Editorial

Dear reader,

Here we are with issue 2 of the RAPTOR newsletter. This publication coincides with the conclusion of 2022, a year of intense activity for the project from the scientific and networking point of view.

Inside this issue

A great work has been done to be able to submit 13 deliverables and achieve all the planned milestones. In addition, collaboration between the ESRs and various actors in the consortium has become very active through online and on-site meetings.

Highlight of 2022 was certainly the RAPTOR school held at Cosylab headquarters in Ljubljana in September. It was 6 extremely intense and productive days, which made the cohesion within the consortium even greater.

In this issue of the Newsletter, we have focused precisely on telling the story of the first and second RAPTOR schools, as we believe that training and educational events are essential to pursue the goal RAPTOR has set: **to successfully bring adaptive particle therapy to the clinic**.

What better occasion then, to announce that the **3rd RAPTOR school** will be held from 10 to 15 September 2023 in Switzerland, the event will be organized back to back with the **4D workshop for particle therapy**. All information will be posted on our social channels shortly.

Without further ado, we now leave you to read this issue of the newsletter and wish you a **happy conclusion to 2022 and an inspiring start to 2023**.

Where to find us:

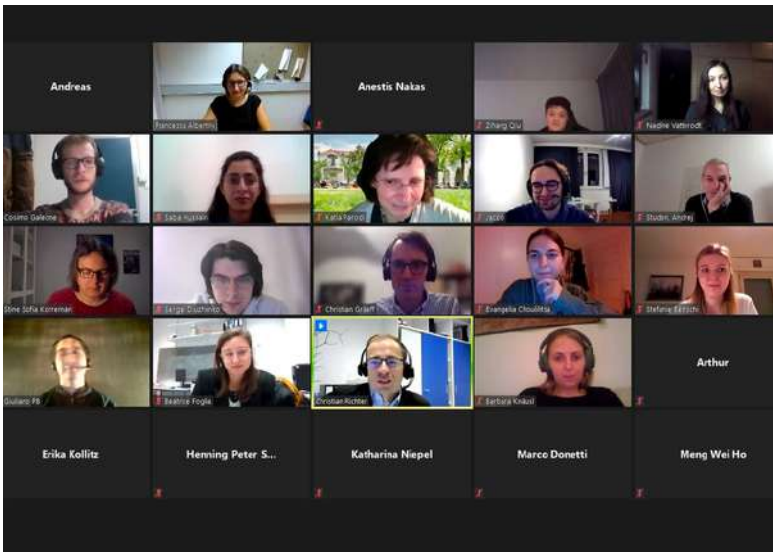
www ESTRO YOUNG CORNER

The First **RAPTOR** *School*

The first RAPTOR school was organized to be held in Munich from 13th to 17th December 2021, but unfortunately, it was conducted virtually due to Covid restrictions. Despite this, the participation was very active among speakers, ESRs and attendees. Specifically, the school counted up to 36 experts that provided insightful talks, along with our 15 ESRs for a total of 95 participants. The school has been accredited by EBAMP as CPD event for Medical Physicists at EQF Level 6 and awarded 72 CPD credit points.

The course aimed at providing a broad introduction to Radiation Therapy (RT) and Particle Therapy (PT) focusing on the integration of three key elements, medical imaging, treatment planning and treatment adaptation, addressed in dedicated lectures of world-renowned experts.
Specifically, the school opened with a dedicated talk on the historical perspective on the developments of proton and light ion therapy, from the pioneering experience at research institutions able to accelerate heavy charge particles up to suitable energies for the treatment of deep-seated tumors, through the first hospital based facilities established in the 1990s, up to the still ongoing exponential growth of state-of-the-art dedicated facilities. Both clinical and physics perspectives of RT/PT were then covered in the first day of the school. The clinical importance of modern technologies, including hypofractionation, in-room imaging and adaptation, towards highly precise dose shaping with a corresponding improvement of normal tissue complications was highlighted, as well as the physics principles on electromagnetic and nuclear interactions of proton and ion beams with matter and their consequences for PT technology.

The value of medical imaging to support treatment planning and adaptation was also revealed, covering topics related to tomographic imaging, with special emphasis on the prediction of the stopping power ratio as prerequisite for accurate range calculation; in-room imaging technologies, to consistently verify the accuracy in dose delivery; time-resolved imaging, to account for organ motion due to respiration; and the basic concepts for the generation of synthetic 3D medical images in multiple contexts, including X-ray imaging, MRI and PET, a key research theme also deeply investigated in RAPTOR to implement daily adaptive PT.



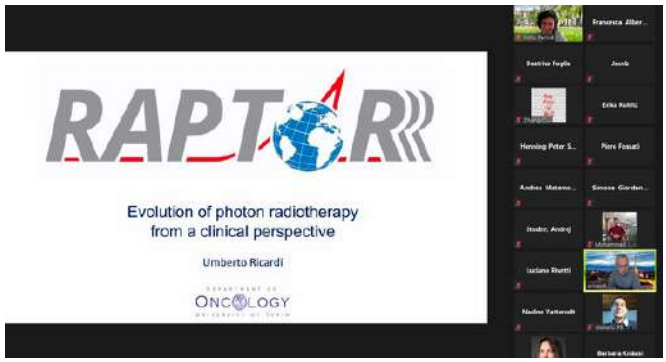
As treatment adaptation consists in adapting the planned dose to the current anatomo-pathological condition of the patient, dedicated talks have also been focused on the recipe to make a robust treatment plan, the basis of biological models in PT planning to account for the higher relative biological effectiveness of particles with respect to conventional RT, and the power of Monte Carlo dose calculations for clinical and research applications.

These scientific lectures were also complemented by more technical training in basic skills relevant to contemporary research in adaptive radiation therapy, such as scripting on modern treatment planning and data analysis. In addition, soft fundamental skills for management, development and scientific communication were also covered.

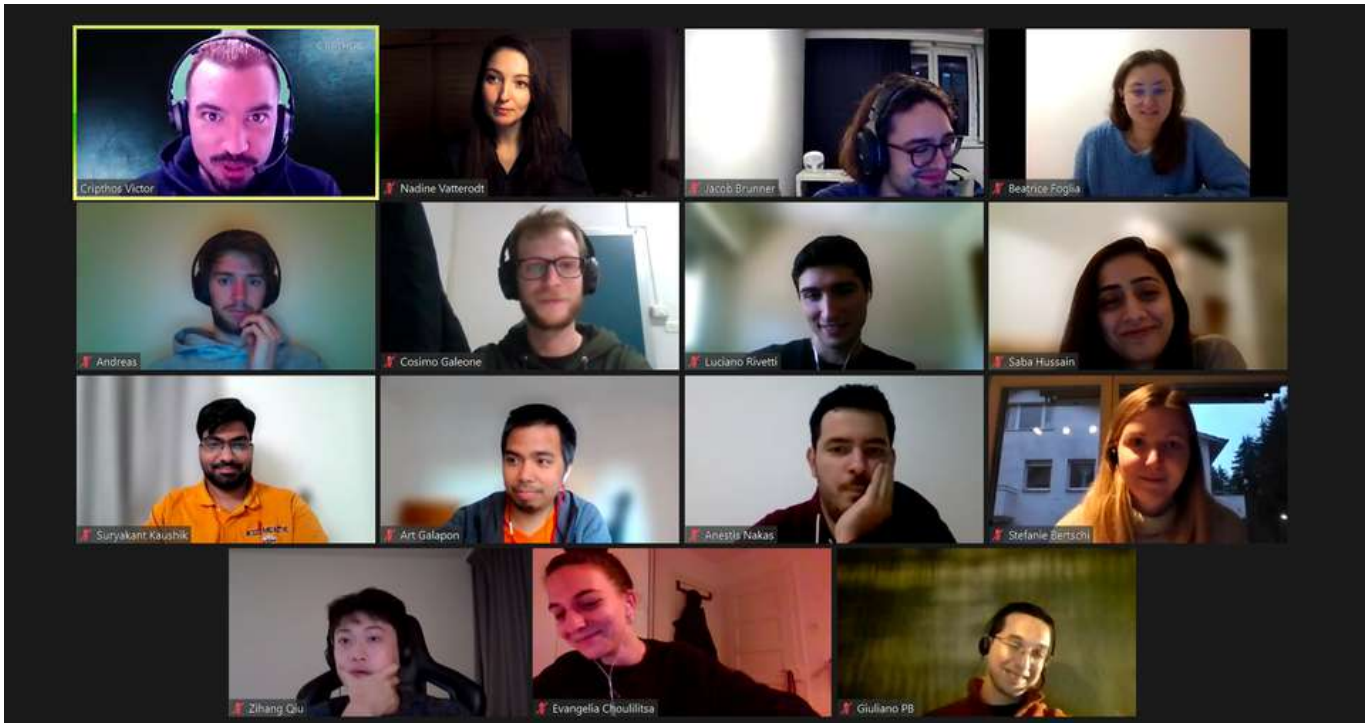
The patient perspective was underlined to provide more information on PT and their access, involving patients in medical decision-making, encouraging them to participate in decisions about their cancer treatment, empowering them as co-creators of their own health. In this scenario, RAPTOR can also make PT treatment modality affordable for the majority of the patients, achieving substantial cost savings and contributing to the democratization of PT.

The participants also received training on Research Data Management which plays a crucial role in every scientific endeavor, especially when patient data are involved. FAIR guiding principles were therefore presented at the first school to make our ESRs aware of the appropriateness of data management and data publication. Parallel to this, we also had the opportunity to discuss publications and Open Access requirements.

In addition to all these activities, a virtual visit of the Radiation Oncology Department of the University Hospital, Ludwig-Maximilian-Universität (LMU) Munich, Munich, Germany was organized, where a new combined MR-linac device is used for advanced adaptive therapy in photon treatments, to show the recent advances of new treatment units able to image anatomical changes that occur before and during treatment in order to adapt the treatment accordingly.



Last but not least, we enjoyed the first school with social activities. Although remotely, we were able to meet and introduce each other, discuss about science and life, and savor the motivation of all the RAPTOR members to achieve RAPTOR objectives and, thus, to push towards clinical implementation of online adaptive particle therapy, paving the way to improved workflows and patient care in PT.



The Second **RAPTOR** *School*

"RAPTOR School – loop requirements" - was held in Ljubljana from the 4th to the 9th of September 2022. It was hosted by Cosylab, one of RAPTOR's founding institutions. The RAPTOR community met at Cosylab for the first time four years ago and it was nice to see the biggest and most prominent experts in the particle therapy (PT) field gather here again, along with up-and-coming scientists.

The school has been accredited by European Board for Accreditation in Medical Physics (EBAMP) as a CPD event for Medical Physicists at the EQF Level 7 and has been awarded 76 CPD credit points. The school hosted 24 expert speakers, along with 15 ESRs, principal investigators and attendees from various RAPTOR beneficiaries and partner institutions. Moreover, to support external students' participation in the RAPTOR school, two scholarships have been awarded.

The main objectives of the 2nd RAPTOR School were to provide advanced scientific knowledge to translate and valorize ideas and concepts into novel clinical tools to increase the efficiency, cost-effectiveness, and innovation capacity of the rapidly emerging PT field. The school was explicitly designed to educate a new generation of entrepreneurial and innovative scientists who will have a long-term impact on advanced adaptive PT. In addition to the technical and scientific classes, soft fundamental skills for entrepreneurship, intellectual property, and certification management were addressed.

The School opened with the talk of Cosylab's CEO and co-founder, Dr Mark Plesko, on entrepreneurship. Dr Plesko recalled his personal example of how a group of physicists grew a scientific project into the world's leading company in their field, what was behind their success and how they overcame the challenges along the way. Mark also gave some common-sense advice on how to start a company, motivating the audience to translate their research into products that can significantly impact the clinic.

Following the School's main objective, advanced knowledge in adaptive PT was provided, revealing modern approaches in each step of the adaptation loop. The current state of treatment and accelerator control systems and what is required to move towards online adaptation workflow were also discussed. The importance of treatment log files collected by these systems for patient specific quality assurance was highlighted along with a broad introduction to the rationale and current clinical practice of PT quality assurance procedures and their applicability for real-time treatment adaptation.

Dedicated talks were focused on logfile-based dose reconstruction for moving targets as a tool for treatment verification and reduction of 4D dose calculation uncertainty. The basic principles, implementation, and role of prompt gamma imaging technique in online adaptive workflow for independent treatment verification were revealed. The key ingredient for online adaptation, as well as for conventional particle therapy, is patient imaging. The deformable image registration (DIR) techniques are essential for adaptive workflow since they allow automated contour propagation and dose accumulation on daily patient geometry. The dedicated talk addressed the basics and mathematical foundation of DIR, and various clinical applications with a specific focus on DIR validation aspects. Moreover, several talks have discussed the basics of AI and deep learning algorithms and their applications to clinical imaging.

Since adaptive workflow requires fast and accurate dose calculation, the physics aspects of Monte-Carlo (MC) dose calculation algorithms were covered. MC algorithms are computationally expensive, so the lecture was focused on simplifications in modelling various physical processes to allow optimal trade-offs between speed and calculation precision. During these talks, the importance of modelling radiobiological effects for protons and heavy ions was highlighted to account for the higher relative biological effectiveness.

A specific talk was dedicated to applications of Machine and Deep Learning for treatment planning. Considering the amount of data generated during online adaptive treatment, it is needed to safely store data and analyze it. In this respect, the acquisition and handling of Big Data in a clinical environment and a broad introduction to Biostatistics were covered during the School. Besides many lectures on mathematical and physical topics, clinical perspectives on daily and online adaptive particle therapy were covered, since particle therapy is a multidisciplinary field, and it is always important for researchers to understand realistic clinical needs.

In addition to the scientific lectures, soft fundamental skills relevant to entrepreneurship and translation of research into the clinical environment have been addressed, such as medical device regulations, intellectual property rights, industrialization, certification, healthcare economics, and challenges of operation of particle therapy facility. A dedicated roundtable was organized, presenting three career paths: a scientist at an institute, a medical physicist in a clinic, and a manager in a company. The ESR could see the benefits and challenges in each of these distinct roles.

On Friday, a special event, “RAPTOR beyond RAPTOR”, was organised. The main goal was to define the next steps in the RAPTOR consortium. We discussed how we could enlarge the consortium and what would be the next scientific breakthroughs we would have to achieve.

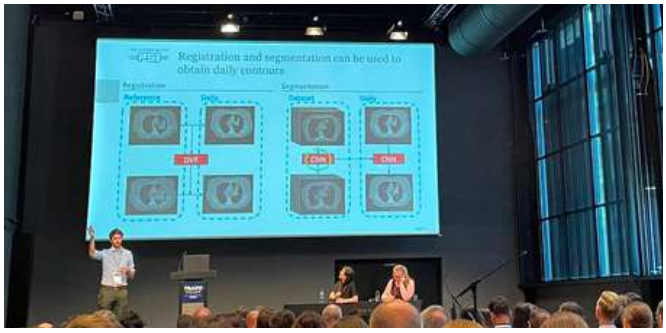
One of the RAPTOR Schools' highlights was a public talk by Dr Thomas ‘Rock’ Mackie, a renowned scientist and an innovator in the radiation therapy, titled "Innovations in medical physics". The talk was held at the Josef Stefan Institute (JSI). Dr Mackie told us stories about different start-ups he was involved in and what questions a successful startup should answer.

Yet, the school was not only about lectures, but we were also able to enjoy social activities. In contrast to the first RAPTOR school, which unfortunately had to be held virtually due to the COVID restrictions, a particular highlight of this latest School was extensive networking between participants. We visited one of the most famous Slovenian spots, a fairy-tale town called Bled. The trip concluded with a nice dinner in a local restaurant.

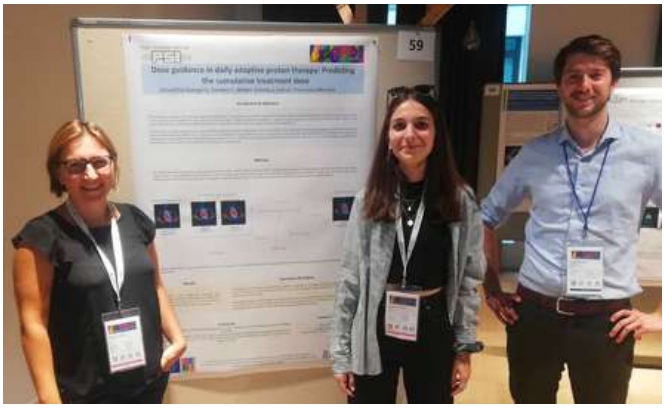
In addition, we also held a dedicated poster session, where RAPTOR ESRs shared their scientific advances with other participants. This session turned to stimulate extensive scientific discussions, development of further cooperation, and strengthening connections within the consortium.

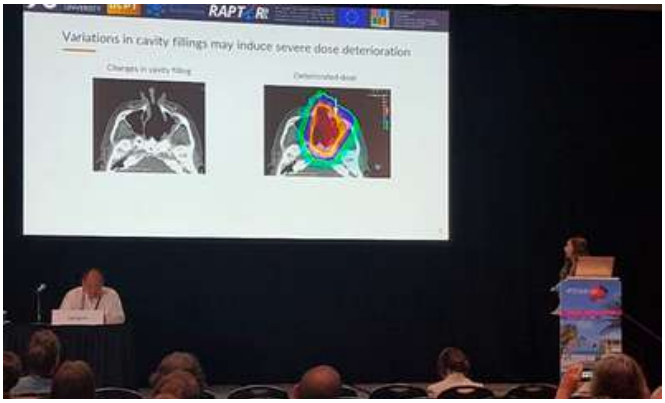
Scientific *Contributions*

The scientific contributions of the ESRs in this first year were diverse. We made contributions in the three work packages.

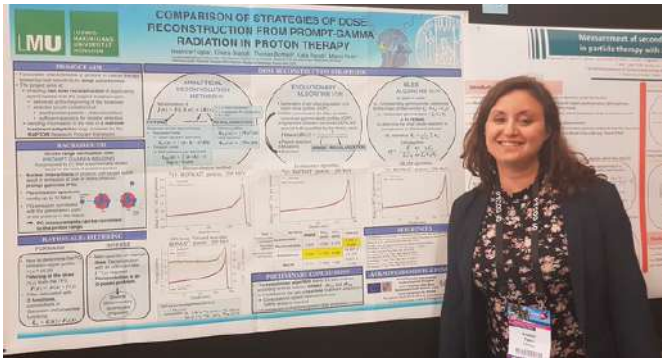


In the **work package 2**, Andreas Smolders (ESR1) was selected for a publication and an oral talk in the **Workshop on Biomedical Imaging Registration** (WBIR), for a small paper at **Medical Imaging in Deep Learning** (MIDL) and an oral presentation in the **Scientific Association of Swiss Radiation Oncology** (SASRO) meeting. The work he presented in WBIR focused on the development of a probabilistic unsupervised deep learning method for predicting the variance of a given deformable vector field (DVF). The work presented at MIDL showed that a deep learning (DL) model that doesn't use Monte-Carlo samplings can be used to generate probability maps of the daily structures faster than DL models which need them. The work he presented at SASRO was focused on the performance analysis of a daily contour segmentation method which uses a patient specific neural network.





In the **work package 3**, Nadine Vatterodt (ESR7) was selected for an oral presentation at **Particle Therapy Co-Operative Group** (PTCOG) annual conference. In this work she compared the dosimetric potential of including anatomical error scenarios to account for changes in nasal cavity filling against the conventional robust optimization for sinonasal cancer. Evangelia Choulilitsa (ESR10) presented a poster in the SASRO meeting. In this work she analyzed two approaches for predicting the total delivered treatment dose as part of a DAPT workflow.



In the **work package 4**, Beatrice Foglia (ESR14) was selected for a poster exhibition at PTCOG. Her work focused on the comparison of three dose reconstruction approaches using prompt gamma distributions. Jacob Brunner (ESR12) presented a poster in the **Drei-Verbände-Tagung** meeting. The research he presented aimed to characterize additively manufactured materials for the design of an E2E test phantom fulfilling the requirements for ion beam therapy. Moreover, they evaluated the printing quality and tissue equivalency of the materials.

We are proud of the wide-ranging conference contributions by the RAPTOR community, especially given that our ESRs started their projects very close to most conference submission deadlines for 2022. We expect that the scientific contributions in 2023 increase significantly.

Secondment
Reports

Andreas Smolders, *Paul Scherrer Institute*

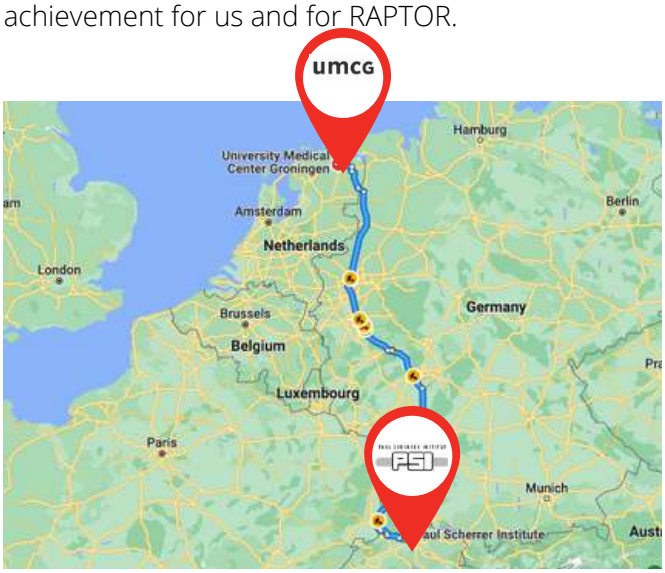
Who: Andreas Smolders, collaborating with Gabriel Guterres Marmitt, Stefan Both, Arthur Galapon and Giuliano Perotti Bernardini
Where: University Medical Center Groningen, Groningen, Netherlands
When: July - August 2022
Why: the use of deformable registration software not available at home institute

How would you describe your secondment in one word?
Revisitable

What did you take home from your secondment?
An article to finish

Which song describes your secondment best?
Noodgeval – Goldband

Originating from Belgium, going to the Netherlands was closer to going home than going far away. I was happy to be able to speak my mother tongue and communicate freely with the open and enthusiastic Dutch people. The group at UMCG immediately made me feel home by answering all my questions, helping me out with my research and, most importantly, taking me out to the best bars in town. We danced on a rooftop, swam at the Groningen 'beach', swam at the actual beach and played pétanque, or 'jeu-de-boules' as they call it. From a social perspective, it could not have been better. Also, for my research, the secondment was worthwhile. Thanks to the great assistance of my colleagues, we could finish what we planned to do in less than half the envisioned time, so I had plenty of time for exploration. Together with Gabriel we restarted an unfinished project on deformable registration uncertainty for dose accumulation. It fitted exactly within the scope of my PhD, and we continued our collaboration after the secondment ended. This has resulted now in the submission of a joined manuscript between our institutes, a great achievement for us and for RAPTOR.

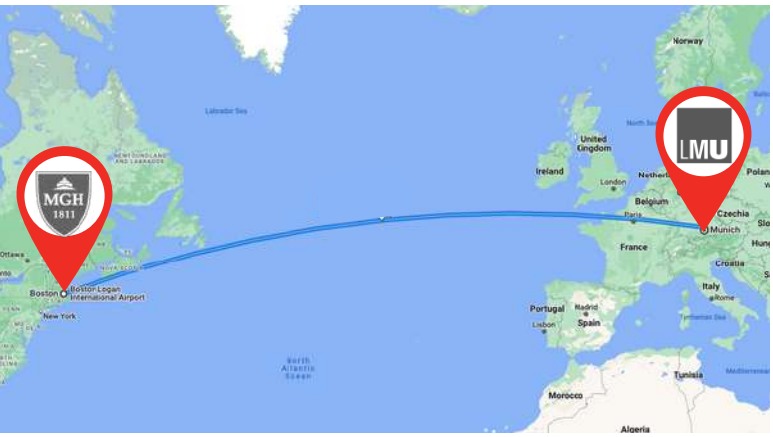


Beatrice Foglia, *Ludwig Maximilian University of Munich*

Who: Beatrice Foglia, collaborating with Thomas Bortfeld and Joost Verburg
Where: Department of Radiation Oncology, Massachusetts General Hospital, Boston, USA
When: June - August 2022
Why: Experimental campaign to acquire data with the PG spectroscopy detector available at MGH. Getting to know how the hospital environment work, more meetings in person with the co-supervisor and conferences attendance.

Going to US has always been a dream, I feel so lucky and grateful to my supervisors and to the RAPTOR consortium for this opportunity. In Boston I met a lot of people belonging to a dynamic and enthusiast group, working on many fields radiation related. I started to learn how an hospital environment works, which was helpful to clear a bit my mind about my future.

I treated a head phantom as if it was a real human patient, which means I had the possibility to put my hands in what comes prior to the proton therapy itself (CT, contouring, treatment planning, ...) and see how medical physicists work. I also gained more experience with experiment and data acquisition, using the prompt gamma spectroscopy detector developed at MGH. These data are useful for my project to make a further step towards the assessment of the dose reconstruction algorithms, which are the main actors of my work.
I also participated to two conferences, where not only I attended interesting talks about innovative topics, but I also understood the importance of networking.



I could have not forgiven myself if I did not visit New York, just a four hour bus drive from Boston, and so I went there. I also had a lot of fun learning US history and visiting many monuments. My colleague Zihang was a great adventure partner and I will never forget the day we went whale watching (and that we actually saw some whales).

How would you describe your secondment in one word?
Lively

What did you take home from your secondment?
Apart from data, pictures and memories

Which song describes your secondment best?
Miley Cyrus – Party in the USA

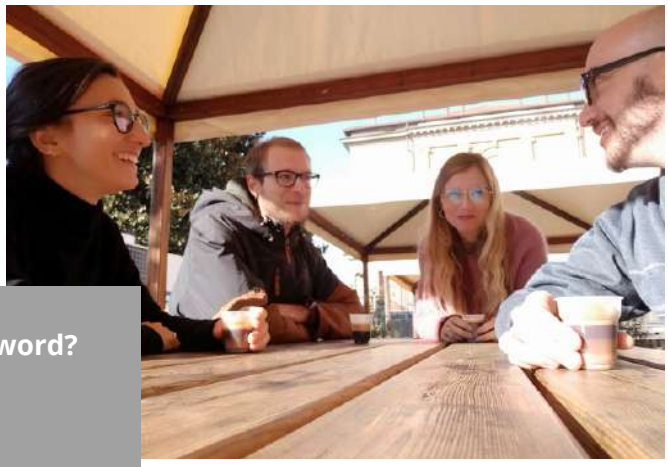
Cosimo Galeone, *GSI*

Who: Cosimo Galeone, collaborating with Simona Giordanengo, Anna Vignati and Felix Mas Milian
Where: University of Torino, Torino, Italy
When: October - December 2021
Why: Getting familiar with a tool developed within the medical physics team of INFN and University of Torino

I spent the first three months of my PhD at the University of Torino. My project is based on a tool developed there, and it was important for me to learn all the details of the algorithm and discuss with the experts who developed the code.

I already knew the team in Torino and I always had total support from them. With the respect to my previous experience in the group, I got to work on a totally different subject and with new students coming from all over. I really like the familiar vibes and the nice people I worked with. They helped me out in the very first stage of the project and thanks to their supervision I have been able to practically start working in a more independent way after this secondment.

I was also very familiar with the city because I did my bachelor and master in Torino. So I had the opportunity to spend time not only with colleagues but also with some old friends from my studies. We watched very nice football matches, amazing concerts and ate the best “polenta” in the mountains.



How would you describe your secondment in one word?
Familiar

What did you take home from your secondment?
Confidence at my new job

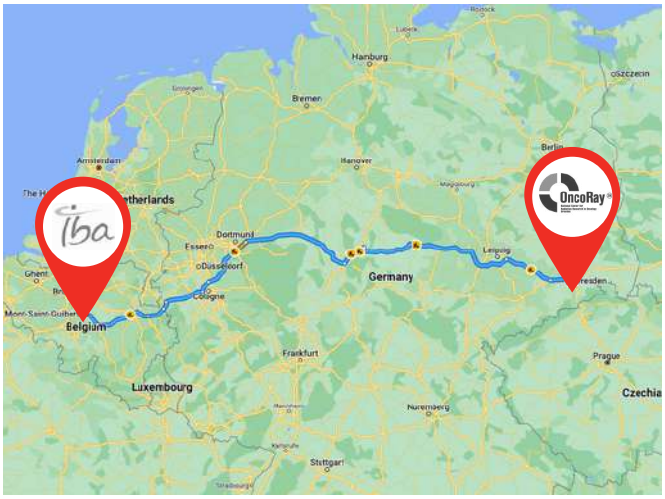
Which song describes your secondment best?
Qui non c’è il mare - Statuto

Stefanie Bertschi, *OncoRay, Dresden*

Even though it was only a short visit of 1 week, it was an amazing stay with a lot of experiences and achievements. I went with the train, which gave me the opportunity to stop in Brussels for a dinner, a short city tour and even some nice concerts at the Brussels Jazz Festival on the 'Grote Markt'.

Who: Stefanie Bertschi collaborating with Guillaume Janssens and Julien Smeets

Where: IBA, Louvain-la-Neuve, Wallonia, Belgium
When: May 2022 (1 week)
Why: Discuss and plan project in detail including further planned secondments and current tasks with second super visor



During the week at IBA, I met my second super visor Guillaume Janssens in person as well as the rest of the R&D team, who gave me a lot of insights in their daily tasks. Together with Guillaume, we defined my project in detail and solved open questions. I was able to test prompt-gamma imaging simulations on cone-beam CTs in preparation for my secondment in Aarhus. Furthermore, I generated our beam model at OncoRay in MC square, which is required for a joint experiment and which also provides us the opportunity for an independent dose calculation. To finish the week, I could join a very interesting tour through the production of the company. I think this week was a great success and I am looking forward to visiting IBA again next year.

How would you describe your secondment in one word?
Insightful

What did you take home from your secondment?
Beam Model in MCsquare

Which song describes your secondment best?
Prove it – Divided By Friday

Zihang Qiu, *University of Amsterdam*

Who: Zihang Qiu, with Thomas Bortfeld, Beatrice Foglia
Where: Massachusetts General Hospital, Boston, USA
When: June - October 2022
Why: Test adaptive planning algorithm on clinical data

This is my second visit to the US, as I lived there for four years for my bachelor's study. But this is my first time living on the east coast. I liked Boston because it is a good blend of old times and new times. On the street, you can see architecture built hundred years ago and, at the same time, modern skyscrapers. You have a lot of activities to do in the town, museum visiting, bar crawling, sports, etc. My favorite is renting a kayak and floating on the Charles River, chilling with music and drinks under the sun. Besides, I have also made many friends in-and-out the office. A special shoutout to Bea and the (Mc) doctors and professors in Nashua for making my visit so enjoyable!

Research-wise, it went surprisingly well. I successfully implemented the adaptive planning algorithm and made replans for a diverse cohort of proton patients that received offline adaptation at MGH. Promising results were obtained. Thanks to everyone that helped me. Besides, I had the chance to get to know the clinical side of radiotherapy. The medical physicists provided me various insights from the clinical perspective, which are useful for my further research. I was also offered the opportunity to interact with the clinical online adaptive photon therapy system operated at MGH, Ethos. I am definitely looking forward to my second visit to MGH.

How would you describe your secondment in one word?
Fun

What did you take home from your secondment?
A lobster toy and a Harvard email address

Which song describes your secondment best?
Vision – Mo'kalamity

Next Events and Important Dates

The 3rd RAPTOR School - Loop Engagement
10 - 15 September 2023
Monte Verità, Ascona, Switzerland
More information here.

The 3rd RAPTOR School will take place in Ascona, Switzerland.
The school is co-sponsored by ETH GRANT "Support for scientific meeting" and will be combined 4D-workshop. **Save the date!**

RAPTOR project has received funding from the European Union's Horizon 2020 Marie Skłodowska-Curie Actions under Grant Agreement No. 955956