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Arteriovenous Shunt Measurement during Endovascular Therapy for Cerebrospinal Lesions

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PURPOSE: To determine (a) whether superselective angioscintigraphy with technetium-99m macroaggregated albumin (99mTc-MAA) can be used for the evaluation of arteriovenous shunting in tumors and vascular malformations of the head and spine and (b) whether the amount of microparticles shunted is related to diagnosis, lesion size, or angiographic pattern. METHODS: Particles of 99mTc-MAA with a calibrated diameter of 25 to 50 μm were delivered intraarterially in feeders of head and spine tumors and vascular malformations in 38 patients. The first estimation of the proportion of particles reaching the lungs was made on-line in the angiography suite using a hand-held lead-shielded detector. Evaluation of the intralesional shunt (pulmonary shunt index, or PSI) was derived from quantitative gamma camera recordings of tumoral and pulmonary activity after the embolization procedure was complete. RESULTS: The PSI value ranged from 48% to 100% for vascular malformations and vascular tumors (n = 11), 82% to 95% for juvenile angiofibromas (n = 4), 63% to 70% for high-grade gliomas (n = 2), 0% to 50% for renal cell carcinoma metastases (n = 4), 0% to 86% for meningiomas (n = 11), and 0% to 36% for paragangliomas (n = 6). Angiographically, the presence of visible arteriovenous channels was predictive of a high PSI. In contrast, the presence of early venous drainage was associated with a wide PSI range. CONCLUSION: Superselective 99mTc-MAA angioscintigraphy of tumors and vascular malformations of the head and spine is a valuable method for quantifying an intralesional arteriovenous shunt before embolization.

Index terms: Arteriovenous malformations, embolization; Interventional materials, embolic agents; Radionuclide imaging; Technetium


Therapeutic endovascular embolization refers to the occlusion of a vessel territory by the selective introduction of embolic agents into the arteriocapillary bed of the lesion. To obtain optimal devascularization, it is essential to deposit the embolic agents as deeply as possible into the tumor or vascular malformation. Complete devascularization of vascular malformations as well as of highly vascularized tumors demands that precapillaries, capillaries, and even the proximal parts of the draining veins are occluded. However, passage of embolic material to normal intracranial arteries (1–3) and passage to the venous system, especially during chemoembolization and radioembolization of malignant tumors, must be avoided.

Polyvinyl alcohol (PVA) microparticles of different sizes are routinely used for preoperative embolization of craniocerebral and spinal lesions. Microspheres are currently being investigated for mechanical embolization (4, 5) or as vehicles for the intraarterial selective delivery of chemotherapeutics or radionuclides in the treatment of cancer (6–9). To achieve effective and safe embolization, it is important to know which would be the smallest particle completely trapped in the capillary bed of a given lesion. This information can be partially ascertained by injecting the embolic agents under fluoroscopic control.

The lungs, being the first organ downstream from the point of injection, will retain any embolic material passing through the lesion. Thus,
measuring the extent of pulmonary trapping for a given particle size will reflect the degree of arteriovenous shunting in the catheterized tissue, as has been shown with tumors in other locations (9–12). The technical improvements in catheterization techniques and the recent development of microcatheters with variable stiffness now permit selective injection in vessels with a luminal diameter as small as 1 to 2 mm. This capability enables the interventional neuroradiologist to study intraläsional shunting safely between dangerous arterioarterial anastomoses.

To measure intraläsional arteriovenous microparticle shunting, we prospectively performed superselective angioscintigraphy with technetium-99m macroaggregated albumin (99mTc-MAA) before embolization in patients with tumors and vascular malformations of the head and spine.

Patients and Methods

Patient Population

Thirty-eight patients undergoing presurgical angiography and embolization for tumors and vascular malformations of the head, neck, and spine were entered into the study (Table). Pretherapeutic and posttherapeutic imaging consisted of multiplanar high-field-strength magnetic resonance (MR) imaging, which normally included contrast-enhanced T1-weighted images, and/or high-resolution computed tomography (CT) before and after embolization. The project was approved by the local ethics commission, and patients gave informed consent to participate in the study.

Angiography, 99mTc-MAA Angioscintigraphy, and Embolization

The following steps were successively undertaken on the day of the procedure:

1) A diagnostic angiographic workup was performed as the first step, including selective and superselective functional neuroangiography to identify the type, number, and geometry of the feeding arteries and to determine the angioarchitecture of the lesion. The procedure was usually performed with local anesthetic administered through the femoral artery using a 4.5F to 5.5F catheter, which allows catheterization of individual feeding arteries in head and neck lesions as well as insertion of a microcatheter for superselective angioangiography and embolization. A dedicated neurointerventional system, equipped with the possibilities of biplane fluoroscopy, road mapping, and digital subtraction angiography (DSA) (matrix, 1024 × 1024), was used.

2) Superselective catheterization of the distal portion of the feeding arteries of the lesion was performed with a microcatheter, usually a Tracker 18 or 10 (Target Therapeutics, Fremont, Calif).

3) Following DSA documentation of the superselective catheterization and of the position of the tip of the microcatheter, we slowly injected approximately 170 MBq of freshly prepared 99mTc-MAA particles (CIS Biointernational, Gif sur Yvette, France) under fluoroscopic control. Ninety-five percent of the 99mTc-MAA particles had a diameter ranging from 25 to 50 μm. None of the particles was larger than 100 μm or smaller than 10 μm, according to the manufacturer. These particles are known to be trapped in the capillary bed of the lungs following peripheral intravenous injection, and they are used routinely at our hospital in pulmonary perfusion studies (13).

4) With the microcatheter in place, we measured the maximum gamma-ray emission (maximum, 3000 cps) over the lesion and over the right lung (anterior and posterior projections) using a portable, lead-shielded probe (235 Isotope Localisation Monitor, Pitman Instruments, Weybridge, England).

5) The tumor selectivity ratio (TSR) was calculated in the angiography suite as TSR = cps over the tumor(cps over the right lung).

6) Embolization of the lesion was performed, usually with glue or PVA particles, mostly in the range of 100 to 500 μm (Contour, Interventional Therapeutics Corp, San Francisco, Calif). Particles as small as 45 μm were used if no radioactivity was detected over the lungs by the former measurement.

7) The procedure was completed by angiography using the original position of the guiding catheter and biplane projections as described in step 1 to control and document the effect of embolization.

8) After removal of the femoral catheter or sheath and femoral compression, the patient was transported to the department of nuclear medicine for scintigraphy of the lesion and the thorax with a gamma camera (Gamma Diagnost, Philips AG, Eindhoven, the Netherlands) attached to a computer system. Two hundred thousand to 300 000 counts were recorded from the image with maximal activity. An identical recording time was used to make the other images.

9) With a dedicated computer program, after correcting the background and considering carefully drawn regions of interest as described elsewhere (11), we calculated the pulmonary shunt index (PSI) as PSI = (activity over the lungs/activity over both tumor and lungs) × 100.

Histologic Diagnosis, Angiographic Characteristics, and Size of the Lesions

Histologic diagnosis was obtained in all patients, except for those with vascular malformations. The lesions were subdivided into three types according to their appearance in the angiographic workup: type 1, visible arteriovenous channels; type 2, presence of early venous drainage, strong parenchymal blush, no visible arteriovenous channels; type 3, presence of a strong parenchymal blush but no visible arteriovenous channels or early venous drainage.
The maximal diameter of the lesion was measured on CT or MR studies except in those patients with dural arteriovenous fistulas (AVFs).

**Results**

Patient data, histologic diagnosis, location of the lesion, catheterized arterial feeder, maximal lesion diameter, angiographic type, and PSI are shown in the Table. Illustrative cases are shown in Figures 1 through 4.

No adverse reactions were observed after intraarterial injection of $^{99m}$Tc-MAA. On-line measurement of gamma-ray emission with the hand-held detector was possible in 24 of the 38 patients. There was a positive correlation between increasing TSR and decreasing PSI ($r =$
Fig 5. A TSR of more than 10 was always associated with a PSI of less than 30%. In one patient with an intramedullary angioma, the measurement was not reliable because of anatomic proximity to the lungs. Data from the hand-held detector were not precise in the remaining cases because the activity exceeded the capacity of the hand-held monitor (3000 cps).

Lesion Type and PSI (Fig 6)

A high PSI (mean, 79%; range, 42 to 100) was found in vascular lesions (three arteriovenous malformations [AVMs], four dural AVFs, two facial angiomas, one vertebral hemangioma, and one hemangioblastoma). For the remaining 27 solid tumors, a wide range of PSI was found. Juvenile angiofibromas had a mean PSI of 90% (range, 82% to 95%). High-grade gliomas, one anaplastic oligodendroglioma, and one glioblastoma, had a PSI of 63% and 70%, respectively (mean, 67%). Patients with metastases of renal cell carcinoma showed a PSI of 0%, 0%, 14%, and 50% (mean, 16%). Glomus tumors had a PSI of 0%, 0%, 3%, 16%, 18%, and 36% (mean, 12%). PSIs were especially low in meningiomas (mean, 12%); however, in two cases, we found a PSI of 27% (mixed fibroblastic and meningothelial type) and 86% (meningothelial type).

Lesion Size and PSI

Overall, there was no significant correlation between the maximal lesion diameter and the PSI. The histologic subgroups were too small to allow statistical analysis. However, even considering the largest subgroup of meningiomas (n = 11), no correlation was found (P = .1752).

Angiographic Characteristics and PSI

Seven lesions had visible arteriovenous channels detected during the angiographic workup (type 1); all of them were AVMs or dural AVFs.
Twenty-two additional lesions showed an early venous drainage and a strong parenchymal blush (type 2): six glomus tumors, four angiofibromas, two high-grade gliomas, two facial angiomas (one capillary venous angioma and one arteriovenous angioma), one hemangioblastoma, five meningiomas, and two renal cell carcinoma metastases. Seven lesions showed a strong parenchymal blush without visible arteriovenous channels or early venous drainage (type 3): five meningiomas, one vertebral hemangioma, and one renal cell carcinoma metastasis.

Mean PSIs were 80%, 42%, and 8% in angio graphic type 1 (range, 60% to 100%, n = 7), type 2 (range, 0% to 95%, n = 22), and type 3 (range, 1% to 50%, n = 7), respectively. Standard deviations were very high (23%, 38%, and 17%, respectively), especially for type 2.

The absence of early venous drainage (type 3) was invariably associated with a PSI of less than 50%. However, lesions with early venous drainage had PSIs ranging from 0% to 100%. In particular, glomus tumors and juvenile angiofibromas, which share the same angiographic characteristics, had strikingly different PSIs, as shown above.

Discussion

Knowing the amount of intral esional arterio venous shunting for a given particle size in a given lesion could help in the choice of embolic agents and in the optimization of mechanical embolization, radioembolization (14), and chemoembolization. To date, evaluation of intral esional shunting is based primarily on angiographic characteristics. With short injections of contrast material, a bolus can be followed through blood vessels of the lesion (bolus tracking), and the transit velocity can be compared with that of the adjacent normal parenchyma.

Faster circulation through the lesion with...
early appearance of draining veins is the result of decreased local cerebrovascular resistance. This may be due to direct communication between arteries and veins or to the presence of enlarged abnormal and/or dilated normal capillaries (15–17). The width of the capillary bed is influenced by the local metabolism; that is, an increased concentration of CO₂ and a low pH can generate luxury perfusion as a consequence of cerebrovascular occlusive lesions (18).

Even with the use of magnification angiography, only blood vessels with diameters as small as 200 μm can be seen directly. Arteriovenous shunts of this or an even larger diameter are often present in AVMs, but they are rare in tumors. With conventional angiography, it is not always possible to define the precise location and size of those large AVFs inside an AVM. Even with superselective catheterization of the single feeder supplying the fistulous compartment of the AVM in combination with magnification and rapid serial digital angiography, it may be difficult to decide whether there is only one large direct or many smaller connections between the artery and draining vein, owing to the high velocity of the blood flow and the immediate opacification of the usually enlarged draining vein.

On the other hand, localized slowing of circulation with delayed emptying of arteries and late filling of veins may be the result of locally increased pressure caused by the space-occupying process itself and the surrounding edema or by restriction of the outflow in the draining veins, as observed in dural high-pressure, low-flow fistulas. This is, therefore, also compatible with the presence of arteriovenous shunts.

Although there is a great deal of histopathologic and electron microscopic data available...
on tumors and vascular malformations, only some is helpful in predicting the extent and size of vascular anastomoses leading to arteriovenous shunting.

Brain scintigraphy with $^{131}$I-MAA was used mainly as a diagnostic tool for brain tumors before the CT era (19–26). With intracarotid injection of $^{131}$I-MAA, Handa et al (27) could estimate the global rate of short-circuited arterial blood. Picard et al (28) embolized 45 extracerebral craniospinal lesions using gelatin sponges marked with iodine-131. The next day, they controlled scintigraphically the embolized area and the thoracoabdominal region. These authors focused mainly on the distribution of the embolization material and they identified three patterns of tumor embolization: centrotumoral, peritumoral, and extratumoral, depending on the selectivity achieved by the catheterization of the vascular pedicles. They did not notice any scintigraphic activity on the thoracoabdominal region in any of the cases. This finding is not surprising if we consider the dry size of the gelatin pieces they used, the smallest measuring approximately $0.5 \times 0.6 \times 0.8$ mm. Conroy et al (29) used the same technique to embolize...
visceral lesions with gelatin sponges marked with technetium-99m. Reflux of this material to the thigh was documented in one case of transarterial embolization of the spleen. Translesional embolization to the lungs was documented in two cases during transvenous treatment of esophageal varices. Using the same embolization agent, Seo et al (30) documented translesional passage to the lungs in one case of dural AVF and no translesional shunting in a hemangioma of the back.

Each of the studies just described is limited by the relatively large size of the catheters used, and thus the reduced selectivity; by a lack of information concerning the real size of the embolic material; and by a lack of quantification of the amount of translesional shunting.

Jack et al (31) refined the method by labeling PVA microparticles (average size, about 0.5 mm) with technetium-99m, and demonstrated complex stability and biodistribution after intravenous and intracarotid injection in animals. These investigators documented the location of the embolic material in and around a large pteryonal meningioma after injection in the distal external carotid artery. In one case of an AVM of the thigh, Sirr et al (32), using a mobile gamma camera installed in the angiographic suite, documented reflux and distal migration of large 99mTc-marked PVA particles in the calf.
but no translesional arteriovenous shunting to the lungs. In one case of a pelvic AVM, migration to the lungs was identified during the procedure, prompting the researchers to modify the position of the catheter to avoid this pulmonary shunting.

To optimize intraarterial chemotherapy of cervicofacial malignancies, Wheeler et al (10) injected $^{99m}$Tc-MAA into the external carotid artery of nine patients. These authors calculated a mean systemic shunt of 23% (range, 11% to 44%), a mean tumor blood flow of 13.6 mL/100 mg per minute, and a ratio of tumor/normal tissue blood flow of 5.6 using a xenon-133 washout technique.

Using microcatheter techniques, we injected $^{99m}$Tc-MAA particles with a diameter of 25 to 50 $\mu$m superselectively into small arteries, which exclusively supplied different cerebrospinal lesions in 38 patients. With this technique, it was possible to see the extension and distribution of the embolic material inside the lesion as well as to measure the pulmonary trapping of the $^{99m}$Tc-MAA particles that shunted through the arteriocapillary bed of the lesions.

We tested the reliability of a portable detector as compared with measurements made with the use of a gamma camera. The positive point about this hand-held system is its practicality: it is easy to handle and not time-consuming, and it allows focused application on the region of interest and rapid calculation of a selectivity ratio. A TSR of more than 10 was always associated with a PSI of less than 30% (see “Results”). However, we used very small microparticles (45 to 150 $\mu$m) only in those instances in which almost no activity was detected over the lungs. The major limitation of this portable detector is that the recording depends on how the probe is held over the region of interest, which makes the measurement somewhat examiner-dependent. However, an estimation of whether an important pulmonary shunt exists or not is always possible. In contrast, a precise TSR cannot be calculated in every case. The use of a movable gamma camera in the angiography suite could overcome these limitations but would probably prolong the procedure.

Performing scintigraphy of tumor and lung with a gamma camera after definite embolization allowed us good visual representation and quantification of microparticle shunting to the lungs. As expected, a high, almost complete pulmonary shunting was seen in AVMs, demonstrating the presence of arteriovenous communications clearly larger than 25 $\mu$m. This was also evident in the patient with exclusively plexiform angioarchitecture (case 2). Angiographically, this was already suspected in most of these lesions on the basis of the appearance of large fistulas and because of the very rapid circulation time with appearance of draining veins during the early arterial phase. Despite the presence of similar visible arteriovenous channels, the PSI was not as high in dural fistulas.

Hemangioblastomas are composed of a fine mesh of blood spaces and capillary channels that may be seen dilated into large sinuses (33–35). In our study, this tumor showed the typical intense parenchymal blush and the rapid appearance of contrast medium in draining veins. A similar angioarchitecture was also found by intraarterial DSA in a capillary venous angioma and in an AVM of the face. We identified an important arteriovenous shunt in both.

Vertebral hemangiomas are usually of the cavernous type and show a slow circulation time at angiography, sometimes with contrast medium stagnating in the tumor and draining veins (17). Despite these angiographic characteristics, we found a significant intralesional shunt in one patient (PSI = 42%). As we recently reported in a smaller series (36), we found a surprisingly low PSI in paragangliomas. Willis and Birrell (37) made an in-depth study of the microvasculature of a paraganglioma of the carotid body with special emphasis on the unique anastomosing pattern in this tumor type. Even if large cavernous and hypertrophic vessels were found in this tumor, no direct communication between arteries and veins exceeding a caliber of 13 $\mu$m was described in their article. Accordingly, our data suggest that potentially no or a low arteriovenous shunt results from injection of particles as small as 25 $\mu$m in diameter, which seems to be a promising result, considering the possible future options of microspheric radioembolization or chemoembolization of this type of tumor. In contrast, a very high PSI was observed in the four patients with juvenile angiofibroma, despite the angiographic similarity between this tumor and paragangliomas.

Glioblastomas have angiographically typical areas of vascular shunts, with a relatively high flow and a vascular bed of moderate size. In arteriography, the contrast medium thus appears early and is washed out early, usually
simultaneously with the appearance of the draining veins, as in our patient with this type of tumor. Our findings in this patient support the hypothesis of an important arteriovenous anastomosis component in these tumors. The same finding characterized one anaplastic oligodendroglioma, which had the same angiographic pattern as glioblastoma. Because of this important arteriovenous shunting, no significantly better potential for cell killing or lower systemic toxicity can be expected after intraarterial chemotherapy in these malignant gliomas as compared with systemic intravenous application. Experimental approaches using chemotherapeutics encased in microspheres (38, 39) might better reach those goals.

In metastases of renal cell carcinoma, we observed 0% to 50% PSI. Two such tumors showed a rapid circulation time with an early appearance of veins; however, in neither tumor was an intralosomal shunt detected with our method. We found very low shunt rates in meningiomas, less than 5% in nine of 11 tumors. Interestingly, four of these tumors had evidence of early venous drainage, but in only two of them was a significant intralosomal shunt detected. These data suggest that particles as small as 25 μm could be used to optimize presurgical embolization in most meningiomas (Fig 4).

In summary, our method identified three groups of lesions according to the amount of intralosomal arteriovenous shunting: those with high PSI, including AVMs and angiofibromas; those with medium-high PSI, including hemangiomas, dural fistulas, and high-grade gliomas; and those with low PSI, including meningiomas, glomus tumors, and renal cell carcinoma metastases. The size of our subgroups was too small to permit general conclusions for every tumor type.

The presence of visible arteriovenous channels at angiography was associated with a high intralosomal microparticle shunting; however, a rapid circulation time as assessed by the presence of early venous drainage at angiography was not a good predictor of intralosomal microparticle shunting in paragangliomas, renal cell carcinoma metastases, and meningiomas. The early venous drainage in these tumors was probably due to the presence of a widespread network of dilated capillaries that were smaller than the particles used.

Conclusion
Superselective angioscintigraphy with 99mTc-MAA allows quantification of the intralosomal arteriovenous shunting of microparticles with a caliber of 25 to 50 μm in tumors and vascular malformations of the head and spine, including those in the central nervous system. The amount of microparticle shunting in tumors seems to be related to the histopathologic diagnosis and to some angiographic characteristics but not to the size of the lesion. Superselective angioscintigraphy and on-line measurement of the pulmonary shunt rate in the angiography suite can be useful complementary tools for determining the ideal size of embolic agents for a given lesion.

References


