From the Core of Red Giant Stars to the Edge of the Tumors







"Anselm Kiefer (German artist) is fascinated by the night sky and its different interpretations throughout history, particularly those describing it as a divine, mysterious kingdom recalling our origins and fate."

GSI-FAIR Colloquium, Darmstadt, 11/02/2025

A. Kiefer (Guggenheim M.)



- Heavy elements nucleosynthesis: How stars make gold (r-process) and lead (s-process)?
- Neutron-capture experiments at CERN n_TOF: Red-Giant stars in the lab
- Enhancing detection sensitivity in neutron capture TOF experiments
- Beyond the limits: r-process neutron-reactions in the lab?
- From stars to tumors: ion-range & dose monitoring in hadron therapy
- Summary & Outlook







[†]Based upon ¹²C. () indicates the mass number of the longest-lived isotope.

For the most precise values and uncertainties visit claaw.org and pml.nist.gov/data. NIST SP 966 (June 2024)

The origin of the elements:

Making Gold (r-process) and Lead (s-process)



Heavy Elements Nucleosynthesis: Making Gold (r-process)





The r-process: all elements at once, in a few seconds





By CDP with ROOT, modSN-Thermotrajectory from AA+GMP'21, NucNet network code, B. Meyer et al., Clemson University FRDM+QRPA (P. Möller) + JINA Reaclib Database

Most recent advanced NS-toolkit:



The r-process: all elements at once, in a few seconds







By CDP with ROOT, modSN-Thermotrajectory from AA+GMP'21, NucNet network code, B. Meyer et al., Clemson University FRDM+QRPA (P. Möller) + JINA Reaclib Database

Important neutron-capture isotopes:



Vescovi+2022



Mumpower+2016



Surman+2014

The r-process: How much gold is produced in one event?





The r-process: How much gold is produced in one event?







The slow neutron-capture process (s-process) mechanism: Fe to Pb-Bi





¹³C(⁴He,n)¹⁶O

²²Ne(⁴He,**n**)²⁵Mg

Many open questions in s-process nucleosynthesis





- C13-pocket
- Rotation
- Metallicity
- Stellar mass
- Thermal gradients





Rotating massive stars: From first stars to gamma ray bursts

André Maeder* and Georges Meynet*

Geneva Observatory, University of Geneva, 51 chemin des Maillettes, CH-1290 Versoix, Switzerland

LETTER

de 10.1056/arti-v10003

Imprints of fast-rotating massive stars in the Galactic Bulge

Criterio: Chieppi d¹ 24, 0, 47 John escht¹²⁴, Georges Meyner¹, Rephari Filoschi⁴ 5, Berrik Barbay², Massa ² graver¹, -Tarbad Devresar¹ 8 Acad² Nacad²



S. Cristallo+2014



How does it work?

Theory: Stellar model







- Heavy elements nucleosynthesis: How stars make gold (r-process) and lead (s-process)?
- Neutron-capture experiments at CERN n_TOF: Red-Giant stars in the lab
- Enhancing detection sensitivity in neutron capture TOF experiments
- Beyond the limits: r-process neutron-reactions in the lab?
- From stars to tumors: ion-range & dose monitoring in hadron therapy
- Summary & Outlook







C. Rubbia et al., *A high resolution spallation driven facility at the CERN-PS to measure neutron cross sections in the interval* from 1 eV to 250 MeV, CERN/LHC/98-02(EET) 1998. CERN n_TOF Collaboration: 150 scientists, 41 institutions worldwide n_TOF + ISOLDE = 75% of PS proton Budget (!)

(CEDNIX)		
OTOF	proton beam momentum	20 GeV/c
	intensity (dedicated mode)	8.5 x 10 ¹² protons/pulse
	repetition frequency	1 pulse/1.2s
	pulse width	б ns (rms)
	n/p	300
	lead target dimensions	80x80x60 cm ³
	cooling & moderation material	N ₂ & H ₂ O (borated)
	moderator thickness in the exit face	5 cm
	neutron beam dimension in EAR-1 (capture mode)	2 cm (FWHM)
Gen.#3 Spallation Target $< P > = 5.4 \text{ kW} \rightarrow 2.2 \text{ E}12 \text{ p/s}$		
P = 1.6 TW		
Period Period		proton beam from the PS

R. Esposito, M. Calviani et al. Phys. Rev. Acc. & Beams 24 (2021)







What we have done at n_TOF?



About 50% related to astrophysics

²⁰⁴Pb: Calibrating AGB models & "defining" the age of our Solar System



²⁰⁴Pb abundance determined by ²⁰⁴Tl(n,γ)











Mimicking stellar nucleosynthesis with a reactor to produce ²⁰⁴Tl

²⁰⁴TI (3.78y) neutron-capture at CERN n_TOF





²⁰⁴Pb abundance determined by ²⁰⁴Tl(n,γ)



A Casanovas-Hoste *et al.* (n_TOF) Physical Review Letters **133**, 052702 (2024) DOI: <u>10.1103/PhysRevLett.133.052702</u>



The uncertainty arising from the 204 Tl(n, γ) cross section on the *s*-process abundance of 204 Pb has been reduced from ~30% down to **+8%/-6%**, and the *s*-process calculations are in agreement with K. Lodders in 2021.

²⁰⁴Pb abundance of pure s-process origin:
→No need for fractionation mechanisms in early Solar system
→No need for invoking gamma-process contributions



G. Gonzalez 2014

M.Pignatari+ 2016

The ⁷⁹Se(n, γ) stellar thermometer









European

Research erc Council



2.8 g of ²⁰⁸Pb 1.0 g of ⁷⁸Se

3 mg of ⁷⁹Se 1.6 MBq of ⁶⁰Co 5 MBq of ⁷⁵Se







Preparation of PbSc targets for 79Sc neutron capture cross section studies

Nadine M. Chiera**, Emilio Andrea Maugeri*, Ivan Danilov*, Javier Babbrea-Correa*, Cesar Domingo-Pardo^b, Ulli Köster⁴, Jorge Lerendegui-Mareo^b, Mario Veicht^{4,4}, Ivan Zivadinovic^{3,4}, Dorothea Schumann³, the n₂TOF collaboration

ted televise autility, Switzerlan Sulling de Auto Corporater - Uningo Superior de Jorea Sulling Lane Langevin, Passe Saie Neproduktiger Nationale de Lancauxe, Rainevinol Régenitedate Nationale Hechardes Status, Serieurbard eier is Averlagione Gemäliger Salverint de Mähele Spain



-

New techniques for enhanced sensitivity in (n,γ) cross-section experiments



Total-Energy Detector with g-ray imaging capability (i-TED):

- Need of very high detection efficiency \rightarrow arrays of large monolithic crystals
- Need of very low neutron sensitivity → Customized design with LaCl₃(Ce) and ⁶Li-HD-PE absorbers

Final i-TED setup @ n_TOF:

3D- Spatial calibration techniques:





Neutron absorbers based on ${}^{6}Li$ enriched HD-PE: No γ -ray emission after neutron absorption by ${}^{6}Li$ (!)

Convolutional Neural Network

3D keras models for the individual crystals

Keras



Crystal read-out and electronics:



V.Babiano et al, NIM-A 931 (2019)

Optical Photons simulation

- P. Olleros *et al.* 2018 JINST13 P03014 **ML-aided 3D-position reconstruction** J. Balibrea et al. NIM-A (2020)
- In total: 20 Position-Sensitive Detectors
- 1150 cm³ of LaCl3(Ce)
- 1280 readout channels (4xKintex FPGA, 20xTOFPET2 **ASIC**s, PETsys)

Testing the gamma-ray vision capability of i-TED

Dynamic image: radioactive source in a remotely controlled XY-gantry imaged at multiple positions



Testing the gamma-ray vision capability of i-TED

Dynamic image: radioactive source in a remotely controlled XY-gantry imaged at multiple positions





High sensitivitY Measurements of key stellar Nucleo-Synthesis reactions









The ⁷⁹Se(n, γ) stellar thermometer

Comparison i-TED vs. Conventional C6D6 detectors





PRELIMINARY RESULTS – DATA ANLYSIS IN PROGRESS-

CDP, NIM-A 825 (2016), V.Babiano et al. NIM-A 953 (2020) V.Babiano-Suarez et al., EPJA, (2022) J. Lerendegui-Marco et al., EPJWC (2023)







- Heavy elements nucleosynthesis: How stars make gold (r-process) and lead (s-process)?
- Neutron-capture experiments at CERN n_TOF: Red-Giant stars in the lab
 - Enhancing detection sensitivity in neutron capture TOF experiments
- Beyond the limits: r-process neutron-reactions in the lab?
- From stars to tumors: ion-range & dose monitoring in hadron therapy
- Summary & Outlook





State-of-the-art TOF neutron-capture measurements: the limit?

EAR1 ⁷⁹Se(n, y), 2022



EAR1 ²⁰⁵Tl(n,γ), 2015



EAR1 ¹⁵¹Sm(n,γ), 2001





Limits in state-of-the-art TOF experiments:

- \rightarrow Sample > 10¹⁸ atoms
- → Sample half-life
- → Sample activity < 10 MBq</p>
- → Sample purity / enrichment
- → Neutron-induced backgrounds
- → Detector count rates < 1 MHz</p>

Important neutron-capture isotopes:



Vescovi+2022



Mumpower+2016



Surman+2014





Journal of Physics: Conference Series 2743 (2024) 012091 doi:10.1088/1742-6596/2748/1/012091

20th International Conference on Ion Sources

PHYSICAL REVIEW ACCELERATORS AND BEAMS 20, 044701 (2017)

Spallation-based neutron target for direct studies of neutron-induced reactions in inverse kinematics

René Reifarth," Kathrin Göbel, Tanja Heftrich, and Mario Weigand Goethe-Universität Frankfurt, Frankfurt am Main, 60438 Frankfurt, Germany

> Beatriz Jurado CENBG, 33175 Gradignan, France

Franz Käppeler Karlsruhe Institute of Technology, 76131 Karlsruhe, Germany

Yuri A. Litvinov GSI Helmholtzzentrum für Schwerionenforschung, 64291 Darmstadt, Germany A high-intensity, low-energy heavy ion source for a neutron target proof-of-principle experiment at LANSCE

> Androw L Couper¹, S Mosby¹, R Reiferth², A Couture¹, E Bennett¹, N Gibson¹, D Gorelov², C Keith¹, A Lovell¹, G Misch¹, and M Mumpower¹

IOP Publishing







M. Grieser et al., Eur. Phys. J Spec. Top. 207, 1 (2012)



- Heavy elements nucleosynthesis: How stars make gold (r-process) and lead (s-process)?
- Neutron-capture experiments at CERN n_TOF: AGB stars in the lab.
 - Gamma-ray imaging: Enhancing the sensitivity in neutron capture TOF experiments
- Breaking the limits: r-process neutron reactions in the lab?
- From stars to tumors: ion-range & dose monitoring in hadron therapy
- Summary & Outlook





Artist: Anselm Kiefer Guggenheim Museum, Bilbao



Therapeutic proton beams for localized tumor treatments

- → Protons: maximum dose deposition at the end of their trajectory (Bragg peak), proposed by R. Wilson in 1946
- \rightarrow Minimize damage to neighbouring tissues
- → Range uncertainties impose conservative safety margins of 3.5% + 3 mm



R. Wilson, R.R. (1946); H. Paganetti, Phys. Med. Biol. 57 (2012); U. Amaldi et al., Rep.Prog.Phys. 68 (2005); Zarifi (2019); PTCOG-2022

PET monitoring

Prompt-Gamma Imaging



→ Range verification via PET (Llacer, 1979)

- Generally based on ¹⁵O (2min), ¹¹C (20min), ¹⁰C (20s)
- Sensitive to tissue stoichiometry and mass density
- Functional character: physiological processes and tumour RF
- In-Beam PET: GSI (Enghardt+20, Parodi+02); Excellent sensitivity (2.5 mm, 10⁸p) with ¹²N (11ms) and tomographic functionality (KVI-Group, Siemens PET heads)
- Advances with secondary C-beams at GSI+LMU groups (BARB) using radioactive beams of (¹⁰⁻¹¹C) [Kostyleva+23, Boscolo+24, etc], and with ¹⁴⁻¹⁵O[Purushothaman+23].

Limitations with "conventional" proton-therapy:

- Delayed (biological washout, organ motion...)
- Not directly coinciding with the Bragg peak
- Low counting statistics (10 Bq/ml) → Low efficiency



- → Range verification via Prompt Gamma Imaging (Stichelbault&Jongen, 2003)
- Slit camera in clinical use (Smeets+12) \rightarrow 1-2 mm (1D)
- Most advanced electronic (Compton) imagers: Kabuki+09; Richard+12; Peterson+10; Kormoll+11; Thirolf+14, Llosa+13; etc
- High yield of high-energy γ-rays (2-6 MeV) at the Bragg peak → reliable signature of the ion-range
- Imaging resolution much more limited than in PET
- Low efficiency (particularly for more than two detection planes)
- Large neutron-induced backgrounds (in-beam)

PET monitoring

Prompt-Gamma Imaging



Combining PET- and Compton-imaging possible?

(1)

K. Parodi, Nucl. Instr. Meth. A (2016) γ-Ray rectastion and Methods in Physics Sevence A we could seve Contents have available as ScienceDirect Proton Nuclear Inst. and Methods in Physics Research, A 签 journal homepage www.abayler.com/locata/nime 8+ Fragment Target Prompt-gamma monitoring in hadrontherapy: A review Nucleus x-Delay 10.00 J. Krimmer*, D. Dauwergne¹1*, J.M. Létang*, É. Testa* We, Developed as Specific International Control (2007) 2020/2020, FCMCC Manaharan, Parma The overlap of the second secon w New? COMERCIAN STREET, AND AND Contents line as its is at ScienceDirect

2.3. Specificity of PG imaging

Table 2 presents the specificities of PG cameras for hadrontherapy with respect to conventional medical imaging. It is clear from these specificities that dedicated cameras are needed, with special features like high energy detection capability and count rate capability, and data acquisition systems that have to be adapted to the beam time structure.

For the particular objective of the precision for the falloff determination in the 1D-profile, the background plays a major role. Indeed, if we describe the falloff features in terms of contrast *C*, falloff width *FW* and background level *B*, it has been shown that the falloff retrieval precision *FRP* is determined by the following equation for homogeneous targets [32]:

$$FRP = \frac{\sqrt{B}}{C} = \frac{1}{\sqrt{N}}$$

where *N* is the number of incident ions. A striking result is that the falloff width has no influence on the *FRP*. This means that the priority when optimizing camera designs is the detection efficiency and the background rejection (shielding, TOF_{result}).

As we will see in Section 4, detection efficiencies of PG cameras – ranging from 10^{-5} (collimated cameras) to 10^{-4} (Compton cameras) – will lead to relatively low numbers of detected PG at spot level for pencil beam scanning systems.



- High detection efficiency → Online real-time proton-range verification
- Low sensitivity to n-induced backgrounds \rightarrow Improved S/B-ratio
- Good performance in the gamma-ray energy range up to 5-6 MeV
- Compact & lightweight → Compatible with clinical environment

Heidelberg Hadrontherapy Center





Hybrid **PGI-PET** technique and **pulsed beams**



- → Clinical proton-beam energy (55-200 MeV)
- → Clinical proton-intensity (10⁸ p/point)



MC-Study: <u>J. Lerendegui-Marco, et al. Nat. Sci. Rep. 12, 2735 (2022)</u> PoC @ 18 MeV: <u>J. Balibrea-Correa, et al. EPJ-Plus (Nov.2022)</u>



55 MeV p-beam 10⁹ p/spot on Graphite Target @ three positions



J. Balibrea-Correa, J. Lerendegui-Marco, et al. (HIT, USe) (publication in review)

55 MeV p-beam 10⁹ p/spot on Graphite Target @ three positions / Compton PGI:



isidelberger innenstrahl Therapiegentrum

J. Balibrea-Correa, J. Lerendegui-Marco, et al. (HIT, USe) (publication in review)

150 MeV p-beam 10⁹ p/spot on PE-Target @ three positions



ridelberzer inner strak i Therapiezentrum

→ Improve geometry → Higher statistics/spot → Suppress background → Better S/B

J. Balibrea-Correa, J. Lerendegui-Marco, et al. (HIT, USe) (publication in review)

First PET-Compton pre-clinical tests at WPE



Universitätsmedizin Essen Universitätsklinikum





PET Calibration:





Prel. Est. < 2mm sensitivity for 1E8 p

Isochronous Normal Conducting Cyclotron (**IBA-ProteusPlus**) @ WPE



First PET-Compton pre-clinical tests at WPE



Universitätsmedizin Essen Universitätsklinikum



Compton PGI: iTED A: +0mm 200 100



Prel. Est. <4mm sensitivity for 1E8 p

 \rightarrow Possible to combine Compton & PET with same apparatus using a cyclotron-based machine \rightarrow Data analysis in progress (!)



Dosimetry with therapeutic <u>neutron fields</u>



AMA





- Regular patient treatment: 2 (Japan)
- Clinical trial: 6 (Japan, China, Korea, Taiwan)
- Commissioning, Development & Construction

- **BNCT** is an emerging treatment that aims at improving the therapeutic ratio for traditionally difficult to treat tumors.
- Clinically: Glioblastoma multiforme, meningioma, head, neck, lung, breast cancers, etc [Malouff+21]

Dosimetry in BNCT presents challenges:

- Neutrons interaction within the body
- Uncertainties associated with the uptake of boron.
- **Current treatment planning:** strong extrapolations of boron uptake by the tumor derived from prior PET scans.

Solution?: online boron-uptake monitoring and spatial distribution via the Compton imaging of the 478 keV line

Challenges:

0

- Very large count rates (MHz at 50 cm)
- Neutron-induced backgrounds

Dosimetry with therapeutic neutron fields

- Highly demanding online 3D-reconstruction
- New algorithms required for guasi-real time imaging

Next steps:

- first tests at clinical facility

PRELIMINARY RESULTS

- WORK IN PROGRESS
- B. Gameiro et al. (2024) https://doi.org/10.48550/arXiv.2411.04785

P. Torres-Sanchez et al. (2024) https://doi.org/10.1016/j.apradiso.2024.111649

J. Lerendegui-Marco et al. (2024) https://doi.org/10.48550/arXiv.2409.05687

ERC POC-Grant: Advanced imaging system for Medical Applications (AMA) (Grant No. 101137646)

Summary & Outlook

VNIVERSITAT ØØVALÈNCIA

CSIC

Thanks to all collaborators and funding agencies

O. Aberle¹ V. Alcayne² S. Amaducci^{3,4} J. Andrzejewski⁵ L. Audouin⁶ V. Babiano-Suarez⁷ M. Bacak^{1,8,9} M. Barbagallo^{1,10} S. Bennett¹¹ F Berthoumieux9 J Billowes¹¹ D. Bosnar¹² A. Brown¹³ M Busso^{10,14,15} M. Caamaño¹⁶ L. Caballero-Ontanava⁷ F. Calviño¹⁷ M. Calviani¹ D Cano-Ott² A. Casanovas¹⁷ F. Cerutti¹ E. Chiaveri^{1,11} N. Colonna¹⁰ G. Cortés¹⁷ M. A. Cortés-Giraldo18 L. Cosentino³ S. Cristallo14,19 L. A. Damone^{10,20} P. J. Davies¹¹ M. Diakaki^{21,1} M. Dietz²⁴ A Ventura³⁴ D. Vescovi^{10,14} V. Vlachoudis¹

C. Domingo-Pardo7 I. Ladarescu⁷ R. Dressler²³ Q. Ducasse²⁴ H. Leeb⁸ E. Dupont⁹ I Durán¹⁶ S J I onsdale²² Z. Eleme²⁵ D. Macina¹ B. Fernández-Domínguez¹⁶ A. Manna^{34,35} A. Ferrari¹ T. Martínez² P Finocchiaro³ A Masi¹ V. Furman²⁶ C. Massimi^{34,35} K. Göbel²⁷ P. Mastinu³⁶ R. Garq²² M. Mastromarco¹ A. Gawlik⁵ E. A. Maugeri²³ S. Gilardoni¹ A. Mazzone^{10,37} I. F. Gonçalves²⁸ F Mendoza² E. González-Romero² A. Mengoni³⁸ C. Guerrero¹⁸ V. Michalopoulou^{21,1} P. M. Milazzo³⁹ F. Gunsina9 H. Harada²⁹ F. Minarone¹ S Heinitz²³ J Moreno-Soto⁹ J. Heyse³⁰ A. Musumarra^{3,40} D. G. Jenkins¹³ A. Negret⁴¹ A. Junghans³¹ R. Nolte²⁴ F. Käppeler³² F. Ogállar42 Y. Kadi¹ A. Oprea⁴¹ A. Kimura²⁹ N. Patronis²⁵ I. Knapová³³ A. Pavlik⁴³ M. Kokkoris²¹ J. Perkowski⁵ Y. Kopatch²⁶ L. Persanti^{10,14,19} M. Krtička³³ C Petrone⁴¹ D. Kurtulgil²⁷ E. Pirovano²⁴

C. Lederer-Woods²² J. Lerendequi-Marco¹⁸

J. Praena42 J. M. Quesada¹⁸

I. Porras⁴²

- D. Ramos-Doval⁶
- T Rauscher^{44,45}
- R. Reifarth²⁷
- D. Rochman²³
- Y. Romanets²⁸
- C Rubbia¹
- M. Sabaté-Gilarte^{18,1}
- A. Saxena⁴⁶
 - P. Schillebeeckx³⁰
 - D. Schumann²³
 - A. Sekhar¹¹
 - A. G. Smith¹¹
 - N. V. Sosnin¹¹
 - P. Sprung²³
 - A. Stamatopoulos²¹
 - G. Tagliente¹⁰
 - J I Tain⁷
 - A. Tarifeño-Saldivia¹⁷ L. Tassan-Got^{1,21,6}
 - Th. Thomas²⁷
 - P. Torres-Sánchez42
 - A. Tsinganis¹
 - J. Ulrich²³
 - S. Urlass^{31,1}
 - S. Valenta³³
 - G Vannini^{34,35}
 - V Variale¹⁰
 - P. Vaz²⁸

The n_TOF Collaboration

European Research Council

ERC-CoG HYMNS Grant Id. 681740 ERC-POC AMA Grant Id. 101137646 ERC-POC GNVISION Grant Id.101113330

HIT

R. Vlastou²¹

A. Wallner⁴⁷

T. Wriaht¹¹

P. Žugec¹²

P. J. Woods²²

