

Radioisotope production in ^{209}Bi photo-activation with a laser induced bremsstrahlung source



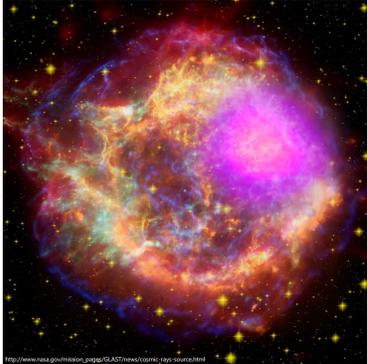
The 4th ELIMED Workshop MEDical and Multidisciplinary Applications of Laser-driven Ion Beams at ELI Beamlines Facility

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The impact of photo-induced reactions

Basic science



Space exploration

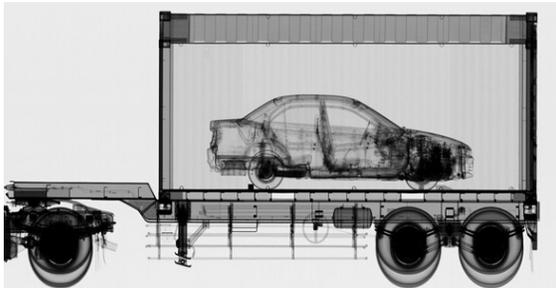


Credits: NASA - <https://www.nasa.gov/image-article/sunita-williams-spacewalk/>

Radiotherapy



National safeguard



Nuclear waste inspection

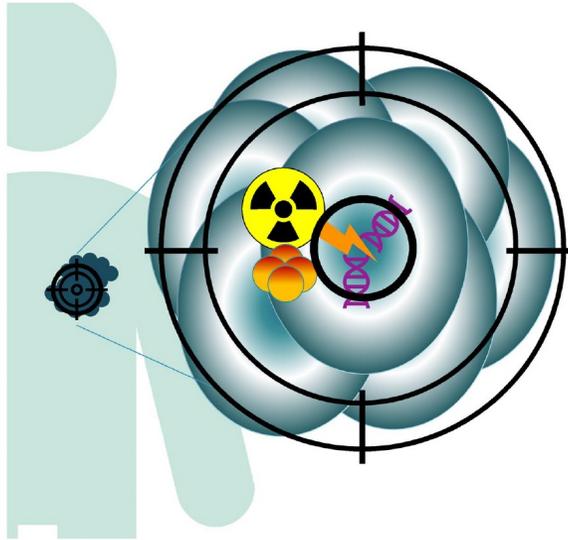


Medical radioisotope production



Medical radioisotopes in targeted alpha therapy

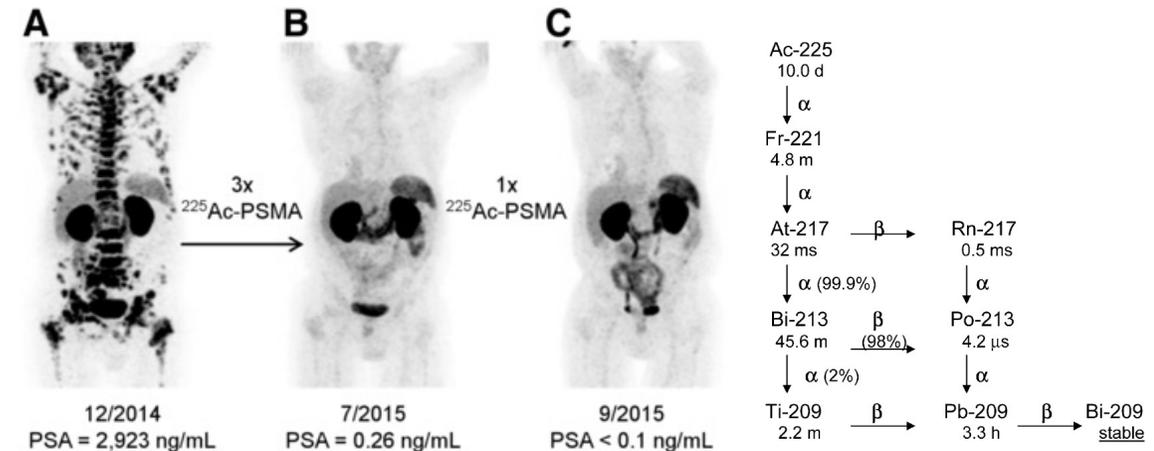
Targeted Alpha Therapy (TAT) delivers high-energy α -emitting radioisotopes directly to cancer cells using targeting molecules (e.g. antibodies or peptides).



TAT causes irreparable DNA double-strand breaks in tumours while minimizing damage to healthy tissue (short range of α -particles).

TAT is particularly effective in treating non-localised tumours (e.g. leukaemia) and advanced tumours with multiple metastases.

^{225}Ac coupled to *PSMA* is particularly effective for metastatic tumours, notably in prostate tumours. It offers significant, often durable, therapeutic effects with manageable toxicity.

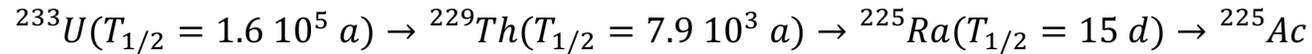


C. Kratochwil et al., J. Nucl. Med. 57, 1941 (2016)

Assuming some 200.000 treatments per year and a dose of 0,3 mCi (10 MBq) per patient, a total production of ^{225}Ac per year of 60 Ci (2,2 TBq) is required.

^{225}Ac production methods

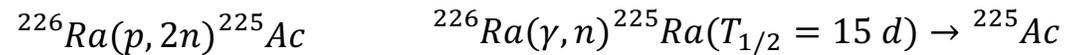
✓ Extraction from ^{233}U .



- Clean separation of ^{225}Ac .

- Limited availability of ^{233}U .
- Some 350 mCi of ^{229}Th available.

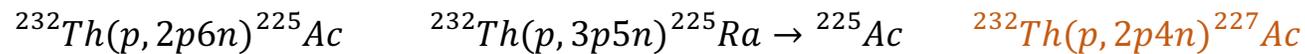
✓ Production from ^{226}Ra .



- Clean separation of ^{225}Ac .

- High toxicity of ^{226}Ra (decay into ^{222}Rn).
- Some 1 kCi of ^{226}Ra available.

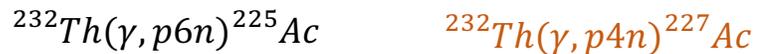
✓ Spallation of ^{232}Th .



- Large production of ^{225}Ac , around 0,25 Ci/day.

- Long-lived contaminant ^{227}Ac .
- Large and expensive facility (100 μA , 200 MeV proton accelerator).

✓ Photo-activation of ^{232}Th .



- Possible low-cost bremsstrahlung facility.

- Long-lived contaminant ^{227}Ac .
- High energy photons (> 50 MeV)
- Lower cross section.

Photon-induced reaction mechanisms

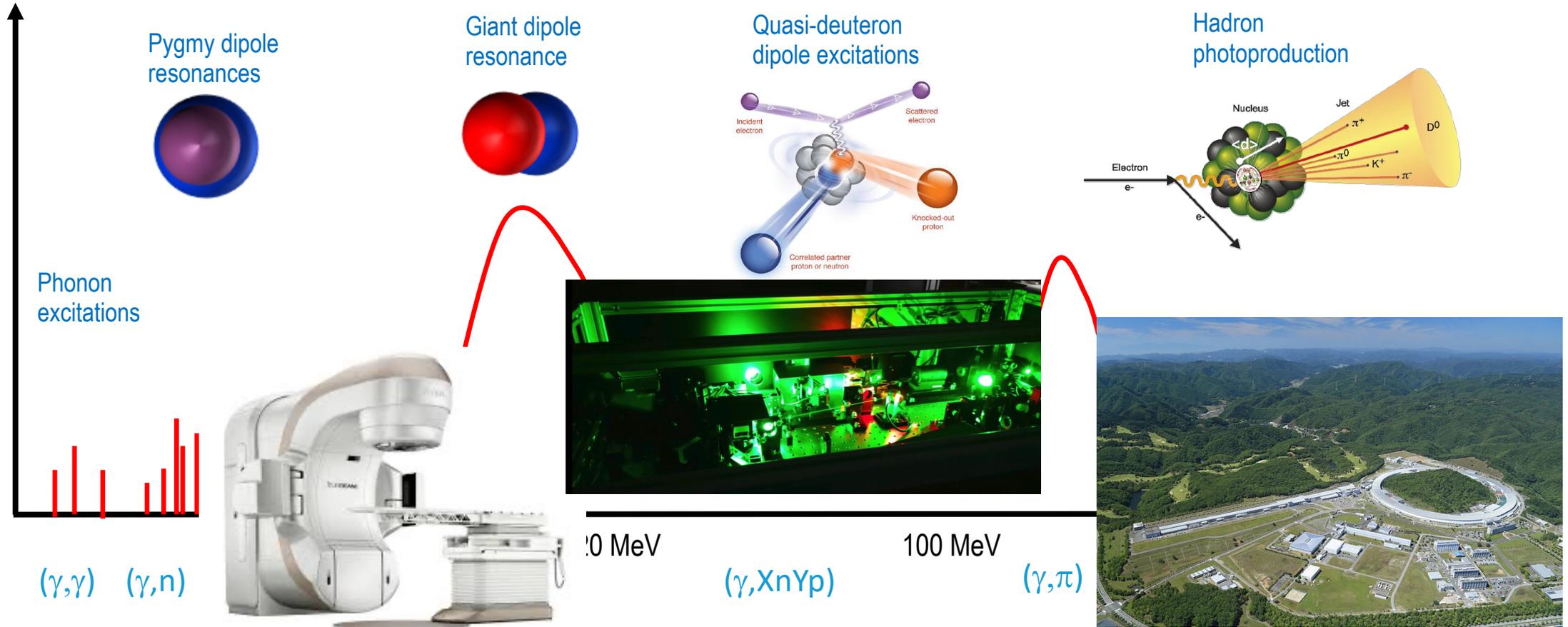
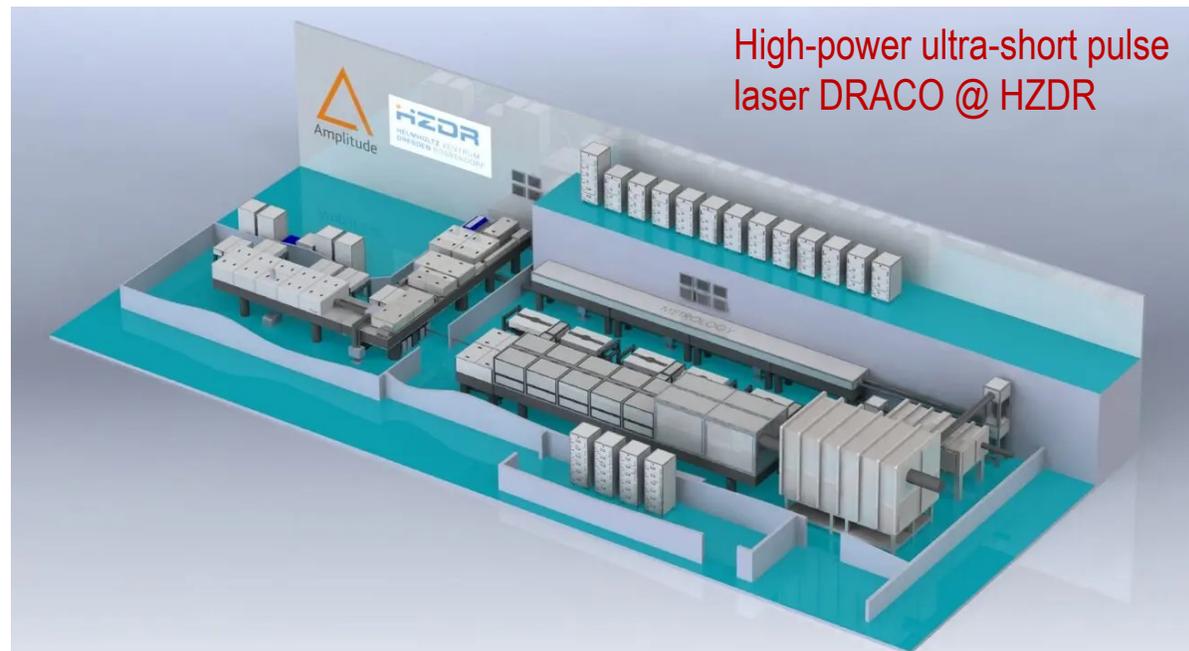
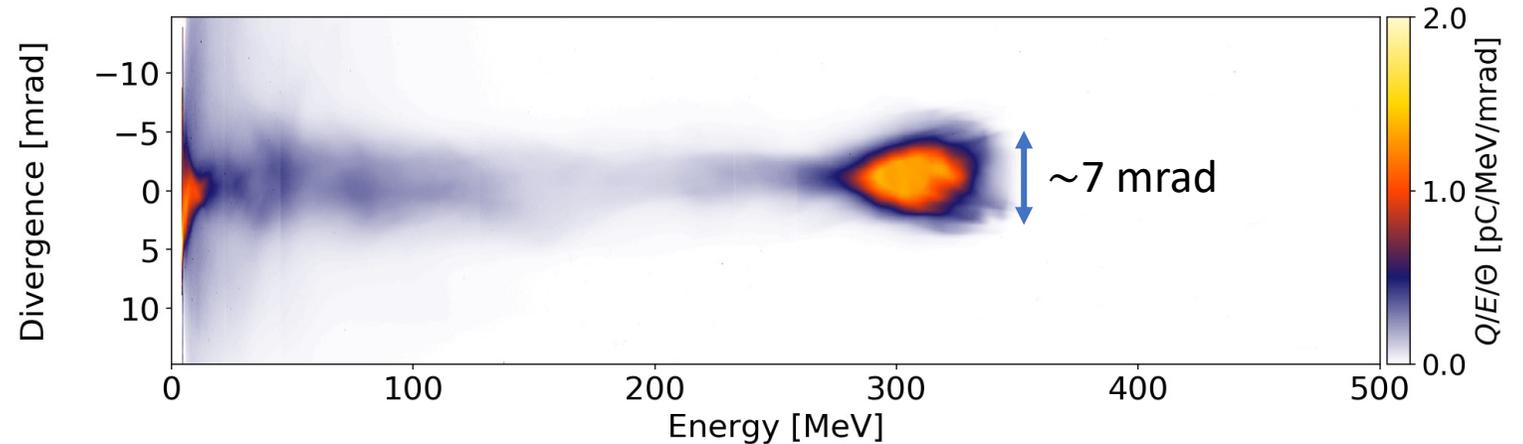
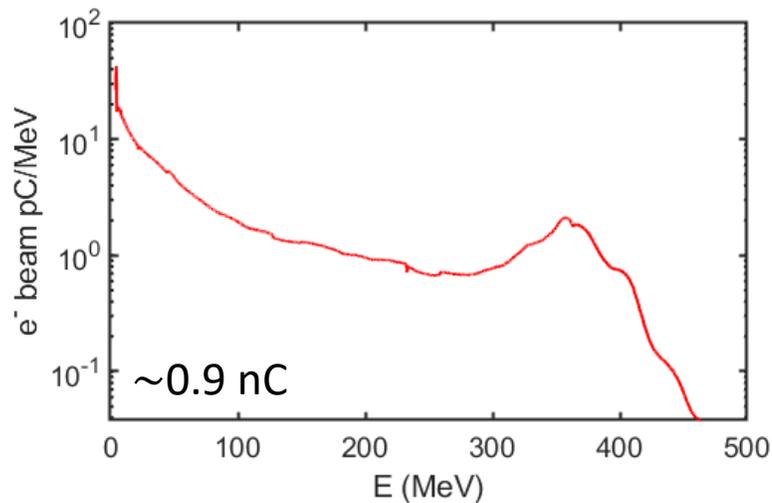
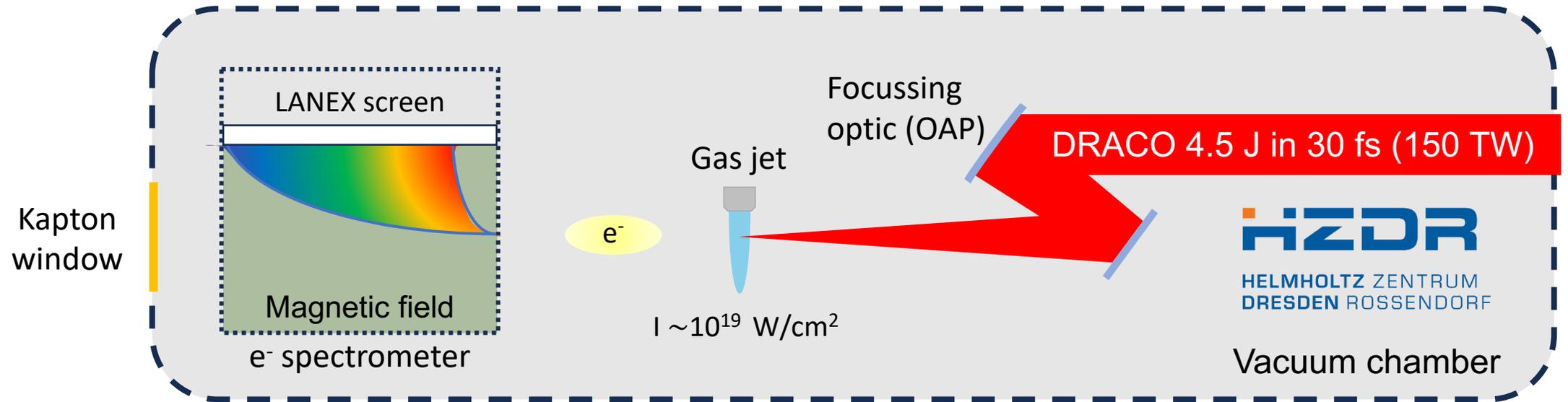


Photo-activation of ^{209}Bi with a laser driven bremsstrahlung source

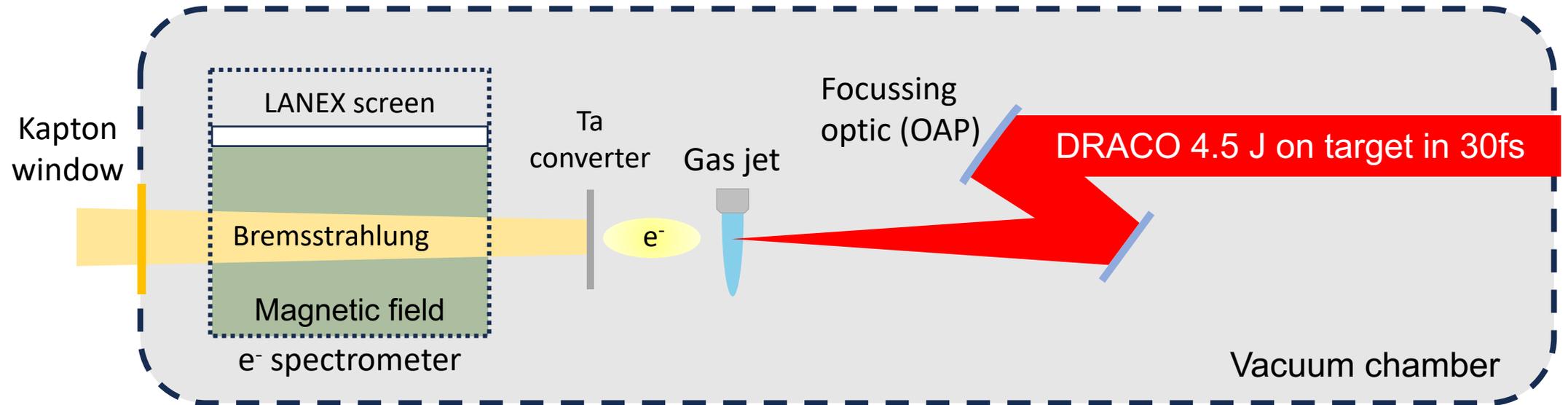
- ✓ Demonstrate the production of radioisotopes with a laser-driven bremsstrahlung source.
- ✓ Measure the production of ^{202}Pb in $^{209}\text{Bi}(\gamma, p6n)$ as a proxy of the reaction $^{232}\text{Th}(\gamma, p6n)^{225}\text{Ac}$.



The laser-driven electron source



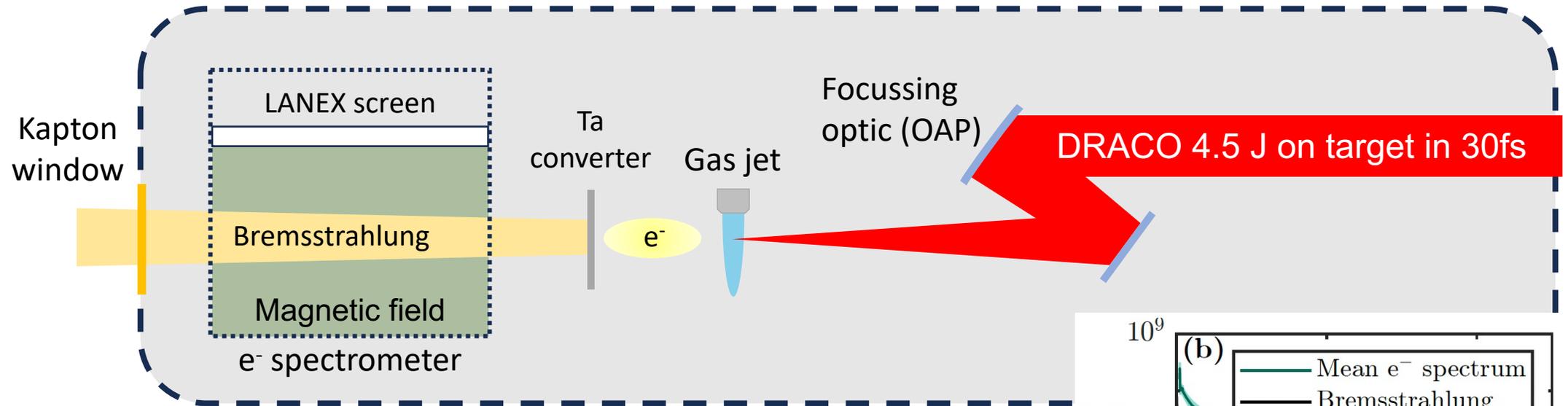
The bremsstrahlung source



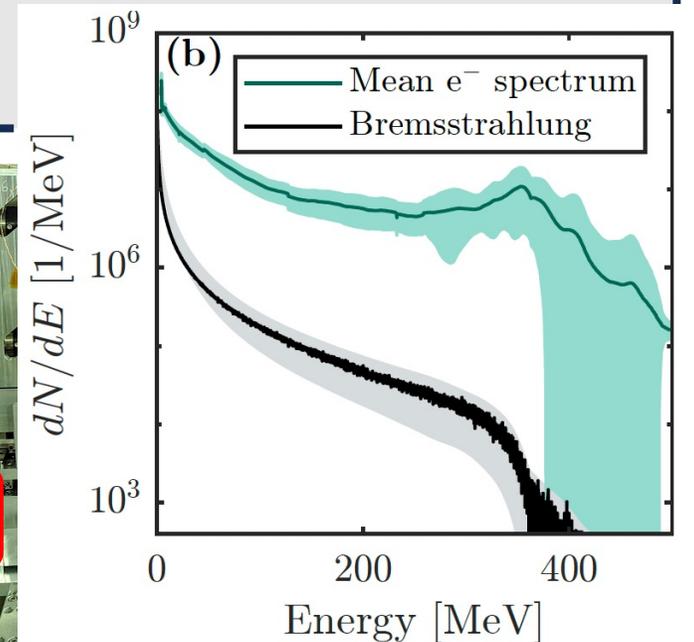
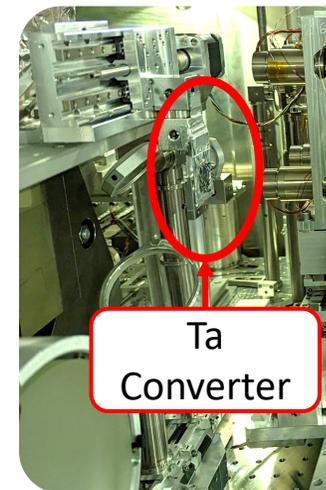
- For bremsstrahlung production a *0.8 mm tantalum* converter was used.
- Electrons were deflected with a magnet.
- Bremsstrahlung spectrum **could not be measured** → Numerical simulation



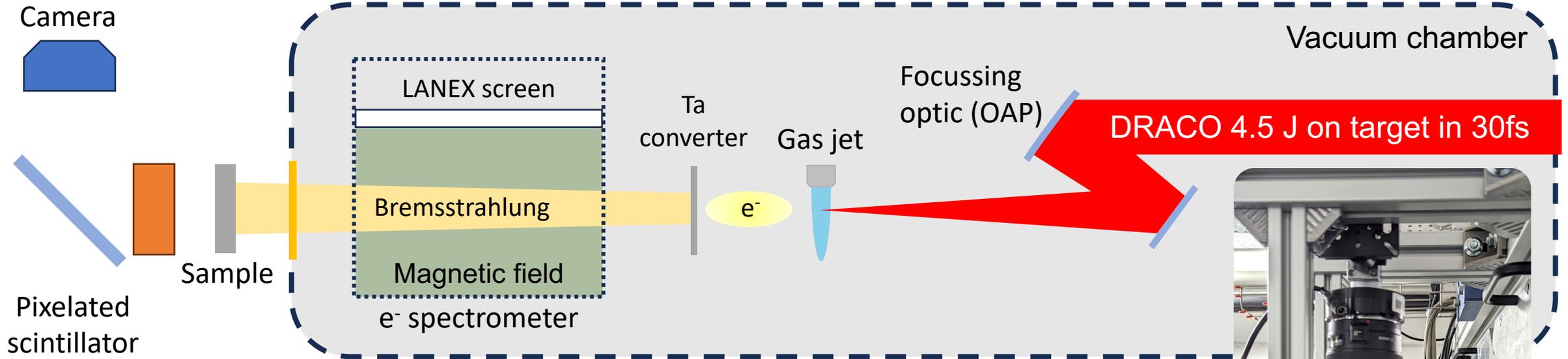
The bremsstrahlung source



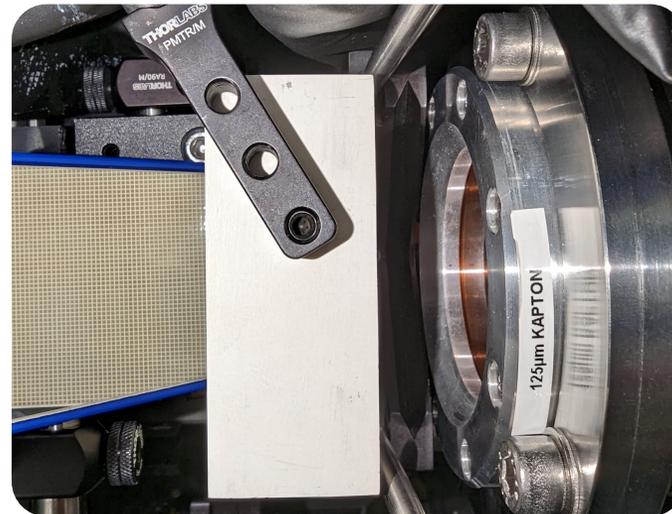
- For bremsstrahlung production a *0.8 mm tantalum* converter was placed.
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The ^{209}Bi sample irradiation

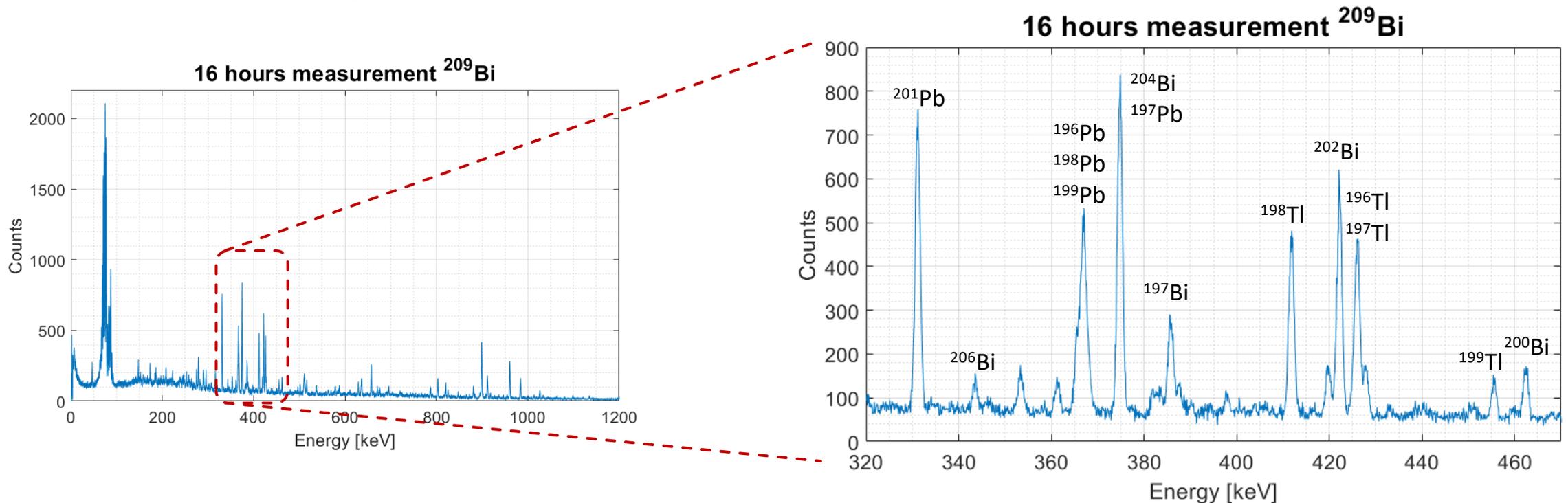


- A ^{209}Bi sample of $25.4 \text{ mm} \times 2 \text{ mm}$ was placed outside the chamber after a $125 \mu\text{m}$ Kapton window.
- Bremsstrahlung pointing measured online with a pixelated scintillator placed after the sample.



The ^{209}Bi sample irradiation

- The ^{209}Bi sample was irradiated for 1 hour at 0.1 Hz (370 shots).
- The sample was successfully activated and measured with a *HPGe* detector.
- Laser-plasma interaction creates an extremely harsh environment → *HPGe* detector must be in a different room (7 min transfer time).
- A short-lived activity of 10-100 Bq was measured.



Observed isotopes in γ -spectrometry

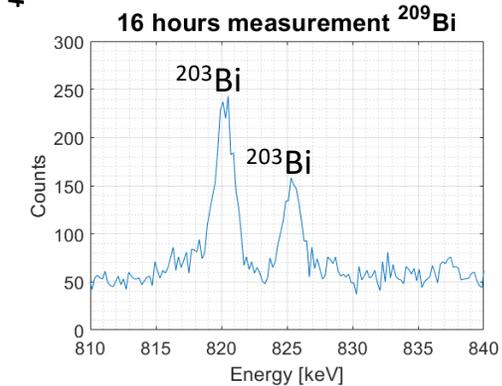
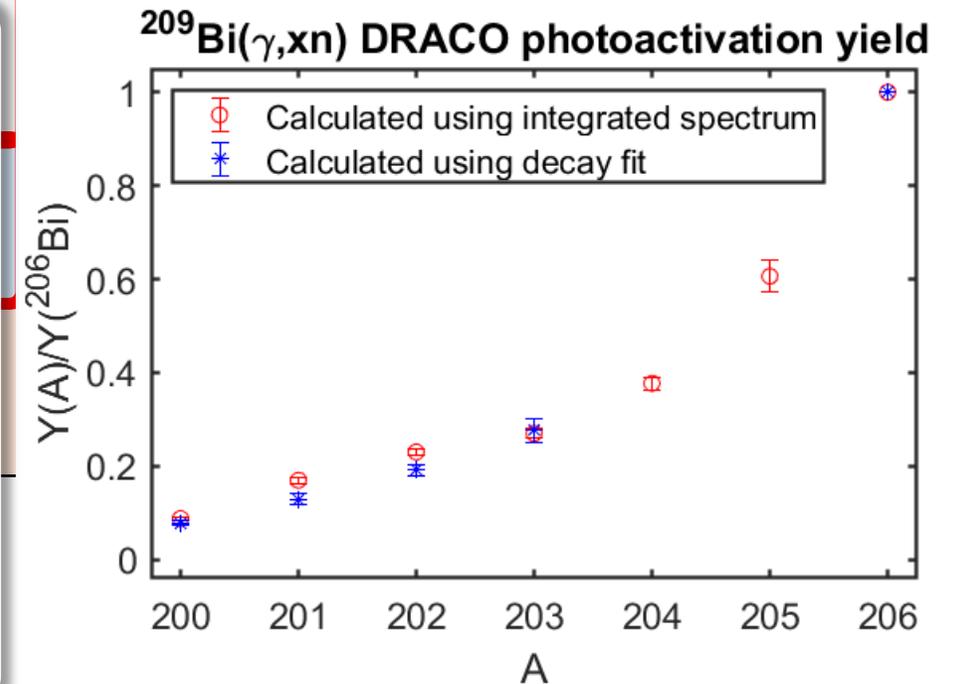
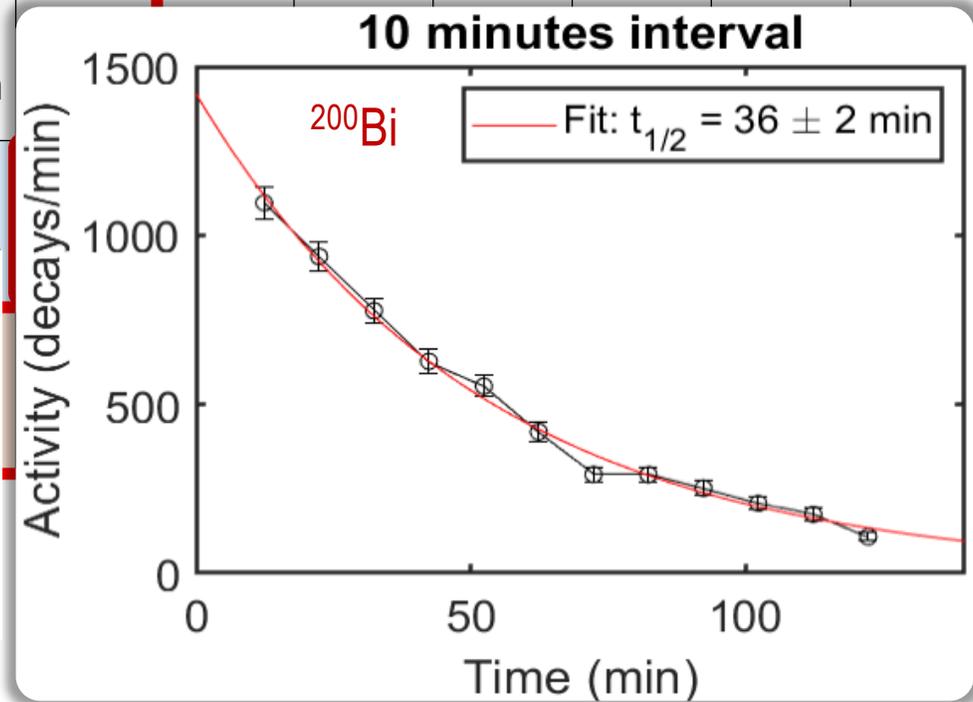
Region of interest of Chart of Nuclides

# Protons (Z)	83	¹⁹³ Bi 63.6 s	¹⁹⁴ Bi 95 s	¹⁹⁵ Bi 183 s	¹⁹⁶ Bi 308 s	¹⁹⁷ Bi 9.3 min	¹⁹⁸ Bi 10 min	¹⁹⁹ Bi 27 min	²⁰⁰ Bi 36 min	²⁰¹ Bi 103 min	²⁰² Bi 1.7 h	²⁰³ Bi 11.8 h	²⁰⁴ Bi 11.2 h	²⁰⁵ Bi 15.3 d	²⁰⁶ Bi 6.2 d	²⁰⁷ Bi 31.6 y	²⁰⁸ Bi 3.7e5 y	²⁰⁹ Bi stable
	82	¹⁹² Pb 3.5 min	¹⁹³ Pb 5.8 min	¹⁹⁴ Pb 11 min	¹⁹⁵ Pb 15 min	¹⁹⁶ Pb 37 min	¹⁹⁷ Pb 8.1 min	¹⁹⁸ Pb 2.4 h	¹⁹⁹ Pb 90 min	²⁰⁰ Pb 21.5 h	²⁰¹ Pb 9.3 h	²⁰² Pb 5.6e4 y	²⁰³ Pb 51.9 h	²⁰⁴ Pb stable	²⁰⁵ Pb 1.7e7 y	²⁰⁶ Pb stable	²⁰⁷ Pb stable	²⁰⁸ Pb stable
	81	¹⁹¹ Tl 5.2 min	¹⁹² Tl 9.6 min	¹⁹³ Tl 22 min	¹⁹⁴ Tl 33 min	¹⁹⁵ Tl 1.2 h	¹⁹⁶ Tl 1.8 h	¹⁹⁷ Tl 2.84 h	¹⁹⁸ Tl 5.3 h	¹⁹⁹ Tl 7.4 h	²⁰⁰ Tl 26.1 h	²⁰¹ Tl 3.4 d	²⁰² Tl 12.3 d	²⁰³ Tl stable	²⁰⁴ Tl 3.8 y	²⁰⁵ Tl stable	²⁰⁶ Tl 4.2 min	²⁰⁷ Tl 4.8 min
	80	¹⁹⁰ Hg 20 min	¹⁹¹ Hg 49 min	¹⁹² Hg 4.9 h	¹⁹³ Hg 3.8 h	¹⁹⁴ Hg 444 y	¹⁹⁵ Hg 10.5 h	¹⁹⁶ Hg stable	¹⁹⁷ Hg 64.1 h	¹⁹⁸ Hg stable	¹⁹⁹ Hg stable	²⁰⁰ Hg stable	²⁰¹ Hg stable	²⁰² Hg stable	²⁰³ Hg 46.6 d	²⁰⁴ Hg stable	²⁰⁵ Hg 5.1 min	²⁰⁶ Hg 8.3 min
		110	111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126
		# Neutrons (N)																

Production of lighter isotopes

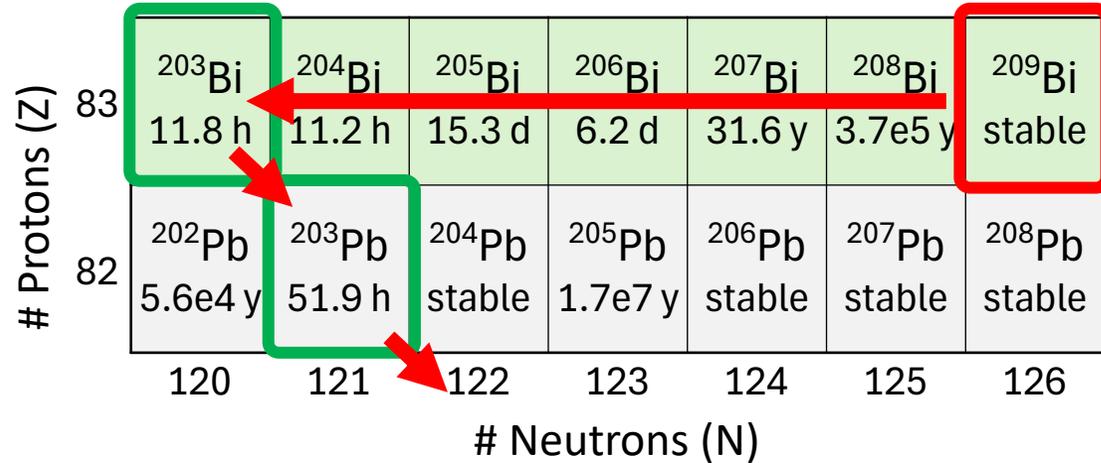
Region of interest of Chart of Nuclides

83	¹⁹³ Bi 63.6 s	¹⁹⁴ Bi 95 s	¹⁹⁵ Bi 183 s	¹⁹⁶ Bi 308 s	¹⁹⁷ Bi 9.3 min	¹⁹⁸ Bi 10 min	¹⁹⁹ Bi 27 min	²⁰⁰ Bi 36 min	²⁰¹ Bi 103 min	²⁰² Bi 1.7 h	²⁰³ Bi 11.8 h	²⁰⁴ Bi 11.2 h	²⁰⁵ Bi 15.3 d	²⁰⁶ Bi 6.2 d	²⁰⁷ Bi 31.6 y	²⁰⁸ Bi 3.7e5 y	²⁰⁹ Bi stable
82	¹⁹² Pb 3.5 min	¹⁹³ Pb 5.8 min	¹⁹⁴ Pb 11 min														
81	¹⁹¹ Tl 5.0 min	¹⁹² Tl 9.0 min	¹⁹³ Tl 22 min														



Production of lighter isotopes

Lead, thallium or mercury isotopes could be produced through the decay of parent nuclei

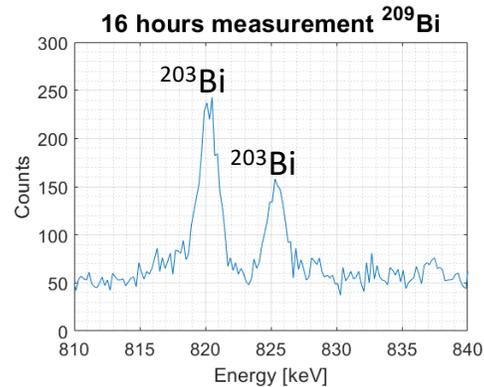
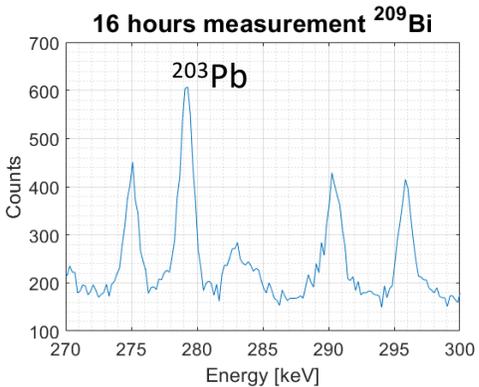


$$\frac{dN_{Bi}}{dt} = q - \lambda_{Bi}N_{Bi}$$

$$\frac{dN_{Pb}}{dt} = \lambda_{Bi}N_{Bi} - \lambda_{Pb}N_{Pb}$$

$$\frac{N_{Pb}(t_{irr})}{N_{Bi}(t_{irr})} = \frac{\frac{\lambda_{Bi}}{\lambda_{Pb}}(1 - e^{-\lambda_{Pb}t_{irr}}) + \frac{\lambda_{Bi}}{\lambda_{Pb} - \lambda_{Bi}}(e^{-\lambda_{Pb}t_{irr}} - e^{-\lambda_{Bi}t_{irr}})}{1 - e^{-\lambda_{Bi}t_{irr}}}$$

q is the constant production rate of ^{203}Bi and t_{irr} the irradiation time.



Estimated fraction of ^{203}Pb produced by the decay of ^{203}Bi :
 $t_{irr} = 60.67 \text{ min}$

Experimental ratio:
(From measured counts)

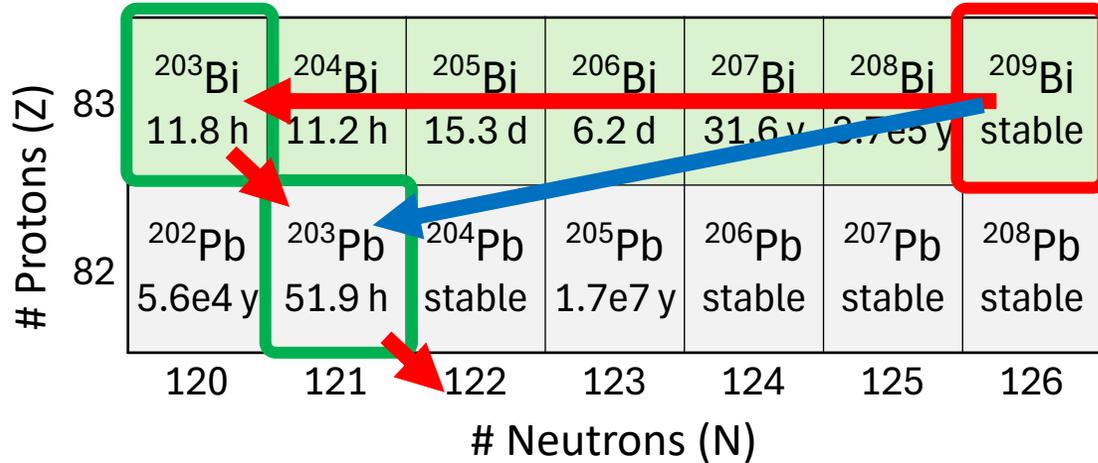
$$\frac{N_{Pb}^{Th}(t_{irr})}{N_{Bi}^{Th}(t_{irr})} = 0.030$$

$$\frac{N_{Pb}^{Exp}(t_{irr})}{N_{Bi}^{Exp}(t_{irr})} = 0.642$$

Not all the production of Pb comes from Bi decay!

Production of lighter isotopes

^{203}Pb can also be produced directly by $^{209}\text{Bi}(\gamma, p5n)^{203}\text{Pb}$ reactions



$$\frac{dN_{Pb}}{dt} = \lambda_{Bi}N_{Bi} + p - \lambda_{Pb}N_{Pb}$$

$p \equiv$ direct production rate of ^{203}Pb
 $q \equiv$ direct production rate of ^{203}Bi

$$\frac{N_{Pb}(t_{irr})}{N_{Bi}(t_{irr})} = \frac{\left(1 - \frac{p}{q}\right) \frac{\lambda_{Bi}}{\lambda_{Pb}} (1 - e^{-\lambda_{Pb}t_{irr}}) + \frac{\lambda_{Bi}}{\lambda_{Pb} - \lambda_{Bi}} (e^{-\lambda_{Pb}t_{irr}} - e^{-\lambda_{Bi}t_{irr}})}{1 - e^{-\lambda_{Bi}t_{irr}}}$$

M. Krmar et al. (EPJ A, 2023)

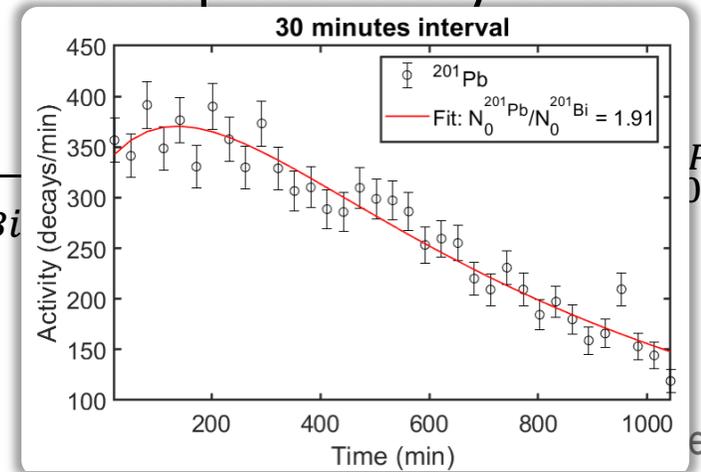
- Analytical method.

$$\frac{N_{Pb}^{Exp}(t_{irr})}{N_{Bi}^{Exp}(t_{irr})} = \left[\frac{N_{Pb}^{Exp}}{N_{Bi}^{Exp}} - \frac{\lambda_{Bi}}{\lambda_{Bi} - \lambda_{Pb}} \frac{e^{-\lambda_{Pb}t_1} - e^{-\lambda_{Pb}t_2}}{e^{-\lambda_{Bi}t_1} - e^{-\lambda_{Bi}t_2}} + \frac{\lambda_{Pb}}{\lambda_{Bi} - \lambda_{Pb}} \right] \frac{e^{-\lambda_{Bi}t_1} - e^{-\lambda_{Bi}t_2}}{e^{-\lambda_{Pb}t_1} - e^{-\lambda_{Pb}t_2}}$$

t_1 and t_2 are the initial and final measurement times after the irradiation time t_{irr}

- Fit of the temporal decay of the activity.

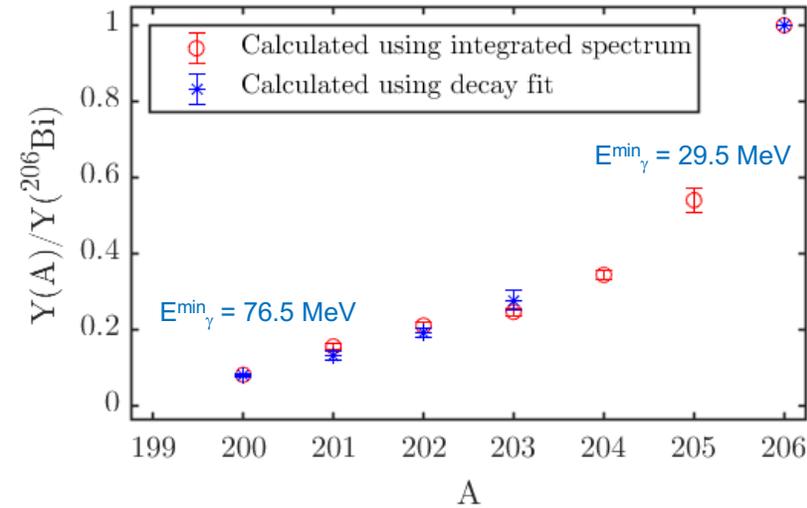
$$A_{Pb} = \frac{\lambda_{Bi}\lambda_{Pb}}{\lambda_{Pb} - \lambda_{Bi}}$$



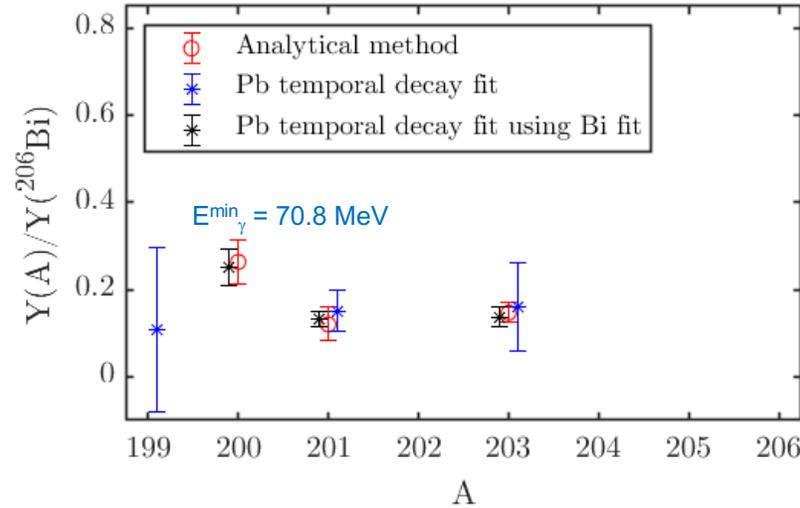
$$A_{Pb} e^{-\lambda_{Pb}t}$$

Direct production yields by photo-activation of ^{209}Bi

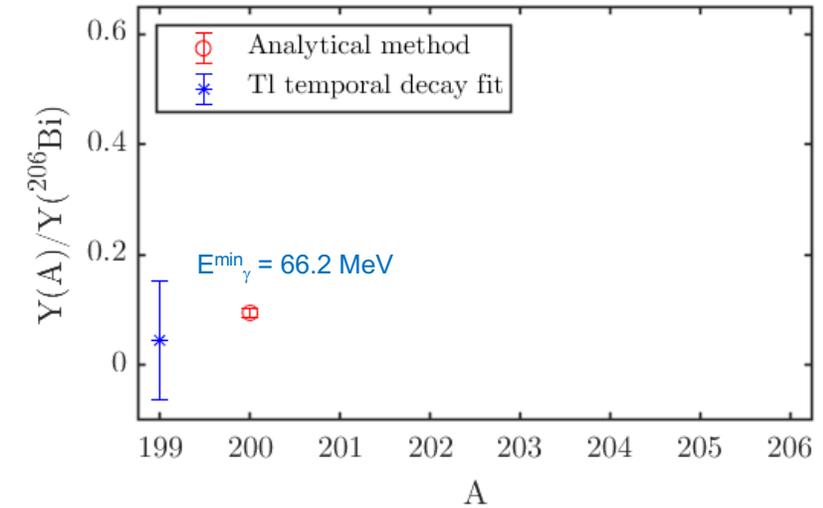
Bismuth isotopes



Lead isotopes

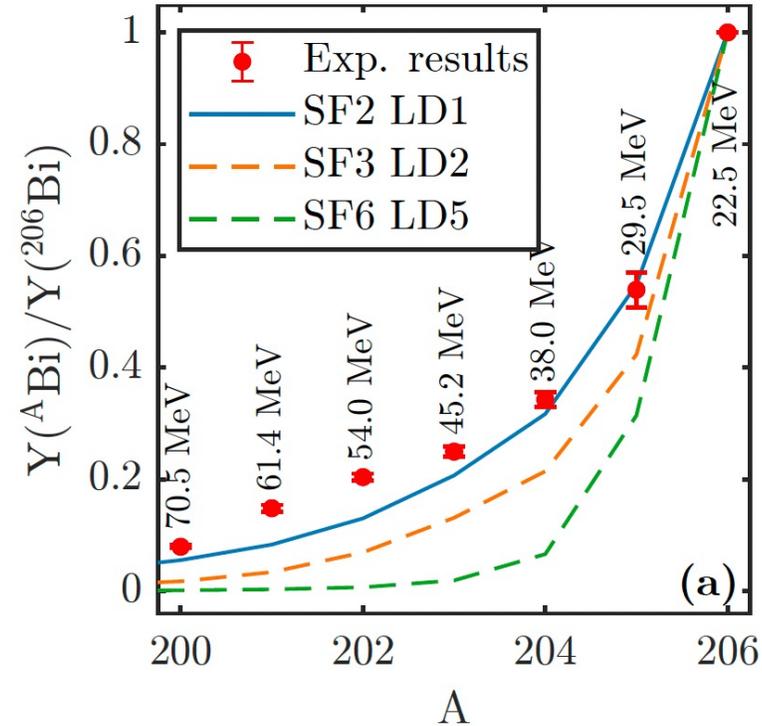


Thallium isotopes



- ✓ Different methods used to obtain the production yields of final nuclei provide similar results.
- ✓ Observing final nuclei with up to ten fewer nucleons than ^{209}Bi indicates that photo-absorption processes involving γ -rays with energies well above the *GDR* regime are occurring.

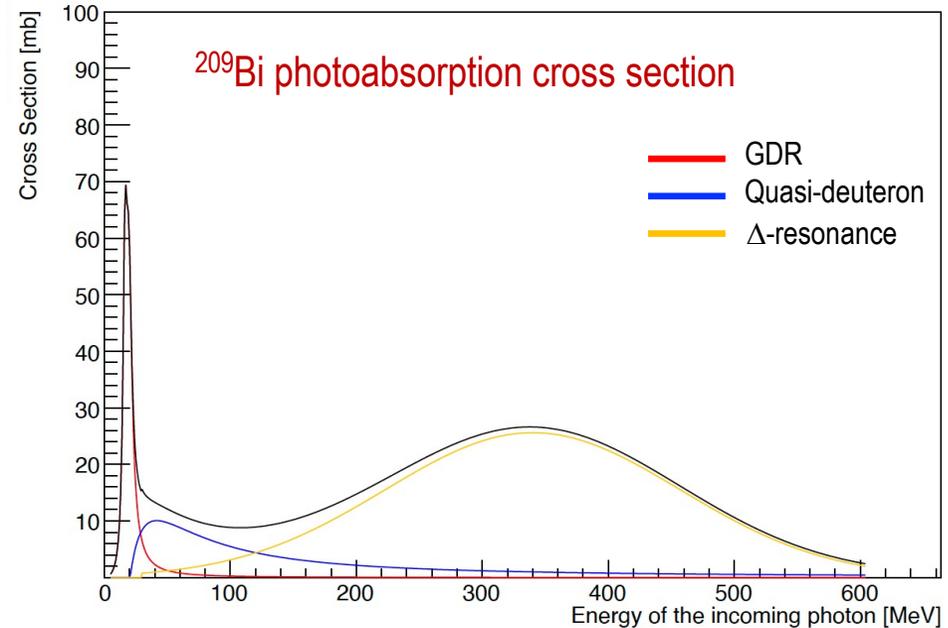
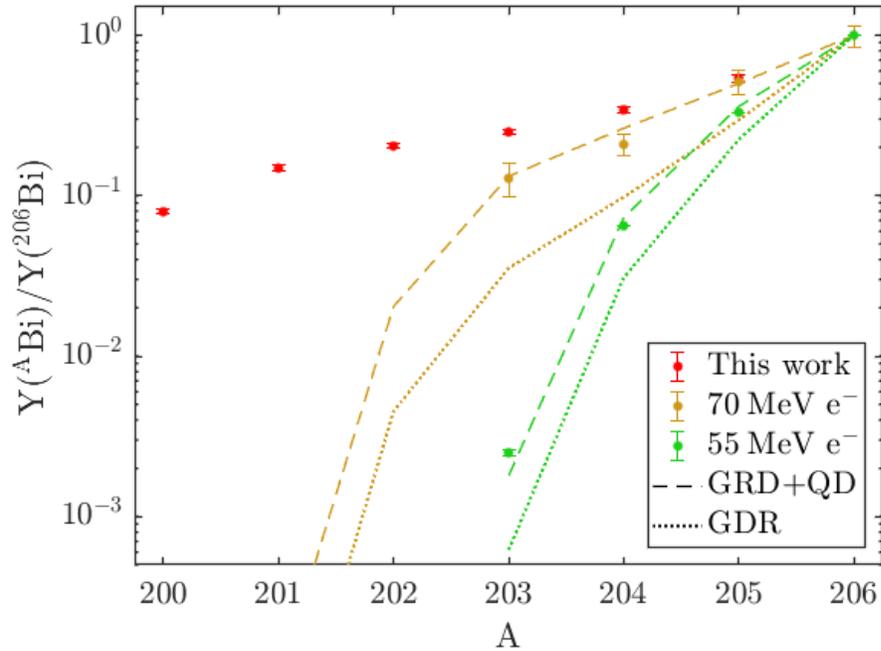
Model calculations with Talys



✓ Although model calculations using the *Talys* code with the default options for describing level densities (*LD1*) and the photon strength function (*SF2*) provide the best description of the data, they underestimate the production of the lighter residual nuclei.

✓ This result may indicate a deficiency in the physics model used by *Talys* to describe photo-absorption above the *GDR* regime, the *quasi-deuteron breakup* or the missing photo-absorption by the excitation of the Δ -resonance.

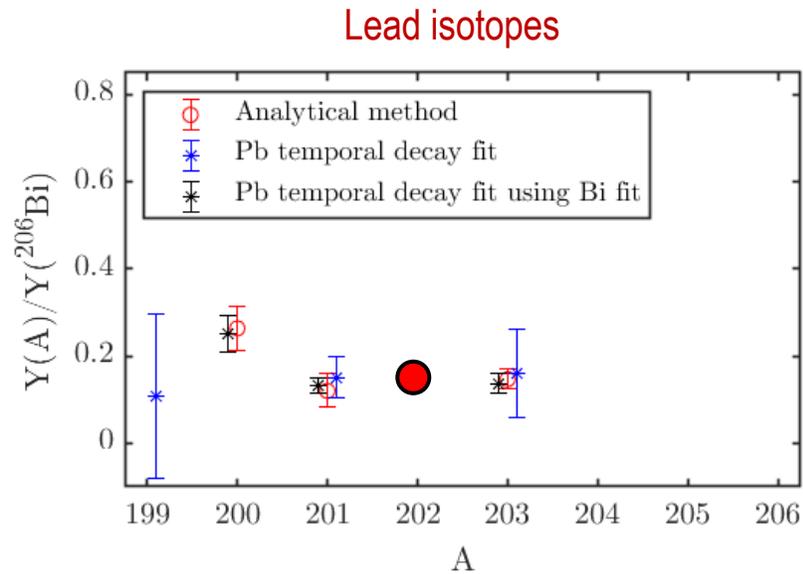
Model calculations with Talys



- ✓ However, *Talys* calculations using the *GDR* and *quasi-deuteron* photo-absorption channels provide a fairly accurate description of the production of residual nuclei in reactions involving bremsstrahlung generated by lower energy-electrons.
- ✓ This could be a clear indication on the role of the Δ -resonance *photo-absorption* mechanism not included in the *Talys* code.

Estimated production of ^{225}Ac in photo-activation reactions

$^{209}\text{Bi}(\gamma, p6n)^{202}\text{Pb}$, as a proxy of $^{232}\text{Th}(\gamma, p6n)^{225}\text{Ac}$



Assuming a production rate $R(^{225}\text{Ac}) = R(^{202}\text{Pb}) = 3654 \text{ nuclei/min}$, and using $T_{1/2}(^{225}\text{Ac}) = 1484,8 \text{ min}$, the activity of ^{225}Ac generated in 1 hour will be:

$$N(t = 60) = \frac{R}{\lambda} (1 - e^{-\lambda t}) = 2,2 \cdot 10^5 \text{ nuclei}$$

$$A = \lambda N = 0,18 \text{ Bq/h}$$

Estimated production of ^{225}Ac in photo-activation reactions

Accelerator	Proton energy on target [MeV]	Beam current [μA]	Rep. rate [Hz]	Yield [kBq/h]
INR (Russia)	145	120	-	488.4
Brookhaven (USA)	185	80	-	592
Los Alamos (USA)	90	180	-	133.2
TRIUMF (Canada)	110	60	-	88.8
Arronax (France)	65	180	-	33.3
150 TW system	-	0.000 09	0.1	0.000 18
150 TW HRR system	-	0.09	100	0.177
150 TW HRR system optimised	-	0.405	100	25.5

Possible optimisations of the laser-driven source:

- Converter thickness: $0,8 \rightarrow 3 \text{ mm}$, 60% gain.
- Close-coupling converter-sample: 244% gain.
- Electron-beam charge: $0,9 \rightarrow 4 \text{ nC}$, 430%, gain.
- **Pulse rate: $0,1 \rightarrow 100 \text{ Hz}$.**

Expected activity: $25,5 \text{ kBq/h}$

Although an optimised laser-driven source could produce activities of a few MBq of ^{225}Ac in a few days, commercial production would require laser systems with operating at a pulse rate above 100 Hz .

Summary

- ✓ We have investigated the production of ^{225}Ac using a laser-driven bremsstrahlung source using as a proxy the reaction $^{209}\text{Bi}(\gamma, p6n)^{202}\text{Pb}$.
- ✓ We have performed an experiment to validate this technology.
 - We used the *DRACO* laser system at *HZDR* to accelerate electrons and to produce bremsstrahlung up to 350 MeV.
 - This laser-driven bremsstrahlung source was used to photo-activate a ^{209}Bi sample.
- ✓ Twenty-five different isotopes of *Bi*, *Pb*, *Tl* and *Hg* were identified, many of which were produced by direct photon-induced reactions. The difference in neutron and proton numbers relative to ^{209}Bi , for many of them, indicates that they were produced in a gamma absorption energy domain well above the *GDR*.
- ✓ Model calculations performed using the *Talys* code clearly underestimate the production of the lighter isotopes. These results indicate the need for a better understanding of the photon-nucleus interaction above the *GDR* domain.
- ✓ The measured production of ^{201}Pb and ^{203}Pb was used to estimate an expected activity of ^{225}Ac of 0,18 Bq/h which would increase to 25,5 kBq/h with an optimized laser-driven source, indicating that a competitive commercial source should run above 100 Hz.

The team



A. Alejo, **A. Bembibre**



J. Benlliure

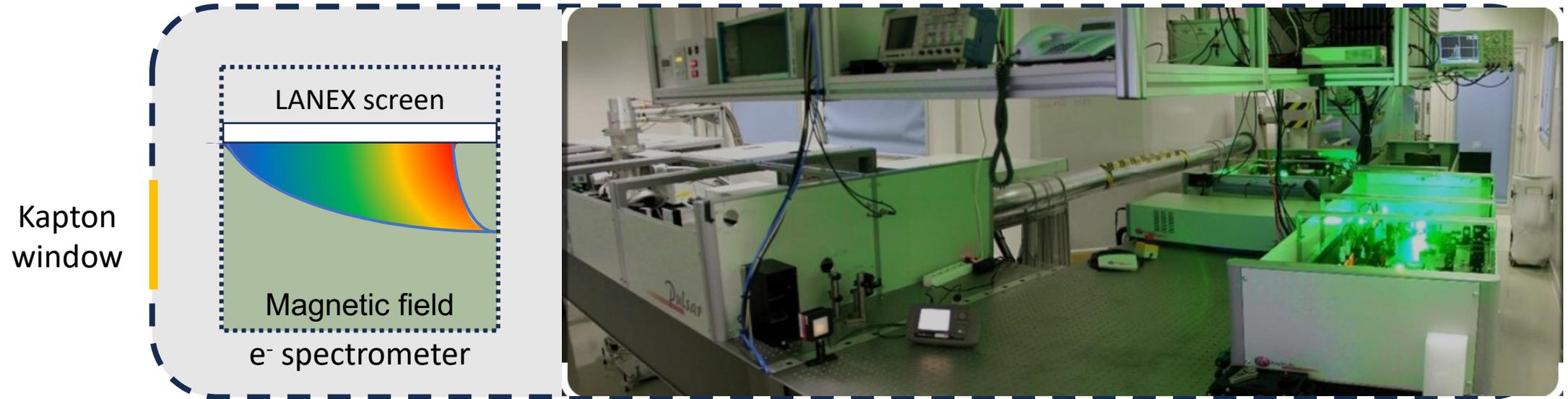


HELMHOLTZ ZENTRUM
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A. Irman, Y.-Y. Chang, F.
Herrmann, M. Laberge, J.
Metzkes, S. Schöbel, K. Zeil, P.
Ufer, T. Cowan, U. Schramm

The laser-driven electron source



Electron spectrometer before and after irradiation for beam characterisation.

