SPECT Evaluation of Arterial Perfusion in Regional Chemotherapy

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Simultaneous emission and transmission tomography was performed after the injection of [^{99m}Tc]MAA in 30 patients undergoing intra-arterial chemotherapy to nonhepatic sites to determine the accuracy of catheter placement. The transmission and emission data were reconstructed in transverse, and optionally, coronal and sagittal planes. The correlation of the emission scan with the reconstructed transmission data allowed accurate anatomical localization of the infusate distribution. In seven patients, catheter placement resulted in perfusion to nontumor sites, and hence required repositioning. MAA accumulation was seen in the lungs of all patients, regardless of tumor site, indicating arterio-venous shunting of the MAA. The degree of uptake in the lungs was quantified from planar anterior/posterior thorax images in terms of injected dose in ten patients, with values of 5–50% of injected dose present in the lungs. The technique provides a noninvasive means of accurately determining regional perfusion of chemotherapeutic agents delivered intra-arterially.

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Regional chemotherapy delivered by intra-arterial catheters has been used in a variety of tumors since the early 1960s (*1–9*) both as primary therapy and as an adjunct to surgery and/or radiotherapy. Despite over 20 years experience with this technique its efficacy remains controversial (*10–12*). Clearly, for maximal tumor response, precise delivery of the chemotherapeutic agent to the tumor is essential. As demonstrated by Kaplan et al. (*13*), only radionuclide infusions permit accurate assessment of tumor perfusion by the catheter as they can be injected at rates that mimic chemotherapy infusion. Scintigraphic techniques have been used mainly in hepatic regional chemotherapy (*14–17*) and more recently in extrahepatic sites (*8, 18*). It is customary in hepatic studies to perform a technetium-99m (^{99m}Tc) sulfide colloid scan prior to perfusion scintigraphy in order to obtain an anatomic outline on which to orient the perfusion data.

In nonhepatic studies, such simple localisation is not possible and the perfusion data are overlaid on skeletal radiographs (*8*) or contrast angiograms (*18*). Single photon emission computed tomography (SPECT) has recently been applied to infusion studies (*19*), with computed x-ray tomography providing the reference anatomic data. We have developed a technique by which scintigraphic data and anatomic reference data can be acquired simultaneously (*20*). We have applied this technique, using [^{99m}Tc]macroaggregated albumin (MAA) scintigraphy and the superimposition of perfusion and anatomic data, to allow more precise prediction of perfusion than previously possible.

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MATERIALS AND METHODS

Thirty patients with histologically proven nonhepatic tumors were selected for this study and their characteristics are listed in Table 1. Regional chemotherapy was used prior to surgery with or without radiotherapy.

Arterial catheters were placed in the nearest accessible artery to the tumor, with position being checked by the injection of 2 ml of Patent Blue over a 10-sec period. The resultant skin discolouration allowed prediction of the approximate distribution of chemotherapy. Contrast angiography was also performed where possible. In the patients with head and neck tumors angiography was not possible, due to the fine bore of the arterial catheter. Perfusion scintigraphy was performed on all patients within 24 hr of catheter insertion.

Procedure

The patient was placed on a cantilevered scanning bed. A gadolinium-153 flood source was attached to the head of a

TABLE 1
Patient Characteristics

Region	Tumor type	M	F
Head and neck	Carcinoma	5	5
	Sarcoma	3	
	Melanoma		1
Breast	Carcinoma, Stage III		3
Abdomen and pelvis	Carcinoma	2	
	Sarcoma	2	
Limbs	Sarcoma	6	3
Total		18	12
		=30	

rotating gamma camera (GE 400 AT, International General Electric, Milwaukee, WI). Fifty megabequerels (1.2 mCi) of ^{99m}Tc-labeled MAA (MAA Technescan, Mallinkrodt Inc., St. Louis, MO) in a 2.0-ml saline suspension was introduced into the intra-arterial pump line and was subsequently infused slowly at the proposed rate of the chemotherapy. Data were acquired by dual radionuclide collection on the tomographic gamma camera interfaced to a computer (PDP 11/34, Digital Equipment Corporation, Maynard, MA). A 360° acquisition was collected of 64 angles at 20 secs per angle in a 64 × 64 word matrix, giving 2–4 × 10^5 reconstructed counts/slice over the perfused area. Slice thickness was ~6 mm. At the conclusion of the study, views of the thorax were obtained to estimate the degree of pulmonary uptake of MAA. This was modified in later studies to include a ^{99m}Tc transmission scan of the anterior thorax, performed prior to the injection of MAA, in order to quantify lung uptake. The entire procedure lasted approximately forty minutes.

The transmission study was reconstructed after scatter subtraction using a protocol previously described (*20*), so that an attenuation map of the body was obtained. Both transmission and emission studies were reconstructed with standard convolution backprojection algorithms (Nuclear Medicine Package, ANALOGIC Corp., Wakefield, MA). The emission and attenuation sections were displayed separately, and superimposed, and the combined studies were viewed in transverse, and when indicated, sagittal and coronal planes.

The transmission and emission planar lung studies were analyzed for quantitation of absolute lung uptake following the method of Macey and Marshall (*21*). This involves calculating the activity present in lung regions-of interest from the equation

$$A = \frac{G}{E}\left[\frac{N_o}{N_t}\right]^{1/2},$$

where A = activity (MBq), G = geometric mean of anterior/posterior images, E = sensitivity of camera/collimator system, N_o = unattenuated count rate of the flood source, and N_t = the transmitted count rate through the subject.

All patients had catheters inserted in a radiological procedure with final position verified by Patent Blue staining and, when catheter lumen size permitted, rapid injection of radioopaque contrast. Thus, all patients presenting for perfusion scintigraphy had catheters which were thought to be in anatomically optimal positions.

RESULTS

A total of 45 studies have been performed in 30 patients (18 males, 12 females; age range 15–75 yr). No complications occurred. The findings on perfusion scintigraphy led to catheter repositioning in seven patients. In six of these there was disagreement between the SPECT studies and Patent Blue testing. Tumor perfusion subsequently improved in five cases. Two examples are cited in the following case reports.

Case 1: Comparison with Patent Blue

A 57-yr-old man underwent intra-arterial infusion chemotherapy for a malignant fibrous histiocytoma of the left sternomastoid muscle. Following insertion of a left superficial temporal artery catheter, a Patent Blue infusion indicated satisfactory catheter position, with staining of the skin overlying the tumor (Fig. 1, arrowed). However, the radionuclide study clearly demonstrated predominant perfusion of the left cerebral hemisphere (Fig. 2) with minimal tumor perfusion. The

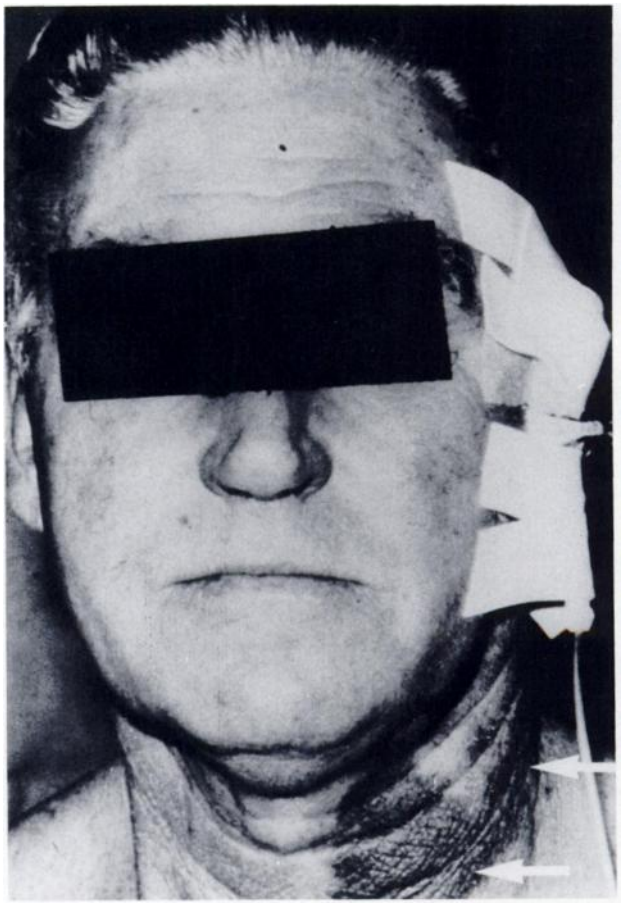

FIGURE 1
57-yr-old male with malignant fibrous histiocytoma of the left sternomastoid muscle. The catheter is situated on the left side of the head and the arrows indicate the Patent Blue stain pattern on the skin.

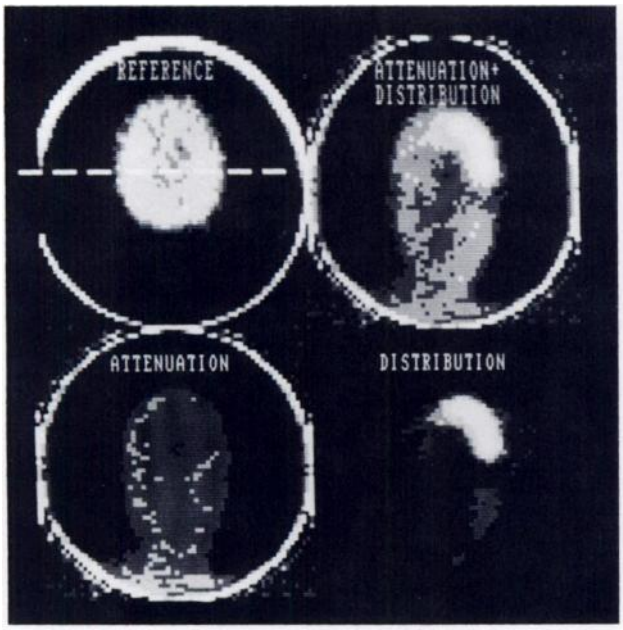

FIGURE 2
Counter-clockwise from top left are seen (i) a reference transverse attenuation slice indicating the level of the coronal sections, (ii) the coronal slice of attenuation (anatomy), (iii) the corresponding coronal slice of MAA distribution (perfusion), and (iv) the attenuation and MAA distributions superimposed. The coronal slices are viewed as from the anterior. Note the abudant perfusion of the left cerebral hemisphere with very little perfusion of the left sternomastoid region.

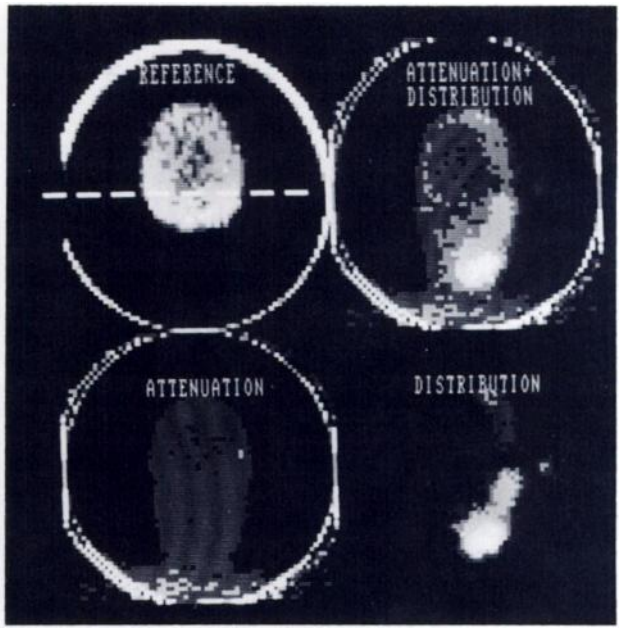

FIGURE 3
After catheter repositioning, the region containing the tumor is seen to be well perfused with a slight degree of scalp perfusion as well on the left side. (The small focus to the left of the body outline is the catheter tip.)

catheter was repositioned, and a later scintigram confirmed satisfactory perfusion of the tumor (Fig. 3).

Case 2: Comparison with Planar Images

A 29-yr-old man with a sarcoma of the left cheek had a catheter inserted via the left superficial temporal artery. Patent Blue staining indicated perfusion of most of the left side of the face. MAA perfusion studies were then performed. Planar images (Fig. 4A) showed that while perfusion was somewhat heterogeneous, it was generally in the correct anatomical area. Tomographic images (Fig. 4B and 4C), however, showed perfusion was predominantly to the nose and mouth. Re-positioning of the catheter was advised. Subsequent perfusion studies were performed after re-positioning. The planar images (Fig. 5A) showed perfusion to be different, but in general to the same region. The tomographic images (Fig. 5B) though, displayed good perfusion of the entire left cheek area and the underlying tissues.

Tumor Arteriovenous Shunting

Arteriovenous (A-V) shunting through the tumor as demonstrated by pulmonary uptake of MAA was present in 11 patients. Quantitation of lung uptake in the last ten patients showed that 5–50% of the injected dose reached the lungs. None of the patients studied had repeat studies to assess the reproducibility of the lung uptake measurement. All patients that had repeat studies had their catheters repositioned before the second study, therefore changing the perfusion and shunting patterns.

DISCUSSION

MAA when infused into an artery will impact in the first distal capillary bed, so that the distribution of a well mixed injection of [^{99m}Tc]MAA will reflect the territory perfused by the injected artery. As noted previously (*13*), the rate of injection is the major determinant of the distribution of the injectate. When MAA is injected at the same rate as the proposed chemotherapy, it will give an accurate indication of drug distribution. For this reason, perfusion scintigraphy is the method of choice in assessing the accuracy of catheter placement for intra-arterial chemotherapy. We have developed this technique further with the addition of SPECT and dual acquisition collections so that more precise positioning of arterial catheters is possible. The simultaneous emission/transmission technique not only provides superior definition of patient contour and anatomy without recourse to such secondary methods as external skin markers, but also displays the data tomographically. Thus it permits direct comparison of tracer distribution with anatomy.

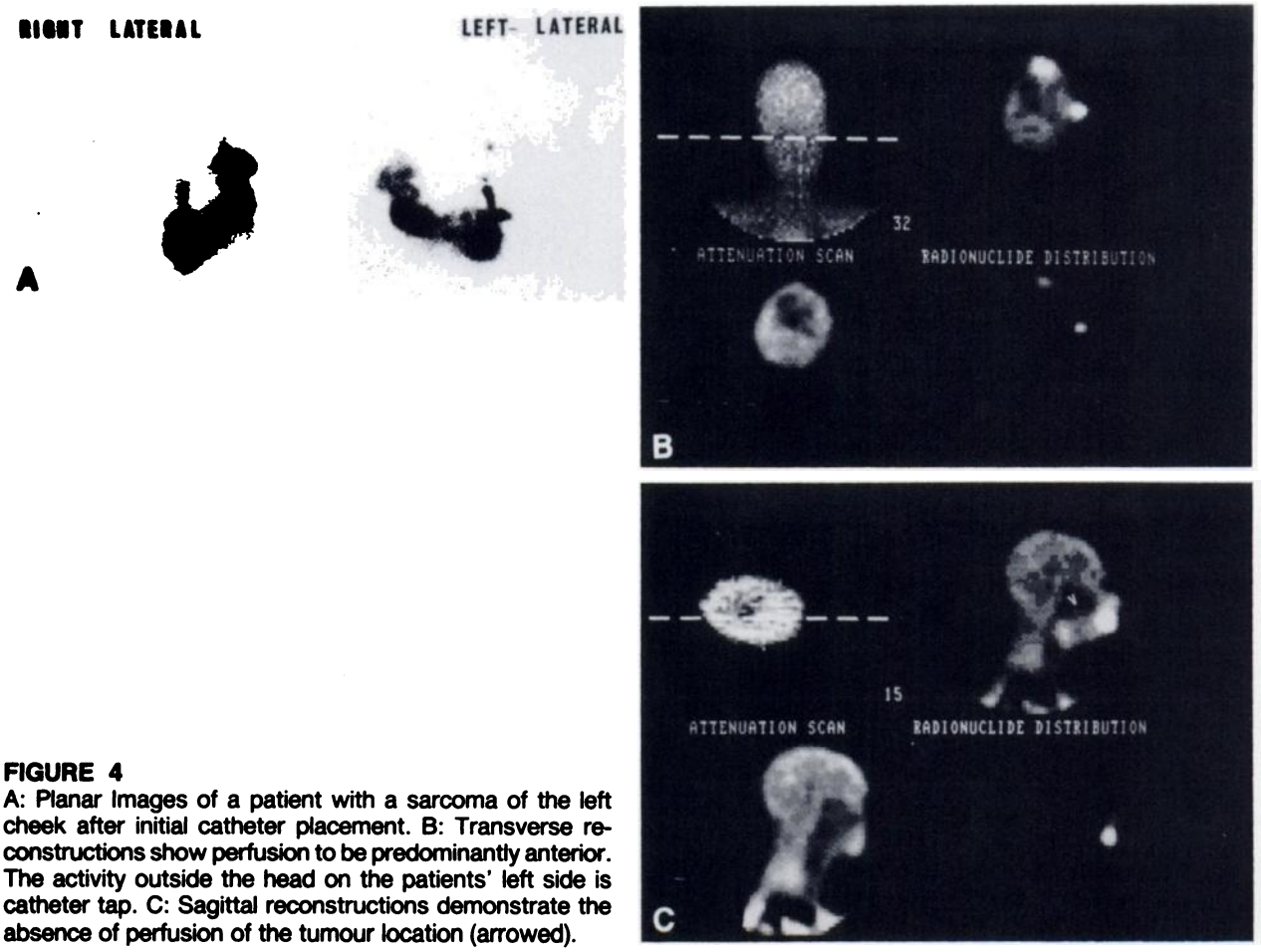

FIGURE 4
A: Planar Images of a patient with a sarcoma of the left cheek after initial catheter placement. B: Transverse reconstructions show perfusion to be predominantly anterior. The activity outside the head on the patients' left side is catheter tap. C: Sagittal reconstructions demonstrate the absence of perfusion of the tumour location (arrowed).

The value of tomographic images is well demonstrated in Case 2. Planar images do not give the same precise localisation of the perfusion as is possible with tomographic methods. This is reinforced by the availability of reconstructed attenuation slices.

In addition, this combined technique is a step towards truly quantitative SPECT as the data from the ^{153}Gd transmission study can be used in an attenuation correction protocol. This method of acquiring attenuation data has not been used previously (*19,22*) for perfusion studies.

Tumor A-V shunting occurred in all the patients in this study. This phenomenon has been previously described by others (*23–25*). The degree of A-V shunting did not correlate with systemic toxicity. This was contrary to the experience of Kaplan (*25*). Bledin (*24*) showed that the incidence of complications using intra-arterial chemotherapy, for hepatic neoplasm, correlated with extra-hepatic localisation of MAA (other than in the lungs). The discrepancy between our results and Kaplans' could be explained by this extra-hepatic deposition of MAA (and therefore chemotherapeutic agent). However, accurate quantitation of A-V shunting is potentially another important variable in determining the efficacy of intra-arterial chemotherapy. Quantitative prediction of A-V shunting will be needed if microspheres labeled with therapeutic agents such as yttrium-90 (^{90}Y) are to be used. The technique outlined here is directly applicable to this purpose.

In conclusion, perfusion scintigraphy with [^{99m}Tc] MAA using SPECT with simultaneous emission and transmission acquisitions permits accurate spatial localisation of arterial perfusion and hence catheter positioning, a prerequisite for successful regional chemotherapy. This technique is safe, simple, and readily repeatable.

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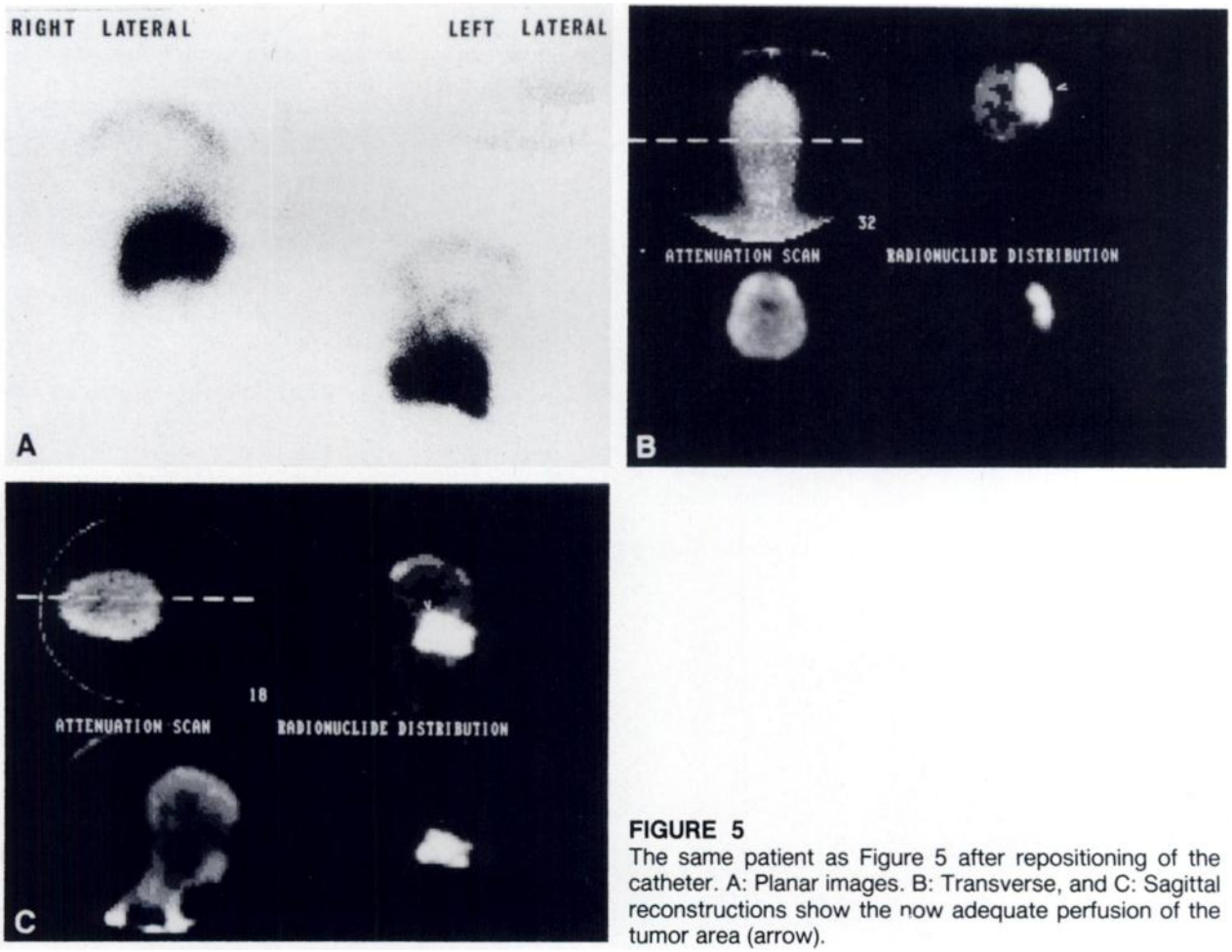

FIGURE 5
The same patient as Figure 5 after repositioning of the catheter. A: Planar images. B: Transverse, and C: Sagittal reconstructions show the now adequate perfusion of the tumor area (arrow).

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