Comparison of Two Systems for the Quantification of Technetium-99m Radiochromatography Procedures

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The use of the dose calibrator and a radiochromatogram scanner were evaluated for the quantification of radiochromatography procedures performed on ^{99m}Tc-radiopharmaceuticals. Reproducibility of measurements was significantly better using the dose calibrator technique. This factor, combined with reduced time and cost considerations, warrants the routine use of the dose calibrator for the quantification of radiochromatography procedures.

The radiochemical purity of a radiopharmaceutical is defined as the fraction of the total radioactivity which is in the desired chemical form. Good clinical nuclear medicine practice necessitates that the radiochemical purity of ^{99m}Tc-radiopharmaceuticals be assured prior to their injection. Subsequently, image interpretation problems associated with alterations in the expected biodistribution of the agent or decreased target-to-background radioactivity ratios, increased costs, and patient radiation exposures incurred with requirements to repeat the examination are avoided.

The most common radiochemical impurities found in ^{99m}Tc-radiopharmaceuticals are free (unbound) [^{99m}Tc]pertechnetate and hydrolyzed-reduced ^{99m}Tc-colloids (*1*). Following intravenous injection, [^{99m}Tc]pertechnetate distributes throughout the vasculature and interstitial fluids and concentrates in the stomach, intestinal tract, thyroid, salivary glands, kidneys, and bladder. Hence, the presence of [^{99m}Tc]pertechnetate as a radiochemical impurity will result in increased background activity corresponding to these organs. Colloidal particles, administered intravenously, are phagocytized by cells of the reticuloendothelial system which are primarily located in the liver and spleen. The presence of ^{99m}Tc-colloid impurities will therefore result in an increase in liver and spleen background activity.

The radiochemical purity of ^{99m}Tc-radiopharmaceuticals is typically analyzed by paper or thin-layer chromatography techniques with quantification of the results performed with radiochromatogram scanners, well-scintillation counters, radionuclide dose calibrators, or scintillation camera systems. In this regard, numerous articles have described and evaluated the various solid supports (i.e., paper, thin-layer, instant thin-layer chromatography strips), solvents, and methodologies used for the chromatography of ^{99m}Tc-radiopharmaceuticals (*1–5*), but few have compared the methods used for quantification (*1*).

This article describes our evaluation of the use of a commercially available radiochromatogram scanner in comparison to a radionuclide dose calibrator for the quantitation of chromatographic quality assurance tests performed on routinely utilized ^{99m}Tc-radiopharmaceuticals. Factors analyzed include reproducibility of the quantification system, time involvement, and associated costs.

MATERIALS AND METHODS

The radiochromatography strips,* obtained from the radiochemical purity analysis of 100 commercially available ^{99m}Tc-radiopharmaceutical kits, were quantitated using both a radiochromatogram scanner† and radionuclide dose calibrator‡.

Chromatography Technique

The radiochemical purity of the ^{99m}Tc-radiopharmaceuticals was analyzed using instant thin-layer chromatography (ITLC)§. Table 1 lists the respective adsorbents and solvents utilized for the determination of [^{99m}Tc]pertechnetate and ^{99m}Tc-hydrolyzed-reduced colloid (if applicable) in each of the ^{99m}Tc-radiopharmaceuticals evaluated. Using a syringe (25-gauge needle), a small drop of the ^{99m}Tc-radiopharmaceutical to be tested was placed at the designated "origin" of the ITLC strip. Typically, this drop had an activity of 10–150 mCi depending on the concentration of the radiopharmaceutical kit. The strip was placed immediately into a glass vial containing the appropriate solvent. Care was taken to avoid immersion of the origin in the solvent. Following its development (migration of solvent), the chromatography strip was removed from the solvent vial with forceps and covered with nonporous cellophane tape to avoid potential contamination problems.

Radiochromatogram Scanner

The taped chromatography strip was correctly positioned on the tray of the radiochromatogram scanner and the strip was scanned to determine the percent of respective radiochemical impurity present (free pertechnetate or hydrolyzed-reduced). The total labeling efficiency of the radiopharmaceutical was determined as follows:

$$100\% - [\%\ [^{99m}\text{Tc}]\text{pertechnetate} + \%\ ^{99m}\text{Tc-HR-colloid}]$$

To evaluate reproducibility, strips were run twice on the radio-

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TABLE 1. Chromatography Systems

^{99m}Tc-Radiopharmaceutical	ITLC Adsorbent	Solvent	Rf ^{99m}Tc-Radiopharmaceutical	Rf ^{99m}Tc Free TcO_4^-	Rf ^{99m}Tc-colloid
^{99m}Tc-sulfur colloid	Silica gel	Acetone	0.0	1.0	—
[^{99m}Tc]pertechnetate	Silica gel	Acetone	1.0	—	0.0
[^{99m}Tc]medronate (MDP)	Silica gel	Acetone	0.0	1.0	—
	Silica gel	0.9% sodium chloride	1.0	—	0.0
^{99m}Tc-pentetate (DTPA)	Silica gel	Acetone	0.0	1.0	—
	Silica gel	0.9% sodium chloride	1.0	—	0.0
^{99m}Tc-disofenin (PIPIDA)	Silica acetate	20% sodium chloride	0.0	1.0	—
	Silica gel	Distilled water	1.0	—	0.0
^{99m}Tc-macroaggregated albumin (MAA)	Silica gel	Acetone	0.0	1.0	—
^{99m}Tc-gluceptate	Silica gel	Acetone	0.0	1.0	—
	Silica gel	0.9% sodium chloride	1.0	—	0.0
^{99m}Tc-pyrophosphate (PYP)	Silica gel	Acetone	0.0	1.0	—
	Silica gel	0.9% sodium chloride	1.0	—	0.0

chromatography scanner. The average length of time required to quantitate two chromatography strips using the radiochromatogram scanner was noted.

Radionuclide Dose Calibrator

Following radiochromatogram scanner quantitation, the chromatography strip was cut midway between the origin and solvent front. The section of the strip corresponding to the expected activity of the ^{99m}Tc-radiopharmaceutical was placed in the dose calibrator (^{99m}Tc setting) and the activity was quantitated. The remaining section of the strip, corresponding to the expected activity of the radiochemical impurity, was added to the dose calibrator and the total activity on the strip was quantitated. Care was taken to ensure reproducible geometry in the positioning of the strips. The percent of respective impurity present was determined as follows:

$$\% \text{ impurity} = \left[1 - \frac{\text{activity } ^{99m}\text{Tc-radiopharmaceutical}}{\text{activity total strip}}\right] \times 100$$

The total labeling efficiency of the radiopharmaceutical was determined as described above. Reproducibility of the dose calibrator technique was evaluated by performing the described process twice for each chromatography strip. The average length of time required to quantitate two chromatography strips using this procedure was noted.

Data Analysis

The two values of total labeling efficiency obtained using the radiochromatogram scanner and the two values obtained using the dose calibrator were tabulated for each ^{99m}Tc-radiopharmaceutical tested. To evaluate relative reproducibility, the differences between the two measurements obtained with the chromatogram scanner were compared to the differences between the two measurements obtained with the dose calibrator using a "paired t-test." In this regard, the null hypothesis assumed that the difference in radiochromatograph scanner measurements minus the difference in dose calibrator measurements was equal to zero.

RESULTS

Time Involvement

Following development and protective taping, 7 min were required to analyze two chromatography strips (i.e., for [^{99m}Tc]pertechnetate and ^{99m}Tc-HR-colloid impurities) and to determine final labeling efficiency using the radiochromatogram scanner. Approximately 1 min was required to assay the four sections of these same two chromatography strips and to determine final labeling efficiency using the dose calibrator.

Reproducibility

The radiochromatogram scanner produced significantly greater variances in two simultaneous measurements of total labeling efficiency on the same ^{99m}Tc-radiopharmaceutical (using the same chromatography strips) than did the dose calibrator. In other words, the previously described null hypothesis was rejected at the 0.01 significance level. In this regard, the greatest difference between two measurements observed with the radiochromatogram scanner was 10.3%, and with the dose calibrator, 3.4%. The radiochromatogram scanner produced measurement differences in excess of 5% in 16 of the ^{99m}Tc-radiopharmaceuticals tested. The average difference in measurements with the radiochromatogram scanner was 2.58% compared to 0.58% for the dose calibrator. In addition, the radiochromatogram scanner produced consistently (83%) lower mean (two measurements) labeling efficiencies than those observed with the dose calibrator.

DISCUSSION

The dose calibrator procedure described represents a less time consuming and more reproducible alternative to the radio-

chromatogram scanner for the quantification of chromatography procedures used for evaluating the radiochemical purity of ^{99m}Tc-radiopharmaceuticals. In addition, although the cost of a dose calibrator is typically greater than that of a commercially available radiochromatogram scanner, all nuclear medicine facilities involved in the administration of ^{99m}Tc-radiopharmaceuticals must have dose calibrators on hand in order to fulfill their Nuclear Regulatory Commission (NRC) dose assay requirements. Hence, the dose calibrator procedure is less costly since it does not require the purchase and maintenance of additional equipment.

The increased variability of simultaneous measurements and the lower mean labeling efficiencies observed with the radiochromatogram scanner may be associated with the relatively prolonged deadtime characteristics inherent to the Geiger-Mueller (G-M) detector utilized in this device. In this regard, the deadtime for a G-M tube is typically 50–200 μsec (*6*). This deadtime results in the loss of true count rate when assaying high activities such as those encountered in the radiochemical purity evaluation of ^{99m}Tc-radiopharmaceuticals. Although this deadtime problem is a well-established consideration regarding the use of G-M tubes, the instruction manual for the radiochromatogram scanner utilized does not specify maximum (or minimum) counting rate capability.

On a similar note, the instruction manual for the radiochromatogram scanner does not outline or propose quality control procedures to ensure correct operation of the instrumentation. In contradistinction, the correct operation of clinically-utilized dose calibrators is evaluated (i.e., constancy of operation, linearity testing, etc.) on a routine basis as required by NRC guidelines and licensing conditions.

It has been stated that a limitation to the use of a dose calibrator for the quantitation of radiochromatography strips is its inability to accurately assay the low activities typically associated with the level of [^{99m}Tc]pertechnetate or ^{99m}Tc-colloid impurities (*1*). This problem can be addressed, to a certain degree, by using the described procedure wherein the level of impurity is determined from assaying the higher activities of the ^{99m}Tc-radiopharmaceutical and the total radiochromatography strip. A dose calibrator problem that cannot be overcome is its inability to differentiate radiochemical impurities (i.e., other than [^{99m}Tc]pertechnetate or ^{99m}Tc-colloids) which may appear at Rf values other than 0 or 1. However, such impurities are not anticipated or frequently encountered with routinely utilized, commercially available ^{99m}Tc-radiopharmaceuticals.

In conclusion, the lack of a radiochromatogram scanner should not preclude the performance of routine quality assurance tests to evaluate the radiochemical purity of ^{99m}Tc-radiopharmaceuticals. The quantitation of these radiochromatography procedures can be conveniently, effectively, and economically performed using a commonly available dose calibrator.

FOOTNOTES

*147 strips, Seprachrom ITLC Chromatography, Gelman Sciences, Ann Arbor, MI.

†Atomaster, Atomic Products Corporation, Center Moriches, NY.

‡Capintec CRC-2N, Capintec Inc., Ramsey, NJ.

§Seprachrom ITLC Chromatography, Gelman Sciences, Ann Arbor, MI.

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