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## **Radioactive Coil Embolization of Intracranial Aneurysms: Minimal Inventory to Reach Target Activities in a Virtual Series of 154 patients**

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# Radioactive Coil Embolization of Intracranial Aneurysms: Minimal Inventory to Reach Target Activities in a Virtual Series of 154 patients

Charbel Mounayer, Michel Potin, Jacques Moret, and Jean Raymond

**BACKGROUND AND PURPOSE:** Recanalization after selective endovascular treatment of intracranial aneurysms with platinum coils has been widely reported in the literature. Beta radiation emitted from  $^{32}\text{P}$  ion-implanted coils can prevent recanalization in animal models. A complete inventory of radioactive coils may not be realistic; our hypothesis was that it might not be necessary to reach target activities in most aneurysms. A limited supply of three or four types of coils may decrease the inventory difficulties related to the use of an isotope with a half-life of 2 weeks.

**METHODS:** We reviewed 154 aneurysms selectively treated with standard coils. We calculated the volumetric activity obtained if all coils (simulation 1) were radioactive with linear activities of 0.13 (scenario I) or 0.26  $\mu\text{Ci}/\text{cm}$  (scenario II). Then, we simulated a treatment with standard coils plus a selection of radioactive coils limited to three (simulation 2) or four types of commonly used coils (simulation 3). Resulting activities were calculated and reported to the lesion volume. For each scenario and simulation, the percentage of lesions, in which the target volumetric activity (0.018  $\mu\text{Ci}/\text{mm}^3$ ) was reached, was reported.

**RESULTS:** Success in reaching target volumetric activities varied from 55–99% according to different simulations. A supply of four types of coils was sufficient to reach target activities in 86–95% of patients commonly treated in our institution. Target activities were difficult to reach in giant aneurysms.

**CONCLUSION:** It is feasible to reach target activities in most lesions by using a limited coil supply.

Endovascular treatment of intracranial aneurysms with platinum coils is safe and effective but too often followed by recanalization and recurrences (1). This propensity for recurrence increases with aneurysm size and is maximal in large and giant aneurysms (2, 3). Even in densely packed aneurysms, volumes are filled only 20–30% with platinum, with the remaining 70–80% occupied by thrombus (4). Recanalization of thrombus after coil occlusion is a cellular process that can be inhibited by in situ beta radiation with  $^{32}\text{P}$  ion-implanted platinum coils, at least in experimental

models (5, 6). A retrospective simulation of 357 clinical aneurysms demonstrated that, if all coils had been ion-implanted with 0.26  $\mu\text{Ci}/\text{cm}$  of  $^{32}\text{P}$ , 92–98% of lesions would have contained volumetric activities shown to be effective in preventing recanalization (7). This previous work presumed that the entire coil inventory could be supplied radioactively at the time of treatment.

More than 200 types of coils can be used to treat clinical aneurysms, and  $^{32}\text{P}$  decays with a half-life of 2 weeks. Although ion implantation is the most reliable way of producing  $^{32}\text{P}$  coils with minimal in vivo leaching of radioactive material, coils have to be prepared in advance. The logistic difficulties related to the production and distribution of such a wide variety of radioactive coils with a short shelf life makes this strategy impractical. One way to deal with this difficulty is to supply a limited variety of radioactive coils. The introduction of nonradioactive coils in combination with radioactive ones does not compromise their efficacy in the prevention of recanalization, provided that the effective volumetric activity (0.018  $\mu\text{Ci}/\text{mm}^3$ ) is achieved (5, 6). Therefore, the purpose of this study was to determine if target volumetric activities could

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be reached in most aneurysms by using a limited coil supply.

To reduce difficulties involved with the inventory of radioactive material, we proposed limiting the radioactive coil supply to selected but commonly used coils. We studied three simulations to determine the types of coils that could permit us to treat the maximal variety of aneurysms using a minimal variety of radioactive coils.

## Methods

### *Patients and Endovascular Treatment*

We retrospectively reviewed 154 aneurysms in 138 consecutive patients treated with standard platinum coils in our department (Fondation Ophtalmologique Rothschild, Paris, France) between December 2001 and April 2003. Eighty-six of the aneurysms (56%) were ruptured and treated within 48 hours after subarachnoid hemorrhage; 44% were unruptured. Treatment was unassisted in 85 aneurysms (55%), but more sophisticated techniques were used in 69 aneurysms (45%), with balloon assistance in 59 (38%), a stent in seven (5%), and an aneurysmal neck-bridge device in three (2%). Aneurysmal volume was determined from 3D images derived from rotational angiography (RA), by using the software provided by the manufacturer (Integris Allura; Philips, Best, the Netherlands). RA was performed by using the floor-mounted frontal plane of a biplanar C arm. The rotational study covered an angular range of 200° during the injection of contrast material. The rotational run was 4 seconds, corresponding to the acquisition of 100 images (25 frames per second). These images were acquired with a 17-cm image intensifier coupled to a 1024-pixel matrix. A 20-mL bolus of 300-mg/mL iodinated contrast material was injected intra-arterially (internal carotid or vertebral arteries) through a 5F catheter connected to an automated angiographic injector (Mark V Plus; Medrad, Indianola, PA). The bolus injection (4 mL/s in 5 seconds) was initiated 1 second before the start of the rotational sweep so that all 100 images were acquired during the injection of contrast material.

Images were transferred to a dedicated workstation (Integris 3D-RA; Philips) for 3D reconstruction. The reconstructions were visualized by using the volume-rendering technique, and the rendering parameters were chosen to achieve an anatomically correct representation of the aneurysm, the parent artery, and the main branches in the absence of background noise. The dimensions of the aneurysm (dome height and width, neck size) were measured on these volume-rendering images. A volume of interest was focused on the aneurysm and the adjacent arterial branches. At this stage, the aneurysm and its surrounding branches were displayed by using the surface-shaded mode to ease 3D manipulation of the volume of interest. By using spherical and planar cutting graphical tools, the aneurysm was progressively isolated from its parent vessel and surrounding arterial branches. Once the aneurysm was totally isolated, the volume of the aneurysm was automatically determined by using the dedicated volumetric software of the workstation. The same neuroradiologists (M.P.) studied the 3D images of all aneurysms and the dimension and volume of the aneurysm.

The packing density of each aneurysm was calculated (coils volume and aneurysm volume). The length and diameter of all coils introduced during each procedure were noted.

### *Virtual Radioactive Embolization of Aneurysm*

We considered two scenarios for each simulation. In scenario I, coils were ion-implanted with 0.26  $\mu\text{Ci}/\text{cm}$  of  $^{32}\text{P}$ , and in scenario II, with 0.13  $\mu\text{Ci}/\text{cm}$ . These linear activities were arbitrarily chosen to represent the activities shown to be more than 90% effective in preventing recanalization in a canine arterial model (0.13  $\mu\text{Ci}/\text{cm}$ ), and the activities that would need to be implanted to offer a 2-week shelf life (0.26  $\mu\text{Ci}/\text{cm}$ ) (5, 6).

### *Simulation 1*

We first simulated conditions wherein all coils were radioactive. We considered that each centimeter of coil positioned into aneurysm had an activity of 0.26  $\mu\text{Ci}$  for scenario I and 0.13  $\mu\text{Ci}$  for scenario II. The total activity was related to the aneurysm volume and compared with the target volumetric activity of 0.018  $\mu\text{Ci}/\text{mm}^3$  (6, 7).

### *Simulation 2*

We selected three types of coils, which in our opinion would be most frequently used in the selective treatment of aneurysms, and we simulated a scenario wherein ion-implanted coils with 0.26  $\mu\text{Ci}/\text{cm}$  of  $^{32}\text{P}$  were used. The types were as follows: 1) diameter of 8 mm, length of 30 cm, and coil activity of 8  $\mu\text{Ci}$  (scenario I) and 4  $\mu\text{Ci}$  (scenario II); 2) diameter of 5 mm, length of 15 cm, and coil activity of 4  $\mu\text{Ci}$  (scenario I) and 2  $\mu\text{Ci}$  (scenario II); and 3) diameter of 3 mm, length of 4 cm, and coil activity 1  $\mu\text{Ci}$  (scenario I) and 0.5  $\mu\text{Ci}$  (scenario II).

### *Simulation 3*

We added to simulation 2 a 2 mm  $\times$  4 cm coil implanted with 1  $\mu\text{Ci}$  (scenario I) or 0.5  $\mu\text{Ci}$  of  $^{32}\text{P}$  (scenario II).

For each intervention, we simulated conditions whereby the operator would always be free to use standard coils to initiate or finish the procedure, but that he or she would attempt to reach the target activities according to the volume of the lesion by substituting a certain number of standard coils with radioactive coils from the limited variety supplied in the different simulations. With respect to procedural feasibility, these simulations were performed with particular attention to rigid requirements. During the virtual replacement of a standard coil with a radioactive one, the diameter of the coil could not be increased. The selection a radioactive coil with a diameter 1 cm smaller was allowed. (For example, a 4-mm-diameter, 8-cm-long standard coil could be replaced by two 3-mm-diameter, 4-cm-long radioactive coils, but a 7-mm-diameter, 30-cm-long bare coil could not be replaced by an 8-mm-diameter, 30-cm-long radioactive coil.) The first coil diameter that the operator used needed to be conserved even if it was shortened. When the first coil used during the procedure was longer by more than 4 cm, its length during the simulation could not be less. (For example, if the first coil had a diameter of 6 mm and a length of 18 cm, it could not be replaced with a 6-mm-diameter, 3-cm-long standard coil and a 5-mm-diameter, 15-cm-long radioactive coil.)

Aneurysms were classified into six groups by volume: Group A was  $<50 \text{ mm}^3$ , group B was 51–100  $\text{mm}^3$ , group C was 101–200  $\text{mm}^3$ , group D was 201–500  $\text{mm}^3$ , group E was 501–1000  $\text{mm}^3$ , and group F was  $>1000 \text{ mm}^3$ . We measured the volumetric activity obtained for each aneurysm and compared the results among each group after the simulations. Results for each simulation were expressed as the percentage of the lesions in which the target volumetric activity of 0.018  $\mu\text{Ci}/\text{mm}^3$  was reached. This level of activity was previously shown to prevent recanalization in animal models (6, 7).

## Results

Results are summarized in Tables 1 and 2. Activities for scenario II were one-half those obtained for scenario I. The target volumetric activity was reached in 97–99% of cases with simulation I (all coils simulated to be radioactive) in both scenarios. Treatment of aneurysms with a limited inventory of three radioactive coils (simulation 2) failed to reach the target volumetric activity in 16% (scenario I) or 45% (scenario II) of cases. The addition of a small radioactive

TABLE 1: Mean volumetric activities after virtual radioactive coil embolization

Aneurysm Volume	Aneurysm No.	Scenario I			Scenario II		
		Simulation 1	Simulation 2	Simulation 3	Simulation 1	Simulation 2	Simulation 3
Group A	56	0.156	0.041	0.108	0.078	0.02	0.054
Group B	38	0.148	0.054	0.089	0.074	0.027	0.045
Group C	26	0.114	0.062	0.083	0.057	0.031	0.041
Group D	20	0.091	0.048	0.056	0.045	0.024	0.028
Group E	8	0.076	0.039	0.041	0.038	0.019	0.02
Group F	6	0.054	0.012	0.014	0.027	0.006	0.007
Total	154	0.131	0.047	0.086	0.065	0.023	0.043

TABLE 2: Efficacy in reaching target activities for each simulation and scenario

Group	Scenario 1			Scenario 2		
	Simulation 1	Simulation 2	Simulation 3	Simulation 1	Simulation 2	Simulation 3
A	56/56 (100)	43/56 (76.7)	54/56 (96.4)	55/56 (98.2)	25/56 (44.6)	51/56 (91)
B	38/38 (100)	35/38 (92.1)	37/38 (97.3)	38/38 (100)	24/38 (63.1)	37/38 (97.3)
C	26/26 (100)	24/26 (92.3)	25/26 (96.1)	25/26 (96.1)	18/26 (69.2)	25/26 (96.1)
D	20/20 (100)	19/20 (95)	20/20 (100)	20/20 (100)	13/20 (65)	16/20 (80)
E	8/8 (100)	7/8 (87.5)	8/8 (100)	8/8 (100)	4/8 (50)	4/8 (50)
F	4/6 (66.6)	2/6 (33.3)	2/6 (33.3)	4/6 (66.6)	0/6 (0)	0/6 (0)
Total	152/154 (99)	130/154 (84.4)	146/154 (94.8)	150/154 (97.4)	84/154 (54.5)	133/154 (86.3)

Note.—Data in parentheses are percentages.

coil (2 mm  $\times$  4 cm) to the inventory permitted us to reach target volumetric activities in 95% (scenario I) or 86% (scenario II) of cases. Target volumetric activity was not easily reached in giant aneurysms regardless of simulation or scenario.

Packing density varied between 8% and 82% (mean, 34.4%) in group A, 16% and 81% (mean, 33.3%) in group B, 7% and 46% (mean, 30.6%) in group C, 17% and 47% (mean, 24.5%) in group D, 18% and 29% (mean, 22.5%) in group E, and 4% and 24% (mean, 16.5%) in group F. Packing densities did not change significantly after virtual replacement of standard coils with radioactive coils.

The mean number of standard coils that were replaced with radioactive ones was  $3 \pm 1.45$  for group A,  $4 \pm 1$  for group B,  $7 \pm 2$  for group C,  $8 \pm 2$  for group D,  $13 \pm 4$  for group E, and  $14 \pm 9$  for group F.

## Discussion

The introduction of detachable coils in the early 1990s revolutionized the endovascular treatment of aneurysms (8). Detachable platinum coils offer several design features that allow their placement into both ruptured and unruptured aneurysms, with a relatively low risk of aneurysm perforation or parent-artery compromise. These design features include tractability, softness, a low profile, radiopacity, low thrombogenicity, and retrievability. However, important limitations have become manifest; these include relatively low rates of complete aneurysm obliteration and high rates of aneurysm recanalization, as compared with those of surgical clip placement (2, 3). Recently, two kinds of bioactive coils were introduced for aneurysm embolization. Matrix coils (Boston Sci-

entific, Natick, MA) consist of platinum coils covered with a bioabsorbable polymeric material (polyglycolic acid/lactide). The goal is to accelerate aneurysm fibrosis and neointima formation (9). The HydroCoil Embolization System (MicroVention, Inc, Aliso Viejo, CA) consists of a synthetic polymeric hydrogel attached to a platinum coil (10). This device is designed to entirely fill the aneurysm cavity with complete or near-complete exclusion of thrombus. In our experience, the mechanical properties of these devices differ from those of standard platinum coils, and their introduction and placement in the aneurysm sac is more difficult. To our knowledge, no reports have compared the clinical benefits, drawbacks, and complications of these coils compared with standard platinum coils. Compared with surgical clip placement, endovascular treatment with standard platinum coils can improve the outcome of patients with ruptured aneurysms (11). Long-term angiographic results are inferior to surgical results, but long-term bleeding episodes remain rare events (1, 11, 12). A modified coil designed to improve long-term angiographic results is needed, but it should not substantially increase the immediate risks of the procedure or decrease the initial success rate and thus jeopardize the benefits of the endovascular approach. In this context, a randomized comparison between standard and modified coils is mandatory before proposing the routine use of these new devices.

In situ beta radiation has recently been proposed as a new strategy to prevent recanalization after endovascular treatment (5). The technique consists of the implantation of  $^{32}\text{P}$  ions on platinum coils by using a dedicated implanter (5). The mechanical properties of the coils are not modified, and the coils can be



delivered similarly to nonradioactive coils through standard microcatheters. This approach was evaluated during the deployment of 242 radioactive coils during pre-clinical studies and during an initial clinical experience in 45 aneurysms (6, 13). This method may offer improved long-term angiographic results without affecting the results or the safety of the initial procedure.

A previous simulation, in which all coils were considered radioactive with activities in the range of 0.26  $\mu\text{Ci}/\text{cm}$   $^{32}\text{P}$ , showed that 92–98% of aneurysms contained volumetric activities effective in preventing recanalization (7). This simulation assumed that the endovascular team disposed of the ion implanter and that coils could be implanted with  $^{32}\text{P}$  ion immediately before each procedure. A more realistic hypothesis is that a limited inventory of coils could be supplied to the endovascular center and that coil activities would progressively decrease according to the half-life of the isotope. This is why we decided to repeat simulations by using a limited inventory of radioactive coils with two scenarios corresponding to activities at the time of delivery (0.26  $\mu\text{Ci}/\text{cm}$ ), and to activities after 2 weeks or one half-life of  $^{32}\text{P}$  (0.13  $\mu\text{Ci}/\text{cm}$ ). We then determined if the target volumetric activity of 0.018  $\mu\text{Ci}/\text{cm}^3$  (6), which was effective in animal experiments, could be reached in each scenario and after each simulation (Table 2). When we considered that all coils were radioactive, our results were similar to those previously reported (7), with dosimetric success in 98.7% of all cases after scenario I and 97.4% after scenario II. In our series, the success rate was higher than that of a similar simulation in a virtual series of patients treated in Montreal; this may be attributed to selection bias in North American centers, with a greater proportion of large aneurysms in centers where surgical clip placement is still frequently used.

With an inventory of three radioactive coils (with a 3-mm diameter for the smallest one in simulation 2), dosimetric success was achieved in 84.4% of cases after scenario I and in only 54.5% after scenario II. Failures were more frequently encountered in small (group A) and giant aneurysms (group F).

To reduce the risk of failure in small aneurysms, we added a fourth radioactive coil 2 mm in diameter (simulation 3). After this last simulation, dosimetric success was achieved in 94.8% in scenario I and 86.3% in scenario II. This proportion was close to the percentage of patients in whom target volumetric activities were reached in the initial clinical experience after radioactive coil embolization of an intracranial aneurysm (13).

Failures commonly occurred when aneurysm volumes exceeded 1000  $\text{mm}^3$  (group F) (7). This difficulty in reaching target activities is directly related to the packing density of coils in large aneurysms that falls dramatically when compared with the one that can be found in small lesions (14). The solution for these large or giant aneurysms could be higher  $^{32}\text{P}$ -activity implantation onto large coils.

Our center has an extensive experience with endovascular treatment of aneurysms. The substitutions that were needed to reach target activities were be-

lieved to be realistic and feasible, with minimal if any potential clinical consequences on the immediate outcome of treatment. This study remains a theoretical exploration of the feasibility of using a limited inventory of radioactive coils. It should, however, provide some guidance in the selection of coils that could be supplied to centers involved in treating similar patient cohorts in preparation for a multicenter, randomized trial comparing radioactive and standard coil embolization of intracranial aneurysms.

## Conclusion

A simulation of radioactive embolization of 154 consecutive intracranial aneurysms shows that a limited inventory of four radioactive coils is sufficient to reach target volumetric activities in 86% of cases.

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