Radiopharmacy

Adaptation of a Multichannel Scaler Device for Radiochromatogram Scanning

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Using an inexpensive device and the multichannel scaling mode (MCS) of a multichannel analyzer (MCA), the determination of radiochemical purity as distinguished by the radiochromatographic technique may be easily and accurately performed.

The availability of the sterile radiopharmaceutical kit has brought tremendous change and expansion to the practice of nuclear medicine. With the Mo-99/Tc-99m generator and the large number of commercially available agents for tagging with Tc-99m, clinicians may now choose from a diverse array of diagnostically specific kits. These kits have definite advantages over the previous on-site method of radiopharmaceutical preparation. In the past, radiopharmaceutical compounding from bulk reagents was generally limited to large medical centers with trained personnel and adequate facilities to perform manufacturing procedures. Under this arragement, it was the responsibility of each nuclear pharmacy or laboratory to verify total quality control of the compounded agent.

Presently, it is the commercial manufacturer's responsibility to establish the quality of each kit ingredient as well as sterility and apyrogenicity in accordance with current Food and Drug Administration guidelines (*1*). Assurance for final radiochemical purity following addition of the radiolabel remains, however, the responsibility of the user who prepares each kit in its final dosage form. Image quality may be significantly compromised by the presence of excessive quantities of radiochemical contaminants due either to improper preparation of these kits or oxidative decomposition following tagging with the radiolabel (*2,3*). Numerous paper and instant thin layer chromatography (ITLC) techniques have been introduced to resolve the presence of radiochemical contaminants accurately (*4–7*). We have adapted a multichannel analyzer (MCA) for use with radiochromatographic analysis techniques to determine radiochemical purity.

Materials and Methods

With minor adaptations, the multichannel scaling mode (MCS) found on most MCA units allows this unit to serve as a radiochromatogram scanner (RCS) as well. The MCS mode allows the instrument to count as a single-channel analyzer with counts, or pulses, recorded into the memory of each channel as a function of time. The time counted in each channel—dwell time—is variable and may be set with an internal timer. A strip transport unit has been designed to move radiochromatography strips past the collimated detector at a constant speed (Fig. 1).

The strip transport component is a 6 in. × 12 in. × ⅜ in. lead base onto which a motor drive unit is mounted (Fig. 2). The motor drive unit consists of a one rpm constant speed motor (Autotrol Corp., Crystal Lake, IL) with a 1-in. diam rubber friction wheel mounted onto the lead base

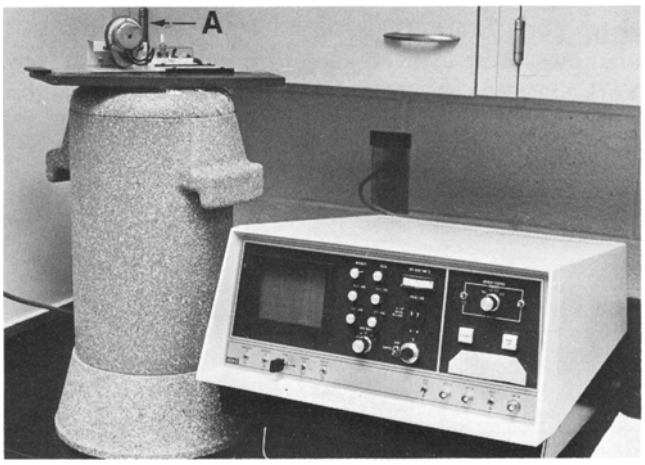

FIG. 1. Photograph of multichannel analyzer with (A) radiochromatogram strip transport unit.

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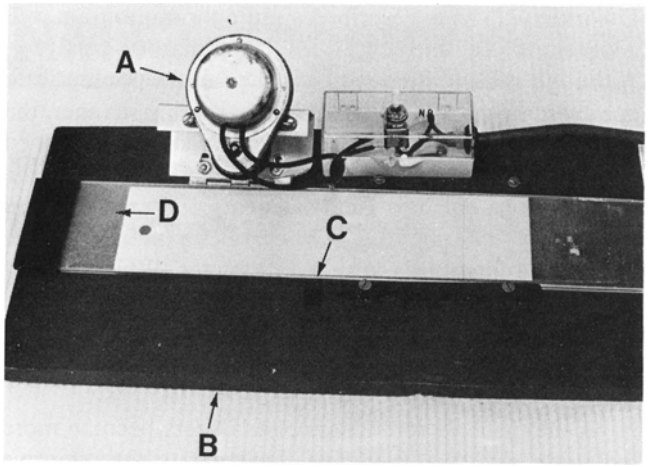

FIG. 2. Close-up photograph of strip transport component with (A) constant-speed motor drive, (B) lead base, (C) collimator slot, and (D) envelope containing radiochromatogram strip.

using a hinged frame. Cut into the base is a 1½ in. × ¼ in. slot which serves as the collimator over which the motor drive advances the radiochromatogram strip. Channel guides are affixed to the base to direct the movement of the strip. To reduce friction of the sliding strip and to prevent possible contamination of the transport unit and the detector, a 12 in. × 2½ in. clear polyvinyl plastic sheet (1 mm thick) was placed in the transport channel. Strips to be analyzed are placed in a 2¼ in. × 12 in. clear styrene plastic envelope (60-mm thick) for additional protection.

The total acquisition time of the MCA in the MCS mode is adjusted to match the time necessary to scan the radiochromatograph strip with this device. The distance versus time relationship of the MCS mode yields counts stored in the memory of the MCA that can be related to distance. The MCA display of counts versus distance is equivalent to the recorder output of a commercial RCS.

The contents of the MCA memory may be printed out as a list of numbers representing counts obtained in each channel during the radiochromatogram strip counting time. By using these figures, it is possible to calculate the radiochemical purity. Alternatively, the optional integrate, intensify and alphanumeric functions found on many smaller MCA units allow the integration of all or any part of the memory and a display of these results on the MCA. For analysis, the integral of counts of any region may be divided by the integral of the entire memory. These regions selected are representative of specific radiochemical components as determined by standard radiochromatographic techniques (*4–7*).

Results

Radiochromatogram scanning with the MCS mode is performed as follows:

1. A window around the photopeak of interest is selected.
2. The MCA is switched to the MCS mode.
3. Dwell time per channel is adjusted so that the total strip length will pass over the collimator during acquisition time (i.e., 0.2-sec dwell time per each of the 1024 channels provides a total scanning time of approximately 205 sec, sufficient time to image a 20-cm strip).
4. The envelope containing the chromatogram strip is now placed into the guide channel of the strip advance unit so that the end of the envelope is under the motor drive with the radiochromatogram strip next to the collimator slot.
5. Acquisition is started and the motor drive is turned on. When the timing cycle is complete, the MCA automatically displays the contents of its memory (i.e., the radioactivity distribution along the chromatrogram strip).
6. A region of interest may be selected along this distribution using the built-in cursor system and the integral of this region easily determined. The percentage represented by this integral as related to the total strip activity may be calculated by dividing the integral of this region by the integral of the entire memory.

Radiochromatogram strips to be analyzed by the MCS mode are prepared by any of several well known chromatographic methods (*4–7*). To illustrate, Tc-99m Sn-DTPA is spotted on a 20 cm × 5 cm ITLC-SC (silica gel) media strip (Gelman Co., Ann Arbor, MI) at a point approximately 3 cm from the edge. The strip is developed in a chamber containing acetone as the solvent. Immediately following development, the strip is allowed to air dry and is then placed into the plastic envelope approximately 8 cm from the lead end. Using acetone as the developing solvent, free unbound pertechnetate migrates with the solvent front to an Rf value of approximately 1.00 (*4*).

Figure 3 shows the grossly impure strip scans of Tc-99m Sn-DTPA preparation as displayed on the MCA unit following MCS scanning. The activity represented in the entire strip or field may be rapidly determined by integration and displayed simultaneously on the MCA with the chromatogram distribution (Fig. 3A). The region representing free unbound pertechnetate may be selected by the movable cursor system with the counts contained in this area also displayed on the MCA in a similar manner (Fig. 3B). The counts in this region may be easily related to the counts of the entire strip and representative percentages may then be calculated (Fig. 3C).

Discussion

Techniques for radiochromatographic evaluation of radiochemical purity are available for the majority of radiopharmaceuticals employed today (*4–7*). Utilizing either paper or ITLC media and specific solvent systems, it is possible to resolve and quantify radiochemical

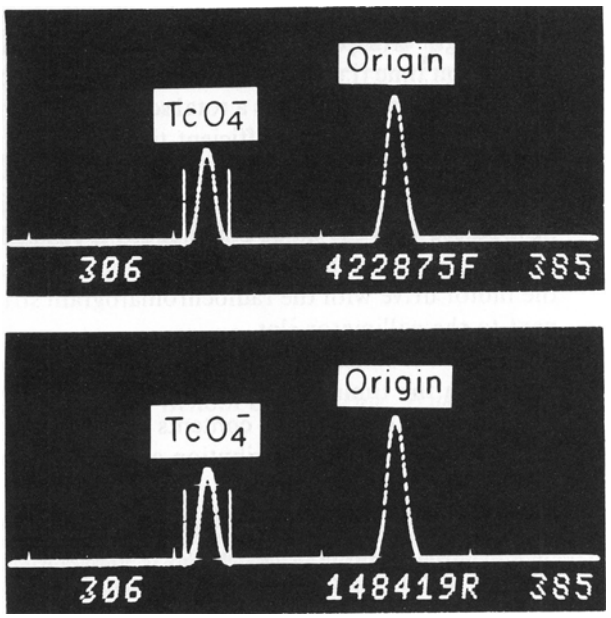

FIG. 3. Multichannel display of Tc-99m Sn-DTPA chromatogram developed in acetone: (A) display showing counts of entire strip or field (F); (B) same display with cursors marking counts of selected region (R) of interest representing free, unbound component (Rf approx. 1.00); (C) to calculate percent radiochemical impurity:

$$\frac{\text{counts in selected region (R)}}{\text{counts in entire strip (F)}} \times 100 = \%\ \text{radiochemial component.}$$

components within a radiopharmaceutical based upon distinguishable migration along the chromatogram. Presently, there are two generally accepted methods to analyze these strips. First, the strip may be cut and each portion counted using standard detection systems (dose calibrator, well counter, etc.). Haney et al. (*8*) described this method for measuring the radiopurity of Tc-99m sulfur colloid. The chromatographic strip is developed with 85% methanol with the strip cut midway between the application point and the solvent front. Activity is determined for each half and the purity of Tc-99m sulfur colloid expressed as the ratio of the net counts of the spotted half of the strip divided by the total net counts of the entire strip. In addition to being time-consuming, the inaccurate cutting of these strips can lead to significant analytical errors.

In the second method, radiochromatogram scanners which scan the entire intact strip and plot radioactivity distribution are used (*9,10*). With the information obtained, proportionate radiochemical purity figures are then calculated. Although scanners of this type portray activity distribution very accurately, the expense of these single purpose instruments generally precludes their purchase by many laboratories and hospitals.

Other systems have been developed for the analysis of radiochromatogram strips (*11,12*). Gutowski and Dworkin (*11*) have described a radiochromatogram well adapter to be used with a single-channel analyzer. Although their system employs the same basic idea as a commercially available radiochromatogram scanner, the radiochromatogram strip either must be advanced manually with counts obtained for each 1-cm unit or the strip must be cut into 1-cm segments and each counted individually. Sunderland (*12*) describes a method using a G–M tube integrated with a rate meter. While both of these methods are definite improvements over the manual cutting and assaying of strip halves, neither offers the simplicty and accuracy of the adapted multichannel system.

As inexpensive multichannel analyzers become more available in nuclear medicine departments, the extensive use of these instruments in nuclear pharmacy quality control is possible. In addition to standard radionuclide quality control, we have demonstrated that the multichannel scaling mode of such instruments can be readily adaptable to *radiochemical* purity determinations. By offering definite advantages over the current methods used to analyze radiochromatograms, the use of the multichannel scaling function extends the practical application of this instrument in nuclear medicine.

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