REPORT on the PIANOFORTE-funded training course

PRO_TREAT PROtecting while TREATING:

from the basic principles of the biological effects of ionizing radiations up to their use in neurodegenerative disease

organized by University of Pavia, Istitut de Radioprotection et de Sûreté Nucléaire and Stockholms Universitet and hosted by the University of Pavia, Pavia, Italy 18 – 22 September 2023

The PRO_TREAT course was organised within the framework of the NECTAR (NEutron Capture enhanced Treatment of neurotoxic Amyloid aggRegates) project funded by European Commission under the H2020 - FETOPEN - 2018 - 2020 call, Grant Agreement #964934.
NECTAR aims to study the efficacy and safety of a possible low-dose and low dose-rate treatment for Alzheimer's disease (AD) based on the use of low-energy neutrons and compounds enriched in ^{10}B and ^{157}Gd that selectively bind to β-Amyloid aggregates, one of the main culprits of AD.
The PRO_TREAT course aimed to provide basic knowledge on multidisciplinary topics needed in scenarios where acute radiation exposure is inevitably linked to low-dose exposure, such as cancer radiotherapy, targeted therapies for cancer and other diseases, as well as Capture Enhanced Neutron Irradiation (CENI) being developed by the NECTAR project. Several subject areas were of interest starting from the physics of ionising radiation, to neutron spectroscopy and microdosimetry up to neurobiology.

PARTICIPANTS, LECTURERS and PRACTICAL ASPECTS for the ORGANIZATION

The PRO_TREAT course was organised for a total number of 12 participants, giving priority to PhD students. The selection was made by evaluating specific documentation (CV, motivation letter and recommendation letter).
A few days before the start of the course, two students informed us that, due to personal reasons, they would not be able to attend the lessons in person, which is why we decided to deliver the entire course in a bimodal manner, both online, using the Zoom platform, and in person. This resulted in 10 in-person and 5 remote students, most of whom were PhD students, 4 MSc students, a postdoctoral researcher, a staff member and an assistant professor.
There was no fee for the course and in-person participants were offered accommodation, lunches and morning and afternoon coffee breaks for the duration of the course.

The lecturers were chosen from among the NECTAR partners in order to deliver targeted and in-depth lectures on all topics of the different scientific areas intertwined in the project.

This partnership has received funding from the European Union's "EURATOM" research and innovation program under the 101061037 grant agreement.

In particular: N. Protti, S. Altieri and V. Pascali from the Physics Department of the University of Pavia, Italy; A. Deagostino, P. Renzi, S. Geninatti, D. Alberti from the Chemistry department and the Biotechnology and Health Sciences department of the University of Turin, Italy; D.Rastelli, S. Pasquato and C. Caprioli from Raylab solutions s.r.l., Italy; A. Pola, D. Bortot and D. Mazzucconi from the Politecnico di Milano, Italy; C. Balducci, E. Micotti, E. Gobbi, G. Forloni and S. Fumagalli from the Mario Negri Institute, Milan, Italy; Y. Perrot from the Institut de Radioprotection et de Sûreté Nucléaire (IRSN), Paris, France; R. Dodel and A. Ross from Essen University Hospital, Essen, Germany; L. Lundholm from the Department of Molecular Biosciences, Stockholm University.
Thanks to the presence of these numerous speakers, it was possible to investigate all the topics at the very base of the NECTAR project, and to delve into various aspects through lectures and hands-on sessions.



PRO_TREAT Course - pictures of the lectures

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COURSE CONTENTS and HANDS-ON SESSIONS

The course was delivered in one-week, full day, through lectures and hands-on sessions. Hands-on gave students the opportunity to delve more deeply into some of the topics. In particular, the first hands-on took place during the second afternoon of the course and focused on the Monte Carlo Geant4 and Geant4-DNA codes. The students were able to carry out Monte Carlo simulations on various scales (from microscopic to macroscopic) using their laptops thanks to a virtual machine that they were provided with before the start of the course.
The third afternoon was devoted to new hands-on sessions focusing on neutron spectroscopy and unfolding. The students were provided with pre-recorded data so that they could work independently.
The last hands-on took place on the fourth afternoon of the course and focused on image analysis. Specifically, during the first half of the lesson, the students worked on images of small animals, while during the last part they analysed images of microglia cells.

During the morning of the last day of the course, the students had the opportunity to visit the Applied Nuclear Energy Laboratory (LENA) where the Triga Mark II nuclear research reactor is housed and where the experimental activity related to the NECTAR project is conducted. Afterwards, the students participated in an online tour of the National Centre for Oncology Hadrontherapy (CNAO) facility located in Pavia.

The detailed programme of the PRO_TREAT course is presented below.

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Monday 18.09.2023:
9-9:45: registration
9:45-10:30: NECTAR overview, N.Protti, Pavia University, Pavia, Italy
10:30-11:00: coffee break
11:00-12:30: Alzheimr's disease and ageing, G.Forloni, Mario Negri Institute for Pharmacological Research, Milano, Italy
12:30-14:00: lunch
14:00-15:00: radiation-matter interaction, S.Altieri, Pavia University, Pavia, Italy
15:00-16:00: NCT principles, V.Pascali, Pavia University, Pavia, Italy
16:00-16:30: coffee break
16:30-17:30: Design and synthesis of NCT therapeutic agents for the targeted delivery of boron and gadolinium, A.Deagostino & P.Renzi, Torino University, Torino, Italy

Tuesday 19.09.2023:
9:00-10:00: neutron spectrometry: theory and measurements, D.Rastelli, Raylab solutions s.r.l., Italy
10:00-11:00: neutron dosimetry, A.Pola, Milano Politecnico, Milano, Italy (1h)
11:00-11:30: coffee break
11:30-13:00: Monte Carlo models for IR-induced damages in biological matter, Y.Perrot, Institut de Radioprotection et de Sûreté Nucléaire, Paris, France
13:00-14:00 lunch
14:00-15:00: Geant4 and Geant4-DNA **hands-on**, Y.Perrot, IRSN, Paris, France & V.Pascali, Pavia University, Pavia, Italy
15:00-16:00: Geant4 and Geant4-DNA **hands-on**, Y.Perrot, IRSN, Paris, France & V.Pascali, Pavia University, Pavia, Italy
16:00-16:30: coffee break
16:30-17:30: Geant4 and Geant4-DNA **hands-on**, Y.Perrot, IRSN, Paris, France & V.Pascali, Pavia University, Pavia, Italy
17:30-18:00: tutorship

Wednesday 20.09.2023:
9:00-9:45: effective vehiculation of B/Gd compounds towards brain, S.Geninatti, Torino University, Torino, Italy
9:45-10:30: in vivo B/Gd concentration measurements by theranostics agents, D.Alberti, Torino University, Torino, Italy
10:30-11:00: coffee break
11:00-11:45: biological models in NECTAR, C.Balducci, Mario Negri Institute for Pharmacological Research, Milano, Italy
11:45-12:30: clinical translation of NECTAR project, R.Dodel, Essen University Hospital, Essen, Germany (on-line)
12:30-13:00: tutorship
13:00-14:00 lunch
14:00-15:30: **hands-on** using pre-recorded data sets of n-spectrometry, S.Pasquato, Raylab solutions, Italy + hands-on using pre-recorded data sets of n-spectrum unfolding, N.Protti, Pavia University, Pavia, Italy

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15:30-16:00: coffee break
16:00-17:30: **hands-on** using pre-recorded data sets on micro- and nanodosimetry, D.Bortot & D.Mazzucconi, Milano Politecnico, Milano, Italy
17:30-18:30: tutorship

Thursday 21.09.2023:
9:00-9:45: biological features of amyloidosis and protein aggregates in AD, M.Gobbi, Mario Negri Institute for Pharmacological Research, Milano, Italy
9:45-10:30: low doses and low dose rates effects, with particular focus on brain tissues, L.Lundholm, Stockholm University, Stockholm, Sweden
10:30-11:00 coffee break
11:00-11:45: ionizing radiation induced immune effects in the brain, A.Ross, Essen University Hospital, Essen, Germany (on-line)
11:45-12:30: Radiotherapy and BNCT of the brain, A.Wittig, Würzburg University, Würzburg, Germany
12:30-13:30: lunch
13:30-15:00: **hands-on** using pre-recorded small animal MRI, E.Micotti and F.Moro, Mario Negri Institute for Pharmacological Research, Milano, Italy
15:00-15:30: coffee break
15:30-17:00: **hands-on** using pre-recorded microscopy images, S.Fumagalli, Mario Negri Institute for Pharmacological Research, Milano, Italy
17:00-18:00: tutorship
Evening: social dinner

Friday 22.09.2023:
9:00-9:30: tutorship
9:30-11:00: final test, presentations/comments on data analysis
11:00-11:30: coffee break
11:30-13:00: LENA TRIGA Mark II reactor on-site tour & CNAO virtual visit

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FINAL EXAM and PARTICIPANTS' EVALUATION FORM

On the last day of the course, the students were given a final test consisting of multiple choice questions. These covered all the topics addressed during the week and were prepared directly by the speakers involved. The students achieved a high score and were awarded a certificate of attendance for the course.

All material used during the lectures and hands-on sessions was made available to the students in a drive folder.

In the days following the end of the course, students were sent a form to fill out anonymously in order to assess the quality of the lectures. This is shown below with the corresponding scores.

QUESTION	AVERAGE SCORE (1-low to 5-high)
What is your general view about the quality of the course?	4.4
Did the content of the course match your expectations?	4.6
Did you have enough basic knowledge to follow the course?	4.7
How much knowledge did you acquire from the course?	4.4
Did you miss certain subjects that you think would have been relevant?	2.2

Report prepared by Nicoletta Protti – PRO_TREAT local Course Director

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