

**NEW DEVELOPMENTS**  
*in imaging and treatment of*  
**INTRACRANIAL ANEURYSMS**



Anjob Nathalie de Gast

# **NEW DEVELOPMENTS IN IMAGING AND TREATMENT OF INTRACRANIAL ANEURYSMS**

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# Chapter 1

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## Introduction

In the past two decades, new techniques in imaging and treatment of intracranial aneurysms have been introduced that greatly influenced clinical practise.

Since the introduction of detachable coils in the early nineties of the last century, the endovascular treatment of intracranial aneurysms has largely overtaken the surgical approach. Coiling has several advantages over surgery: it is less invasive, has better outcome, and can be performed in patients with acutely ruptured aneurysms in poor clinical condition. The only disadvantage of coiling is the possibility of reopening of the aneurysm with time due to coil compaction necessitating additional coil treatment. This occurs in about 10% of coiled intracranial aneurysms and imaging follow up of all coiled aneurysms is mandatory. Follow up angiography is invasive and is associated with patient discomfort and relatively high costs. Non-invasive imaging with sufficient resolution to replace follow up angiography would be welcomed by patients and institutions.

In an attempt to reduce the reopening rate of aneurysms after coiling, several new types of coils, coated with “biologically active” substances, have been developed. These substances were intended to accelerate the natural biological processes involved in cellular proliferation and healing of the aneurysm orifice on the parent artery thereby reducing the risk of reopening.

Parallel to this dramatic change in aneurysm therapy, improvements in imaging of intracranial aneurysms has facilitated diagnosis and follow up. Digital subtraction catheter angiography (DSA) has moved to a higher level owing to the introduction of 3D Rotational Angiography (3DRA). With this technique, high resolution 3D images of the cerebral vessels can be acquired that can be freely rotated. With 3DRA, small aneurysms are more easily depicted and evaluation of local aneurysm anatomy is more reliable. With use of 3DRA, time-consuming evaluation of aneurysm anatomy with multiple 2D projections is redundant. With 3DRA new angiographic insight in anatomic variations such as arterial fenestrations is offered. Another major step forwards is the development of non-invasive angiographic imaging techniques with CT and MR. CT is performed with increasing multi-slice techniques and MR with increasing field strength. With CT Angiography (CTA) and MR Angiography (MRA), imaging of cerebral vessels can be performed without the need for catheterization and with less patient discomfort. Image resolution of CTA and MRA is not yet sufficient for reliable aneurysm depiction and evaluation of anatomy in the acute setting of aneurysm rupture but can play a major role in follow up imaging after treatment and in screening. The increased use of CT and MRI in general has resulted in detection of more asymptomatic intracranial aneurysms. In the decision whether or not to treat these incidentally found aneurysms, risk of rupture has to be balanced against the risk of treatment.

The aim of this thesis is to describe consequences for diagnosis, treatment and imaging follow-up in some aspects of these new developments in imaging and treatment.

In chapter 1, we compared a newly developed coil coated with transforming growth factor- $\beta$  (TGF- $\beta$ ) with a standard platinum coil in a rabbit model for cellular proliferation on the transition of aneurysm and parent artery.

In chapter 2, we clinically evaluated another new type of coil with interwoven polyglycolic/polyactid (PGLA) microfilament threads in 101 aneurysms and results were compared to historical results of aneurysms treated with standard coils.

In chapter 3, we evaluated the clinical results of coiling of 58 asymptomatic aneurysms in 48 patients, discovered on CT or MRI performed for reasons unrelated to the aneurysm. Treatment complications and results of follow-up were compared with natural history of patients with incidental aneurysms that were not treated. In addition, clinical decision making in indication for treatment or non treatment was observed.

In chapter 5, we used a newly installed MRI at 3.0 Tesla as mid term imaging follow up in 39 patients with unruptured large and giant carotid artery aneurysms that presented with symptoms of mass effect and were treated with therapeutic carotid artery occlusion. In particular, we assessed whether aneurysm size decreased with time and sought to find a relation with evolution of clinical symptoms.

In chapter 6, we used a newly developed high resolution 3.0 Tesla MRA protocol to assess the incidence of de novo aneurysm formation and growth of existing untreated aneurysms in 39 patients mid-term after therapeutic carotid artery occlusion for carotid artery aneurysms.

In chapter 7, we used 3D Rotational Angiography to assess the incidence of visible fenestrations of the anterior communicating artery and evaluated the relationship with aneurysms on this location.

In chapter 8, we evaluated whether introduction of 3D Rotational Angiography, among other factors, reduced procedural time of coiling. Procedural time of coiling of 642 aneurysms was assessed and risk factors for long procedural time were sought for.

In chapter 9, a summary of this thesis is provided.



## Chapter 2

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### **Transforming growth factor $\beta$ -coated platinum coils for endovascular treatment of aneurysms: an animal study**

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## ABSTRACT

### OBJECTIVE

To test the hypothesis that coating platinum coils with transforming growth factor  $\beta$  (TGF $\beta$ ) would improve the cellular proliferation within experimental aneurysms relative to uncoated coils.

### MATERIALS AND METHODS

Elastase-induced saccular aneurysms were created in 12 New Zealand White rabbits. These aneurysms were embolized with platinum coils, either “control” (unmodified) coils or “test” (coated with TGF $\beta$ ) coils. Subjects were killed either 2 weeks (n= 3, control; n= 3, test) or 6 weeks (n= 3, control; n= 3, test) after embolization. Aneurysm tissue was embedded in plastic, sectioned, and stained with hematoxylin and eosin. The thickness of tissue covering the coils at the coil-lumen interface was measured by use of a digital microscope, and was compared between groups by use of the Student’s t test.

### RESULTS

Two-week implantation samples demonstrated mean thickness of tissue overlying TGF $\beta$  -coated coils of  $36 \pm 15\mu\text{m}$  and mean thickness of overlying control coils of  $3 \pm 5 \mu\text{m}$ , indicating significantly thicker tissue growth covering test versus control coils ( $P = 0.02$ ). Six-week implantation samples demonstrated mean thickness of tissue overlying TGF $\beta$  -coated coils of  $86 \pm 74 \mu\text{m}$  versus mean thickness overlying control coils of  $37 \pm 6 \mu\text{m}$  this difference did not reach statistical significance ( $P = 0.30$ ). Thickness of tissue covering TGF $\beta$  -coated coils did not change significantly from 2 to 6 weeks ( $P = 0.31$ ). Tissue thickness over control coils increased significantly between 2 and 6 weeks ( $P = 0.002$ ).

### CONCLUSION

TGF $\beta$  -coated platinum coils undergo earlier cellular coverage than standard platinum coils, but differences in coverage between coated and control coils are no longer present at later time points. These data suggest that improvements in intra-aneurysmal cellular proliferation resulting from coil modifications, although significant in the early postembolization phase, may dissipate over time.

### KEY WORDS

Aneurysm, Animal model, Embolization, Growth factors

## INTRODUCTION

Guglielmi detachable coils (GDCs) (Target Therapeutics, Fremont, CA) represent an important advance in minimally invasive therapy of cerebral aneurysms. Numerous reports have demonstrated the clinical efficacy of GDCs in diminishing rates of rehemorrhage in ruptured aneurysms<sup>(9,11,16)</sup>. The relative efficacy of GDCs is influenced by aneurysm size; small aneurysms demonstrate excellent long-term occlusion rates, but large and giant aneurysms demonstrate disappointing rates of stable, aneurysm occlusion<sup>(5,8,10,11,16,21)</sup>.

Because of relatively disappointing results in the treatment of large and giant aneurysms with GDCs, several investigators have proposed modifications to the coil to improve occlusion rates in these aneurysms<sup>(1,3,6,7,12,14,15,17,19,22,23)</sup>. These coil modifications are aimed primarily at increasing the “biological activity” of the GDC, because standard GDCs are relatively biologically inert and fail to induce scar formation in large aneurysms<sup>(8,10,11,16)</sup>. Three classes of biological modification have been proposed previously. First, the addition of a collagen filament to the core of the GDC has been tested in a swine model<sup>(6,7,23)</sup>. Second, tissue allografts, including fibroblasts and smooth muscle cells, have been added to embolic agents to improve cell growth in experimental aneurysms<sup>(15,19,22)</sup>. And last, a number of coil coatings have been proposed to increase biological activity. These coatings include basement membrane and extracellular matrix proteins, proteins involved in the fibrinolytic pathway, and peptide growth factors<sup>(1,3,12,14,17)</sup>. Several of these coatings have demonstrated promise in a swine model of saccular aneurysms, but a recent report in a rabbit model with modulators of the fibrinolytic system demonstrated no improved efficacy in increasing intra-aneurysmal fibrosis as compared with standard coils<sup>(3)</sup>.

Transforming growth factor  $\beta$  (TGF $\beta$ ) is an ubiquitous growth factor that has been demonstrated to increase collagen synthesis, and endothelialization in vivo. These biological functions would be considered beneficial in the setting of coil embolization of aneurysms. TGF $\beta$  has been demonstrated previously to adhere to the surface of platinum coils in vitro<sup>(13)</sup>. In the current study, we explore the histological differences, by use of a rabbit aneurysm model, between standard platinum coils and platinum coils coated with TGF $\beta$ , specifically regarding the rate and degree of cell growth over intra-aneurysmal coils.

## MATERIALS AND METHODS

### ANEURYSM CREATION

All animal experimentation was approved by the animal research committee at our institution. Details of aneurysm creation are available in published reports<sup>(2,4)</sup>. Twelve New Zealand White Rabbits (3-4 kg) were used for this study. Each animal was anesthetized with 60 mg/kg of intramuscularly administered ketamine (Ketavet; Vedco, St. Joseph, MO) and 6 mg/kg xylazine (Traqived; Vedco). Heparin, 100 U/kg, was administered intravenously. By use of sterile technique, a 3-cm longitudinal incision was made in the midline of the neck.

The right common carotid artery (CCA) was exposed for approximately 1.5 cm. Three 3-0 silk sutures were passed around the artery. The distal aspect of the artery was legated with one of the silk sutures. An arteriotomy was performed and a 5-French vascular sheath was passed retrograde into the CCA, with its tip resting approximately 3 cm cephalad to the origin of the CCA. Under fluoroscopic guidance, a 3-French Fogarty balloon catheter (Baxter Healthcare Corp., Deerfield, IL) and a Tracker 10 microcatheter (Target Therapeutics) were passed through the diaphragm of the sheath. The balloon was inflated at the bifurcation of the right CCA and the right subclavian artery. Porcine elastase, 200 U, (Sigma Chemical Co., St. Louis, MO, and Worthington Biochemical, Lakewood, NJ) was mixed with Omnipaque 300 iodinated contrast (Nycomed, Princeton, NJ) and saline. This elastase-contrast-saline mixture was injected through the microcatheter and incubated within the CCA lumen for 20 minutes. The Fogarty balloon was deflated and removed. After the procedure, the animals were allowed to recover for 2 weeks before embolization.

### **COATING OF PLATINUM COILS WITH TGF $\beta$**

Previous studies have demonstrated prolonged adherence of TGF $\beta$  to the surface of platinum coils by simple co-incubation of the coils with the growth factor<sup>(13, 20)</sup>. TGF $\beta$  (Sigma) reconstituted in bovine serum albumin to a concentration 1  $\mu$ g/ml was prepared. Coil samples were incubated in this solution for 2 hours, followed by immediate implantation into aneurysms.

### **ANEURYSM EMBOLIZATION PROCEDURE**

With the elastase-induced aneurysm technique as used in New Zealand White Rabbits, it is impossible to precisely predict the size and shape of resultant aneurysm. For the current study, we specifically chose aneurysms with relatively narrow necks (dome-to-neck ratio  $\geq 1.5:1$ ) to facilitate coil embolizations. Aneurysm sizes were approximately 4 mm diameter for all cases. Before embolization, the animals each were premedicated as indicated previously. Heparin (100 U/kg) was given intravenously to prevent thromboembolic complications. A 4-French vascular sheath was placed in the right common femoral artery. A 4-French catheter was advanced to the origin of the brachiocephalic artery. An external sizing device was placed on the chest to aid in choice of appropriate coils. Digital subtraction angiography was performed. By use of coaxial technique, a Tracker 10 microcatheter was advanced into the aneurysm cavity. GDC embolization of the aneurysms was performed by use of either control (untreated) GDCs (n=6) or TGF $\beta$ -coated T10 coils (n=6), sized appropriately to the diameter of the aneurysm cavity. A single T10 coil, 4 mm x 10 cm, was used for embolization in each case. Because we were highly focused on the interface between the coil and flowing blood within an aneurysm, we chose to use a single coil for embolization to ensure some ongoing intra-aneurysmal flow after coil insertion. After embolization, the microcatheters and guiding catheters were removed, the femoral sheath was removed, and the femoral artery was legated. The skin over the femoral artery was closed with running suture.

## **HISTOLOGICAL EVALUATION**

Animals survived for either 2 weeks ( $n=3$ , control animals;  $n=3$ , TGF $\beta$ -coated coil animals) or 6 weeks ( $n=3$ , control animals;  $n=3$ , TGF $\beta$ -coated coil animals). The animals were killed with a lethal dose of pentobarbital. The aortic arc and the brachiocephalic vessels were removed en bloc and placed in formalin for at least 24 hours. The samples were embedded in methylmethacrylate, sectioned at 30  $\mu\text{m}$  increments, and stained with hematoxylin and eosin. Qualitative histological evaluation was performed by two experienced observers. These observers characterized the cellular infiltration within the aneurysm lumen globally, with particular attention to the type of cellular infiltration (nucleated cells, red blood cells, or thrombus). Detailed characterization of the cells immediately adjacent to the coils also was performed.

## **QUANTITATIVE HISTOPATHOLOGY**

Stained tissue sections were viewed by two experienced observers, blinded to the treatment group, by use of an Olympus BH2 microscope (Olympus Optical Co., Tokyo, Japan) connected to an MTI (Irvine, CA) digital camera. A calibrated slide with 10-m minor units and 100-m major units was used to set the calibration scale. The thickness of tissue overlying two coil loops was measured for each sample. The thickness of tissue was compared between control versus test coils at 2 weeks and at 6 weeks, between control coils at 2 weeks versus control coils at 6 weeks, and between test coils at 2 weeks versus 6 weeks by use of the Student's  $t$  test.

## RESULTS

### QUALITATIVE HISTOPATHOLOGY

Samples of the aneurysms with standard GDCs collected 2 weeks after embolization demonstrated unorganized thrombus involving the majority of the aneurysm cavity. Red blood cells were noted within the central lumina of the coil winds. There was no evidence of cellular proliferation on the implanted coils, within the central lumen of the coils, or across the necks of the aneurysms (Fig. 1).

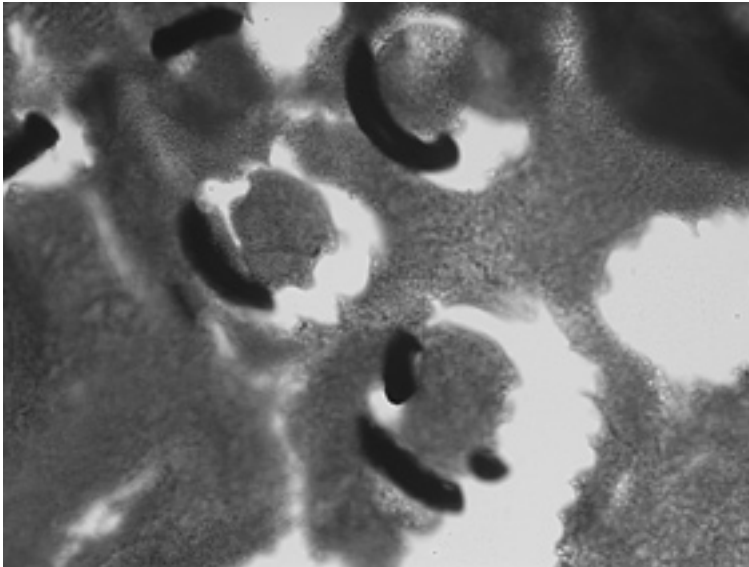


Fig 1. Control coil, 2 weeks after implantation. Coil winds have been displaced slightly from their original position, leaving serrated clear spaces that indicate the initial position of the coil. All tissue surrounding all coil loops consists of red blood cells, without evidence of infiltration by nucleated cells (hematoxylin and eosin; original magnification, x 100).

Conversely, TGF $\beta$ -coated coil samples at 2 weeks demonstrated multiple nucleated cells proliferating over the surface of the coils and within the central lumen of the coils. Measurable tissue was present over the surface of the coils at their point of contact with the aneurysm neck (Fig. 2).



Fig 2. TGF $\beta$ -coated coil, 2 weeks after implantation. Coil winds have been displaced slightly from their original position, leaving serrated clear spaces that indicate the initial position of the coil. There is a measurable thickness of cell growth over the coil loop (arrows). Nucleated cells also are present within the central lumen of the coil (hematoxylin and eosin; original magnification, x 100).

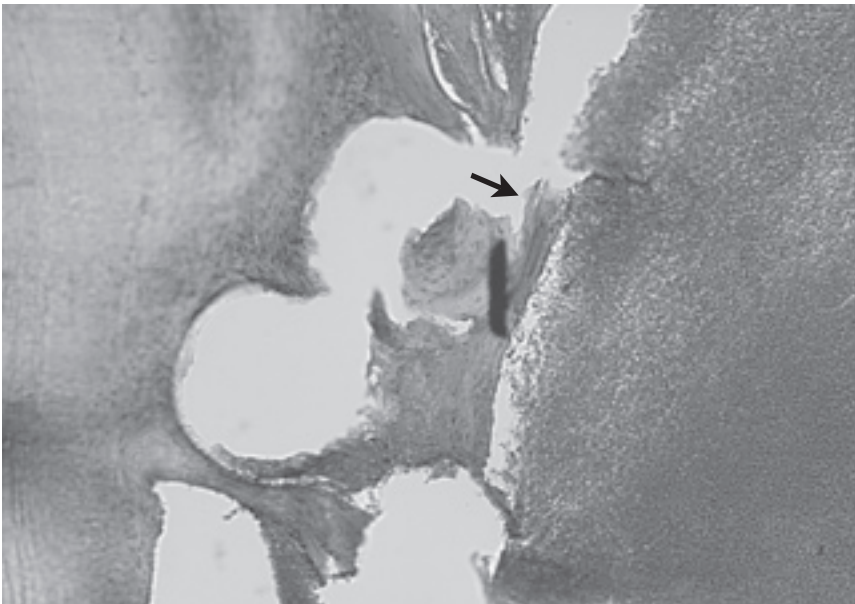


Fig 3. Control coil, 6 weeks after implantation. There is a measurable thickness of cell growth over the coil loop (arrows). Nucleated cells also are present within the central lumen of the coil (hematoxylin and eosin; original magnification, x 100).

Among the samples of the aneurysms with standard GDCs collected 6 weeks after embolization, coil winds were found primarily along the periphery of the aneurysms. As such, it was straight forward to compare similar portions of the aneurysm in different cases.

Although most of the aneurysm lumens were filled with involuting thrombus, measurable areas of cellular proliferation were present over the surface of the coils in these 6-week control samples (Fig. 3). Qualitative histopathology findings for the 6-week TGF $\beta$ -coated GDCs were nearly identical to those observed in the 2-week TGF $\beta$ -coated samples.

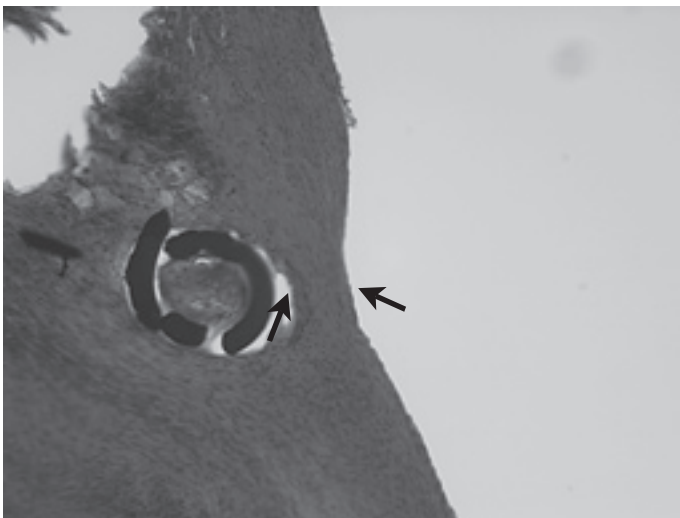


Fig 4. TGF $\beta$ -coated coil, 6 weeks after implantation. Cell growth is observed over the surface of the coil (arrows) (hematoxylin and eosin: original magnification, x 100).

Specifically, there were multiple nucleated cells proliferating over the surface of the coils and within the central lumen of the coils. Measurable tissue was present over the surface of the coils at their point of contact with the aneurysm neck (Fig. 4).

#### QUANTITATIVE HISTOPATHOLOGY

We noted a statistically significant difference at 2 weeks in the thickness of the cellular layer covering the TGF $\beta$ -coated coils (mean thickness,  $36 \pm 15 \mu\text{m}$ ) versus that of covering control coils (mean thickness,  $3 \pm 5 \mu\text{m}$ ) ( $P = 0.02$ ). Cellular coverage was nearly completely absent over all coil loops in the control samples at 2 weeks, and a measurable thickness of tissue was noted over all TGF $\beta$ -coated coils at 2 weeks.

At 6 weeks after implantation, the control coils demonstrated a significant increase in thickness covering the coils as compared with control coils at 2 weeks ( $37 \pm 6 \mu\text{m}$  at 6 wk versus  $3 \pm 4 \mu\text{m}$  for control coils at 6 and 2 wk, respectively;  $p = 0.002$ ). TGF $\beta$ -coated coils demonstrated a trend toward increased thickness from

2 to 6 weeks, but this difference did not reach statistical significance. Notably, there was no statistically significant difference at 6 weeks between the thickness covering control coils versus that covering TGF $\beta$ -coated coils ( $37 \pm 6 \mu\text{m}$  versus  $86 \pm 74 \mu\text{m}$  for control and TGF $\beta$ -coated coils, respectively;  $P=0.30$ ).

## DISCUSSION

In this study, we compared the “biological activity,” defined as the degree of cellular proliferation around and within coils, of standard platinum coils with that of platinum coils coated with TGF $\beta$  in a rabbit model of secular aneurysms. TGF $\beta$  was chosen for this study because it is a growth factor that plays a prominent role in wound healing and because it binds nonselectively to various inorganic surfaces, including platinum coils<sup>(13,20)</sup>. We demonstrated that coating with TGF $\beta$  improves cellular coverage early after coil implantation as compared with standard coils. However, the difference in degree of cellular proliferation over coils dissipated over time; in our model, no difference was observed between TGF $\beta$  coated coils and control coils at 6 weeks.

Numerous authors have proposed methods for increasing the “biological activity” of platinum coils to improve occlusion rates in cerebral aneurysms. Collagen and other basement membrane coatings, collagen filaments, growth factors and other proteins, polymers, and cells have been added to platinum coils to improve fibrotic reaction to implanted coils<sup>(6,7,17,23)</sup>. Although some of these techniques demonstrated promise in preclinical testing, none has reached clinical application. Most of these coil modification techniques were tested in a swine model of aneurysms; this model evidently undergoes spontaneous thrombosis and fibrosis even without treatment. To our knowledge, none of the preclinical testing in swine of modified platinum coils has included an untreated control arm, rendering it impossible to interpret histological findings in treated aneurysms. A recent report used a surgically created aneurysm in rabbits to test the efficacy of plasminogen activation inhibitor in improvement of intra-aneurysm healing<sup>(3)</sup>. These latter authors failed to demonstrate improvement in cellular proliferation over the coils by use of plasminogen activation inhibitor coatings.

We hypothesize that thin coatings of bioactive substances on platinum coils are unable to effect metabolic changes at any significant distance from the coil surface. Because only a small minority of the volume of a coil-embolized aneurysm contains coil, and the majority of the volume represents blood, it is reasonable to assume that improvements in healing must reach long distances relative to coating thickness. Our TGF $\beta$  coating was able to improve cellular coverage at early time points after embolization, but these differences did not persist. We hypothesize that more durable improvements may occur with the use of bioactive substances that either permeate further into the thrombus surrounding the coil loops or are produced during a prolonged period of time. Although our study failed to demonstrate prolonged “bioactivity” within experimental aneurysms by use of a TGF $\beta$  coating, we remain optimistic that TGF $\beta$ , when delivered in larger amounts or in a more prolonged fashion than in

this study, may improve intra-aneurysmal fibrosis. As stated above, we chose to focus on TGF $\beta$  among many available growth factors, not only because it plays a prominent role in wound healing but also because it has been demonstrated to bind nonselectively to various inorganic surfaces<sup>(18,20)</sup>. TGF $\beta$  is released from platelet  $\alpha$ -granules and influences many of the cells involved in wound healing. TGF $\beta$  enhances epithelial cell coverage<sup>(12)</sup> and stimulates fibroblasts to produce Type I collagen and fibronectin<sup>(17)</sup>. All of these biological actions are considered by us to be desirable within coil-embolized aneurysms. Prolonged delivery of growth factors may be achieved either by binding the proteins to various nonmetallic carriers or by implantation of tissue allografts that have been biologically modified to produce and secrete the protein<sup>(12, 14)</sup>.

Our study had several important limitations. As observed with many protocols that use metallic implants, detailed immunohistochemical processing is difficult or impossible. Because of these severe limitations in tissue processing, we have not attempted to identify the cell types observed proliferating adjacent to implanted coils. We have simply identified nucleated versus no nucleated cells. The former probably represent fibroblasts, smooth muscle cells, or inflammatory cells, and the latter almost certainly represent red blood cells in various stages of breakdown. Even within this limitation, we consider it useful to identify any type of nucleated cell adjacent to implanted coils, if the control coils fail to demonstrate such findings. Another limitation of this study was the small sample size. Even with the small sample size, however, we were able to demonstrate statistically significant differences between test and control coils at an early time point. Furthermore, our study was performed by use of a rabbit model of aneurysms that may not perfectly simulate human intracranial aneurysms. Among the many animal models available, however, the model used herein has numerous advantages. It shares the morphological features observed in humans, with parent arteries of approximately 3 to 4 mm and aneurysm cavities of approximately 6 mm, and it arises at a prominent vessel curve. The wall is arterial, rather than venous as observed in other animal models of aneurysms, and there is no local surgery around the aneurysm cavity. Last, we did not include angiographic follow-up as a part of this study. Our primary interest was to analyze the histological reaction to the coated coil rather than coil morphology.

A further limitation of our study was that we could not match packing density exactly in each aneurysm, and the degree of packing density probably is an important determinant in the biological response to implanted coils. We remain highly focused on the interaction between the coil surface and the intra-aneurysmal tissue, and our model of a single coil allows clear identification of this interaction. Numerous coil winds were readily assessed regarding thickness of overlying tissue in each sample. Another reason to purposely “under pack” the aneurysm cavities is that biological modifications probably will have most impact in large and giant aneurysms, in which dense packing is impossible in most cases. Because our animal model usually results in small aneurysms, we used the “underpacked” small aneurysm as a surrogate for moderately packed large and giant aneurysms.

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## Chapter 3

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### **Results of 101 aneurysms treated with PGLA microfilament NEXUS coils compared with historical controls treated with standard coils**

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## **ABSTRACT**

### **BACKGROUND AND PURPOSE**

Polyglycolic/polylactic acid (PGLA) addition to bare platinum coils is intended to reduce reopening rate of coiled intracranial aneurysms. Nexus coils are standard complex platinum coils with interwoven PGLA microfilament threads. We present the clinical results of coiling of 101 intracranial aneurysms with Nexus coils.

### **PATIENTS AND METHODS**

Results of coiling of 101 aneurysms treated with Nexus coils were compared with historical results of coiling of 120 aneurysms with GDC 10 coils and 115 with Cordis TruFill coils using identical methodology. Complication rate, mean aneurysm volume, packing density, incomplete aneurysm occlusion at 6 months and retreatment rates were compared.

### **RESULTS**

Initial occlusion in aneurysms treated with Nexus coils was (near) complete in 97 aneurysms and incomplete in 4 aneurysms. There were no permanent procedural complications (0 in 95 patients, 0%, 97.5% CI 0.0-3.3%). Mean aneurysm volume was 180.2 mm<sup>3</sup> (median 71, range 5-1624 mm<sup>3</sup>). Mean packing was 19.4% (median 18.3%, range 7.5-38.9%). Six months angiographic follow up in 87 of 101 aneurysms showed incomplete occlusion in 14 (16%) and 12 of those (14%) were additionally coiled. Mean packing of 19.4% of Nexus coils was significantly lower than 22.9% for GDC 10 and 29.7% for Cordis TruFill coils. Other clinical results were not statistically different.

### **CONCLUSION**

PGLA microfilament Nexus coils are safe to use with clinical results comparable to those of standard platinum coils. Handling properties are not optimal. This study gives further evidence of lack of beneficial effect of PGLA addition to reduce recurrence rate.

## INTRODUCTION

Endovascular treatment of intracranial aneurysms with bare platinum coils has become an accepted alternative to surgery <sup>(1)</sup>. The most significant drawback of this technique is the possibility of aneurysm reopening over time occurring at an incidence of around 10%. In particular, large and giant aneurysms and initially incompletely occluded aneurysms are at risk for reopening <sup>(2-4)</sup>. Animal models and human studies have shown that the biologic response of intracranial aneurysms to bare coils is complex, requiring stability of the initial occlusion for a considerable period of time for a stable and durable treatment result. As for now, high packing density is the only proven factor predictive of stable occlusion <sup>(2)</sup>. Recently, coating the surface of bare platinum coils with a co-polymer consisting of polyglycolic/poly(lactic acid) (PGLA) was proposed in an attempt to accelerate the biologic response to coils with intended reduction of reopening rate. After an experimental study in 26 swine and a registry of 100 patients <sup>(5,6)</sup>, Boston Scientific (Fremont, CA) introduced the first PGLA coated coil (Matrix) on the market in 2003, later followed by other manufacturers. Matrix coils have a thick PGLA coating over a platinum core with different physical properties (softness, surface smoothness and other) from standard bare platinum coils resulting in different handling. The Nexus PGLA microfilament coil was introduced by EV3 (Irvine, CA) in 2005. Nexus coils are standard bare platinum coils with additional PGLA microfilament threads interwoven in the primary coil. The concept of microfilament threads was chosen by the manufacturer in order to maintain the physical properties of the standard bare platinum coil. In this study, we present our results with coiling of 101 intracranial aneurysms with Nexus microfilament coils. In addition, we compare the results of Nexus coils with historical data from our institution of two types of bare platinum coils <sup>(7)</sup>.

## PATIENTS AND METHODS

### DESCRIPTION OF COILS

Nexus coils have a thickness of 0.010 inch and are available in helical and two different complex shapes (Morpheus and Tetris). Nexus coils have PGLA microfilament threads interwoven in the primary coil (fig 1). In addition, the coils have a nitinol inner core intended to make the coil resistant to stretch and compaction.



*Fig1 Schematic representation of complex shaped Nexus coil with interwoven PGLA microfilament threads.*

## **PATIENTS**

Between May 15, 2006 and May 5, 2007, 101 aneurysms in 95 patients were treated with Nexus coils. Patients were not consecutive; in the same period another 23 aneurysms were treated with other types of coils for the following reasons: in the beginning and ending of the study period stock of Nexus coils was incomplete (12 aneurysms), operator preference for (thicker) GDC 18 coils in aneurysms of 10-20 mm (7 aneurysms), and conversion from Nexus coils to other types of coils (4 aneurysms). There were 39 men and 56 women with a mean age of 53.6 years (median 53, range 14-89 years). Of 101 aneurysms, 77

had ruptured and 24 had not. Of 24 unruptured aneurysms, 12 were incidentally discovered, 8 were additional to another ruptured aneurysm and 4 presented with symptoms of mass effect. Of 77 patients with a ruptured aneurysm, Hunt and Hess (HH) grading at the time of treatment was HH I-II in 41, HH III in 16, HH IV-V in 20 patients. Timing of treatment after SAH was 0-3 days in 55 patients, 4-7 days in 13 patients and >7 days in 9 patients.

Location of 101 aneurysms was anterior communicating artery in 34, middle cerebral artery in 20, posterior communicating artery in 15, ophthalmic artery in 10, basilar tip in 7, posterior inferior cerebellar artery in 5, pericallosal artery in 4, anterior choroideal artery in 2, superior cerebellar artery in 2, posterior cerebral artery in 1 and vertebral artery in 1. Mean aneurysm size was 6.6 mm (median 6, range 2-16 mm).

### **COILING PROCEDURE AND COMPLICATION REGISTRATION**

Coiling of aneurysms was performed on a biplane angiographic unit (Integris BN 3000, Philips Medical Systems, Best, The Netherlands) with the patient under general anaesthesia. The aim of coiling was to obtain a dense packing of the aneurysm, until not one coil could be placed. After location of the aneurysm on 2D angiography, 3D Rotational Angiography was performed of the vessel harbouring the aneurysm. From 3D images, coil projection was assessed and measurements of aneurysm diameter and aneurysm volume were performed. Used types of coils, number and lengths of coils and total volume of inserted coils was assessed for every aneurysm and packing, defined as coil volume / aneurysm volume x 100% was calculated. Coil volume was calculated with a spreadsheet provided by the manufacturer containing volumes per cm of every type of coil. Angiographic occlusion was dichotomized in (near) complete occlusion (90-100%) or incomplete occlusion (<90%).

Complications leading to temporary or permanent neurological deficit or death were recorded. In addition, all technical complications related to the Nexus coils were recorded, regardless of clinical impact.

### **SUPPORTING DEVICES**

One aneurysm was coiled with a temporary supporting balloon (Hyperform, EV3, Irvine, CA), one aneurysm was coiled after placement of a neck bridging device (TriSpan, Boston Scientific, Fremont, CA) and 5 aneurysms were coiled after stent placement (Enterprise, Cordis Neurovascular, Miami Lakes, FL).

### **ANTICOAGULATION PROTOCOL**

During coiling of ruptured aneurysms, no heparin was administered apart from the heparin in the pressure bags (1000 U per 500 ml saline). During coiling of unruptured aneurysms not additional to another ruptured aneurysm, 2500 U heparin was administered before insertion of the micro catheter. After the procedure, no anticoagulation was given in small aneurysms with complete occlusion. In larger and wide necked aneurysms, subcutaneous heparin in therapeutic dosage was prescribed for 48 hours.

Patients with unruptured aneurysms treated with stent assisted coiling were preloaded with Clopidogrel 75 mg and Aspirin 80 mg and this was continued for 3-6 months after the procedure. Patients with acutely ruptured aneurysms treated with stent assisted coiling received intravenous Aspirin 500 mg before placement of the stent. In all patients treated with stents, response to antiplatelet medication was tested with VerifyNow P2Y12 Assay (Accumetrics, San Diego, CA) before stent placement.

When thrombus formation on the coil mesh was angiographically visible or when coil loops protruded outside the aneurysm in the parent artery, intravenous infusion of a glycoprotein IIb/IIIa antagonist (tirofiban, Aggrastat, Merck & Co., Inc., Whitehouse Station, NJ), was started for 24-48 hours duration.

### **CLINICAL AND ANGIOGRAPHIC FOLLOW UP**

Patients who survived the hospital admission period were scheduled for a follow up visit at 6 weeks and for angiographic follow up at 6 months. Results of angiographic follow up were classified in the same way as initial angiographic occlusion. Need for additional treatment was assessed in a weekly meeting with neuroradiologists, neurologists and neurosurgeons. Outcome according to the Glasgow Outcome Scale (GOS) was assessed at 6 months.

### **COMPARISON WITH HISTORICAL DATA OF BARE PLATINUM COILS**

Results of coiling of 101 aneurysms with Nexus coils were compared with historical results of coiling of 120 aneurysms with GDC 10 coils and 115 aneurysms with Cordis TruFill coils using identical methodology <sup>(7)</sup>.

Mean aneurysm volume, packing, incomplete aneurysm occlusion at 6 months follow up angiography and retreatment rates for Nexus coils were compared with both GDC 10 coils and Cordis TruFill coils. Differences were statistically analyzed using the unpaired t test for comparison of means and Chi-square test for comparison of proportions. P values < 0.05 were considered significant.

## RESULTS

### INITIAL ANGIOGRAPHIC RESULTS AND PACKING

Initial occlusion was (near) complete in 97 aneurysms and incomplete in 4 aneurysms. Mean aneurysm volume was 180.2 mm<sup>3</sup> (median 71, range 5-1624 mm<sup>3</sup>). Mean packing was 19.4% (median 18.3%, range 7.5-38.9%). Of 95 patients, 58 (61%) were prescribed anticoagulation after the procedure.

In 101 aneurysms, 426 coils were used (mean 4.2, median 3, range 1-14). The 426 coils had a total length of 5,776 cm and total coil volume was 3,088 mm<sup>3</sup>. Of 5,776 cm total length of coils, 2,775 cm (48%) was from helical coils, 2,372 cm (41%) was from complex Morpheus coils and 629 cm (11%) was from complex Tetris coils. Inserted coil length per mm<sup>3</sup> aneurysm volume was 0.32 cm (total coil length 5,776 / total aneurysm volume 18,201).

### CLINICAL COMPLICATIONS

There were no complications leading to transient or permanent morbidity or mortality (0 in 95 patients, 0%, 97.5% CI 0.0-3.3%).

### TECHNICAL COMPLICATIONS AND CONVERSIONS

Coil loops protruding from the aneurysm in the parent vessel occurred in 11 patients, in two patients with angiographic visible thrombus formation on the coils. Aggrastat infusion was administered in 7 of 11 patients. In all cases, malposition of coil loops occurred after correct placement of the first coil and was caused by insertion of additional coils that displaced loops of previously inserted coils (figs 2 and 3).

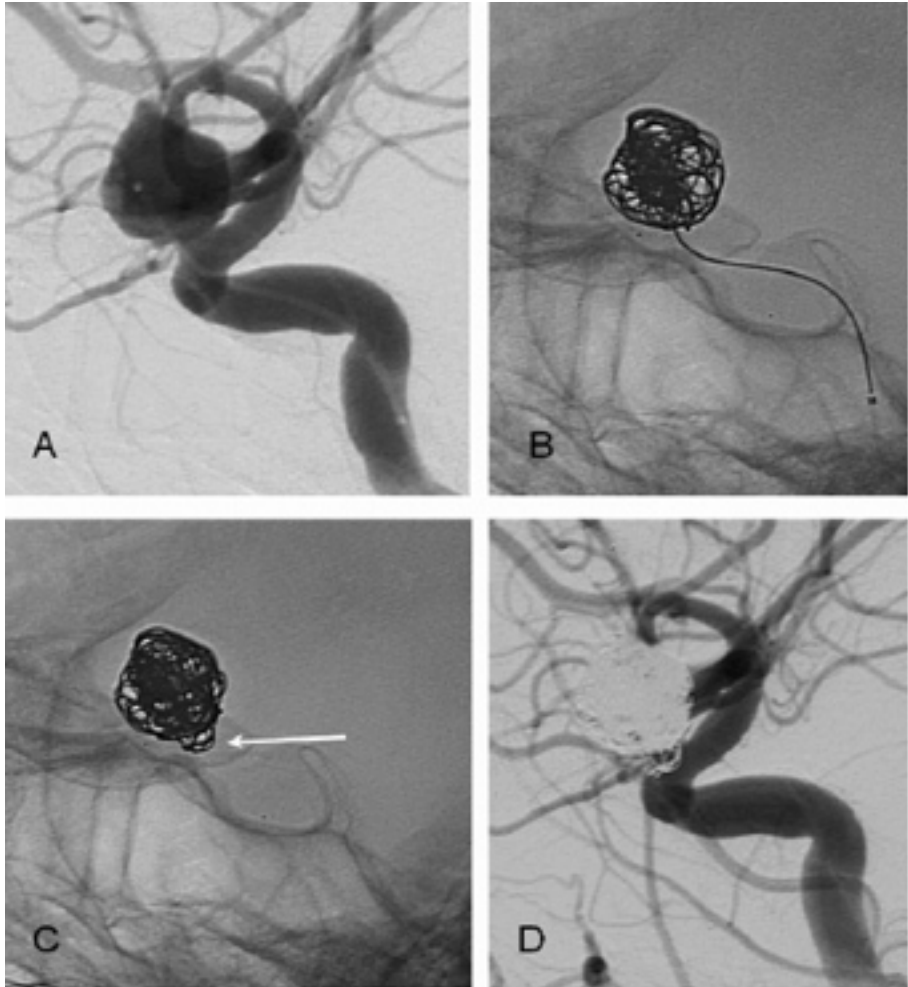


Fig 2 50-year-old woman with an incidentally discovered unruptured ophthalmic aneurysm.

*A: Lateral internal carotid angiogram demonstrates 9 mm ophthalmic aneurysm.*

*B: After insertion of three 8x30 Nexus Morpheus coils an adequate basket is formed.*

*C: After failed attempt to deliver and withdrawal of a 7x30 Nexus Morpheus coil: coil loops of previous coils protruding in the parent artery (arrow).*

*D: Final result with coil loops in carotid artery. The patient received Aggrastat infusion for 48 hours. Good clinical outcome.*

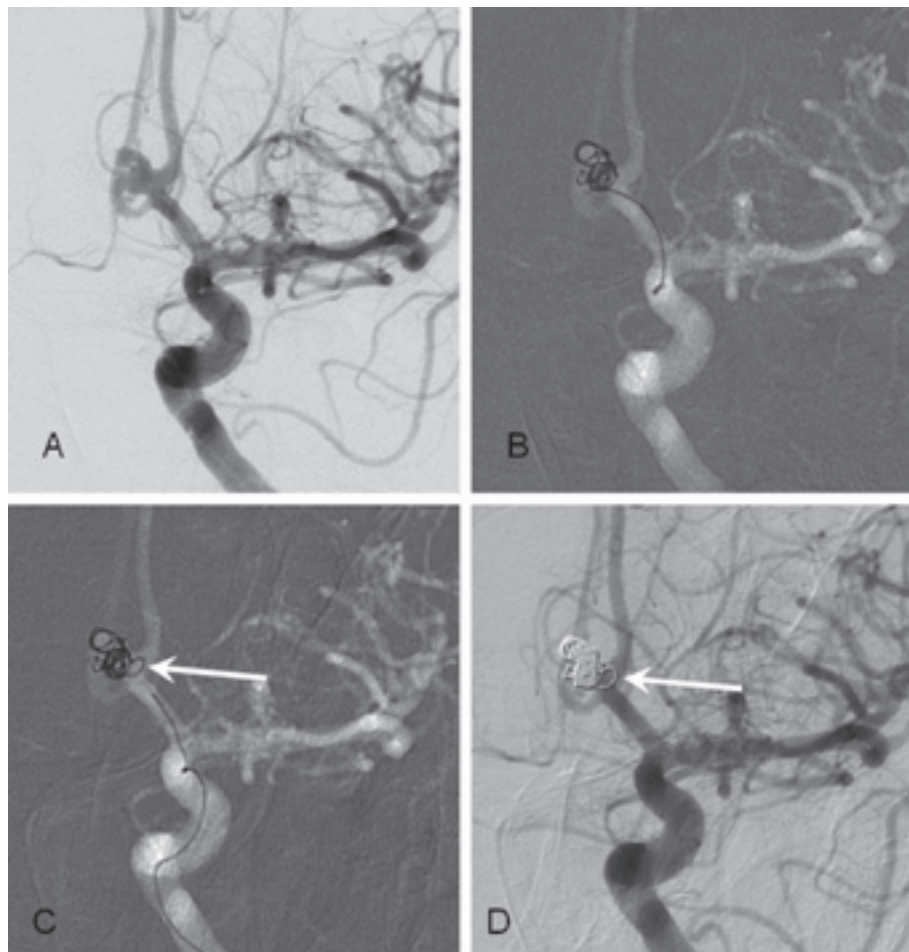


Fig 3 62-year-old man with grade III SAH from anterior communicating artery aneurysm.

*A: Internal carotid angiogram shows bilobated 5 mm anterior communicating artery aneurysm.*

*B: First coil (5x15 Morpheus) forms adequate basket.*

*C: during insertion of the second coil (2x8mm helical), suddenly a coil loop protruded in the parent artery (arrow). After withdrawal of this coil in the micro catheter, the protruding loop persisted proving this was a displaced loop of the first coil.*

*D: final result with persisting protrusion of the coil loop (arrow). Aggrastat infusion was started. Good clinical outcome.*

In four aneurysms intended to be treated with Nexus coils, this proved impossible and these aneurysms were treated with other types of coils. In two wide necked aneurysms (one 7 mm middle cerebral artery aneurysm and one 10 mm anterior communicating aneurysm) treated with balloon assisted coiling, the first inserted Nexus coil did not retain its shape after insertion with balloon assistance but retook its original shape after deflating the balloon resulting in protrusion of loops in the parent artery (fig. 4). Both aneurysms were treated with GDC 18 coils. In one 2 mm anterior communicating artery aneurysm, a 2 mm helical Nexus coil could not be delivered and this aneurysm was treated with a 2 mm GDC 10 Ultrasoft coil. Finally, first inserted 10 mm Nexus Morpheus coil in a 12 mm middle cerebral artery aneurysm could not be placed satisfactory and this aneurysm was treated with GDC 18 coils.

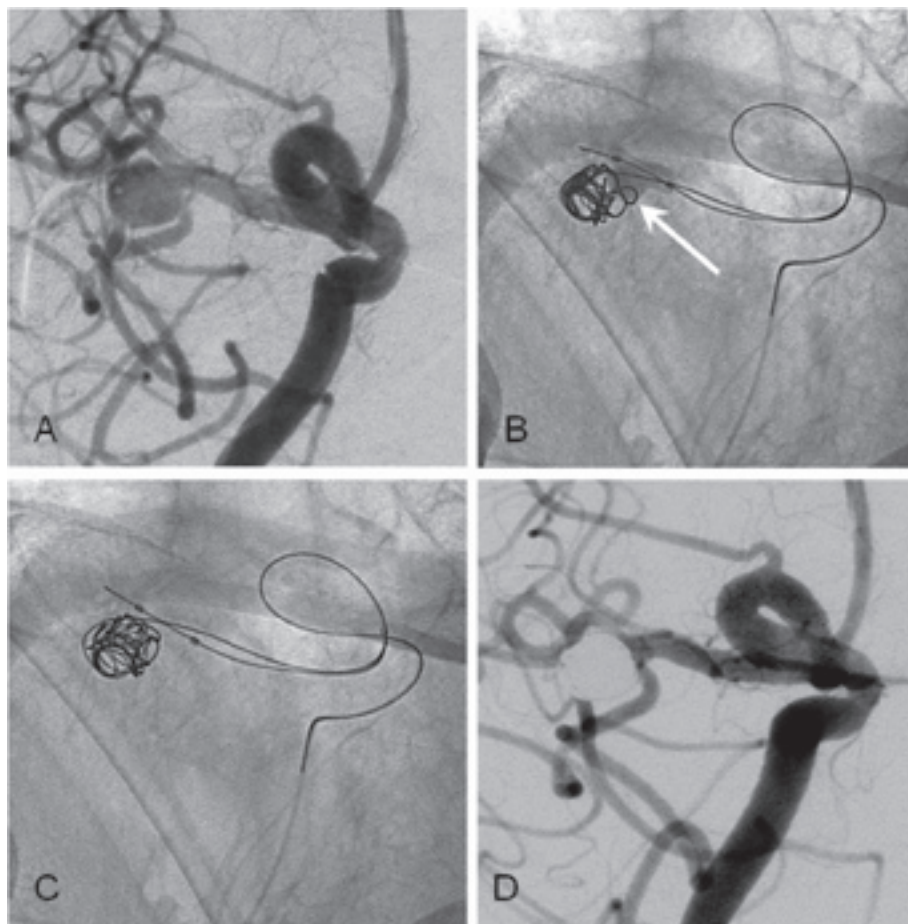


Fig 4 57-year-old woman with grade II SAH from a middle cerebral artery aneurysm.  
A: internal carotid angiogram shows wide necked 7 mm middle cerebral artery aneurysm.  
B: Adequate placement of the first coil (7x21 Morpheus) with assistance of Hyperform 7 mm balloon (EV3, Irvine, CA).  
C: after deflation of the balloon expansion of the coil with protrusion into the parent artery. This coil was withdrawn.  
D: Final result after balloon assisted treatment with GDC 18 coils (Boston Scientific, Fremont, CA).

### CLINICAL FOLLOW UP

Clinical follow up at 6 months was available for all patients. Of 77 patients with ruptured aneurysms, 7 died in the hospital from initial impact of SAH or vasospasm (GOS 1). Two patients were in a nursing home (GOS 3), 4 patients had non disabling neurological deficits (GOS 4) as a result of vasospasm and 64 patients had good outcomes (GOS 5). All 18 patients with unruptured aneurysms were neurologically intact.

### ANGIOGRAPHIC FOLLOW UP

Angiographic follow up at 6 months was available for 82 patients with 87 aneurysms (86%). Thirteen patients (with 14 aneurysms) had no follow up angiography for the following reasons: death after SAH in 7, refusal in 5 and advanced age (78 years) in 1 patient. Occlusion status for 87 aneurysms at 6 months was (near) complete in 73 (84%) and incomplete in 14 (16%) aneurysms. Of 14 incompletely occluded aneurysms, 12 were additionally coiled. In 2 aneurysms, both for 80% occluded, further follow up is scheduled. Overall retreatment rate was 12% (12 of 101) and retreatment rate for aneurysms with angiographic follow up was 14% (12 of 87). Additional coilings were without complications.

### COMPARISON WITH HISTORICAL DATA OF BARE PLATINUM COILS

Results of comparison of Nexus coated coils with GDC 10 coils and with Cordis TruFill coils are displayed in Table. Mean packing of 19.2% of Nexus coils was significantly lower than 22.9% of GDC 10 coils ( $P < 0.0001$ ) and 29.7% of Cordis TruFill coils ( $P < 0.0001$ ). All other parameters (including proportion of incompletely occluded aneurysms at follow up and retreatment rates) were statistically not significantly different.

	Nexus	GDC 10	Cordis TruFill	p value Nexus-GDC 10 / Nexus-Cordis TruFill
number of aneurysms	101	120	115	
mean aneurysm volume	180 mm <sup>3</sup>	128 mm <sup>3</sup>	162 mm <sup>3</sup>	10/57
mean packing	19.4% (median 18.3, range 8-39 %)	22.9 % (median 21.8, range 9-48 %)	29.7 % (median 29.6, range 15-57 %)	< 0.0001/< 0.0001
morbidity / mortality	0% / 0%	2.5% / 0.8%	0.9% / 0%	0.18/0.97*
number of initial incompletely occluded aneurysms	4 (4.0%)	4 (3.5 %)	3 (2.6 %)	1 2/85
incomplete aneurysm occlusion at 6 months	14 of 87 (17%)	22 of 99 (22.2%)	15 of 95 (15.8%)	43/96
number of retreatments	12 of 101 (11.9%)	16 of 120 (13.3%)	9 of 115 (7.8%)	0.91/0.43
number of incompletely occluded aneurysms at 6 months left untreated	2 (2.0%)	6 (5.0%)	6 (5.2%)	0.41/0.38

*Table Comparison of clinical results of Nexus PGLA microfilament coils with both GDC 10 and Cordis TruFill bare platinum coils. \* combined morbidity/mortality compared*

## DISCUSSION

In this study, we found that results of treating aneurysms with PGLA microfilament Nexus coils are similar to those of two types of standard bare platinum coils. In other words, a beneficial effect of PGLA addition on stability at follow up could not be demonstrated. Nexus coils were safe to use: no neurological complications occurred in 95 patients with 101 aneurysms. The significantly lower packing of Nexus coils compared to both GDC 10 coils and Cordis TruFill coils had no significant effect on reopening and retreatment rates in this relatively small aneurysm groups, although there was a trend to lower retreatment rate for Cordis TruFill coils. Technical complications occurred rather frequently, in our opinion predominantly related to the inner nitinol core of the coil, intended to make the coil resistant to compaction and stretch. Nitinol has the propensity to regain its original shape after being forced into a different shape. In clinical practise, this physical property of the coil resulted in displacement of loops of already inserted coils during placement of additional coils resulting in coil loops protruding in the parent artery (figs 2 and 3). In our experience, we have not encountered this phenomenon with the use of other types of (bare platinum) coils. In patients with coil loops protruding outside the aneurysm in the parent artery, we administered an intravenous infusion of a glycoprotein IIb/IIIa antagonist for 24-48 hours, since Nexus coils have additional PGLA microfilaments with possible increased thrombogenicity. With this protocol, no permanent thromboembolic complications occurred.

Another disadvantage of the physical property of the nitinol core is the dire performance in balloon assisted treatment. The first inserted Nexus coil usually did not retain its shape after insertion with balloon assistance but retook its original shape after deflating the balloon resulting in protrusion of loops in the parent artery, thereby neutralizing the intended effect of balloon assistance (fig.4). In these cases, treatment was continued with other types of coils with good results.

The coil manufacturer (EV3, Irvine, CA) has recently introduced a new range of coils of several thicknesses, from 0.0115-0.0145 inch (Axium) dependant on the loop diameter. This new coil is intended to replace the current available Nexus range. The new Axium coil has no nitinol core and will be available as bare platinum coil and as microfilament coil with either PGLA or nylon.

In general, the results of this study are comparable to studies with other types coils with PGLA addition such as Matrix and Cerecyte coils<sup>(8-18)</sup>. As in our study, a beneficial effect of PGLA in terms of better stability at follow up was absent or not significant in previous studies<sup>(8-18)</sup>.

Should we continue to use these PGLA coils to treat intracranial aneurysms? In our opinion<sup>(19-21)</sup>, supported by others<sup>(22-24)</sup>, the answer to this question is a clearly no for the following reasons. First and most important, clinical results of coils with PGLA addition are not better than those of bare platinum coils. Second, in some PGLA coils (Matrix), coating modifies physical coil properties, negatively affecting ease of handling. Third, PGLA coils are more expensive.

Large prospective randomized trials, instigated by coil manufacturers <sup>(24)</sup>, comparing performance of PGLA coils and standard coils are not warranted, based on current available data.

## **CONCLUSION**

PGLA microfilament Nexus coils are safe to use with results comparable to those of standard platinum coils. Handling properties are not optimal. This study gives further evidence of lack of beneficial effect of PGLA addition to reduce recurrence rate.

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# Chapter 4

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## Coiling of truly incidental intracranial aneurysms

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## **ABSTRACT**

### **BACKGROUND AND PURPOSE**

The purpose of this study is to report the morbidity, mortality, and angiographic results of coiling of asymptomatic incidental aneurysms and compare the characteristics of these aneurysms with other asymptomatic incidental aneurysms that were not treated.

### **PATIENTS AND METHODS**

During a 10-year period, 97 patients without previous subarachnoid hemorrhage, presented with incidentally found intracranial aneurysms. In 48 patients, 58 aneurysms were coiled. The mean size of the 58 coiled incidental aneurysms was 10.9 mm (median, 9 mm; range, 3–40 mm). Twenty-six of 58 coiled aneurysms (44.8%) were  $\geq 10$  mm.

### **RESULTS**

Permanent morbidity of coiling was 2.1% (1 of 48), mortality was 0%. Compared with untreated patients with incidental aneurysms, coiled patients were younger and more often had multiple aneurysms. Aneurysms of coiled patients more often had a small neck, were more often located on the carotid artery, and were less often located on the middle cerebral artery. Of 46 aneurysms with angiographic follow up, 45 were completely or near completely occluded. To obtain these results, 3 aneurysms were coiled more than once. Coiled incidental aneurysms did not rupture during a median follow-up period of 28.5 months. Mean hospital stay per patient was 2.5 days.

### **CONCLUSION**

Coiling of incidental intracranial aneurysms has a low complication rate in selected aneurysms and patients. Coiling should be the first treatment option in incidental aneurysms suitable for this technique.

## INTRODUCTION

The widespread use of imaging of the brain with CT scanning and MR imaging enhances the chance of discovering an intracranial aneurysm unrelated to the presenting symptoms of the patient. Bleeding from an intracranial aneurysm may have devastating consequences, but the chance of rupture of an incidentally discovered aneurysm is generally low and is mainly dependent on size and location. In making the decision whether to treat an unruptured aneurysm, many factors have to be considered: location, size, and morphology of the aneurysm, patient age and life expectancy, and the skills and experience of the treating physician.

Unruptured aneurysms can be classified as symptomatic (by mass effect) or asymptomatic. Most asymptomatic unruptured aneurysms are additional aneurysms discovered in the diagnostic work-up of another ruptured aneurysm. Truly incidental aneurysms form a specific subset of unruptured aneurysms with a lower chance of rupture than additional or symptomatic unruptured aneurysms<sup>(1-3)</sup>. Most reports about endovascular treatment of unruptured aneurysms contain data about all 3 types of unruptured aneurysms<sup>(4-7)</sup>. In this study, we report our experience during 10 years with coiling of 58 incidental aneurysms in 48 patients and compare patient and aneurysm characteristics with 53 incidental aneurysms in 41 patients who were not treated during the same period.

## PATIENTS AND METHODS

### GENERAL

Between January 1995 and April 2005, 97 patients presented with incidentally found aneurysms. All patients were discussed in a multidisciplinary working group consisting of 2 neurosurgeons, 2 neurologists, and 2 neuroradiologists.

Asymptomatic aneurysms, diagnosed on imaging studies performed for symptoms unrelated to the presence of the aneurysm in patients without a history of subarachnoid hemorrhage, were classified as incidental. Imaging studies included CT scanning, MR imaging, and angiography performed for a variety of symptoms: headache, transient ischemic attacks, carotid artery stenosis, seizures, multiple sclerosis, tinnitus, dizziness, collapse, meningioma, memory disturbances, suspected metastases, etc. In patients with an incidental aneurysm diagnosed on CT or MR imaging and for whom treatment was considered, a complete angiogram was performed; in the past 4 years, this included a 3D rotational angiogram. After completion of the angiographic imaging, the possibility of and need for treatment were discussed in the working group and the consensus opinion was discussed with the patient in the outpatient clinic. In general, coiling was the first treatment option for all aneurysms in the posterior circulation and for aneurysms with a well-defined neck in the anterior circulation. Surgery was considered in aneurysms not suitable for coiling or endovascular parent vessel occlusion, generally wide-necked aneurysms in the anterior circulation. The working group tried to balance the benefit and risk

of treatment against the presumed annual risk of bleeding from the aneurysm. Multiple patient and aneurysm factors were taken into consideration: patient age, general medical condition, comorbidity and wish for treatment, aneurysm size, location, anatomy, and presence of intraluminal thrombus or calcifications.

## PATIENTS

Of the 97 patients presenting with an incidental aneurysm, 56 (57.1%) were treated, 48 with coil embolization, 7 with surgical clipping, and one with parent vessel balloon occlusion. The 48 patients with incidental aneurysms that were coiled are the subject of the present study. There were 38 women and 10 men with a mean age of 53.6 years (median age, 52 years; range, 26–75 years). Of the 48 patients, 19 (39.6%) had multiple incidental aneurysms for a total of 85 aneurysms: 8 patients had 2 aneurysms, 8 patients had 3 aneurysms, 2 patients had 4 aneurysms, and one patient had 8 aneurysms. Of these 85 aneurysms in 48 patients, 66 were treated, 58 with coil embolization and 8 with surgical clipping: 8 patients had 2 treated incidental aneurysms, 2 patients had 3 treated aneurysms, and one patient had 7 treated aneurysms. In 6 patients, 2 incidental aneurysms were coiled in the same session, and in one patient 4 aneurysms were coiled in the same session. The mean size of the 58 coiled incidental aneurysms was 10.9 mm (median, 9 mm; range, 3–40 mm). Twenty-six of 58 coiled aneurysms (44.8%) were 6–10 mm. Locations were the ophthalmic artery<sup>(15)</sup>, basilar tip<sup>(14)</sup>, posterior communicating artery (8), anterior communicating artery (6), middle cerebral artery (5), carotid tip (4), posterior cerebral artery (2), posterior inferior cerebellar artery (2), superior cerebellar artery (one), and basilar trunk (one). During the same period, 184 other unruptured aneurysms were treated by endovascular means in our hospital: 97 were additional to another ruptured aneurysm, and 87 presented with symptoms of mass effect. Thus, the proportion of incidental aneurysms was 24% (58 of 242) of endovascularly treated unruptured aneurysms.

## COILING PROCEDURE

Coiling of aneurysms was performed with the patient under general anesthesia and systemic heparinization. Heparin was continued intravenously or subcutaneously for 48 hours after the procedure, followed by low-dose aspirin for 3 months orally. Coiling was performed with Guglielmi detachable coils (Boston Scientific, Fremont, Calif) or TruFill DCS coils (Cordis, Miami, Fla). Some large aneurysms were coiled with very long mechanically detachable coils (Detach 18; Cook Inc., Copenhagen, Denmark). The aim of coiling was to pack the aneurysm as densely as possible until not a single additional coil could be placed. Wide-necked aneurysms were coiled with a temporary supporting balloon (Sentry; Boston Scientific) or after placement of a permanent supporting device (TriSpan or Neuroform stent; Boston Scientific). Complications of coiling were recorded. Initial angiographic results of coiling were classified as complete occlusion (98%–100%), near-complete occlusion (90%–98%), or incomplete occlusion (< 90%).

## **DURATION OF HOSPITAL STAY**

Patients with incidental aneurysms scheduled for coiling or additional coiling were admitted in the neurosurgical ward in the morning, coiling was performed in the afternoon, and discharge was the next afternoon in uncomplicated procedures. Duration of hospital stay was recorded in all patients.

## **FOLLOW-UP**

Patients with coiled incidental aneurysms were scheduled for an outpatient clinic visit at 6 weeks and a follow-up angiogram after 6 months. Results of angiographic follow-up were classified in the same way as the initial postembolization occlusion. Incomplete occlusion at any point in time was considered an indication for further therapy, unless clinical or anatomic factors dictated otherwise. Results and consequences of angiographic follow-up were discussed in the working group. During the meeting, decisions were made for the need for additional treatment or extended angiographic follow-up. Patients with aneurysms with complete or near-complete occlusion at 6-month follow-up angiography were generally discarded from further angiographic follow-up. When additional treatment was performed, the result was evaluated in the weekly meeting and 6-month follow-up angiogram after additional treatment was scheduled.

In April 2005, a telephone survey was done by one of us (A.d.G.) for all treated patients with an outpatient clinic visit more than 6 months earlier. Patients or their next of kin were asked about general health, hospital admissions, and episodic headaches that might be contributing to subarachnoid hemorrhage.

## **UNTREATED PATIENTS**

Of the 97 patients with incidental aneurysms, 41 were not treated. The main reasons for not treating the 41 patients included unfavorable aneurysm anatomy (wide neck) in 29, patient refusal in 3, near-complete thrombosis in 2, small aneurysm size (5 mm) in 2, advanced patient age in 2, failed surgical clipping in one, location in the cavernous sinus in one, and one 65-year-old man with a 30-mm basilar trunk dissecting aneurysm discovered on MR imaging performed for transient ischemic attacks in the right carotid artery territory who died of subarachnoid hemorrhage shortly before scheduled treatment. There were 23 women and 18 men, with a mean age of 60.6 years (median age, 63 years; range, 46–74 years). Of the 41 patients, 7 (17%) had multiple aneurysms, for a total of 53 aneurysms: 4 patients had 2 aneurysms and 3 patients had 3 aneurysms. The mean size of the aneurysms was 9.2 mm (median, 8 mm; range, 3–30 mm). The locations of 53 aneurysms were the middle cerebral artery (15), anterior communicating artery (9), basilar tip (9), cavernous sinus (5), posterior communicating artery (4), ophthalmic artery (3), superior cerebellar artery (2), carotid tip (2), posterior cerebral artery (one), basilar trunk (one), pericallosal artery (one), and vertebral artery (one).

## COMPARISON OF TREATED AND UNTREATED PATIENTS

For patients with coiled versus untreated incidental aneurysms, the following patient and aneurysm characteristics were compared: mean patient age, mean aneurysm size, proportion of wide-necked aneurysms, proportion of patients with multiple incidental aneurysms, and proportion of aneurysms located on anterior cerebral artery, middle cerebral artery, carotid artery, and vertebrobasilar artery. Statistical analysis was performed by using a *t* test for comparison of means and a  $\chi^2$  test for comparison of proportions (MedCalc statistical software, Mariakerke, Belgium).

## RESULTS

### COMPARISON OF TREATED AND UNTREATED PATIENTS

In the Table, the characteristics of 48 patients with 58 incidental aneurysms that were coiled and of 41 patients with 53 incidental aneurysms that were not treated are summarized. Mean age of 53.7 years of 48 coiled patients was significantly lower than mean age of 60.6 years in 41 untreated patients. Mean aneurysm size did not differ for both groups. Eight of 58 coiled aneurysms (13.8%) had a wide neck versus 29 of 53 (54.7%) untreated aneurysms. This difference was statistically significant. Of the 48 coiled patients, 19 had multiple incidental aneurysms (39.6%) versus 7 of 41 untreated patients (17.1%). This difference was also statistically significant. Aneurysms located in the carotid artery were significantly more often coiled, whereas aneurysms located in the middle cerebral artery were—to a statistically significant degree—more often left untreated.

Characteristics of 48 patients with 58 incidental aneurysms that were coiled and of 41 patients with 53 incidental aneurysms that were not treated.			
	48 Patients with 58 Coiled Aneurysms	41 Patients with 53 Untreated Aneurysms	P Value
Mean age	53.6 y (median 52, range 26-75)	60.6 y (median 63, range 46-74)	.0006
Multiple aneurysms	19/48 (39.6%)	7/41 (17.1%)	.035
Mean aneurysms size	10.9 mm (median 9, range 3-40)	9.2 mm (median 8, range 3-30)	.461
Aneurysms with wide neck	8/58 (13.8%)	29/53 (54.7%)	<.0001
Location on carotid artery	27/58 (47%)	13/53 (25%)	.010
Location on middle cerebral artery	5/58 (9%)	15/53 (29%)	.014
Location on anterior cerebral artery	6/58 (10%)	10/53 (19%)	.309
Location on posterior circulation	20/58 (34%)	14/53 (27%)	.472

### COMPLICATIONS

One thromboembolic complication leading to permanent right-sided apraxia occurred in a 40-year-old woman during coiling of an 8 mm left carotid ophthalmic and a 6 mm left posterior communicating artery aneurysm in the same session. All other treatments were without complication. Permanent morbidity rate was 2.1% (1 of 48; 95% confidence interval [CI] 0.01%-12.03%). There was no mortality of treatment (0%; 97.5% CI 0%-7.4%).

## **DURATION OF HOSPITAL STAY**

Hospitalization was 2 days for 57 coiling procedures in 47 patients and 5 days for the one patient who suffered a thromboembolic complication. Mean hospital stay per patient, including additional coil treatments, was 2.5 days.

## **CLINICAL FOLLOW-UP**

All 48 coiled patients had clinical follow-up of a median 28.5 months (mean, 35.1 months; range, 2-112 months), totaling 1688 months (140.6 patient-years). A 68-year-old man died of pneumonia 6 months after coiling of a basilar tip aneurysm. A 70-year-old woman had mild aphasia after clipping of an additional incidental 15 mm left middle cerebral artery aneurysm. All other patients were alive and neurologically intact at the time of follow-up, and there were no hospital admissions or episodes of headache that could be attributed to subarachnoid hemorrhage.

## **ANGIOGRAPHIC RESULTS**

Of the 58 aneurysms treated in 48 patients, 6 wide-necked aneurysms were coiled with the aid of a temporary supporting balloon and one with the aid of a stent. One 14 mm basilar tip aneurysm was initially coiled with the aid of a TriSpan supporting device and 6 months later was additionally coiled after placement of a stent. Initial postembolization occlusion in 58 coiled aneurysms was complete occlusion in 49, near-complete occlusion in 6, and incomplete occlusion in 3 aneurysms. Two of the 3 incompletely occluded aneurysms were additionally coiled, one 16 mm basilar tip aneurysm was additionally coiled with the aid of a stent, and one 26-mm partially thrombosed basilar tip aneurysm was additionally coiled 5 times during a 3-year period. One 10-mm ophthalmic aneurysm that was 80% occluded remained stable on follow-up and was not additionally treated. Follow-up angiography at 6 months was performed in 42 patients with 46 coiled aneurysms (6 patients with 12 coiled aneurysms are scheduled for follow-up). One initial completely occluded 30 mm basilar tip aneurysm showed reopening and was additionally coiled for 4 times during a 2-year period to obtain a stable, almost-complete occlusion.

## **DISCUSSION**

In this study we found that coiling of incidental aneurysms has a low complication rate in selected patients and aneurysms. Selection was biased toward younger patients and aneurysms with well-defined necks. Aneurysms located on the carotid artery were treated significantly more often, and aneurysms on the middle cerebral artery were more often not treated. This may reflect the difference in morphology of aneurysms located at these sites: carotid artery aneurysms are usually sidewall aneurysms, whereas most middle cerebral artery aneurysms are located at bi- or trifurcations of arteries. Moreover, if carotid artery aneurysms are wide-necked, coiling with balloon protection of the carotid artery is relatively straight forward, whereas balloon protection in the middle cerebral

artery aneurysms is hazardous. In the present study, none of coiled aneurysms ruptured during a median follow-up period of 28.5 months, but longer follow-up is necessary to establish the efficacy of coiling of incidental aneurysms. Although selection was biased toward suitability of aneurysms for coiling, almost half of the coiled incidental aneurysms were  $\geq 10$  mm and in 9 procedures coiling was possible only with assistance of balloon protection of the parent artery or placement of a stent or TriSpan device. Despite these more challenging treatments, the complication rate was low. The natural history of unruptured intracranial aneurysms is still unclear and is influenced by many factors, such as previous subarachnoid hemorrhage from another aneurysm, history of cigarette smoking, coexisting medical conditions, and aneurysm characteristics such as size, location, and morphology <sup>(1-3,8-11)</sup>. In the International Study of Unruptured Intracranial Aneurysms (ISUIA) <sup>(1)</sup>, 5-year cumulative rupture rates for patients who did not have a history of subarachnoid hemorrhage with aneurysms located in the internal carotid artery, anterior communicating artery, anterior cerebral artery, and middle cerebral artery were 0%, 2.6%, 14.5%, and 40% for aneurysms  $<7$  mm, 7–12 mm, 13–24 mm, and  $\geq 25$  mm, respectively, compared with rates of 2.5%, 14.5%, 18.4%, and 50%, respectively, for the same size categories involving posterior circulation and posterior communicating artery aneurysms. On the other hand, adverse outcomes after surgery or coiling of unruptured aneurysms are in the range of 25% and 10%, respectively <sup>(1,5,7)</sup>. These data have to be considered in balancing the risk of rupture against the risk of complications of elective treatment in patients presenting with unruptured aneurysms. In a study using life expectancy analysis based on ISUIA data to determine the circumstances under which treatment of unruptured aneurysms may be beneficial <sup>(9)</sup>, life years are lost at all ages by treating incidental anterior circulation aneurysms  $<7$  mm. For all other unruptured aneurysms the number of life-years saved by treatment depends on patient age at the time of treatment: 2-40 years are saved in patients aged 20 years, but benefits fall to 0 in patients 45-70 years of age, depending on the size and location of the aneurysm. Truly incidental aneurysms are considered to carry the lowest risk of rupture among unruptured aneurysms <sup>(1)</sup> and treatment of these aneurysms should therefore have the lowest possible risk of procedural complications. Endovascular coil treatment of unruptured aneurysms is generally associated with lower risks than surgical treatment <sup>(2,4-7,12,13)</sup>. Moreover, coiling of unruptured aneurysms is associated with significantly lower costs and shorter hospital stay <sup>(5)</sup>. Mean duration of hospital stay per patient was 2.5 days in our patients. In our opinion, when treatment of an incidentally found intracranial aneurysm is considered, coiling should be the first treatment option. When an aneurysm is unsuitable for coiling, surgical treatment may be considered as an alternative. Long-term efficacy in preventing rupture of coiling of incidental aneurysms is not yet established; longer follow-up studies are needed.

## ACKNOWLEDGMENTS

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# Chapter 5

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## Midterm clinical and magnetic resonance imaging follow-up of large and giant carotid artery aneurysms after therapeutic carotid artery occlusion

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## **ABSTRACT**

### **OBJECTIVE**

The purpose of this study was to evaluate aneurysm size and clinical symptoms midterm after therapeutic carotid artery occlusion in 39 patients with large or giant carotid artery aneurysms.

### **METHODS**

Between January 1996 and August 2004, 39 patients with large or giant carotid artery aneurysms were treated with therapeutic carotid artery occlusion and had clinical and magnetic resonance imaging follow-up of at least 3 months (mean, 35.9 mo; median, 29 mo; range, 3–107 mo; 117 patient-yr). Initial clinical presentation was mass effect caused by the aneurysm in 32 (82%) of the 39 patients. Three patients presented with subarachnoid hemorrhage (SAH) and one presented with epistaxis; two aneurysms were an incidental finding and one was additional to another ruptured aneurysm.

### **RESULTS**

There were no early or late complications of therapeutic carotid artery occlusion. All aneurysms seemed to have thrombosed completely after carotid artery occlusion as observed on early and late magnetic resonance imaging (MRI) and magnetic resonance angiographic (MRA) follow-up studies. At the time of the most recent MRI follow-up study, 29 (74%) of the 39 aneurysms involuted totally, two aneurysms decreased to 25% of the original diameter, two aneurysms decreased to 50%, and five aneurysms decreased to 75%. Two aneurysms remained unchanged in size after 49 and 58 months, respectively. At the most recent clinical follow-up evaluation, symptoms of mass effect were cured in 19 (60%), improved in 10 (31%), and remained unchanged in 3 (9%) of the 32 patients.

### **CONCLUSION**

Therapeutic carotid artery occlusion was a simple, safe, and effective treatment for large and giant carotid artery aneurysms. Almost all aneurysms involute completely or substantially decrease in size. Alleviation of symptoms of mass effect was achieved in most patients.

### **KEY WORDS**

Aneurysm, Follow-up, Magnetic resonance imaging, Therapeutic carotid artery occlusion

## INTRODUCTION

Large and giant carotid artery aneurysms are located extradurally in the cavernous sinus or intradurally in its supraclinoid segments. Clinical presentation is usually with symptoms of mass effect on one or more of the adjacent cranial nerves (CN) II–VI resulting in diplopia, ophthalmoparesis, decreased visual acuity, trigeminal neuralgia, or a combination thereof. Rupture may result in SAH, carotid cavernous fistulae, or epistaxis, depending on aneurysm location.

For large and giant aneurysms of the internal carotid artery, therapeutic carotid artery balloon occlusion is a simple, safe, and effective therapy in patients who can tolerate sacrifice of the carotid artery<sup>(6,13,16)</sup>. Tolerance to internal carotid artery occlusion can be evaluated reliably by angiographic test occlusion, even in patients under general anesthesia<sup>(1,8,14,15)</sup>. The aim of therapeutic carotid artery occlusion is thrombosis of the internal carotid artery, including the aneurysm. In this study, we evaluated aneurysm size and clinical symptoms midterm after therapeutic carotid artery occlusion in 39 patients with large or giant carotid artery aneurysms.

## PATIENTS AND METHODS

### PATIENTS

Between January 1996 and August 2004, 52 patients were treated with carotid artery balloon occlusion for large or giant carotid aneurysms. Technical and clinical aspects of carotid artery occlusion in these patients have been published in previous articles<sup>(14,15)</sup>. During the same period, another 26 patients with carotid artery aneurysms intended to be treated with carotid artery occlusion did not tolerate the test occlusion. Of these 26 patients, four with cavernous sinus aneurysms symptomatic only by abducens palsy were not treated at all. Seven patients had bypass surgery preceding carotid artery occlusion. Fifteen aneurysms were coiled, two of them after placement of a stent and six with the aid of a supporting balloon. In June 2005, a follow-up survey was completed by the 52 patients with aneurysms treated with carotid artery balloon occlusion without preceding bypass surgery. Eight patients died during the follow-up period: one patient died shortly after carotid occlusion of the initial SAH, one patient died of trauma, two elderly patients died in the hospital from pneumonia and multiple organ failure, one patient died in the hospital as a result of chronic obstructive pulmonary disease, one patient died of lung cancer, one patient died in the hospital from cardiac infarction, and one patient died at home of old age. None of these patients died as a result of SAH. Of the 44 surviving patients, seven could not be located in June 2005 but had previous follow-up data. The remaining 37 patients were contacted and asked to complete a phone questionnaire about the evolution

of their clinical symptoms after carotid artery occlusion and their current state of health. Follow-up MRI and MRA on a 3.0 Tesla system (Philips Intera RIO; Philips Medical Systems, Best, The Netherlands) were offered to all 37 patients

and were eventually performed in 26. Basic ophthalmological assessment was performed at the same time. Of the 11 patients who refused long-term MRI follow-up, the seven patients who could not be located, and the eight patients who had died, previous clinical and MRI follow-up data for 3 months or longer was available in the medical records of 13, allowing these patients to be included in the analysis. Thus, the final study group consisted of 39 patients with large or giant carotid artery aneurysms treated with therapeutic carotid artery occlusion and with clinical and MRI follow-up of at least 3 months (mean, 35.9 mo; median, 29 mo; range, 3–107 mo; 117 patient yr). There were 32 women and 7 men with a mean age of 56 years (range, 26–78 yr) at the time of carotid artery occlusion. The location of the large and giant carotid artery aneurysms was the carotid cavernous sinus in 28 of the patients, the carotid hypophyseal segment in four, the carotid ophthalmic segment in three, the carotid supraclinoid segment in three, and the internal carotid bifurcation in one.

The initial clinical presentation was mass effect caused by the aneurysm in 32 (82%) of the 39 patients. Oculomotor dysfunction with intact visual acuity was present in 27 patients with large or giant cavernous sinus aneurysms, including isolated abducens palsy in five patients and ophthalmoparesis in 22 patients (in two patients with additional trigeminal neuralgia). Decreased visual acuity was the presenting symptom in four patients with carotid ophthalmic or hypophyseal aneurysms; one patient with an internal carotid bifurcation aneurysm presented with hemiparesis. Retro-orbital pain accompanied symptoms of mass effect in 18 of the 32 patients. Three patients presented with SAH and were treated with carotid artery occlusion more than 3 weeks after SAH, two of them after initial coiling in the acute phase of SAH. One patient presented with epistaxis. Two aneurysms were an incidental finding and one aneurysm was additional to another ruptured aneurysm. Seven (18%) of the 39 aneurysms contained intraluminal thrombus at the time of presentation. The presence of intraluminal thrombus was assessed from both cross-sectional imaging and angiography. This study was approved by the ethical committees of both participating hospitals.

### **INITIAL AND FOLLOW-UP MRI PROTOCOL**

In all 39 patients, MRI was performed before carotid artery occlusion. MRI was repeated 2 to 5 days after carotid artery occlusion and again 3 months later. Extended MRI follow-up (>3 mo) was performed in 35 of the 39 patients. MRI was performed on a 0.5-, 1.0-, or 1.5-Tesla system (Philips T5, T10, or T15; Philips Medical Systems) and consisted of transverse and coronal T1 weighted images and transverse T2 weighted images. In 26 patients, midterm MRI scanning was performed on a 3.0-Tesla system.

Initial and follow-up MRI studies were compared by two experienced neuroradiologists (WJvR, MS) in consensus. Thrombosis of the aneurysm after carotid artery occlusion was assessed by typical signal changes of the aneurysmal lumen on MRI scans over time, including loss of flow void and the appearance of T1-weighted hyperintensities (Fig. 1). Aneurysm diameter on follow-up MRI scans was categorized as 100, 75, 50, 25, or 0% of the initial

aneurysm diameter. Differences in aneurysm size reduction, dichotomized as 50% or more and less than 50%, were assessed for supraclinoidal aneurysms and cavernous sinus aneurysms. The evolution of clinical symptoms was categorized as worsened, unchanged, improved, or cured. All patients and their family physicians were informed regarding the imaging findings.

### **STATISTICAL ANALYSIS**

Aneurysm size reduction for aneurysms with initial intraluminal thrombus was compared with size reduction of aneurysms without initial intraluminal thrombus using Fisher's exact test. Differences in aneurysm size reduction, dichotomized as 50% or more and less than 50%, were compared for supraclinoidal aneurysms and cavernous sinus aneurysms using the  $\chi^2$  test. In 32 patients, the relationship between aneurysm size reduction at the most recent follow-up examination and clinical symptoms of mass effect was assessed as follows: the proportion of aneurysms with almost complete obliteration (0 or 25% of the initial aneurysm diameter) was assessed for patients with clinical cure, for patients with improved symptoms, and for patients with unchanged symptoms. The  $\chi^2$  test was used to identify statistical relations.

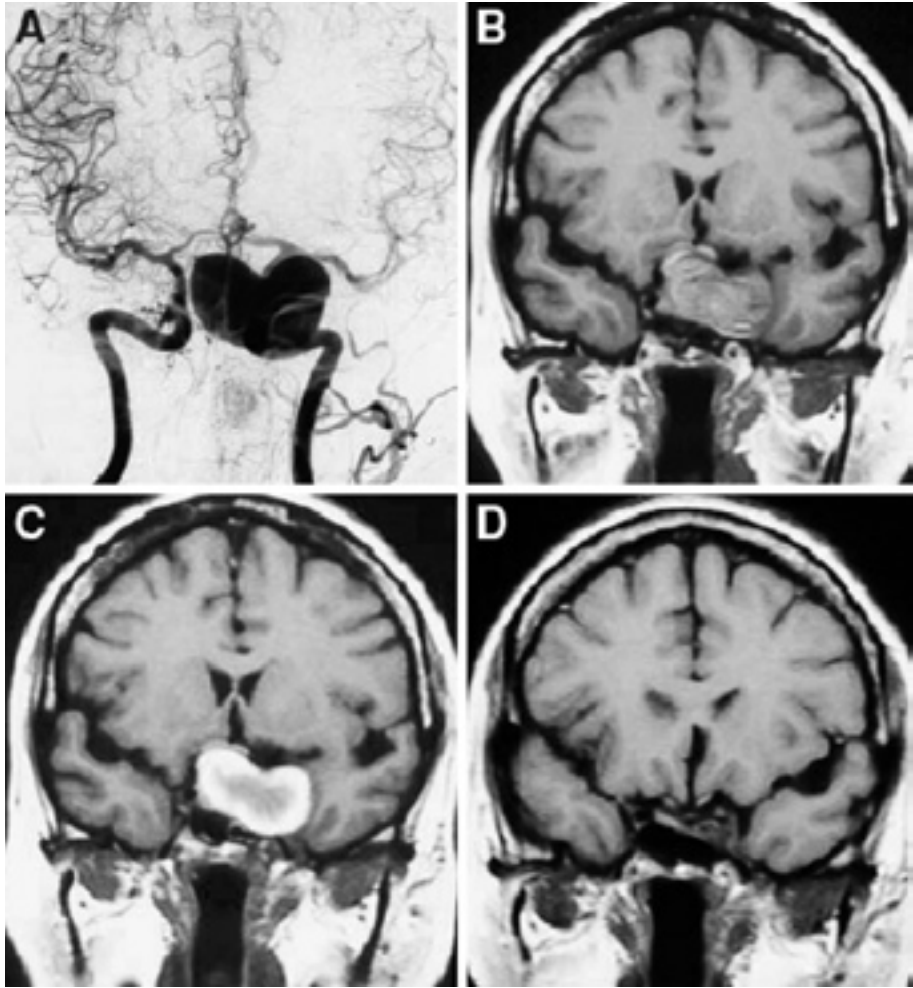


Fig 1. This 51-year-old woman presented with decreased visual acuity. A, bilateral internal carotid artery angiogram demonstrating a giant carotid ophthalmic aneurysm. B, coronal T1-weighted MRI scan obtained 5 days after left internal carotid artery balloon occlusion showing complete aneurysm thrombosis. Note the mass effect on the optic chiasm. C, MRI scan obtained 2 weeks later showing unchanged aneurysm size. D, MRI scan obtained after 4 months showing complete aneurysm involution. At the time of the last clinical follow-up examination (50 mo after carotid artery occlusion), vision had markedly improved.

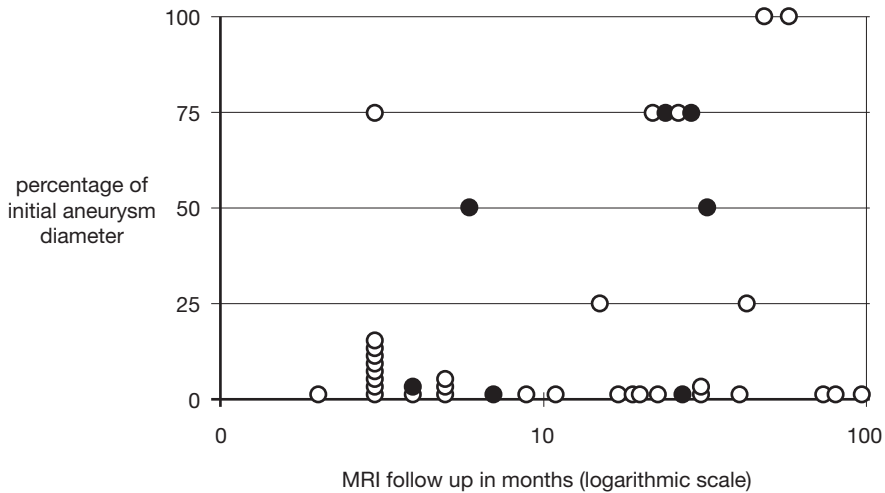


Fig 2. Graph showing the reduction in aneurysm size over time for 39 large and giant carotid artery aneurysms treated with carotid artery balloon occlusion. For 29 aneurysms that involuted totally, the x axis indicates the shortest available follow-up MRI scan with complete involution; for the 10 other aneurysms, the x axis indicates last follow-up MRI scan. Multiple circles with the same coordinates are piled. Solid circles, aneurysms with initial intraluminal thrombus; open circles, aneurysms without initial intraluminal thrombus.

## RESULTS

### ANEURYSM SIZE REDUCTION

All aneurysms seemed to have thrombosed completely after carotid artery occlusion as seen on early and late MRI scans and magnetic resonance angiography follow-up. At the time of the last MRI follow-up, 29 of the 39 aneurysms (74%) were totally involuted, two decreased to 25% of the original diameter, two decreased to 50%, and five decreased to 75%. Two aneurysms remained unchanged in size after 49 and 58 months, respectively. A reduction in aneurysm size related to the MRI follow-up period is illustrated in Fig 2. Complete aneurysm involution was obvious within 3 months for nine aneurysms, within 12 months for another nine aneurysms, and between 17 and 98 months for the remaining 11 aneurysms. Seven (64%) out of 11 supraclinoidal aneurysms and 25 (89%) out of 28 cavernous sinus aneurysms had a reduction of 50% or more in diameter size during the follow-up period. This difference was not significant ( $P = 0.17$ ). Three (43%) out of seven aneurysms with initial intraluminal thrombus and 26 (81%) out of 32 aneurysms without initial intraluminal thrombus involuted completely. This difference was not statistically significant ( $P = 0.11$ ). Illustrative cases are presented in Fig 1, 3, and 4.

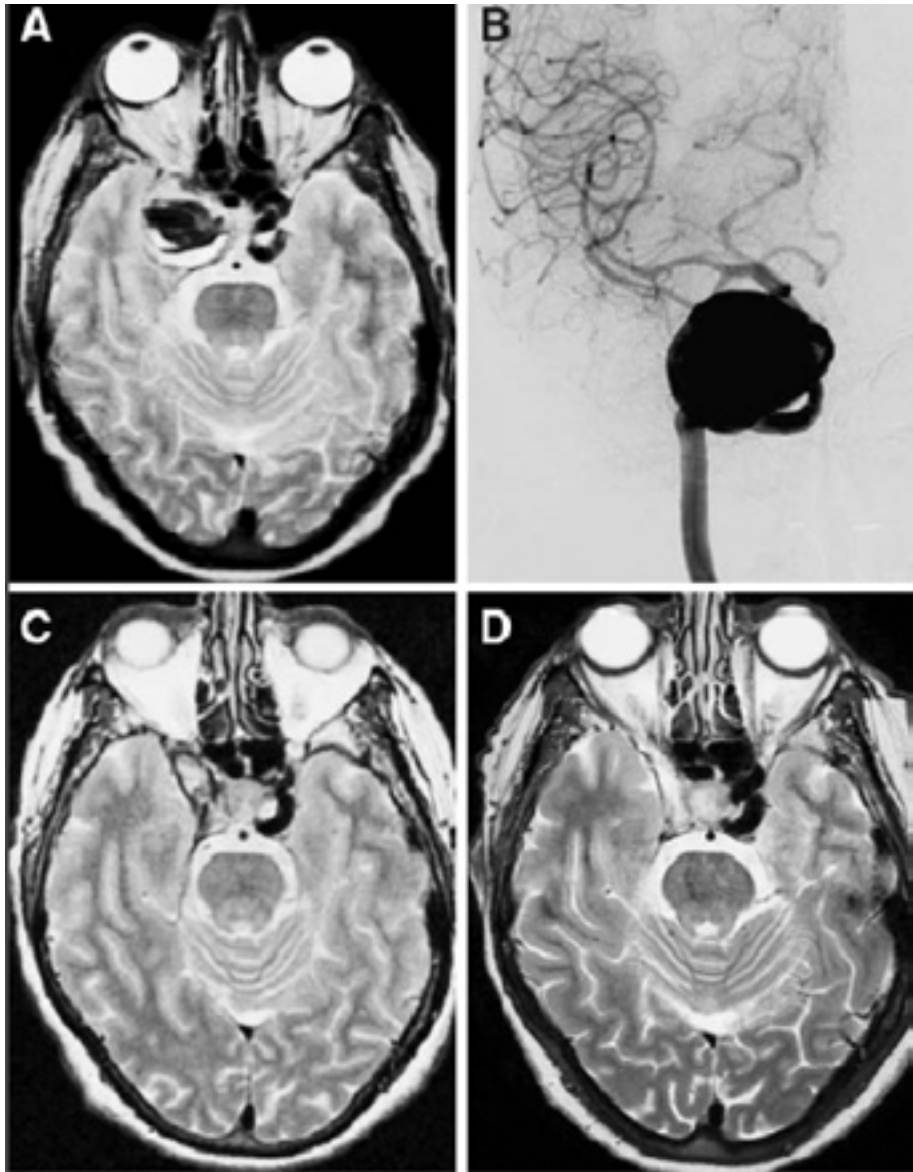
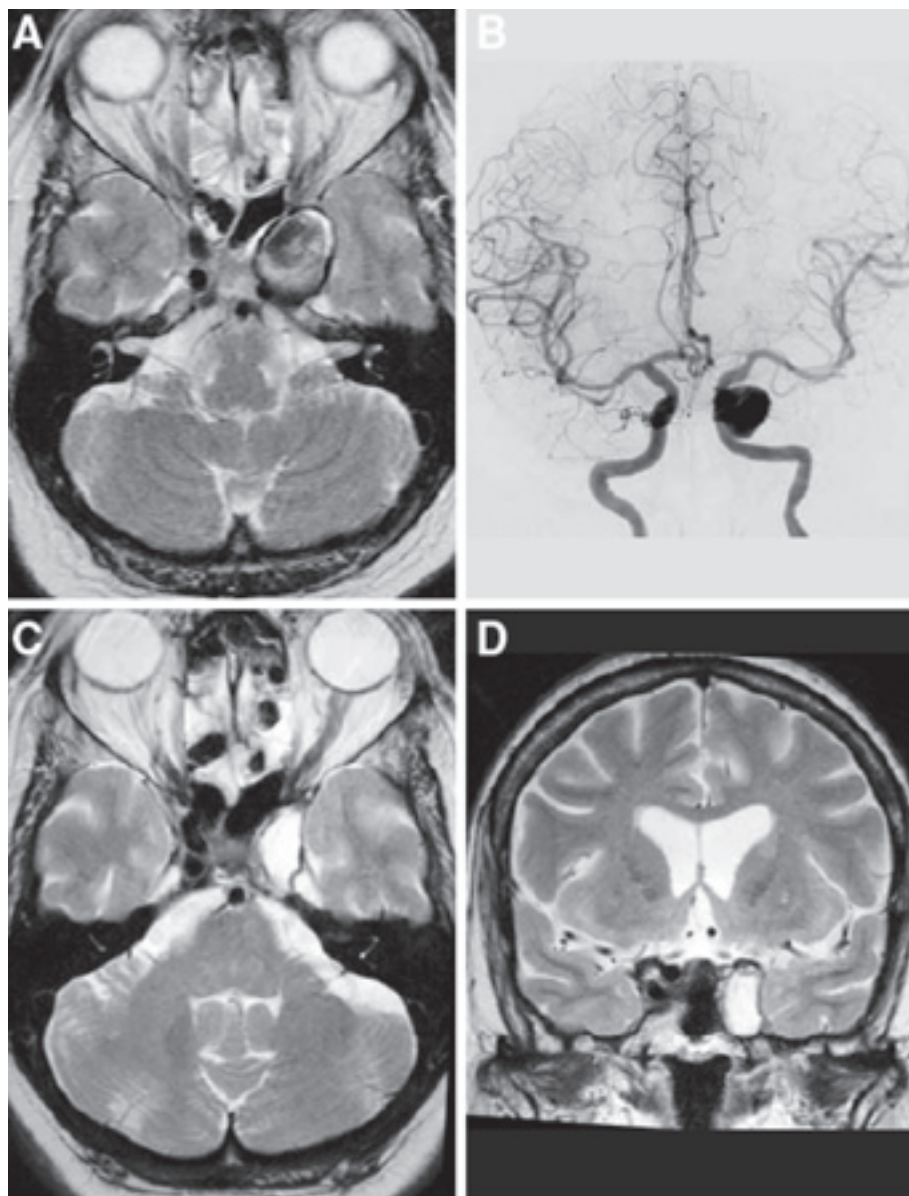


Fig 3. This 69-year-old woman presented with acute right-sided ophthalmoplegia. A, transverse T2-weighted MRI scan demonstrating a giant cavernous sinus aneurysm with flow effects. B, angiography showing the giant right cavernous sinus aneurysm. C, MRI scan obtained 3 months later showing that the aneurysm has markedly decreased in size. D, MRI scan obtained 16 months after carotid artery occlusion showing that the aneurysm is involuted completely. The patient's ophthalmoplegia was cured.



*Fig 4. This 71-year-old woman presented with acute complete left ophthalmoplegia. A, transverse T2-weighted MRI scan showing a large left cavernous sinus aneurysm with intraluminal thrombus. B, bilateral internal carotid artery angiogram showing the lumen of the cavernous sinus aneurysm. C and D, transverse and coronal MRI scans obtained 32 months after left internal carotid artery occlusion showing a decrease in aneurysm size to 50% of the original diameter. The patient's ophthalmoplegia was cured.*

## CLINICAL FOLLOW-UP

There were no early or late complications of the therapeutic artery occlusion<sup>(14, 15)</sup>. At the time of the last clinical follow-up evaluation, symptoms of mass effect were cured in 19 (60%), improved in 10 (31%), and unchanged in three (9%) out of 32 patients. Although four patients reported worsening of symptoms in the first several weeks after carotid artery occlusion, none of the patients had aggravation of existing symptoms or new clinical symptoms at the time of the last follow-up evaluation. The relationship between the initial type of clinical symptoms and evolution during the follow-up period is listed in Table 1. Accompanying retro-orbital pain was cured in all 18 patients. For most patients with clinical improvement or cure, this was obvious in the first year after carotid artery occlusion.

The proportion of aneurysms with almost complete involution was 89% (17 out of 19) in patients with clinical cure, 80% (8 out of 10) in patients with improved symptoms, and 100% (3 out of 3) in patients with unchanged symptoms. These differences were not significant ( $P > 0.9$ ).

## DISCUSSION

In this study, we found that alleviation of the symptoms of mass effect is achieved in the vast majority of patients treated with therapeutic carotid artery occlusion for large and giant carotid artery aneurysms. None of the patients in this series had new clinical symptoms or aggravation of existing symptoms during the follow-up period. In addition, most aneurysms involuted totally or decreased substantially in size over time, particularly in the first year after carotid artery occlusion. Aneurysm size reduction over time was independent of the presence of intraluminal thrombus at presentation and on location (supraclinoid versus cavernous sinus). Similar good outcomes have also been reported in previous studies<sup>(1,3,6,8,16)</sup>.

Although a relationship between aneurysm size reduction and improvement of symptoms of mass effects seems likely, we were unable to identify a definite relationship: some aneurysms in cured patients were unchanged in size and some patients with totally involuted aneurysms had unchanged symptoms of mass effect. Apparently, mere thrombosis of the aneurysm may be sufficient to alleviate the symptoms of mass effect. On the other hand, when cranial nerve damage is permanent, clinical symptoms remain unchanged even after complete aneurysm shrinkage. A limitation of our retrospective study, although relatively large and with midterm follow-up data, is the wide variation in follow-up intervals: imaging and clinical findings at various points in time could have been present at an earlier stage. Moreover, we were unable to use a validated questionnaire to determine the clinical status of the patients, and medical records were not always complete (i.e., the duration of symptoms at the time of presentation to our hospital was not always known).

Most of our patients had symptomatic aneurysms located in the cavernous sinus. There is some controversy regarding whether or not to treat these aneurysms

because their natural history is relatively benign <sup>(3,5,7,13)</sup>. The favorable long term results obtained with therapeutic carotid artery occlusion combined with the absence of complications may justify this treatment for both symptomatic and asymptomatic large and giant cavernous sinus aneurysms in patients who can tolerate carotid artery sacrifice. We generally do not treat patients with asymptomatic cavernous sinus aneurysms who cannot tolerate carotid artery occlusion.

**Table 1. Evolution of clinical symptoms of mass effect at the last follow-up evaluation for 32 patients with large or giant carotid artery aneurysms treated with carotid occlusion**

	No. of patients	Cured	Improved	Unchanged
Isolated abducens palsy	5	4	0	1
Ophthalmoparesis <sup>a)</sup>	22	15	5	2
Visual field deficit	4	0	4	0
Hemiparesis	1	0	1	0
Total	32	19 (60%)	10 (31%)	3 (9%)

**TABLE 1**

<sup>a)</sup> Two patients presented with additional trigeminal neuralgia that was cured in both patients at the time of the last follow-up evaluation.

In recent years, new endovascular techniques for occlusion of carotid aneurysms with sparing of the patency of the internal carotid artery became available in clinical practice: coiling of aneurysms with a protective balloon or stent and filling of the aneurysm with a liquid embolic agent (Onyx; Microtherapeutics, Irvine, CA). These methods are technically more challenging and complications such as thromboembolic events, in-stent thrombosis, stent malpositioning, carotid dissection, or migration of Onyx may occur <sup>(4,9,10,11)</sup>. Moreover, when coils are used to occlude large and giant aneurysms, compaction is likely over time and repeat treatment is necessary <sup>(15)</sup>. In our practice, these techniques are restricted to patients with intradural aneurysms or symptomatic cavernous sinus aneurysms who cannot tolerate carotid artery occlusion.

There is some concern that hemodynamic changes in the circle of Willis predispose to the formation of new aneurysms on the anterior communicating artery or on the contralateral carotid artery many years later. In our patient group, 26 patients had midterm (mean, 50 mo) follow-up magnetic resonance angiography at 3 Tesla; no new aneurysms were found in these patients <sup>(2)</sup>. However, longer term follow-up data will be needed to draw definitive conclusions regarding new aneurysm formation.

## **CONCLUSION**

Therapeutic carotid artery occlusion is a simple, safe, and effective treatment for large and giant carotid artery aneurysms. Almost all aneurysms involute completely or substantially decrease in size, and most aneurysms do so in the first year after carotid occlusion. Alleviation of symptoms of mass effect is achieved in most patients. Aggravation of clinical symptoms did not occur.

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## Chapter 6

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### **Long term 3T-MRA follow-up after therapeutic occlusion of the internal carotid artery to detect possible de novo aneurysm formation**

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## **ABSTRACT**

### **BACKGROUND AND PURPOSE**

The purpose of this study was to assess the incidence of de novo aneurysm formation, the incidence of subarachnoid hemorrhage (SAH) and growth of existing untreated aneurysms in 52 patients after therapeutic carotid artery balloon occlusion for carotid aneurysms.

### **PATIENTS AND METHODS**

Between January 1996 and August 2004, 52 patients were treated with carotid artery balloon occlusion for carotid aneurysms. In June 2005, all patients, their next of kin or family physicians were contacted and asked for episodes of headaches or hospital admissions that could be attributed to (SAH). In addition, magnetic resonance imaging (MRI) and magnetic resonance angiographic (MRA) at 3 Tesla were performed in 26 of 44 surviving patients after a mean follow-up period of 50.2 months (median 43.5, range 14-107 months). MRI and MRA studies were compared with the digital subtraction angiograms at the time of carotid artery occlusion.

### **RESULTS**

During clinical follow up of mean 50.3 months (median 42.5, range 0-107 months), no episodes of SAH were reported. In the 26 patients with follow up MR, no de novo aneurysms were detected (0%, 97.5 Confidence Interval 0-13.2%). Five existing untreated small aneurysms in 5 patients had not enlarged after a mean follow up of 40 months.

### **CONCLUSION**

Therapeutic carotid artery occlusion is not associated with a higher risk for development of new aneurysms or enlargement of existing untreated aneurysms over time.

## INTRODUCTION

Therapeutic carotid artery balloon occlusion is a simple, safe and effective method in the treatment of carotid aneurysms not suitable for surgical clipping or selective occlusion with coils<sup>(1-4)</sup>. After carotid occlusion, hemodynamic alterations will occur in the circle of Willis with increased flow over the contralateral carotid artery and anterior and/or posterior communicating arteries. There is some concern, expressed in anecdotal reports, that these hemodynamic changes predispose for the formation of de novo aneurysms or enlargement of existing untreated aneurysms exposing the patient to a risk of subarachnoid hemorrhage (SAH)<sup>(5-9)</sup>. In this study, we used MRI and MRA at 3.0 Tesla<sup>(10)</sup> to assess the incidence of de novo aneurysm formation and the occurrence of enlargement of existing untreated aneurysms long term after therapeutic carotid artery balloon occlusion. In addition we assessed the incidence of (SAH) during a follow up period of mean 50.3 months.

## MATERIALS EN METHODS

### PATIENTS

Between January 1996 and August 2004, 52 patients were treated with carotid artery balloon occlusion for carotid aneurysms. In June 2005, a follow up survey was performed. During the follow up, 8 patients had died: one patient died shortly after carotid occlusion of initial SAH, one patient died of trauma and 6 elderly patients died of cardiac or pulmonary disease. None of these patients had died of SAH. Of the remaining 44 surviving patients, 37 were contacted and asked for episodes of headaches or hospital admissions that could be attributed to (SAH). Seven patients could not be traced, but previous follow up was available in medical records.

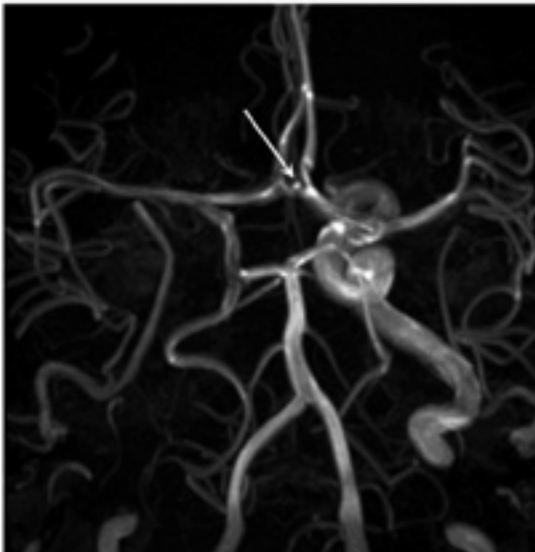
Follow up MRA was offered to these 37 patients and 28 (76%) agreed to participate in this study. Between January and June 2005, MRI and MRA were performed in 26 of 28 patients. In two patients, MR imaging could not be performed because of claustrophobia in one and severe cervical kyphosis in the other patient. There were 21 women and 5 men with a mean age of 60.6 years (range 28- 81 years). The mean follow-up period of 26 patients after carotid occlusion was 50.2 months (median 43.5, range 14-107 months, total 1310 months). Clinical follow up of all 52 patients, including the deceased patients and patients that could not be traced but who had a previous follow up, was 2616 months (mean 50.3 months, median 42.5, range 0-107 months).

This study was approved by the ethical committees of the participating hospitals.

### MRI PROTOCOL

MRI and MRA was performed on a 3.0-Tesla system (Philips Intera R10, Philips Medical Systems, Best, The Netherlands) using the sensitivity encoding (SENSE) phased array head coil (MRI Devices, Gainesville, Florida, USA).

The MR protocol included axial and coronal T2-weighted fast spin echo, coronal T1-weighted spin echo and high resolution MOTSA 3D-TOF MRA sequences. Imaging parameters for the T1-weighted spin echo sequence were 570/12 (TR/TE), 256x256 matrix (reconstructed to 512x512), 180-mm field of view, 90% rectangular field of view, 3-mm thick sections with 0.3-mm gap. Parameters for the T2-weighted fast spin echo sequence were 3394/80 (TR/TE), 400x400 matrix (reconstructed to 512x512) 230-mm field of view, 70% rectangular field of view, 3-mm thick sections with 0.5-mm gap. For the MOTSA 3D-TOF MR sequence the parameters were as follows: 3D fast field echo T1-weighted sequence, 21/4 (TR/TE) flip angle 20°, 512x512 matrix (reconstructed to 1024x1024), 200-mm field of view, 85% rectangular field of view, 1.0-mm thick sections, interpolated to 0.5-mm, 160 slices acquired in 8 chunks. The measured voxel size of the MOTSA 3D-TOF MR sequence was 0.39 x 0.61 x 1 mm and the reconstructed voxel size 0.2 x 0.2 x 0.5 mm. MRI and MRA studies were interpreted by two experienced neuroradiologists in consensus and were compared with the digital subtraction angiograms at the time of carotid artery occlusion to assess the incidence of de novo aneurysm formation and growth of additional aneurysms. All patients and their family physicians were informed on the imaging findings.



*Fig 1 Follow up MRA in a 71 year old woman 28 months after right carotid artery balloon occlusion for a giant cavernous sinus aneurysm. An additional 1.7 mm anterior communicating artery aneurysm (arrow) was unchanged in size.*

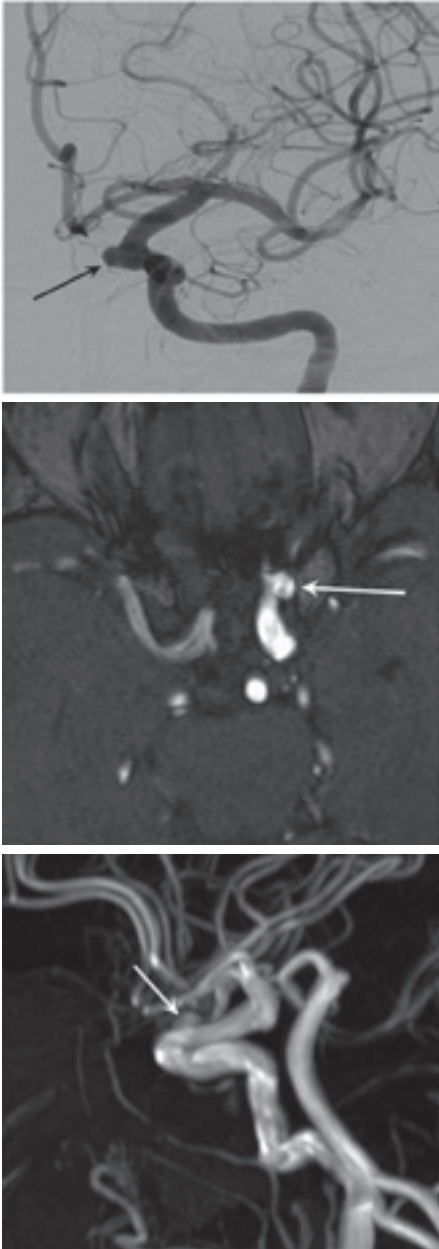


Fig 2

*A: left internal carotid angiogram at the time of right internal carotid artery occlusion for a giant ophthalmic aneurysm in a 43 year old woman shows additional small mirror ophthalmic aneurysm with a wide neck.*

*B and C: MRA MIP and source images after 27 months demonstrates unchanged size.*

## RESULTS

In the 26 patients, no de novo aneurysms (0%, 97.5% Confidence Interval 0-13.2%) were identified on MRA after a mean follow up of 50.2 months (median 43.5, range 14-107 months, 109 patient years). Five of 26 patients had one untreated additional small (2-5mm) aneurysm (fig 1 and 2) and none of these 5 aneurysms had enlarged in size after a mean follow up of 40 months (range 21-60 months, 16.6 patient years). During clinical follow up of all 52 patients of mean 50.3 months (median 42.5, range 0-107 months, 218 patient years), no episodes of headache or hospital admissions that could be attributed to SAH occurred.

## DISCUSSION

There is some concern that increased hemodynamic stress in the circle of Willis after therapeutic balloon occlusion predisposes to the formation of de novo aneurysms or enlargement of existing aneurysms. Since no systematic follow up data are available, frequency is not well established and publications are anecdotal<sup>(5-9)</sup>. In a review<sup>(6)</sup> of 19 articles published between 1962 and 2000 describing 30 cases with angiographically proven de novo aneurysm formation after carotid occlusion, incidence varied from 0.7 to 3.4% with an average of 2%. On the other hand, in other reviews of therapeutic carotid artery occlusion, no mention is made of similar cases, so cumulative incidence may be lower than 2%<sup>(6)</sup>, with unknown annual incidence rate. The interval between carotid occlusion and the onset of symptoms due to de novo aneurysms specified in 28 cases varied from 3 to 25 years with an average of 9.6 years with 20 of 28 (74%) between 3 and 10 years. The location of 27 de novo aneurysms was the anterior communicating artery in 11 (41%), the carotid artery in 14 (52%) and the vertebral artery in two (7%).

The incidence of de novo aneurysm formation and recurrent SAH in patients with aneurysms treated by clipping was recently established in large prospective studies<sup>(11,12,13)</sup>. In these studies, CT angiography was used to detect de novo aneurysms and enlargement of existing aneurysms long term after surgical clipping of a ruptured aneurysm. In 610 patients, 19 definitive de novo aneurysms were found in 14 patients (after a mean interval of 9.1 years) and 42 probable de novo aneurysms were found in 34 patients. This corresponds to an overall incidence of de novo aneurysm formation between 2.3 and 10% and an annual incidence between 0.37 and 1.20%. Of 19 definitive de novo aneurysms, 12 (63%) were located on the middle cerebral artery, 2 (11%) on the anterior communicating artery, and 5 (26%) on the carotid artery. Of these 19 aneurysms, 18 (95%) were smaller than 5 mm. In the same study, 4 of 18 (22%) existing aneurysms had enlarged in the first 5 years of follow up and 13 of 53 (25%) in the first 10 years. In a study of 752 patients with previously clipped ruptured aneurysms<sup>(13)</sup>, the cumulative incidence of recurrent SAH was 3.2% in the first 10 years after initial SAH and was 22 times higher than expected in populations with comparable age and gender.

In view of the relatively high incidence between 2.3 and 10% of de novo aneurysm formation in patients with clipped aneurysms and the cumulative incidence of recurrent SAH of 3.2% in the first 10 years, it is unlikely that the reported estimated incidence of symptomatic or asymptomatic de novo aneurysm formation after carotid artery occlusion of less than 2% can be attributed to carotid artery occlusion alone. In fact, all patients with diagnosed aneurysms have a much higher risk of new aneurysm formation and (recurrent) SAH than the general population and there is no solid evidence that therapeutic artery occlusion increases this risk. Our prospective study, although small and with limited follow up, confirms this assumption. Balloon or coil occlusion of the carotid artery is generally used in symptomatic large and giant carotid aneurysms and is a simple, safe and effective treatment. Tolerance to carotid occlusion can be tested reliably by clinical and angiographic test occlusion protocols <sup>(1,14)</sup>. Fear of inducing new aneurysm formation by hemodynamic stress is no argument to refrain from this simple therapy and to proceed to other therapies with much higher complication rates such as direct surgical clipping, bypass surgery or endovascular treatment with coils or liquid embolics with assistance of a supporting balloon or endovascular stent <sup>(15-18)</sup>. These therapies should be restricted to patients who cannot tolerate carotid artery occlusion. In conclusion, therapeutic carotid artery occlusion is not associated with a higher risk for development of new aneurysms or enlargement of existing untreated aneurysms over time.

#### **ACKNOWLEDGEMENT**

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# Chapter 7

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## **Fenestrations of the anterior communicating artery: incidence on 3D angiography and relationship to aneurysm**

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**AJNR AM J NEURORADIOL 2008; 29: 296-8**

## **ABSTRACT**

### **BACKGROUND AND PURPOSE**

Demonstration of fenestrations of the anterior communicating artery (AcomA) with conventional digital subtraction angiography is very uncommon. The purpose of this study was to assess the incidence of visible fenestrations of the AcomA on 3D rotational angiography (3DRA) and to evaluate the relationship between fenestrations of the AcomA and aneurysms of the AcomA.

### **MATERIALS AND METHODS**

We systematically reviewed 305 datasets of 3DRA of the internal carotid artery in 305 patients with aneurysms of the anterior circulation on a dedicated workstation for the presence of fenestrations on the AcomA.

### **RESULTS**

In 78 of 305 3DRAs, only the ipsilateral A2 segment was visible; thus, the AcomA could not be evaluated. Of the remaining 227 3DRAs, a fenestration of the AcomA was present in 12 (5.3%; 95% CI, 3.0%–9.1%). Of 12 fenestrations of the AcomA, 10 (83%) were associated with 1 or more aneurysms of the AcomA. Of 305 patients, 133 had an aneurysm on the AcomA, and in 127 of these, the AcomA was visible. Of 127 AcomA aneurysms with a visible AcomA, 10 were associated with fenestration, which accounted for an incidence of AcomA fenestrations with AcomA aneurysms of 7.9% (95% CI, 4.2%–14.0%). The proportion of fenestrations of the AcomA with aneurysms of the AcomA was 4.4% (10/227), and the proportion of AcomA fenestration with an aneurysm at another location was 0.9% (2/227). This difference was statistically significant ( $P=.040$ ). Even in retrospect, 11 of 12 fenestrations were not visible on 2D DSA images.

### **CONCLUSION**

In selected patients with aneurysms of the anterior circulation, fenestrations in the AcomA were found with 3DRA in 5.3% of datasets. Most fenestrations were associated with 1 or more aneurysms of the AcomA.

## INTRODUCTION

The anterior communicating artery (AcomA) is a small connecting artery between the paired anterior cerebral arteries and provides an important anastomotic channel for collateral circulation through the circle of Willis. In the embryologic stage, the AcomA develops from a multichanneled vascular network that coalesces to a variable degree by the time of birth <sup>(1)</sup>. A wide variety exists in the anatomy of the AcomA complex. A common variation is aplasia or hypoplasia of one A1 segment. In this variation, the other A1 continues as two A2 segments and an AcomA can hardly be defined <sup>(2)</sup>. In large autopsy and surgical series, single, double, or even triple fenestrations of the AcomA are reported in approximately 40% of specimens <sup>(3-5)</sup>. Despite this frequent occurrence in anatomic studies, angiographic demonstration of fenestrations of the AcomA is very uncommon. With recent advances in 3D rotational angiography (3DRA), high-resolution images are obtained that can be freely rotated. In this study, we systematically reviewed 305 datasets of 3DRA of the internal carotid artery in 305 patients with aneurysms of the anterior circulation to assess the incidence of visible AcomA fenestrations and to evaluate the relationship between AcomA fenestrations and AcomA aneurysms.

## PATIENTS AND METHODS

### 3D ROTATIONAL ANGIOGRAPHY

In our practice, all patients with suspected intracranial aneurysms in whom treatment is considered, an intra-arterial digital subtraction angiography (IA-DSA) is performed on all cerebral vessels. When an aneurysm is apparent or suspected on IA-DSA, additional 3DRA is performed on the vessel harboring the aneurysm to evaluate its anatomy and to determine the type of treatment (coiling, surgery, or occlusion of the parent vessel). In patients with aneurysms allocated to coiling, 3DRA is repeated under general anesthesia immediately before coiling to find out the best working projection. We performed angiographic imaging on a biplane neuroangiographic unit (Integris BN 3000 Neuro; Philips Medical Systems, Best, the Netherlands). 3DRA was performed with an 8-second 180° rotational run with acquisition of 200 images and with an injection of 3 to 4 ml of contrast material per second through a large-lumen 6F guiding catheter in the internal carotid artery. On a dedicated workstation, 3D reconstructions can be made in a matrix of maximum 512 <sup>(3)</sup>. All raw 3DRA datasets are stored on the hard drive of the workstation or on a compact disc. Raw datasets stored on compact discs can be reloaded in the workstation for real-time evaluation.

### PATIENTS

Between March 2004 and May 2007, 305 patients with intracranial aneurysms of the anterior circulation had 3DRA of one of the carotid arteries. All of these 305 3D datasets were reevaluated on the workstation for the presence of fenestrations and aneurysms on the AcomA.

### STATISTICAL ANALYSIS

In patients with a visible AcomA, we compared the proportion of fenestrations of the AcomA associated with an aneurysm of the AcomA with the proportion of fenestrations of the AcomA associated with an aneurysm at another location, using the  $\chi^2$  test. In patients with a visible AcomA, we compared the proportion of AcomA aneurysms with AcomA fenestrations with the proportion of aneurysms at other locations with AcomA fenestrations, using the  $\chi^2$  test.

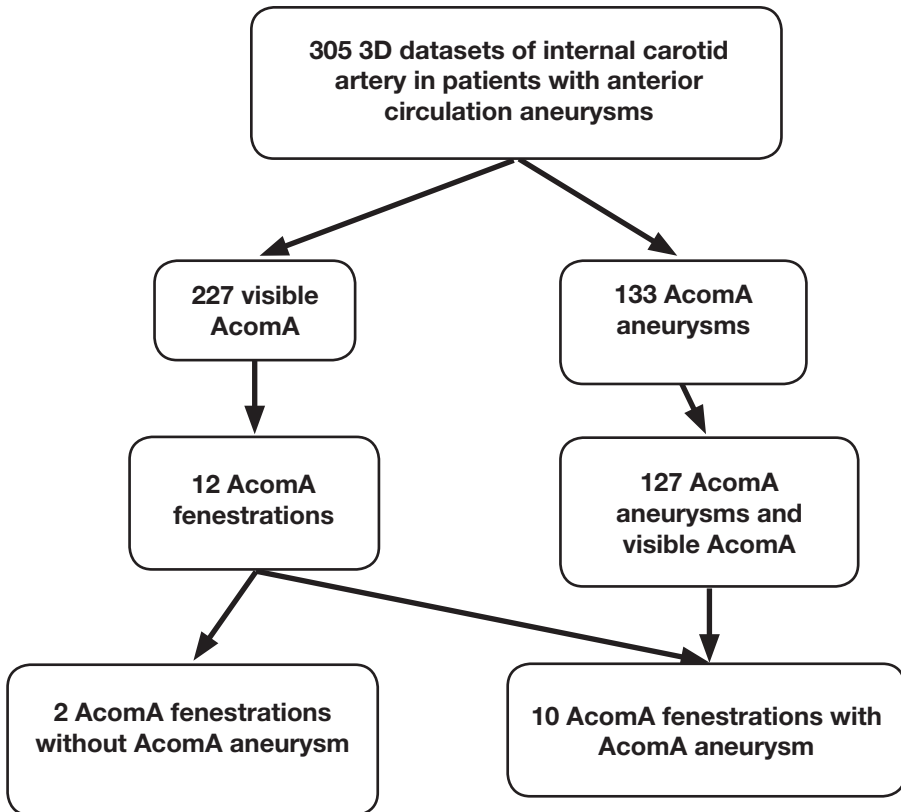


Fig 1. Diagram showing relationship of aneurysms of the AcomA and fenestrations of the AcomA in 305 patients with aneurysms of the anterior circulation.

### RESULTS

Results are summarized in Fig 1. In 78 of 305 3DRAs, only the ipsilateral A2 segment was visible; thus, the AcomA could not be evaluated (an AcomA aneurysm without a visible AcomA was defined as an aneurysm on the transition

from A1 to A2). Of the remaining 227 3DRAs with good visibility of the AcomA, a fenestration was present in 12 (5.3%; 95% CI 3.0–9.1%) (Fig 2). Of 12 fenestrations of the AcomA, 10 (83%) were associated with 1 or more aneurysms of the AcomA. Of 305 patients, 133 had an aneurysm on the AcomA, and in 127 of these, the AcomA was visible. Of 127 AcomA aneurysms with a visible AcomA, 10 were associated with a fenestration accounting for an incidence of AcomA fenestrations with AcomA aneurysms of 7.9% (95% CI 4.2–14.0%). Even in retrospect, 11 of 12 fenestrations were not visible on 2D DSA images. The proportion of AcomA fenestration with an AcomA aneurysm was 4.4% (10/227), and the proportion of AcomA fenestration with an aneurysm at another location was 0.9% (2/227). This difference was statistically significant ( $P=.040$ ). The proportion of AcomA aneurysms associated with fenestration was 7.9% (10/127), and the proportion of aneurysms at other locations associated with fenestration of the AcomA was 2.0% (2/100). This difference was not statistically significant ( $P=.096$ ).

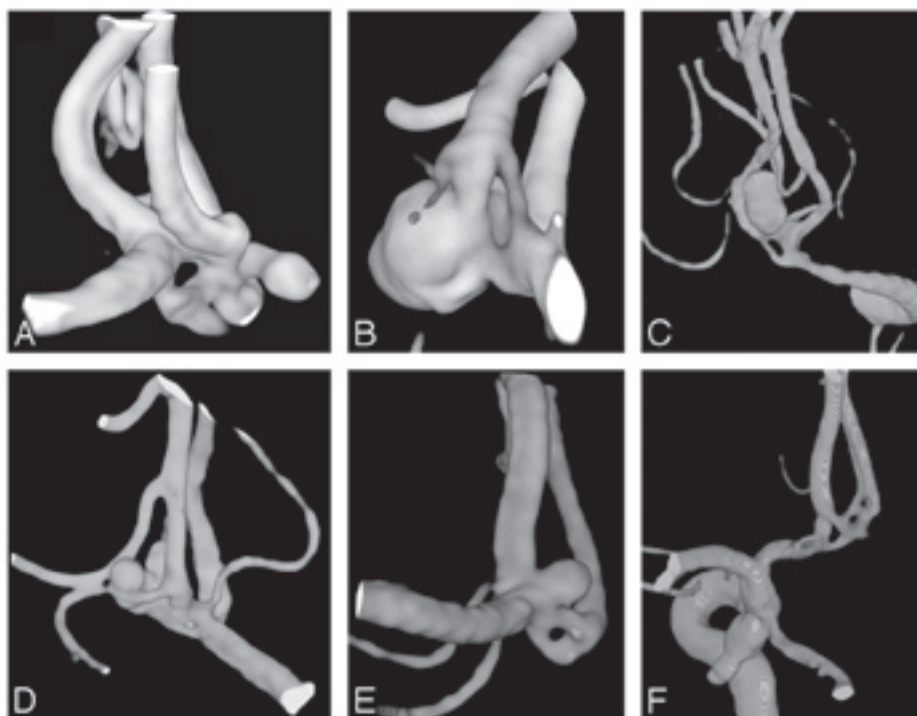


Fig 2. A–F, Examples of fenestrations of the AcomA. A, Fenestration with three A2s and three small aneurysms. B,C, Simple fenestration with aneurysm. D, Multiple fenestrations with 2 aneurysms. E, Simple fenestration with an aneurysm. F, Multiple fenestrations with an aneurysm of the posterior communicating artery.

## DISCUSSION

In our study, we found that fenestrations of the AcomA were discernible in 12 (5.3%) of 227 3DRA datasets with a visible AcomA. Of these 12 fenestrations, 10 were associated with 1 or more aneurysms of the AcomA. In a reverse fashion, of 127 aneurysms of the AcomA with a visible AcomA, 10 (7.9%) were associated with fenestration. There is a wide variety in fenestrations of the AcomA from simple duplication (Fig 2C) to stepladder-like configurations (Fig 2F). Our study is the first with systematic imaging assessment of fenestrations of the AcomA. Although AcomA fenestrations were significantly more often associated with AcomA aneurysms than with aneurysms at other locations in our patient group, a definite relationship cannot be established. First, only a small proportion of expected fenestrations of the AcomA (40% in anatomic studies) are visible on 3DRA. Second, no 3DRA data are available from patients without aneurysms. The introduction of 3DRA has greatly improved the imaging quality of cerebral vessels and plays an important role in treatment planning and measurements of intracranial aneurysms<sup>(6-9)</sup>. This improvement of imaging quality is illustrated by the fact that, in retrospect, only 1 of 12 fenestrations of the AcomA was visible on 2D IA-DSA. In a review by Sanders et al<sup>(10)</sup> of 5190 cerebral angiograms, 37 fenestrations were found, but none of these were on the AcomA. Because the frequency of fenestrations on the AcomA in large surgical and autopsy series is approximately 40%, a substantial proportion of fenestrations remain invisible on 3DRA with current available resolution. This is not surprising because in many fenestrations, bridging arteries are too thin (0.1–0.3 mm) to become perceptible on 3DRA. In anatomic studies, important perforating arteries supplying the optic chiasm, infundibulum, subcallosal area, and preoptic area of the hypothalamus may arise from the AcomA, also from fenestrated AcomAs<sup>(3,4)</sup>. This possibility of the presence of perforators implies that with coiling of aneurysms on a fenestrated, double, or triple AcomA, sparing the patency of all channels of the AcomA should be recommended, despite the fact that occlusion of the channel harboring the aneurysm would have no consequences for blood flow to the A2 and A1 segments. In some patients with an aneurysm on a fenestrated AcomA, the anatomy is quite complex (Figs 2A and 2D), and accurate 3D images are helpful in recognizing anatomic landmarks during surgery and general appreciation of anatomy.

## CONCLUSION

In selected patients with aneurysms of the anterior circulation, fenestrations of the AcomA were found with 3DRA in 5.3% of datasets. Most fenestrations were associated with 1 or more aneurysms of the AcomA.

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# Chapter 8

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## How long does it take to coil an intracranial aneurysm?

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## **ABSTRACT**

### **INTRODUCTION**

The change in the treatment of choice for intracranial aneurysms from clipping to coiling has been associated with an important change in logistics. The time needed for coiling is variable and depends on many factors. In this study, we assessed the procedural time for the coiling of 642 aneurysms and tried to identify predictors of a long procedural time.

### **METHODS**

The procedural time for coiling was defined as the number of minutes between the first diagnostic angiographic run and the last angiographic run after embolization. Thus, induction of general anesthesia and catheterization of the first vessel were not included in the procedural time. A long procedural time was defined as the upper quartile of procedural times (70–158 min). Logistic regression analysis was performed for several variables.

### **RESULTS**

The mean procedural time was 57.3 min (median 52 min, range 15–158 min). More than half of the coiling procedures lasted between 30 and 60 min. Multiple logistic regression analysis identified the use of a supportive device (OR 5.4), procedural morbidity (OR 4.5) and large aneurysm size (OR 3.0) as independent predictors of a long procedural time. A poor clinical condition of the patient, the rupture status of the aneurysm, gender, the occurrence of procedural rupture, and aneurysm location were not related to a long procedural time. The mean time for the first 321 coiling procedures was not statistically significantly different from mean time for the last 321 procedures.

### **CONCLUSION**

With optimal logistics, coiling of most intracranial aneurysms can be performed in one to two hours, including patient handling before and after the actual coiling procedure.

### **KEYWORDS**

Intracranial aneurysms, Coiling Procedural time.

## INTRODUCTION

Coiling of intracranial aneurysms has become the treatment of choice and has partly replaced neurosurgical clipping in most neurosurgical centers<sup>(1-3)</sup>. This change in treatment modality has been associated with an important change in logistics: patients are no longer treated in the operating room but in the radiology department. Coiling of intracranial aneurysms has to fit into the program of the angiography suite and an anesthetic team has to leave the operating room complex to assist in coiling. Since many aneurysms are treated acutely after subarachnoid hemorrhage (SAH), planning may be difficult. The time slot needed for coiling is variable and depends on many factors such as complexity of the aneurysm, the number of aneurysms that should be treated, the experience and skills of the treating endovascular team and local preferences. In this study, we assessed the procedural time for coiling of 642 aneurysms and tried to identify predictors of a long procedural time.

## PATIENTS AND METHODS

### PATIENTS

From January 1998 to September 2005, 817 aneurysms were coiled. The starting point of the study was chosen because of the installation of a new biplane angiographic unit (Integris 3000 BN Neuro, Philips Medical Systems, Best, The Netherlands) at the end of 1997. We excluded 65 patients (with 146 aneurysms) with more than one aneurysm coiled in the same session. Of the remaining 671 aneurysms, 642 had complete imaging data available for review. The time of each angiographic run was printed on the images automatically. The procedural time for coiling was defined as the number of minutes between the first diagnostic angiographic run and the last angiographic run after embolization. Thus, induction of general anesthesia and catheterization of the first vessel were not included in the procedural time. In the vast majority of patients, 3-D rotational angiography (3DRA) of the vessel harboring the aneurysm was performed<sup>(4)</sup>. Many patients with acute SAH confirmed on CT scan were immediately transferred to the angiography suite and underwent complete diagnostic angiography and coiling of the aneurysm under general anesthesia. Only in patients with unruptured aneurysms, diagnostic angiography was usually available before coiling, and in these patients only 3DRA was performed during the process of coiling. Of the 642 patients, 178 were men and 464 were women with a mean age of 52.9 years (median 52 years, range 19–83 years). Of the 642 aneurysms, 523 had ruptured and 119 had not. Among the 523 patients with a ruptured aneurysm at the time of treatment, clinical condition was Hunt and Hess (HH) I/II in 337, HH IV/V in 68, and HH III in 118. The mean aneurysm size was 8.0 mm (range 2–55 mm). The aneurysm was located in the posterior circulation in 154, in the anterior cerebral artery in 246, in the middle cerebral artery in 46, and in the carotid artery in 196 patients. The type of coil used was mostly Guglielmi detachable coils (GDC; Boston Scientific, Fremont, Calif.), followed by TruFill/Orbit coils (Cordis

Neurovascular, Miami Lakes, Fl.) and straight coils 50 cm long (Cook Detach, Cook, Copenhagen, Denmark) for large and giant aneurysms <sup>(5)</sup>. A supportive device was used during coiling in 60 aneurysms, a supportive balloon in 55, a TriSpan in 4, and a stent in 1 aneurysm <sup>(6)</sup>. In 26 aneurysms a procedural rupture occurred. Complications leading to permanent neurological deficit or death occurred in 40 patients <sup>(7, 8)</sup>.

### **STATISTICAL ANALYSIS**

To assess possible predictors of a long procedural time, we defined a long procedural time as the upper quartile of the procedural times (70–158 min) and performed logistic regression analysis for the following variables: male gender, age greater than the median age of 52 years, ruptured aneurysm, aneurysm size in the upper quartile (10–55 m), occurrence of procedural rupture, HH grade III–V, occurrence of procedural morbidity defined as complications leading to death or permanent neurological deficit <sup>(7, 8)</sup>, use of a supportive device, location on the anterior cerebral artery, carotid artery or middle cerebral artery, and location in the posterior circulation. Subsequently, to identify independent predictors, multiple logistic regression analysis was performed for all significant predictors. To assess whether recent technical developments had influenced procedural time, we compared the mean procedural time of the first 321 aneurysms with the mean procedural time of the last 321 aneurysms using a t test. In addition, we assessed whether the implementation of 3DRA in October 2000 had influenced procedural time.

## RESULTS

The mean procedural time was 57.3 min (median 52 min, range 15–158 min). More than half of the coiling procedures lasted between 30 and 60 min (Fig. 1), 49 procedures (7.6%) lasted less than 30 min, and 68 procedures (10.6%) lasted more than 90 min. Median and mean procedural times with ranges and standard deviations for aneurysm coiling procedures in relation to patient and aneurysm characteristics are summarized in Table 1. The predictors of a long procedural time are displayed in Table 2. The use of a supportive device was the strongest predictor of a long procedural time (OR 5.4), followed by the occurrence of procedural morbidity (OR 4.5), a large aneurysm size (OR 3.0), and patient age (OR 1.5). A poor clinical condition of the patient, rupture status of the aneurysm, gender, occurrence of procedural rupture, aneurysm location, and implementation of 3DRA had no influence on procedural time. Multiple logistic regression analysis identified the use of a supportive device, occurrence of procedural morbidity, and large aneurysm size as independent predictors of a long procedural time. The mean procedural time for the first 321 coil procedures was 56.5 min (median 51 min, range 18–158 min) and for the last 321 this was 58.1 min (median 54 min, range 15–124 min). This difference was not significant (*t* test, *P*=0.40)

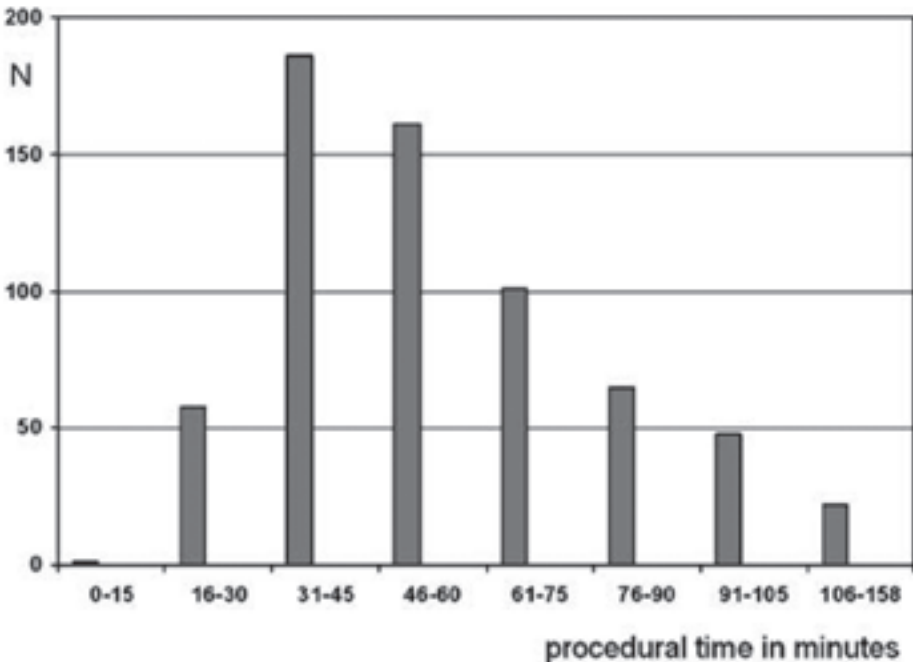


Fig. 1 Procedural times in minutes for 642 coiling procedures displayed as number of procedures in 15-min time periods.

Table 1 Procedural times for all 642 aneurysms in relation to patient and aneurysm characteristics

Variable	No. of aneurysms	Procedural time (min)			Standard deviation
		Median	Mean	Range	
All aneurysms	642	57.3	52.0	15–158	24.1
Use of supportive device	60	80.5	80.2	35–150	30.7
Procedural morbidity	40	72.5	75.6	28–158	30.7
Aneurysm size in upper quartile (10–55 mm)	163	64	70.5	25–158	26.4
Age more than median 52 years	321	55	60.7	17–158	25.0
Hunt and Hess grade III–V	186	54	59.2	18–122	22.6
Ruptured aneurysm	523	52	58.1	16–158	24.6
Male gender	182	55	60.4	17–131	23.8
Procedural rupture	26	50	53.8	16–107	21.3
Aneurysm location					
Middle cerebral artery	46	53	61.8	19–131	26.8
Posterior circulation	154	54	61.7	22–146	27.1
Anterior cerebral artery	246	53.5	57.1	16–112	21.2
Carotid artery	196	48	53.1	15–158	23.9
Implementation of 3-D angiography					
Before	167	52	58.6	18–158	25.5
After	475	52	56.9	15–146	23.7

## DISCUSSION

In this study the mean procedural time for coiling was 57 min. Most procedures were performed within 1 h. Procedural time was defined as the time between the first and the last angiographic run, since this time period could easily be assessed from time prints on the images. The time for patient preparation, anesthetic care, insertion of angiographic sheet and catheterization of the first vessel were not included in the procedural time. In our department, this additional time is usually between 30 and 45 min. This means that the typical time needed for coiling of an intracranial aneurysm is around one and a half hours, varying from one to two hours.

A long procedural time was associated with the use of a supportive device, occurrence of procedural morbidity and large aneurysm size. Although coiling of middle cerebral artery aneurysms tended to take more time and coiling of carotid artery aneurysms tended to take less time, these differences were not statistically significant. The strongest predictor of a long procedural time was the use of a supportive device, mostly a supportive balloon<sup>(6)</sup>. When the use of a supportive device is not anticipated from the beginning of the procedure, an additional guiding catheter must be placed in the groin and navigated to the vessel harboring the aneurysm, or the guiding catheter has to be changed for a catheter with larger inner lumen. In addition, the balloon catheter has to be prepared and navigated across the neck of the aneurysm, this may be time consuming since 0.010-inch guidewires are usually difficult to steer. Another predictor of a long procedural time was large aneurysm size. In larger aneurysms a higher number of coils can usually be inserted and the accumulated electrolytic detachment time thus increases. The last predictor of a long procedural time was the occurrence of morbidity (not the occurrence of procedural rupture). Most morbidity is caused by thromboembolic complications. Several actions may be undertaken when such a complication occurs, such as mechanical thrombus fragmentation and selective injection of thrombolytic drugs, which both lead to a longer procedural time.

It is of note that no difference in procedural time was found between the earlier and later procedures, despite the technical advances in microcatheters and guidewires and increased experience. In both groups, there was no difference in mean aneurysm size (8.7 versus 7.2 mm), use of a supportive device (both 30) or occurrence of morbidity (both 20). We did not include the first 3 years of coiling in our hospital because the time was not printed on the images by the angiographic equipment used during that period. The mean procedural time may have been longer on the steep side of the learning curve during those first 3 years.

In our high-volume department, logistics have been optimized. In patients scheduled for coiling, an intravenous line and urinary catheter are placed on the ward, the treating endovascular team is experienced, a biplane angiographic unit with 3DRA is available, all catheters and devices needed are available in the angiography room, micro-catheters and guidewires are prepared by technicians,

and in recent years the puncture site is closed with a dedicated device. For coiling of large and giant aneurysms, we use for the most part mechanically detachable coils 50 cm long. All anesthetists involved in coil procedures are experienced, without residents in training. Our time slot for anesthesia is in the afternoon from 1300 to 1600 hours with a “deadline” at 16.30, after which time an anesthetist on call has to be notified to take over care. With these logistics we normally plan two patients, and regularly treat three patients within this time slot.

Both of the senior authors (M.S. and W.J.v.R) have performed many coil procedures in four other hospitals in The Netherlands. The procedural time may differ greatly between centers, depending on many factors such as availability of single- or biplane angiographic equipment and 3DRA, the experience of the operator, supporting technicians and anesthetic team, and local preferences such as liberal or restricted use of supportive devices.

*Table 2* Odds ratios with 95% confidence intervals for different variables for the upper quartile of procedural times (70–158 min)

Variable	Odds ratio	95% CI
Use of supportive device	5.40	3.11–9.34
Procedural morbidity	4.49	2.33–8.64
Aneurysm size in upper quartile (10–55 mm)	3.03	2.06–4.45
Age more than median age	1.47	1.02–2.10
Hunt and Hess grade III–V	1.32	0.88–1.97
Ruptured aneurysm	1.41	0.87–2.30
Male gender	0.79	0.54–1.16
Procedural rupture	0.73	0.27–1.98
Aneurysm location		
Middle cerebral artery	1.81	0.97–3.40
Posterior circulation	1.30	0.87–1.95
Anterior cerebral artery	0.93	0.65–1.35
Carotid artery	0.68	0.46–1.02
Implementation of 3D angiography	1.11	0.74–1.66

## CONCLUSION

With optimal logistics, coiling of most intracranial aneurysms can be performed in one to two hours, including patient handling before and after the actual coiling procedure.

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# Chapter 9

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## Summary

## CHAPTER 1

In Chapter 1 we describe the background and aim of the study.

## CHAPTER 2

In Chapter 2, we compared coils coated with transforming growth factor- $\beta$  (TGF- $\beta$ ) to standard platinum coils in an experimental setting. TGF- $\beta$  coil modifications are aimed primarily at increasing the “biological activity” of the coil, because standard platinum coils are biologically inert and fail to induce sufficient scar formation. TGF- $\beta$  is a ubiquitous growth factor that has been demonstrated to increase collagen synthesis, and endothelialization in vivo. These biological functions are considered beneficial in the setting of coil embolization of aneurysms. In 12 New Zealand White rabbits elastase-induced saccular aneurysms were embolized with standard platinum coils or with TGF- $\beta$  coated coils.

The aneurysms embolized with TGF- $\beta$  coated coils underwent earlier cellular aneurysm neck coverage than those embolized with standard coils, but differences in coverage between coated and control coils were no longer present at later time points.

We concluded that these data suggest that improvements in intra-aneurysmal cellular proliferation resulting from coil modifications, although significant in the early postembolization phase, dissipate over time.

## CHAPTER 3

In Chapter 3, we compared clinical and angiographic results of embolization of 101 intracranial aneurysms with Nexus coils to historical results of coiling of 120 aneurysms with GDC 10 coils and 115 with Cordis TruFill coils (both standard platinum coils) using an identical methodology.

Nexus coils are standard complex platinum coils with interwoven PGLA microfilament threads. Polyglycolic/polylactic acid (PGLA) addition to bare platinum coils is intended to reduce the reopening rate of coiled intracranial aneurysms. Initial occlusion in aneurysms treated with Nexus coils was (near) complete in 97 aneurysms and incomplete in 4 aneurysms. There were no permanent procedural complications (0 in 95 patients, 0%, 97.5% CI 0.0-3.3%). Mean aneurysm volume was 180.2 mm<sup>3</sup> (median 71, range 5-1624 mm<sup>3</sup>). Mean packing was 19.4% (median 18.3%, range 7.5-38.9%). Six months angiographic follow up in 87 of 101 aneurysms showed incomplete occlusion in 14 (16%) and 12 of those (14%) were additionally coiled.

The mean packing of 19.4% of Nexus coils was significantly lower than 22.9% for GDC 10 and 29.7% for Cordis TruFill coils. Other clinical results, including reopening and retreatment rates, were not statistically different.

We concluded that there was no reduction in the reopening rate in aneurysms treated with Nexus coils.

## CHAPTER 4

In Chapter 4, we evaluated the morbidity, mortality, and angiographic results of coiling of asymptomatic incidental aneurysms and compared the characteristics of these patients and aneurysms with those of patients with incidental aneurysms that were not treated. During a 10-year period, 97 patients without a previous subarachnoid hemorrhage, presented with incidentally found intracranial aneurysms. In 48 of these patients, 58 aneurysms were coiled. Permanent morbidity of coiling was 2.1% (1 of 48) and mortality was 0%. Of 46 aneurysms with angiographic follow up, 45 were completely or near completely occluded. To obtain these results, 3 aneurysms were coiled more than once. Coiled incidental aneurysms did not rupture during the median follow-up period of 28.5 months. Compared to untreated patients with incidental aneurysms, coiled patients were younger and more often had multiple aneurysms. Aneurysms of coiled patients more often had a small neck, were more often located on the carotid artery, and were less often located on the middle cerebral artery.

We concluded that coiling of incidental intracranial aneurysms has a low complication rate in selected aneurysms and patients.

## CHAPTER 5

In Chapter 5, we used 3.0 Tesla Magnetic Resonance Imaging to evaluate aneurysm size in relation to evolution of clinical symptoms in 39 patients with large or giant carotid artery aneurysms treated with therapeutic carotid artery occlusion. These patients had clinical and magnetic resonance imaging (MRI) follow-up of at least 3 months (mean, 35.9, median 29, range 3–107 months, 117 patient-years). Clinical presentation was mass effect caused by the aneurysm in 32, subarachnoid hemorrhage in 3, and epistaxis in 1 patient. Two aneurysms were an incidental finding and 1 was additional to another ruptured aneurysm.

All aneurysms seemed to have thrombosed completely after carotid artery occlusion as observed on early and late MRI and MRA follow-up studies. At the time of the latest MRI follow-up, 29 (74%) of the 39 aneurysms were obliterated totally, two aneurysms decreased to 25% of the original diameter, two aneurysms decreased to 50%, and five aneurysms decreased to 75%. Two aneurysms remained unchanged in size after 49 and 58 months. At the latest clinical follow-up evaluation, symptoms of mass effect were cured in 19 (60%), improved in 10 (31%), and remained unchanged in three (9%) of the 32 patients.

We concluded that therapeutic carotid artery occlusion is a simple, safe, and effective treatment for large and giant carotid artery aneurysms. Almost all aneurysms involuted completely or substantially decreased in size over time. Alleviation of symptoms of mass effect was achieved in most patients.

## CHAPTER 6

In Chapter 6, we used 3.0 Tesla Magnetic Resonance Angiography to assess the incidence of the novo aneurysm formation and growth of existing untreated aneurysms in patients after therapeutic carotid artery occlusion for carotid aneurysms. 3.0 Tesla MRA and MRI was performed in 26 of 44 surviving patients after a mean follow-up period of 50.2 months (median 43.5, range 14-107 months). MRI and MRA studies were compared with digital subtraction angiograms at the time of carotid artery occlusion. During a clinical follow-up of 50.3 months (median 42.5, range 0-107 months), no episodes of SAH were reported. In the 26 patients with follow-up MRA, no de novo aneurysms were detected (0%, 97.5 CI 0-13.2%). Five existing untreated small aneurysms in 5 patients had not enlarged after a mean follow-up of 40 months.

We concluded that therapeutic carotid artery occlusion is not associated with a higher risk for development of new aneurysms or enlargement of existing untreated aneurysms over time.

## CHAPTER 7

In Chapter 7, we assessed the incidence of visible fenestrations of the anterior communicating artery (AcomA) on 3D rotational angiography (3DRA) and evaluated the relationship between fenestrations of the AcomA with aneurysms at this location. With conventional digital subtraction angiography, demonstration of fenestrations of the AcomA is very uncommon. On a dedicated workstation, we systematically reviewed 305 3DRA datasets of the internal carotid artery in 305 patients with aneurysms of the anterior circulation for the presence of fenestrations on the AcomA. In 78 of 305 3DRAs, only the ipsilateral A2 segment was visible; thus, the AcomA could not be evaluated. Of the remaining 227 3DRAs, a fenestration of the AcomA was present in 12 (5.3%; 95% CI 3.0%-9.1%). Of 12 fenestrations of the AcomA, 10 (83%) were associated with one or more aneurysms of the AcomA. Of 305 patients, 133 had an aneurysm on the AcomA, and in 127 of these, the AcomA was visible. Of 127 AcomA aneurysms with a visible AcomA, 10 were associated with fenestration, which accounted for an incidence of AcomA fenestrations with AcomA aneurysms of 7.9% (95% CI 4.2%-14.0%). The proportion of fenestrations of the AcomA with aneurysms of the AcomA was 4.4% (10/227), and the proportion of AcomA fenestration with an aneurysm at another location was 0.9% (2/227). This difference was statistically significant ( $P=.040$ ). Even in retrospect, 11 of 12 fenestrations were not visible on 2D DSA images.

We concluded that in selected patients with aneurysms of the anterior circulation, fenestrations in the AcomA are found with 3DRA in 5.3% of datasets. Most fenestrations were associated with one or more aneurysms of the AcomA.

## CHAPTER 8

In Chapter 8, we assessed the procedural time for the coiling of 642 aneurysms and tried to identify predictors of a long procedural time. In particular, we were interested whether implementation of 3DRA in October 2001 had resulted in a decrease of procedural time. The time needed for coiling an intracranial aneurysm is variable and depends on many factors. In this study, the procedural time for coiling was defined as the number of minutes between the first diagnostic angiographic run and the last angiographic run after embolization. The mean procedural time was 57.3 min (median 52 min, range 15-158 min). More than half of the coiling procedures lasted between 30 and 60 min. Multiple logistic regression analysis identified the use of a supportive device (OR 5.4), procedural morbidity (OR 4.5) and large aneurysm size (OR 3.0) as independent predictors of a long procedural time. A poor clinical condition of the patient, the rupture status of the aneurysm, gender, the occurrence of procedural rupture, and aneurysm location were not related to a long procedural time. The mean time for the first 321 coiling procedures was not statistically significantly different from mean time for the last 321 procedures. Implementation of 3DRA had no influence on procedural time.

We concluded that with optimal logistics, coiling of most intracranial aneurysms can be performed in one to two hours, including patient handling before and after the actual coiling procedure.



# Hoofdstuk 10

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## Samenvatting in het Nederlands

## HOOFDSTUK 1

In hoofdstuk 1 wordt het doel van dit proefschrift beschreven.

## HOOFDSTUK 2

In hoofdstuk 2, vergeleken wij coils “gecoat” met “transforming growth factor- $\beta$ ” (TGF- $\beta$ ) met standaard platina coils in een diermodel. TGF- $\beta$  coil modificaties beogen de “biologische activiteit” van de coil te verhogen: standaard platina coils zijn biologisch inert en induceren littekenvorming en endothelialisatie onvoldoende. TGF- $\beta$  is een alomvattende groeifactor die, althans in vivo, collageen synthese en endotheelvorming stimuleert. Dit biologische proces lijkt waardevol bij endothelialisatie van de nek na embolisatie van aneurysma’s met coils.

De aneurysma’s geëmboliseerd met TGF- $\beta$  gecoate coils ondergingen eerder cel proliferatie ter hoogte van de nek van het aneurysma dan de aneurysma’s gecoild met standaard coils, maar het verschil in proliferatie tussen gecoate en standaard coils werd niet meer gezien op latere tijdstippen.

Wij concludeerden dat de coil modificatie initieel de intra-aneurysmatische cel proliferatie verbetert, maar dat dit effect na verloop van tijd verdwijnt.

## HOOFDSTUK 3

In hoofdstuk 3, vergeleken wij klinische en angiografische resultaten van 101 intracraniale aneurysma’s geëmboliseerd met Nexus coils met de historische resultaten van 120 aneurysma’s gecoild met Guglielmi Detachable Coils 10 (GDC 10) en 115 aneurysma’s gecoild met Cordis Trufill coils (beiden standaard platina coils).

Nexus coils zijn standaard platina coils met verweven “polyglycolic/polylactic acid (PGLA)” microvezels. PGLA zou cellulaire activiteit en endothelialisatie van de nek na coiling stimuleren en daardoor zou minder vaak heropening optreden. In aneurysma’s behandeld met Nexus coils was de initiële occlusie (bijna) compleet bij 97 aneurysma’s en incompleet bij 4 aneurysma’s. Er waren geen permanente procedurele complicaties (0 in 95 patiënten, 0%, 97.5% CI 0.0-3.3%). Het gemiddelde volume van de aneurysma’s was 180.2 mm<sup>3</sup> (mediaan 71, spreiding 5-1624). De gemiddelde vullingsgraad was 19.4% (mediaan 18.3%, spreiding 7.5-38.9%). Angiografisch vervolg na zes maanden bij 87 van de 101 aneurysma’s liet incomplete occlusie zien bij 14 (16%) en 12 hiervan (14%) werden additioneel gecoild. De gemiddelde vullingsgraad van 19.4% van de Nexus coils was significant lager dan de 22.9% van de GDC 10 en de 29.7% van de Cordis Trufill coils. Andere klinische parameters, inclusief proportie heropening en herbehandeling, waren niet significant verschillend.

Wij concludeerden dat er geen reductie in de proportie van heropening was in de aneurysma’s behandeld met PGLA Nexus coils.

## HOOFDSTUK 4

In hoofdstuk 4 beschreven wij de morbiditeit, mortaliteit en angiografische resultaten van het coilen van asymptomatische incidenteel gevonden aneurysma's en vergeleken de karakteristieken van deze patiënten en aneurysma's met die van patiënten met incidenteel gevonden aneurysma's die niet waren behandeld. Gedurende een periode van 10 jaar, presenteerden 97 patiënten zonder een voorafgaande subarachnoïdale bloeding, zich met een toevallig gevonden aneurysma. In 48 van deze patiënten werden 58 aneurysma's gecoild. Permanente morbiditeit als gevolg van de coiling was 2.1% (1 van de 48) en de mortaliteit was 0%. Van de 46 aneurysma's die angiografisch werden vervolgd na 6 maanden, waren 45 compleet of bijna compleet afgesloten. Drie aneurysma's werden meer dan één maal gecoild. De gecoilde aneurysma's ruptuurden niet gedurende een gemiddelde vervolgduur van 28.5 maanden.

Vergeleken met onbehandelde patiënten met een toevallig gevonden aneurysma, waren gecoilde patiënten jonger en hadden zij vaker meerdere aneurysma's. Aneurysma's van gecoilde patiënten hadden vaker een smalle nek, waren vaker gelokaliseerd op de arteria carotis en minder vaak op de middelste cerebrale arterie. Wij concludeerden dat het coilen van een incidenteel gevonden aneurysma een laag complicatie risico heeft in geselecteerde aneurysma's en patiënten.

## HOOFDSTUK 5

In hoofdstuk 5 gebruikten wij 3.0 Tesla MRI en MRA om bij patiënten met een groot of reuze aneurysma van de arteria carotis, behandeld met een therapeutische afsluiting van de carotis, de evolutie van de klinische symptomen te beoordelen in relatie tot de aneurysma grootte. Deze patiënten hadden klinische en MRI vervolg studies van minstens 3 maanden (gemiddeld 35.9, mediaan 29, spreiding 3-107, 117 patiënt jaren). De klinische presentatie was massa werking door het aneurysma bij 32 patienten, een subarachnoïdale bloeding bij 3 en een neusbloeding bij 1 patiënt. Twee aneurysma's waren toevallig gevonden en 1 was additioneel aan een ander geruptureerd aneurysma.

Zowel op vroege als late MRI en MRA vervolg studies bleken alle aneurysma's volledig gethromboseerd na de carotis afsluiting. Ten tijde van de laatste MRI vervolg studie, waren 29 (74%) van de 39 aneurysma's volledig verschrompeld, de grootte van 2 aneurysma's was afgenomen tot 25% van de originele diameter, van 2 aneurysma's tot 50% en van 5 aneurysma's tot 75%. Twee aneurysma's bleven onveranderd in grootte na 49 en 58 maanden. Bij het laatste klinische onderzoek van de 32 patiënten, waren 19 (60%) genezen van de symptomen van massa werking, 10 (31%) waren verbeterd en 3 (9%) waren onveranderd.

Wij concludeerden dat therapeutische arteria carotis afsluiting een simpele, veilige en effectieve behandeling is voor grote en reuze aneurysma's van de carotis. Bijna alle aneurysma's verschrompelden volledig of verminderden substantieel in grootte na verloop van tijd. Genezing of verlichting van de symptomen van massa werking trad op in het merendeel van de patiënten.

## HOOFDSTUK 6

In hoofdstuk 6 gebruikten wij 3.0 Tesla MRI en MRA om de incidentie van nieuwvorming van aneurysma's en groei van bestaande onbehandelde aneurysma's te onderzoeken bij patiënten met een aneurysma van de carotis behandeld met therapeutische afsluiting van dit vat. De hemodynamische veranderingen na de carotisafsluiting zouden kunnen predisponeren voor nieuwvorming van aneurysma's. MR werd verricht in 26 patiënten na gemiddeld 50.2 maanden (mediaan 43.5, spreiding 14-107) na de carotis afsluiting. MRI en MRA beelden werden vergeleken met digitale subtractie angiografieën op het moment van de carotis afsluiting. Subarachnoidale bloedingen kwamen niet voor tijdens een vervolg van gemiddeld 50.3 maanden (mediaan 42.5, spreiding 0-107). Bij de 26 patiënten met vervolg MRA werden geen nieuw gevormde aneurysma's waargenomen (0%, 97.5% CI 0-13.2%). Vijf bestaande maar niet behandelde kleine aneurysma's bij 5 patiënten waren niet groter geworden na een gemiddeld vervolg van 40 maanden. Wij concludeerden dat therapeutische arteria carotis afsluiting niet geassocieerd is met een hoger risico voor het ontstaan van nieuwe aneurysma's of groei van bestaande onbehandelde aneurysma's op de middellange termijn.

## HOOFDSTUK 7

In hoofdstuk 7 onderzochten wij het voorkomen van zichtbare fenestraties van de arteria communicans anterior (AcomA) met 3D rotatie angiografie (3DRA). Tevens onderzochten wij de relatie tussen fenestraties van de AcomA met aneurysma's op deze locatie. Met conventionele digitale subtractie angiografie (2D DSA) is visualisatie van fenestraties van de AcomA uiterst ongewoon. Op een speciaal 3D werkstation, herbeoordeelden wij 305 3DRA onderzoeken van de arteria carotis interna van 305 patiënten met een aneurysma van de voorste circulatie op de aanwezigheid van fenestraties van de AcomA. In 78 van de 305 3DRA's was alleen het ipsilaterale A2 segment zichtbaar, zodat de AcomA niet kon worden beoordeeld. In de resterende 227 3DRA's was een fenestratie van de AcomA zichtbaar bij 12 (5.3%; 95% CI 3.0-9.1%). Van de 12 fenestraties van de AcomA, waren 10 (83%) geassocieerd met één of meer aneurysma's van de AcomA. Bij 133 van de 305 onderzochte patiënten met een voorste circulatie aneurysma was het aneurysma gelokaliseerd op de AcomA en bij 127 was de AcomA zichtbaar. Tien van de 127 AcomA aneurysma's met zichtbare AcomA hadden een fenestratie. De incidentie van AcomA fenestraties bij een AcomA aneurysma was daarmee 7.9% (95% CI 4.2-14.0%). De proportie fenestraties met een aneurysma van de AcomA was 14.4% (10 van de 227) en de proportie AcomA fenestraties met een aneurysma op een andere locatie was 0.9% (2 van de 227). Dit verschil is statistisch significant ( $P=0.040$ ). Zelfs retrospectief waren 11 van de 12 fenestraties niet zichtbaar op 2D DSA. Wij concludeerden dat in geselecteerde patiënten met een aneurysma van de voorste circulatie, bij 5,3% fenestraties van de AcomA worden gevonden met 3DRA. De meeste fenestraties gaan gepaard met één of meer aneurysma's van de AcomA.

## HOOFDSTUK 8

In hoofdstuk 8 onderzochten wij de tijd die nodig was voor coilen bij 642 aneurysma's en welke factoren een lange procedure tijd veroorzaakten. Wij waren in het bijzonder geïnteresseerd of de implementatie van 3DRA in oktober 2001 had bijgedragen aan de reductie van de procedure tijd. Met 3DRA is de ideale coil projectie sneller te vinden. De procedure tijd werd gedefinieerd als het aantal minuten tussen de eerste diagnostische run en de laatste run na embolisatie. Een lange procedure tijd werd gedefinieerd als de bovenste quartiel. De gemiddelde procedure tijd was 57.3 minuten (mediaan 52, spreiding 15-158). Meer dan de helft van de coil procedures duurde tussen 30 en 60 minuten. Met multipele logistische regressie analyse bleek dat het gebruik van een steunballon (OR 5.4), het optreden van procedurele morbiditeit (OR 4.5) en grote aneurysma's (OR 3.0) onafhankelijke voorspellers zijn van een lange procedure tijd. Een slechte klinische conditie van de patiënt, het al of niet geruptureerd zijn van het aneurysma, het geslacht van de patiënt, het ontstaan van een ruptuur tijdens de procedure en de locatie van het aneurysma hadden geen voorspellende waarde van een lange procedure tijd. De gemiddelde duur van de coilings voor de implementatie van 3DRA verschilde niet van de gemiddelde duur van de coilings daarna. Implementatie van 3DRA heeft dus geen invloed gehad op de procedure tijd.

Wij concludeerden dat onder optimale logistieke omstandigheden coiling van de meeste intracranieële aneurysma's, inclusief periprocedurele zorg, moet kunnen worden verricht in 1 à 2 uur.



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## **CURRICULUM VITAE** *ANJOB DE GAST*

Anjob de Gast was born on March 30th 1972 in Groningen, the Netherlands. After graduating from the Atheneum in 1992, she studied Biology for 2 years at the University of Utrecht before starting her medical training at the same University in 1994. In 1998, she performed 3 months of scientific research at the department of Radiology and Neurosurgery at the University of Virginia, Charlottesville, USA. After her clinical internship, partially completed in Pretoria, South Africa, she did a one-year residency at the Department of Neurosurgery of the Academical Medical Centre in Amsterdam. She started her Radiology residency at the St. Elisabeth Ziekenhuis in Tilburg in 2002 (head: K.H. Schuur, MD, PhD) and was Board certified in 2007. During her Radiology residency, she conducted the studies leading to the present thesis. In 2007, she was appointed as a radiologist at the VieCuri Medisch Centrum voor Noord-Limburg.

Anjob de Gast is married to Harry Laurent. They have a daughter, Eline and their second child is expected in July 2008.

