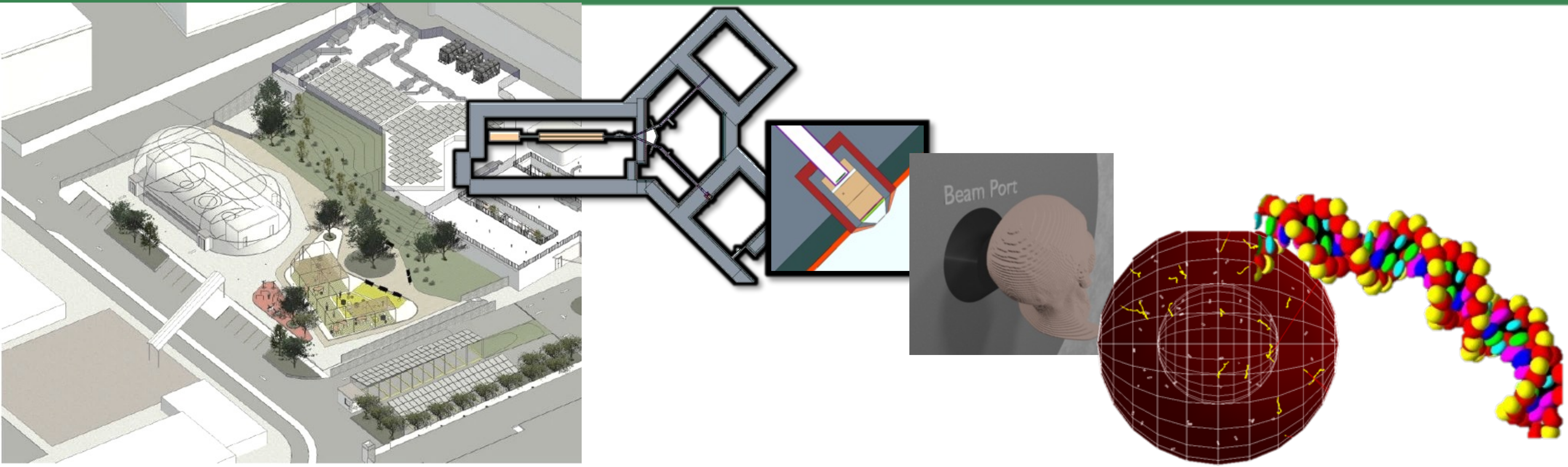
Ministero dell'Università e della Ricerca

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

PNC
Piano nazionale per gli investimenti complementari al PNRR
Ministero dell'Università e della Ricerca

Anthem
AdvaNced Technologies for Human-centEred Medicine



Translational BNCT: Coupling Experimental Radiobiology with Model-Based Dosimetry

Postuma Ian – ian.postuma@infn.it

SIRR International Day: 2025 - Simulation and Biological Damage prediction - 6.10.2025 - Catania

S. Bortolussi, I. Postuma, S. Fatemi, B. Marcaccio, R. Ramos, C. Pezzi, G. Garini, A. Kourkoumeli Charalampidi, A. Lanza, C. Ferrari, L. Cansolino, E. Delgrosso, U. Anselmi Tamburini, M. P. Demichelis, P. Sommi, A. Pisent, E. Fagotti, L. Bellan, F. Grespan, C. Baltador, J. Esposito, P. Mastinu, V. Conte, A. Selva, A. Bianchi, Y. Ong, P. Mereu, M. Nenni, C. Mingioni, E. Nicoletti, T. Bencivenga, A. Retico, D. Imperio, L. Panza, L. Gialanella, A. D'Onofrio, L. Bagnale, D. Pistone, G. Porzio, R. Buompane, C. Sabbarese, M.R. Masullo, A. Passarelli, L. Manti, S. Pacifico, E. Nigro, S. Piccolella, A. Capuano, L. Altucci, V. Carafa, M. Crepaldi, C. Papulino, E. Martinelli, N. Del Gaudio, S. Cappabianca, M. Barbieri, L. Sciciola, G. De Matteis, S. Di Giacomo, S.J. Gonzalez, A.M. Portu, G.A. Santa Cruz, I. Porras, P. Torres-Sánchez, Y-H. Liu, D. Shu, J. Pan, M. Ying, C. Geng, X. Tang, K. Chatzipapas, P. Cirrone, S. Fattori, G. Cuttone, S. Paleari, G. Paolisso and **V. Vercesi**

Ministero dell'Università e della Ricerca

Italiadomani
PIANO NAZIONALE DI RIPRESA E RESILIENZA

PNC
Piano nazionale per gli investimenti complementari al PNRR
Ministero dell'Università e della Ricerca

Anthem
AdvaNced Technologies for Human-centEred Medicine

南京航空航天大学
1952
NUAA

Dan Beninson
Instituto de Tecnología Nuclear

UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Università degli Studi di Napoli
Federico II

CNEA
Comisión Nacional de Energía Atómica

CONICET

UNIVERSITAS GRANATENSIS
1531
UNIVERSIDAD DE GRANADA

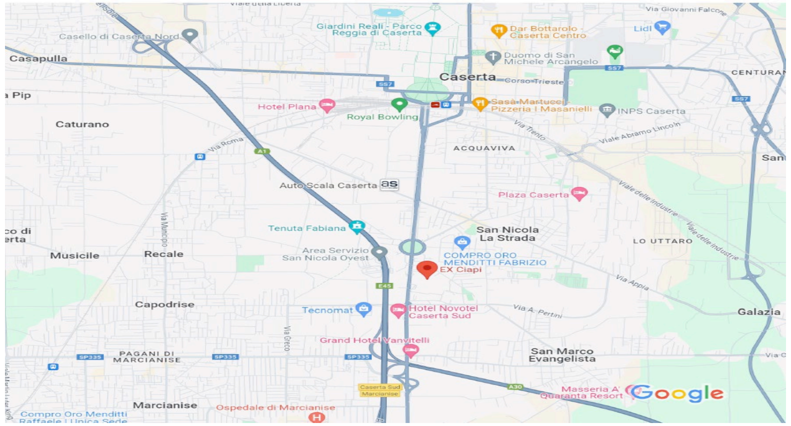
UNIVERSITÀ DI PAVIA

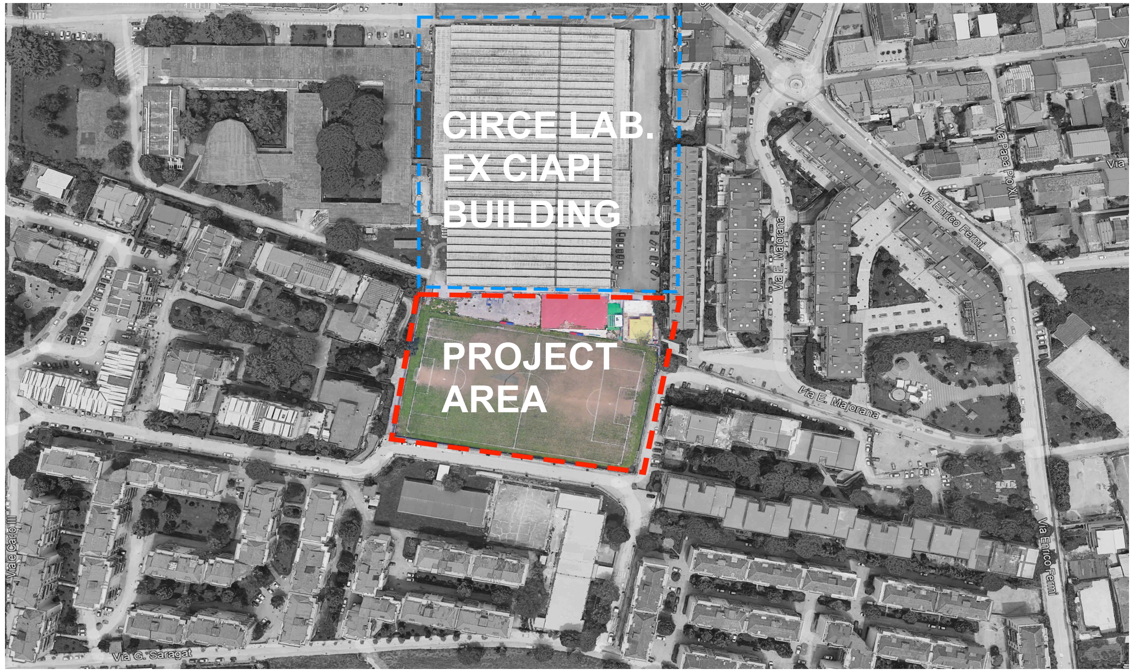
NEUBORON
中硼医疗

ALCOTEC

厦门弘爱医院
XIAMEN HUMANITY HOSPITAL

Design of a new building for BNCT near Caserta, in San Nicola La Strada. The project area is adjacent the *CIAPI* building where the CIRCE laboratory of the University of Campania Luigi Vanvitelli is placed together with some other INFN installations.





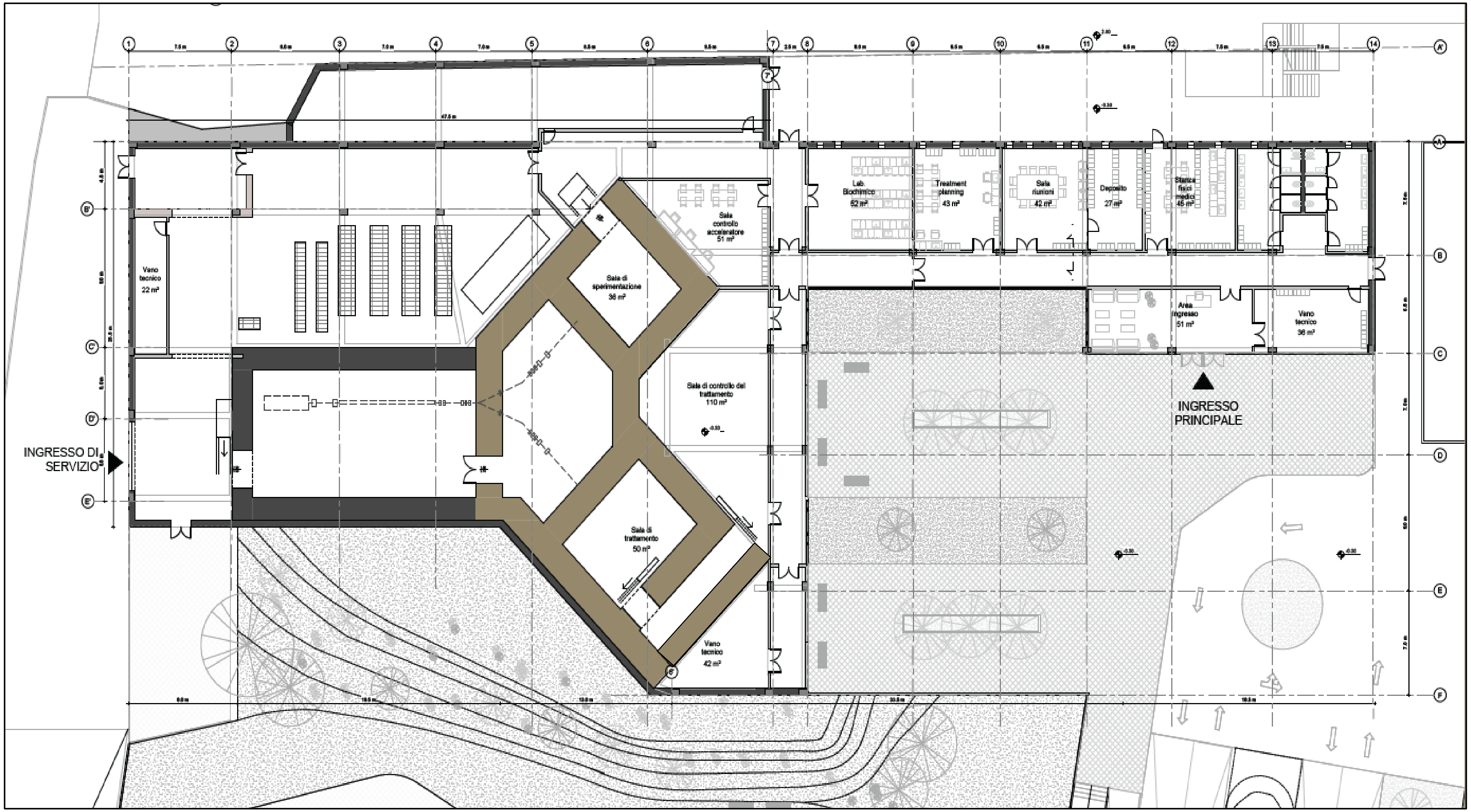
The Centre will be the first facility of this kind in all the central and southern Italy (6 clinical centres treating patients in the world, more than 20 in construction for research and/or clinics) and the only one fully based on public funds

Università degli Studi della Campania Luigi Vanvitelli

ALCOTEC

INFN
Istituto Nazionale di Fisica Nucleare

FUNCTIONAL LAYOUT–PHASE1



The proposed *technical solutions* are intended to be indicative and will be carefully evaluated during the final and/or executive development phase of the project.

Ministero dell'Università e della Ricerca | Italiadomani PIANO NAZIONALE DI RIPRESA E RESILIENZA | PNC Piano nazionale per gli investimenti complementari al PNRR Ministero dell'Università e della Ricerca | Anthem AdvaNced Technologies for Human-centEred Medicine

Prot. n. 160185 del 11/09/2025

PROGRAMMA REGIONALE FESR

PR CAMPANIA FESR 2021-2027 - ASSE 1 - OBIETTIVO SPECIFICO 1.1
AZIONE 1.1.4

Schema

Accordo di Collaborazione
per la realizzazione dell'intervento
"Realizzazione del bunker necessario all'attuazione del progetto "ANTHEM"

- con DGR n. 437 del 6 agosto 2024 - programmazione risorse, è stato programmato l'importo massimo di € 10.000.000,00 (dieci milioni/€), a valere sulle risorse del PR Campania FESR 2021/2027, Obiettivo Specifico 1.1 "*sviluppare e rafforzare le capacità di ricerca e di innovazione e l'introduzione di tecnologie avanzate*" - Azione 1.1.4 *"sostenere la sperimentazione diffusa e la domanda di innovazione della PA per la definizione di prodotti innovativi a beneficio di imprese e cittadini"*, a favore dell'Università della Campania "Luigi Vanvitelli", per la realizzazione del bunker destinato ad accogliere l'impianto di terapia a cattura di neutroni con boro (BNCT), realizzato nell'ambito del progetto "ANTHEM", finanziato con il Decreto del Ministro dell'Università e della Ricerca n. 1983/2022;

Letto confermato e sottoscritto per la Regione

PASQUALE MANDUCA
Regione Campania
Dirigente
11.09.2025 11:14:51
GMT+02:00

Approvati dal CdA dell'Università Vanvitelli a luglio 2025

Convenzione con Regione Campania per il trasferimento dei fondi

Gara d'appalto integrato per la costruzione dell'edificio

Bando pubblicato 1° di Ottobre sulla Gazzetta Europea

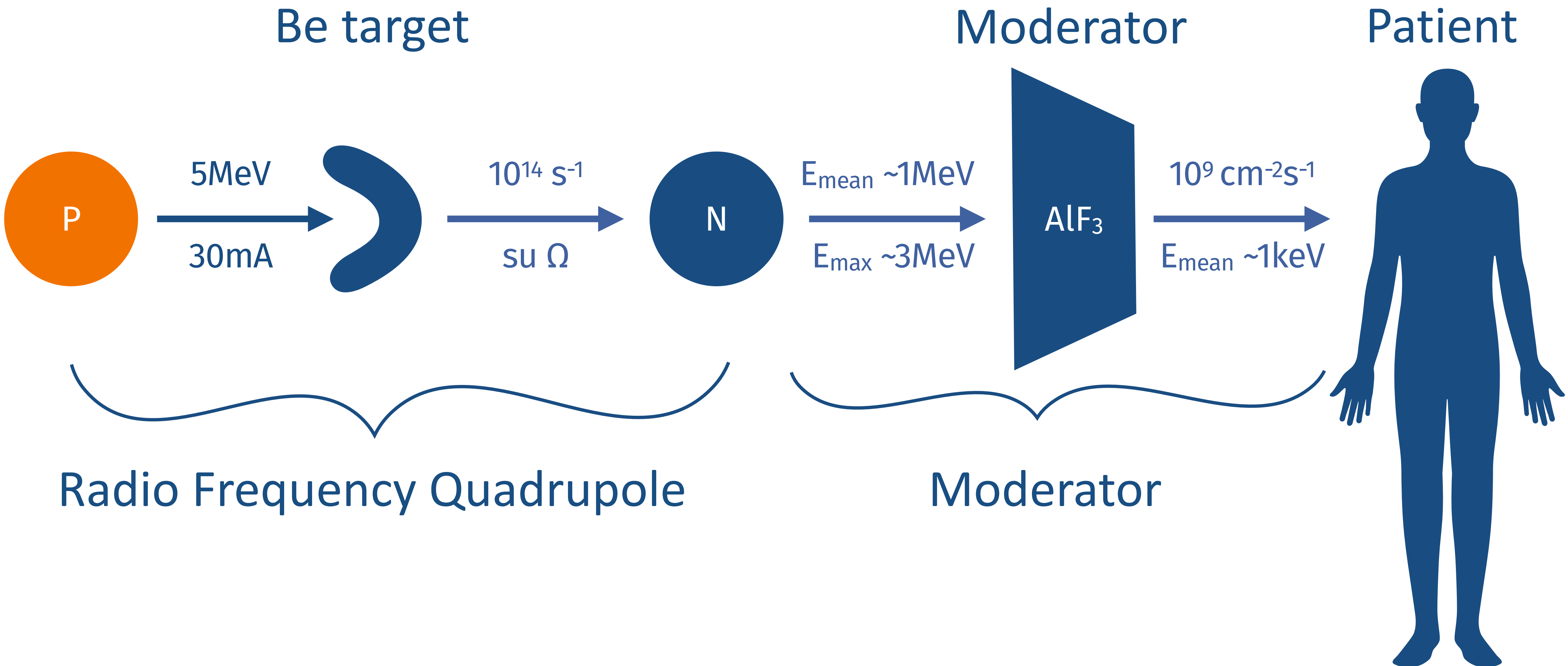
638716-2025 - Gara

See the notice on TED website

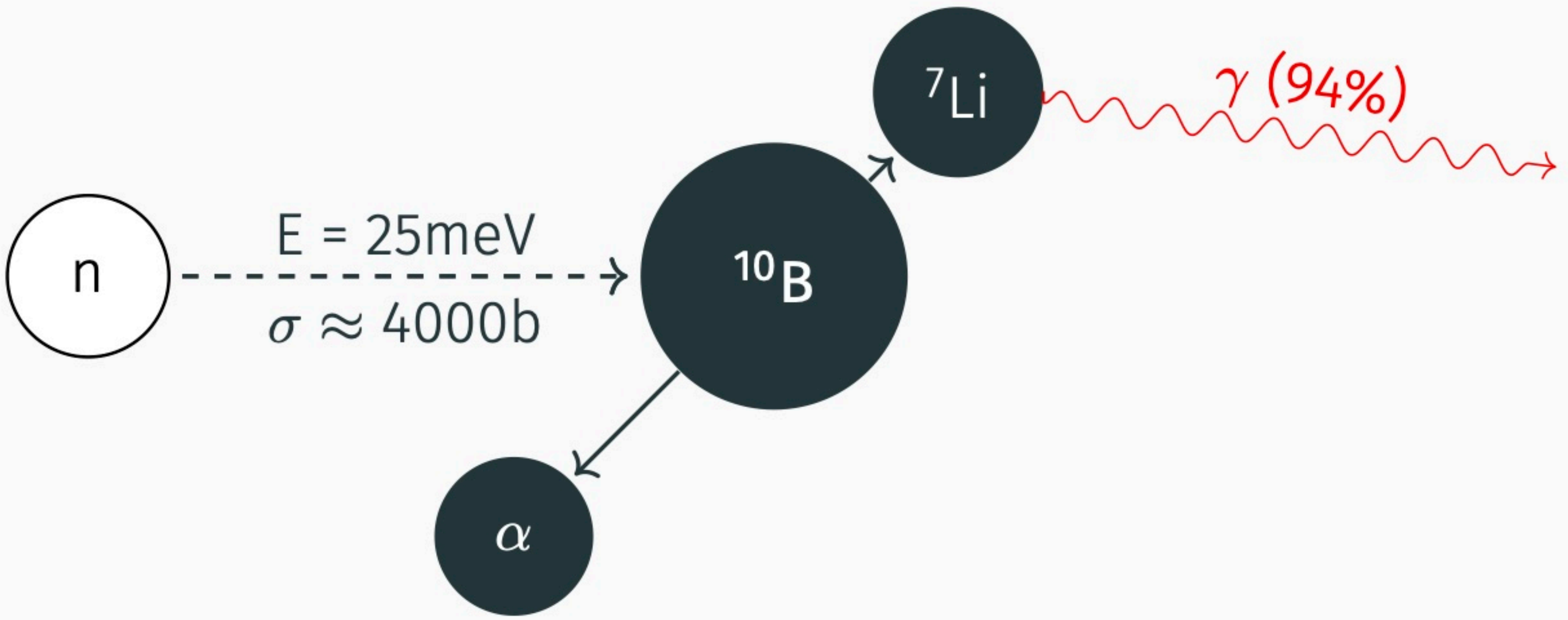
Italia – Lavori di costruzione di laboratori – Realizzazione dell'edificio destinato alla Boron Neutron Capture Therapy (BNCT), presso l'immobile ex CIAPI, nel Comune di San Nicola la Strada (CE), nell'ambito del progetto di ricerca ANTHEM (Advanced Technologies for Human-centrED Medicine), in esecuzione delle iniziative di ricerca per tecnologie e percorsi innovativi in Ambito sanitario e assistenziale - Decreto Direttoriale n. 931 del 6-06-2
OJ S 187/2025 30/09/2025
Bando di gara o di concessione – regime ordinario
Lavori

Parere definitivo MASE in arrivo

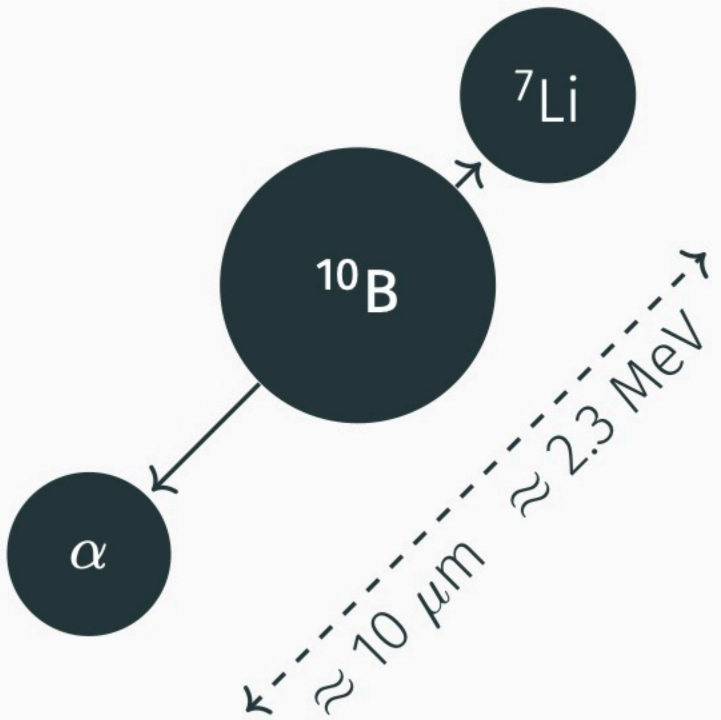
BNCT @ INFN



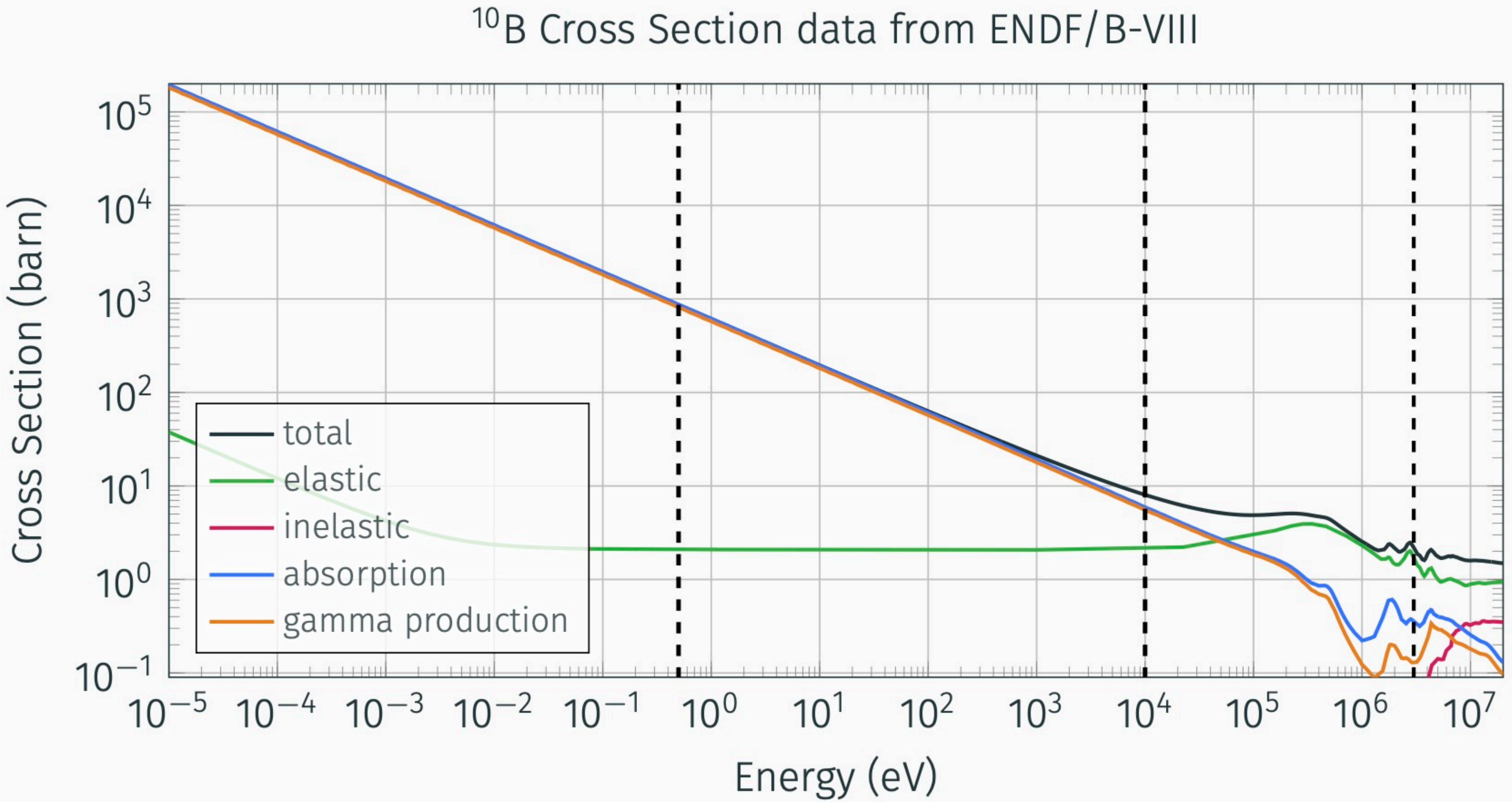
Be target
Moderator
Patient
P
5MeV
30mA
10^{14} s^{-1}
su Ω
N
E_{mean} ~1MeV
E_{max} ~3MeV
AlF_3
10^9 $cm^{-2}s^{-1}$
E_{mean} ~1keV
Radio Frequency Quadrupole
Moderator



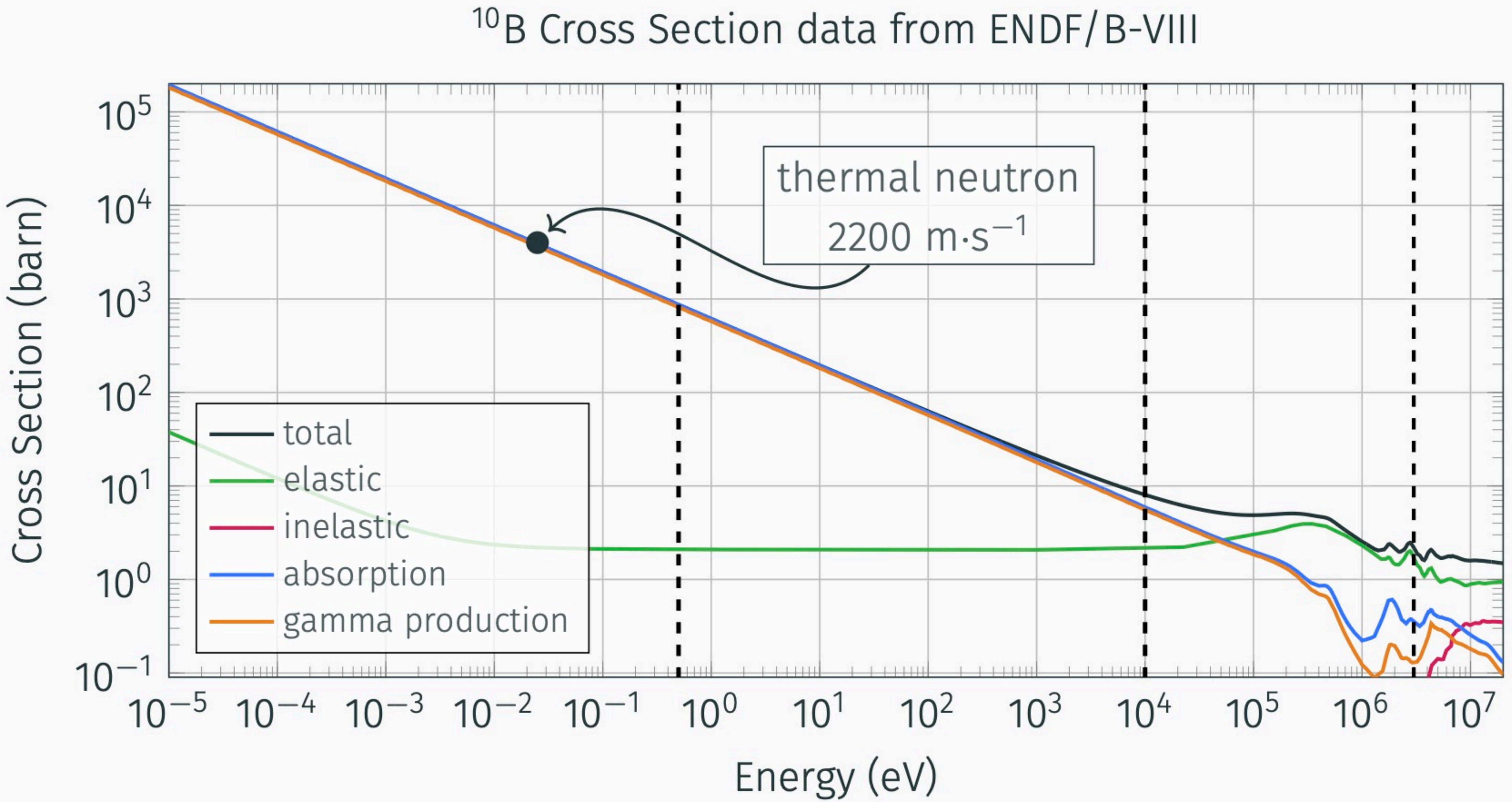
n
E = 25meV
σ ≈ 4000b
10B
7Li
γ (94%)
α



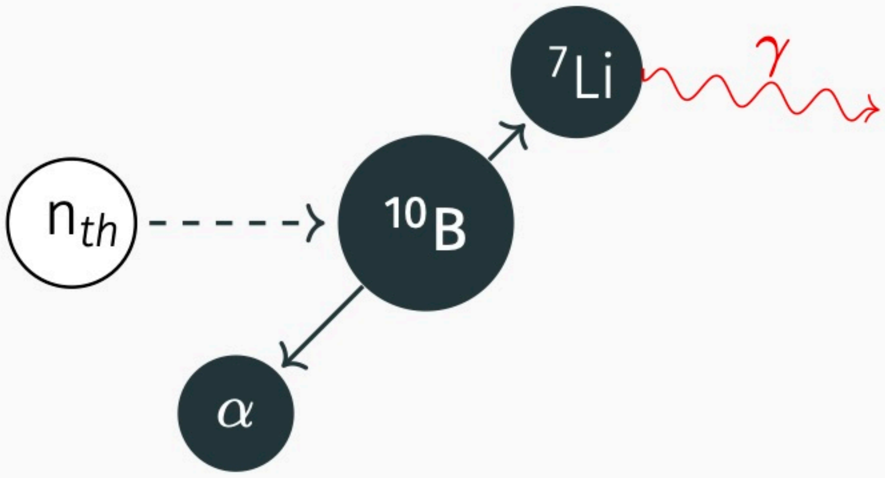
^{7}Li
^{10}B
α
$\approx 10\ \mu m \quad \approx 2.3$ MeV



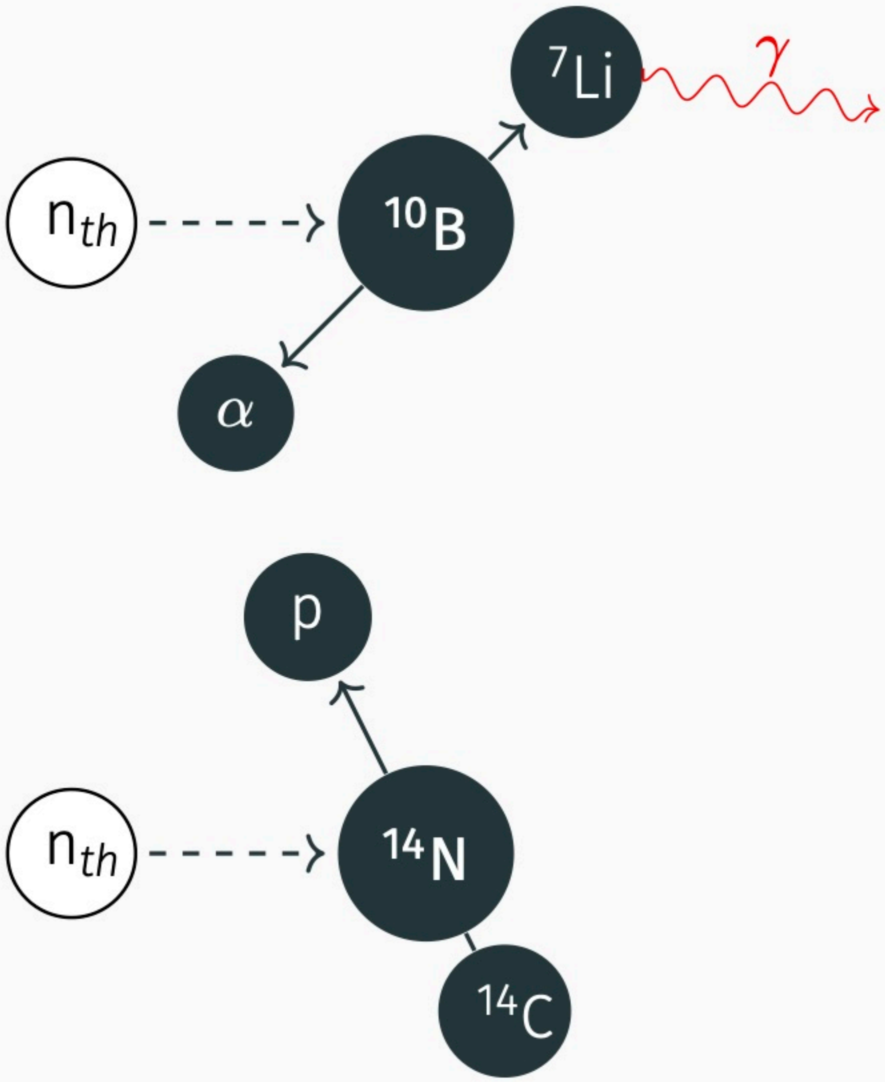
^{10}B Cross Section data from ENDF/B-VIII
Cross Section (barn)
Energy (eV)
total
elastic
inelastic
absorption
gamma production
10^{5}
10^{4}
10^{3}
10^{2}
10^{1}
10^{0}
10^{-1}
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6} 10^{7}



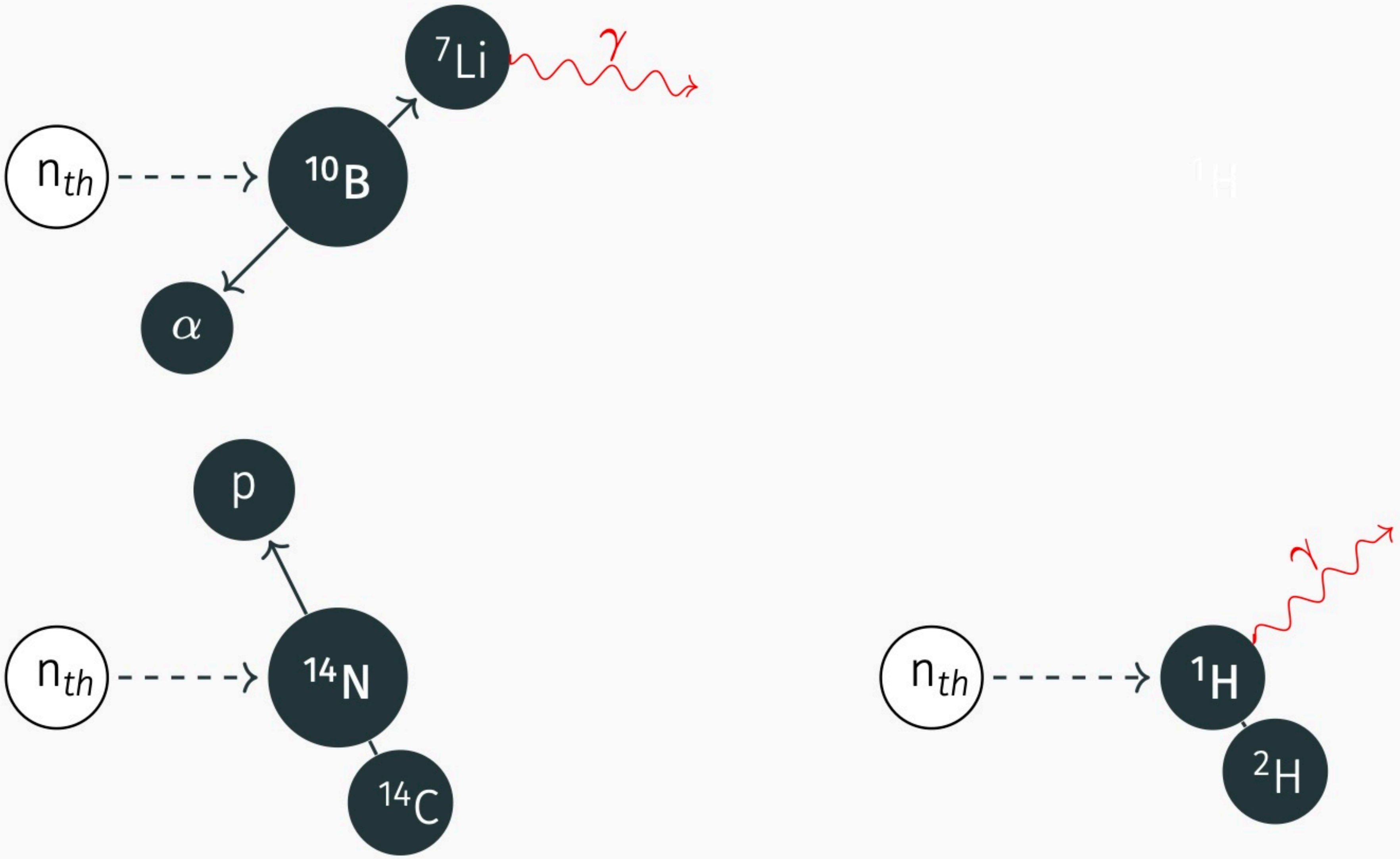
^{10}B Cross Section data from ENDF/B-VIII
thermal neutron
2200 m·s^{-1}
Cross Section (barn)
Energy (eV)
total
elastic
inelastic
absorption
gamma production
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
10^{5}
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6} 10^{7}



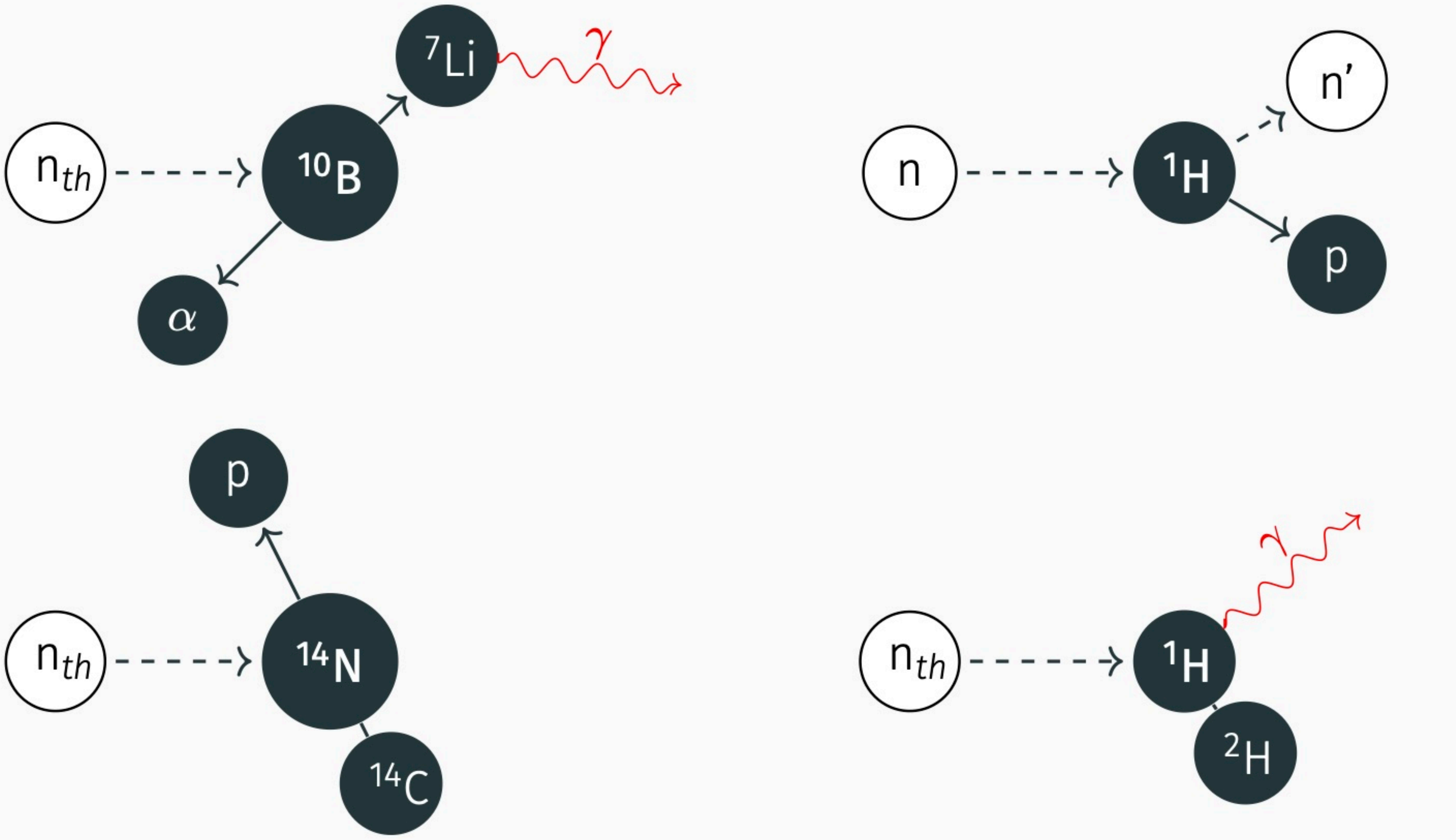
n th
10B
7Li
γ
α



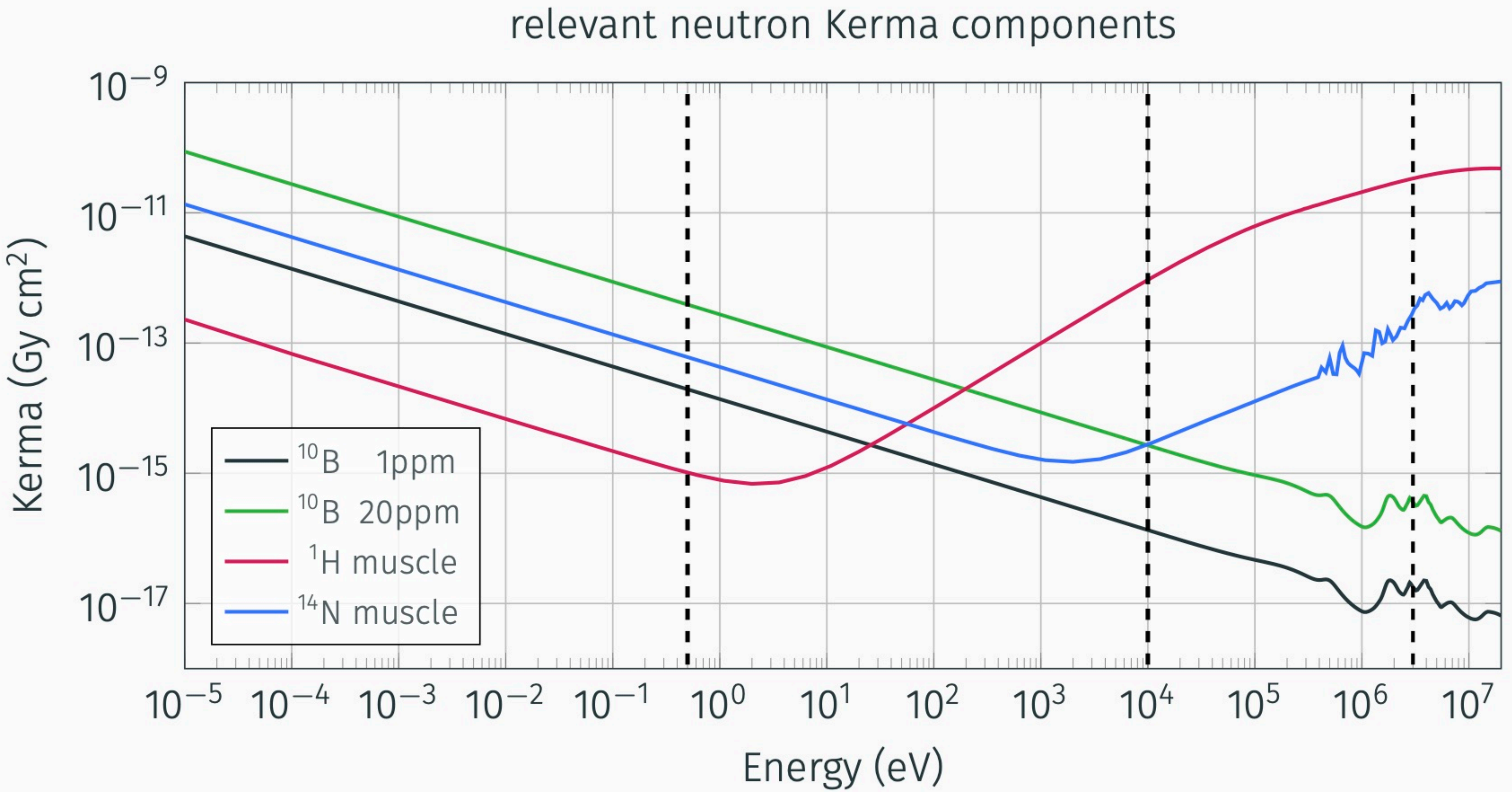
n_{th}
^{10}B
^{7}Li
γ
α
p
n_{th}
^{14}N
^{14}C



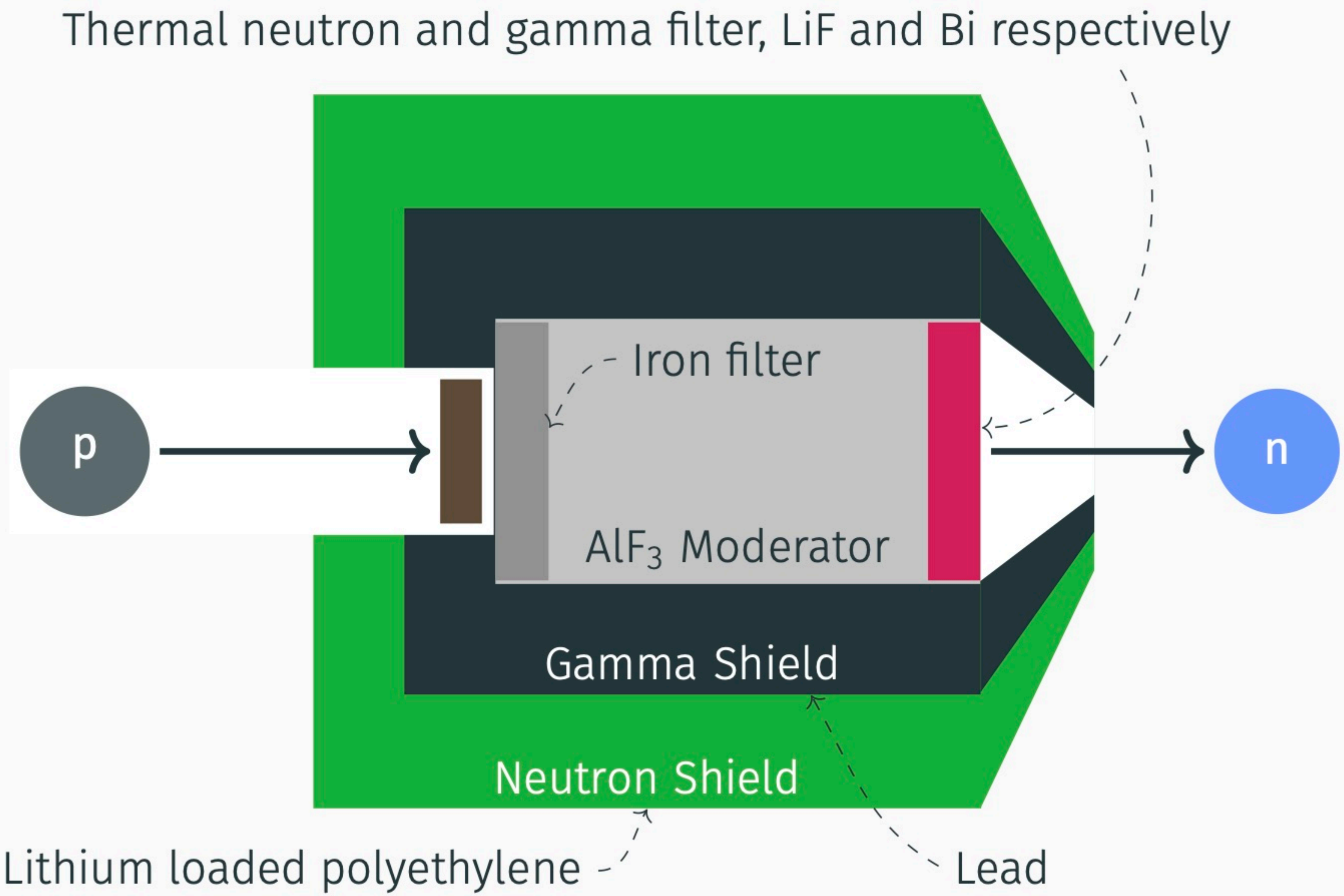
n_{th}
^{10}B
^{7}Li
γ
α
p
n_{th}
^{14}N
^{14}C
n_{th}
^{1}H
^{2}H
γ

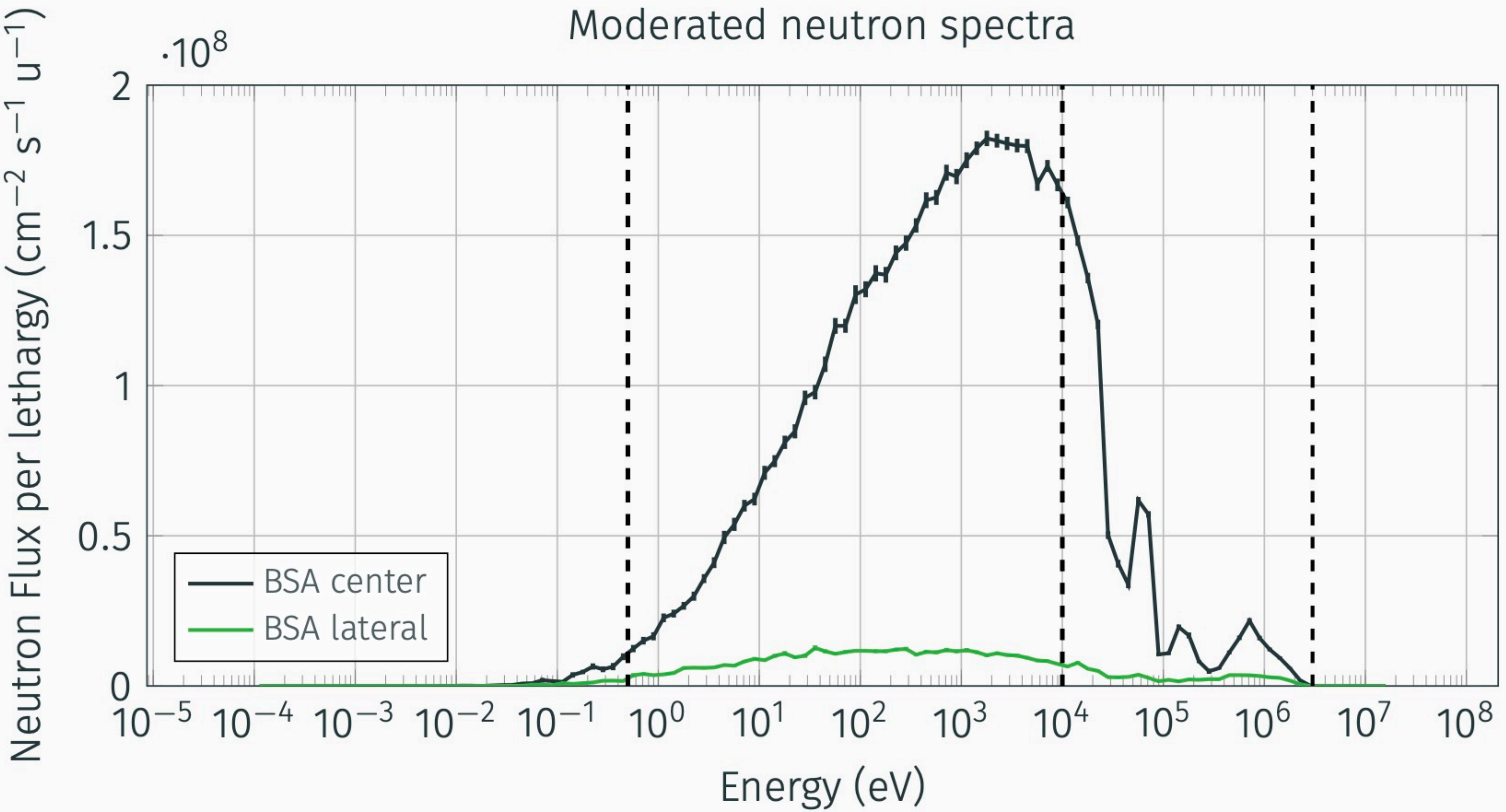


n_{th}
^{10}B
^{7}Li
γ
α
n
^{1}H
n'
p
p
n_{th}
^{14}N
^{14}C
γ
n_{th}
^{1}H
^{2}H

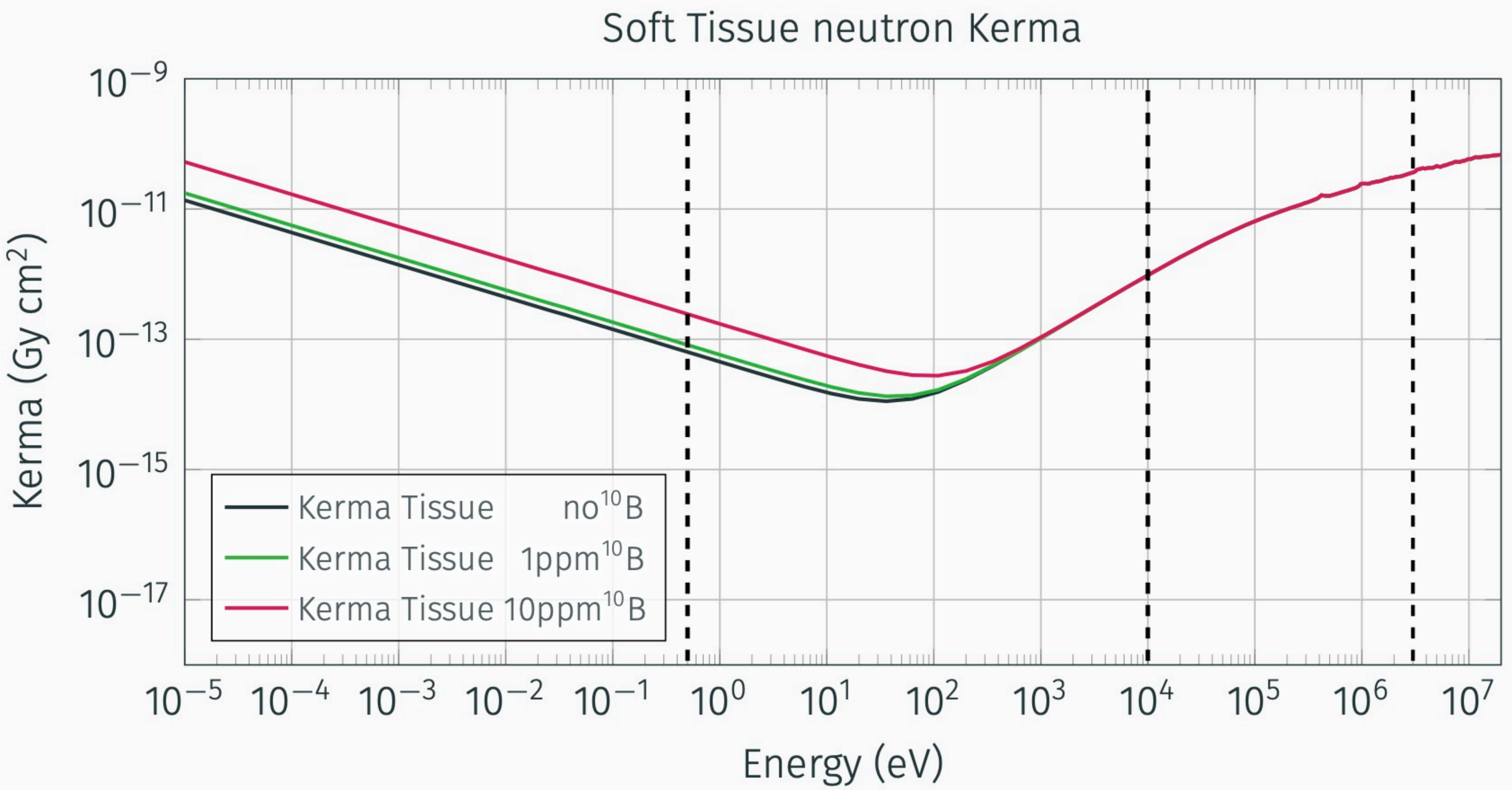


relevant neutron Kerma components
Kerma (Gy cm^2)
Energy (eV)
10^{-9}
10^{-11}
10^{-13}
10^{-15}
10^{-17}
10^{-5}
10^{-4}
10^{-3}
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
10^{5}
10^{6}
10^{7}
^{10}B 1ppm
^{10}B 20ppm
^{1}H muscle
^{14}N muscle


Thermal neutron and gamma filter, LiF and Bi respectively
Iron filter
p
n
AlF₃ Moderator
Gamma Shield
Neutron Shield
Lithium loaded polyethylene
Lead



Moderated neutron spectra
·10^8
2
1.5
1
0.5
0
Neutron Flux per lethargy (cm^−2 s^−1 u^−1)
BSA center
BSA lateral
10^−5 10^−4 10^−3 10^−2 10^−1 10^0 10^1 10^2 10^3 10^4 10^5 10^6 10^7 10^8
Energy (eV)



Soft Tissue neutron Kerma
Kerma (Gy cm^2)
10^{-9}
10^{-11}
10^{-13}
10^{-15}
10^{-17}
Kerma Tissue no^{10}B
Kerma Tissue 1ppm^{10}B
Kerma Tissue 10ppm^{10}B
10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 10^{0} 10^{1} 10^{2} 10^{3} 10^{4} 10^{5} 10^{6} 10^{7}
Energy (eV)

Biological effectiveness of BNCT

$$\mathrm{D}_W = \sum_{i=1}^{i=4} D_i W_i$$

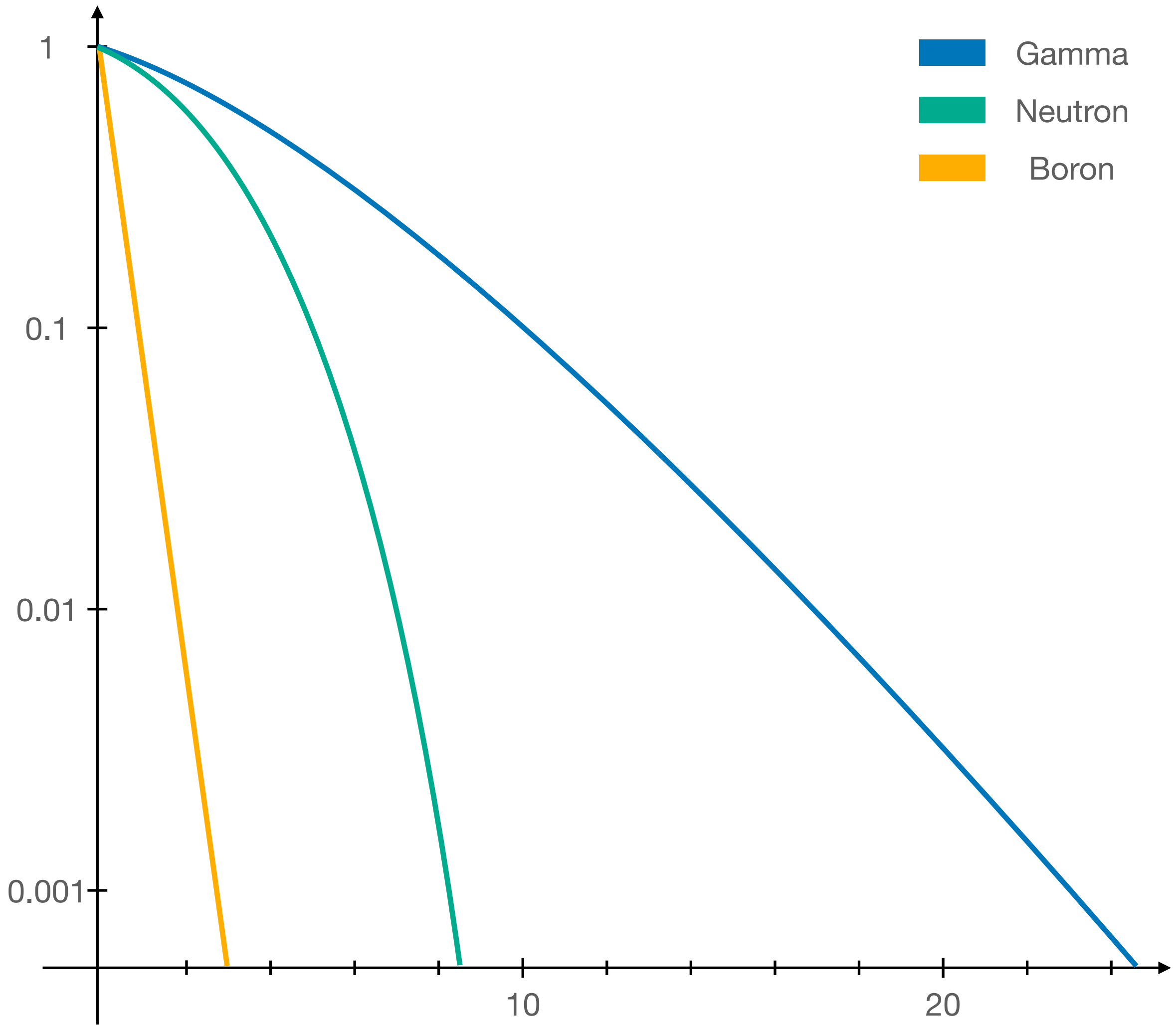
Biological effectiveness of BNCT

$$D_W = \sum_{i=1}^{i=4} D_i W_i$$

In BNCT, there is a mixed radiation field. Therefore, each contribution to the absorbed dose must be multiplied by the corresponding biological weighting factor. Currently, this biological weighting factor for radiation is assumed to be constant. The dose contributions in BNCT are:

D_1 = dose from neutron capture on ^{10}B
D_2 = dose from neutron capture on ^{14}N
D_3 = dose from elastic neutron scattering
D_4 = dose from photons

W1 depends on the type of cell and the microscopic distribution of boron. W2 and W3 are usually considered equal, while W4 is assumed to be 1.

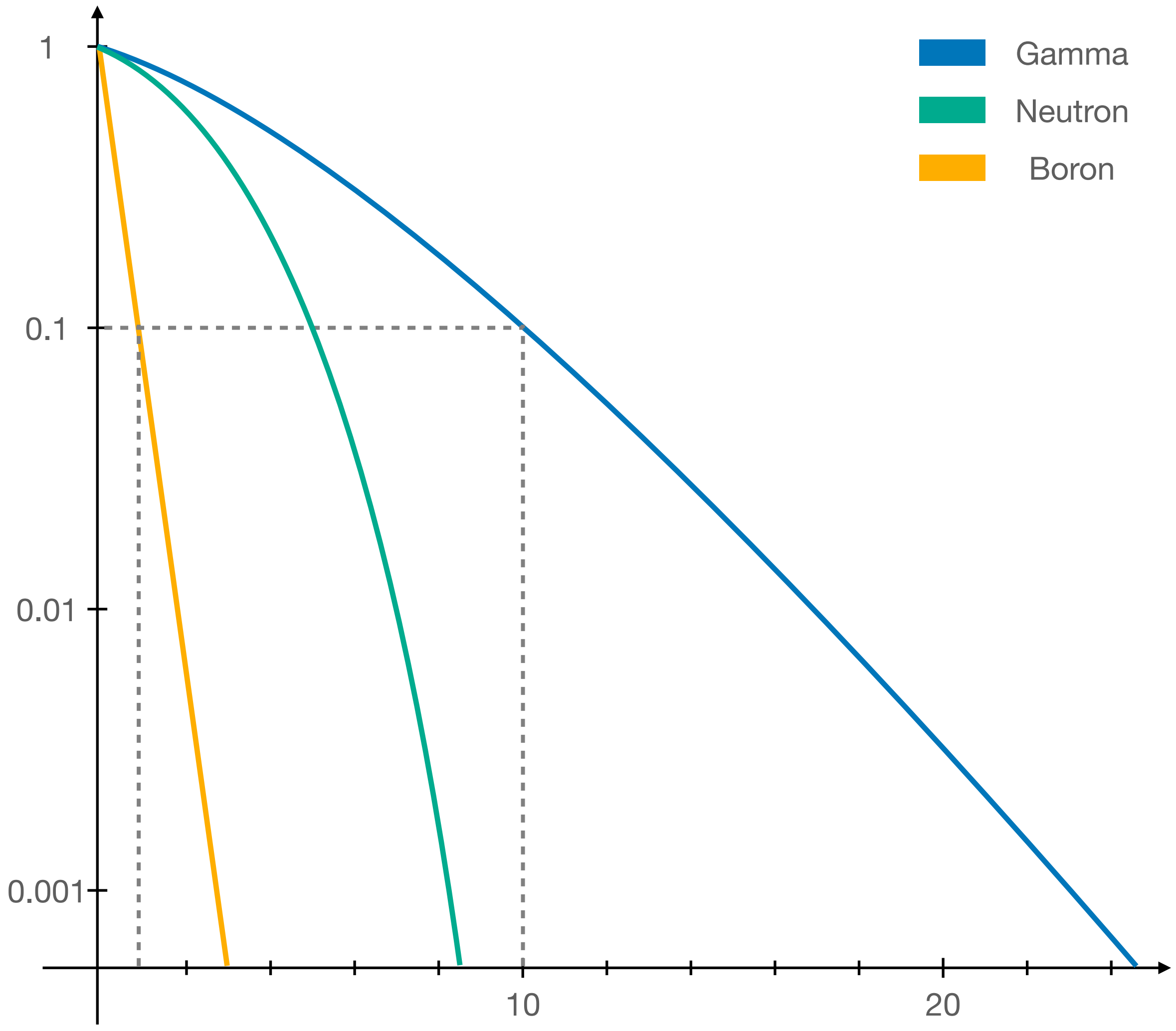


$$w_i = \frac{D_R(S = 0.1)}{D_i(S = 0.1)}$$

$\mathbf{D_R}$ is the reference radiation (gamma).

$\mathbf{D_i}$ is the comparison radiation.

$\mathbf{W_i}$ is the radiobiological weighting factor for that radiation.



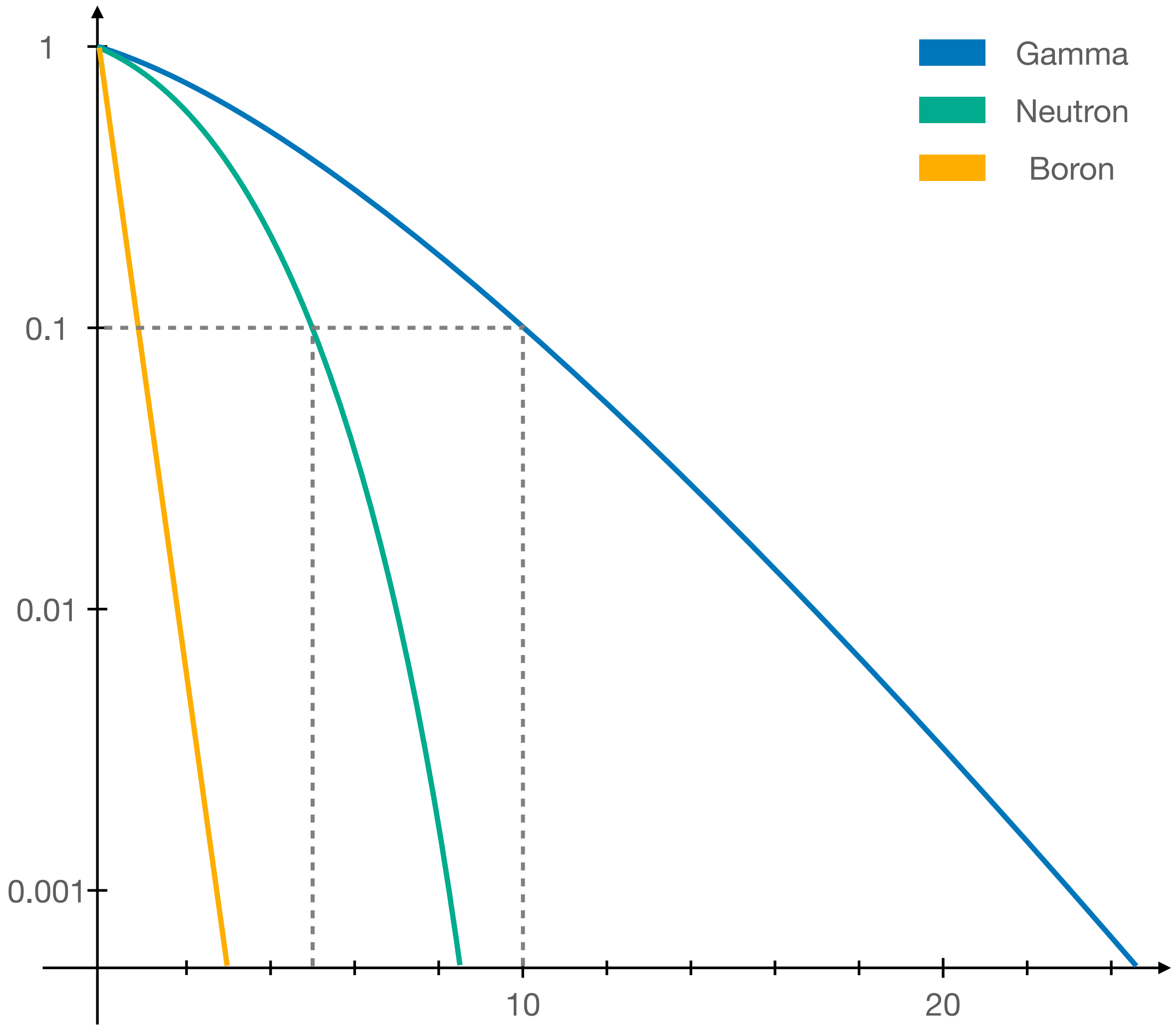
$$w_i = \frac{D_R(S = 0.1)}{D_i(S = 0.1)}$$

D_R is the reference radiation (gamma).

D_i is the comparison radiation.

W_i is the radiobiological weighting factor for that radiation.

$W_{boro} = 10 / 1 = 10$



$$w_i = \frac{D_R(S = 0.1)}{D_i(S = 0.1)}$$

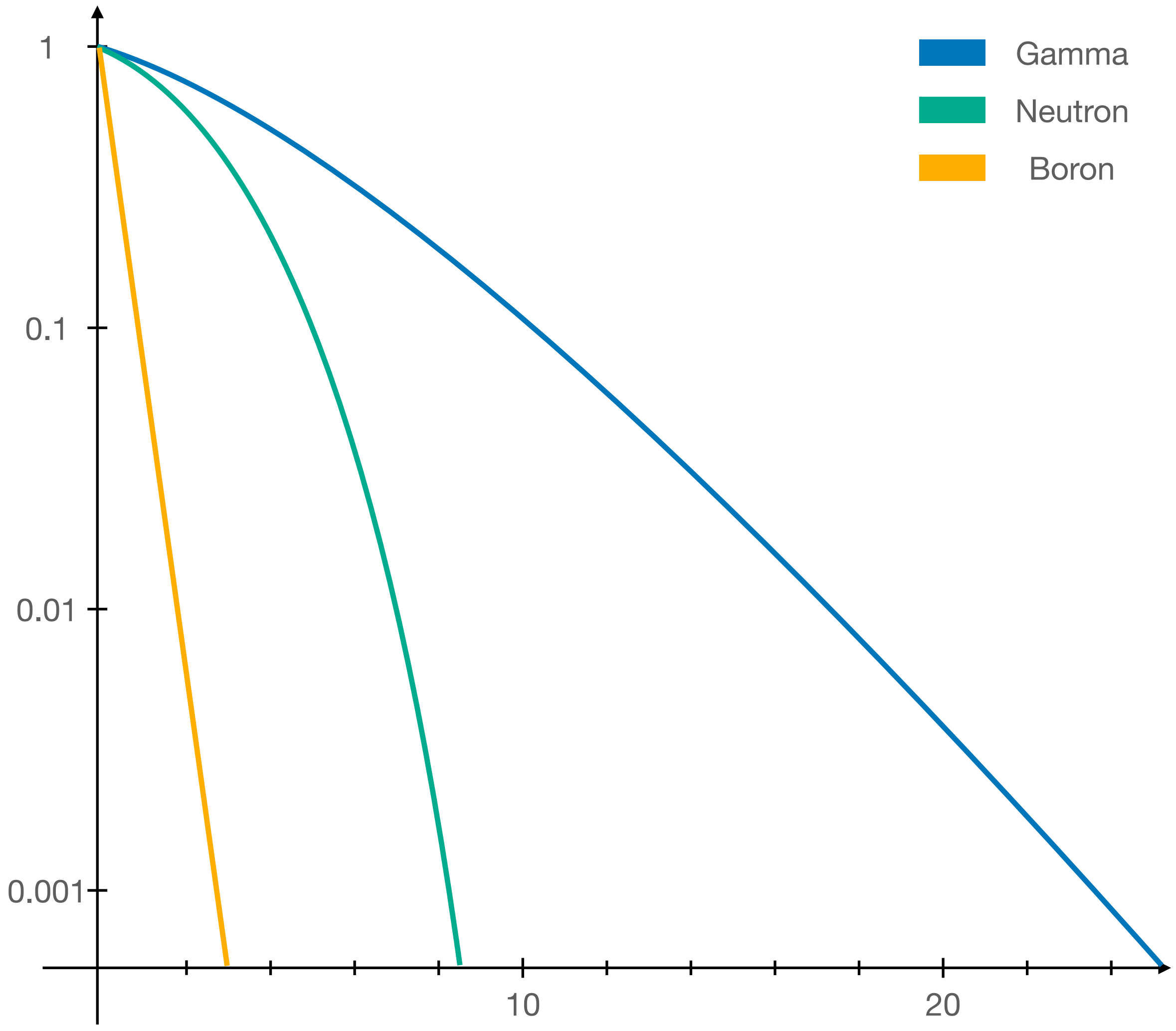
$\mathbf{D_R}$ is the reference radiation (gamma).

$\mathbf{D_i}$ is the comparison radiation.

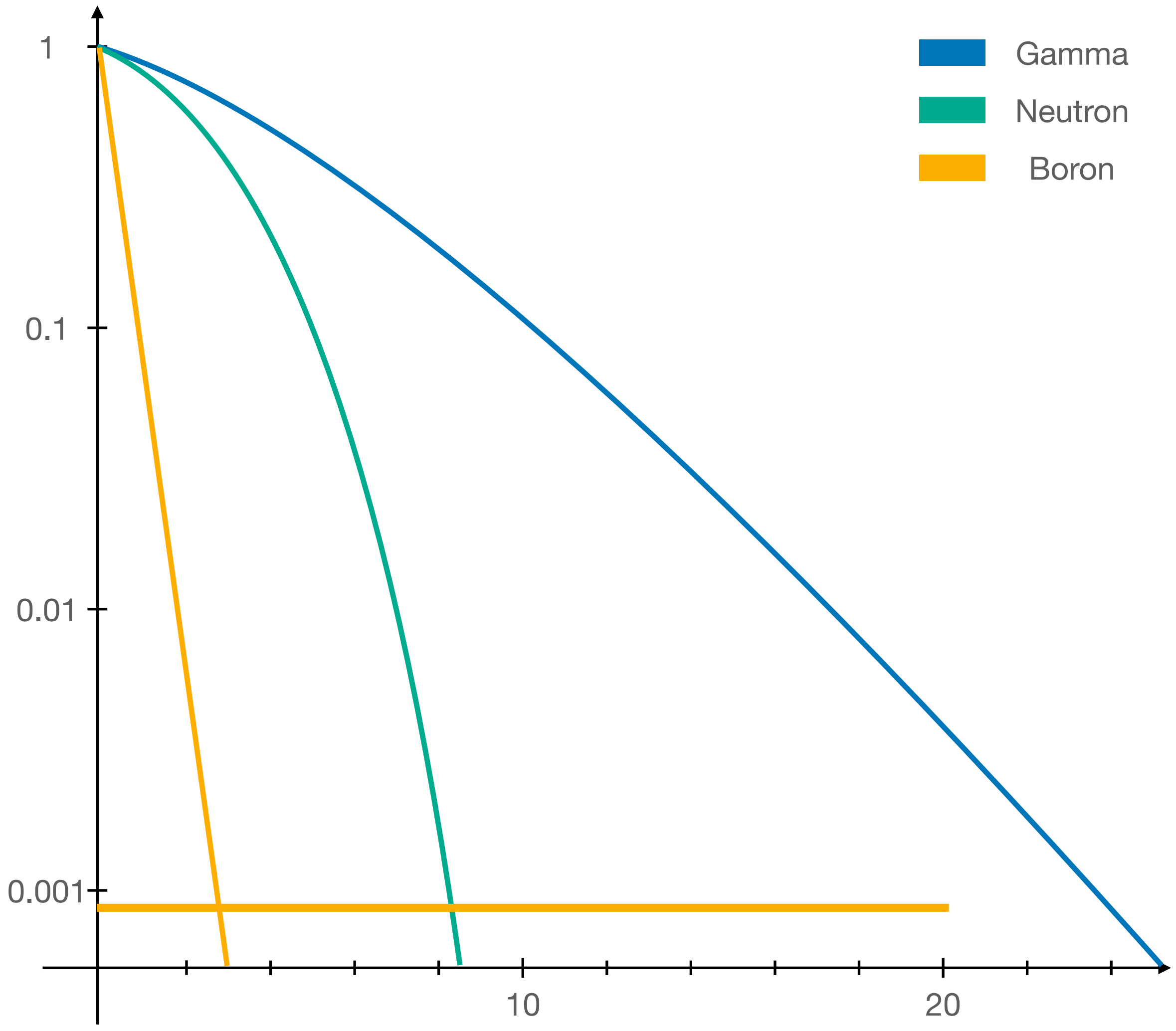
$\mathbf{W_i}$ is the radiobiological weighting factor for that radiation.

$W_{boro} = 10 / 1 = 10$

$W_{neutron} = 10 / 5 = 2$



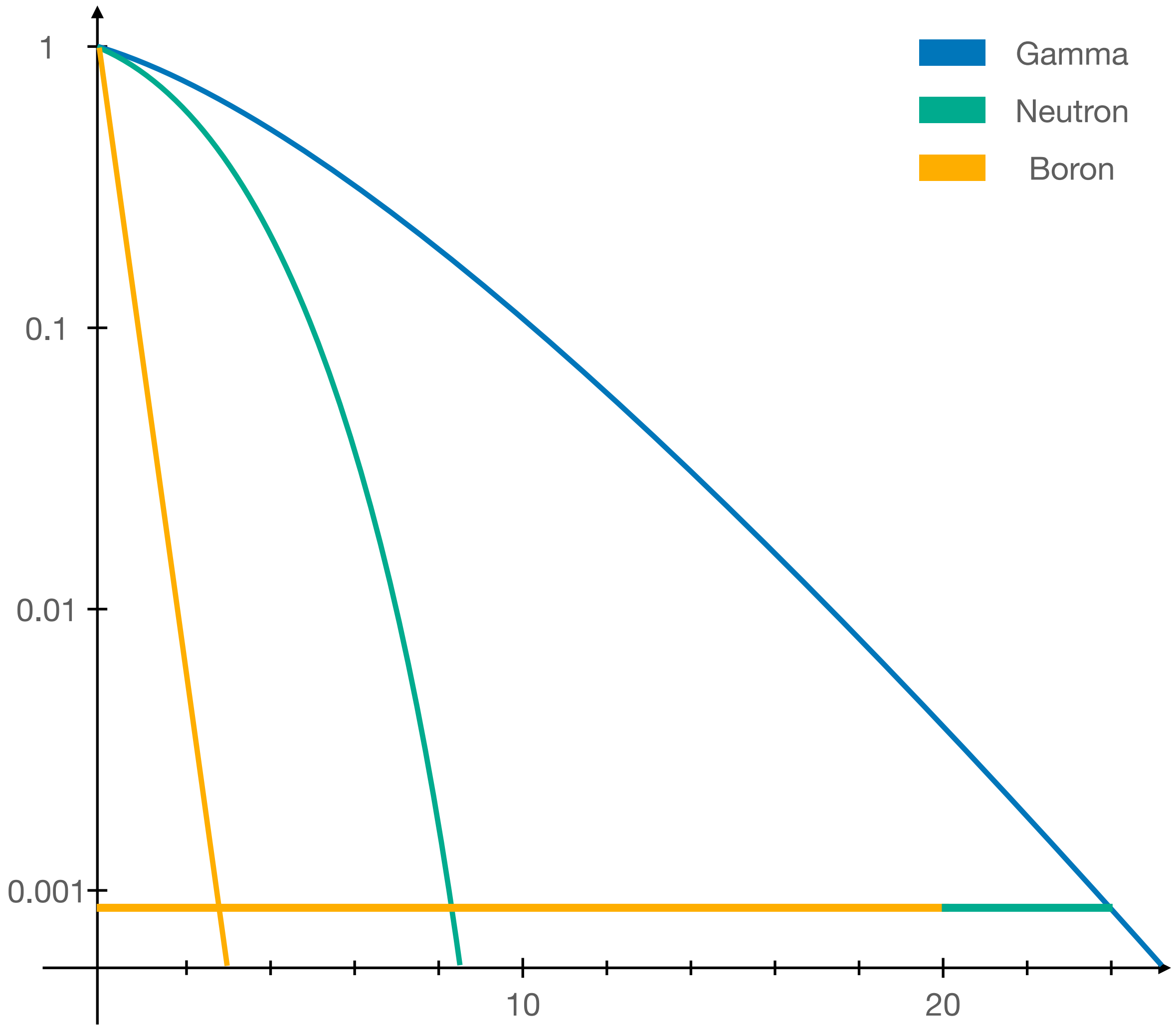
Now, let's consider a mixed radiation field composed of neutron scattering and neutron capture on boron. Suppose 50% of the energy is deposited by scattering, while the remaining 50% comes from the reaction on boron. If we deliver a total dose of 4 Gy, what weighted dose would we obtain?



$D_{boro} * W_{boro}$

Now, let's consider a mixed radiation field composed of neutron scattering and neutron capture on boron. Suppose 50% of the energy is deposited by scattering, while the remaining 50% comes from the reaction on boron. If we deliver a total dose of 4 Gy, what weighted dose would we obtain?

$D_{boro} * W_{boro} = 10 * 2 = 20\ Gy_{w}$

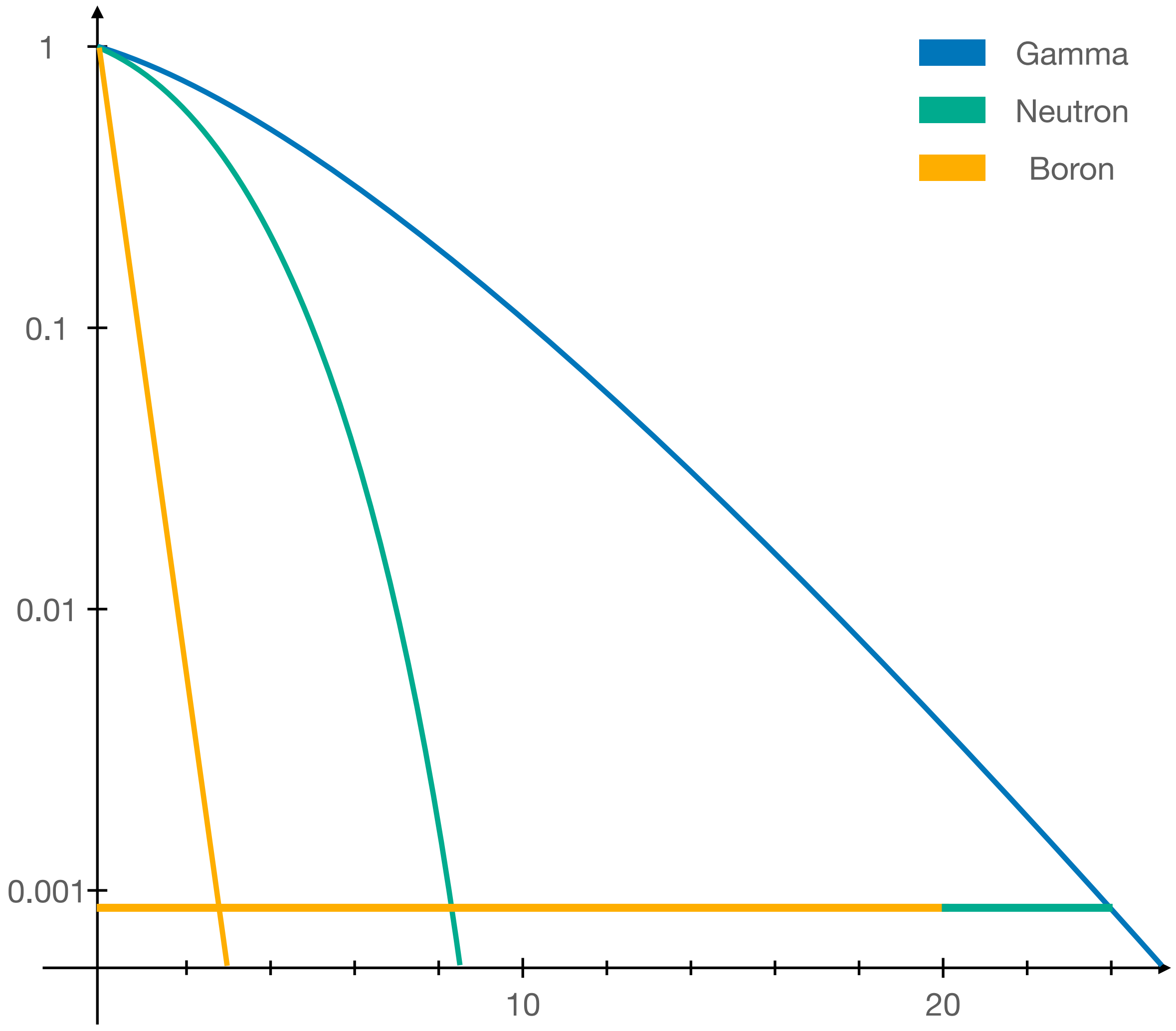


$D_{boro} * W_{boro}$ $D_{neutron} * W_{neutron}$

Now, let's consider a mixed radiation field composed of neutron scattering and neutron capture on boron. Suppose 50% of the energy is deposited by scattering, while the remaining 50% comes from the reaction on boron. If we deliver a total dose of 4 Gy, what weighted dose would we obtain?

$$D_{boro} * W_{boro} = 10 * 2 = 20\ Gy_{w}$$

$$D_{neutron} * W_{neutron} = 2 * 2 = 4\ Gy_{w}$$



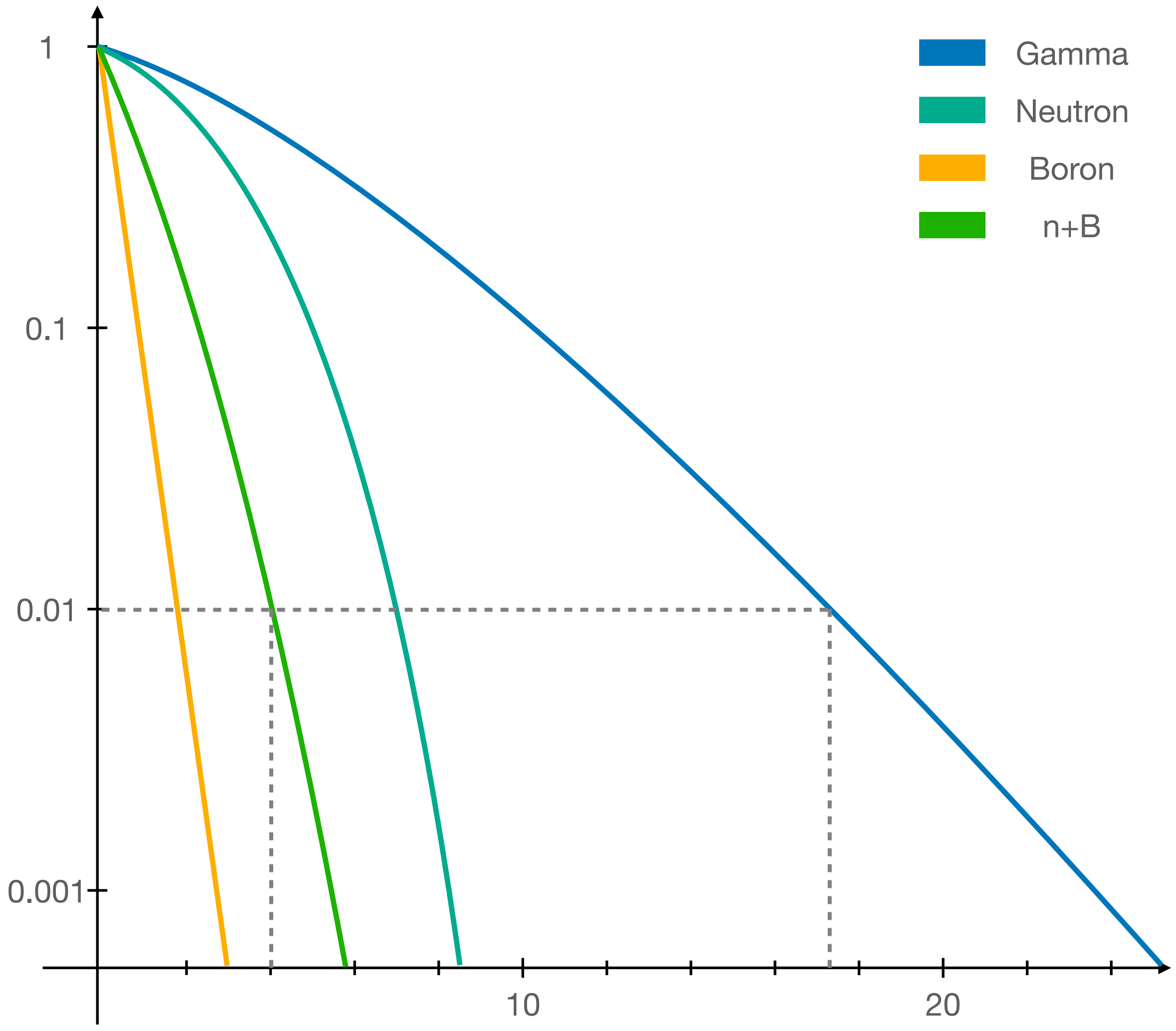
$D_{boro} * W_{boro}$ $D_{neutron} * W_{neutron}$

Now, let's consider a mixed radiation field composed of neutron scattering and neutron capture on boron. Suppose 50% of the energy is deposited by scattering, while the remaining 50% comes from the reaction on boron. If we deliver a total dose of 4 Gy, what weighted dose would we obtain?

$D_{boro} * W_{boro} = 10 * 2 = 20\ Gy_w$

$D_{neutron} * W_{neutron} = 2 * 2 = 4\ Gy_w$

D_w is 24 Gy_w. Which corresponds to a cell survival fraction of just less than 0.001.

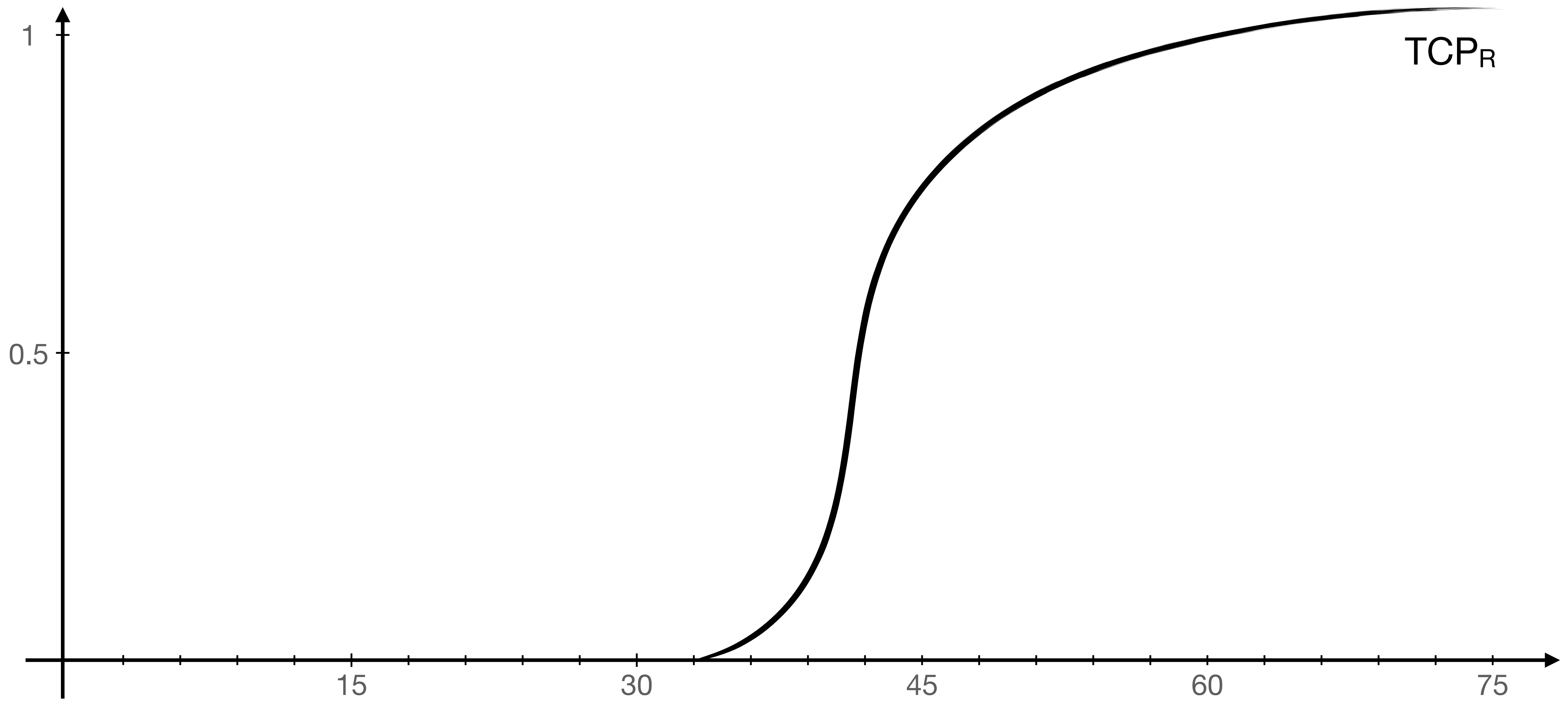


The reality is that a linear propagation of dose (i.e., using fixed weighting factors) is not accurate. If we consider the curve representing the combination of dose (50% from neutron scattering and 50% from neutron capture on boron), we observe that it lies roughly midway between the curves of the individual radiation types.

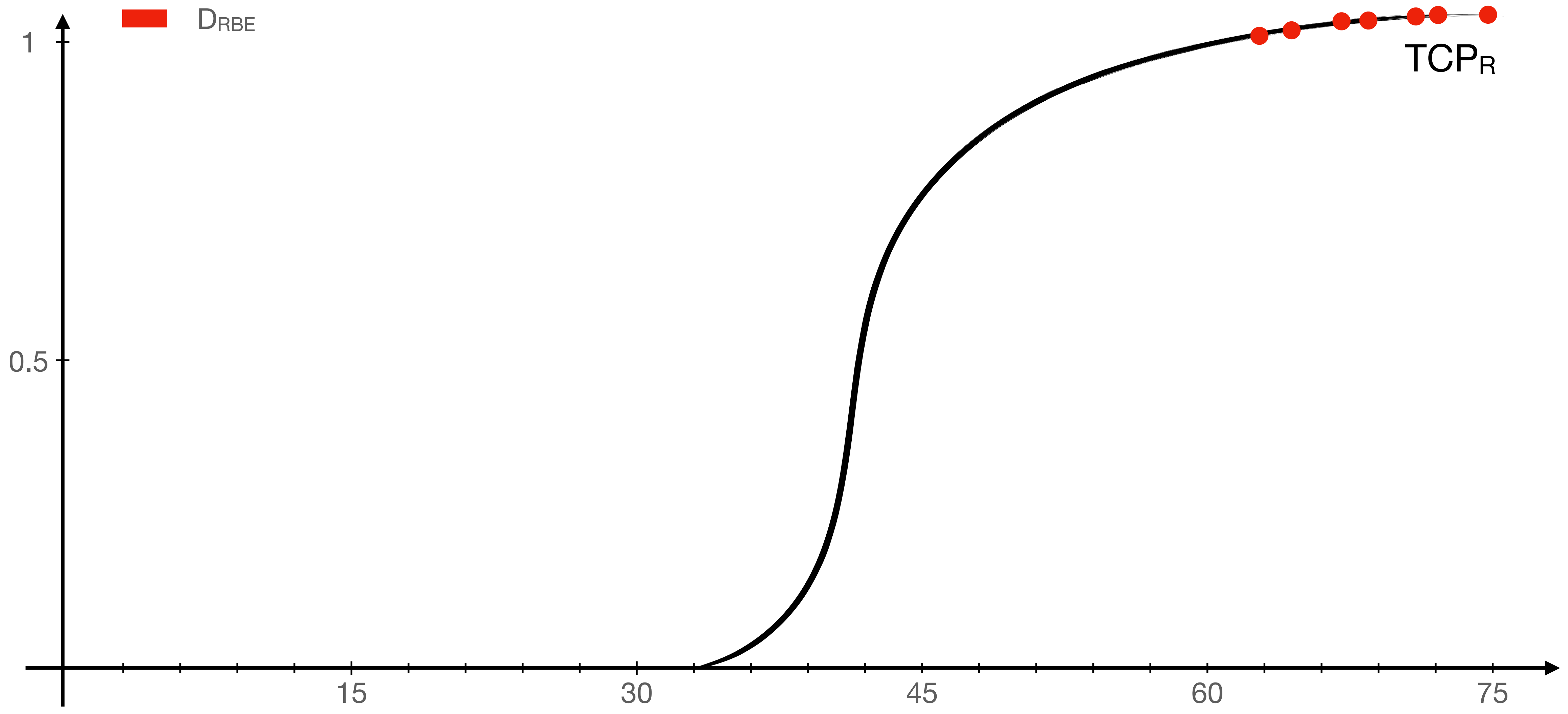
Thus, for 4 Gy of mixed field dose, if we look at the n+B curve, we obtain a cell survival rate of 1e-2. This survival corresponds to an equivalent dose of approximately 17 Gy of photons. In this case, we have 17 Gy_{isoE}, as the dosimetry is isoeffective with respect to photons.

Compared to the previous situation (dose weighted with fixed weighting factors), the dose is lower. Specifically, using fixed weighting factors overestimates the dose by about 140% at just 4 Gy of mixed field. As the dose increases, this discrepancy continues to grow.

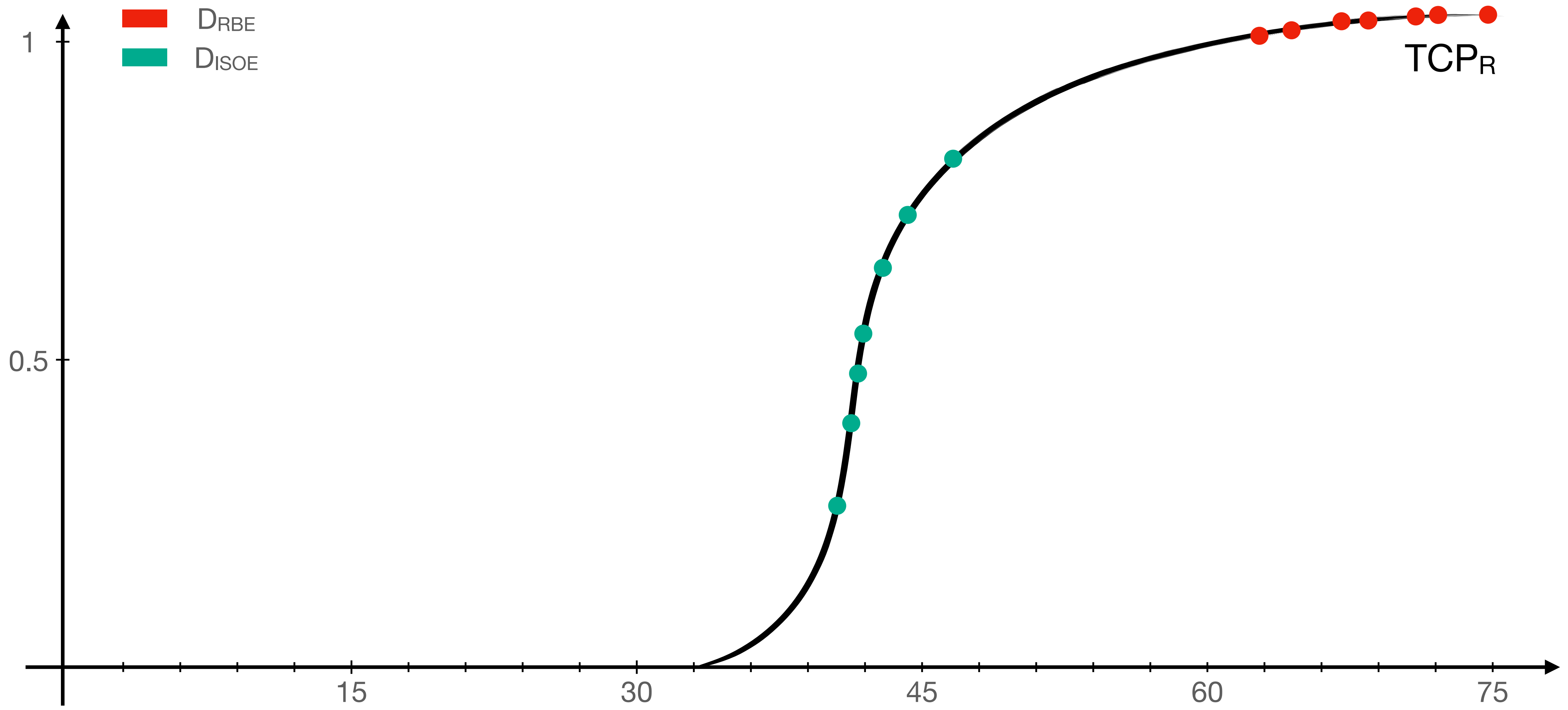
This means that in the tumor (where doses are higher), **the overestimation of dose using fixed-factor dosimetry becomes significant**!



1
0.5
15
30
45
60
75
TCP$_R$



DRBE
TCPR
1
0.5
15
30
45
60
75



D_RBE
D_ISOE
TCP_R
1
0.5
15
30
45
60
75

Biological effectiveness of BNC

$$\cancel{D_W = \sum_{i=1}^{i=4} D_i W_i}$$

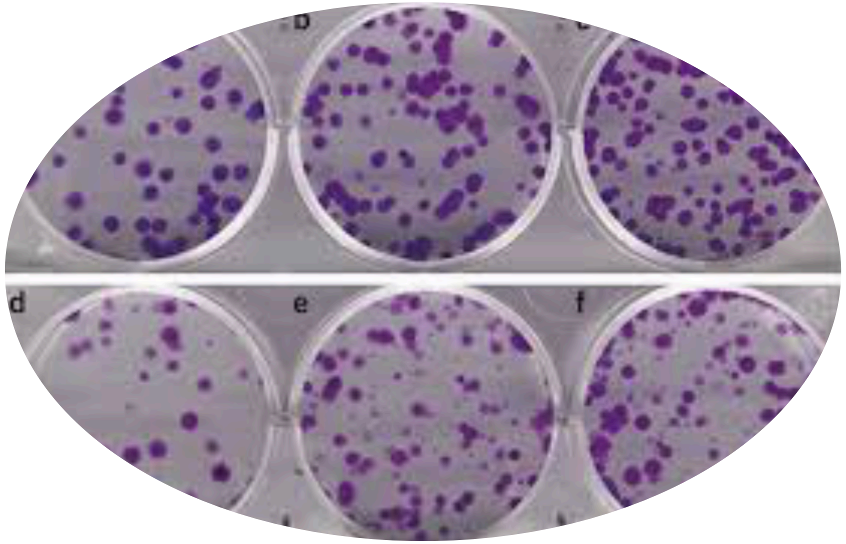
$$D_{isoE} = \frac{\alpha_R}{2G_R\beta_R}\left(\sqrt{1 + \frac{4G_R}{\alpha_R(\alpha/\beta)_R}\left(\sum_{i=1}^{4}\alpha_i D_i + \sum_{i=1}^{4}\sum_{j=1}^{4} G_{ij}\sqrt{\beta_i\beta_j}D_i D_j\right)} - 1\right)$$

Biological effectiveness of BNC

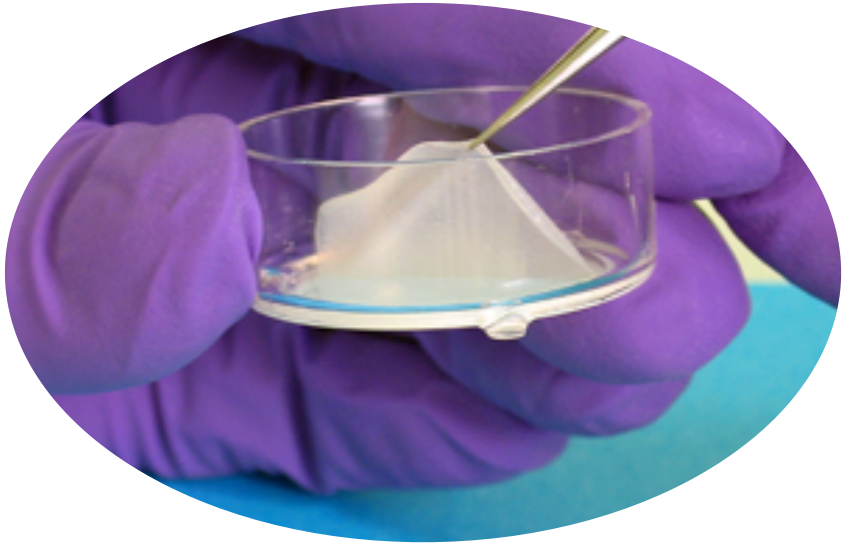
$$\cancel{\mathrm{D}_W = \sum_{i=1}^{i=4} D_i W_i}$$

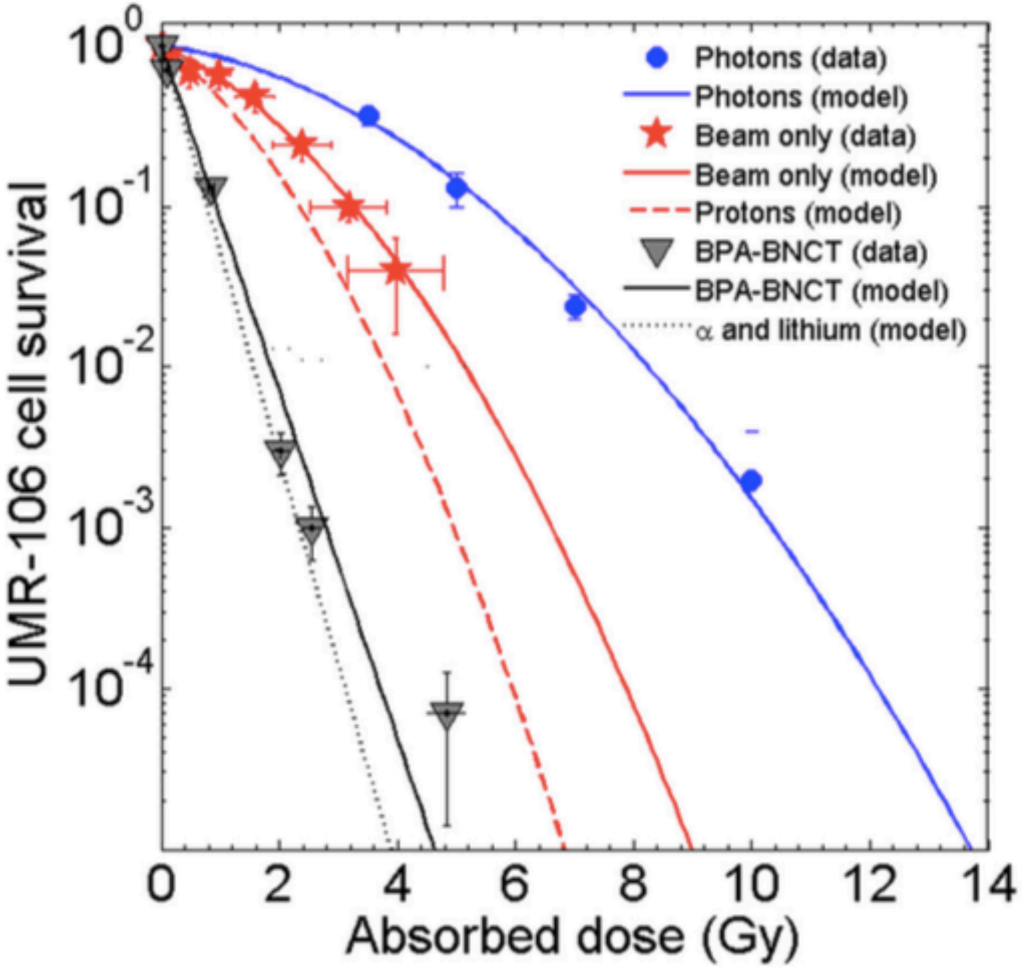
$$\mathrm{D}_{isoE} = \frac{\alpha_R}{2G_R\beta_R}\left(\sqrt{1 + \frac{4G_R}{\alpha_R(\alpha/\beta)_R}\left(\sum_{i=1}^{4}\alpha_i \mathrm{D}_i + \sum_{i=1}^{4}\sum_{j=1}^{4} G_{ij}\sqrt{\beta_i\beta_j}\,\mathrm{D}_i\mathrm{D}_j\right)} - 1\right)$$

González, Sara J. et al. Radiation research 178.6 (2012): 609-621.

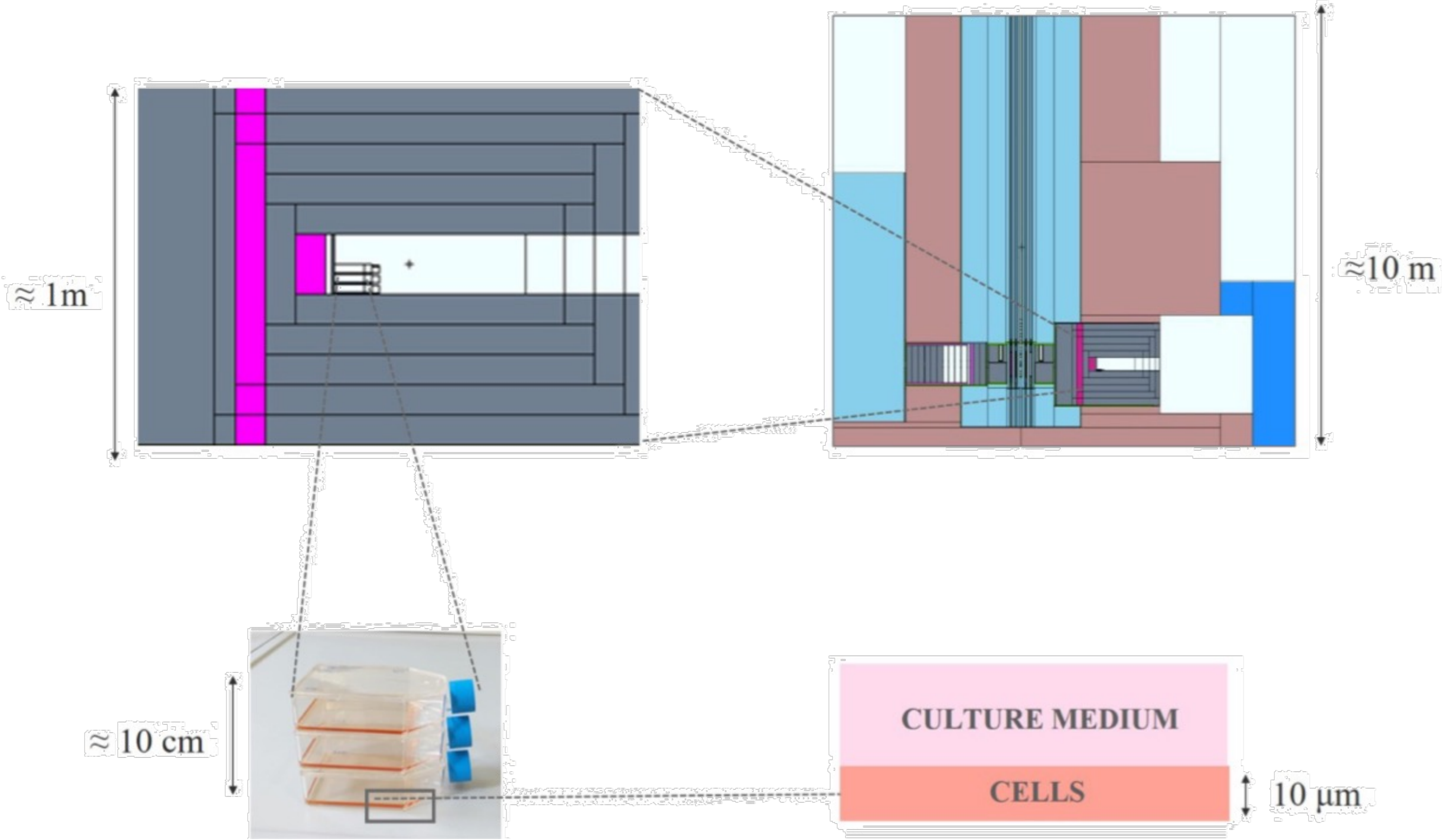


b
d
e
f





Photons (data)
Photons (model)
Beam only (data)
Beam only (model)
Protons (model)
BPA-BNCT (data)
BPA-BNCT (model)
α and lithium (model)
UMR-106 cell survival
10^{0}
10^{-1}
10^{-2}
10^{-3}
10^{-4}
0
2
4
6
8
10
12
14
Absorbed dose (Gy)

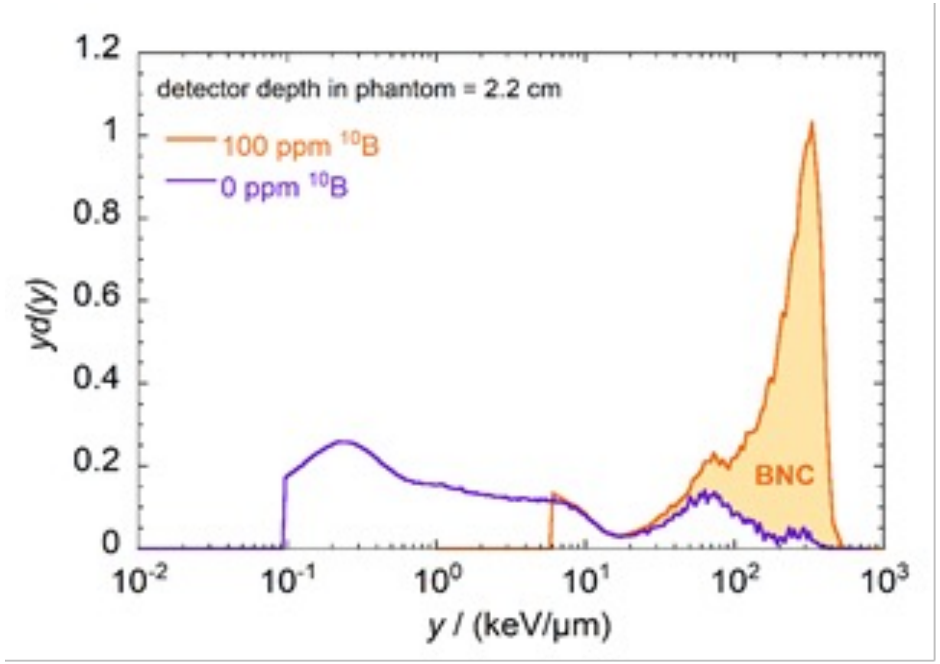


Msc thesis, Matteo Ferrari 2017 & Barbara Marcaccio 2021

BNCT Microdosimetry

Bridging the gap between the physical characteristics of radiation and its biological effects

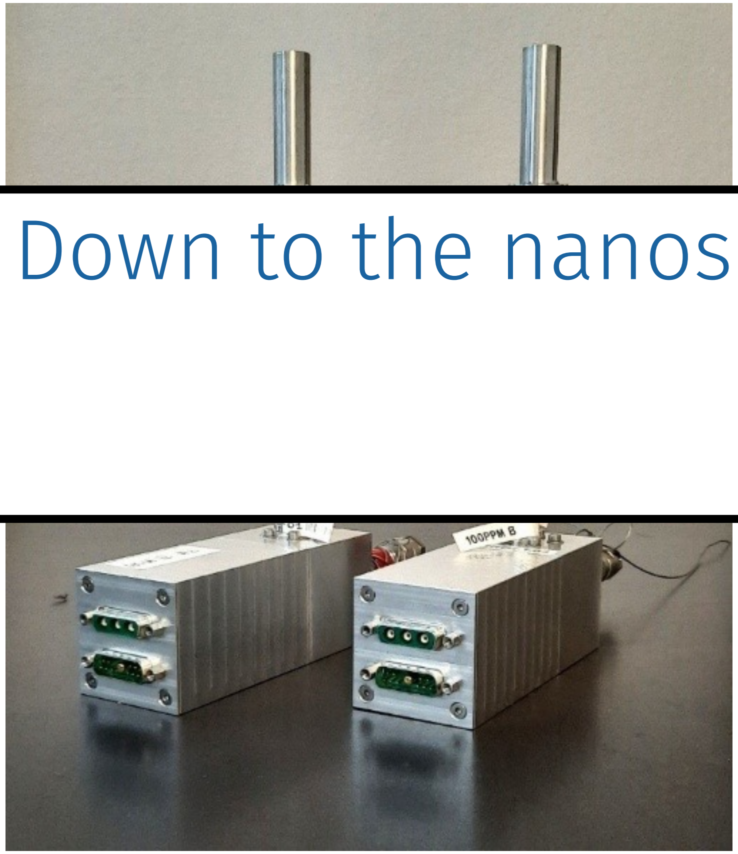
mini-TEPC
(Tissue Equivalent Proportional Counters)



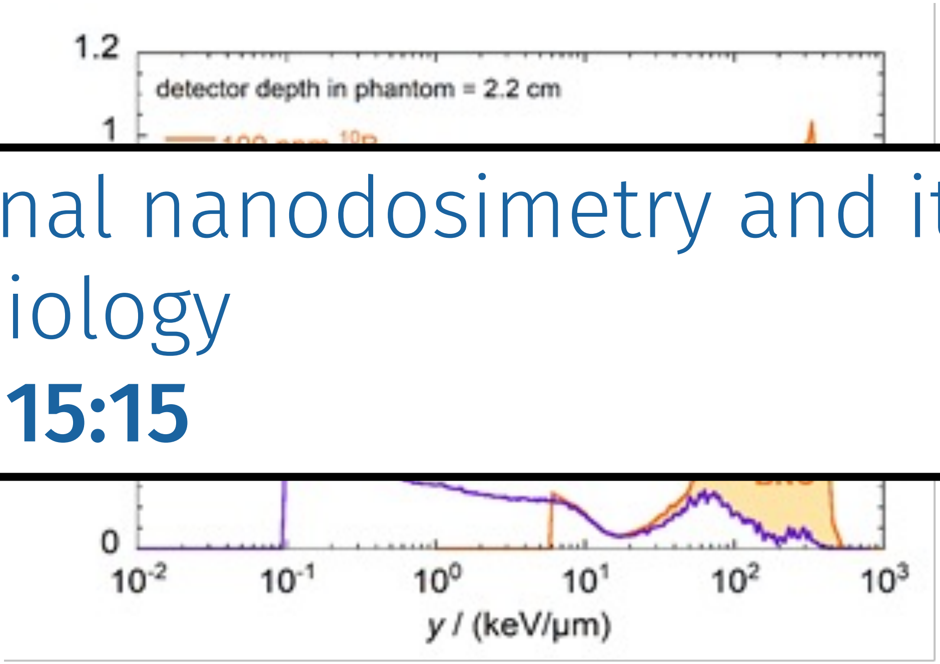
Analyse the quality of the beam and the characteristic of its interaction at sites with the size of a cell. **High innovation potential in BNCT dosimetry and treatment planning!**

BNCT Microdosimetry

Bridging the gap between the physical characteristics of radiation and its biological effects



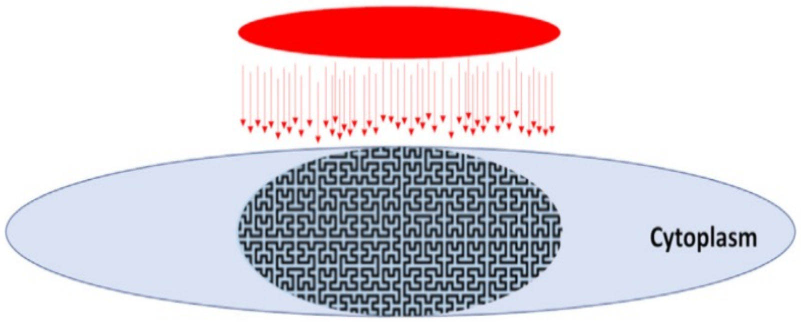
mini-TEPC
(Tissue Equivalent Proportional Counters)

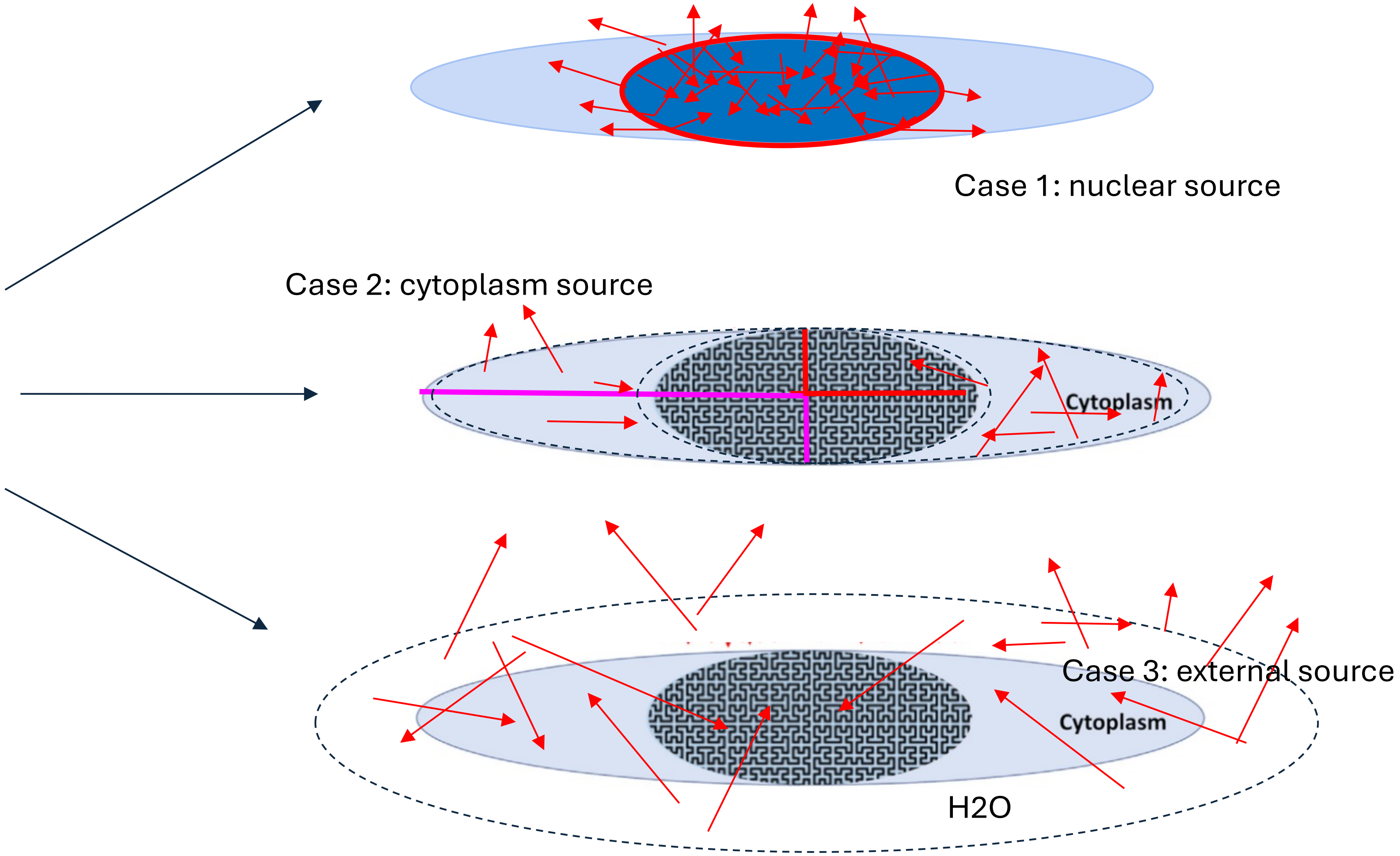


Down to the nanoscale: computational nanodosimetry and its link with radiobiology
Anna Selva @ 15:15

Analyse the quality of the beam and the characteristic of its interaction at sites with the size of a cell. **High innovation potential in BNCT dosimetry and treatment planning!**

Geant4DNA simulations of intra and intercellular particle source



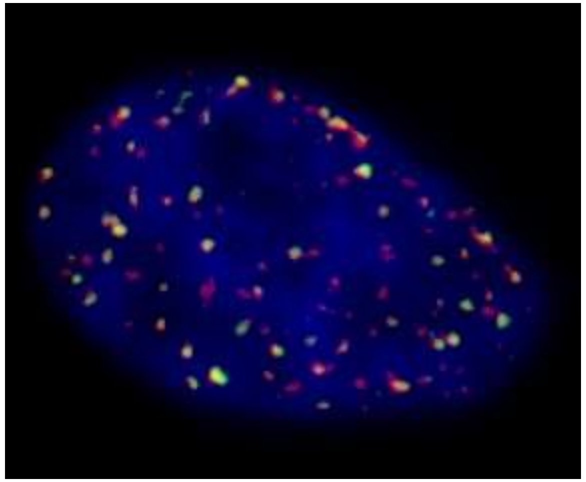


Particle source location in different volumes

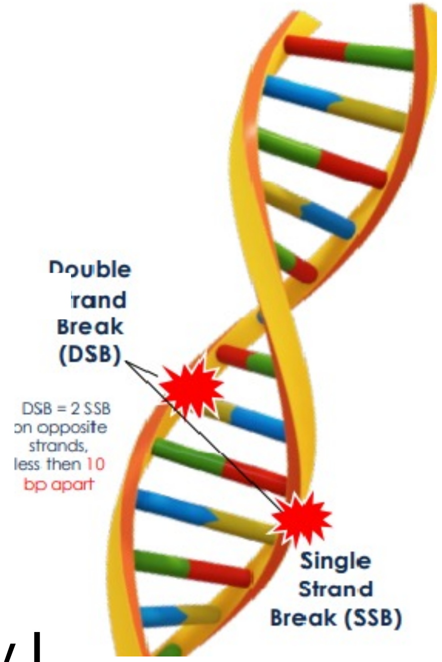
PhD Thesis of Laura Bagnale

From experimental validation to predictive results

MSc thesis -> number of foci per cell at different time points



F. Fede, MSc thesis, supervised by L. Manti.



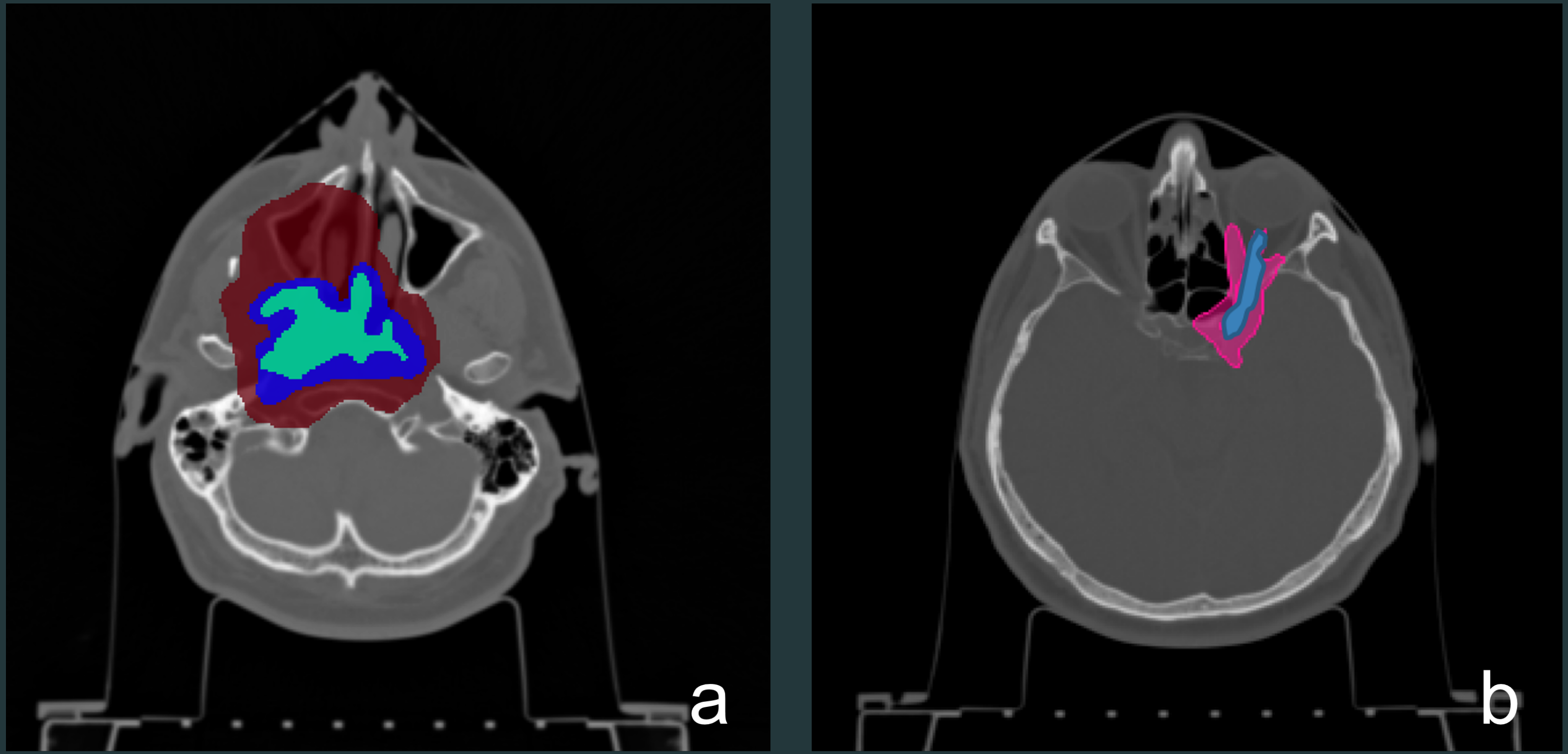
Geant4-DNA -> same conditions

By editing the output parameters

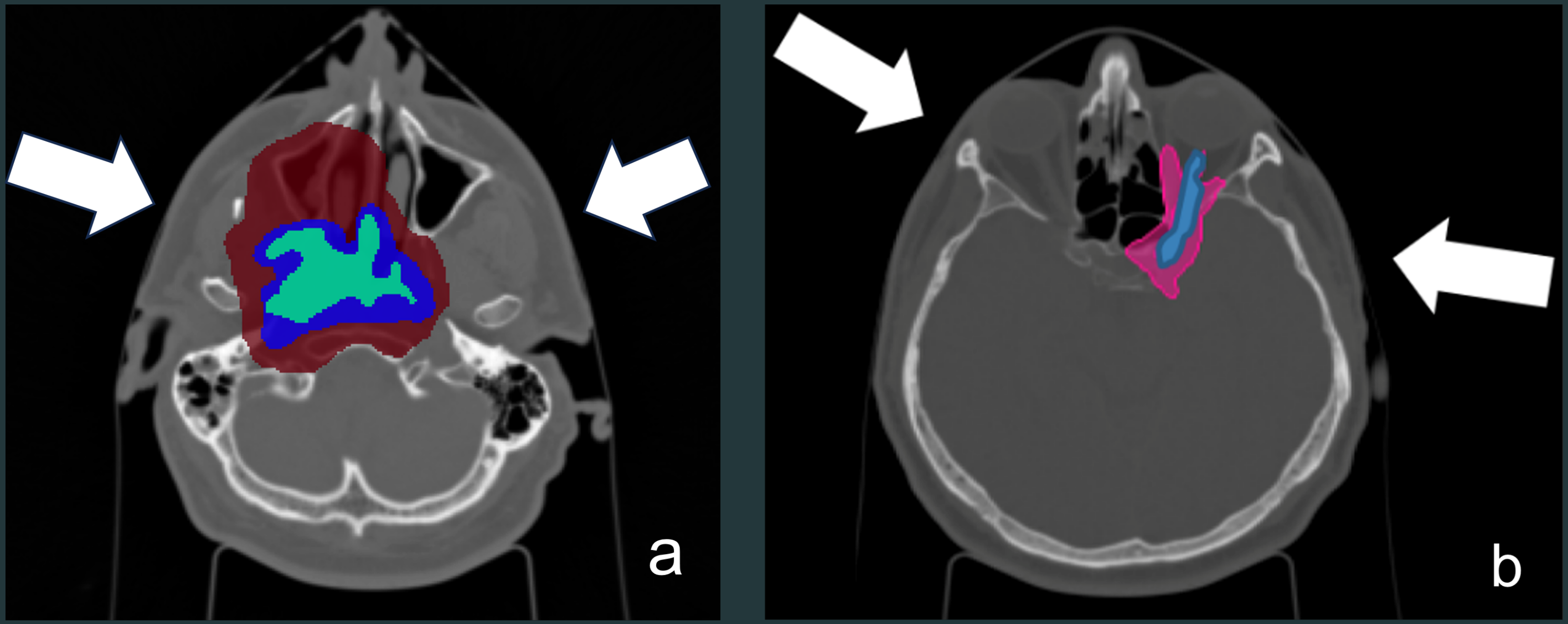
```
Dose Absorbed (Gy): 4.93656
Particle : alpha        Energy (MeV) : 1.47     Number of Primaries : 1669
  Output Damage :
             Species Hits (Gy-1 Mbp-1)
        EaqBaseHits    : 0.532618         error %: 0.0011207
        EaqStrandHits : 0         error %: -nan
        OHBaseHits     : 0.301552         error %: 0.00239989
        OHStrandHits  : 0.109351         error %: 0.00229696
        HBaseHits      : 0.0105935        error %: 0.00394312
        HStrandHits    : 0        error %: -nan

             Damage yield (Gy-0.5 1 cell)
        SSB            : 33.3228          error %: 0.0116192
        SSB+           : 9.92594          error %: 0.0138146
        2SSB           : 21.0673          error %: 0.012474
        SSB total      : 64.316
        DSB            : 11.0401          error %: 0.0130569
        DSB+           : 3.95012          error %: 0.0149066
        DSB++          : 15.1928          error %: 0.0132309
        DSB total      : 30.1829

             Breaks yield (Gy-0.5 1 cell)
        SSB direct     : 0.81028          error %: 0.0236456
        SSB indirect   : 56.3145          error %: 0.0117989
        SSB mixed      : 7.19124          error %: 0.00180369
        SSB total      : 64.316           error %: 0.0118208
        DSB direct     : 0.506425         error %: 0.0316802
        DSB indirect   : 16.8133          error %: 0.0124208
        DSB mixed      : 2.7347           error %: 0.0183804
        DSB hybrid     : 10.1285          error %: 0.0128825
        DSB total      : 30.1829          error %: 0.0123043

        SSB/DSB        : 2.13087
```

MC for clinical applications ?

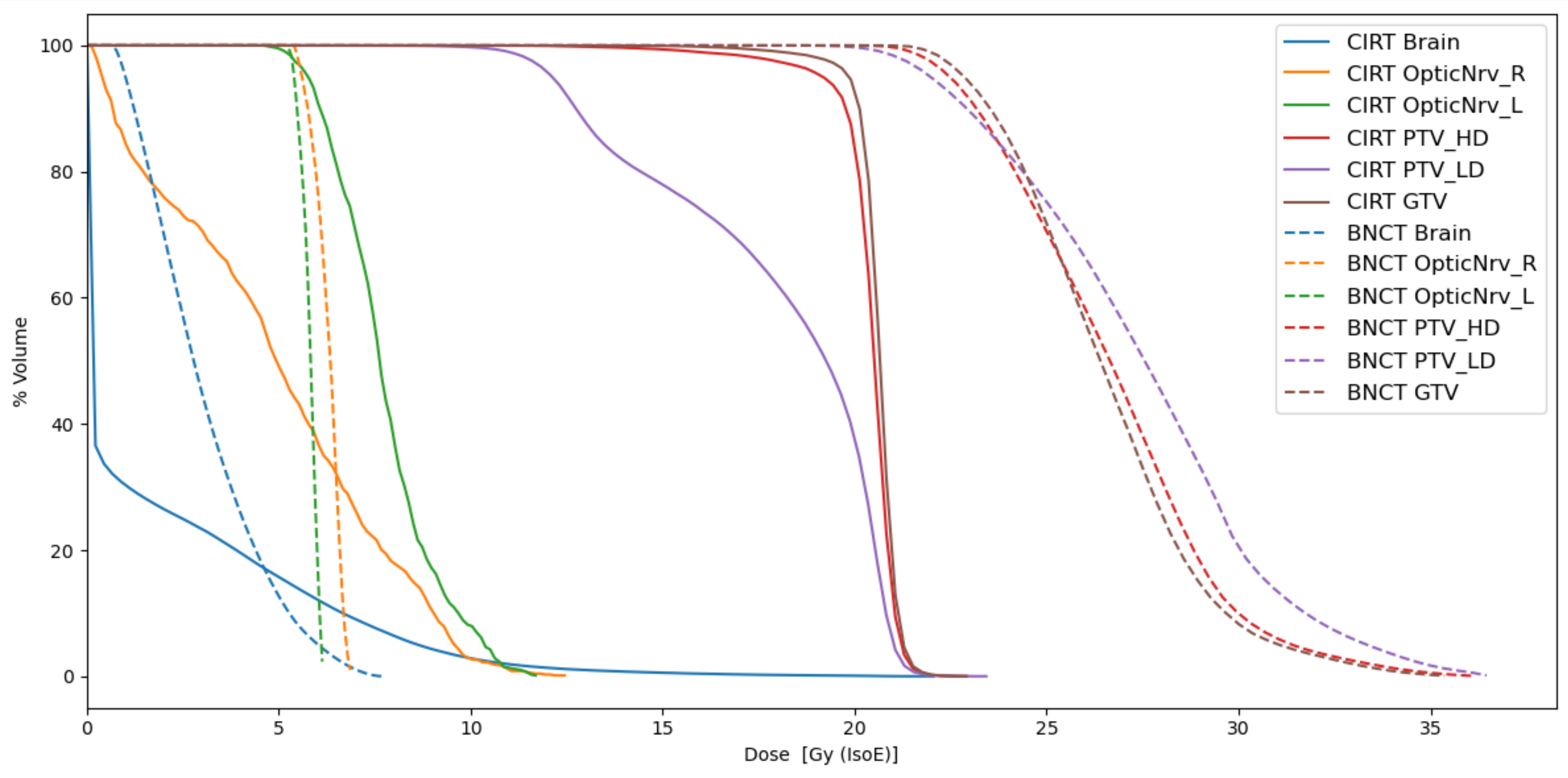
From the development of the facility to Treatment Planning Simulations



CIRT is reported in photon-equivalent units, converting absorbed dose through the Local Effect Model (LEM). Then we translated carbon ion dose values into single fraction doses using BED formalism.

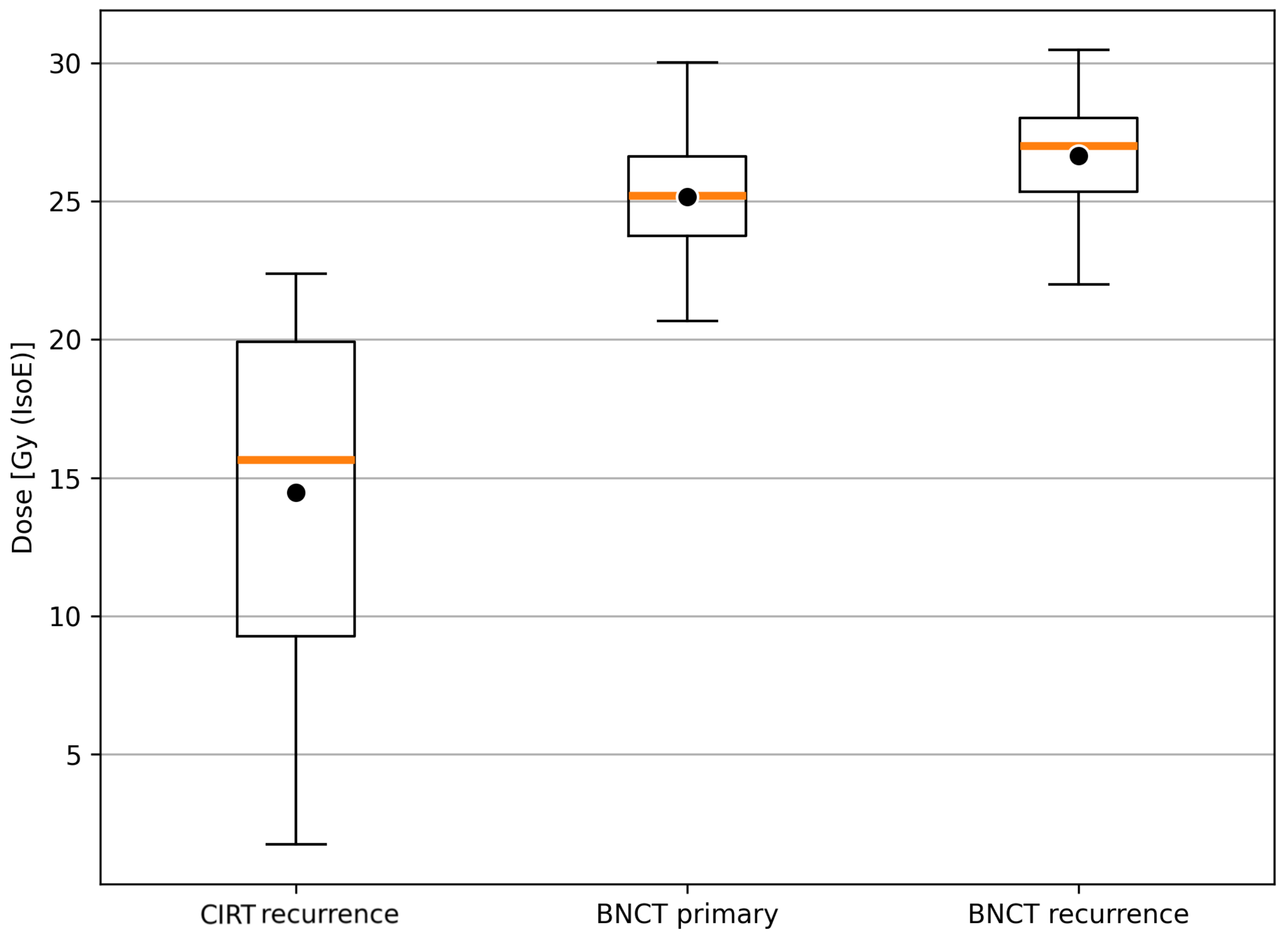


BNCT simulations of the primary tumour and recurrence were carried out by using the IT_STARTS software.
The computed Isoeffective dose is equivalent to a single photon fraction.



DVH of the CIRT and of the BNCT treatment. Gy(IsoE) of x-axis indicates Gy (IsoE, C12, BED) for CIRT and Gy (IsoE, BNCT) for BNCT.

Dose distribution in the ROI corresponding to the recurrence volume for: **CIRT**, **BNCT** treatment of the primary **tumour** and **BNCT** treatment of the **recurrence**.



Deepening the dose-effect relation in BNCT

GIOCONDA

- New boron carriers
- New boron imaging methods
- New biological assays
- New biological models

Input for models of photon-equivalent dose, TCP, NTCP

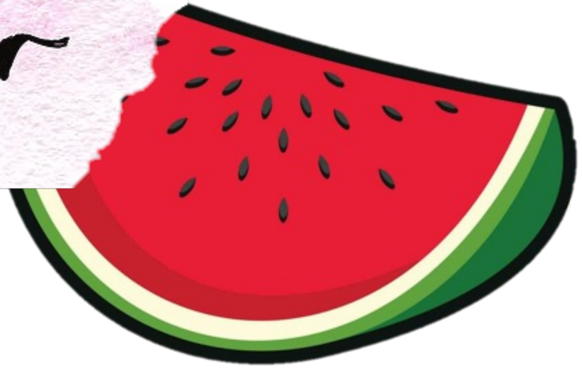
Photon Isoeffective Dose model

Microdosimetry

Artificial Intelligence methods in treatment planning

Towards more effective BNCT treatment planning

Hope
is the only
thing stronger
than fear



Anthem
AdvaNced Technologies for Human-centEred Medicine

Pistone, Daniele et al. “Cellular irradiation with 583 keV protons at the CIRCE tandem accelerator: a dosimetric and radiobiological investigation for BNCT applications” **Journal of Instrumentation**. (2025)

Imperio, Daniela et al. “A Novel Closo-Ortho-Carborane-Based Glucosamine Derivative as a Promising Agent for Boron Neutron Capture Therapy” **Pharmaceuticals**. (2025)

Pezzi, Cristina et al. “Dosimetric comparison of the BNCT treatment planning performances when using a nnU-NET to automatically segment Glioblastoma Multiforme” **Health and Technology**. (2025)

Marcaccio, Barbara et al. “Towards an adequate description of the dose-response relationship in BNCT of glioblastoma multiforme” **Medical Physics**. (2025)

Postuma, Ian, et al. "Using the photon isoeffective dose formalism to compare and combine BNCT and CIRT in a head and neck tumour." **Scientific Reports**. (2024)

Selva, Anna, et al. “A new boron-doped gas microdosimeter for clinical Boron Neutron Capture Therapy” **Applied Radiation and Isotopes**. (2025)

Wu, Yan, et al. "Optimization of Subcellular Boron Distribution Measurement Using UV-C Imprint and Neutron Autoradiography in Boron Neutron Capture Therapy." **Radiation Measurements** (2024).

Perotti Bernardini, Giuliano Franco, et al. "Comparison of Photon Isoeffective Dose Models Based on In Vitro and In Vivo Radiobiological Experiments for Head and Neck Cancer Treated with BNCT." **Radiation Research** (2022).

Viegas, Ana Mailén Dattoli, et al. "Detailed dosimetry calculation for in-vitro experiments and its impact on clinical BNCT." **Physica Medica**. (2021)