The Utility of Technetium-99m DTPA Inhalational Scans in Artificially Ventilated Patients

S. Patrick Butler, Philip O. Alderson, Robin L. Greenspan, David G. Doctor, and Vincent J. DeFillipi

Division of Nuclear Medicine, Department of Radiology, Columbia University, New York, New York

Technetium-99m diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) radioaerosol scans performed on 21 consecutive artificially ventilated patients were compared to 50 similar scans performed on patients breathing without mechanical assistance. All patients were referred for evaluation of suspected pulmonary embolism. The comparison revealed increased extrathoracic tracheal and mediastinal tracheal deposition but less central bronchial deposition in the artificially ventilated patients. Peripheral penetration in both groups of patients was excellent. Within the artificially ventilated group, peripheral penetration of activity seemed equally good in patients receiving positive-end expiratory pressure ventilation (n = 14) and those ventilated with normal pressures (n = 7). The frequency of regions in which aerosol activity (A) was present in the same zone as a perfusion (P) defect was the same in the controls and artificially ventilated patients (12% against 14%) but the frequency of the reverse type of mismatch (i.e., P > A) was significantly higher in the artificially ventilated group (42% against 14%, $p < 0.001$). The results suggest that [^{99m}Tc]DTPA aerosol scans in artificially ventilated patients are associated with good peripheral penetration of activity and frequently yield valuable clinical information.

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Radioaerosols were introduced for ventilation scanning many years ago (*1,2*). Recently, technical improvements in delivery systems have resulted in substantially increased clinical utilization. In fact, radioaerosols currently are considered comparable to radioactive gases as adjuncts to perfusion imaging in patients suspected of pulmonary embolism (*3,4*). In the past, a major criticism of radioaerosol inhalation scans has been excessive central bronchial deposition and relatively poor peripheral penetration of aerosol. With current delivery systems, this appears to be less of a problem. In artificially ventilated patients, however, radioaerosols have been less readily accepted. It generally has been felt that the central deposition tendencies of radioaerosols are likely to be accentuated in this patient group. This did not seem the case in our clinical experience, however. In order to investigate this situation further, a retrospective study was undertaken to evaluate the characteristics and quality of radioaerosol inhalation studies in a group of artificially ventilated patients.

MATERIALS AND METHODS

All 387 aerosol inhalational scans performed at Columbia-Presbyterian Medical Center from October 1985 to January 1988 were reviewed. Twenty-one of these scans were performed on 20 artificially ventilated patients. From the remaining 366 scans, 50 scans from 50 different patients were randomly selected to serve as a typical group of non-ventilator dependent patients whose aerosol deposition patterns after inhalation during tidal ventilation could be compared to those seen in artificially ventilated patients. The clinical characteristics of both the comparison group and the artificially ventilated group are given in Table 1. The medical conditions that necessitated ventilatory support were varied: five patients were postcardiorespiratory arrest, five were postoperative and the remainder had respiratory failure (left ventricular failure in four patients, generalized sepsis in three patients, drug abuse in two patients and chronic obstructive airways disease in one patient).

For the routine aerosol inhalation scan, 1110 MBq (30 mCi) of technetium-99m-labeled diethylenetriaminepentaacetic acid ([^{99m}Tc]DTPA) (Medi-Physics Inc., NJ) in a volume of 2 ml of 0.9% saline was placed in either a Cadema (Cadema Medical Products, Middletown, NY) or a Syntevent (Synaco Inc., Palo Alto, CA) nebulizer that was aerated at 10 l per minute of 100% oxygen from a compressed air tank. The patient was placed in the supine position over the gamma camera and was instructed to inhale until a count rate of 100,000 cpm was reached (3 to 5 minutes). Typically, this resulted in ~28 MBq (750 μCi) of activity being deposited in the patient's lungs (*5*). Six aerosol images (the anterior, posterior, left anterior oblique (LAO), right anterior oblique (RAO), left posterior oblique (LPO) and right posterior oblique (RPO) projections) then were acquired using the same conventional large field-of-view gamma camera (Picker Dyna Camera 4, Picker Inc., Northford, CT). Each image contained

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For reprints contact: Philip O. Alderson, MD, Dept. of Radiology, Div. of Nuclear Medicine, 622 West 168th St., New York, NY 10032.

TABLE 1
Clinical Details of Tidal Respiration Group and Artificially Ventilated Patients

	Tidal respiration group	Artificial ventilation group
Male: female ratio	1:3	3:1
Age (mean)	57 yr	61 yr
Range	31–93 yr	31–82 yr
Principal diagnosis		
Carcinoma	8	6
Coronary artery disease	5	6
Chronic airways disease	5	1
Postop minor surgery	5	0
Pneumonia	4	2
Postop orthopaedic	3	0
SLE	2	0
Pulmonary embolism	2	0
Deep venous thrombosis	2	0
Peripheral vascular disease	2	1
Drug abuse	0	2
Other	6	2
No diagnosis available	6	0

~100,000 counts and required 2 to 3 min of imaging time. Perfusion imaging then was performed in the same six projections after injection of 148 MBq (4 mCi) of [^{99m}Tc] macroaggregated albumin (MAA) (Mallinckrodt, St. Louis, MO). Each perfusion view contained 500,000 counts with a count rate exceeding by at least four times that obtained during inhalation scanning alone.

All ventilatory support was provided by the same type of volume-cycled ventilator (Bennett Ventilation Model MA-1, Puritan Bennett Corp., Los Angeles, CA) with a tidal volume of between 700 to 900 ml. Positive end expiratory pressures (PEEP) up to 12 mm water (mean 4 mm water) were used in some patients (see below). The aerosol apparatus was connected "in series" with the ventilator during the study in the manner recommended by the manufacturers. The nebulizer is placed in the ventilator circuit and is not aerated until the entire circuit is closed. In this way, the possibility of contamination of the area with radioaerosol is minimized. Similarly, at the conclusion of the inhalation of the radioaerosol, the generation of radioaerosol is stopped before the nebulizer is removed from the respiratory circuit so that the possibility of radioaerosol contamination is minimized. Removing the nebulizer from the circuit takes 10–20 sec. At all times the nebulizer unit is adequately shielded. The ventilator's parameters were not changed (including PEEP) and no additional endotracheal suctioning was performed on these patients prior to scanning. A respiratory care technologist was present throughout the inhalation of radioaerosol—even for scans done on emergencies on off-hours shifts—and controlled the patient's ventilation.

For the purposes of review, scans were randomized and then analyzed by two experienced nuclear medicine physicians who were unaware of whether the scan was that of an artificially ventilated patient. Disagreements were resolved by consensus. The review was designed to determine if there were any significant, reproducible differences between aerosol deposition patterns in patients being artificially ventilated and those breathing normally.

All scans were graded for extrathoracic tracheal activity, mediastinal tracheal activity, central bronchial deposition and peripheral penetration by using four-part scales. In each case, if the feature in question was absent, the image was graded "0". Conversely, if the feature was present, it was subjectively graded as 1+ to 3+ positive. The 3+ grade was used when the intensity of the feature in question exceeded that of general lung activity itself; 2+ was used when activity was about equal to that of the lung; 1+ was used when activity was definitely present but less than that in the lungs. Peripheral penetration was determined by visually comparing the ventilation scan to the perfusion scan and estimating the limitation of penetration, using the outermost edges of the perfusion scan (excluding local defects) to define the lung borders. Penetration of activity was graded as "excellent" when the aerosol scan and perfusion scan were superimposable; as "good" when the outer margins of the aerosol scans were equal to perfusion scans in distance from the hila, but were more faint; as "fair" when there was only faint activity in the peripheral third of the lung; and "poor" when penetration was markedly decreased. In addition, comparison with the perfusion scan was utilized to note the occurrence of regional discrepancies in aerosol-perfusion activity. When aerosol activity was visualized in the region of a perfusion defect, it was described as a conventional aerosol-perfusion defect (A-P mismatch). When perfusion activity was seen in a region without or with substantially reduced aerosol activity, it was defined as a reverse A-P mismatch.

After all scans were graded, the grade 1–2 abnormalities in each category were grouped and considered "mild" with the grade 3–4 abnormalities also being grouped and considered "marked". These two groups were compared using a chi-square analysis to determine if there were any significant differences between the two groups with respect to the parameters mentioned above.

RESULTS

All 21 scans of the artificially ventilated patients were of sufficient quality for diagnostic interpretation. The scan of one of the tidal ventilation patients had to be excluded from the analysis of local A-P concordance because of poor peripheral penetration of activity but was included in the other comparisons. The statistical analysis demonstrated significantly more extrathoracic tracheal ($p < 0.01$) and mediastinal tracheal deposition ($p < 0.001$) in the artificially ventilated group but significantly less ($p < 0.001$) central bronchial (i.e., perihilar) deposition than in controls (Table 2). Peripheral penetration was excellent in both groups of patients. Only 10% of the artificially ventilated patients had moderate decreases in peripheral penetration and none had severe limitations.

In the artificially ventilated patient group, the count rate over the thorax in the first image of the ventilation scan was 2.30k cts/sec with an s.d. of 1.16k cts/sec. In the last image, the count rate was 2.43k cts/sec with an s.d. of 0.99k cts/sec. In addition, the count rates in

TABLE 2
Radioaerosol Deposition Patterns in Tidal Ventilation and Artificially Ventilated Patients

Finding	Grade	Tidal vent (%)	Artif. vent (%)	p Value
		(n = 50)	(n = 21)	
Tracheal deposition	0	6%	10%	
	1	50	14	
	2	30	29	
	3	14	47	<0.01
Mediastinal deposition	0	42%	29%	
	1	30	5	
	2	22	24	
	3	6	42	<0.001
Central bronchial deposition	0	20%	57%	
	1	36	34	
	2	32	9	
	3	12	0	<0.001
Peripheral penetration	Exc	48%	76%	
	Good	24	14	
	Fair	12	10	
	Poor	6	0	=0.50
Mismatches		12%	14%	=0.45
Reverse mismatches		14%	42%	<0.001

those patients on PEEP were not significantly lower in the last image as compared to the first image (2.22k cts ± 0.91; 2.78k cts ± 0.87).

Two-thirds of the artificially ventilated patients (n = 14) were on PEEP. Some differences were noted between the radioaerosol deposition patterns in this group and the remainder of the artificially ventilated group. Tracheal deposition was more common ($p < 0.05$) in patients on PEEP, but central bronchial deposition was less common ($p < 0.05$) as shown in Table 3. Peripheral penetration was equally good in patients with or without PEEP. The frequency of A-P discordance of either the conventional or reverse type was not significantly different in artificially ventilated patients receiving or not receiving PEEP.

Conventional A-P mismatch occurred in 14% of artificially ventilated patients and 12% of the tidal ventilation group, but reverse A-P mismatch occurred in 43% of the artificially ventilated patients and in only 14% of the tidal ventilation patients ($p < 0.001$). The chest radiographs of those patients with reverse mismatch were reviewed; at the site of reverse mismatch, four patients (44%) had an infiltrate, one (11%) had atelectasis plus an infiltrate, one (11%) pulmonary oligemia, one pleural effusion (11%) and two (22%) had a clear radiograph. Bronchial obstruction from mucus or other causes was found after being suggested by the radioaerosol findings in two of these nine patients even though it was unsuspected clinically.

One such patient was a 70-yr-old man who underwent a cholecystectomy. Postoperatively, the patient developed fever and upper abdominal pain and surgical re-exploration revealed a perforated small bowel. During anaesthetic induction for the second operation, the patient started vomiting vigorously and intubation was difficult. The patient was artificially ventilated postoperatively and, 48 hr following surgery, rapid atrial fibrillation/flutter occurred. An aerosol-perfusion lung scan was performed to exclude pulmonary embolism. The chest radiograph (Fig. 1A) showed a large infiltrate at the right lung base with an accompanying smaller infiltrate at the left lung base. In the aerosol-perfusion study (Fig. 1B, C, D, E) radioaerosol activity in the tracheobronchial tree revealed an inappropriate proximity between the carina (arrow) and lung bases, i.e., it suggested that the bases were symmetrically hypoventilated. In addition, the perfusion study demonstrated relatively preserved perfusion at the left and right bases. Thus, there were significant reverse aerosol-perfusion mismatches involving both left and right lung bases, with the left being larger than the right. Bronchoscopy revealed copious secretions throughout the bronchial tree. The secretions were removed and intensive chest physiotherapy with repeated tracheobronchial suctioning was initiated. Prior to the bronchoscopy, the arterial gases were pH 7.41, pO_2 86 mmHg, pCO_2 35 mmHg on an inspired oxygen concentration of 75%. Thirty-six hours after bronchial cleansing, the patient was extubated with arterial gases of pH 7.40, pO_2 100 mmHg and pCO_2 37 mmHg on a face mask of 50% oxygen.

TABLE 3
Effect of PEEP on Radioaerosol Deposition Patterns in Artificially Ventilated Patients

	PEEP (n = 14)		No PEEP (n = 7)		
	Mild	Marked	Mild	Marked	p Value
Tracheal deposition	2	12	3	4	<0.05
Mediastinal deposition	5	9	4	3	N.S.*
Central bronchial deposition	14	0	5	2	<0.05
Peripheral penetration	12	2	6	1	N.S.

* Not significant.

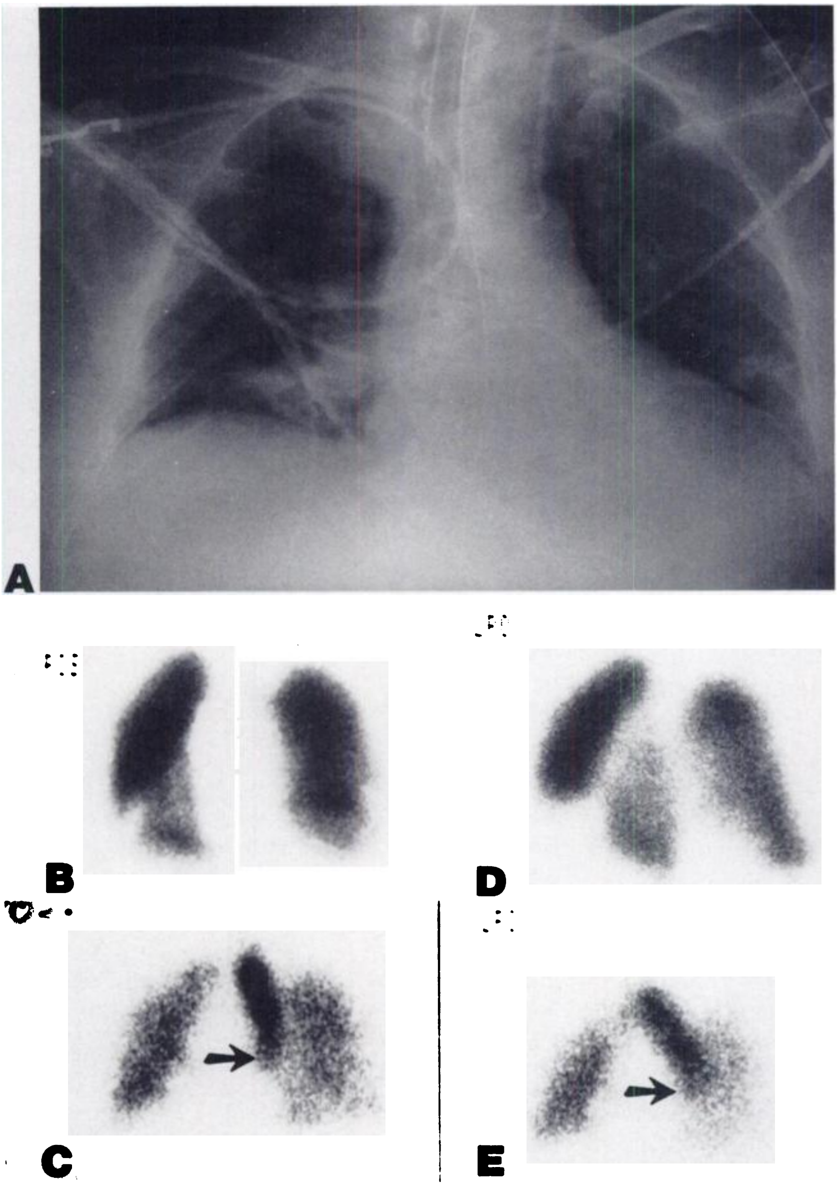

FIGURE 1
70-yr-old man was artificially ventilated following abdominal exploration with sudden onset of atrial fibrillation/flutter and hypoxia 48 hr after surgery. A: An AP chest radiograph demonstrating findings including a large right basilar infiltrate with a smaller left basilar infiltrate. B: Posterior [^{99m}Tc]MAA perfusion scan with accompanying [^{99m}Tc] DTPA radioaerosol scan (C). LPO projections of same scans (D) and (E). In the inhalation study, radioaerosol activity in the tracheobronchial tree revealed an inappropriate proximity between the carina (arrow) and lung bases, i.e., it suggested that the bases were symmetrically hypoventilated. In addition, the perfusion study demonstrated relatively preserved perfusion at the left and right bases. Thus there were significant reverse ventilation perfusion mismatches involving both left and right lung bases, with the left being larger than the right. Clinical improvement followed bronchial cleansing bilaterally.

DISCUSSION

Potential problems with radioaerosol inhalation studies in patients receiving mechanical ventilation include difficulties with radioaerosol administration, poor peripheral penetration of radioaerosol activity, and image artifacts that might be associated with radioaerosol inhalation by a patient on a ventilator.

With respect to radioaerosol administration, the "in series" placement of the nebulizer unit into the breathing circuit allows the ventilator to drive the aerosol into the patient's lungs. There are several theoretical reasons why a radioaerosol propelled into the lungs by a ventilator might work well. First, the respiratory rate of the ventilator is slow (12–14 breaths per min) and this permits a slow regular input of radioaerosol into the lung. Central bronchial deposition has been attributed to turbulent flow in the large airways resulting in excessive central deposition. A slow inflow rate should result in less turbulent flow, and thus less bronchial deposition. Second, the tidal volume is relatively large (700–900 ml), which permits greater lung expansion and could aid aerosol penetration. In addition, in two-thirds of our patients the scans were performed while the patients were on PEEP, which is designed to force air into the lungs and keep the lungs expanded between inspiration and expiration. This, too, should assist radioaerosol penetration.

The results of the current study suggest that changes in radioaerosol distribution patterns related to the presence of mechanical ventilation are predictable. Significantly increased extrathoracic tracheal and mediastinal tracheal deposition is likely to be seen. This probably is the result of adherence of the radioaerosol to the inner surface of the endotracheal tubing, and may be facilitated by the presence there of bronchial mucous secretions. Central bronchial deposition was not significant and peripheral penetration was excellent; no patient had a major limitation in penetration and only 10% had moderate limitation. In all the artificially ventilated patients, scans were of such quality that all perfusion defects could be correlated with regional ventilation to assess whether the perfusion defect was matched or not.

Other studies (*6*) of radioaerosol inhalation in patients on artificial ventilation have recommended the use of insoluble tracers rather than [^{99m}Tc]DTPA. The potentially rapid clearance of [^{99m}Tc]diethylenetriaminepentaacetic acid (DTPA) in certain lung disorders was cited as a reason for this choice. Our experiences with DTPA were excellent, however. Technetium-99m DTPA deposited in the lung is absorbed across the alveolar epithelium and excreted through the kidneys. In normal patients, the half clearance time of this tracer varies from 60–90 min (*7*). The theoretically rapid clearance that may be seen in some patients has not been a problem in our experience. Our patients inhale radioaerosol while under the gamma camera and imaging is commenced as soon as an acceptable count rate is obtained. The entire procedure time for the routine six views (each of 100,000 cts) is 15–20 min. In our artificially ventilated group, the count rates obtained in the sixth image were not significantly prolonged from those in the first image. Accordingly, we believe that [^{99m}Tc]DTPA is an adequate radioaerosol for evaluation of most artificially ventilated patients.

The high frequency (42%) of reverse A-P mismatch in the artificially ventilated group in the current study is interesting. Such discordance has been seen in ventilation-perfusion studies (*8–11*) and has been attributed to a failure of hypoxic vasoconstriction in the affected lung segment. It has been shown experimentally (*12*) that alveolar hypoxia results in significant vasoconstriction of the regional pulmonary vasculature in a normal lung. For unknown reasons (*13*) this normal autoregulation may fail in lungs affected by pneumonia, atelectasis, bronchial obstruction (*14*), chronic obstructive airways disease (*15*), and respiratory alkalosis (*16*). Carvalho et al. (*17*) recently reviewed their experience with reverse ventilation-perfusion (V-P) mismatch in a general hospital population using krypton-81m as the ventilation agent. The incidence of reverse V-P mismatch in their group was 12%, which compares closely with the 14% frequency seen in the control group in this study.

It is tempting to postulate that PEEP contributed to the high frequency of reverse A-P mismatch in our population, but this cannot be deduced from the data presented here. It has been shown in animal models that PEEP can cause redistribution of the blood flow to a nonventilated lobe (*18*), as PEEP increases the vascular resistance of the normally ventilated lung and permits increased blood flow through the relatively lower resistance of the non-ventilated lung. Thus, PEEP could result in, or contribute to, a worsening of systemic oxygenation by causing an increased blood flow to a nonventilated lung. Such a tendency toward increased reverse A-P mismatch was not seen in the PEEP subset of our population, however.

The present study has demonstrated that inhalational radioaerosol lung scanning in artificially ventilated patients results in scans of an excellent quality. The "in series" set-up is easy. The nebulizer units are commercially available and can easily be adapted before being installed into the ventilator circuit. In addition, significant pathophysiological events can be demonstrated with such scans and can lead to important changes in patient management. The findings suggest that inhalational lung scanning in artificially ventilated patients is not only feasible, but valuable.

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15 30

Selected manuscripts from the issues of the Journal of Nuclear Medicine published 15 and 30 years ago.
Edited by F.F. Mand

JANUARY 1960

Radiosulfur Labeled Congo Red Dye

Charles T. Knorpp, Mary H. Rennie, Donald R. Korst

Congo red, an organic dye with an affinity for amyloid tissue, has been used to diagnose amyloidosis by photometric determination of plasma clearance. The dose of organic dye used has been known to produce serious side effects and sensitivity in patients. An attempt has been made to appreciably reduce the amount of dye used in the test, by incorporating a radioactive label in the molecule.

Congo red dye containing ^{35}S was prepared by the coupling of tetrazotized benizidine with sodium naphthionate. Naphthionic acid was prepared by the thermal rearrangement of 1-napthionic acid sulfate, the latter material containing the S325 isotope.

The labeled Congo red dye distribution then was studied in normal rats. Plasma clearance tests using 12 mg of labeled dye seemed to parallel liver function, and attempts to block the removal of the Congo red by saturating the reticuloendothelial system with bromsulphalein resulted in increased retention of the Congo red as compared with normal subjects. ■

JANUARY 1975

Clinical Experience with [^{99m}Tc]DMSA: A New Renal Imaging Agent

Hirsch Handmaker, Bradford W. Young, Jerold M. Lowenstein

A variety of radiopharmaceuticals have been proposed to improve the quality of renal images presently being recorded with radiomercurial compounds. Technetium-99m-dimercaptosuccinic acid (DMSA) is an agent that provides superior images of renal parenchyma with virtually no undesirable urinary excretion.

Sixty-five patients were studied using [^{99m}Tc]DMSA and a gamma scintillation camera. In all but three patients, the images obtained were of sufficient quality to satisfy the clinical question asked.

It has been suggested that the use of radionuclide scintigraphy may be valuable in the evaluation of acute and chronic pyelonephritis, and in five patients with this disease cortical defects and scars clearly were seen.

As indicated by the variety of agents evaluated for renal imaging in the past decade, no one compound has been found to be ideal. It seems clear that ^{99m}Tc compounds have decided advantages because of their physical characteristics. Difficulties have arisen as a result of the chemical forms of these compounds with regard to availability, difficulty in preparation, high soft-tissue background, urinary excretion, or poor handling in p atients with altered renal function. Many of these difficulties have been reduced or eliminated with the use of [^{99m}Tc]DMSA. ■

JANUARY 1990

Half-Life

Hirsch Handmaker

"That was a different time, a very different time," Hirsch Handmaker remembers, when prompted to recall the clinical environment from which his paper emerged.

"It was a time when pessimism about medical practice and the survivability of nuyclear medicine did not exist. A time when there was still a great deal of excitement about the tracer principle, about linking well suited isotopes to chemical compounds to permit imaging of organs and functions previously inaccessible."

Working with H. Saul Winchell, Handmaker and other researchers were exploring a wide variety of unique radiopharmaceuticals when they were made aware of the "leap" of T.S. Lin. Lin, who was familiar with the use of DMSA for the treatment of renal complications resulting from the use of antimony in the treatment of a serious schistosomiasis infestation in China, extrapolated that DMSA might be used for imaging the renal cortex when labeled appropriately.

Handmaker and his associates then compiled compelling clinical data for the use of [^{99m}Tc]DMSA. But there were problems, familiar problems.

"While some things change, others stay the same," Handmaker noted. "There was a great deal of enthusiasm and scientific zeal, but there was also the FDA, and they were as cautious and slow-moving as they are today regarding radiopharmaceuticals. Though we had what we believed to be more than enough evidence to convince our clinical colleagues of its safety and efficacy, the FDA was very slow to act to approve the agent."

Fifteen years later, Handmaker has the satisfaction of knowing that [^{99m}Tc]DMSA remains an important radiopharmaceutical for the evaluation of renal cortical function and integrity. ■