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Short Communication

A convenient configuration for safe and efficient radio-HPLC of ^{99m}Tc-radiopharmaceuticals*

C. VAN NEROM,†§ G. BORMANS,‡ B. CLEYNHENS,† M. DE ROO† and A. VERBRUGGEN‡

†*Department of Nuclear Medicine, University Hospital Gasthuisberg, B-3000 Leuven, Belgium*
‡*Laboratory of Radiopharmaceutical Chemistry, Institute of Pharmaceutical Sciences, U.Z. Gasthuisberg, B-3000 Leuven, Belgium*

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Introduction

Almost 90% of all nuclear medicine procedures are based on a ^{99m}Tc-labelled compound as tracer agent [1]. Due to the short physical half-life of ^{99m}Tc (6.02 h) these radiopharmaceuticals have to be prepared and analysed in the hospital just before use. Most of the older ^{99m}Tc-radiopharmaceuticals are highly polar compounds for which simple TLC methods are most appropriate for efficient and rapid quality control [2]. However, high-performance liquid chromatography (HPLC) has become an indispensable technique for the development of newer, more lipophilic ^{99m}Tc-compounds and their routine analysis after introduction for clinical use [3].

HPLC of radioactive compounds requires particular precautions and the use of special equipment for the handling of ionizing radiation. Radioactive parts of the system should be adequately shielded to protect the operator against the potentially harmful effect of the radiation. Frequent changing of columns or loops must be avoided as it involves a serious risk of radioactive contamination. However, the analysis of different compounds requires the use of different columns. Finally, the use of radiometric detection method and an appropriate integrating technique is required, especially for ^{99m}Tc-agents which possess a high specific activity and are usually analysed in picogram quantities.

Shielding

Materials with high density and a high atomic number afford the most efficient shielding against gamma radiation. Lead (d = 11.34 g cm^{-3}, Z = 82) is commonly used as the shielding material in the practice of radiopharmacy and nuclear medicine. The half-value thickness of lead for the 140.5 keV gamma rays of ^{99m}Tc is 0.17 mm.

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§To whom correspondence should be addressed.

In radio-HPLC of ^{99m}Tc-radiopharmaceuticals, shielding of all parts from injector to waste container with 3–6 mm of lead is sufficient for the safe handling of up to 3.7 GBq of ^{99m}Tc. It may be necessary to apply such high activities on the column in preparative work, e.g. for the isolation of sufficient activities of products which are formed in relatively small amounts or when preparative HPLC is used to obtain a very pure ^{99m}Tc-radiopharmaceutical.

The injector and column(s) can efficiently be shielded using the housing unit described in this paper. The detector, usually a NaI(T1) crystal with a photomultiplier tube or a Geiger–Müller tube, is adequately shielded against background radiation by surrounding it with a closed lead castle of thickness 1–5 cm. The stainless steel or Teflon tubing with the column eluate enters and leaves the lead castle through 2 mm holes above the detector. Finally the waste disposal container is placed in a 0.6 cm lead cylinder that has been made by folding sheet lead in such a way as to shield the container completely with the exception of the opening.

Shielded Housing Unit for Multiple HPLC-columns

Daily quality control of a wide range of ^{99m}Tc-radiopharmaceuticals by radio-HPLC requires the possible use of different columns with a variety of stationary phases. However, frequent column changing must be avoided since it enhances the risk of damaging the expensive materials and, in particular, involves a serious risk of radioactive contamination. This problem can be overcome by the use of a column-switching valve that permits easy selection of the desired column.

An efficient shielding of the injector and columns has been used with combination of five columns with a six-port column-switching valve in a convenient HPLC-housing unit for safe radio-HPLC of ^{99m}Tc-radiopharmaceuticals, both on the analytical and preparative scales (Fig. 2). It consists of a 60 × 49 × 20 cm metal box with a central panel, holding five HPLC-columns connected to a Valco N6 injector and an Alltech CST6UW column-switching valve. The sixth selection port permits rapid flushing for changing solvents. The columns can be surrounded with a thermostatic water jacket. The walls of the box are shielded with 3 mm of lead. The front wall however is a door of lead glass, equivalent to 6 mm of lead, that allows visual inspection and gives easy access to the columns. The rear wall can also be opened to permit loop changing.

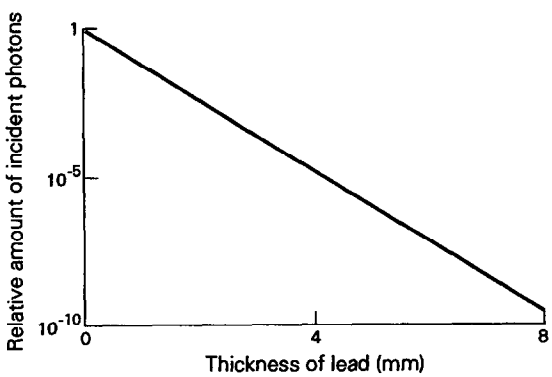

Figure 1
Fraction of 140 keV gamma rays passing through lead shields of different thickness.

The effectiveness of the system for reduction of the absorbed radiation dose to the operator has been evaluated with different activities of ^{99m}Tc. Table 1 lists the measured radiation dose rate at a distance of 0.5 m in front of the box with and without shielding during radio-HPLC of up to 1.85 GBq of a ^{99m}Tc-compound.

Table 1
Measured radiation dose rate 0.5 m in front of the column housing unit during radio-HPLC of different activities of ^{99m}Tc-compounds

Activity of ^{99m}Tc (MBq)	Radiation dose rate at 0.5 m* (mSv h^{-1})	
	Without shielding	In shielded unit
37	38×10^{-4}	8×10^{-4}
370	32×10^{-2}	8×10^{-4}
1850	18×10^{-1}	1×10^{-3}

*Maximum permissible dose = 25×10^{-3} mSv h^{-1} [4].

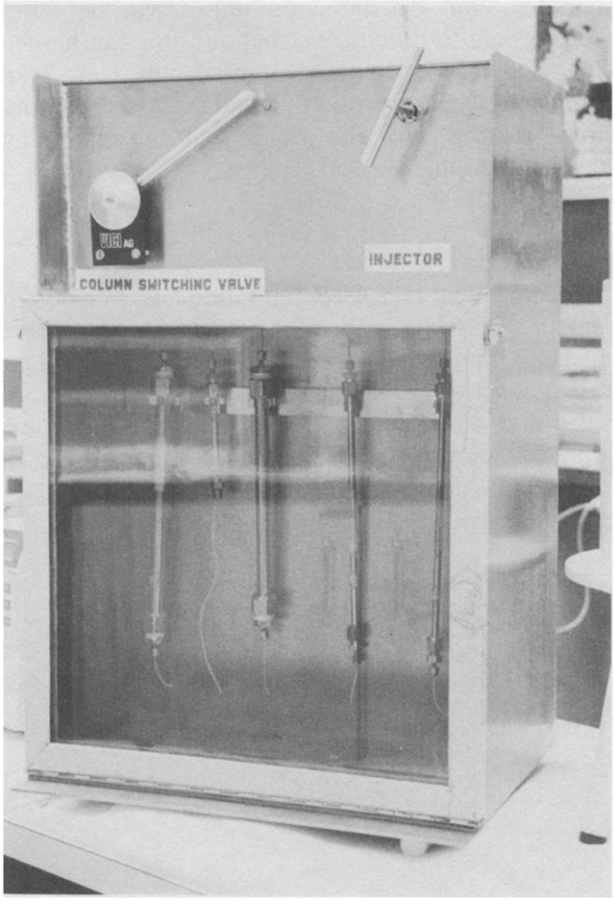

Figure 2
Photograph of the shielded column housing unit with injector and column-switching valve.

Detection and Integration

To monitor the radioactivity in the column eluate two types of radiometric detector are in general use. The first type is a thallium-activated sodium iodide scintillation detector, coupled to a photomultiplier tube and connected to a high voltage supply, pre-amplifier, amplifier and discriminator or single channel analyser. This solid detector absorbs gamma radiation most efficiently and is indicated in the analysis of low activities. A very high sensitivity is obtained with such a NaI(Tl) detector when the eluate tubing is wrapped around the crystal or conducted as a loop through the crystal well. On the other hand, to accurately monitor high activities with this scintillation detector it is necessary to interpose between the crystal and the eluate tubing one or two lead disks of 3 mm thickness with a central hole of 2–6 mm, depending on the activity level. Geiger–Müller counters are much less sensitive for gamma radiation and therefore they can be used over a wide range of activities up to GBq-amounts of ^{99m}Tc without problems of loss of counts due to the dead-time of the detector system electronics. The combination of these two detectors, installed serially after the column, allows convenient detection of ^{99m}Tc in an activity range of 370 Bq–3.7 GBq.

Two systems are available for integration of the radioactivity pulse signal. The amplified and discriminated pulses can be fed into a ratemeter where they are transformed to a voltage signal and this can be handled by a classic integrator. In the multichannel system the amplified pulses are stored in successive memory channels during consecutive preset time intervals ("dwell time") and the resulting radiochromatogram is then analysed by a built-in integrating program (e.g. Ramona-4 radio chromatographic system).

Conclusion

A convenient HPLC configuration has been designed for the safe and efficient analysis and preparative isolation of ^{99m}Tc-radiopharmaceuticals. The radiation dose to the operator is minimized by the use of adequate shielding in a column housing unit. The risk for radioactive contamination is drastically reduced by the use of a column-switching valve that allows easy selection of the desired column. Finally, the combination of two types of radiometric detector enlarges the detection range to cover Bq to GBq activities.

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