MINI-PAPER CHROMATOGRAPHY SYSTEMS FOR TECHNETIUM-99M SESTAMIBI AND TECHNETIUM-99M MERTIATIDE

To the Editor: In a recent article, Zimmer and Spies (*1*) discussed some of the available quality control methods for the newer radiopharmaceuticals, including technetium-99m sestamibi (^{99m}Tc-sestamibi) and technetium-99m mertiatide (^{99m}Tc-MAG$_3$). The miniaturized paper chromatography system that was investigated by Zimmer and Spies for determining the radiochemical purity (RCP) of ^{99m}Tc-sestamibi involves the use of a single strip of Whatman 31ET paper (Whatman Chromatography Products, Clifton, NJ) and ethyl acetate (*1*). According to this report (*1*), ^{99m}Tc-sestamibi migrates with the developing solvent to the solvent front (S_f) while the other ^{99m}Tc impurities remain at the origin. However, due to the streaking problem of this chromatographic quality control system, the authors suggest that the cut line for the paper strip be located at a relative front (R_f) value of 0.2–0.25 (*1*).

We have developed a mini-paper chromatography (MPC) system (1 cm × 8.5 cm; Solvent Saturation Pads, Gelman Sciences, Ann Arbor, MI) for analyzing RCP values of ^{99m}Tc-sestamibi and have published this method in *The Journal of Nuclear Medicine* (*2*). As shown in Table 1, this MPC system also allows ^{99m}Tc-sestamibi to migrate with the mobile phase to the S_f. Therefore, the %RCP of a ^{99m}Tc-sestamibi preparation can be determined with a single-strip chromatographic paper. The average time for developing the chromatographic paper of this MPC system is ~2 min (*2*). Although a considerable streaking is also noted with this paper chromatography system (*2*), the trailing pattern of the ^{99m}Tc-sestamibi does not fall below the R_f value of 0.5.

Our previous study indicates that the RCP results from our MPC system and the recommended Al_2O_3-coated thin-layer chromatography system (TLC) (*3*) are in good agreement for measuring the ^{99m}Tc-sestamibi preparations with different RCP values (i.e., 71%–99%) (*2*). One important feature of our MPC method is that this chromatographic system underestimates slightly the RCPs of ^{99m}Tc-sestamibi preparations in the intermediate range (i.e., 83%–92%) (*2*). This RCP range is considered critical in the evaluation of this new paper chromatography system since the ^{99m}Tc-sestamibi preparations have been tested to be safe and effective in human clinical trials if the RCP of the ^{99m}Tc-sestamibi product is ≥90% (*3*). Based upon this minimum acceptance level of RCP value (i.e., 90%), our MPC method may occasionally reject a ^{99m}Tc-sestamibi kit that would be acceptable by the suggested TLC method. However, it would be very unlikely for our MPC system to accept a ^{99m}Tc-sestamibi kit preparation that is rejected by the Al_2O_3-coated TLC method.

Zimmer and Spies indicate in their paper (*1*) that a number of attempts have been made to develop a rapid TLC or MPC procedure to evaluate the RCP of ^{99m}Tc-MAG$_3$, but the efforts have not been very successful. DuCret et al. (*4*) and Taylor et al. (*5*) have used some paper chromatography methods to determine the RCP values of ^{99m}Tc-MAG$_3$ products. However, we have found that their methods are time consuming (it takes 15–20 min to develop the paper strips).

Nonetheless, a dual-strip MPC system (1 cm × 8.5 cm; Solvent Saturation Pads, Gelman Sciences, Ann Arbor, MI) for determining the RCP of ^{99m}Tc-MAG$_3$ has been developed in our laboratory, and this rapid quality control method (2–3 min) was published in the September 1991 issue of the *Journal of Nuclear Medicine Technology* (*6*). The detailed descriptions of this MPC system and R_f values for different ^{99m}Tc components in a ^{99m}Tc-MAG$_3$ preparation are indicated in Table 1. As stated in our paper (*6*), the RCP results measured by our MPC method and the recommended Sep-Pak® C18 cartridge (Millipore Corp., Milford, MA) method (*7*) are closely correlated in a wide range of RCP values (i.e., 67%–99%) (*6*).

Joseph C. Hung
Mayo Clinic
Rochester, Minnesota

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2. Hung JC, Wilson ME, Brown ML, Gibbons RJ. Rapid preparation and quality control method for technetium-99m-2-methoxy isobutyl isonitrile (technetium-99m-sestamibi). *J Nucl Med* 1991;32:2162–2168.

TABLE 1. MPC Systems for ^{99m}Tc-Sestamibi and ^{99m}Tc-MAG$_3$

Compound	Solvent	R_f Bound ^{99m}Tc	R_f Free ^{99m}Tc	R_f H-R* ^{99m}Tc
^{99m}Tc-sestamibi	$CHCl_3$/THF† (1:1)	0.5–1.0	0	0
^{99m}Tc-MAG$_3$	$CHCl_3$/CH_3COCH_3/THF† (1:1:2)	0	0.5–1.0	0
	0.9% NaCl	0.5–1.0	0.5–1.0	0

This mini-paper chromatography system uses Solvent Saturation Pads (1 cm × 8.5 cm) as the stationary phase (support media).

* H-R ^{99m}Tc = Hydrolyzed reduced ^{99m}Tc; includes the insoluble ^{99m}Tc tin colloid and ^{99m}Tc-dioxide.

† $CHCl_3$ = chloroform; THF = tetrahydrofuran; CH_3COCH_3 = acetone.

3. Cardiolite® package insert. Du Pont Merck Pharmaceutical Co., Billerica, MA. November 1991.
4. DuCret RP, Boudreau RJ, Gonzalez R, Carpenter R, Tennison J, Kuni KC. Clinical efficacy of ^{99m}technetium mercaptoacetylglycine kit formulation in routine renal scintigraphy. *J Urol* 1989;142:19–22.
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6. Hung JC, Wilson ME, Brown ML. Rapid preparation and quality control of technetium-99m MAG_3™. *J Nucl Med Technol* 1991;19:176–179.
7. TechneScan MAG_3™ Technical product data. Mallinckrodt Medical, Inc., St. Louis, MO. June 1990.

CAUTION URGED IN USING MICROWAVED TECHNETIUM-99M SESTAMIBI

To the Editor: We read with great interest the letter from Wilson, Hung, and Gibbons of the Mayo Clinic (*J Nucl Med Technol* 1992;20:180) regarding a "Simple Procedure for Microwaved Technetium-99m Sestamibi Temperature Reduction." In their letter, the authors suggest that if a unit dose of Cardiolite (Du Pont Pharma, Billerica, MA) is withdrawn from the vial in a shielded 3-ml syringe just after heating, the temperature of the dose will be acceptable for intravenous injection in about 3 minutes.

While we do not dispute these findings, it has recently come to our attention that Cardiolite image quality may become moderately compromised by stomach uptake under the following combination of conditions: dilution of Cardiolite in the vial immediately after heating, followed by withdrawal of the patient dose from the vial while the contents are still hot.

We have yet to determine which of the above parameters is the culprit, or whether both are in fact necessary to produce the appearance of the stomach in the resulting images. We are presently investigating this phenomenon to determine the specific cause.

Although the benefits of more rapid preparation and quality control of Cardiolite are tempting, particularly for patients in the acute setting, we urge caution in adopting procedures that differ from the description in the package insert.

David Pendleton
Technical Services Manager
Du Pont Pharma
North Billerica, Massachusetts

Tim Threadgill
Sr. Program Manager
Clinical Services
Syncor International Corp.
Chatsworth, California