



REPORT NUMBER 16

MUHC -Technology Assessment Unit

The Use of Matrix Coils in the Treatment of Cerebro-vascular Aneurysms

A Technology Assessment

by

The Technology Assessment Unit (TAU)

of the McGill University Health Centre (MUHC)

June 23 2004

**This analysis was prepared for the Technology Assessment Unit (TAU)
of the McGill University Health Centre (MUHC)**
by

**Vania Costa, MUHC TAU
James Brophy, Department of Medicine of the MUHC**

and approved and adopted by the committee of the TAU:

**Juliana Arnoldo, Jeffrey Barkun, Andre Bonnici, James Brophy, James Hanley,
John Johnston, Marilyn Kaplow, Maurice McGregor, Gary Pekeles,
Judith Ritchie, Fred Salevsky, Gary Stoopler.**

And consultants:

**Dr. Donatella Tampieri, Director, Diagnostic and Interventional Neuroradiology,
MNI/H**

Dr. John Penrod, Centre for the Analysis of Cost Effective Care

Report available at www.mcgill.ca/tau/

Invitation. This document was designed to assist decision-making in the McGill University Health Centre. Others are welcome to make use of it with acknowledgment. More important, to assist us in making our own evaluation, it would be *deeply appreciated* if potential users could inform us whether it has influenced policy decisions in any way, and even if it has not, whether it has been helpful in informing decision makers.

e-mail: james.brophy@mcgill.ca
maurice.mcgregor@mcgill.ca

Executive Summary

Cerebro-vascular aneurysms are present in 0.5% to 6% of the adult population. If a cerebro-vascular aneurysm ruptures it causes subarachnoid hemorrhage, which is associated with a 40%-60% case-fatality rate. Treatment alternatives for ruptured and unruptured aneurysms include surgical clipping and endovascular coiling, the latter may also be combined with balloon remodelling or stents, for aneurysms with wider necks.

Treated aneurysms may recanalize, usually within 18 months of the treatment. The rate of recanalization varies widely according to the degree of aneurysm occlusion after treatment, aneurysm location, size, and shape. Recent studies with endovascular coils showed a mean recanalization rate of approximately 23%, a re-treatment rate in the first two years of 15% and re-rupture rates of approximately 1.1% in patients treated with bare platinum coils such as the Guglielmi Detachable Coils (GDC). The Matrix coil is a newer technology that has the same indications as the GDCs. It consists of a platinum coil coated with a bioabsorbable polymer that is expected to improve the rate of aneurysm exclusion from the circulation, as a result of greater cellular reaction, which in turn, is expected to result in less recanalization and consequently less repeat procedures. However, precise reliable estimates of the comparative efficacy of these two coils in preventing future re-interventions are simply not presently available from the peer reviewed medical literature.

The additional cost per aneurysm treated with Matrix coils compared to GDCs is approximately CDN\$ 1,252, assuming that the procedures, including complication rates, are otherwise constant. If the 40 patients presently treated annually with GDCs in the Montreal Neurological Institute/Hospital (MNI/H) were to be treated with Matrix coils, the estimated extra cost to the MUHC would be CDN\$ 50,080. This amount may realistically vary between \$23,360 and \$65,808 due to the uncertainty surrounding any efficacy benefit.

Recommendation

In conclusion, the TAU considers that although unpublished reports are promising, up to this time, additional health benefits with the Matrix coils have not been demonstrated. The TAU has previously considered such issues and has come to the conclusion that leadership in an academic hospital is not best demonstrated by adopting the use of “leading edge” technologies before the benefits have been clearly established. Leadership is better demonstrated by refusing to adopt such technologies as the accepted standard of care and by encouraging research to clarify the issue.

Consequently, despite the relatively low budget impact, the TAU does not recommend the purchase of the Matrix coils for routine patient care at this time. In addition, the TAU strongly encourages further research with this technology and notes that due to the low budget impact of the Matrix coil and its presumed safety, the burden of proof required to demonstrate its clinical superiority need not be extensive.

Finally, as with all health technology assessments (HTAs), this position will need to be re-evaluated as more evidence becomes available.

Table of Contents

| | |
|---|----|
| 1. Introduction | 7 |
| 2. Background | 7 |
| 3. Treatment modalities | 8 |
| 4. Matrix Coils | 8 |
| 5. Use of endovascular coils | 10 |
| 6. Literature review | 10 |
| 6.1 Method | 10 |
| 6.2 Results with GDCs | 11 |
| 6.3 Results with Matrix Coils | 15 |
| 7. Analysis of Cost | 17 |
| 8. Discussion | 18 |
| References..... | 20 |
| | |
| Appendix 1 List of databases used in the literature search | 23 |
| Appendix 2 Hunt and Hess and Glasgow Outcome Scale | 24 |
| Appendix 3 Characteristics of the studies included in the report..... | 25 |
| Appendix 4 Clinical results with GDC | 29 |
| Appendix 5 Total procedural costs with Matrix and GDC coils..... | 32 |
| | |
| Appendix 6 Total cost of treatment with Matrix coils and GDCs within 1-2 years after the initial procedure | 34 |

The use of Matrix Coils in the treatment of Cerebro-vascular Aneurysms

1. Introduction

In March 2004, Mr. Victor Simon requested that the Technology Assessment Unit (TAU) evaluate the use of Matrix Coils as a treatment for brain aneurysms. At the meeting of April 6th 2004, the Committee of the TAU approved the preparation of this report.

The objective of this report is to compare the use of the Matrix Detachable Coil with the Guglielmi Detachable Coil (GDC), which up to now has been the standard treatment used in the MUHC, in regard to its long-term efficacy and costs.

2. Background

An aneurysm is an outward bulging of an artery due to weakening of the artery's wall, and brain aneurysms are estimated to be present in anywhere from 0.5% to 6% of the adult population¹. While most aneurysms are asymptomatic and may be incidentally found with imaging studies, some are discovered because they produce symptoms such as headaches or cranial neuropathies, which are a consequence of nerve or brain tissue compression ^{1,2}. An intracranial aneurysm may also rupture before it is discovered, causing subarachnoid hemorrhage (SAH), a cause of stroke that presents with a 40% to 60% case-fatality rate ³, and a 10% to 20% chance of the patient being dependent after the event¹. A Canadian study showed an estimated age-standardized annual rate of hospitalization for subarachnoid hemorrhage in 1991-1992 of 0.01% for women and 0.008% for men in the general population ⁴, although other causes were included, principally, arterio-venous malformations.

The risk of bleeding from an unruptured aneurysm is estimated to be between 1%-2% per year⁵, however, once subarachnoid hemorrhage has occurred, the rate of re-bleeding is approximately 4% in the first 24 hours, and 19% within the first two weeks ³. Vasospasm may also occur 5-20 days after the rupture of the aneurysm, at a rate of 20%-50% ³. A study of the natural history of unruptured aneurysms showed that in small aneurysms, < 10mm, the risk of rupture seems to be increased with a previous history of subarachnoid hemorrhage from a different aneurysm when compared to patients without such a history, (0.5% per year versus 0.05% per year

respectively over a 7.5-year period). Larger unruptured aneurysms had a yearly rupture rate of 1% regardless of a previous history of hemorrhage⁶. The location of the aneurysm may also predict the risk of rupture, as aneurysms located in the tip of the basilar artery are more likely to rupture compared to other locations both in patients with or without a prior history of hemorrhage in a different aneurysm⁶.

3. Treatment modalities

Until recently, aneurysms were generally treated by surgical clipping of their neck, in an attempt to exclude them from the circulation thereby decreasing the risk of bleeding¹. In 1991, Guido Guglielmi described a technique of excluding aneurysms from the circulation with an endovascular approach, using electrolytically detachable platinum coils, called Guglielmi Detachable Coils (GDC)¹. The GDC is a soft platinum helical coil introduced into the aneurysm through the femoral artery using a microcatheter, and detached from a stainless-steel microguidewire by an electrical discharge^{7 1}. Initially, endovascular treatment of aneurysms was reserved for patients deemed unsuitable for surgery, or in poor medical condition⁸. Although the use of endovascular coiling has been increasing, and it is now often the procedure of choice^{1 9} the aneurysm may still undergo recanalization, characterized by a re-opening of its neck .

Newer coils coated with bioactive materials such as fibroblast growth factor, collagen or polyglycolic acid/lactide (Matrix coil)¹⁰, or radioactive coils¹¹ have been developed. Endovascular coiling may be combined with other percutaneous techniques including balloon remodeling or stents in aneurysms with a wider neck¹⁰, but this evaluation is limited to the Matrix coil.

4. Matrix Coils

The Matrix Detachable coil was approved by the FDA in 2002¹², and it has also received approval from Health Canada¹³. They consist of platinum coils covered with an absorbable copolymer, the polyglycolic-polylactic acid (PGLA), which is absorbed by the body within 90 days¹⁴. Matrix coils have the same indications as GDCs, namely, treatment of intracranial aneurysms in patients that are at very high risk for treatment with surgical techniques, or that are inoperable because of the aneurysms' morphology, location, or the patients' medical condition^{15 16}.

More than one coil is used to exclude the aneurysm from the circulation¹. Figure 1 illustrates the insertion of the coils into the aneurysm.



Figure. Schematic diagram of a microcatheter and GDC within an aneurysm.

Figure 1 – Insertion of an endovascular coil into the aneurysm. Image from a publication by R.A. Willinsky⁷.

Matrix coils are used endovascularly in the same fashion as GDCs, and are expected to provide advantages over the GDCs as a result of enhanced cellular reactions provoked by its bioabsorbable polymer coating¹⁷. Treatment of an aneurysm with a bare platinum GDC coil elicits a sequential biocellular process that produces organized connective tissue, which is analogous to the wound healing mechanism of a vessel wall¹⁷. Incorporating bioabsorbable polymers as a coating to the bare platinum coil may induce more intense cellular reactions, thereby accelerating the clot organization in the aneurysm and leading to additional scarring and retraction¹⁷. Bioabsorbable polymeric materials (BPMs) are not expected to promote an intense foreign body reaction as they are gradually absorbed and do not leave residues in the implantation site¹⁷. In theory the more local connective tissue formation occurs, and the more organized the clot, the more resistant will the aneurysm be to the pressure exerted by the blood circulation, lowering the chance of recanalization¹⁷. The maturation of collagen fibers causes the aneurysm to retract, which may reduce its size, therefore decreasing the aneurysm compression of cranial nerves or brain parenchyma¹⁷.

A lower coil packing density has been associated with a greater contact between the coil and the circulation at the neck of the aneurysm, which may cause coil compaction¹⁸, increasing the risk of recanalization¹⁹. Nonetheless, despite observing a lower packing density with Matrix coils

compared to GDCs, Murayama et al. believe that this did not prevent the formation of scar tissue at 3 months after the procedure¹⁷.

5. Use of Endovascular Coils

According to the Committee on Cerebrovascular Imaging of the American Heart Association Council on Cardiovascular Radiology, the decision to treat the aneurysm endovascularly or surgically depends on factors such as aneurysm location and size, neck size, comorbidities, contraindications to radiologic contrasts¹, and implicitly, local expertise. Aneurysms located in the posterior cerebral circulation, and in the cavernous segment of the internal carotid artery are difficult to be treated with surgery, and are therefore more suitable for treatment with coils. Aneurysms in the middle cerebral artery, on the other hand, are more difficult to treat endovascularly than with surgery¹. Larger aneurysms are associated with more complications regardless of the treatment chosen. A meta-analysis of surgical clipping of unruptured aneurysms showed a higher mortality and morbidity for giant aneurysms ($>25\text{mm}$)²⁰, and larger aneurysms are associated with less complete occlusion and consequently a more frequent need for further coiling procedures in patients treated with GDC¹. Paradoxically, aneurysms with a very small diameter ($<3\text{ mm}$) have been associated with a higher risk of rupture when treated with GDCs¹. Aneurysms with a larger neck size have also been associated with a less complete aneurysm occlusion¹. With regards to comorbidities, surgical treatment may be more appropriate if a large parenchymal hematoma with mass effect is present, as it may be evacuated by surgery¹. On the other hand, patients with a higher Hunt-Hess score (see appendix 2 for details), or with evidence of significant brain-swelling without a mass lesion, may be more favorably treated with coils than surgery, although a higher risk of complications is expected compared with patients without these conditions¹.

6. Literature review

6.1 Method

The literature search was performed by using the Medline, Pubmed, Cochrane, and health technology agencies databases. A list of these health technology agencies databases is provided in Appendix 1. The search terms included: matrix, coils, absorbable polymers, Guglielmi, GDC, aneurysm, brain, neurological, neuro-angiography, and endovascular, used in different

combinations. There were no restriction for dates of publication or languages, however, only articles published in English, French, German, Italian, Spanish, and Portuguese would be reviewed.

6.2 Results with GDC

Literature review

The literature search conducted using the keywords mentioned above, with the exception of the terms matrix and absorbable polymers, yielded more than 300 articles published with GDCs after 1996. In order to estimate the efficacy and complications of these coils, we have summarized the results of articles with GDCs published in the last 3 years, i.e., since January 2001, and that had at least 100 patients. We have decided to limit our review to more recent and larger studies, as they were more likely to reflect current installation techniques in high performance centers, and were therefore, most comparable to the MUHC. Earlier studies also have a higher possibility of learning curve inconsistencies¹. Nonetheless, two systematic reviews including earlier studies are also included in our report. Due to the variations in pathological and clinical presentations of the patients included in the studies, and also as larger studies are generally a closer estimate of the population value, we have decided to use articles with a larger number of patients, i.e., more than one hundred. It should be born in mind that this was not an attempt to undertake a formal systematic review of GDC coils but only to provide a stable reference point for this technology.

Two systematic reviews of the literature published after 1996 were found^{21 22}. Their results and those from 2 randomized trials comparing GDC with surgical clipping are included in this report^{21 22 23-25}.

Results with GDCs

A summary of the results of these studies is presented below, and more details are shown in Appendix 4. Results are given for ruptured and unruptured aneurysms analysed as one group, unless otherwise specified. Several studies evaluating GDCs have been published, however, they mostly consist of case series and observational studies, conducted prospectively or retrospectively with varying indications as well as pathologic and clinical presentation^{8,26-30}.

In the studies selected, most of the patients were female, 71% on average, and the weighted average for age among the studies was around 52 years^{8,26-30}. The aneurysms were present in the posterior or anterior circulation of the brain, and were of varying sizes^{8,26-30}.

Technical failures occurred, on average, in 4% of the patients with ruptured and unruptured aneurysms^{8,26-30}. Ng et al. reported an overall failure rate of 10%, however, this rate was higher in wider neck aneurysms, 30%, compared to narrow neck aneurysms, 8% ($p < 0.0001$)²⁷. Complete occlusion of the aneurysm immediately after the GDC was deployed occurred in 64% of the aneurysms on average, with a large variation in the results ranging from 46% to 90% of the aneurysms^{8 27 26 30 29}. Sluzewski et al. and Henkes et al. reported aneurysm occlusion rates greater than 90% in 92% and 87% of the patients respectively^{29 30}. According to some authors, the rate of complete aneurysm occlusion was associated with the aneurysm and neck size^{26 27}, as well as the hospital where the patient was treated³¹. There was no procedure-related mortality in patients with unruptured aneurysms in two studies^{8 27}, whereas the rate reported in patients with ruptured aneurysms was around 3%^{27 29}. A meta-analysis showed a 100% occlusion of the aneurysms in 60.8% of the patients after endovascular treatment with coils, and a 2.1% rate of procedure-related deaths in patients included in studies deemed as high-quality by the authors of the meta-analysis²¹. A systematic review of the literature reported a 1.4% procedural mortality, and a 5.1% procedural morbidity after treatment of aneurysms located in the posterior circulation with endovascular coils²².

In four recent studies, the average rate of recanalization of treated aneurysms was 23.2%, with a follow-up of approximately 1-2 years^{8 26 27 28}. There was a large variation in the rates of recanalizations reported in the studies selected, as it may vary with the size of both the aneurysm and the neck²⁶. A literature review from Germany also shows that the rate of aneurysm recanalization is dependent on the degree of occlusion, i.e., it may range from 0 to 14% in completely occluded aneurysms, 7-50% in aneurysms with small remnants, and greater than 50% in aneurysms with large remnants after initial treatment³².

On average, 15% of the patients who underwent GDC coiling needed a second procedure on the same aneurysm within approximately 2 years of the first procedure^{27 28 29}. The types of

secondary procedures were coiling, used in approximately 41% of the re-treatments, surgical clipping, used in approximately 35% of the re-treatments, and endovascular balloon occlusion of the parent artery, used in 24% of the cases^{27 28 29}.

Re-rupture of the aneurysm occurred, on average, in 1.1% of the patients after 1-2 years of follow-up^{26 28 29}, occurring mostly in aneurysms that were ruptured prior to the initial treatment^{8 26 27 28 29}. Ng et al. reported a higher rate of intraprocedural ruptures in patients who had ruptured aneurysms at presentation, 16%, compared to patients with unruptured aneurysms, 1.3% ($p<0.001$)²⁷. Apparently, the rate of re-rupture depends at least partially on the type of follow-up, as with regular imaging the risk is lower.

Roy et al. reported a 4.3% treatment-related permanent morbidity rate in 116 patients with unruptured aneurysms, evaluated by the Modified Rankin Scale (details in Appendix 2)⁸. Ng et al. reported a 5.1% and a 8.6% procedure-related morbidity rate in patients with unruptured and ruptured aneurysms respectively, after treatment with endovascular coils²⁷. Procedure-related morbidity was defined as neurologic deficit that lasted more than 7 days²⁷. Sluzewski et al. reported that after a mean follow-up of 37 months after the treatment with GDC, 94% of the patients with unruptured aneurysms remained independent, defined as score 4 or 5 measured by the Glasgow Outcome Scale (GOS) (details in Appendix 2)²⁹. Ng et al. observed that two years after the GDC treatment, 84% of the patients with ruptured aneurysms, and 70% of the patients with unruptured aneurysms had a good outcome, defined as GOS scores 4 or 5²⁷.

Procedural complications with GDC, other than mortality, occurred on average in 14.9% of the patients with ruptured and unruptured aneurysms^{8 26 27 30}. According to Henkes et al., the most common complications that occurred during the coiling procedure were embolic events, 6%, aneurysm perforation and thrombosis, 3.1% each, coil malposition, 2.5%, and other less common complications included vasospasm, vessel dissection, increased mass effect, occlusion of the parent artery, reaction to contrast medium³⁰. In this study, only 0.2% of the complications that occurred during the procedure were not dependent on the coiling procedure³⁰.

Henkes et al. observed a trend for patients with ruptured aneurysm to experience better outcomes after treatment with endovascular coils if the treatment was performed earlier, i.e., less than 3 days after the subarachnoidal hemorrhage, compared to 3-10, 11-30, or more than 30 days after its onset, however the differences in results were not statistically significant³⁰.

Part of the variation in the results observed across the studies may be explained by different anatomical locations of the aneurysm, different aneurysms and neck sizes, and different proportions of patients with ruptured/unruptured aneurysms across the studies, as well as different lengths of follow-up between studies, and physicians' with different grades of experience in the procedure.

One randomized study comparing coiling and surgical clipping for the treatment of aneurysms was found in the literature. The ISAT trial²³ included 2143 patients with ruptured brain aneurysms and showed that the use of GDC resulted in an absolute reduction of 6.9% (95% CI, 2.5% , 11.3%) in the risk of death or dependence one year post-treatment. On the other hand, case fatality rates were similar between GDC and surgical clipping, 8.1% (95% CI, 6.3% , 10.2%), and 10.1% (95% CI, 8.1% , 12.4%) respectively²³. A larger proportion of patients in the GDC group needed additional endovascular or surgical procedures on the same aneurysm compared to patients in the surgical clipping group, 121 patients (12.6%) in the GDC group, and 33 (3.5%) of the patients in the surgical clipping group²³. In the GDC group, 63% of the additional procedures were surgical clipping, compared to 12% in surgical clipping group²³. According to the authors, these results are generalizable to patients that were similar to the ones included in the trial, i.e., SAH patients who were suitable for either treatment modality, in good clinical grade, and with small anterior circulation aneurysms²³. Another randomized study comparing GDC (n=52) and surgical clipping (n=57) in 109 patients with ruptured aneurysms did not show any difference in neurologic disability (GOS), survival, or re-bleeding between the two groups 12 months after the initial treatment^{24,25}. Angiographic evaluation performed shortly after the treatment showed better results with surgery than with endovascular treatment, but there was a trend towards a higher procedure-related mortality in the surgical clipping group, 4% and 2% respectively²⁴, although this difference was not statistically significant. A meta-analysis including studies that evaluated surgical clipping as a treatment for unruptured brain aneurysm published between 1970 and 1996 showed an overall

postoperative mortality rate of 2.6% (95% confidence interval (CI) 2% , 3.3%), and a permanent morbidity rate of 10.9% (95% CI, 9.6% , 12.2%)²⁰. According to the authors, the mortality rate was lower in more recently published studies, and both morbidity and mortality rates were associated with the size and location of the aneurysm²⁰.

6.3 Results with Matrix Coils

Literature review

Animal studies

Two animal studies with Matrix coils were found in the literature^{12,17}. In the first study, which compared GDCs with Matrix coils in 12 Yorkshire swine, initial occlusion and separation of the aneurysm from the parent artery was improved with the Matrix coil¹⁷. In the second animal study using 26 Yorkshire swine, a greater neointimal thickness at the aneurysm neck level, thrombus organization, and a smaller area was observed with the Matrix coil compared to GDC¹². Surprisingly, coil packing densities have been lower with the Matrix coils, which may cause coil compaction¹⁸, and theoretically increases the risk of recanalization¹⁹.

Clinical results

With the exception of abstracts and results presented in scientific meetings, no clinical studies with Matrix coils were found in the peer-reviewed literature. No technology assessment report on the Matrix coils was found. We have confirmed these findings with the product manufacturer (Boston Scientific). Additionally, according to the letter of approval of the Food And Drug Administration, the Matrix Coil was approved based on expected equivalence to other marketed devices¹⁶, rather than specific clinical information provided with the device. Therefore, the information on Matrix coils in this report comes from abstracts or oral presentations at scientific meetings as well as local expert opinion (Dr. Donatella Tampieri, Director of Diagnostic and Interventional Neuroradiology – MNI/H).

In June 2003, it was estimated that Matrix coils have been used in 400 patients throughout the world³³. The Montreal Neurological Institute (MNI/H) treats more than 100 patients with aneurysms a year, and approximately 40 of these receive endovascular treatment. Dr. Tampieri (Director of Diagnostic and Interventional Neuroradiology – MNI/H) has summarized her personal

experience with Matrix coils, and information reported during scientific meetings as follows: providing an increased amount of mature, intra-aneurysmal connective tissue, an increase in neck tissue thickness, and a reduction in the size of the aneurysm, Matrix coils probably lead to a lower rate of recanalizations and repeat procedures.

However, no formal comparisons of the GDC and Matrix coil have been reported in the peer-reviewed literature.

The following paragraphs summarize the information presented orally in scientific meetings as reported by Dr. Tampieri (Director of Diagnostic and Interventional Neuroradiology – MNI/H). Additional information from published studies including abstracts is not fully available.

Observational studies report lower rates of recanalization and re-treatment with the Matrix coils compared to historical GDCs treated controls, i.e., 19% recanalization rate with aneurysms with a neck remnant treated with Matrix coils compared with 50% with GDCs after 18 months of follow-up (F. Vinuela, presented at the Japanese Society of Intravascular Neurology Meeting – Nov. 2003). Chaloupka et al. reported a 15.3% rate of re-treatment with Matrix coils compared to 29.6% with GDCs (J. Chaloupka et al., presented at the American Society of Interventional and Therapeutic Neuroradiology Meeting (ASITN) – Feb. 2004). Alexander et al. reported a 3.9% rate of re-treatment in 51 out of 101 patients treated with Matrix coils who had a 6-month follow-up, no information about the remaining 50 patients was given (M. Alexander, presented at the ASITN Meeting – Feb. 2004). Partial results from the ACTIVE study, a registry trial including patients treated with Matrix Coils, showed a rate of recanalization of 11% in 88 patients at both 3 and 12 months follow-up (Presented at the ASITN Meeting – Feb. 2004). Both Chaloupka et al. and Murayama et al. reported a lower coil packing density in the aneurysms treated with Matrix coils^{34 35}, which has been reported to increase the contact between the circulation and the coil¹⁸, and theoretically lead to a higher risk of recanalization¹⁹. However, to date, this does not appear to have caused any clinical difficulties³⁵. Another study reported that only 4 out of 14 aneurysms (29%) treated with GDC showed complete or near complete occlusion after a 1 year follow-up, whereas in 16 patients who received a combination of the GDC and Matrix systems, none showed any evidence of recanalization after 6 months³⁶. However, the population and angiographic characteristics included in this study³⁶ were

not well described. Technical complications have been only sporadically reported and no firm conclusions may be drawn^{34 35}.

The MNI experience with both coils has not yet been systematically analyzed. Dr. Tampieri (Director of Diagnostic and Interventional Neuroradiology – MNI/H) estimates that in her practice, approximately 20-25% of GDC patients present with aneurysm recanalization, and 16-20% need to be re-treated within 18 months of the initial treatment. With Matrix coils, she estimates that 15% of the patients need to be re-treated during the same time frame. In absolute terms, this might mean 1-5 fewer repeat procedures per 100 patients treated.

7. Analysis of cost

Matrix and GDC coils come in different sizes and shapes, with an average cost of CDN\$ 1,021 and CDN\$ 800 for the Matrix and GDC coils respectively.

The number of Matrix/GDC coils used to treat each aneurysm depends on the aneurysm size and averages 6 per aneurysm, regardless of the aneurysm being ruptured or unruptured at presentation (Mrs. Patricia Smith, Neuroradiology Department, MNI/H).

The total cost of the endovascular coiling procedure with Matrix coils is CDN\$9,810, and CDN\$ 8,558 with GDCs. Appendix 5 contains detailed information on total procedural costs with Matrix and GDC coils. We have also assumed that complication rates do not differ between the two alternatives, although precise information on this issue is lacking.

On the basis of these assumptions, the estimated additional cost to the MUHC of treating one aneurysm with Matrix coils instead of GDCs would be CDN\$1,252. If all 40 GDC endovascular coiling procedures done at the MNI/H each year were replaced by Matrix coils, the total difference in cost per year to the MUHC would be CDN\$50,080, without taking into account further re-hospitalization and complications.

Due to the lack of clinical and comparative data for Matrix coils published in the peer-reviewed literature, we have assumed that the procedural complication rates, procedural duration

and length of stay in hospital would be similar with the two treatments. For the same reason, we could not formally calculate the long-term cost impact of the use of Matrix coils compared to GDCs. However, as an attempt to roughly estimate the additional long-term impact of replacing GDCs by Matrix coils for the treatment of brain aneurysms, we have used the rates of re-treatment obtained from expert opinion and non-comparative published studies. Appendix 6 has detailed information on how this calculation was done. The additional long-term cost of replacing 40 GDC coils by Matrix coils varied from CDN\$23,360 to CDN\$65,808, largely depending on the assumptions regarding future savings or reduced re-interventions due to possible improved efficacy.

8. Discussion

Based on results from animal studies^{12 17}, and clinical information presented in scientific meetings, a decrease in the rate of aneurysm recurrence with Matrix coils compared to GDC may be expected. However, due to the absence of any published clinical studies of this technology, it is not possible at this point, to be sure that these benefits will be observed in clinical practice. One author investigated the use of a combination of GDC and Matrix coils to treat the same aneurysm, with apparently satisfactory preliminary results³⁶. If these results are confirmed, the strategy may combine the advantages of both systems with a lower cost compared to Matrix coils alone, but again this remains to be proven.

Thus, although at present, this appears to be a promising and innovative technology, it would be premature to adopt the use of Matrix coils as a first choice treatment in the MUHC in the absence of published peer-reviewed reports. Should its clinical efficacy be confirmed, it could become the standard treatment at a relatively low cost. If all 40 patients presently treated each year with GDCs in the MUHC were treated with Matrix coils, the estimated extra purchase cost would be CDN\$ 50,080 with potential offsetting savings from reduced repeat procedures.

Given that efficacy has not been established, formal cost-effectiveness analyses have not been performed. There was a wide variation in the estimated additional long-term cost of replacing GDCs for Matrix coils for the treatment of brain aneurysms, as calculated by using re-treatment

rates derived from different sources. This variation further demonstrates the imprecision/instability of the evidence currently available for the superiority of one treatment over the other. Clearly, if improved efficacy with reduced recanalization is demonstrated, the reduction in secondary procedures will help offset the additional acquisition cost of the Matrix coil. In addition to comparative trials, it is also necessary to investigate if the combination of Matrix and GDC coils will provide equal or improved efficacy at lower costs.

Recommendation

In conclusion, the TAU considers that although unpublished reports are promising, up to this time, additional health benefits with the Matrix coils have not been demonstrated. The TAU has previously considered such issues and has come to the conclusion that leadership in an academic hospital is not best demonstrated by adopting the use of “leading edge” technologies before the benefits have been clearly established. Leadership is better demonstrated by refusing to adopt such technologies as the accepted standard of care and by encouraging research to clarify the issue.

Consequently, despite the relatively low budget impact, the TAU does not recommend the purchase of the Matrix coils for routine patient care at this time. In addition, the TAU strongly encourages further research with this technology and notes that due to the low budget impact of the Matrix coil and its presumed safety, the burden of proof required to demonstrate its clinical superiority need not be extensive.

Finally, as with all health technology assessments (HTAs), this position will need to be re-evaluated as more evidence becomes available.

References

1. Johnston SC, Higashida RT, Barrow DL, Caplan LR, Dion JE, Hademenos G, et al. Recommendations for the endovascular treatment of intracranial aneurysms: a statement for healthcare professionals from the Committee on Cerebrovascular Imaging of the American Heart Association Council on Cardiovascular Radiology. *Stroke* 2002; 33:2536-44.
2. Johnston SC, Wilson CB, Halbach VV, Higashida RT, Dowd CF, McDermott MW, et al. Endovascular and surgical treatment of unruptured cerebral aneurysms: comparison of risks. *Ann Neurol* 2000; 48:11-9.
3. Pruvost JP, Leclerc X, Ares GS, Lejeune JP, Leys D. Endovascular treatment of ruptured intracranial aneurysms. *J Neurol* 1999; 246:244-9.
4. Ostbye T, Levy AR, Mayo NE. Hospitalization and case-fatality rates for subarachnoid hemorrhage in Canada from 1982 through 1991. The Canadian Collaborative Study Group of Stroke Hospitalizations. *Stroke* 1997; 28:793-8.
5. Murayama Y, Vinuela F, Duckwiler GR, Gobin YP, Guglielmi G. Embolization of incidental cerebral aneurysms by using the Guglielmi detachable coil system. *J Neurosurg* 1999; 90:207-14.
6. Anonymous. Unruptured intracranial aneurysms--risk of rupture and risks of surgical intervention. International Study of Unruptured Intracranial Aneurysms Investigators. *N Engl J Med* 1998; 339:1725-33.
7. Willinsky RA. Detachable coils to treat intracranial aneurysms. *CMAJ* 1999; 161:1136
8. Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. *Stroke* 2001; 32:1998-2004.
9. Murayama Y, Vinuela F, Tateshima S, Gonzalez NR, Song JK, Mahdavieh H, et al. Cellular responses of bioabsorbable polymeric material and Guglielmi detachable coil in experimental aneurysms. *Stroke* 2002; 33:1120-8.
10. Pelz D, Lylyk P, Negoro M. Interventional neuroradiology. *Stroke* 2004; 35:381-2.
11. Raymond J, Roy D, Leblanc P, Roorda S, Janicki C, Normandieu L, et al. Endovascular treatment of intracranial aneurysms with radioactive coils: initial clinical experience. *Stroke* 2003; 34:2801-6.
12. Murayama Y, Tateshima S, Gonzalez NR, Vinuela F. Matrix and bioabsorbable polymeric coils accelerate healing of intracranial aneurysms: long-term experimental study. *Stroke* 2003; 34:2031-7.
13. Health Canada - Medical Devices Active License Listing. <http://cpe002078d58dac-cm00803785ace5.cpe.net.cable.rogers.com/mdall/english/Device.cfm?ID=110134&DeviceName=MATRIX%20D%202D%20SHAPE%20COILS>. Last accessed on May 12th 2004
14. Boston Scientific - Matrix Coils Device Overview. http://www.bostonscientific.com/med_specialty/deviceDetail.jhtml?task=tskBasicDevice.jhtml§ionId=4&relId=5,230,231,232&deviceId=14025&clickType=SpecMainPromo. Last accessed on May 12th 2004
15. Boston Scientific - Matrix Coils - Instructions for use. http://www.bostonscientific.com/common_templates/singleDetailList.jhtml?task=tskDeviceStat

ement.jhtml§ionId=4&relId=5,230,231,242,243&deviceId=14025. Last accessed on May 12th 2004

16. Food and Drug Administration - Device Evaluation Information.
<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=5814>. Last accessed on May 12th 2004
17. Murayama Y, Vinuela F, Tateshima S, Song JK, Gonzalez NR, Wallace MP. Bioabsorbable polymeric material coils for embolization of intracranial aneurysms: a preliminary experimental study. *J Neurosurg* 2001; 94:454-63.
18. Kawanabe Y, Sadato A, Taki W, Hashimoto N. Endovascular occlusion of intracranial aneurysms with Guglielmi detachable coils: correlation between coil packing density and coil compaction. *Acta Neurochir (Wien)* 2001; 143:451-5.
19. Byrne JV, Sohn MJ, Molyneux AJ, Chir B. Five-year experience in using coil embolization for ruptured intracranial aneurysms: outcomes and incidence of late rebleeding. *J Neurosurg* 1999; 90:656-63.
20. Raaymakers TW, Rinkel GJ, Limburg M, Algra A. Mortality and morbidity of surgery for unruptured intracranial aneurysms: a meta-analysis. *Stroke* 1998; 29:1531-8.
21. Brilstra EH, Rinkel GJ, van der Graaf Y, van Rooij WJ, Algra A. Treatment of intracranial aneurysms by embolization with coils: a systematic review. *Stroke* 1999; 30:470-6.
22. Lozier AP, Connolly ES Jr, Lavine SD, Solomon RA. Guglielmi detachable coil embolization of posterior circulation aneurysms: a systematic review of the literature. *Stroke* 2002; 33:2509-18.
23. Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised trial. *Lancet* 2002; 360:1267-74.
24. Koivisto T, Vanninen R, Hurskainen H, Saari T, Hernesniemi J, Vapalahti M. Outcomes of early endovascular versus surgical treatment of ruptured cerebral aneurysms. A prospective randomized study. *Stroke* 2000; 31:2369-77.
25. Vanninen R, Koivisto T, Saari T, Hernesniemi J, Vapalahti M. Ruptured intracranial aneurysms: acute endovascular treatment with electrolytically detachable coils--a prospective randomized study. *Radiology* 1999; 211:325-36.
26. Murayama Y, Nien YL, Duckwiler G, Gobin YP, Jahan R, Frazee J, et al. Guglielmi detachable coil embolization of cerebral aneurysms: 11 years' experience. *J Neurosurg* 2003; 98:959-66.
27. Ng P, Khangure MS, Phatouros CC, Bynevelt M, ApSimon H, McAuliffe W. Endovascular treatment of intracranial aneurysms with Guglielmi detachable coils: analysis of midterm angiographic and clinical outcomes. *Stroke* 2002; 33:210-7.
28. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, et al. Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. *Stroke* 2003; 34:1398-403.
29. Sluzewski M, van Rooij WJ, Rinkel GJ, Wijnalda D. Endovascular treatment of ruptured intracranial aneurysms with detachable coils: long-term clinical and serial angiographic results. *Radiology* 2003; 227:720-4.

30. Henkes H, Fischer S, Weber W, Miloslavski E, Felber S, Brew S, et al. Endovascular coil occlusion of 1811 intracranial aneurysms: early angiographic and clinical results. *Neurosurgery* 2004; 54:268-80; discussion 280-5.
31. Vinuela F, Duckwiler G, Mawad M. Guglielmi detachable coil embolization of acute intracranial aneurysm: perioperative anatomical and clinical outcome in 403 patients. *J Neurosurg* 1997; 86:475-82.
32. Raabe A, Seifert V, Schmiedek P, Steinmetz H, Bertalanffy H, Steiger HJ, et al. [Recommendations for the management of unruptured intracranial aneurysms]. *Zentralbl Neurochir* 2002; 63:70-6.
33. News Communication . http://www.muhc.ca/media/news/2003/06_18_cza/. Last accessed on May 12th 2004 2003;
34. Chaloupka JC. LS. Single-Center Experience with Matrix Detachable Coils in More than 100 Aneurysms: technical Evaluation and Outcomes . Abstract.
35. Murayama Y. Matrix Detachable Coils for Brain Aneurysms: Preliminary Clinical Results. 2004; Abstract.
36. Wolf MJ. Matrix Coil System for Intracranial Aneurysms - a 12-Month Angiographic and Clinical Follow-up. Abstract.
37. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet* 1975; 1:480-4.
38. Lai SM, Duncan PW. Evaluation of the American Heart Association Stroke Outcome Classification. *Stroke* 1999; 30:1840-3.
39. Regie de l'Assurance Maladie du Quebec. Manuals - Medical Specialties . <http://www.ramq.gouv.qc.ca/fr/professionnels/medspe/manuel/man150.shtml> . Last access on May 12th 2004

Appendix 1

List of databases used in the literature search

- Pubmed
- Medline
- Cochrane database

Health Technology Assessment Agencies:

- CHSPR – Centre for Health Services and Policy Research (UBC) British Columbia
- HSURC – Health Services Utilization and Research Commission (Saskatchewan)
- ICES – Institute for Clinical Evaluative Sciences
- MCHP – Manitoba Centre for Health Policy
- INAHTA database – International Network of Agencies for Health Technology Assessment

Members of INAHTA (agencies included in the INAHTA database):

AÉTMIS - Agence d'évaluation des technologies et des modes d'intervention en santé

AHFMR - Alberta Heritage Foundation for Medical Research

ANAES - L'agence nationale d'accréditation et d'évaluation en santé

ASERNIP-S- Australian Safety & Efficacy Register of New Interventional Procedures - Surgery

CAHTA - Catalan Agency for Health Technology Assessment and Research

CCOHTA – Canadian Coordinating Office for Health Technology Assessment

CÉDIT – Comité d'évaluation et de diffusion des innovation technologiques

CMT – Center for Medical Technology Assessment (Sweden)

DACEHTA – Danish Centre for Evaluation and Health Technology Assessment

DIMDI – German Institute of Medical Documentation and Information

DSI – Danish Institute for Health Services Research

FinOHTA – Finnish Office for Health Care Technology Assessment

ITA – Institute of Technology Assessment ((Austria)

MSAC – Medical Services Advisory Committee (Australia)

NCCHTA - National Coordinating Centre for Health Technology Assessment

NHS QIS - NHS Quality Improvement Scotland

NHS – National Horizon Scanning Centre

N.I.C.E. – National Institute for Clinical Excellence

SBU – The Swedish Council on Technology Assessment in Health Care

SNHTA – Swiss Network for Health Technology Assessment

TA-SWISS – Center for Technology Assessment

Websites:

- FDA (www.fda.gov)

Appendix 2

Glasgow Outcome Scale, Hunt and Hess Scale and the Modified Rankin Scale

The Glasgow Outcome Scale (GOS) was designed in order to measure the disabilities resulting from brain damage³⁷. The scores range from 1 to five, as follows³⁷:

- 1 – Death
- 2 – Persistent vegetative state
- 3 – Severe disability (conscious but disabled)
- 4 – Moderate disability (disabled but independent)
- 5 – Good recovery

The Hunt and Hess (HH) scale was designed to measure the neurologic deficit in patients with subarachnoid hemorrhage, the scoring is as follows:

- 1 - Asymptomatic, mild headache, slight nuchal rigidity
- 2 - Moderate to severe headache, nuchal rigidity , no neurologic deficit other than cranial nerve palsy
- 3 - Drowsiness / confusion, mild focal neurologic deficit
- 4 - Stupor, moderate-severe hemiparesis
- 5 - Coma, decerebrate posturing

Information from the Strokecenter (http://www.strokecenter.org/trials/scales/hunt_hess.html)

The Modified Rankin Scale is used to measure disability and handicap, with grading ranging from 0 (no symptoms at all), to 5 (severe disability)³⁸.

Appendix 3

Summary of the studies used in the report

Roy et al. studied 116 patients with 226 unruptured aneurysms treated with GDC coils between August 1992 and June 1999 in the Notre Dame Hospital in the province of Quebec⁸. The patients included had been referred from neurosurgical centers because of contraindications to surgery, surgical failure, or because endovascular treatment was considered a better approach compared to surgery and conservative treatment⁸. Patients presenting with extradural, giant or aneurysms smaller than 3 mm were not included, as well as patients in whom parent vessel occlusion had been the treatment of choice⁸. Seventy-eight percent of the patients were women, and the mean age was 51 years. From the 226 aneurysms, 101 were excluded from the analysis as they were treated either with surgical clipping or endovascular balloon occlusion, therefore, 125 were included in the analysis⁸. Aneurysms location included the ophthalmic segment (40%), basilar bifurcation (14%), middle cerebral artery (11%), posterior communicating artery (9.6%), anterior communicating artery (8%), and other locations (16.8%)⁸. Sixty-eight percent of the aneurysms were small (<10 mm), and 62.4% of the aneurysms had a neck of less than 4 mm⁸. Approximately 15% of the patients did not have angiographic follow-up during the 2-12-month period after the treatment, the reason for this was not specified in the article. Outcomes evaluated included degree of aneurysm occlusion evaluated angiographically, complications, rates of aneurysm recanalization and rupture, and mortality⁸.

Ng et al. retrospectively reviewed the clinical information of 144 patients with 160 ruptured or unruptured aneurysms treated with endovascular coils between July 1992 and August 1998 in one hospital²⁷. Sixty-two percent of the patients were female, and the mean age was 52 years²⁷. Sixty percent of the patients were in Hunt & Hess grades I or II²⁷. Fifty percent of the patients were treated for a ruptured aneurysm²⁷. Seventy-three percent of the patients that were alive at 6 months had a follow-up evaluation beyond 6 months after the treatment, and 53% had a follow-up evaluation after 2 years²⁷. The outcomes of ruptured and unruptured aneurysms were analysed separately²⁷. The angiograms done after the treatment were analysed by two experienced neuroradiologists according to the authors²⁷. The degree of occlusion of the aneurysm, complications, neurologic status of the patient (HH, GOS), recanalization, re-rupture, and mortality rates were evaluated²⁷.

Henkes et al. evaluated the early outcomes of 1,811 ruptured or unruptured aneurysms that were treated with endovascular coils between November 1992 and January 2003³⁰. According to the authors, the neuroradiologists who treated the patients were experienced³⁰. The outcomes evaluated were degree of aneurysm occlusion, complications, and neurological deficit measured by the GOS scale³⁰. Seventy percent of the patients were female, and the mean age was 52 years, 55% of the aneurysms were ruptured at the time of treatment³⁰. Aneurysms were located in the middle-cerebral artery in approximately 43% of the cases, in the internal carotid artery in 31%, in the anterior cerebral artery in 22%, and in the posterior artery in 3% of the cases, the mean size of the aneurysm was 8.5mm³⁰.

Sluzewski et al. evaluated the outcomes of 160 consecutive patients with ruptured aneurysms treated with GDCs between 1995 and 2000²⁹. Initially, patients were referred for coil treatment due to high risk for surgery, but the indication for treatment was broader later in the study²⁹. The mean follow-up was 37 months²⁹. The outcomes evaluated were neurologic status (GOS), degree of aneurysm occlusion, complications, and mortality rate²⁹. Sixty-nine percent of the patients were women, 43% of the aneurysms were located in the posterior circulation, 26% in the anterior circulation, 22% in the carotid artery, and 9% in the middle-cerebral artery²⁹. Sixty-one percent of the aneurysms were smaller than or equal to 10 mm²⁹. Twenty-four percent of the patients alive refused to undergo repeat angiography at the 6 or 18 months follow-up visit²⁹.

Murayama et al. have studied 818 patients presenting with 916 aneurysms treated with GDCs at a medical center between 1990 and 2002²⁶. The patients were divided into two groups according to treatment period, 1990-1995, and 1996-2002, i.e., before and after FDA approval respectively²⁶. The main outcomes evaluated were treatment complications, degree of aneurysm occlusion, mortality rate, and neurologic status²⁶. Only patients from the second group were included in our report as this would probably be a closer approximation of the current clinical practice. Seventy-one percent of the patients were female, 43% of the patients were between 51 and 70 years of age, and 49% of the patients presented with ruptured aneurysms at the time of treatment²⁶. Forty percent of the aneurysms in the second group were smaller than 10mm and had a small neck

(≤ 4 mm)²⁶. Seventy-one percent of the aneurysms were located in the anterior circulation²⁶.

There were 588 patients with 665 aneurysms in the second group²⁶.

Raymond et al. reported the outcomes of 466 patients with 501 ruptured aneurysms treated with GDCs between August 1992 and May 2002 at one institution in the province of Quebec²⁸. Patients whose aneurysms would be difficult to treat surgically, or who had failed an attempted surgery, or in whom treatment with coils was considered a better approach than surgery or conservative treatment were referred for endovascular treatment with GDCs²⁸. The patients were followed for an average of 31 months²⁸. Their mean age was 54 years, and 74% were female²⁸.

The ISAT was an international, multicenter, randomised study comparing surgical clipping and GDC embolization in patients with ruptured aneurysms²³. From the 9,559 patients screened, 7,416 were excluded due either to patient refusal, in 671 patients, or other reasons not specified, 6745 patients²³. From the 1,073 patients randomised to receive endovascular treatment, 9 (0.8%) were treated by surgical clipping, and 38 (3.6%) of the 1,070 patients initially randomised to surgery received endovascular treatment²³. The reasons for crossovers were clinical, patient preference, and technical failure in the GDC group²³. The baseline characteristics seemed to be similar in both groups, except for the mean time between the aneurysm rupture and the treatment, which was longer in the surgery group, 1.7 days, compared to the endovascular group, 1.1 days ($p < 0.0001$)²³. The authors judged the randomised patients as being in a very good clinical condition, and the aneurysms were predominantly small and in the anterior circulation²³. For these reasons, the results of this study is generalisable mainly to a similar patient population, as mentioned by the authors²³.

It is important to acknowledge that the results presented in the articles refer to the patients that were not lost to follow-up, i.e., even after excluding the patients who died, approximately 24%-27% of the patients from two studies did not have a follow-up angiography^{27 29} therefore, the results may represent an overestimate of the benefits of the treatment.

The definition of neurologic morbidity may have varied slightly from study to study, for instance, Ng et al. defined procedure-related morbidity as a neurological deficit that lasted for

more than 7 days and that was attributed to the procedure²⁷, while Roy et al. defined morbidity as either temporary or permanent⁸. For this reason, in the results section, the rates of the neurologic evaluation from different studies were not pooled together into one estimate, but were given separately.

The degree of occlusion obtained through angiography is visually graded³⁰, which may result in discrepancies between the studies.

Appendix 4 – Table with Characteristics and Results of the Studies with GDC used in the report

| Study Characteristics | | | | | | | |
|---|---------------------------|-------------------------------|-----------------------|---|---|--|--|
| Study N. patients/ aneurysms Follow-up | Comparative randomized | Prospective /retrospective | Years of treatment | Inclusion / Exclusion Criteria | Patient characteristics | Location | Size |
| Roy et al.⁸ 116pt / 130 an Mean follow-up: 32 months Unruptured | No | Prospective | 92-99 | Preference for endovascular (EV) treatment Exclusion: Giant or < 3 mm MCA | Female – 78% Age – 50.6 | Ophthalmic – 40% Basilar bifurc. – 14.4% Posterior – 9.6% Anterior – 8% Middle – 11% | Aneurysm <= 10 mm – 68% Neck <= 4mm – 62% |
| Ng et al.^{27*} N=79 Follow-up: 24 months Unruptured | No | Prospective | 92-98 | - | Female: 62% Age: 52 HH I-III – 87% | Anterior communicating artery most frequent | Narrow neck: 81% |
| Ng et al.^{27*} N=81 Follow-up: 24 months Ruptured | No | Prospective | 92-98 | | Female: 62% Age: 52 HH I-III – 87% | Anterior communicating artery most frequent | Narrow neck: 81% |
| Raymond et al²⁸. N=466 (501) Mean follow-up: 31 months Ruptured | No | Retrospective | 92-02 | Failed or not suitable for surgical tx | Female: 74% Age: 54 HH I-III – 85% | Basilar bif – 27% Ophthalmic – 18% Anterior – 14% Posterior – 11% | Mean size of neck: 4.3 mm |
| Sluzewski et al²⁹. N=160 Mean follow-up: 37 months Ruptured | No | Prospective | 95-00 | High surgical risk at first and then aneurysm suitable for coil treatment | Female: 69% Age: 50 HH I-III – 87% | Anterior – 26% Posterior – 43% Carotid – 22% MCA – 9% | Aneurysm <= 10mm – 61% |
| Murayama et al.²⁶ 588 pt (group B) Mean f-up: 11 months Ruptured/unruptured | No | Prospective | 96-02 | Similar referral as neurosurgical, but more pts with anterior | Female: 71% Age: 41% < 50y SAH: 49.4% HH I-III – 75% | Posterior – 29% Anterior - 71% | Aneurysm <= 10 mm – 63% Neck <= 4mm – 36.5% |
| Henkes et al.³⁰ N=1811 Ruptured / unruptured | No | Retrospective | 92-03 | - | SAH: 55.5% HH I-III: 72.4% | Posterior - 3.3% Anterior – 22.5% Middle – 43.5% Internal carotid – 30.5% | Mean size: 8.5mm Neck: 3.9mm |

*The results of the patients included in the study by Ng et al.²⁷ were divided into ruptured and unruptured aneurysms in our analysis.

Study Results

| Study N. patients /aneurysms follow-up | Procedural failures / complications | Occlusion (immediate – f-up) | Mortality | Neurologic evaluation | Need for 2 nd procedure | Recanalization | Rupture |
|--|--|--|--|--|--|--|----------------------|
| Roy et al.⁸ 116/130 Follow-up: 32 months Unruptured aneurysms | Failures – 5.6% Complications – 12% | Immediate Complete: 90% | Immediate: 0 (procedure-related) | Morbidity > 1 month: 5.2% (4.3% tx related) | - | Residual neck – 12% (not occluded) 8% (occluded) | 0 (SAH) |
| Ng et al.²⁷ * 79 patients follow-up: 24 months Unruptured aneurysms | Failure: 8% Complications: - | Immediate: Complete:46% Neck remnants:16% (higher in narrow neck) Rupt - unrupt Long-term: 44% evolved to occlusion at 6-12m | Immediate: 0 (procedure related) In-hospital: 0 | Immediate: 5.1% procedure related morbidity rate Independence: 100% 6 months: Independence:98% 2 years: Independence:94% | 16/129* (12%) (3% surgery, 8% GDC, 0.9% balloon) *patients with follow-up | 6-12m: 23% of compl - recanalization 1st year: 28% deter. of degree of occlusion 1-2nd yr: 20% showed features of recan. | 0 |
| Ng et al²⁷* 81 follow-up: 24 months Ruptured aneurysms | Failure : 10% (higher in narrow neck) Complications: 21% (ruptured / unruptured) | Immediate: Complete:46% Neck remnants:16% (higher in narrow neck) Rupt - unrupt Long-term: 44% evolved to occlusion at 6-12m | Immediate: 2% (procedure related) 1.2% overall 11% in-hospital death | Immediate: 2.5% procedure related 8.6% morbidity rate H I-II: 88% 2 years: HH I-II: 85% | Follow-up: 11.9% (3% surgery, 8% GDC, 0.9% balloon) | 6-12months: 23% of compl - recanalization 1st year: 28% deter. of degree of occlusion 1-2nd yr: 20% showed features of recan. | Re-bleeding: 1.5% |

SAH: subarachnoid hemorrhage

*The results of the patients included in the study by Ng et al. ²⁷ were divided into ruptured and unruptured aneurysms in our analysis.

Study Results (continuation)

| Study / N Follow-up | Procedural failures / complications | Occlusion (immediate – f-up) | Mortality | Neurologic evaluation | Need for 2nd procedure | Recanalization | Rupture |
|---|--|--|--|---|---|---|--------------------------------|
| <i>Raymond²⁸</i> 466/501 f-up: 31months Ruptured aneurysms | Failure: 4% Complications: - | - | - | - | 18% (4% - surgical clipping 5.6% - parent vessel occlusion 8.4% coil) | 33.6% | Re-bleeding: 0.8% |
| <i>Sluzewski²⁹</i> 160 36 months 126 (with f-up) Ruptured aneurysms | Failure : 8.7% Complications : 4% of complications with death or dependency | Immediate : Complete :71% Near complete (90- 98%): 22% Long-term: Complete:59% Near complete (90- 98%): 25% | Immediate : 3.1% (procedure related) 6m – 9.4% Long-term : 11.3% 0.6% (recurrence of bleeding) | Immediate : Dependent: 0.6% (procedure related) Long-term : Good outcome (4-5): 84.4% Dependent (3): 4.4% | 6 months 3.1% (2.5-surg / 0.6-balloon occl) 18 months 11% (10.3% - coil / 0.7% sur) | - | Re-bleeding: 1.2% |
| <i>Murayama²⁶</i> N=588 Follow-up: 11 months Ruptured /Unruptured aneurysms | Failure – 5% Complications – 7% | Immediate: Complete occl – 55% (dependent on aneurysm and neck size) | Immediate: 1.1% (procedural complications) In-hospital: 4.1% SAH:6.4% Unrupt:0.8% | Immediate Unchanged - 91% <i>Morbidity rate</i> SAH- 7.2% Unruptured:4.5% Long-term Clinical outcome Improved – 17% Unchanged – 69% Neurologic deficit – 5% | - | Recanalization Small aneur/neck Overall: 17.2% Small aneur / wide neck -20% Large 35% Giant – 59% | <i>Delayed rupture</i> 1.6% |
| <i>Henkes³⁰</i> N=1811 Ruptured /Unruptured aneurysms | Failure: 2.9% Complications: 17.4% | Complete:65.8% >90%: 86.5% | 1.3% (due to coil treatment) | Immediate: No deficit: 74.6% Coil-related morbidity: Transient deficit – 5.3% Mild deficit – 2.3% Severe: 2.8% | - | - | - |
| Weighted average of results of the studies selected | Failure: 4% Complications: 14.9% | Immediate: Complete: 64% | Immediate: 1.3% (procedure- related) 4.4% (in- hospital) | - | 15% (surgery: 35%, GDC 41%, balloon occlusion 24%) | 17% | 1.1% |

HH: Hunt and Hess score

Appendix 5 – Total procedural costs with Matrix and GDC coils

The estimated cost for the treatment of one aneurysm with Matrix coils and GDCs is given in the table below.

Estimated cost of treatment of one ruptured or unruptured aneurysm with Matrix coils and GDCs (costs in Canadian dollars).

| Item | Matrix Coil | | | GDC | | |
|----------------------|----------------------------|--|----------------|----------------------------|-----------|----------------|
| | Units | Unit cost | Total cost | Units | Unit cost | Total cost |
| Coil (Matrix / GDC) | 6 | \$1,021 (\$1,075 without the 5% discount) | \$6,126 | 6 | \$800 | \$4,800 |
| Guidewire | 2 | \$209 (\$220 without the 5% discount) | \$418 | 2 | \$220 | \$440 |
| Other materials* | - | - | \$1,147 | - | - | \$1,199 |
| 1 X-ray technologist | 3.5 hours x 1 technologist | \$40/hour | \$140 | 3.5 hours x 1 technologist | \$40/hour | \$140 |
| 2 nurses | 3.5 hours x 2 nurses | \$50/hour | \$350 | 3.5 hours x 2 nurses | \$50/hour | \$350 |
| ICU stay | 2 days | \$814.34 | \$1,628.68 | 2 days | \$814.34 | \$1,628.68 |
| Total cost | | | \$9,810 | | | \$8,558 |

*other materials include: 1 catheter (\$427.5), 2 rotating hemostatic valves (\$332.5), basic angiography set up (\$237.5), 2 connecting cables (\$98), and 3 bottles of contrast media (\$51)

The costs of equipment used in the Matrix coils procedure presented in the table include a 5% discount on the Matrix coil and other equipment purchased from Boston Scientific. This discount will be given by Boston Scientific during one year, if Matrix coils rather than GDCs are purchased by the hospital (information provided by Dr. Donatella Tampieri, Director of Diagnostic and Interventional Radiology – MNI/H). Costs of equipment used in the GDC procedure do not include the discount as this is only applicable if Matrix coils are purchased.

Patients who presented with a ruptured aneurysm at the time of treatment usually stay in the hospital for an additional 4-7 weeks compared to unruptured aneurysms, according to the information from Mrs. Josée Beloin (Nurse, Department of Neuroradiology – MNI/H).

Information on the cost of hospital stay was provided by the Finance department of the MUHC (Mr. Gilles Gaudet), and the information on the length, material, and personnel required for the procedure were provided by the Neuroradiology department of the MUHC (Mrs. Patricia Smith / Mrs. Josée Beloin). The total cost of the endovascular coiling of an aneurysm with Matrix Coils including the 5% discount is \$9,810, and \$8,558 with GDCs. Additional costs of treating procedure-related complications and technical failures were not included due to the lack of this type of information in patients treated with Matrix coils.

Physicians' and anesthesiologists fees according to the Regie de l'Assurance Maladie du Quebec³⁹ are as follows:

| Procedure | Physicians' fee |
|---|-----------------|
| Cranial arterial embolisation (code 9439) | \$410 |
| General anesthesia for blocking a major nerve for diagnostic and therapeutic procedures (code 0986) | \$308 |
| Total for physicians' fees | \$718 |

Including physicians' fees, the total cost of the endovascular coiling procedure is estimated to be \$10,528 and \$9,276 for the Matrix and GDC coils respectively.

Appendix 6 – Total cost of treatment with Matrix coils and GDCs within 1-2 years after the initial procedure

Despite the lack of information on efficacy and long-term outcomes from randomized comparisons between Matrix coils and GDCs in the peer-reviewed literature, we have attempted to evaluate the long-term impact of adopting the use of Matrix coils within 2 years after the initial procedure by using information provided by experts and non-comparative studies. We acknowledge that we may be introducing biases in our results by using information not derived from randomized studies specifically designed to compare these two technologies. This is a concern especially given the large variations in outcomes in aneurysms of different sizes and locations, and in patients with different characteristics. Moreover, the populations from which the estimates were derived may not be homogeneous. In order to minimize this bias, we have performed sensitivity analyses using information on long-term outcomes obtained from the different sources, such as expert opinion and non-comparative published studies.

Tables 1 through 4 present the long-term cost impact of replacing GDCs by Matrix coils. The long-term re-treatment rate with Matrix coils of 15% remained constant in the different scenarios, and was provided by Dr. Donatella Tampieri (Director of Neuroradiology, MNI/H) based on information released in scientific meetings. For GDCs, the long-term re-treatment rate varied in each scenario, and was derived from the rate for different hospitals provided by Dr. Donatella Tampieri (Director of Neuroradiology, MNI/H), i.e., 25%, for Table 1, personal experience from Dr. Donatella Tampieri (Director of Neuroradiology, MNI/H) at the MNI/H, i.e., 18% (ranging from 16%-20%), for Table 2, the average rate obtained from our literature review for GDCs, i.e., 15%, for Table 3, and for Table 4, the results of patients treated with GDC on a randomized controlled trial that compared GDCs with surgical clipping in patients with ruptured aneurysms, the ISAT trial²³, were used, i.e., 12.6%.

As can be seen in Tables 1 through 4, the additional cost of using Matrix coils instead of GDCs in the 40 patients treated annually at the MNI/H varied from CDN\$23,360 to CDN\$65,808 for the first two years after the initial treatment. This wide variation reflects the imprecision of the currently available information on the comparison between the two treatments, consequently, these results should be interpreted with extreme caution. Additionally,

as previously mentioned, the populations from which the rates were derived are possibly heterogeneous, and the re-treatment rate for Matrix coils was not obtained from the peer-reviewed literature, but from information presented orally at scientific meetings, with no supporting abstract. We haven't included the risk of re-bleeding in our cost calculations as this occurs mostly in aneurysms that were ruptured before the initial treatment, and as the actual rate of ruptured aneurysms treated in the MNI/H may vary. We have not included the rates of failures and treatment complications in the cost calculations due to lack of such information for Matrix coils.

We have also assumed that all patients were alive after the initial treatment, and therefore at risk of requiring an additional treatment procedure. Considering a 4.4% in-hospital mortality rate (Appendix 3), this would result in a -2% to 5% alteration in the cost difference between the two treatment modalities across the different scenarios.

All costs shown are in Canadian dollars.

Table 1 - Total cost of treatment with Matrix Coils and GDCs.

Rates of additional procedures for GDCs for different hospitals according to expert opinion, Dr. Donatella Tampieri (Director of Neuroradiology, MNI/H).

| | Cost per procedure (Appendix 5) | Initial cost for 40 patients | Re-treatment rates (1-2 years) | Cost of re-treatment* (re-treatment rate *40 patients* procedure cost) | Total cost for the first 1-2 years (initial + recurrence costs) for 40 patients |
|---|---------------------------------|------------------------------|--------------------------------|--|---|
| Matrix Coils | \$9,810 | \$392,400 | 15% | \$58,860 | \$451,260 |
| GDC | \$8,558 | \$342,320 | 25% | \$85,580 | \$427,900 |
| Difference in cost with Matrix coils | | | | | + \$23,360 |

*We assumed that aneurysms that required re-treatment were treated with endovascular coils.

Table 2 - Total cost of treatment with Matrix Coils and GDCs.

Rates of additional procedures with GDCs at the MNI/H according to expert opinion, (Dr. Donatella Tampieri, Director of Neuroradiology, MNI/H).

| | Cost per procedure (Appendix 5) | Initial cost for 40 patients | Re-treatment rates (1-2 years) | Cost of re- treatment* (re- treatment rate *40 patients* procedure cost) | Total cost for the first 1-2 years (initial + recurrence costs) for 40 patients |
|---|--|---|---|---|--|
| Matrix Coils | \$9,810 | \$392,400 | 15% | \$58,860 | \$451,260 |
| GDC | \$8,558 | \$342,320 | 18% | \$61,618 | \$403,938 |
| Difference in cost with Matrix coils | | | | | + \$47,322 |

*We assumed that aneurysms that required re-treatment were treated with endovascular coils.

Table 3 - Total cost of treatment with Matrix Coils and GDCs.

Rates of additional procedures for GDCs were taken from the literature review (section 6.2).

| | Cost per procedure (Appendix 5) | Initial cost for 40 patients | Re-treatment rates (1-2 years) | Cost of re- treatment* (re- treatment rate *40 patients* procedure cost) | Total cost for the first 1-2 years (initial + recurrence costs) |
|---|--|---|---|---|--|
| Matrix Coils | \$9,810 | \$392,400 | 15% | \$58,860 | \$451,260 |
| GDC | \$8,558 | \$342,320 | 15% | \$51,348 | \$393,668 |
| Difference in cost with Matrix coils | | | | | + \$57,592 |

*We assumed that aneurysms that required re-treatment were treated with endovascular coils.

Table 4 - Total cost of treatment with Matrix Coils and GDCs.

Rates of additional procedures for GDCs were taken from the ISAT trial²³.

| | Cost per procedure (Appendix 5) | Initial cost for 40 patients | Re-treatment rates (1-2 years) | Cost of re- treatment* (re- treatment rate *40 patients* procedure cost) | Total cost for the first 1-2 years (initial + recurrence costs) for 40 patients |
|---|--|---|---|---|--|
| Matrix Coils | \$9,810 | \$392,400 | 15% | \$58,860 | \$451,260 |
| GDC | \$8,558 | \$342,320 | 12.6% ²³ | \$43,132 | \$385,452 |
| Difference in cost with Matrix coils | | | | | + \$65,808 |

*We assumed that aneurysms that required re-treatment were treated with endovascular coils.