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RT/2016/32/ENEA

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M. Capogni, A. Pietropaolo, L. Quintieri

Riassunto

Il ^{99m}Tc è un radionuclide ampiamente usato in tutto il mondo per diagnosi di tipo SPECT (*Single Photon Emission Computed Tomography*) grazie alla sua breve vita media (circa 6 h) e all'emissione di fotoni di bassa energia (140 keV), particolarmente idonei per la strumentazione diagnostica utilizzata. In campo medico, il ^{99m}Tc viene principalmente fornito attraverso il suo precursore ^{99}Mo, che ad oggi viene ricavato essenzialmente come prodotto di fissione di *target* irraggiati in reattori nucleari. Nel 2009 l'Agenzia per l'Energia Nucleare (NEA), a fronte dell'evidenza di un'imminente carenza a livello mondiale di ^{99m}Tc, ha costituito un gruppo di lavoro di alto livello sulla sicurezza nella produzione di radioisotopi medici (HLG-MR) allo scopo di studiare tutti i possibili canali di produzione di ^{99}Mo/^{99m}Tc nel breve, medio e lungo periodo. Come risultato di questa accurata indagine, il HLG-MR ha rilasciato un rapporto che evidenzia come la carenza di produzione di ^{99m}Tc sia principalmente dovuta alla ben consolidata, ma vetusta, catena di produzione, essenzialmente basata su reattori nucleari di vecchia generazione. Il HLG-MR ha anche prodotto una rassegna di differenti tecnologie per la produzione di ^{99}Mo/^{99m}Tc, basata rispettivamente su: a) bersagli HEU (Uranio altamente arricchito) e LEU (Uranio a basso arricchimento) nei reattori a fissione; b) attivazione di ^{98}Mo mediante neutroni termici in reattori nucleari; c) produzione diretta da ciclotroni; d) reazioni di fotofissione in ^{238}U; e) foto produzione di ^{99}Mo e f) reazioni indotte da neutroni veloci.
Nel presente rapporto tecnico, si descrive l'uso di ^{99m}Tc in medicina nucleare focalizzando l'attenzione sulla recente e ben documentata vasta richiesta e critica carenza di tale radionuclide a livello mondiale. Viene, in particolare, discusso il metodo di generazione del ^{99m}Tc per mezzo della reazione ^{100}Mo(n,2n)^{99}Mo. Proprio con riferimento a quest'ultimo canale di produzione, in ENEA è stato recentemente condotto uno studio di fattibilità di produzione del ^{99}Mo, come descritto in dettaglio nel seguito. L'attività di ^{99}Mo, ottenuta irraggiando con neutroni da 14 MeV un bersaglio di Molibdeno naturale presso l'impianto *Frascati Neutron Generator* (FNG), sito nel Centro Ricerche ENEA di Frascati, è stata accuratamente determinata mediante misure riferibili ai campioni nazionali di attività dell'*Istituto Nazionale di Metrologia delle Radiazioni Ionizzanti* (INMRI) presso il Centro Ricerche Casaccia dell'ENEA (Santa Maria di Galeria, Roma). I risultati dell'attività specifica di ^{99}Mo ottenuta in ENEA sono stati confrontati con quelli documentati da un gruppo di ricerca giapponese, che ha usato la stessa tecnica, mostrando un ottimo accordo entro le incertezze di misura.
L'intero esperimento svolto in ENEA e le stime predittive estrapolate dai risultati sperimentali sono state supportate con simulazioni Monte Carlo effettuate con il codice Fluka.
I modelli Monte Carlo sono stati validati attraverso il confronto delle stime di attività prodotte a ENEA-FNG con i corrispettivi valori misurati presso l'ENEA-INMRI, avvalendosi della riferibilità ai campioni primari di attività sviluppati e custoditi nella sezione Radioattività dell'Istituto.
Al fine di confrontare in modo quantitativo l'efficienza di produzione del ^{99}Mo attraverso i metodi implementati nelle diverse tipologie di impianti (acceleratori e reattori), è stata introdotta un'adeguata Figura di Merito (*FoM*) basata sull'attività di ^{99}Mo prodotta dall'impianto e la potenza dello stesso. Ciò ha consentito di valutare l'efficienza di produzione di ^{99}Mo a FNG, permettendo di estrapolare questo dato all'impianto di nuova concezione di neutroni a 14 MeV quale è la *New Sorgentina Fusion Source* (NSFS). Infine, ma non meno importante, è stata introdotta una FoM finanziaria, da considerarsi come un parametro di costo delle varie *facility* prese in esame per la produzione di ^{99}Mo e l'attività prodotta settimanalmente per questo radionuclide.

Parole chiave: Carenza di ^{99m}Tc; produzioni di ^{99}Mo/^{99m}Tc; fasci di neutroni a 14 MeV

Abstract

^{99m}Tc 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. In medicals, ^{99m}Tc is mostly provided through its precursor ^{99}Mo.
In 2009 the Nuclear Energy Agency (NEA) formed the High-Level Group on Security of Supply of Medical Radioisotopes (HLG-MR), in order to study the supply chain of ^{99}Mo/^{99m}Tc in the world for short, medium and long term period. The HLG-MR delivered a report highlighting how the shortage of ^{99m}Tc supply was mostly due to the well-established but aged production chain essentially based on old nuclear reactors. A review of different technologies for producing ^{99}Mo/^{99m}Tc was also provided by the HLG-MR based respectively 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.
In this technical report, the use of ^{99m}Tc in nuclear medicine is discussed focusing on the recently documented great worldwide demand and shortage of this radionuclide. The specific method for producing ^{99m}Tc via ^{100}Mo(n,2n)^{99}Mo reaction is discussed in detail as it was investigated also in ENEA. The ^{99}Mo activity achieved by means of 14 MeV neutron irradiation on natural Molybdenum sample at the Frascati Neutron Generator (FNG) facility, at the Research Centre of ENEA-Frascati, was accurately assessed, by tracing it to the standards provided by the Italian National Institute of Ionizing Radiation Metrology (INMRI), located at the Research Centre of ENEA-Casaccia. The results of ^{99}Mo specific activity obtained at ENEA were then compared with those documented in feasibility studies of a Japanese research group, which used the same technique, showing a good agreement within the uncertainties of measurements. 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 laboratories, Radioactivity
section.
A Figure of Merit (FoM) was then introduced in order to compare the performances of the different methods (accelerator or neutron based) used for ^{99}Mo production. The FoM was obtained by taking into account the ^{99}Mo activity produced and the power of the facility used. This allowed to evaluate the ^{99}Mo efficiency production at FNG and to extrapolate the obtained data to the new infrastructure for generating 14 MeV neutron which is New Sorgentina Fusion Source (NSFS).
Last, but not the least, a financial FoM was introduced in order to take into account the cost parameter of each facility considered for ^{99}Mo production respect to the weakly activity produced for this radionuclide.

Keyword: *^{99m}Tc shortage; ^{99}Mo/^{99m}Tc production; 14 MeV neutron beams*

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Misura ciò che è misurabile, e rendi misurabile ciò che non lo è.
(Galileo Galilei)

1. ^{99m}Tc in Nuclear Medicine and global shortage

Metastable Technetium-99 (^{99m}Tc) is the principal radionuclide used worldwide in medical diagnostics with more than 30 million procedures per year, accounting for 80 to 85% of all Nuclear Medicine diagnostics [1,2]. ^{99m}Tc was discovered by E. Segré and C. Perrier at the University of Palermo in 1937 and it was obtained by bombarding natural Molybdenum with 8 MeV deuterons in the 37-inch cyclotron of Ernest Orland Lawrence's Radiation Laboratory [3].
The short half-life of ^{99m}Tc (about 6h) and the related 140 keV gamma-ray make it well suited to medical imaging, using conventional gamma cameras such as SPECT[1].
^{99m}Tc can be obtained from the decay of Molybdenum-99 (^{99}Mo) that has a half-life of 66 hours. The decay scheme of ^{99}Mo [4] is shown in Figure 1.

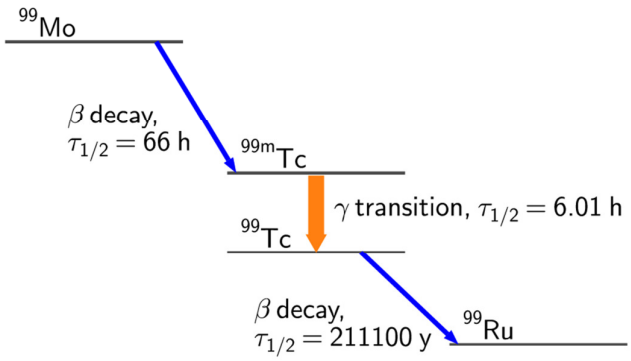

Figure 1 – *Decay scheme of ^{99}Mo*

Molybdenum does not occur free in nature. Its abundance in the Earth's crust is estimated to be about 1-1.5 parts per million. Seven naturally occurring non-radioactive isotopes of Molybdenum exist with the following percentages: ^{92}Mo (14.8%), ^{94}Mo (9.3%), ^{95}Mo (15.9%), ^{96}Mo (16.7%), ^{97}Mo (9.6%), ^{98}Mo (24.1%) and ^{100}Mo (9.6%). At present, ^{99}Mo is almost exclusively provided from the fission of ^{235}U targets (by using primarily highly-enriched Uranium) irradiated in a few number of research nuclear reactors in the world.

1.1. First medical applications and worldwide expansion

The first ^{99m}Tc generator (see Figure 2) was developed at the Hot Lab Division of the Brookhaven National Laboratory (BNL, USA) in 1958 primarily by Walter Tucker and Margaret Greene [5]. Powell Richards, at the same laboratory, suggested in 1960 to use ^{99m}Tc as medical tracer. The first US medical application of this radiopharmaceutical appeared on August 1963 [6,7]. The development and improvement of new diagnostic instruments, such as the gamma camera, produced also a large expansion of the use of radiopharmaceuticals for medical diagnostic applications around the world:

- **USA**: Between 1963 and 1966 the demand for ^{99m}Tc grew exponentially and by 1966 the production and distribution were transferred to private companies, such as Nuclear Consultants, Inc. (St. Louis, Missouri) and Union Carbide Nuclear Corporation (Tuxedo, New York). From 1967 to 1980, ^{99}Mo was produced for Mallinckrodt Nuclear Company at the Missouri University Research Reactor (MURR) using radiative thermal neutron capture on ^{98}Mo, by means of ^{98}Mo (n,γ)^{99}Mo reaction.

[1] Single Photon Emission Computed Tomography

Figure 2 – *the first ^{99m}Tc generator in 1958.*

The process of ^{99}Mo production by irradiation of highly enriched uranium (HEU) targets in nuclear reactors was then investigated by Union Carbide which developed, at the Cintichem facility [8], the process based on 93% highly enriched ^{235}U deposited as uranium dioxide (UO_2) on the inner side of a cylindrical target. At the end of the 1970s, $2x10^5$ Ci (7.4×10^{15} Bq, expressed in the correct SI units) of total fission product radiation (of which about 6% is ^{99}Mo) were weekly extracted using the so-called Cintichem chemical isolation process. Thus considering the percentage of 6% this results in $4.4x10^{14}$ Bq of ^{99}Mo.

- **Europe**: In May 1963, Scheer and Maier-Borst were the first to introduce in Europe the use of ^{99m}Tc for medical applications. In 1968, Philips-Duphar (later Mallinckrodt, presently Covidien) marketed the first ^{99m}Tc generator produced in Europe and distributed it from the High Flux Reactor (HFR) in Petten (the Netherlands).

- **Argentina**: In 1967 Argentina started the first commercial production of ^{99}Mo/^{99m}Tc generators, with the ^{99}Mo produced at CNEA's RA-1 Enrico Fermi reactor (40 kW thermal power). Besides its domestic market, CNEA supplies ^{99}Mo to other South American countries [9].

- **Australia and New Zealand**: In 1967 ^{99m}Tc procedures were carried out in Auckland, with ^{99}Mo initially supplied by Amersham, UK, then by the Australian Nuclear Science and Technology Organization (ANSTO) [10].

- **Canada**: In 1970, the National Research Universal (NRU) reactor facility (135 MW power) started the ^{99}Mo production and by 1978 the reactor provided ^{99m}Tc processed by AECL's radiochemical division. The AECL was, successively privatized in 1988 as Nordion (presently MDS Nordion [11]). In the 1990s, a substitution for the aged NRU reactor to produce radioisotopes was planned. The Multipurpose Applied Physics Lattice Experiment (MAPLE) was designed as a dedicated isotope-production facility. Initially, two identical MAPLE reactors were going to be built at Chalk River Laboratories, each capable of supplying 100% of the world's medical isotope demand. However a problem related to the a positive power reactivity coefficient, of the MAPLE 1 reactor, led to the cancellation of the project in 2008.

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 as shown in Figure 3 [12]. The 6-day Ci is the accepted term used to quantify ^{99}Mo activity for medical purposes and is defined as the amount of ^{99}Mo activity remaining six days after the end of processing (EOP)[2]. The global demand for ^{99}Mo is divided according the following ratios: 53% North America, 23% Europe, 20% Asia and 4% the rest of the world [12].

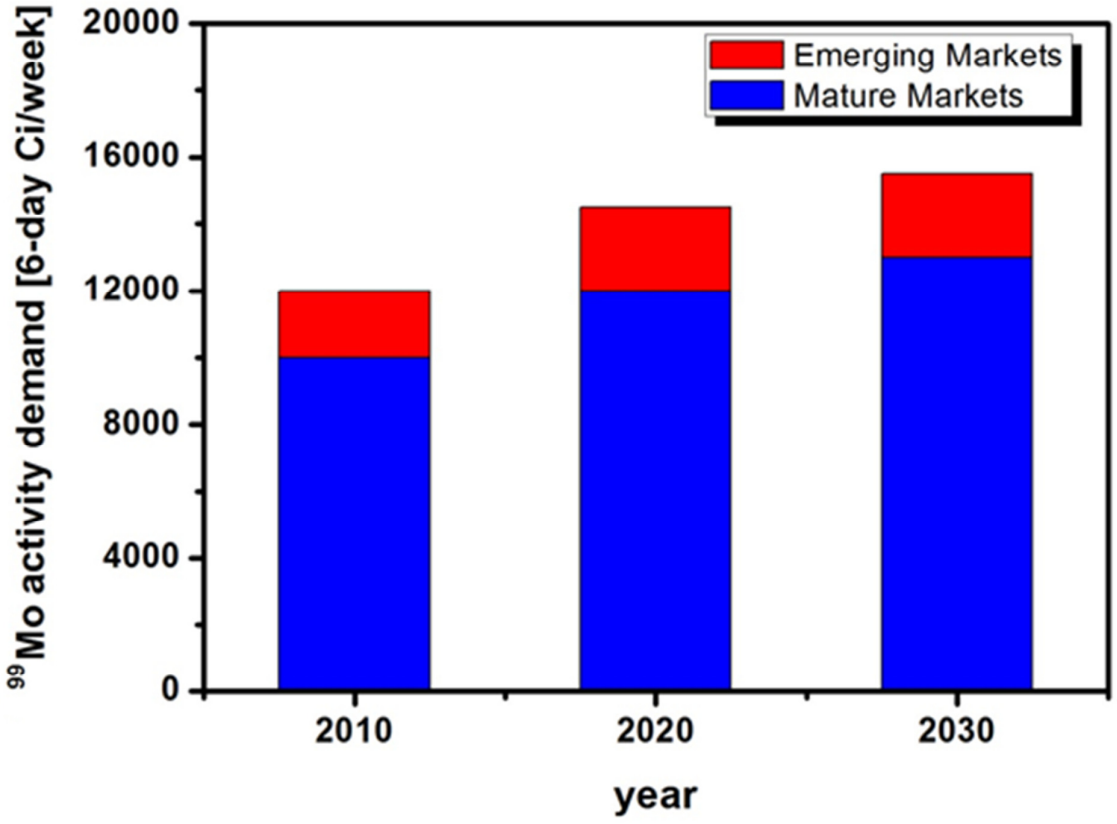

Figure 3: *World ^{99}Mo demand for the next 15 years: quantities are expressed in 6-day Ci activity per week.*

A number of factors may influence the future demand of ^{99m}Tc, namely:
- growing population and urbanisation will drive an increase in access to imaging;
- ageing population and changing prevalence of medical conditions including malignancy will influence demand;
- increased availability of SPECT and SPECT-CT cameras;
- new PET (Positron Emission Tomography) tracers may have an influence, but because of the high cost of PET imaging the relative impact is expected to be low in the short to medium-term.

1.2. Global shortage of ^{99m}Tc

Global shortage of ^{99m}Tc emerged in the late 2000s because the two main reactors (NRU and HFR), 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 production methods.

[2] EOP is defined as the end of preparation of the chromatographic column ready for distribution

In April 2009, the Organization of Economic Co-operation and Development (OECD) and the Nuclear Energy Agency (NEA) constituted the High-Level Group on the security of supply of Medical Radioisotopes (HLG-MR) with the following duties:
- review the total ^{99}Mo supply chain from Uranium procurement from targets to patient delivery;
- identify weak points and issues in the supply chain in the short, medium and long-term;
- recommend options to address vulnerabilities to help ensuring stable and secure supply of radioisotopes.

The world level problem of ^{99m}Tc shortage was clearly outlined in the Paula Gould's paper, appeared on Nature journal in 2009 [13], where it is stressed that "*all five commercial nuclear reactors that use neutron-induced fission of highly enriched ^{235}U to make ^{99}Mo are more than 40 years old and cracks are beginning to emerge*". It is also underlined that the problem of shortfall of ^{99m}Tc, due to the temporary shutdown of the aged nuclear reactors in 2009, arose because both radioisotopes (^{99}Mo and ^{99m}Tc) cannot be stockpiled. This induced physicians to postpone diagnostic procedures or to switch to older diagnostic techniques, thus exposing patients to higher doses of radiation. In the same paper, the author underlines that the Canadian Chalk River reactor (NRU), which produces close to one-third of current global supplies, is scheduled to end production of isotopes in the next few years. At present, just a few nuclear reactors around the world 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. Table 1 and figure 4 provide a complete landscape of the worldwide ^{99}Mo production from reactors [14].

Table 1*: Main characteristic of worldwide reactors used for ^{99}Mo production*

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

(a) 6-day Ci at the End of Process (EOP).

(b) Fuel elements and targets are classified as either Low enriched Uranium (LEU) with < 20% ^{235}U ad High Enriched Uranium (HEU) with < 20% ^{235}U (in some cases greater than 95%).

(c) Does not account for increase in capacity since April 2010 with the installation of additional irradiation capacity.

(d) These reactors started production in 2010 so some data are not available.

(e) The LVR-15 reactor uses HEU at 36% enrichment in ^{235}U.

(f) The OPAL reactor started ^{99}Mo production in 2009 mostly for domestic use.

(g) In 2010 the fuel element changed into LEU.

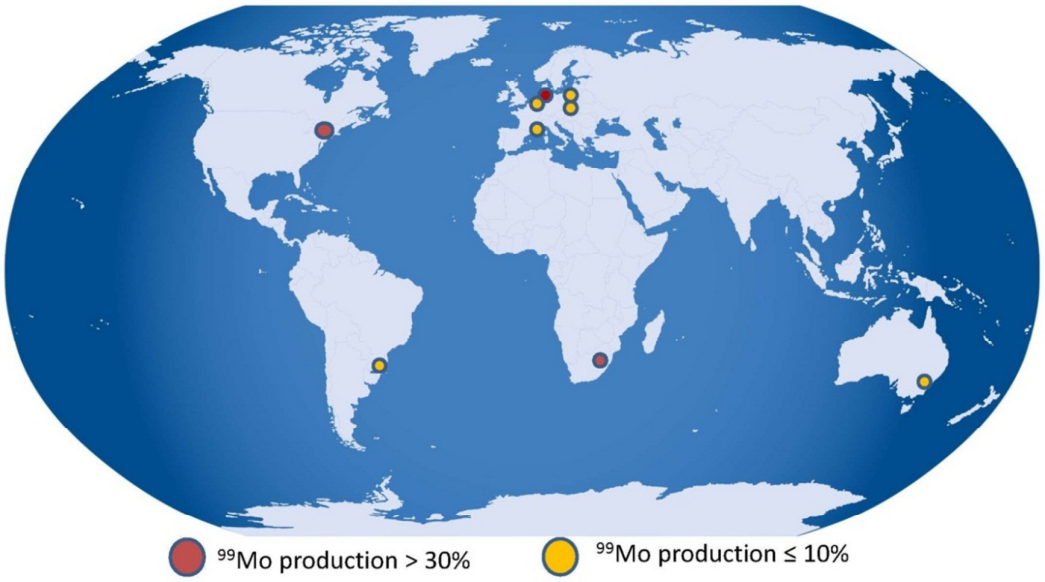

Figure 4 – *Present ^{99}Mo suppliers in the world [15]. Red points indicate a fraction of the total worldwide production greater than 30%, yellow points below 10%.*

2. ^{99m}Tc production methods

Whilst irradiation facility relying on fission reactors have generally been used to produce ^{99}Mo, accelerator-based methods may be used for producing either ^{99}Mo or directly ^{99m}Tc. As a matter of fact, direct ^{99m}Tc production restricts the distance between production site and final users with respect to the case of ^{99}Mo, because of their very different half-lives. The choice between these different approaches thereby has a direct and strong effect on the supply chain and the related infrastructures. Indeed, ^{99}Mo may be produced far from the end-users, whilst ^{99m}Tc most likely must be used within a few hour transport time from its site of production.

Three general methods of radionuclides productions have been identified:

a) Thermal or fast neutron beams to transmute target nuclides, which in turn decay emitting electrons or gammas;

b) Accelerated charged-particle beams which usually produce neutron-deficient isotopes that decay by electron capture and emissions of x-rays, γ-rays and positrons;

c) Gamma-ray beams for radioisotope photo-production.

In the case of ^{99}Mo production, accelerator-based technologies, not requiring Uranium target, may rely on the following physical processes:

a) Photonuclear reactions on ^{100}Mo: ^{100}Mo(γ,n) ^{99}Mo;

b) Direct production of ^{99m}Tc by bombarding ^{100}Mo enriched target with accelerated protons: ^{100}Mo(p,2n) ^{99m}Tc;

c) Inelastic reactions on ^{100}Mo induced by accelerator-driven fast neutrons: ^{100}Mo(n,2n)^{99}Mo.

In the following two neutron based methods are described, namely fission in reactors and inelastic reaction in accelerator driven facilities. The former is nowadays the main production method worldwide, while the latter is the alternative method discussed in this report.

2.1 Nuclear fission reactor-based production

The main ^{99}Mo production route is based on fission of highly enriched uranium (HEU) targets [16,17] in nuclear reactors of moderate to-high power (*i.e.* > 1 MW), where intense thermal neutrons fluxes are available.
^{99}Mo can be separated from the original HEU target by means of chemical processes.
The advantages and disadvantages of the nuclear reactor based method may be summarised as follows:

Advantages:

- Intense fluxes of neutrons typically available
- High efficiency of ^{99}Mo fission fragment production
- High ^{99}Mo specific activity
-

Disadvantages:

- Large capital costs for building
- Difficult licensing procedures
- Significant waste stream
- Long lasting infrastructure construction time
- Large capital costs for decommissioning the facility

In Figure 5, the supply chain of the ^{99}Mo/^{99m}Tc is shown starting from the source to the end-users.

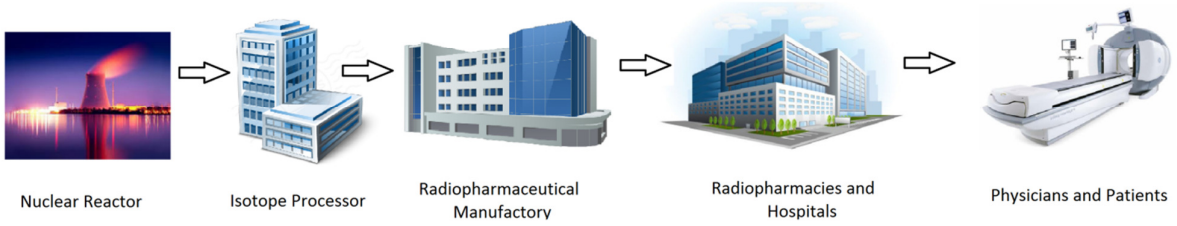

Figure 5 – *Supply chain of ^{99}Mo/^{99m}Tc: from the reactors to the Hospitals [18]*

Highly enriched uranium (HEU) is preferably used by main manufacturers (see Tab. I), nevertheless nuclear non-proliferation and security concerns have led to an increased worldwide request to migrate from weapon grade HEU towards low-enriched uranium (LEU).
In this framework, the OPAL reactor in Australia is already using low-enriched target plates when making ^{99}Mo and runs on low-enriched Uranium fuel, which cannot be diverted to weapons.

2.2 Inelastic fast neutron reactions on ^{100}Mo

^{100}Mo(n,2n)^{99}Mo reaction with 14 MeV neutrons [19] has been identified as a feasible and effective alternative method to fission reactors.
Indeed, the ^{100}Mo(n,2n)^{99}Mo cross section is appreciable and exhibits a maximum around 14 MeV as shown in Figure 6.

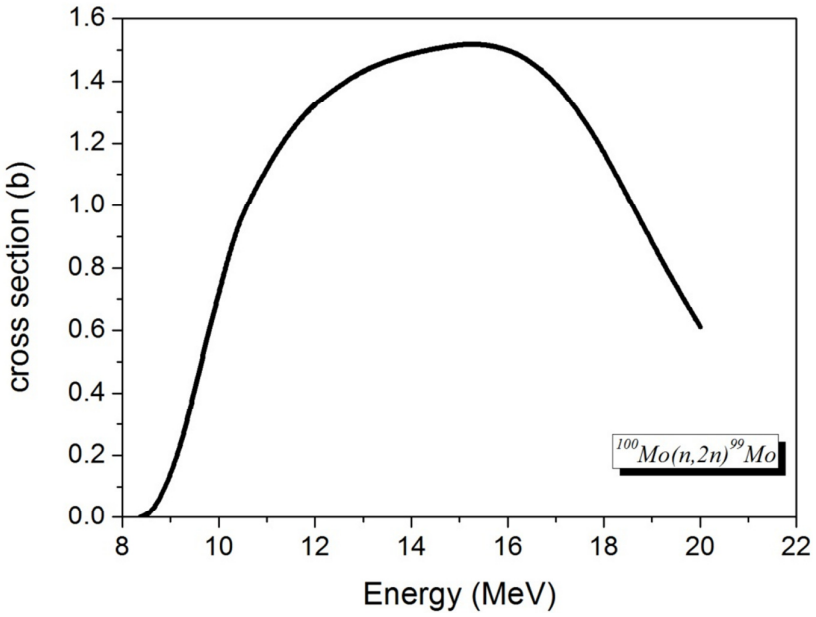

Figure 6: *Cross section of the nuclear reaction $^{100}Mo(n,2n)^{99}Mo$ as a function of the neutron energy.*

This approach was tested in 2015 from a Japanese group, which provided a first complete assessment of ^{99m}Tc production and the characterization of the radiochemical chain to produce the radiopharmaceuticals by 14 MeV neutron beam. They succeeded in separating ^{99m}Tc from a 7.9 g of MoO_3 sample, enriched 99.98% ^{100}Mo. The 14 MeV neutron beam was provided by the D-T reaction at the Fusion Neutronics Source of Japan Atomic Energy Agency. The measured absolute total activity was about 21 MBq [20], *i.e.* a ^{99}Mo specific activity of about 4 MBq g^{-1}. Moreover, the radiopharmaceutical they produced using a thermo-chromatographic separation technique (and used for a SPECT on mice) fulfils the US pharmacopeia requirements [21].
In Italy a 14 MeV neutron sources operates at the Frascati Research Centre of ENEA, namely *Frascati Neutron Generator* (FNG) [22].

3. ^{99}Mo production at the ENEA *Frascati Neutron Generator* (FNG) and perspectives on the *New Sorgentina Fusion Source* (NSFS).

The ENEA *Frascati Neutron Generator* (FNG) is an accelerator driven continuous neutron source [22]. It relies on Deuteron-Tritium (DT) reactions in turn producing almost monochromatic 14 MeV neutrons with a maximum neutron emission rate of 10^{11} s^{-1}. The deuterons are accelerated by means of an electrostatic accelerator up to 300 kV and 1 mA current and directed onto a Titanium target loaded with Tritium, where D-T fusion reactions take place. The neutron yield is determined by means of an absolute measurement, the so-called associated alpha particle technique. Indeed the D-T reaction produces in the final state a neutron and an alpha particle following the reaction $D+T \rightarrow n+\alpha+Q$, where Q=17.1 MeV is the energy released in the reaction (in the form of 14.1 MeV kinetic energy of neutron and 3.6 MeV kinetic energy of α). The measurement of the number of alpha particles by means of an energy calibrated silicon detector, subtending a small and well defined solid angle to the fusion target, provides the absolute number of neutrons produced at the target. Simulations, benchmarked by means of experimental measurements, provide a neutron yield and flux determination within an uncertainty of 3%. The FNG neutron spectrum and the corresponding neutron fluxes are plotted in Figure 7.

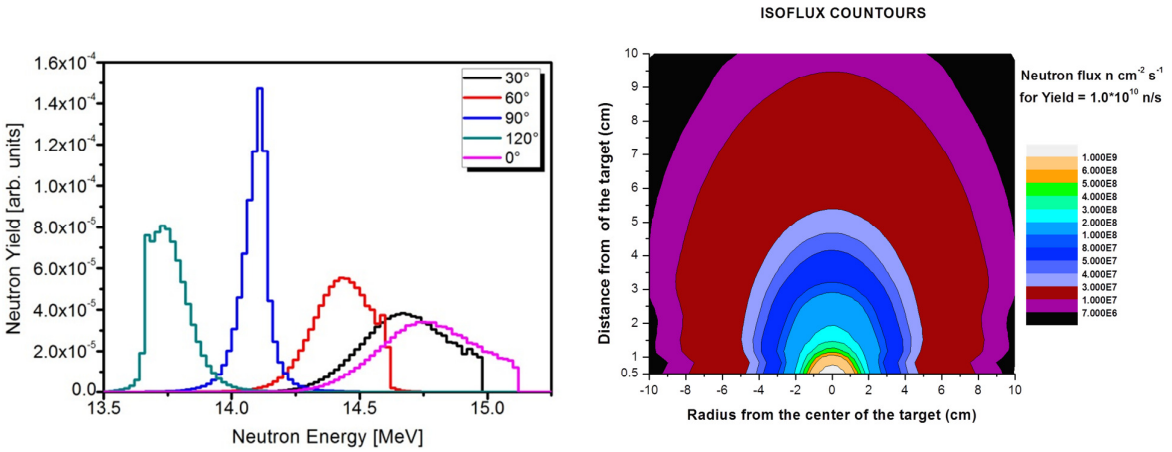

Figure 7: *(left) FNG Neutron spectra as a function of the angle; (right) iso-flux map of FNG.*

New Sorgentina Fusion Source (NSFS) [23,24] is a project of an intense 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 4-5 10^{15} s^{-1}.
Deuterons, accelerated at about 200 kV and 20 A current, impinge onto a rotating target where Tritium is implanted onto Titanium tablets (about 10 x 20 cm^2) positioned on the outer layer of a stainless steel wheel (see Figure 8). Rotation and cooling of the target is mandatory to cope with the high power density deposition (20 kW cm^{-2}). Together with the deuteron beam, a triton beam with the same characteristics is directed onto the target to implant Tritium nuclei into the target to maintain fusion reactions. To enhance the neutron flux a double wheel configuration is designed so to provide an "intense flux volume" (about half a litre in the original design) where the average neutron fluence rate (peaked around 14 MeV) should be about 10^{13} s^{-1} cm^{-2}.

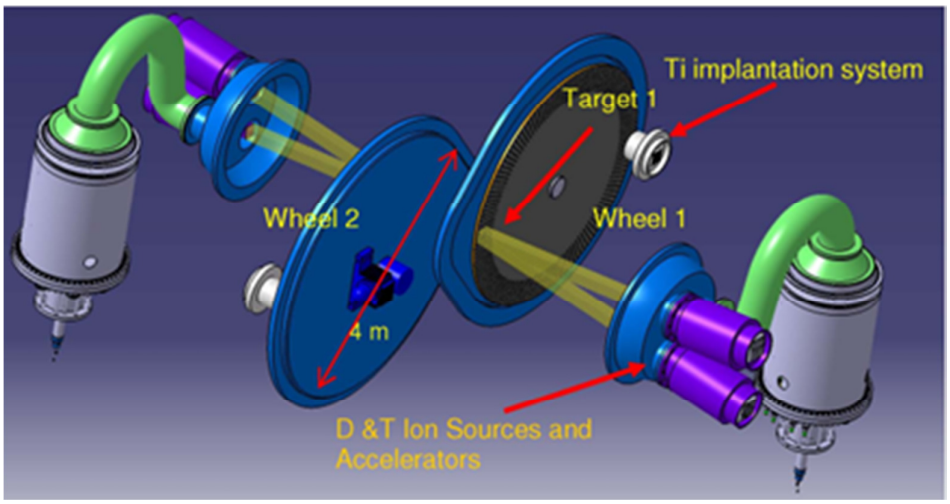

Figure 8: *3D schematic representation of SORGENTINA's targets and accelerators*

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 and unique laboratory in the European context to test and validate the NSFS's capabilities and performances.
Indeed, a preliminary methodological approach has been already assessed that involved both experimental measurements and Monte Carlo (MC) computations, as described in detail in the following.

3.1 Experimental ^{99}Mo production and activity measurements at ENEA

As far as measurements are concerned, a natural Molybdenum sample was irradiated at ENEA-FNG for about 15 minutes with an isotropic neutron source emission rate of 2.89×10^{10} s^{-1} . The obtained first results show that a ^{99}Mo specific activity of about (2.30 ± 0.04) kBq g^{-1} [25] was produced, in good agreement (within 7%) with the MC predictions.

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:

- use of an energy well-defined neutron source, determined by the *D+T* reaction, with a well-defined emission rate, determined by the absolute technique of the associated alpha particle;
- MC calculations to optimize the experimental set-up and irradiation;
- accuracy and traceability at high metrological level of the ^{99}Mo and ^{99m}Tc activity measurements and MC benchmarking.

Our results, after a proper normalization in order to take into account the different experimental conditions, are coherently comparable to those published in reference [19], providing a consistent and reliable estimation of the measured specific activities.

3.2 Monte Carlo predictions for NSFS

Starting from the results achieved at ENEA, by using the ENEA-FNG facility for the ^{99}Mo production, an extrapolation of the achievable ^{99}Mo activity at NSFS has been derived, considering that the NSFS source can be operated in continuous mode, providing a neutron emission rate of at least 10^{15} s^{-1} (reliably 4.0×10^{15} s^{-1}). Moreover, in support of this extrapolation, several MC simulations have been performed as well, to predict the ^{99}Mo total activity obtained with targets of different geometry, made of pure ^{100}Mo, for several irradiation profiles (i.e. neutron rates and time windows of irradiation), at different cooling times after the neutron beam shutdown. The activities of all other radionuclides produced during the irradiation have been also estimated. In order to provide “reliable” and “conservative” predictions of the ^{99}Mo production capabilities at NSFS, a preliminary study has been carried out to identify the most important physical operative constraints that could actually limit the operability of NSFS (by identifying a reasonable duty-cycle). The irradiation modalities are, in fact, mainly related to the thermo-mechanical issues that a ^{100}Mo target can experience when the maximum NSFS neutron emission rate is used for a long irradiation time (without using any cooling system), attempting to maximize the ^{99}Mo activity. The optimization of the target and the definition of an adequate irradiation duty cycle (with respect to main features of the facility) require to couple the nuclear analysis with the thermo physical one. A detailed treatment of engineering design aspects is out of the intent of this report. Nevertheless, two experimental configurations have been assessed, on the base of a conservative and “well-posed” hypotheses, that allow to identify reasonable limits of productivity range, in terms of ^{99}Mo activity, for NSFS. The goal is to maximize the (weekly) production of ^{99}Mo: once chosen the material target, several other parameters can affect the total amount of ^{99}Mo activity, such as the target mass, the geometrical source-target set-up (*i.e* the distance), the irradiation time and the neutron emission rate of the facility. Supposing an operative neutron emission rate of 10^{15} s^{-1} and identifying an optimum irradiation time of 22 hours (from the decay time curve of the transient equilibrium between ^{99}Mo, precursor, and ^{99m}Tc, daughter, as shown in figure 9), two experimental scenarios can be established as delimiting the predictable NSFS ^{99}Mo production capabilities:

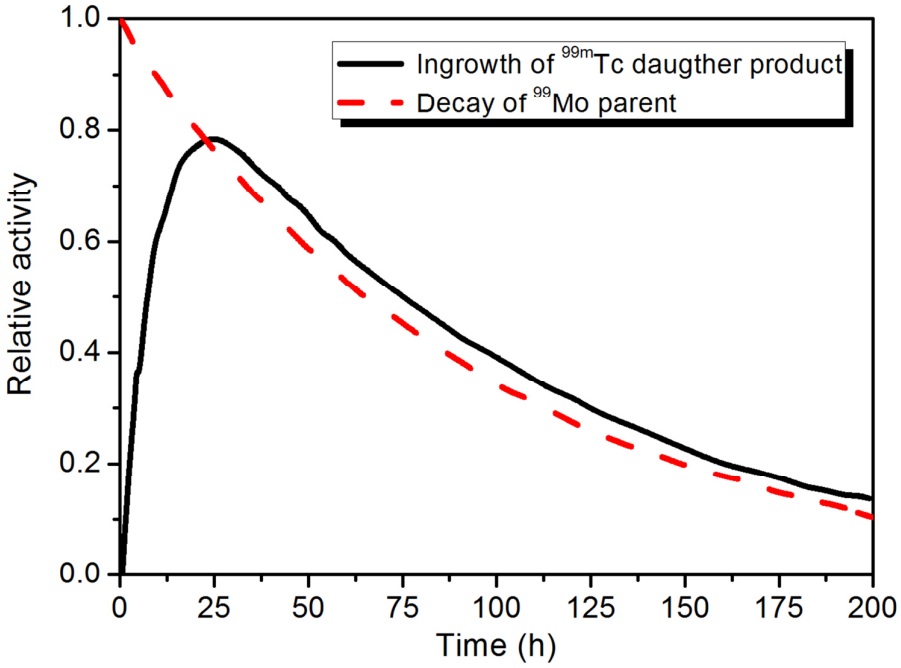

Figure 9: *Trend of the relative activity of ^{99}Mo formed during ^{100}Mo irradiation and ^{99m}Tc. The crossing point of ^{99}Mo decay curve and the ingrowth of the ^{99m}Tc daughter product is the best irradiation time.*

(a) An "optimistic" scenario that fixes the upper limit of ^{99}Mo weekly activity that could be provided by NSFS (about 75 TBq).

This value has been obtained by supposing to fill the irradiation volume between the two NSFS target wheels (0.5 litres) with a solid ^{100}Mo target (corresponding to almost 6 kg), irradiating it continuously for 22 h with a neutron emission rate of 1 10^{15} s^{-1}. In this case, without taking into account any thermo physical parameters, but relying only on nuclear considerations (estimation of reaction rates), a maximum activity of 25 TBq has been estimated by MC simulations at the End Of Irradiation (EOI). This value, extrapolated on a weekly based duty cycle, means almost 75 TBq per week. The hypothetical weekly duty cycle used to derive the total ^{99}Mo activity presumes to have only three days per week allocated for irradiation (leaving the rest of the time for technical operations). 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 (2900 K). This result was obtained making extremely conservative assumptions on the target heat transfer, *i.e.* adiabatic boundary conditions on a bulk target external surface. The energy deposited in the target, that causes the heating of the target itself, is mainly due (more than 80%) to the electromagnetic radiation ensuing the inelastic interaction of neutrons with the target nuclei. In figure 10, charged particles (e^-, e^+, p, α, *etc*) and gamma rays, produced inside the target, are shown together with the deposited energy density (total and electromagnetic one, respectively): all values are per primary particle[3]. The estimations have been obtained by Fluka (version 2011.2c.3) code [26], supposing a uniform and isotropic irradiation with 14 MeV neutrons coming from the NSFS wheel surfaces. More realistically, the temperature distribution inside the target should be evaluated taking into account the heat transfer by irradiation and possible target cooling systems, if eventually foreseen. Anyway, this issue will be properly addressed in an upcoming work, not being a principal concern of this report.

[3] The effective rate of particle produced and the expected power density deposition in the target are obtained by multiplying the values shown in the figure by the real rate of primary particle emitted by the source.

(b) A "pessimistic" scenario that fixes the lower limit of ^{99}Mo weekly activity that could be provided by NSFS (about 40 TBq).

If 3 kg of ^{100}Mo (*i.e.* half of the volume of the previous case) were irradiated for 22 h with a neutron emission rate of 1×10^{15} s^{-1}, NSFS would be able to produce 13.5 TBq at EOI. This implies that, considering a duty cycle made of 3 irradiations of 22 h each, in 6 days, almost 40 TBq can be produced weekly. This lower limit of the ^{99}Mo production for NSFS has been identified by choosing a target configuration for which the maximum temperature is kept lower than a safe margin of 2500 K (i.e. about 400 K below the Mo melting point) during all the irradiation time. 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.

Finally, 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.

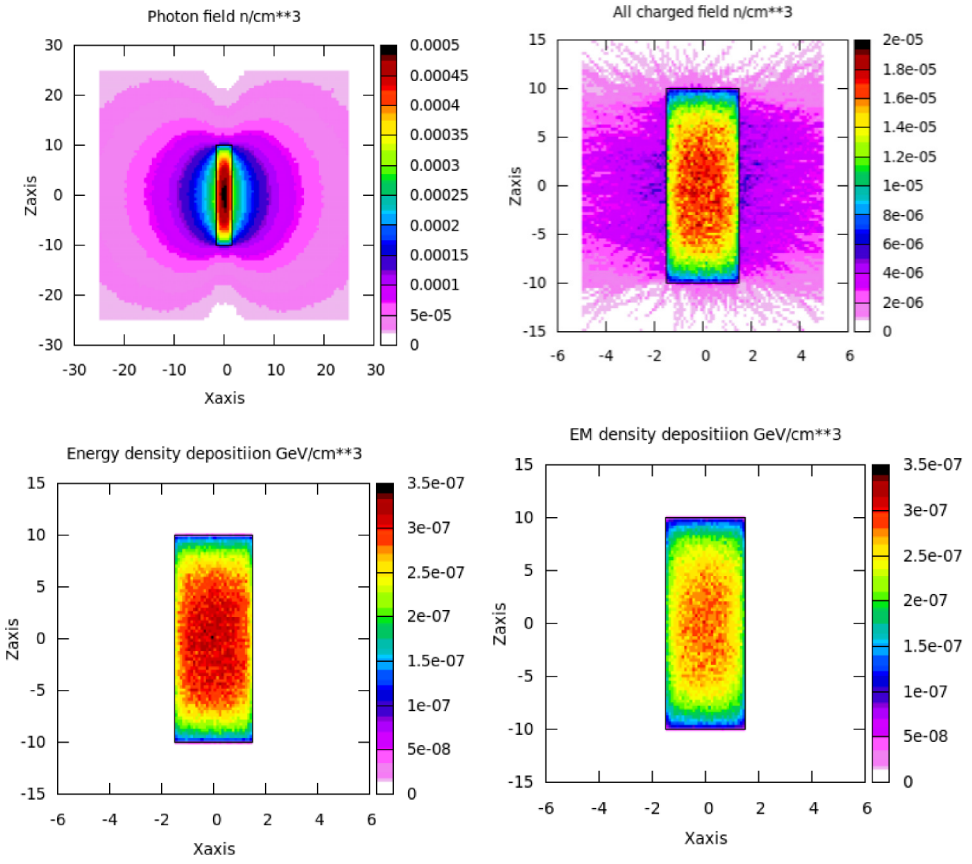

Figure 10: ^{100}Mo *target for NSFS (3x10x20 cm^3) irradiated uniformly with 14 MeV neutrons: (a. upper left): gamma density, (b. upper right): total charged particle density, (c. lower left): total energy deposition; (d. lower left) electromagnetic energy deposition. Data obtained by using MC Fluka code. All the results are per unit primary particle.*

In Table II, the activity of all long-lived residual nuclei produced in a target of ^{100}Mo at the end of 14 MeV neutron irradiation is reported, together with the data on the production reactions and the concerned main decay channels.

Table II: *Activities [Bq] of residual nuclei at the End of Irradiation (EOI) time of 3 kg of* ^{100}Mo *with an isotropic 14 MeV neutron field (total emission rate* 1×10^{15} s^{-1} *from both the* 10x20 cm^2 *NSFS wheels). Refs. [27] for decay data and [28] for cross section values, respectively.* A_T *is the total activity,* A_S *the specific activity, RC is the reaction channel,* σ *is the cross section evaluated at 14 MeV, DN is the daughter nucleus, DM is the decay mode,* E_γ *the gamma-ray energy and* I_γ *the intensity of gamma-ray emission*

Z	Nuclei	A_T [Bq]	A_S [Bq g^{-1}]	RC	σ [b]	DN	$T_{1/2}$	DM	E_γ [keV]	I_γ
40	^{97}Zr	7.4×10^{10} (3%)	2.6×10^{7}	^{100}Mo(n,α)^{97}Zr	2×10^{-3}	^{97}Nb$_{41}$	16.7 h	β$^-$	743.4	0.93
41	^{97}Nb	7.0×10^{10} (3%)	2.4×10^{7}	^{97}Zr decay	-	^{97}Mo$_{42}$	72.0 m	β$^-$	657.9	0.98
	^{99}Nb	4.1×10^{8} (47%)	1.4×10^{5}	^{100}Mo(n,np)^{99}Nb	3×10^{-4}	^{99}Mo$_{42}$	15.0 s	β$^-$	137.7	0.81
	^{100}Nb	6.0×10^{10} (4%)	2.1×10^{7}	^{100}Mo(n,p)^{100}Nb	4×10^{-3}	^{100}Mo$_{42}$	2.9 s	β$^-$	535.6	0.95
42	^{99}Mo	1.4×10^{13} (0.1%)	4.7×10^{9}	^{100}Mo(n,2n)^{99}Tc	1.5	^{99}Tc$_{43}$	65.9 h	β$^-$	739.5	0.12
	^{101}Mo	4.6×10^{11} (1%)	1.6×10^{8}	^{100}Mo(n,γ)^{101}Mo	1×10^{-3}	^{101}Tc$_{43}$	14.6 m	β$^-$	589.1	0.19
43	^{99}Tc ^{99m}Tc	3.5×10^{4} (0.1%) 7.9×10^{12} (0.1%)	12 2.7×10^{9}	^{99}Mo decay	- -	^{99}Rb$_{44}$	2×10^{5} y 6 d	β$^-$	140.5	0.89
	^{100}Tc	4.6×10^{11} (1%)	1.6×10^{9}	^{101}Mo decay	-	^{101}Rb$_{44}$	14.2 m	β$^-$	306.8	0.89

3.3 Technical and financial Figures of Merit

Referring to Table 1 and considering the nominal thermal power of the different reactors, a Figure of Merit (*FoM*) can be then defined as follows:

$$FoM = \frac{A_W}{NP_{th}} \qquad (\text{Bq MW}^{-1}) \tag{1}$$

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 (and indirectly of the costs). The *FoM*, as defined above, can be assumed as an efficiency parameter for the specific production facility. In Table III the comparison in terms of calculated *FoMs* is made among the main fission reactors listed on Tab. I and NSFS (which is an accelerator-driven neutron

source). In Table IV a comparison is made also between an electron Linac-based facility for photo-production of ^{99}Mo and NSFS, the NP_{th} in the case of Linac being the e-beam delivered power.

Table III: *Nominal Power (NP_{th}), weekly activities and related Figures of Merit (FoM) for fission reactors and accelerator driven 14 MeV neutron source (NSFS as reference term). For reactors, NP_{th} represents the thermal power, whilst in case of NSFS is the D/T beam power.*

Fission Facilities	*Age Facility* **[year]**	NP_{th} **[MW]**	A_W **[Bq]**	*FoM* $[A_W/NP_{th}]$ **[Bq MW^{-1}]** 10^{12}
HFR-PETTEN [29]	55	45	$1.8\ 10^{14}$	4.0
SAFARI-PELINDABA [30]	51	20	$9.2\ 10^{13}$	4.6
NRU-CHALK RIVER [31]	59	135	$1.8\ 10^{14}$	1.3
OPAL-SYDNEY [32]	10	20	$4.6\ 10^{13}$	2.3
D-T Fusion sources				
NSFS	-	16	$4.0 \div 7.5\ 10^{13}$	$2.5 \div 4.7$

Table IV: *Delivered Power (DP), weekly activities and related Figures of Merit (FoM) for accelerator driven photo-production sources [33,34] and 14 MeV neutron sources (NSFS as reference term).*

Accelerator driven	**Delivered Power *DP* [MW]**	A_w **[Bq]**	**FOM [*Aw/DP*] [Bq MW^{-1}]** 10^{12}
Photonuclear (γ,n)*	0.1	$1\ 10^{12}$	10*
Neutron Inelastic Scattering (n,2n)	16.0	$4.0 \div 7.5\ 10^{13}$	$2.5 \div 4.7$

Data extrapolated by the activity values claimed in [33] and considering a 100% duty cycle

In the calculation of the *FoM* for NSFS, a "preliminary designed" power of 16 MW has been assumed. A more calibrated choice of the deuteron beam parameters (especially incident energy) may certainly result in an enhancement of irradiation performance. Thus, the *FoM* values calculated for NSFS may be considered as a conservative and slightly underestimated.

As far as photo-production (e-Linac) facilities is concerned, a typical configuration of the electron beam was considered delivering an average power around 100 kW with an electron energy E_e=35 MeV.

Although the *FoM* for the photo-production facility is a factor more than two higher with respect to NSFS, nevertheless, in order to achieve the same weekly activity, a rescaled number of Linac-based facilities should work in parallel.

In figure 11, the calculated *FoM*s reported in Table IV and V are plotted as a function of the weekly activity. In the same plot the weekly demands for USA, Canada and Italy have been also highlighted. It is worthy to stress that the Italian weekly activity has been obtained by interpolating the USA and Canada referenced values, according the respective populations.

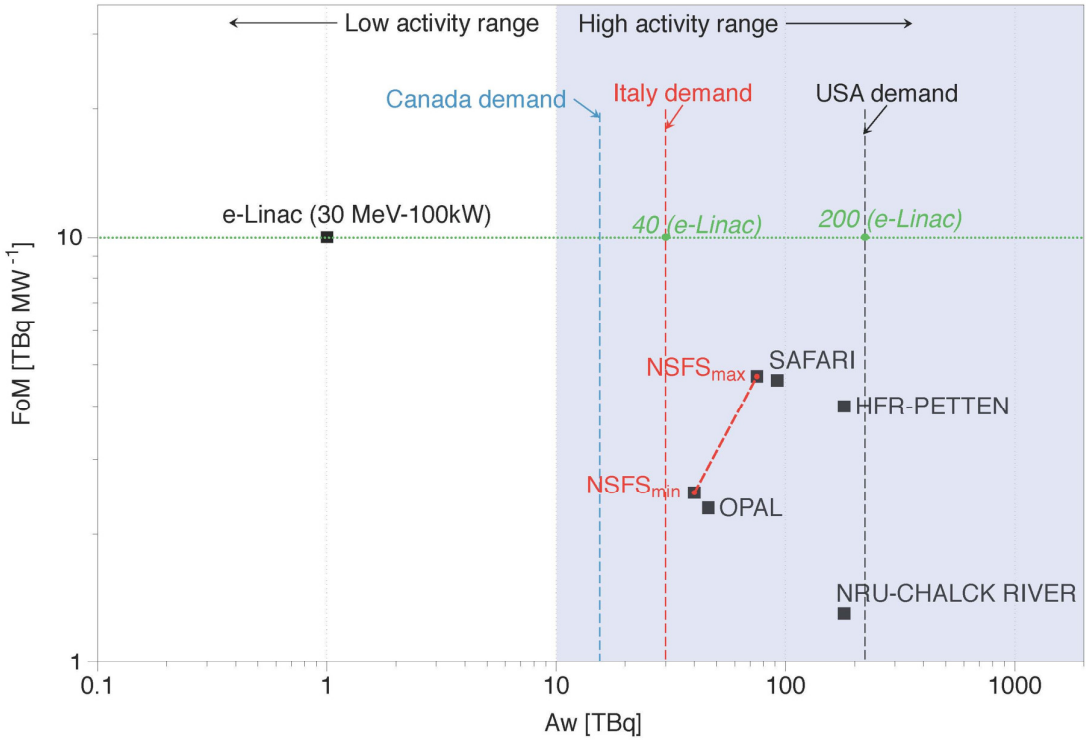

Figure 11: *Figure of Merit (FoM), defined as the ^{99}Mo weekly activity per unit facility nominal power. Nuclear fission reators FoM compared to accelerator-driven neutrons sources (see Tab. I for reference). Vertical dashed lines show the ^{99}Mo demand for the indicated countries.*

In Figure 12, the normalized *FoM* (FoM_N) for Table III only are plotted, the normalization factor being the SAFARI's *FoM*

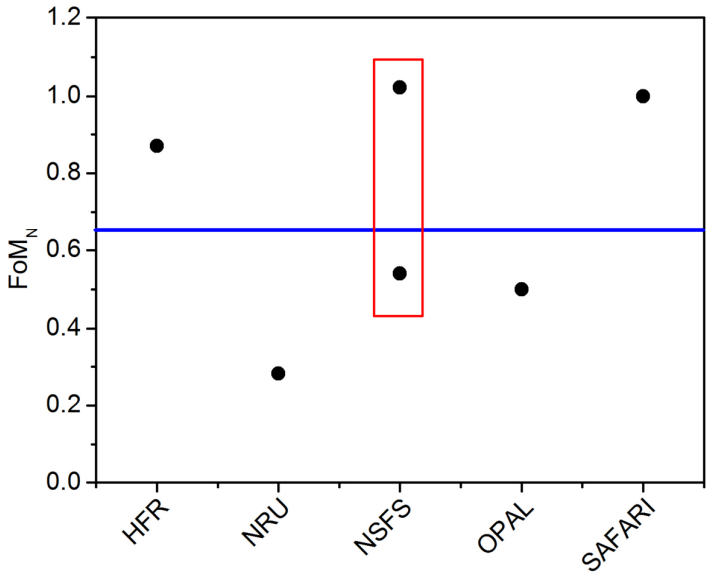

Figure 12: *Normalized FoM (FoM_N) for the main fission reactors and NSFS, the normalization value being the FoM of SAFARI fission reactor (see Table 1). The continuous blue line marks the average FoM over the whole set of fission reactors in the plot. The rectangle embeds the minimum and maximum value of the FoM for NSFS (see text for details).*

Together with the *FoM* defined in Eq. (1), that identifies the technical and operational performances of the facility, it could be useful to introduce a financial Figure of Merit, hereafter called ε, that describes the cost parameter of the facility, in terms of the ^{99}Mo weekly activity produced normalized to an estimation of the overall weekly costs of the facility [35], indicated as C_W.

$$\varepsilon = \frac{A_W}{C_w} \quad (\mathrm{Bq\,M\,€^{-1}}) \tag{2}$$

In figure 13, the ε values are shown for the facilities listed in Table III.

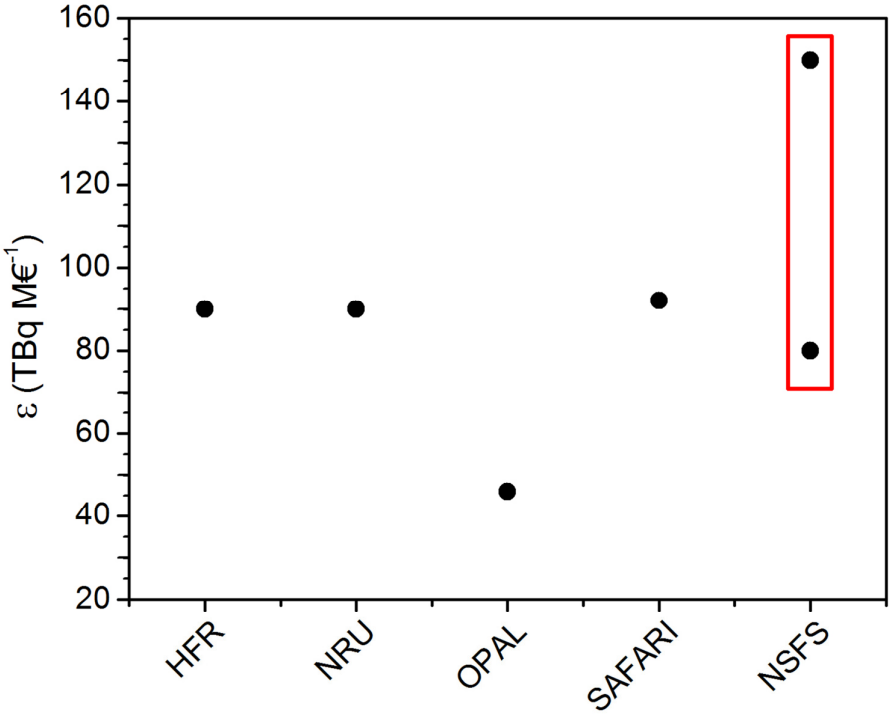

Figure 13: *Cost parameter for the different neutron based facilities for ^{99}Mo production.*

Due to the lack of official data for the overall cost of the reactor facilities listed in Table III, ε was estimated relying on the information related to the annual cost of a research fission reactor of the same power class (P_{th}=58 MW). As a matter of fact the initial cost of NSFS may be about one order of magnitude lower than the one for a medium power research reactor.

It is noteworthy to highlight that, together with ^{99}Mo, NSFS would be capable of producing a series of other radionuclides interesting for medical applications using inelastic reactions of 14 MeV neutrons,. Although out of the scopes of the present report, following Ref. [36] a list of possible radionuclides that could be produced at NSFS is provided in Table V.

Table V: *Short-lived (T_i < 1 day) radionuclide production yields at saturation with neutron fluence rate 10^{10} cm^{-2} s^{-1} 14 MeV neutrons by (n, 2n) reactions [30].*

Target	Radionuclide	T_i	Yield [Bq g^{-1}]×3.710^4
^{19}F	^{18}F	108 min	406
^{45}Sc	^{44}Sc	4.0 h	670
^{59}Co	^{58}Co	9.15 h	1103
^{63}Cu	^{62}Cu	9.7 m	1285
^{65}Cu	^{64}Cu	12.8 h	2382
^{64}Zn	^{63}Zn	34.8 min	417
^{70}Zn	^{69}Zn	57 min	3008
^{69}Ga	^{68}Ga	60.3 min	2246
^{71}Ga	^{70}Ga	21.1 min	2190
^{76}Ge	^{75}Ge	83 min	2579
^{80}Se	^{79m}Se	3.9 min	1372
^{82}Se	^{81}Se	57 min	1896
^{79}Br	^{78}Br	64 min	1911
^{87}Rb	^{86m}Rb	1.0 min	1735
^{86}Kr	^{85m}Kr	4.4 h	651
^{95}Ru	^{96}Ru	1.65 h	1029
^{110}Pd	^{109}Pd	15.5 h	2935
^{106}Ag	^{107}Ag	24 min	1514
^{113}In	^{112m}In	21 min	1904
^{112}Sn	^{111}Sn	35 min	1870
^{136}Xe	^{135}Xe	9.15 h	2025
^{191}Ir	^{190}Ir	3.2 h	1653
^{198}Pt	^{197}Pt	18 h	922
^{200}Hg	^{199m}Hg	43 min	639
^{181}Ta	^{180}Ta	8.1 h	1011
^{150}Nd	^{149}Nd	1.73 h	1855
^{165}Ho	^{164m}Ho	8.06 h	1138

4. The situation of radiopharmaceutical industry in Italy

An extensive production of radiopharmaceuticals (such as [^{18}F] FDG, ^{64}Cu, ^{124}I and other isotopes of iodine) by using biomedical cyclotrons started in Italy more than ten years ago in many Radiopharmaceuticals Production Centers (RPCs), located in different regions of the country. At the same time an intensive research program [37, 38, 39] started at ENEA-INMRI for developing and maintaining new primary standards of short-lived radionuclides, which are typically used in Nuclear Medicine (NM) for diagnostic and therapy, in order to face with a growing request for calibrating instruments, such as dose calibrators based on well-type ionization chambers, typically used in the RPCs and in Nuclear Medicine Departments (NMDs). In order to harmonize around the world the activity measurements of short-lived radionuclides used in NM, a large standardization program was promoted by the Consultative Committee of Ionizing Radiation (CCRI) – Section II (Radionuclides) under the auspices of the *Bureau International des Poids et Mésures* (BIPM). In particular, in order to assure the traceability of the activity measurements of short-lived radionuclides carried out around the world, a transfer instrument (TI) for linking a particular National Metrological Institute (NMI) to the International Reference System (SIR) for short-lived gamma emitters [40] was developed by BIPM. By using the BIPM SIR-TI, ENEA-INMRI was

linked to the BIPM-SIR both for ^{18}F [41] and ^{99m}Tc. In Figure 14, the degrees of equivalence of the activity measurements for different NMIs of the world for the specific case of ^{99m}Tc [42] are shown.

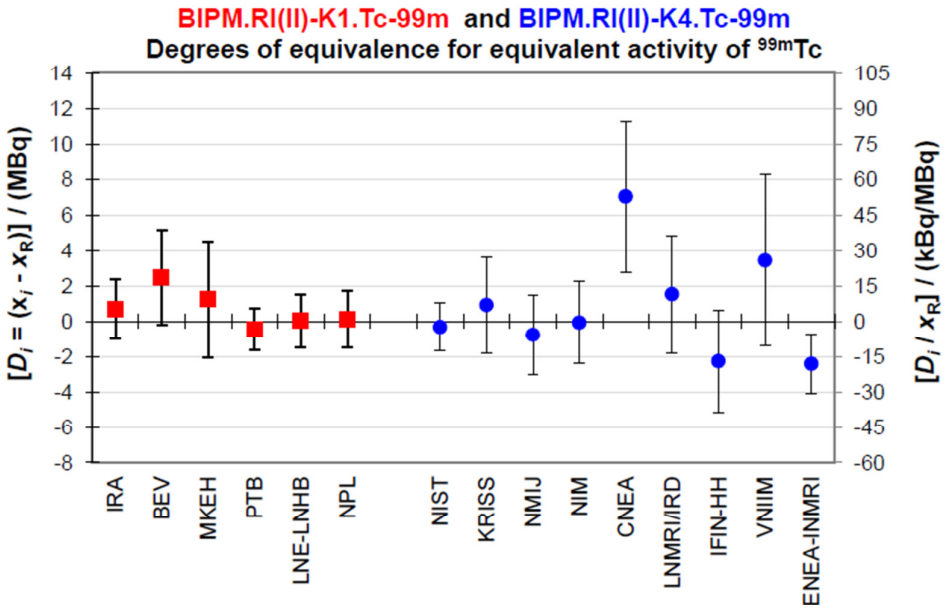

Figure 14: *Degrees of equivalence of ^{99m}Tc activity for different NMIs in the world*

In this way, an unbroken metrological chain for activity measurements performed at high metrological level was then implemented and maintained in Italy by ENEA-INMRI, for many radionuclides, ^{99m}Tc included, used as radiopharmaceuticals, which links the activity measurements of short-lived radionuclides performed at the NMDs and/or RPCs with the ENEA-INMRI primary activity standards.
The experimental test performed at ENEA-FNG laboratory for producing ^{99}Mo, and so on ^{99m}Tc, by using natural Molybdenum has been carried out at a high metrological level on the activity measurements, taking into account both the characteristics of the ENEA-FNG neutron beam, described in the paragraph above, and the ENEA-INMRI radioactivity standards. The set of measurements so produced allowed to validate with high accuracy the MC, based on Fluka code, developed and used in the studying phase of the entire experiment.

5. Conclusions and future perspectives

The production of ^{99m}Tc using methods alternative to nuclear fission reactors was identified as a social-driven issue to be addressed after the unexpected crisis in 2009, due to the aging of reactors devoted to this activity.
In this context, the use of 14 MeV neutrons to produce ^{99m}Tc exploiting $^{100}Mo(n,2n)^{99}Mo$ reaction is clearly identified as a valuable solution, if really intense sources to feed an intensive radiopharmaceutical production were available.
Recently an experimental assessment of this approach has been proposed by a Japanese research group and also in ENEA, that is one of the few worldwide research institutions presently possessing a 14 MeV D-T neutron source, namely the *Frascati Neutron Generator* (FNG),a similar experiment has been successfully carried out by using a well-defined characterization procedure, based on

accurately calibrated neutron beam characteristics, MC simulations and high level traceability of the activity measurements to the national radioactivity primary standards.
The achieved results 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 radioisotope production classical chain, based on nuclear fission reactors, in terms of a proper defined figure of merit (*FoM*).
It is found that NSFS' *FoM* is appreciably close to that of the main (but aged) nuclear fission reactors in the global landscape that cover a quite large fraction of the present ^{99m}Tc market.
Furthermore, as being NSFS an accelerator driven facility, a comparison has been done also with e-LINAC facilities for radioisotope production by photo-neutron reaction ^{100}Mo(γ,n)^{99}Mo.
In this respect it is found that NSFS is absolutely competitive when high ^{99}Mo activity production is considered.
Apart of technical considerations on the ^{99m}Tc production methods, it is worth to briefly focus on more social concern on the distribution of this radiopharmaceutical. Approximately 30 million doses are used each year worldwide and most authorities agree that there will be a continued growth in demand for ^{99}Mo (precursor of ^{99m}Tc) in the medium term. Estimates [12] highlight that in the short/medium term, ^{99m}Tc is expected to remain the major market player, although the relative proportion of the radiopharmaceutical market occupied by ^{99m}Tc is expected to decrease (from 85% to 72%).
It is important to make a consideration about the Italian and world ^{99m}Tc request and the possible position of the NSFS in this framework.
The weekly request of ^{99m}Tc in US is estimated to be 220 TBq [43], while for Canada [33] it is about 15.5 TBq. For other countries such as those hosting the reactors in Table I a possible gauging might be made rescaling for the population. Without entering into details, it can be confidently stated that the suite of these old reactors can cover a great fraction of the world demand. In this context the previsions for NSFS indicate a capability of about 27% of the US demand, a full fulfilment of the Canadian. In the Italian landscape it is possible to confidently stated that NSFS would completely satisfy the internal market with the possibility to provide the radiopharmaceutical for a fraction of the remaining global market.

Focusing on the Italian scenario, it is worth mentioning that, the *Ospedale Pediatrico Bambino Gesù* (OPBG), in Rome, as an example, needs about 3 GBq per week of ^{99}Mo or diagnostic purposes [44]. In this regard, considering the lower limit for NSFS ^{99}Mo production (see Tab. II) more than 10 000 hospitals requiring the same amount of ^{99}Mo could be supplied.
A further example is the *Ospedale San Camillo-Forlanini*,in Rome, where about 8.5 TBq/year of ^{99m}Tc are used, that is 0.2 TBq/week [45]. In this regard, considering the lower limit for NSFS ^{99}Mo production (see Tab. II), about 200 hospitals requiring the same amount of ^{99}Mo could be supplied.

However, it is important to put in evidence that ^{99}Mo produced by nuclear fission reactors is distributed worldwide, after a chemical-based extraction process, by means of chromatographic columns that can be considered as a standardized device for the purpose. ^{99}Mo produced by means of 14 MeV neutrons needs a different distribution device.
An efficient device that works with ^{99}Mo produced with e-Linac using ^{100}Mo(γ,n)^{99}Mo and thus also with ^{100}Mo(n,2n)^{99}Mo was developed by NORTHSTAR and is called TECHNEGEN. The discussion of this device is out of the scope of this report and the reader is referred to Ref. [46] for a thorough description.
In summary, it can be foreseen that the intense neutron yield of NSFS would be fully exploitable to produce a large weekly activity of ^{99}Mo using ^{100}Mo(n,2n)^{99}Mo inelastic reactions, fulfilling in some extent the requirement strongly expressed by international organizations of finding viable, suitable and secure alternative production chains in the short, medium and long term that are alternative to that based on aged nuclear fission reactors.

The report, finally, highlights the potentiality of ENEA facilities for testing with high accuracy and precision a method for ^{99m}Tc production alternative to the classical nuclear fission reactor chain. It is desirable that this road, now opened, will be profitably covered for interesting future applications and research developments in the field of radiopharmaceutical production, with the specific attention to the ^{99m}Tc case. Moreover, it is also desirable to evaluate the capability of the ENEA nuclear fission reactors for ^{99m}Tc production.
In this way a complete survey on the ENEA facilities that can provide directly or indirectly a support for this kind of investigation can be fully achieved, promoting, at the same time, a synergic collaboration for sharing wide competences, know-how and expertise that exist in ENEA.

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