^{99}Mo/^{99m}Tc Generator Shortage: Free, Web-Based Software

The current shortage of ^{99}Mo/^{99m}Tc generators is unfortunately nothing new, although it is probably the worst ever. In the past 3 y, several reactors have been offline for extended periods of time for a variety of reasons (regulatory disputes, leakages of coolant, routine maintenance, etc.). It is worth noting that among the available ^{99}Mo production sites, all 5 nuclear reactors producing significant commercial quantities (High Flux reactor, Petten, The Netherlands; National Research Universal reactor, Chalk River, Ontario, Canada; BR-2 at Fleurus, Belgium; SAFAR-1 at Pelindaba, South Africa; and Osiris at Saclay, France) and using neutron-induced fission of high-enriched ^{235}U (*1*) are elderly (42–51 y old) (*2*) and nearing time for decommissioning. The need for extraordinary maintenance at these sites is becoming routine and is increasing as time goes on. This leads to a "lack of access to a reliable, consistent supply of the most important medical isotope," as noted by Robert Atcher, PhD, MBA, past president of SNM in 2009 (*3*). ^{99m}Tc is used in about 70,000 medical imaging procedures each day (*4*). Notably, this shortage will probably be worse in the United States and Japan (the 2 largest consumers of isotopes), because they have no domestic production of ^{99}Mo. Reactors (including the OPAL reactor in Australia, the CNEA Ra-3 reactor in Argentina, and others) currently using low-enriched ^{235}U as a substrate (of less concern because it is not considered to be weapon grade [*5*]) will probably be unable to provide enough isotopes to meet worldwide demand because of the lesser yield.

Because isotopes cannot be stockpiled, a number of solutions have been proposed, such as using PET isotopes as substitutes for ^{99m}Tc, using ^{201}Tl as a substitute for myocardial imaging, building new reactors, upgrading/updating current reactors, using non-reactor-based technologies (*6*), local production using accelerators firing high-intensity beams of photons, and others. None of these alternatives seems conclusive. As reported in a press release from the European Association of Nuclear Medicine (*7*), ^{99}Mo shortage should be considered as a chronic disease rather than a short-term problem, and this could lead to higher costs for isotopes in addition to unreliable delivery dates and quantities provided.

While awaiting regulatory, political, and administrative decisions to solve the ^{99m}Tc production problem conclusively and untangle this highly fragmented supply network, is there something that could be done to "soften the fallout" of the ^{99m}Tc shortage?

- Resolution recovery software and hardware that enable lower amounts of the isotope to be administered are now commercially available and will partially solve the problem, but it will take time and money to equip all nuclear medicine departments worldwide.
- Changing patient scheduling to combine maximum activity with a higher number of procedures is probably a good idea, but working on weekends or late at night to maximize generator use would have to be negotiated with doctors, nurses, administrative staff, and technicians and adapted to local regulations.
- Precisely calculating the theoretical and estimated yield of the ^{99}Mo/^{99m}Tc generator enables a rational use of available activity, also enabling a selection of the type and number of procedures to perform.

In our view, this last point is easy to achieve for all departments by using an "ad hoc" instrument. Although the calculations needed to perform such operations are well known (*8*) (and sometimes implemented in commercial software), as far as we are aware no freely available, easy-to-use Web-based system is able to calculate the theoretical/estimated generator yield precisely, taking elution efficiency into account. Such a system should enable the yield of multiple elutions of the generator on the same day as the first elution to be calculated.

We aimed to construct a free, Web-based software for performing such calculations, using the Apache Web server (www.apache.org) and PHP (www.php.net). After inputting the link (www.rad.unipd.it/nucmed/decay/), the user is prompted to complete a form that is currently provided in American/English and Italian.

The system is simple to use and requires only 5–6 values, which are: generator calibration date; generator arrival date; ^{99}Mo (in GBq) calibration activity declared by manufacturer; number of hours after first elution when second elution is to be performed (and, if a third elution is needed, the number of hours after the second elution when the third elution is to be performed); and elution efficiency (0.9 is the predefined value). If necessary, a generator label (ID), chosen by the user, can be added to distinguish a given generator from a similar one. When the user presses "calculate," a table appears presenting calculations from the generator arrival date to 15 d after its calibration date. For each date presented, the calculations performed are as follows:

- ^{99}Mo activity, considering decay since calibration date;
- Theoretical yield (Ty) of generator (representing the theoretical amount of ^{99}Mo decaying into ^{99m}Tc), calculated as:

$$\mathrm{Ty} = (^{99}\mathrm{MoA}) \times \mathrm{D} \times \mathrm{R},$$

where ^{99}MoA = ^{99}Mo activity at the specified date; D is a decay factor; and R is the ^{99m}Tc/^{99}Mo ratio as a fraction. Detailed information on the calculations appears when the user presses the "Info & disclaimer" button;

- Estimated yield (Ey) of the generator (first elution), representing the ^{99m}Tc that can actually be "extracted" from the generator. Of course, Ey depends on the generator's elution efficiency, which is usually >95% (*9*). It is strongly recommended that every nuclear medicine service adjust the proposed (0.9) elution efficiency to fit its own real value.
  Ey was calculated as follows:

$$\mathrm{Ey} = \mathrm{Ty} \times \mathrm{E},$$

where E is the elution efficiency. The generator's theoretical and estimated yields are calculated twice, as if the generator were eluted 24 or 48 h before (although elution after 48 h is not advisable [and is even explicitly forbidden in some countries, as in Italy (*10*)], the information may be helpful for training purposes);

- Second/third elution: the yield (estimated) of the generator after N (and, if necessary, N + X) hours after the first elution, where N (and, if necessary, N + X) is selected by the user. This value is useful for optimizing the generator's use, so as to establish the exact yield of a generator at various elution times after the first elution;
- Yield (estimated) on the day after the last elution. This value is useful because it represents the yield of a generator on the next day, considering losses from first + second + third elutions (performed on a given day).

In a second form (accessible by pressing a button on the left-hand side of each row), the user can see the decay of the eluted ^{99m}Tc and perform multiple subtractions of activity at selected times.

If the ^{99}Mo contamination level (in MBq) at the time of elution is reported in the form, then after selecting the contamination limits (0.15 KBq of ^{99}Mo/MBq of ^{99m}Tc as stated by the U.S. Nuclear Regulatory Commission in 10 CFR 35, or ^{99}Mo < 0.1% as stated by the *Farmacopea Ufficiale della Repubblica Italiana* in 1985), the estimated contamination of ^{99}Mo (at different times) and the maximum allowable ^{99}Mo activities are shown.

This program has been used successfully on a daily basis at our department for the last 6 mo to calculate yields, and—for an elution with a saline volume of at least 5 mL—only very slight deviations from the calculated values have been observed. The system has recently been adopted as a tool on the official Web site of the Italian Association of Nuclear Medicine and Molecular Imaging (www.aimn.it, accessed by pressing "servizi" and then "tools").

In conclusion, we are sharing the program free of charge in the hope that it will be clinically useful to optimize multiple generator elutions, to monitor ^{99}Mo contamination levels, and also for educational purposes.

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