

**ORIGINAL  
RESEARCH**

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# Single-Center Experience of Cerecyte Coils in the Treatment of Intracranial Aneurysms: Initial Experience and Early Follow-Up Results

**BACKGROUND AND PURPOSE:** Endovascular treatment of intracranial aneurysms using platinum coils is effective, but uncommonly aneurysms recur. New-generation coils, such as Cerecyte, aim to address this problem. This study examines the safety and efficacy of these coils in the treatment of a cohort of ruptured and unruptured aneurysms

**MATERIALS AND METHODS:** Sixty-seven patients with 68 aneurysms were included in the study. Of these, 51 were treated exclusively with the new polyglycolic acid (PGA)-containing coils, and 17 were treated with a combination of new PGA-containing and other coils. Initial and follow-up angiograms were graded according to the 3-point scale of occlusion. Follow-up angiography was available in 46 cases at 6 months. Based on occlusion grading at initial and follow-up angiography, aneurysms were classified into stable, improved, and worsened (recanalized) groups.

**RESULTS:** Of the exclusive new-coil cohort, 36 cases (70.6%) were initially completely occluded (grade 1), 12 (23.5%) showed filling at the neck (grade 2), and 3 (5.9%) showed contrast within the neck and sac (grade 3). Analysis of the follow-up angiograms showed 24 (70.6%) had stable occlusion, 3 (8.8%) had improved occlusion, and 7 (20.6%) had worsening occlusion. Data for cases treated with new PGA-containing coils together with bare platinum coils were also analyzed separately. Intraprocedural adverse events were noted in 4 cases (7.8%), but there were no clinical sequelae. There were no rebleeds in the follow-up period.

**CONCLUSION:** New PGA-containing coils show no excess in procedural and periprocedural complications over bare platinum coils, and the recanalization rate is comparable with bare platinum coils in the short term.

**W**e report the early results of 68 aneurysms treated with PGA-modified coils. Cerecyte (Micrus, Sunnyvale, Calif) coils incorporate a strand of polyglycolic acid (PGA) polymer that has been shown to accelerate aneurysm fibrosis and neointima formation in animal studies.<sup>1</sup> Endovascular coiling has been the treatment of choice for most intracranial aneurysms since the publication of the International Subarachnoid Aneurysm Trial (ISAT). This showed a significant decrease in immediate morbidity and mortality compared with neurosurgical clipping in those aneurysms previously deemed suitable for either management. Follow-up of patients treated with endovascular coiling has, however, shown that a minority of cases undergo compaction of the coil ball and recanalization or regrowth of the treated aneurysm. These patients are at risk of recurrent subarachnoid hemorrhage. To combat the risk of recurrence, new devices and technologies have been developed. These include the use of nondetachable balloons and expandable stents to allow improved treatment of wide-necked aneurysms and, more recently, new coils. These coils incorporate a polymer with properties that are supposed to improve aneurysm occlusion.

## Methods

Seventy-two patients with a total of 77 aneurysms were treated using new PGA-containing coils between September 2004 and March 2006. Of these, 51 patients (51 aneurysms) were treated exclusively using new PGA-containing coils, and 21 had new PGA-containing coils in conjunction with other types of coils. Cases where the new coil was used in conjunction with another type of PGA, polylactic acid copolymer (PGLA)-containing coil or with HydroCoils (MicroVention, Aliso Viejo, Calif) have been excluded. A single aneurysm in a fenestrated basilar artery was treated with new PGA-containing coils in combination with a Neuroform stent (Boston Scientific, Natick, Mass). This case has also been excluded from subsequent analysis, as has a case in which the patient went for surgical clipping immediately postcoiling, resulting in a total of 67 patients with 68 aneurysms being assessed. Fifty-one patients were female, and 16 were male. Age range was 14-81 years.

Diagnostic angiography and embolization were performed using an Integris Allura biplane fluoroscopy unit or an Integris V3000 single plane unit (Philips Medical Systems, Best, the Netherlands). Aneurysm dimensions were measured in at least 2 planes with standard software, either by using the guide catheter as a reference or from reformatted rotational 3D angiograms. Aneurysms were divided into narrow or wide-necked groups, where a wide neck was defined as an aneurysm neck diameter greater than 4 mm and/or neck:dome ratio greater than 1:2.

Embolization was performed by a consultant neuroradiologist. Postembolization angiograms, including the working projection and 2 further views, were performed as standard at the completion of the procedure.

During some procedures, coils of the desired length, shape, or softness were not immediately available in the new PGA-containing

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coil type and other types needed to be used in conjunction with the new coil. Other coils used were Ultipaq (Micrus) in 9 aneurysms, Guglielmi detachable coils (Boston Scientific) in 6, Microplex (Microvention) in 4, and detachable coils (Cook, Bjaeverskov, Denmark) in 1 case. In 5 cases, 2 coil types were used in combination with new PGA-containing coils. In these cases, new PGA-containing coils were used in combination with other coils, and the proportion of the new PGA coils ranged from 38% to 92%. The total length of PGA-containing coil deployed was between 2 and 143.5 mm.

HydroCoils (Microvention) were used in 7 cases and Matrix coils (Boston Scientific) in 2. These were excluded from the analysis and will not be discussed further.

In 45 cases, 6-month follow-up was available. One of these was performed using MR angiography, the others using conventional digital subtraction angiography, by using the work projection and at least 2 additional views.

The postembolization and follow-up angiograms were analyzed by 2 consultant neuroradiologists (D.M. and V.J.). In cases of discrepancy, the opinion of a third consultant neuroradiologist (A.G.) was obtained, and the majority decision was accepted. Angiograms were graded according to a 3-point scale of complete obliteration of the aneurysm, near-complete occlusion with contrast filling the neck of the aneurysm, without contrast within the body of the aneurysm, and finally incomplete occlusion with filling of both the neck and body of the aneurysm. Data analysis was performed separately for all of the cases treated exclusively with new PGA-containing coils and those where more than 1 type of coil was used, using an Excel spreadsheet (Microsoft, Redmond, Wash).

## Results

The aneurysms treated with new PGA-containing coils were not specifically selected and are representative of the caseload at our institution. Most cases were acutely ruptured aneurysms (60 [88.2%]), and most of these were World Federation of Neurological Surgeons (WFNS) grade 1 (39 [65.0%]). The remainder of the acute cases were graded as follows: WFNS grade 2 (2 [3.3%]), grade 3 (12 [20.0%]), grade 4 (3 [5.0%]), and grade 5 (4 [6.7%]). Nine cases were unruptured, incidental aneurysms.

The maximum diameter of the aneurysms ranged between 2 and 12.5 mm (mean, 5.8 mm). Thirty-two (47.1%) measured 5 mm or less, 35 (51.5%) were between 5 and 10 mm, and 1 was greater than 10 mm in diameter (1.4%). Twenty-seven aneurysms (39.7%) were wide necked, with either a neck diameter of greater than 4 mm or a neck:dome ratio greater than 2, of which 1 required balloon remodeling.

The cohort treated exclusively with the new coil included aneurysms between 2 and 12.5 mm (mean, 5.1 mm). Twenty (39.3%) were wide necked, with 3 cases requiring balloon remodeling. In the cohort treated with mixed coil types, the mean aneurysm size was 5.5 mm (range, 2–9 mm), and 6 (37.5%) were wide necked.

In the cohort of cases exclusively treated with new PGA-containing coils, the results are as follows: Postembolization occlusion was complete in 36 (70.6%), near complete in 12 (23.5%), and incomplete in 3 (5.9%). Thirty four of these 51 patients have undergone 6-month follow-up angiography with the following results: complete occlusion in 24 (70.6%), near complete in 5 (14.7%), and incomplete in 5 (14.7%; Table 1).

**Table 1: Occlusion grades in aneurysms treated only with PGA-containing coils at end of coiling procedure and at 6-month follow-up angiography where performed**

Exclusive Cerecyte	Initial Result (Total = 51), n (%)	6-Month Follow-Up (Total = 34), n (%)
Complete occlusion	36 (70.6)	24 (70.6)
Near-complete occlusion	17 (23.5)	5 (14.7)
Incomplete occlusion	3 (5.9)	5 (14.7)

**Table 2: Occlusion grades in aneurysms treated with a mixture of PGA-containing and bare platinum coils at end of coiling procedure and at 6-month follow-up angiography where performed**

Mixed Cerecyte	Initial Result (Total = 15), n (%)	6-Month Follow-Up (Total = 12), n (%)
Complete occlusion	12 (70.6)	8 (66.7)
Near-complete occlusion	5 (29.4)	1 (8.3)
Incomplete occlusion	0 (0.0)	3 (25.0)

Twenty-four cases (70.6%) showed stable occlusion, 3 cases (8.8%) showed improvement in occlusion grade, and 7 cases (20.6%) showed worsening of the occlusion grade. Of those cases that had worsened, 3 had moved from grade 1 to grade 2, 2 cases had moved from grade 2 to grade 3, and 2 cases had moved from grade 1 to grade 3.

In the exclusive new PGA-containing coil cohort, 4 patients (7.8%) had adverse events during the procedure, including 1 aneurysm rupture. Three minor thromboembolic events occurred (5.9%), requiring saline flushing only. There were no clinical sequelae.

At the end of the coiling procedure, occlusion grade for the mixed coil cohort was as follows: complete occlusion in 12 (70.6%), near complete in 5 (29.4%), and incomplete in 0 (0.0%). Twelve aneurysms have been followed up at 6 months, and the grading is as follows: complete occlusion in 8 (66.7%), near complete in 1 (8.3%), and incomplete in 3 (25.0%; Table 2). Thus, 6 cases (50.0%) demonstrated stable occlusion, with no change in grade over 6 months, 2 cases (16.7%) showed an improvement in grade, and 4 cases (33.3%) showed deterioration in grade over the 6-month follow-up period.

Complications or adverse events were angiographically noticed during the procedure in 4 cases. Two cases in which the aneurysm was ruptured during attempted placing of a final bare platinum coil resulted in no clinical sequelae. One case of thromboembolism to the A2 segment of the anterior cerebral artery required treatment with intravenous abciximab (Reo-Pro), and there was 1 further case in which thromboembolism to the callosomarginal artery caused mild flow restriction treated with saline flushing and hypertension, with subsequent oral aspirin therapy. Both of these cases had transient lower limb weakness that resolved completely within 48 hours.

There were no instances of coil stretching. There have been no rebleeds in this cohort during the follow-up period to date. Of the 3 deaths, 1 was due to myocardial infarction, 1 due to sepsis, and 1 due to the original subarachnoid hemorrhage.

## Discussion

Since the publication of the ISAT data,<sup>2,3</sup> endovascular treatment of intracranial aneurysms has become the accepted best practice in most aneurysms, where vascular access and aneurysm morphology allow. Although ISAT did show a decrease

in early mortality and morbidity with this technique, it also demonstrated that a minority of cases undergo recanalization and that these cases are at increased risk of recurrent subarachnoid hemorrhage, with the attendant morbidity. This confirms the finding of other, smaller studies.<sup>4-10</sup> In an attempt to reduce the rate of recanalization, coils that incorporate a gel or polymer that aims to improve on the ability of bare platinum to successfully and permanently occlude the aneurysm have recently become available. However, it remains to be proven that these modified coils actually reduce recurrence.

HydroCoils have a layer of hydrogel polymer surrounding the platinum core that expands after deployment, resulting in a greater packing attenuation than that achieved by bare platinum coils.<sup>11</sup> The other types of new-generation coils use a PGA polymer with or without lactic acid copolymer (PGA or PGLA) with a platinum coil. PGLA is widely used in absorbable sutures and as a cellular scaffold in tissue engineering and is known to be safe to use in humans. Animal studies on induced aneurysms have shown histologic evidence of accelerated fibrosis and neointima formation after treatment with PGLA-containing coils.<sup>1</sup> This is thought to be a result of improved adhesion of inflammatory cells and spindle cells to the PGLA, allowing increased collagen deposition and thrombus organization in the occluded aneurysm.<sup>12</sup> Previous *in vivo* studies have shown that altering the proportions of PGA and polylactic acid (PLA) in a PGLA copolymer affects the rate of breakdown of the polymer and the degree of associated tissue reaction.<sup>13</sup> Pure PGA has a half-life of 5 months and elicits a mild inflammatory reaction, whereas a 50:50 ratio copolymer has a half-life of 1 week and a more intense reaction. Cerecyte coils contain pure PGA monomer, and Matrix coils (Boston Scientific) have a 90:10 PGA:PLA polymer. Studies have reported a radiolucent separation of coil from opacified blood on angiographic follow-up of aneurysms treated with bioactive coils that is assumed to represent neointima.<sup>14</sup> Matrix coils have coating of PGLA on the surface of the coil, and Nexus coils (ev3, Irvine, Calif) have PGLA fibers extending from the platinum core. Cerecyte coils have a PGA thread within the primary wind of the coil. This results in a coil that has handling characteristics identical to bare platinum, and, so, unlike the other coils, there is no need to change operating practice or undergo a learning curve when changing from bare platinum coils.

Several studies showed that the first PGLA-containing coil to be available, Matrix, had worse initial and late occlusion rates than bare platinum,<sup>14-16</sup> and this was suggested to be because the coils were slightly stiffer and developed more friction when being deployed through the microcatheter, leading to increased compartmentalization and reduced packing of the aneurysms. It is impossible to know whether these factors masked any effect of the PGLA. With the new PGA-containing coils being so similar to bare platinum coils in clinical practice, any differences seen should be due to the effect of the PGA. Compared with historical bare-platinum results, however, we are not taking into account the effects of other improvements in endovascular treatment. With this in mind, our institution is involved in the randomized, multicenter Cerecyte Coil Trial that aims to compare new PGA-containing and bare platinum coils.

The caveats about comparing with historical studies not-

withstanding, our results are encouraging. The original ISAT article found initial occlusion rates of 66%, with 26% of cases having a neck remnant and 8% with incomplete occlusion and filling of the aneurysm sac.<sup>2</sup> Another large study using bare platinum coils<sup>5</sup> showed initial occlusion in 72.6%, subtotal occlusion in 25.0%, and incomplete occlusion in 2.4%. There is a degree of subjectivity in the grading of angiographic findings postembolization, and the grading system that we have used is similar to that of Raymond et al,<sup>4</sup> who showed initial occlusion in 35.9% of cases, a residual neck in 46.3%, and residual aneurysm in 13.8%, with failure to treat in 4.0% again by using bare platinum coils. These results are comparable with our own results of complete occlusion in 70.6% of the exclusive new PGA-containing coil cohort, near complete occlusion in 23.5%, and incomplete occlusion in 5.9%. This suggests that there is little difference in the initial deployment between the bare platinum coils used in the previous studies and the new PGA-containing coils.

This is also borne out by the low rates of morbidity and lack of mortality in our cohort. There were no cases of coil stretching and only a single case of aneurysm rupture, which was asymptomatic, in the exclusive new PGA-containing coil cohort. Our period of follow-up is short, but as yet there have been no cases of rebleeding. One theoretical drawback of PGLA-containing coils is that increased thrombogenicity could lead to an increase in thromboembolic complications. In our experience, there has been no excess of thromboembolic events (5.9%) related to new PGA-containing coils.

The main aim of PGLA-containing coils is to increase long-term stability of embolized aneurysms, with a reduction of recanalization and rebleeding. For the cohort treated exclusively with new PGA-containing coils, we showed a 20.6% recurrence rate (near complete in 8.8% and incomplete in 11.8%). In the study of Raymond et al,<sup>4</sup> who originally described the grading criteria, the recurrence rates were 33.6%, with major recurrence in 20.7%. Our results appear considerably better, which may in part be because of the effect of the PGA component of the coil. There are several other variables, however, the most important of which is probably the duration of follow-up. In our study, follow-up has been short (6 months). In the study by Raymond et al,<sup>4</sup> recurrence was demonstrated at a mean of 12.31 months, with major recurrences appearing at a mean of 16.49 months; at 6 months only 46.9% of all of the recurrences had been detected. The size of the aneurysms treated is also important, as seen in a recent paper looking specifically at coiling of small aneurysms.<sup>17</sup> Initial occlusion rates were not recorded, but the recanalization rate was 25.8% of cases at 6 months. Allowing for the subjective nature of recurrence interpretation and grading, similar results have been reported by other centers. Cognard et al<sup>6</sup> reported a 14% recurrence rate in initially completely occluded aneurysms treated with bare platinum coils and a 33.3% recurrence rate in those aneurysms with initial subtotal occlusion. Our small cohort of patients treated with a mix of PGA-containing and bare platinum coils showed a higher rate of recanalization over the 6-month follow-up (33.3%). Although the groups are too small to allow concrete conclusions to be drawn, this finding could represent increased aneurysm stability in cases treated with a greater proportion of PGA-containing coils.

There have been few published data regarding Cerecyte coils. One published abstract quotes stable or improved occlusion in 90% of a cohort of 145 patients treated with Cerecyte coils and a 9.6% rate of recurrence requiring retreatment at 6-month follow-up. It states that these results were better than the same centers' results with bare platinum coils.<sup>18</sup> A recent article<sup>19</sup> looked at initial aneurysm treatment and early follow-up in 25 aneurysms. Four cases were also treated with bare platinum coils, and 2 cases were stent assisted. Initial occlusion rates were 68%, with 88% occlusion on 6-month follow-up angiography. Interestingly, this study measured coil packing attenuation and found it to be lower in the Cerecyte cohort than in published bare-platinum series. The authors felt that the high persistent occlusion rate despite a low packing attenuation may represent a beneficial effect of the PGA. Our data show a similar initial occlusion rate but a slightly increased rate of recanalization. Not all of the follow-up angiograms have been performed on our cohort, however, and our recanalization rate may change slightly in the future.

### Conclusion

Cerecyte coils are safe to use in acutely ruptured and unruptured intracranial aneurysms. The handling characteristics are similar to those of bare platinum coils allowing similar rates of initial aneurysm occlusion to be obtained. In a short follow-up period, recurrence rates are comparable with those demonstrated in studies of bare platinum coils. A randomized, controlled trial is necessary to assess the benefit of new PGA-containing coils over existing bare-platinum technology.

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