Technology Brief: Update

Cerecyte (bioactive) coils for the treatment of intracranial aneurysms

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REGISTER ID  WP087

NAME OF TECHNOLOGY  CERECYTE (BIOACTIVE) COILS

PURPOSE AND TARGET GROUP  FOR USE IN NEUROSURGICAL PROCEDURES TO TREAT INTRACRANIAL ANEURYSMS (RUPTURED AND UNRUPTURED); THE BIOACTIVE COMPONENT AIDS TO REDUCE INCOMPLETE OCCLUSION AND RECANALISATION OF THE ANEURYSM

STAGE OF DEVELOPMENT (IN AUSTRALIA)

☐ Yet to emerge  ☐ Established
☐ Experimental  ☐ Established but changed indication or modification of technique
☐ Investigational  ☐ Should be taken out of use
☒ Nearly established

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☒ Yes  ARTG number  133001, 133002, 133088, 133089, 144816, 154322, 164326
☐ No
☐ Not applicable

INTERNATIONAL UTILISATION

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2012 SAFETY AND EFFECTIVENESS ISSUES

Study description

A total of two studies evaluating the safety and efficacy of Cerecyte coils were included in this update (Murphy and Pryor 2010 and Castro et al 2008). The study by Murphy and Pryor (2010) was a conference abstract presented at the 7th Annual Meeting of the Society of Neurointerventional Surgery. Castro et al (2008) was a registry study that was not included in the original brief.

The aim of the retrospective, non-randomised comparative study by Murphy et al (2010) was to compare chemically inert bare platinum endovascular coils with second generation ‘bioactive’ endovascular coils for the treatment of cerebral aneurysms (level III-3 intervention evidence). In this study, the medical records of patients treated with bare platinum or biologically active coils between 2002 and 2009 were retrospectively reviewed for information regarding coil manufacturer, treatment details, follow-up angiographic date and outcome. A total of 90 cases were selected for inclusion, 50 aneurysms were treated using Micrus bare platinum coils and 40 aneurysms were treated using Micrus Cerecyte coils. Two cases were excluded from the analysis in each group due to aneurysm characteristics, partial thrombosis and fusiform anatomy. The mean aneurysm volume in the bare platinum coil group was 217.96 mm³, with 20 aneurysms smaller than 7 mm and 28 aneurysms measuring 7 mm or greater. In the Cerecyte group, the mean aneurysm volume was 587.70 mm³, with 18 aneurysms smaller than 7 mm and 20 aneurysms measuring 7 mm or greater. No further information on patient characteristics was provided.

The data assessed included initial occlusion rates, recanalisation rates, packing density and follow-up assessment of coil performance and stability. Short term follow-up data (6 and 12 months) were available for 70% (26/37) and 51% (19/37) of Cerecyte patients and 71% (32/45) and 58% (26/45) of bare platinum patients, respectively. Long term follow-up data (3 and 5 years) were available for 41% (15/37) and 2.7% (1/37) of Cerecyte patients and 49% (22/45) and 24% (11/45) of bare platinum patients, respectively. The mean length of follow-up for the Cerecyte and bare platinum groups was 29 months and 38 months, respectively.

Castro et al (2008) assessed the safety and efficacy of Cerecyte coils for the treatment of small ruptured and unruptured intracranial aneurysms. This Spanish Registry for Embolisation of Small Intracranial Aneurysms with Cerecyte Coils (SPAREC) was a non-randomised, prospective, multi-centre registry which commenced in May 2005 (level IV intervention evidence). Aneurysms <10 mm were classified as small with either a narrow neck (<4 mm) or a wide neck (>4 mm). In this
study, exclusion criteria included stent-assisted procedures, retreatment, patients treated with non-Cerecyte bioactive coils, non-saccular aneurysms, and pseudoaneurysms.

A total of 47 patients with 48 small cerebral aneurysms (26 ruptured, five with III cranial nerve paresis, and 17 incidental) who were treated at various centres between May 2005 and September 2007 were included in the study. There were 29 cases of narrow neck aneurysms and 19 cases of wide neck aneurysms. The ruptured aneurysms were Hunt-Hess grade I in nine patients, grade II in 11, grade III in five, and grade IV in one. No further information on patient characteristics was provided.

All procedures were performed using a transfemoral approach under general anaesthesia. Standard endovascular treatment procedures were used, and aneurysms were occluded with coils packed as densely as possible. The combination of Cerecyte coils with bare platinum coils, as well as balloon-assisted coiling was allowed at the discretion of the attending physician at each centre. Balloon-assisted coiling was used in a total of 29 (60.4%) cases. Clinical and angiographic follow-up was performed in all 48 cases for a full 6 months.

Outcomes that were assessed included aneurysm sac volume, volumetric percentage occlusion (VPO) and the percentage of bioactive coils (PBC) against all coils employed. Two external interventional neuroradiologists assessed the initial and follow-up angiographic results, which were rated according to the Raymond scale:

- Complete occlusion: no contrast filling of the aneurysm.
- Neck remnant: a small amount of contrast filling at the aneurysm neck.
- Incomplete occlusion: any amount of contrast filling in the aneurysm dome.

The authors defined recanalisation as any worsening in the Raymond scale grade, together with any increase in remnant size despite an unchanged Raymond scale grade, to make sure that no unfavourable change in angiographic stability during follow-up would go unnoticed. Recanalisation was categorised as major where any increase in size made retreatment with coils theoretically feasible. Procedural complications and neurological events during the perioperative and follow-up period were also recorded.

2012 Safety

Murphy et al (2010) reported that an adverse clinical outcome and treatment-related death occurred in 2.1% (1/48) of patients in the bare platinum group; however, no such complications were observed in the Cerecyte group.

In the study by Castro et al (2008), a total of five patients (10.4%) experienced technical complications. Four local thromboembolic complications (8.3%) were resolved with medication without clinical consequences, while one case of
asymptomatic coil protrusion into the parent vessel (2.1%) was also recorded. In addition, one patient experienced a clinical complication (2.1%), suffering a new neurological deficit due to occlusion of the anterior choroidal artery during repair of a ruptured anterior choroidal aneurysm, with severe hemiparesis. No deaths related to the procedure were reported.

2012 Effectiveness

In the study by Murphy et al (2010), the authors reported that the rate of persistent complete occlusion was similar between the two groups, with a rate of 35.4% (17/48) in bare platinum group and 39.5% (15/38) in the Cerecyte group; however, no statistical analyses were provided. The rate of progressive occlusion was 19.4% (6/31) in the bare platinum group, compared with 43.5% (10/23) in the Cerecyte group. The authors reported that a statistical comparison of the two groups made at final follow-up showed no statistical difference between the two groups (P=0.0542).

The initial mean packing density in the bare platinum group was 23.07 ± 11.88% (n=45) and 28.68 ± 18.38% in the Cerecyte group (n=33); however, no statistical analyses were provided. On follow-up angiography, aneurysmal recanalisation was demonstrated in three (17.6%) cases in the bare platinum group, compared with one case (6.6%) in the Cerecyte group; however, no statistical analyses were provided.

Castro et al (2008) reported that no early bleeding or rebleeding was observed in any of the 48 cases during follow-up. In two small aneurysms (3 mm in diameter), the initial use of a 3 mm spherical Cerecyte coil was unsuccessful, due to issues related to microcatheter pull-out. As a result, conventional 3 mm platinum coils were deployed in these cases, which improved microcatheter stability.

With regard to the immediate 30-day clinical outcome, 46 patients (97.8%) were neurologically unchanged or improved immediately after the procedure. However, the one patient with occlusion of the anterior choroidal artery who suffered severe hemiparesis was rated as moderately to severely disabled at discharge, with a Modified Rankin Scale (mRS) score of 4. By mid-term follow-up, the crural paresis in this patient had improved; however, the brachial paresis remained severe, with an unchanged mRS score of 4. In the five cases that presented with III cranial nerve paresis at baseline no immediate worsening was observed, and at 30-day follow-up, four patients had improved while one patient remained unchanged. By mid-term follow-up, cranial nerve paresis was fully resolved in four patients, but remained unchanged in one patient.

With regard to the immediate angiographic outcome, complete occlusion was achieved in 33 aneurysms (68.7%), a neck remnant was observed in 12 aneurysms
(25%) and incomplete occlusions were observed in 3 aneurysms (6.25%). At 6 months follow-up, 33 aneurysms (68.7%) remained completely occluded, a neck remnant was observed in 13 aneurysms (27.1%) and incomplete occlusions were observed in 2 aneurysms (4.16%). At 6 months follow-up, the angiographic stability rate was 66%, as 33 aneurysms maintained the same Raymond sac occlusion scale grade. At this same time point, 8 aneurysms exhibited progressive occlusion (16.7%), achieving an improved Raymond sac occlusion scale grade compared with immediately after the procedure. In addition, a further 8 aneurysms (16.7%) exhibited some degree of recanalisation. Of these, 6 aneurysms (12.5%) that were initially completely occluded developed residual necks (minor recanalisations) and were left untreated, while one residual neck (2.1%) and one initially complete occlusion (2.1%) developed into incomplete occlusions (major recanalisation), and required treatment. Therefore, the retreatment rate in this study was 4.2%.

Following the procedure, the overall mean VPO was 25.2%. Where aneurysms were treated with balloon-assisted coiling, the mean VPO was 27.8% compared with 21.8% in cases treated using only conventional coil packing (P<0.01). At six months follow-up, the VPO was 23.9% in aneurysms that were angiographically unchanged, compared with 27.2% in aneurysms that underwent progressive thrombosis, and 26.4% in aneurysms where recanalisation occurred. No statistically significant differences between these three groups were observed (P>0.05).

At six months follow-up, the PBC was 75.1% in aneurysms that were angiographically unchanged, compared with 93.8% in aneurysms that underwent progressive thrombosis, and 74.3% in aneurysms where recanalisation occurred. The PBC was significantly higher in the progressive thrombosis group compared with the angiographically stable and recanalisation groups (P<0.05 for both); however, no statistically significant difference between the angiographically stable and recanalisation groups was observed (P>0.05).

2012 COST IMPACT

One study was identified that evaluated the relative cost of various embolic materials, including bioactive coils, used for the treatment of wide-necked intracranial aneurysms (Simon et al 2010). The cost of a bioactive coil on average ranged from $US 1,984 for a 3 mm aneurysm, to $US 172,179 for a 25mm aneurysm. Specifically, the cost of a Helipaq 18 Cerecyte coil ranged from $US 1,130 for a 3 mm aneurysm, to $US 94,530 for a 25mm aneurysm. The authors concluded that larger outer diameter helical coils, hydrocoils and liquid embolics provide a relative cost saving compared with standard, spherical or bioactive coils when aneurysm size, shape, packing density and embolic agent were controlled and standardised, and
that this cost differential increases as the size of the aneurysm being treated increases.

2012 Ethical, Cultural or Religious Considerations

No issues were identified from the retrieved material.

2012 Other Issues

The study by Murphy and Pryor (2010) reported that one author had a competing interest, and listed Micrus Endovascular Corporation, the manufacturer of Cerecyte coils. Castro et al (2008) reported that the study was supported in part by Micrus Endovascular Corporation; however, the authors reported having no financial interest in the results of the study or any affiliation with the device manufacturer.

Searches of clinical trial registers indicate that there are currently 2 ongoing clinical trials evaluating Cerecyte coils; importantly however, neither trial is specifically comparing Cerecyte coils to other endovascular coils (Table 1). In addition, the results of the Cerecyte Coil Trial are yet to be published. This is a prospective, randomised trial of 500 patients enrolled at 23 centres worldwide, who have been treated with Cerecyte or bare platinum coils for ruptured and unruptured intracranial aneurysms.

Table 1: Ongoing and currently recruiting clinical trials involving Cerecyte coils

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<thead>
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<th>Estimated date of completion</th>
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<td>NCT01195129 (ongoing but not recruiting)</td>
<td>USA</td>
<td>Prospective, multicentre, randomised trial of 799 patients receiving either non-Hydrocoils (Cerecyte or Platinum) or Hydrocoils 18 month follow-up period.</td>
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<tr>
<td>NCT01340612 (recruiting)</td>
<td>Canada</td>
<td>Prospective, randomised trial of an estimated 600 patients receiving either endovascular coiling (including Cerecyte coils) or endovascular stenting with or without endovascular coiling (including Cerecyte coils) 12 month follow-up period.</td>
<td>April 2016</td>
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2012 Summary of Findings

The results from a small, single centre, single physician, retrospective, non-randomised study suggest that Cerecyte coils are associated with lower recanalisation rates and higher packing attenuation, when compared with bare platinum coils, up to 3 years follow-up; however no statistical analyses were provided for these comparisons. Importantly, no complications were reported in patients who were treated with Cerecyte coils. In addition, a small, multicentre
registry study assessing patient outcomes after treatment with Cerecyte coils reported that the majority of patients were neurologically unchanged or improved up to 6 months follow-up. Additionally, no cases of bleeding or rebleeding were reported up to 6 months follow-up. A low rate of clinical complications was observed in this study, while technical complications (10.4%) were generally resolved with medication and without clinical consequences. There is currently a lack of long-term, follow-up data from prospective, randomised trials assessing the safety and efficacy of Cerecyte coils for the treatment of intracranial aneurysms; however, at least one such trial is currently ongoing.

**2012 HealthPACT Assessment**

The evidence base assessing the safety and effectiveness of Cerecyte bioactive coils is limited. In addition, the significant cost of these coils is likely to limit their diffusion into clinical practice in Australia. Therefore, HealthPACT have recommended that no further assessment of this technology is warranted.

**2012 Included Studies**

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**2012 References**


PRIORITISING SUMMARY 2010

REGISTER ID S000126

NAME OF TECHNOLOGY CERECYTE (BIOACTIVE) COILS

PURPOSE AND TARGET GROUP FOR USE IN NEUROSURGICAL PROCEDURES TO TREAT INTRACRANIAL ANEURYSMS (RUPTURED AND UNRUPTURED); THE BIOACTIVE COMPONENT WAS INTRODUCED WITH AN AIM TO REDUCE INCOMPLETE OCCLUSION AND RECANALISATION OF THE ANEURYSMS POST-PROCEDURE

STAGE OF DEVELOPMENT (IN AUSTRALIA)

☐ Yet to emerge
☐ Experimental
☐ Investigational
☒ Nearly established

☐ Established
☐ Established but changed indication or modification of technique
☐ Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☒ Yes
☐ No
☐ Not applicable

ARTG number 133001

INTERNATIONAL UTILISATION

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2010 IMPACT SUMMARY

The Cerecyte® microcoil (Micrus Endovascular Corporation, San Jose, California) is a bare platinum coil with polyglycolic acid (PGA) running through its lumen. It is employed by neuroradiologists in minimally invasive endoscopic treatments for patients with intracerebral aneurysms (ruptured and unruptured). PGA was added to the traditional bare platinum coil to reduce incomplete aneurysm occlusion and recanalisation, complications that have been associated with the use of endovascular coils.

2010 BACKGROUND

An aneurysm is an abnormal localised dilation of any vessel. Due to various histopathologic and haemodynamic factors, aneurysms generally occur in arteries supplying blood to the brain (Vega et al 2002). Intracranial aneurysms can be classified as saccular (developing from defects in the muscular layer of arteries), fusiform (developing from ectatic, tortuous cerebral arteries) or dissecting (resulting from cystic medical necrosis or a traumatic tear of an artery); the most common of these are saccular aneurysms (accounting for approximately 90% of all intracranial aneurysms) (Vega et al 2002). Patients with suspected or confirmed asymptomatic or symptomatic intracranial aneurysms have two options of invasive treatment: open craniotomy or endovascular treatment (Vega et al 2002).

Following publication of the International Subarachnoid Aneurysm Trial (ISAT), endovascular platinum coil treatment has become the therapy of choice for most patients with ruptured intracranial aneurysms (where vascular access and aneurysm morphology allow), and it has become a preferred treatment for those with unruptured aneurysms as well (Bendszus et al 2007; Butteriss et al 2008). Criteria that favor an endovascular approach can include: (1) older patient age (>50 years); (2) aneurysm size; (3) aneurysm location, i.e. posterior circulation; (4) aneurysm unruptured or, if ruptured, presence of vasospasm; (5) aneurysm poor grade; and (6) operator preference and/or availability (Linfante et al 2009).

Endovascular techniques have reduced length of hospital stay, hospital costs, and neurological complications and adverse outcomes (Veznedaroglu et al 2008). However, an ongoing concern is the long-term durability of endovascular treatment including whether the risk of rebleeding/bleeding can be lowered to that following surgical clipping (Bendszus et al 2007).

The frequency of angiographic aneurysm recurrence following coil occlusion is 17% to 33%, although the actual rebleed rate is low (Bendszus & Solymosi 2006). Ideally the recurrence rate can be decreased, although attempts to lower the recurrence rate must not be accompanied by increased complications. This challenge has been
addressed via innovations in coil technology. New technologies include 3D coils, the liquid embolic agent Onyx, intravascular stents, increased packing density with the use of HydroCoils, radioactive coils, and bioactive modified coils such as Cerecyte (Geyik et al 2010).

The Cerecyte coil consists of a regular bare platinum coil with PGA running through the lumen of the primary platinum wind, which also provides stretch resistance when placing coils into the aneurysm (Bendszus & Solymosi 2006). PGA is a polymer shown to accelerate aneurysm fibrosis and neointima formation in animal studies, thus accelerating occlusion and preventing recanalisation of an aneurismal sac (Butteriss et al 2008). The PGA also maintains the soft properties of bare platinum systems, which minimises the risk of use and allows increased coil-packing density (Veznedaroglu et al 2008). It also results in a coil that has handling characteristics identical to bare platinum so there is no need to change operating practice or undergo a learning curve when changing from bare platinum coils (Butteriss et al 2008).

Figure 1: Micrus® Endovascular CERECYTE® Microcoil.

2010 CLINICAL NEED AND BURDEN OF DISEASE
Intracranial aneurysms are fairly common and sufferers are often asymptomatic until the time of rupture. Subarachnoid haemorrhage associated with aneurismal rupture is potentially lethal, with an associated mortality rate as high as 50% (Vega et al 2002). In patients who survive initial haemorrhage many have permanent disability (Vega et al 2002). A systematic review of studies involving more than 56,000 patients reported that unruptured intracranial aneurysms occur in 3.6% to 6% of the general population (Rinkel et al 1998). Risk factors for the formation of aneurysms include a family history (with 8% to 9% of persons with two or more relatives who have had a subarachnoid haemorrhage or aneurysm likely to experience an intracranial aneurysm themselves), various inherited disorders, age greater than 50 years, female gender, current cigarette smoking and cocaine use (Vega et al 2002).
Endovascular embolisation of intracranial aneurysms with detachable coils is associated with lower morbidity and mortality rates compared with traditional microsurgical clipping; however, recanalisation of the aneurysm sac after coil embolisation occurs in 20% to 40% of patients (Linfante et al. 2009).

2010 Diffusion

Cerecyte coils were approved by the United States (US) Food and Drug Administration (FDA) in February 2004 with three subsequent modifications (FDA 2010). A letter to the manufacturer of Cerecyte coils (Micrus Endovascular Corporation) from the FDA in 2008 states that the Micrus Microcoil Delivery System is intended for endovascular embolisation of intracranial aneurysms, as well as other neurovascular abnormalities such as arteriovenous malformations and arteriovenous fistulae (FDA 2008). The letter also states the coils are intended for arterial and venous embolisations in the peripheral vasculature (FDA 2008). Cerecyte coils were also approved for use by Health Canada in 2001 (Health Canada 2010) and according to the Cerecyte Clinical Trial website have received European approval (Cerecyte Clinical Trial 2006).

Most recently, in February 2009, Cerecyte coils were approved for use in Australia (Australian Register of Therapeutic Goods number 133001) as a Class III device for endovascular embolisation of intracranial aneurysms (Therapeutic Goods Administration 2009).

2010 Comparators

Various coil technologies have been developed for the treatment of intracerebral aneurysms. The reference standard is bare platinum coils but manufacturers have introduced a variety of coil types specifically designed to promote ‘aneurysm healing’ following cerebral aneurysm coiling or to improve the durability and angiographic results of coiling including those integrating PGA or combined PGA/polylactic acid (PGLA), nylon/Dacron/PGLA fibres and hydrogel coating (White & Raymond 2009).

2010 Safety and Effectiveness Issues

Five studies were eligible for inclusion in this summary (Table 1). All were observational with three of the five including a comparison group in the analysis.

Table 1: Published Cerecyte coil studies

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<td>2005-08</td>
<td>Pair analysis of Cerecyte vs bare platinum coils</td>
<td>Retrospective analysis of Cerecyte vs bare platinum coils</td>
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<td>54; 55</td>
<td>Prospective case series vs historical controls with bare platinum coils</td>
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**Study profiles**

Geyik et al (2010) conducted a retrospective matched pair analysis, where outcomes for 74 patients with 80 aneurysms treated with Cerecyte coils were compared with database information for 80 patients with 80 aneurysms treated with bare platinum coils. Matching was based on aneurysm size, location, neck size, initial occlusion grade and clinical presentation (ruptured or unruptured) – risk factors that have the most significant impact on recurrence rate. In both groups, sex distribution was about equal, mean age was 54 years (range, 18-68), most aneurysms were in the anterior communicating artery or the middle cerebral artery, and 55% of aneurysms had ruptured. Under general anaesthesia, patients had embolisation procedures that were technically similar regardless of coil type. Follow-up included angiography interpreted by blinded neurointerventionalists.

In the study by Linfante et al (2009), a database prospectively collected information on patients with ruptured or unruptured aneurysms who were treated with Cerecyte coils (n=63). These data were retrospectively compared with information on patients treated with bare platinum coils over the same time period (n=65). Patients received treatment under general anaesthesia and endovascular access was via a standard transfemoral approach. Aneurysms were coiled as densely as possible with Cerecyte and/or bare platinum coils according to operator judgment and coil availability. Aneurysm occlusion was estimated by two independent reviewers using the three-point Raymond classification system (Table 2). Age range was 25 to 87 years, 68% of patients were female, and 40% had ruptured aneurysms.

Butteriss et al (2008) reported a case series of 51 patients who were treated with Cerecyte coils for ruptured or unruptured intracerebral aneurysms. Most patients were female and most aneurysms had ruptured. Results were classified by the Raymond class (Table 2) and clinical follow-up was performed at six months.

Veznedaroglu et al (2008) reported a case series analysing results for 81 patients (89 aneurysms) who received Cerecyte coil treatment for ruptured (65%) or unruptured...
aneurysms over a 12-month period. Mean patient age was 50 years and 83% of aneurysms were located in the anterior circulation.

Finally, Bendszus et al (2007) conducted a prospective case series enrolling 54 patients (55 aneurysms) to receive Cerecyte coils. For analysis, patients were matched by aneurysm size and location to historical controls who had received bare platinum coils from 2002 to 2004. About half the patients were women and mean age was 50 years (standard deviation, 10 years). The same interventionalists treated all patients, surgical protocols were identical, and study analysts were blinded as to treatment.

2010 Safety

The devices were generally deemed to be safe. Geyik et al (2010) did not report safety data. In Linfante et al (2009) there were two cases of intraoperative rupture in each group (with no long-lasting sequelae) plus one arterial dissection in the bare platinum group. Intraprocedural abciximab was required for clot-on-coil management in 15% of patients with Cerecyte versus 10% with bare platinum coils. Butteriss et al (2008) reported four patients (8%) with adverse events during the procedure including one aneurysm rupture and three minor thromboembolic events (6%) requiring saline flushing with no clinical sequelae. Veznedaroglu et al (2008) reported one thromboembolic event that led to a permanent neurological deficit. The earliest study, Bendszus et al (2007) reported that there was no procedure-related permanent morbidity or mortality.

2010 Efficacy

In the study by Geyik et al (2010), initial treatment results were similar in both groups. However, at 6-month follow-up, results were superior in the Cerecyte group with Raymond Class I results (Table 2) achieved in 86% of patients versus 64% for bare platinum coils ($P=0.002$). Occlusion was also more durable in the Cerecyte group as seen on follow-up angiograms: among those with initial Raymond Class I results, 91% had stable occlusion versus 75% in the bare platinum group. Retreatment rates were 6% versus 13% in the Cerecyte and bare platinum groups, respectively.

<table>
<thead>
<tr>
<th>Class</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Complete obliteration of aneurysm (no residual neck &amp; no contrast within the aneurysm sac)</td>
</tr>
<tr>
<td>II</td>
<td>Residual neck (any remaining portion of the original defect in the arterial wall but without any contrast present within the aneurysm sac)</td>
</tr>
<tr>
<td>III</td>
<td>Residual aneurysm (any contrast present within the aneurysm sac)</td>
</tr>
</tbody>
</table>

Table 2: Raymond Classification Scheme (Source: Wong et al 2007)
Initial outcomes reported by Linfante et al (2009) were also similar between the groups with 49% of patients with Cerecyte achieving Raymond Class I versus 41% with bare platinum coils (P=0.39). Follow-up at 12 months (only 54% and 43% of patients were available, Cerecyte versus bare platinum) showed that recanalisation had occurred in 11% versus 23% of patients (P=0.17).

Butteriss et al (2008) reported complete occlusion in 71% of patients (36/51), near complete in 24% (12/51), and incomplete in 6% (3/51) initially. Six-month follow-up for 34 patients (68% of all patients) showed complete occlusion in 71% (24/34), near complete in 15% (5/34), and incomplete in 15% (5/34). With respect to stability at six months follow-up, 71% (24/34) of patients showed stable occlusion, 9% (3/34) improved, and 21% (7/34) worsened.

In the case series study by Veznedaroglu et al (2008), immediate postoperative angiographic occlusion was deemed complete (Raymond Class I; Table 2) in 45% (40/89) of aneurysms and partial with residual neck remnant (Class II) in 48% (43/89) of aneurysms, and incomplete (Class III) in 3% (3/89). Follow-up angiography at a mean of 11.4 months (median 8 months) identified recurrences requiring retreatment in six aneurysms (7%); five of these six were initially treated in the first month of Cerecyte coil use.

Bendszus et al (2007) also reported similar initial results between patients treated with bare and Cerecyte coils. At six-month follow-up, results were marginally superior for Cerecyte (Table 3).

Table 3: Six-month efficacy outcomes for Bendszus et al (2007)

<table>
<thead>
<tr>
<th>Class</th>
<th>Cerecyte (n[%])</th>
<th>Bare coils (matched historical controls) (n[%])</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>43 (78%)</td>
<td>34 (62%)</td>
<td>0.045</td>
</tr>
<tr>
<td>II</td>
<td>10 (18%)</td>
<td>14 (25%)</td>
<td>NR</td>
</tr>
<tr>
<td>III</td>
<td>2 (4%)</td>
<td>7 (13%)</td>
<td>NR</td>
</tr>
<tr>
<td>Retreatment</td>
<td>1 (2)</td>
<td>6 (11%)</td>
<td>0.056</td>
</tr>
</tbody>
</table>

2010 Cost Impact
No economic studies or cost information were identified in the included literature. A reference to cost occurs in a systemic review of coated-coil technologies, i.e. the authors state that many of these devices are sold at a substantial cost premium ‘despite the lack of grade 1 evidence for equivalent safety and improved efficacy compared with the proved bare platinum coil technology’ (White & Raymond 2009).

2010 Ethical, Cultural or Religious Considerations
No issues were identified in the included literature.
2010 Other Issues

As noted above, available evidence is observational. However, the Cerecyte Coil Trial (CCT) is a prospective randomised controlled trial (RCT) comparing Cerecyte coils with bare platinum coils (Cerecyte Clinical Trial 2006). The trial’s primary objective is to determine if Cerecyte coils improve the proportion of patients with angiographic occlusion of intracranial aneurysms at six months by 50%, from a rate of 75% to 87.5%. Coordinated by Oxford University, the trial has enrolled 500 patients at 24 centres in six countries (Canada, Germany, Japan, Turkey, United Kingdom and US) since its launch in 2005. The last patient was enrolled late in 2009 and outcomes will be tracked up to 24 months. The study sponsor is Micrus Endovascular Corporation (recently purchased by Johnson & Johnson) and both arms of the trial employ devices made by this company. Preliminary results (six-month) were reported at a May 2010 conference, at which point the devices in both arms were performing well (freedom from disability: Cerecyte 95%, bare 99%; investigator-reported angiographic occlusion rate: Cerecyte 85%, bare 87%) which researchers found to be superior to the results reported in The International Subarachnoid Aneurysm Trial (ISAT) (Business Wire 2010).

An RCT sponsored by the University of Virginia (NCT01195128) is comparing treatment of patients with cerebral aneurysms using the Hydrogel coil (Microvention Inc., Tustin, California) in one study arm with treatment with the Cerecyte coil or a bare platinum coil in the other study arm (clinicaltrials.gov 2010). Planned enrolment at 11 US sites is about 1000 patients, follow-up will extend to 18 months and reporting is expected in 2012. Cost of treatment is included as a planned outcome. If the data are sufficient, post-hoc comparisons between results with Cerecyte versus bare platinum coils will be carried out although this is not the primary aim of the RCT (personal communication, Claire McKinley, University of Virginia, 4 October 2010).

With respect to study funding, one lead author (Dr. Martin Bendszus) has been a paid consultant and speaker for Micrus Endovascular, although the study report claims that Micrus ‘had no influence on the data collection, analysis, or writing of the manuscript’ (Bendszus et al 2007). Two study reports reported that the authors had no conflicts of interest (Butteriss et al 2008; Geyik et al 2010) and the remaining two reports included no financial disclosure information (Veznedaroglu et al 2008, Linfante et al 2009).

2010 Summary of Findings

From the limited literature available (five small observational studies), Cerecyte coils appear to be safe with occlusion/recanalisation rates that are as good or better than bare platinum coils (the traditional standard) for treatment of ruptured and
unruptured intracerebral aneurysms. The technology was approved several years ago in a number of countries and appears to be in at least limited use. Cost data were not available in order to determine the financial impact of switching to Cerecyte (or its competitors) from bare platinum coils. At least one multicentre RCT will report within the next year or two, thus adding to the evidence base for this technology.

**2010 HealthPACT Assessment**

The Cerecyte coil is seeing limited use in several countries based on small observational studies that have shown it to be safe and at least as effective as bare platinum coils for the treatment of ruptured or unruptured intracranial aneurysms. A large RCT of Cerecyte coils is currently underway at 24 centres in six countries. As results from the observational studies do not unequivocally establish its benefits over bare platinum coils, decision makers may wish to defer an opinion until the RCT results are available. Based on this it is recommended that the technology be monitored for 12 months.

**2010 Number of Studies Included**

Total number of studies 5
Level III-3 evidence 3
Level IV evidence 2

**2010 References**


2010 SOURCES OF FURTHER INFORMATION


**2010 Search Criteria to be Used**

Cerecyte coil  
Bioactive coil  
Platinum coil AND polyglycolic acid  
Intracranial aneurysm