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HIGH LET SPECTRAL AND MICRODOSIMETRIC CHARACTERIZATION OF SECONDARIES IN THE TREATMENT OF ALZHEIMER'S DISEASE WITH NEUTRON CAPTURE THERAPY

<u>M. Hervé¹</u>, Y. Perrot¹, C. Villagrasa¹ & N. Protti^{2,3}

¹Institut de Radioprotection et de Sûreté Nucléaire (IRSN), Ionizing Radiation Dosimetry Laboratory (LDRI) Fontenay-aux-Roses, France. ²University of Pavia, Department of Physics, Pavia, Italy. ³National Institute of Nuclear Physics INFN, Pavia Unit, Pavia, Italy.

ETSOF

FRAMEWORK

Alzheimer disease (AD) neurodegenerative dementia (affecting the central nervous system & leading to cell death)



55 million affected today (2019 evaluation) up to 139 million by 2050⁽¹⁾

No cure to this day ...

BUT : eradication of amyloids (A β aggregates) associated with reduction of cognitive & functional decline



NECTAR = NEutron Capture-enhanced Treatment of neurotoxic Amyloid aggRegates <u>*https://fisica.unipv.it/NECTAR-EU-FETOpen*</u>

Curative treatment based on neutron capture therapy targeting AD A β aggregates



(1) World Health Organization figures from World Alzheimer report 2022











 $10\mathbf{B}$

Auger electron + X rays

- Internal conversion electron $158Gd + \gamma + 7.9 MeV$

 $A\beta$ fibril (nm- μ m)



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 $^{157}Gd + n \rightarrow$



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V GEANT4 INTERNATIONAL USER CONFERENCE AT THE PHYSICS-MEDICINE-BIOLOGY FRONTIER - OCTOBER 2022

THE NECTAR PROJECT

Main goals :

- Synthetize a Gd/B enriched molecule able to bind selectively with A β aggregates inside the brain
- In vitro depolymerization of the Aβ folded structures (from oligomers to plaque) with high LET particles irradiation
- **micro- & nano-dosimetric** calculations & measurements to understand the depolymerization process
- In vitro & in vivo **irradiation of AD biological models** to obtain a proof of concept for the developed Gd/B carrier
- Identifying **dose limits** (threshold & rate) to define the frame of a treatment plan



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MONTE CARLO MODELLING IN NECTAR

Main Goal : modelling high LET secondaries effects

- Fully characterize the production of the secondaries
- Determine the dosimetric impact
 - Secondaries characterization (specific energy, lineal energy)
 - Energy deposit at nm scale
- Consider various experimental condition (boron concentration, target size, neutron source...) → to validate the simulation approach & to perform the correlation with biological effects on the target





GEANT4 for neutrons : High precision package with thermal scattering process



FIRST SIMPLIFIED SIMULATION SET UP

Source :

Neutron flux of the Pavia TRIGA Mark II research reactor

- Target : *plaque aggregate* **100 µm** radius sphere filled with water (inside water world)
- Boron concentration : 100 ppm (¹⁰B)
- Characteristic quantity : energy deposit per neutron source & unit mass inside the target



From : V. Pascali - Monte Carlo simulations ranging from microscopic up to macroscopic level for the irradiation of protein aggregates exploiting neutron capture reactions - 2021





FROM ENERGY DEPOSIT TO SPECIFIC ENERGY [z = ε (energy deposit) / m (target mass)]





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MONOENERGETIC BEAMS – 10 eV NEUTRONS

Neutron source @ 10 eV

- Population below Q = 2.31MeV peak : α particles & ⁷Li that are exiting the target
- Very low Gy bin : neutron elastic scattering on hydrogen or oxygen in water





SPECIFIC ENERGY AS FUNCTION OF THE INITIAL NEUTRON ENERGY



Neutron energy $\nearrow \rightarrow$ number of events where all the energy available is not deposit in the target \checkmark

Neutron capture on ¹⁰B is located deeper in the target $\rightarrow \alpha$ particles & ⁷Li stay in the volume



PERSPECTIVES

[On going work and following steps

Secondaries discrimination & associated effects on microdosimetric values

Target specification, different size models & boron concentration

Nanodosimetry calculations with GEANT4-DNA ↔ depolymerization process

[In parallel : work/discussion with experimentalist on the project to obtain validated & possible experimental conditions





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THANK YOU FOR YOUR ATTENTION

Contact info: marine.herve@irsn.fr

