A Simple Automated System for the Routine Production of ^{99m}Tc by Methyl-Ethyl-Ketone Extraction

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SUMMARY

A relatively simple, automated system for the rapid, efficient and safe routine production of ^{99m}Tc04 from ^{99}Mo03 by the methyl-ethyl-ketone (MEK) extraction technique is described. The 4 phases of the extraction process — bubbling of air, phase separation, drawing off of ^{99m}Tc in MEK, and evaporation to dryness, are controlled by an automatic timer, suction-pressure pump and solenoid switches. The eluate was found to contain neither bacterial organisms or pyrogens nor significant levels of alumina and radio-isotopic impurities. With this system it is possible to make use of locally produced ^{99}Mo, even of low specific activity for the routine production of ^{99m}Tc in any concentration required.

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Due to the excellent properties of technetium 99m (^{99m}Tc) a marked increase has been experienced in recent years in the application of this radio-isotope in nuclear medicine. At the same time there has been a considerable increase in the use of the gamma camera for dynamic studies undertaken separately, or as part of another study, e.g. a brain scan.

The most widely used source of ^{99m}Tc is the ^{99}Mo/^{99m}Tc ion-exchange generator from which sodium pertechnetate is eluted. When using the gamma camera for dynamic studies, low-volume doses of ^{99m}Tc are essential. The eluate from a conventional ^{99}Mo/^{99m}Tc generator may prove unsuitable for this purpose unless a concentration procedure is used. Low yields have also been reported, as well as a relative hazard of ^{99}Mo breakthrough and alumina leakage.[1-3]

Conditions in South Africa at present necessitate the importation of generators, mainly from Europe. Since ^{99}Mo can be produced by the South African Atomic Energy Board, with considerable decrease in cost, the possibility was investigated of using locally produced ^{99}Mo and an extraction process as a routine source of ^{99m}Tc.

We developed a relatively simple, automated system for the rapid, efficient and safe routine production of ^{99m}Tc04 from ^{99}Mo03 by the methyl-ethyl-ketone (MEK) extraction technique, this being a further development of other manual systems previously described.[4-7]

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MATERIAL AND METHODS

Apparatus

The apparatus shown in Fig. 1 was set up on top of a layer of 50-mm lead bricks in a fume cupboard equipped with an extraction fan and fluorescent lighting. The same thickness lead bricks were used to construct a castle around the glass container with ^{99}Mo. A sliding lead door was used to gain access to the lead pot and Teflon tap at the bottom of the container. The rest of the apparatus was surrounded by a 5-mm lead shield with a swing door for access. The Mo03 solution in 5M NaOH is contained in a glass vessel with inlets for solutions and air, and a suction outlet.

The apparatus and the separation level between MEK and the aqueous phase is viewed by a system of mirrors, while a simple periscope offers a better view of the separation level and aids in fine adjustments of the suction tube. A combined vacuum pressure pump is used to bubble air through the MEK/^{99}Mo mixture and to draw off the MEK layer containing the ^{99m}Tc-pertechnetate through an alumina filter, the operation being controlled by solenoid valves. The extracted ^{99m}Tc is evaporated to dryness by a current of warm air supplied by a commercial type heat-blower via a funnel. The recondensed evaporated MEK is trapped in a glass collector.

The four phases of the extraction process: bubbling of air, separation, drawing-off of ^{99m}Tc in MEK, and evaporation to dryness, are controlled by an automatic timer (Fig. 2). The timer is equipped with a safety device which prevents the onset of a cycle unless the timer is returned to the proper start of the cycle, i.e. the bubbling of air. The MEK layer cannot be drawn off unless the receptacle in which it is to be evaporated is properly fitted, since the vacuum needed for this step can only be produced in a closed system.

Loading and Unloading

Loading is accomplished by pressure filling of the vessel (Fig. 3). About 200 mCi ^{99}Mo is supplied in a multidose vial as Mo03 dissolved in 7,5M NaOH. The loading system is flushed with a sterile water or 2,5M NaOH solution to adjust the final NaOH concentration in the column to 5M NaOH. Pressure filling is employed to minimise radiation exposure to personnel. The long and short needles used are fixed into permanent positions and the lead pot has special guides to ensure quick and accurate positioning of its lid to minimise adjustments and radiation exposure. Unloading is accomplished by opening the

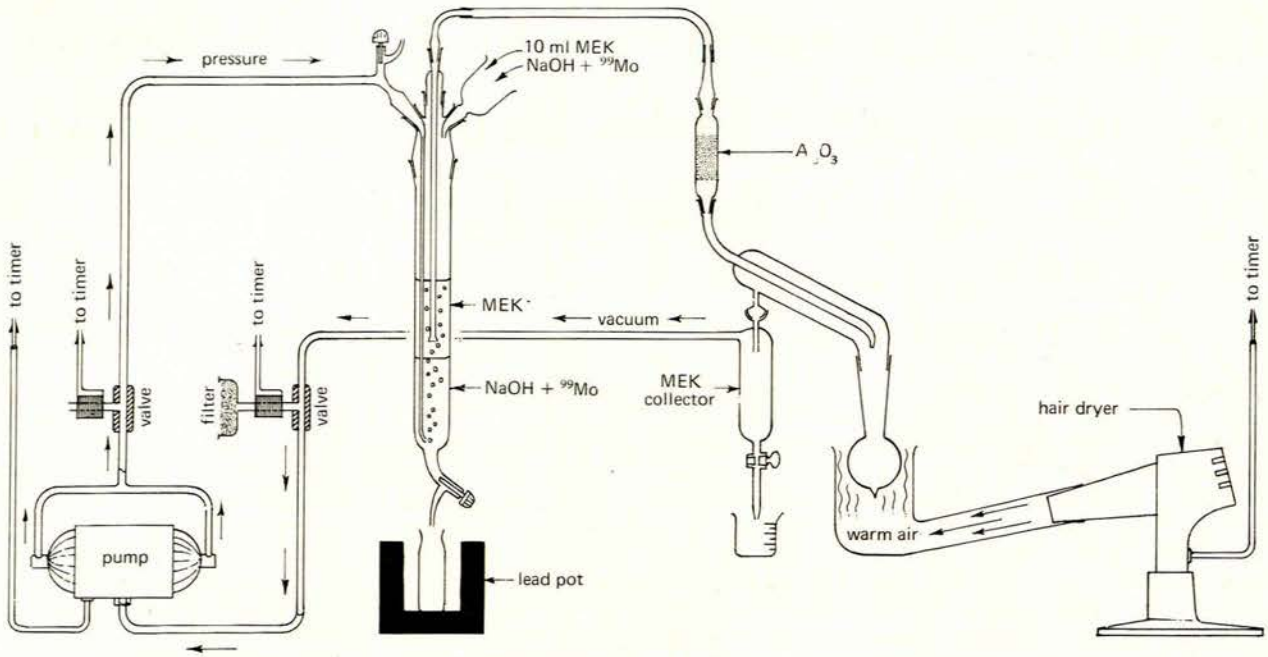

Fig. 1. System for producing ^{99m}Tc by MEK extraction.

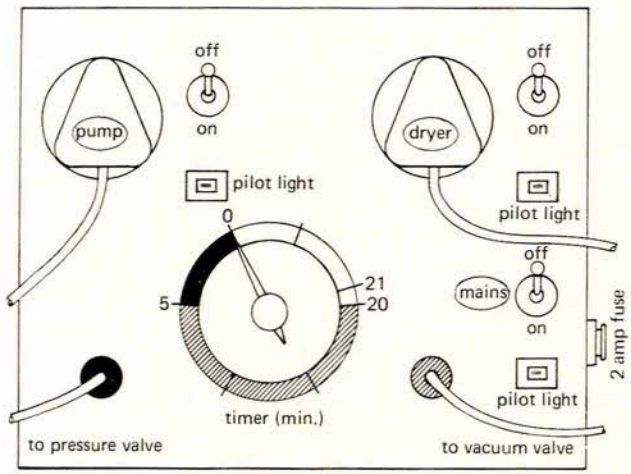

Fig. 2. Automatic timer controlling the phases of the extraction process.

Teflon tap at the bottom of the column (Fig. 1). The lead pot containing the receptacle for the used ^{99}Mo fits into a special guide to ensure quick positioning.

Operation

After loading the column, the suction tube is adjusted to 2 mm above the filling level. About 10 ml double-distilled MEK is added through the filling funnel and the 4 phases of the extraction process controlled automatically by the timer. A phase separation period of 15 min is allowed following a 5-min mixing of the organic and aqueous components. One minute after suction is commenced the heater-blower is switched on, a drying period of about 20 min at 70°C being allowed. The extraction is completed in well under an hour. The technetium

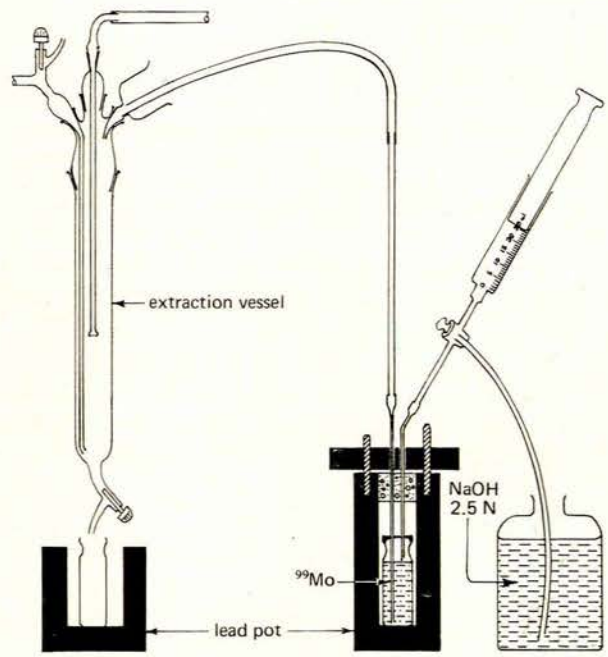

Fig. 3. System for loading and unloading the extraction vessel.

is redissolved in the appropriate volume of saline, and sterilised by Millipore filtration.

Analysis of Aluminium and Radio-active Contamination

The aluminium content of extractions dissolved in 5 ml saline was determined spectrophotometrically. Molybdenum

breakthrough was determined in a calibrated ionisation chamber using a lead pot with a calibrated thickness (Picker Dose Calibrator). Gamma-ray spectroscopy with a solid state detector and a multichannel analyser was performed on aliquots 2 weeks after extraction.

Sterility and Pyrogen Contamination

Sterility of several aliquots was determined by both aerobic and anaerobic culture. The presence of pyrogens was tested for by the South African Bureau of Standards, employing standard techniques.

RESULTS

This system has been in routine operation for 6 months, and supplies ^{99m}Tc of high quality. The efficiency of the system was usually about 60%. The first extraction from a new batch of molybdenum, however, was lower than this.

Alumina levels were constantly less than 1 μg/ml, i.e. less than 5 μg per elution. The level of ^{99}Mo in the elution has always been much lower than 10^{-3} of the ^{99m}Tc activity present. No significant levels of long-lived radioisotopic impurities were found, nor were any bacterial growth or pyrogens recovered from the eluate. Personnel radiation was kept at levels below 1 mrem/hour at operational distances from the system.

DISCUSSION

The main advantages of a solvent extraction technique over the column type generator for the separation of ^{99m}Tc from the parent ^{99}Mo are summarised in Table I.

TABLE I. ADVANTAGES OF MEK EXTRACTION

Cheaper than generators
Use of locally produced ^{99}Mo
Low ^{99}Mo contamination
Low alumina contamination
High specific activity ^{99m}Tc
Constant concentrations ^{99m}Tc

With this system it is possible to make use of ^{99}Mo produced in South Africa without the cost and complexities of producing a generator. This, added to the savings in the cost of air freight from European countries, results in approximately a 50% reduction in the per millicurie price of ^{99m}Tc.

Not only is the product cheaper, but it also contains less ^{99}Mo contamination than the generator-produced ^{99m}Tc, resulting in a lower radiation dose to the patient. The low levels of alumina contamination are essential for the preparation of various labelled compounds, e.g. sulphur colloid and labelled red blood cells.[5] For dynamic studies (brain, cardiac) it is essential to use high specific activity ^{99m}Tc, which can only be obtained from a fresh generator. Critical volumes are often used in ^{99m}Tc-preparations, often necessitating a high concentration of ^{99m}Tc, a goal not easily obtainable with a generator.[9]

The relatively simple automated system we have developed offers several distinct advantages over other systems in current use. The potential hazards and the complexity of repeatedly transferring heavily shielded ^{99}Mo manually between the extraction chamber and the storage reservoir are eliminated, since a single vessel is used for both of these functions.[4] Radiation exposure to the operator is further reduced by the system of pressure-loading the column. Since the extraction process is automated, it saves operator time and reduces radiation exposure, which is further minimised by inspection of the separation level by means of a periscope. Although the addition of H_2O_2 is claimed to increase the initial yield,[4] we have found that although the addition of H_2O_2 in saline does increase the ^{99m}Tc yield, it should not be used in this system due to the formation of a foamy layer on top of the organic phase. This layer contains a relatively large volume of the aqueous phase, causing ^{99}Mo contamination of both the alumina filter and the eluant. The presence of traces of H_2O_2 in the dried eluant also interferes in the preparation of compounds for which reduced ^{99m}Tc is essential. If ^{99}Mo contamination of the system does occur, we have found that it is still possible to simply flush the system clean and return it to an operational state with little delay. It is essential not to raise the temperature of the drying vessel above 70°C, since this causes decomposition of MEK, resulting in a dark-yellow eluant which is unsatisfactory for the production of ^{99m}Tc compounds.

Although the percentage of ^{99}Mo contamination may be further reduced by using ^{97}Mo in 7M NaOH, we have found a 5M NaOH solution more practical, since the specific gravity of a 7M NaOH precludes proper mixing of the aqueous-organic phases in this system. This reduces the yield of the ^{99m}Tc considerably. It is essential to use only Teflon or glass tubes and connexions throughout, since MEK dissolves the commonly-used plastic tubes.

It is essential that ^{99}Mo breakthrough be checked after each elution. This can be accomplished easily and satisfactorily with commercially available equipment.

In an editorial comment it has been stated by Quinn[10] that this type of system has been a source of pertechnetate for radiopharmaceutical manufacturing for several years, and that he could not recommend anything more strongly. This type of system is easy to set up and offers a significant financial saving in the USA. By automating the system, we have managed to further simplify the extraction process and to reduce the manual steps involved, resulting in a reduction of operator time and radiation exposure to the operator.

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