

How to produce scandium-44 efficiently ?

Research studies at SUBATECH laboratory and GIP ARRONAX (France)

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1. Introduction

- 3 isotopes of scandium present physical characteristics compatible with nuclear medicine purpose:
 - **Sc-47** ($T_{1/2} = 3.351$ days, $\beta^- = 100\%$, $\gamma = 68\%$) \rightarrow targeted **radiotherapy**.
 - **Sc-43** ($T_{1/2} = 3.891$ hours, $\beta^+ = 88.1\%$) \rightarrow **diagnosis**.
Katharina A. Domnanich talk.
 - **Sc-44g** ($T_{1/2} = 3.97$ hours, $\beta^+ = 94\%$, $\gamma = 99.9\%$) \rightarrow **diagnosis**.
Jerzy Jastrzębski talk (with α) and this talk (with p and d). (available as $^{44}\text{Ti}/^{44}\text{Sc}$ generator.)
- **Theranostic** approach possible with scandium.

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Special emphasis on Sc-44 characteristics :

- Sc-44g is a positron emitter with a half-life between that of Ga-68 and Cu-64.
 \rightarrow good candidate for PET imaging.
- Two states : **Sc-44m** ($T_{1/2} = 58.6$ hours)

Internal Transition
98.8 %

\swarrow

γ 270 keV

Sc-44g ($T_{1/2} = 3.97$ hours)

}

- Possibility to produce the **Sc-44m/Sc-44g generator**.

- Production in cyclotron.

2. The different Sc-44 applications

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- An isomeric state Sc-44m exists and mainly decays to Sc-44g through IT.
 - Huclier S. et al (Nantes) have demonstrated that Sc-44m/Sc-44g ***in-vivo* generator (3)** is feasible.
 - Interesting to enlarge the use of Sc-44g to antibody labelling.

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→ Our selected target: calcium-44.

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- Data for Ca-44(p,n)Sc-44 reaction are available in literature.
- No data for the deuteron route

→ **Exp. cross section measurements has been carried out at the ARRONAX cyclotron.**

3. The ARRONAX cyclotron

3.1 Study of the Ca-44(d,2n) reaction



Accelerator for the
Research in
Radiochemistry and
Oncology at
Nantes
Atlantique
X

Reaction: Ca-44(d,2n)Sc-44

$E_{\text{threshold}} = 6.9 \text{ MeV}$

Delivered particles	Energy (MeV)	Max. intensity (μA)	Dual beam
Protons	30-70	2 x 350	Yes
Deuterons	15-34	2 x 50	Yes
α particles	67.4	70	No

→ Deuterons beam energy delivered by ARRONAX permits to cover all the energy range of interest

3. The ARRONAX cyclotron

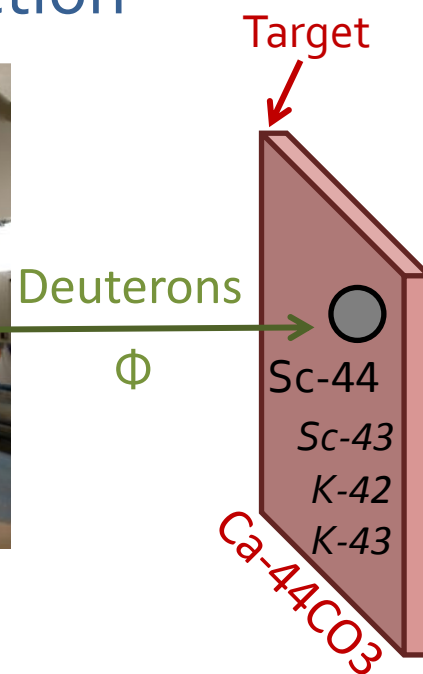
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Target form:
Ca-44CO₃ deposit
on Al foil

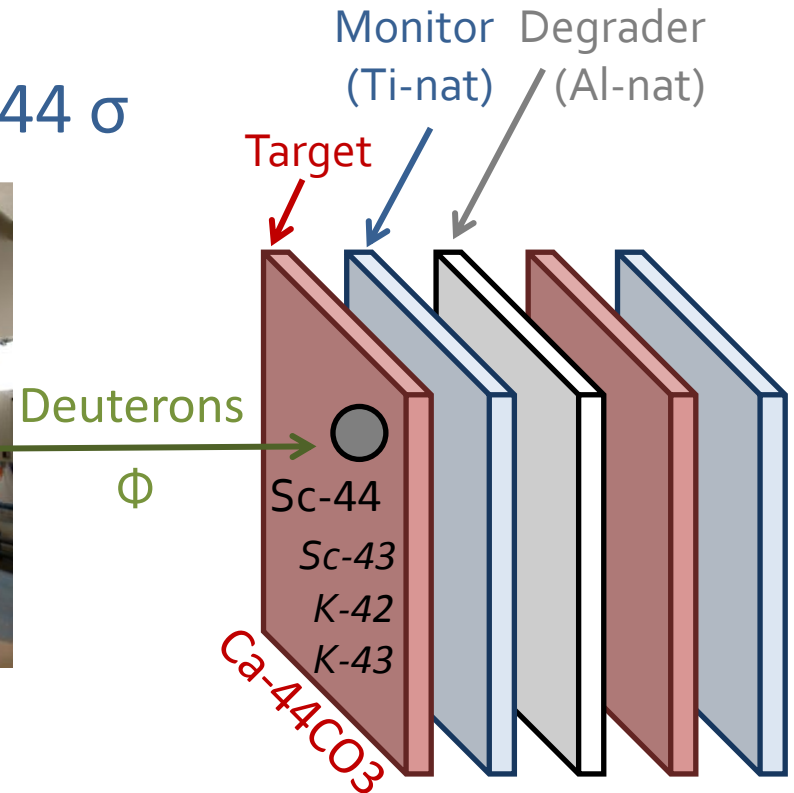


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3.2 Experimental method for Sc-44 σ



- For prod. cross section determination → “stacked-foils” technique

Condition : $\Phi = \Phi'$

$$\sigma = \underbrace{\sigma'}_{\text{Cross section recommended by the IAEA}} \frac{\text{Act} \cdot A \cdot \chi' \cdot \rho' \cdot \text{ef}' \cdot (1 - \exp(-\lambda' \cdot t_{\text{irr}}))}{\text{Act}' \cdot A' \cdot \chi \cdot \rho \cdot \text{ef} \cdot (1 - \exp(-\lambda \cdot t_{\text{irr}}))}$$

Cross section recommended by the IAEA

In our case Ti-nat(d,x)V-48

— Produced radionuclide

— Target characteristics

— Irradiation conditions

4. γ spectrum analysis

- High purity Ge detector used to determine the activity in each foils.
- HPGe calibrated in energy and efficiency with certified Eu-152 γ source.
- Three different counting measurements, in the same conditions, to validate the activity values.



High purity Ge detector

4. γ spectrum analysis

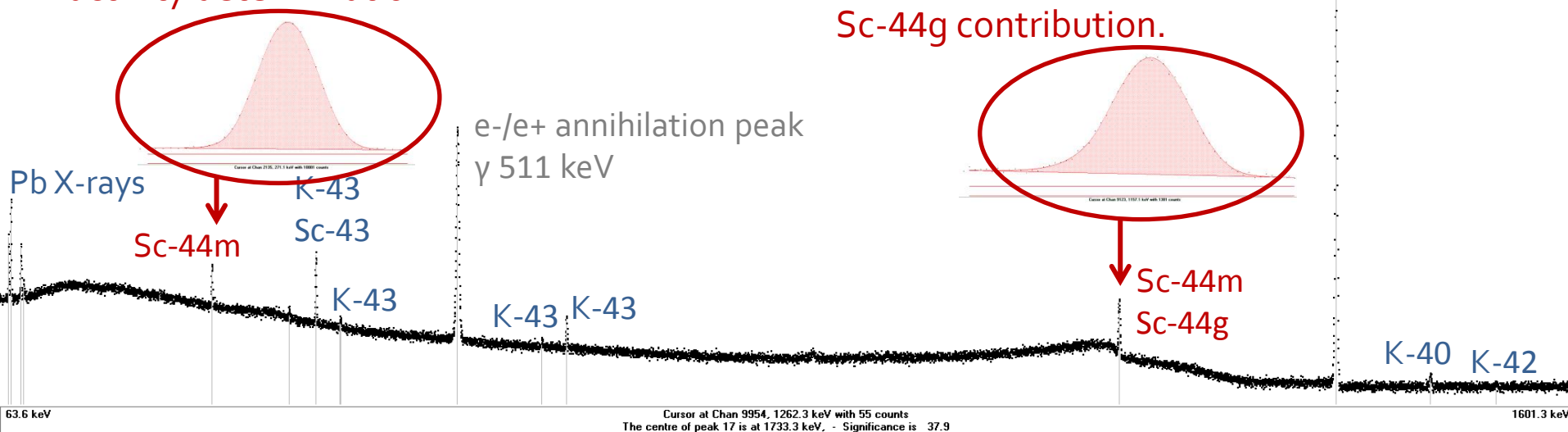
- High purity Ge detector used to determine the activity in each foils.
- HPGe calibrated in energy and efficiency with certified Eu-152 γ source.
- Three different counting measurements, in the same conditions, to validate the activity values.



High purity Ge detector

This peak helps for Sc-44m activity determination.

This peak permits to deduce Sc-44g contribution.

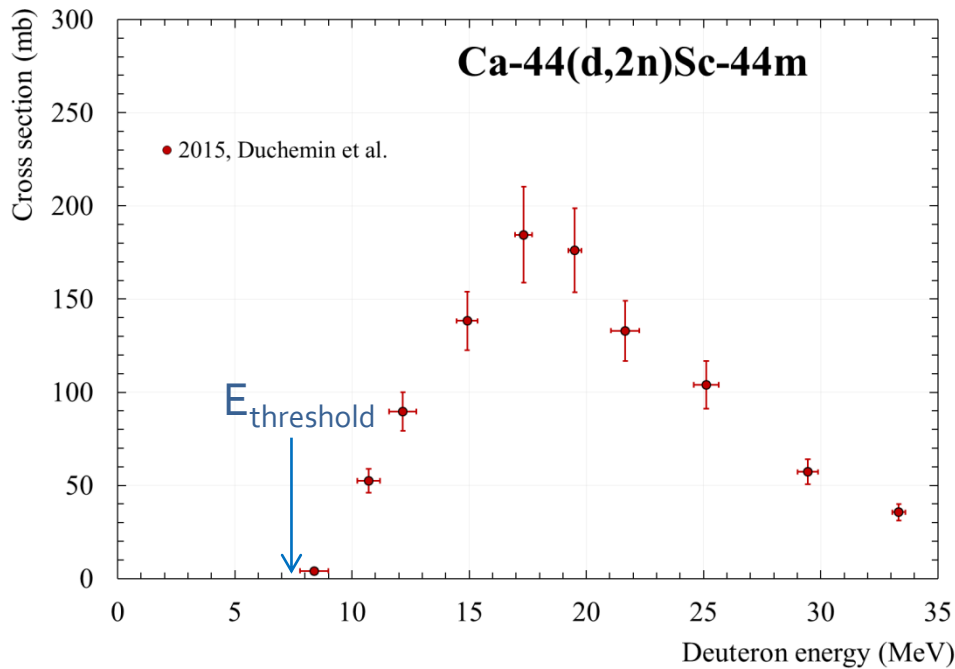


Sample:- taken on 12-Aug-2014 at 8:30
From Detector 2, Live Time is 4160, True Time is 4340 seconds, Collected on 12-Aug-2014 at 8:30
Using NORMAL Defaults file 1, Calibration from Spectrum data file

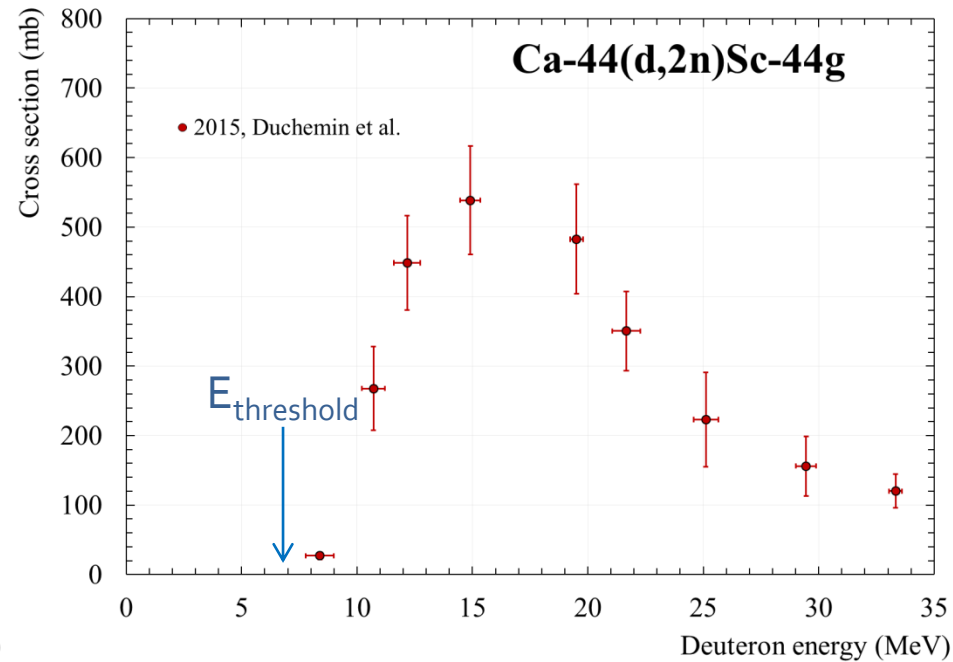
34 MeV deuterons

5. Sc-44 production cross sections

→ Sc-44m : $T_{1/2} = 58.6$ hours



→ Sc-44g : $T_{1/2} = 3.97$ hours



→ First data available in the literature for the Ca-44(d,2n) production route.

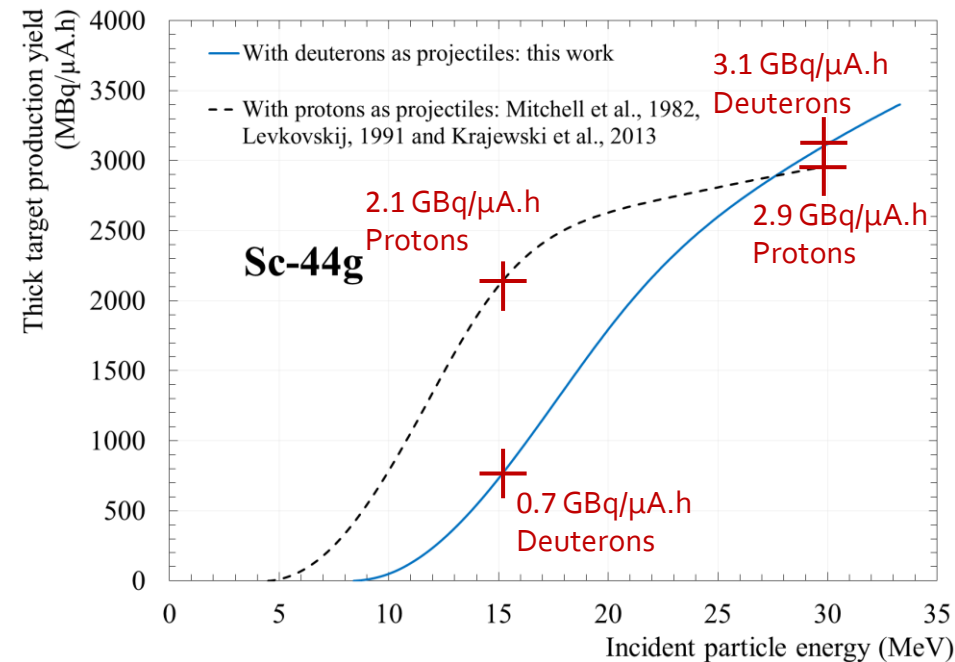
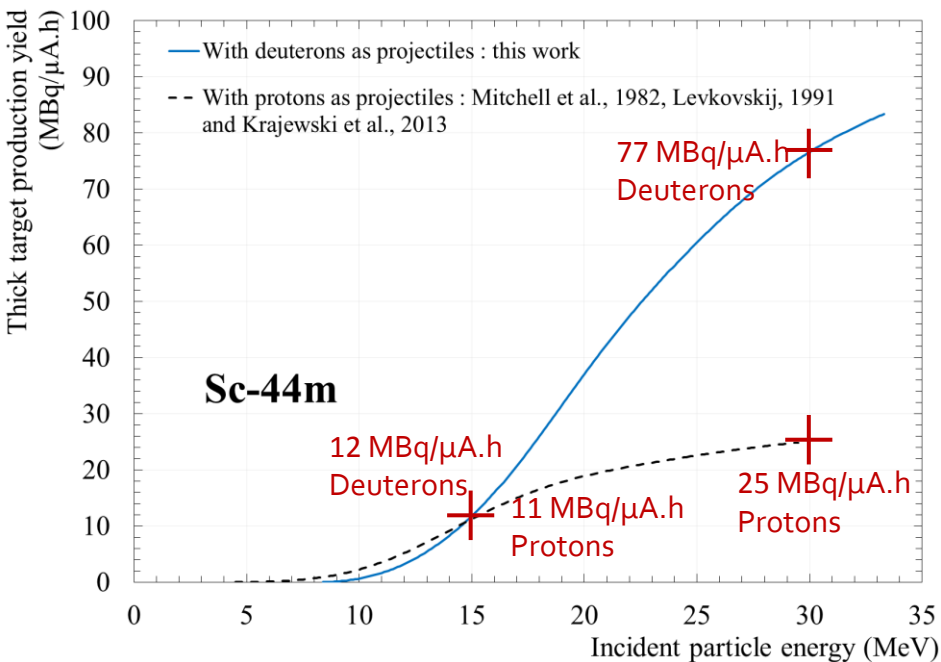
→ In addition, data on Sc-43, K-42 and K-43 have been obtained.

Results published in *Physics in Medicine and Biology* **60** (2015) **6847-6864**

6. Sc-44 Thick Target production Yields (TTY)

→ Comparison with Ca-44(p,n) production route

N.B.: in the case where the target is entirely composed by Ca-44 atoms.



Results published in *Physics in Medicine and Biology* **60** (2015) **6847-6864**

7. Conclusion on the best Sc-44 production routes with protons and deuterons.

Cyclotron type	Scenario	Sc-44g for PET using small molecules as vectors	Sc-44g for 3 γ imaging developed at SUBATECH laboratory (Xenon group)	Production of the Sc-44m/Sc-44g <i>in-vivo</i> generator paired with antibodies as vectors
		Needs: - High Sc-44g activity - Limit the Sc-44m act. <i>(additional dose to the patient)</i>	Needs: - Limit Sc-44m and Sc-43 act. <i>(dose + background)</i>	Needs: - High Sc-44m activity - Limit Sc-44g and Sc-43 act.
15 MeV protons		++	++	-
15 MeV deuterons		-	+	+
30 MeV protons		+	--	-
30 to 35 MeV deuterons		--	-	++

Results published in *Physics in Medicine and Biology* **60** (2015) **6847-6864**

Thank you for your attention

Special thanks to the members of the PRISMA group (SUBATECH) and of the GIP ARRONAX.

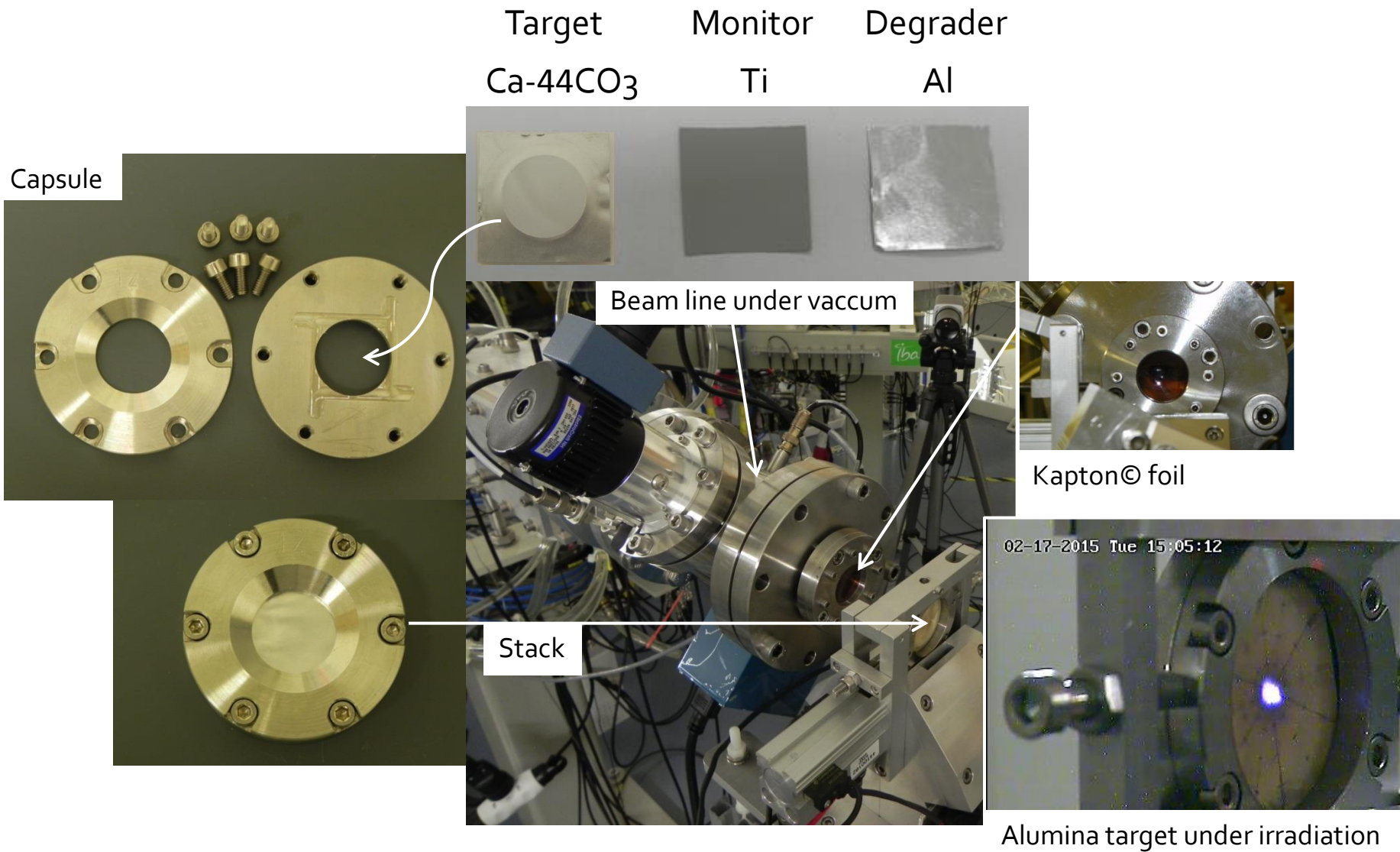
The ARRONAX cyclotron is a project promoted by the Regional Council of Pays de la Loire financed by local authorities, the French government and the European Union. This work has been, in part, supported by a grant from the French National Agency for Research called "Investissements d'Avenir", Equipex Arronax-Plus n° ANR-11-EQPX-0004 and Labex n° ANR-11-LABX-0018-01.

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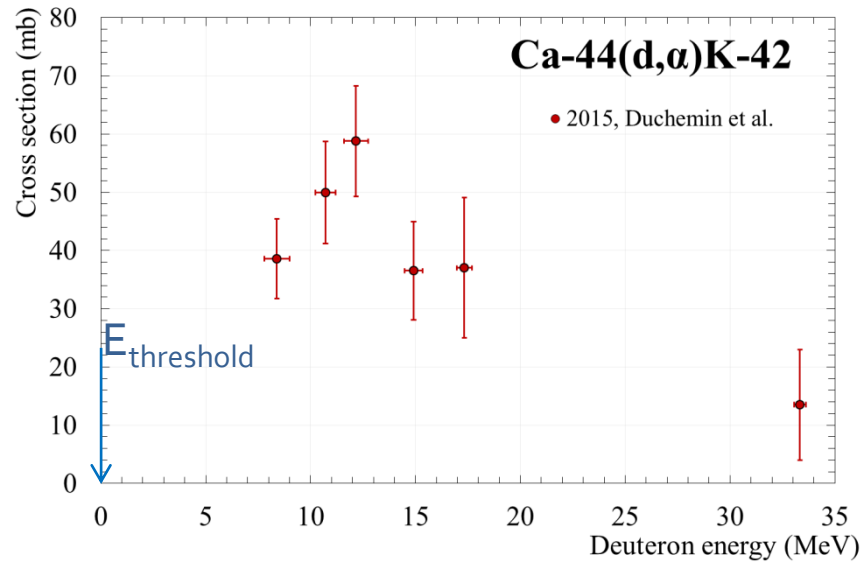
The experimental set-up



Production cross sections

Others radionuclides detected

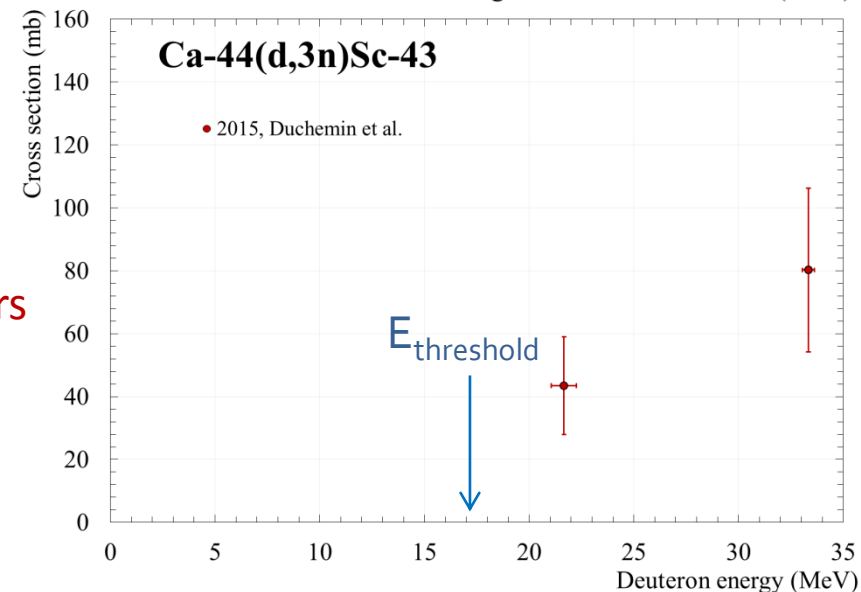
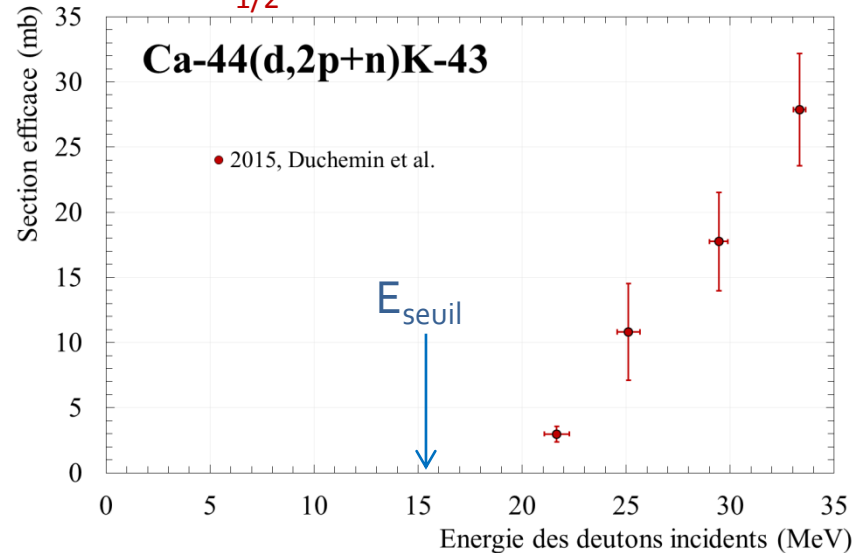
→ K-42 : $T_{1/2} = 12.26$ hours



→ Sc-43 : $T_{1/2} = 3.89$ hours

→ Sc-43 no chemically separable from Sc-44

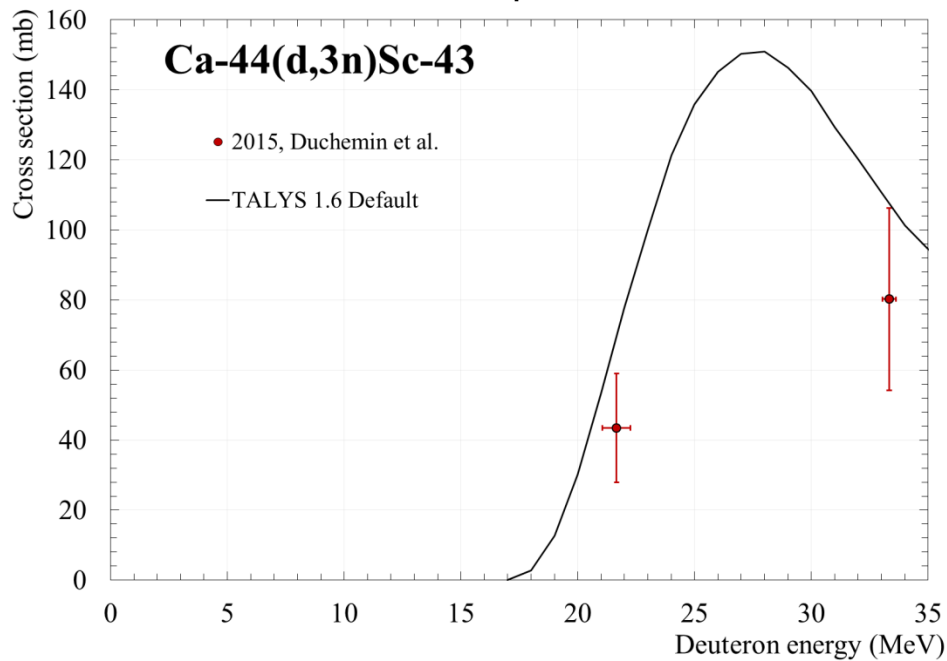
→ K-43 : $T_{1/2} = 22.3$ hours



Sc-43 Thick Target production Yields (TTY)

→ Sc-43 can not be chemically separated from Sc-44. Its production has to be controlled.

→ Ca-44(d,3n)Sc-43 production cross section data.



*The TALYS code is nuclear reaction program that included theoretical models by default.

→ TTY comparison with proton route.

