

# Badanie wytwarzania radioizotopów medycznych w Środowiskowym Laboratorium Ciężkich Jonów

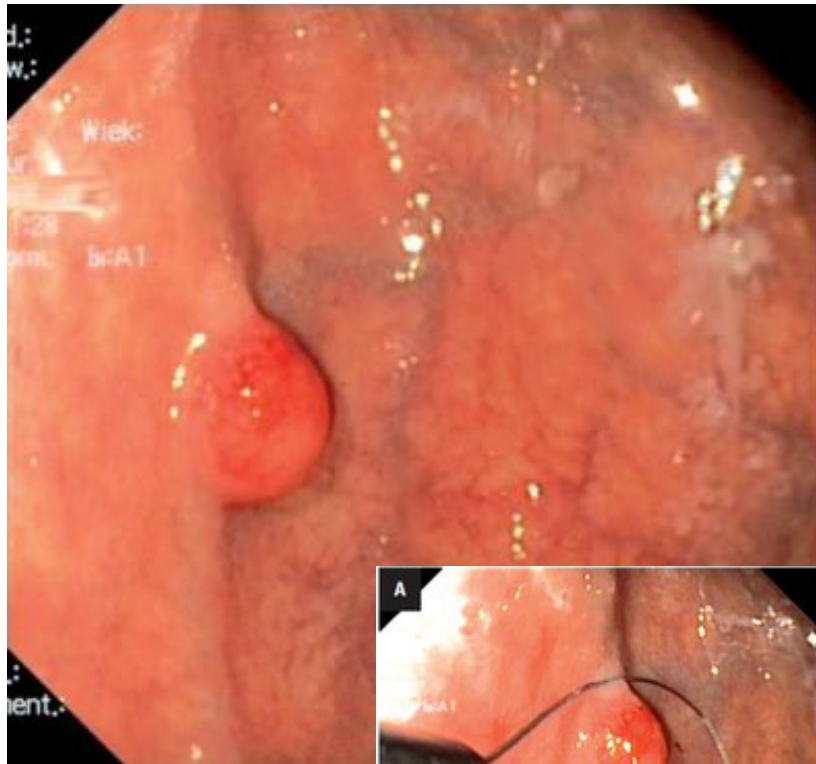
Mateusz Sitarz<sup>1,2</sup>

opiekunowie: prof. Jerzy Jastrzębski<sup>1</sup>, dr Agnieszka Trzcńska<sup>1</sup>, prof. Tomasz Matulewicz<sup>2</sup>

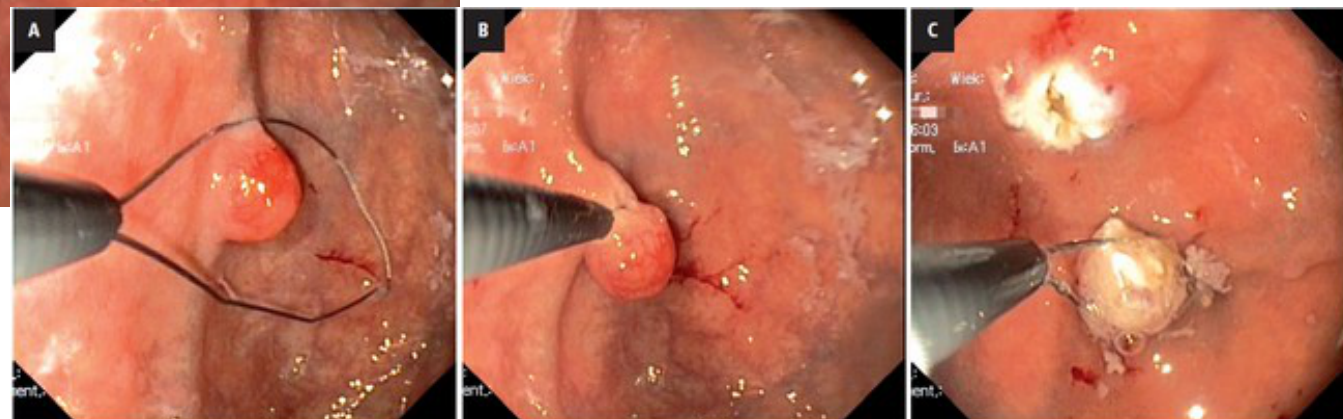
<sup>1</sup> *Środowiskowe Laboratorium Ciężkich Jonów UW*

<sup>2</sup> *Wydział Fizyki Uniwersytetu Warszawskiego*

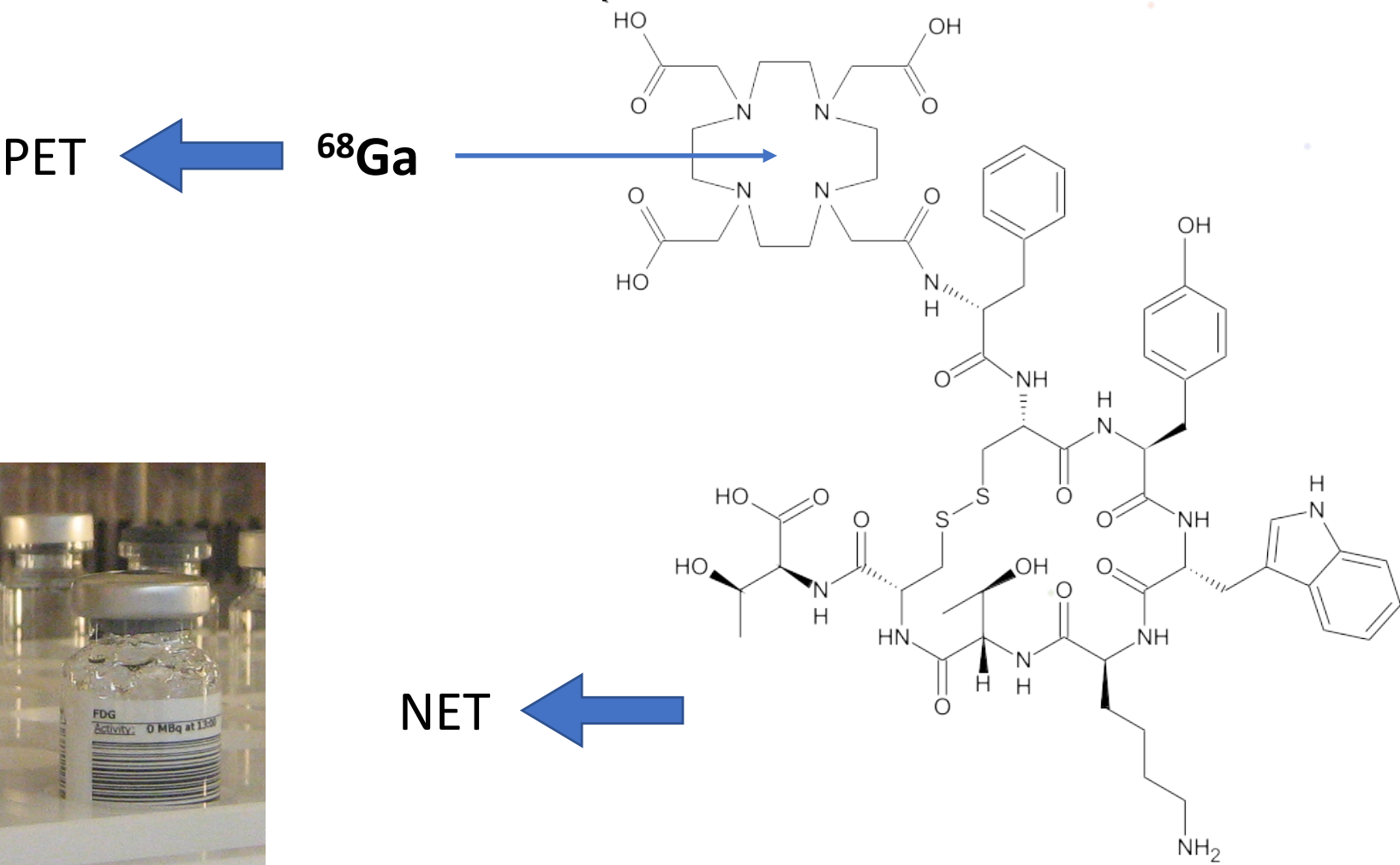
# Nowotwory neuroendokryne (NET)



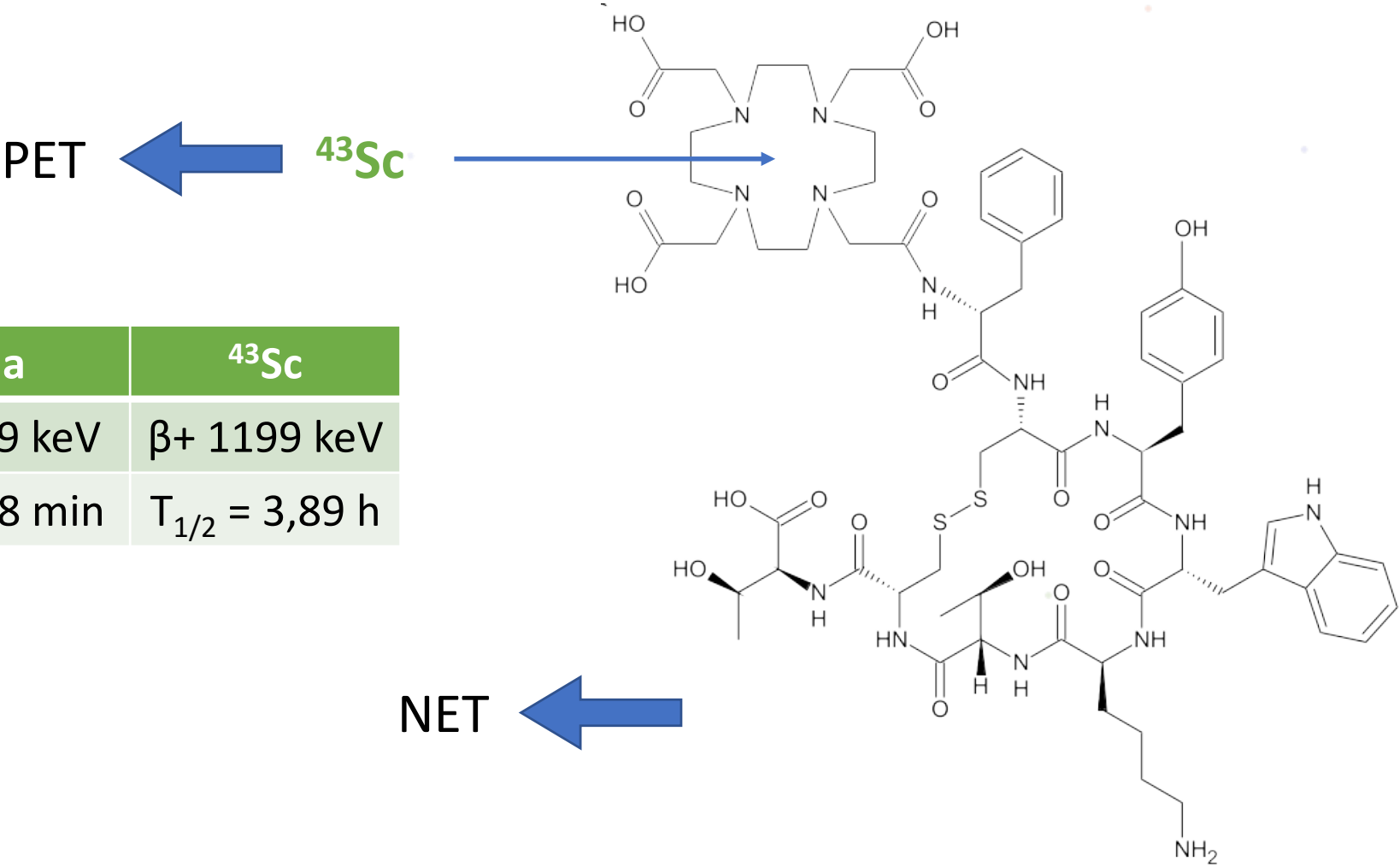
Nadekspresja receptora somatostatyny



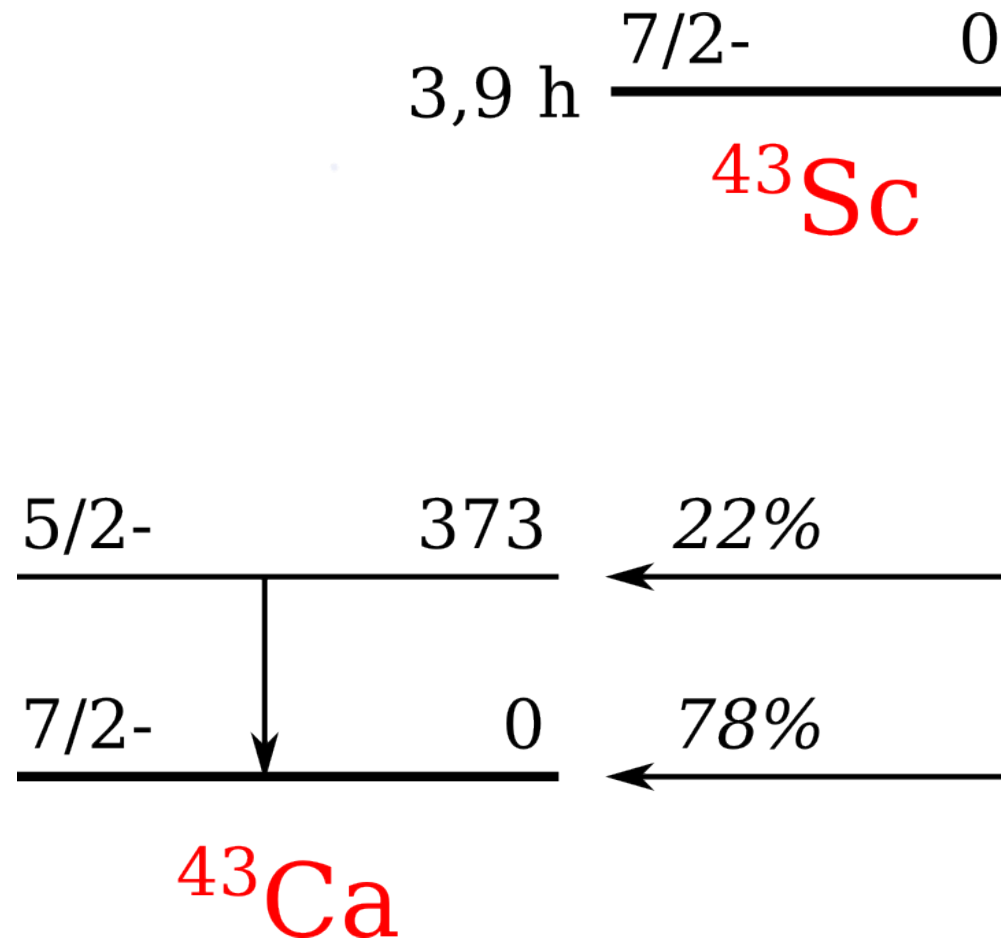
# Diagnoza NET i DOTA-TATE



# Diagnoza NET i DOTA-TATE



# Radioizotop $^{43}\text{Sc}$

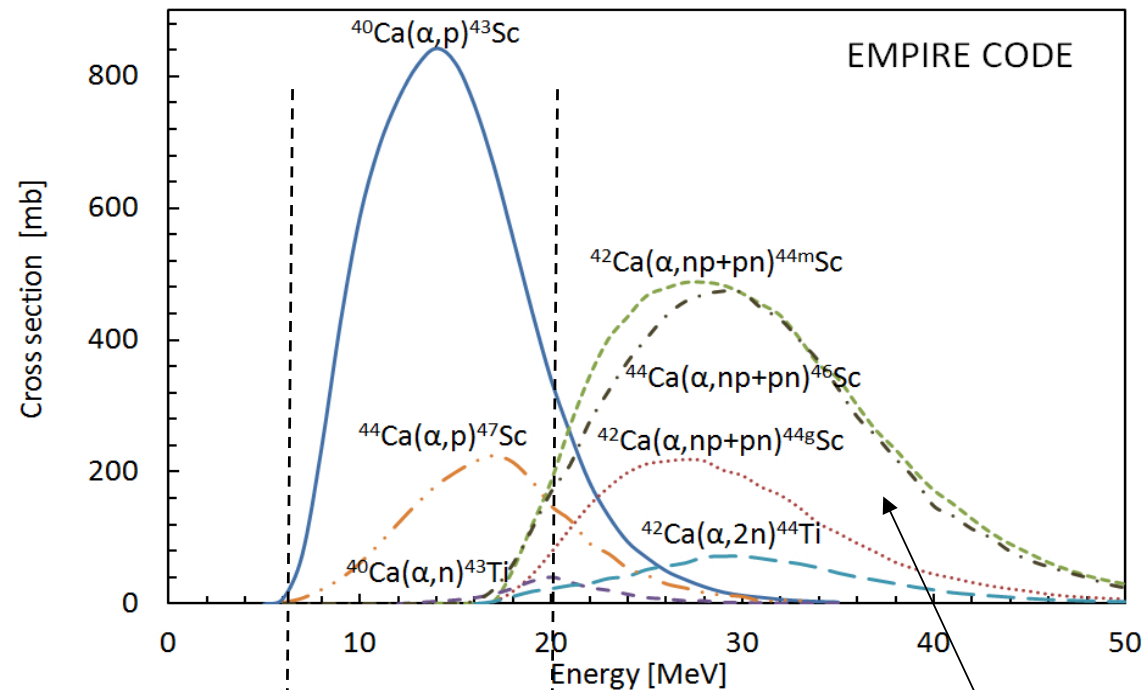


# Produkcja $^{43}\text{Sc}$



$^{42}\text{Ti}$ 199 MS ε: 100.00%	$^{43}\text{Ti}$ 509 MS ε: 100.00%	$^{44}\text{Ti}$ 60.0 Y ε: 100.00%	$^{45}\text{Ti}$ 184.8 M ε: 100.00%	$^{46}\text{Ti}$ STABLE 8.25%	$^{47}\text{Ti}$ STABLE 7.44%	$^{48}\text{Ti}$ STABLE 73.72%
$^{41}\text{Sc}$ 596.3 MS ε: 100.00%	$^{42}\text{Sc}$ 681.3 MS ε: 100.00%	$^{43}\text{Sc}$ 3.891 H ε: 100.00%	$^{44}\text{Sc}$ 3.97 H ε: 100.00%	$^{45}\text{Sc}$ STABLE 100%	$^{46}\text{Sc}$ 83.79 D β-: 100.00%	$^{47}\text{Sc}$ 3.3492 D β-: 100.00%
$^{40}\text{Ca}$ >3.0E+21 Y 96.94% 2ε	$^{41}\text{Ca}$ 1.02E+5 Y ε: 100.00%	$^{42}\text{Ca}$ STABLE 0.647%	$^{43}\text{Ca}$ STABLE 0.135%	$^{44}\text{Ca}$ STABLE 2.09%	$^{45}\text{Ca}$ 162.61 D β-: 100.00%	$^{46}\text{Ca}$ >0.28E+16 Y 0.004% 2β-

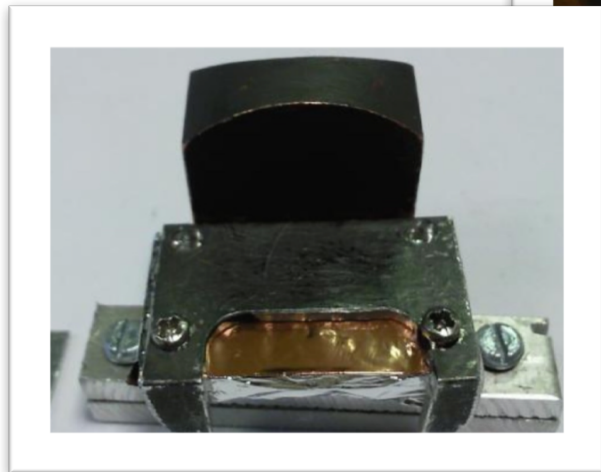
# Produkcja $^{43}\text{Sc}$



tarcza z  $^{40}\text{Ca}$  do naświetlania  
energią  $20 \rightarrow 6$  MeV

zanieczyszczenia  
radioizotopowe

# Produkcja $^{43}\text{Sc}$

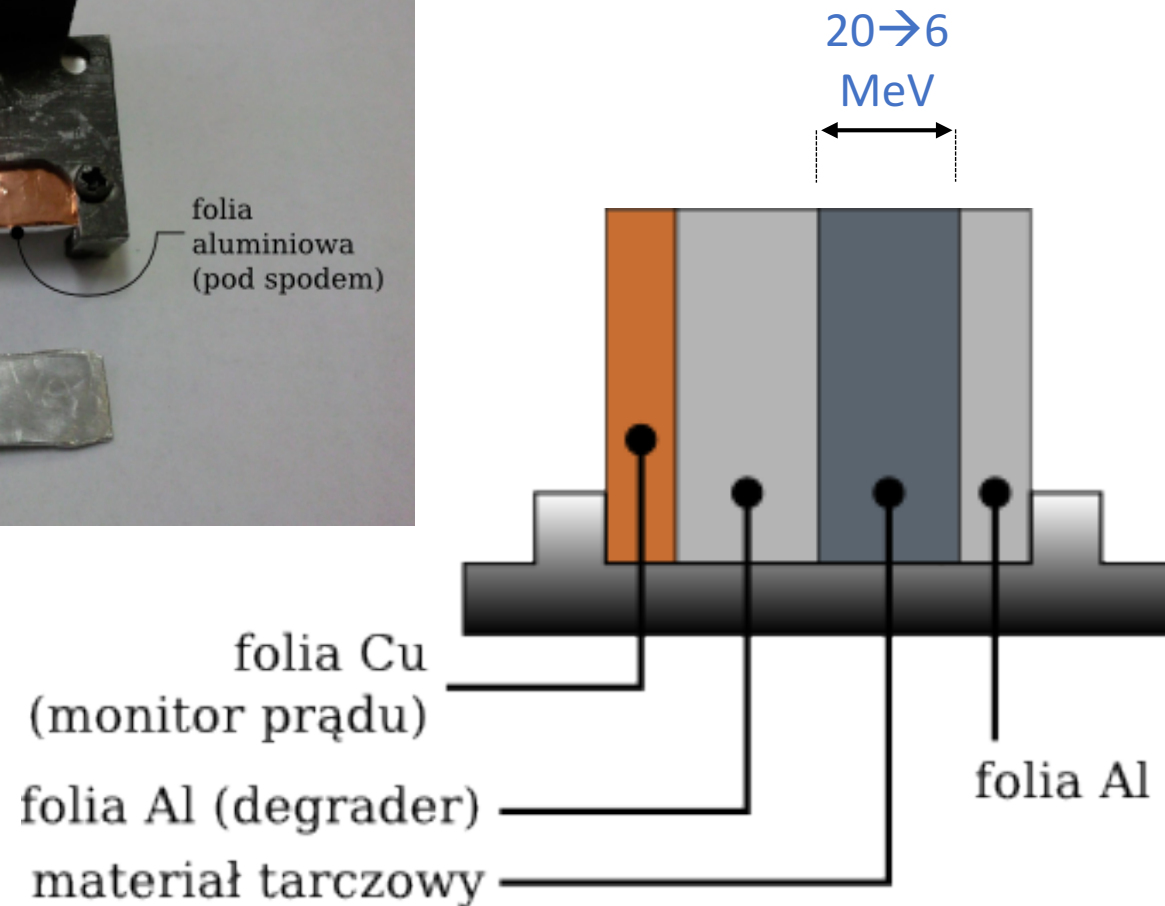
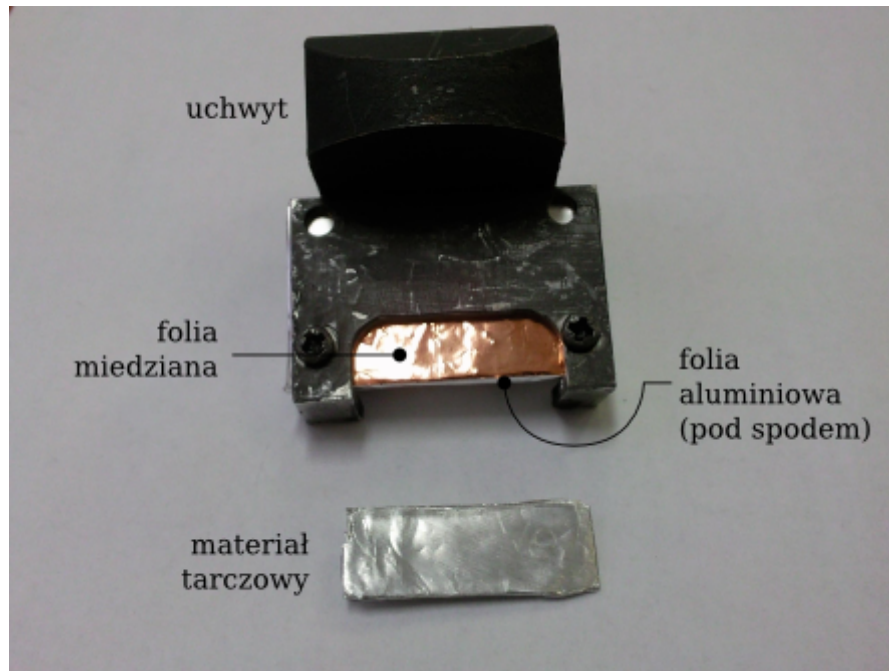


09.03.2017

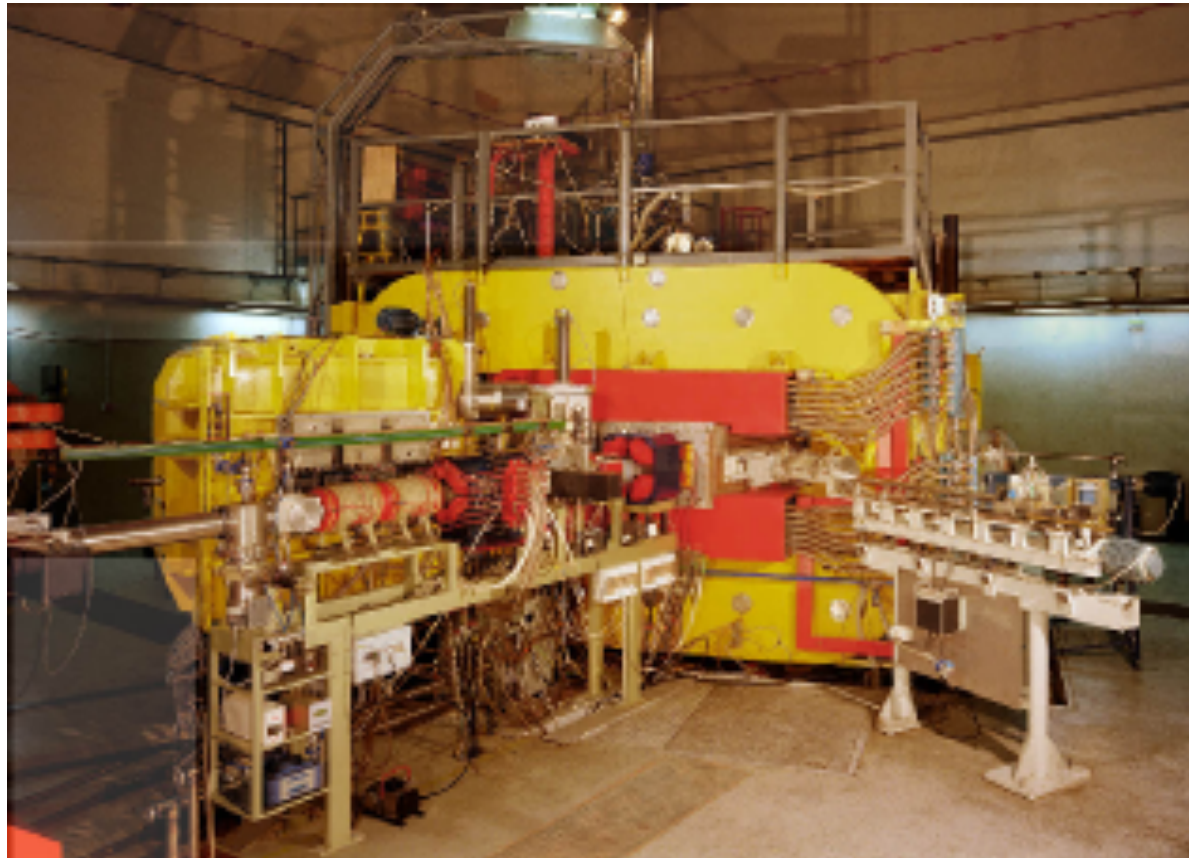
seminarium fizyki jądra atomowego



# Produkcja $^{43}\text{Sc}$

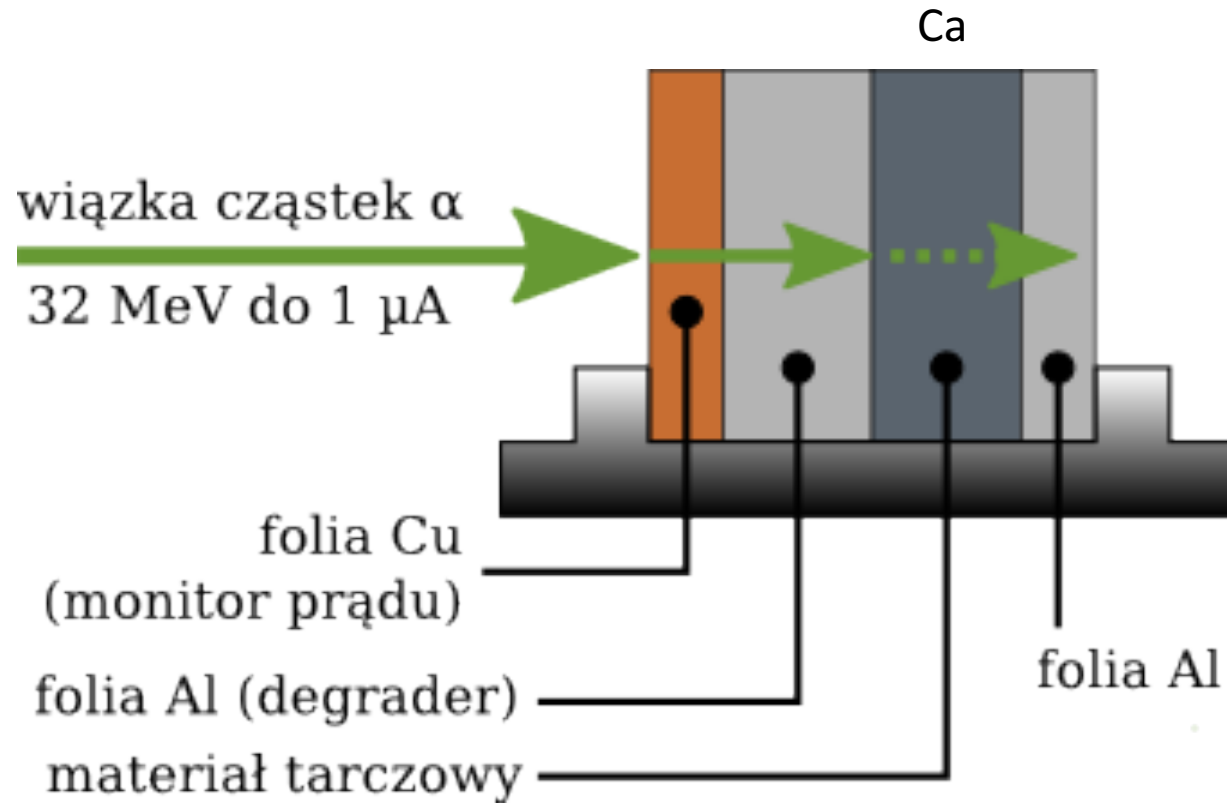


# Produkcja $^{43}\text{Sc}$



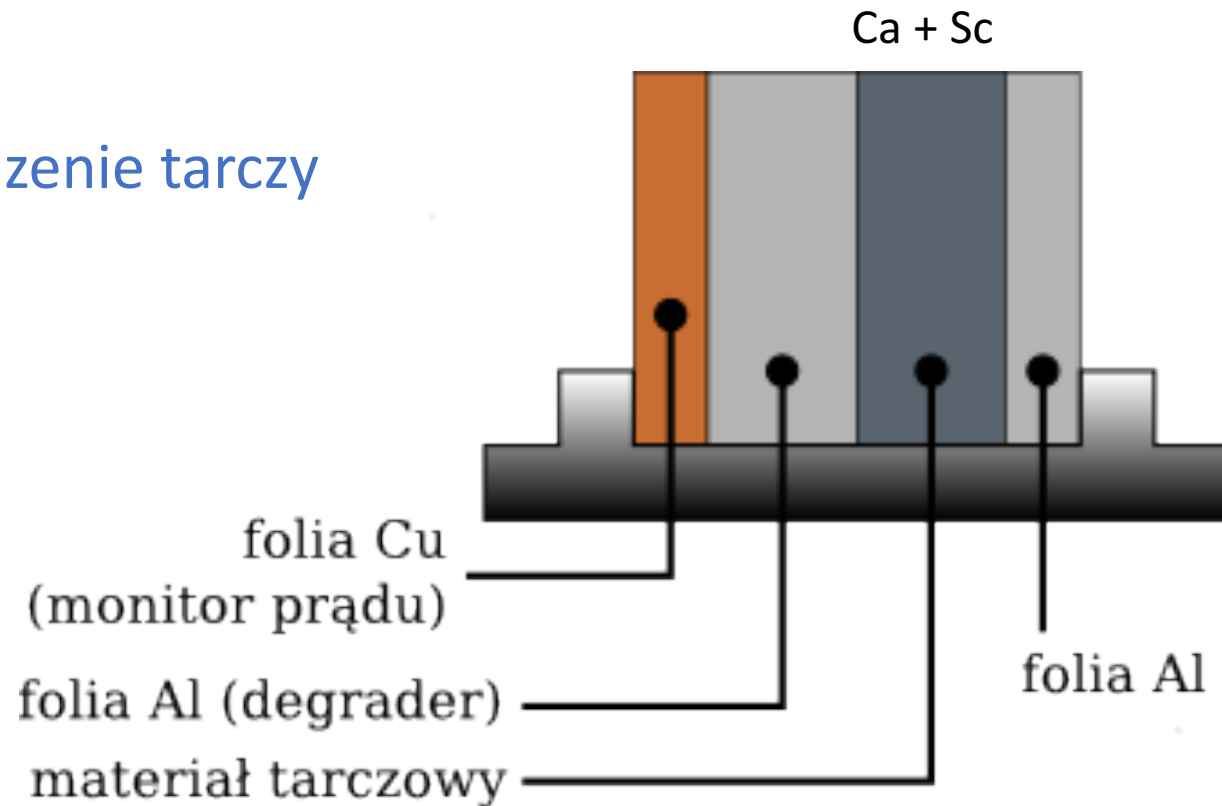
**U-200P** cząstki  $\alpha$  32 MeV  
wiązka wewnętrzna  $\sim 1 \mu\text{A}$   
Środowiskowe Laboratorium Ciężkich Jonów

# Produkcja $^{43}\text{Sc}$

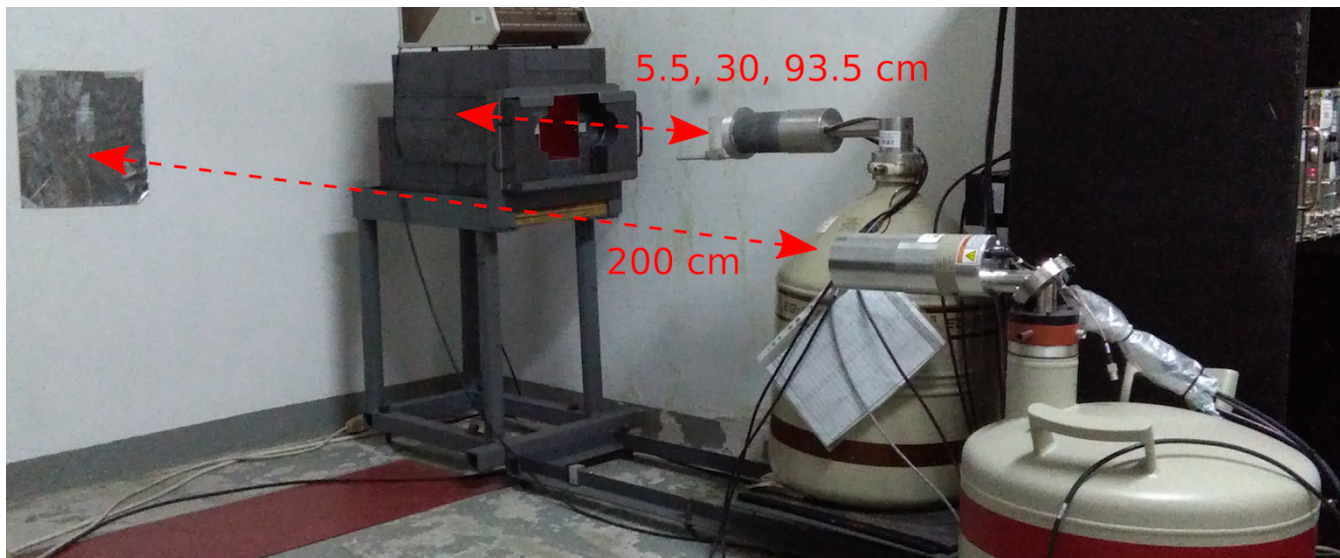
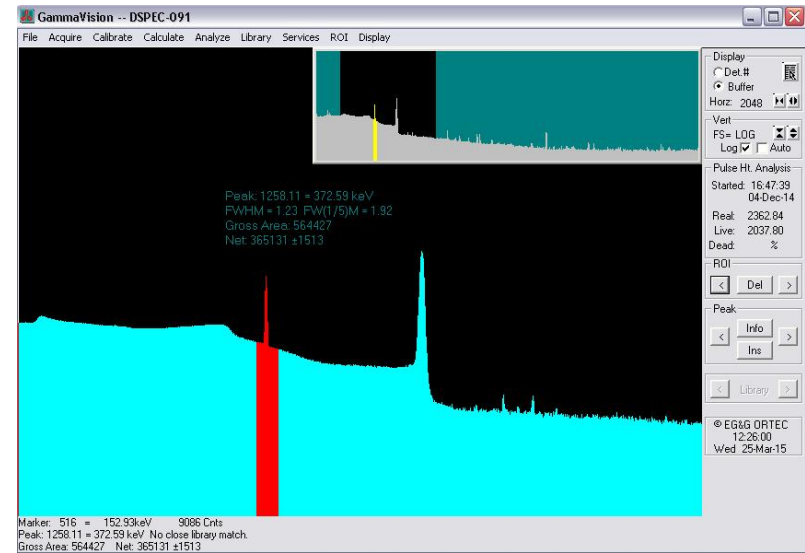
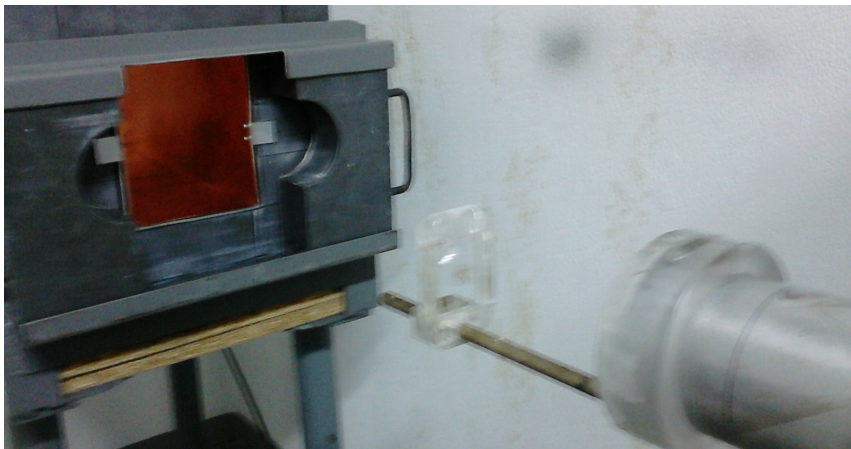


# Produkcja $^{43}\text{Sc}$

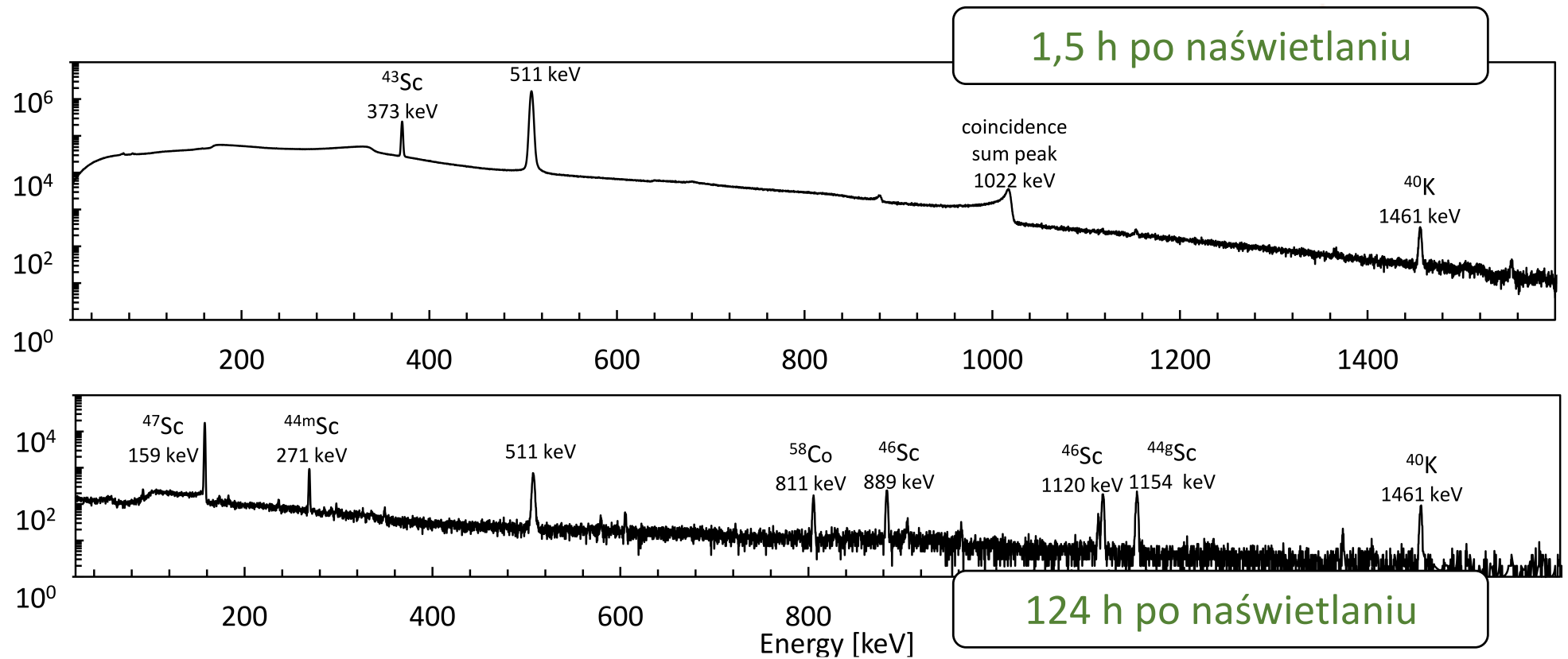
- chłodzenie tarczy



# Akwizycja i analiza



# Produkcja $^{43}\text{Sc}$



Widmo  $^{\text{nat}}\text{CaCO}_3$  naświetlanego cząstkami  $\alpha$  o energii 30 MeV

# Akwizycja i analiza

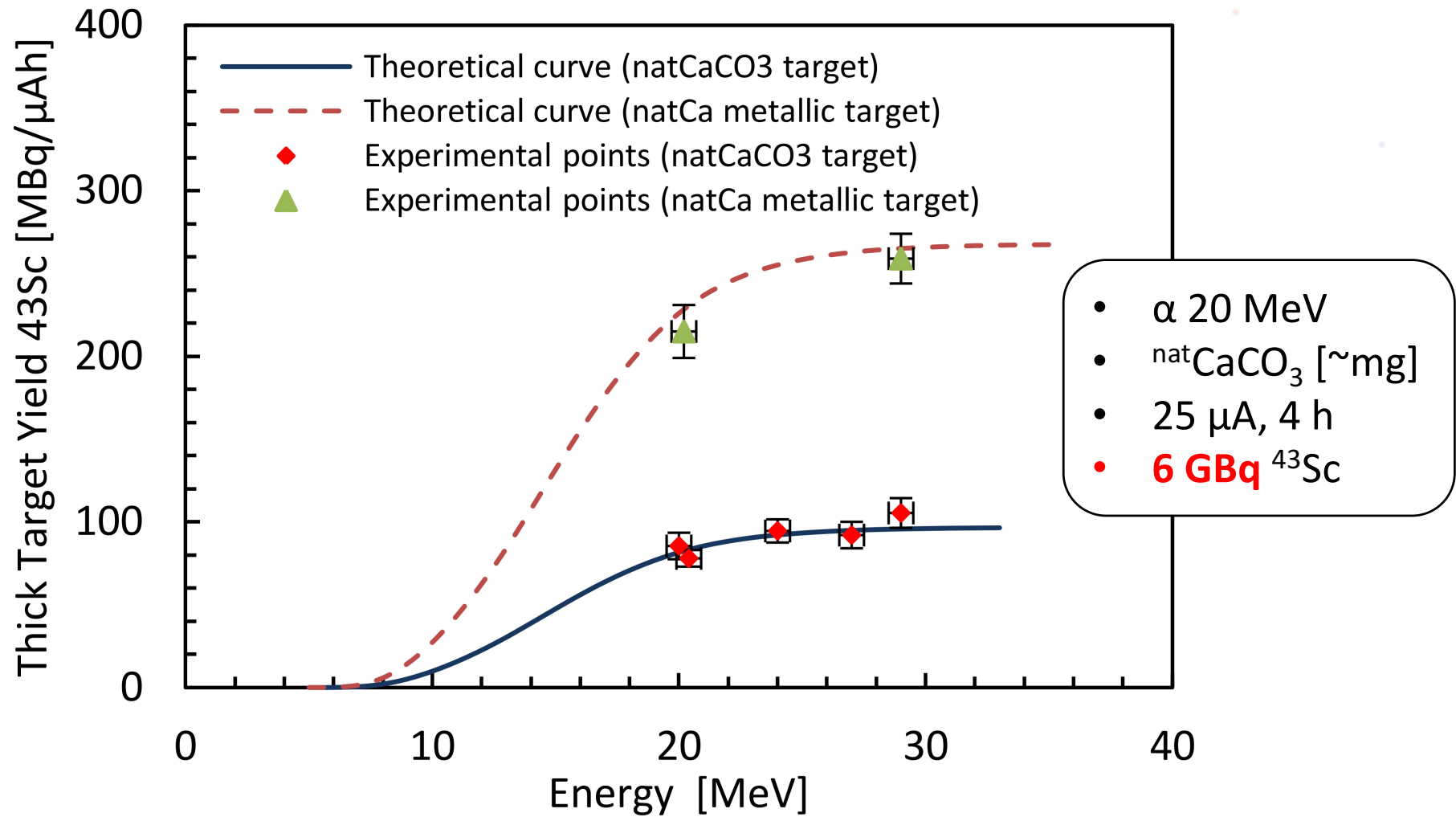
## Eksperyment

- $A_{EOB}$  – activity End Of Bombardment
- $I$  – beam current ( $\sigma$  IAEA monitor reactions)
- $TTY = \frac{A_{EOB}}{I \tau (1 - \exp(-\lambda t_{irr}))}$  – thick target yield [MBq/ $\mu$ Ah]

## Teoria

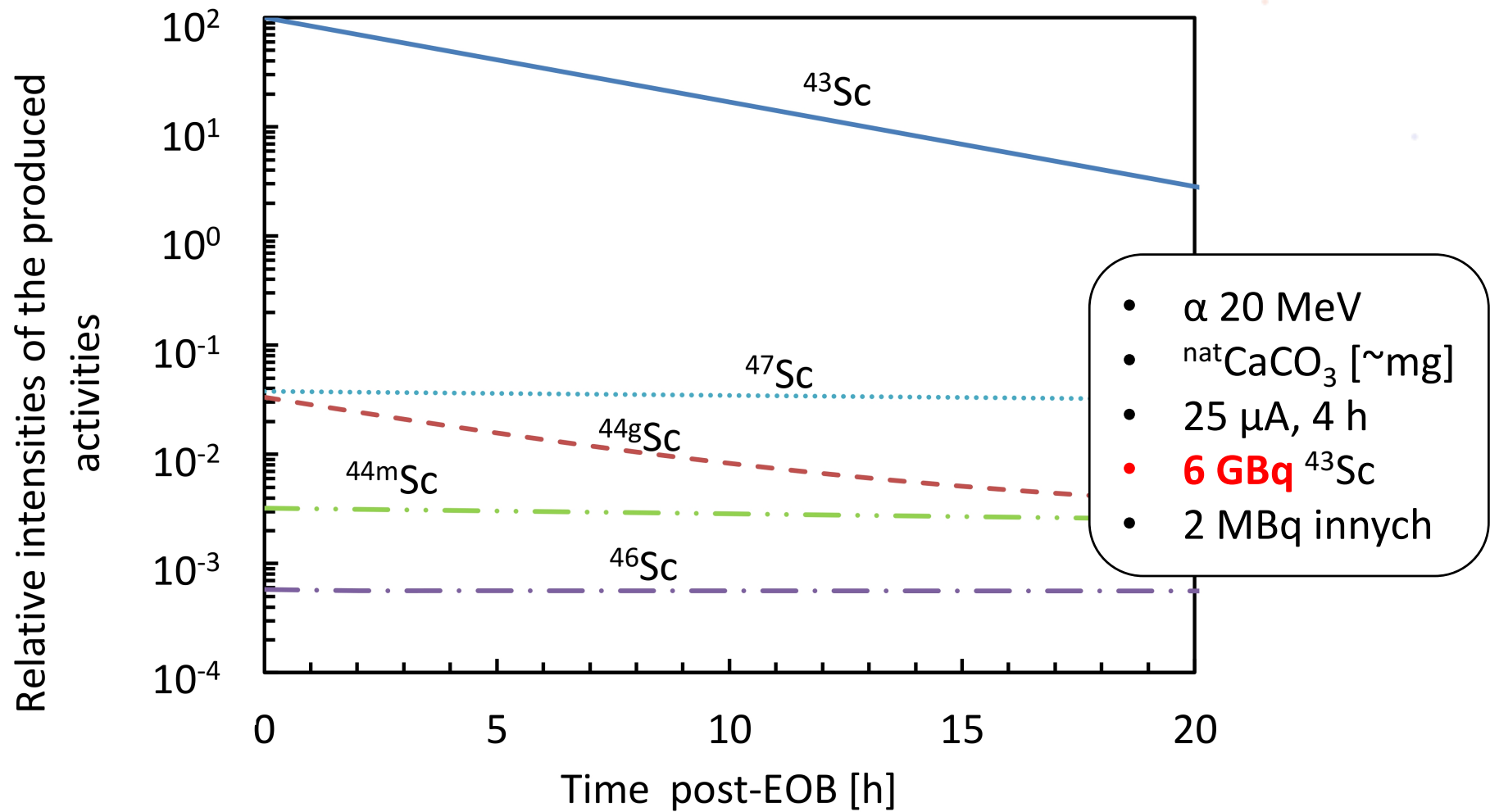
- $\frac{dN_{prod}}{dt} = -\lambda N_{prod} + \sigma \phi N_{tarczy}$
- $TTY = \frac{H N_A}{M} \frac{1}{Z e} \frac{1}{\tau} \int_{E_1}^{E_2} \frac{\sigma(E)}{dx/dE} dE$

# Produkcja $^{43}\text{Sc}$



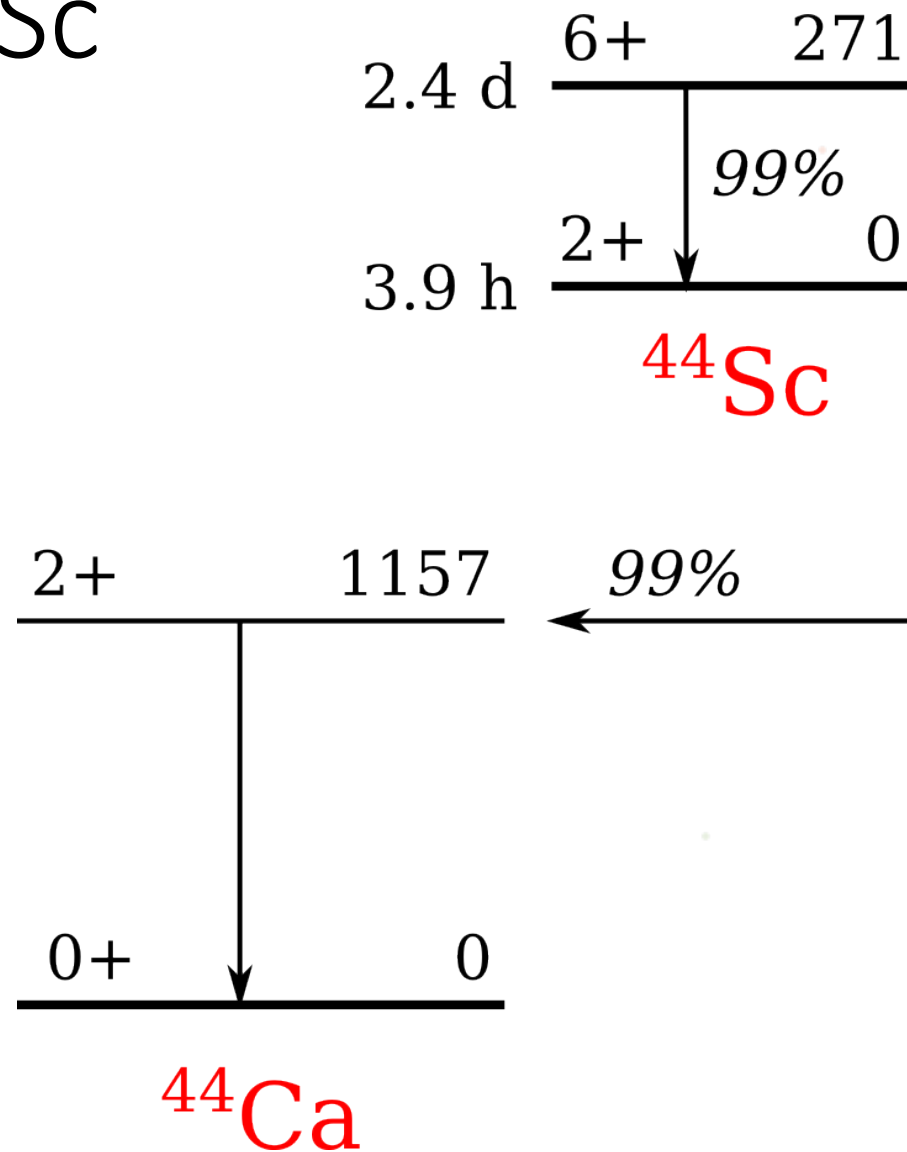


# Produkcja $^{43}\text{Sc}$

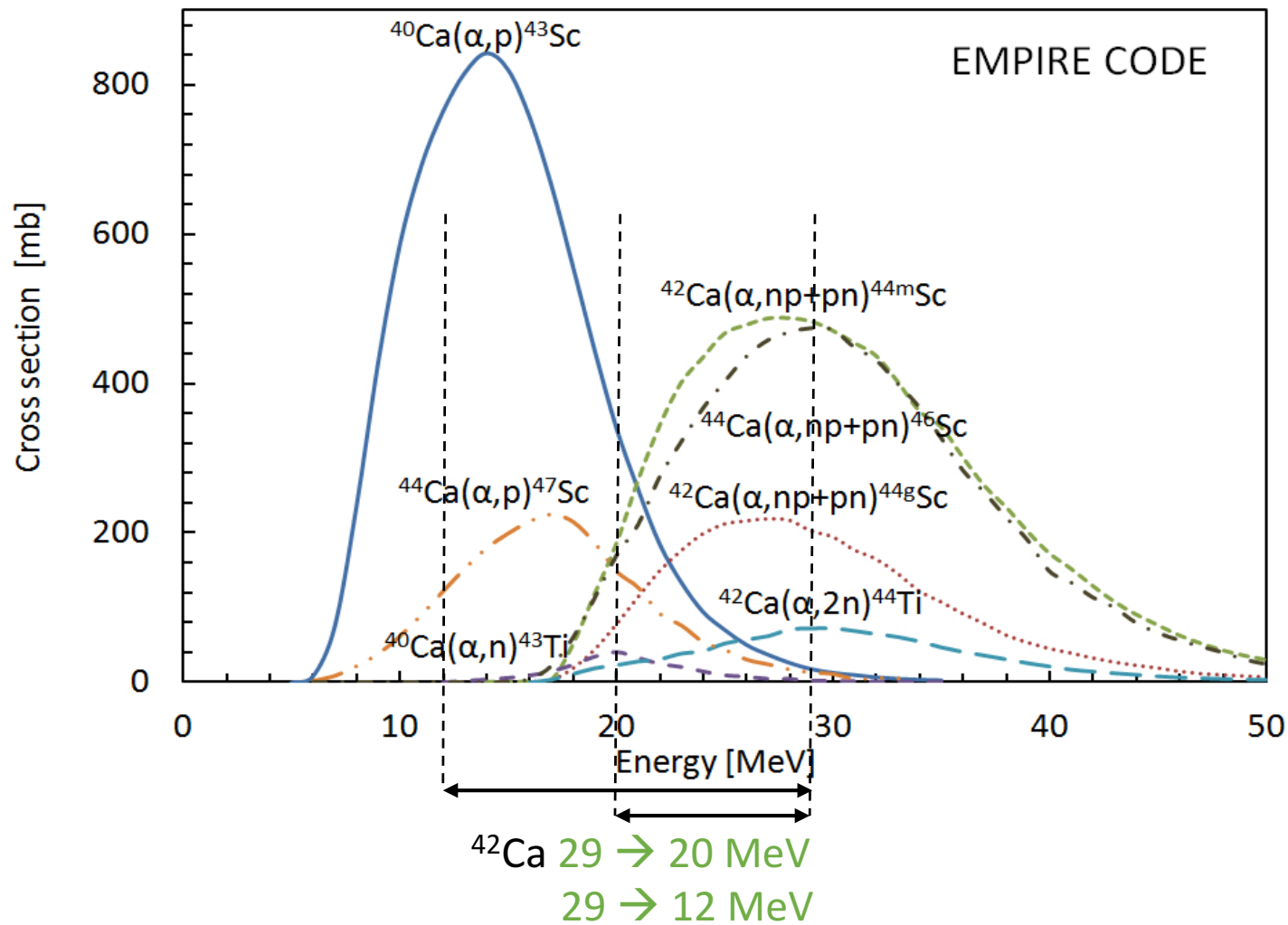


# Radioizotop $^{44}\text{Sc}$

- three photon PET  
(C. Grignon et al. 2007)
- in vivo generator



# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ wiązką $\alpha$

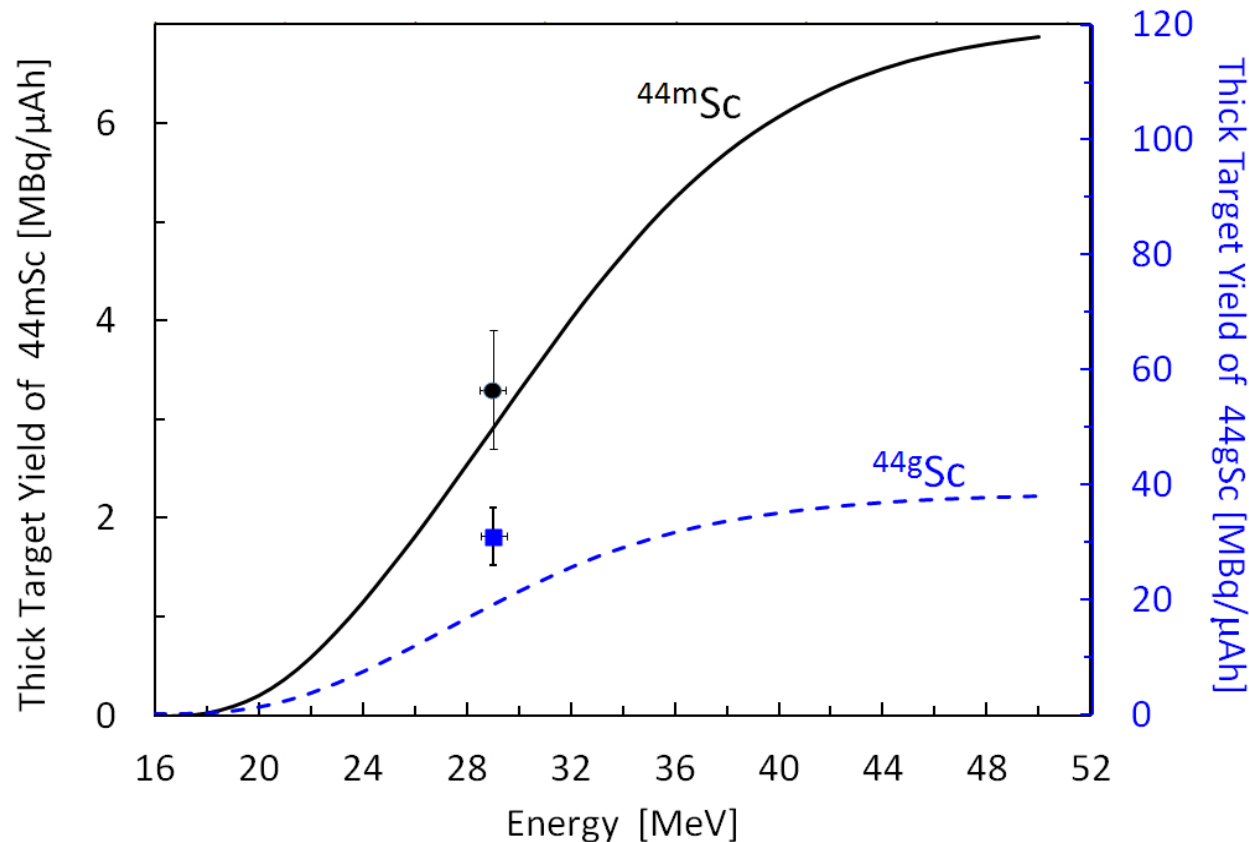


# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ wiązką $\alpha$



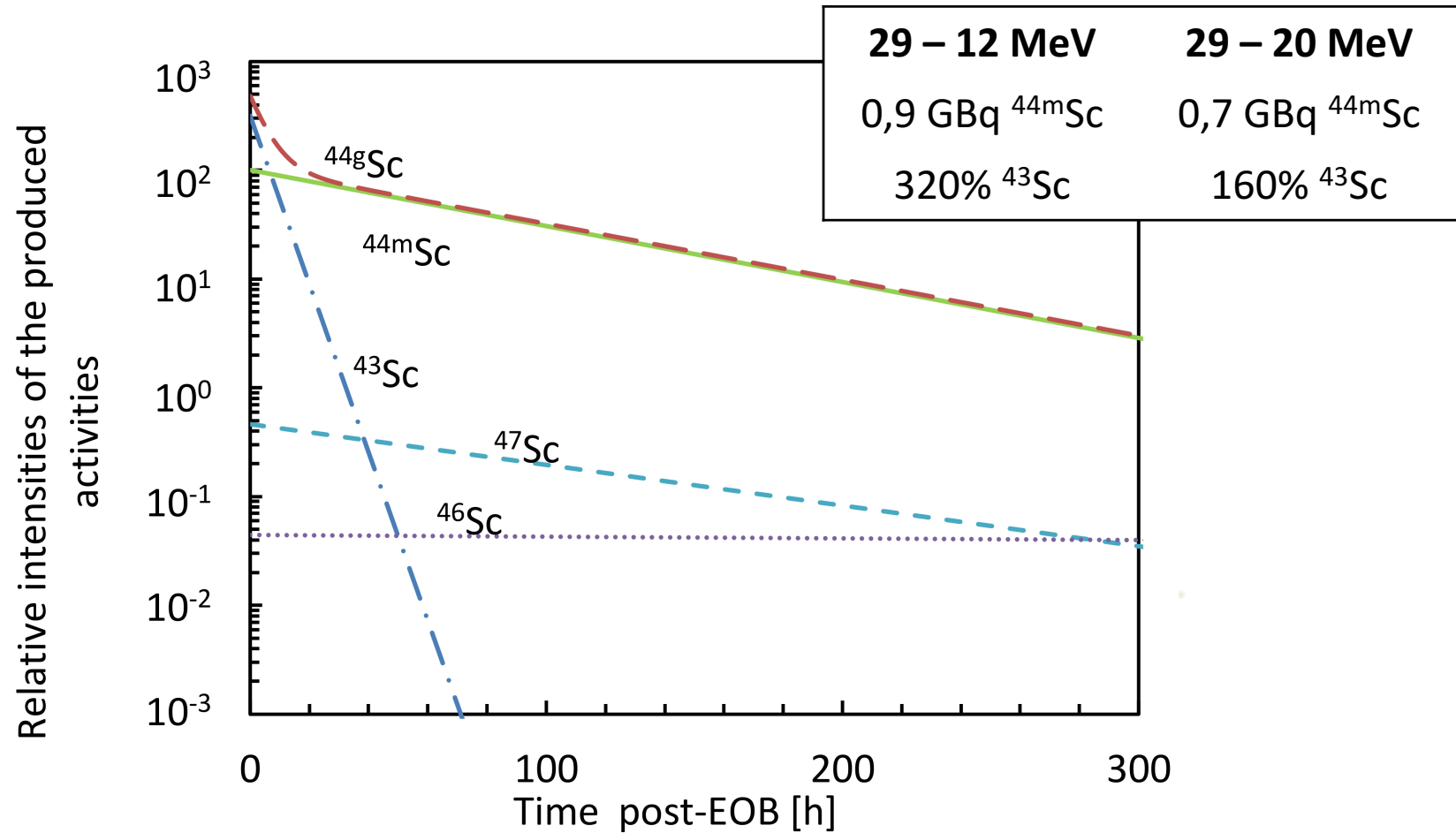
	$^{\text{nat}}\text{CaCO}_3$	oferty ISOFLEX ( $\text{CaCO}_3$ )	
$^{40}\text{Ca}$	96,9%	99,99%	1,4 \$/mg
$^{42}\text{Ca}$	0,65%	68% 95,9%	43 \$/mg 81 \$/mg
$^{44}\text{Ca}$	2,1%	99,2%	23 \$/mg
$^{48}\text{Ca}$	0,19%	69,2% 97,1%	89 \$/mg 230 \$/mg

# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ wiązką $\alpha$

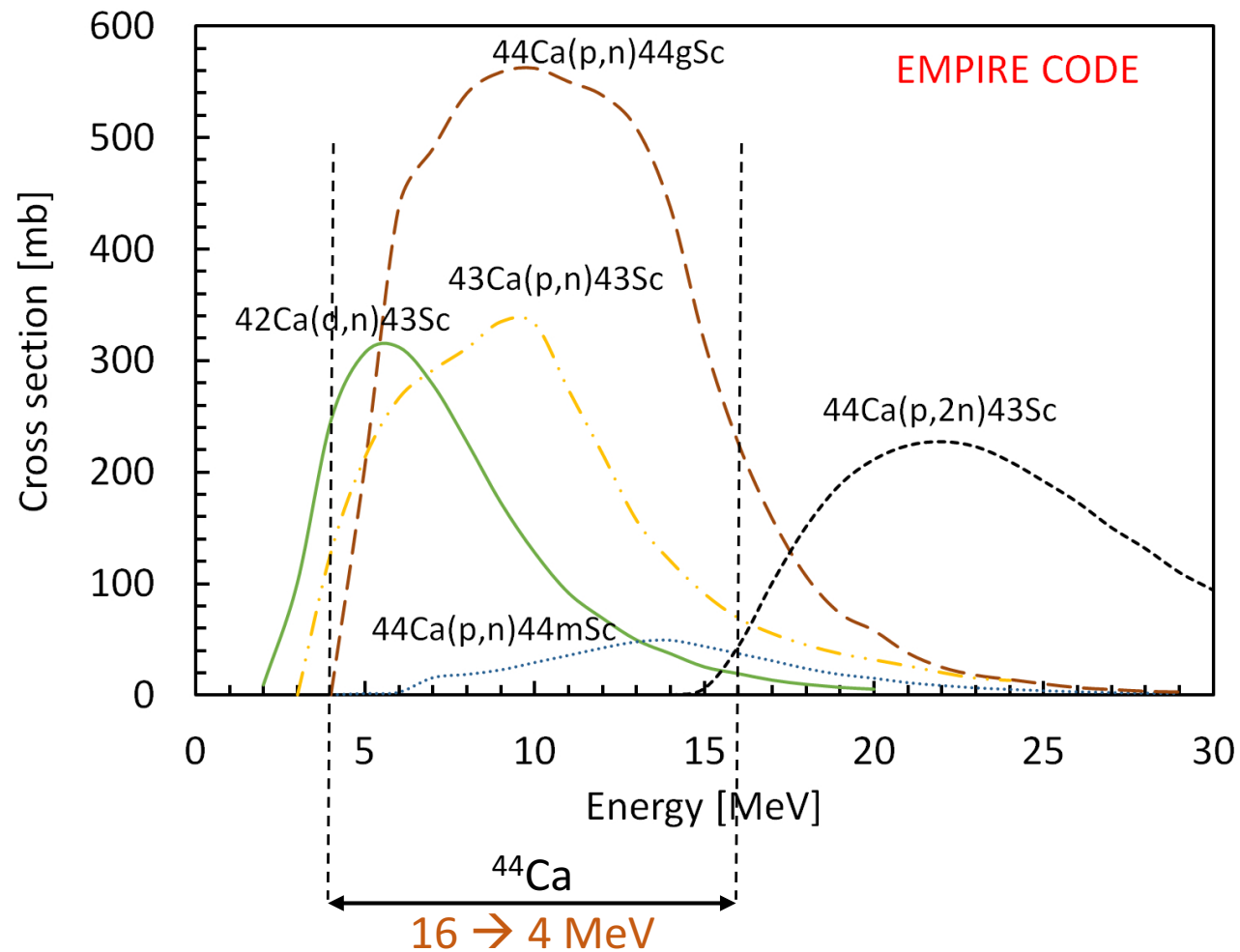


- $^{42}\text{CaCO}_3$  (68%)
- 25  $\mu\text{A}$ , **12 h**
- **0,9 GBq**  $^{44m}\text{Sc}$
- 4 GBq  $^{44}\text{Sc}$

# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ wiązką $\alpha$



# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami



# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami

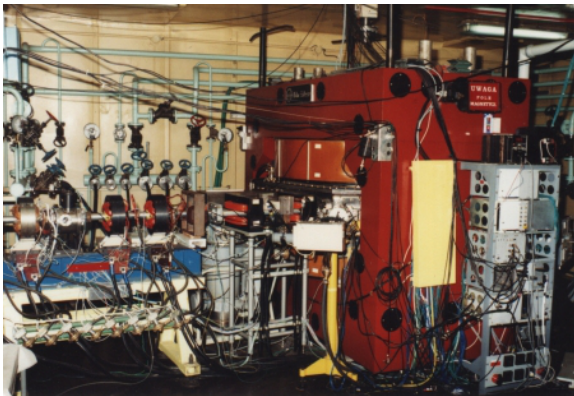


**$^{44}\text{CaCO}_3$  (94,8%  $^{44}\text{Ca}$ )**  
25%  $\text{CaCO}_3$  + 75% grafit





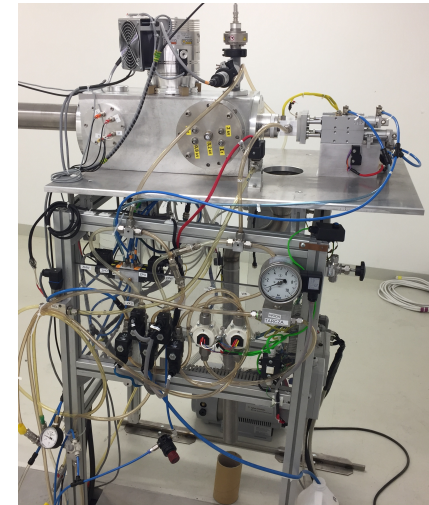
# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami



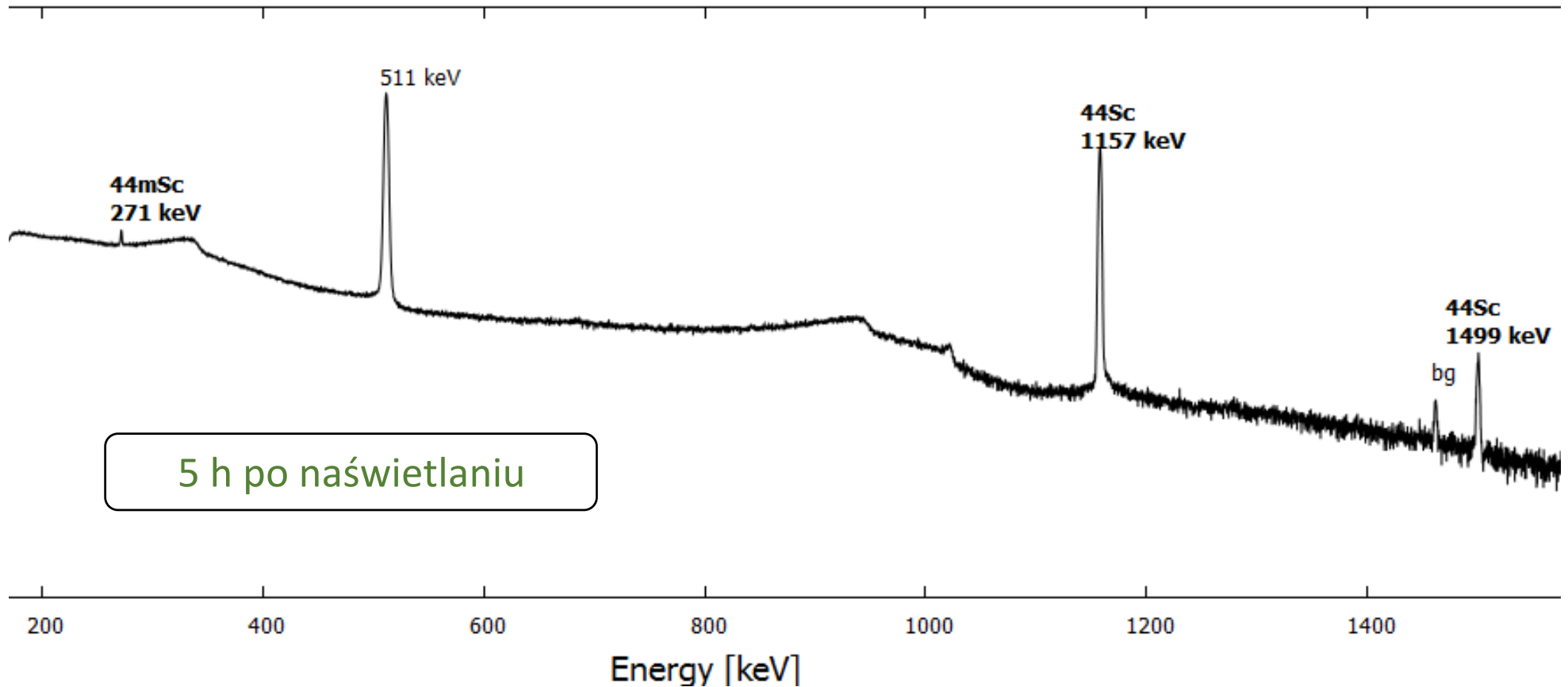
**C30** protony **28 MeV**  
wiązka zewnętrzna  $\sim 10$  nA  
Narodowe Centrum Badań Jądrowych



**PETtrace** protony **16,5 MeV**  
wiązka zewnętrzna  $25 \mu\text{A}$   
Środowiskowe Laboratorium Ciężkich Jonów

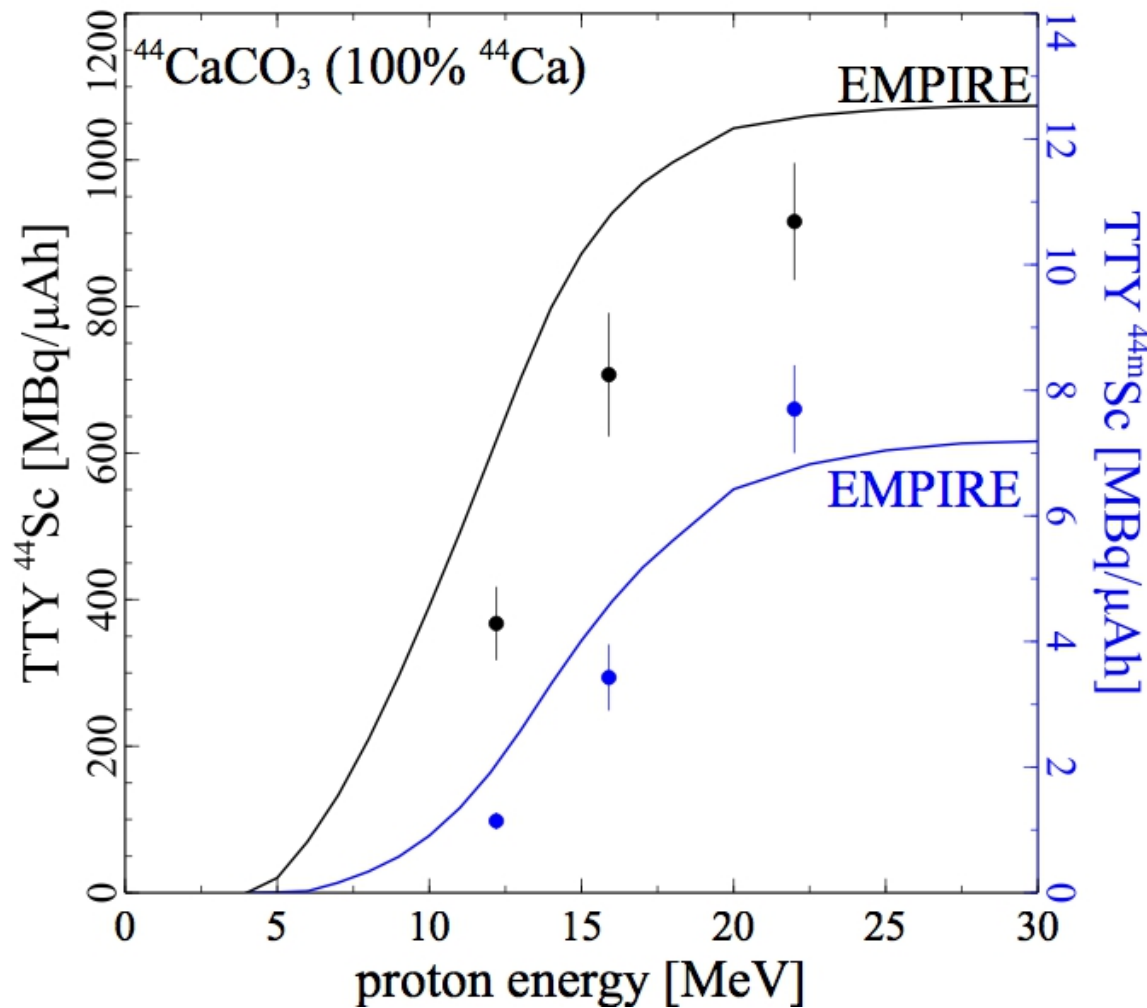


# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami



Widmo  $^{44}\text{CaCO}_3$  (94,8%) naświetlanego protonami o energii 16 MeV

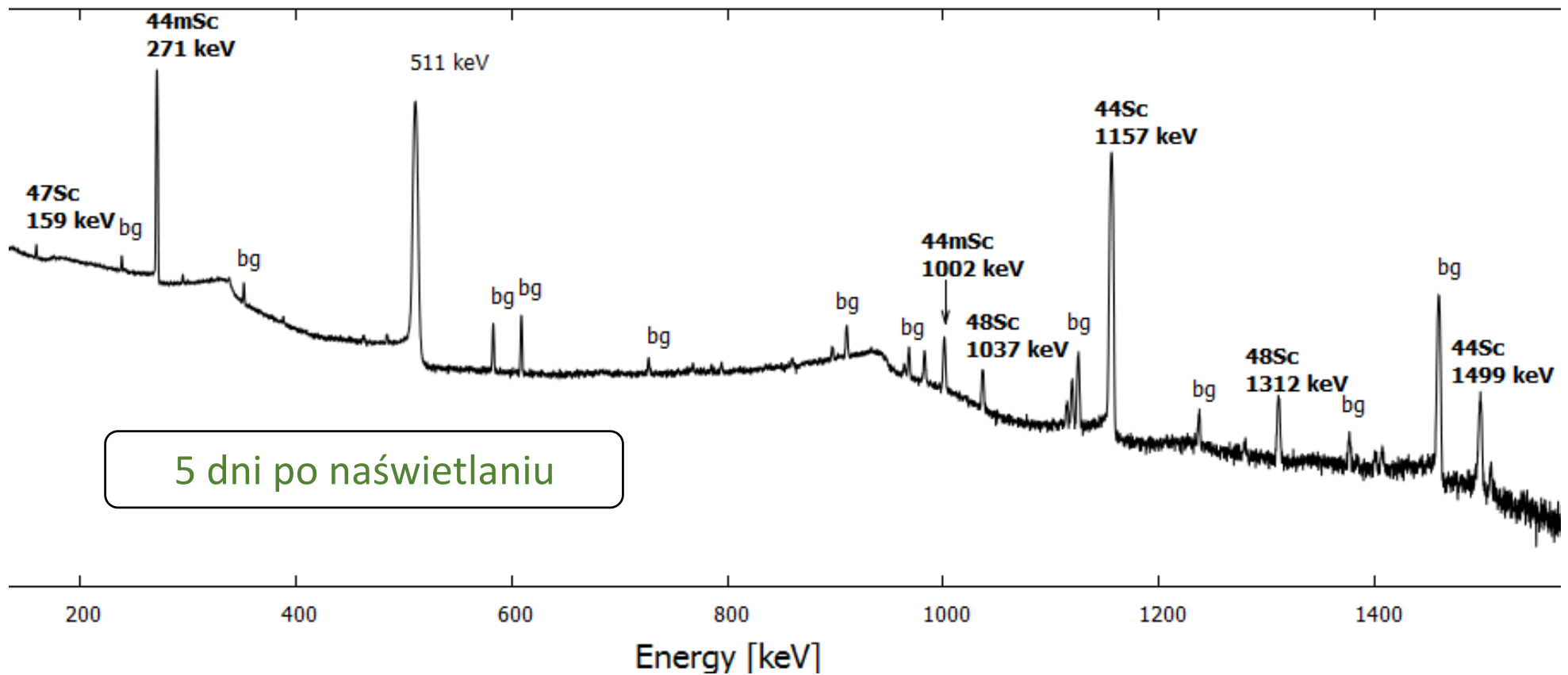
# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami



- 16 MeV
- $^{44}\text{CaCO}_3$  (94,8%)
- 25  $\mu\text{A}$ , 12 h
- **0,9 GBq  $^{44m}\text{Sc}$**

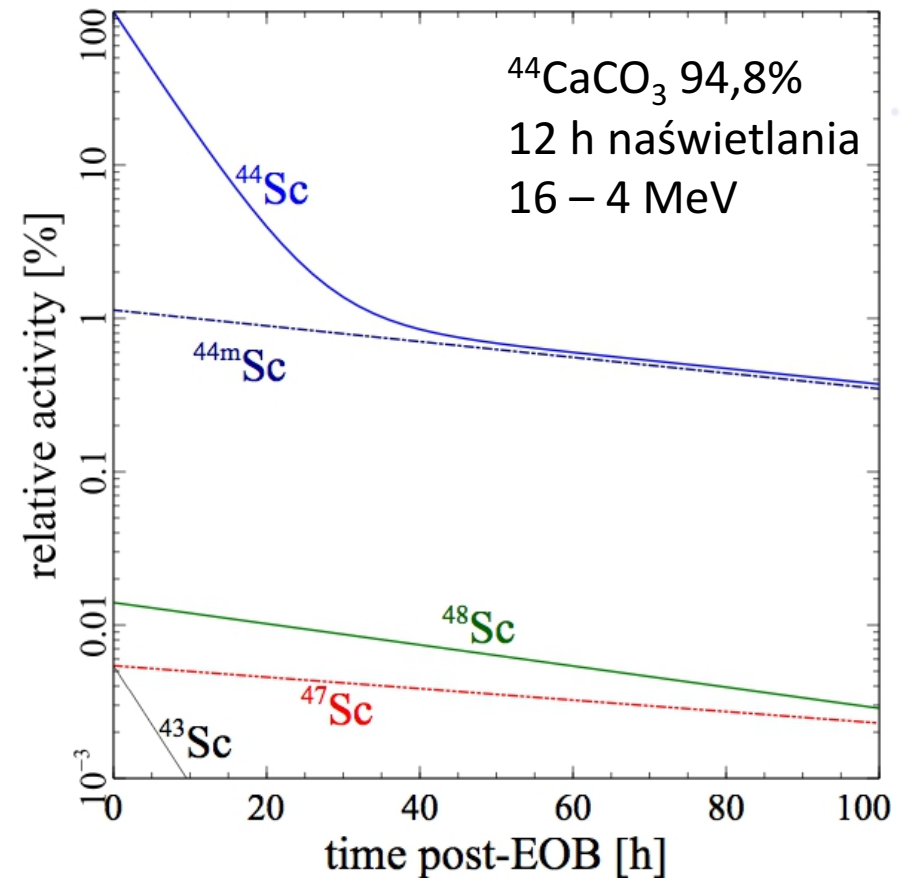
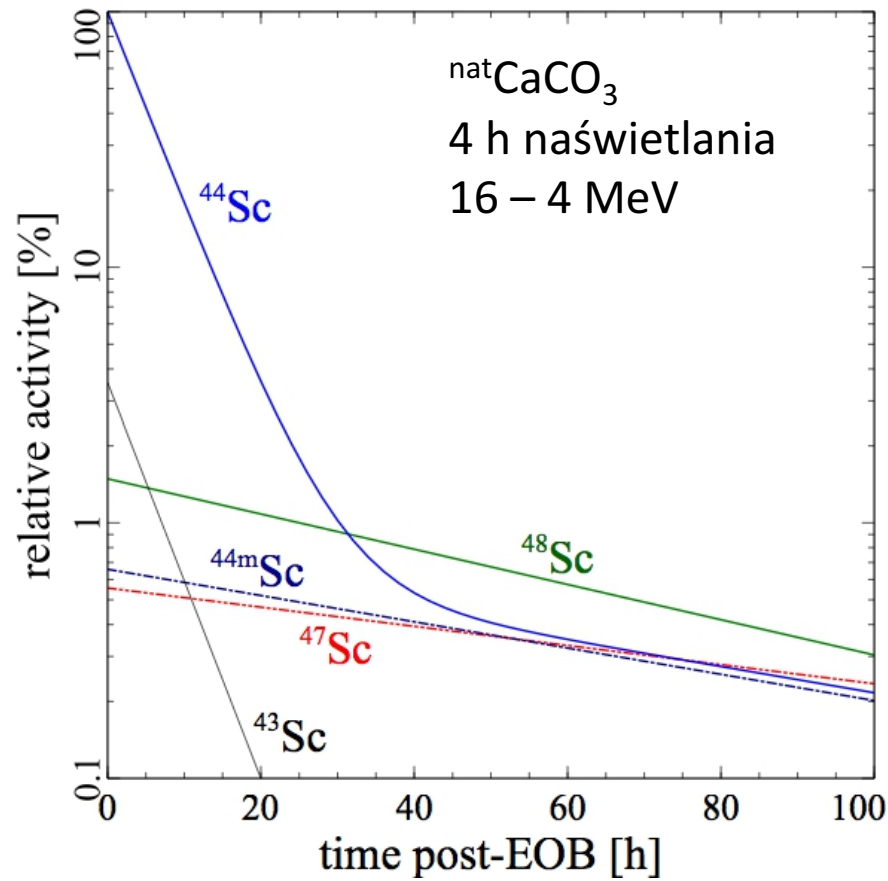
- 16 MeV
- nat $^{44}\text{CaCO}_3$
- 25  $\mu\text{A}$ , 2 h
- **1,1 GBq  $^{44}\text{Sc}$**

# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami

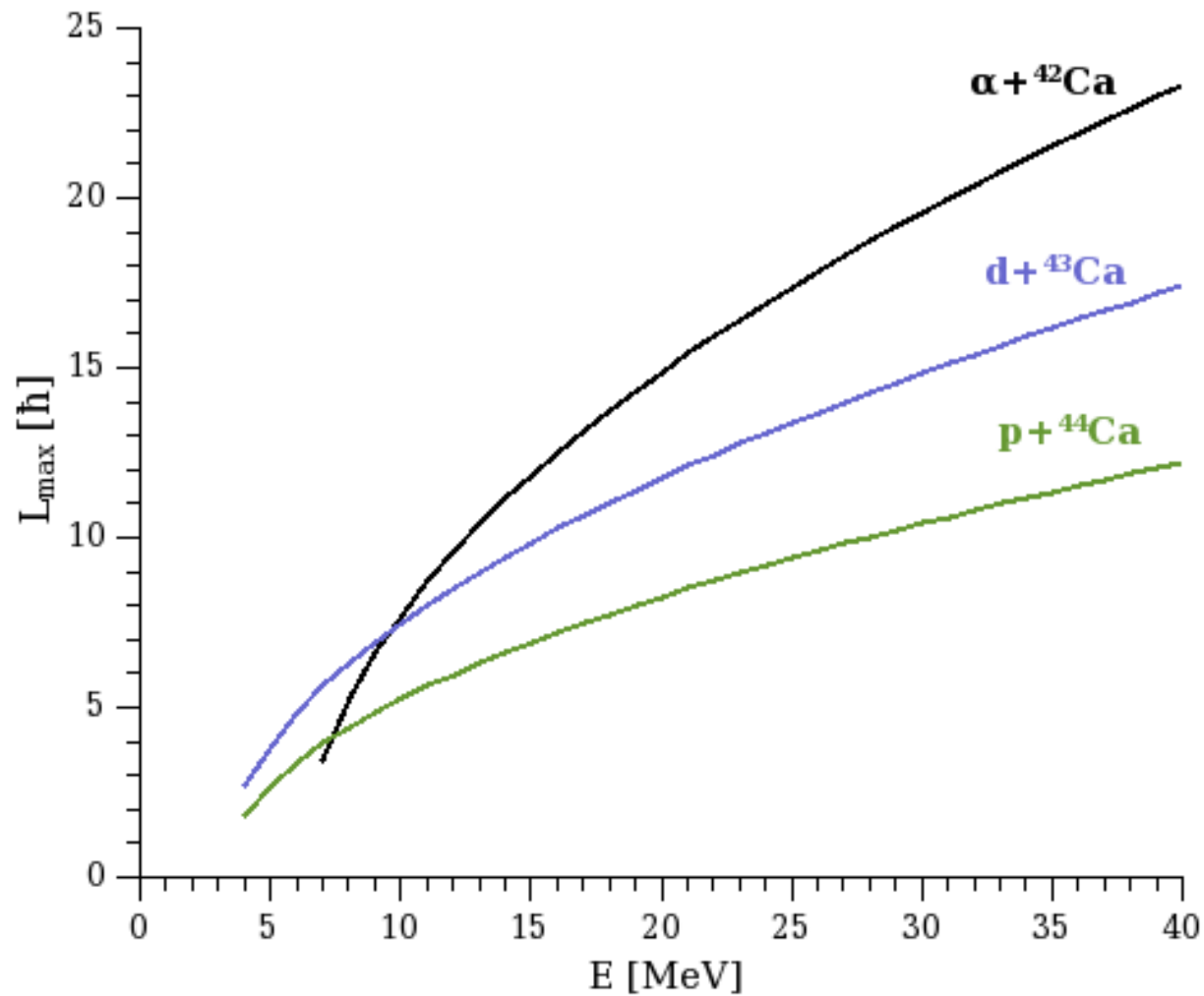


Widmo  $^{44}\text{CaCO}_3$  (94,8%) naświetlanego protonami o energii 16 MeV

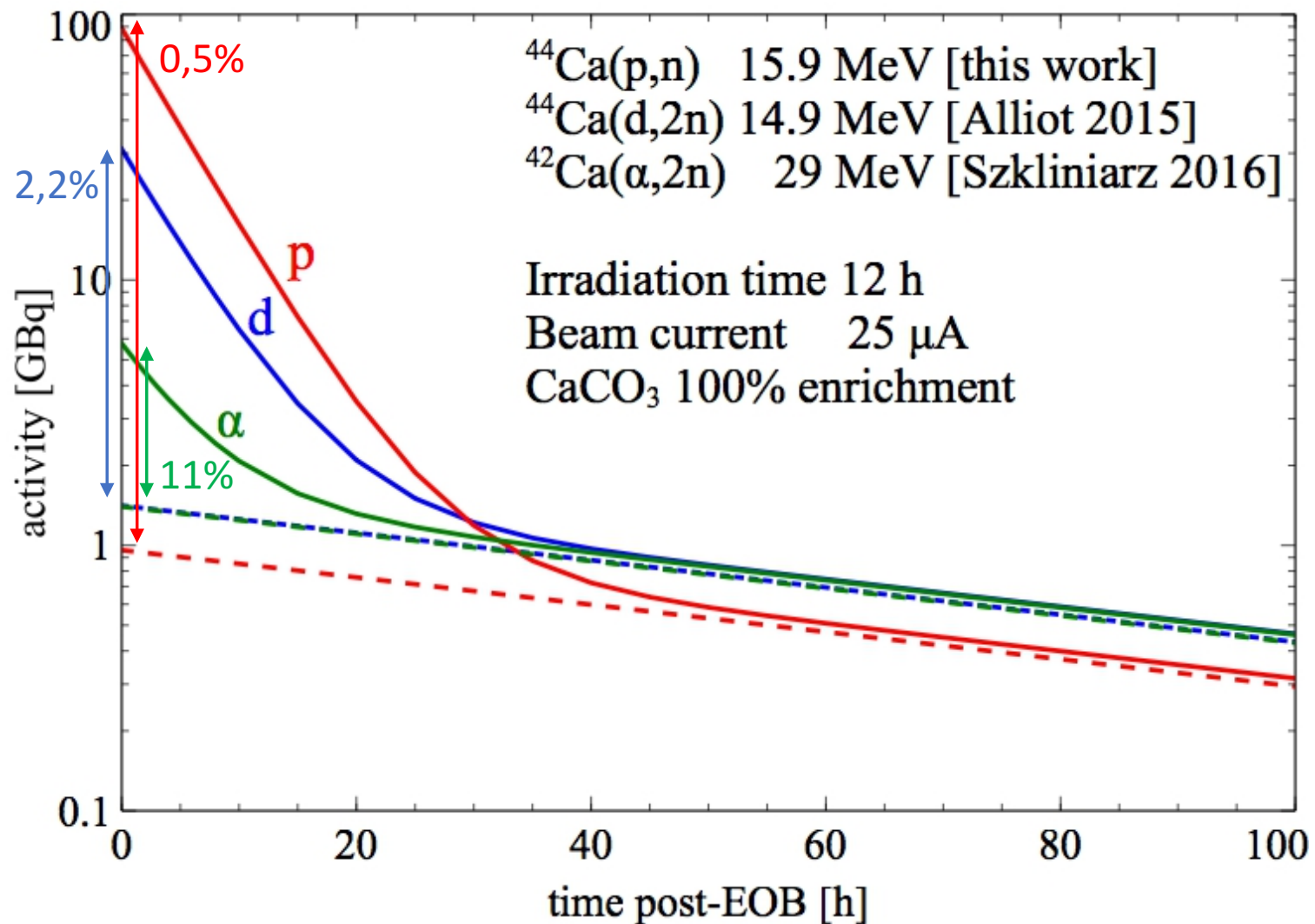
# Produkcja $^{44m}\text{Sc}/^{44}\text{Sc}$ protonami



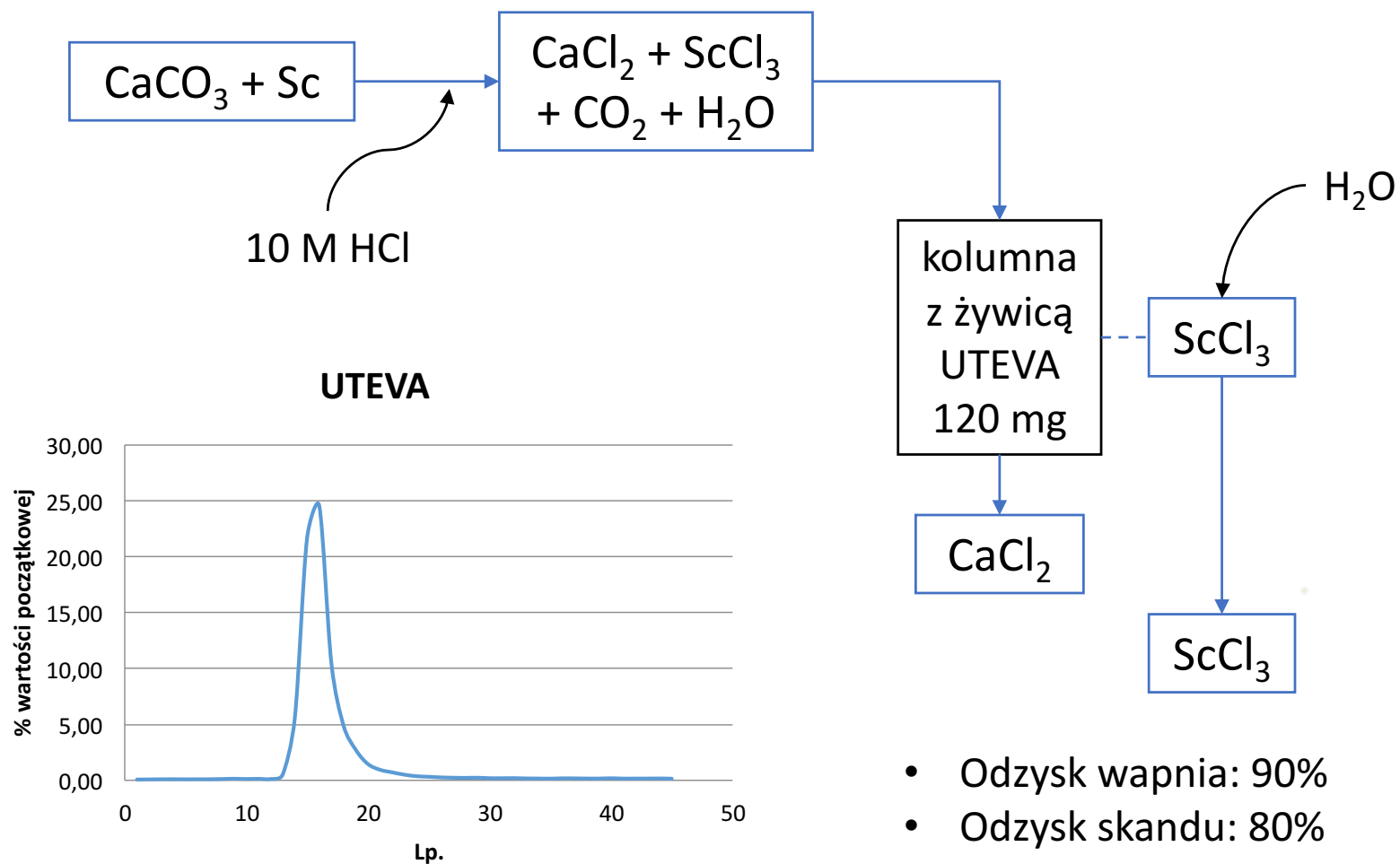
# Różne drogi produkcji $^{44m}\text{Sc}/^{44}\text{Sc}$



# Różne drogi produkcji $^{44m}\text{Sc}/^{44}\text{Sc}$



# Proces rozdzielania Sc/Ca



dzięki uprzejmości Rafała Walczaka i Aleksandra Bilewicza z IChTJ



# Odzysk wapnia



Usunięcie nadmiaru HCl  
przez odparowanie z  
 $\text{HNO}_3$



Wytrącenie  $\text{CaCO}_3$  w  
wodzie i 1 M  $(\text{NH}_4)_2\text{CO}_3$



Odfiltrowanie osadu



Suszenie

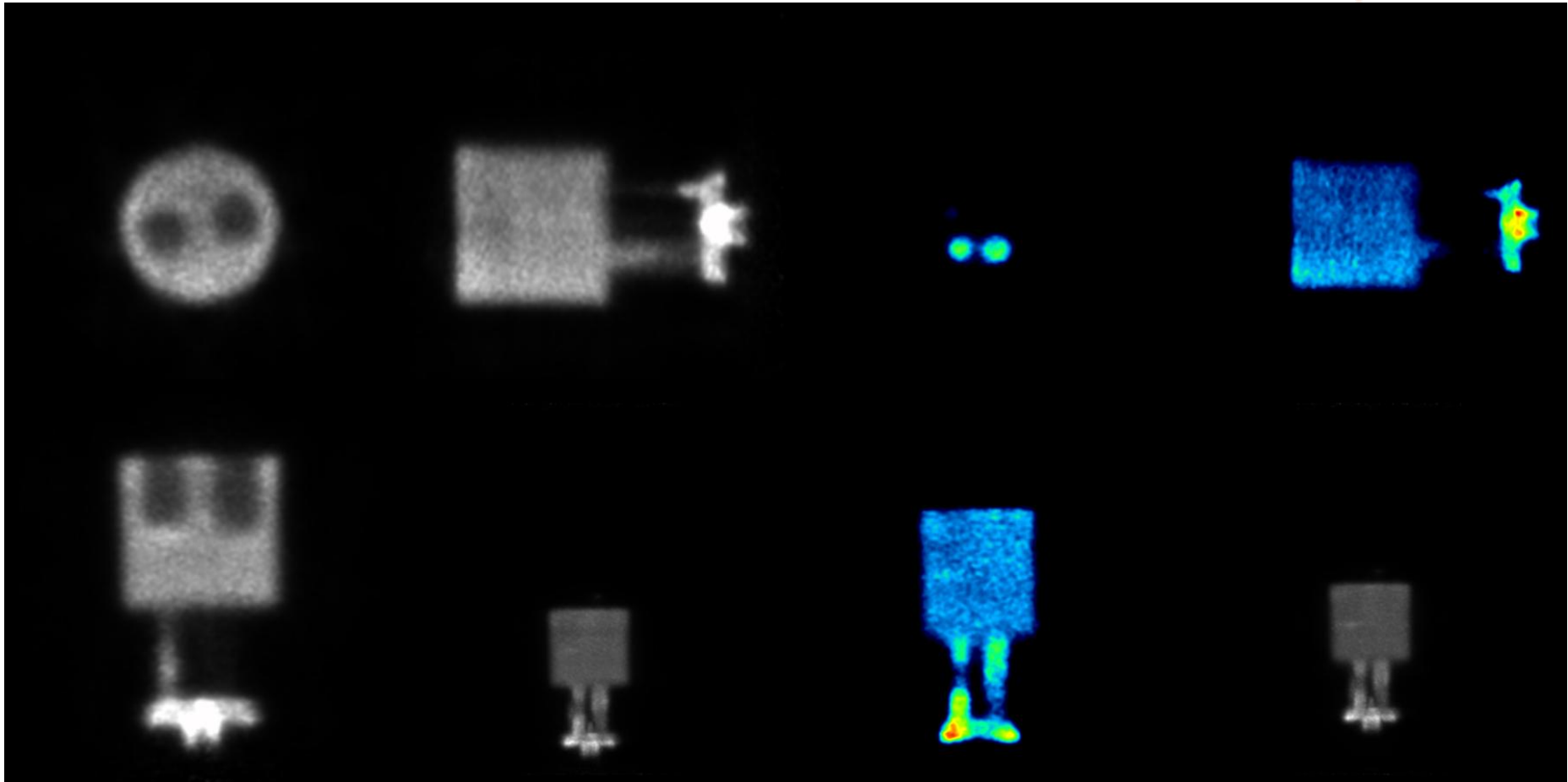
dzięki uprzejmości Rafała Walczaka i Aleksandra Bilewicza z IChTJ

09.03.2017

seminarium fizyki jądra atomowego

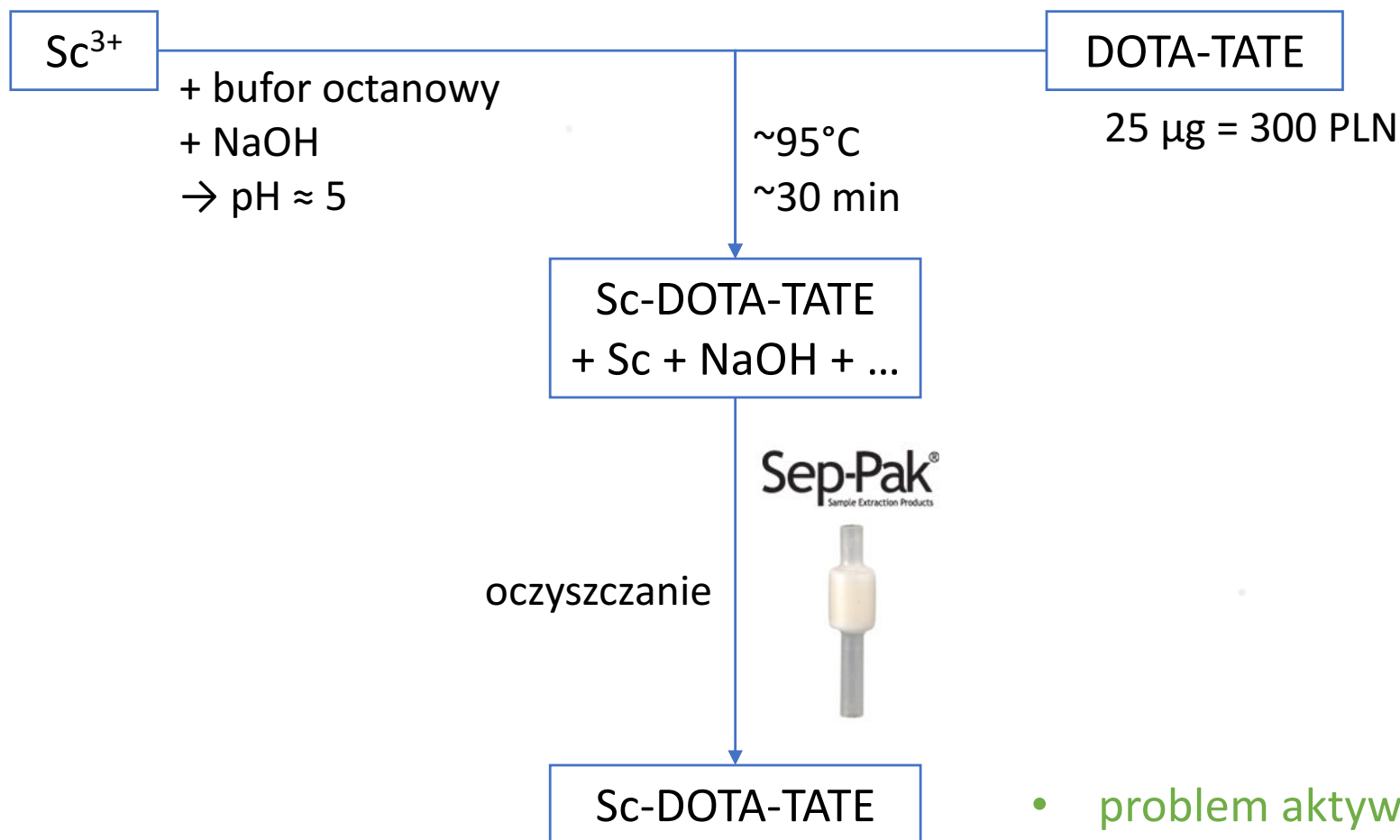
33

# PET/CT



dzięki uprzejmości Łukasza Chedy, Krzysztofa Kiliana i Zbigniewa Rogulskiego z CNBCh UW

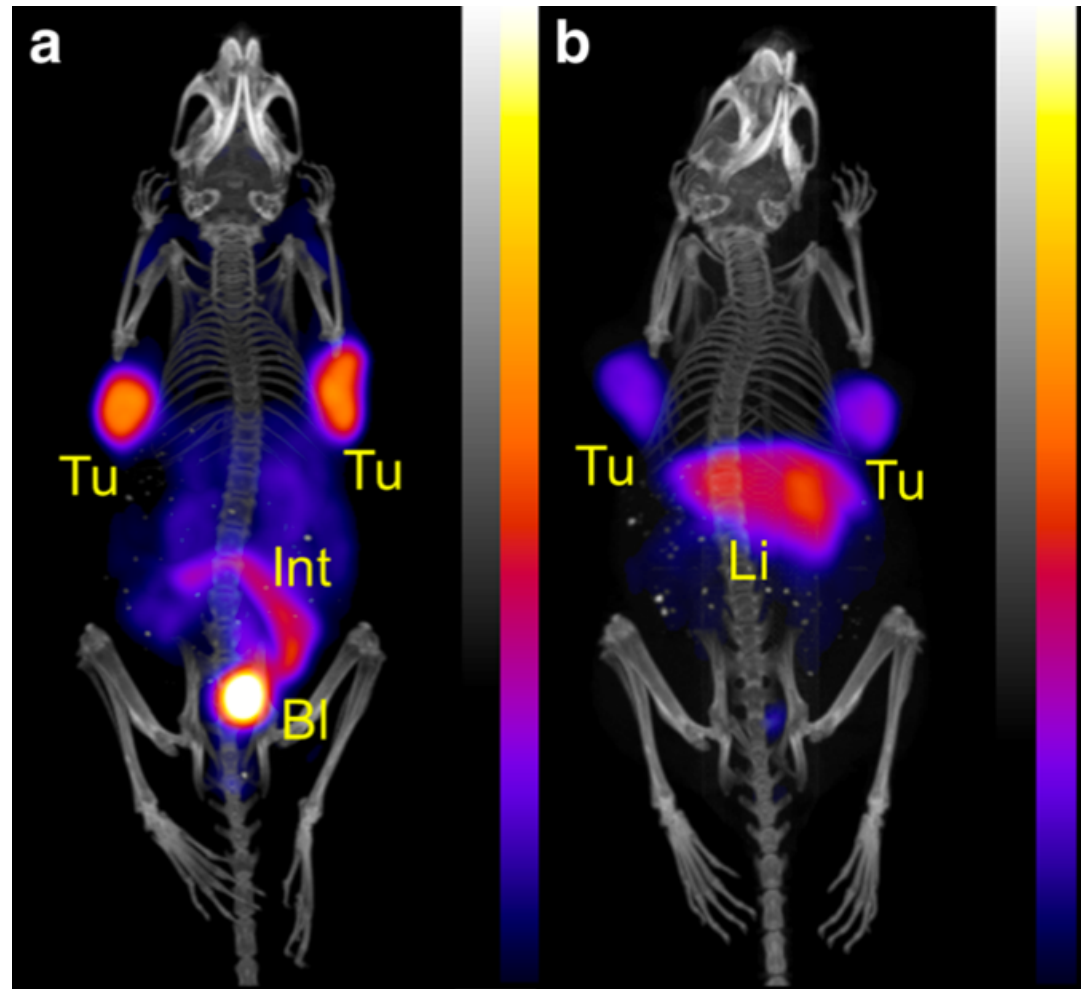
# Proces znakowania Sc-DOTATATE



- problem aktywności właściwej

# PET/CT

3 h po wstrzyknięciu  
10 MBq / 1 nmol  
PET = 20 min  
CT = 1,5 min

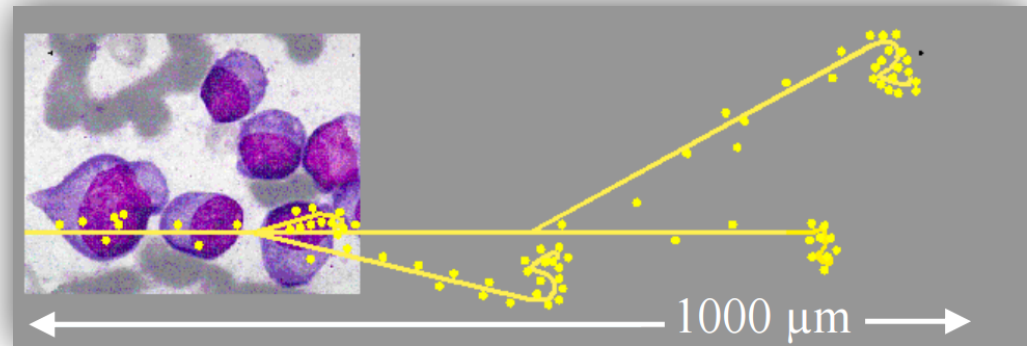
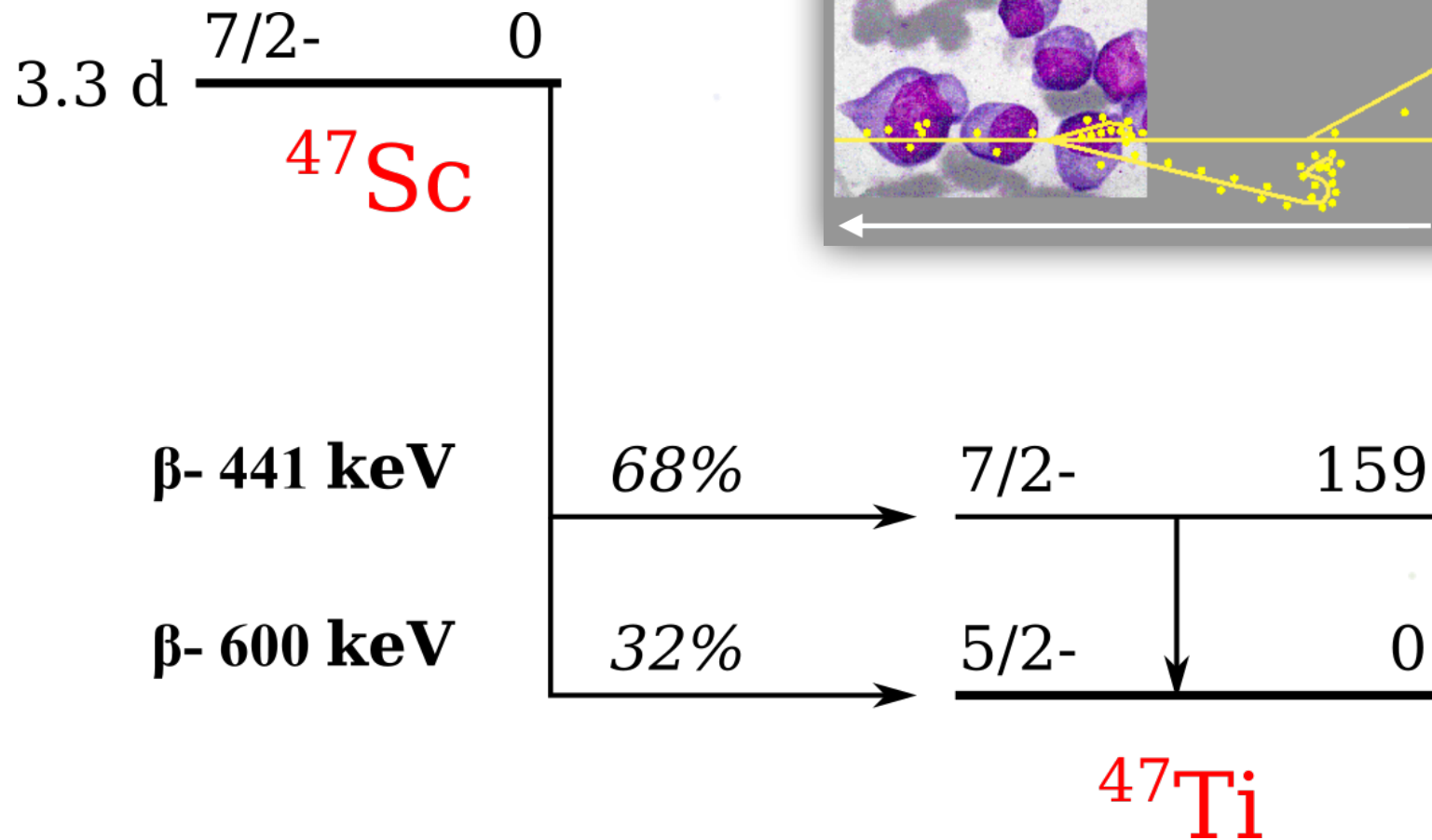


$^{44}\text{Sc}$ -DOTA-RGD

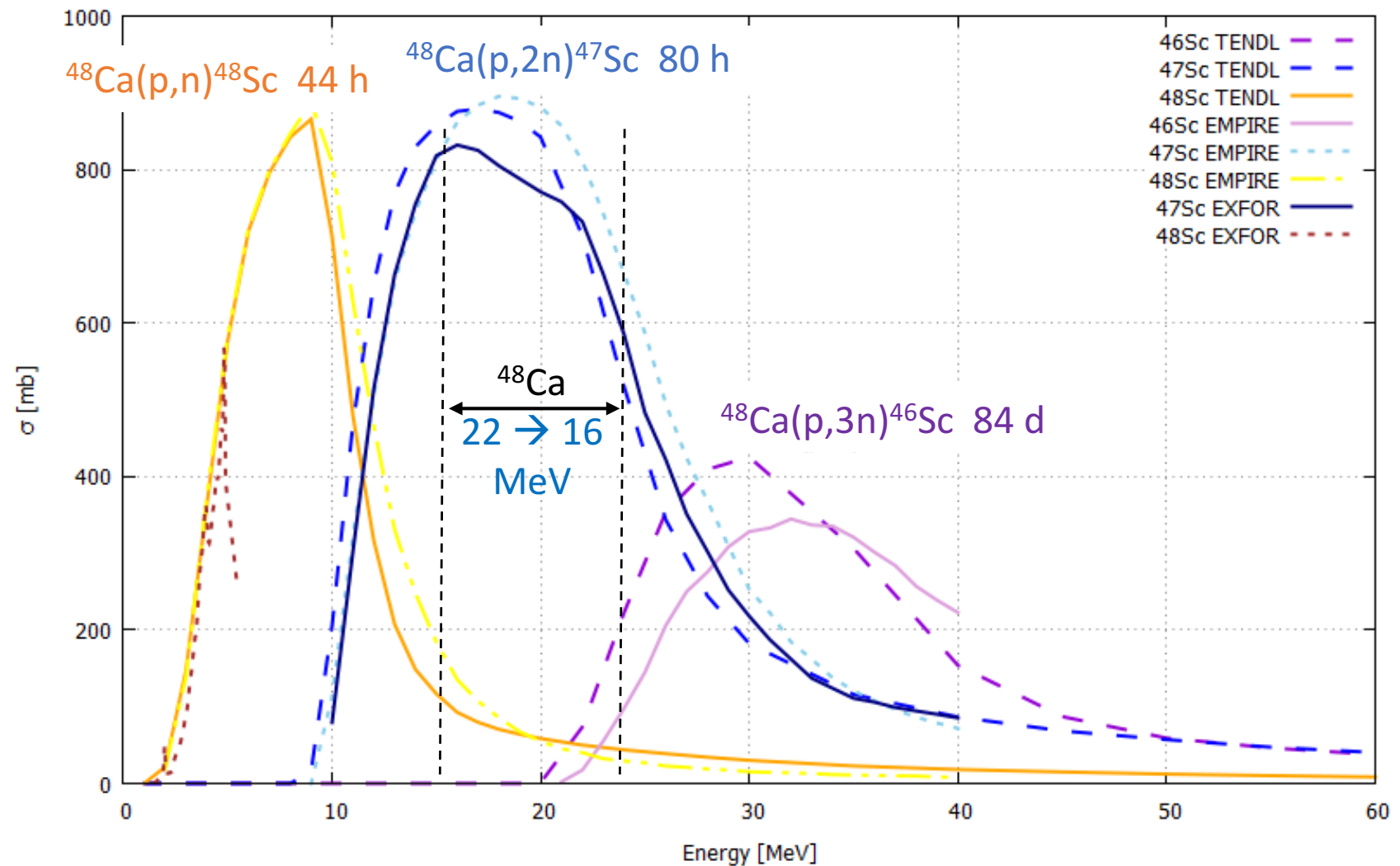
$^{68}\text{Ga}$ -DOTA-RGD

Domnanich et al. EJNMMI Radiopharmacy and Chemistry (2016) 1:8

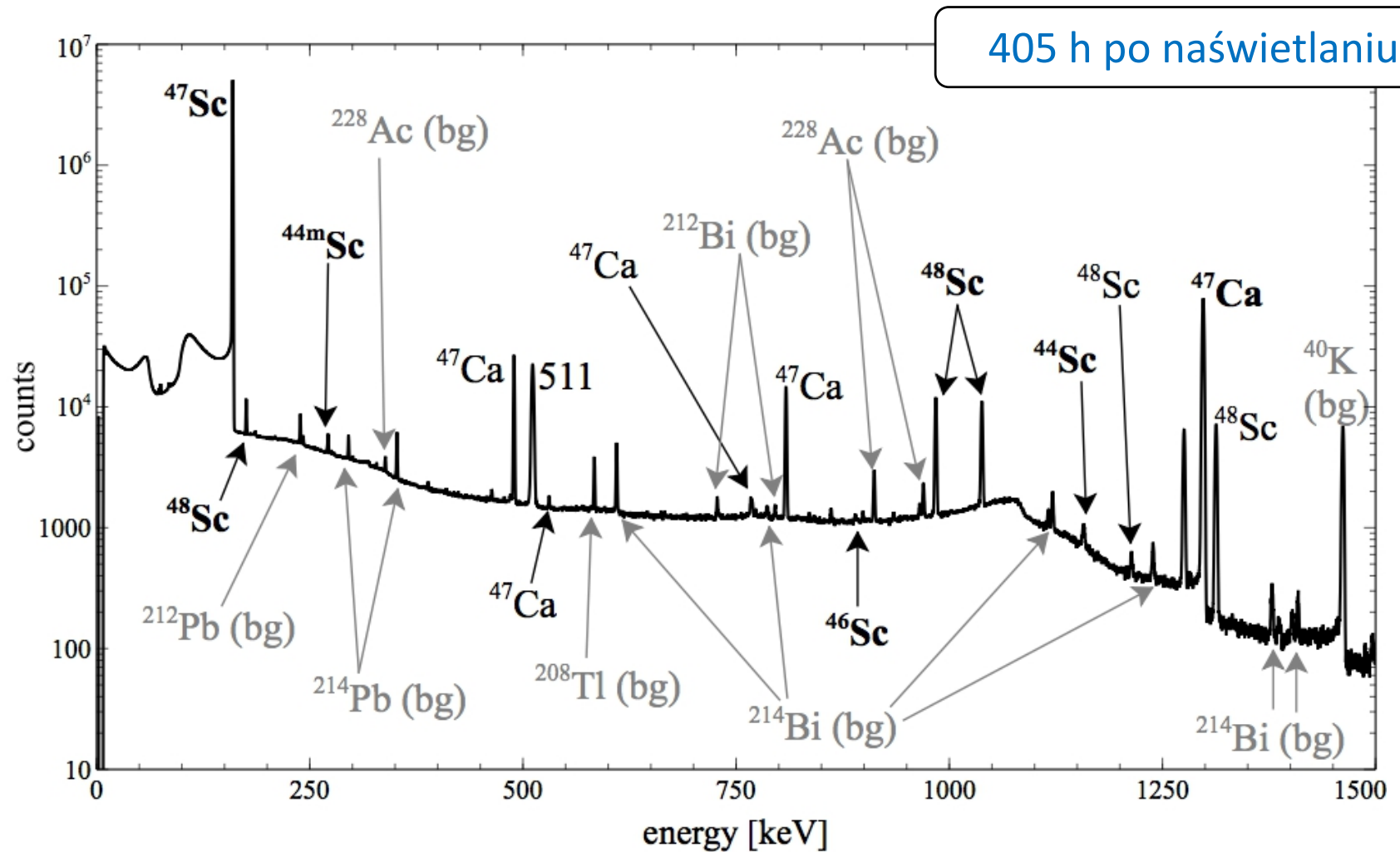
# Radioizotop $^{47}\text{Sc}$



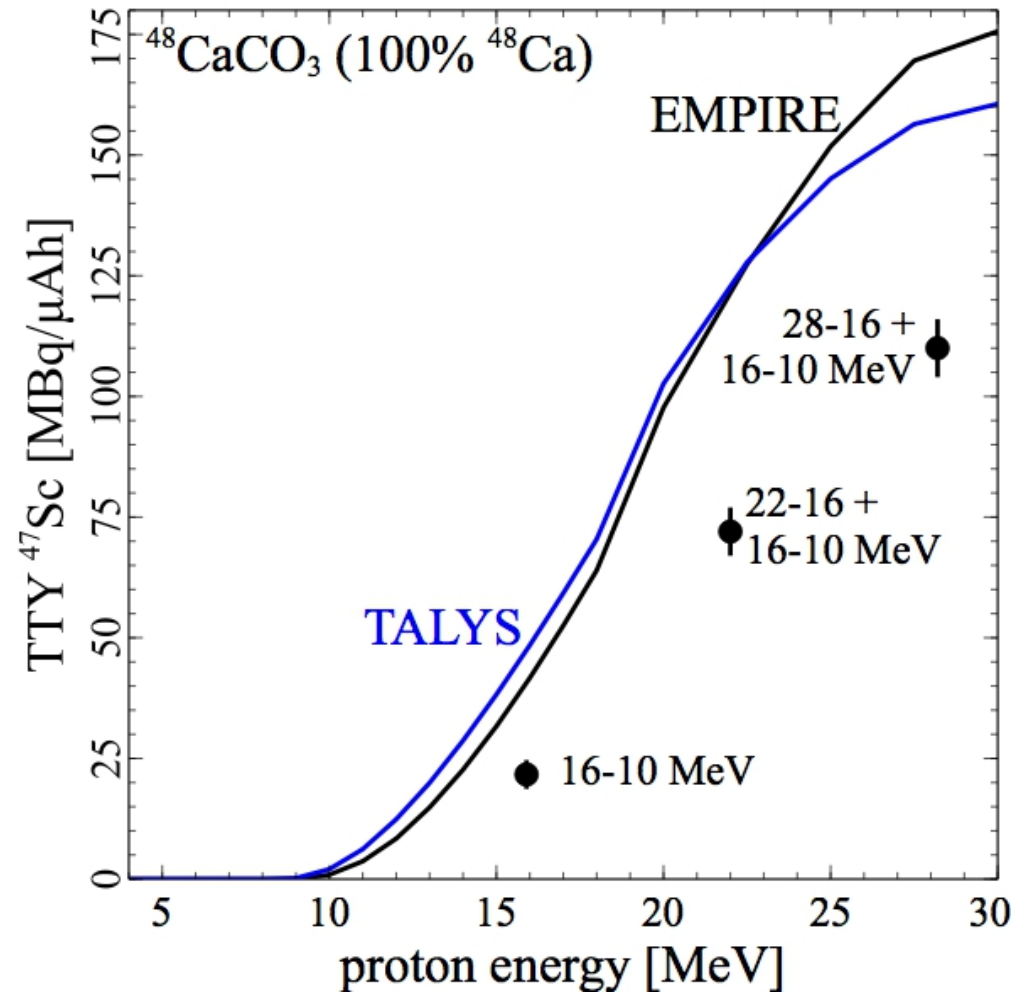
# Produkcja $^{47}\text{Sc}$



# Produkcja $^{47}\text{Sc}$



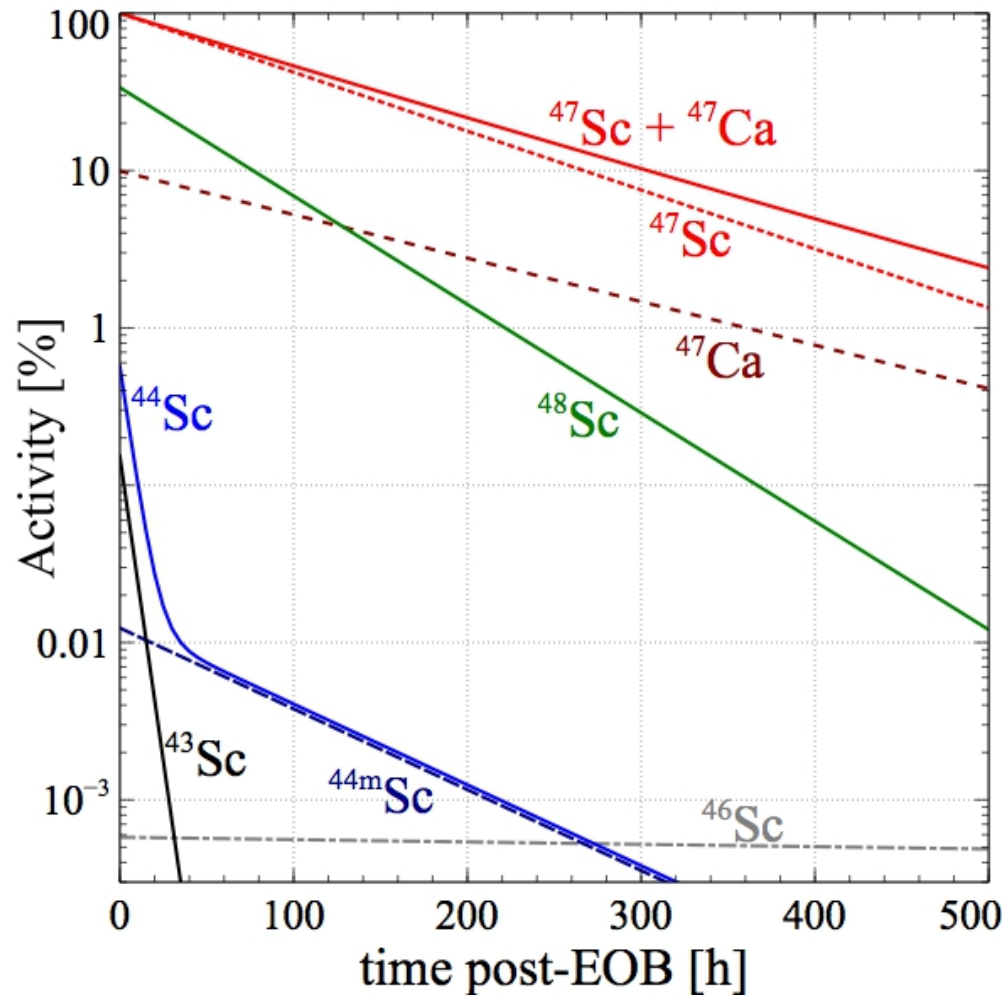
# Produkcja $^{47}\text{Sc}$



- 22 – 16 MeV
- $^{48}\text{CaCO}_3$  (97,1%)
- 25  $\mu\text{A}$ , 10 h
- **7,3 GBq  $^{47}\text{Sc}$**



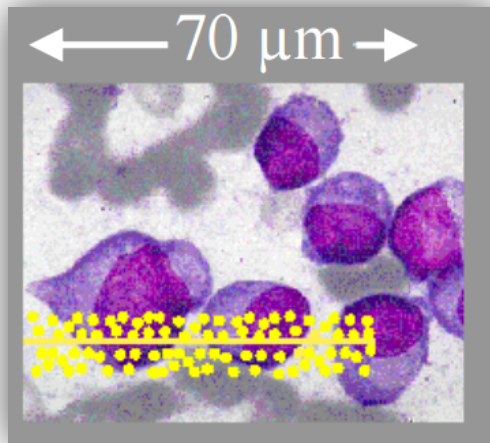
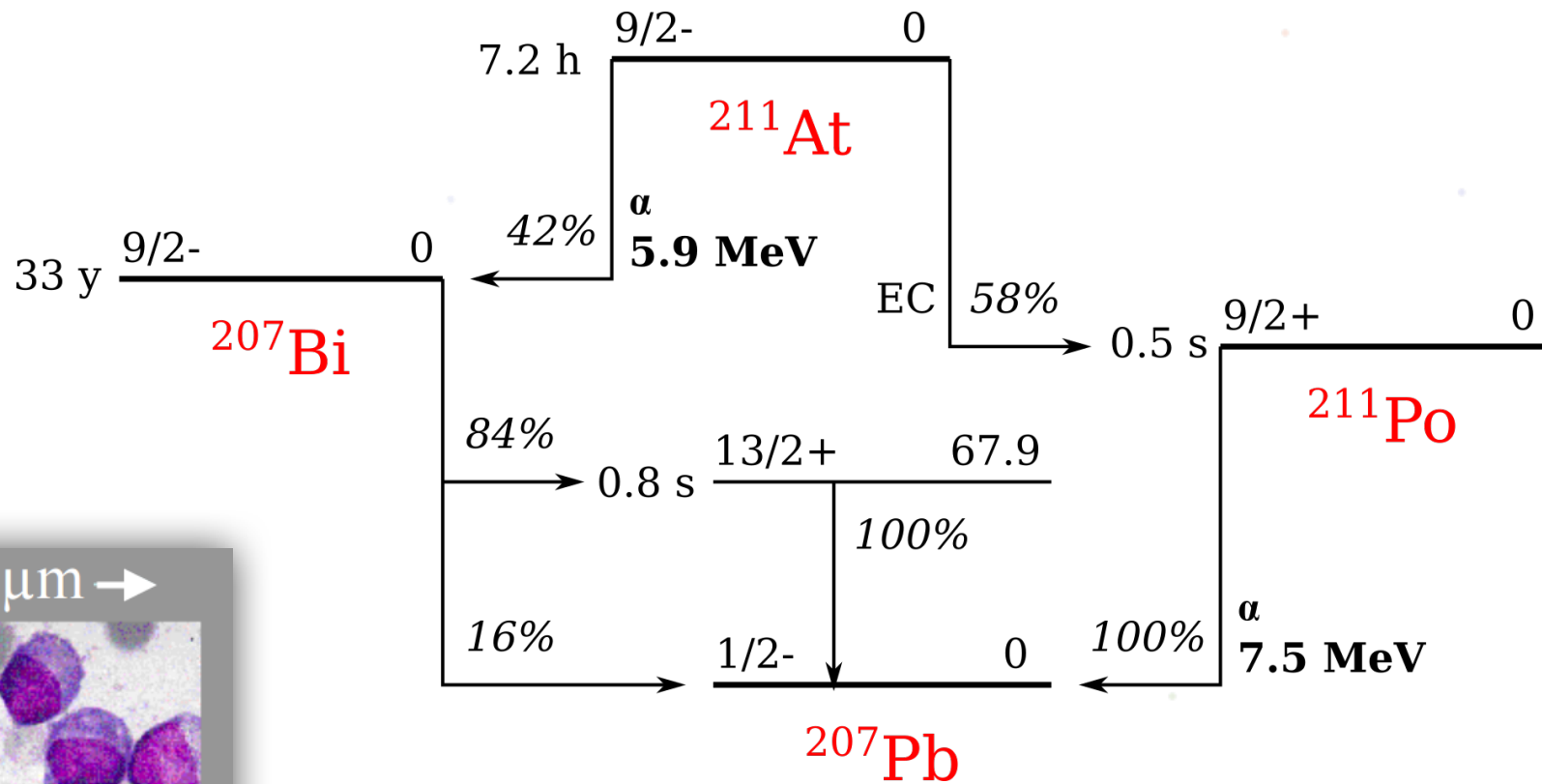
# Produkcja $^{47}\text{Sc}$



- 22 – 16 MeV
- $^{48}\text{CaCO}_3$  (97,1%)
- 25  $\mu\text{A}$ , 10 h
- **7,3 GBq  $^{47}\text{Sc}$**

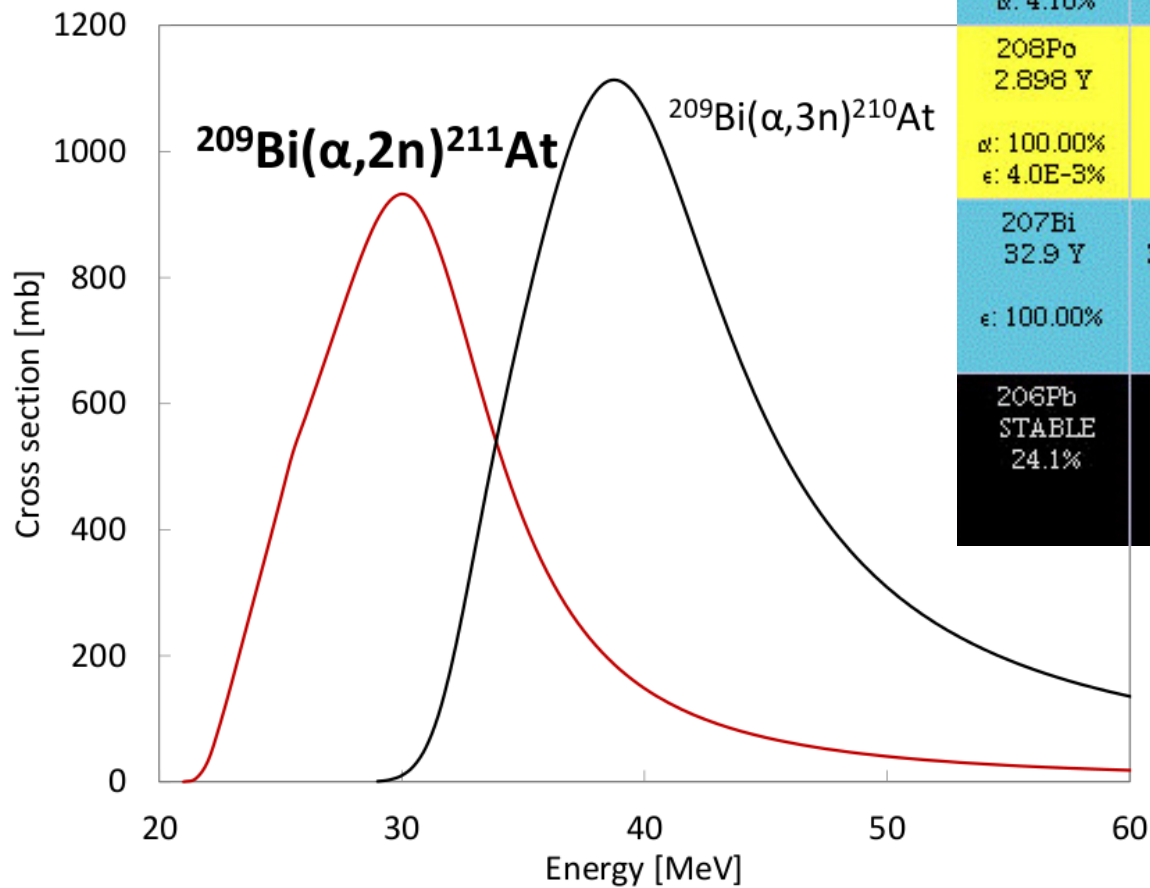
	po 420 h
$^{47}\text{Sc}$	0,5 GBq
$^{48}\text{Sc}$	1%
$^{46}\text{Sc}$	0,012%
$^{47}\text{Ca}$	16%

# Radioizotop $^{211}\text{At}$



- 100 keV/ $\mu\text{m}$
- DSB

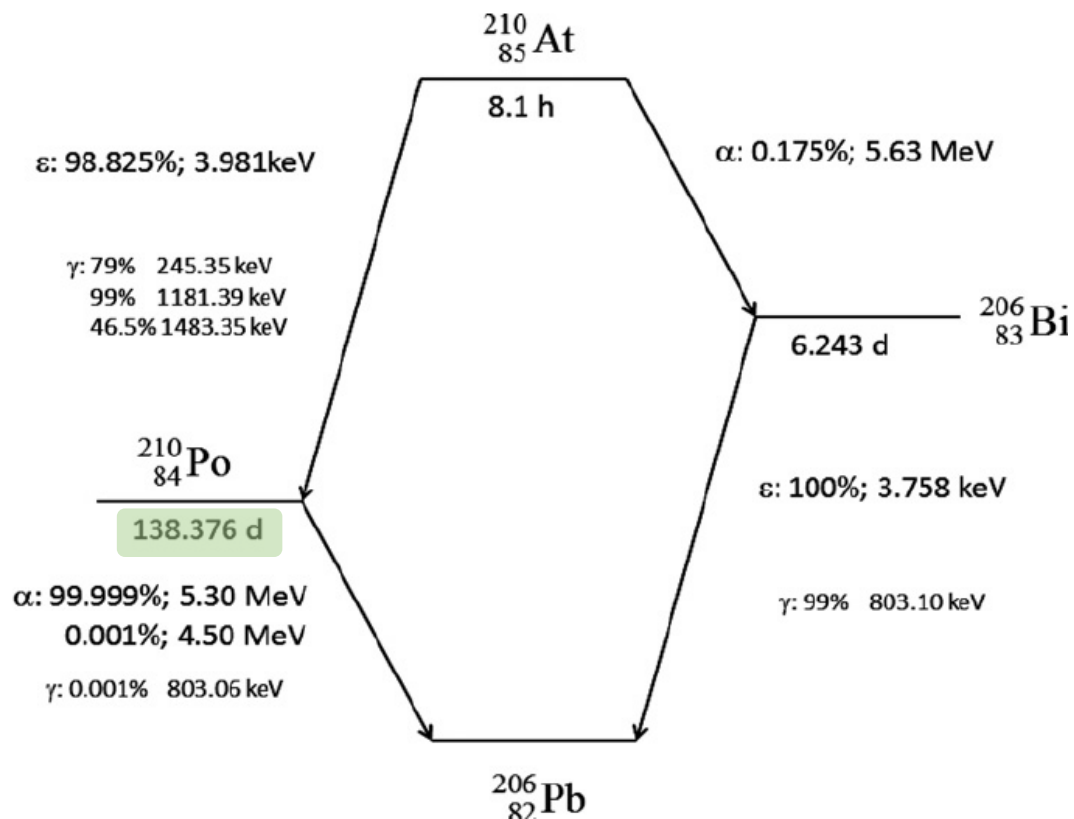
# Produkcja $^{211}\text{At}$



$^{210}\text{Rn}$ 2.4 H	$^{211}\text{Rn}$ 14.6 H	$^{212}\text{Rn}$ 23.9 M	$^{213}\text{Rn}$ 19.5 MS	$^{214}\text{Rn}$ 0.27 $\mu\text{s}$
$\alpha$ : 96.00% $\epsilon$ : 4.00%	$\epsilon$ : 72.60% $\alpha$ : 27.40%	$\alpha$ : 100.00%	$\alpha$ : 100.00%	$\alpha$ : 100.00%
$^{209}\text{At}$ 5.41 H	$^{210}\text{At}$ 8.1 H	$^{211}\text{At}$ 7.214 H	$^{212}\text{At}$ 0.314 S	$^{213}\text{At}$ 125 NS
$\epsilon$ : 95.90% $\alpha$ : 4.10%	$\epsilon$ : 99.82% $\alpha$ : 0.18%	$\epsilon$ : 58.20% $\alpha$ : 41.80%	$\alpha$ : 100.00% $\epsilon$ : < 0.03%	$\alpha$ : 100.00%
$^{208}\text{Po}$ 2.898 Y	$^{209}\text{Po}$ 102 Y	$^{210}\text{Po}$ 138.376 D	$^{211}\text{Po}$ 0.516 S	$^{212}\text{Po}$ 0.299 $\mu\text{s}$
$\alpha$ : 100.00% $\epsilon$ : 4.0E-3%	$\alpha$ : 99.52% $\epsilon$ : 0.48%	$\alpha$ : 100.00%	$\alpha$ : 100.00%	$\alpha$ : 100.00%
$^{207}\text{Bi}$ 32.9 Y	$^{208}\text{Bi}$ 3.68E+5 Y	$^{209}\text{Bi}$ STABLE 100%	$^{210}\text{Bi}$ 5.012 D	$^{211}\text{Bi}$ 2.14 M
$\epsilon$ : 100.00%	$\epsilon$ : 100.00%		$\beta^-$ : 100.00% $\alpha$ : 1.3E-4%	$\alpha$ : 99.72% $\beta^-$ : 0.28%
$^{206}\text{Pb}$ STABLE 24.1%	$^{207}\text{Pb}$ STABLE 22.1%	$^{208}\text{Pb}$ STABLE 52.4%	$^{209}\text{Pb}$ 3.253 H	$^{210}\text{Pb}$ 22.20 Y
			$\beta^-$ : 100.00%	$\beta^-$ : 100.00% $\alpha$ : 1.9E-6%

EMPIRE evaporation code

# Toksyczność $^{210}\text{At}$



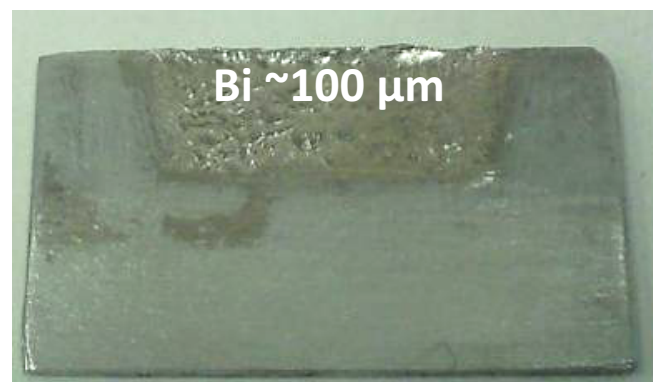
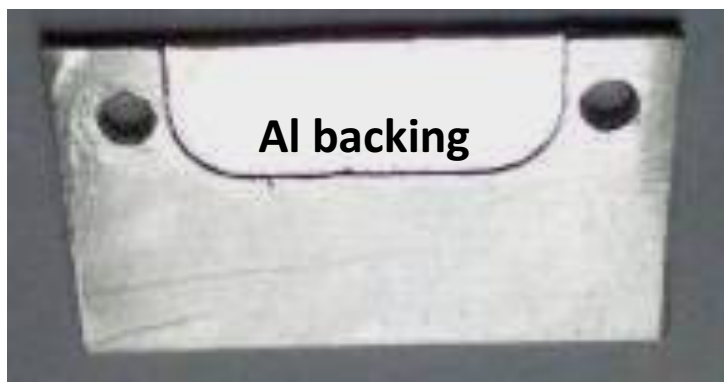
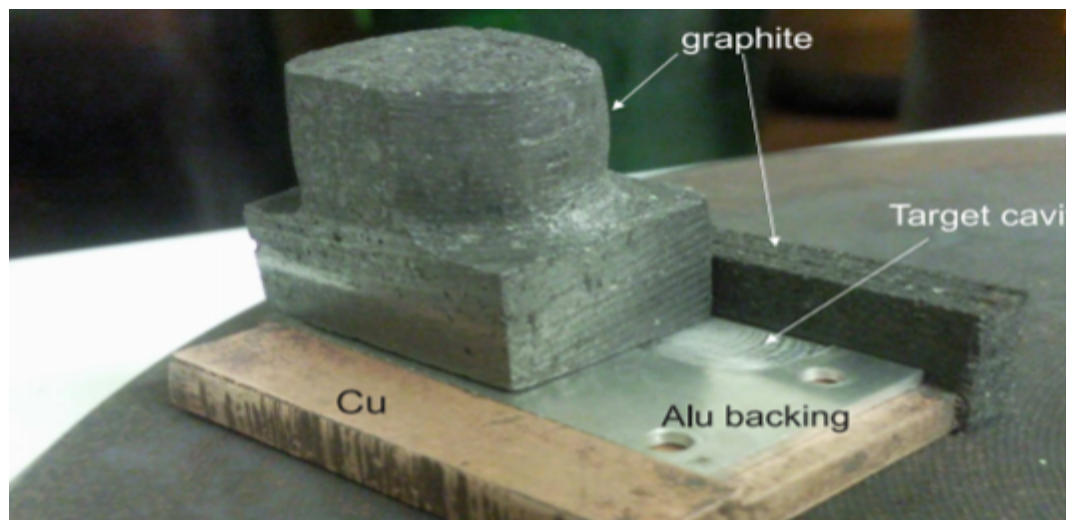
## WAGOWY CZYNNIK TKANKI ( $w_T$ )

Rozporządzenie Rady Ministrów z dn. 18 stycznia 2005r.

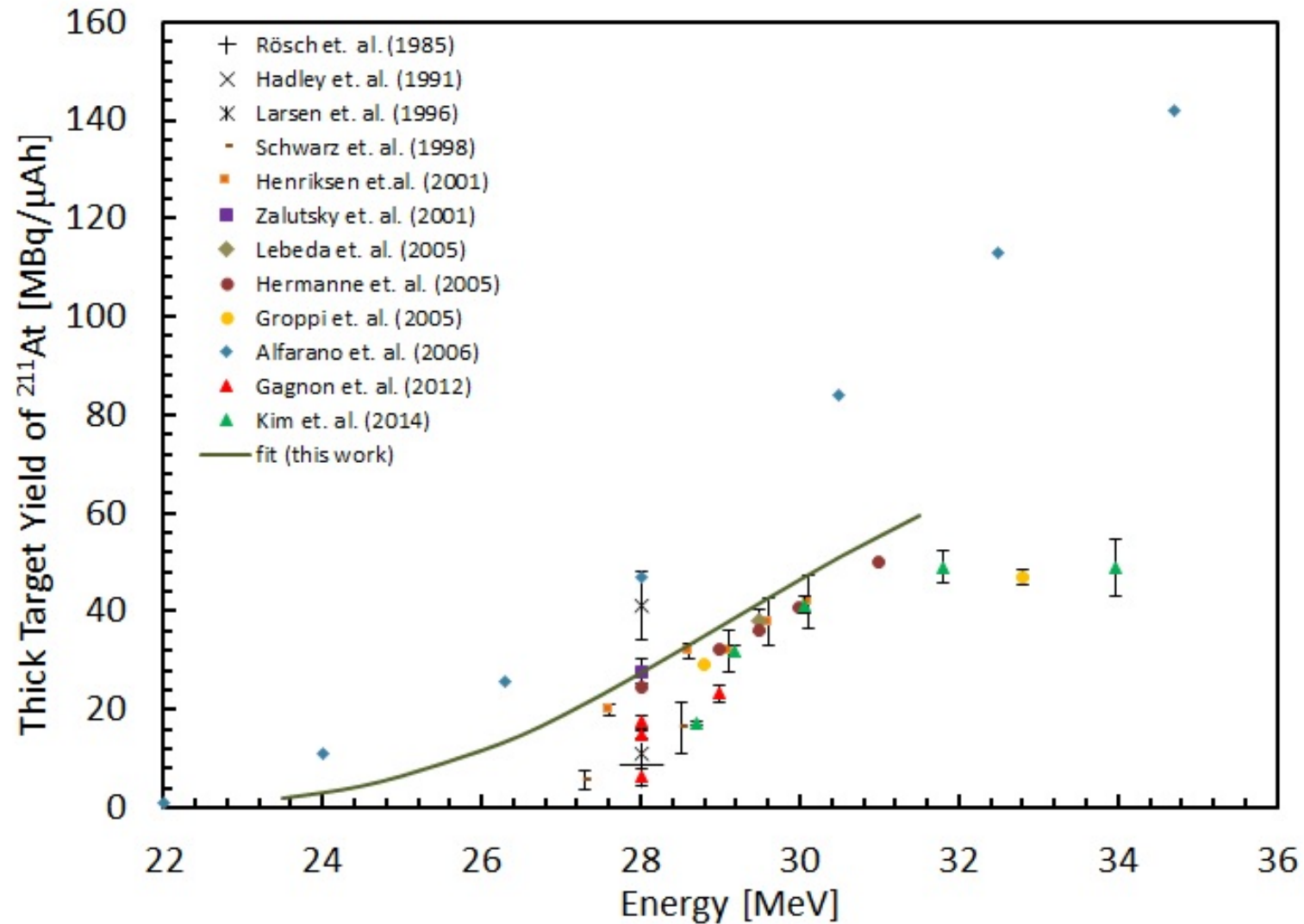
Dz. U. z dn. 3 lutego 2005r. poz. 168

Tkanka (narząd), T	$w_T^{1)}$	$w_T$ ICRP2007
Gonady	0,20	0,08
Czerwony szpik kostny	0,12	0,12
Jelito grube	0,12	0,12
Płuco	0,12	0,12
Żołądek	0,12	0,12
Pęcherz moczowy	0,05	0,04
Gruzoły piersiowe	0,05	0,12
Wątroba	0,05	0,04
Przełyk	0,05	0,04
Tarczycyca	0,05	0,04
Skóra	0,01	0,01
Powierzchnia kości	0,01	0,01
Pozostałe	0,05 <sup>2), 3)</sup>	0,012

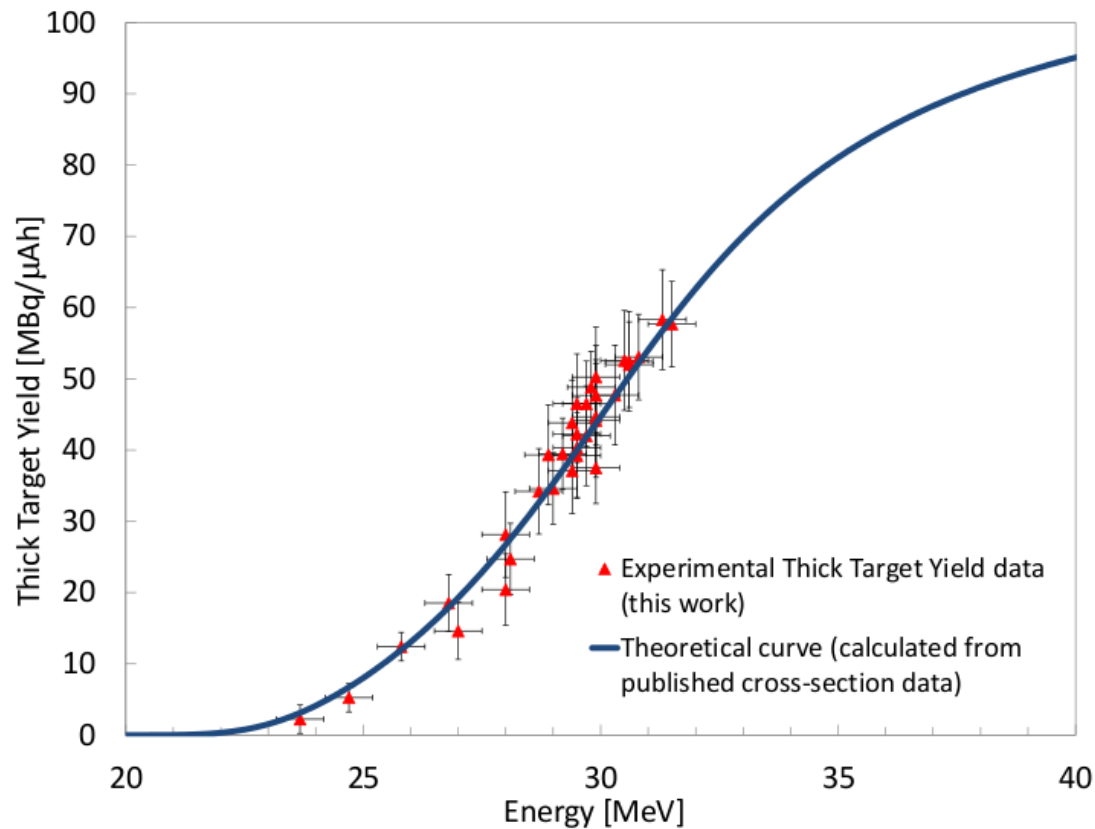
# Produkcja $^{211}\text{At}$



# Produkcja $^{211}\text{At}$



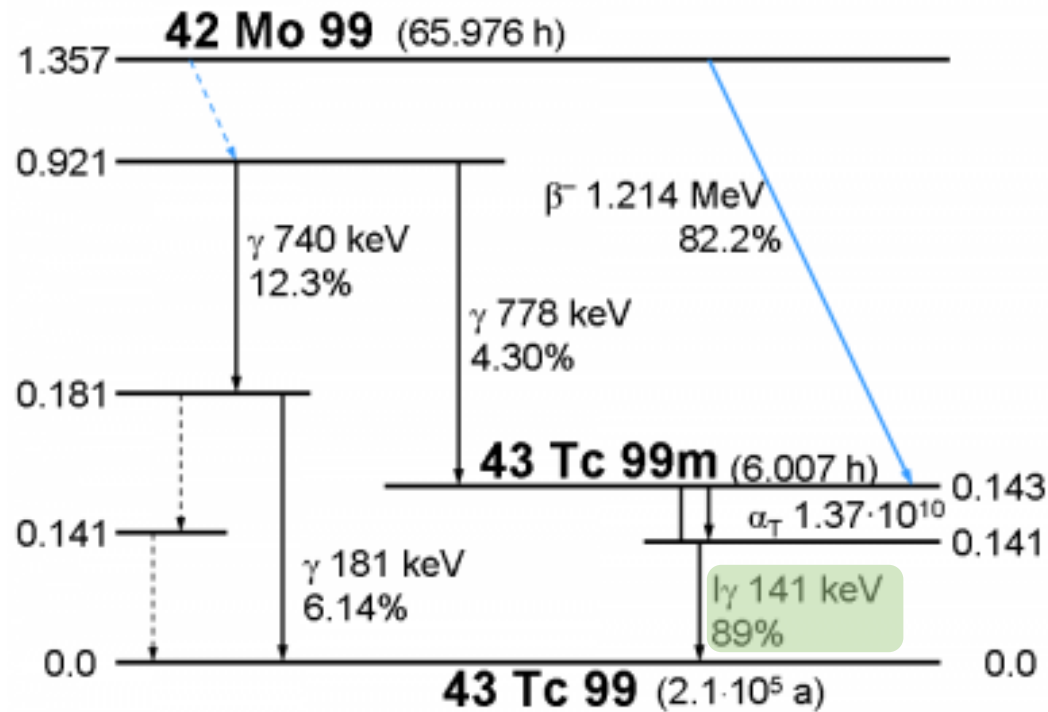
# Produkcja $^{211}\text{At}$



wiązka	$\alpha$
tarcza	$^{nat}\text{Bi}$
reakcja	$^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$
naświetlanie	7 h, 25 $\mu\text{A}$
EOB	<b>4,7 GBq</b> (29 MeV)
$^{210}\text{At}$	0,03%

oszacowane dla prądu 25  $\mu\text{A}$

# Radioizotop $^{99m}\text{Tc}$



LA PHYSIQUE AU CANADA / Vol. 66, No. 1 ( jan. à mars 2010 )

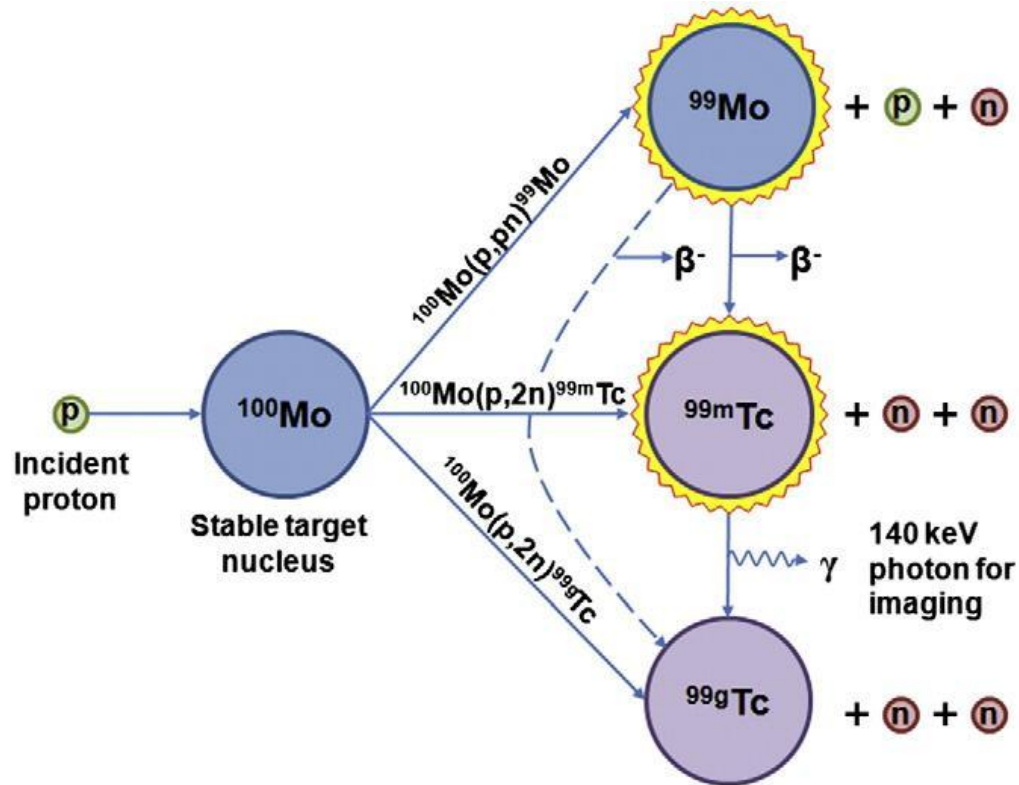
## A SHORT TERM SOLUTION TO THE MEDICAL ISOTOPE CRISIS VIA DIRECT PRODUCTION OF Tc-99M AT LOW ENERGY: A PIECE OF THE PUZZLE

BY THOMAS J. RUTH, TRIUMF

The recent unexpected shutdown of the Chalk River, Canada reactor has caused a major disruption in the supply of the most important radionuclide used in medicine today, Mo-99. Mo-99 is the source of **Tc-99m used in more than 80%** of all nuclear medicine imaging procedures. There are only 5 reactors that are presently used in the production of Mo-99 and all of these reactors are over forty years old, the one in Chalk River, the NRU, is 52 years old. The NRU and the HFR reactor in the Netherlands account for more than 60% of the world's supply. The NRU is closed because of a heavy water leak in the containment vessel releasing tritiated water into the holding tank. The HFR reactor had a leak in a coolant pipe earlier in 2009 and is due for an extended shutdown in 2010 to repair this leak.



# Produkcja (cyklotronowa) $^{99m}\text{Tc}$



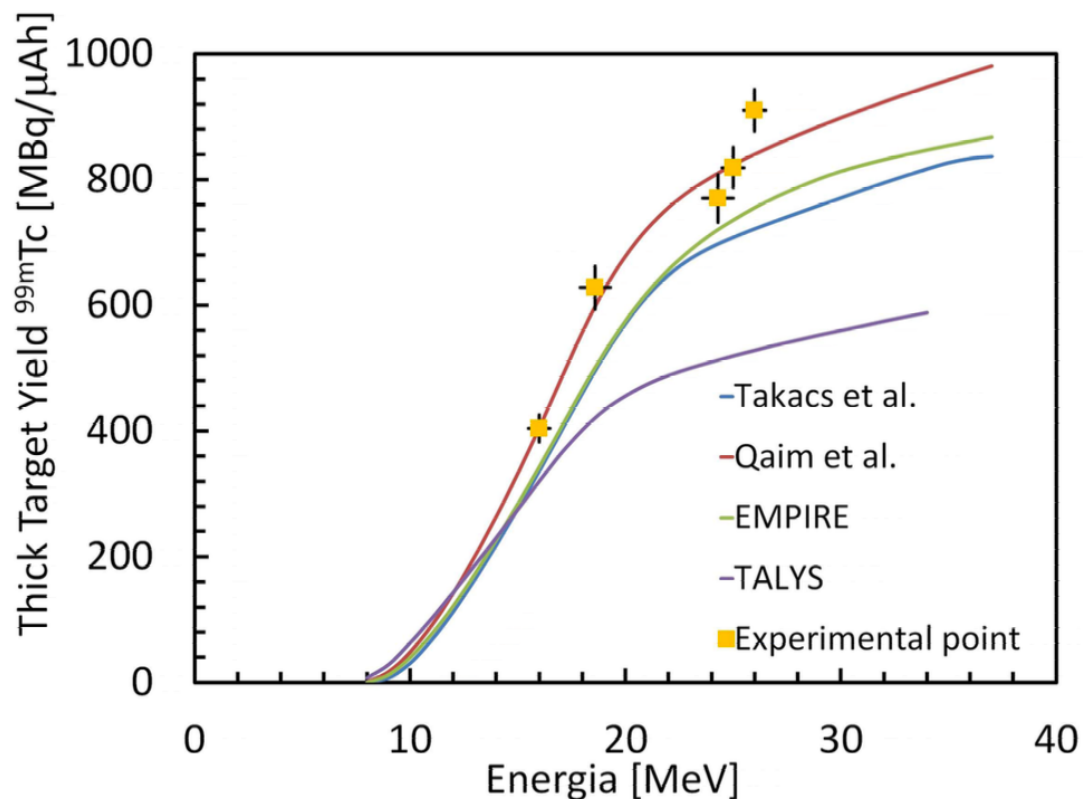
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# Produkcja (cyklotronowa) $^{99m}\text{Tc}$



wiązka      protony

tarcza       $^{100}\text{Mo}$  (99.815%)

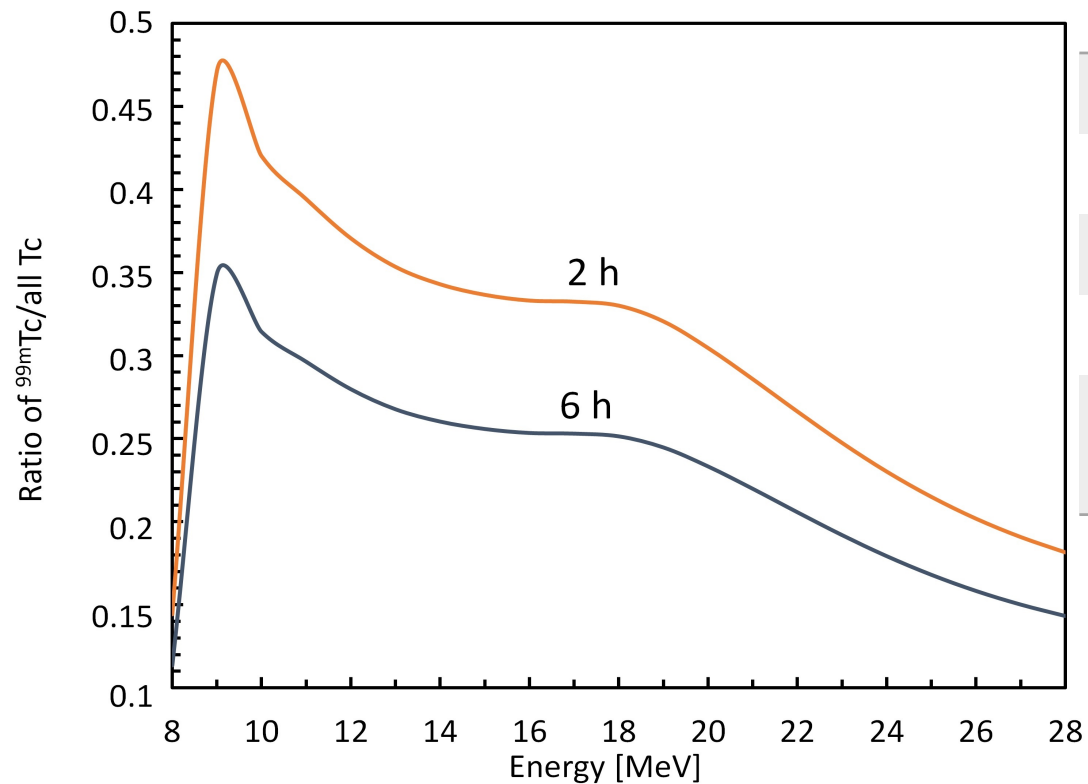
reakcja       $^{100}\text{Mo}(p,2n)^{99m}\text{Tc}$

naświetlanie      6 h, 40 μA

EOB      **64 GBq (16→8 MeV)**  
**150 GBq (26→8 MeV)**

oszacowanie dla prądu 40 μA

# Produkcja (cyklotronowa) $^{99m}\text{Tc}$



wiązka      protony

tarcza       $^{100}\text{Mo}$  (99.815%)

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oszacowanie dla prądu 40  $\mu\text{A}$

# Podziękowania

## **Środowiskowe Laboratorium Ciężkich Jonów**

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Agnieszka Trzcińska

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## **Uniwersytet Śląski**

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Wiktor Zipper

## **Instytut Chemii i Technik Jądrowych**

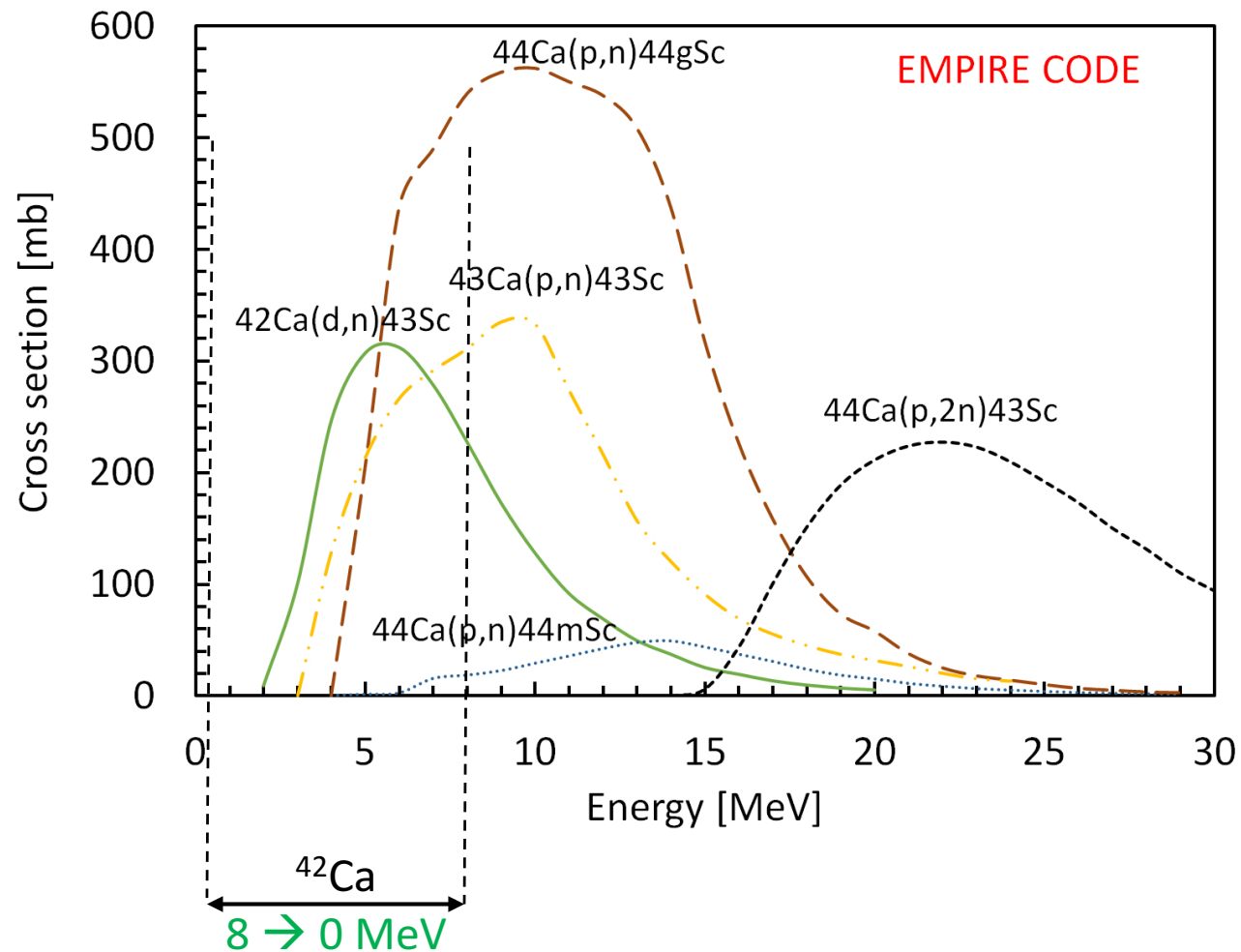
Aleksander Bilewicz  
Agnieszka Majkowska  
Rafał Walczak



# Źródła

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- "DOTATATE" by Anypodetos - Own work, based on File:Octreotide.svg. Licensed under CC0 via Wikimedia Commons - <http://commons.wikimedia.org/wiki/File:DOTATATE.svg#mediaviewer/File:DOTATATE.svg>
- [http://i00.i.aliimg.com/photo/v0/150411098/limestone CaCO3 calcium carbonate powder.jpg](http://i00.i.aliimg.com/photo/v0/150411098/limestone_CaCO3_calcium_carbonate_powder.jpg)
- K. Gagnon et al., Nuclear Medicine and Biology 38 (2011) 907–916

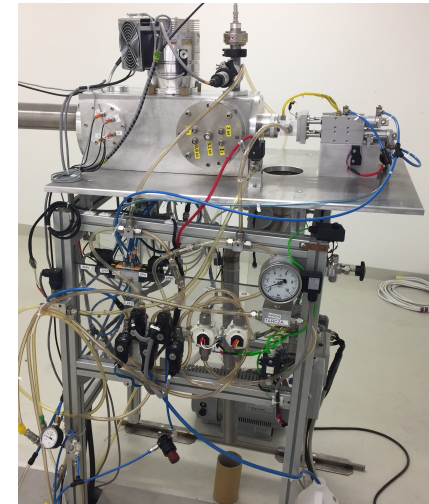
# Produkcja $^{43}\text{Sc}$ deuteronami



# Produkcja $^{43}\text{Sc}$ deuteronami



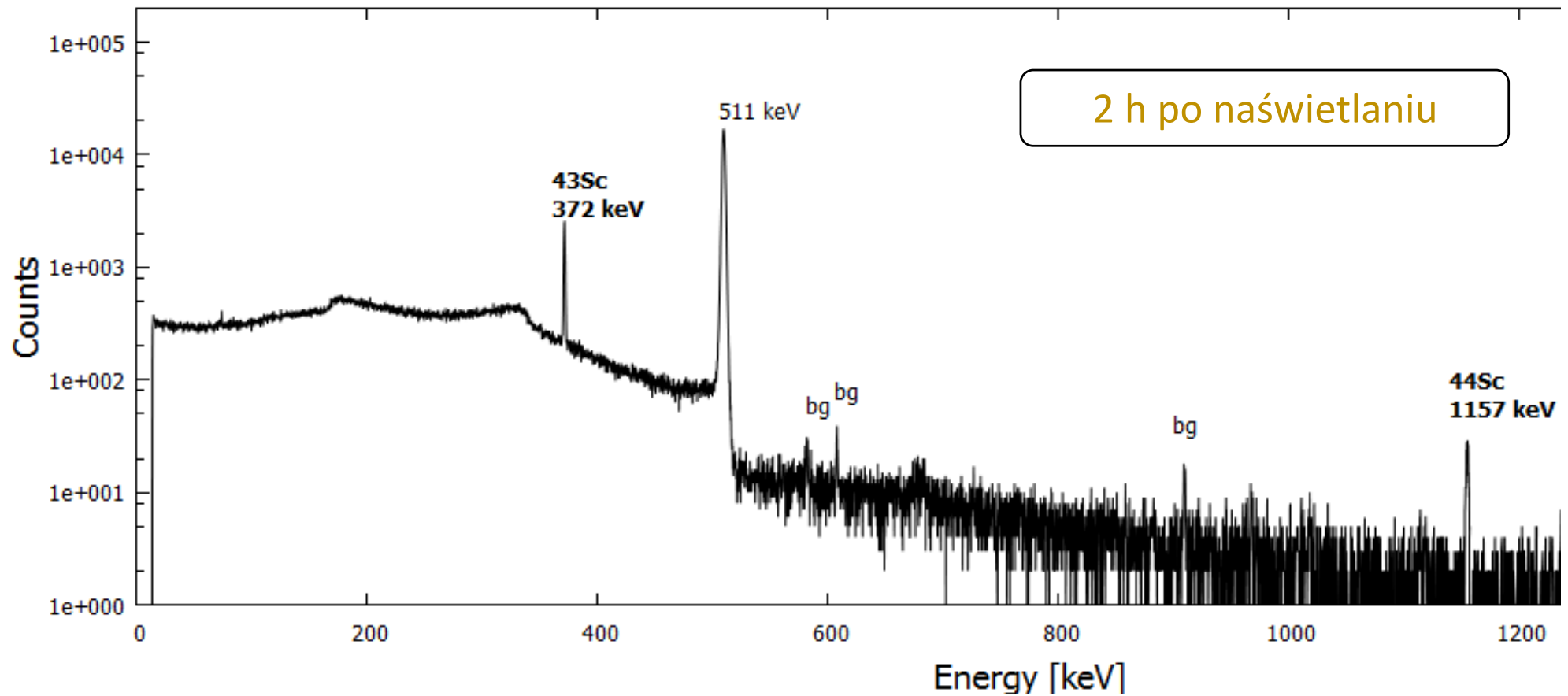
$^{42}\text{CaCO}_3$  (68%  $^{42}\text{Ca}$ )  
25%  $\text{CaCO}_3$  + 75% grafit



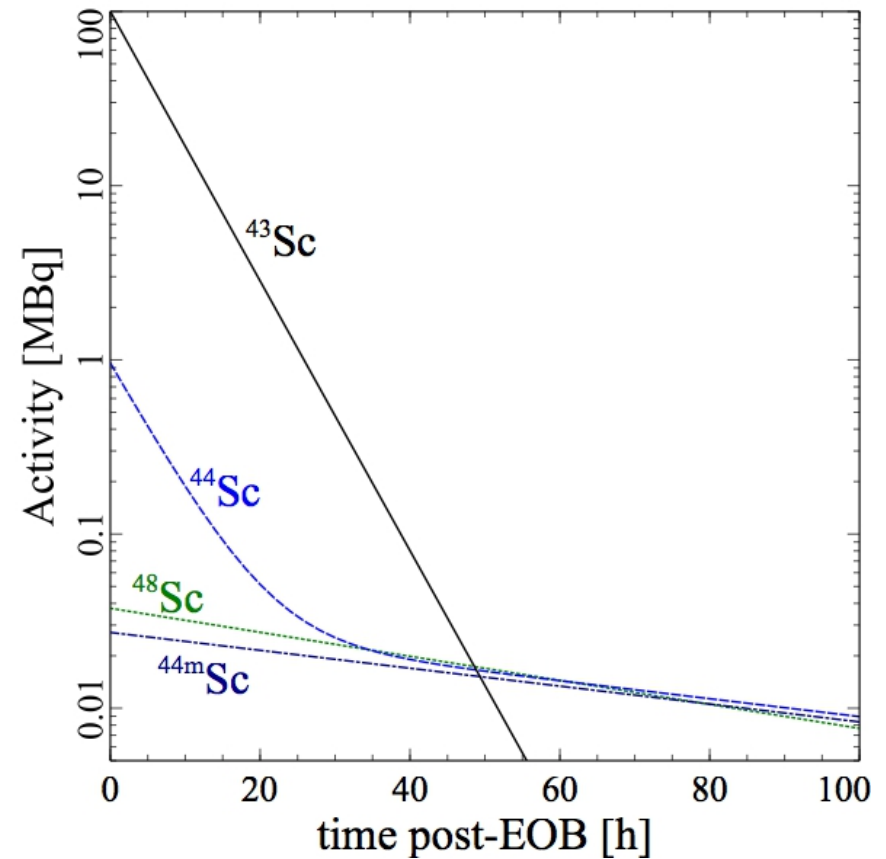
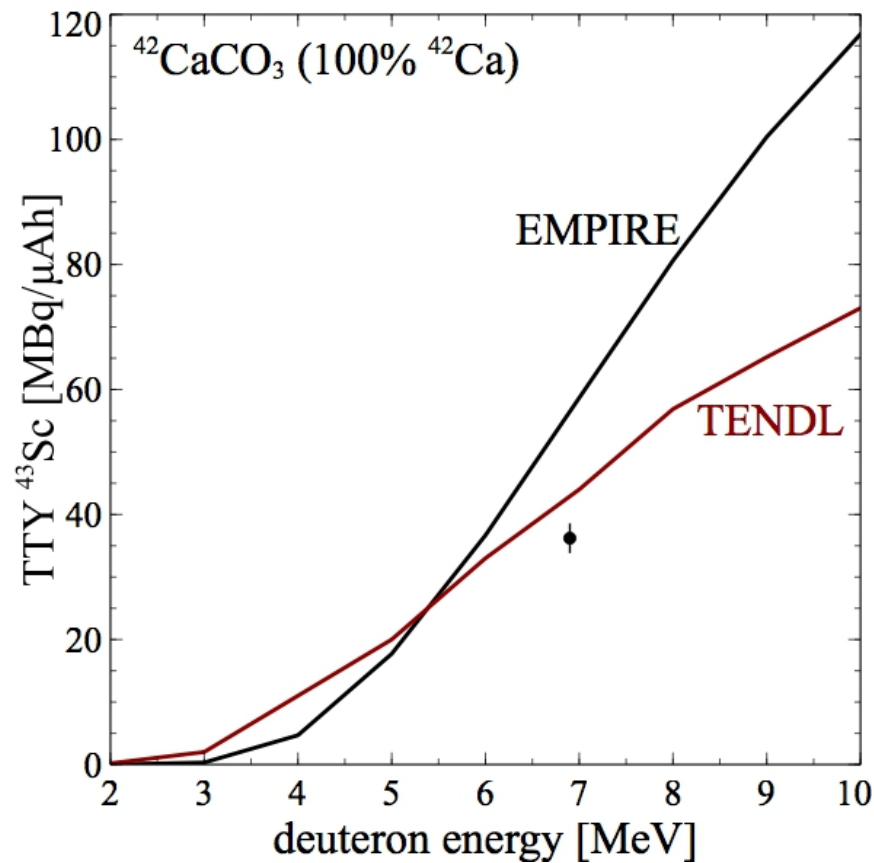
**PETtrace** deuterony 8,4 MeV  
wiązka zewnętrzna 0,5  $\mu\text{A}$   
Środowiskowe Laboratorium Ciężkich Jonów



# Produkcja $^{43}\text{Sc}$ deuteronami



# Produkcja $^{43}\text{Sc}$ deutronami



$^{42}\text{CaCO}_3$  (68%), 4 h,  $1 \mu\text{A} = 74 \text{ MBq } ^{43}\text{Sc}$