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14 MeV neutrons for medical application: a scientific case for $^{99}\text{Mo}/^{99}\text{Tc}^{\text{m}}$ production

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Abstract. $^{99}\text{Tc}^{\text{m}}$ is a widely used radionuclide for SPECT (Single Photon Emission Computed Tomography) diagnostics thanks to its short half-life (about 6h) and the low-energy gamma ray emission (140 keV) well suited for diagnostic devices. The specific method for producing $^{99}\text{Tc}^{\text{m}}$ via $^{100}\text{Mo}(n,2n)^{99}\text{Mo}$ reaction, as it was investigated in ENEA, is discussed in detail in this paper. The ^{99}Mo activity achieved by means of 14 MeV neutron irradiation on natural Molybdenum sample irradiated at the Frascati Neutron Generator (FNG) facility, at the Research Centre of ENEA-Frascati, was accurately assessed, by tracing it to the activity standards provided by the Italian National Institute of Ionizing Radiation Metrology (INMRI), located at the Research Centre of ENEA-Casaccia. The whole experiment carried out in ENEA was supported by simulations performed with the Fluka Monte Carlo code, whose predictions have been benchmarked against the experimental data collected at ENEA-FNG, relying on the traceability to the activity standards developed and maintained at the ENEA-INMRI Radioactivity laboratories.

1. Introduction

Metastable Technetium-99 ($^{99\text{m}}\text{Tc}$) is the principal radionuclide used worldwide in medical diagnostics with more than 30 million procedures per year, accounting for more than 80% of all Nuclear Medicine diagnostics [1,2]. The short half-life of $^{99\text{m}}\text{Tc}$ ($T_{1/2} = 6.0067$ (10) h [3]) and the related 140 keV gamma-ray make it well suited to medical imaging, using conventional gamma cameras such as Single Photon Emission Computed Tomography (SPECT). $^{99\text{m}}\text{Tc}$ can be obtained from the decay of Molybdenum-99 (^{99}Mo) ($T_{1/2} = 2.7479$ (6) d [4]). The known different technologies for producing $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ are based on: a) HEU (Highly Enriched Uranium) and LEU (Low Enriched Uranium) targets in fission reactors; b) ^{98}Mo thermal neutron activation in nuclear reactors; c) direct cyclotron production; d) photo-fission reactions on ^{238}U ; e) ^{99}Mo photo-production and f) fast neutron-induced reactions. Presently the almost complete supply of ^{99}Mo is provided by method a).

In 2010, the global demand for ^{99}Mo was estimated to be about 1.2×10^4 6-day Curie (6-day Ci) per week (444 TBq per week) and it is continuously growing. Global shortage of $^{99}\text{Tc}^{\text{m}}$ emerged in the late 2000s because the two main reactors (NRU in Canada and the High Flux Reactor-HFR in The



Netherlands), capable to provide about two-thirds of the world's supply of ^{99}Mo , were shut down repeatedly for extended maintenance periods. These events highlighted vulnerabilities in the classical supply chain of medical radionuclides based on nuclear reactors. At present, just a few nuclear reactors around the world can provide ^{99}Mo . Many of these are old and soon will stop their medical isotopes production, consequently leaving the world vulnerable to the shortage of this and several other radiopharmaceuticals. A complete landscape of the worldwide ^{99}Mo production from reactors is provided in reference [5]. Table 1 shows a list of the main production sites and their main features.

Table 1: Main characteristics of worldwide reactors used for ^{99}Mo production.

Site	Location	operation days	Weekly Nominal production (6-day Ci)	Weekly % of world demand	Fuel/Target	First Commissioning
BR-2	Belgium	140	5200	25-65	HEU/HEU	1961
HFR	The Netherlands	300	4880	35-70	LEU/HEU	1961
MARIA	Poland	-	700-1500	-	HEU/HEU	1974
LVR-15	Czech Republic	-	> 600	-	HEU ^e /HEU	1957
NRU	Canada	300	4680	35-70	LEU/HEU	1957
OPAL	Australia	290	1000-1500	-	LEU/LEU	2006
OSIRIS	France	180	1200	10-20	LEU/HEU	1966
SAFARI-1	South Africa	305	2500	10-30	LEU/HEU	1965
RA-3	Argentina	230	240	<2	LEU/LEU	1967

1.1. Feasibility study of ^{99}Mo production at the ENEA-FNG and perspectives on the New Sorigentina Fusion Source (NSFS).

$^{100}\text{Mo}(n,2n)^{99}\text{Mo}$ reaction with 14 MeV neutrons [6] has been identified as a feasible and effective alternative method to the nuclear fission reactors for the $^{99}\text{Tc}^m$ production. Indeed, the $^{100}\text{Mo}(n,2n)^{99}\text{Mo}$ cross section is appreciable and exhibits a maximum around 14 MeV. This approach was tested in 2015 from a Japanese group, which provided a first complete assessment of $^{99}\text{Tc}^m$ production and the characterization of the radiochemical chain to produce the radiopharmaceuticals by 14 MeV neutron beam. The Frascati Neutron Generator (FNG) in ENEA is an accelerator driven continuous neutron source [7]. It relies on Deuteron-Tritium (D-T) fusion reactions, producing almost monochromatic 14 MeV neutrons with a maximum neutron emission rate of 10^{11} s^{-1} . A natural Molybdenum powder sample (density 1.94 g/cm^3) was irradiated at FNG for about 15 minutes with a FNG neutron emission rate of $2.89 \times 10^{10} \text{ s}^{-1}$. The obtained results show that a ^{99}Mo specific activity of about $(2.32 \pm 0.05) \text{ kBq g}^{-1}$ [8] at the reference time was produced, in good agreement (within 7%) with the Monte Carlo (MC) predictions, based on the Fluka code (version 2011.2c.3). In this context, the measurements performed at ENEA have to be considered as a mandatory step to build and assess a valuable procedure that allows computational and experimental verification of the ^{99}Mo production using 14 MeV neutron beams, in a controlled and reliable way. Indeed, it is important to highlight the peculiarities of the applied procedure: (1) use of an well-defined energy neutron source, determined by the D+T reaction, with a well-defined emission rate, determined by the absolute technique of the associated alpha particle; (2) MC calculations to optimize the experimental set-up and irradiation; (3) accuracy and traceability at high metrological level of the ^{99}Mo and $^{99}\text{Tc}^m$ activity measurements and MC benchmarking. Indeed, the activity measurements of ^{99}Mo and ^{99m}Tc were carried out by using a high-energy resolution HPGe spectrometer owned by the Italian National Institute of Ionizing Radiation Metrology (ENEA-INMRI), which was previously calibrated with long-lived multi-gamma-emitting radionuclides (such as ^{152}Eu) and with the ^{99m}Tc primary standard. In this way all the performed activity measurements are traceable to the activity standards maintained in ENEA-INMRI.

The results obtained at ENEA-FNG, after a proper normalization in order to take into account the different experimental conditions, are coherently comparable to those published by the Japanese group in reference [4], providing a consistent and reliable estimation of the measured specific activities. Indeed, properly considering the experimental conditions of the two experiments the specific activity obtained in Ref. [4] and at FNG are the same within experimental errors.

New Sordani Fusion Source (NSFS) [9,10] is a project of an intense double rotating targets 14 MeV neutron source, based on D-T fission reactions driven by deuteron accelerators and featuring a yield about 5×10^4 times higher than FNG, reaching in such a way an emission rate of about $4\text{--}5 \times 10^{15} \text{ s}^{-1}$. NSFS main features make this facility a potential and interesting infrastructure for an extensive radiopharmaceutical production. In this framework, FNG can be considered as a useful laboratory in the European context to test and validate the NSFS's capabilities and performances. Indeed, a preliminary methodological approach has been already assessed involving both experimental measurements and Monte Carlo (MC) computations, as described in detail in the following.

1.2. Monte Carlo predictions for NSFS

Accurate and realistic predictions of the ^{99}Mo activity producible at NSFS by irradiating ^{100}Mo , have been obtained by MC simulations, taking properly into account the geometry of possible and “optimized” targets (w.r.t thermal issues) and identifying reasonable irradiation profiles (i.e. neutron rates and a realistic duty cycle). A conservative approach has been adopted to estimate the maximum obtainable ^{99}Mo activity at NSFS. Supposing an operative neutron emission rate of 10^{15} s^{-1} and identifying an optimum irradiation time of 22 hours (coming mainly from thermo-physical considerations on the melting Molybdenum temperature but matching also the decay time curve of the transient equilibrium between ^{99}Mo , precursor, and $^{99}\text{Tc}^m$, daughter radionuclide), two experimental scenarios can be established as delimiting the predictable NSFS ^{99}Mo production capabilities:

(a) An “optimistic” scenario that fixes the upper limit of ^{99}Mo weekly activity that could be provided by NSFS (about 75 TBq). This has been obtained by supposing to fill the irradiation volume between the two NSFS target wheels (0.5 liters) with a solid ^{100}Mo target (corresponding to almost 6 kg) and irradiating it continuously for 22 h with a neutron emission rate of 10^{15} s^{-1} . Anyway, the evaluated total power deposited in the target in this configuration would cause the maximum temperature of the target to exceed the Molybdenum melting point temperature (2900 K). This result was obtained assuming conservatively adiabatic heat transfer boundary conditions on the bulk target external surface.

(b) A “pessimistic” scenario that fixes the lower limit of ^{99}Mo weekly activity that could be provided by NSFS (about 40 TBq). This assumes 3 kg of ^{100}Mo (i.e. half of the volume of the previous case) irradiated for 22 h with a neutron emission rate of 10^{15} s^{-1} . With this constraint, it has been found the maximum admissible volume of a ^{100}Mo target that could be irradiated continuously for 22 h, without melting, that is a plate with the same planar surfaces of the previous case but thickness one half. Thus, the range 40-75 TBq can be referred as a reliable range, that confidently includes the designed performances of NSFS.

In a more realistic target layout (made of multiple piled ^{100}Mo sheets, properly dimensioned and distributed over the irradiation volume, e.g. each having 1 mm thickness) the weekly activity predicted by MC simulations, as expected, lies within the envisaged NSFS working range.

1.3. ^{99}Mo production: FoM definition

Referring to Table 1 and considering the nominal thermal power of the different reactors, a Figure of Merit (FoM) can be defined as $FoM = \frac{A_w}{NP_{th}}$, A_w being the weekly activity of ^{99}Mo (measured in

Bq), and NP_{th} (measured in MW) is the facility nominal power that corresponds, respectively, to the nominal thermal power for reactors and the delivered beam power for accelerator driven facilities. The nominal thermal power and the delivered beam power are the specific parameters representative of the

facility performances with respect to the achievable ^{99}Mo activity. The FoM , as defined above, can be assumed as an efficiency parameter for the specific production facility. Figure 2 reports the $FoMs$ for the main reactors in Table 1 as compared to NSFS for which NP_{th} is 16 MW and $25 < A_w < 75$ TBq.

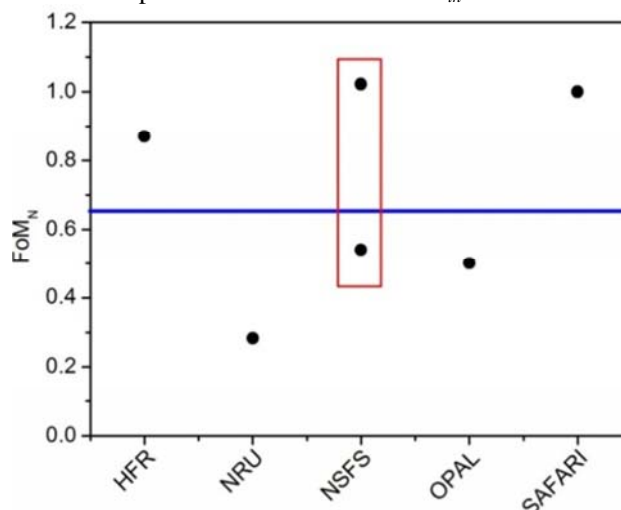


Figure 1: Normalized FoM (FoM_N) for the main fission reactors and NSFS, the normalization value being the FoM of SAFARI fission reactor (see Table 1). The continuous blue line marks the average FoM over the whole set of fission reactors in the plot. The rectangle embeds the minimum and maximum value of the FoM for NSFS (see text for details).

2. Conclusions and perspectives

The production of $^{99}\text{Tc}^m$ using methods alternative to nuclear fission reactors was identified as a social-driven issue to be addressed after the unexpected crisis in 2009. In this context, the use of 14 MeV neutrons to produce $^{99}\text{Tc}^m$ exploiting $^{100}\text{Mo}(n,2n)^{99}\text{Mo}$ reaction is clearly identified as a valuable solution, if really intense sources to feed radiopharmaceutical production were available. An experimental assessment of this approach was carried out in ENEA using a well-defined characterization procedure, based on accurately calibrated 14 MeV neutron beam delivered by FNG, MC simulations and high level traceability of the activity measurements to the national radioactivity primary standards at ENEAS-INMRI. The achieved results and the benchmarked predictive models allow for making a reliable extrapolation of the performances of New Sorgentina Fusion Source (NSFS) for the production of ^{99}Mo , providing a comparison with the radiopharmaceutical production classical chain, based on nuclear fission reactors, in terms of a proper defined figure of merit (FoM).

It is found that the FoM of NSFS is appreciably close to that one of the main (but aged) nuclear fission reactors in the global landscape which cover a quite large fraction of the present $^{99}\text{Tc}^m$ market.

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