Embolization of Cerebral Aneurysms with Spherically Shaped Detachable Microcoils (MicruSphere Microcoil System) A Single Centre Experience

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Summary

We present our initial experience of concentric-filling technique using MicruSphere 3D coils (Micrus Endovascular, San Jose, CA) in the treatment of intracranial aneurysms.

149 intracranial saccular aneurysms in 142 consecutive patients (mean age 56.6 ± 12.7 , ruptured in 54 (36.2%)) were treated with the concentric-filling technique. The mean aneurysm volume was $169.0 \pm 363.0 \text{ mm}^3$. Neck remodeling technique was used in 120 (80.5%). Procedure-related problems were recorded. Initial embolization results were evaluated, and the coil packing density was calculated. Clinical and angiographic follow-ups were performed after six months. Any changes in embolization status were classified as 'improved', 'unchanged', or 'worse'.

The overall packing density was 40.1% (range 10.5-90.9%). The permanent morbidity and mortality rates were 4.0% and 1.3%, respectively. The initial Raymond and Roy classification results were class 1 in 37 aneurysms (24.8%), class 2 in 50 (33.6%), and class 3 in 62 (41.6%). On the mean follow-up examination of 8.2 months in 103 patients (72.5%), there were one transient ischemic attack, one minor stroke, and one instance of rebleeding. Angiographic follow-up in 101 aneurysms (67.8%) showed the change in embolization status as 'improved' in 42 aneurysms (41.6%), 'unchanged' in 42 (41.6%), and 'worse' in 17 (recanalisation rate, 16.8%).

The concentric-filling technique using MicruSphere 3D coils was effective in achieving high packing density which in turn resulted in stable embolization in the majority of the aneurysms. Longer follow-up is warranted to determine the durability of these results.

Introduction

Achieving a high packing density is one of the most important technical goals in the treatment of intracranial aneurysms with detachable coils. There have been several reports showing that a higher coil packing density was correlated with a successful initial angiographic outcome and a lower rate of aneurysm recanalisation on follow-up despite some past arguments to the contrary^{1,2}.

The initial framing coil and subsequent filling coils are very important to maximise the packing density. For a framing coil, many prefer a coil with a three-dimensional (3D) configuration because of its conformability to the aneurysm sac and its higher degree of retention within a wider-necked aneurysm. Various coil-loop designs have been applied for better conformability without losing the robust 3D characteristics^{3,4}.

The MicruSphere microcoil (Micrus Endovascular, San Jose, CA) is one of the 3D detachable coils which may be able to provide a good structural frame along the inner wall of

Figure 1 Photographic depiction of the concept of the 'concentric-filling technique'. Two coils are placed in an open space. A second coil (pink in colour) is placed within the initial framing coil (light blue in colour) while retaining its 3-dimensional configuration leaving a roughly spherical space in the centre.

an aneurysm and neck opening, while maintaining the empty inner space⁵. The original design of the coil began with the anatomically conformable 3D (ACT) detachable platinum coil from the same company. The feasibility of using the ACT coil as a framing coil had already been documented⁶. The empty inner space of the framed sac permits the placement of consecutive framing coils of smaller diameters. This series of consecutive 3D coils results in a concentric, shell-like arrangement of several 3D coils. This technique is labeled the 'concentric-filling' technique or the 'coil-in-coil' technique and is also known as the 'Russian-doll' technique (Figure 1).

It is believed that this peculiar concentric arrangement of 3D coils can minimize potential empty spaces left between coil loops and thus provide a firm frame for filling the remaining spaces. The purpose of this study is to report our initial experience of concentric-filling technique using MicruSphere 3D coils for the treatment of intracranial saccular aneurysms.

Materials and Methods

Patients

From March 2005 to December 2006, 149 intracranial saccular aneurysms in 142 consecutive patients were treated with MicruSphere Microcoils. Patient demographics are summa-

rized in Table 1. The average patient age was 56.5 years, ranging between 23 and 87 years. The patients were predominantly female (83.8%). Fifty-four patients (36.2%) had subarachnoid haemorrhage (SAH). Patients with ruptured aneurysms were clinically assessed using the Hunt and Hess (HH) grading scale. Upon admission, SAH patients were assigned the following HH grades: grade I in 9/54 (16.7%) patients; grade II in 18/54 (33.3%) patients; grade III in 13/54 (24.1%) patients; grade IV in 7/54 (13.0%) patients; and grade V in 7/54 (13.0%) patients. Among the patients with unruptured aneurysms, the majority (80%) were diagnosed incidentally or following a patient complaining of a headache. In the remaining patients, five presented with cranial nerve palsy, five with visual disturbance, four with transient neurological deficit, one with seizure, one with mass effect, two with retro-orbital pain, and one with tinnitus.

Aneurysm Characteristics

One-hundred-eighteen (79.2%) aneurysms were located in the anterior circulation and 31 (20.8%) were in the posterior circulation (Table 2). As shown in Table 3, in this series there was a range of aneurysm sizes with domes less than 4 mm (very small) to more than 25 mm (large). There were 19 tiny aneurysms (dome <4 mm) (12.8%), 63 (42.3%) small-dome (dome <10 mm) and narrow-necked (<4 mm) aneurysms. Forty-two (28.2%) had a small dome and wide neck (dome <10 mm, neck ≥4 mm). There were 24 (16.1%) large aneurysms (dome ≥10 mm) and one (0.7%) giant aneurysm (dome ≥25 mm).

Embolization Procedure

All procedures were performed in the angiography suite equipped with biplane angiographic machines (Siemens Axiom Artis, Erlangen, Germany) while the patient was under general anesthesia. Informed consent was obtained for each patient. For the elective procedures, patients were pretreated with aspirin (325 mg daily) and clopidogrel (75 mg daily following a 300-mg loading dose, Plavix; Sanofi-Aventis) starting five to ten days before the procedure if the use of a stent was anticipated. In cases of ruptured aneurysm, the loading dose of clopidogrel was given together with aspirin via an oro-gastric tube immediately before the stent-assisted embolization. All proce-

Table 1 **Basic demographics of the patients and lesion characteristics.**

No. of patients			142
Female (%)		119 (83.8%)	
Age	Mean $\pm$ S.D (yr)	56.5 $\pm$ 12.7	
	Range (yr)	23-87	
No. of treated aneurysms			149
Ruptured (%)		54 (36.2%)	
Hunt and Hess grade (%)			
	I	9 (16.7%)	
	II	18 (33.3%)	
	III	13 (24.1%)	
	IV	7 (13.0%)	
	V	7 (13.0%)	
Unruptured (%)		95 (63.8%)	
	Incidental and/or headache	76	
	Cranial nerve palsy	5	
	Visual disturbance	5	
	Transient neurological deficit	4	
	Seizure	1	
	Mass effect	1	
	Retro-orbital pain	2	
	Tinnitus	1	
Location of aneurysms			
Anterior circulation (%)		118 (79.2%)	
	Cavernous ICA	6	
	Ophthalmic and paraophthalmic	20	
	Superior hypophyseal	21	
	PCoA	27	
	AChA	2	
	ICA terminal	4	
	MCA bifurcation	10	
	ACA A1	2	
	ACoA	24	
	ACA A2	2	
Posterior circulation (%)		31 (20.8%)	
	BA trunk	4	
	PICA	5	
	SCA	4	
	Basilar tip	18

Figure 2 Initial angiographic results according to the size of the aneurysm. Tiny: aneurysm with a dome < 4 mm, SS: small-dome (< 10 mm) and narrow-necked (< 4 mm) aneurysm, SW: small-dome (< 10 mm) and wide-necked (≥ 4 mm) aneurysm, large: aneurysm with a dome ≥ 10 mm including giant aneurysm.

dures were performed under systemic heparinization regardless of the aneurysm rupture. The target-activated clotting time was twice that of the baseline.

We used the same embolization technique previously described^{7,8}. Stent (Neuroform; Boston Scientific Corp., Fremont, CA) or bal-

loon-assisted (Hyperform or Hyperglide; EV3 Endovascular, Irvine, CA) embolization was performed in aneurysms with a relatively wide neck. There was no strict indication regarding the use of MicroSphere Microcoils, and the selection of the coils during the embolization procedures was based on the physician's preference.

The MicroSphere microcoil is a spherically shaped detachable coil. The first distal loop is 25% smaller in diameter than the remaining loops. The coil loops deploy in 90-degree, full-loop increments, thus providing a predictable coil deployment. The 3D coil was designed to provide a structural framework within the aneurysm walls and neck while retaining an open inner core. This characteristic is balanced with the coil's ability to conform anatomically to aneurysms of various shapes and sizes (Figure 1).

A 3D coil was used for the initial framing in every aneurysm, even in the smallest aneurysms as the loop diameter of the smallest 3D coil available was as small as 2 mm. To achieve a Russian-doll-like concentric filling of the

Table 2 Summary of the size and volume of the aneurysms and the various coils used for embolization.

Aneurysm size		
	Tiny (dome < 4 mm) (%)	19 (12.8%)
	Small dome and narrow neck (dome < 10 mm, neck < 4 mm) (%)	63 (42.3%)
	Small dome and wide neck (dome < 10 mm, neck ≥ 4 mm) (%)	42 (28.2%)
	Large aneurysm (dome ≥ 10 mm)	24 (16.1%)
	Giant (dome ≥ 25 mm)	1 (0.7%)
Volume (mm ³)	Mean $\pm$ S.D. (range)	169 $\pm$ 363.0 (8.4 – 2563.5)
Embolization techniques		
	Balloon-assisted (%)	69 (46.3%)
	Stent-assisted (%)	40 (26.9%)
	Use of both balloon and stent (%)	11 (7.4%)
Coil volume (mm ³)	Mean $\pm$ S.D. (range)	52.6 $\pm$ 98.8 (3.0 – 746.8)
Surface-modified coils (%)		36 (24.5%)
	Cerecyte coils	29
	Matrix coils	6
Hydrocoils (%)		18 (12.1%)

coils, successive smaller-size 3D coils were used in the filling phase of the embolization procedure. After detaching the first framing coil, successive 3D coils with one-step smaller diameters, were deployed to fill the inner core space in concentric coil-in-coil fashion. We tried to use as many 3D coils as possible. Residual space which seemed not to fit for the 3D coils, was filled with standard and/or soft helical coils (Helipaq and Ultipaq; Micrus Endovascular, San Jose, CA).

There were several patients who were treated with the combined use of other types of detachable coils based on the physicians' preference. Surface-modified coils (Matrix; Boston Scientific Corp. or Cerecyte; Micrus Endovascular) were used in some patients. Hydrocoils (Microvention) were used for the filling of several large aneurysms.

Analysis and Statistics

The study was performed under the approval of local institutional review board. Information on each patient's clinical condition was obtained by retrospective review of the medical records. Angiographic images were reviewed through the PACS and/or 3D data sets which were stored in the separate storing device. The size of the aneurysm was primarily measured in three dimensions using 3D angiograms. 2D angiographic images were used if the 3D images were unavailable. All aneurysms were assumed to have an elliptical shape, and the distance was measured in three representative dimensions. A representative set of frontal and lateral angiographic images was used for the 2D angiographic images. Aneurysm volume was calculated using a web-based calculation software program (www.angiocalc.com).

Procedure-related complications were recorded and the associated mortality and morbidity were analyzed on an aneurysm basis. The initial embolization results were evaluated using the Raymond and Roy angiographic classification of coil embolization⁹. The coil-packing density was also calculated. Subgroup analysis was performed in terms of aneurysm size. The difference in packing density in terms of coil type used was also analyzed.

The mean hospital stay and immediate clinical outcome were analyzed on an individual patient basis using the Glasgow outcome scale (GOS) of 1 (deceased) to 5 (able to return to work).

Figure 3 This histogram shows the difference in coil packing density according to the size (dome and neck) difference of the aneurysms. SS: small dome and narrow neck, SW: small dome and wide neck.

Follow-up clinical and angiographic examinations were obtained six months after initial treatment. The clinical outcome was evaluated in terms of symptom recurrence. The angiographic findings were analyzed in terms of the stability of embolized aneurysms. The follow-up status of each aneurysm was categorized as 'improved' (decrease of residual neck and/or sac filling), 'unchanged' (no angiographic change from the initial status) or 'worse' (increase of aneurysm filling including recanalization). The influence of combined coil types on the angiographic results, as seen on follow-up, was analyzed. In addition to reporting the retreatment rate, the modified Raymond and Roy classification was used to evaluate the angiographic outcome immediately post-treatment and at follow-up.

Results

The most common procedure-related complication was acute thrombosis which occurred during or immediately after completion of the embolization at the aneurysm-parent artery interface or within the stent lumen (Table 3). This thrombus formation was noted in 16 aneurysms (10.7 %), five of which were in-stent thromboses following insertion of the Neuroform

stent. Thrombus formation was frequent in ruptured aneurysms (20.4% vs. 7.4%, $p = 0.034$, Fisher exact test), however, the filling defects disappeared with prompt use of weight-based, intravenous administration of abciximab after which there were no clinical consequences. Other procedure-related problems and related morbidity and mortality are summarized in Table 3. Most of the incidents were asymptomatic or with transient symptoms. The morbidity and mortality were noted in six (4.0%) and two (1.3%) patients.

Initial angiographic embolization results according to the Raymond and Roy classification, were class 1 in 37 (24.8%), class 2 in 50 (33.6%), and class 3 in 62 aneurysms (41.6%) (Table 4). The initial angiographic embolization classification as a function of aneurysm size is shown in Figure 2.

The overall coil packing density was 40.1% (range, 10.5-90.9%). There was a trend toward decreased packing density with increase of the

size of the aneurysm sac (Figure 3). In cases of combined use of other types of coil, the mean coil volume percentages of the surface-modified coils ($n=35$) and Hydrocoils ($n=18$) were 59.0% (range, 6.5 – 93.5%) and 61.1% (range, 29.1 – 60.6%), respectively. Their corresponding packing densities were 35.1% (range, 12.7 – 55.1%) and 46.6% (range, 14.9 – 76.0%), respectively. The mean packing density of the 120 aneurysms embolized without use of any surface-modified coil, was 41.3% (range, 10.5 – 90.9%).

The mean patient hospital stay was 7.6 days (median: 2; range: 2-49), and the immediate clinical outcome according to the Glasgow outcome scale (GOS) was GOS 5 in 108 patients (76.1%), GOS 4 in 15 (10.6%), GOS 3 in 11 (7.7%), GOS 2 in four (2.8%), and GOS 1 in four patients (2.8%).

On clinical follow-up of 103 patients (72.5%) at a mean interval of 8.2 months after the initial procedure (range: 0.7-26 months), there were

Table 3 Procedure-related problems and related morbidity and mortality rates.

Problems	Frequency (% per aneurysm)	Transient symptom	Permanent morbidity	Mortality
Acute thrombosis in the stent or aneurysm/parent artery interface	16 (10.7%)	0	0	0
Thromboembolism	9 (6.0%)	4	4	1
Intraprocedural rupture of the aneurysm	3 (2.0%)	0	1	1
Parent artery occlusion	2 (1.3%)	0	0	0
Cranial nerve palsy	2 (1.3%)	1	1	0
Coil loop prolapse	4 (2.7%)	0	0	0
Groin/retroperitoneal Hematoma	3 (2.0%)	3	0	0
Total (%)	39 (26.2%)	8 (5.4%)	6 (4.0%)	2 (1.3%)

Table 4 Follow-up angiographic change according to the initial Raymond and Roy classification.

Initial Raymond and Roy classification	Improved	Unchanged	Worse	Final Raymond and Roy classification
Class 1 ($n=28$)	NA	26	2	60 (59.4%)
Class 2 ($n=33$)	13	11	9	27 (26.7%)
Class 3 ($n=62$)	29	5	6	14 (13.9%)
Total	42 (41.6%)	42 (41.6%)	17 (16.8%)	101 (100%)

one transient ischemic attack, one minor stroke, and one instance of rebleeding. Angiographic follow-up was obtained for 101 aneurysms (67.8%) at a mean of 8.3 months after the initial procedure (range: 0.7-26 months). The results of their angiographic change on follow-up according to the initial Raymond and Roy classification are summarized in Table 4. The category of 'worse' is also equivalent to recanalization and was noted in 17 aneurysms which included two cases initially ranked as class 1, nine cases as class 2, and six cases as class 3. The overall recanalization rate was 16.8%. Recanalization was observed in ten (13.9%) out of 72 unruptured cases and seven (24.1%) out of 29 ruptured cases ($p=0.245$). There were no significant differences in the recanalization rate between the cases of stent assistance (8/33, 24.2%) and that without assistance (9/68, 13.2%) ($p=0.256$).

However, the majority of the aneurysms remained in a stable state (41.6%) or showed improvement of the embolization status (41.6%) on this mid-term angiographic follow-up examination. The final Raymond and Roy angiographic classification was class 1 in 59.4% of our patients, class 2 in 26.7%, and class 3 in 13.9%. In this series, 11 aneurysms were re-treated (repeated embolization in ten and surgical clipping in one) due to worsening of the embolization status in ten aneurysms and persistent residual sac in one.

Discussion

Embolization of ruptured or unruptured intracranial aneurysms using the 'concentric-filling' technique with 3D MicroSphere coils was effective in achieving a higher packing density. The average packing density of approximately 40% that we achieved in this series was higher than that in any other report based on the use of conventional bare coils. Higher packing density can be achieved by inserting a higher volume of coils in the aneurysm sac. However, if non-hydrogel-coated coils are used, the likelihood of obtaining a higher packing density merely by increasing the total length of a certain coil would be minimal even using coils made of thicker coil wire or softer finishing coils^{10,11}.

This study hypothesized that higher packing density could be maximized by minimizing potential dead spaces between the coil wires within the conglomerated coil mesh. The character-

istics of the MicroSphere coils provided a thin, shell-like configuration of deployed coil mesh, thereby leaving a virtually smaller sac volume which could be filled and contracted with subsequent use of another 3D coil of one-size smaller diameter. We believe that this "Russian doll"-like configuration of the coil mass would yield a smaller dead space than the coil mass made by random deposition of coils. We thought that this coiling configuration was the major reason for the higher packing density in our series. This theory is consistent with previous data published by Vallee et al who reported that when three or more 3D coils were first positioned in the aneurysm the packing density increased¹².

It is notable that the overall rate of aneurysm occlusion or improvement of embolization status appeared improved on follow-up angiography. This has not been consistently documented even though we have frequently observed this phenomenon in our practice. Berenstein et al. reported approximately a 28% improvement in the angiographic embolization status on follow-up in their series with Hydrocoils¹³. In our series, we observed frequent late improvement of the embolization status which significantly outweighed the rate of recanalization. This improvement was noted in 41.6% of our study group while recanalization was noted in 16.8%. We believe that this difference may be attributed to the accelerated aneurysm healing process after coil embolization secondary to the changes in the local hemodynamics and the resulting endothelial response¹⁴.

Endovascular treatment of wide-neck aneurysms is challenging because of the coil prolapse which can be minimized or prevented either by using a neck-remodeling technique with balloon catheters¹⁵ or by one of the currently available, self-expandable stents or with complex 3D coils⁴. The use of more than two microcatheters has been proposed as an alternative method for increasing the stability enhancement of the initial framing coils¹⁶. Among those methods, we preferred using the stent-assisted technique.

We do not believe that the relatively frequent occurrence of thrombus formation in our series was related to the use of a specific type of coil. This acute complication occurred almost three times more frequently in patients with ruptured aneurysms. It is believed that improvement of the image quality has helped to

increase the early detection of small filling defects at the coil-parent artery interface or in the stent. As reported by Song et Al. prompt use of intravenous abciximab can successfully dissolve a thrombus¹⁷. In our series this was possible in every patient without any adverse clinical consequences.

There are several limitations to our study. The most important limitations are its retrospective nature and the lack of follow-up data in approximately one-third of our study patients. The aneurysm volume measurement method is also believed to have been inconsistent due to the retrospective nature of our study. However, as there was no significant difference between volume assessments using conventional DSA images and that using the dedicated 3D volume calculation software embedded in the post-processing equipment (Leo-

nardo; Siemens Medical System, Erlangen, Germany), we believe that the lack of 3D data sets in some of the patients had little impact on the measured packing density. The other study limitations are the predominance of female patients and the higher percentage of unruptured aneurysms in our series.

Conclusions

According to our study, 3D MicruSphere Microcoils were effective in achieving a good coil packing density in either ruptured or unruptured aneurysms using a concentric filling technique. Therefore, improvement of embolization status was frequently noted on follow-up angiography. Our initial clinical outcome and mid-term angiographic follow-up results are comparable to those of other reports.

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