

# ***Target development for the production of Cu-67 and Tb-149 for future radiotherapy treatment at GIP ARRONAX***

***4th Nuclear Technologies for Health Symposium***

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**<sup>2</sup> GIP ARRONAX**

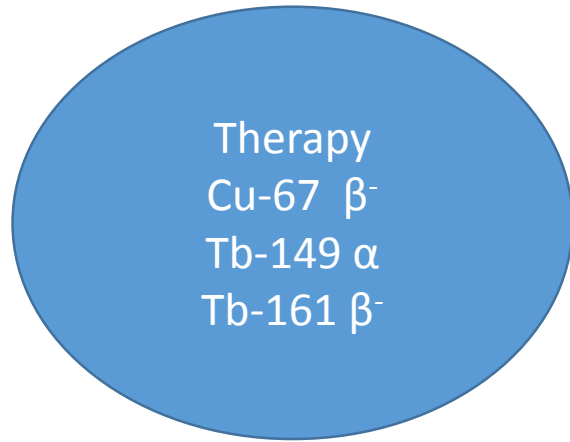


**Thomas Sounalet \***

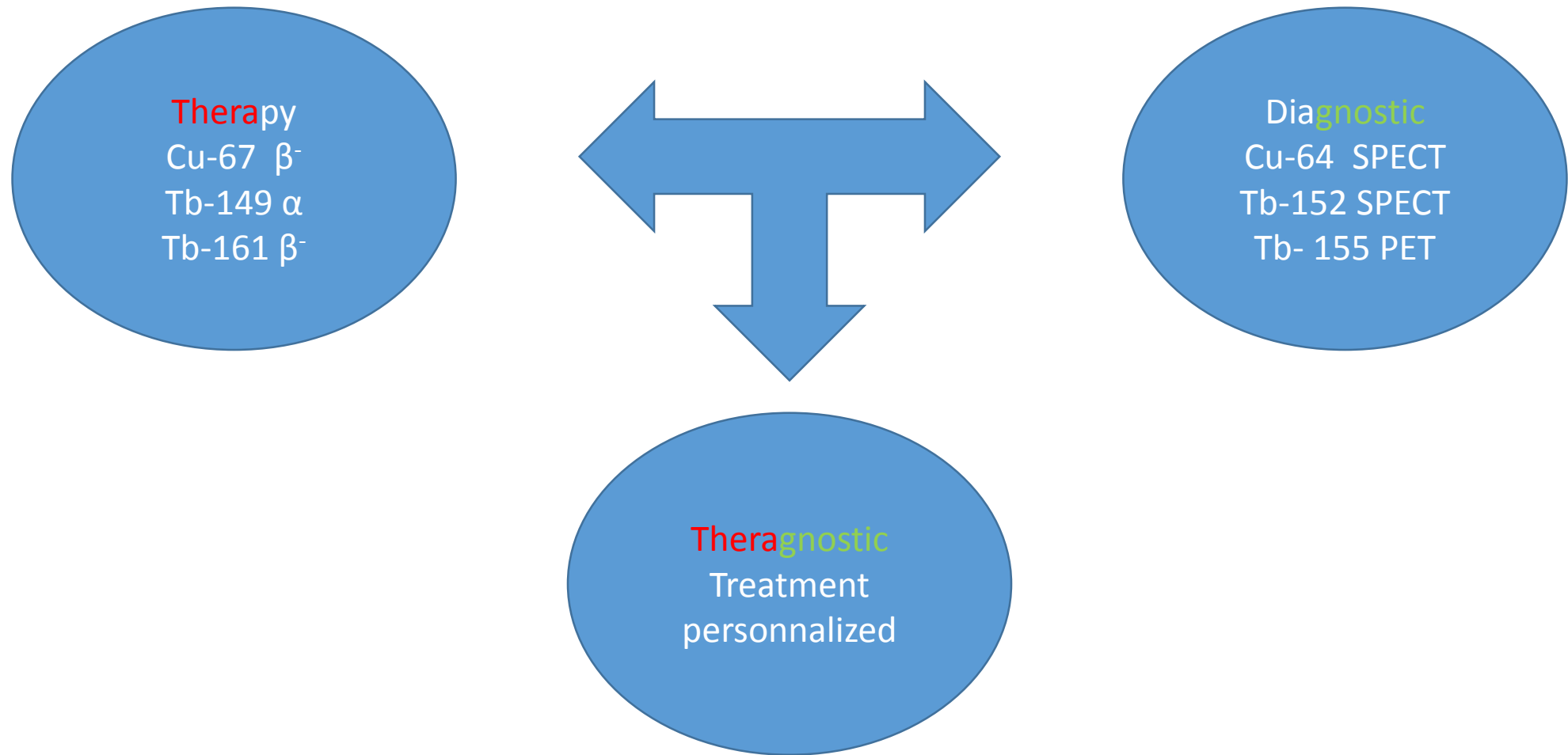
**\* Corresponding author**

# ***Target development for the production of Cu-67 and Tb-149 for future radiotherapy treatment at GIP ARRONAX***

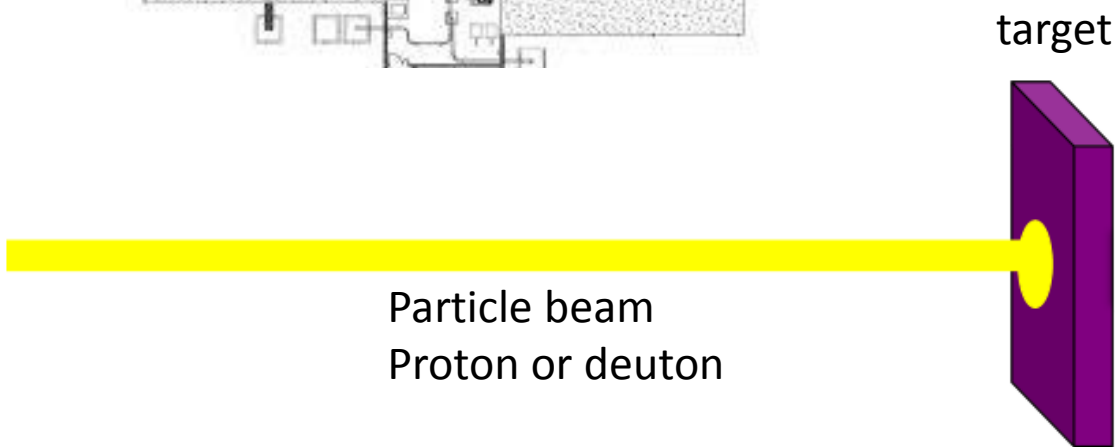
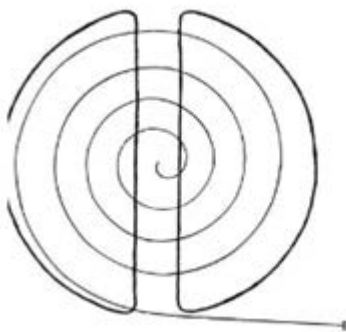
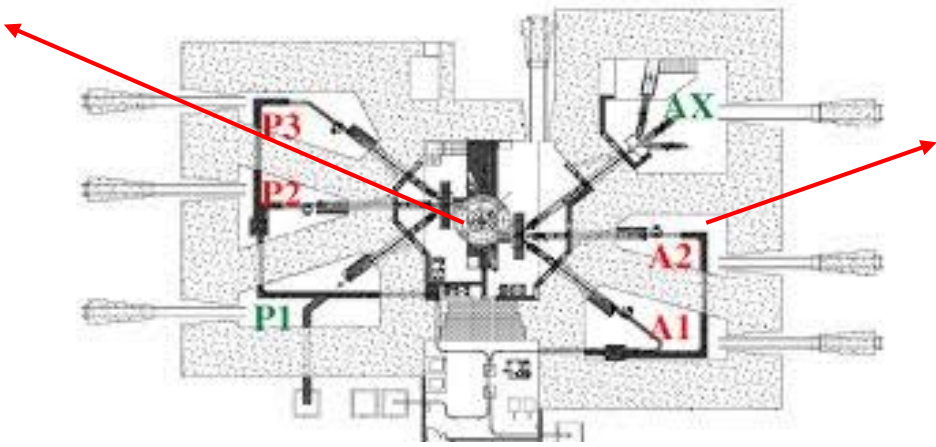
I have prepared subtitles for you because my accent is very strong. Indeed, I am hard of hearing. My presentation is titled : Target development for the production of Cu-67 and Tb-149 for future radiotherapy treatment at GIP ARRONAX



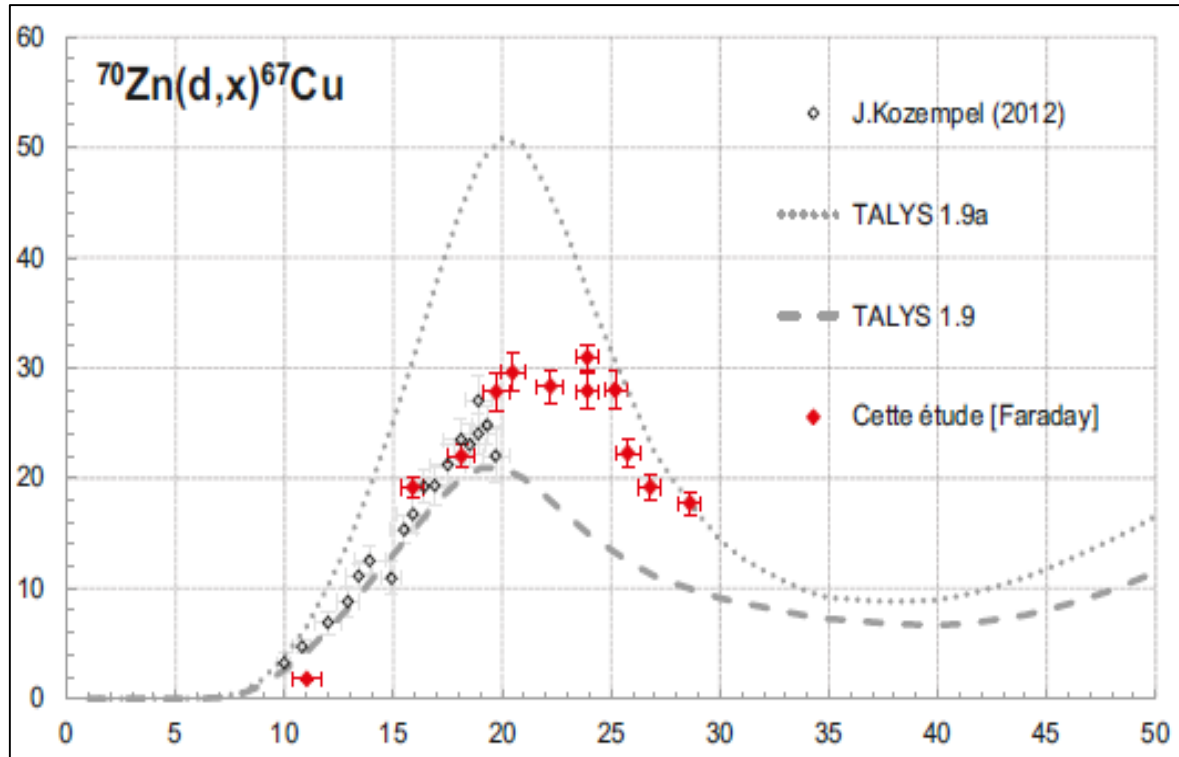
The radioisotopes Cu-67, Tb-149 and Tb-161 emit respectively  $\beta^-$ ,  $\alpha$  and  $\beta^-$  with their energies respectively 141 KeV, 3,9 MeV and 157 KeV and their half life periods 61,83 h, 4,118 h and 6,89 d. Their emissions are adapted for therapy and allow to destroy tumour cells.



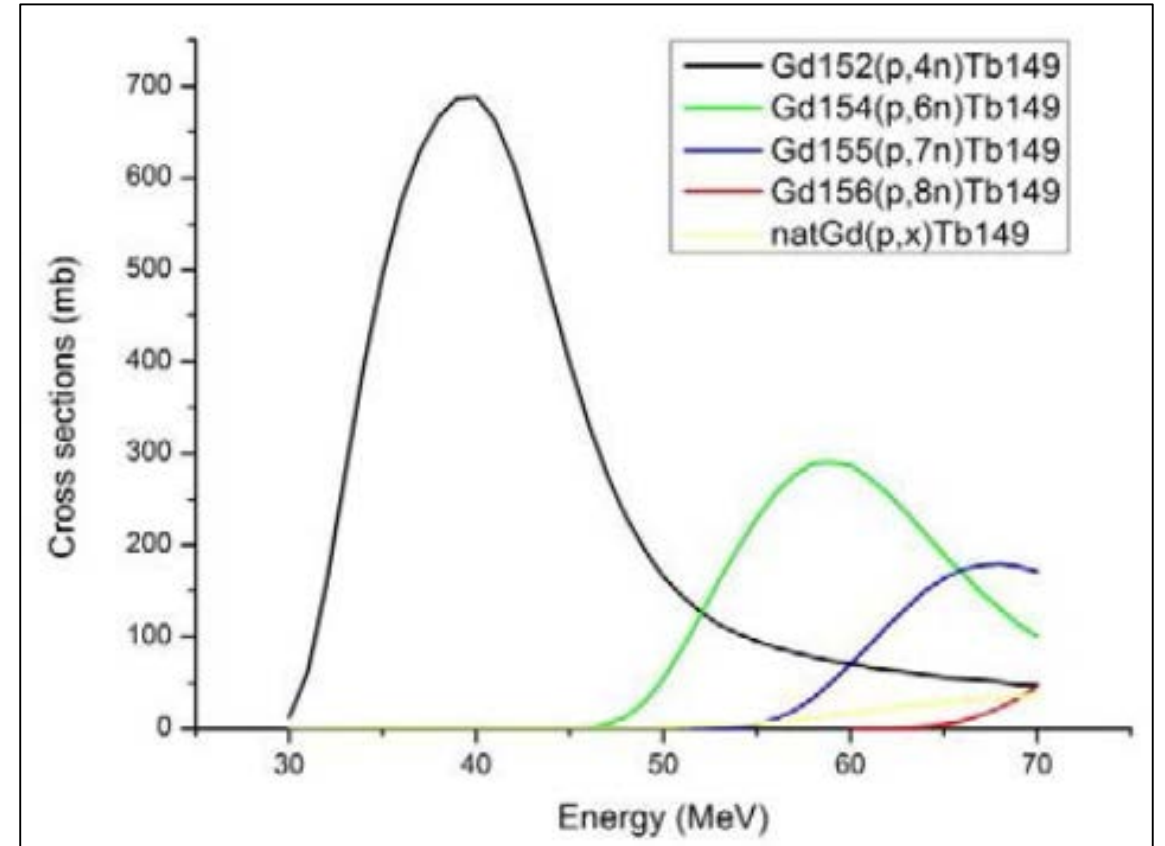
These radioisotopes can be utilized in theragnostic by using Cu-64 for SPECT and Tb-152 for SPECT and Tb-155 for TEP. The radioisotope Cu-64 is already used in France and are produced by ARRONAX. The production of Tb-152 and Tb-155 is ongoing in research, like for Tb-161. That is why we are interested in producing Cu-67 and Tb-149 to complete with these other radioisotopes to increase the use of theragnostic treatment.



The radioisotopes Cu-67 and Tb-149 are produced artificially by bombarding the particle beam with protons and deuterons which are accelerated in the cyclotron ARRONAX. The targets produced, Cu-67 and Tb-149 are held in the irradiation station. These targets are stable elements. But how do we choose these stable elements?

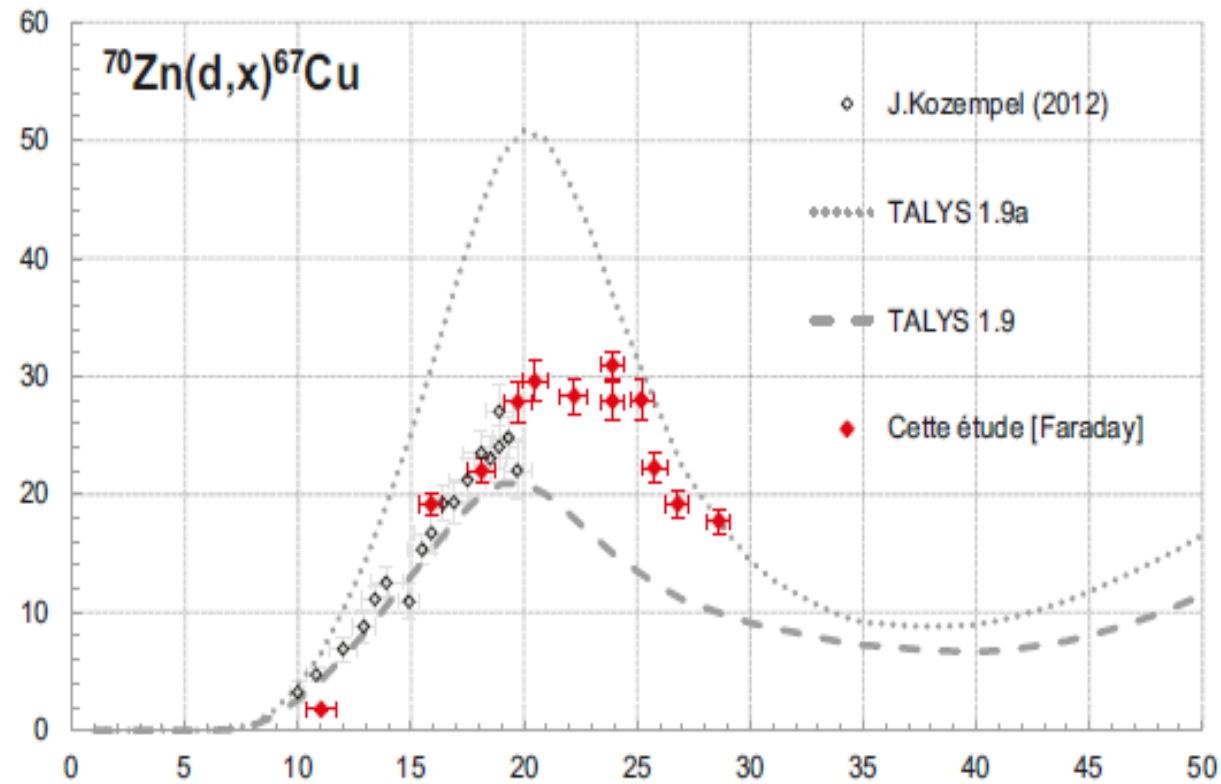


Ref : PhD Etienne Nigrón Radioactives isotopes produced by unconventional means (2019)



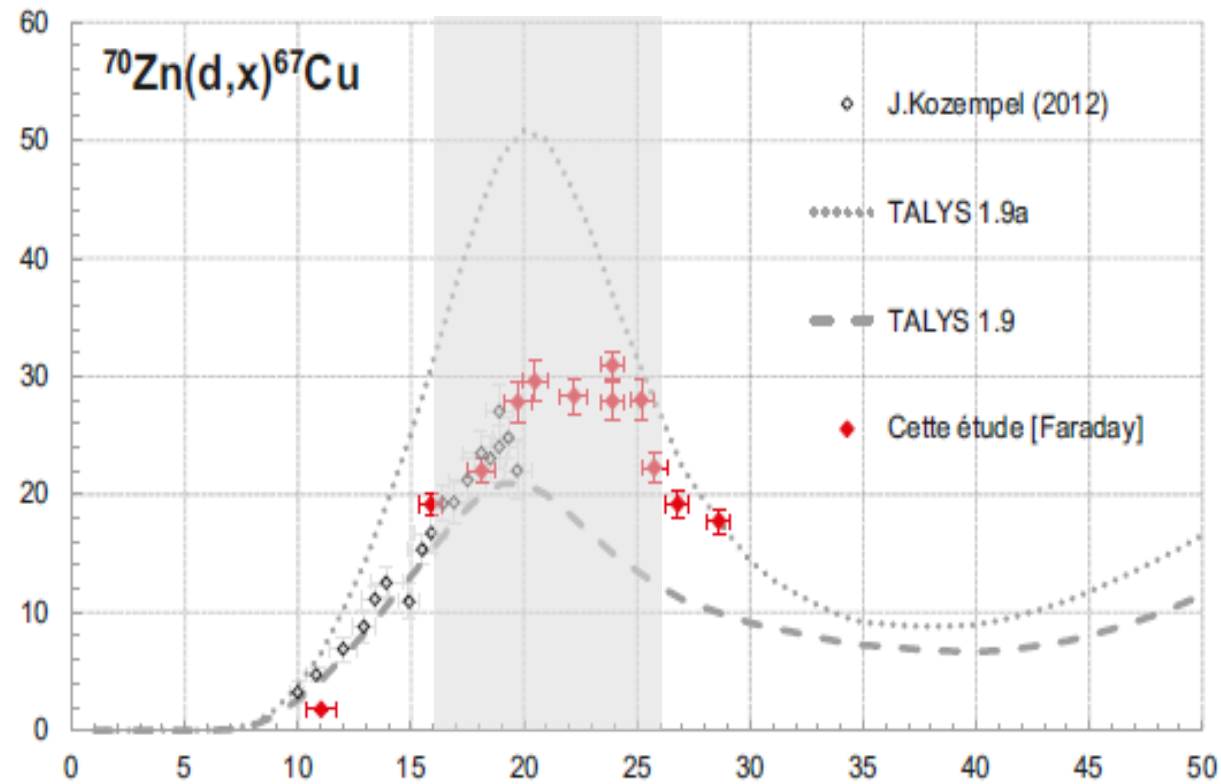
Ref : R. Formento Cavaier et al. / Physics Procedia 90 ( 2017 ) 157 – 163

To define which stable elements allow to produce Cu-67 and Tb-149, several experimental studies named “measure of cross section”, are conducted. These experiments allow us to determine the activity of Cu-67 and Tb-149 in function of particle energy.



Ref : PhD Etienne Nigrón Radioactives isotopes produced by unconventional means

Since 2019 we have found an interesting new pathway for producing Cu-67 : by using Zn-70 with deuteron irradiation to produce Cu-67.

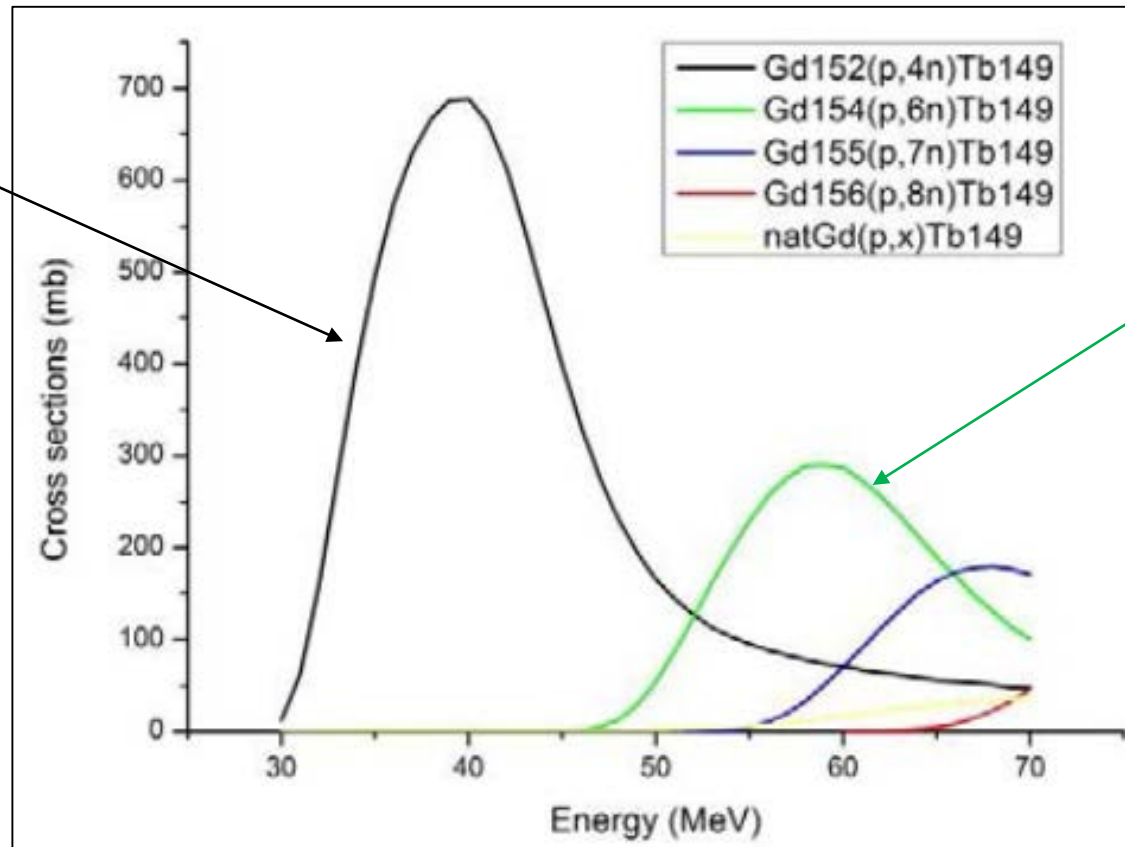


Ref : PhD Etienne Nigrón Radioactives isotopes produced by unconventional means

The Cu-67 production is calculated from energy irradiation 26 MeV to 16 MeV, assuming the intensity irradiation is 80  $\mu\text{A}$  and the duration irradiation 72h, the activity produced is 24,1 GBq.



Gd152(p,4n)Tb149



Gd154(p,6n)Tb149

Ref : R. Formento Cavaier et al. / Physics Procedia 90 ( 2017 ) 157 – 163

To produce Tb-149, contrary to the study of the production Cu-67, there aren't any experimental databases, only theoretical cross sections have been effected. The calculation found that two stable elements are interesting to use: Gd-152 or Gd-154, both with proton irradiation. The Tb-149 production hasn't been calculated.

Zn-70	0,61%
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Gd-152	0,20%
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Gd-154	2,18%
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These 3 stable elements have a very low natural abundance : 0,61% for Zn-70 and 0,20% and 2.18% for respectively Gd-152 and Gd-154. These low values don't allow the production of radio-isotopes of interest in highly quantities.

Zn-70	0,61%
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Gd-152	0,20%
--------	-------

Gd-154	2,18%
--------	-------

Enrichment



Zn-68 Gd-154	> 60%	Gd-152	34%
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So, it is necessary to use enriched elements to increase the production of interest radioisotopes. The expected enrichment of Zn-70 and Gd-154 is more than 60% but for Gd-152, the expected enrichment is 34%, this value is low, the production will not be high if we use Gd-152. Gd-154 is much more interesting than Gd-152.

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Enrichment



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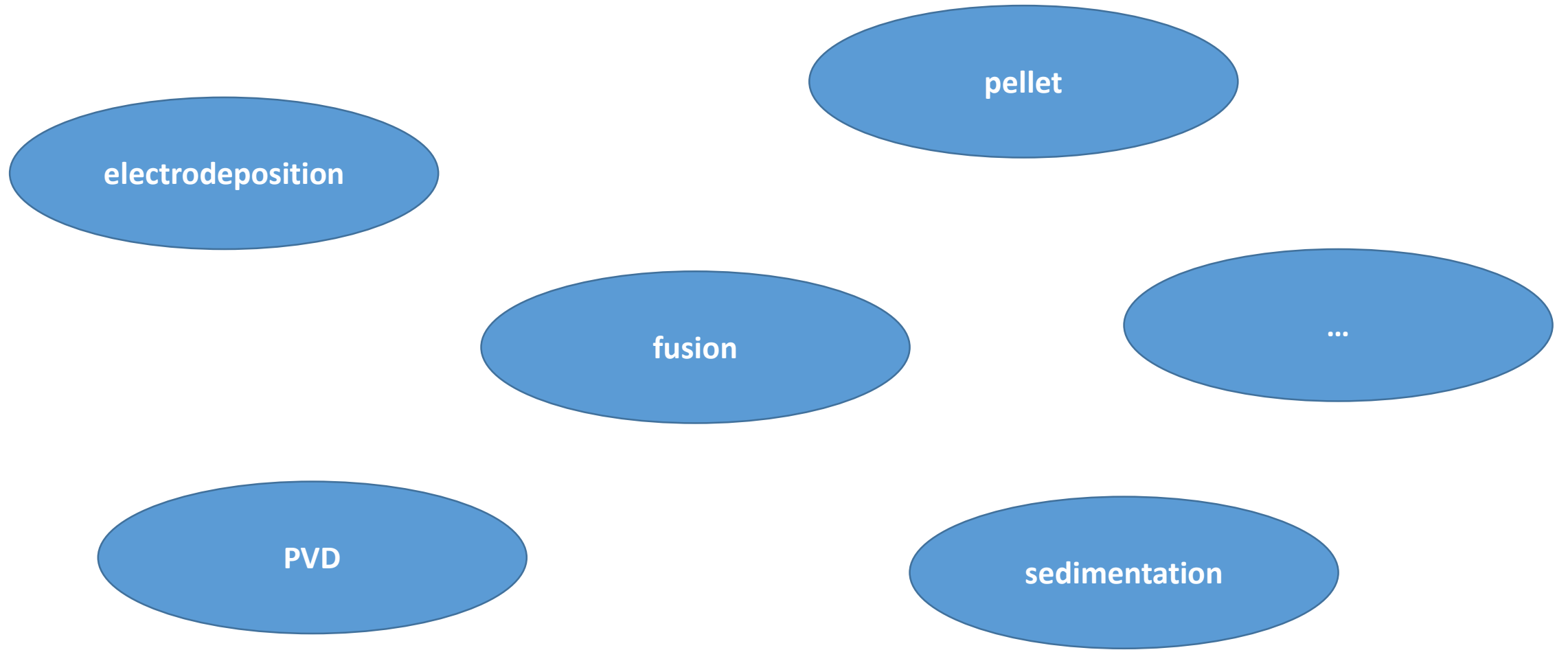


metallic oxide

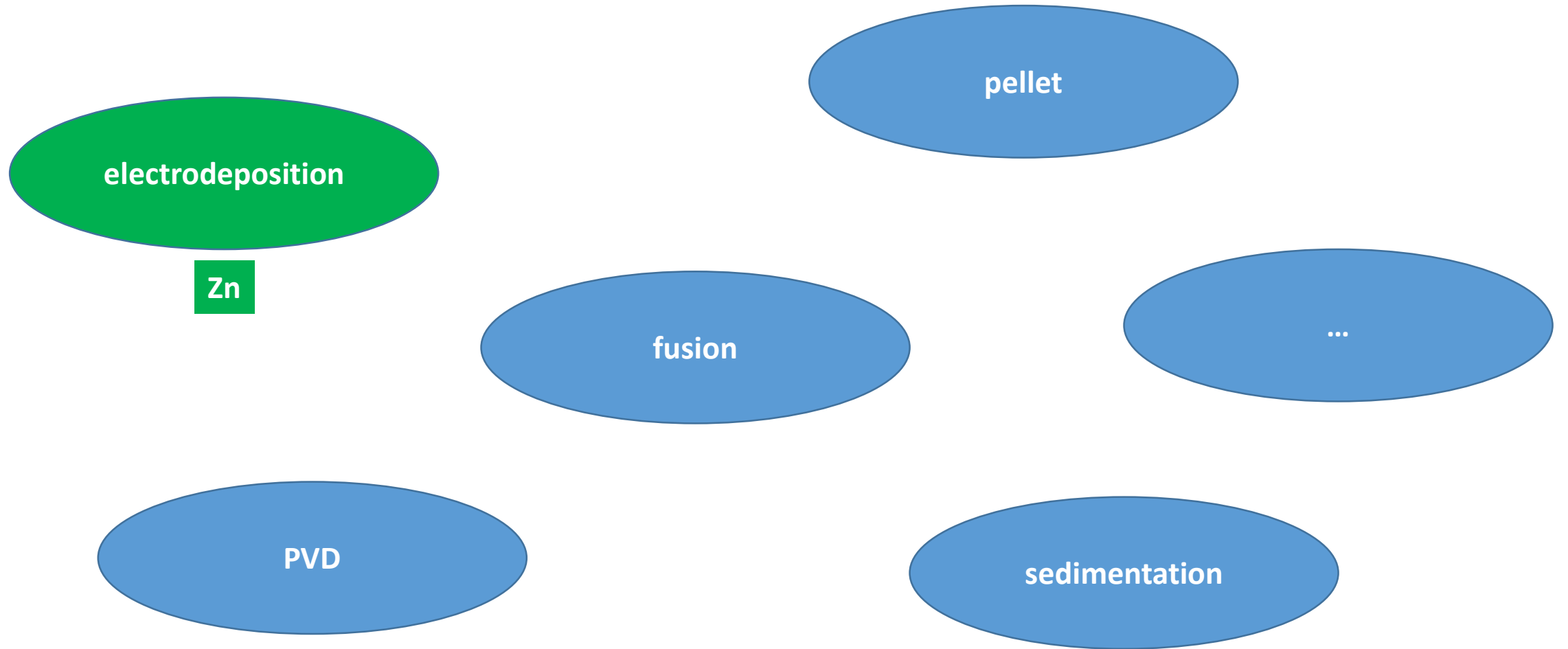


metallic powder

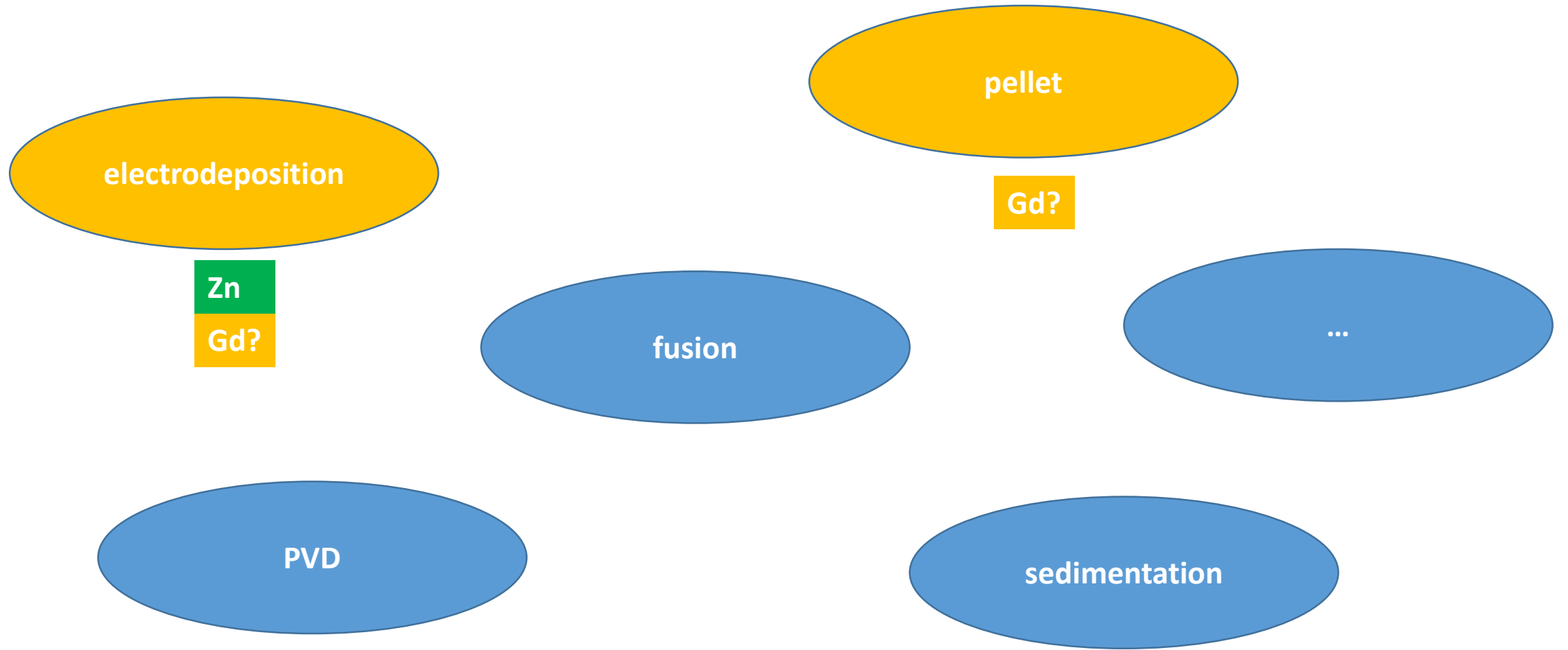
All stable enrichment elements have only two physical forms: metallic oxide or metallic powder. These physical states aren't adapted for producing the radioisotopes of interest in high quantities, it is necessary to make the targets Zn-70 and Gd-154 under solid form.



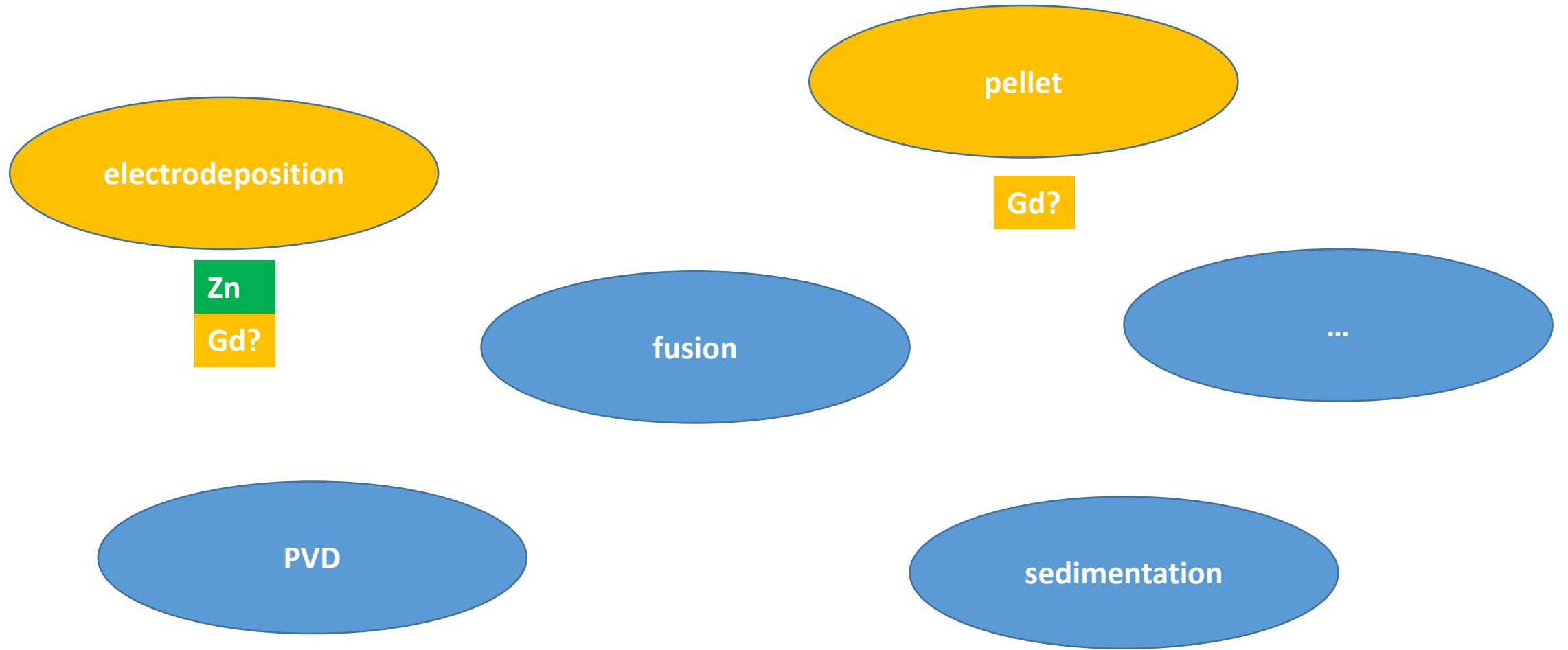
There are several methods to obtain the solid targets. The most used to manufacture the targets are electrodeposition, fusion, pellet, PVD and sedimentation. Each method has advantages and disadvantages as well as a cost.



The target Zn-70 is made by electrodeposition. We have chosen this technique because this technique has been used for more than a decade and works well.



As for Gd-154, we are researching the best adapted method for manufacturing because the studies on the Gd target are poor in literature. In our present work, we have focused on electrodeposition and pellet.

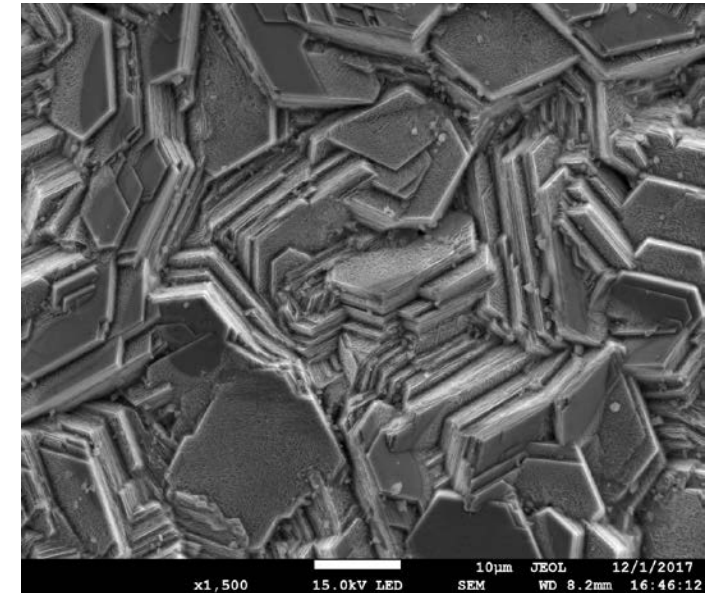


The enriched elements are very expensive. All experiments are worked with natural elements

The enriched elements are very expensive. For all experiments, we have used natural elements.

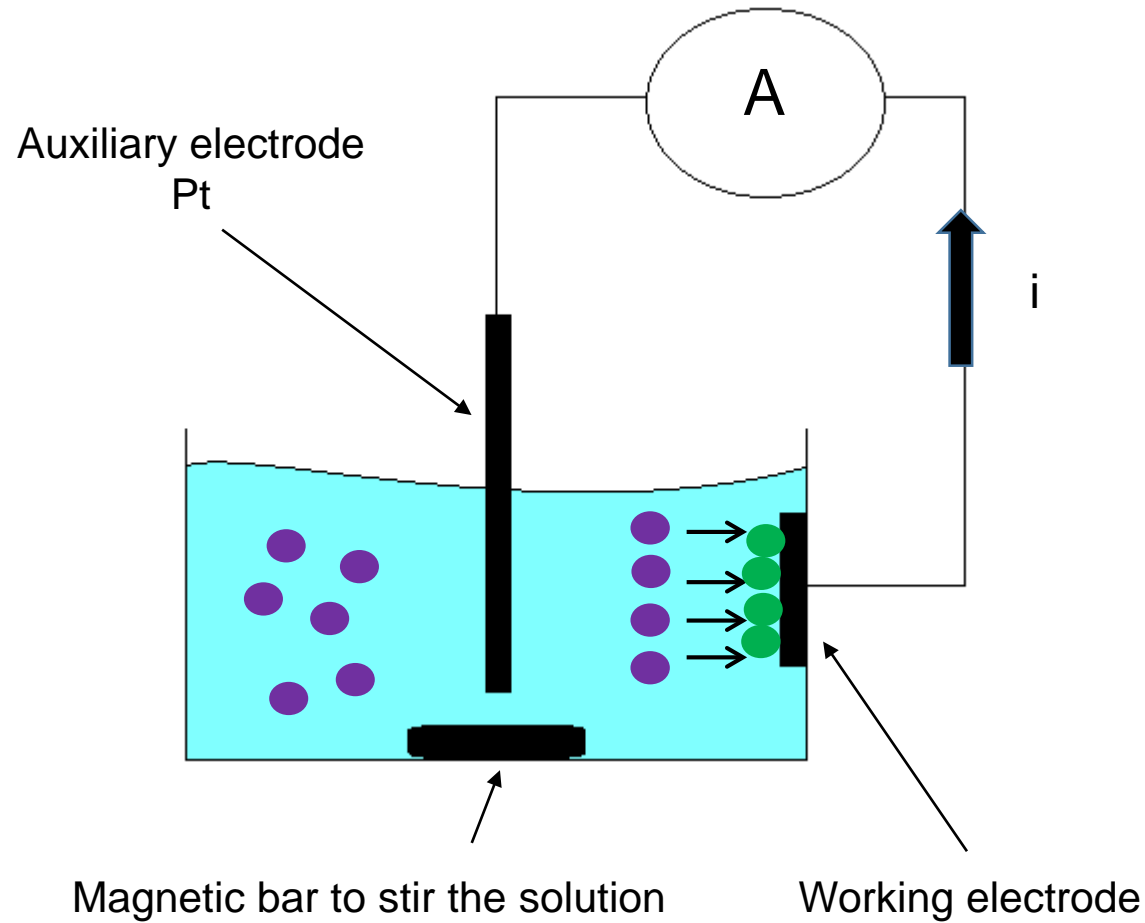


## Production of Cu-67 from Zn-70



Here we can see the target for the production of Cu-67 from Zn-70. For all experiments, we used natural Zn. The target of Zn is obtained by electrodeposition.

# Production of Cu-67 from Zn-70



Electrodeposition parameters to study :

- ❖ Concentration of species
- ❖ pH of solution
- ❖ Temperature of solution
- ❖ Intensity or potential to apply
- ❖ Agitation speed of the solution

What is electrodeposition? It is a technique that involves reducing species present in a solution on a conductive substrate. Our interest is to reduce a metal cation  $\text{Zn}^{2+}$  on a substrate by applying a potential or an intensity to the working and auxiliary electrodes. We thus obtain a metallic deposit Zn on the working electrode. Here, we use gold backing because it is noble.

## Production of Cu-67 from Zn-70



$S = 4 \text{ cm}^2$   
 $e = 250 \text{ }\mu\text{m}$   
 $t = 8\text{h}$

Parameters of electrodeposition :  $\text{ZnSO}_4$ ,  
 $C_m(\text{Zn}^{2+}) = 30 \text{ g/L}$  ; pH 2 ;  $J = - 20 \text{ mA/cm}^2$  ;  
 $T^\circ\text{C} = 30^\circ\text{C}$

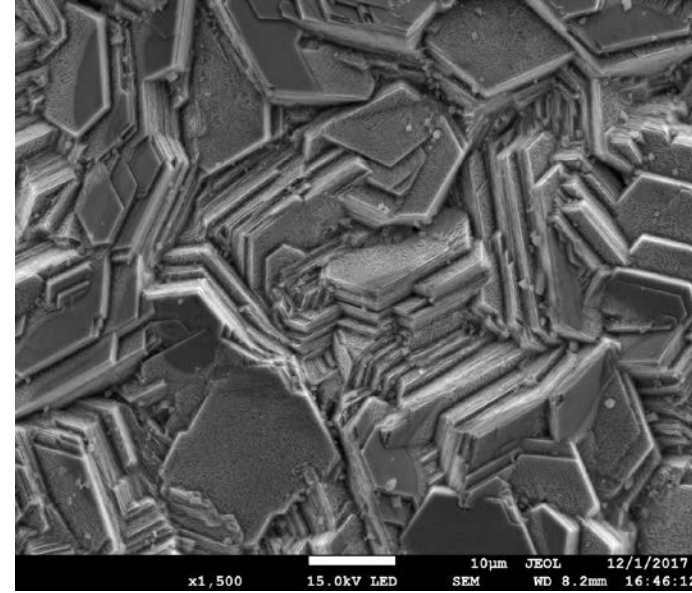
In this photo we can see a Zn deposit after 8h of electrodeposition, a thickness of  $250 \text{ }\mu\text{m}$  and a surface  $4 \text{ cm}^2$  is obtained. It is visibly metallic grey and compact.

# Production of Cu-67 from Zn-70



S = 4 cm<sup>2</sup>  
e = 250 μm  
t = 8h

Parameters of electrodeposition : ZnSO<sub>4</sub>,  
C<sub>m</sub>(Zn<sup>2+</sup>) = 30 g/L ; pH 2 ; J = - 20 mA/cm<sup>2</sup> ;  
T°C = 30°C



MEB (x1500)

Deposits were analyzed through SEM to observe how their crystallographic structures evolved. We can see that the structures are hexagonal and are homogeneous over the entire surface. These structures are typical of Zn deposition. The quality of this target meets our requirements, it is well suited for the production of Cu-67.

## Target of Gd for the production of Tb-149



**Don't work in aqueous solutions because Gd deposits will be highly oxidized**



**Poor quality of Gd deposit**

For the production of Tb-149, it is not recommended to work in aqueous solutions because it is known that Gd is easily oxidized during electrodeposition. An oxidized deposit means a deposit of poor quality and is thus unusable.

## Target of Gd for the production of Tb-149



Don't work in aqueous solutions because Gd deposits will be highly oxidized



Poor quality of Gd deposit



How do we obtain the target of Gd?

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How do we obtain the target of Gd?



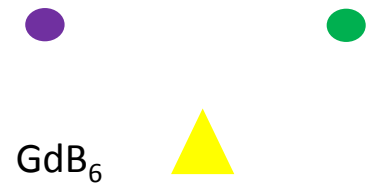
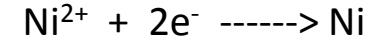
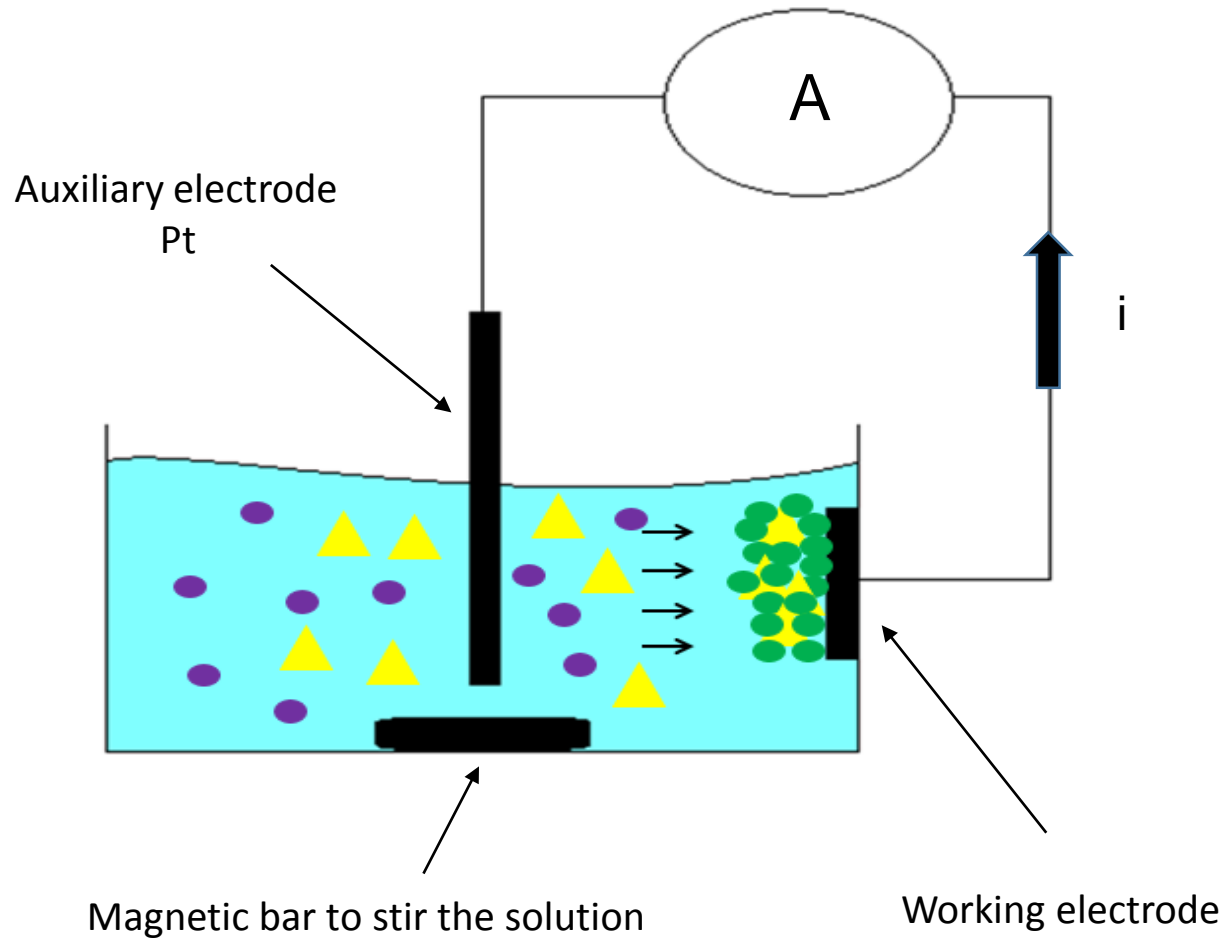
by trapping the powder of Gd or salt Gd in Ni deposit. This technique is called **EMMC** (electrodeposited metal matrix/metal particle composites) and this target is obtained by electrodeposition



by obtaining a pellet of salt Gd

To obtain a target Gd, we have the choice between 2 solutions : by trapping the powder of Gd or salt Gd in nickel deposit. This technique is called EMMC (electrodeposited metal matrix/metal particle composites) and this target is obtained by electrodeposition, or by obtaining a pellet of salt Gd. A PhD student, Yizheng Wang, has been working on these studies since September 2019.

# Production of Tb-149 from Gd-154

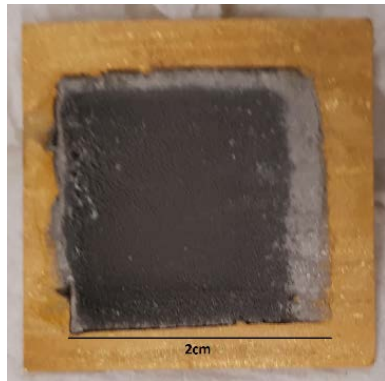


Trapping of Gd compound, GdB<sub>6</sub>, in Ni matrix

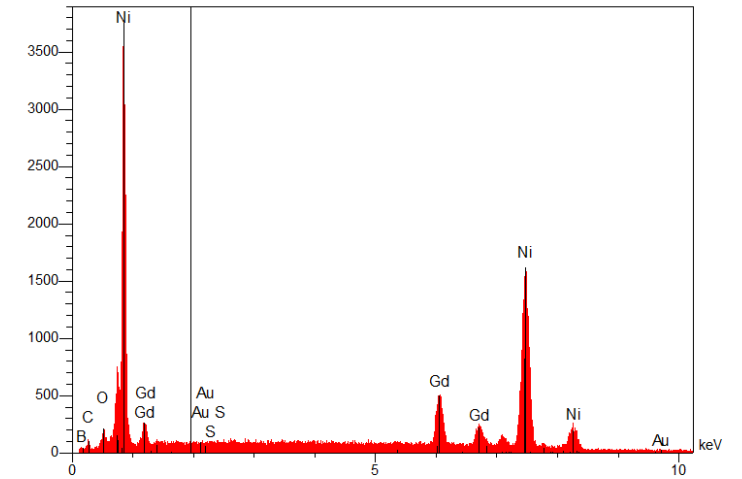
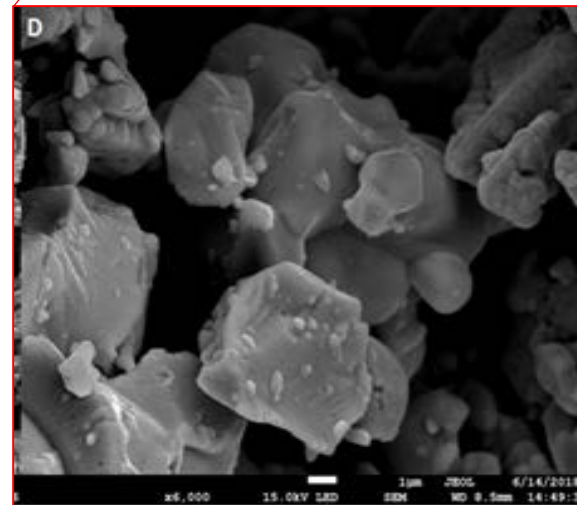
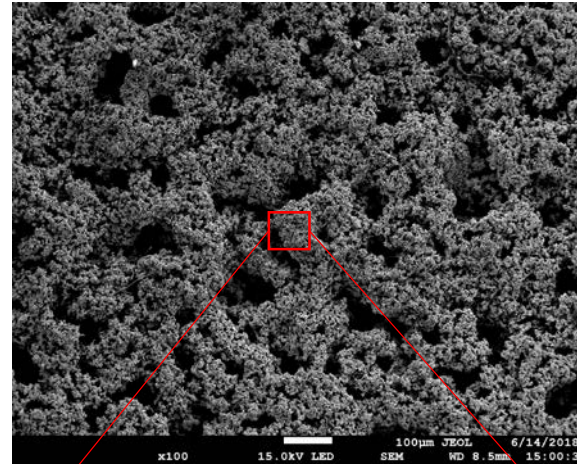
Contrary to what we have seen before, here it is not a question of reducing the gadolinium particles. It is the Ni cations that will be reduced. The particles are "washed away" by these cations towards the substrate and at the moment of the reduction of the Ni cations, the particles are trapped between the Ni atoms. And so, the particles are in the Ni deposit.



# Production of Tb-149 from Gd-154

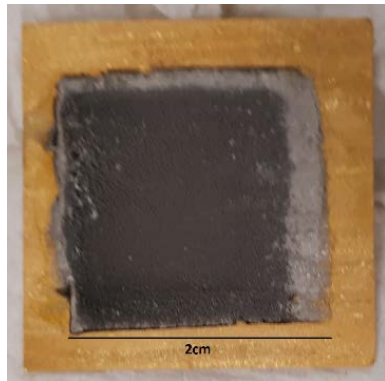


Area of coating = 4 cm<sup>2</sup>  
Thickness of Ni substrate : 50 μm

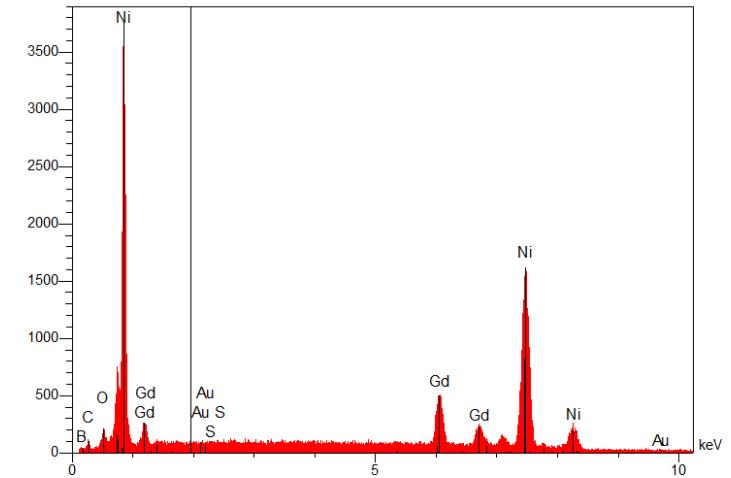
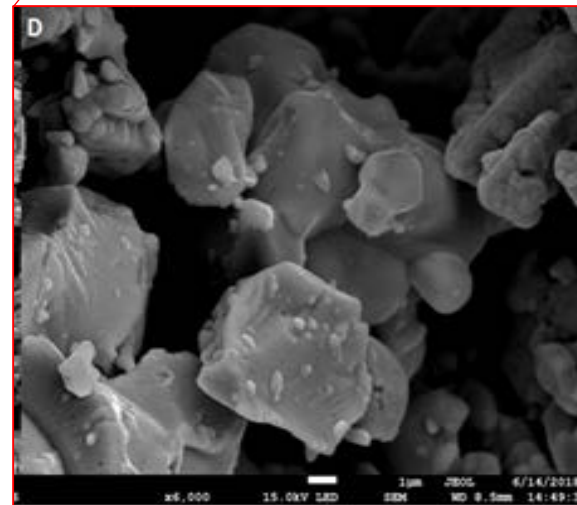
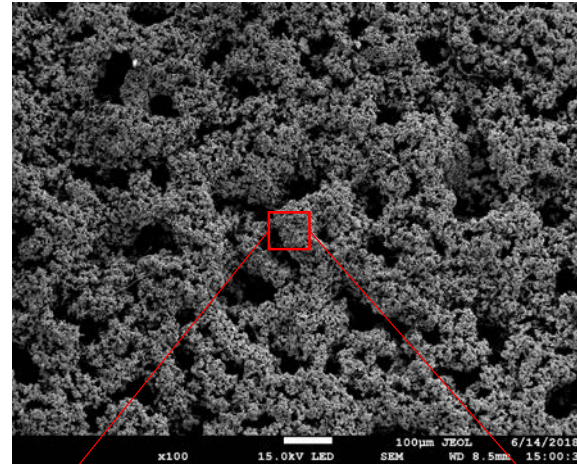


The deposit is black because the salt of GdB<sub>6</sub> is black. The deposit adhered to the support.

# Production of Tb-149 from Gd-154

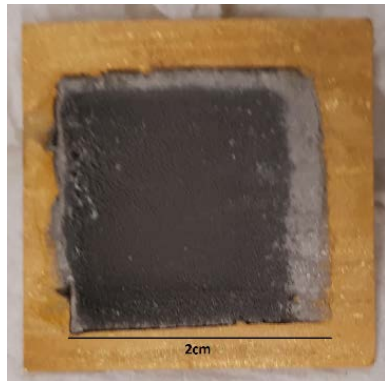


Area of coating = 4 cm<sup>2</sup>  
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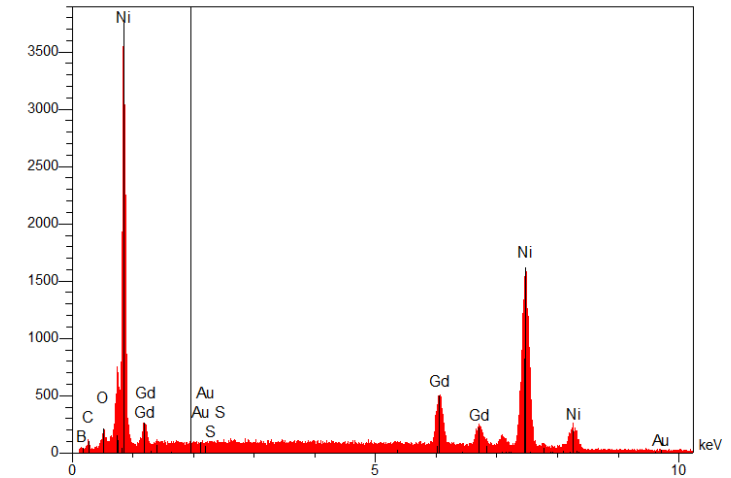
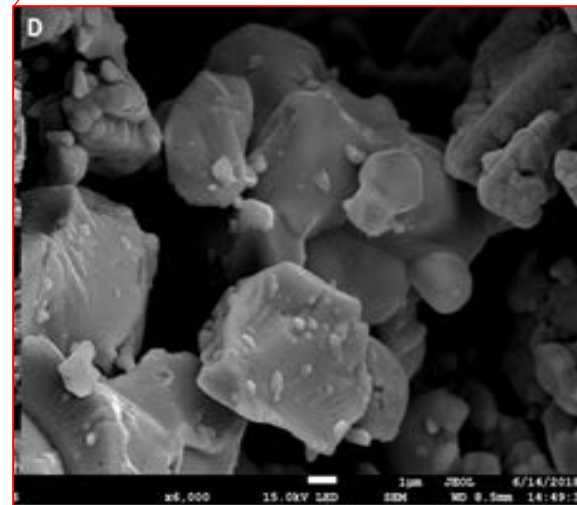
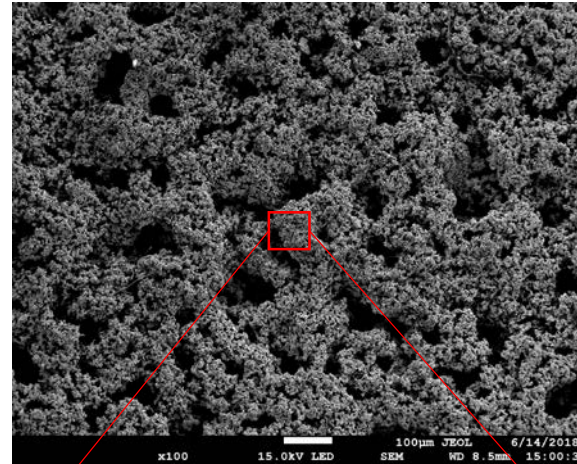


Here it has been analysed by MEB-EDX, the photo taken by MEB, on the top middle, shows a certain structural irregularity of the deposit and at the bottom middle, at a higher magnification, we can see in 3D the hexagonal structure of GdB<sub>6</sub> trapped in Ni. The spectrum at the right, shows that there is a presence of Gd and Ni. Despite the irregular structure of the deposit, impurities are absent.

# Production of Tb-149 from Gd-154



Area of coating = 4 cm<sup>2</sup>  
Thickness of Ni substrate : 50 μm



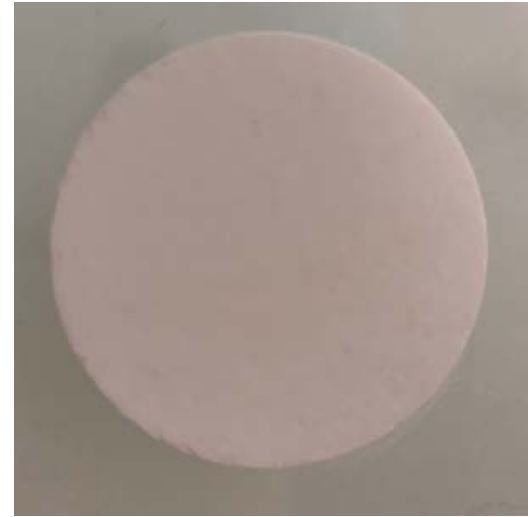
**ICP : 22% of Gd in Ni matrix**

The analysis by ICP allowed to quantify the mass proportion of Gd in the Ni matrix and gives 22 %. This proportion is interesting and can be improved within the structural state of the deposit, by varying the different parameters such as the current density, the concentration of nickel and GdB6, the temperature of the solution and so on.

## Production of Tb-149 from Gd-154



$\text{GdF}_3$   
e = 1,66 mm  
diameter : 2cm



$\text{GdCl}_3$   
e = 1,54 mm  
diameter : 2cm

Another solution for making the targets is to make pellets. In the figures above, to the left we see a pellet of fluoride gadolinium and to the right a chloride gadolinium. These pellets are compact and solid. But more studies are necessary to know if these pellets are suited for the production of Tb-149, especially to determine their molten temperatures. Indeed, the pellets must not melt during irradiation.

## Conclusion

✓ Zn target for the production of Cu-67 is ready



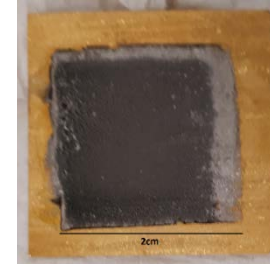
To conclude, the parameters to make Zn deposit are defined and the coating quality is very good. We are able to make Zn target with high thickness and thus high activity of Cu-67. The target of Zn is ready.

## Conclusion

✓ Zn target for the production of Cu-67 is ready



✓ Using pellets or EMMC for the production of Tb-149 is promising.



✓ The pellets can be used for the production Tb-161, Tb-152 and Tb-155



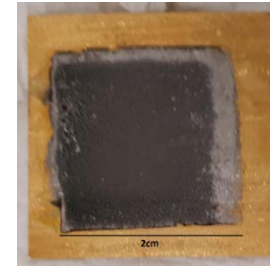
For the Gd targets, we are able to make different targets like EMMC and pellets and these targets can be used for the production of Tb-149. Furthermore, these manufacturing methods can be used for the production of Tb-161, Tb-152 and Tb-155. Yizheng Wang, a PhD student is studying which among these targets are the best suited for these productions.

## Conclusion

✓ Zn target for the production of Cu-67 is ready



✓ Using pellets or EMMC for the production of Tb-149 is promising.



✓ The pellets can be used for the production Tb-161, Tb-152 and Tb-155



But we are missing experimental cross section databases to determine the produced activity. These steps are fundamental and their research is ongoing.

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# Thank you for your attention

Thank you to :

C.Alliot<sup>1</sup>, G.Arnaud<sup>2</sup>, R.Formento Cavaier<sup>3</sup>, F.Haddad<sup>1,2</sup>, N.Michel<sup>1,2</sup>, I.Zahi<sup>3</sup>, Y.Wang<sup>1,2,4</sup>

<sup>1</sup> GIP ARRONAX, Nantes, France

<sup>2</sup> laboratory Subatech, IN2P3-CNRS, Nantes, France

<sup>3</sup> AAA, Saint-Genis-Pouilly, France

<sup>4</sup> PhD student

And thank you to the whole team of GIP ARRONAX and Subatech

If you have questions, I propose that you write them on a paper and we discuss them during the break.