Nuclear data program for NCT at the n_TOF Collaboration at CERN

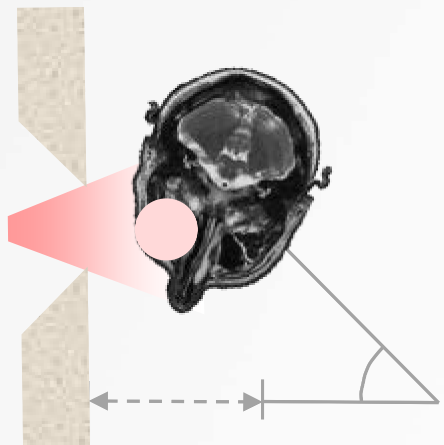
M. Sabaté-Gilarte[1,2], F. Ogállar[2,3], J. Praena[3], I. Porras[3], P. Torres-Sánchez[3], J.M. Quesada[1] and The n_TOF Collaboration[4].

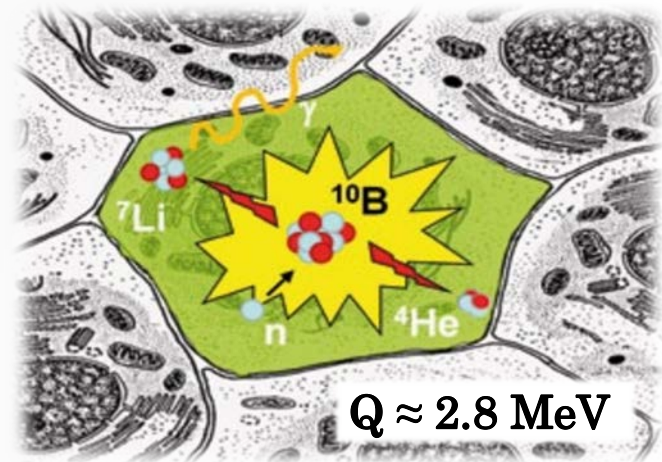
1. University of Seville (Spain) 2. CERN (Switzerland)
3. University of Granada (Spain) 4. www.cern.ch/ntof

The Neutron Capture Therapy (**NCT**) is an experimental binary radiation therapy design for treating **highly resistant tumours** to chemotherapy and conventional radiotherapy due to their morphology, location and/or risks.

1. A stable isotope is injected into the patient, accumulating in cancer cells: typically ^{10}B.

2. Tumour region is irradiated with neutrons, inducing **(n,α)** reaction in ^{10}B.

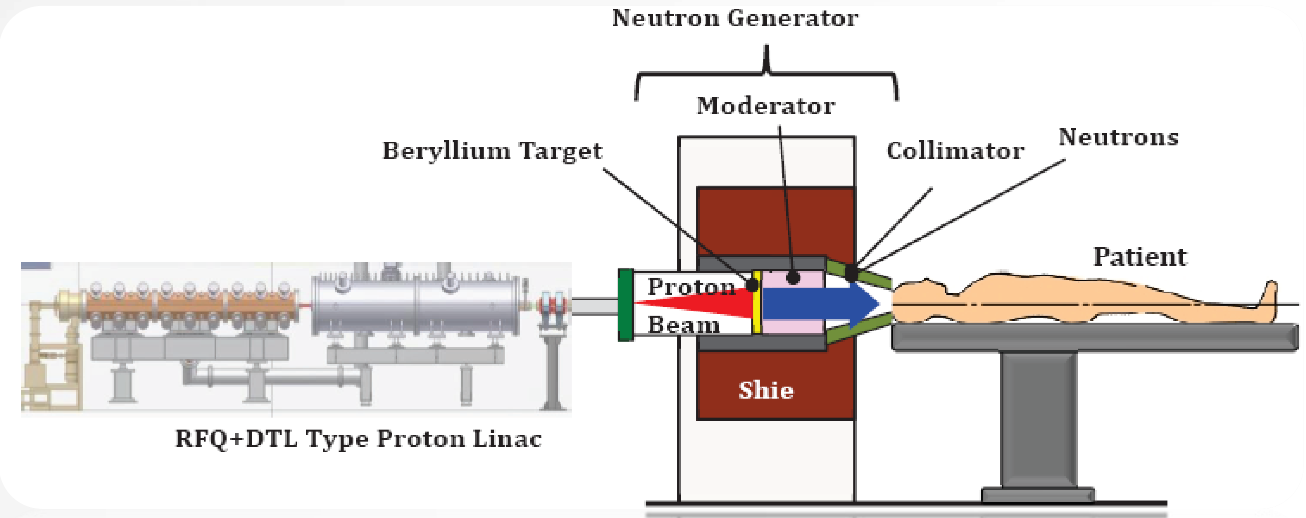




- Neutrons are moderated in tissue and arrive to the tumour with thermal energy, maximizing the reaction probability.
- Energy deposition range (5-9 μm) ~ cell size.
- One day of treatment.

A **neutron beam** is necessary to perform the treatment:

- **Nuclear reactors**: has been the only way for a long time, limiting the therapy potential:
  1. Logistic problems.
  2. Not optimized neutron beam.
- Accelerator-Based neutron sources for NCT:
  1. Open the possibility to implement this therapy in hospitals.
  2. Development in Russia, Italy, UK, Israel, Japan or Argentina.
  3. From reactor beams to more versatile and safety AB-BNCT beams.



Better therapeutic outcome by increasing the delivered dose to the tumour.

Increasing neutron irradation.

Exploring other possible compounds besides ^{10}B. Requirements:

- High (n, lcp) cross section.
- lcp with high LET (Linear Energy Transfer).
- Range of the lcp in the order of the tumour cells.

Better therapeutic outcome by increasing the delivered dose to the tumour.

Exploring other possible compounds besides ^{10}B. Requirements:

- **High (n, lcp) cross section.**
- **lcp with high LET (Linear Energy Transfer).**
- **Range of the lcp in the order of the tumour cells.**

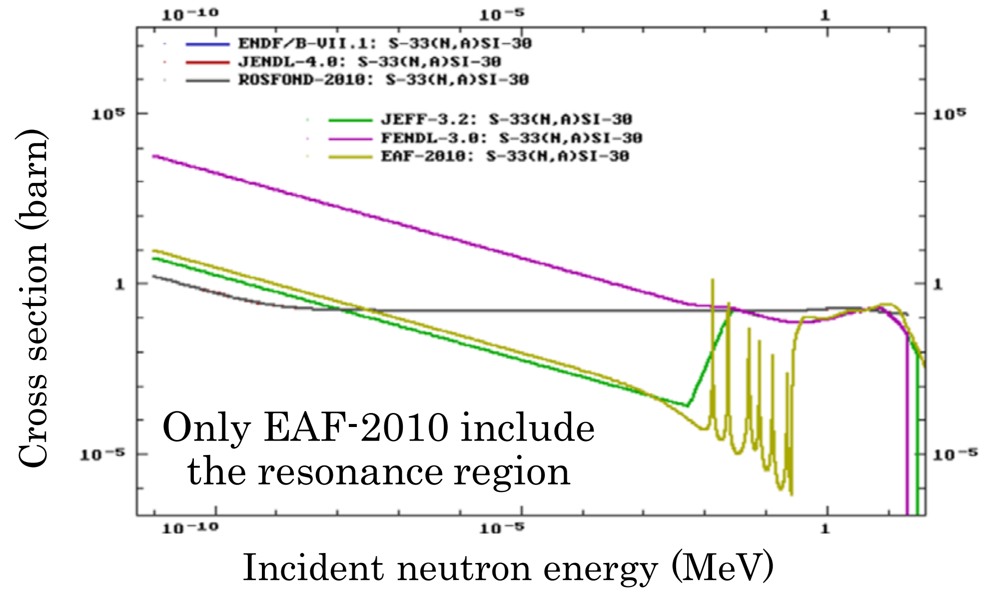
^{33}S in AB-BNCT:

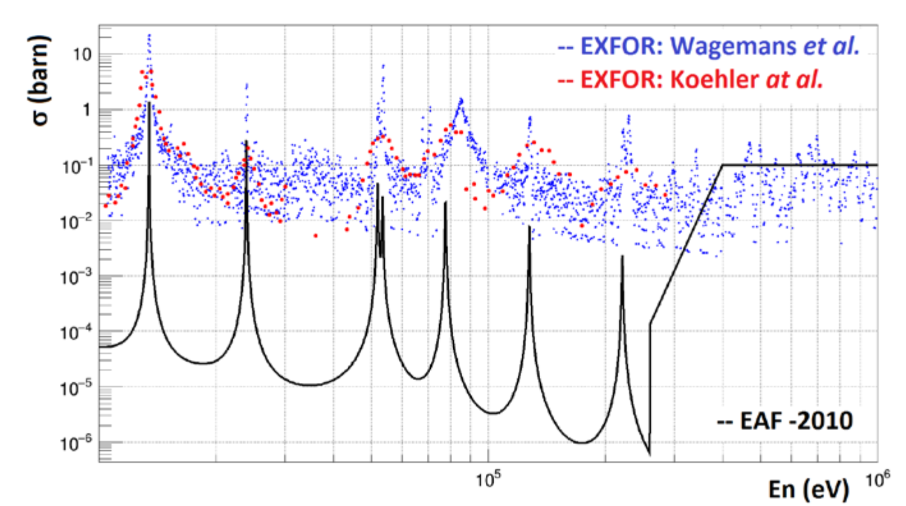
- Proposed in 2008 as possible cooperative target to ^{10}B.
- ^{33}S stable isotope of sulphur (0.75%).
- $^{33}S(n, \alpha)$ most probable neutron-induced reaction channel: $Q \approx 3.5$ MeV
- Resonance region above 10 keV with higher cross section than $^{10}B(n, \alpha)$.

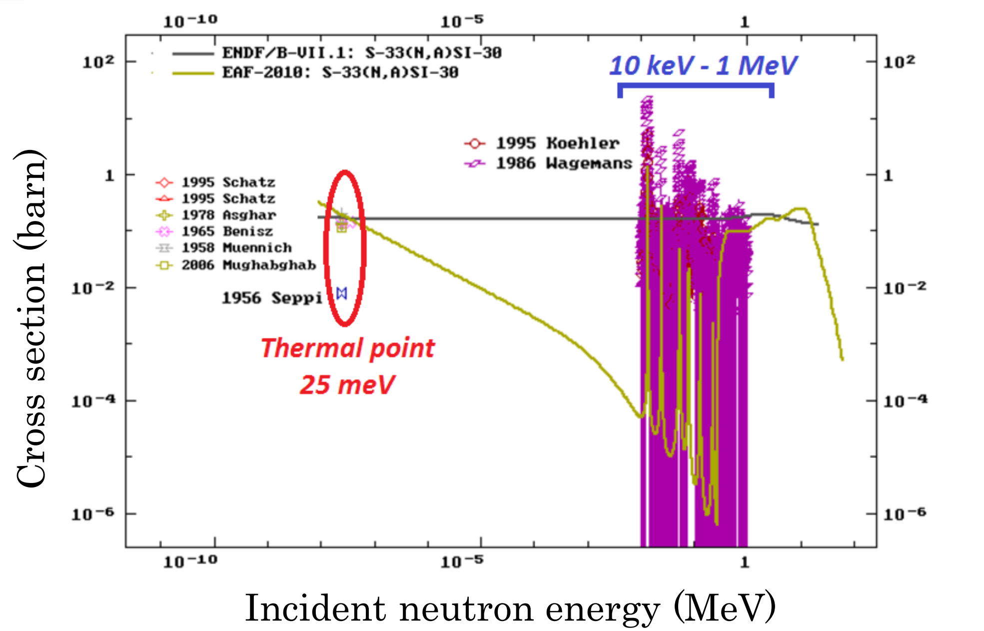
$^{33}S(n,\alpha)$: Nuclear data status

To perform the dose calculations and investigate further the potentials of ^{33}S, we need the reaction **cross section**.

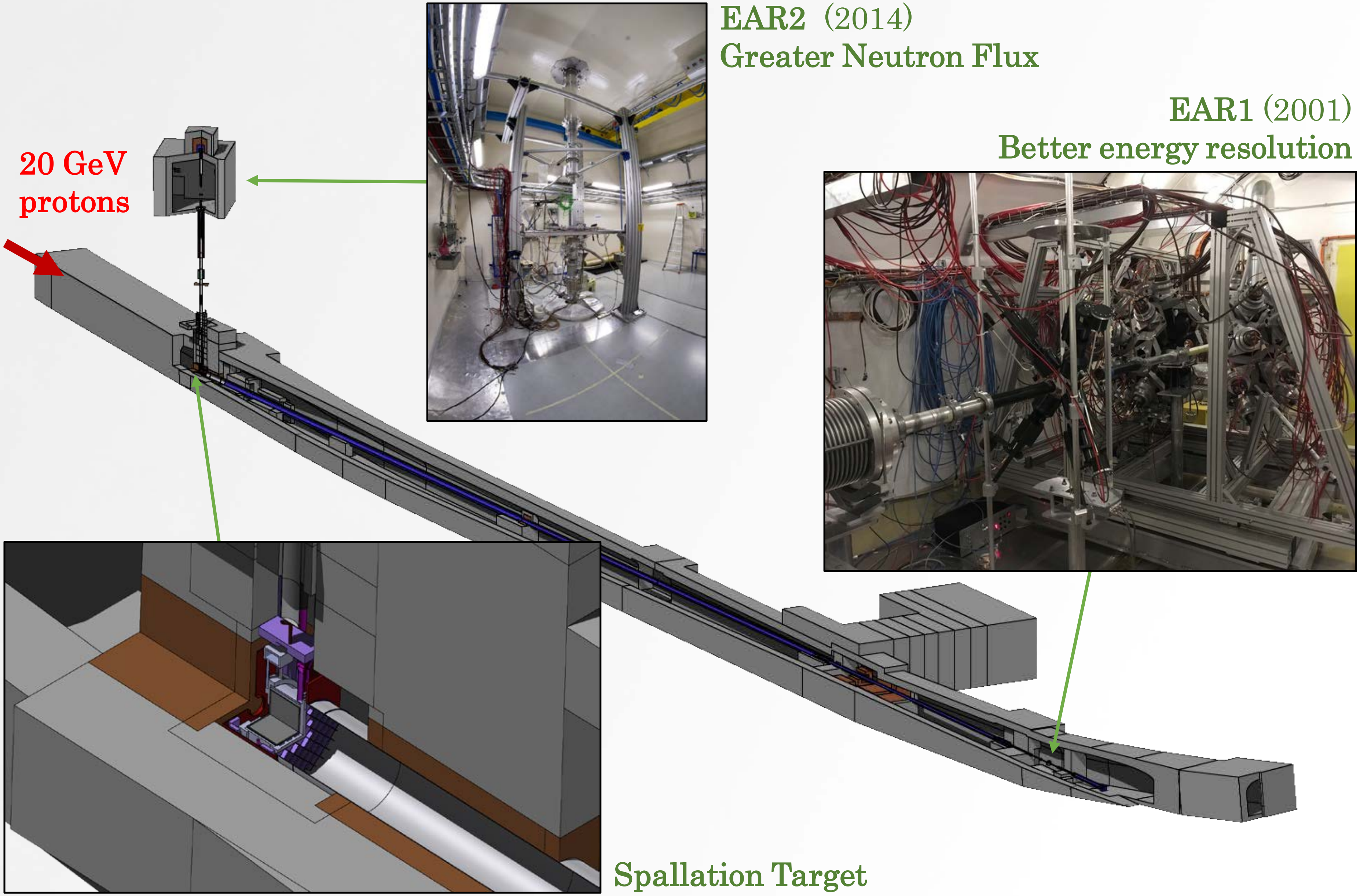
- The results of Wageman *et al.,* (n,a), and Coddens *et al.*, transmission, measurements show discrepancies in the Γ_{α}. For the first resonance it is of a factor 2.
- No experimental data from thermal to 10 keV. Low energy resonances (< 10 keV) may exist in view of the work performed for the reverse reaction.







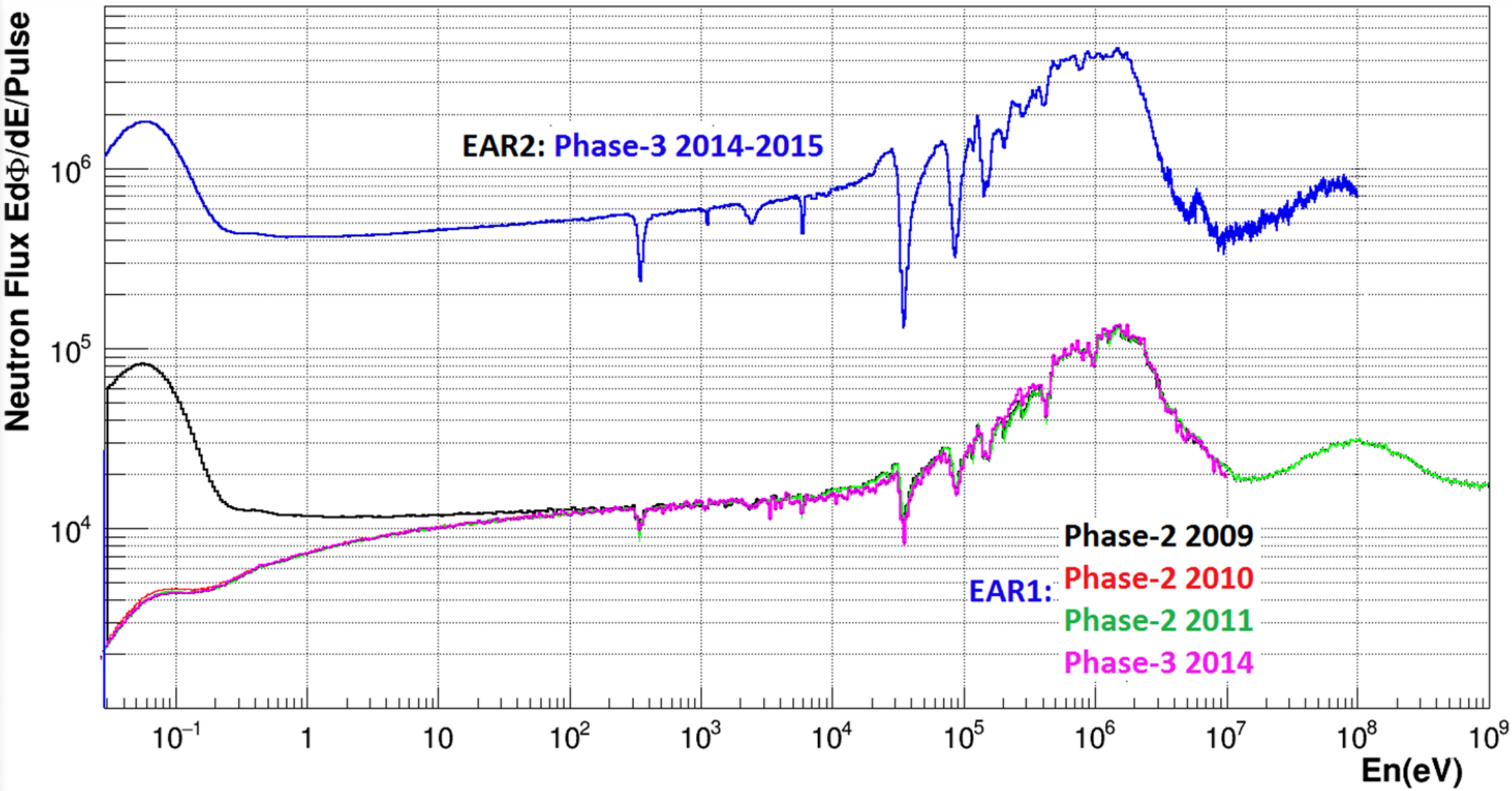
20 GeV protons



EAR2 (2014)
Greater Neutron Flux

EAR1 (2001)
Better energy resolution

Spallation Target

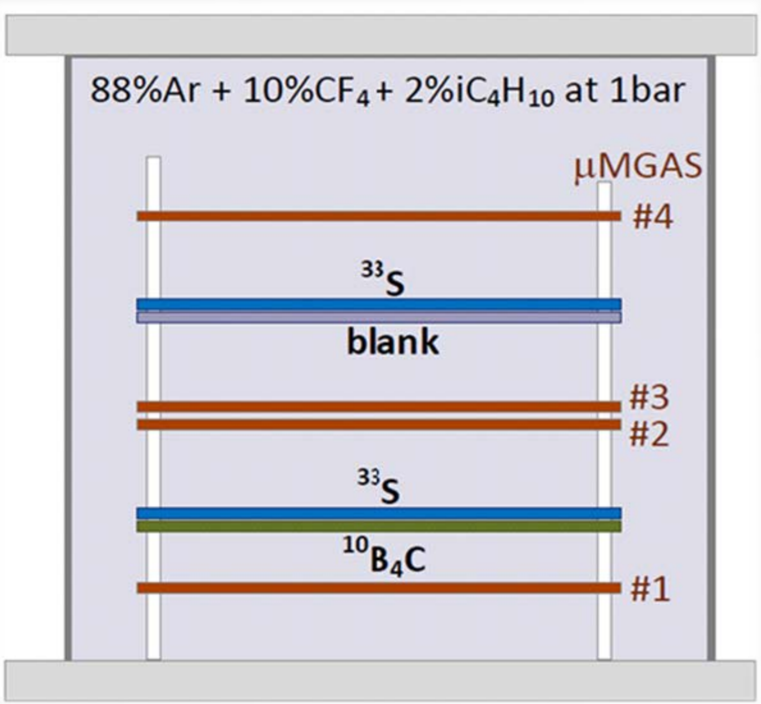

Neutron Flux EdΦ/dE/Pulse
EAR2: Phase-3 2014-2015
EAR1:
Phase-2 2009
Phase-2 2010
Phase-2 2011
Phase-3 2014
10^4
10^5
10^6
10^{-1}
1
10
10^2
10^3
10^4
10^5
10^6
10^7
10^8
10^9
En(eV)

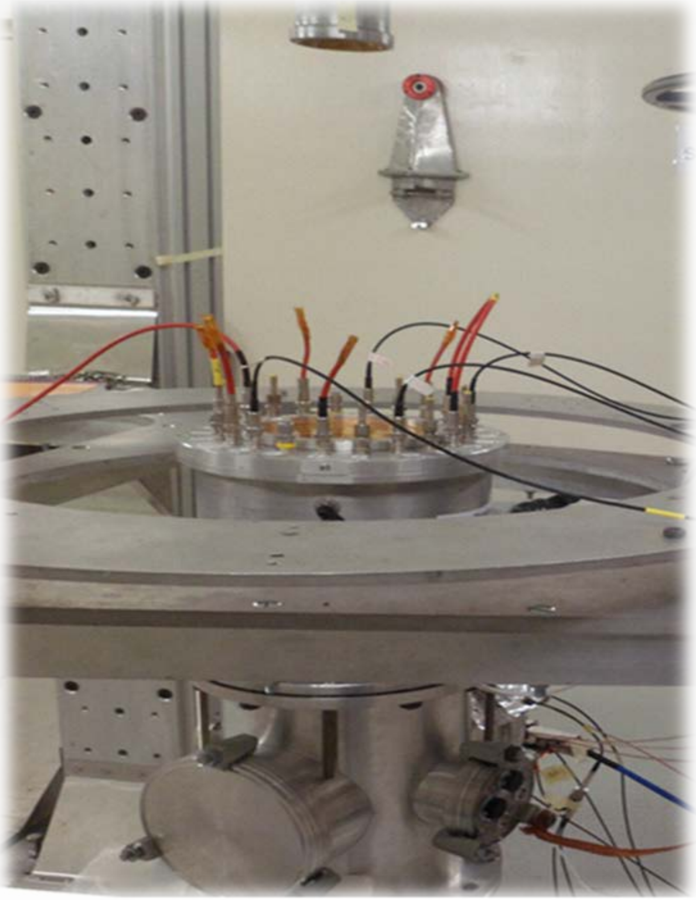
$^{33}S(n,\alpha)$ in n_TOF: 2015

- 4 gaseous detectors: µMGAS:
- Back-to-back configuration:
  - Det 1: 20 nm $^{10}B_4C$ onto Mylar.
  - Det 2: 2.59e-7 atm/barn ^{33}S.
  - Det 3: blank (^{33}S backing).
  - Det 4: 3.76e-7 atm/barn ^{33}S.

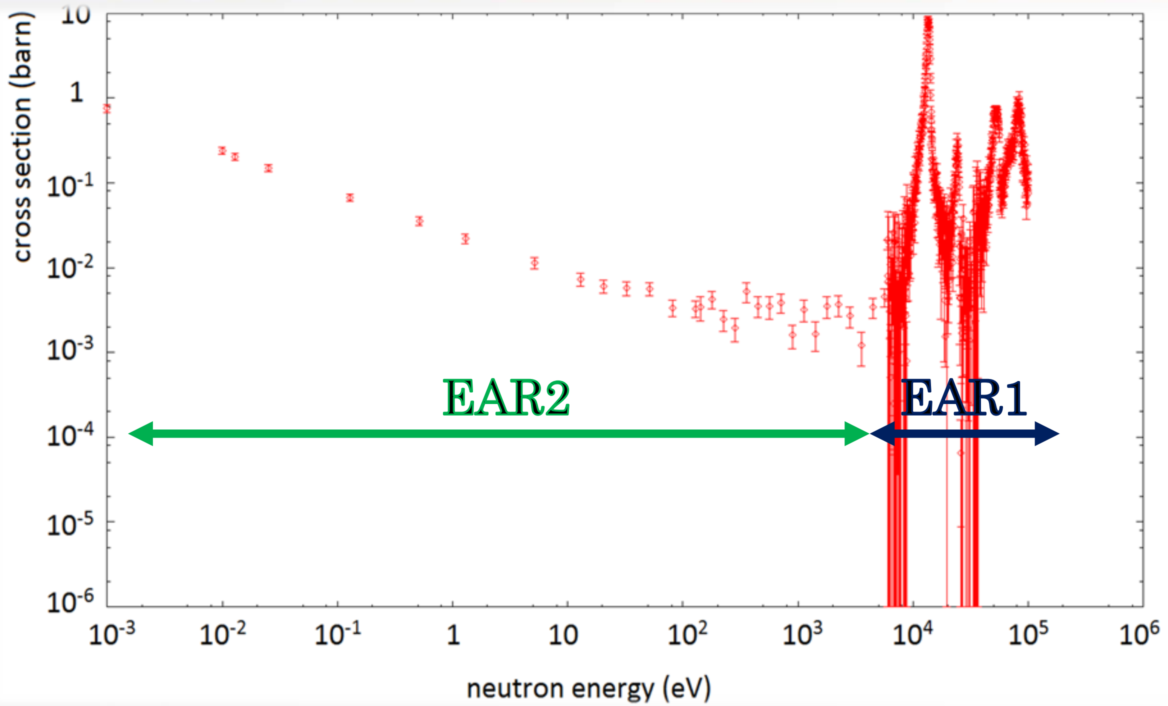
Spokespersons:
- J. Praena (UGR, Spain)
- I. Porras (UGR)

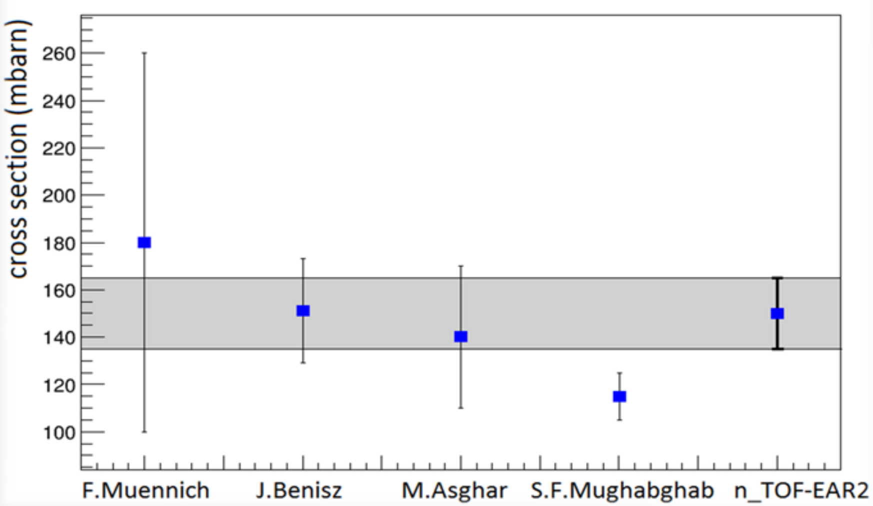
Data analysis:
- M. Sabaté-Gilarte (CERN and US, Spain)





$^{33}S(n,\alpha)$ in n_TOF: results

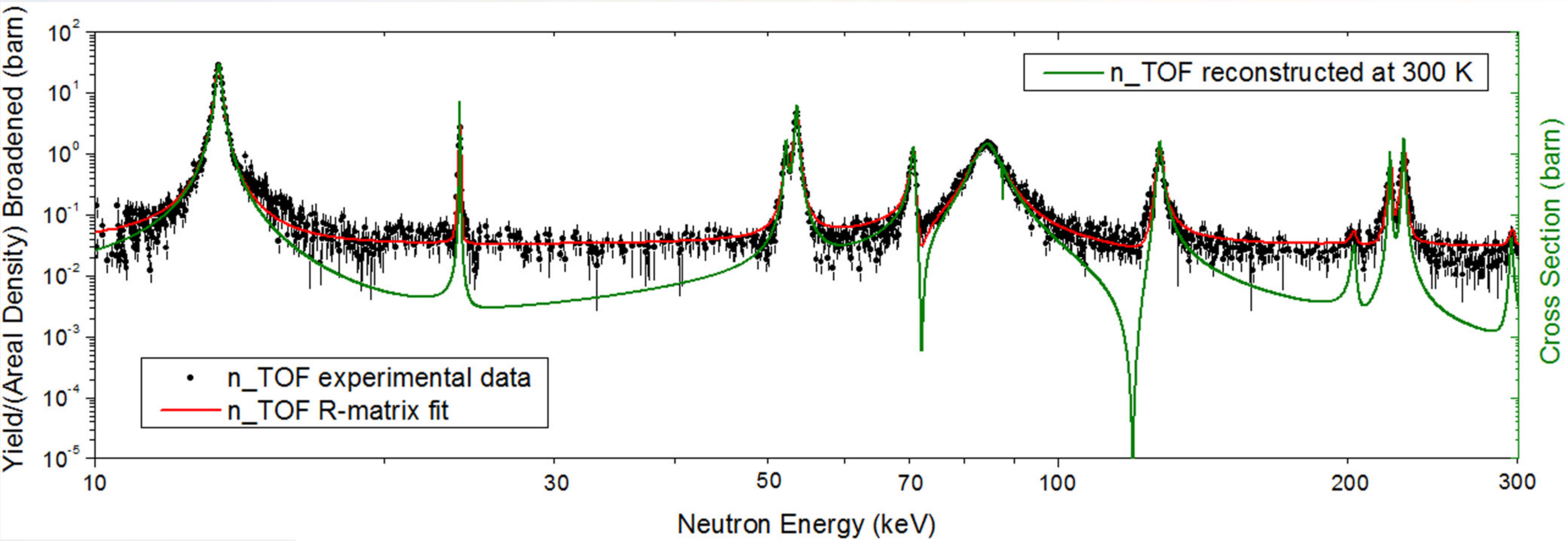




Thermal point: 25.3 meV

year	Author	σ (mbarn)
1958	F. Muennich	180 ± 80
1965	J. Benisz	151 ± 22
1978	M. Asghar	140 ± 30
2006	S.F. Mughabghab	115 ± 10
2016	**This work**	**150 ± 15**

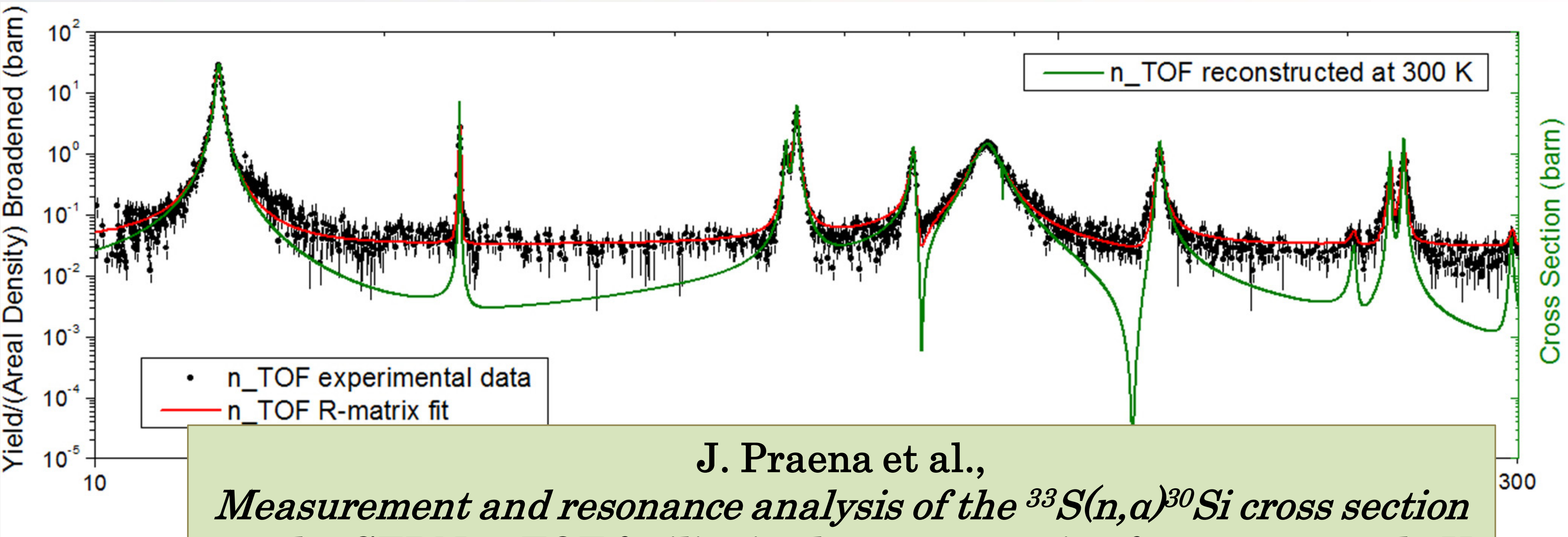
$^{33}S(n,\alpha)$ in n_TOF: results EAR1



E_n (keV)	J^{π} [a]	Γ_γ [b] (eV)	Γ_n [c] (eV)	Γ_α (eV)			$g\Gamma_n\Gamma_\alpha/\Gamma$ (eV)		
				n_TOF	ORNL	Geel	n_TOF	ORNL	Geel
13.45	2^+	0.25 ± 0.05	75 ± 1	100 ± 5	83 ± 3	41 ± 5	27.0 ± 0.4	24.6 ± 0.5	16.4 ± 1.1
23.95	3^-	1.45 ± 0.10	16.0 ± 0.9	2.2 ± 0.4		2.5 ± 0.3	1.57 ± 0.09		1.86 ± 0.16
52.12	2^+	0.25 ± 0.05	349 ± 6			18 ± 2			10.5 ± 1.2
53.60	3^-	1.6 ± 0.3	68 ± 3	320 ± 10	120 ± 11	83 ± 13	47 ± 3	38 ± 2	32.6 ± 2.0
70.86	1^-	0.68 ± 0.15	65 ± 10	580 ± 20	170 ± 50	107 ± 63	22 ± 4	18 ± 3	15.1 ± 1.9
81.36	2^+	0.95 ± 0.06	705 ± 19			4 ± 2			2.5 ± 1.2
84.88	1^-	0.8 ± 0.09	720 ± 25 [d]	4500 ± 100	3900 ± 300	3970 ± 600	232 ± 8	370 ± 20	374 ± 24
87.63	1^-	2.14 ± 0.14	28 ± 5 [d]	1 ± 0.2		10 ± 5	0.34 ± 0.06		3.6 ± 1.8
127.66	1^-	1.7 ± 0.4	360 ± 40	950 ± 110	520 ± 120	127 ± 60	98 ± 11	80 ± 11	58 ± 6
203.32	3^-	2.2 ± 0.2	2090 ± 42	5 ± 2		14 ± 5	4.4 ± 0.09		12 ± 4
221.38	2^+	1.4 ± 0.4	690 ± 70	140 ± 14	280 ± 100	55 ± 20	73 ± 8	120 ± 30	32 ± 14
223.17	0^+	0.68 ± 0.12	4400 ± 900			900 ± 300			93 ± 25
228.73	3^-	0.84 ± 0.13	760 ± 50	230 ± 30	230 ± 60	203 ± 27	150 ± 11	150 ± 30	140 ± 14
295.95	2^+	2.2 ± 0.15	2090 ± 100	15 ± 5	—	—	9.3 ± 0.5	—	42 ± 10

[a] Determined by ORNL except 295.95 keV, which is tentative (see text for details).
[b] Determined by ORNL from the (n,γ) data of Auchampaugh *et al.* [9].
[c] Determined by ORNL except where it is indicated (see text for details).
[d] Γ_n ORNL values: 1330 ± 80 eV for 84.88 keV and 280 ± 20 eV for 87.63 keV.

$^{33}S(n,\alpha)$ in n_TOF: results EAR1



J. Praena et al.,
Measurement and resonance analysis of the $^{33}S(n,\alpha)^{30}Si$ cross section at the CERN n_TOF facility in the energy region from 10 to 300 keV
Phys. Rev. C **97**, 064603 (2018)

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81.36	2^+	0.95 ± 0.06	705 ± 19			4 ± 2			2.5 ± 1.2
84.88	1^-	0.8 ± 0.09	720 ± 25[d]	4500 ± 100	3900 ± 300	3970 ± 600	232 ± 8	370 ± 20	374 ± 24
87.63	1^-	2.14 ± 0.14	28 ± 5 [d]	1 ± 0.2		10 ± 5	0.34 ± 0.06		3.6 ± 1.8
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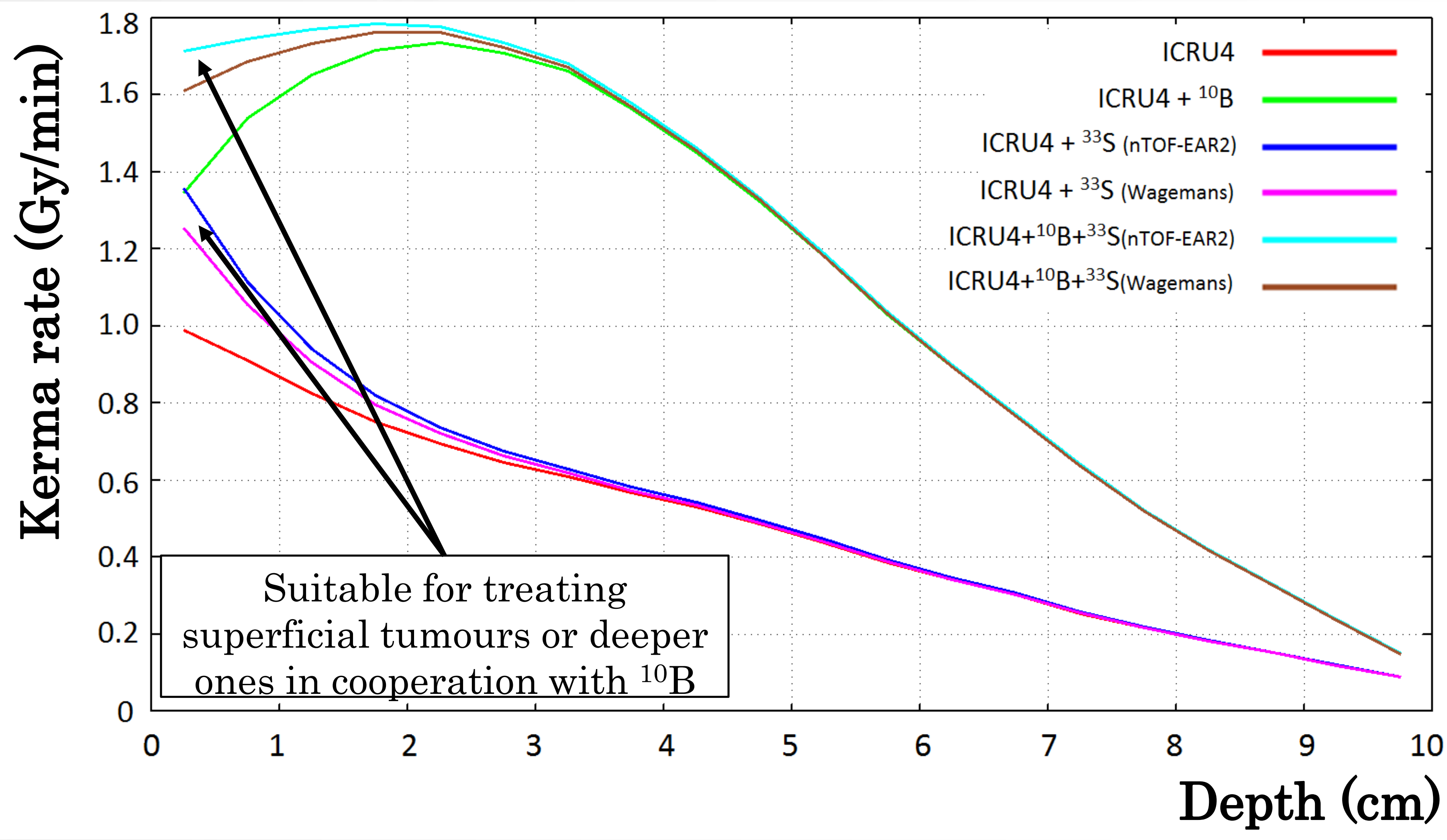


Kerma rate (Gy/min)
Depth (cm)
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
0
1
2
3
4
5
6
7
8
9
10
ICRU4
ICRU4 + 10B
ICRU4 + 33S (nTOF-EAR2)
ICRU4 + 33S (Wagemans)
ICRU4+10B+33S(nTOF-EAR2)
ICRU4+10B+33S(Wagemans)
Suitable for treating superficial tumours or deeper ones in cooperation with 10B

Improve the treatment by increasing the delivered dose to the tumour.

Increasing neutron irradation.

Exploring other possible compounds besides ^{10}B. Requirements:

- High (n, lcp) cross section.
- lcp with high LET (Linear Energy Transfer).
- Range of the lcp in the order of the tumour cells.

Improve the treatment by increasing the delivered dose to the tumour.

Increasing neutron irradation.

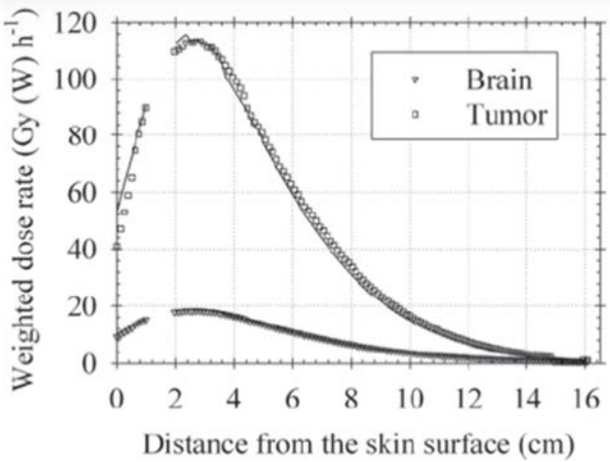


Figure 14 SERA (line) and JCDS (symbol) calculations for the total depth distributions in brain and tumor for the anterior field, using a 14 cm diameter circular FiR 1 beam. The boron dose (D_B) was calculated for 19 mg/g (ppm) of ^{10}B in brain and 66.5 μg/g (ppm) ^{10}B in tumor.

The effect of neutrons in healthy tissue is much lower than in tumour ^{10}B-load; **however, the dose in healthy tissue is the limiting factor in whatever radiotherapy treatment.**

Because of uncertainties, a large safe margin is applied for treatment planning.

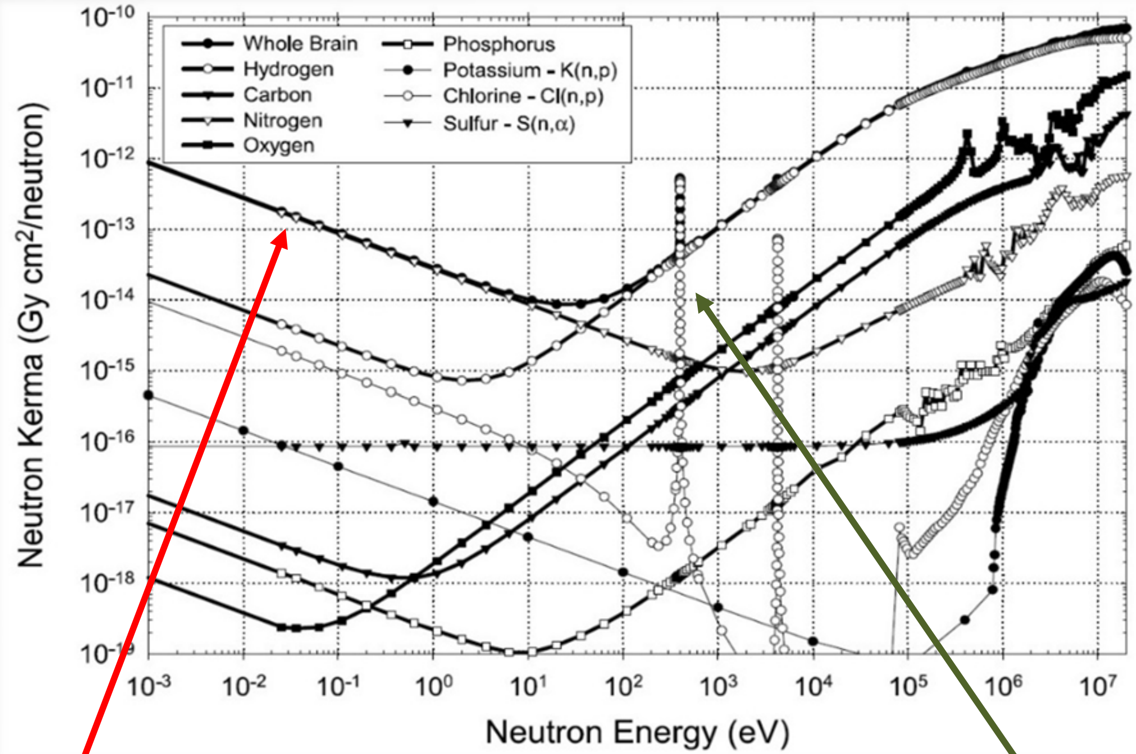
↓

With more precise dose calculations, we could control better the delivered dose to the different tissues, optimizing the treatment.

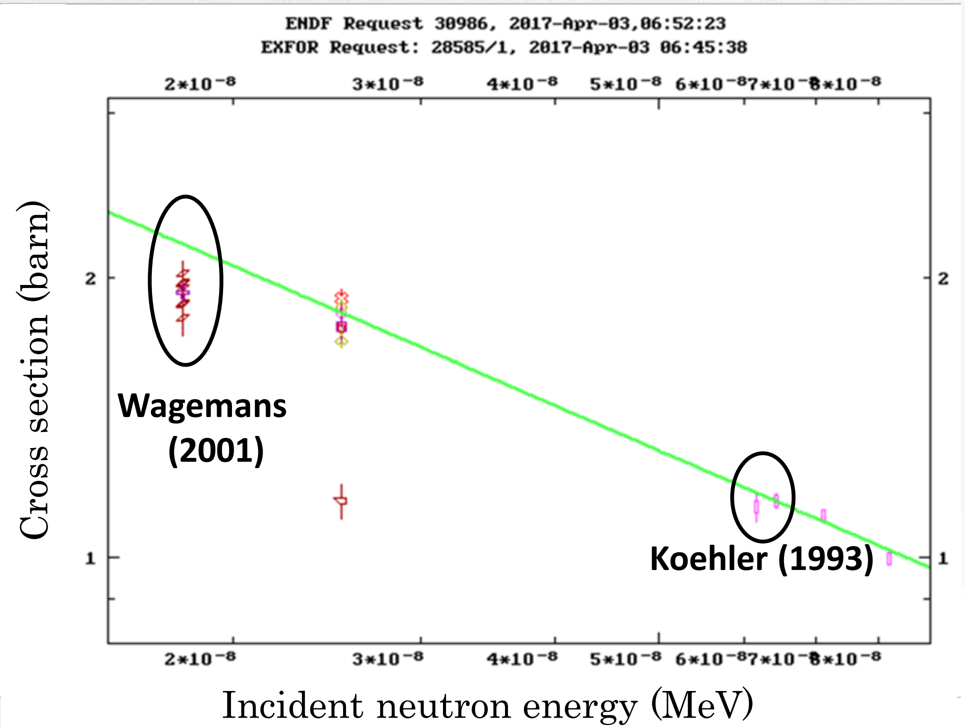
↓

More precise dose calculations require a better knowledge of the cross section of the neutron-induced reactions.

Kerma factor is a magnitude used in dosimetry which takes into account the concentration of each isotope and the cross-section: $K \propto N \cdot \sigma$



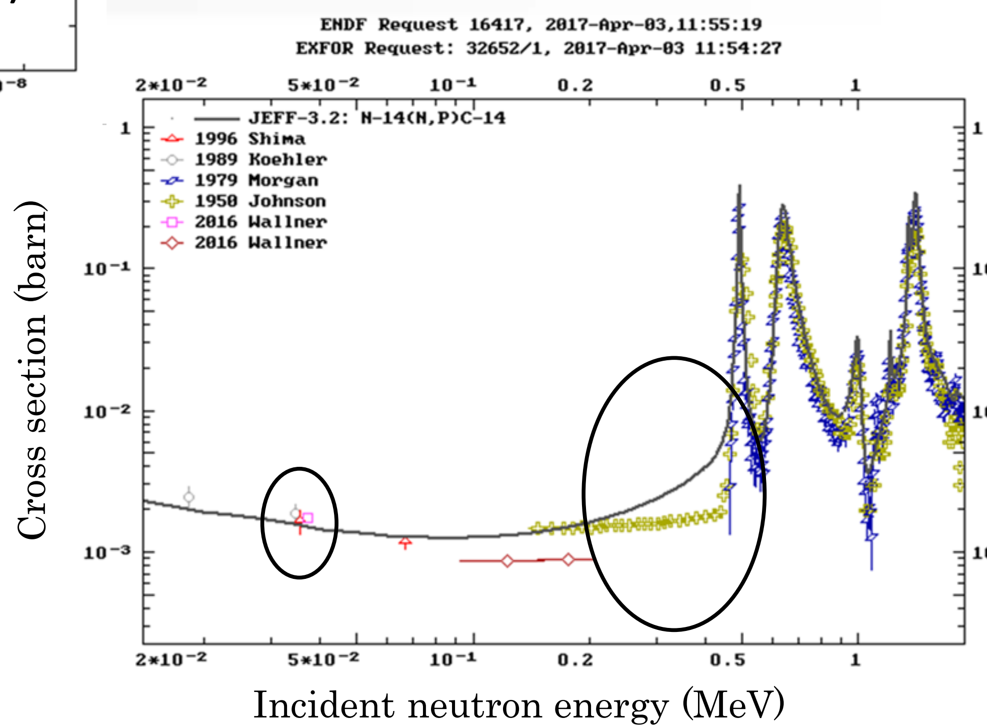
- The contribution of $^{14}N(n,p)$ is the most important for E_n below 50 keV.
- Due to the resonances in $^{35}Cl(n,p)$, this reactions has bigger effect than ^{16}O and ^{12}C for epithermal neutrons.

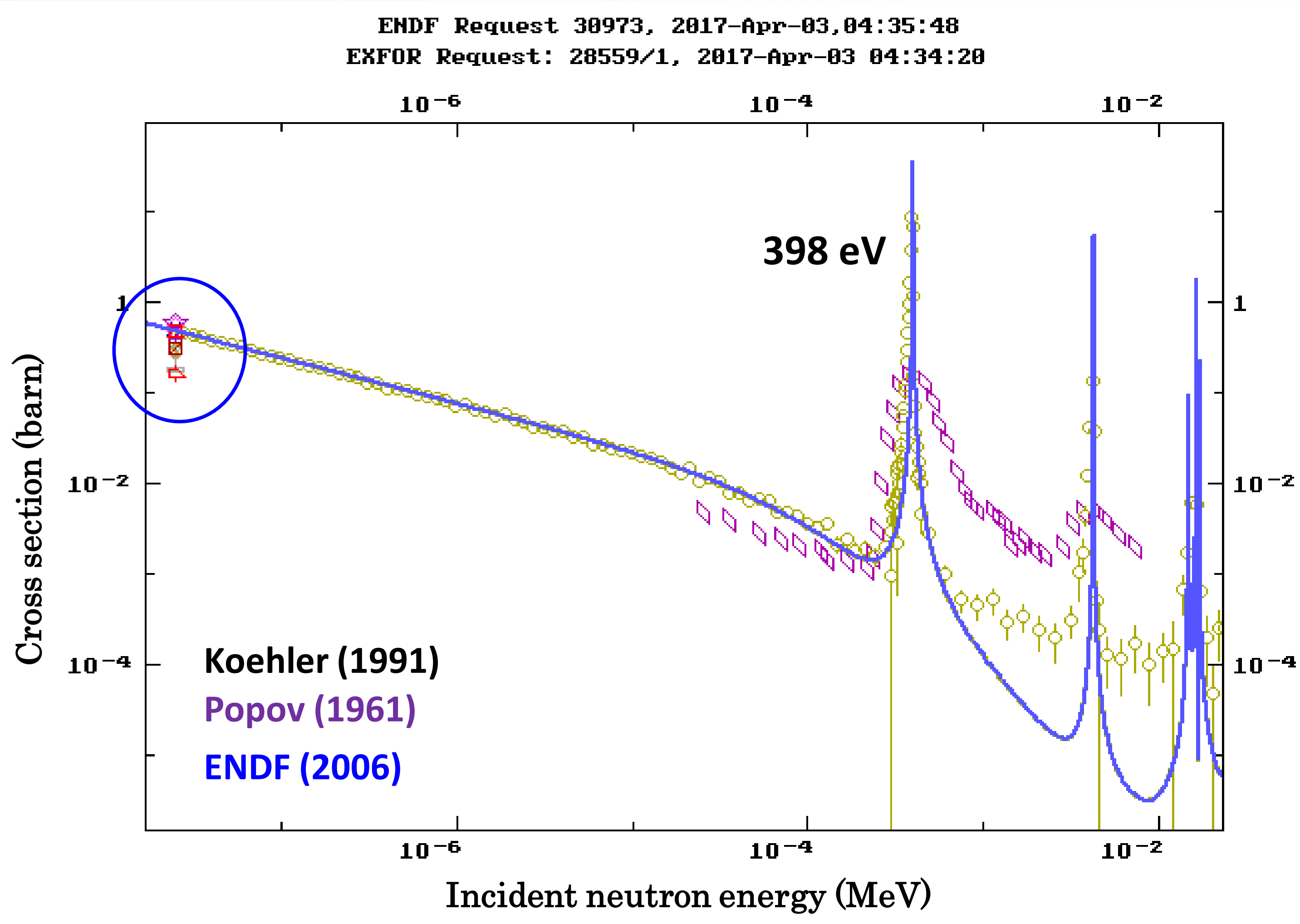


Koehler (1993) reached near thermal value. Wagemans (2001) measured the **thermal** cross-section finding >10% differences, they mentioned the need of a "careful new evaluation".

Wallner *et al.*, Gledenov *et al.* and Shima *et al.* in agreement with Koehler and JEFF-3.2.

Morgan measured 493-keV **resonance** with a strength lower than Johnson. Wallner *et al.* shows a further reduction of Morgan in a factor 3.3.



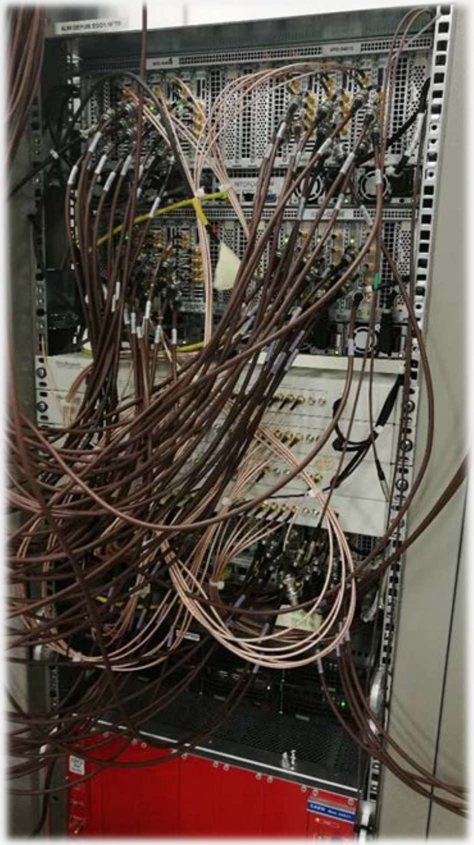


Evaluations are based on Koehler at thermal, in the energy range below 398-keV and in the resonances it is based in Druyts.

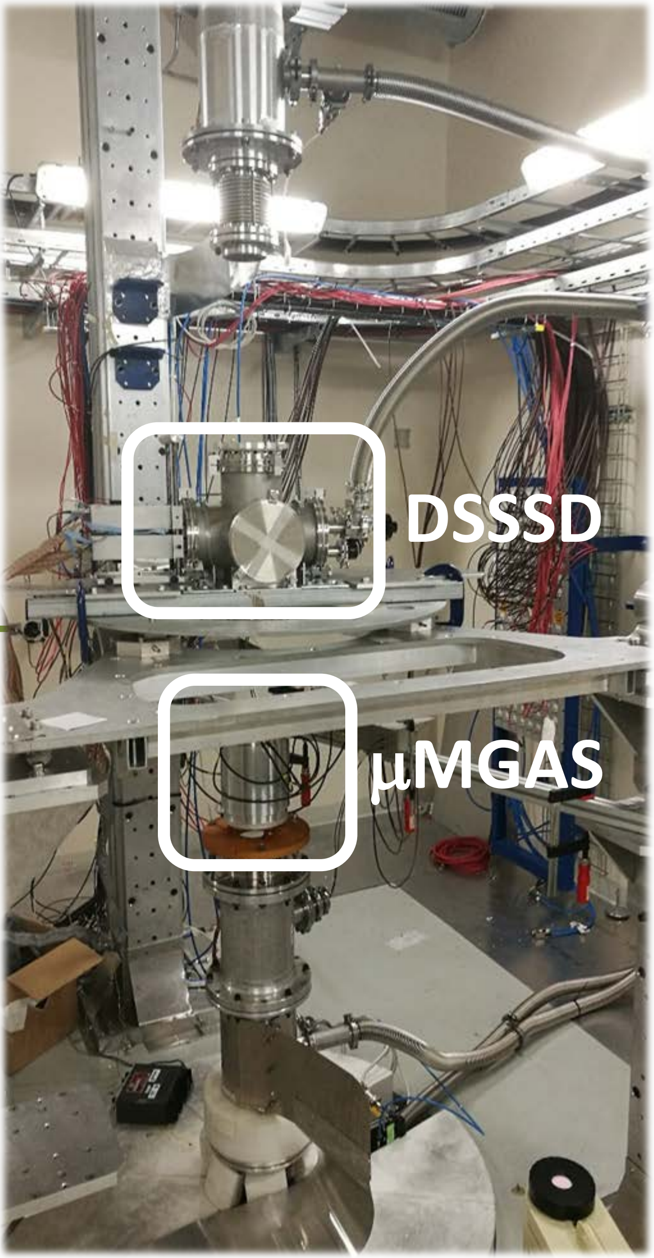
Thermal value in the evaluation is 483 mb while Druyts *et al.* measured 440 mb and Gledenov *et al.* obtained 575 mb.

Spokespersons: **J. Praena (UGR),**
C. Lederer-Woods (UE, UK) and
M. Sabaté-Gilarte (CERN and US)

BNCT

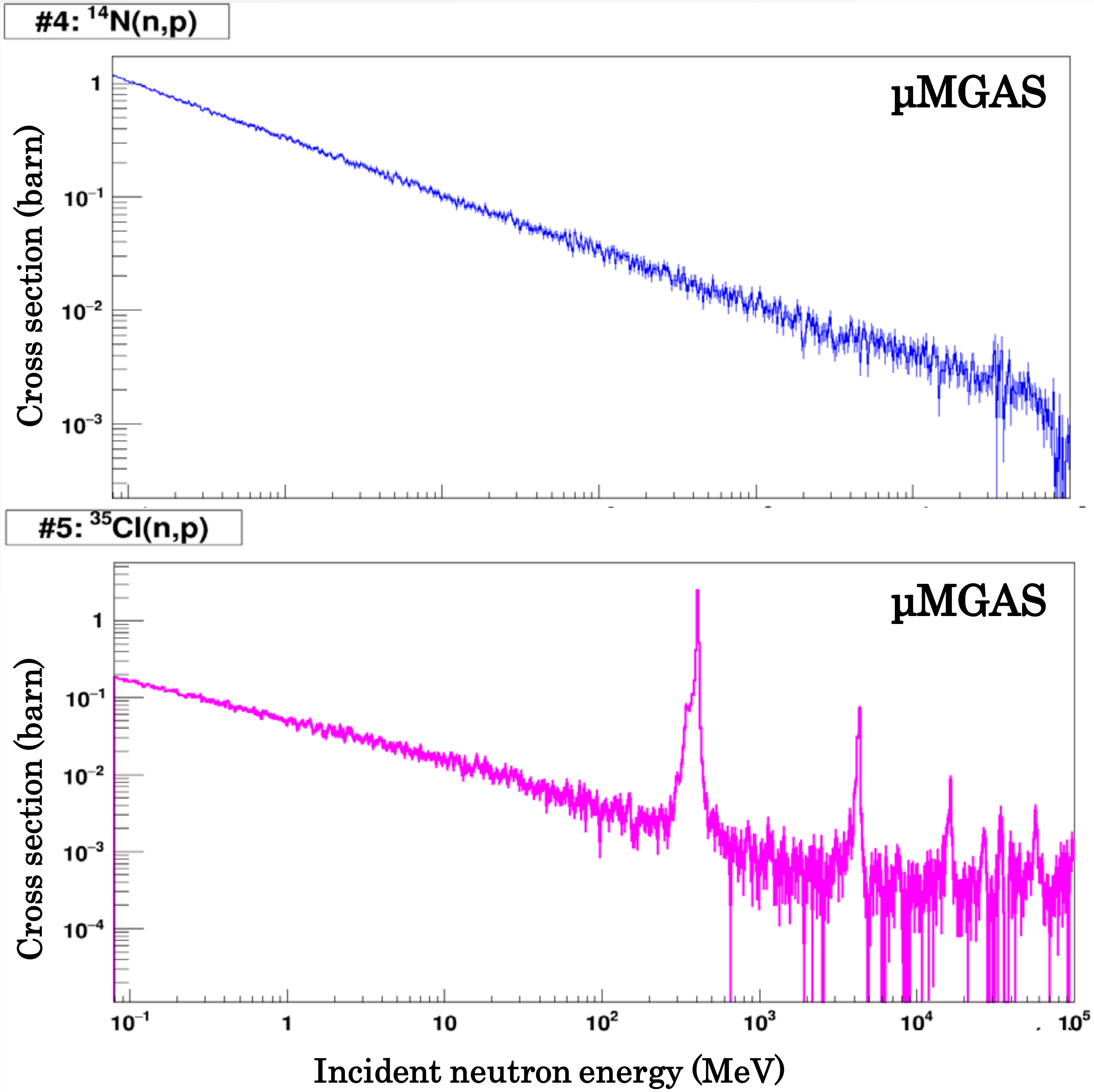


64 + 6 +1 =
71 channels!



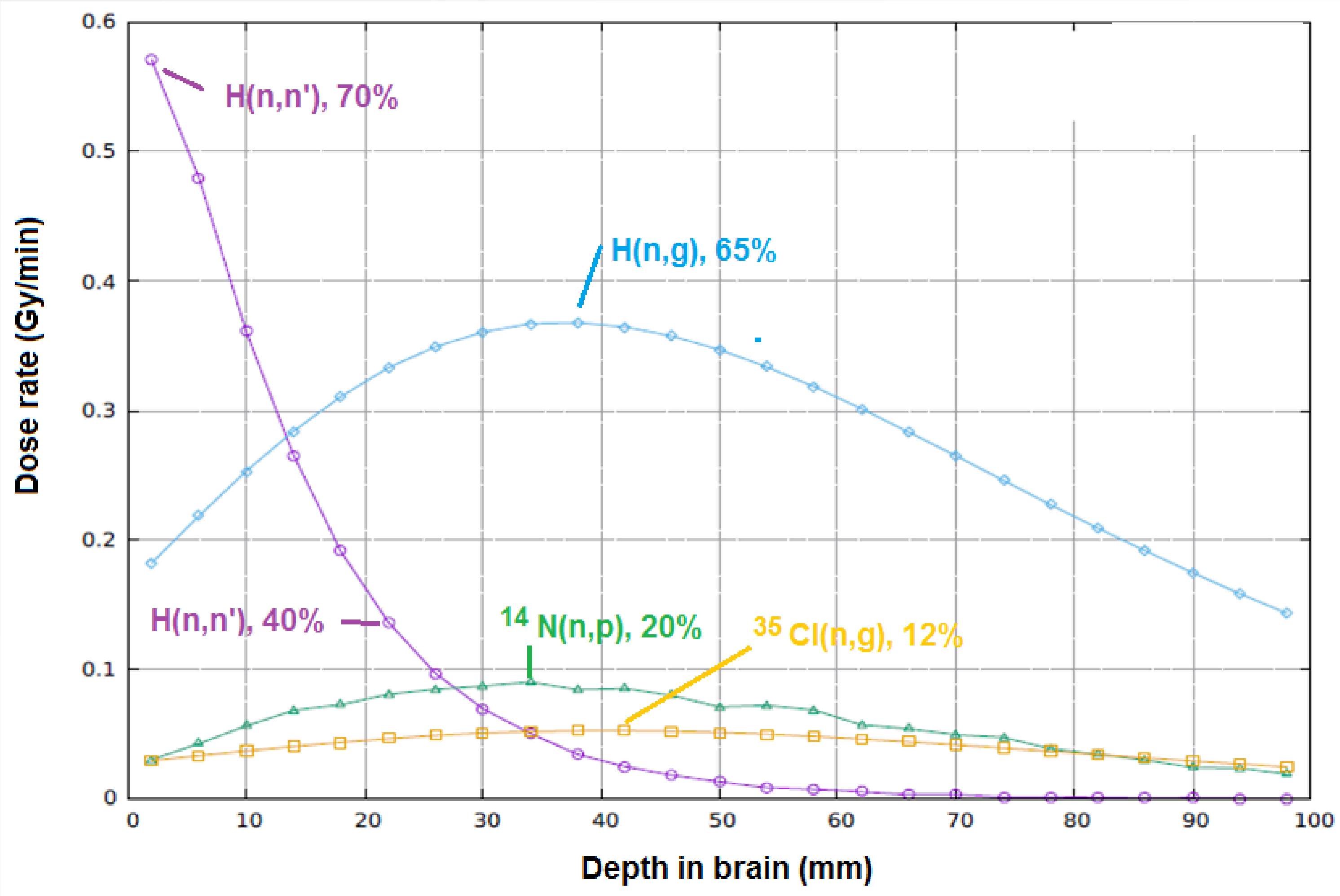
The combination of both set-ups, MMGAS and DSSSD, allows understanding possible anisotropies in the angular distribution of the reaction.

$^{14}N(n,p)$ & ^{35}Cl (n,p): ultra preliminary analysis

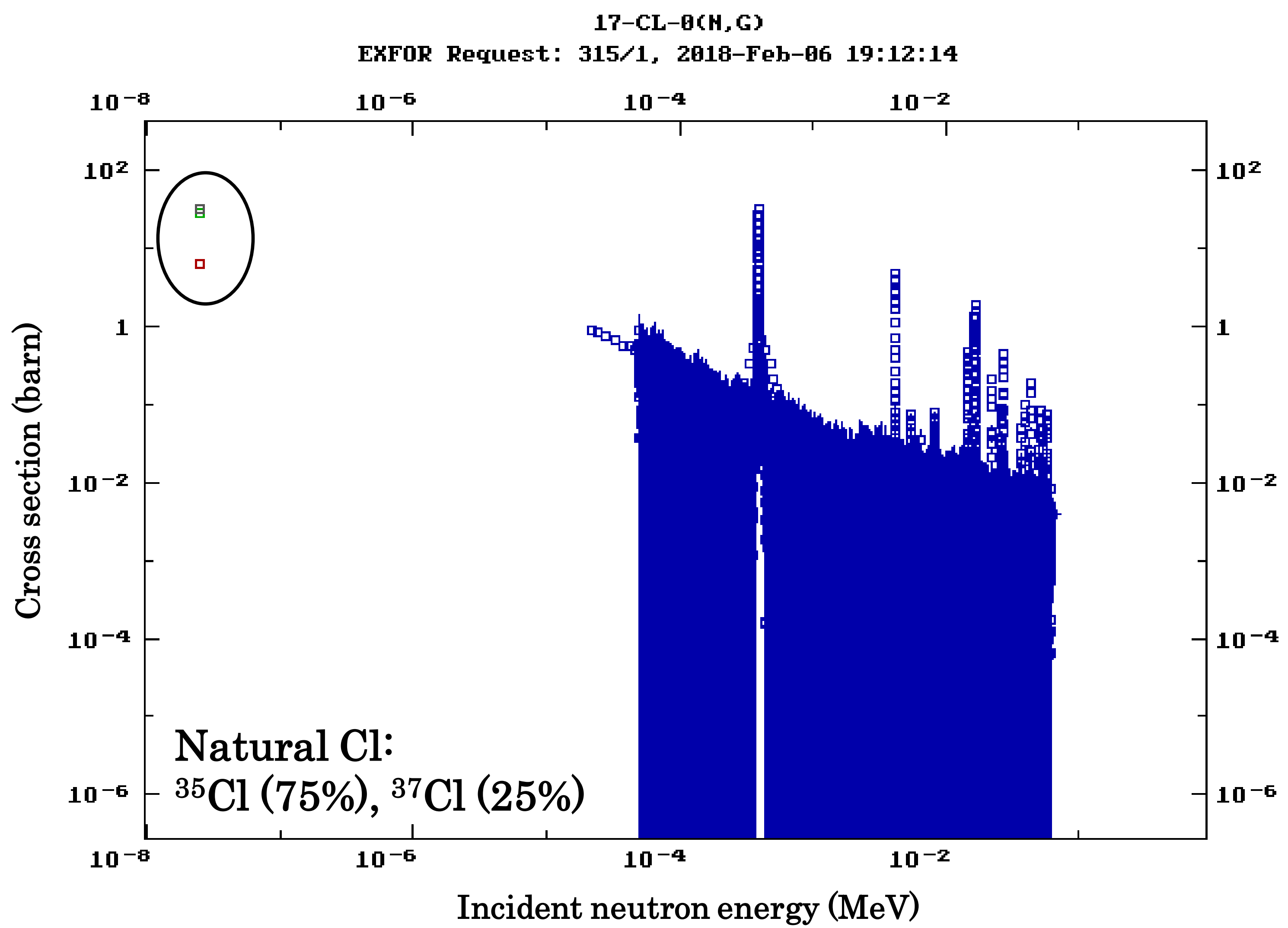


NCT: ^{35}Cl (n,γ) in healthy tissue dosimetry

- Cl is present in brain and in skin at 0.3%.
- From Monte Carlo simulations we obtained that it is important for dose calculations in **healthy tissue**



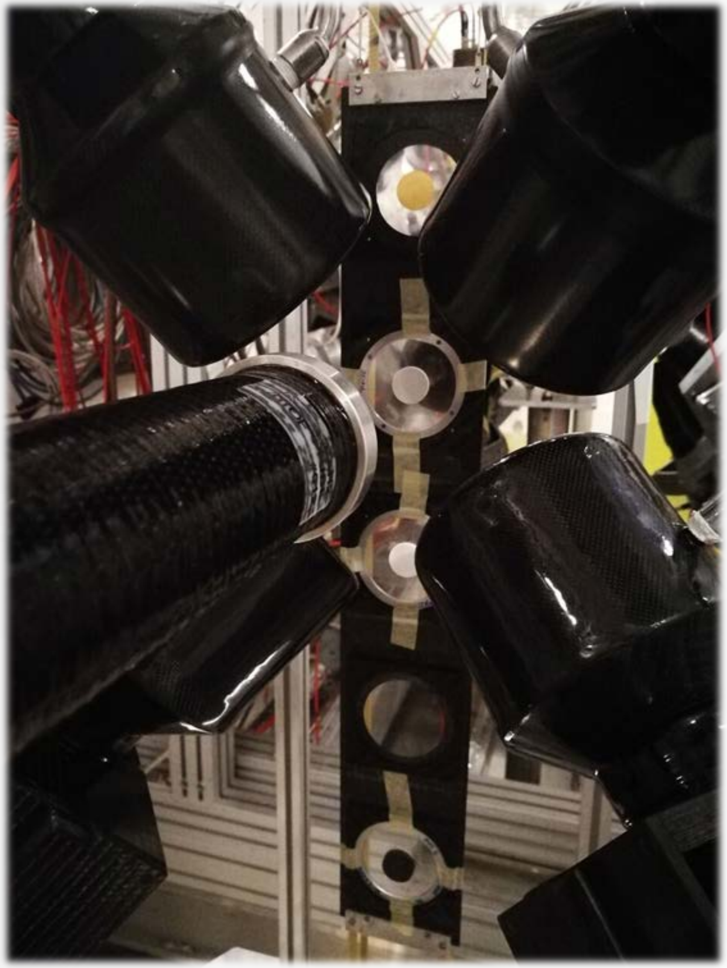
^{35}Cl (n, γ): status of the data



- Only **one capture measurement** in resonances region:
  K. H. Guber, R. O. Sayer, T. E. Valentine, et al, *Phys. Rev. C* 65, 058801 (2002)
- Discrepances in the measurements at **thermal point**.

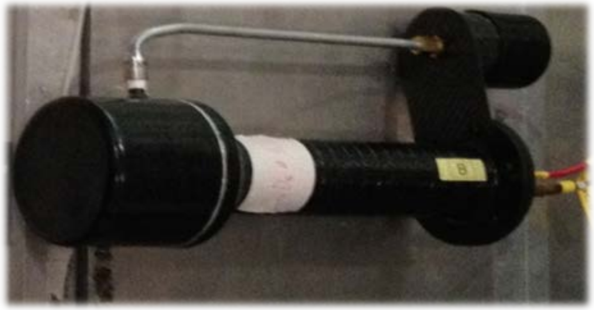
BNCT

Spokespersons: I. Porras (UGR)
T. Wright (UMAN, UK)

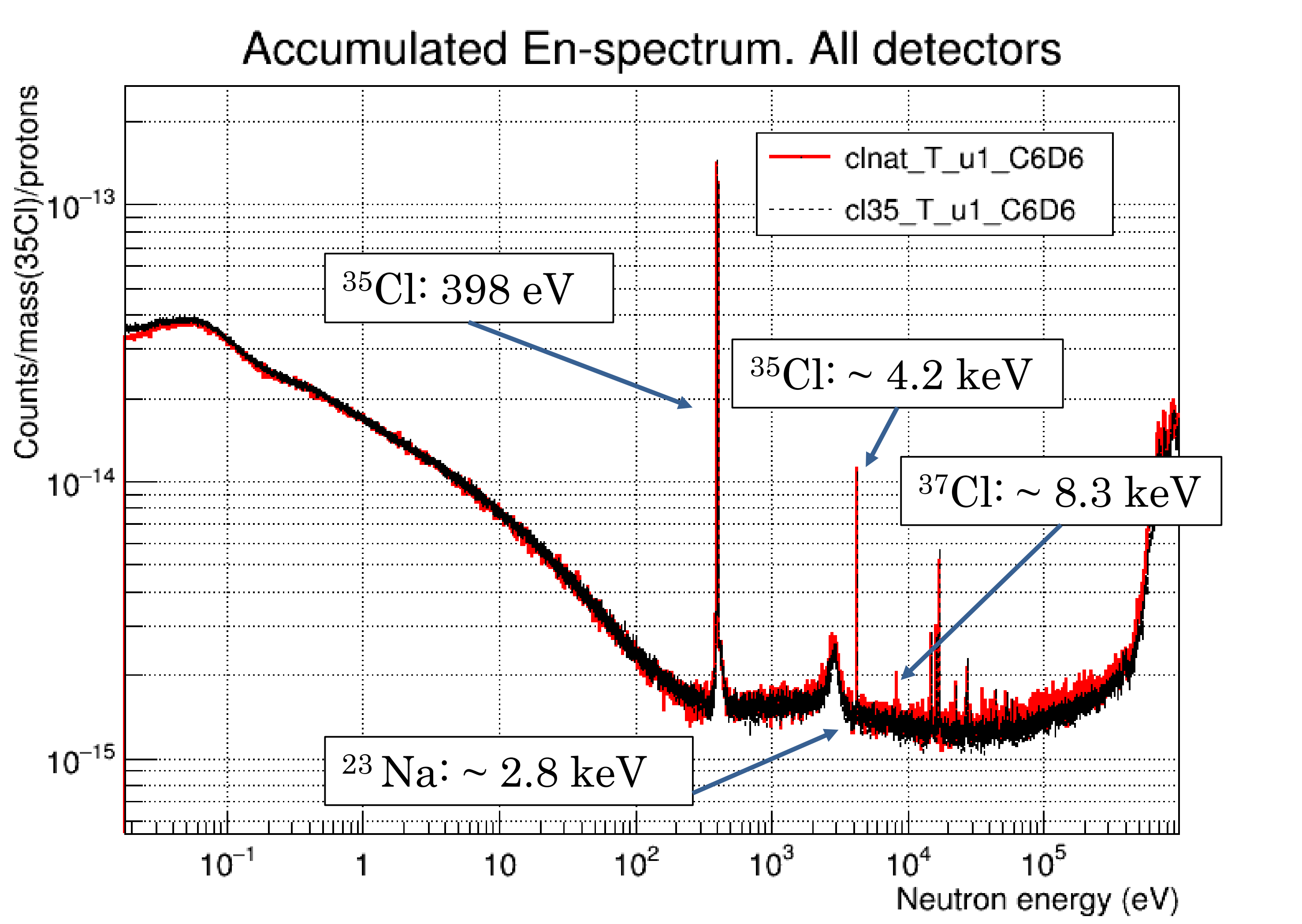


4 x **C6D6** detectors, widely used for capture measurements in n_TOF.

- 1 sample of Nat-Cl
- 1 simple of ^{35}Cl



The data analysis is still to be done.



Courtesy of Samuel Bennett (UMAN)

- NCT face a new era due to the development of accelerator-bassed NCT beams. Treatments can be improved from different perspectives:
  - Alternative and cooperative isotopes.
  - More accurate dosimetry calculations, including new contributions.
    - Neutron-induced cross section measurements
  - More effective chemical compounds to load tumour cells with ^{10}B.
  - Improve the knowledge of biological factors.
  - Etc.

- n_TOF: was the ideal facility to perform our neutron-induced cross section measurements:
  - **^{33}S(n,α)**: analysis finalised and partially published. Potential of enhancing the delivered dose to superficial tumours
  - **^{14}N(n,p)**, **^{35}Cl(n,p)** and **^{35}Cl(n,γ)**: analysis is in process. Results will be used to perform more accurate dosimetry calculations. This will ideally allow the NCT community to plan treatments capable of increasing the dose delivered to tumours, improving the chances of survival.

Thank you!

Nuclear data program for NCT at the n_TOF Collaboration at CERN

M. Sabaté-Gilarte[1,2], F. Ogállar[2,3], J. Praena[3], I. Porras[3], P. Torres-Sánchez[3], J.M. Quesada[1] and The n_TOF Collaboration[4].

1. University of Seville (Spain) 2. CERN (Switzerland)
3. University of Granada (Spain) 4. www.cern.ch/ntof

MANCHESTER 1824 The University of Manchester

THE UNIVERSITY OF EDINBURGH

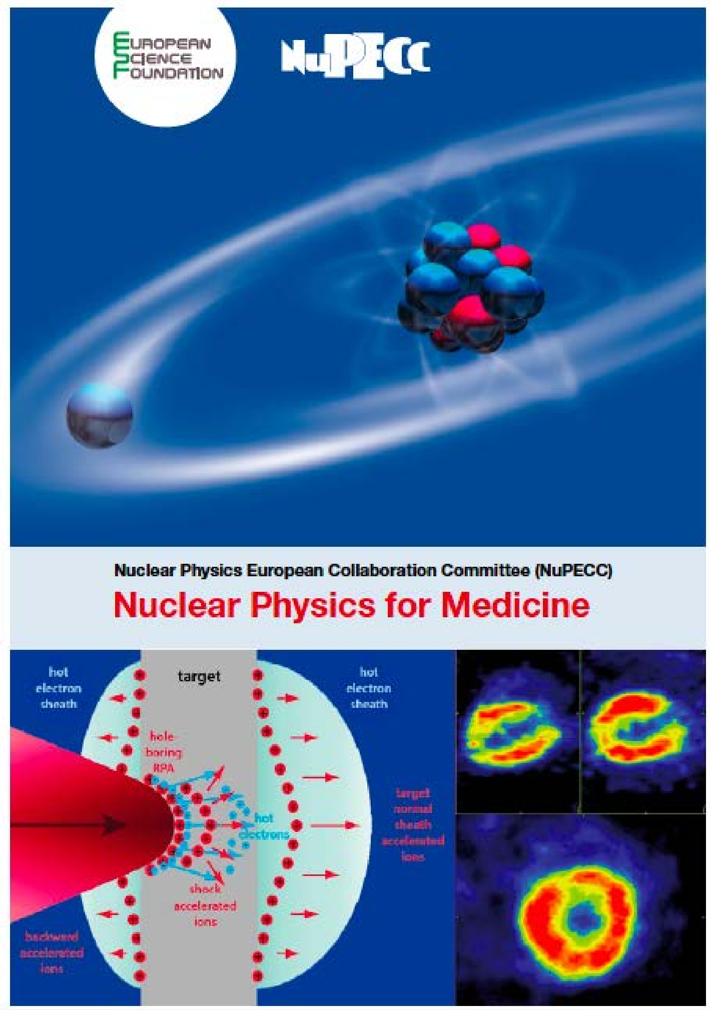
UNIVERSIDAD DE SEVILLA

UNIVERSIDAD DE GRANADA

CERN

nTOF

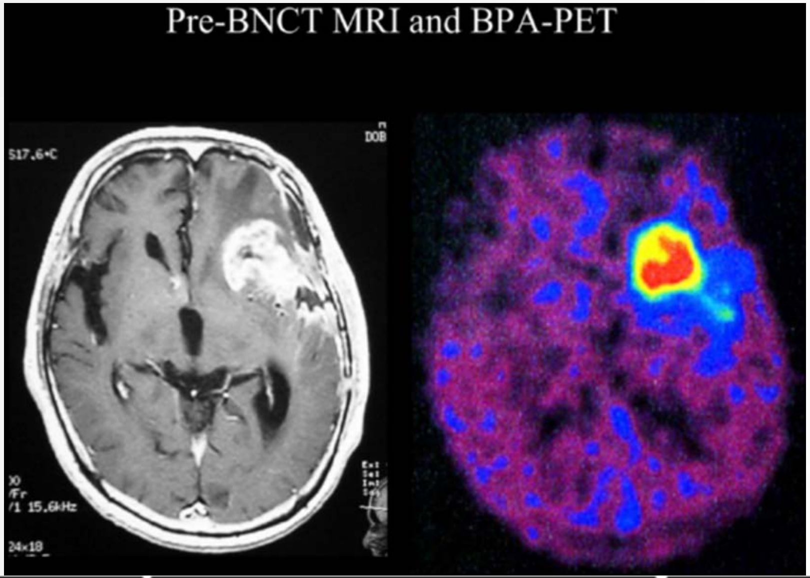
Importance of BNCT

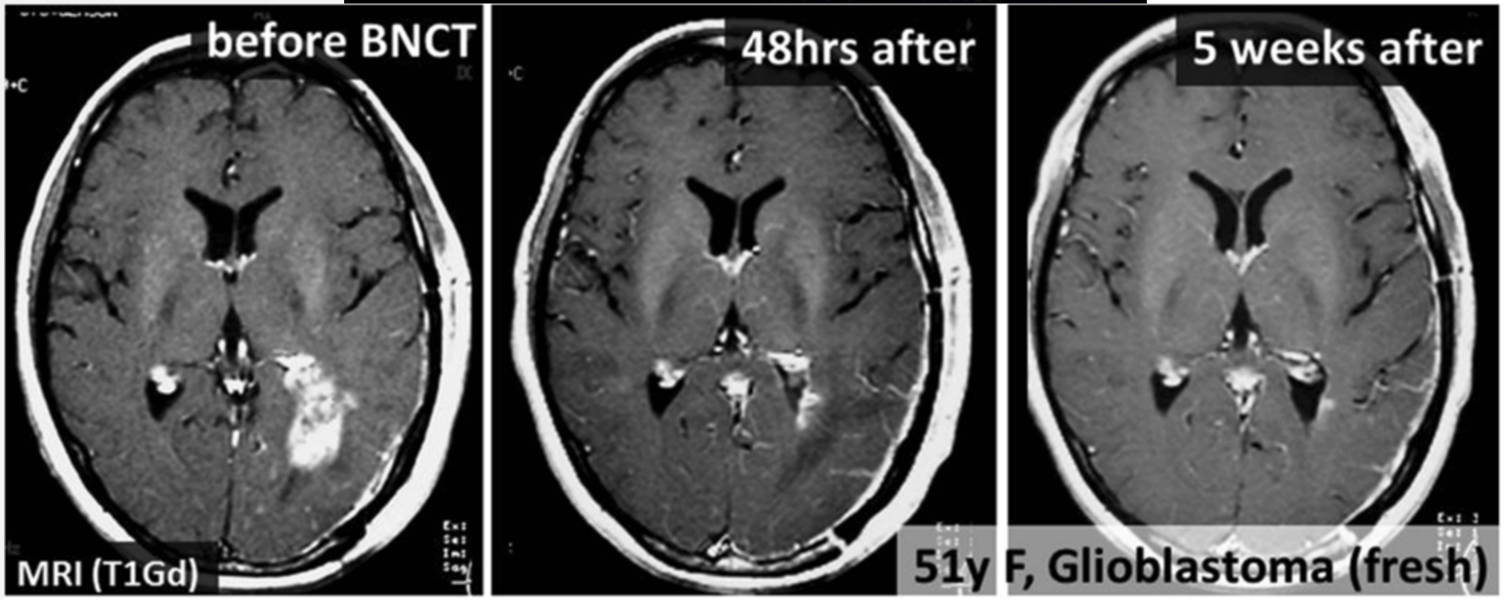


Chapter I
Hadrontherapy

Conveners: **Marco Durante** (GSI) – **Sydney Galès** (Orsay, FAIR, ELI)

BNCT: unique RT option for infiltrative tumours





BNCT: survival curves

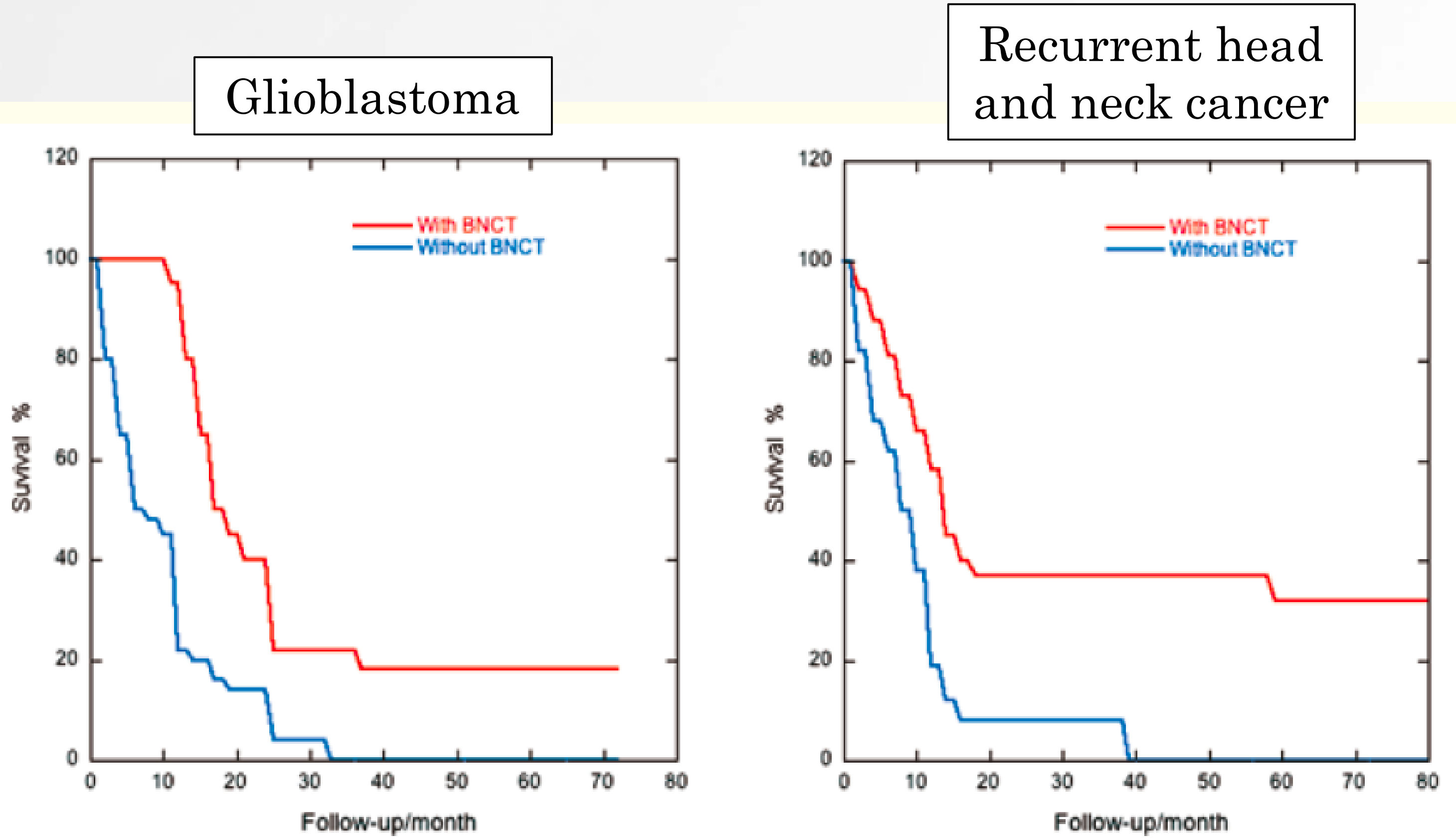
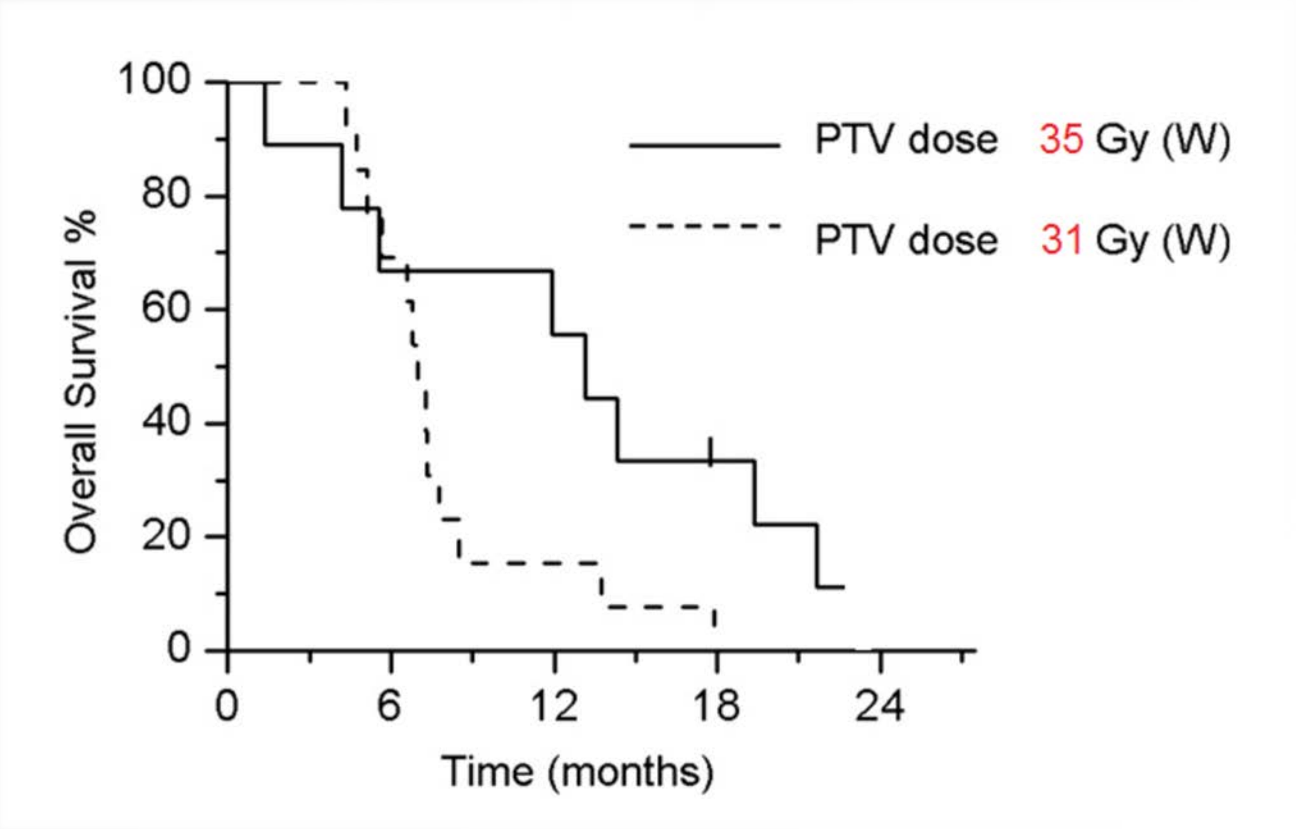


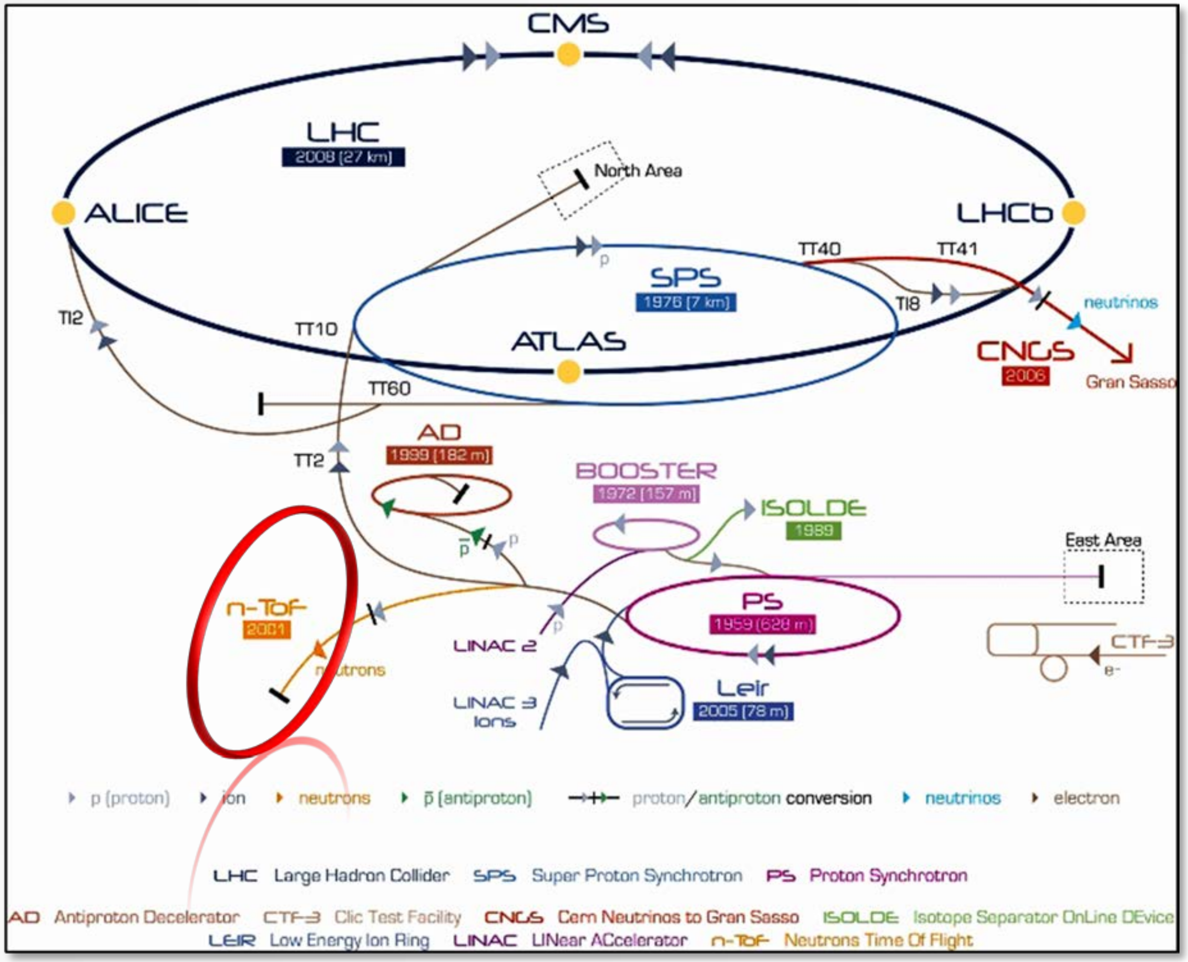
Figure 10.2. Left side, Kaplan–Meier plot of the overall survival for all newly diagnosed glioblastoma treated and not treated with BNCT [from Kawabata *et al.* (2009). Survival benefit from boron neutron capture therapy for the newly diagnosed glioblastoma patients. *Appl. Radiat. Isot.* **67**: S15-18]. Right side, Kaplan–Meier survival plots of patients with recurrent head and neck cancer treated with and without BNCT [from Kato *et al.* (2009). Effectiveness of boron neutron capture therapy for recurrent head and neck malignancies. *Appl. Radiat. Isot.* **67**: S37-42].

Adjusting delivered dose may improve outcome



The n_TOF facility at CERN

- Nominal proton intensity:
  7×10^{12} p/pulse
- Proton pulse width:
  7 ns (r.m.s.)
- Low repetition rate:
  < 0.8 Hz
- Wide energy spectrum:
  < 25 meV to 1 GeV
- Neutrons per proton:
  300
- High instantaneous flux:
  10^5-10^7 n/cm^2/pulse



The n_TOF beam lines

EAR1

- In operation since 2001.
- Horizontal beam line located at 185 m downstream from the spallation target.
- High energy resolution allowing to resolve resonances in the keV-MeV neutron energy range.
- Measuring neutron capture and neutron-induced fission cross-sections of interest in nuclear technology and astrophysics for more than 10 years.

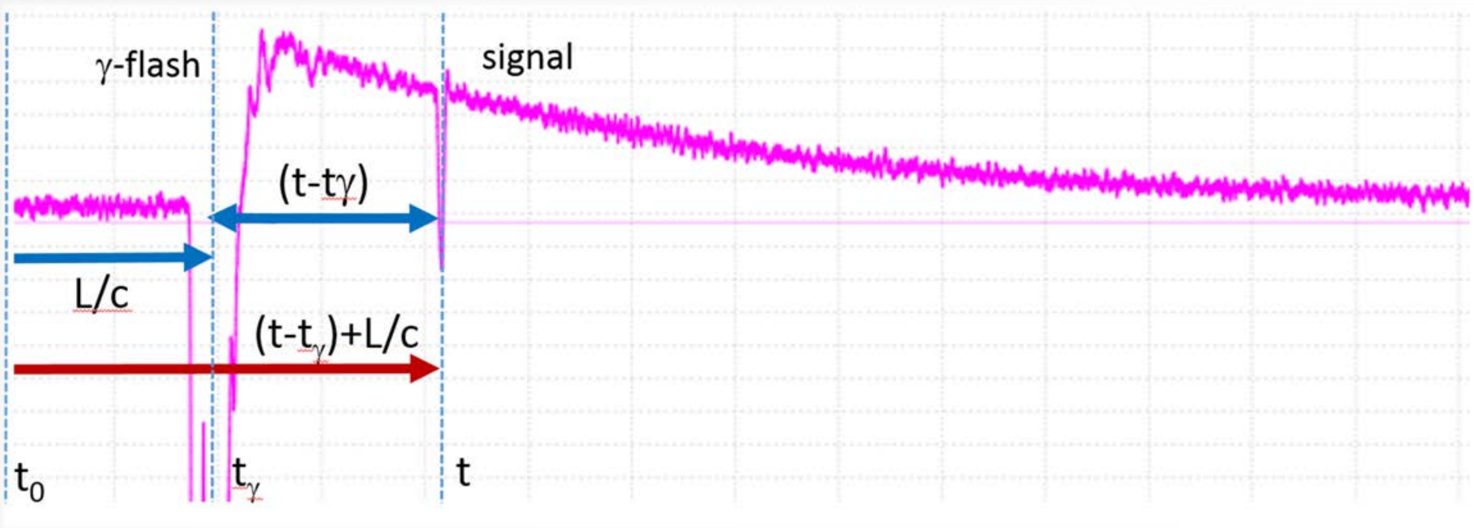
EAR2

- In operation since 2014.
- Vertical beam line above the ground placed at 19.5 m from the target.
- Running in parallel with EAR1.
- Neutron fluence increased by a factor 40 on average.
- Optimized to measure small samples (<1mg) as well as radioactive isotopes with very short half-lifes.
- Low cross section measurements.
- Shorter time scale measurement.

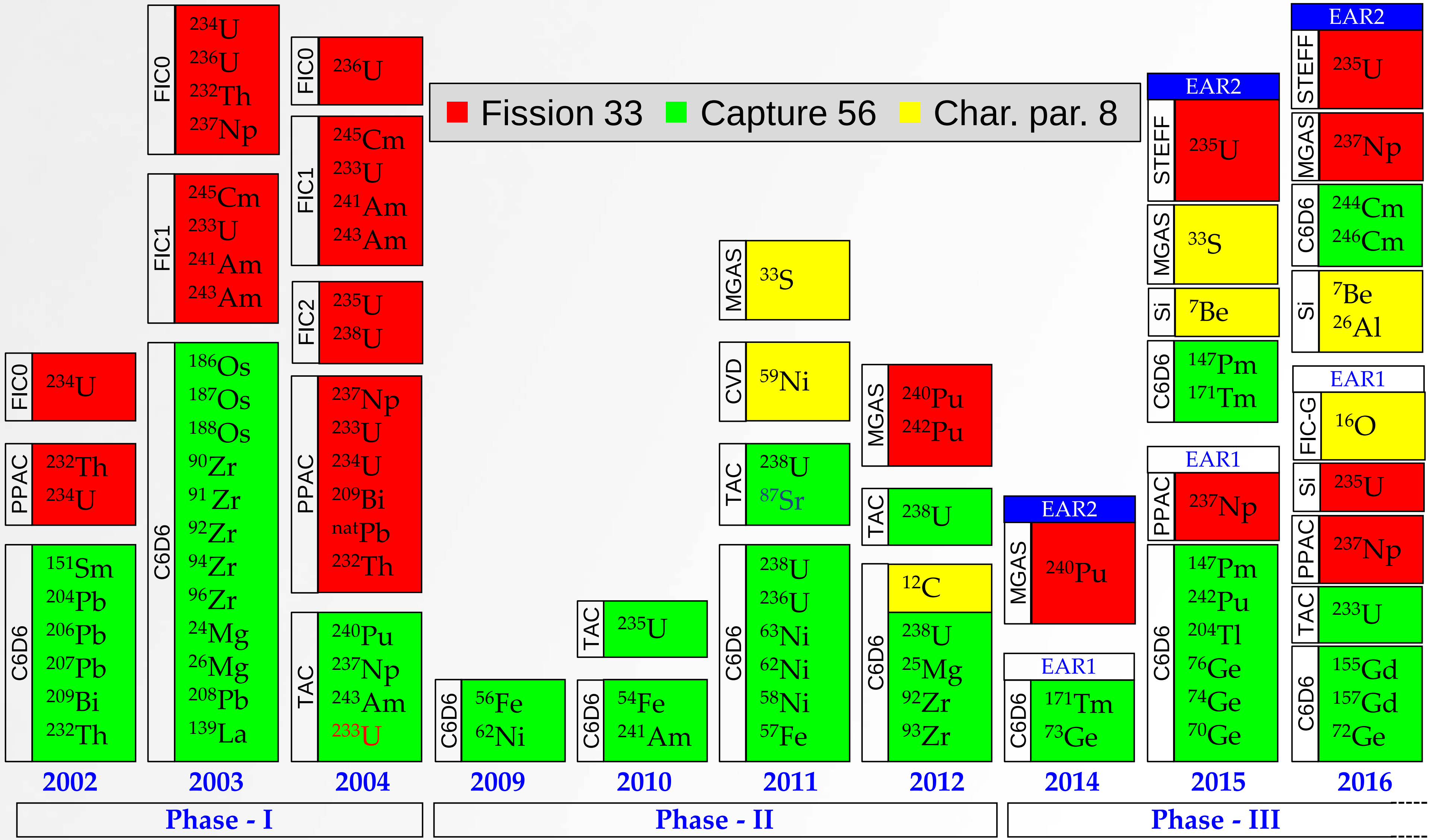
Time-of-flight technique

•TOF determination:

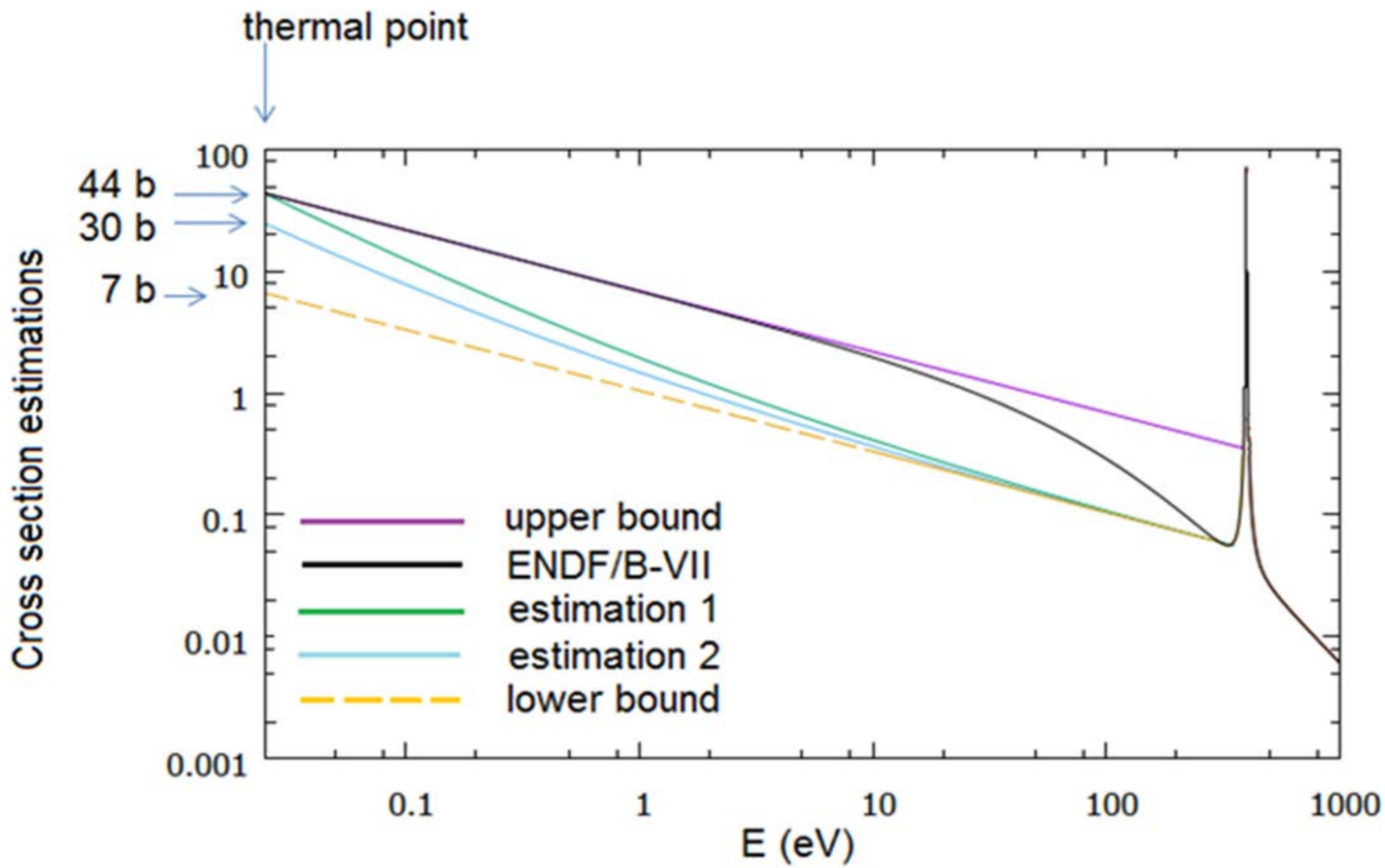
t : arrival time of the signal to the detection system
t_γ : time of the γ-flash
L : geometrical distance between the detection system and the spallation target
c : the speed of light



Program of measures since 2001



ENDF: Use **bound state** to fit the thermal value of Mughabghab.
-75 eV to -180 eV reported from different authors.
Different possibilities for low energy behaviou:



	Dose ^{35}Cl (n,γ)	%Dose ^{35}Cl(n,γ)	Total Dose
Upper bound	0.516	**12.446**	4.1830
ENDF/B-VII	0.514	**12.410**	4.1439
Estimation 1	0.551	**13.196**	4.1421
Estimation 2	0.325	**8.167**	3.9803
Lower bound	0.081	**2.162**	3.7660