Abstract — The paper is devoted to the production of technetium-99m from the extraction of the generator. In the Tomsk Polytechnic University, create several types of extraction systems.

Keywords — Nuclear medicine, generator technetium-99m, molybdenum-99.

I. INTRODUCTION

His technetium-99m pharmaceuticals, daughter products of $^{99}$Mo radionuclide decay; occupy a prominent place among pharmaceuticals used in medical diagnostics. In order to separate a $^{99}$Mo/$^{99m}$Tc genetically bound dyad, generators of three main types are used: chromatographic (sorption), sublimation and extraction ones. In contradistinction to the former two generator types, the extraction generators are stationary setups designed for centralized supply of big cities and regions with the technetium-99m pharmaceuticals.

II. EXTRACTION OF TECHNETIUM-99M GENERATORS

The NPI at TPU first generator was designed and manufactured in 1986. While investigating its principal scheme, the following tasks were being solved:

1. Development of a single system, that would fully remotely control the process of pharmaceutical production;
2. Decrease in the liquid communications quantity;
3. Placement of the electrically controlled mechanisms outside the active zone;
4. Increase of the extractive substance bleeding reliability and effectiveness.

As a result of research and development, a new generator of coaxial type was first manufactured [1-3]; it was designed for exploitation in normal chambers of research reactors. The external view of the generator together with the control board is given in Fig. 1.

Fig. 2 shows the installation principal schematic. Its base is the generator column 1, made of quartz glass. In contradistinction to well-known constructions, it combines several units in a single body: the input throat with the cover 2, the column for molybdenum oxide dissolution and subsequent extraction 3, the water phase level regulator 4 with the dosing syringe 27, the unit for extractive substance evacuation 5, and the filtering column 6 with sorbent $\text{Al}_2\text{O}_3$.

The dissipating ring for better mixing of the extractive substance is installed into the middle of the column 3. The supporting equipment remained in the active zone is the evaporator 7 with the refrigerator 8, and the container for removal of the used water phase 9 with the shut-off faucet 10, controlled by the manipulator. It is used once per week. As a result of such a layout, the quantity of connecting communications was decreased significantly, all manual operations at the radiation dangerous stages were avoided, and the process control was simplified.

Located outside the “hot” chamber are the container 11 for supplying the operation solutions and extractive substance to the extractor, container 12 for the saline solution, collector for dissolution of the sodium pertechnetate solution, device for the pharmaceutical prepackaging 14 with the phials 15, and the external container for removal of the used water phase 17 (to be used twice per year). The generator is controlled from the outer board 18 by means of the single air-vacuum system, which consists of the vacuum pump 19, needle valve 20, manometer 21 and eight electromagnetic valves K$_1$-K$_8$, started using the program that consists of 7 commands. The solutions and received products are supplied to the generator containers by creating small air underpressure ranged from $-0.01$ to $-0.2 \text{ kg/cm}^2$ in a given container.

The generator is loaded with the irradiated dry powder of
natural composition molybdenum oxide \((\text{MoO}_3)\) in the amount of 14-20 g; it is subsequently dissolved directly in the extraction column. The process of irradiation takes place in the dismountable anodized aluminum pen-cases, on which the shut-off valves are installed. The pen-cases are opened using a special device, installed over the input throat 2.

Fig. 2. Schematic of the extraction generator with the coaxial column

The \(^{99m}\text{Tc}\) is extracted by methylethylketone (MEK) from the formed water phase in amounts of 10-15 ml. Some portion of the water phase (3-4 ml) is taken by the syringe 27 into the level regulator 4 in advance. The extractive substance, having passed bottom-up through the solution, freely enters the apertures 5 in the extractor upper part, and then passes along the extractor outer walls onto the porous partition 26 of the column with the sorbent \((\text{Al}_2\text{O}_3)\) 6. When extraction is over, the water phase is taken back into the column from the level regulator, so the extractive substance remains are displaced. Simultaneously, hot \((t=96^\circ\text{C})\) and cold water is supplied to the evaporator 7 and refrigerator 8 cases, respectively. By switching the \(K_2\) valve on, the air is depressed in the MEK evaporator 7 and refrigerator 8 cases, respectively. By shut-off valves are installed. The pen-cases are opened using a dismountable anodized aluminum pen-cases, on which the extraction column. The process of irradiation takes place in vacuum communications, introduced directly into the hot chamber. Absence of regulative and shut-off electrically controlled valves on them significantly increases its reliability. The unit adjusting the water phase level in the extractor provides the completeness of the extractive substance bleeding. The value of its losses is 2-3 ml with the total volume equal to 100-110 ml. This setup has no analogues among the known generator systems.

The generator setup presented has 3 liquid and 3 air-vacuum communications, introduced directly into the hot chamber. Absence of regulative and shut-off electrically controlled valves on them significantly increases its reliability. The unit adjusting the water phase level in the extractor provides the completeness of the extractive substance bleeding. The value of its losses is 2-3 ml with the total volume equal to 100-110 ml. This setup has no analogues among the known generator systems.

The process of extraction in the generator presented can be described by the equation [4]:

\[
dN = kN \, dV_o/V,
\]

where \(dV_o\) is the extractive substance portion volume, which absorbs \(^{99m}\text{Tc}\) in the \(dN\) amount; \(V\) is the water phase volume; \(k\) is some constant meaning the distribution coefficient.

Taking into account the fact that the technetium-99m nuclei quantity \(N\) and its activity \(A\) are connected by the ratio \(N=A/\lambda_2\) [5], where \(\lambda_2\) is the \(^{99m}\text{Tc}\) decay constant, one can obtain after integration of the equation (1):

\[
A = A_o \exp(-kV_o/V),
\]

where \(A_o\) is the \(^{99m}\text{Tc}\) initial activity in the generator water phase.

The ratio \(A/A_o \cdot 100 = B_T\) characterizes the \(^{99m}\text{Tc}\) yield value.

The experimental dependence of \(B_T\) on the MEK volume that has passed through the coaxial generator column is shown in Fig. 3.

It follows from the given dependence that in order to achieve the yield exceeding 80\%, the passed extractive substance volume should approximately be equal to the water phase volume, i.e., to 100-110 ml.

In the version considered, the average duration of \(^{99m}\text{Tc}\) pharmaceutical production is 112-115 min., where 55-60 min. is the time, during which the extractive substance is distilled. In order to increase the extraction effectiveness and decrease
the extractive substance volume, the generator of a new type [6] was developed, which is based on the principle of repeated extraction in the closed small volume. The generator apparatus schematic is given in Fig. 4. Like the generator with the coaxial column, it is remotely controlled with the same principle of solutions supply. All periphery, including the evaporator, pertechnetate bleeding unit, container for wastes etc., is not changed as well.

The principal difference of the installation from the previous generator is the two extraction columns 1 and 2 connected in series. The both columns have neckings in the central part 3, dissipating rings 4 and spongy filters 5 in the lower part. The column 2 has also the intake 6, connected to the evaporator 8 through the filtering column (Al₂O₃) 7.

The generator operational principle is as follows. The first column is loaded with the irradiated MoO₃ oxide (the procedure is described above), which is then dissolved by supplying solutions from the container 9 with the further MEK extraction through the formed water phase. The water phase is leveled according to the mark on the necked part of the column 1.

When the first extraction is over, the contents of the first column are supplied into the column-extractor 2 through the lower branch pipe 10 with the B₄ valve opened. In this case, the water phase passes there first, and then the whole amount of the extractive substance repeatedly passes through it and is collected over the water phase. The twin extraction cycle, described above, can be repeated several times by means of providing alternate air depression in the columns 1 and 2 through the valves K₁ and K₂, respectively. The extractive substance is finally extracted from the system through the intake, the end of which is located in the necked part of the column 2 at the boundary of the water and organic phases. The rest operations, starting from the MEK evaporation, pharmaceutical preparation and water phase removal, are the same as in the coaxial generator.

On account of the repeated extraction method, the actual contact of the extractive substance with the water phase is achieved, that is comparable to the process that takes place in the straight-through column of 6-8 fold larger dimensions. In order to estimate the expected efficiency of technetium-99m extraction by small volumes of the extractive substance, the series of model experiments for determining technetium-99m distribution coefficients in the systems with different proportions of the water and organic phases was carried out. For calculations, the known ratio was used [7]:

\[ E = \frac{100D}{D + V/V₀} \]  \quad (3)

where \( E \) is the extraction degree, %; \( D \) is the distribution coefficient.

The experimental values of \( D \) for various volumes of the extractive substance \( V₀ \) (at the fixed water phase volume \( V = 90\text{ml} \)) are given in Table 1. The expected values of the ⁹⁹ᵐTc content amount in the organic phase after \( n \) extractions, are given in the same table; they are calculated using the expression [4]:

\[ E = 100\left[1-\left(1+DV/V₀\right)^n\right]^{-1} \]  \quad (4)

<table>
<thead>
<tr>
<th>( V, \text{ml} )</th>
<th>( \text{Expected ( n ) extractions} )</th>
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<tr>
<td>( V₀, \text{ml} )</td>
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<tr>
<td>40</td>
<td>0.32</td>
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<td>50</td>
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<td>60</td>
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<td>90</td>
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<td>70</td>
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The data from Table 1 show that to achieve the ⁹⁹ᵐTc extraction level of the order of 90%, 40 ml of MEK will suffice for the 8-extraction cycle, 50 ml will do for the 6-extraction cycle. However, these experimental values were not fully confirmed in practice. In particular, the radionuclide...
yield vs the quantity of the extraction cycles experimental
dependences given in Fig. 5, show that:

1. for the 4-extraction cycle, the calculation data agree well
with the experimental values of the technetium yield over the
whole range of the chosen extractive substance volumes;
2. using MEK in the amount of 50-60 ml, satisfactory yield
values of 80-85% are achieved at the 8-extraction cycle;
3. extraction at the V_e/V ≤ 0,5 volume ratio does not ensure
the yield exceeding 70% at any number of extractions.

The decrease of the extraction yield with the increase of the
cycle quantity, observed in the experiment, is, apparently,
connected with the processes of the phases mutual dissolution,
especially typical for methyl ethyl ketone.

It should be noted that the multi-stage extraction principle
was not used in known generator devices up to the moment.
Its application, together with the decrease of the installation
dimensions, has allowed us to decrease the extractive
substance volume almost twice and, consequently, decrease
the time of the pharmaceutical preparation for more than 30
min. in comparison with the coaxial generator as well as with
other generators with straight-through columns.

In addition to the devices described, on the basis of the
generator with the extraction repeated cycle, the generator
with the additional extractor (AE) was developed. It is used as
two coupled installations and intended for centralized supply
of big cities and regions. Besides, the generator mobile
version together with the transportable extractor for direct use
in radiological laboratories [8] was developed. The design of
this portable installation provides the possibility of self-
regulation over the water and organic phases boundary in the
closed extractor; in this connection, it can be used as a "black
box". The installation is designed for loading of up to 1-1,5
Curie of 99Mo. Presently, it is used for production of
technetium-99m pharmaceutical in the Regional Hospital,
Kemerovo.

Spare extractors for the generator stationary part (the stand
with the evaporator and the remote control board) are
delivered by means of automobile transport twice per month
directly from the IRT-T reactor.

Table 2 shows general operational characteristics of the
technetium-99m generators developed at the NPI at TPU.

The technetium-99m extraction generators described above
allow production of the pharmaceutical "Sodium pertechnetate,
99mTe" as a solution for injections with the following characteristics:
- description: uncoloured clear liquid;
- contents: technetium-99m without carrier - 740-1480
mBecquerel;
- sodium chloride - 8,7 - 9,3 mg;
- water for injections - up to 1 ml;
- radiochemical purity > 99,0%;
- methyl ethyl ketone content < 0,05%;
- pH - 5,0 - 7,0;
- radionuclide admixtures: 99Mo< 2·10^{-2} %, other
radionuclides less than 1·10^{-4} %.
- chemical (non-active) admixtures (μg/ml): molybdenum -
0,2; copper - 0,1. The rest - less than the level of their
detection by the emission spectral analysis method.

Hence, as a result of 15-year investigations at the TPU
reactor, the complex of extraction technologies and remotely
controlled devices has been developed and employed for
regional use. Similar centralized generators can be
implemented at the reactors of Ekaterinburgh, Kransnoyarsk,
Chelyabinsk with minimum expenses, that would allow to
solve the problem of supplying these big cities with high
informative pharmaceuticals, as well as to decrease their first
cost by 2-3 times.

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