix for 52 days postembolization but still had a fatal aneurysm rerupture. A plain x-ray film of the skull showed coil remodeling.

Discussion

The Matrix coil is the first generation of commercially approved bioactive, bioabsorbable coil for the endovascular treatment of intracranial aneurysms. In animal studies, the combined use of bioabsorbable copolymer (PGLA) and a platinum coil appeared to accelerate intraneurysm clot maturation, promoting the development of connective tissue and neointimal formation, and thus eliminating the aneurysm from the parent artery lumen. Such connective tissue is stronger than immature thrombus and therefore can resist the blood flow mechanical forces that elicit coil compaction and aneurysm recanalization.

Mechanical Performance of the Matrix Coil

The use of Matrix coils in patients revealed some mechanical characteristics that differed from those of the GDCs; these mechanical differences were not obvious when the Matrix was tested in the preclinical, good laboratory practice animal study. As a general principle, the Matrix coil is softer and has less memory than the GDC-18 system. It is possible to deliver and withdraw the Matrix coil into an aneurysm as many times as needed, but this action requires gentle manipulation to avoid untoward coil stretching. There is intrinsic increased friction during coil delivery.
into the aneurysm sac that is related to the surface design of the copolymer coating. This friction is more noticeable during coil retraction into the microcatheter. Predelivery hydration of the Matrix in normal saline and gentle coil insertion and withdrawal minimize coil damage. The radiopacity of the Matrix is sufficient to obtain appropriate fluoroscopic visualization of the coil throughout the embolization procedure.

In the ACTIVE group, we could not achieve sufficient aneurysm packing in 25% of the aneurysms (four of 16). Insufficient packing was more noticeable in wide-necked aneurysms because of our inability to use the balloon-assisted technique, which was proscribed by the ACTIVE protocol. We were extremely conservative technically to avoid complication in the absence of appropriate adjunctive tools. The increased friction while delivering the first-generation Matrix coils was a significant factor. At the beginning of our clinical experience, this limiting factor could not be neutralized by using other types of coils (ACTIVE protocol restriction). With additional experience it was possible to overcome this mechanical factor by increasing the use of 3D Matrix coils, positioning the catheter tip closer to the aneurysm outflow zone, and mixing different types of coils according to the location of the microcatheter tip. The increased use of the 3D coils reinforced the Matrix scaffold and decreased early compartmentalization. Early compartmentalization does not allow homogeneous coil delivery throughout the aneurysm and forces the physician to reposition the microcatheter in the lesion.

Anatomical Evolution of Aneurysms Embolized With Matrix Coils

In a previous series of aneurysms treated using GDCs, the rate of recanalization from a neck remnant was 48%. In the present series of aneurysms embolized with Matrix coils, lesions with a neck remnant showed a 15% rate of recanalization. No recanalization was demonstrated on midterm follow-up angiography performed in patients with aneurysms that had been completely occluded with Matrix

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**Fig. 4.** A: Angiogram obtained in a 65-year-old woman who had presented with a ruptured right basilar artery–superior cerebellar artery aneurysm, demonstrating a 5.5 × 4-mm aneurysm (neck 4 mm). The aneurysm was embolized with three Matrix coils. B: Immediate postembolization angiogram showing a neck remnant and slight coil protrusion into the parent artery. C: Three-month postembolization angiogram demonstrating complete obliteration. D: Three-dimensional digital subtraction angiogram obtained 12 months postembolization revealing complete obliteration with a clear border between the coil mass and the parent artery.
coils. These midterm anatomical results represented some improvement compared with those obtained using standard GDCs. Results can be improved in wide-necked and large aneurysms by increasing the use of Matrix Stretch-Resistant coils and by using balloon-assisted technology combined with intracranial stents. The additional use of bare platinum coils in the aneurysm inflow zone may also reduce coil friction. All these technical additions permit increased Matrix coil packing density and anchoring throughout an aneurysm cavity. The biological properties of the Matrix work when it is surrounded by a clot. If the intraneurysm biomechanical forces of blood flow are not overcome by dense coil packing, a clot will not form and the Matrix-induced biological reaction will not occur.

Polyglycolic/poly-L-lactic acid has relatively slow in vitro and in vivo degradation and bioabsorption times, eliciting a mild to moderate inflammatory response. The risk of PGLA producing an intense and uncontrollable inflammatory response in an aneurysm with stenosis of the parent artery has not been seen in animal studies or in the present clinical series. In four patients, midterm follow-up angiography studies demonstrated perfect reconstitution of the parent artery at the neck level of the aneurysm. This type of angiography finding has been observed in a preclin-
Histological examinations of vascular specimens from swine showed that this linear angiography separation was produced by the anatomical reconstruction of the parent artery wall by mesenchymal tissue covered with neointima. There was complete and permanent exclusion of the aneurysm cavity from the parent artery. This angiography finding has not been described in aneurysms completely occluded with bare platinum coils.22,26

Clinical Safety

Data from this study show technical complications and immediate and midterm clinical outcomes similar to those in patients treated with GDCs.23 The PGLA coating on the platinum core did not increase coil thrombogenicity or aneurysm perforation. The contact of Matrix coils with small arteries, such as the ACoA and the anterior and middle cerebral arteries, did not elicit untoward in situ thrombosis and occlusion of these arteries. These findings substantiate the preclinical results obtained in the animal laboratory. The neurointerventional physician does not need to change the GDC postembolization pharmacological regimen (aspirin and Plavix for the same indications) from that used in aneurysms embolized with bare platinum coils. Appropriate manipulation of the Matrix coil while delivering or withdrawing it from an aneurysm decreases the chances of coil stretching or aneurysm rupture. If the physician notices increased friction during the early phases of Matrix delivery, it would be better to discontinue the coil delivery and avoid forcing the Matrix coil into the aneurysm and to instead use bare platinum coils. Combining coils improves aneurysm packing and decreases risk.

Conclusions

The use of Matrix bioactive, biodegradable coils in patients with aneurysms leads to clinical outcomes similar to those in patients treated with GDCs. In the present study, midterm anatomical outcomes showed moderate improvement in the recanalization rate when compared with the rate associated with GDCs. The angiography findings of complete anatomical reconstitution of the arterial wall at the neck level of the aneurysm have not been previously observed in aneurysms embolized using bare platinum coils. This anatomical outcome is related to the specific biological response elicited by the contact of PGLA with the aneurysm thrombus. Note, however, that the first generation of Matrix coils produces increased friction when delivered into an aneurysm compared with that produced by GDCs. This technical factor can be neutralized by appropriately positioning the microcatheter tip in the aneurysm and by using the Matrix Stretch-Resistant coil and/or GDC Ultra-soft finishing coils. The next generation of Matrix coils with a better surface design may address these mechanical limitations.

Disclosure

Drs. Murayama and Viñuela invented the biodegradable coil, including the detachable coil, and are consultants for Boston Scientific, Inc.

References

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