# Partition of Calibrated Tris-acryl Gelatin Microspheres in the Arterial Vasculature of Embolized Nasopharyngeal Angiofibromas and Paragangliomas

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**PURPOSE: To determine the location of calibrated tris-acryl gelatin microspheres (TGMs) in the arterial vasculature of nasopharyngeal angiofibromas (NAFs) and paragangliomas (PGs).**

**MATERIALS AND METHODS: Forty-nine specimens (25 PGs and 24 NAFs) treated operatively after embolization with TGMs of various sizes (100–300 $\mu$m to 900–1200 $\mu$m) were stained with hematoxylin and eosin saffron and analyzed at an objective magnification of 10 or 20 with a micrometric eyepiece (magnification, ×12.5). The diameter of occluded vessels, their localization (intra- or extratumoral), and the number and diameter of TGMs they contained were determined.**

**RESULTS: Embolized vessels ($N = 1125$) were measured: 440 in PGs and 685 in NAFs. Vessels were 89% intratumoral and 11% extratumoral. The diameter of the occluded vessels increased significantly with the size range of TGMs used for embolization for each tumor type ($P < .0001$). Intratumoral occluded vessels were significantly smaller than extratumoral vessels ($P < .0001$). Distribution of TGMs within the vascular network (intratumoral or extratumoral location) were similar for NAFs and PGs. The intratumoral and extratumoral dissemination of TGMs was different when comparing 100–300-$\mu$m TGMs versus 500–700-$\mu$m TGMs ($P = .0006$) as well as 300–500-$\mu$m TGMs versus 500–700-$\mu$m TGMs ($P = .0001$).**

**CONCLUSIONS: The size of the vessels occluded by TGMs and their intra- or extratumoral location directly depend on the size of the injected TGMs. The vessels located inside the tumors were smaller than those located outside the tumors. A threshold for the intratumoral penetration of TGMs in the vasculature can be proposed from these data. There was no evidence of different behavior of TGMs in NAFs versus PGs.**

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**Abbreviations:** NAF = nasopharyngeal angiofibroma, PG = paraganglioma, TGM = tris-acryl gelatin microsphere

CALIBRATED tris-acryl gelatin microspheres (TGMs; Embospheres; Biosphere Medical, Roissy Charles de Gaulle, France) were developed (1) to address some of the perceived shortcomings of other embolization particles such as polyvinyl alcohol foam particles, which are difficult to calibrate and the behavior of which can be unpredictable during embolization (2,3). Conversely, TGMs do not aggregate (4) and are more homogeneously distributed in the vasculature (5). Theoretically, the calibration of TGMs should permit interventional radiologists to adapt the caliber of microspheres to the size of the vessels to be occluded so an accurate targeting can be obtained.

In a recent study (6), we demonstrated that a controlled embolization of tumors and arteriovenous malformations was achievable with TGMs by choosing the size of injected TGMs, as the size of the occluded vessels was consistently in good agreement with the size of TGMs used during the embolization procedure. For a given pathologic condition, it should be possible to determine the optimal range of

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TGM caliber to be injected to control their penetration in the tumoral tissue. As a first step, histopathologic data are required to determine the actual distribution of calibrated TGMs within the vascular network of each tumor type.

In the present study, we conducted a pathologic evaluation of the localization (ie, site of occlusion) of TGMs in surgical specimens obtained from patients previously treated with embolization for nasopharyngeal angiofibromas (NAFs) or paragangliomas (PGs). The objectives of the present study were to histologically determine (i) whether TGMs were actually present in the tumor specimens, (ii) whether there was correlations between the size of TGMs used for embolization and the size of TGMs found in specimens or the diameter of the occluded vessels, (iii) the proportion and intra- or extratumoral location of TGMs after embolization, and (iv) whether, for any of these three items, there was a difference between NAFs and PGs.

## MATERIALS AND METHODS

### Patients

We retrospectively reviewed the files of 49 patients with NAF ($n = 24$) or PG ($n = 25$) who were treated with embolization with calibrated TGMs (Embospheres; Biosphere) in our institution between 1987 and 2003 and then treated operatively. Some of these patients have been described in a previous study (6).

All the histologic slides were reviewed for the presence of TGMs. The charts and embolization reports of all patients were reviewed for clinical data, dates of embolization, and TGM sizes used. The present study reports data obtained retrospectively on histopathologic material and did not require approval by the institutional review board.

### Embolization Technique

Patients underwent superselective angiography for embolization under fluoroscopic guidance. The objective of embolization was to perform the most complete, best achievable preoperative vessel occlusion with the highest degree of safety for the patient. All patients underwent embolization according to the same protocol, which took into account the following items:

1. Selective angiography was followed by superselective catheterization of the arterial feeders with various types of standard microcatheters.
2. Embolization was achieved with TGMs of the following size ranges: 100–300 μm, 300–500 μm, 500–700 μm, 700–900 μm, and 900–1,200 μm. Sizes were increased step by step, according to each artery and the corresponding angiographic blush. Embolization began with 100–300-μm TGMs except in arteries that were more likely for extracranial/intracranial anastomosis. In these arteries, embolization began with 300–500-μm TGMs.
3. Dilution of TGMs was adapted to the size of microspheres and their concentration in the vial. TGMs were suspended in a 50:50 mixture of saline solution and contrast medium. To get a homogeneous solution, injection in the microcatheter was achieved with a 3-mL Luer-lock syringe connected by means of a three-way stopcock to a 10-mL Luer-lock syringe filled with the solution containing the TGMs, and the suspension was smoothly agitated to maintain TGMs homogeneously suspended in the medium.

Embolization procedures differed slightly between the two pathologic conditions as a result of differences in the vasculature of the tumors. PGs are mostly fed by the ascending pharyngeal artery and the stylomastoid artery, which may show anastomosis to intracranial arteries. NAFs are fed by branches of the internal maxillary artery, which are less likely to show anastomosis to intracranial arteries. These anastomoses are not seen at the beginning of the embolization but appear during the procedure. Therefore, because of the higher risk of anastomosis with PGs than with NAFs, embolization of PGs is initiated with larger TGM calibers than are used for NAFs.

### Slide Review and Measurements

After variable delays after embolization, patients were treated operatively and 49 specimens were obtained. Specimens were fixed in formalin and embedded in paraffin. Sections 4 μm thick were stained with hematoxylin and eosin saffron stain and observed with an optical microscope (Diaplan; Leitz, Stuttgart, Germany).

The presence of TGMs was checked in all slides of each specimen. The embolized vessels were divided in three classes: (i) vessels containing one TGM, (ii) vessels containing two to five TGMs, and (iii) vessels containing more than five TGMs. In the specimens containing TGMs, the diameter of the occluded vessels and the number and diameter of TGMs present in each vessel were analyzed (when several TGMs were found in one vessel, the diameters of the smallest and largest microspheres were measured). The location of the occluded vessels were also determined, with TGMs being found within the tumoral tissue or in peritumoral tissues.

Measurements were performed at an objective magnification of 10 or 20 with a ×12.5 eyepiece containing a calibrated micrometer. In each specimen, all embolized vessels (ie, vessels containing embolic agent) were measured.

The diameter of occluded vessels was determined as follows (**Fig 1**). When one microsphere was present in the lumen of the vessel, the vessel diameter was measured as the internal diameter of the vessel lumen if the vascular section was transverse (**Fig 1a**) or as the smallest axis of the ellipse if the section was oblique (**Fig 1b**). When a foreign body reaction was present around the microsphere, the measured diameter of the vessel comprised the thickness of the cellular reaction and therefore appeared larger than the diameter of the microsphere. In case of longitudinal section of the vessel (**Fig 1c**), the vessel diameter was measured at the level of the largest microsphere present in the vessel. When a cluster of TGMs was found in the vessel (**Fig 1d**), the internal diameter of the vessel was measured as the smallest axis of the ellipse.

### Statistical Analysis

Continuous variables were expressed as means ± SD. Statistical analyses were performed on StatView