Fabrication and characterization of Gd targets for the production of terbium radionuclides for nuclear medicine

PhD hours presentation – 9th session

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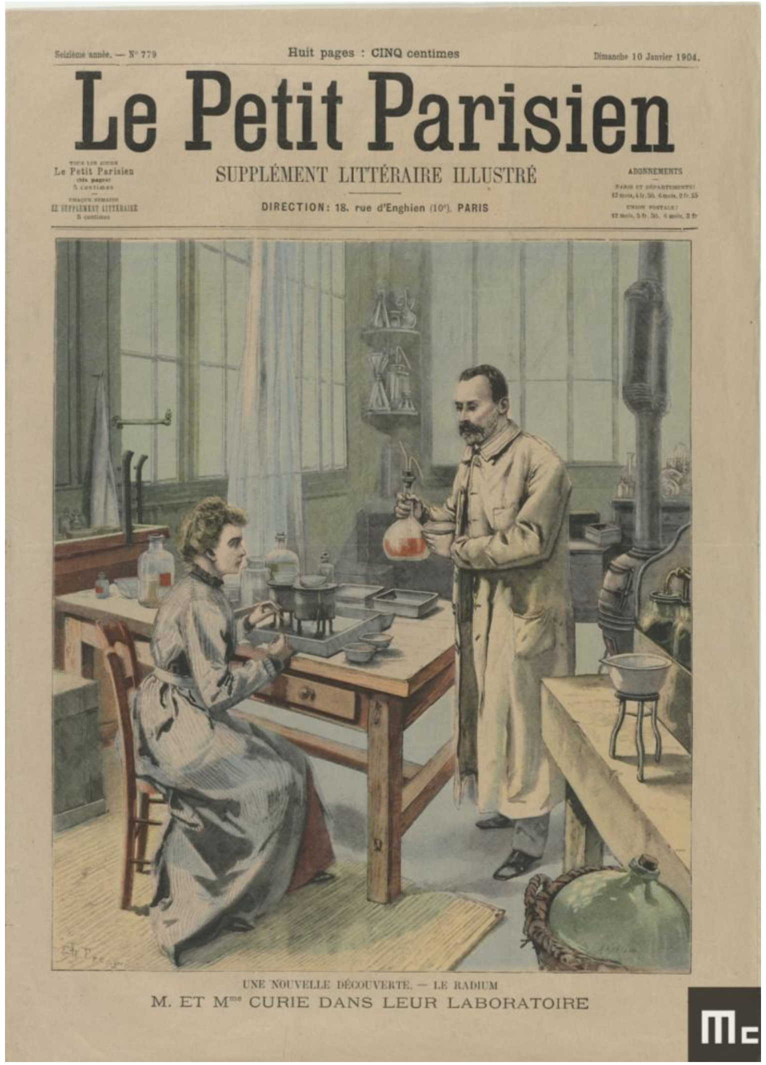
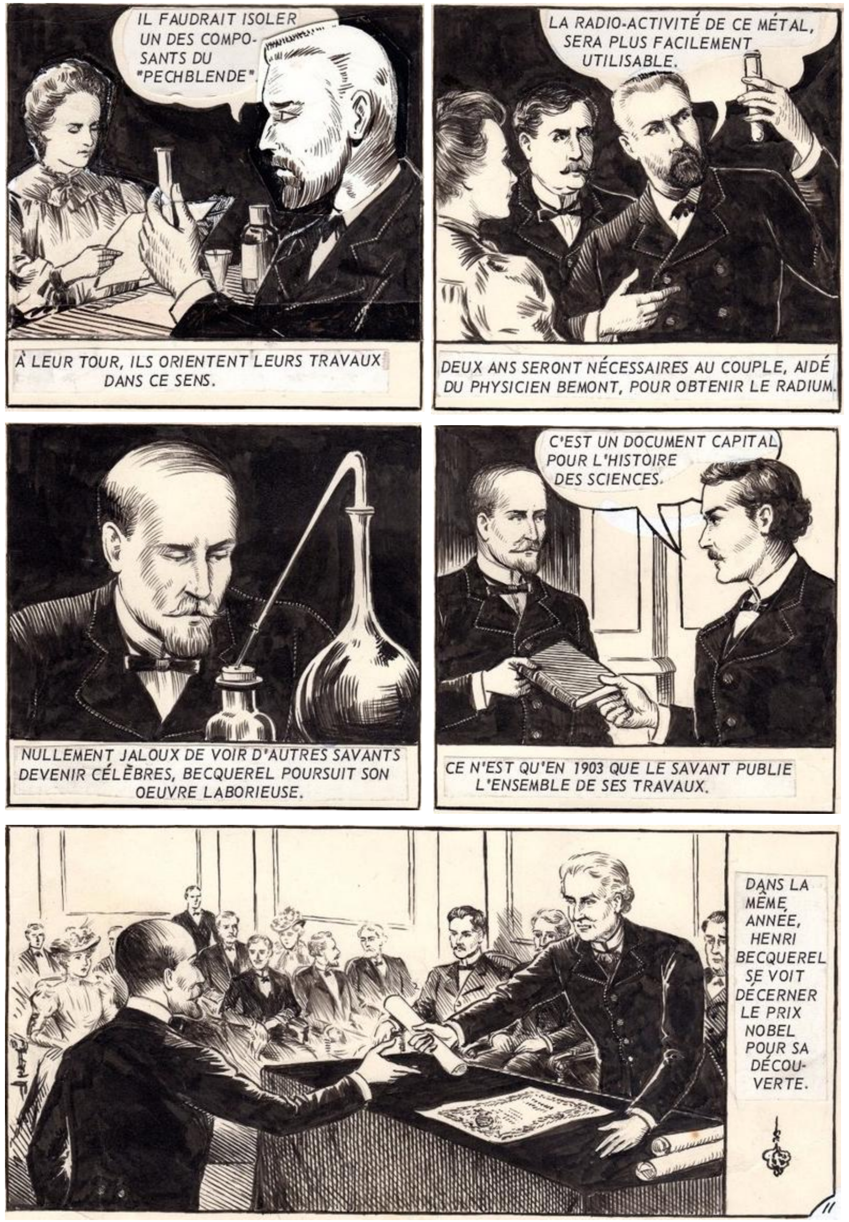
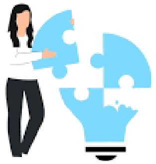
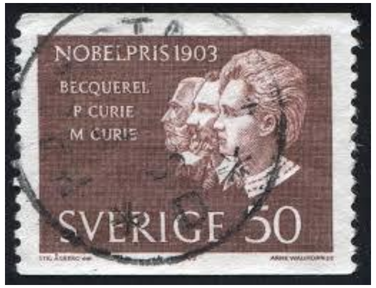
Contents:

- Centralizing the attention to the discover of radioactivity and radioactive elements;
- This field has involved into a crucial component of modern healthcare;
- Either as an independent technique or in conjunction with other medical procedures.



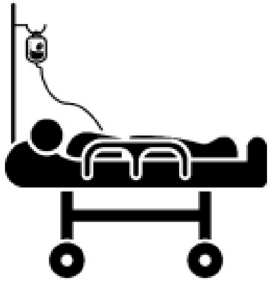






Cherry, Sorenson, & Phelps, 4th edition, 2012.

➢ This evolution has been supported by significant advancements in theragnostic approaches.



THERANOSTICS

Therapeutic

RadioTherapy
Alpha/beta/Auger

Diagnostic

RadioImaging
PET/SPECT

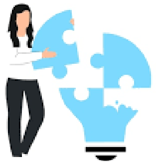
α therapy → TAT = high energy and short range = effectively destroy cancer cells with minimal damage → ^{149}Tb

β therapy → Have a longer range and are commonly used in treating larger tumor masses → ^{161}Tb

Auger electron → Are low-energy electrons that have an extremely short range = for targeting microscopic clusters of cancer cells = with high precision → ^{161}Tb

SPECT Single-photon Emission Computed Tomography → Is uses gamma-emitting radionuclide → ^{155}Tb

PET Positron Emission Tomography → Is uses positron-emitting → ^{152}Tb



Hutton & Nuyts, 2002; Hernandez et al., 2022; Duchemin et al., 2021; Müller et al., 2012; Naskar & Lahiri, 2021.

The production process:

Protons particles

Deuterons particles

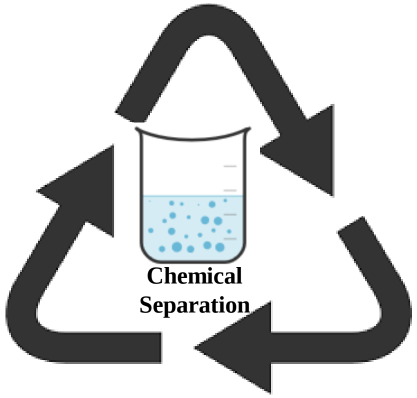
Alpha particles

Particles

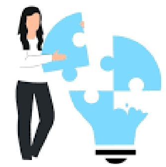
$Gd_{enriched}$ targets

production of **Tb** radionuclides

- Is an element of great interest in nuclear medicine due to its unique properties that make it ideal for both diagnosis and therapy;



- High purity of Terbium.



C. Muller, et al. J Nucl Med 53:1951-9 (2012) doi: https://doi.org/10.2967/jnumed.112.107540.

Obtain thin and thick targets of Gd, ideally under the metallic form, for the production of Tb radionuclides **(namely the isotope ^{155}Tb);**

- Thin targets = explore electrodeposition technique in organic media;
- Thick targets = explore pelletezing technique.

Study and development of chemical separation using an ion extraction chromatography and/or exchange chromatography;

Optimize radioisotope production process with different light charges (protons or deuterons or alpha).

Methodology of MP
(for cross section measurements):

1. **Bulk electrolyte** = with a homogeneous part;

↓

2. The **diffusion** and **convection** zone = the ions go closer to the electrode and a concentration difference started;

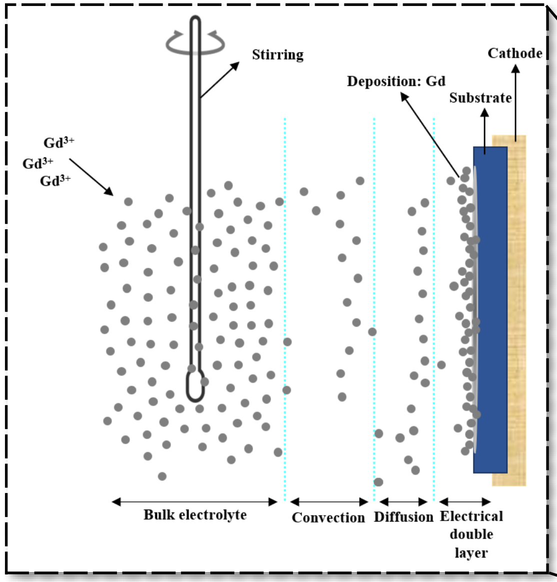
↓

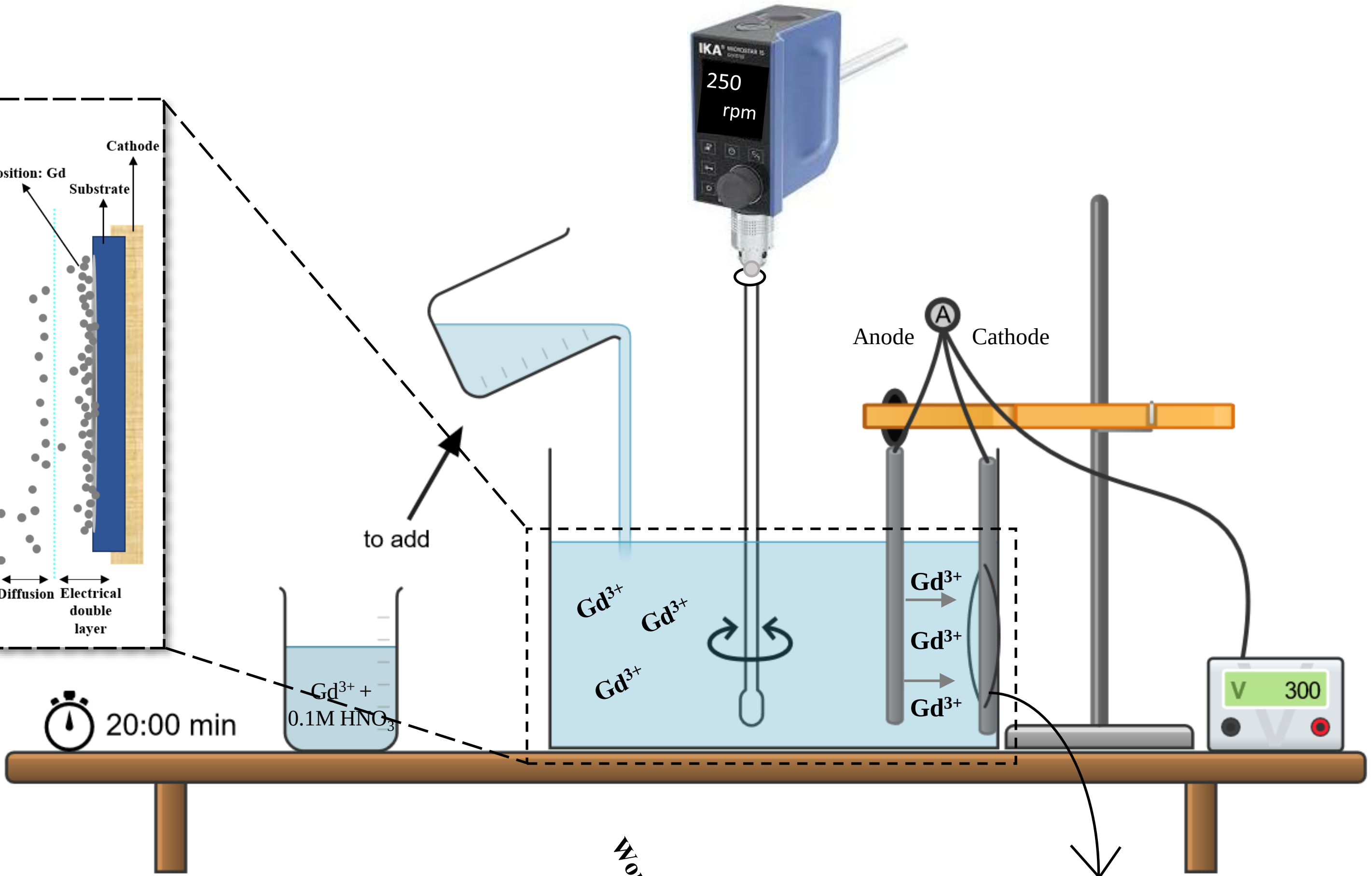
3. The **electrical double layer** = compose by a layer of adsorbed ions + a diffuse layer of ions in the electrolyte;

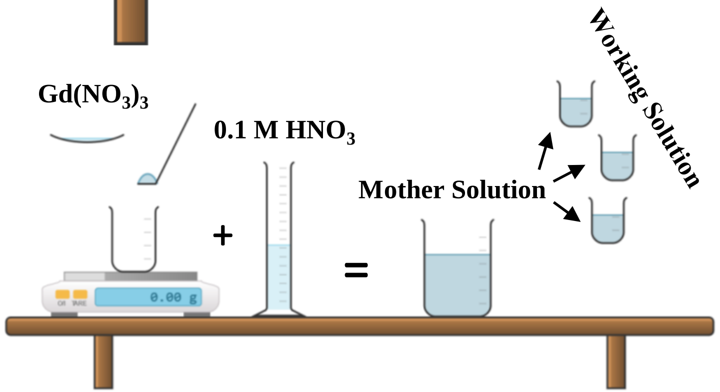
↓

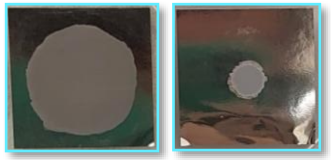
4. The **deposition** =

- thermodynamically applying an electrical potential to the cathode, reducing the free energy of the system, and creating a driving force for the reduction reaction;
- + in kinetic ratio as a function of the current density of the system.



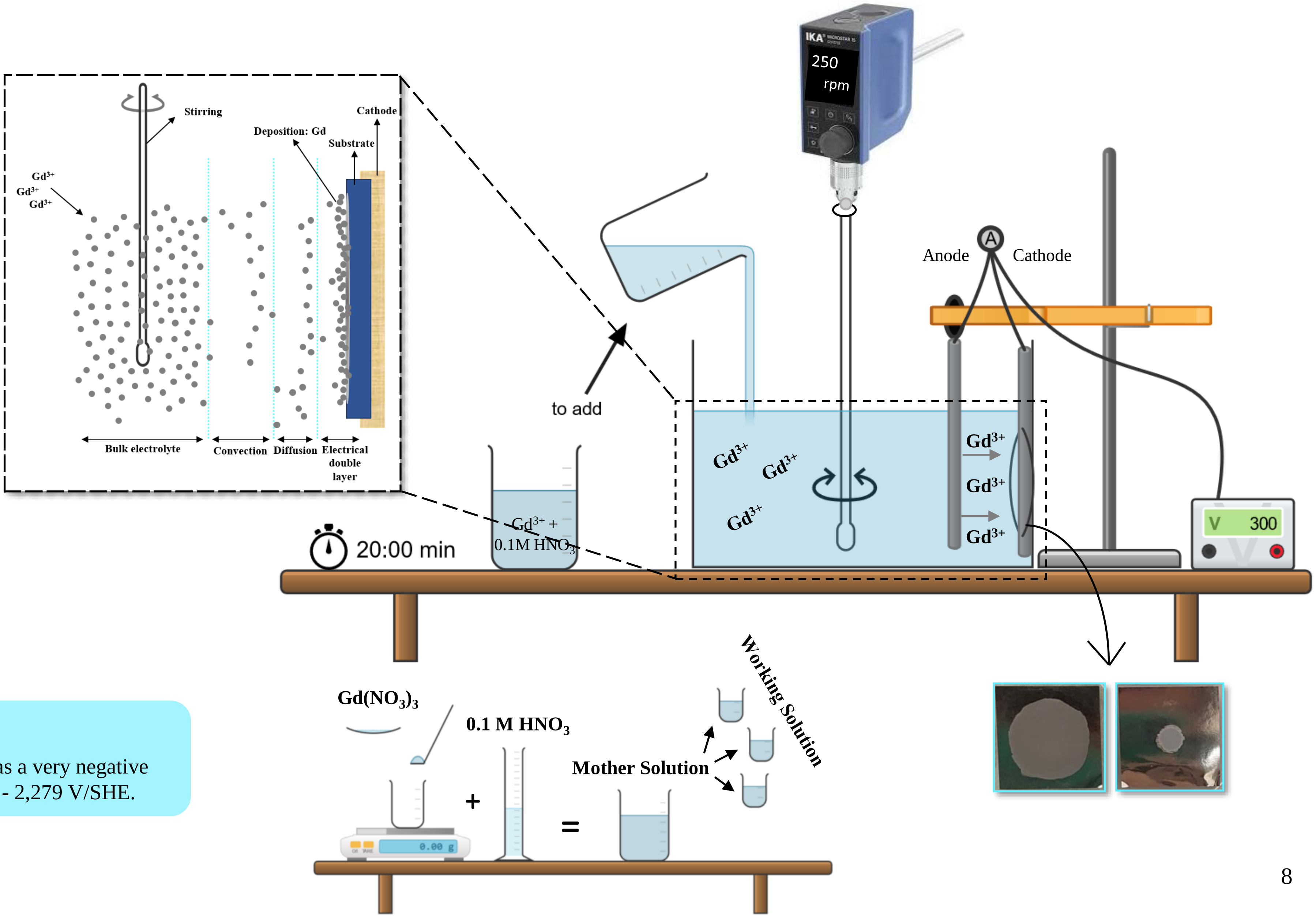






Methodology of MP
(for cross section measurements):

Parameters:
• Substrate
• Substrate thickness
• Time of process
• Temperature
• m(Gd)$_{\text{electrolyte solution}}$
• Voltage
• Current dentity
• Deposit diameter
• Stirring speed
• Solvent
• Distance between electrodes



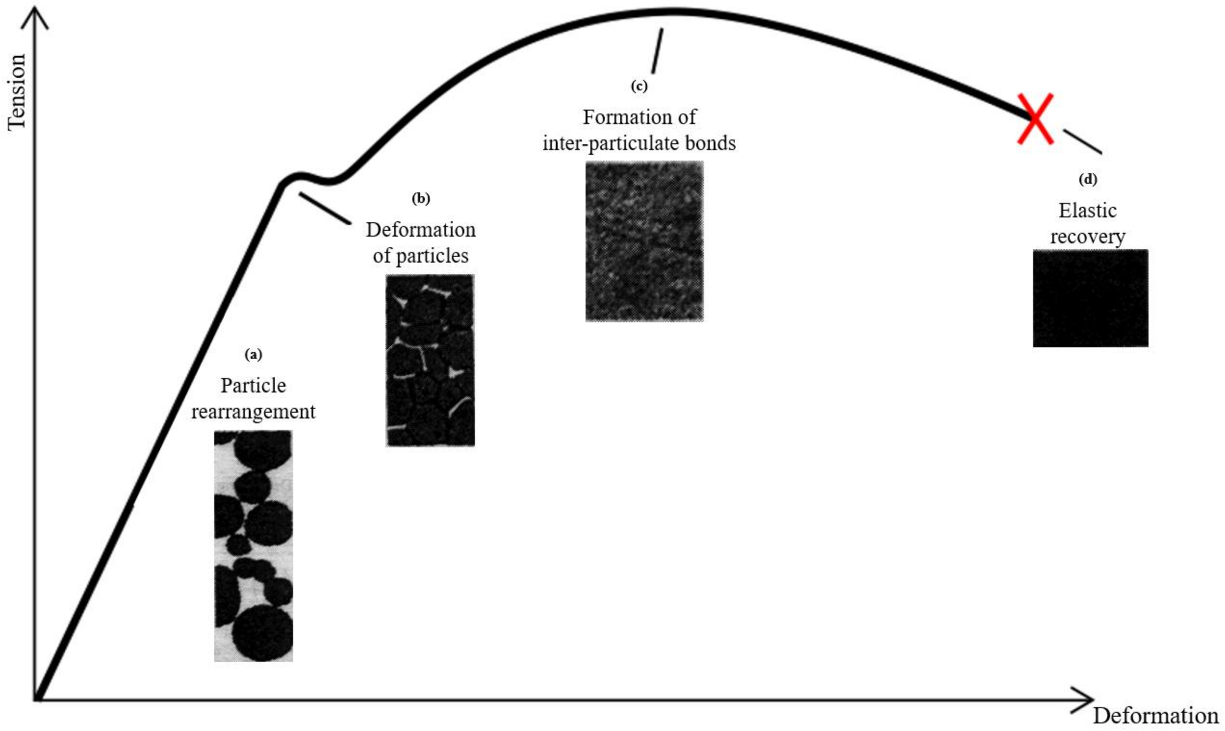
Why Molecular Plating?

possible to obtain a metallic element which has a very negative standard potencial electrode E°(Gd3+/Gd)= - 2,279 V/SHE.

Methodology of Pelletizing (for production):

➢ This technique involves transforming fine particles of a material into pellets through agglomeration.

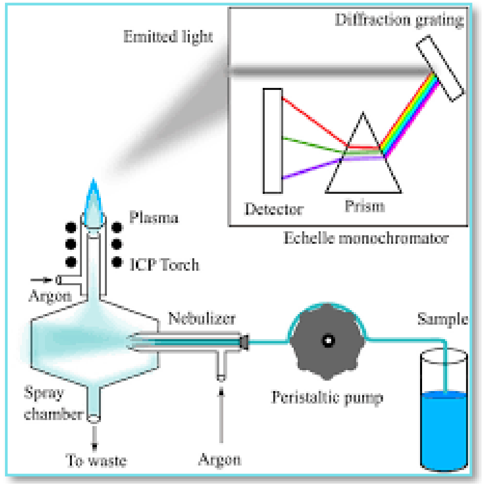
Hydraulic press
Pression max = 950 MPa



Example of Gd_2O_3 Pellet
Thickness = 1.07mm (for example)

Why Pelletezing?

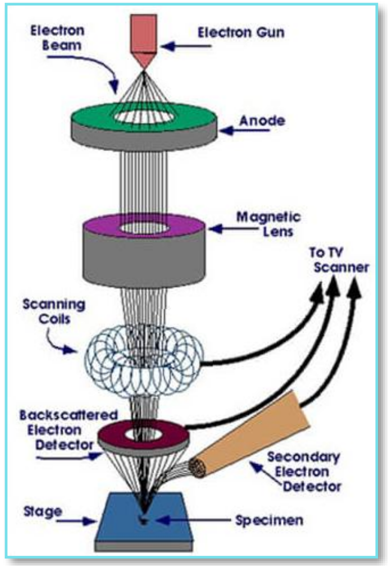
simple process and to obtain dense targets.



- Determines the concentration of chemical elements by exciting atoms in a high-temperature plasma.

- The emitted light is analyzed to identify and quantify elements based on their characteristic emission wavelengths.

- An analytical balance, like this one, determines the mass of a sample by measuring the gravitational force acting on it.



Characterization of the deposit:

Mass Measurements

SEM analysis

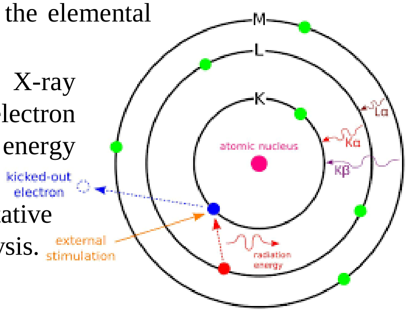
- Uses a focused electron beam to scan the surface of a material, generating high-resolution images based on electron-sample interactions.

- It provides detailed morphological and structural information.

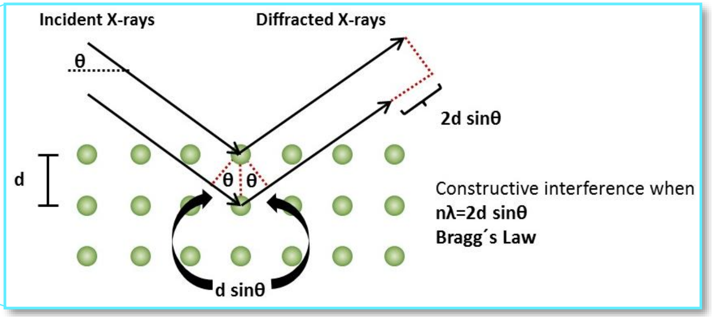
EDS analysis

- Works alongside SEM to identify the elemental composition of a sample.

- It detects characteristic X-ray emissions generated by electron transitions between atomic energy levels (K, L, M shells) and specific transitions (α, β), allowing qualitative and quantitative elemental analysis.



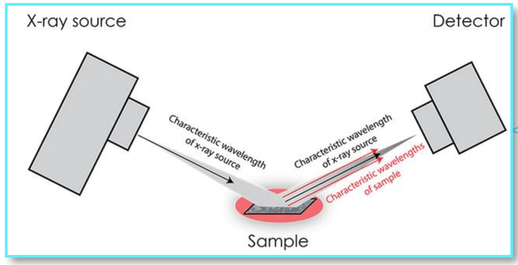
XRD analysis



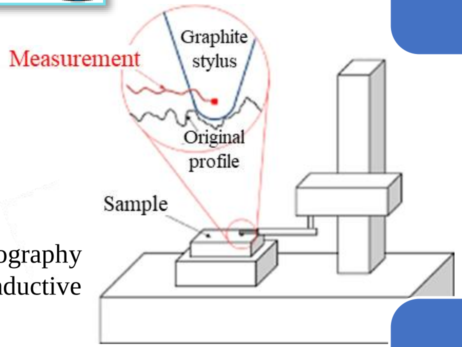
$$n\lambda = 2d.\sin\theta$$

- n is a constant;
- λ is the wavelength of the X-ray;
- d is the interplanar distance;
- θ is the diffraction angle.

- Works by directing X-rays at a material, and as these rays interact with the atomic planes in the crystal, they are scattered at specific angles, producing a diffraction pattern that reveals the material's atomic structure based on Bragg's law.



Profilometry analysis

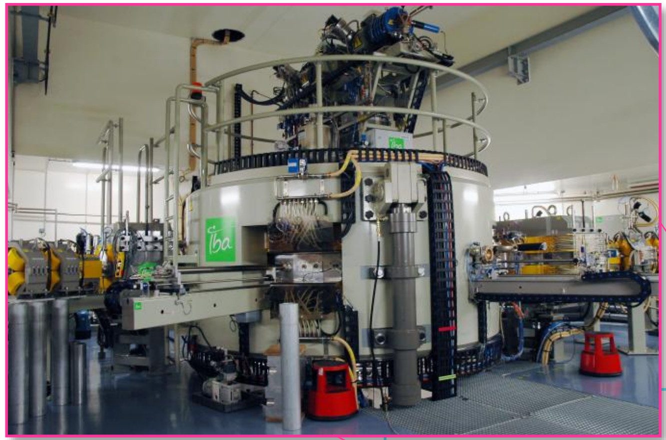


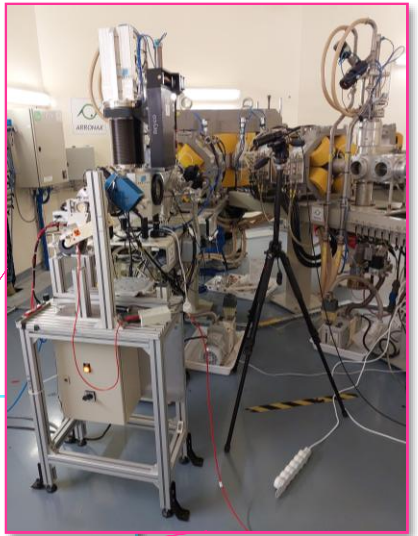
- Measures surface topography and roughness using a conductive graphite probe.

- This method enables high-resolution scanning by detecting variations in surface height and texture finally providing the thickness of the samples.

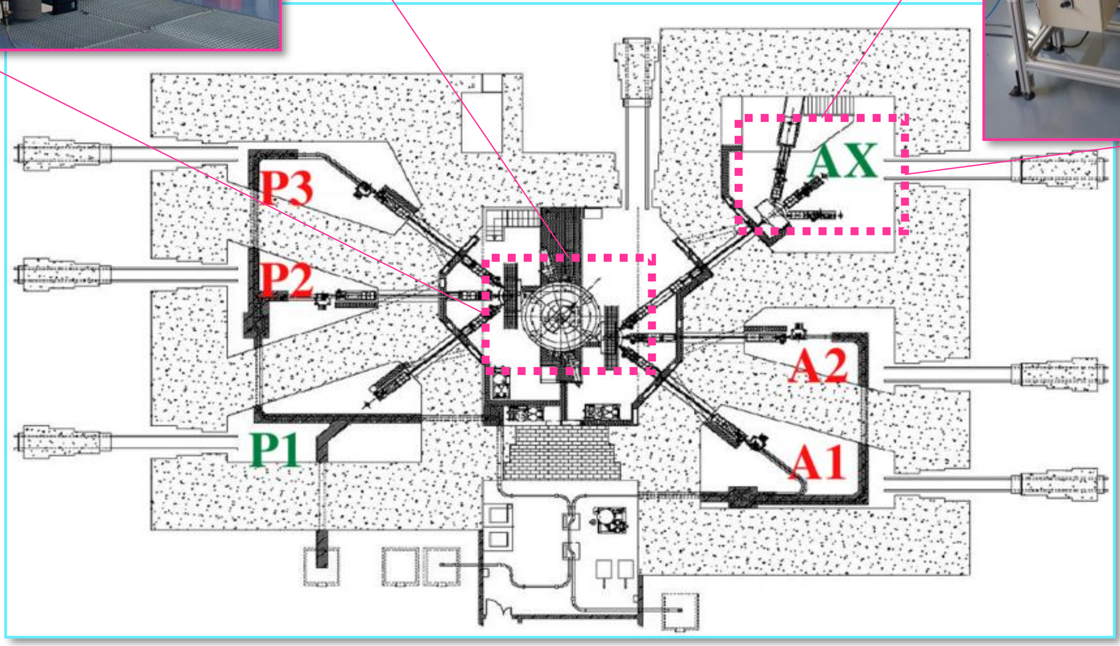
ICP-OES analysis

Experiments:





Irradiation experiment: to evaluate the feasibility of the MP methodology



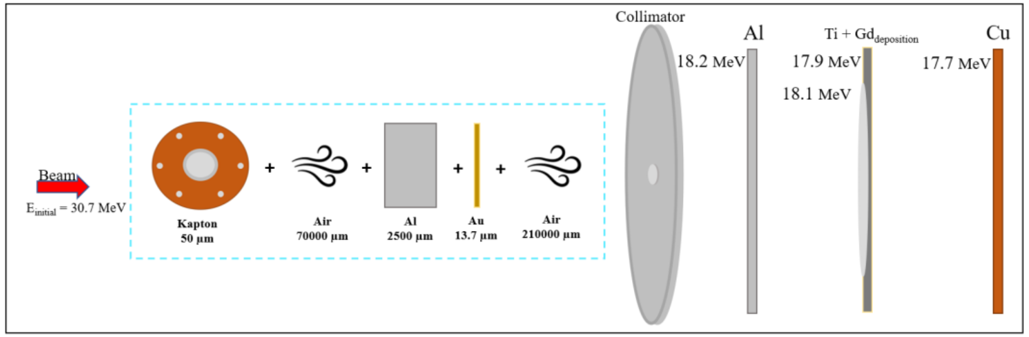
Additional experiments conducted by MP methodology + pelletizing methodology (experiments in progress)

- Protons: 30-70 MeV, up to 375 µA;
- Alpha particles: 67.4 MeV, up to 35 µA;
- Deuterons: 17-35 MeV, up to 80 µA.

Irradiation experiment: to evaluate the feasibility of the MP methodology

Samples manufacturing parameters	
Substrate:	Ti foil
Time of process:	3h20min
Temperature:	18-21 °C
$C_{electrolyte\ solution}$:	0.07 $mg.ml^{-1}$
Current dentity:	10.5 $mA.cm^{-2}$
Deposit diameter:	0.6 cm
Stirring speed:	250 rpm
Solvent:	Isopropanol

Irradiation parameters	
Date:	Dec/2024
Technique:	Stacked foils
Time of irradiation:	40 min
Particles:	Protons
Beam current:	150 nA
Monitor:	Ti and Cu foil
Catcher:	Al foils Thichness Al_1 = 13.2 µm Thickness Al_2 = 13.0 µm
Energy:	18.2 MeV



- Simulations with SRIM program;
- Considered half the thickness of each foil = to determine the energy loss for each foil;
- Inputs: material, thickness and density;
- Outputs: the loss of energy and energy with each foil.

- Reaction of interest: $^{nat}Gd(p,x)^{155}Tb$ → half-life = 5.32 days
- Competitive reaction: $^{nat}Gd(p,x)^{156}Tb$ → half-life = 5.35 days

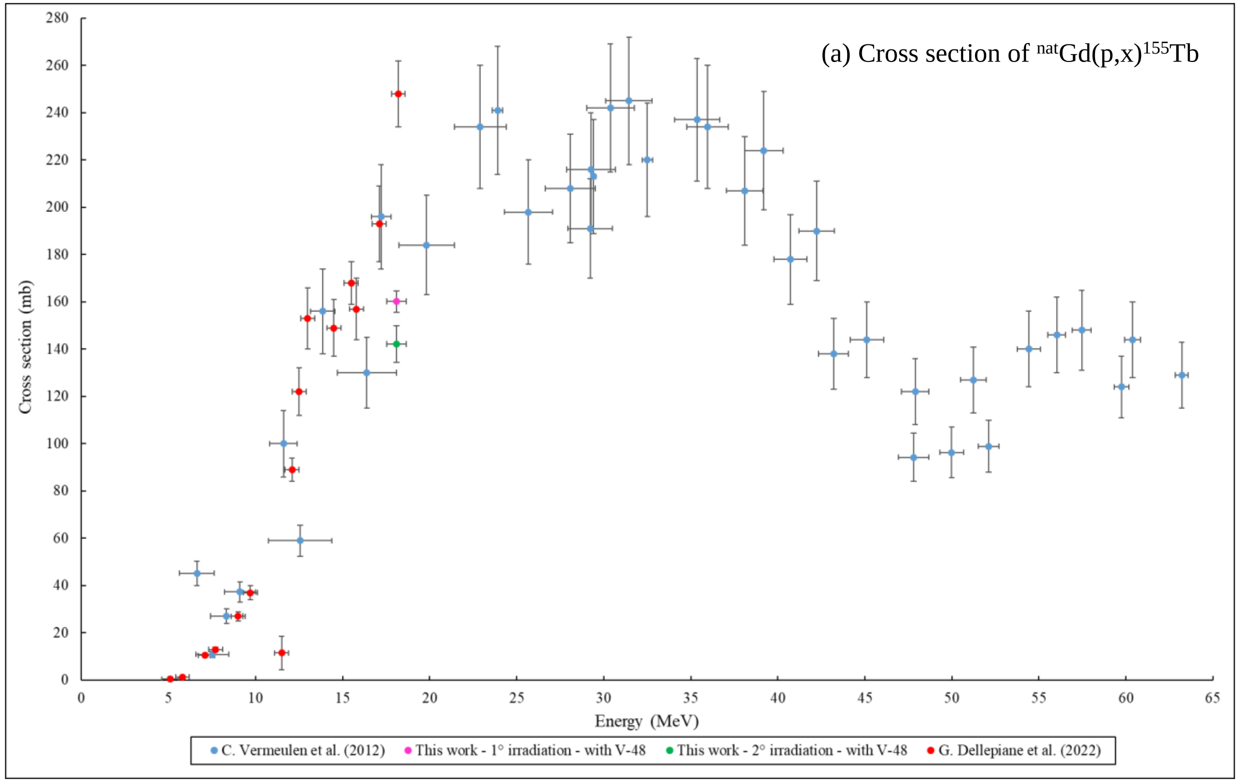
- 1° counting: 3-4 days after irradiation
  $^{nat}Gd(p,x)^{155}Tb$, ^{156}Tb → determine the activity of ^{155}Tb, ^{156}Tb
- 2° counting: 48-50 days after irradiation
  $^{nat}Ti(p,x)^{48}V$ → determine the activity of ^{48}V (half-life = 15.97 days)
  $^{nat}Cu(p,x)^{65}Zn$ → determine the activity of ^{65}Zn (half-life = 243.93 days)

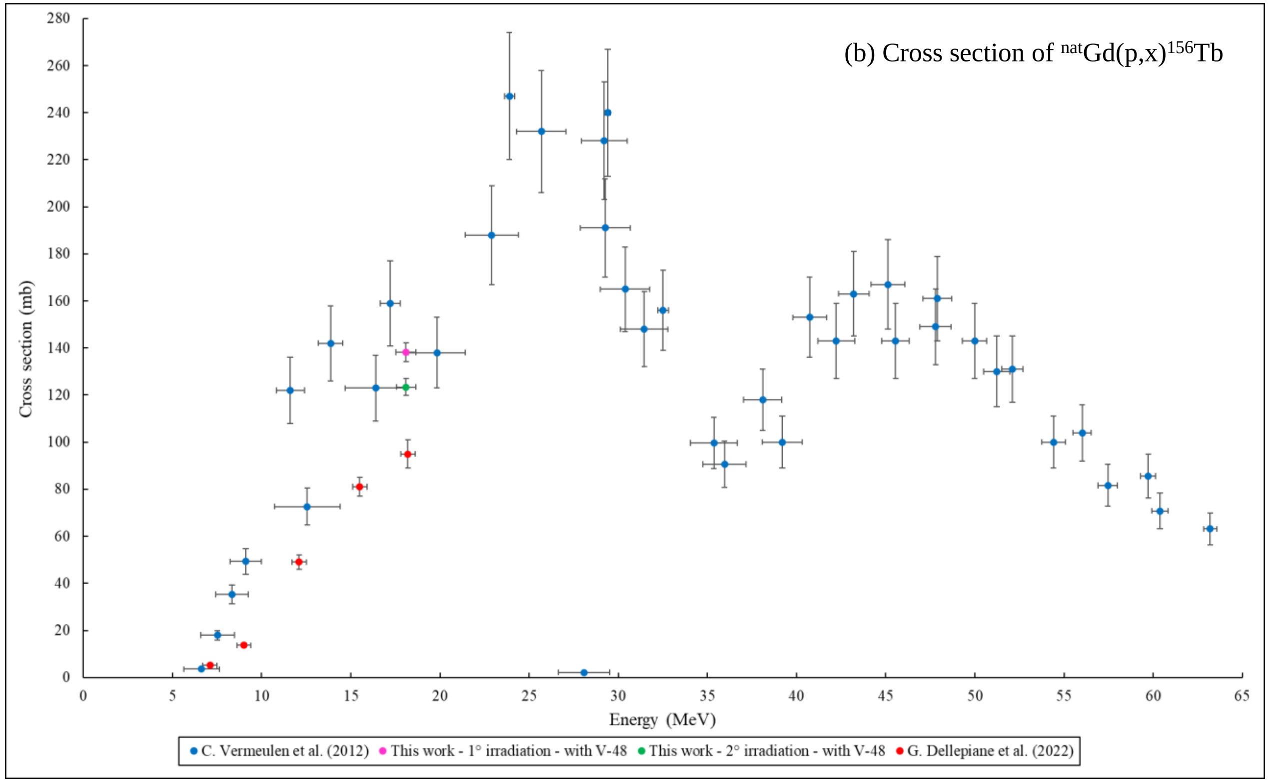
$$\sigma(E) = \frac{Act \cdot A}{\phi_{sample} . N_A . P . \left(\frac{m_2}{s}\right) . (1 - e^{-\lambda t})}$$

$\sigma(E)$ = the energy efficient section (cm^2)
Act = the activity of $^{155}Tb/^{156}Tb$ (Bq)
A = molar mass of $^{155}Tb/^{156}Tb$ ($g.mol^{-1}$)
Φ = the flow of projectiles as determined by monitor (particules·s^{-1})
λ = the radioactive constant of the radionuclides (s^{-1})

P = purity
m_2 = mass of (Gd) obtained by ICP-OES analysis (g)
S = surface of deposit (cm^2)
t = the irradiation time (s)
N_A = Avogadro's number (mol^{-1})

Irradiation experiment: to evaluate the feasibility of the MP methodology





- m(Gd) of sample of the first irradiation = 1.33 ± 0.01 mg;
- m(Gd) of sample of the second irradiation = 1.47 ± 0.01 mg;
- Its notice that our points follows others points from Vermeulen et al. and Dellepiane et al. including their uncertainties, concluding that our values are good consistence with these authors.

Aditional experiments :

1. Varying the speed of mechanical agitation:

Goal: to optimize the homogeneity of the electrolyte solution and, consequently, the deposits.

Speed:	Result:
50 and 150 rpm	Inhomogeneous and extremely thin deposition layer
250 rpm	Very homogeneous surface
500 and 1000 rpm	Very strong the speed and inhomogeneous deposition were obtained

2. Varying the solvent:

Goal: to ensure better compatibility with the manufacturing system.

Solvent:	Result:
Methanol	Without good adhesion to the substrate
DMF	Inhomogeneous surface
Isobutanol	Homogeneous surface and good adhesion
Isopropanol	
Ethanol	Homogeneous surface, but high volatitily

3. Varying the substrate thickness:

Goal: to assess whether there is a difference in using thicker or thinner substrates.

Solvent:	Substrate thickness:	Average mass*:
Isopropanol	125 µm	1.53 ± 0.03 mg
	20 µm	1.51 ± 0.01 mg
Isobutanol	125 µm	0.78 ± 0.02 mg
	20 µm	0.80 ± 0.02 mg

*mass of Gd obtained by ICP-OES analysis

- The results display well-defined that there are not difference using thicker or thinner substrates.

Aditional experiments:

4. Varying the voltage:

Goal: to optimize the efficiency of the process of electrodeposition.

Voltage:	Result:
300 V	Process time = 20 min $T_{initial} \approx$ 19-20°C $T_{final} \approx$ 19-20°C
500 V	Process time = 20 min $T_{initial} \approx$ 19-20°C $T_{final} \approx$ 48°C

5. Varying the m(Gd) add to the working solution:

Goal: to optimize the deposition yield.

m(Gd):	Result:
2 mg	Yield of deposition = 73.5±1.3 %
10 mg	Yield of deposition = 17.5±1.2 %

6. Varying the process time:

Goal: evaluate which behavior has the longest processing time.

Process time:	Result:
20 min	Yield of deposition = 44.97±1.4 % $T_{final} \approx$ 20-25°C
40 min	Yield of deposition = 83.32±1.0 % $T_{final} \approx$ 42-45°C

- The results display well-defined that is better to work with m(Gd) = 2 mg and 20 min of process time.

Solvent	m(Gd) working solution (mg)	m deposit (mg)	m(Gd) deposited (mg)	yield of deposition (%)
30 ml isobutanol	2.112	1.46±0.02	0.80±0.01	37.4±1.7
15 ml isobutanol + 15 ml isopropanol	2.112	1.5±0.4	0.8±0.3	38.7±12.4
28 ml isobutanol + 2 ml isopropanol	2.112	1.8±0.1	0.97±0.01	46.2±1.8
2 ml isobutanol + 28 ml isopropanol	2.112	1.9±0.1	0.9±0.1	43.7±4.6
30 ml isopropanol	2.112	2.64±0.07	1.55±0.03	73.5±1.3

Characterization of the deposit:

Mass Measurements

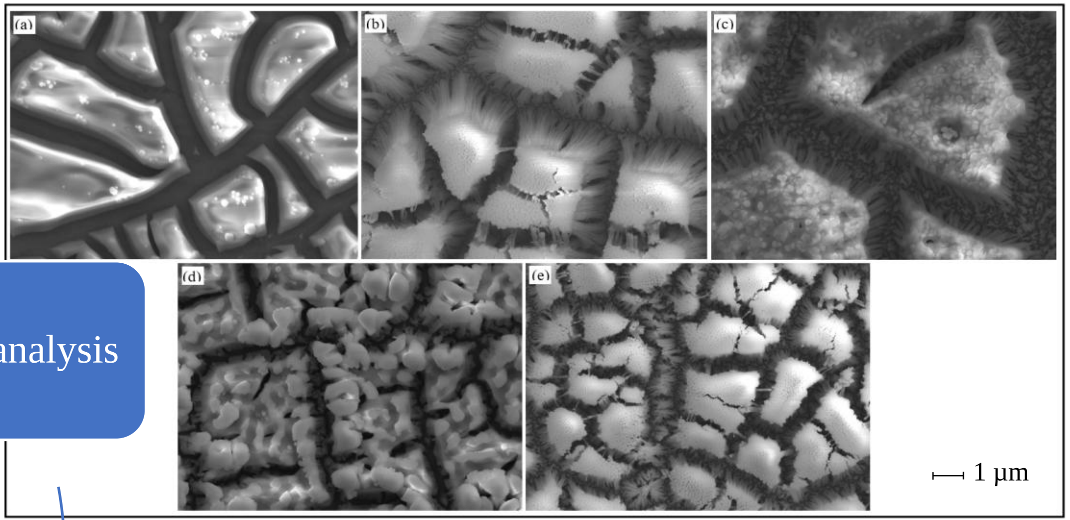
SEM analysis

EDS analysis

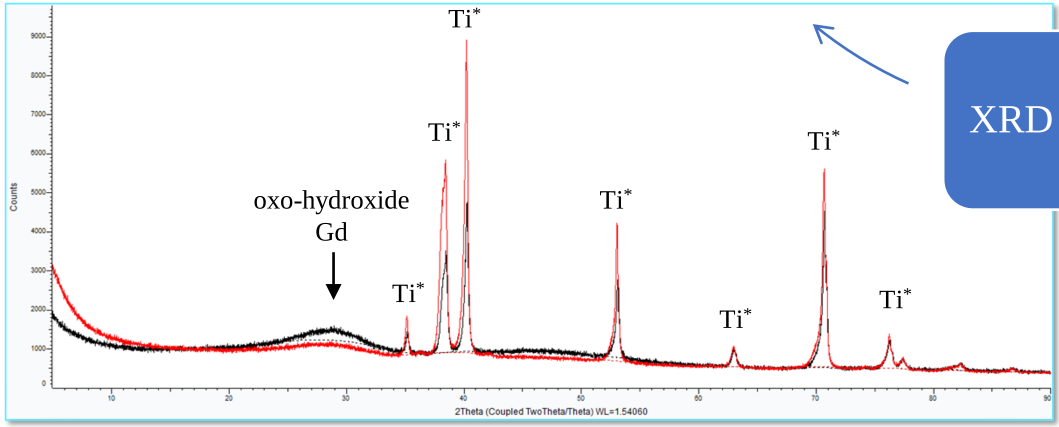
XRD analysis

Profilometry analysis

ICP-OES analysis

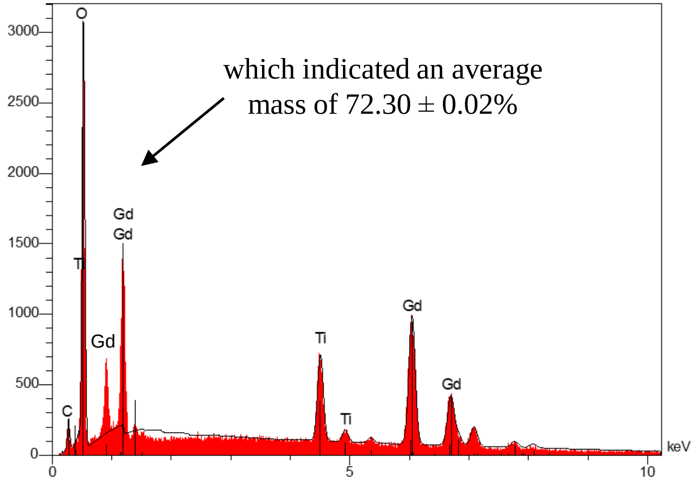


SEM results at 4000x magnification: (a) 100% isobutanol, (b) 100% isopropanol, (c) 50/50% isobutanol + isopropanol, (d) 93.3/6.7% isobutanol + isopropanol, (e) 93.3/6.7 % isopropanol + isobutanol

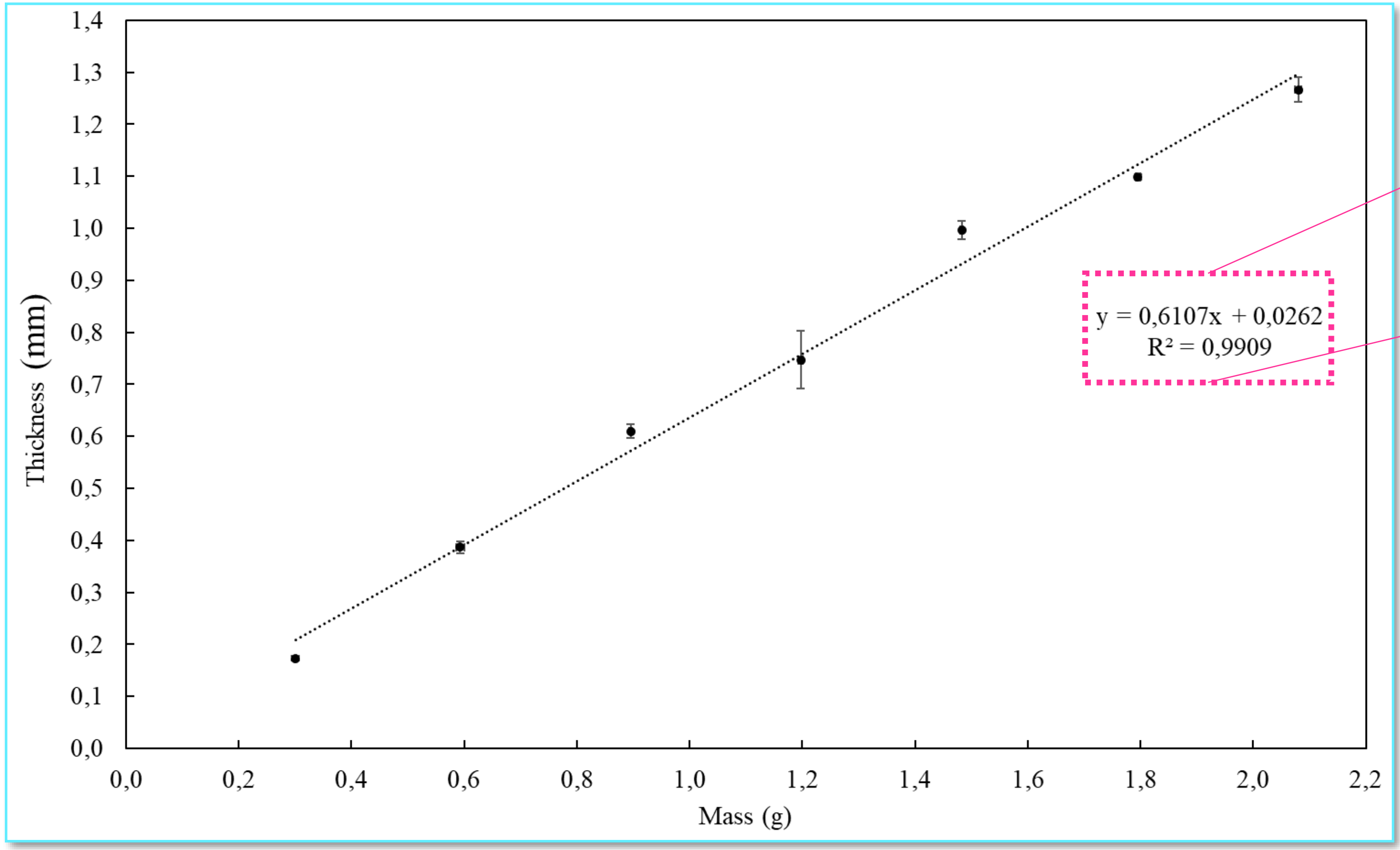


*peaks from Ti - hexagonal form

- Sample with isopropanol
- Sample with isobutanol



Pelletizing technique: experiments in progress



- Optimization between x = mass (g) and y = thickness (mm)

➢ Pressed under 600 bar for 60s;

➢ We are looking to optimize the process to obtain well-densified pellets for irradiation studies.

Work completed:

Thin target:

- Improve the quality of Gd deposit and characterize Gd deposit to understand under which chemical form it is made;
- Irradiate a natural Gd thin target, manufactured by MP, with deuterons and protons, and compare the results with those from different authors to confirm the feasibility of our technique;
- Characterize the targets obtained, accurately measuring the effective production cross sections of Tb-155 and different impurity radioisotopes;

Follow-up:

Thin target:

- Continue developing experiments focused on the MP methodology and further improve the characterization of the obtained Gd deposits;
- Expand the possibilities of applying this target manufacturing method to other chemical elements.

Thick target:

- Obtain Gd_2O_3 pellet to prepare the future production;
- To explore $^{155}Gd(\alpha,4n)^{155}Dy \rightarrow {}^{155}Tb$ and $^{156}Gd(\alpha,5n)^{155}Dy \rightarrow {}^{155}Tb$ nuclear reactions are designed;
- Expand the possibilities of applying this target manufacturing method to other chemical elements.

Chemical separation:

- Study and develop chemical separation techniques for a cyclic process.

Thank you very much for your attention!