New developments in imaging and treatment of intracranial aneurysms

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Chapter 3

Results of 101 aneurysms treated with PGLA microfilament NEXUS coils compared with historical controls treated with standard coils

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ABSTRACT

BACKGROUND AND PURPOSE
Polyglycolic/polyactic acid (PGLA) addition to bare platinum coils is intended to reduce reopening rate of coiled intracranial aneurysms. Nexus coils are standard complex platinum coils with interwoven PGLA microfilament threads. We present the clinical results of coiling of 101 intracranial aneurysms with Nexus coils.

PATIENTS AND METHODS
Results of coiling of 101 aneurysms treated with Nexus coils were compared with historical results of coiling of 120 aneurysms with GDC 10 coils and 115 with Cordis TruFill coils using identical methodology. Complication rate, mean aneurysm volume, packing density, incomplete aneurysm occlusion at 6 months and retreatment rates were compared.

RESULTS
Initial occlusion in aneurysms treated with Nexus coils was (near) complete in 97 aneurysms and incomplete in 4 aneurysms. There were no permanent procedural complications (0 in 95 patients, 0%, 97.5% CI 0.0-3.3%). Mean aneurysm volume was 180.2 mm³ (median 71, range 5-1624 mm³). Mean packing was 19.4% (median 18.3%, range 7.5-38.9%). Six months angiographic follow up in 87 of 101 aneurysms showed incomplete occlusion in 14 (16%) and 12 of those (14%) were additionally coiled. Mean packing of 19.4% of Nexus coils was significantly lower than 22.9% for GDC 10 and 29.7% for Cordis TruFill coils. Other clinical results were not statistically different.

CONCLUSION
PGLA microfilament Nexus coils are safe to use with clinical results comparable to those of standard platinum coils. Handling properties are not optimal. This study gives further evidence of lack of beneficial effect of PGLA addition to reduce recurrence rate.
INTRODUCTION

Endovascular treatment of intracranial aneurysms with bare platinum coils has become an accepted alternative to surgery (1). The most significant drawback of this technique is the possibility of aneurysm reopening over time occurring at an incidence of around 10%. In particular, large and giant aneurysms and initially incompletely occluded aneurysms are at risk for reopening (2-4). Animal models and human studies have shown that the biologic response of intracranial aneurysms to bare coils is complex, requiring stability of the initial occlusion for a considerable period of time for a stable and durable treatment result. As for now, high packing density is the only proven factor predictive of stable occlusion (5). Recently, coating the surface of bare platinum coils with a co-polymer consisting of polyglycolic/polylactic acid (PGLA) was proposed in an attempt to accelerate the biologic response to coils with intended reduction of reopening rate. After an experimental study in 26 swine and a registry of 100 patients (5,6), Boston Scientific (Fremont, CA) introduced the first PGLA coated coil (Matrix) on the market in 2003, later followed by other manufacturers. Matrix coils have a thick PGLA coating over a platinum core with different physical properties (softness, surface smoothness and other) from standard bare platinum coils resulting in different handling. The Nexus PGLA microfilament coil was introduced by EV3 (Irvine, CA) in 2005. Nexus coils are standard bare platinum coils with additional PGLA microfilament threads interwoven in the primary coil. The concept of microfilament threads was chosen by the manufacturer in order to maintain the physical properties of the standard bare platinum coil. In this study, we present our results with coiling of 101 intracranial aneurysms with Nexus microfilament coils. In addition, we compare the results of Nexus coils with historical data from our institution of two types of bare platinum coils (7).

PATIENTS AND METHODS

DESCRIPTION OF COILS

Nexus coils have a thickness of 0.010 inch and are available in helical and two different complex shapes (Morpheus and Tetris). Nexus coils have PGLA microfilament threads interwoven in the primary coil (fig 1). In addition, the coils have a nitinol inner core intended to make the coil resistant to stretch and compaction.
PATIENTS
Between May 15, 2006 and May 5, 2007, 101 aneurysms in 95 patients were treated with Nexus coils. Patients were not consecutive; in the same period another 23 aneurysms were treated with other types of coils for the following reasons: in the beginning and ending of the study period stock of Nexus coils was incomplete (12 aneurysms), operator preference for (thicker) GDC 18 coils in aneurysms of 10-20 mm (7 aneurysms), and conversion from Nexus coils to other types of coils (4 aneurysms). There were 39 men and 56 women with a mean age of 53.6 years (median 53, range 14-89 years). Of 101 aneurysms, 77
had ruptured and 24 had not. Of 24 unruptured aneurysms, 12 were incidentally discovered, 8 were additional to another ruptured aneurysm and 4 presented with symptoms of mass effect. Of 77 patients with a ruptured aneurysm, Hunt and Hess (HH) grading at the time of treatment was HH I-II in 41, HH III in 16, HH IV-V in 20 patients. Timing of treatment after SAH was 0-3 days in 55 patients, 4-7 days in 13 patients and >7 days in 9 patients.

Location of 101 aneurysms was anterior communicating artery in 34, middle cerebral artery in 20, posterior communicating artery in 15, ophthalmic artery in 10, basilar tip in 7, posterior inferior cerebellar artery in 5, pericallosal artery in 4, anterior choreoidal artery in 2, superior cerebellar artery in 2, posterior cerebral artery in 1 and vertebral artery in 1. Mean aneurysm size was 6.6 mm (median 6, range 2-16 mm).

COILING PROCEDURE AND COMPLICATION REGISTRATION
Coiling of aneurysms was performed on a biplane angiographic unit (Integris BN 3000, Philips Medical Systems, Best, The Netherlands) with the patient under general anaesthesia. The aim of coiling was to obtain a dense packing of the aneurysm, until not one coil could be placed. After location of the aneurysm on 2D angiography, 3D Rotational Angiography was performed of the vessel harbouring the aneurysm. From 3D images, coil projection was assessed and measurements of aneurysm diameter and aneurysm volume were performed. Used types of coils, number and lengths of coils and total volume of inserted coils was assessed for every aneurysm and packing, defined as coil volume / aneurysm volume x 100% was calculated. Coil volume was calculated with a spreadsheet provided by the manufacturer containing volumes per cm of every type of coil. Angiographic occlusion was dichotomized in (near) complete occlusion (90-100%) or incomplete occlusion (<90%).

Complications leading to temporary or permanent neurological deficit or death were recorded. In addition, all technical complications related to the Nexus coils were recorded, regardless of clinical impact.

SUPPORTING DEVICES
One aneurysm was coiled with a temporary supporting balloon (Hyperform, EV3, Irvine, CA), one aneurysm was coiled after placement of a neck bridging device (TriSpan, Boston Scientific, Fremont, CA) and 5 aneurysms were coiled after stent placement (Enterprise, Cordis Neurovascular, Miami Lakes, FL).

ANTICOAGULATION PROTOCOL
During coiling of ruptured aneurysms, no heparin was administered apart from the heparin in the pressure bags (1000 U per 500 ml saline). During coiling of unruptured aneurysms not additional to another ruptured aneurysm, 2500 U heparin was administered before insertion of the micro catheter. After the procedure, no anticoagulation was given in small aneurysms with complete occlusion. In larger and wide necked aneurysms, subcutaneous heparin in therapeutic dosage was prescribed for 48 hours.
Patients with unruptured aneurysms treated with stent assisted coiling were preloaded with Clopidogrel 75 mg and Aspirin 80 mg and this was continued for 3-6 months after the procedure. Patients with acutely ruptured aneurysms treated with stent assisted coiling received intravenous Aspirin 500 mg before placement of the stent. In all patients treated with stents, response to antiplatelet medication was tested with VerifyNow P2Y12 Assay (Accumetrics, San Diego, CA) before stent placement.

When thrombus formation on the coil mesh was angiographically visible or when coil loops protruded outside the aneurysm in the parent artery, intravenous infusion of a glycoprotein IIb/IIIa antagonist (tirofiban, Aggrastat, Merck & Co., Inc., Whitehouse Station, NJ), was started for 24-48 hours duration.

CLINICAL AND ANGIOGRAPHIC FOLLOW UP
Patients who survived the hospital admission period were scheduled for a follow up visit at 6 weeks and for angiographic follow up at 6 months. Results of angiographic follow up were classified in the same way as initial angiographic occlusion. Need for additional treatment was assessed in a weekly meeting with neuroradiologists, neurologists and neurosurgeons. Outcome according to the Glasgow Outcome Scale (GOS) was assessed at 6 months.

COMPARISON WITH HISTORICAL DATA OF BARE PLATINUM COILS
Results of coiling of 101 aneurysms with Nexus coils were compared with historical results of coiling of 120 aneurysms with GDC 10 coils and 115 aneurysms with Cordis TruFill coils using identical methodology.\(^7\)

Mean aneurysm volume, packing, incomplete aneurysm occlusion at 6 months follow up angiography and retreatment rates for Nexus coils were compared with both GDC 10 coils and Cordis TruFill coils. Differences were statistically analyzed using the unpaired t test for comparison of means and Chi-square test for comparison of proportions. P values < 0.05 were considered significant.
RESULTS

INITIAL ANGIOGRAPHIC RESULTS AND PACKING
Initial occlusion was (near) complete in 97 aneurysms and incomplete in 4 aneurysms. Mean aneurysm volume was 180.2 mm³ (median 71, range 5-1624 mm³). Mean packing was 19.4% (median 18.3%, range 7.5-38.9%). Of 95 patients, 58 (61%) were prescribed anticoagulation after the procedure. In 101 aneurysms, 426 coils were used (mean 4.2, median 3, range 1-14). The 426 coils had a total length of 5,776 cm and total coil volume was 3,088 mm³. Of 5,776 cm total length of coils, 2,775 cm (48%) was from helical coils, 2,372 cm (41%) was from complex Morpheus coils and 629 cm (11%) was from complex Tetris coils. Inserted coil length per mm³ aneurysm volume was 0.32 cm (total coil length 5,776 / total aneurysm volume 18,201).

CLINICAL COMPLICATIONS
There were no complications leading to transient or permanent morbidity or mortality (0 in 95 patients, 0%, 97.5% CI 0.0-3.3%).

TECHNICAL COMPLICATIONS AND CONVERSIONS
Coil loops protruding from the aneurysm in the parent vessel occurred in 11 patients, in two patients with angiographic visible thrombus formation on the coils. Aggrastat infusion was administered in 7 of 11 patients. In all cases, malposition of coil loops occurred after correct placement of the first coil and was caused by insertion of additional coils that displaced loops of previously inserted coils (figs 2 and 3).
Fig 2 50-year-old woman with an incidentally discovered unruptured ophthalmic aneurysm.

A: Lateral internal carotid angiogram demonstrates 9 mm ophthalmic aneurysm.
B: After insertion of three 8x30 Nexus Morpheus coils an adequate basket is formed.
C: After failed attempt to deliver and withdrawal of a 7x30 Nexus Morpheus coil: coil loops of previous coils protruding in the parent artery (arrow).
D: Final result with coil loops in carotid artery. The patient received Aggrastat infusion for 48 hours. Good clinical outcome.
Results of 101 aneurysms treated with PGLA microfilament NEXUS coils compared with historical controls treated with standard coils

Fig 3 62-year-old man with grade III SAH from anterior communicating artery aneurysm.

A: Internal carotid angiogram shows bilobated 5 mm anterior communicating artery aneurysm.
B: First coil (6x15 Morpheus) forms adequate basket.
C: During insertion of the second coil (2x8mm helical), suddenly a coil loop protruded in the parent artery (arrow). After withdrawal of this coil in the micro catheter, the protruding loop persisted proving this was a displaced loop of the first coil.
D: Final result with persisting protrusion of the coil loop (arrow). Aggrastat infusion was started. Good clinical outcome.
In four aneurysms intended to be treated with Nexus coils, this proved impossible and these aneurysms were treated with other types of coils. In two wide necked aneurysms (one 7 mm middle cerebral artery aneurysm and one 10 mm anterior communicating aneurysm) treated with balloon assisted coiling, the first inserted Nexus coil did not retain its shape after insertion with balloon assistance but retook its original shape after deflating the balloon resulting in protrusion of loops in the parent artery (fig. 4). Both aneurysms were treated with GDC 18 coils. In one 2 mm anterior communicating artery aneurysm, a 2 mm helical Nexus coil could not be delivered and this aneurysm was treated with a 2 mm GDC 10 Ultrasoft coil. Finally, first inserted 10 mm Nexus Morpheus coil in a 12 mm middle cerebral artery aneurysm could not be placed satisfactory and this aneurysm was treated with GDC 18 coils.
Fig 4 57-year-old woman with grade II SAH from a middle cerebral artery aneurysm. 
A: Internal carotid angiogram shows wide necked 7 mm middle cerebral artery aneurysm.
B: Adequate placement of the first coil (7x21 Morpheus) with assistance of Hyperform 7 mm balloon (EV3, Irvine, CA).
C: After deflation of the balloon expansion of the coil with protrusion into the parent artery. This coil was withdrawn.
D: Final result after balloon assisted treatment with GDC 18 coils (Boston Scientific, Fremont, CA).

CLINICAL FOLLOW UP
Clinical follow up at 6 months was available for all patients. Of 77 patients with ruptured aneurysms, 7 died in the hospital from initial impact of SAH or vasospasm (GOS 1). Two patients were in a nursing home (GOS 3), 4 patients had non disabling neurological deficits (GOS 4) as a result of vasospasm and 64 patients had good outcomes (GOS 5). All 18 patients with unruptured aneurysms were neurologically intact.
ANGIOGRAPHIC FOLLOW UP
Angiographic follow up at 6 months was available for 82 patients with 87 aneurysms (86%). Thirteen patients (with 14 aneurysms) had no follow up angiography for the following reasons: death after SAH in 7, refusal in 5 and advanced age (78 years) in 1 patient. Occlusion status for 87 aneurysms at 6 months was (near) complete in 73 (84%) and incomplete in 14 (16%) aneurysms. Of 14 incompletely occluded aneurysms, 12 were additionally coiled. In 2 aneurysms, both for 80% occluded, further follow up is scheduled. Overall retreatment rate was 12% (12 of 101) and retreatment rate for aneurysms with angiographic follow up was 14% (12 of 87). Additional coilings were without complications.

COMPARISON WITH HISTORICAL DATA OF BARE PLATINUM COILS
Results of comparison of Nexus coated coils with GDC 10 coils and with Cordis TruFill coils are displayed in Table. Mean packing of 19.2% of Nexus coils was significantly lower than 22.9% of GDC 10 coils (P<0.0001) and 29.7% of Cordis TruFill coils (P<0.0001). All other parameters (including proportion of incompletely occluded aneurysms at follow up and retreatment rates) were statistically not significantly different.

<table>
<thead>
<tr>
<th></th>
<th>Nexus</th>
<th>GDC 10</th>
<th>Cordis TruFill</th>
<th>p value Nexus-GDC 10 / Nexus-Cordis TruFill</th>
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<tr>
<td>number of aneurysms</td>
<td>101</td>
<td>120</td>
<td>115</td>
<td></td>
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<tr>
<td>mean aneurysm volume</td>
<td>180 mm³</td>
<td>128 mm³</td>
<td>162 mm³</td>
<td></td>
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<tr>
<td>mean packing</td>
<td>19.4% (median 18.3, range 8-39 %)</td>
<td>22.9 % (median 21.8, range 9-48 %)</td>
<td>29.7 % (median 29.6, range 15-57 %)</td>
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<tr>
<td>morbidity / mortality</td>
<td>0% / 0%</td>
<td>2.5% / 0.8%</td>
<td>0.9% / 0%</td>
<td>0.18/0.97*</td>
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<tr>
<td>number of initial incompletely occluded aneurysms</td>
<td>4 (4.0%)</td>
<td>4 (3.5 %)</td>
<td>3 (2.6 %)</td>
<td>1.2/85</td>
</tr>
<tr>
<td>incomplete aneurysm occlusion at 6 months</td>
<td>14 of 87 (17%)</td>
<td>22 of 99 (22.2%)</td>
<td>15 of 95 (15.8%)</td>
<td>43/96</td>
</tr>
<tr>
<td>number of retreatments</td>
<td>12 of 101 (11.9%)</td>
<td>16 of 120 (13.3%)</td>
<td>9 of 115 (7.8%)</td>
<td>0.91/0.43</td>
</tr>
<tr>
<td>number of incompletely occluded aneurysms at 6 months left untreated</td>
<td>2 (2.0%)</td>
<td>6 (5.0%)</td>
<td>6 (5.2%)</td>
<td>0.41/0.38</td>
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</table>

Table Comparison of clinical results of Nexus PGLA microfilament coils with both GDC 10 and Cordis TruFill bare platinum coils. * combined morbidity/mortality compared
DISCUSSION

In this study, we found that results of treating aneurysms with PGLA microfilament Nexus coils are similar to those of two types of standard bare platinum coils. In other words, a beneficial effect of PGLA addition on stability at follow up could not be demonstrated. Nexus coils were safe to use: no neurological complications occurred in 95 patients with 101 aneurysms. The significantly lower packing of Nexus coils compared to both GDC 10 coils and Cordis TruFill coils had no significant effect on reopening and retreatment rates in this relatively small aneurysm groups, although there was a trend to lower retreatment rate for Cordis Trufill coils. Technical complications occurred rather frequently, in our opinion predominantly related to the inner nitinol core of the coil, intended to make the coil resistant to compaction and stretch. Nitinol has the propensity to regain its original shape after being forced into a different shape. In clinical practise, this physical property of the coil resulted in displacement of loops of already inserted coils during placement of additional coils resulting in coil loops protruding in the parent artery (figs 2 and 3). In our experience, we have not encountered this phenomenon with the use of other types of (bare platinum) coils. In patients with coil loops protruding outside the aneurysm in the parent artery, we administered an intravenous infusion of a glycoprotein IIb/IIIa antagonist for 24-48 hours, since Nexus coils have additional PGLA microfilaments with possible increased thrombogenicity. With this protocol, no permanent thromboembolic complications occurred.

Another disadvantage of the physical property of the nitinol core is the dire performance in balloon assisted treatment. The first inserted Nexus coil usually did not retain its shape after insertion with balloon assistance but retook its original shape after deflating the balloon resulting in protrusion of loops in the parent artery, thereby neutralizing the intended effect of balloon assistance (fig.4). In these cases, treatment was continued with other types of coils with good results.

The coil manufacturer (EV3, Irvine, CA) has recently introduced a new range of coils of several thicknesses, from 0.0115-0.0145 inch (Axium) dependant on the loop diameter. This new coil is intended to replace the current available Nexus range. The new Axium coil has no nitinol core and will be available as bare platinum coil and as microfilament coil with either PGLA or nylon.

In general, the results of this study are comparable to studies with other types coils with PGLA addition such as Matrix and Cerecyte coils (8-18). As in our study, a beneficial effect of PGLA in terms of better stability at follow up was absent or not significant in previous studies (8-18).

Should we continue to use these PGLA coils to treat intracranial aneurysms? In our opinion (19-21), supported by others (22-24), the answer to this question is a clearly no for the following reasons. First and most important, clinical results of coils with PGLA addition are not better than those of bare platinum coils. Second, in some PGLA coils (Matrix), coating modifies physical coil properties, negatively affecting ease of handling. Third, PGLA coils are more expensive.
Large prospective randomized trials, instigated by coil manufacturers (24), comparing performance of PGLA coils and standard coils are not warranted, based on current available data.

**CONCLUSION**

PGLA microfilament Nexus coils are safe to use with results comparable to those of standard platinum coils. Handling properties are not optimal. This study gives further evidence of lack of beneficial effect of PGLA addition to reduce recurrence rate.
REFERENCES


22. Cloft HJ: Have you been smoking something that is biologically active? AJNR Am J Neuroradiol 2006;27:240-2
