Direct targets for the production of medical radionuclides: an update ^{155}Tb as a case study

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The famous 'Swiss army knife' of nuclear medicine

^{149}Tb

$T_{1/2}$ = 4 h
Eα = 4 MeV, $E_{\beta+}$ = 638 keV

Applied in "Alpha therapy"

(Muller, 2017; Umbricht 2019)

^{152}Tb

$T_{1/2}$ = 18 h
Mean $E_{\beta+}$ = 1,14 MeV

Applied in PET/CT

(Muller, 2016; Baum 2017)

65 158.925
Tb
Terbium
[Xe] $4f^9 6s^2$
Lanthanides

^{161}Tb

$T_{1/2}$ = 7 d
Mean $E_{\beta-}$ = 154 keV

An alternative to ^{177}Lu
Applied in β therapy
(Lehenberger, 2011; Gracheva, 2019)

^{155}Tb

$T_{1/2}$ = 5 j
E_{γ}= 87 MeV (32%)
E_{Auger}= 87 keV (37%)

Applied in SPECT + Auger therapy
(Muller, 2014; Baum 2017)

Production and availability of Tb radionuclides

^{161}Tb

Can be produced in nuclear reactors in large quantity and with good quality

$^{160}Gd(n,\gamma)^{161}Gd \rightarrow ^{161}Tb$

Available through PRISMAP

Soon available from TerThera ?

TERTHERA

$^{149,152,155}Tb$

Produced by spallation: limited quantity, many impurities and complex procedure

→ need for Mass separation / chemistry (low efficiency at the moment)

Alternative : low to medium energy cyclotron and **Gd targets**

Potentially less impurities but **enriched Gd targets required**

- ^{152}Gd (p, 4n)^{149}Tb (enrichment of ^{152}Gd: 30%)
- ^{152}Gd (p, n) ^{152}Tb
- ^{155}Gd (p, n) ^{155}Tb, ^{155}Gd (d, 2n) ^{155}Tb (enrichment: 90%)

Production and availability of Tb radionuclides

^{161}Tb

Can be produced in nuclear reactors in large quantity and with good quality

^{160}Gd(n,γ)^{161}Gd → ^{161}Tb

Available through PRISMAP

Soon available from TerThera ?

^{149,152,155}Tb

Produced by spallation: limited quantity, many impurities and complex procedure

→ need for Mass separation / chemistry

Low efficiency to separate impurities

Alternative : low to medium energy cyclotron and **Gd targets**

Potentially less impurities but **enriched Gd targets required**

- ^{152}Gd (p, 4n)^{149}Tb (enrichment of ^{152}Gd: 30%)
- ^{152}Gd (p, n) ^{152}Tb
- ^{155}Gd (p, n) ^{155}Tb, ^{155}Gd (d, 2n) ^{155}Tb (enrichment: 90%)

Manufacturing of enriched Gd targets

P.O.C. to be done through the production of ^{155}Tb using ^{155}Gd

1 **Cross section measurement of the reaction $^{155}Gd(d,n)^{155}Tb$ to estimate production yield**

- Make very thin targets (10-20 μm)

2 **Manufacture a complete and uniform Gd-containing target for the routine production of Tb**

- Make thicker targets (≥ 100 μm)

Manufacturing of thin targets: Co-electrodeposition

Starting material: enriched Gd_2O_3 from Trace Science

Isotopes	Gd-155	Gd-156	Gd-157	Gd-158	Gd-160
Proportion (%)	**92.8**	5.7	0.8	0.5	0.2

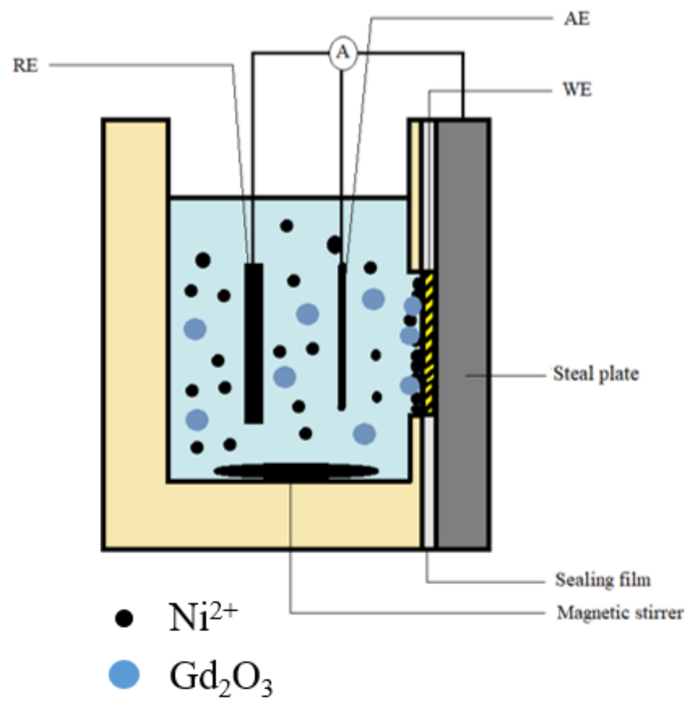
WHY?

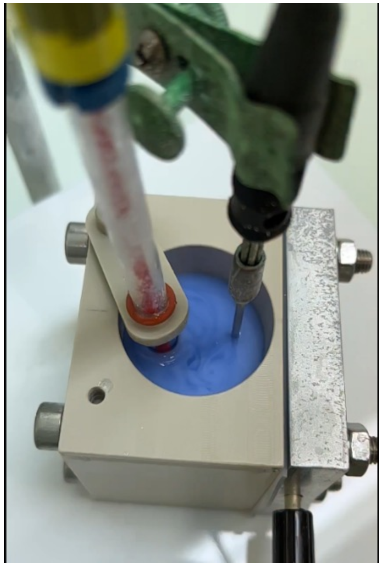
The reduction potential of Gd^{3+}/Gd is too negative (-2,3 V/ENH) to obtain an adhered deposit in aqueous solutions because of the HER.

HOW?

Insoluble Gd_2O_3 particles are mixed in the alkaline Ni plating bath, by applying a potential, the Gd_2O_3 particles will move with Ni^{2+} and trapped in the Ni metal matrix (mechanical process).

Manufacturing of thin targets: Co-electrodeposition



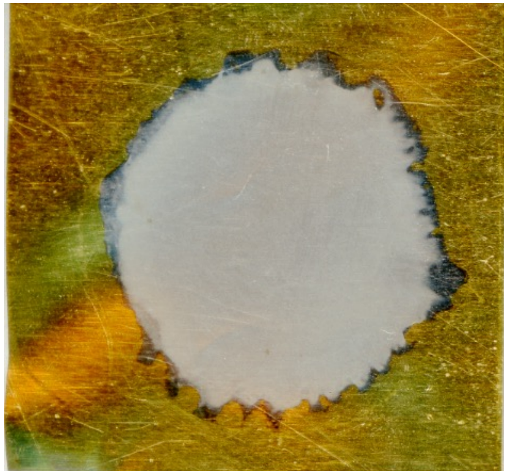


WHAT?

A Ni-Gd_2O_3 composite target with a thickness of 10-20 μm can be obtained.

Manufacturing of thin targets: Co-electrodeposition

Quality control:

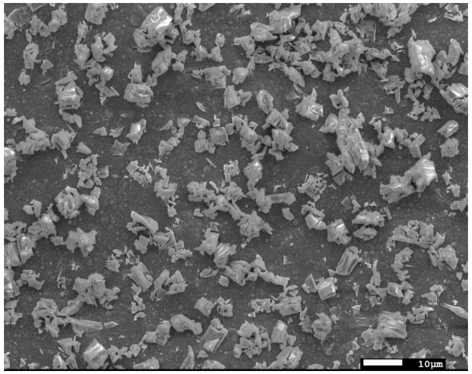


co-electrodeposition for 1**h** **on an** Gold backing

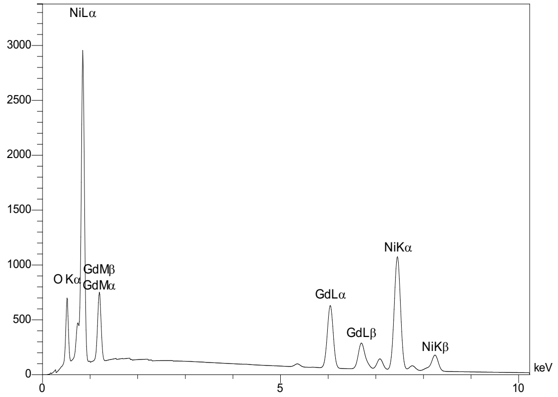
Thickness: 13 µm

Gd content: 3 mg

Morphological analysis: SEM



E= 15kV, x1000



E = 15kV, x100

Composition obtained from EDX and ICP-OES analysis are consistent. The ICP-OES gives a content of about 3 mg of Gd.

From 1 g of Gd_2O_3 powder, 10 targets were made, 0.6 g of powder left.

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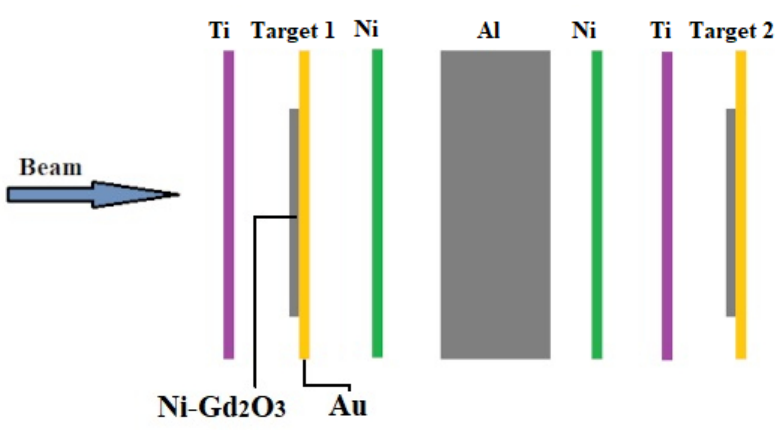
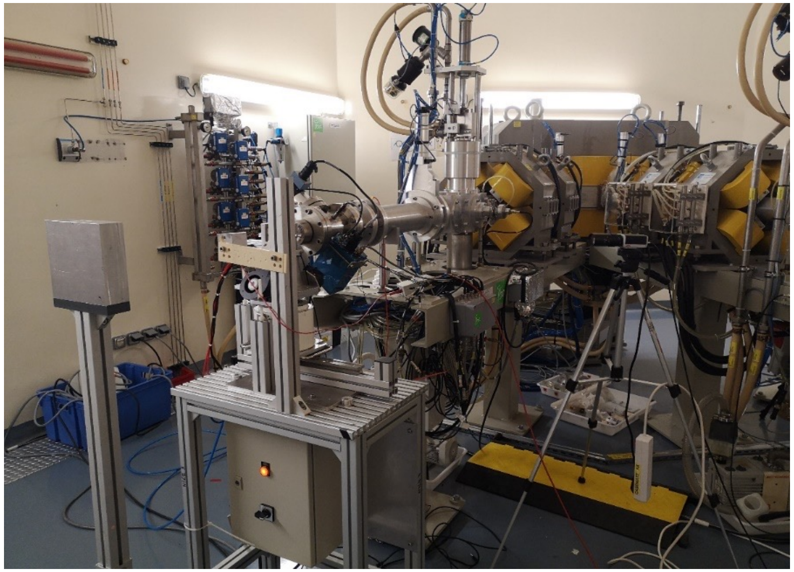
Cross section measurement using stacked-foils

Target: Ni/Gd_2O_3 composite target deposited on the Au substrate
Monitor: Ti and Ni foils (to measure ^{48}V and ^{58}Co)
Degrader: Al foils



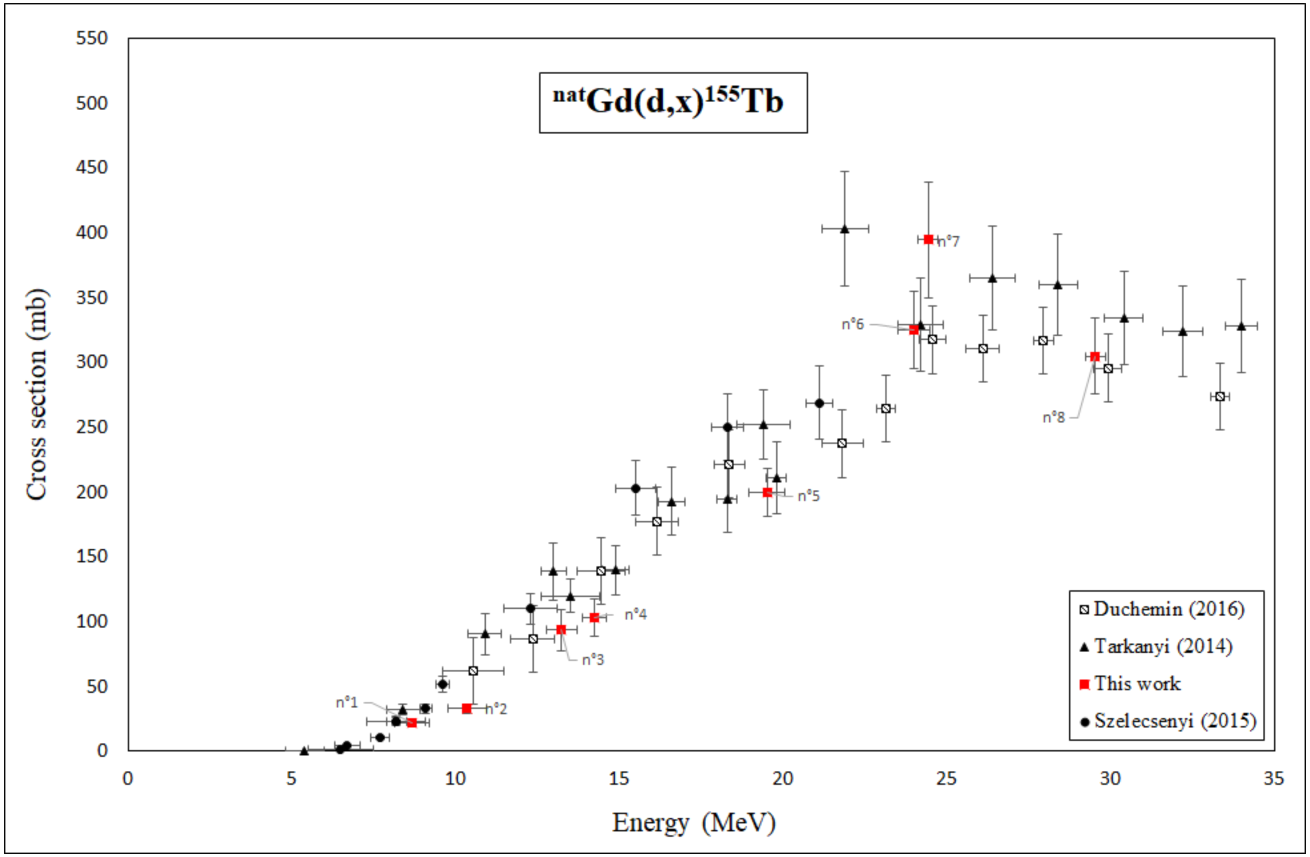
Schematic view of a stack



Beam line used at ARRONAX cyclotron facility

Cross section measurement using the stacked-foils

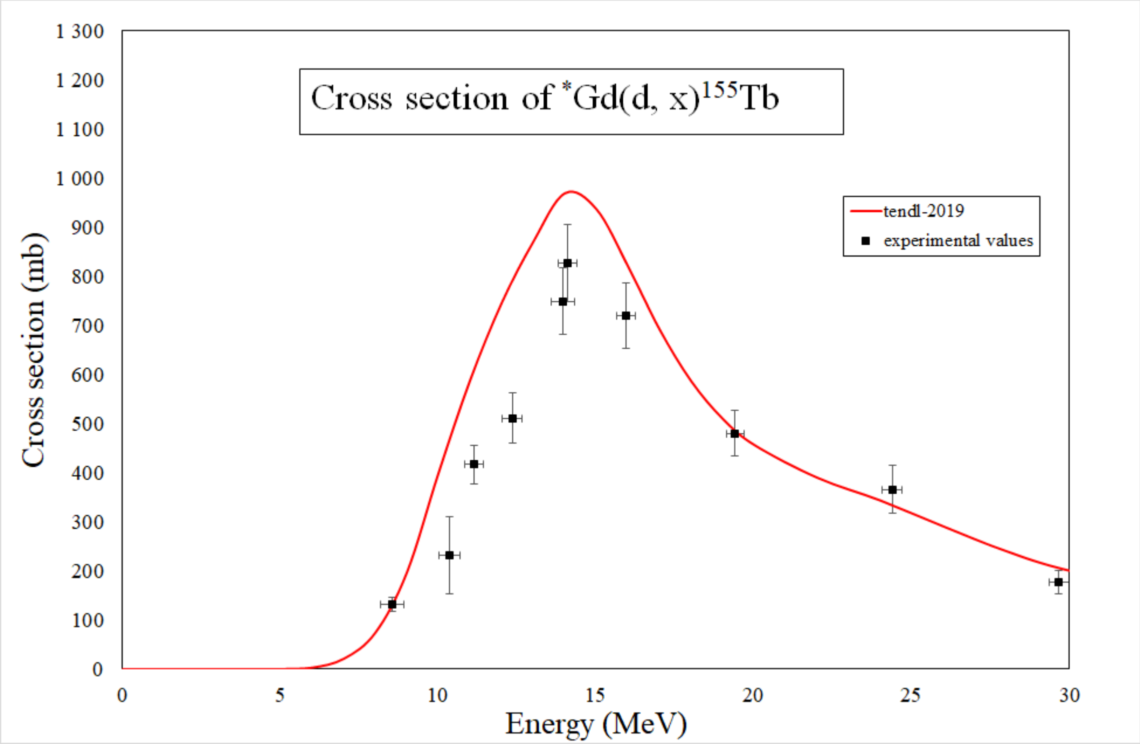
Eight targets made with natural Gd_2O_3 powder were used to measure the σ of $^{nat}Gd(d,x)^{155}Tb$:

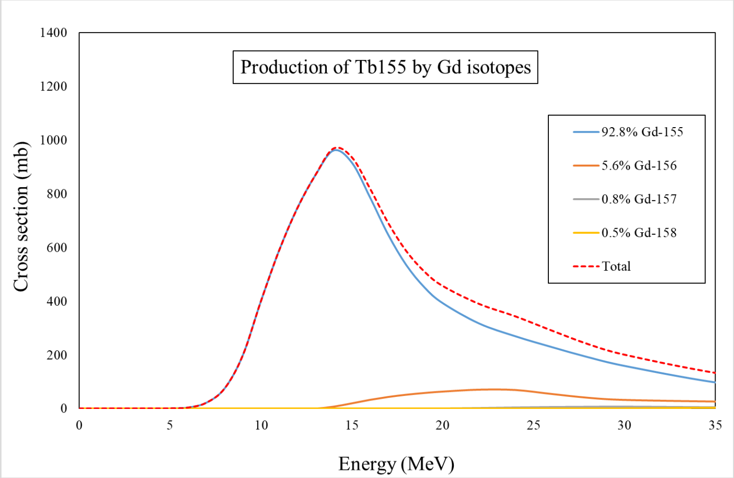


Ours measured values (red) are consistent with existing data.
→ The co-deposition method can be used with enriched material

Cross section measurement using the stacked-foils

The co-depostion technique have been used to prepare enriched Ni/$^{155}Gd_2O_3$





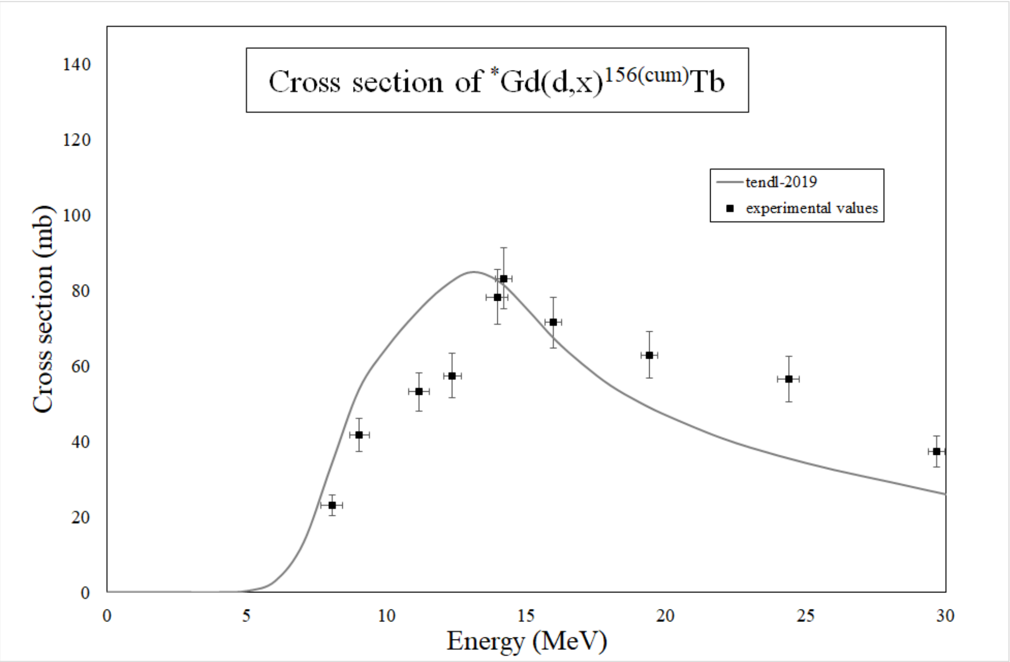
Our enriched 155Gd contains 5.7% of 156Gd.

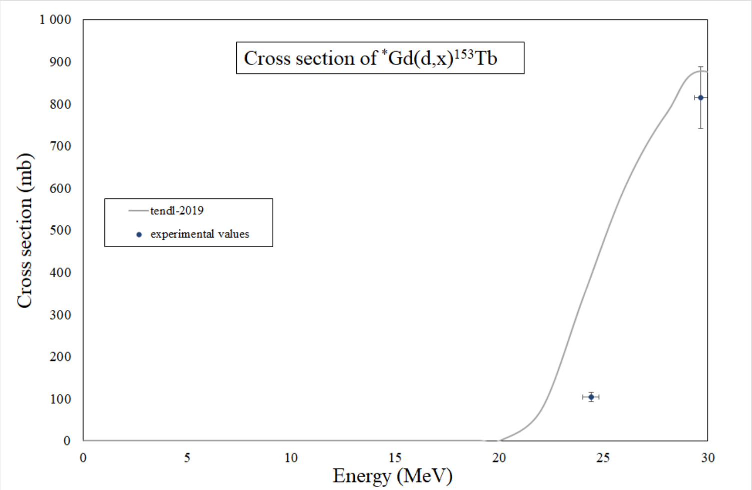
The contribution of ^{156}Gd(d,x)^{155}Tb starts above 13 MeV.

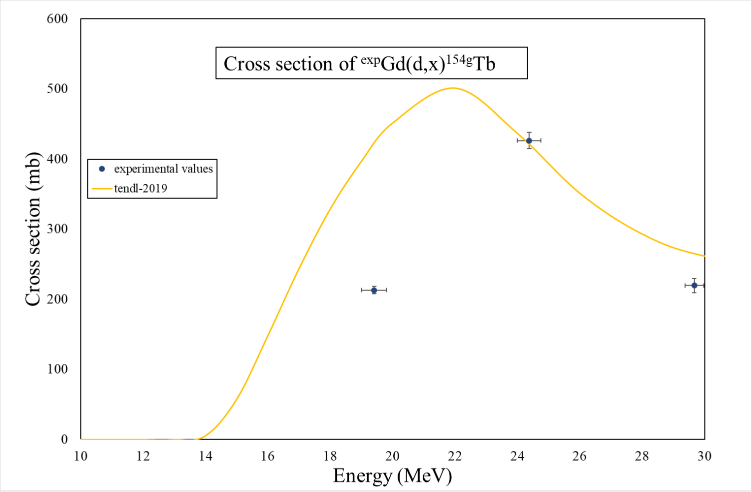
→ 4 measured cross section values corresponds to ^{155}Gd(d,2n)^{155}Tb other contain traces of ^{156}Gd contribution.

Cross section measurement using the stacked-foils

Measured Cross sections for $^{153,154,156}Tb$

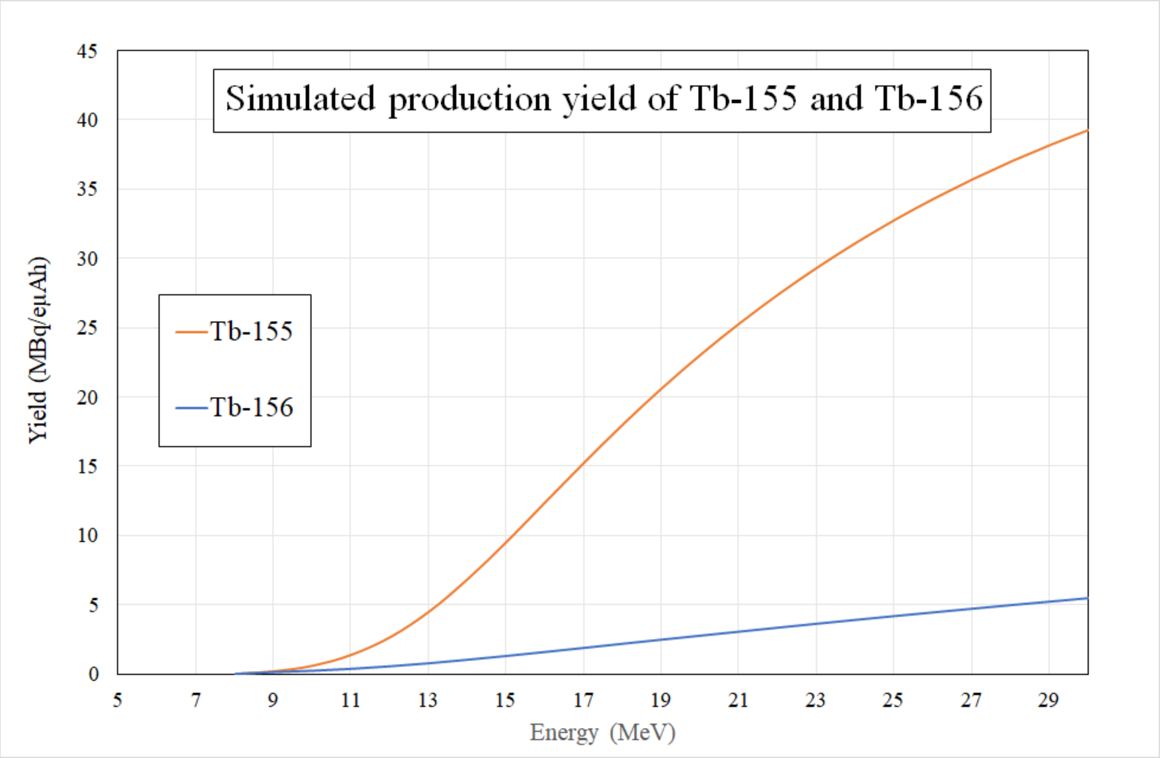






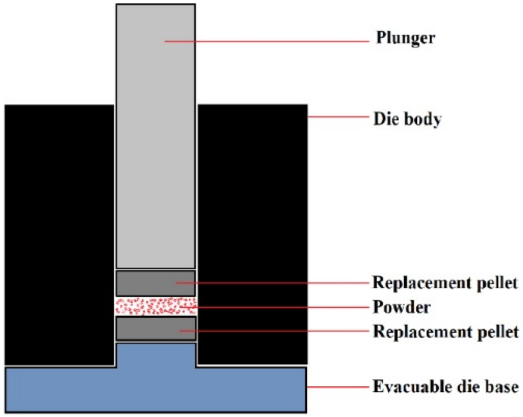
Estimated production yields

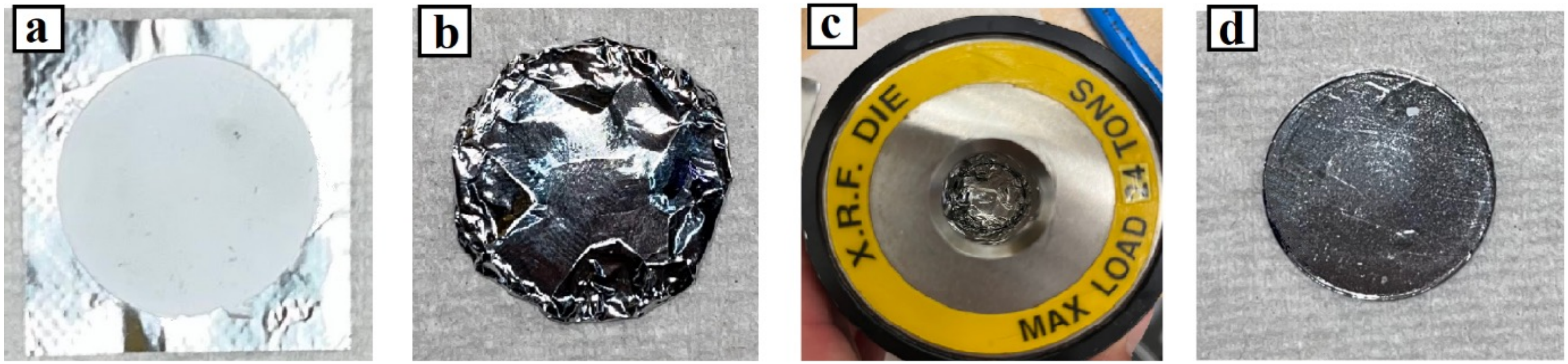
From the measured values, one can estimate the production yield of both ^{155}Tb and ^{156}Tb which can not be avoided



The purity of ^{155}Tb varies from 60% to 89% when energy varies from 9 to 15 MeV.
If one get 100% pure ^{155}Tb, purity can reach 95%
Higher production yield with deuteron but lower purity

Manufacturing of thick targets: the pelletizing method

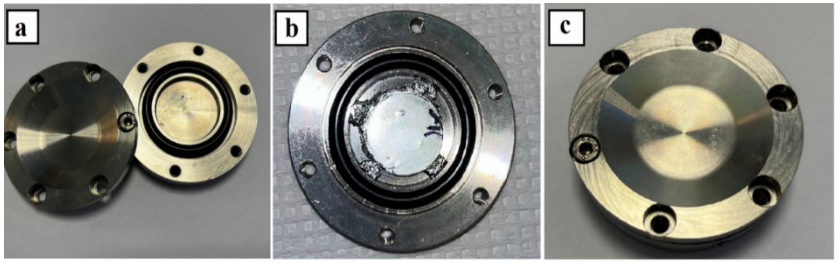




^{155}Gd Mass = 0.6 g, thickness = 0.4 mm, aluminum shell

Manufacturing of thick targets: the pelletizing method

Experiment:

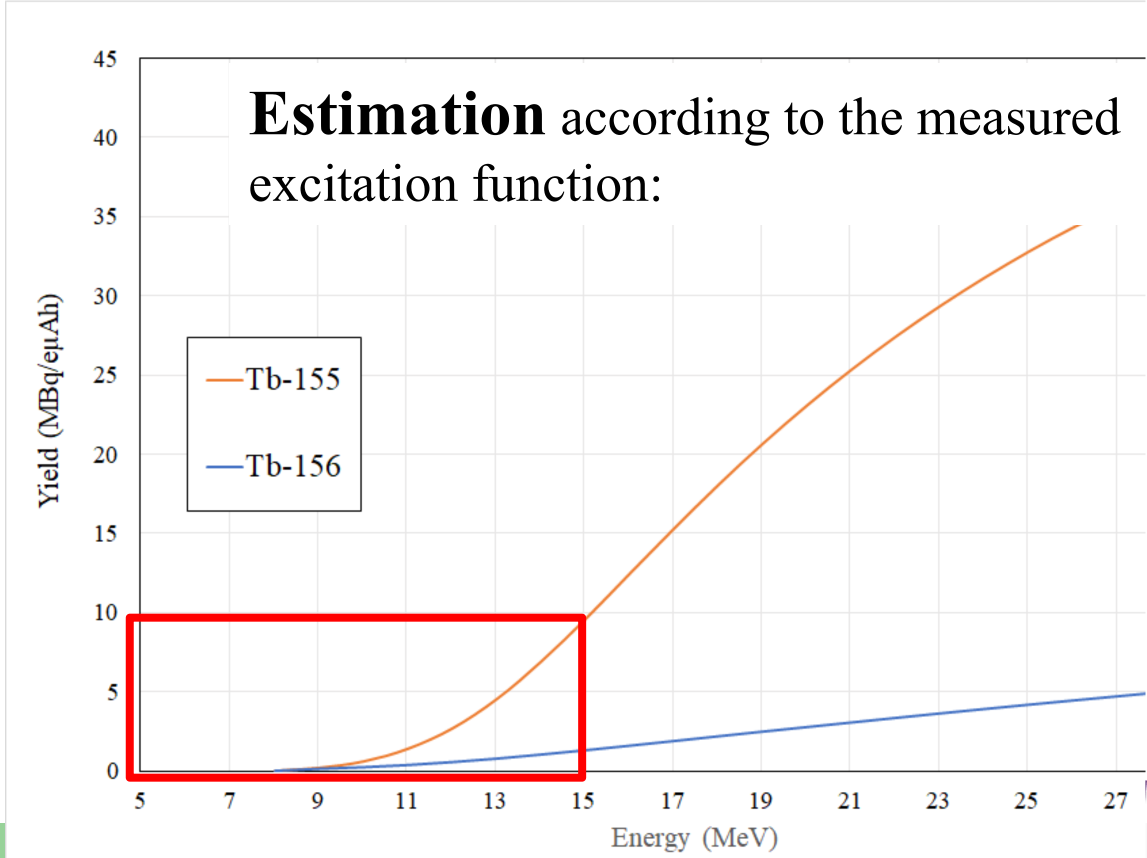


$E_{incident}$ = 15.1 MeV
$E_{outgoing}$ = 8.6 MeV
I = 500 nA for 1 h

Production yield:

- Tb-155: 10.2 ± 0.7 MBq/μAh
- Tb-156: 1.3 ± 0.1 MBq/μAh

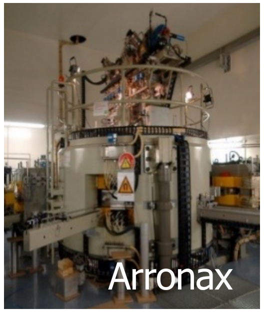
Purity of Tb-155: 89%
(10 d after EOB)

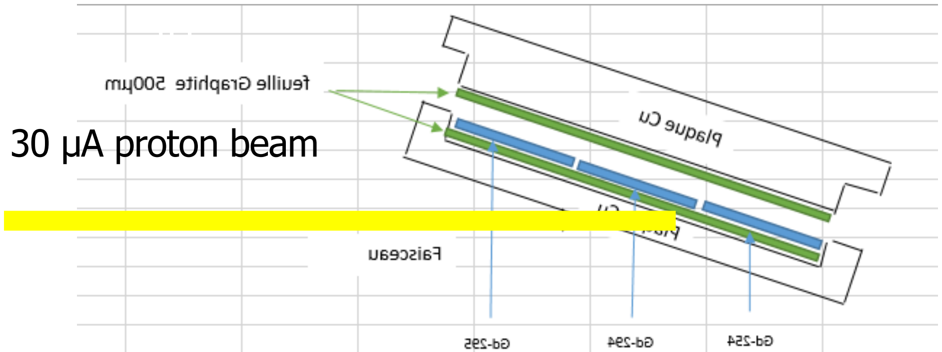


To get a very pure product, it can be interesting to couple low-medium energy cyclotron with mass separation technique

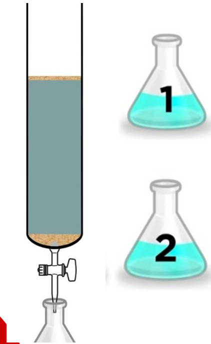
Again ^{155}Tb has been used for POC

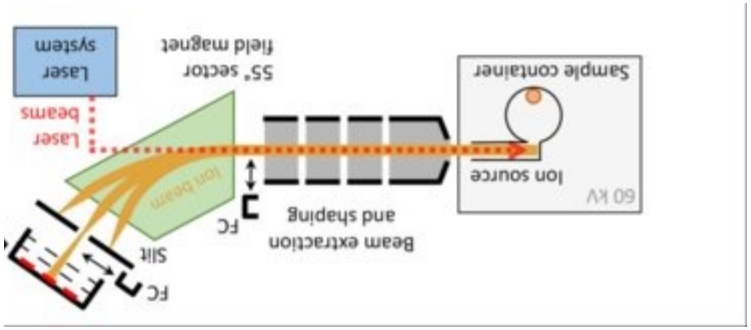
The whole process





Extraction/
purification





Pure ^{155}Tb

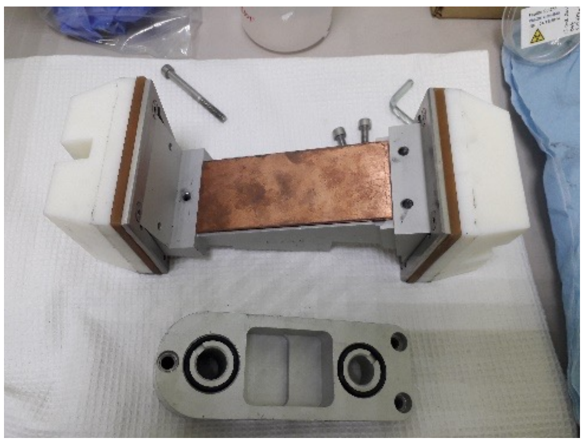
Targettry

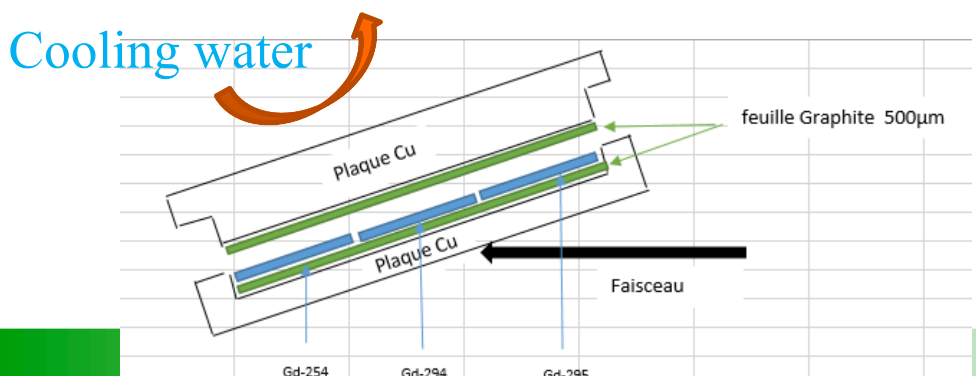
We are using our tilted rabbit (15° with respect to the beam direction)

Energy is fixed at 55MeV to enter the Gd at 34 MeV

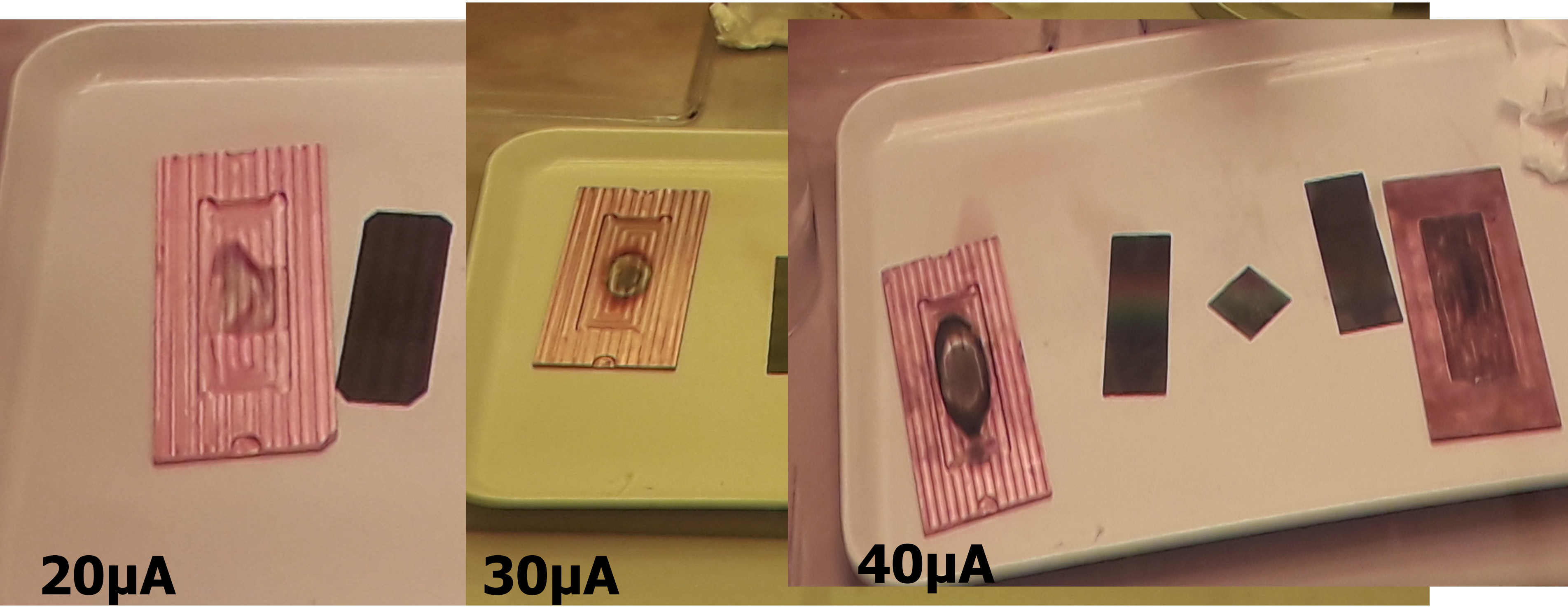
Graphite is used to protect Gd (3 foils of 25µm thick) from Cu

I=30µA for 9 h proton beam on target





Irradiation conditions

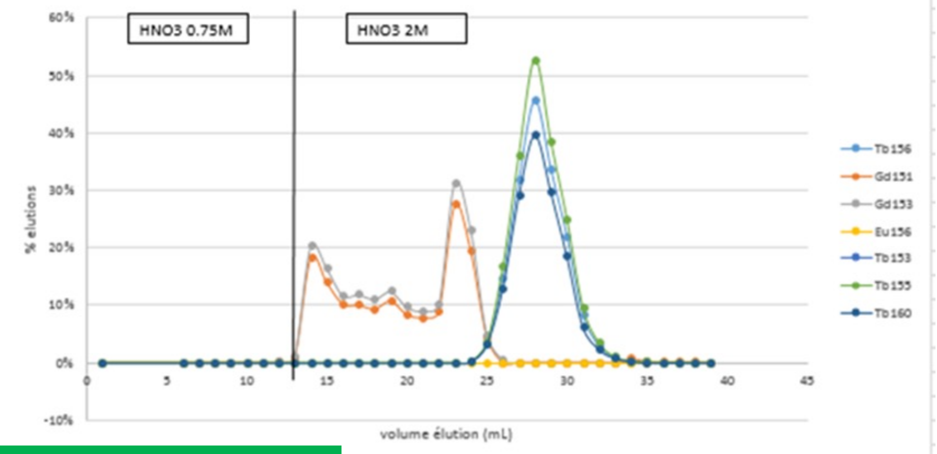


Irradiations have been performed @ 30 µA

Gd/Tb separation 1 Tb :100 Gd

Use of LN (TRISKEM) resin as proposed by NPL in its work for MEDICIS

Process have been done twice to improve Gd/Tb separation



Atomic ratio at departure time from the facility

initial Tb155/Gd ratio greater than 1:1000000

	Tb155/Gd	Tb155/Tb159	Tb159/Gd
08-juil-20	1/23	1/175	1/0,1
29-juil-20	1/7	1/96	1/0,07
30-sept-20	1/29	1/49	1/0,4
27-oct-20	1/2	1/62	1/0,03

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Conclusions and perspectives

Enriched gadolinium targets can be prepared from oxide:

- ✓ Thin targets obtained by co-deposition allowed to performed cross section measurements
- ✓ Thick targets made by pelletizing allows for production
- ✓ Experiments shows that production yield with deuteron is higher than that obtained from proton.
- ✓ However, with deuteron beam and the available ^{155}Gd enrichment, ^{155}Tb represent 89% of the radioactive Tb present in the final product
- ✓ Higher purity can be obtained with proton irradiation
- ✓ Purity improvement can be obtained using mass separation

Perspectives:

^{155}Tb was used as POC. Further work will be done for other ^{149,152}Tb isotopes produced from ^{152}Gd, ^{154}Gd or ^{155}Tb.

Thank you for your attention

The **ARRONAX** project is supported by:

- the **Regional Council of Pays de la Loire**
- the **Université de Nantes**
- the **French government** (CNRS, INSERM)
- the **European Union**.

This work has been, in part, supported by a grant from the French National Agency for Research called "Investissements d'Avenir", Equipex Arronax-Plus noANR-11-EQPX-0004, Labex IRON noANR-11-LABX-18-01, ISITE NExT no ANR-16-IDEX-007.

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008571 (PRISMAP).

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