Evaluation of the Microwave Heating Technique as an Alternative Method for Preparing Technetium-99m-Sulfur Colloid

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Objective: The purpose of this study was to retrospectively evaluate microwave heating preparations of ^{99m}Tc-sulfur colloid during a 4-wk period.

Methods: The ^{99m}Tc-SC kit preparation was performed according to the package insert with microwave heating modifications.

Results: During the first 2 wk, patient studies (n = 14) showed excellent images, however during the last 2 wk patient studies (n = 18) demonstrated lung uptake with clumping (n = 16). The average radiochemical purity of the microwaved ^{99m}Tc-SC preparations for the first and second 2-wk periods were 98.9% ± 0.9% (n = 9) and 99.3% ± 0.4% (n = 9), respectively. Eight of 18 microwaved ^{99m}Tc-SC kits were used in 16 patient studies which showed lung uptake. The ^{99m}Tc radioactivity of the prepared ^{99m}Tc-SC ranged from 51–241 mCi for the first 2 wk, and 62–242 mCi during the last 2 wk. There is no particular day of the week associated with the use of ^{99m}Tc eluates. The preparation and injection of the microwaved ^{99m}Tc-SC were all randomly performed by different nuclear medicine technologists. When comparing lot numbers of the cold kits, two kits came from one lot number, whereas 16 kits from another lot number.

Conclusions: Our findings showed the microwave heating method may not be an optimal method to prepare ^{99m}Tc-SC, although the reason for the lung uptake is not clear.

Key Words: technetium-99m-sulfur colloid; liver-spleen imaging; microwave heating; altered biodistribution

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Technetium-99m-sulfur colloid (^{99m}Tc-SC) is a standard radiopharmaceutical used for liver-spleen scintigraphy. The standard radiolabeling method for ^{99m}Tc-SC requires a 5-min heating interval in a boiling water bath (*1*), plus 5–15 min to preheat the water bath. The microwave heating technique is potentially simpler and faster (e.g., 20 sec) (*2*). In our laboratory, microwave preparations of ^{99m}Tc-SC were evaluated during a 4-wk period. The first 2 wk, patient studies (n = 14) showed excellent images, while during the last 2 wk, patient studies (n = 18) showed lung uptake with clumping (n = 16). We retrospectively looked into the cause of lung uptake of ^{99m}Tc-SC.

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MATERIALS AND METHODS

Preclinical Evaluation of the Microwaved ^{99m}Tc-SC Preparations

Sulfur Colloid Cold Kit Formulation. The ^{99m}Tc-SC kit (Medi-Physics, Inc., Arlington Heights, IL) was used for the preparation of ^{99m}Tc-SC in this study. The kit consists of one reaction vial containing 0.5 ml of 1.0 N HCl and two reagent syringes. Syringe A contains 1.1 ml aqueous solution of 1.9 mg sodium thiosulfate anhydrous and syringe B contains 5.3 mg gelatin in 2.1 ml buffer solution of 177 mg sodium acetate anhydrous.

Microwave Heating Method. The preparation was performed according to the package insert (*1*) with the exception of the microwave heating modification (*2*). The ^{99m}Tc used to prepare microwaved ^{99m}Tc-SC was tested and contained less than 10 μg Al/ml ^{99m}Tc (*3*). After the thiosulfate syringe was injected into the reaction vial containing 15.3–422 mCi ^{99m}Tc, a 20-ml syringe was used to withdraw air from the vial until a vacuum was created. The reaction vial then was placed in a shielded microwave oven with a styrofoam block placed over the aluminum vial seal to prevent sparking during the microwave heating process (see Appendix A). The oven had a power output of 650 W at a frequency of 2,450 mHz. The ^{99m}Tc-SC was microwaved for 15 sec at 452 watts, after which the liquid in the reaction vial was visually noted to be boiling (i.e., 100°C). The rest of the procedure continued as in the package insert (*1*).

Radiochemical Purity Analysis. Radiochemical purity (RCP) of microwaved ^{99m}Tc-SC was determined with thin-layer chromatography using Whatman 31 ET paper (Whatman Lab Sales, Hillsboro, OR) as the stationary phase and acetone as the mobile phase. The relative front (R_f) values for

^{99m}Tc-SC and free ^{99m}Tc are 0.0 and 1.0, respectively. According to the United States Pharmacopeia (USP) 23/National Formulary (NF) 18 (*4*), not less than 92% of the total radioactivity should be found as ^{99m}Tc-SC at the point of application (i.e., R_f = 0.0).

Particle Size Evaluation. Particle size distribution of the microwaved ^{99m}Tc-SC preparation was determined by electron microscopy and digital image analysis.

The particle size of microwaved ^{99m}Tc-SC was determined by using negatives from a transmission electron microscope. A microwaved ^{99m}Tc-SC sample was absorbed onto plastic-coated copper grids (200–300 mesh) and allowed to air dry. The grid surface was then washed with distilled water to remove any water-soluble salts, such as sodium pertechnetate, sodium chloride or phosphate buffer. Electron microscope negatives of the particles were recorded at a magnification of 20,000×. An appropriate magnification calibration specimen was also recorded at 20,000× to be used for the subsequent digital image analysis.

Images were digitized and particles measured on a VIDAS image analysis system (Kontron Elektronik, Munich, Germany) using Kontron Elektronik software. Negatives from the electron microscope were placed on a lightbox and input to the system with a Hamamatsu new vicon video camera (Hamamatsu Photonics, Hamamatsu City, Japan) equipped with a Zeiss 100 mm macro lens (Carl Zeiss, Inc., Oberkochen, Germany).

Clinical Evaluation of the Microwaved ^{99m}Tc-SC Preparation

Approvals from the Institution. Approvals from our Institutional Review Board and Radiation Control Committee were obtained before initiating the patient study to evaluate the microwaved preparation of ^{99m}Tc-SC for standard liver-spleen scanning.

Patient Inclusion Criteria. All patients referred to nuclear medicine for clinically indicated liver-spleen imaging were initially asked verbally if they would allow us to use ^{99m}Tc-SC prepared with the microwave heating method. If patients did not agree to this alternate preparation method, a liver-spleen imaging procedure was performed with ^{99m}Tc-SC prepared by the standard boiling water bath method (*1*).

Microwaved ^{99m}Tc-SC Preparations for the Patient Studies. All of the procedures for the preparation of microwaved ^{99m}Tc-SC were the same as the radiolabeling procedure for the preclinical study, except the added ^{99m}Tc activity was kept below 250 mCi (i.e., 51–242 mCi).

RCP Testing. The RCP testing method was identical to the one used in the preclinical evaluation of the microwaved heating method for ^{99m}Tc-SC preparation. Each microwaved ^{99m}Tc-SC preparation for patient studies was confirmed to exceed the RCP acceptance level of 92% (*4*) before its clinical use.

Imaging Procedure. The procedure for liver imaging began with an intravenous injection of 6 mCi of microwaved ^{99m}Tc-SC. A large field of view planar gamma camera with a low-energy high-resolution collimator was used. The imaging procedure began 15 min after the administration of microwaved ^{99m}Tc-SC. The imaging views were anterior, anterior with marker, right anterior oblique, right lateral, posterior and left lateral. All images were acquired for one million total counts per image except for the left lateral view which was acquired for the same time as the right lateral view.

TABLE 1
RCP Values of Microwaved ^{99m}Tc-SC*

Post-Preparation Time	RCP (%)
5 min	98.5 ± 1.1
15 min	98.8 ± 0.9
30 min	98.7 ± 1.1
1 hr	98.7 ± 1.0
2 hr	98.8 ± 0.7
3 hr	98.8 ± 0.8
4 hr	98.8 ± 0.9
5 hr	98.9 ± 1.0
6 hr	98.8 ± 1.0

*The radioactivity of the microwaved ^{99m}Tc-SC preparations ranged from 15.3–422 mCi; n = 7.

RESULTS

The RCP values of the microwaved ^{99m}Tc-SC for the preclinical evaluation are listed in Table 1.

Electron microscopy and digital imaging analysis of the microwaved ^{99m}Tc-SC samples (Fig. 1) showed that the average particle size for the microwaved ^{99m}Tc-SC was 0.21 ± 0.06 μm (n = 313).

During the first 2 wk of our study, the patients' images (n = 14) were excellent but during the last 2 wk, the patients' images (n = 18) showed lung uptake with clumping (n = 16) (Fig. 2).

Eight of 18 microwaved ^{99m}Tc-SC kits were used in 16 patient studies which showed lung uptake. When comparing lot numbers of the ^{99m}Tc-SC kits, two kits came from one lot number (week 1) whereas 16 kits came from another lot number (weeks 1–4).

Different ages of ^{99m}Tc eluate (i.e., 10–326 min) from a 3-Ci wet-column generator were used to prepare ^{99m}Tc-SC in our study (Table 2). Technetium-99m eluate from a daily milked generator (i.e., 24-hr ingrowth time) or from a long-ingrowth time generator (i.e., >72 hr) was also randomly used in this study (Table 2). All ^{99m}Tc eluates were checked and contained <10 μg Al per ml ^{99m}Tc prior to the preparation of ^{99m}Tc-SC. The ^{99m}Tc radioactivity for the preparation of ^{99m}Tc-SC ranged from 51–241 mCi for the first 2 wk, and 62–242 mCi during the last 2 wk (Table 2). The average ^{99m}Tc activity of the prepared ^{99m}Tc-SC kit for the first and second 2 wk were 180.3 ± 69.7 mCi and 203.8 ± 57.1 mCi, respectively. The ^{99m}Tc volume ranged from 0.41–2.97 ml during the first 2 wk, and 0.61–2.44 ml during the last 2 wk (Table 2).

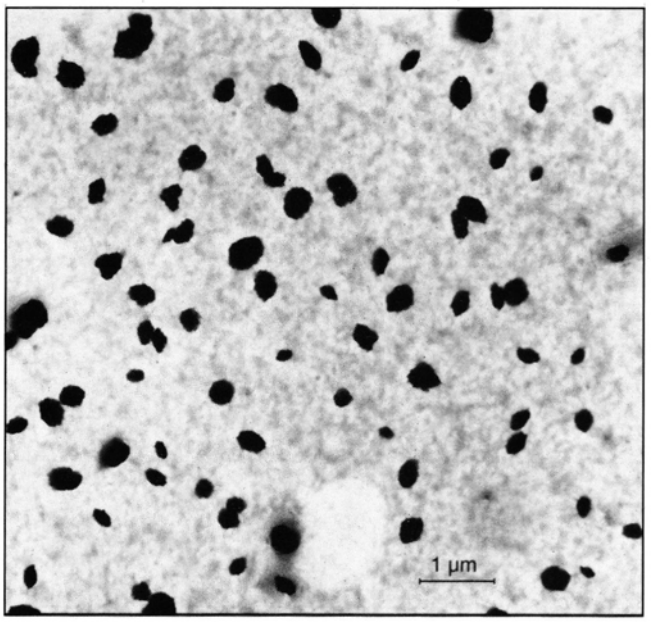

FIGURE 1. Electromicrograph of the microwaved ^{99m}Tc-SC preparation.

The volume of 0.9% NaCl used to dilute ^{99m}Tc source ranged from 0.33–3.66 ml during the first 2 wk and 1.86–3.69 ml during the last 2 wk (Table 2).

The average RCP values of the microwaved ^{99m}Tc-SC preparation for the first and second 2 wk periods were 98.9 ± 0.9% (n = 9) and 99.3 ± 0.4% (n = 9), respectively.

The ^{99m}Tc-SC preparations were randomly performed by different nuclearmedicine technologists (n = 6) (Table 3), and the patients' injections were randomly performed by different nuclear medicine technologists (n = 7) (Table 4).

The patient histories of all 16 studies with lung uptake were reviewed and no information indicated that the patients were taking antacid products containing aluminum.

DISCUSSION

Our preclinical evaluation of the microwaved ^{99m}Tc-SC preparations with the use of RCP testing (Table 1) and electron microscopy/digital image analysis techniques (Fig. 1) indicated that ^{99m}Tc-SC prepared in a microwave oven should be acceptable. The RCP values exceed the USP23/NF18 RCP acceptance level (i.e., ≥92%) (*4*) and the size of the microwaved ^{99m}Tc-SC was within the normal SC particle size range (*5*). However, when the microwaved ^{99m}Tc-SC preparations were used in clinical patient studies during a 4-week evaluation, we noted lung uptake of microwaved ^{99m}Tc-SC in the last 2 wk.

When comparing the 4-wk data, we looked into sources of Al^{3+} ion (*6–8*), including ^{99m}Tc eluate and antacids containing aluminum, and excessive temperature and boiling time (*9,10*). In addition, we evaluated the lot numbers of the cold kits, in-growth time and age of the generator eluate, the day and time of milking the wet-column

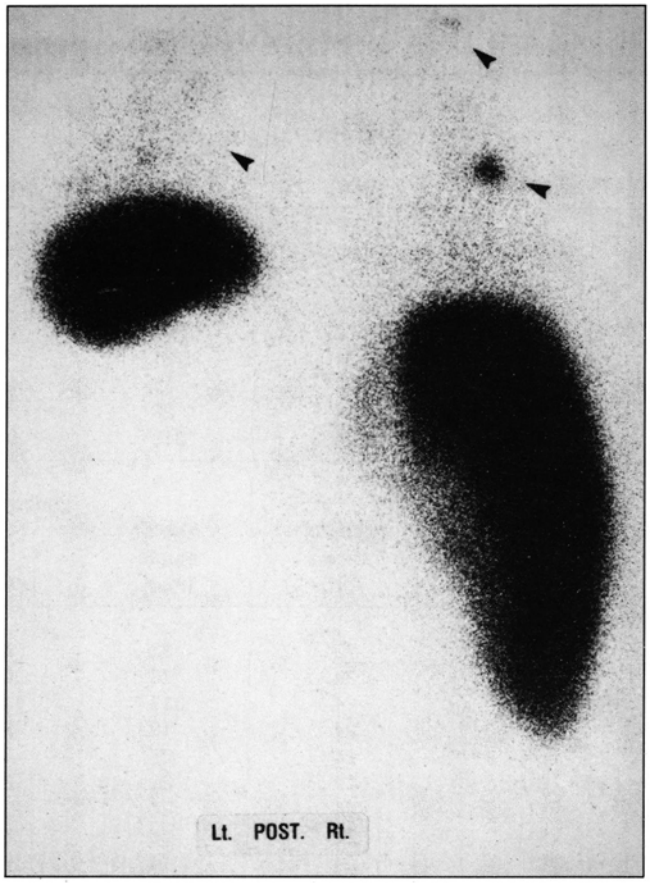

FIGURE 2. Liver-spleen scan with microwaved ^{99m}Tc-SC demonstrating uptake of ^{99m}Tc-SC in both lungs.

generator, added ^{99m}Tc radioactivity and ^{99m}Tc volume, 0.9% NaCl volume used to dilute the ^{99m}Tc activity, the nuclear medicine technologists who prepared the ^{99m}Tc-SC kits, and the nuclear medicine technologists who injected the patients.

The majority of patients with increased lung uptake had received injections by Technologist 1 (Table 4). However, this nuclear medicine technologist is experienced and routinely does patient injections with no problems. During the 4-week period, Technologist 1 injected two patients for good images during the first 2 wk, which led us to believe the problem was not caused by the injection technique but perhaps by the particle size.

According to the USP 23/NF 18 (*4*) and the package insert of ^{99m}Tc-SC (*1*), the particle size of ^{99m}Tc-SC does not need to be determined. The results we obtained from our preclinical study suggest that the particle size of the ^{99m}Tc-SC prepared with the microwaved heating method should be within acceptable size range (*5*). Therefore, the particle size was not examined during the 4-week time period. One possibility is that during the second 2 wk, the particle size increased, possibly due to excessive temperature in the microwave oven. This did not occur during the first 2 wk when the same procedure and settings on the microwave oven were used.

TABLE 2
^{99m}Tc Source for the Preparation of Microwaved ^{99m}Tc-SC

Preparation	Ingrowth time (hr)	Age of eluate (min)	First 2-wk Period: Time of preparation	^{99m}Tc volume (ml)	^{99m}Tc activity (mCi)	0.9% NaCl dilution (ml)
1	72	30	6:30 am	0.64	201.0	3.66
2	24	25	6:25 am	0.83	189.0	3.47
3	24	24	6:24 am	2.38	239.0	0.92
4	72	29	6:29 am	0.70	218.0	3.60
5	72	326	11:26 am	0.41	72.0	2.89
6	24	21	6:42 am	1.10	241.0	3.20
7	24	41	6:41 am	1.65	208.0	2.65
8	24	29	6:29 am	1.55	204.0	2.75
9	24	310	11:30 am	2.97	51.0	0.33

Preparation	Ingrowth time (hr)	Age of eluate (min)	Second 2-wk Period: Time of preparation	^{99m}Tc volume (ml)	^{99m}Tc activity (mCi)	0.9% NaCl dilution (ml)
1*	72	38	6:38 am	0.80	240.0	3.50
2*	24	28	6:28 am	1.42	242.0	2.88
3	24	313	11:13 am	0.63	62.0	3.67
4*	24	10	6:21 am	1.70	231.0	2.60
5*	24	27	6:27 am	2.44	228.0	1.86
6*	72	29	6:14 am	0.63	191.0	3.67
7*	24	24	6:24 am	1.04	229.0	3.26
8*	72	26	6:26 am	0.61	182.0	3.69
9*	24	14	6:29 am	1.05	229.0	3.25

*Lung uptake.

CONCLUSION

Our findings showed the microwave heating technique method may not be an optimal method to prepare ^{99m}Tc-SC, although the reason for the lung uptake of the microwaved ^{99m}Tc-SC is not clear.

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TABLE 3
Number of Microwaved ^{99m}Tc-SC Kits Prepared by Nuclear Medicine Technologist

Nuclear medicine technologist	No lung uptake: First 2-wk period	No lung uptake: Second 2-wk period	Lung uptake: First 2-wk period	Lung uptake: Second 2-wk period
1	3	0	0	4
2	1	0	0	0
3	1	0	0	0
4	3	0	0	3
5	1	1	0	0
6	0	0	0	1

TABLE 4
Number of Patients Injected by Nuclear Medicine Technologist

Nuclear medicine technologist	No lung uptake: First 2-wk period	No lung uptake: Second 2-wk period	Lung uptake: First 2-wk period	Lung uptake: Second 2-wk period
1	2	1	0	13
2	3	0	0	0
3	1	1	0	1
4	4	0	0	0
5	3	0	0	0
6	1	0	0	0
7	0	0	0	2

APPENDIX A

Technical specifications of Kenmore microwave oven, Model No. 565.89627 (Sears, Roebuck and Co., Chicago, IL):

Power input: 120 V,12 A
Power output: 650 W
Microwave frequency: 2,450 MHz
Outer dimensions: 10 15/16″ H × 20 11/16″ W × 15 13/16″ D
Cavity dimensions: 6 5/8″ H × 14″ W × 15″ D
Cavity volume: 0.8 ft^3
Weight: 36.5 lb

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