Cyclotron solid targets preparation for medical radionuclides production in the framework of LARAMED project

H Skliarova¹, S Cisternino¹, G Cicoria², E Cazzola³, G Gorgoni³, M Marengo², J Esposito¹

¹ National Institute of Nuclear Physics, Legnaro National Laboratories (INFN-LNL), Legnaro (PD), Italy.
² University Hospital “S. Orsola–Malpighi”, Medical Physics Department, Bologna, Italy.
³ IRCCS Sacro Cuore Don Calabria Hospital, Cyclotron and Radiopharmacy Department, 37024 Negrar (VR), Italy.

E-mail: hanna.skliarova@sckcen.be

Abstract. LARAMED project aims to set up an advanced science and technology facility to develop new and efficient methods to produce medical radioisotopes at Legnaro National laboratories of National Institute of Nuclear Physics. Waiting for the facility full operation, LARAMED group has already started working on the cyclotron production of several conventional and emerging radionuclides. Suitable target preparation is one of the most critical aspects in cyclotron production of radioisotopes. LARAMED group has investigated a set of non-classical techniques for metallic target preparation. Magnetron sputtering technique developed for ultra-thick film deposition was applied for the preparation of the Mo solid targets for ⁹⁹mTc production, and Y ones for ⁸⁹Zr production. Spark plasma sintering method provides efficient sintering of powders and good bonding of metallic pellet to a backing. Like magnetron sputtering, it was tested for nat,¹⁰⁰Mo and natY targets, as well as for natCr targets preparation aimed at ⁵²Mn production. The High energy Vibration Powders Plating technique was instead applied for natural (Mo, Ti) and enriched ⁴⁸Ti metallic powders with >95% deposition efficiency. All three techniques tested provided the cyclotron solid targets with high thermomechanical performance under the beam (1kW/cm²).

1. Introduction

LARAMED (LAboratory of RAdioisotopes for MEDicine) is a new research infrastructure, under construction at Legnaro National laboratories of National Institute of Nuclear Physics (INFN-LNL). The core of this infrastructure is the new, high-performance, BEST Theratronics Ltd. 70p cyclotron (70 MeV, 750 μA), which will be dedicated not only to nuclear physics study but also in beam time sharing to medical physics research. LARAMED project has been established for performing R&D on cyclotron-based radioisotope production having medical interest, starting from cross-section measurements of potentially useful nuclear reactions, targets development and realization, optimization of the irradiation conditions, target processing, radiochemical separation and purification, radioisotope labeling of biologically active molecules and recovery of enriched materials to close the production cycle. Albeit LARAMED facility is currently bringing to completion, research activities on the most relevant radioisotopes in nuclear medicine are being pursued: cyclotron production of conventional radionuclides, such as ⁹⁹mTc (TECHN-OSP and E-PLATE projects) and ⁸⁹Zr (in collaboration with Sacro
Emerging radionuclides such as $^{67}$Cu (COME project), $^{47}$Sc (PASTA project) and $^{52}$Mn (METRICS project) were studied, along with the development of high power target (TERABIO granted-project).

Targets needed for each given application (in this work, nuclear cross-section measurements and radioisotope production) have particular restrictions, like suitable backing material, acceptable thickness range, etc. The common techniques so far used for solid target manufacturing include pressing, sintering, electrodeposition, lamination, etc. [1,2]. But, whatever the target preparation methods adopted, the following requirements should be met: thermomechanical resistance under the beam at chosen irradiation conditions, adequate target uniformity and a minimum amount of impurities.

For the cyclotron production of radioisotopes, suitable target design and preparation is one of the main technological challenges. In order to achieve the highest nuclear reaction yield, the production should be performed at maximum proton currents. That means that the target system should provide an, as high as possible, heat removal efficiency. Conventional solid target system consists of the target material deposited on a backing plate cooled by water from the backside and, possibly, by helium gas flow from the front side (Fig. 1).

In order to improve the heat dissipation, the target and the backing plate should be made of materials with the maximum thermal conductivity, by adopting a method providing good thermo-mechanical contact between them. Additionally, the chemical inertness of the backing plate in the target dissolution conditions should be also considered. When using isotopically enriched materials, as precursors for radionuclides’ production, the request of providing a high-efficiency target preparation method must, therefore, be taken into account, in order to optimize the related costs.

![Figure 1. Utilized cyclotron target stations: (a) TEMA Sinergie (target slit Ø32×2 mm); (b) ACSI TR19 (target slit Ø24×2 mm).](image)

For different radionuclides production, the LARAMED group at INFN-LNL has studied a set of standard (hydraulic manual pressing, pressing forwarded by sintering) and non-standard techniques for metallic target preparation, like magnetron sputtering (MS) [2,3], High energy Vibration Powders Plating (HIVIPP) and Spark Plasma Sintering (SPS): the current article presents an overview of the non-standard methods.

The radionuclides of interest included the conventional $^{99m}$Tc, used in the majority of all diagnostic SPECT scans all over the world, $^{89}$Zr used in research for in vivo imaging of antibodies, nanoparticles and other large bioactive molecules [4], and emerging theranostic radionuclide $^{47}$Sc [5]. The utilized routes for the cyclotron-based production of these radionuclides were presented in Tab. 1. It should be noted that the target thickness for the nuclear cross-section measurement is much lower than the one for the radioisotope production. The last one depends on the favorable cyclotron energy range, providing maximum yield of radioisotope of interest and minimum impurities, the maximum beam energy of the available cyclotron, and the cross-section of the nuclear reaction used for production of the radioisotope of interest. Since $^{48}$Ti targets were used only for the nuclear cross-section evaluation, they were much thinner than others and were not requiring the dissolution after the irradiation (see Tab. 1).
Table 1. Production routes of radionuclides of medical interest.

| Radionuclide of interest | $^{99m}$Tc [6] | $^{89}$Zr [7,8] | $^{47}$Sc [9] |
|--------------------------|-----------------|-----------------|----------------|
| Nuclear reaction         | $^{100}$Mo(p,2n)$^{99m}$Tc | $^{89}$Y(p,x)$^{89}$Zr | $^{48}$Ti(p,x)$^{47}$Sc |
| Cyclotron energy range   | 10-22 MeV       | 4.6-14 MeV      | 10-40 MeV      |
| Precursor material       | $^{100}$Mo      | nat Y           | $^{48}$Ti      |
| Desired target thickness | 0.25-0.8 mm     | 0.15-0.7 mm     | 1-50 μm        |
| Target dissolution media | H$_2$O$_2$ conc. | HCl conc.       | -              |

2. Magnetron sputtering

MS is a very flexible physical vapor deposition technique, well-known for deposition of thin metallic films. It is not used for thick film deposition because of tensile or compressive stress always present in the films [10]. Here, a method to deposit dense stress-free films of refractory metal, achieving hundreds of microns thickness, directly onto a target backing plate, has been developed.

Natural molybdenum (99.99%), natural yttrium (99.9%) sputtering targets and argon (99.99% purity) were used for the deposition onto different substrates: copper (Ø32 mm × 1 mm), sapphire (Ø13 mm × 0.5 mm) and CVD diamond (Ø13 mm × 0.4 mm) for molybdenum deposition, and niobium 99.9% purity (Ø24 mm × 0.5 mm) for yttrium.

The films were deposited by direct current MS with a 2" planar magnetron source. The depositions were performed simultaneously onto 5/7 substrates, positioned onto a planar substrate holder, with a distance of 6 and 7 cm from the cathode. The sputtering materials were deposited on a spot of 10 mm in diameter in the center of each substrate (backing plate) defined by an appropriate mask. For Mo, a heated sample holder by an IR 450 W lamp was used and the temperature was controlled by a K-type thermocouple. The MS parameters, including sputtering gas pressure, substrate temperature and multilayer deposition mode, were optimized in order to minimize residual stress in the film, avoiding the stress-associated problems (e.g. cracking, adhesion problems, etc. [11]).

The combination of optimized sputtering parameters, high temperature of the sample holder (500 ºC), 1.6×10$^{-2}$ mbar working pressure and multilayer deposition, allowed to deposit high density and stress-free 100 μm thick Mo layers on both metallic (copper) and non-metallic (sapphire and CVD diamond), high thermal conductivity and chemical inertness backing (Fig. 2).

![Figure 2. Sputtered targets: Mo deposited on copper (a), Mo deposited on sapphire (b) and on CVD diamond (c) brazed to copper; Y deposited on niobium (d).](image-url)

Stress-free Y films of more than 50 μm, directly deposited onto 0.5 mm thick niobium backing (Fig. 2d), were obtained by the optimization of the sputtering pressure only (1.4×10$^{-2}$ mbar). Since yttrium is very sensitive to oxidation, the multilayer technique was not applied in order to avoid an introduction of oxide layers between metallic ones, that can promote the increase of the intrinsic stress (causing further possible delamination), instead of stress relaxation. The heating of the sample holder in the case of Y sputtering is not required, since the melting temperature ($T_m$) of Y is lower in respect to Mo, and
the homologous temperature $T_h=0.2 \ (-300 \degree C)$ [10] is reached due to the interaction of the substrate-holder with the plasma during the sputtering process.

Thermomechanical stability of MS deposited targets has been tested under the proton beam of two different medical cyclotrons: the GE PETtrace cyclotron, placed in Sant’Orsola Hospital of Bologna for Mo-based target, and the ACSI TR19 cyclotron at Sacro Cuore Don Calabria Hospital of Neglar for Y-based ones, by using the available solid target stations (Fig. 1). Tests have been realized at 15.6 MeV and 12.7 MeV respectively, increasing beam currents with 10 $\mu$A steps for 1-2 min irradiation, starting from 20 $\mu$A up to 70 $\mu$A. Visual control of the target after each irradiation was performed.

All the Mo target prototypes, realized by 100 $\mu$m thick Mo film deposition by MS, directly onto copper backing (Fig. 2a) as well as onto non-metallic substrate, brazed to copper support (Fig. 2b, c), showed excellent thermomechanical stability under the beam. Excellent adhesion (no delamination) and no film damage were indeed observed after each irradiation run. The integrity of Y targets during irradiation was also not compromised, despite a visible dark spot in the center of the target corresponding to the beam profile. Thus, all targets realized by MS have supported up to 1 kW/cm² heat power density, which is comparable [12] or exceeding the performance of the commercially available targets.

More details on MS deposited cyclotron solid targets are presented in the previous works by the authors [2,3,13].

3. E-PLATE project: Electrostatic Powder pLating for Accelerator TargEts

The High High energy Vibration Powders Plating (HIVIPP) method is based on the powders motion in an electric field. In the current work, the standard set-up described in works of I. Sugai was used [14] for the HIVIPP deposition of $^{nat}$Mo and $^{48}$Ti materials in the framework of E-PLATE (Electrostatic Powder pLating for Accelerator TargEts) project at INFN-LNL.

The deposition process was carried out in vacuum ($1 \times 10^{-3}$mbar) in a quartz cylinder (Ø14 mm/Ø20 mm internal and 1-2 cm height) with steel electrodes mounted at its top and bottom. Substrates (target backing) were positioned in contact with the electrodes. The powders, guided by an electric field, were implanted onto two metallic substrates during the one deposition.

HIVIPP method was applied for $^{nat}$Mo powders (99.5% purity, 170 mesh), $^{nat}$Ti powders (99% purity, 325 mesh) and $^{48}$Ti powders (99.35% enrichment, <10 $\mu$m powder size, TRACE) for the deposition onto aluminum of 100 $\mu$m/25 $\mu$m (99% purity) and copper 0.25 mm (99% purity) foil substrates (Fig. 3).

The HIVIPP deposition was realized under an electric field applied of 5-15 kV/cm, keeping the current less than 10 $\mu$A. The deposition time (10-50 h) varied, depending upon the type of powders and cylinder metalization during the deposition. The primary deposit quantity analysis was realized by weighting the substrates before and after deposition. The thickness of HIVIPP deposit calculated assuming the bulk material density resulted of about 1-3 $\mu$m for $^{nat}$Mo, 5-10 $\mu$m for $^{nat}$Ti, 0.5-4 $\mu$m for $^{48}$Ti. The weighting results have been then proven by the Elastic Backscattering (EBS) analysis.

![Figure 3. HIVIPP deposition $^{nat}$Ti on 100 $\mu$m Al foil (a); $^{48}$Ti 25 $\mu$m Al foil (b); $^{nat}$Mo on 100 $\mu$m Al foil (c); $^{nat}$Mo on 250 $\mu$m Cu foil (d).](image)

Extremely low losses (~5%) during target preparation make the HIVIPP technique very attractive for the enriched materials deposition. Indeed, a batch of $^{48}$Ti-48 enriched targets was realized using...
HIVIPP technique and was successfully used for the cross-section measurement experiments at the ARRONAX facility (Nantes, France) in the framework of the INFN project PASTA (2017-2018).

In order to prove the thermomechanical stability of HIVIPP deposited $^{99m}$Mo targets on Cu backing, the irradiation tests have been performed by ACSI TR19 cyclotron (Negrar) at 17.6 MeV proton beam at increasing the beam current in each following irradiation from 10 to 50 µA. No visual modification or damage of the targets occurred during irradiation. The fact that the HIVIPP deposited targets withstand the heat power density of ~1 kW/cm$^2$, guarantees that, from the point of view of target quality, HIVIPP technique can be a promising solution not only for nuclear physics experiments but also for the production of the radioisotopes.

4. Spark Plasma Sintering (SPS)

The Spark Plasma Sintering (SPS) technique uses a uniaxial pressure, combined with a pulsed direct electrical current under vacuum (see Fig. 4). The mechanism may be described as a kind of micro-spark discharge in the gap between neighboring powder particles, combined with the Joule heating.

![Figure 4.](image)

Figure 4. (a) Dr. SINTER$^\text{®}$ model SPS1050 machine of Sumitomo; (b) Spark Plasma Sintering in “open mode” - without a die.

In the current work, for different radionuclides’ production, the following targets were prepared: $^{99m}$Mo, $^{100}$Mo and $^{99}$Cr on copper-based backing with gold interlayer; $^{nat}$Y on niobium backing (Fig. 5).

The target materials included $^{nat}$Mo powders (99.95% purity, ~60 µm), $^{100}$Mo powders (99.05% isotopic enrichment, Isoflex), $^{nat}$Cr powders (99.5% purity) and Y disks (99% purity) Ø12 mm and 0.15 mm thick. Instead, 1.5 mm thick copper discs (99.9% purity) of Ø32 mm and 1.7 mm thick Ø23.5 mm and niobium discs (99.9% purity) corresponding to the cyclotron target station slits were used as backing. The 25 µm thick gold foil (99.95% purity) was used as a chemically inert protective interlayer.

![Figure 5.](image)

Figure 5. SPS targets starting from powders: $^{nat}$Mo on Cu (a); $^{100}$Mo on Cu with Au protective layer (b); $^{nat}$Cr on Cu with Au protective layer (c); and Y foil bonded to Nb (d).

SPS targets were realized in two steps: the 0.3-0.4 mm thick pellet preliminary pressed in Ø10/15 mm standard hydraulic press die at 600/800 MPa (in case of Y target a ready to use foil was used) were then press-bonded to a corresponding backing at ~10 MPa using Dr. SINTER$^\text{®}$ SPS1050 (Sumitomo Coal & Mining Ltd.) machine, without additional SPS die directly by graphite electrodes covered by graphite foils. Different current levels were used during the sintering keeping under control the temperature of the lower punch during the process in respect to the backing type used: 850°C for Cu-based and 1000°C for Nb-based backing.
NaMo SPS targets on copper-based backing were tested under 70 µA, 15.6 MeV proton beam (heat power density >1 kW/cm²) at PETtrace (Bologna) for 1 min short test and also for 30 min long irradiation test. The irradiation tests for thermomechanical stability of Cr and Y prototype targets manufactured by SPS were performed at the ACSI TR19/300 cyclotron (Negrar) at the maximum proton beam energy (18.8 MeV) at 10, 25 and 50 µA proton beam currents respectively. Targets were visually inspected to control the integrity and the adhesion of the pellet/foil to the target backing. No visible damage/modification appeared after the irradiation up to the maximum allowed beam current. Thus, excellent thermomechanical stability of SPS cyclotron solid targets has been proven.

5. Conclusion
All three techniques, MS, HIVIPP, and SPS, were successfully tested for the preparation of cyclotron solid targets. We showed that MS can be a powerful technique for natural target materials attached to non-metallic backing, but it should be avoided for the enriched isotopes due to high losses during deposition. Both HIVIPP and SPS are instead high-efficiency target preparation methods, covering a different range of target thicknesses requested for different application. In particular, HIVIPP may be used to provide uniform, low and medium thickness, targets for nuclear physics experiments and cross-section measurements. Instead, SPS is not applicable for target manufacturing with a thickness lower than several hundreds of microns, due to the geometrical restrictions but it can be successfully used for thick target preparation (Tab. 2).

| Target preparation method | MS | HIVIPP | SPS |
|---------------------------|----|--------|-----|
| Target thickness          | 0.1 µm-1 mm | 0.1-10 µm | >150 µm |
| Density, % of bulk        | >95% | <80%   | ~95% |
| Efficiency, %              | <20% | 95%    | >90% |
| Backing                   | Any | El. conductive | Metal |

Table 2. Comparison of target preparation techniques used.

References
[1] IAEA 2017 Cyclotron Based Production of Technetium-99m. (Vienna)
[2] Skliarova H et al. 2018 Molecules 24 25.
[3] Skliarova H et al. 2019 Instruments 3 21.
[4] van de Watering F C J et al. 2014 BioMed Res. Int. 2014 1-13.
[5] Qaim S M et al. 2018 J. Radioanal. Nucl. Chem. 318 1493-1509.
[6] Esposito J et al. 2013 Sci. Technol. Nucl. Install. 2013 1-14.
[7] Infantino A et al. 2011 Appl. Radiat. Isot. 69 1134-1137.
[8] Kasbollah A et al. 2013 J. Nucl. Med. Technol. 41 35-41.
[9] Pupillo G et al. 2019 Proc. of the 15th Int. Conf. on nuclear reaction mechanisms (Varenna) 341 348.
[10] Thornton J A et al. 1974 J. Vac. Sci. Technol. 11 666-670.
[11] Detor A J et al. 2009 Acta Mater. 57 2055-2065.
[12] Queern S L et al. 2017 Nucl. Med. Biol. 50 11-16.
[13] Palmieri V et al. 2019 Patent WO/2019/053570.
[14] Sugai I et al. 1997 Nucl. Instrum. Methods Phys. Res. Sect. Accel. Spectrometers Detect. Assoc. Equip. 397 81–90.