The eJournal of the European Society of
Minimally Invasive Neurological Therapy

The impact of first and second generation Hydrogel Coil Technology on Cerebral Aneurysm Treatment: A single practice experience

EJMINT Original Article, 2015: **1506000254** (2nd February 2015)

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Abstract

INTRODUCTION: Bare platinum coils have demonstrated safety and efficacy in the treatment of intracranial aneurysms; however, a persistent and important limitation occurs in the form of delayed recanalisation. The authors report their multiple-hospital, single-practice experience with the use of first and second-generation hydrogel coils for the treatment of ruptured and unruptured cerebral aneurysms. METHODS: During a period of 44 months, 101 consecutive patients with 104 ruptured or unruptured intracranial aneurysms were treated by a two-physician team covering several hospitals. Hydrogel coils, both first (Hydrocoil®) and second (HydroFrame®, HydroFill® and HydroSoft®) generation, were exclusively used in this patient cohort. Retrospective analysis of clinical and angiographic data was performed. RESULTS: Procedural morbidity and mortality were 5 % and 0 % respectively. No patient developed hydrocephalus or aseptic meningitis. The rates of immediate post-procedure total occlusion were 94 %, of neck remnants 6 % and incomplete occlusion 0 %. Long-term (>12 months) angiographic follow-up was obtained in 95 patients (94 %). No recanalisations were observed in any of those patients, whether treated with stent-assisted coiling, balloon assisted coiling or with coils only, including patients who had presented with recurrent, recanalised aneurysms. CONCLUSION: In our patient population, the safety profile of Hydrogel coils was found to be similar to that of non-coated platinum coils. Moreover, significantly improved obliteration rates, both early and delayed, were observed in our patient population, possibly from enhanced long-standing separation of the intra-aneurysmal environment from the parent artery.

Presented at the LINC (Live Interventional Neuroradiology Conference) Houston 2012 Meeting, December 12, 2012, Houston, TX

Keywords: endovascular, coils, cerebral aneurysms, Hydrogel, single practice

Introduction

In the United States, it is currently estimated that the fastest growing group of patients with aneurysms is that of patients with previously ruptured aneurysms, which were previously treated with endovascular coil therapy [1]. The most important determinant of endovascular aneurysm therapy is long-term obliteration, which impacts major clinical correlates such as re-haemorrhage rates, follow-up cost and morbidity and re-treatment cost and morbidity, such that the superiority of coil therapy over surgical clipping has been recently questioned [2]. Since long-term aneurysm obliteration has been a major limitation of endovascular coil aneurysm therapy, considerable research is understandably conducted in this area, which has led to newer generation coils, including coated coils [3-6]. Hydrogel coated coils (Microvention TERUMO, Tustin, CA, USA) have demonstrated lower recanalisation rates than bare platinum coils [7-11]. This report documents the experience of a relatively large single practice with Hydrogel coils, first and second generation combined, with early and long-term follow-up data.

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Patients and Methods

Between March 2009 and December 2012, a total of 101 consecutive patients with 104 aneurysms were treated exclusively with Hydrogel coils (Table 1). Institutional Review Board (IRB) approval was requested and waived, since treatment is considered standard therapy and therefore does not require specific consent. Sixty-two patients were female (61 %), and 39 were male (39 %), ranging in age between 32 and 90 years (mean=57).

All patients were evaluated by a multidisciplinary team prior to treatment. Sixty-seven aneurysms were treated electively, and 37 ruptured aneurysms were treated emergently. Five aneurysms in the unruptured group were in patients with recurrent aneurysms several months after coil therapy using bare platinum coils. These involved the basilar terminus (n=2), the lateral wall of the basilar artery (n=1), the left posterior communicating artery (n=1) and the right middle cerebral artery bifurcation (n=1); all 5 aneurysms had initially presented with subarachnoid haemorrhage (SAH) and therefore treatment for recurrence was indicated (Table 1).

Aneurysm characteristics were evaluated in each patient toward the best treatment strategy. Maximum aneurysm dimension ranged between 2 and 23 mm (mean 7 mm; SD ± 9 mm). Seventeen (16 %) aneurysms were categorised as small (<5 mm), 59 (57 %) as medium-sized (5-15 mm) and 28 (27 %) as large (>15 mm). The majority of unruptured aneurysms treated were larger than 6 mm. Forty (39 %) aneurysms had a narrow neck, defined either as having a neck a neck ≤ 4 mm or a neck-to-dome ratio <50 %), and 64 aneurysms (61 %) were broad-based (neck ≥ 4 mm or neck-to-dome ratio >50 % (Table 1).

Hydrogel coils of all kinds were exclusively used in this series of patients. Coils were generally selected at the operator's discretion. First generation Hydrocoils (HES) were used exclusively in the first 18 patients (19 %) in this cohort. Second generation HydroFrame, HydroFill and HydroSoft coils were used in combination in the remaining 84 (83 %) patients. The finishing coils used in 9/18 patients in the group of patients treated with HES coils were bare platinum coils, while Hypersoft coils (non-hydrogel containing platinum coils) were used in 45/84 patients treated with second generation Hydrogel coils.

In each one of our patients, it was estimated that at least 85 % of coils delivered were polymer-coated.

Endovascular procedures

All procedures were performed under general anaesthesia with intravenous heparin anticoagulation. Patients for whom stent placement was planned received pre-operative dual antiplatelet therapy for 3-5 days consistent with daily 75 mg of clopidogrel and 81 or 325 mg of aspirin. Femoral arterial access was used in all patients, usually with a 6 French arterial sheath. All procedures were performed on biplane angiography equipment, either Axiom Artis (Siemens, Erlangen, Germany) or Allura Xper (Philips, Best, The Netherlands). Balloon remodelling was used in 31 patients (30 %), using either a Hyperform (eV3 Neurovascular, Irvine, CA, USA) or a Scepter balloon (Microvention Terumo, Tustin, CA, USA). Stents were used in 46 patients (44 %) using either a Neuroform (Stryker Boston Scientific, Natick, MA, USA) or Enterprise (Enterprise VRD, Codman Neurovascular, Johnson & Johnson, Miami, FL, USA) device.

Patient follow-up

All patients were followed clinically at 3-6 months intervals after treatment for 18 months, then yearly. In all patients, MRI and MRA were obtained within 9-12 months of treatment, then at 36 months. Patients with ruptured aneurysms were scheduled for follow-up angiography at 6 months, 12 months and 36 months of treatment. In case of significant aneurysm recanalisation, our standard practice is to discuss and perform re-treatment. In patients with previously unruptured aneurysms, angiographic follow-up was obtained at 12 months, then between 24 and 36 months.

In all patients, angiographic evaluation up to 7 years post-treatment was planned. Long-term (>12 months) angiographic follow-up was obtained in 95 patients. Average follow-up length was 14 months in this series.

Angiograms were obtained with oblique views in projections as close as possible to those used during aneurysm treatment; 3D rotational angiograms were commonly, although not consistently, obtained for the sake of radiation reduction if the clinical information provided by standard views was sufficient.

Angiographic studies were reviewed by two neurointerventionalists with significant experience (over 15 years each). The Roy-Raymond classification was used to assess angiographic results [12].

Results

Clinical outcomes and complications

The 1-year follow-up mark was used to assess clinical outcomes in all patients. Three patients admitted with SAH - with WFNS (World Federation of Neurosurgical Societies) grades ranging between IV and V - expired (mRs 6). All other patients (n=34) with ruptured aneurysms had mRs of 0-2 at 1-year year follow-up, with gradual functional recoveries post-SAH.

All patients treated for unruptured aneurysms (n=67), including 5 patients with a prior history of SAH who had recurrent aneurysms and had made full recoveries, had mRS of 0-1 at 1-year.

Intraoperative complications included 2 intraoperative aneurysm ruptures, both basilar apex aneurysms, 1 recurrent 2 years after coiling with bare platinum coils, the other previously untreated. In both cases, aneurysm rupture was thought to have been caused by advancing the microwire within the aneurysm. Both patients had good outcomes with full recovery, one requiring a ventriculoperitoneal shunt. There were also 3 intraoperative thromboembolic events, all which fully resolved with the intra-arterial administration of a glycoprotein IIb/IIIa inhibitor (Integrilin). Therefore, in this series, intraoperative morbidity was 5 % and mortality 0 %.

Delayed, asymptomatic occlusion of the internal carotid artery occurred in 1 patient with a large cavernous aneurysm extending into the sella turcica, thought to be related to extensive atheromatous disease, use of a stent and poor compliance with clopidrogrel. This patient had 2 minor haemodynamic ischaemic events without permanent sequelae, after which she received an EC-IC bypass, which resulted in full recovery.

Angiographic results

Immediate angiographic results using the Roy-Raymond grading system demonstrated Class 1 (complete) occlusion in 95 aneurysms (94 %) and Class 2 (persistent neck opacification in 1 projection without aneurysm sac filling) in 6 patients (6 %); there were no Class 3 (aneurysm sac opacification) findings.

Long-term (>12 months) angiographic results were available in all but 5 patients, of whom 3 had expired, and 2 had relocated. In all patients in whom delayed angiographic data (n=96) was available, no recanalisations were observed.

Discussion

Endovascular therapy for cerebral aneurysms, both ruptured and unruptured, has represented a major breakthrough, showing superiority over surgical clipping after SAH in the form or long-lasting survival benefits [13]. Although in the low numbers, however, the recurrence of haemorrhagic events has clearly been shown to be significantly more common after coil aneurysm therapy compared to surgical clipping [13-14] such that the superiority of coil embolisation over clip ligation has been recently questioned for patients 40 years old and younger [2]. Additionally, in partially clipped, previously ruptured aneurysms, the surgical literature reports repeat SAH rates of 71-79 % within a mean of 10 years (range: 4–20 years) [15-16].

For the largest part, recurrent haemorrhagic events are related to high rates of aneurysm recanalisation after treatment with bare platinum coils, as it has been shown that even if dense packing is obtained at the time of treatment, the aneurysm sac is filled at best with 20-30 % of metal, and 70-80 % with thrombus, leading to recanalisation when the thrombus fails to organise [17].

Among the various modifications to coil design, hydrogel coils have shown the most promise so far. The hydrogel polymer initially expands to create volumetric aneurysm occlusion rates that are far superior to (up to 3 times over) those obtained with dense packing with bare platinum coils, reportedly at a mean of 68 % (range=50-75 %) [3]. In addition, there is experimental evidence of superior long-term obliteration rates [6]. The inert hydrogel biomaterial therefore prevents the setting of a large thrombus within the aneurysm which could possibly promote recanalisation. Furthermore, at a later stage, intra-aneurysmal dehydration contributes to thrombus resorption, leading to a decrease in mass effect. In clinical practice, although challenged in one small clinical study [18], the efficacy of Hydrogel coils was clearly demonstrated in several trials. The HELPS study, a prospective, randomised controlled trial with a blinded independent core lab review comparing the HydroCoil® to bare platinum coils, enrolled 499 patients in 24 countries, in whom 18-month follow up data was provided, showing statistically significant decreases in aneurysm remnants and recanalisation rates in the HydroCoil® arm [7]. The HEAL study [8] showed interestingly that when over 75 % of aneurysm coil length was hydrogel-coated, late (6 month) recanalisation rate was 0 %. Reported results with the use of second generation (HydroFill®, HydroSoft®) coils are similarly good, especially if stenting is performed in combination with coils [10].

Such positive results compare much favorably with lack of superiority over bare platinum coils demonstrated with PGA/PGLA coated coils [19-20].

In our patients, no recanalisation was observed. Although certain practice patterns may have contributed to such a result, i.e., liberal use of stents and balloon remodelling, and consistency in obtaining as tight coil packing as possible, we believe that, in addition to volumetric expansion, the biological interaction between the hydrogel polymer and the aneurysm sac may contribute to separating the obliterated aneurysmal contents from the parent arterial lumen. The presence of a thick lucent line at the aneurysm base has been described [21], which may constitute a continuous layer of hydrogel or a combination of thrombus and hydrogel along the aneurysm neck and extending well beyond it.

Chemical aseptic meningitis has been reported initially as a possible complication of polymer polyglycolic-lactic acid (PGLA)-coated coil [22], and later as a complication of hydrogel coils [23]. None of our patients with an unruptured aneurysm displayed either complaints or evidence of meningitis, aseptic or other.

Hydrocephalus has also been reported to occur after the use of hydrogel coils, either as a consequence of aseptic meningitis [24], or de novo, at a concerning rate of 14 % [25]. However, hydrocephalus and peri-aneurysmal oedema were also reported to occur with bare platinum coils [26-29], so the hydrogel cannot be directly incriminated as the underlying mechanism. Not a single patient in our series, whether presenting with an unruptured or ruptured aneurysm, developed hydrocephalus thought to be attributable to the hydrogel coils. The only patients who developed hydrocephalus requiring a shunt were patients with ruptured intracranial aneurysms, whose admission CT scans showed both evidence of severe SAH and ventriculomegaly.

This study has several limitations. The most obvious limitation is a retrospective, non-randomised design. However, we believe that the nature of the work, i.e., single practice consecutive case series, confers to this study "real-life" characteristics which reproduce the practice conditions of a growing number, if not the majority, of practices. Another limitation resides in self-assessed angiographic results; all results were assessed by 2 observers, both with significant neurointerventional experience (over 15 years each), and reviewed at monthly neurovascular conferences with colleagues from various specialties including neurosurgery, neurology and vascular surgery. Lastly, the use of coils which have a relatively recent track record, and the apparent inhomogeneous coil distribution, might be considered potential limitations. However, we believe that sufficient data on the efficacy of Hydrogel coils exists in the form of large trials [7-9], and that there is consistency in using polymer-coated coils.

Conclusion

In our single practice experience, the use of Hydrogel coils to treat intracranial aneurysms, both ruptured and unruptured, has been correlated with excellent and durable aneurysm obliteration rates. We believe that delayed gel expansion contributes to delayed separation of the intra-aneurysmal environment from the parent artery, therefore promoting long-lasting results.

Conflict of interest

We declare that we have no conflict of interest.

References

1. Origitano TC. Current options in clipping versus coiling of intracranial aneurysms: to clip, to coil, to wait and watch. *Neurosurg Clin N Am* 2008; 19:469–476

2. Mitchell P, Kerr R, Mendelow D, Molyneux A. Could late rebleeding overturn the superiority of cranial aneurysm coil embolization over clip ligation seen in the International Subarachnoid Aneurysm Trial? *J Neurosurg* 108:437–442, 2008

3. Kallmes DF, Fujiwara NH. New expandable hydrogelplatinum coil hybrid device for aneurysm embolization. *AJNR* 23:1580-1588, 2002

4. Yoshino Y, Niimi Y, Song J, Silane M, Berenstein A. Endovascular treatment of intracranial aneurysms: comparative evaluation in a terminal bifurcation aneurysm model in dogs. *Journal of Neurosurgery*; 101: 996–1003, December 2004

5. Tsumoto T, Niimi Y, Berenstein A. Evaluation of the new HydroSoft coil in a canine model of bifurcation aneurysm. *J Neurosurg* 111:11-16, 2009

6. Killer M, Kallmes D, Jones R, Ding Y, Vestal M, Hauser T, Virmani R, Cruise G. Long-term angiographic and histological results of a new hydrogel-containing filling coil in experimental rabbit aneurysms. *Minim Invasive Neurosurg*. 2010 Jun;53(3):97-105. doi: 10.1055/s-0030-1252059. Epub 2010 Aug 31.

7. White PM, Lewis SC, Nahser H, Sellar RJ, Goddard T, Gholkar A; HELPS Trial Collaboration. HydroCoil Endovascular Aneurysm Occlusion and Packing Study (HELPS Trial): Procedural Safety and Operator-Assessed Efficacy Results. *AJNR Am J Neuroradiol* Feb:29 (2) 217-223, 2008

8. Cloft H, for the HEAL Investigators. HydroCoil for Endovascular Aneurysm Occlusion (HEAL) study: 3-6 month angiographic follow up results. *AJNR* 28:152-154, 2007

9. Park JH, Kang HS, Han MH, Jeon P, Yoo DS, Lee TH; Korean HydroSoft Registry Investigators. Embolization of intracranial aneurysms with HydroSoft coils: results of the Korean multicenter study. *AJNR* 32:1756-1761, 2011

10. Toma A, Niimi Y, Ortiz R, Fifi J, Paramasivam S, Berenstein A. Embolization of Intracranial Aneurysms with the HydroSoft and HydroFrame Coils: A Single-Center Experience. *JNET* 6:87-97, 2012

11. Speirs JW, Burke TH, Lee SY, Ala BD. The next generation HydroCoil: initial clinical experience with the HydroFill embolic coil. *J Neurointerv Surg*. 2013 Nov;5 Suppl 3:iii72-iii75. doi: 10.1136/neurintsurg-2012-010643. Epub 2013 Apr 23.

12. Roy D, Milot G, Raymond J. Endovascular treatment of unruptured aneurysms. *Stroke*. 2001 Sep;32(9):1998-2004.

13. Molyneux AJ, Kerr RS, Yu LM, Clarke M, Sneade M, Yarnold JA, Sandercock P; International Subarachnoid Aneurysm Trial (ISAT) Collaborative Group. International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion. *Lancet*. 2005 Sep 3-9;366(9488):809-17.

14. Molyneux AJ, Kerr RS, Birks J, Ramzi N, Yarnold J, Sneade M, Rischmiller J; ISAT Collaborators. Risk of recurrent subarachnoid haemorrhage, death, or dependence and standardised mortality ratios after clipping or coiling of an intracranial aneurysm in the International Subarachnoid Aneurysm Trial (ISAT): long-term follow-up. *Lancet Neurol*. 2009 May;8(5):427-33.

15. Lin T, Fox AJ, Drake CG. Regrowth of aneurysm sacs from residual neck following aneurysm clipping. *J Neurosurg* 1989; 70:556–560

16. Giannotta SL, Litofsky NS. Reoperative management of intracranial aneurysms. *J Neurosurg* 1995; 83:387–393

17. Bavinzski G, Talazoglu V, Killer M, Richling B, Gruber A, Gross CE, Plenk H Jr. Gross and microscopic histopathological findings in aneurysms of the human brain treated with Guglielmi detachable coils. *J Neurosurg* 1999;91:284– 293.

18. van Rooij WJ, Sluzewski M. Durability of treatment of intracranial aneurysms with hydrocoils is not different from standard platinum coils. *Stroke*. 2006 Dec;37(12):2874; author reply 2875. Epub 2006 Oct 19.

19. Piotin M, Pistocchi S, Bartolini B, Blanc R . Intracranial aneurysm coiling with PGLA-coated coils versus bare platinum coils: long-term anatomic follow-up. *Neuroradiology*. 2012 Apr;54(4):345-8.

20. van Rooij WJ, de Gast AN, Sluzewski M. Results of 101 aneurysms treated with polyglycolic/polylactic acid microfilament nexus coils compared with historical controls treated with standard coils. *AJNR Am J Neuroradiol*. 2008 May;29(5):991-6.

21. Arthur AS, Wilson SA, Dixit S, Barr JD. Hydrogel-coated coils for the treatment of cerebral aneurysms: preliminary results. *Neurosurg Focus*. 2005 Feb 15;18(2):E1.

22. Meyers PM, Lavine SD, Fitzsimmons BF, Commichau C, Parra A, Mayer SA, Solomon RA, Connolly ES Jr. Chemical meningitis after cerebral aneurysm treatment using two second-generation aneurysm coils: report of two cases. *Neurosurgery* 2004;55:1222

23. Im SH, Han MH, Kwon BJ, Jung C, Kim JE, Han DH. Aseptic meningitis after embolization of cerebral aneurysms using hydrogel-coated coils: report of three cases. *AJNR Am J Neuroradiol*. 2007 Mar;28(3):511-2.

24. Marchan EM, Sekula RF Jr, Ku A, Williams R, O'Neill BR, Wilberger JE, Quigley MR. Hydrogel coil-related delayed hydrocephalus in patients with unruptured aneurysms. *J Neurosurg*. 2008 Aug;109(2):186-90.

25. Horie N, Kitagawa N, Morikawa M, Tsutsumi K, Kaminogo M, Nagata I. Progressive perianeurysmal edema induced after endovascular coil embolization. Report of three cases and review of the literature. *J Neurosurg*. 2007 May;106(5):916-20.

26. Deshaies EM, Adamo MA, Boulos AS. A prospective single-center analysis of the safety and efficacy of the hydrocoil embolization system for the treatment of intracranial aneurysms. *J Neurosurg*. 2007 Feb;106(2):226-33.

27. White JB, Cloft HJ, Kallmes DF. But did you use HydroCoil? Perianeurysmal edema and hydrocephalus with bare platinum coils. *AJNR Am J Neuroradiol*. 2008 Feb;29(2):299-300. Epub 2007 Nov 16.

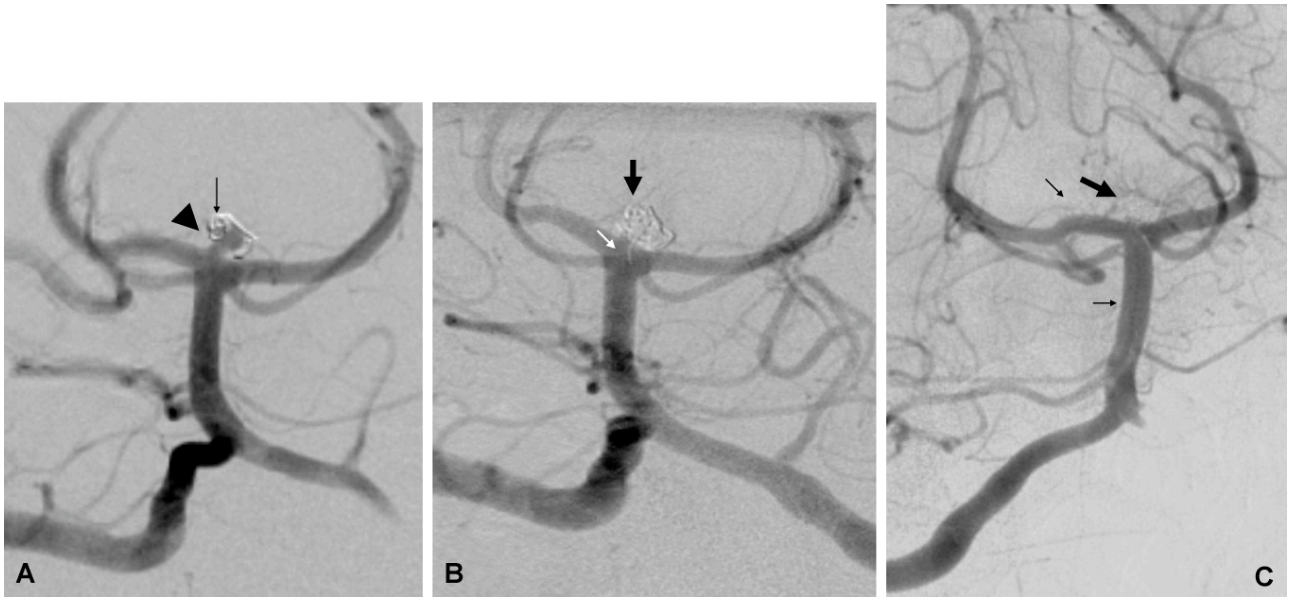
28. Misaki K, Uchiyama N, Mohri M, Hirota Y, Hayashi Y, Hamada J. Unusual delayed hydrocephalus after bare platinum coil embolization of an unruptured aneurysm. *Neurol Med Chir (Tokyo)*. 2010;50(7):581-5.

29. Ozaki M, Murayama Y, Ebara M, Takao H, Abe T. Delayed hydrocephalus after embolization of unruptured aneurysms using bare platinum coils: report of 2 cases. *AJNR Am J Neuroradiol*. 2011 Nov-Dec;32(10):E188-90. doi: 10.3174/ajnr.A2317. Epub 2011 Jan 13.

Figures

Figure 1 - Example of recurrent basilar apex aneurysm re-treated with HydroCoils.

59 y.o. female with recurrent SAH from a re-ruptured basilar apex aneurysm 2 years after treatment with bare platinum coils; note significant coil compaction (1A, small arrow). Immediate post-treatment angiogram shows total aneurysm occlusion (1B, arrow); a coil loop protrudes at the aneurysm base (1B, small white arrow), prompting Enterprise stent placement. Two-year follow-up shows persistent total aneurysm obliteration (1C, arrow), and patent stent (1C, small arrows).



Tables

Table 1 - Demographic, clinical and treatment data.

Patients			101
	Female		62 (61%)
	Male		39 (39 %)
	Age		Mean= 57, Range= 32-90
Aneurysms			104
	SAH		37 (36 %)
		• Grade I	15
		• Grade II	10
		• Grade III	7
		• Grade IV	3
		• Grade V	2
	Unruptured		67 (64 %; includes 5 recurrent s/p prior SAH)
		• Headaches	28
		• Cranial nerve deficit	10
		• Family history	8
		• Asymptomatic	21
	Aneurysm location		
		Anterior circulation (N=81; 78 %)	PCom (20), ACom (17), Paraclinoid ICA (16), ICA-Ophth (14), ICA terminus (8), ICA below skull base (3), MCA bifurcation (3)
		Posterior circulation (N=23; 22 %)	Basilar terminus (12), PICA (5), Lateral wall Basilar (4), SCA (2)
	Aneurysm size		
		Small (<5 mm)	17 (16 %)
		Medium (5-15 mm)	59 (57 %)
		Large (>15 mm)	28 (27 %)
	Aneurysm neck		
		Broad-based	64 (61 %)
		Narrow neck	40 (39 %)
Treatment			
	Coils	HES	18 (17 %)
		Hydroframe, HydroFill, Hydrosoft	84 (83 %)
	Adjunctive technique		
		Stent	46 (44 %)
		Balloon	31 (30 %)