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Transcatheter Infusion of ^{99m}Tc MAA for Predicting Response of Intra-arterial Chemotherapy in Osteogenic Sarcoma

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Abstract—*Ten patients with histologically proven osteogenic sarcoma received multiple courses of intra-arterial chemotherapy. Patients received* 2-3 mCi ^{99m}Tc *macroaggregated albumin (MAA) infused through indwelling arterial catheters prior to, during and after the chemotherapy, and static images of tumor beds and lungs were taken and compared with contrast angiographic findings. Of the* 31 *studies to evaluate tumor vascularity,* 26 *agreed and five showed discrepancies. In general, decreased tumor vascularity, as represented by reduced MAA uptake by the tumor, corresponded to decreased tumor size and to increased tumor calcification seen on radiographs. Twenty-six of the* 31 *lung-imaging studies also revealed agreement between decreasing tumor vascularity, based on decreasing MAA tumor uptake, and decreasing lung uptake of the radioactivity. Decreased lung uptake of the activity on the last follow-up study in eight patients corresponded to reduced tumor involvement and improved patient performance status.*

INTRODUCTION

MAJOR advances in the treatment of osteosarcoma have been enhanced by the transcatheter intra-arterial infusion of chemotherapy, which allows higher concentrations of drugs to accumulate during the first-pass through the tumor bed [1-4]. Conventional radiography and angiography have been used to evaluate the response of tumor to intra-arterial chemotherapy [4]. ^{99m}Tc-macro-aggregated albumin (MAA) perfusion scintigraphy has also been used to optimize the catheter position for arterial chemotherapy and assess the tumor perfusion [5, 6]. There has been a suggestion that MAA study may be helpful in predicting the patient's response to chemotherapy [7, 8]. This report describes our experience in predicting response of the tumor to intra-arterial chemotherapy by using the ^{99m}Tc MAA infusion study in patients with osteogenic sarcoma.

MATERIALS AND METHODS

Ten patients (six men and four women), ranging in age from 16 to 55 yr and having histologically proven osteogenic sarcoma (femur involved in nine patients and tibia in one), were selected for this study. Using the femoral approach, we inserted an arterial catheter into the artery supplying the tumor of each patient. A total of 31 contrast angiographic studies were performed with an injection rate of 5-6 ml/sec before, during and after chemotherapy courses. ^{99m}Tc MAA infusion studies were done within 3 hr after angiographic examinations; 2-3 mCi of ^{99m}Tc MAA (10-90 μM) in 0.5 ml were introduced into the arterial catheter which was connected to the mechanical pump that was to propel MAA particles into the perfused region at the same rate (usually 20-40 ml/hr) at which the chemotherapy (*cis*-platinum) was to be delivered. The tumor perfusion pattern was visually evaluated and correlated with contrast angiograms. Uptake of radioactivity by the lungs was quantitatively measured to assess the degree of arteriovenous (AV) shunting within the perfused bed by analysis of lung activity. Lung activity counts were divided by administered dose of ^{99m}Tc after subtraction of background (conveniently head) activity. This provided a practical quantitative assessment of serial changes of lung uptake of the

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radioactivity. Numerical changes of normalized uptake of the lung activity from the first and last studies were evaluated and correlated with tumor vascularity as well as patient's performance. The patient's performance status was subjectively evaluated from the range of motion of the affected extremity and the patient's degree of pain.

RESULTS

Twenty-six of thirty-one studies in ten patients with osteogenic sarcoma revealed agreement between tumor vascularity and tumor perfusion pattern (Table 1). Decreased tumor vascularity seen on angiographic examination during or after the courses of chemotherapy was represented by reduced MAA tumor uptake and corresponded to reduced tumor extent and to the increased calcifications seen on radiographs. Five studies revealed discrepancies. Two MAA perfusion scans revealed increased tumor perfusion, while angiograms demonstrated decreased vascularity. In our osteogenic sarcoma series we have observed significant shunting of the radioactivity to the lung in all patients, and there was good correlation between decreasing lung activity and improvement in patient's clinical status. Twenty-six of thirty-one lung imaging studies also revealed agreement between decreasing tumor vascularity and decreasing lung activity. Decreased lung uptake generally corresponded to reduced tumor involvement and improved patient performance status.

Table 2 shows changes of normalized lung radioactivity uptake from the first and last studies. Eight of ten patients eventually had decreased lung uptake activity corresponding to disease improvement. A representative case is illustrated in Figs 1-4.

Table 1. Correlation of tumor perfusion pattern on an MAA infusion study and tumor vascularity on contrast angiography in 31 studies involving 10 patients with osteogenic sarcoma

Correlation	Tumor perfusion on the MAA study		Tumor vascularity on angiography
Agreed 26	decreased	10	
	no change	14	
	increased	2	
Disagreed 5	decreased	2	1 no change 1 increased
	no change	1	decreased
	increased	2	both decreased

Table 2. Changes of normalized lung radioactivity uptake from the first and last studies in 10 patients with osteogenic sarcoma

Patient	Study*	Counts/min		Administered dose (mCi)	Normalized lung radioactivity to dose
		Lungs	Head		
1	F	1072	35	3.2	324
	L	400	45	2.6	136
2	F	1100	45	2.4	439
	L	870	50	3.2	256
3	F	2500	600	4.9	387
	L	200	25	2.8	62
4	F	3000	32	3.0	989
	L	380	45	2.9	115
5	F	1500	35	3.6	406
	L	940	60	2.9	303
6	F	950	60	3.1	287
	L	450	35	2.8	148
7	F	1600	35	2.8	558
	L	935	45	2.9	306
8	F	830	30	2.9	276
	L	930	45	3.2	257
9	F	550	35	5.2	99
	L	330	30	3.1	96
10	F	1050	35	2.9	350
	L	1250	40	2.8	432

*F = First; L = last.

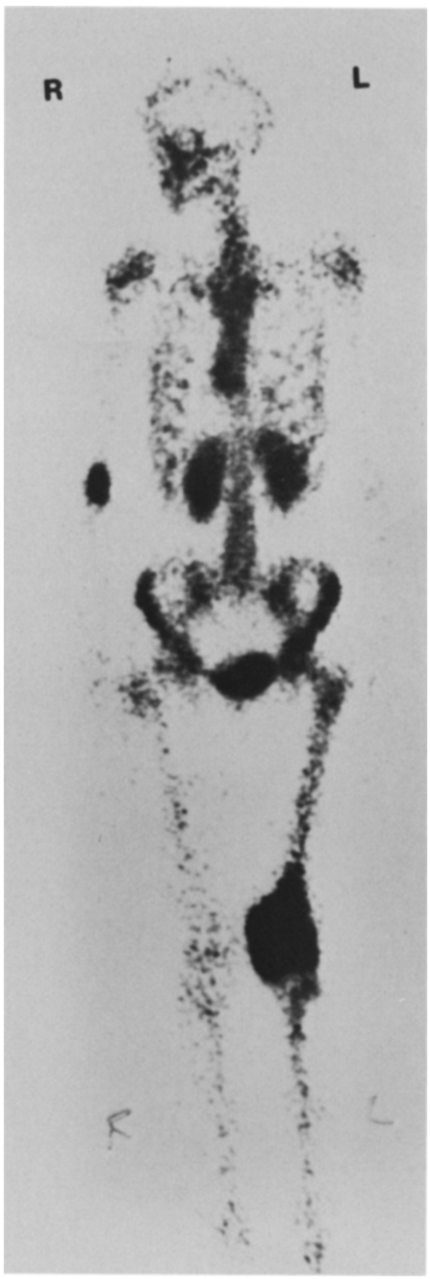

Fig. 1. Anterior whole-body bone image with ^{99m}Tc MDP shows markedly increased radioactivity in the left distal femur, corresponding to the area of biopsy-proven osteogenic sarcoma.

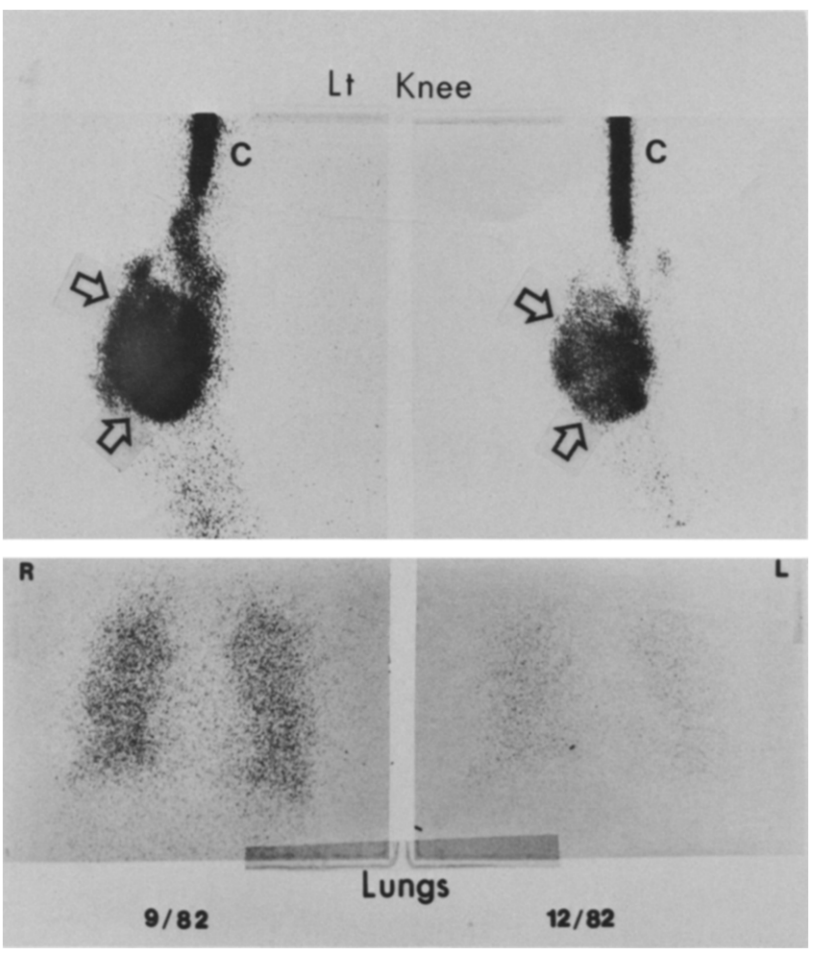

Fig. 2. Images of left knees (upper row) and lungs (lower row) with ^{99m}Tc *MAA infusion prior and after* 3 months *of intra-arterial chemotherapy demonstrate significantly decreased tumor perfusion (diminished radioactivity relative to the activity retained in the arterial catheter) as well as lung radioactivity. Arrows indicate tumor perfusion. C denotes activity in the catheter.*

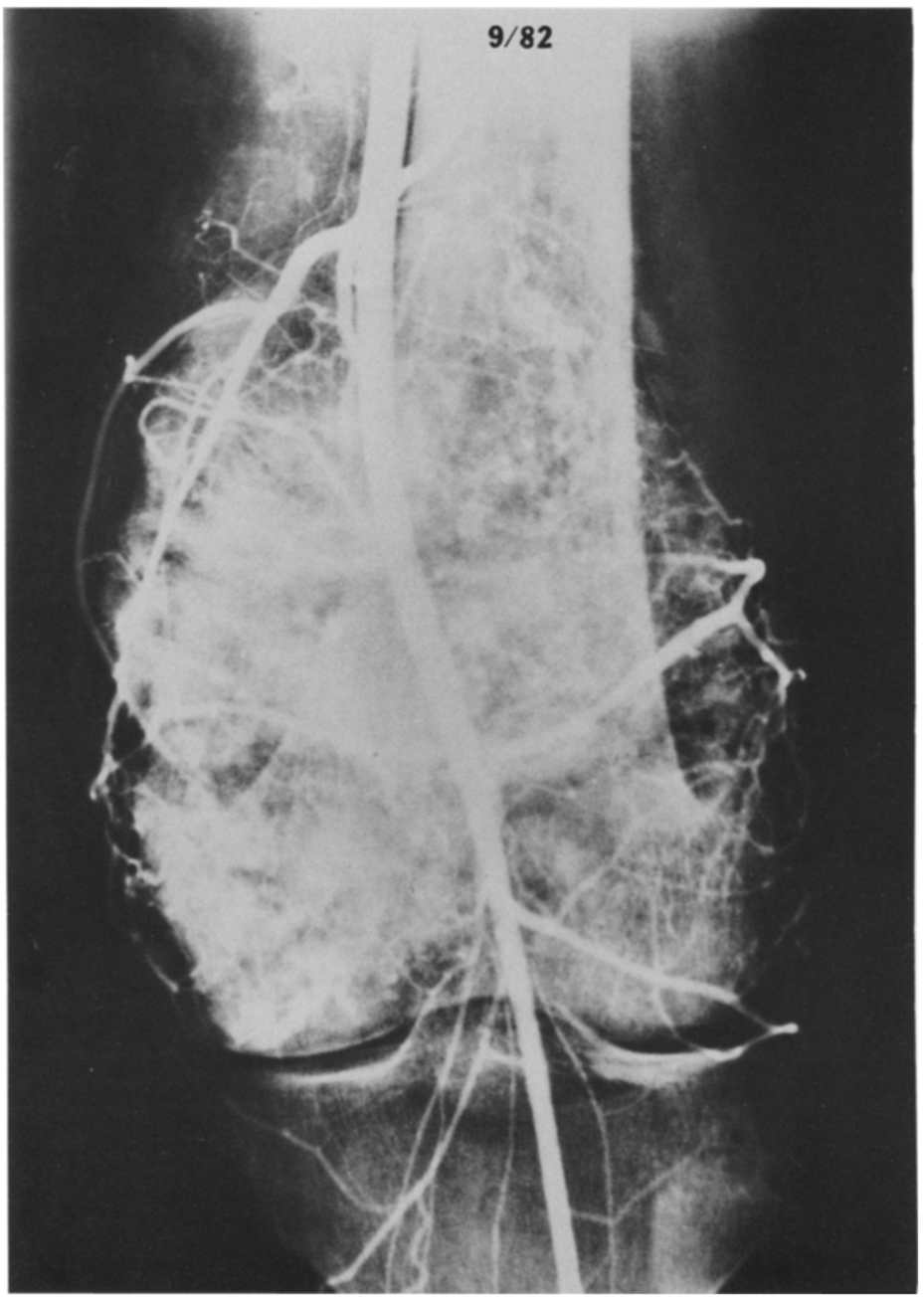

Fig. 3.

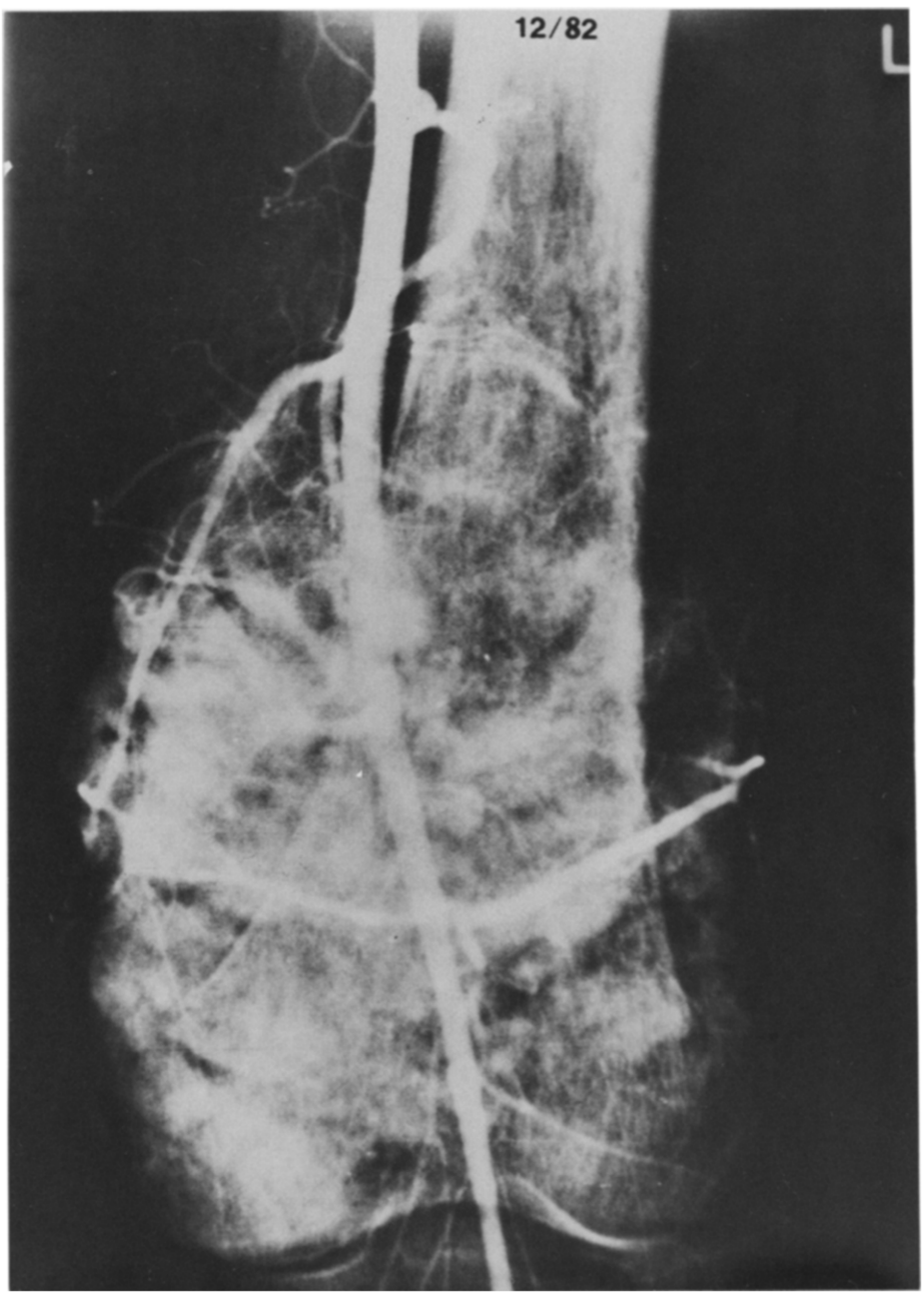

Fig. 4.

Fig. 3 and 4. Corresponding contrast angiogram also reveals significantly decreased tumor vascularity after intra-arterial chemotherapy.

DISCUSSION

Intra-arterial *cis*-platinum chemotherapy in combination with adriamycin has been used in patients with osteogenic sarcoma prior to surgery and placement of custom-fitted prostheses or limb preservation [2]. It has also been shown to provide definite drug-induced tumor response due to improved drug delivery. Higher drug concentration is retained in the tumor bed during the first-pass procedure without increasing systemic toxicity [9]. This has resulted in improvement of the therapeutic index.

^{99m}Tc MAA injected at the same rate as the chemotherapy infusion allows for physiologic assessment of tumor perfusion patterns [10] and more accurately evaluates the region of perfusion than does arteriography [5]. Vascular spasm and streaming effect by the angiography may cause changes in the perfusion pattern.

In general, there is good correlation between tumor vascularity demonstrated by conventional angiography and perfusion pattern demonstrated by radionuclide angiography. After 2–3 courses of intra-arterial *cis*-platinum chemotherapy for osteogenic sarcoma the perfusion pattern includes reduced MAA uptake in the tumor bed and decreased tumor size. This would indicate definite drug-induced tumor response. The perfusion pattern changes corresponded well to observed tumor vascularity and the increased tumor calcifications seen on radiographs.

In this investigation we have observed an increase in AV shunting in peripheral tumors that exceeds that which may occur in normal extremities [11] and decreased AV shunting correlated with response to therapy. This same phenomenon has been observed in cases of hepatic neoplasm. Bledin *et al.* [12] found that there is a predicted response of the tumor to chemotherapy based on decreased radiotracer activity in the lung as the tumor decreased in size.

Tumor vascularity may show no significant changes during chemotherapeutic follow-ups, but we have observed further improvement in patient status with decreasing lung activity. In two follow-up studies there has been increased MAA tumor uptake in the perfusion pattern but discordant decreased vascularity by contrast angiography. The increased tumor perfusion pattern has corresponded to increased MAA pulmonary uptake. Therefore the radionuclide studies indicate that the tumor does not respond to chemotherapy or the presence of recurrent tumor. Angiographically subtle changes in vascularity and tumor calcifications may be difficult to properly evaluate the tumor response. It would imply that tumor vascularity, as represented by MAA tumor perfusion pattern and shunting of MAA radioactivity to the lung, appear to be a better parameter in assessing tumor non-reponsiveness or recurrence.

In conclusion, tumor vascularity and shunting of activity to the lung ^{99m}Tc MAA appear valuable in assessing tumor response in osteogenic sarcoma patients undergoing intra-arterial chemotherapy.

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