ENLIGHT

HITRI plus
Heavy Ion Therapy Research Integration

HIGHLIGHTS
December 2021

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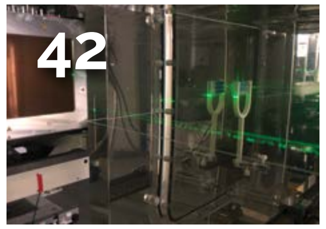

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HITRI*plus*

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HITRI *plus*

Heavy Ion Therapy Research Integration

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— *Management Board Pillar* —

About HITRI*plus*

Heavy Ion Therapy Research Integration plus (HITRI*plus*) (https://hitriplus.eu/) project is a research project funded by the European Commission under the HORIZON 2020 programme H2020-INFRAIA-2020-1. The project, which started the 1st of April 2021, is looking to integrate and propel biophysics and medical research on cancer treatment with heavy ions beams while jointly developing its sophisticated instruments. Moreover, HITRI*plus's* wider objective is to provide radiation oncologists with a cutting-edge tool to treat the fraction of tumours that are not curable with X-rays or protons or have better survival rates or lower recurrences with ions.

Coordinator's role

The management of the project is ensured by CNAO, supported by CERN, GSI, and SEEIIST.

CNAO (National Centre for Oncological Hadrontherapy) is a clinical facility, established and funded by the Italian Ministry of Health and Lombardy Region, to use hadrontherapy for cancer treatments. To date, more than 3500 patients successfully completed the treatment. The CNAO Foundation is also a Centre of Research and Development, whose activities aim to provide continual improvements in the capacity to cure.

CNAO, as HITRI*plus* Coordinator, manages and monitors the project progress of pillar-WPs against contract. As we will see later on, in WP1 CNAO ensures the implementation of the project and the contractual obligations towards the European Commission. This activity implies the overall technical, administrative, financial and legal coordination of the project. In the first place, the role and activities of the overall coordinator concern the monitoring and management of the agreed deliverables and milestones in the contract and secondly, the smooth running of the project as a whole. Directly interconnected to the project management are the activities that will ensure compliance with the HITRI*plus* ethics requirements needed for patients, human cell lines, patient personal data and animal experiments in case they will performed with the research accesses (WP13).

The general set-up of the HITRI*plus* project management consists of three functional and hierarchical layers: The General Assembly, the Coordinator, the Technical Project Board interfacing the WPs thematically organised in three types of activities: Networking, Transnational Access, Joint Researches Activities.

Another important commitment of the Project Coordinator (PC) is the responsibility for the technical management and scientific coordination of the project, assisted by the Deputy Project Coordinator from CERN. The PC chairs the Technical Project Board meetings, leads the Central Project Office, defines the principles for internal and external communication, monitor the overall progress of the project, follow and verify the deliverables, represent the project vis-à-vis the European Commission, be responsible for preparing contractual reports, organise and transmit relevant project information, manage potential conflicts, communicate with external stakeholders, and monitor and promote gender equality. Not only the administrative and financial tasks and responsibilities but also includes managing the financial administration of the overall project expenses and reporting the overall budgetary situation of the project to the European Commission.

CNAO facility in Pavia, Italy

The Technical Project Board (TPB) represents the technical focal point for the project activities. The TPB is chaired by the Coordinator and consists of the three WP Coordinators selected by the Coordinator to represent their own Pillar.

Consortium

The consortium of HITRI*plus*, made by 22 Institutes from 14 European countries, consists of 2 major European heavy-ion physics laboratories, 4 European ion therapy centres, 8 world-class research institutions, 5 leading universities, 3 innovative SME's (two of which are from the South-East Europe region). Some partners have been active in the field of heavy-ion therapy for many years and form the core of Europe's expertise and capacity in this field. Their commitment to the HITRI*plus* project is clearly evidenced by the substantial voluntary co-funding that each of them is willing to bring into the project. Their combined knowledge and background, grounded in the experience of running four state-of-the-art treatment facilities and committed user communities, constitutes the core of this proposal. Some Consortium partners have also previously been involved in challenging European projects.

The HIT, CNAO, MEDA, MIT facilities are central players for the clinical and research activities and the related networking and favour the trans-national access of patients and medical professionals. These facilities also provide the technological, medical, research and economic benchmarks against which the South-East European International Institute for Sustainable Technologies (SEEIIST) will base the new RI in the SEE countries. Their expertise is also crucial to the project's effort to create a fu-

European Commission

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

The consortium consists of 2 major European heavy ion physics laboratories, 4 European ion therapy centres, 8 world-class research institutions, 5 leading universities, 3 innovative SME's (two of which from SEE region). The management of the project is ensured by CNAO, supported by CERN, GSI, and SEEIIST.

ture medical user community in the SEE countries. Together with GSI, which has extensive expertise in biophysics, medical physics, radio-biology and heavy-ion accelerator systems and that was the place where first European patients were treated with heavy ion therapy, they will allow access to the international research community to the heavy ion beams and related research infrastructures.

CERN's expertise lies in designing, constructing and operating accelerators and their subsystems, including superconducting magnets, synchrotrons, ion sources, beam dynamics, control systems and diagnostics. In these activities, CERN will partner with the accelerator design team of SEEIIST and CNAO, and specifically for the linac design with the crucial expertise of BEVA, a spin-off company of Frankfurt University. RTU will contribute to the gantry design with its expertise in mechanical engineering. The activity on superconducting magnets will access the competencies of the main European players in the field, with a consolidated tradition of collaboration in the CERN projects (LHC, HL-LHC) and in other European initiatives (ARIES, EUCARD2): INFN, CERN, PSI, CIEMAT, CEA, UU and Wigner RCP. The SME SENTRONIS will contribute to designing and building magnetic measurement instrumentation for magnet characterisation. CSL is a worldwide renowned company for the control system, with specific expertise in the control of medical accelerators, having designed for example the control system of MEDA. It will exploit this experience and jointly with MEDA and the research centre IJS will design and develop modular accelerator and therapy control systems.

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Sandro Rossi, CNAO

Author:
Angelica Facoetti, CNAO

— *Joint Research Activities pillar* —

The objective of the JRA pillar

The HITRI*plus* Joint Research Activities (JRA) aims to develop advanced beam delivery techniques to improve the quality of the beam delivered to patients and to experimenters, by enhancing the control of the beam properties and of the dose delivered. On the accelerator side, the goal of the HITRI*plus* JRA's consists in developing new technologies to increase beam intensity for faster dose delivery, and to reduce the dimensions and cost of the accelerator and of the gantry used to control the position of the beam on the patient. The improvement in both accelerator and gantry will be allowed by extensive use of superconductivity to generate higher magnetic fields and will take place in close connection with European industry that is a world leader in the field, to prepare both elements for an industrialisation phase followed by possible commercialisation by a company or a consortium of companies identified in the frame of this Starting Community.

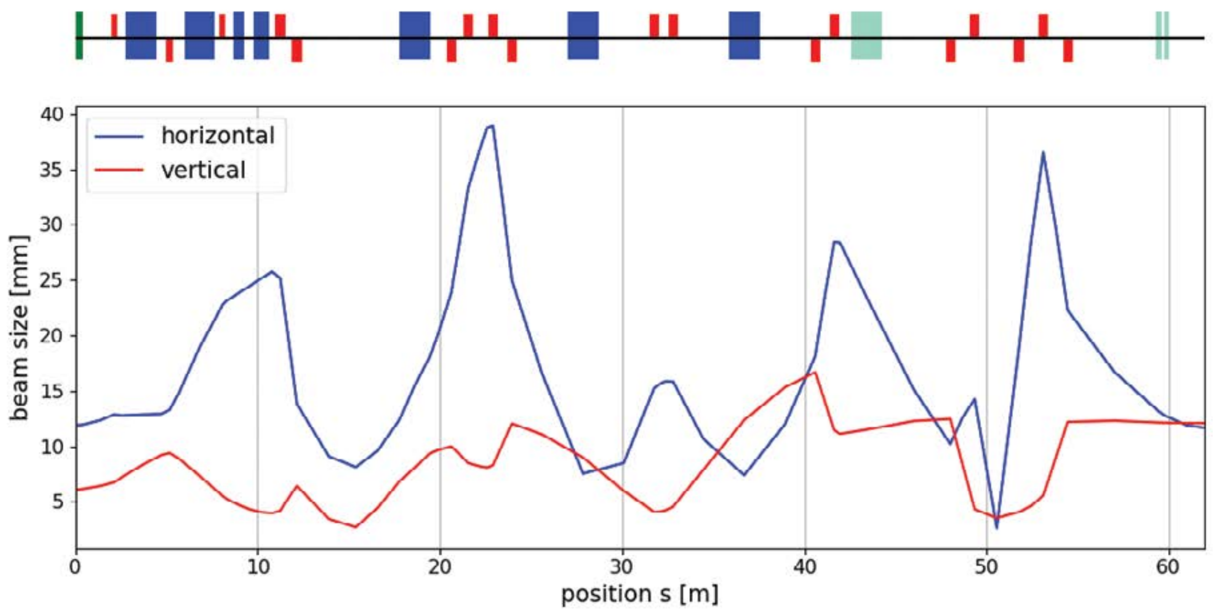
With this in mind, HITRI*plus* will help to foster the economic development of Europe through joint technological developments and allow faster transfer of the innovative outcome of the JRA activities to the industrial partners for exploitation. In parallel, the advances in clinical and medical physics research and gained expertise will be transferred beyond the four current therapy facilities and throughout Europe, through the targeted education and training programme provided in HITRI*plus*. In addition, and thanks to the strong engagement of SEEIIST, many opportunities will open to integrate into this starting research community new talents from the SEE.

Structure

The JRA pillar is structured with WPs that have a double goal:

General 3D view of the SEEIIST facility

Perspective



Horizontal and vertical beam size evolution for beam line tr1h. The beam size is given for Carbon at 400 MeV/u and for beam spot on patient of 10 mm. The dark blue are dipole magnets, red are quadrupole magnets and this turquoise are inactive dipole magnets or fast scanning magnets.

> ***At the end of HITRIplus, a new, optimized and up-to-date design of a novel infrastructure will be available, to become the basis of SEEIIST and of all future ion therapy centres to be realized in Europe and possibly in other regions of the world.***

first to improve and upgrade the systems already in use at the European facilities and secondly to provide the basic components of a future next-generation design. Thus, they will aim to promote research and technological development both in terms of applications of ions in the medical field, with the study of new components of ion accelerators, such as for example new sources, new linear accelerators and new dose distribution systems, both for industry through the development of new superconducting magnets (synchrotron carriers) more efficient and with lower production costs. At the end of HITRI*plus*, a new, optimized and up-to-date design of a novel infrastructure will be available, to become the basis of SEEIIST and of all future ion therapy centres to be realized in Europe and possibly in other regions of the world. Strong coordination of the JRA WPs is required to come to a shared and integrated picture of the different technologies and deliverables, which will rely on the CERN experience in dealing with new technologies and management of distributed groups.

The JRA pillar is composed of 6 WPs: improved accelerator and gantry design (WP7), superconducting magnet design (WP8), advanced beam delivery (WP9), multiple energy extraction systems (WP10), controls and safety (WP11), radiobiological dosimetry and Quality Assurance (QA, WP12).

The JRA pillar coordinator is Maurizio Vretenar (CERN) who is also the scientific coordinator of WP7. CERN has coordinated several large FP7 and H2020 Integrating Activity projects for accelerator and detector infrastructures (EuCARD/EuCARD-2/ARIES and AIDA/AIDA-2020).

Expected results and Impact

HITRI*plus* will produce a complete design for a new generation of superconducting magnets for medical accelerators and gantries that can operate at a 3 T dipole field and 1 T/s ramp rate. These magnets will be used to design a superconducting synchrotron with a circumference about half that of existing ion therapy synchrotrons, and a gantry with a weight below 100 tons and a cost not higher than twice that of proton gantries. Injection systems will be developed, to bring the accelerated carbon ions intensity to 10^{10} ions per pulse, an order of magnitude higher than present systems. Additionally, it will prepare accelerators for extraction of different beam energies, will develop new multi-platform software tools to integrate accelerator and beam delivery control, and will develop a chair system for patient positioning on the ion beam.

In addition, the project aims at promoting a wider, simplified and efficient access to the best research infrastructures. In particular, The JRA's will contribute by improving the facilities so that users will always have access to the best possible research infrastructure.

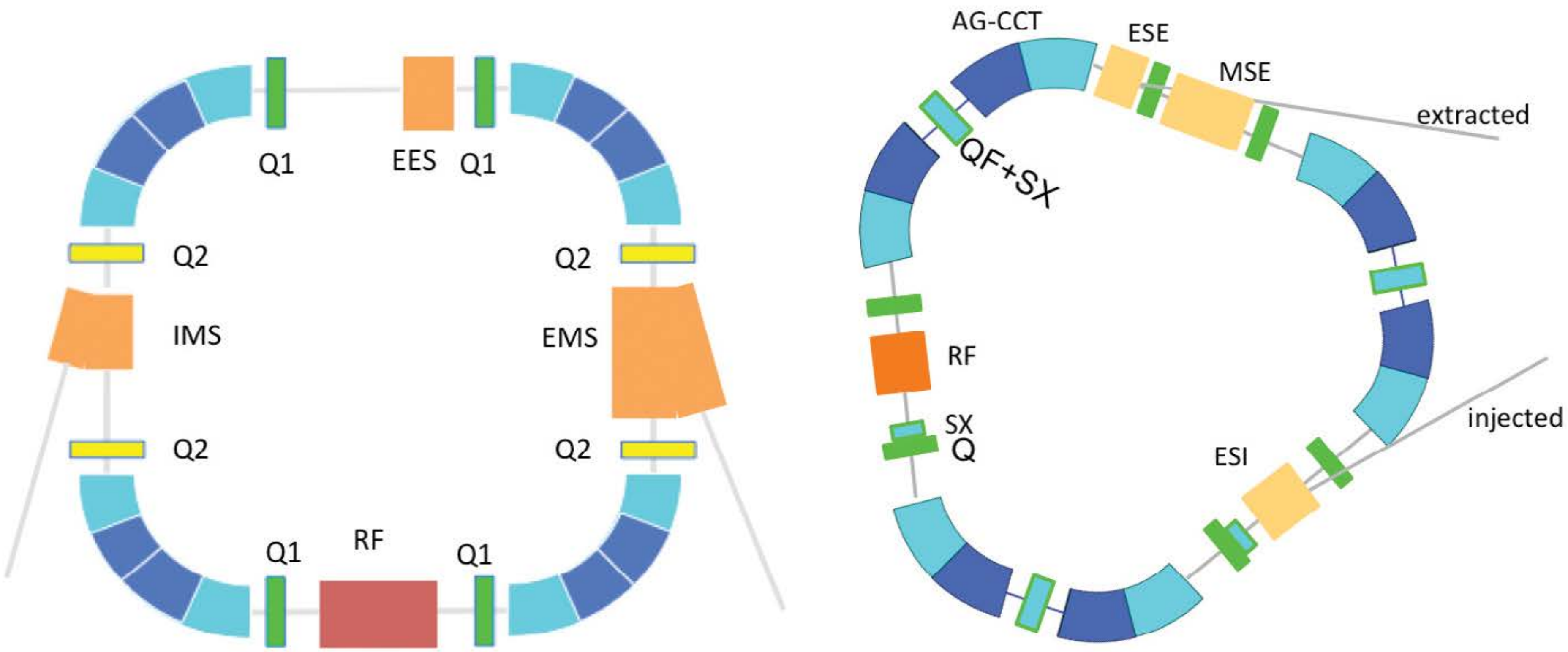
In fact, there is also another important impact, HITRI*plus* is focusing on - Operators of related infrastructures develop synergies and complementary capabilities, leading to improved and harmonised services. Economies of scale and improved use of resources across Europe are also released due to less duplication of services, common development and the optimisation of operations. Standards produced in HITRI*plus*' JRA will be used for QA, and round-robin experiments will be conducted to ensure inter-comparability between the capabilities of TA providers.

A point often overlooked that may be considered as an obstacle is the cost implications of ion therapy treatments. That's why an effort will be made in the JRA's WP7-8 to reduce the construction and operation cost of the accelerator, reduce treatment costs and increase the availability of ion therapy.

Fostering entrepreneurship

Furthermore, HITRI*plus* has a dedicated WP on innovation, technology transfer, industry relations led by CERN for improving the possibilities for helping to identify innovation and generating a market value using the research in the JRA pillar. Some developments such as superconducting magnets and gantry will make market breakthroughs for possible start-up companies.

Author:
Maurizio Vretenar, CERN

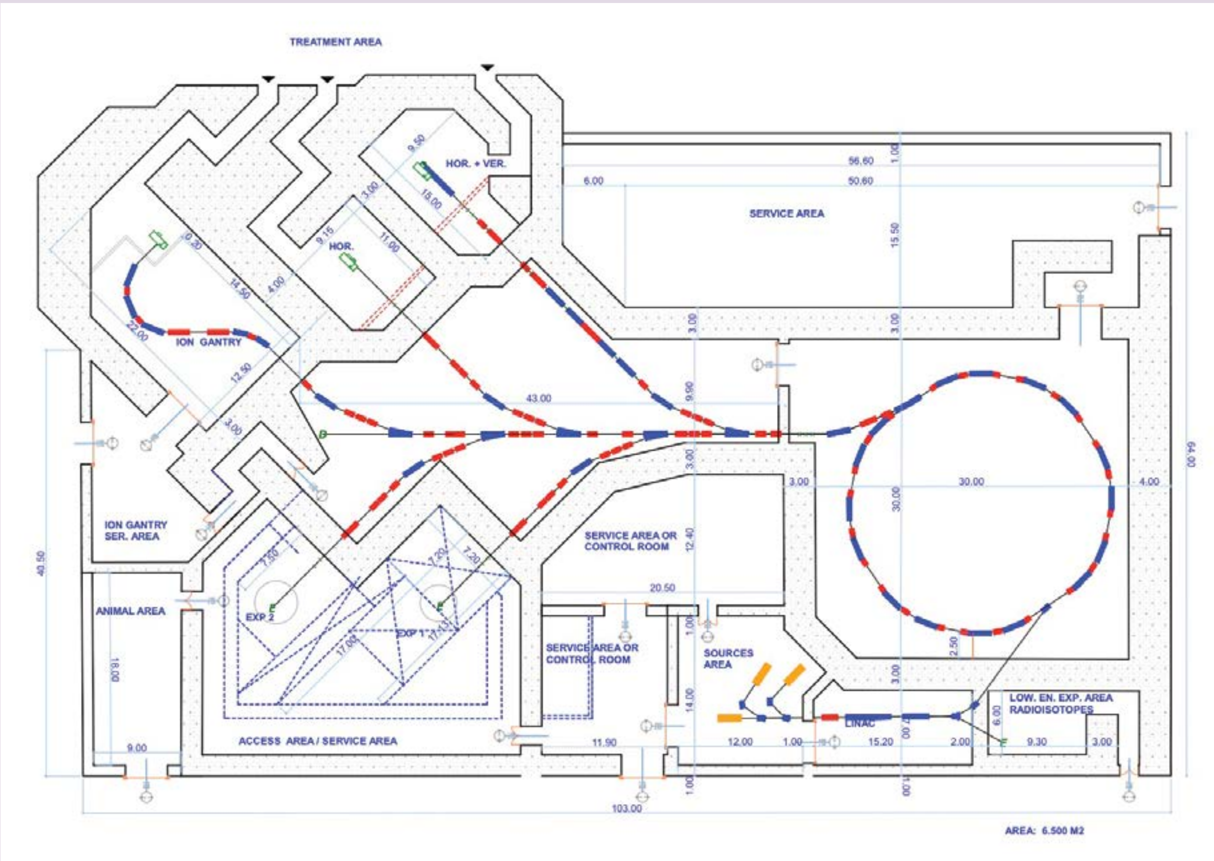


Possible layouts of the compact synchrotron, based on superconducting magnets.

WP 7: Advanced accelerator and gantry design

WP7 will develop solutions to enhance the performance of existing and future accelerators for heavy ion research and therapy: multiturn injection for higher beam intensity up to 10 10 carbon ions per pulse, improved extraction and beam transport, and a new linac injector for higher intensity and parallel production of isotopes for research and therapy. The WP will combine the accelerator solutions with the superconducting (SC) magnets developed in WP8 to define the advanced conceptual design of a compact and innovative SC heavy-ion synchrotron capable of operating with multiple ion species, from helium to argon, and including protons for testing and calibration. This accelerator design is intended to become the reference for any new ion therapy research facility including the one proposed for the SEE region. A simplified version of the compact SC accelerator with single- or double-ion operation at fixed parameters will be proposed as reference for a new generation of compact ion therapy accelerators to be built by European industry to address the global ion therapy market. Additionally, WP7 will convert the most promising of the existing conceptual designs for superconducting gantries into a detailed technical design integrating all components, and prepare for a final industrialisation and production phase by the European industry.

The accelerator and gantry design work will be done in close collaboration with the European heavy ion therapy research centres, to profit from their operational experience and to integrate with the design licensing and operational requirements.



SEEIIST bunker layout

Networking Activities Pillar

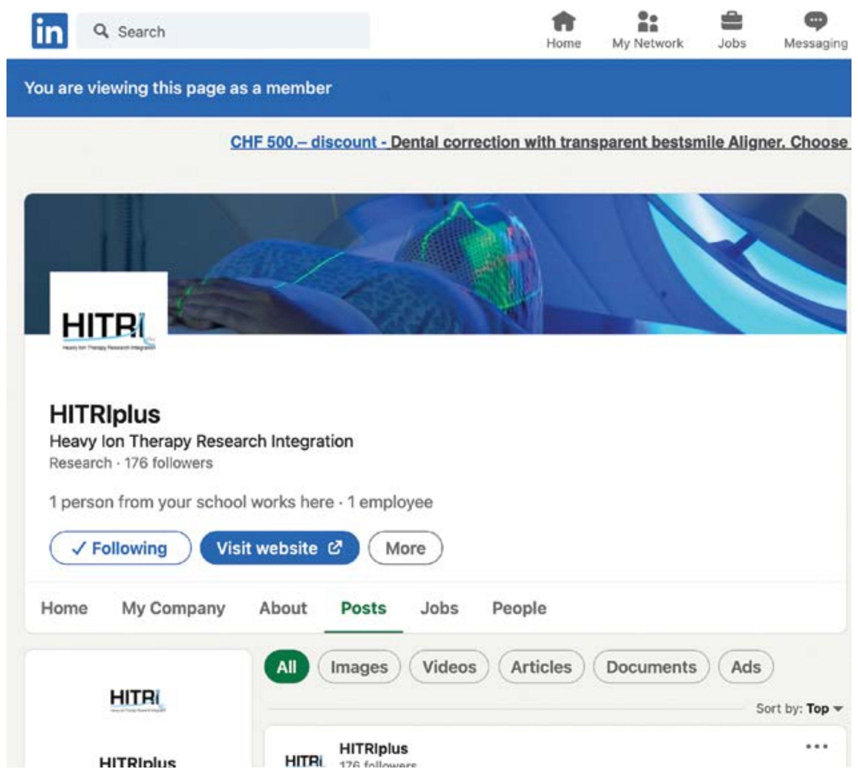
To reach its ambitions, HITRI*plus* needs to realise substantial breakthroughs in community building, promoting experimental programmes, clinical networking, technological developments, and the definition of common standards. For this purpose, the Networking Activities pillar plays a very important role in the entire project.

Structure

The Networking Activities (NA) pillar is organized in four WPs that act as services for the other two pillars Joint Research Activities (JRA) and Transnational Access (TA). The transversal action of NA is intended to go across JRA and TA, giving inputs, defining procedures and rules, but also getting results, information and feedback. The mutual process cross-feeds and permeates the whole project and favours exchange integration among WPs. This same process guarantees visibility and openness to the external world. WP2 on Communication and WP3 on Clinical Networking in NA are particularly important for TA because they contribute to open the access of the facilities to the external medical and research communities. In addition, WP3 contributes to defining the clinical content of the information spread outside the project via the communication activities of WP2.

Not only the NA pillar is essential for the entire project but its influence on the JRA is as well bi-directional: one way to favour the essential collection of input data and specifications from the potential users; the other way to share the outcome results of the single WPs with the existing infrastructures in HITRI*plus* to improve their performances at the advantage of the users. Last but not least, the overall outcome of the JRA consists of a novel design of a new generation RI facility that will be at disposal of the

Graphical presentation of the components showing how they inter-relate.



LinkedIn: HITRIplus

EU community and in particular of SEEIIST.

The Networking Activities Pillar consists of the following WPs: communication, dissemination and outreach (WP2), clinical networking (WP3), innovation technology transfer and industry relations (WP4), education and training (WP5);

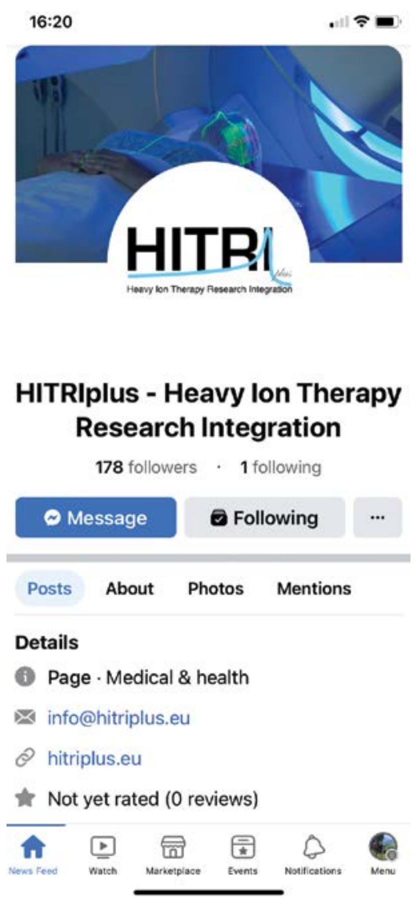
As we have already mentioned, the Networking WPs are transversal and useful to TA and JRA pillars. But Clinical Networking is fundamental to establish a "common language" among the medical doctors of the facilities and between them and the rest of the clinical community. Furthermore, it is also important to establish tools to exchange information and standards. It is a fundamental channel to open the existing facilities to the external communities of users, both clinicians and researchers.

Education and training in this sense are of paramount importance to spread the achievements and create a diffuse culture through the organised involvement of the young generation of students and early-stage researchers. What is interesting for the project and concerning this extending community is the fact that the Networking coordination is assigned to SEEIIST, one of the main perspective users for the Networks' outcome.

Prof. Manjit Dosanjh, SEEIIST Scientific Advisor, Molecular Radiobiologist, is in charge of the Networking Pillar and WP2 supported by the SEEIIST Administrative Unit and in close collaboration with the CERN EU office.

Networking and community building

Networking Activities Pillar is intended to promote the heavy ion therapy facilities to medical researchers all over Europe in particular by raising awareness about the tumour types that could be treated, and to catalyse the collaboration between the different scientific communities (oncologists, radiologists, biologists, biomedical engineers, physicists and accelerator experts), which is necessary for successful development and improvements in ion therapy at national and European levels.



Facebook: HITRIplus - Heavy Ion Therapy Research Integration

> ***"Key to the ion therapy research is engaging with the broader health care community, formed by other professionals such as nurses, planners, bioengineers and radiographers who bring another perspective to the research that is much more patient-centric.***

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A European registry of patients treated with carbon ion radiation therapy would provide real-world data that could supplement classical trials to build a more solid evidence-based medicine.

Key to the ion therapy research is engaging with the broader health care community, formed by other professionals such as nurses, planners, bioengineers and radiographers who bring another perspective to the research that is much more patient-centric. Participation of several European hospitals will allow the clinical translation of the research, for patient benefit, from "bench to bedside", again using HITRI*plus*' NA and TA.

Working in eminent academic institutes, participating in the workshops organised by the NAs of HITRI*plus*, and interacting with industrial partners will expand the job opportunities for PhD students and a new generation of researchers in the academic, health and industrial sectors after completion of the project.

Focus on the South-East Europe Community

Wider, simplified and efficient access to the best research infrastructures is one of the goals of the project. Therefore, the HITRI*plus* Consortium covers 14 European countries, and via the SEEIIST is connected to institutions and researchers in eight SEE countries. Through the HITRI*plus* networking and communication platform, the ion therapy user community will be able to choose the best site for the research they want to perform. In particular, SEE researchers will have access to the best European infrastructure in the field.

Moreover, HITRI*plus* will focus on the needs of its users and will provide a Network Facilitator digital platform.

Dissemination

Regarding dissemination, HITRI*plus* aims to provide timely information about the results from the NA, TA and the JRA activities to the medical and scientific community, and in particular for the JRAs to the European industry.

From the first year of the research activities, HITRI*plus* partners will already present their results at dedicated science conferences for accelerators, particle therapy, radiobiology and cancer treatment, such as (1) PTCOG: Particle Therapy Co-Operative Group annual meeting and (2) ESTRO (European Society for Radiation Oncology) meetings etc. Such participation will help to establish networking activities within the scientific community and make the project much more visible and known.

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Perspective

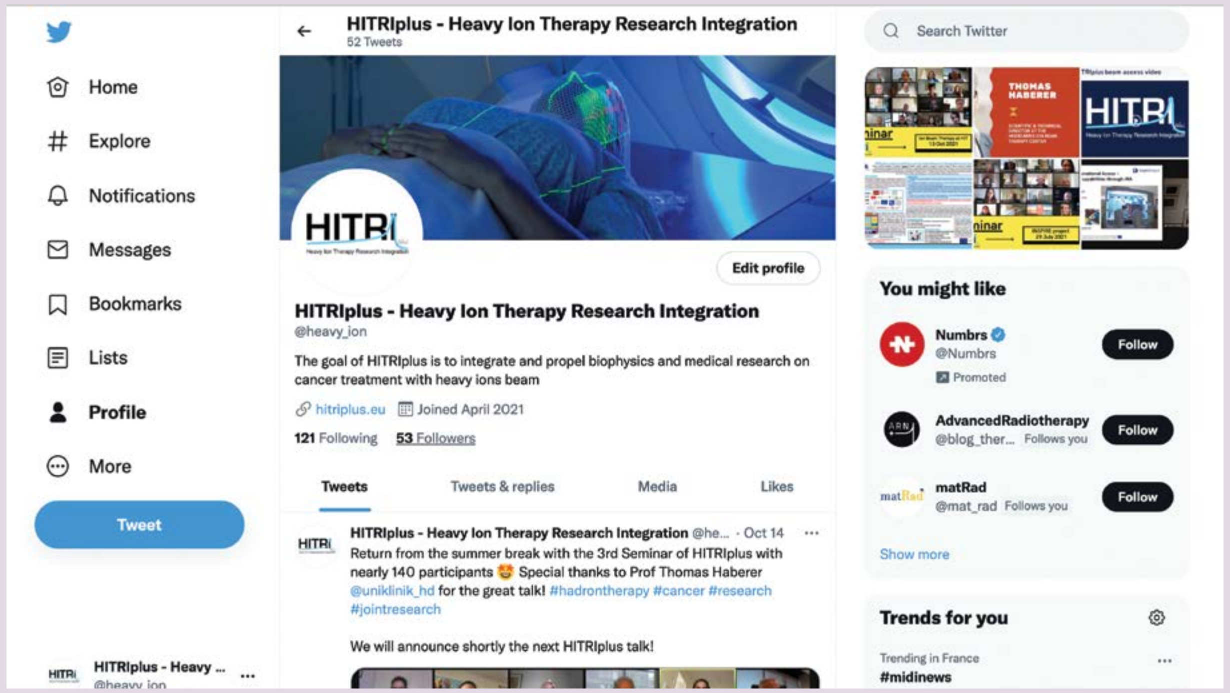
WP 2: Networking and Communication, Dissemination and Outreach

The Dissemination, Communication and Outreach Work Package is central for the Networking Activities Pillar coordinated by SEEIIST. The activities included in this WP are organising and implementing efficient communications inside and outside the consortium. A team of communication experts from CNAO and SEEIIST association is working to enhance the internal synergies, produce outreach materials and provide added value by allowing information flow to/from other projects and the general public as well as within the HITRI*plus*. WP2 will equally support the management for internal communication and follow-up of HITRI*plus* results.

HITRI*plus* recognises the importance of communicating to the public at large and implements WP2 to promote initiatives, develop outreach material, and organize the wide spectrum of outreach. The calendar of the outreach events will be as well available in regards to the developing coronavirus pandemic but meanwhile online events have already been put in place.

Speaking of concrete deliverables, during these first couple of months that the project has been launched the HITRI*plus* Website has been now published. It is a showcase website that gives detailed information about all participating institutions and the latest status of all network activities. The institutional HITRI*plus* website is online since the middle of September and it is a central collection point of debates, talks, courses, papers and posters presented by members of the consortium. A professional video has been produced reflecting the Transnational access and last but not least, one of the tasks that the communication team promised to deliver is this dedicated HITRI*plus* Highlights issue that you are now reading distributed via email and published on the website.

One of the major priorities of WP2 is that HITRI*plus* project participants and users can communicate with a range of audiences, taking into account their specific needs and modes of communication. In that sense, HITRI*plus* outreach activities are destined to impact a large part of the population. What's more, they take into consideration ethical issues.



Twitter: @heavy_ion

Perspective

Aerial view of GSI/FAIR campus. © D. Fehrenz/GSI/FAIR

Transnational Access Pillar

Transnational Access (TA) is the key pillar of the project, joining for the first time the research programmes of the four European ion therapy centres (CNAO, HIT, Marbourg, MedAustron), and linking them to the biophysics research with ions of the GSI laboratory.

Structure of Transnational Access

The HITRI*plus* research and clinical TA represents a unique opportunity for bringing together, for the first time ever, the four heavy-ion centres in operation in Europe, opening them in a coordinated way to the medical and research community. A fifth facility providing access is GSI, which contributes by opening its biophysics research programme.

The TA is organised under one WP - to promote access to the existing facilities of the research and clinical communities (WP6).

The Clinical Access will give the opportunity to the hospitals and oncological institutes in Europe to refer patients to the existing hadrontherapy facilities and share clinical prospective investigations and patient follow up.

The Research Access will attract universities, research centres, and hospitals, which will connect all the groups to perform research activities in the experimental rooms of the existing carbon ion facilities and at GSI. Performing research at a clinical facility will allow researchers to meet different clinical professionals.

The TA Coordination is ensured by GSI (Marco Durante) thanks to its wide experience in research programmes and in successfully running TA activities.

Marco Durante is the Director of the Biophysics Department of GSI, a Full Professor of the Technical University of Darmstadt and Vice-Chair of the Particle Therapy Cooperative Group (PTCOG).

Objective

The first objective of HITRI*plus* (expressed by its TA) consists in integrating and opening up the clinical and research programmes at the four therapy facilities, and in connecting them to the successful biophysics research programme of the GSI laboratory. Biophysicists, medical physicists, medical doctors, pharmaceutical companies, industry and experts developing specialised instrumentation, will all have access to the best European infrastructure for the treatment of cancer with heavy ions. The open access to the therapy facilities, sustaining the patient treatments, will considerably contribute to the creation of evidence-based medicine on heavy-ion treatments. It will favour more efficient recruitment of the European eligible patients and will allow a coherent approach in comparing the clinical trials outcomes. Concerning biophysics research, opening up these infrastructures to external researchers will allow the exchange of information, optimisation of resources, and the establishment of common methods and standards. The TA will pave the way for an enlargement of

Particle accelerator facility of GSI/FAIR. © J. Hosan/HA HessenAgentur the research community, in particular in the direction of South-East Europe favoured by the ongoing SEEIIST programme that will provide connections with the Research Institutions in the area, which will be able to access the best infrastructures gaining an experience that will be vital to the SEEIIST programme.

The goal of HITRI*plus* is to provide to more than 150 users a total of 50 clinical access units (patients) and 448 research units (hours) distributed among its five TA facilities. 20-30% of the users are expected to come from SEE countries institutions that will take part for the first time in ion therapy-related research.

Furthermore, the two crucial elements for the project are: define (in the Networks) and implement (in the Transnational Access) an advanced experimental programme to improve the quality of radiation therapy treatments to cancer patients.

Aiming for new users

HITRI*plus* will offer access to five state-of-the-art infrastructures providing high-quality services, enabling users to conduct excellent research in trans-European collaboration. This will allow research capabilities and expertise in the field to grow and will expand the potential of researchers and clinicians that do not normally have access to heavy-ion technology. In particular, it will expand this research towards the SEE region. Excellence will be ensured by selecting and supporting the best scientific and innovative experiments according to criteria of equality, transparency, fairness and meritocracy.

Treatment Facility at GSI. © A. Zschau/GSI/FAIR

Treatment Facility at GSI. © G. Otto/GSI/FAIR

Cell research in the laboratory of biophysics department. © J. Hosan/GSI/FAIR

Cell research in the laboratory of biophysics department. © J. Hosan/GSI/FAIR

The HITRI*plus* Starting Community initiative aims at gathering a wide multidisciplinary consortium to address both critical issues in a collaborative and structured way. This need is widely recognized, and the international ion therapy community requires coordinated access to the existing facilities for radiobiology research and physics research, offering extended blocks of beam time, with beams suitable for multidisciplinary clinically oriented research. The TA offered by the existing facilities

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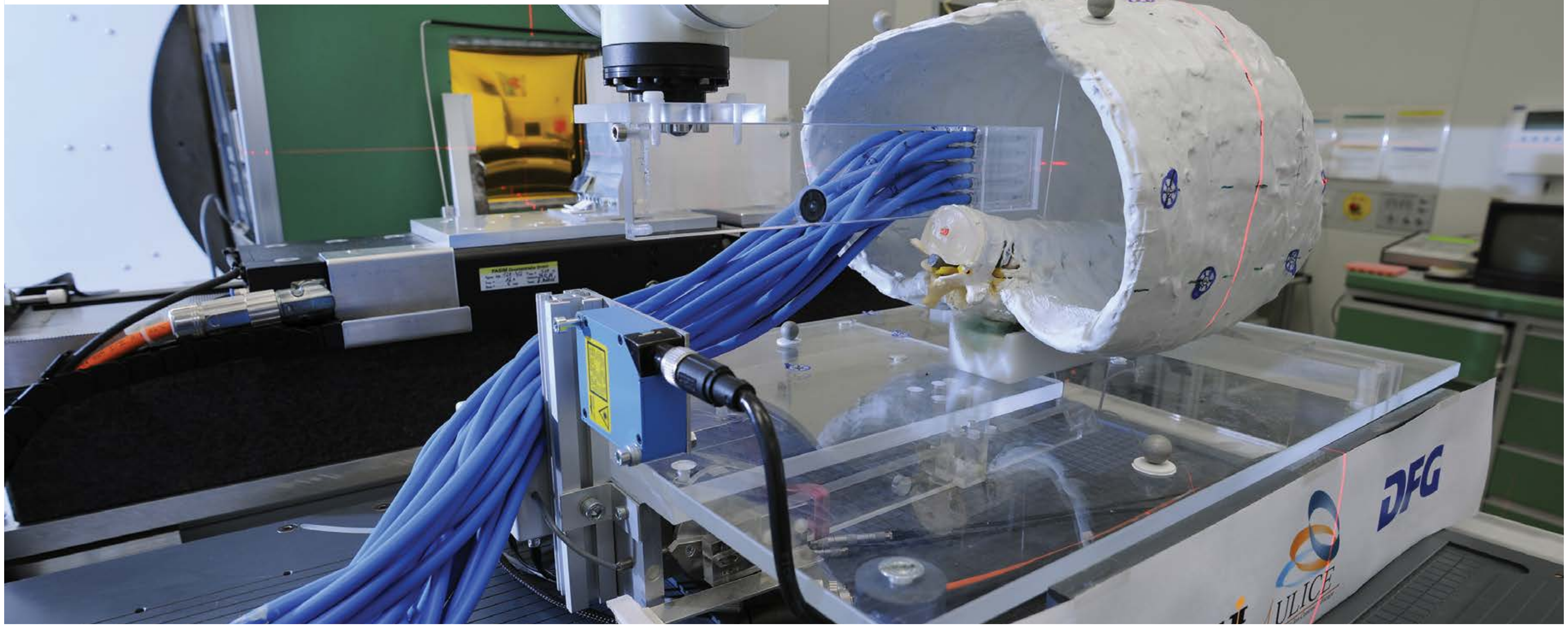
is responding to this need by providing beam time for systematic radiobiology experiments to better characterize the RBE and its complex dependencies, allowing also improvements of the biophysical models that are required to implement these dependencies in the treatment planning procedures.

The facilities

Whereas two out of the four clinical facilities engaged in HITRI*plus* Transnational Access were already present in ULICE (EC funded project), only one (HIT) was offering at the time a limited research programme with carbon ions; the other (CNAO) started its carbon-ion programme only at the end of ULICE. The TA of HITRI*plus* is now based on a consolidated basis of four running facilities routinely treating patients with carbon ions, and this Integrating Activity is focused exclusively on the new challenges and opportunities in radiobiology, biophysics and medicine offered by heavy ions.

“The open access to the therapy facilities, sustaining the patient treatments, will considerably contribute to the creation of evidence-based medicine on heavy-ion treatments.



Thorax Phantom at GSI/FAIR. © G. Otto/GSI/FAIR

Particle accelerator facility of GSI/FAIR. © J. Hosan/GSI/FAIR

Access to cutting-edge technologies

High quality inter-disciplinary and multi-sectoral clinical and research opportunities are now opened for a wider number of users in order to provide cutting-edge cancer research and training of future experts in the ion therapy field.

Author:
Marco Durante, GSI

WP 6: Transnational access

WP6 is dedicated to providing Transnational Access (TA) to research rooms in Heavy Ion centres in Europe.

It brings together, for the first time ever, the four heavy-ion centres in operation in Europe and opens them in a coordinated way to the medical and research community. Moreover, their programme will be integrated with the biophysics programme at GSI. The WP includes two Access programmes.

The Clinical Access will allow the radiation oncologists to work together with their European colleagues and non-European colleagues in multicentre prospective comparative studies to improve the knowledge both in heavy ion therapy and in classical radiation oncology through clinical research practice.

The Research Access, in direct contact with the real needs of the therapy and of the patient, the researchers will have a clear perception of the feasibility to translate the research from bench to bedside. Industrial partners will be encouraged to take part in the research programme, to be involved in the development of new clinical procedures and new medical devices.

The rest of the work packages under HITRI plus

Heavy Ion Therapy Research Integration

WP 3: Clinical networking

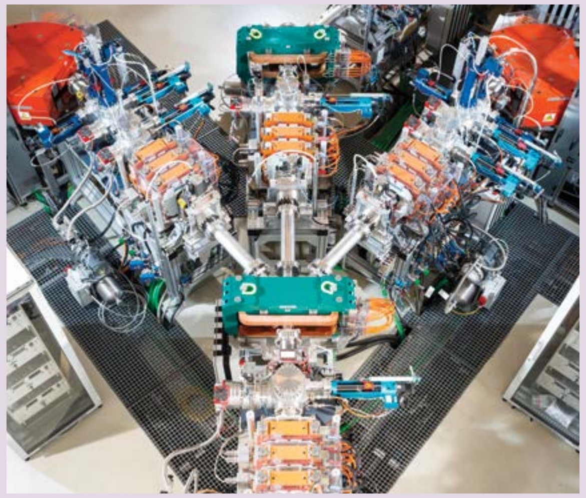
The main objective of this WP is a trial design for innovative use of heavy-ion radiation therapy. This will be accomplished through a review of preclinical data to identify promising novel approaches to exploit the heavy-ion radiation therapy advantages and the design of one trial as a template for bringing innovative heavy-ion radiation therapy approaches in the clinics. Another objective is the creation of a European registry of heavy-ion radiation therapy patients by collecting data on rare cancers treated with heavy-ion radiation therapy. WP3 has the goal of reaching a European-wide agreement for OARs (Organs At Risk) dose constraints with heavy-ion radiation therapy. This will be accomplished by reviewing existing data on OARs dose constraints in use in the clinical facilities and performing pooled data analysis to validate them. Last but not least, WP3 has the task to outline clinical research protocols to favour clinical TA according to the modalities set forth in WP6.

Proton gantry © Kästenbauer/Ettl

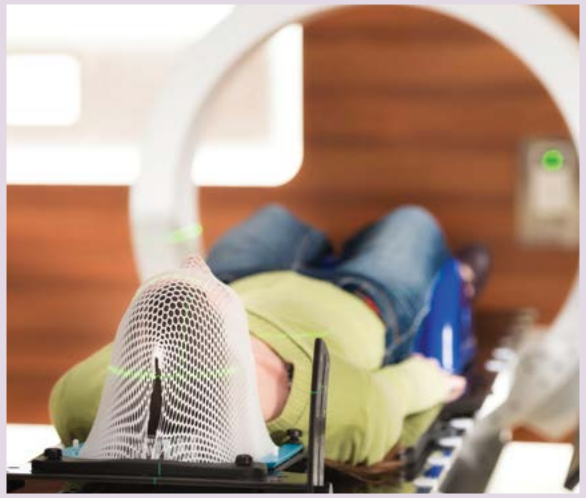
Furthermore, WP3 has been created with

MedAustron building © Kästenbauer/Ettl the aim to involve the medical user community; the starting point for the design requirements of the next-generation facilities will be jointly defined based on oncologists' needs as well as those of researchers. In WP3 and through WP2 the medical user community will be constantly involved and invited to provide feedback. This will also allow HITRI*plus* to establish the training needs that will contribute toward a sustained uptake of the medical potential of each ion therapy facility. The common data sets provided by WP3 are expected to bring evidence on the potential of carbon ion therapy.

Innovative robotic system and imaging ring for patient positioning and monitoring © Kästenbauer/Ettl



Accelerator facility – close-up © Kästenbauer/Ettl



Patient Treatment © Kästenbauer/Ettl

Synchrotron – Core of the accelerator facility © Kästenbauer/Ettl

WP 4: Innovation, technology transfer, industry relation

The objective of this WP is to define and implement a roadmap for the exploitation and industrialisation of the HITRI*plus* technologies and innovations. In order to do this, the generated IP will be tracked and managed from the beginning of the project, and an adequate dissemination and exploitation plan will be drawn up for each technological innovation. Given the highly collaborative, trans-national nature of the HITRI*plus* project, such plans will look beyond traditional IP protection approaches, such as patenting and will also consider open innovation schemes such as co-development with industries open-access licensing schemes. The HITRI*plus* innovations will be broadly disseminated to the industry through a variety of channels, including using well-established networks of industry and technology transfer professionals, industrial exhibitions at relevant conferences, and dedicated "HITRI*plus* meets industry" events. Technology-transfer opportunities arising from these dissemination actions will be proactively followed up.

WP4 is coordinated by CERN, with GSI and INFN participating: all WP4 partners have dedicated Technology Transfer offices with the necessary experience to support the work plan and to achieve these objectives. A dedicated Technology Overview Committee, composed of the WP4 participants and the leaders of the JRA work packages (WP7-WP12), will help streamline the internal communication about new technology disclosures.

CERN coordinates the WP4 "Innovation, Technology Transfer, Industry Relations" and act as a liaison between the beneficiaries to ensure that ownership of new IP is protected.

WP 5: Education and Training

The objective of WP5 is to educate and provide hands-on experience to a new generation of researchers in heavy ion therapy so that they acquire appropriate skills allowing them to optimally access and exploit (even virtually) all the essential tools of European heavy ion therapy research infrastructures. In addition, WP5 provides researchers from academia and industry of a multidisciplinary background, including researchers not necessarily directly involved in heavy ion therapy, with updated and appropriate knowledge on heavy ion therapy research and the activities and potential of the major European heavy ion therapy and research infrastructures. Postgraduate students, postdocs, oncology practitioners, and researchers from a wider

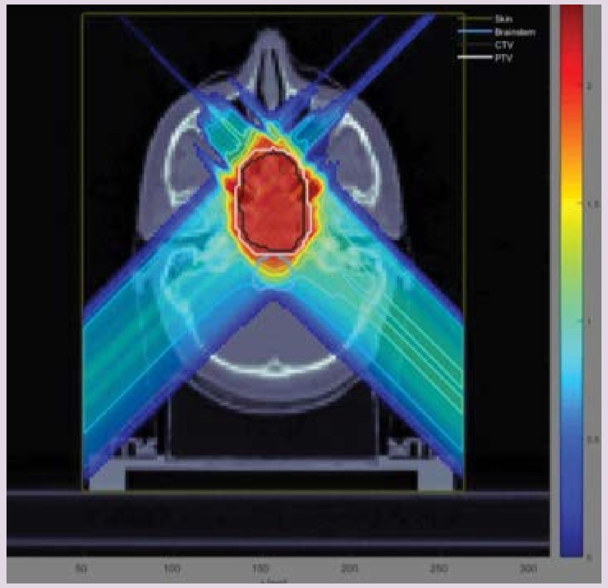


Figure 1: matRad an open source tool kit for dose calculation and optimisation

multidisciplinary community will be attracted, educated and trained to form part of this starting heavy ion therapy research community through specialised courses, masterclasses, e-learning courses, secondments and internships.

The Education and Training WP5 will include training on clinical practice of heavy ion therapy; accelerator technology and beam physics for heavy ion therapy; accelerated heavy ions in radiobiology and medical physics; heavy ion therapy data platform; safety aspects of heavy ion therapy; compliance to European regulations and standards; certification strategies of medical accelerators; medical physics commissioning; and clinical practice of particle therapy.

University of Malta is leading this work package and is working closely with SEEIIST (UKIM, CMSM), GSI, CERN and CNAO towards education and training. SEEIIST (UKIM) is leading a task focused on the organisation of two specialised one-week courses whilst GSI is leading a task focused on the organisation of a one-weeklong masterclass school. UM will lead a task to provide e-learning courses on heavy ion therapy and another task that focuses on the organisation of secondments and Internships in heavy ion therapy research infrastructures.

Figure 2: N. Sammut, Y. Foka and M. Sapinksi in a questions and discussions sessions after one of the lectures.

WP 8: Superconducting Magnet Design

Why superconducting magnets for an ion gantry is a challenge? At present two gantries are in operation… However, size, complexity and, last not least, their cost strongly suggest studying alternative routes to make an ion gantry at the hand of all carbon therapy centres. The possibility of non-coplanar treatment is recognized as a key feature for particle therapy to be competitive. And the technology, we believe, is almost there. In LHC we have superconducting magnets that work in the eight-tesla regime. However, the environment for the gantry is tougher if complexity and cost must be kept low, avoiding the use of liquid helium and employing a very light structure. Seven research Institutes: CEA (Fr), CERN, CIEMAT (Es), INFN (Milano and Genova, It), PSI (Ch), Wigner RCP (Hu), Uppsala University (Se), and one company: Sentronis (Rs) associated via the SEEIIST, are working together in HITRI*plus*-WP8 to develop a superconducting magnet as a demonstrator of a novel generation gantry. The demonstrator makes use of a special layout first employed in the accelerator by CERN for the High Luminosity LHC, the Canted Cosi-neTheta or CCT layout, to reach 5 tesla without direct coolant and with a strong curvature given by a bending radius of 1.5 m, a value never approached so far. The challenges are big but the determination to face them is not less!

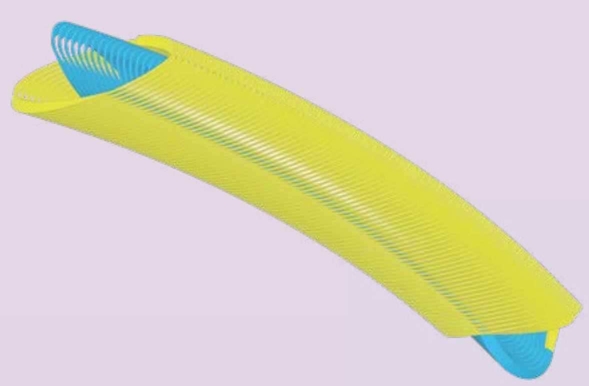


Figure 1: Sketch of a Curved CCT dipole of 4.5 T to which is superimposed a small quadrupole component of 5 T/m. Credit to INFN-Milano-LASA.

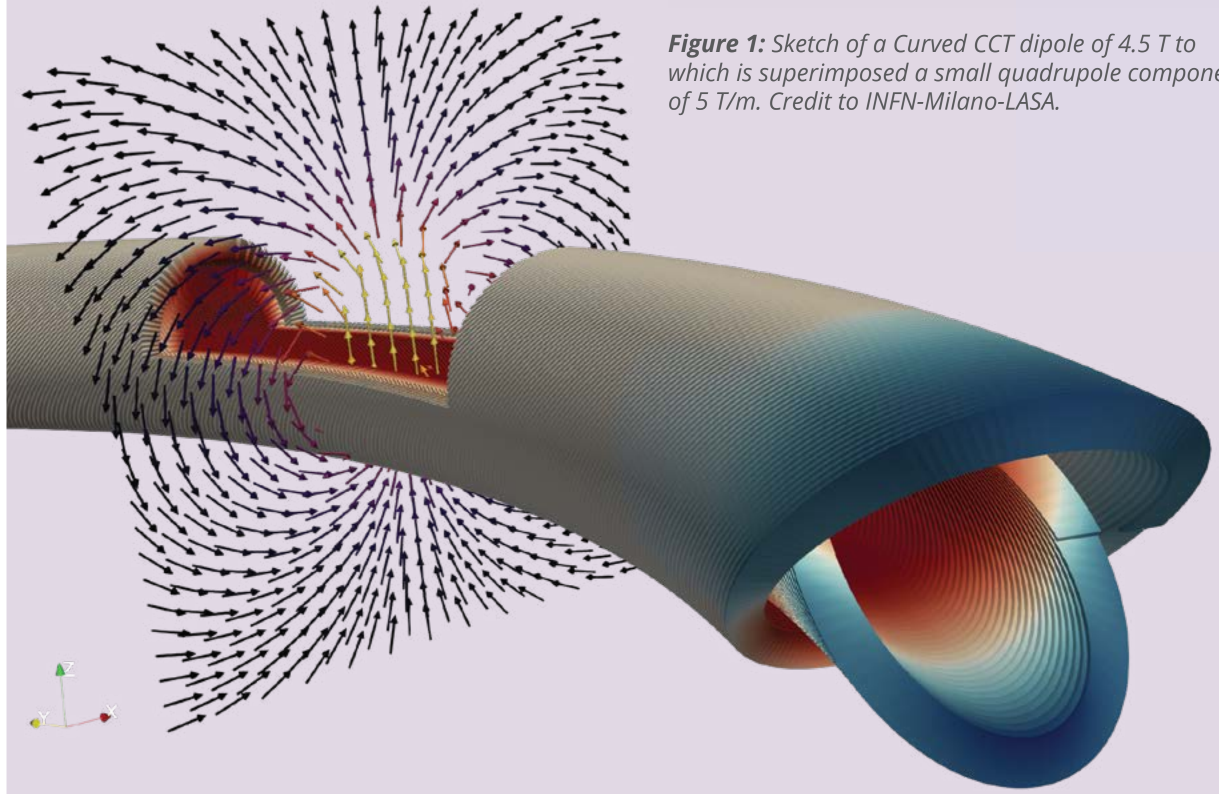
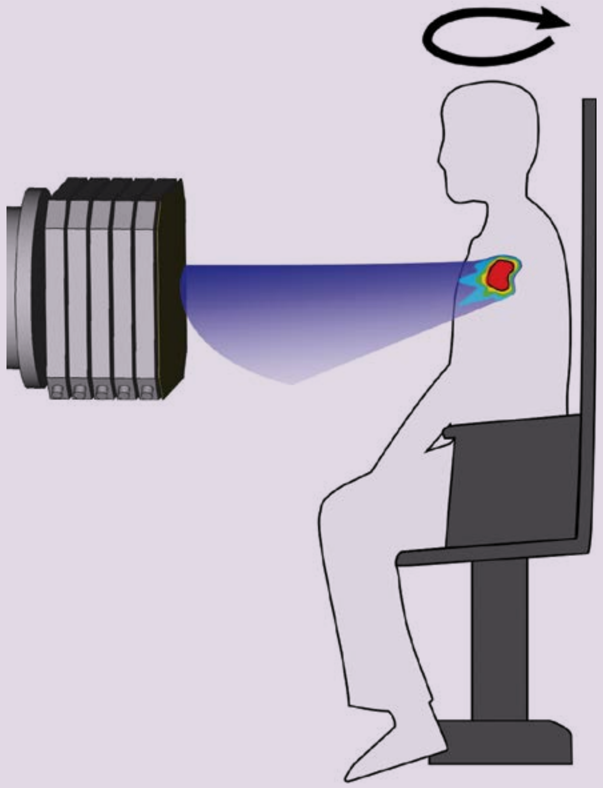


Figure 2: Sketch of the curved CCT dipole wit evidenced the field line generating multiple higher order component because of the curvature. Credit to Wigner RCP (Budapest).

WP 9: Beam Delivery

In addition to gantries becoming more compact and cheaper, the existing and future fixed beam lines should be exploited for the best possible patient care, by providing a means of more flexible beam delivery. In WP9, a patient chair and associated vertical imaging will be investigated to enable particle arc therapy. Novel detector technology will be used to speed-up beam delivery, and potentially allow a combination of flash and arc therapy. The basis of this study will be the CNAO dose delivery system, which is in clinical use at CNAO and MedAustron and was recently installed at GSI.

In order to exploit different beam angles for optimal treatment without relying on a gantry, the designs of patient positioning systems has to be re-evaluated: within this WP, robotic patient chairs and robotic couches will be investigated in combination with complementing imaging technology. In search for advanced treatment strategies, like heavy ion arc therapy, the flexibility offered by the patient positioning will be exploited, for example, by assessing the feasibility of continuous couch/chair motion during therapy. A simulation environment for particle arc therapy, to be implemented in GSI's treatment planning software TRiP98, will enable to investigate arc therapy in different case studies as well as the impact of different parameter scenarios. Additional simulations will consider also gantry based arc therapy, following input from WP7. A small-scale demonstrator based on a rotational stage will be constructed after considering different treatment scenarios, beam types, compatibility issues and input parameters from WP7, and first experimental tests of arc therapy will be conducted at GSI. Results of this WP will inform WP7 and WP10 for further design optimization as well as the upgrade of dose delivery and nozzle design necessary for advanced beam delivery strategies. Novel beam detectors, including a fast Gas Electron Multiplier (GEM) position detector, will enable faster irradiation and better capabilities to treat moving targets, paving the way for heavy ion FLASH therapy. As final part of this WP, a prototype GEM system will be installed at GSI to perform a demonstration test of high-dose-rate arc therapy using the developed rotational stage.



A schematic image of the chair.

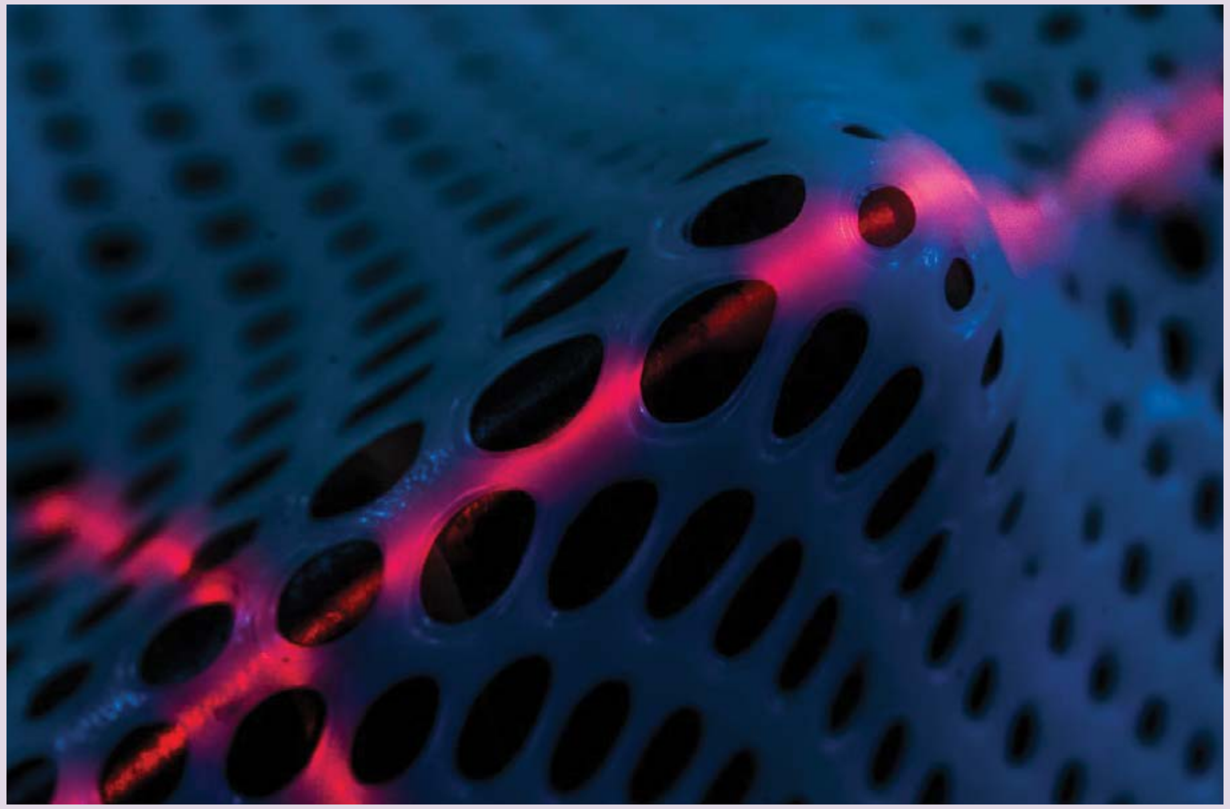
Christian Graeff, WP9 Leader: is the Deputy Director of the Biophysics Department of GSI since 2018 and leader of the Medical Physics group in this department since 2012.

WP 10: Multiple Energy Extraction System

The duty cycle at the existing heavy ion therapy centres is non-optimal and the treatment duration is unnecessarily long. In order to reduce the total treatment time, it is desirable to shorten the phases without beam extraction. Multiple energy operation is a possible future mode of operating the synchrotron, which is going to be investigated by WP10, headed by UKHD/HIT.

A beam characteristics library will be built by defining and combining the existing phase space definitions of new ion species, higher intensities to increase the delivered dose rates, higher energies for some research aspects and a more flexible extraction timing to better support the treatment of moving organs. Furthermore, the multiple energy operation and timing requirements for synchronization capabilities of the next-generation accelerator control system will be defined in coordination with WP11. The supply, distribution and quasi-real-time generation of patient data systems will be designed in hardware and software after discussions with WP11. Using these results and the outcome of WP7, an architectural model of the accelerator multiple energy extraction system that is capable of multiple energy operation will be conceptually designed as a module to be incorporated in the accelerator and treatment control systems of WP11. The results of WP10 will be used as input for WP11 and WP9.

Treatment room at HIT.



The cancer treatment with Ion Beams at Heidelberg Ion Beam Center (HIT) is gentle, more precise and more effective than conventional cancer treatment such as radiotherapy.

Heidelberg Ion Beam Therapy Centre gantry.

Perspective

WP 11: Controls and Safety

The goal of WP11 is to analyse and determine the best solutions for an upgrade of current and future facilities in terms of performance and cost. Using experience from past research results in previous projects, as well as clinical users' experience, future trends and market needs, a novel design for the control software and safety systems will be elaborated. Existing state-of-the-art solutions for machine and treatment room controls and patient safety systems will be used as a baseline on top of which novel solutions will be proposed – unique solutions which will facilitate both research and clinical users at the same time.

In addition, the machine controls will be designed to ensure fast commissioning and machine QA, optimise ease of use for non-clinical personnel, maximise the reliability of the accelerator and lower the operational cost. This will be done by designing a universally compatible modular design with optimised workflows which will allow easy adaptation and upgrading to work with upcoming technologies like adaptive oncology treatments. The system control requirements and the treatment control system architecture will be optimised by first studying all existing treatment room control systems, and then developing a system that will allow easy integration of all the other systems and can be used ergonomically by the machine operators. Input will be regularly exchanged with other WPs, in particular WP7, to ensure this modular software's performance will meet all other subsystem requirements. The high-level system engineering requirements and basic architecture of the patient safety systems will be designed by following the relevant European regulations and international standards.

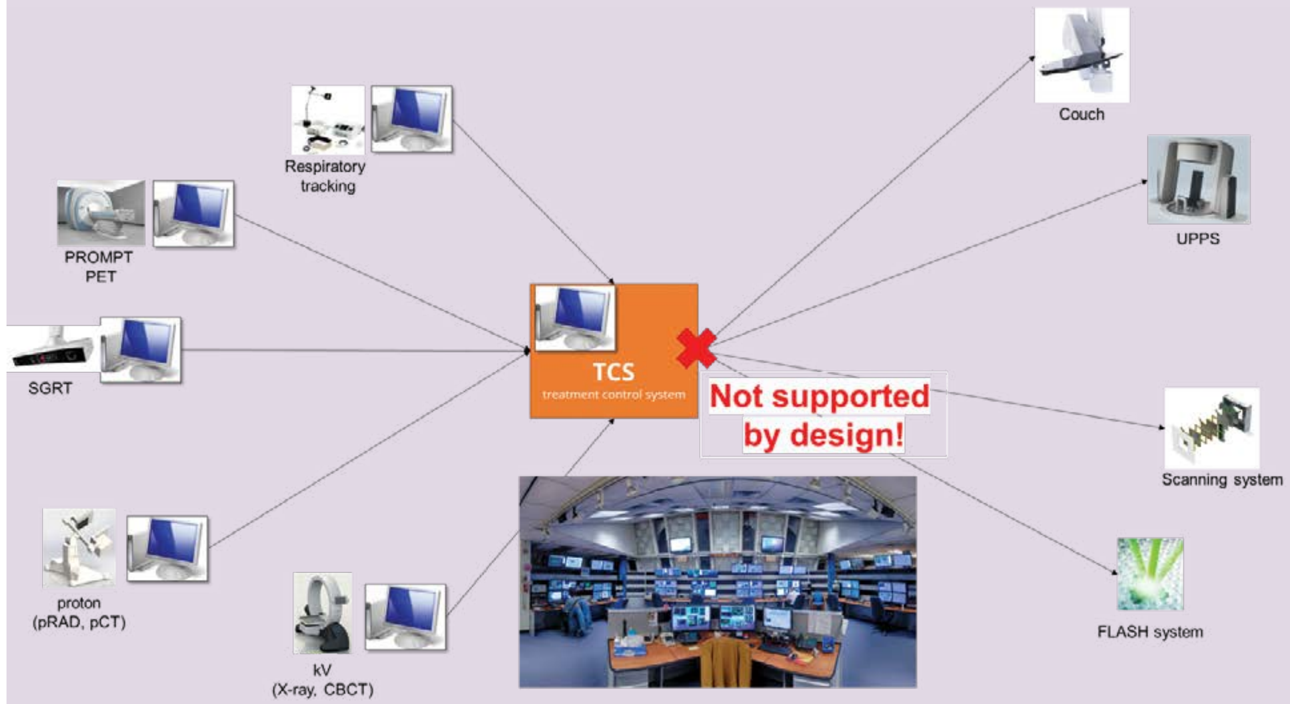


Figure 1: *"Current treatment control systems for particle therapy are lacking in modularity and therefore they have to be customized for each specific system configuration"*

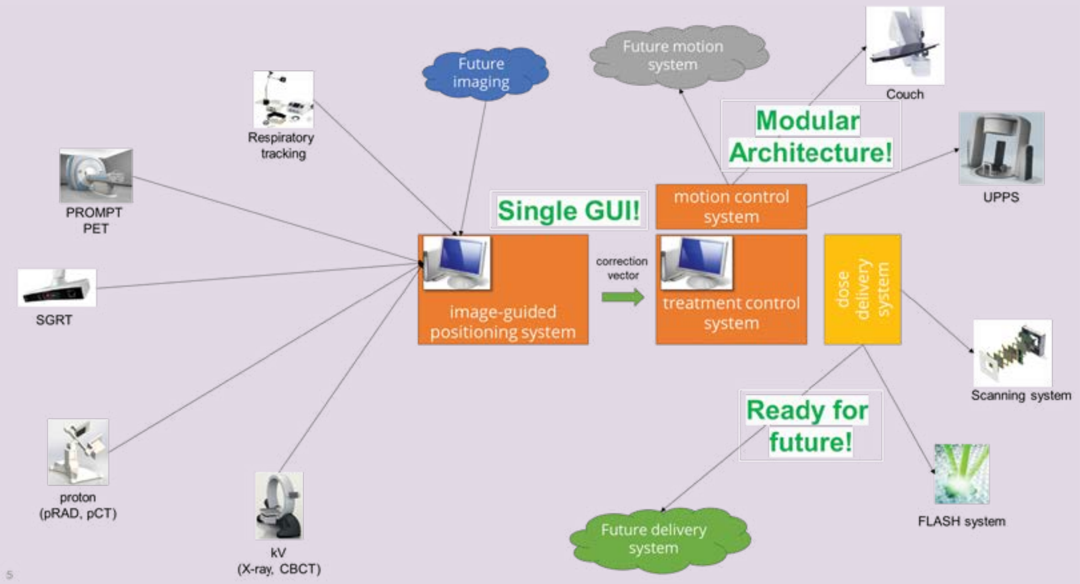


***Figure 2:** "Future treatment control systems for particle therapy shall be modular to support different treatment modalities and room configurations."*

WP 12: Radiobiological Dosimetry and QA

One main aim in radiobiology is to establish associations between various physical doses and their effects induced on cellular level. This requires a characterization of the radiation source in terms of field size, ion energy and type as well as an applied number of particles, since these factors and their characteristics affect the radiation dose and its distribution substantially. Research centres conduct their own studies and implement their own models for dosimetry. Treatment planning and beam application techniques vary between the European ion-beam therapy centers, and to be able to meaningfully evaluate and compare their research results, standardization of radiation dosimetry is a very important step. It requires precise dose measurements and

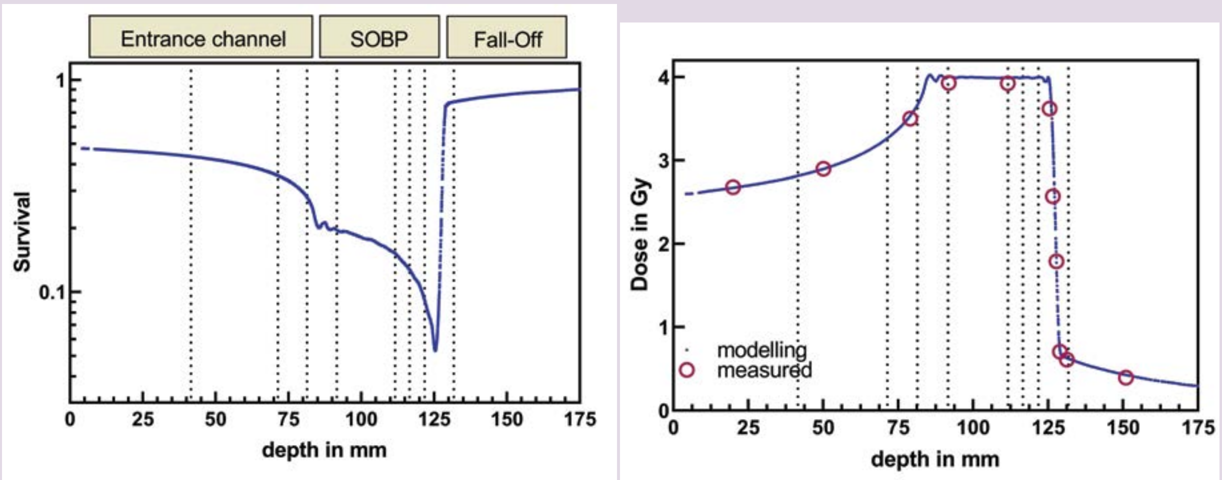


***Figure 1:** Example for modelling treatment plans using TRIP98. The blue curve represents survival for a SOBP geometry of 60x80x40 mm. Dashed lines mark the positioning of the cells for the in vitro experiment, which is supposed to cover entrance channel, SOBP and Fall-off. A) Expected survival for the model cell line. B) Corresponding dose-depth-distribution.*

***Figure 2:** Treatment room, which is also used for radiobiological experiments.*

detailed information about how measurements were performed. WP12 aims to create a standard operating procedure, consisting of a detailed treatment plan and an elaborated experimental radiobiological part, that utilizes a specifically designed phantom to irradiate adherent cells at various positions within a carbon-ion spread-out Bragg peak (Fig.1). Modelling of the joint results with Monte Carlo engines and available models (f.i. RayStation, FRoG, LEM IV, UNIVERSE) will be carried out in order to harmonize the planning process and deliver uniform results in all facilities. The characterization of mixed radiation fields will further improve the quantification of the physical uncertainties influencing biological read-outs. Overall, this project fosters a culture of cooperation between the participants to generate common standards for radiobiological dosimetry and encourage future joint research.

Partners:

- CNAO: Angelica Facoetti, Giuseppe Magro
- GSI: Olga Sokol
- HIT: Andrea Mairani
- MedAustron: Dietmar Georg, Sylvia Kerschbaum-Gruber, Giulio Magrin
- UMR: Kilian-Simon Baumann, Ulrike Schötz

Figure 3: *Prof. Rita Engenhart-Cabillic Director*

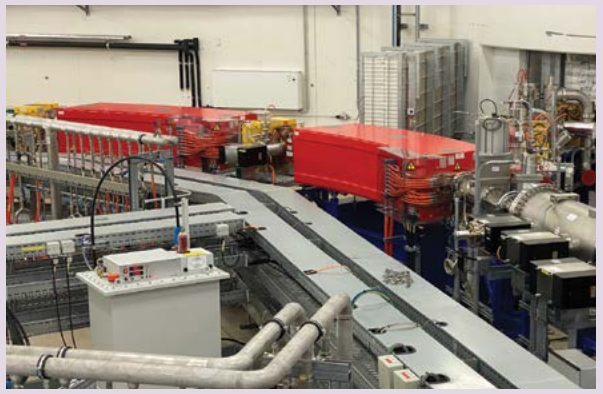


Figure 4: *Accelerator technique*

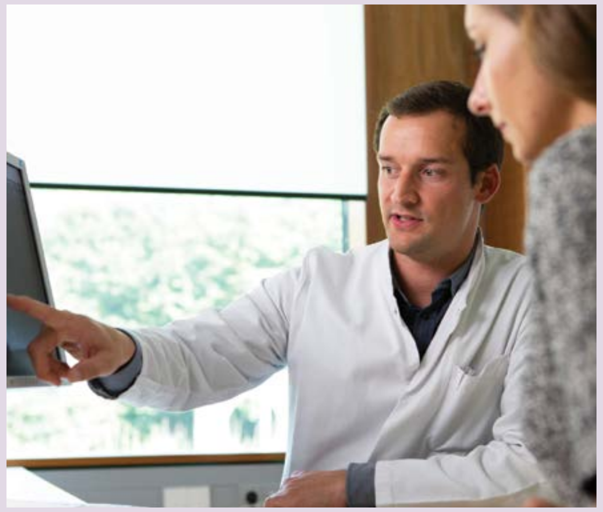


Figure 5: *Consultation with Dr. med. Fabian Eberle.*

Figure 6: *Prof. Klemens Zink (scientific director) and Dr. Kilian Baumann (medical physicist)*

Figure 7: *Work group Molecular Radiobiology. From left to right: Prof. Ekkehard Dikomey (guest professor), Dr. Ulrike Schötz (group leader), Dinesh Tiwari (PhD student), Stefanie Preising (technician), PD Dr. Florentine Subtil (senior scientist), Leoni Piepke (technician), Dr. Ann Parplys (senior scientist)*

Heavy Ion Therapy

Masterclass School

The EU-funded HITRI*plus* project (Heavy Ion Therapy Research Integration) started formally on the 1st of April 2021 holding its kick-off meeting on the 13th of April. It was a well-attended event where a good overview of HITRI*plus's* interesting projects and plans was presented. These also include training and education for capacity building in fields related to heavy-ion cancer treatment through three full-week courses and a programme of internships.

The first HITRI*plus* course, the Heavy Ion Masterclass (HITM) school, took place on the 17th-21st of May 2021. It was coordinated by GSI, where carbon therapy was pioneered in Europe in the 90's, and it had strong support and contributions from HITRI*plus* partners and DKFZ, the German cancer research centre in Heidelberg. It was initially planned to be hosted in the UNSA University of Sarajevo, with the aim to further strengthen ongoing collaborations with an emphasis on capacity building in the South-East European region. However, due to the covid pandemic, it took place online which made it easily accessible literally worldwide.

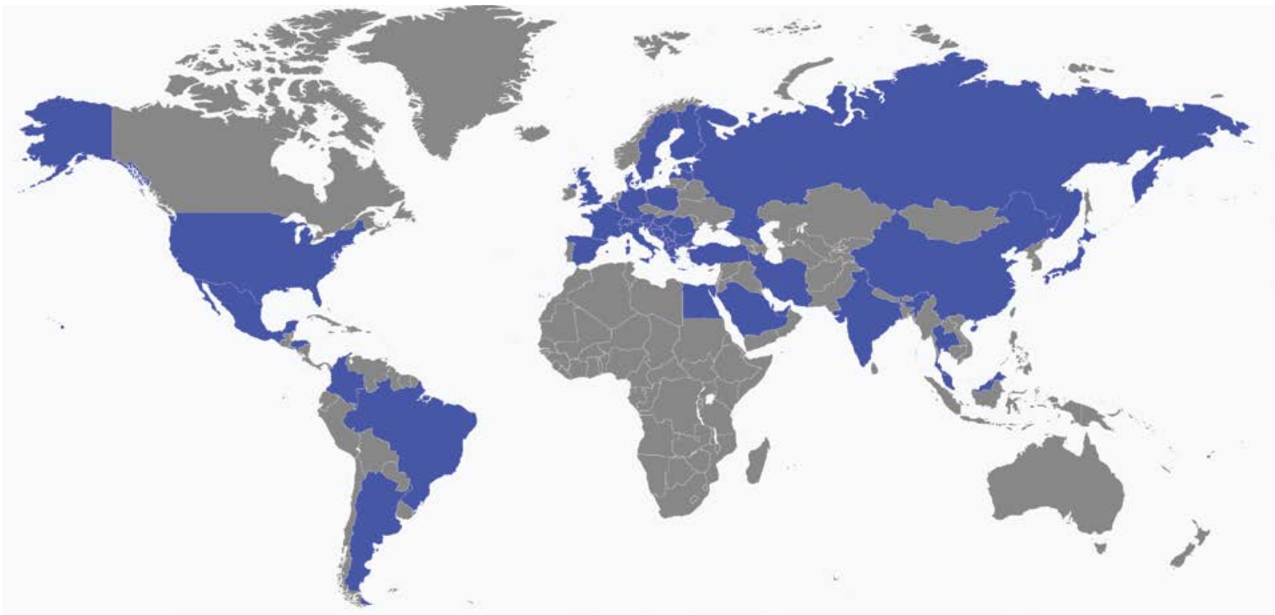
As shown by detailed analysis of available statistics, over a thousand participants, ranging from undergraduate students to practitioners, followed all or parts of the programme, facilitated by provisions to overcome difficulties due to time-zone differences. These unexpected and unprecedentedly high numbers, as well as the received comments, show an increasing interest in heavy-ion therapy research and related training and education. It also demonstrates an enormous potential, represented by the young students and early-stage researchers that will become the new generation of expert scientists in related emerging fields,

Visiting the treatment room at CNAO.

where often there is a lack of specialized personnel.

The scientific programme of the school was shaped to target such emerging topics, consciously addressing diversity aspects, providing role models, and highlighting the importance of developments for fundamental research that find applications in medicine and in particular in cancer diagnostics and treatment. Focusing on the treatment planning, which is practically the prescription of the therapeutic dose, it also covered everything entailed to deliver the beam to the tumour target; starting from the ion source, up to the accelerating and beam delivering elements, and including the biological response of cancerous and healthy tissues. The participants from different fields greatly appreciated this multidisciplinary approach, which started from basic concepts, included state-of-the-art practices and methods, and involved discussions of open points and needed research, as well as future plans for upcoming upgrades and developments. While well-structured overview lectures provided the necessary broad panorama, specialized presentations and hands-on sessions focused on the treatment planning details. These were based on the matRad open-source professional toolkit, developed by the DKFZ German cancer research centre in Heidelberg, specifically for training and research. Expert matRad tutors from DKFZ and LMU guided participants, with enthusiasm and patience, from the step-by-step installation of the needed software to the execution of involved treatment planning cases, demonstrating the benefits, but also the challenges, of heavy-ion therapy compared to different treatment modalities. Despite the demands related to specialized software and computing power, necessary for realistic computations, some 200 participants delivered their hands-on results demonstrating their dedication, motivation, but also their stamina, required for this intense full-week course; and which was awarded appropriate certificate of attendance.

To enhance effectiveness and facilitate the assimilation of information, the course used several proven pedagogical elements, inspired by the newly developed Particle Therapy Masterclasses (PTMC) https://indico.cern.ch/event/840212/ which is integrated into the International Masterclasses https://physicsmasterclasses.org/index.php?cat=schedule programme of IPPOG https://ippog.org. The day started with short informative videos of the European heavy-ion therapy centres and research infrastructures, to stimulate curiosity but also to give a visual impression and facilitate participants to relate the lectures of specific topics to the broader picture. It also included real-time virtual visits to these labs, ranked by participants among the most exciting components of the course. The important role of particle accelerators for particle physics research and then their optimization for particle therapy was apparent. The course offered numerous opportunities for interaction with experts and many of them participated in dedicated sessions, where students presented their results and research projects, but also to the evening social events chatting with interested participants, with a glass of wine in hands, exploiting a powerful interactive platform.

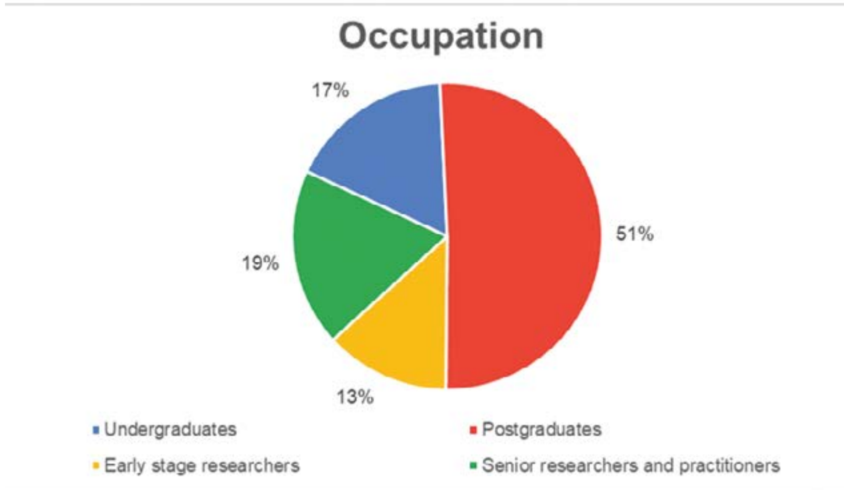


The course had literally worldwide reach. Based on the data delivered by the majority of registrants, 495 came from European countries and over 470 registrants came from non-European countries.

The young students that contributed to the HITM school organization were rewarded with a visit trip at the CNAO heavy-ion therapy facility, the coordinator of the HITRIplus project, and enjoyed detailed explanations by experts on the treatment planning and the accelerator complex.

The social events made a strong impression as they provided the feel of real-life interactions while at the same time bringing to participants valuable information through a career path fair where institutes such as CERN, CNAO, Cosylab, GSI/FAIR, MedAUSTRON presented career opportunities. This event was complemented with a contribution to entrepreneurship by CERN KT, highlighting medical applications, which triggered interesting discussions and drew enthusiastic comments. An important contribution came from the ENLIGHT coordinator who presented the ENLIGHT network and opportunities through its collaborators worldwide and was complemented by a discussion on epidemiology and cancer statistics.

Despite the online mode, a multitude of interactive means was efficiently used and stimulated interesting “question-and-answer” exchanges throughout the lectures but also during the social events. In particular, the opening presentation by the ENLIGHT coordinator, using also one of the ENLIGHT videos, fired the interest of participants and triggered stimulating discussions. All the material of the school, including recordings, is available for in-depth consulta-



Out of about 300 participants that provided information on their occupation status, half of them are postgraduate students (including Masters and PhDs) while the other half represents undergraduates, early-stage researchers and senior researchers or practitioners.

tion via the school agenda making up for the lack of "in-person" interactions.

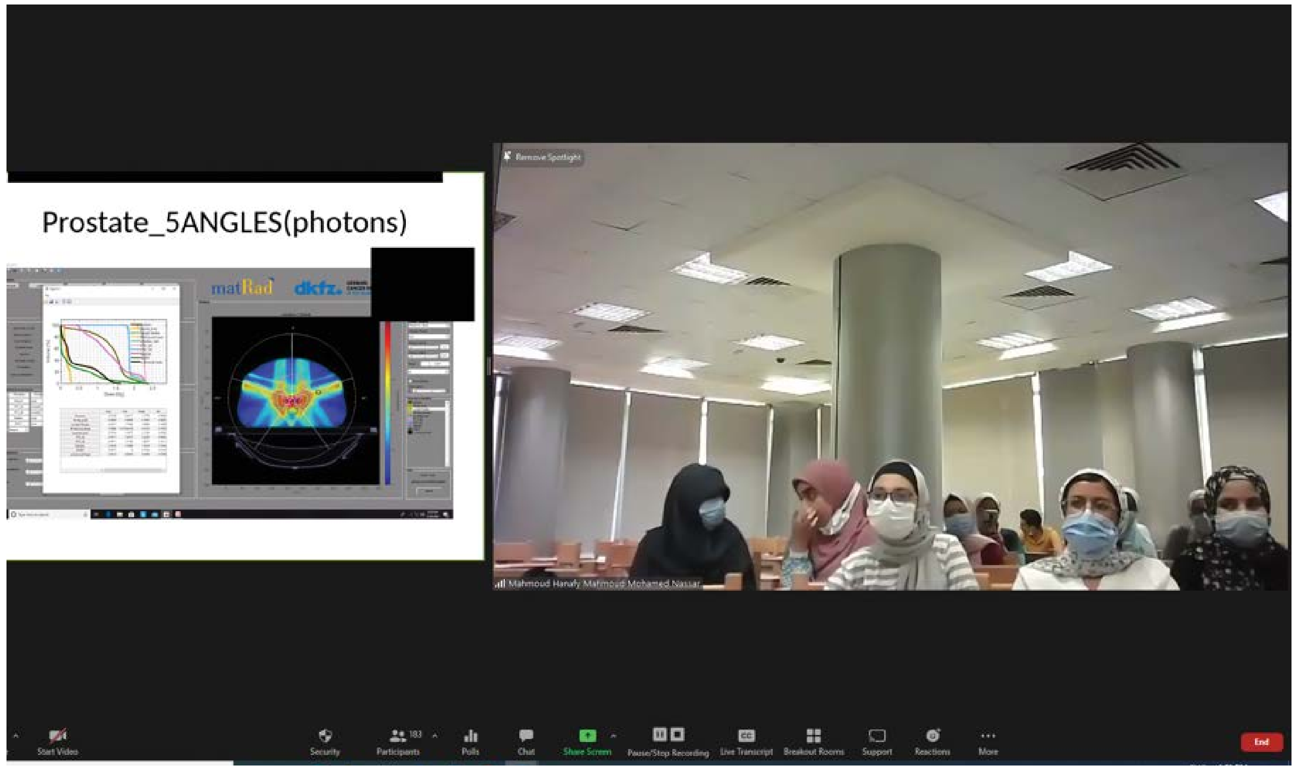
This holistic approach had a big impact on participants, almost equally distributed in European and non-European countries, who were clearly thankful for the opportunity to attend this high-quality school by top experts and for the enormous benefits for their education and future projects. Several of them are also motivated, not only to pursue their careers in related fields but also to get actively involved as tutors at their home institutes in future PTMC events for the younger generations. This upcoming promising experts' workforce will become the backbone for building and operating future heavy-ion therapy and research facilities that are greatly needed to fight and contain cancer all over the world.

Within the HITRI*plus* project, promising early-stage researchers will be candidates to be further supported by the upcoming HITRI*plus* schools on clinical and medical aspects, as well as by HITRI*plus* internships, so that they can optimally access the existing European heavy-ion therapy centres and contribute to relevant research projects, upgrades and future developments. Trained by prominent experts of the heavy-ion therapy field, this group of upcoming next-generation experts will bring their acquired knowledge and know-how to their countries and efficiently support, in a sustainable way, cutting-edge future developments.

The HITRI*plus* collaborators, including research infrastructures, universities, industry partners, the four existing European heavy-ion therapy centres and SEEIIST the South-East European Institute for Sustainable Technologies, motivated by the success of and the response to this first course are preparing already the next courses based on the uplifting received feedback of numerous grateful participants.

The HITRI*plus* project has received funds from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548.

Author:
Yiota Foka (GSI),
HITM chair on behalf
of the HITM Organisers



A surprising addition to the school was the initiative of the University of Benha, Egypt, that organized the participation of some 80-100 students, from different faculties to the full week course, as part of their curriculum, in a formal way, with the presence of the director of the university at the opening session. The students followed the courses from an auditorium via a single connection and worked on the hands-on exercises in smaller groups. They presented their hands-on results in the students' sessions every day. The active participation of female students and the presentations of their hands-on results were stunning, giving an inspiring example to follow.

BEHIND THE SCENES OF TNA BEAM ACCESS VIDEO

An interview with the filmmaker Stefano Conca Bonizzoni

Stefano Conca Bonizzoni, film director and documentarian, has always faced the challenge of social cinema, participating in various international Festivals.

Stefano's cinema is introspective cinema, stuffed with humanity, the same one that he tried to emphasize in a world far from his own, the world of science and in particular of high technology related to the treatment of tumours.

Stefano was chosen to make the video of the HITRIplus project concerning TNA and the access to the beam, and for his first time, he accessed the five major European Centres capable of producing carbon ions for scientific research: CNAO, GSI, HIT, MEDA and MIT, discovering closely how particle accelerators work, different than those used at CERN for quantum physics, and built to treat complex tumours.

Let us discover with him what was going on behind the scenes.

The film-maker Stefano Conca Bonizzoni and his assistant Anna Recalde.

Stefano Conca Bonizzoni on a documentary set.

Before being contacted for this project, were you aware of the existence of these Centers and what idea did you have regarding the physics of quantum at the service of oncology?

I did not know that there could be such advanced technology in cancer treatment. My knowledge of the subject stopped at common radiotherapy and I had never explored the subject any further.

From social cinema to science, what urged you to face the challenge in a field very far from yours?

In fact, this is not the first time that I happen to report a scientific project in an audiovisual language, but in this case, it has been completely different. It was a mixture of curiosity, aesthetic experience and sacredness spirit that pushed me to enter these “cathedrals” of medicine.

It's lucky no one in my close family suffers from cancer. However, some statistics immediately reveal a shocking fact. Every day, in Italy only, a malignant tumour is diagnosed to 1000 people. This was the first element, unique and fundamental in this work, that I dare call a “mission”: to be able to tell with the camera about a scarcely known technology that offers a very effective alternative to one of the most lethal contemporary plagues.

From Italy to Germany, to Austria, how did you choose to direct the works and coordinate the film shootings and the interviews in the five centres?

The centres are located near the Universities or near Hospitals and Institutes of Care, often inserted in innovative architectures inspired by the Bauhaus, and surrounded by gardens recalling the concept of the third landscape theorized by the French writer and landscape designer Gilles Clément. Even if each centre is a world in itself, there is a thin fil rouge that links them to one other, and that's what helped me coordinate the film shootings and editing, and what I tried to emphasize in the video.

Dr. Monica Necchi - CNAO - Responsible Expansion Project.

How did you feel when you stepped for the first time into the particle accelerators bunkers?

Particle accelerators are like Stargates standing on the ground. Underground or in the woods. Monolithic technologies with amazing sizes that treat one person at a time.

From the outside, you don't fancy what to expect.

The feeling entering, especially in the treatment rooms, is to be in the spacecraft of “2001: Odyssey in space.” Here technology does not rebel against man to conserve itself, but is completely at his service, to cure him or to find solutions for.... living on Mars. Every single film shot could in fact be taken from a sci-fi movie, which would start with this wording, I leave it to you to choose the date :

“In a planet torn apart by the struggle for resources and bent by increasingly violent climate disasters, a handful of physicists, doctors and scientists have abandoned megalopolis for the woods. Here, all together, they have built megalithic coloured circles to accelerate particles almost to the speed of light. To treat men, one at a time. And in the meantime, they ran tests with the accelerator to make life possible in space. It is estimated that the first clone to set foot on Mars and live there today attends primary schools. “

Dr. Piero Fossati - MedAustron - Head of Carbon Ion Program.

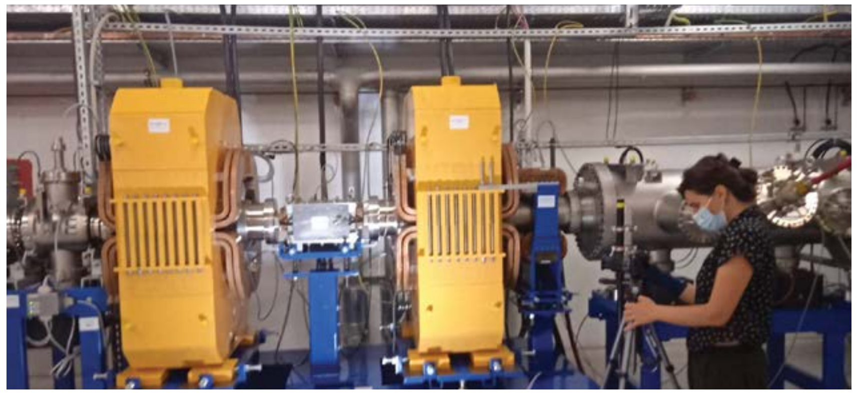
What was the greatest difficulty in making this video and what were instead the moments that you remember most vividly?

The greatest difficulty was organizational: moving among the various centres, due to the restrictions of the pandemic. My assistant Anna Recalde supported me as a phonic operator in this project, and I, have come to constantly take a Covid test a day during the film shootings. The risk was too high for the patients and the doctors of the facility.

On the other hand, there is no single moment I remember with more intensity. Every centre was fascinating, as a separate universe, unique and not replicable. CNAO, GSI, HIT, MEDA and MIT are human, scientific and clinical machines, aimed at new horizons.

For each one of them, it was like discovering something for the first time, understanding how much technology can support medicine: a detail of the particle accelerator, a mechanism of the bed in the treatment room, a detail of the control room.

What these centres undoubtedly have in common is efficiency, competence and professionalism, but especially teamwork. Physicians, physicists, bioengineers, radiology technicians work together in synergy, striving for a common goal: expanding therapeutic skills. Worlds where physics, research and medicine join together in a field as delicate and socially impactful as oncological care.



Anna Recalde on the set of beam access video.

To make this video I have interviewed and collaborated with many of them, and I thank each one of them for the participation and the valuable support they have provided. I would also like to thank the HITRI*plus* WP2 Team for the work coordination, without them the realisation of this project would not have been possible.

The beam access video can be discovered at the following link: **https://www.hitriplus.eu/transnational-access/**

Author:
Silvia Meneghello, CNAO

INSPIRE PROJECT

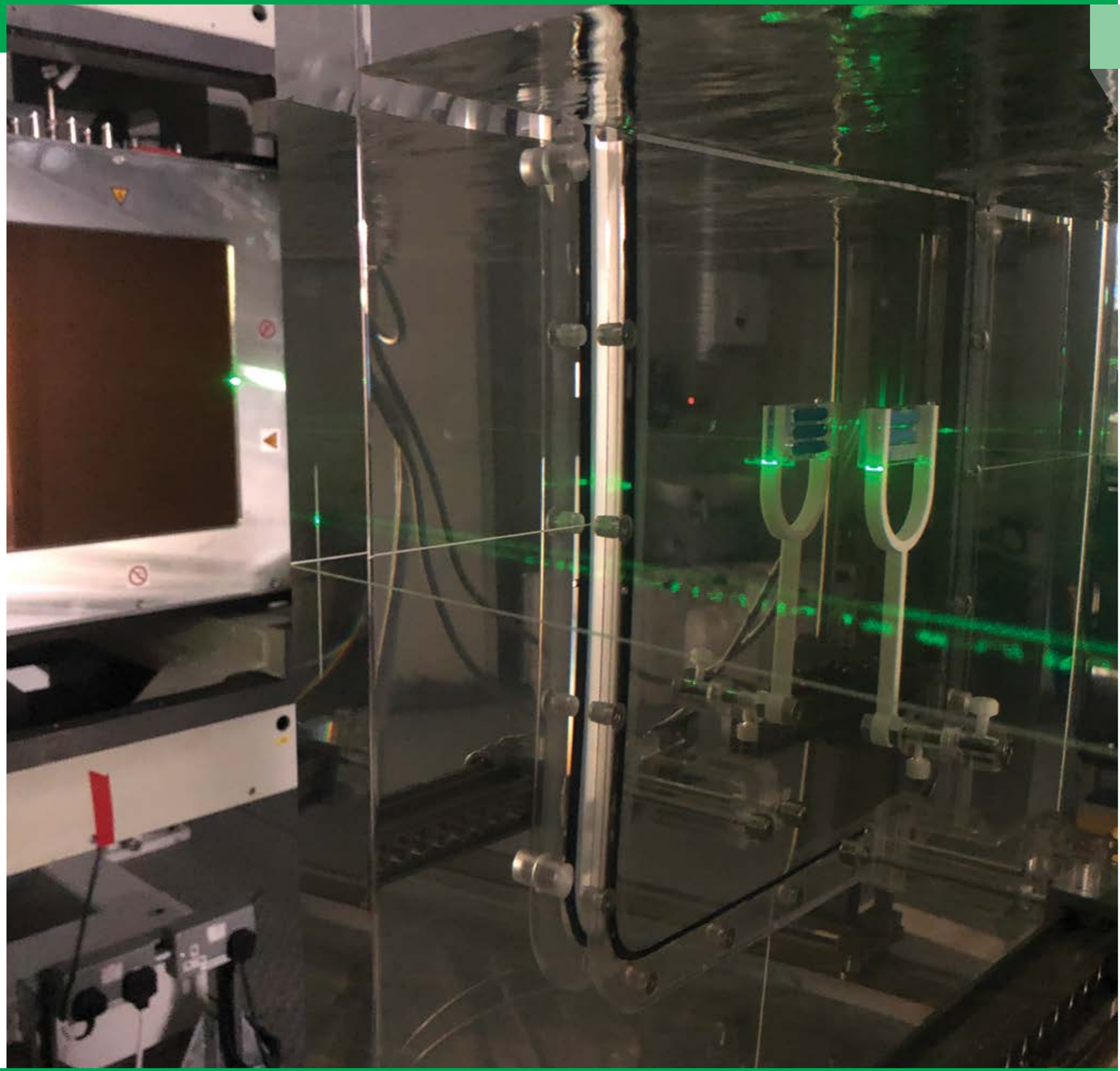
INSPIRE provides an infrastructure that brings together research activities in clinical proton therapy (PT) centres with research and industrial research in this field across Europe. INSPIRE has 17 partners and includes the 2 major manufacturers of proton therapy equipment (Varian and IBA) and 11 clinical centres for proton therapy across Europe. INSPIRE also includes GSI and the low energy cyclotron at UMCG so there is also a component of research with heavier ions to complement proton therapy within INSPIRE.

INSPIRE provides a route for researchers across Europe and internationally to access the research rooms of clinical PBT centres and to also access heavier ions at GSI and UMCG through INSPIRE's Transnational Access (TNA) Gateway. INSPIRE's capabilities and how to access its facilities can be found at https://protonsinspire.eu/. This website also contains the latest news about INSPIRE and copies our Newsletters, publications, software and databases.

A paper which outlining the radiobiology capabilities of the TNA providers in INSPIRE and how these capabilities are being enhanced through INSPIRE's Joint Research Activities (JRA) has been published in the journal Frontiers https://doi.org/10.3389/fphy.2020.565055.

FLASH beams available through INSPIRE

In recent years ultra-high dose rate radiotherapy (FLASH RT) has become an area of significant international interest as FLASH beams appear to spare normal tissue damage whilst still retarding tumour growth. FLASH beams can be delivered using photon, proton and electron beams and the effects observed appear to be agnostic of radiation quality. Through INSPIRE's JRA activities most TNA providers in INSPIRE have demonstrated that they are capable of delivering PBT FLASH beams (UMCG and GSI are also capable of delivering FLASH beams of heavier ions) so that FLASH beams of protons and heavier ions are now available through INSPIRE's TNA.



Inspire dosimetry audit.

Developing INSPIRE's Capabilities:

Collaboration has been a key part of INSPIRE. This is demonstrated by the inter-comparison and benchmarking studies which have taken place in INSPIRE's JRA linking in to Networking activities in such as Quality Assurance and Standards. Some examples are described below:

> **INSPIRE has an Innovation Gateway which enables access to clinical proton beams so that research can be accelerated to higher technology readiness levels, working with industry and working with the clinic to translate research into clinical practice.**

InspireProject

01

A joint experiment led by Dr Olga Sokol at GSI to access the variations in the proton Relative Biological Effectiveness (RBE) measurements at different European centres is underway with a phantom designed by GSI. This is a two-step study includes a preparatory X-ray survival curve experiment in tissue culture flasks as well as a main experiment, where a phantom containing cell plates at different depths within the Bragg peak (provided by GSI) is irradiated with proton beams (for two different SOBP geometries). The goal of the study is to estimate the difference in the cell survival, and thus proton RBE, measured along the SOBP at different centres, when the variations in the biological setup and protocols are minimized. Each centre has purchased the same cell line (V79-4, Chinese hamster lung fibroblast) and receives a phantom together with the instructions on cell preparation and post-processing. After agreeing on the proton field geometries, the centres perform the irradiations of the phantom, followed by the cross comparison of the results. Experiments have now been completed at GSI and are underway in Manchester at The Christie, at Institut Curie in Paris, at the proton centres in Prague, Czech Republic and Krakow in Poland and at Technische Universität Dresden, who additionally produced a local copy of the phantom. Further experiments will be starting soon at the proton therapy centre in Sweden and in Aarhus in Denmark. Due to the lower energies available at low energy cyclotron at UMCG a separate phantom is being designed which will also look at RBE variations with protons and heavier ions at lower energies.

02

An international benchmarking study led by Technische Universität Dresden TUD and involving eight European PT institutions within INSPIRE used suitable treatment planning systems with their centre-specific beam model to create treatment plans. Dose distributions D1.1 and DRBE assuming constant and variable RBE (Relative Biological Effectiveness), respectively, and LET (Linear Energy Transfer) were compared amongst the institutions. The harmonization of LET calculations allows for consistent multi-centric analysis and reporting of tumour control and toxicity after PT in view of a variable RBE. It may in the future serve as a basis for a harmonized variable RBE dose prescription in proton therapy.

03

Together with UMCG (PT centre in Groningen), PSI (PT centre in Switzerland) have started a project to study inter-centre variability for PT pencil beam scanning planning of head and neck cancers. A representative nasopharynx case has been selected and PSI will now distribute this to INSPIRE partners and the wider ESTRO Taskforce European Particle Therapy Network so it can be planned at each centre and the plans compared.

04

An INSPIRE dosimetry audit in conjunction with the EURADOS collaboration (led by Dr Marie Davidkova in Prague) is underway. This utilises PBT spot scanning beams and the team at IFJ-PAN in Krakow has contributed to the development of the audit procedure. Three types of detectors: thermo-luminescent (capsules with TLD powder), alanine pellets and radio photoluminescent (RPL) detectors have been selected for the audit. Each centre has irradiated the different detectors with the same prescribed plan and detectors will be used to compare dosimetry for PBT spot scanning between centres. This will give an indication of dosimetric differences between centres and help in the interpretation of results from radiobiological experiments, such as the inter-comparison experiment described above.

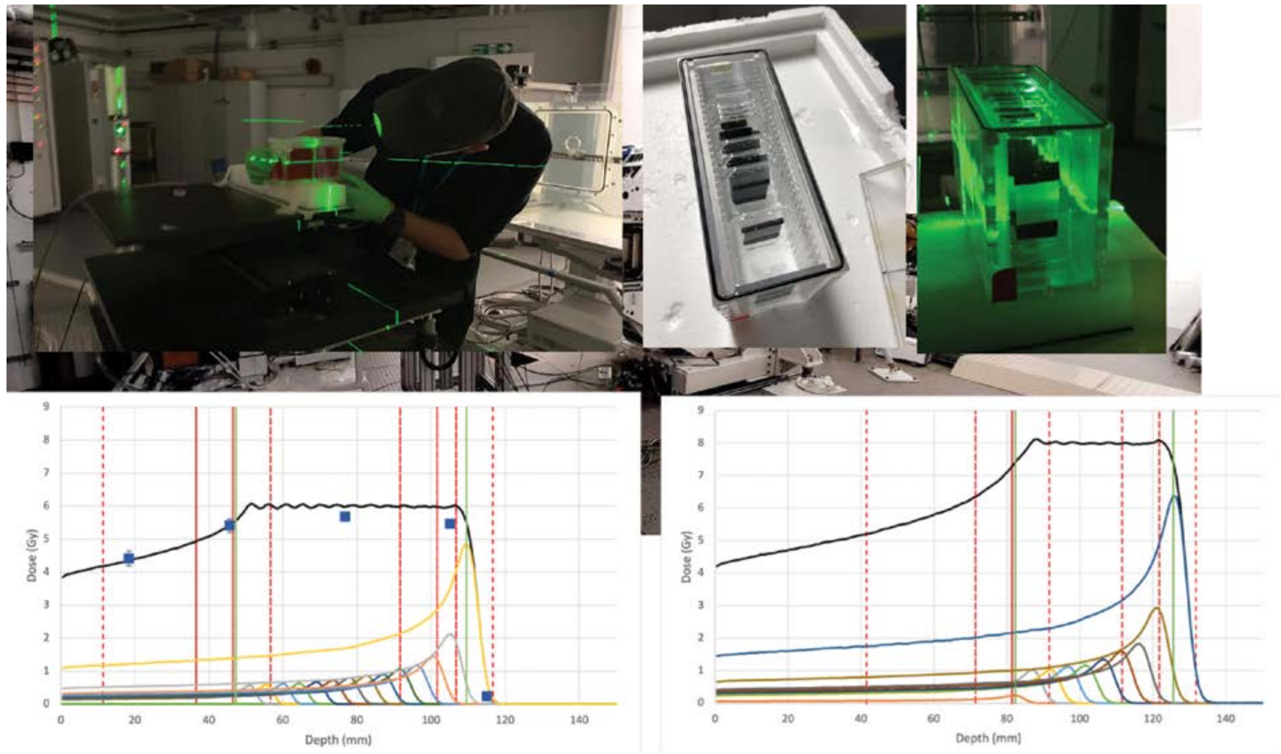


Figure 1 a. *INSPIRE radiobiology inter-comparison experiment with 2 SOBP at 6 and 8 Gy being undertaken in Manchester.*

Innovation Gateway and working with industry

INSPIRE has an Innovation Gateway which enables access to clinical proton beams so that research can be accelerated to higher technology readiness levels, working with industry and working with the clinic to translate research into clinical practice, below are some examples of INSPIRE's Innovation Gateway and how INSPIRE engages with industry.

VARIAN have continued to develop their new detector technology for FLASH PBT. A first full beam monitor system has been tested on a clinical gantry and is being used in the world's first FLASH PBT clinical trial FAST-01 in Cincinnati. In addition, a commercial product "FLEX", has been developed for FLASH PBT research. VARIAN are now developing a product through INSPIRE's Innovation Gateway with the Danish Clinical PBT centre in Aarhus that can also be used clinically at both FLASH and conventional-dose rates.

Figure 1 b.*INSPIRE radiobiology inter-comparison experiment with 2 SOBP at 6 and 8 Gy being undertaken in Manchester.*

Features

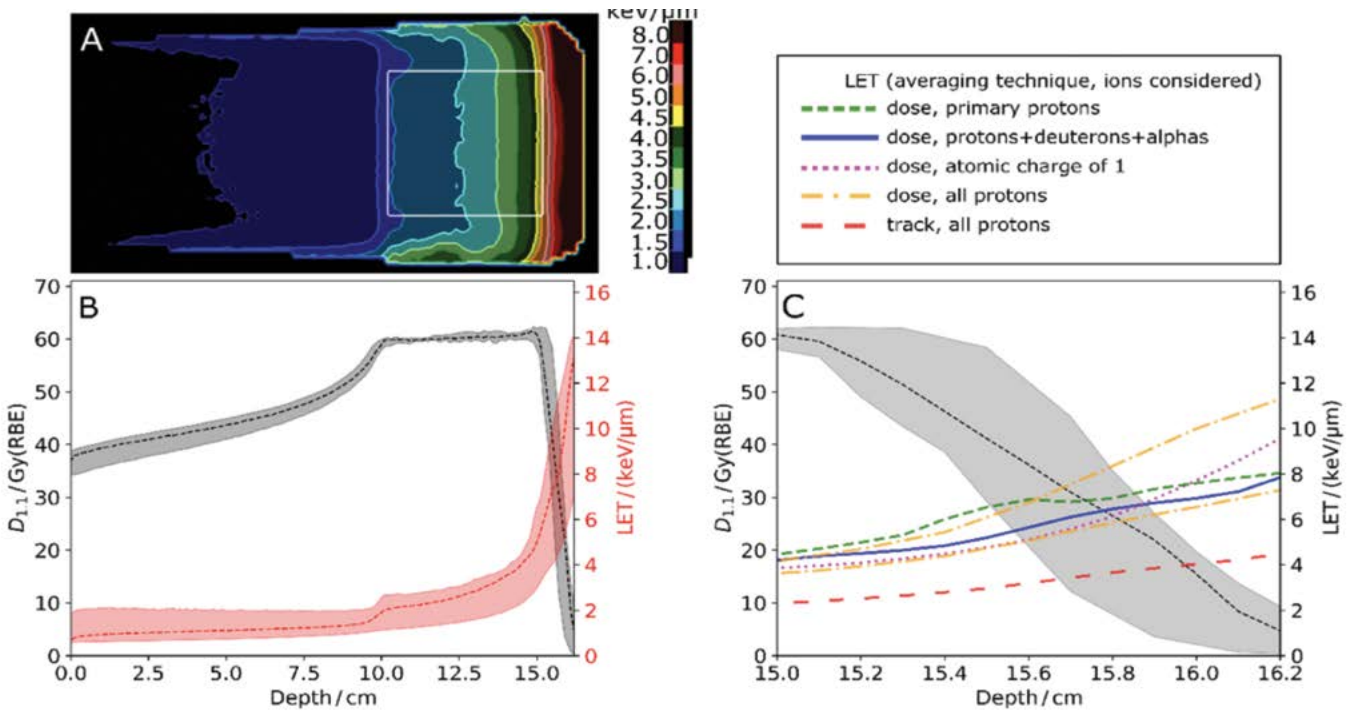


Figure 2: *A) Example of a linear energy transfer distribution (LET, dose-averaged, all protons), corresponding to the dose distribution in Figure 1A. Line profiles of the six institutions along beam central axis are depicted in B) for biologically equivalent dose with relative biological effectiveness of 1.1 (D1.1, grey, upper) and non-harmonised LET distributions (red, lower). Median (dashed) D1.1 and LET are shown together with their minimum and maximum values (shaded area) showing inter-institutional variability between the six institutions. C) Magnification of the distal area in B) with a detailed depiction of LET line profiles for all six institutional non-harmonised LET calculations.*

TUD have been working with SME ADVACAM and EMPIR project UHDPulse through INSPIRE's Innovation Gateway on FLASH dosimetry.

The CAPTAIN normal tissue complication probability (NTCP) database developed by IBA and UMCG is now available online. The platform was first installed at UZL in Belgium and has also been deployed in the Baptist Health South Florida (BHSF) proton therapy centre (USA) with a new collaboration targeting the implementation of new NTCP models for rectal cancer. The number of models available on CAPTAIN has increased and newer versions of the UMCG models have been integrated. Work between UMCG and IBA involves NTCP-models for multiple tumour sites being developed. To leverage these results and translate these models into an EU-wide inventory is the next step and work in this field is ongoing.

Figure 3 *Manchester beam line with hypoxia end station.*

In Manchester, the PT research room at The Christie have taken delivery of a customised hypoxia end station. This enables experiments (in vitro 2D and 3D) to be conducted at different oxygen tensions. This was designed in collaboration with Don Whitley Scientific (DWS) and Thermo Fischer Scientific (TFS). DWS are the supplier of the hypoxia cabinet and TFS supplied the 6-axis robot through FANUC. This cabinet allows the group to perform high-throughput, highly repeatable experiments in a controlled oxygen environment. The cabinet also contains a Wellwash Versa plate washer for automated liquid handling and cell fixation, allowing to control experimental timepoints accurately.

Patents

Three patents are in process or have been granted following work conducted through INSPIRE

- Experiments to explore drug delivery and radiation combinations have been undertaken by IFJ-PAN in Krakow and a patent application has been successful based on gold nano-peanuts for drug delivery

- A device that is capable of irradiating small animals on a clinical machine with a gantry has been developed by Unamur and is the subject of a patent application.

- GSI in collaboration with TIFPA (PT centre in Italy) have developed a new small portable hypoxia chamber for in vitro irradiations in acute hypoxia. Currently, this is being compared with a chamber, and its eligibility for a patent application is under discussion.

Training the next generation

INSPIRE is working with the founders of the first two FLASH Workshops (Institut Curie, in Paris and CHUV in Lausanne), UHDPulse and Kenes on a new conference series Flash Radiotherapy and Particle Therapy (FRPT) https://frpt-conference.org/ which will take place virtually and in-person in Vienna on 1-3rd Dec 2021. FRPT is joining with the Green Journal and Physica Medica so that the top papers from FRPT can be published in these journals. All of the abstracts will be published in Physica Medica. INSPIRE partners are also involved in hosting major conferences for example Aarhus is hosting BIGART in 2021 and ESTRO in 2022.

INSPIRE has also been involved in a number of virtual events for example over 1000 people attended an online Open Nights outreach event in Krakow in 2021. The world's first online Proton School was held in Manchester at The Christie over a period of 6 weeks Nov-Dec 2020 and attracted over 100 delegates from all over the world. PSI held its prestigious and internationally acclaimed winter school online for the first time in January 2021.

For more information on INSPIRE please visit our website https://protonsinspire.eu/

Author:
Karen Kirkby,
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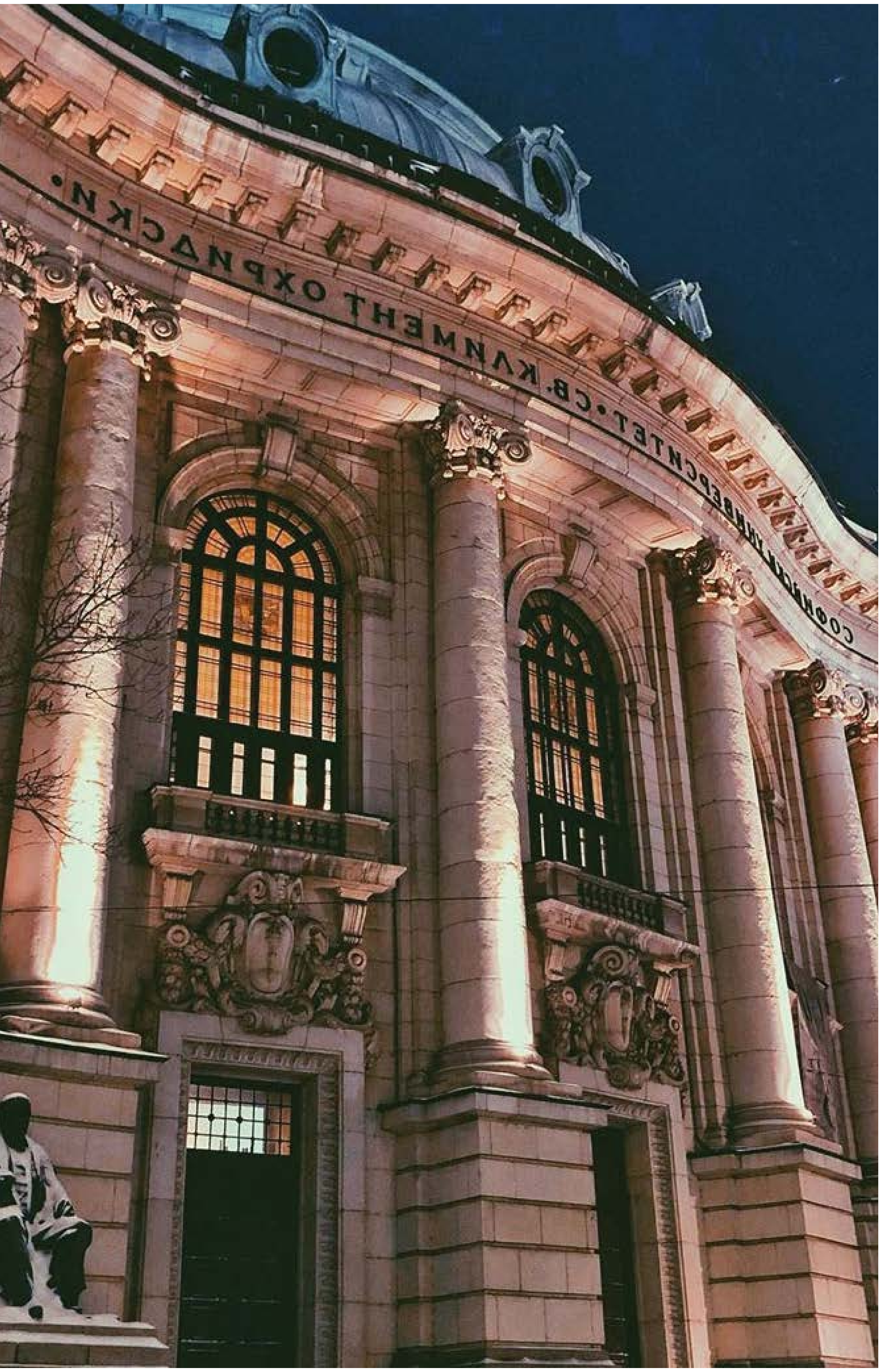
SNEZHINA DIMITROVA

PhD student in Biophysics at Sofia University “St. Kliment Ohridski”



The main entrance of Sofia University “St. Kliment Ohridski”, the oldest high education institution in Bulgaria founded in 1888.

1. Background: Tell us something about yourself, your education, career: Where do you study and what? Do you do research?

My name is Snezhina Dimitrova, 28 years old from Sofia, Bulgaria. I am currently a PhD student in Biophysics at Sofia University “St. Kliment Ohridski”. I have a strong interest in the field of Medical Physics and in 2012 I enrolled the “Medical physics” Bachelor program at Sofia University. During my BSc studies, I was fascinated by the unique properties of the Hadron therapy and its application in cancer treatments. I successfully defended a BSc thesis on “Hadron therapy”. Then I enrolled on the MSc program in Medical physics and I my involvement in this field became even stronger. I have performed some GEANT4 simulations of proton and heavy ions beams hitting a water phantom and successfully defended my MSc thesis - “Monte Carlo simulation of linear energy transfer of protons and light ions”.

Since July, 2018 I have been enrolled as a PhD student in Biophysics at the Atomic Physics Department at the Faculty of Physics of Sofia University “St. Kliment Ohridski”. The subject of my PhD is “Mechanisms of reaction to ionizing radiation of living matter”.

Currently, my work consists of Geant4 simulation of proton and carbon ions interactions in water and DNA damage. In the course of my training I started doing in-depth research on a new type of treatment for tumors with FLASH therapy.

2. Where would you like to study if you had a choice? Why?

If I had to choose where to study again, I would choose the same university. But as a next step for development, I would choose a university abroad, which offers a specialty Radiobiology. The reason for my choice is that research in this field abroad is at a higher level.

3. Current research: What projects are you working on? Are they part of your current education? What are the challenges for you?

The main project I am working on is the completion of my doctoral studies, in addition to the SEIISST project. I am also part of several other projects in the field of biophysics.

The biggest challenge is the absence of places in my country to do the experimental part of my research.

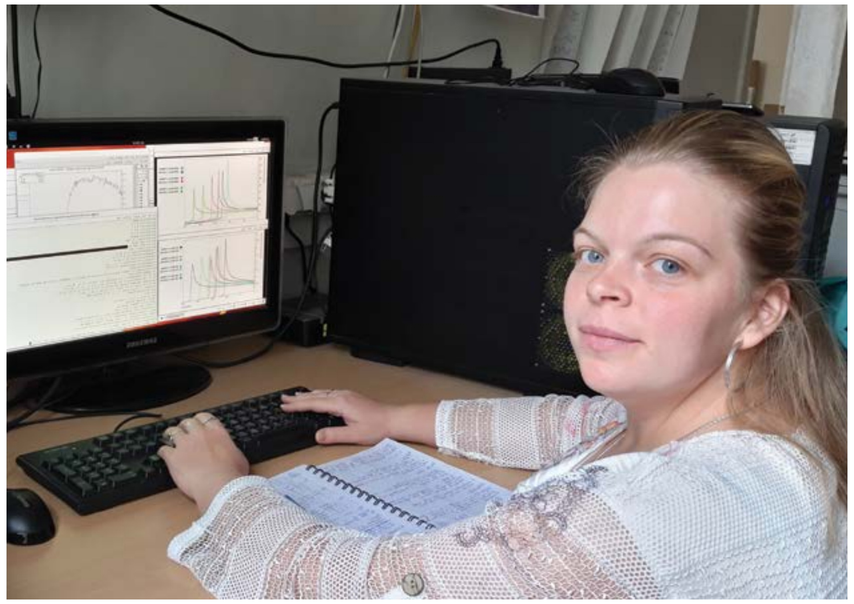
4. What was the most interesting thing you learned during the HITRIplus Heavy Ion Therapy Masterclass school?

During the HITRI*plus* Heavy Ion Therapy Masterclass school, the most interesting thing for me was the practical part. Introduction to MatRad software and its application.

What do you think are the key challenges facing the medical physicists in your country?

The biggest challenge for medical physicists in Bulgaria is the absence of realization. Unfortunately, jobs are very few and difficult to reach.

In addition, in the training of medical physicists the practical part is not included. The university offers more theory than practice.



5. Which is/are your dream(s) for future research and future career? Where do you see yourself 10 years from today?

My dream is the realization of the SEEIIST project. From the beginning I am part of the Bulgarian group that works on SEEIIST project. My job is to estimate the number of patients and the distribution of available protocols by tumour locations. I am doing it with great interest and pleasure. It really brings me satisfaction to know that I contribute to this project. The establishment of a centre like this will help the professional and scientific development of each of the participating countries. I would like to be a part of it.

After 10 years I see myself as a good specialist in the field of medical physics and especially in the field of radiotherapy with protons and carbon ions, and why not Flash therapy at the SEEIIST centre.

6. What do you think of radiation therapy for cancer and particle therapy?

Each therapy has its advantages and disadvantages. All types of therapy such as radiation therapy, chemotherapy, surgery and proton and ion therapy are complementary. Hadron therapy used the properties of charged particles to give off almost all their energy in a very narrow spatial area. This allows the tumour to be attacked with minimal damage to the surrounding tissues. By regulating their energy, the depth to which the main part of their energy will be given. Due to the specific properties of ionization, the healthy tissue in front of the tumour is irradiated minimally, and the one behind it remains virtually unaffected. The effectiveness of this method is significantly higher than X-ray irradiation, and the probability of creating a problem in surrounding tissues is many times lower. In 30% of cases, X rays cannot affect radiation-resistant tumours, and radiation damages not only the tumour itself but also the tissue in front of and behind it.

RIKO HOASHI

a graduate student of Tohoku University in Japan

1. Background: Tell us something about yourself, your education, career: Where do you study and what? Do you do research?

Born in Japan, in 1998. I'm majoring in medical engineering and quantum science at Tohoku University in Japan.

I have experienced the Great East Japan Earthquake in 2011 when I was an elementary school student. Japan has faced a serious accident at the nuclear power plant in Fukushima Prefecture which was triggered by a great tsunami. Distrust of nuclear power generation and fear of radiation has spread throughout the country since the accident.

Now, most people of the prefecture can live a normal life, but they're still suffering from harmful rumours arising from misunderstandings of radioactive contamination.

I want to acquire an accurate understanding of the effects of radiation on the human body and want to tell particularly not the professional person the versatility of radiation, not just dangerous.

So, I'm interested in radiotherapy and engaged in proton therapy research at the Cyclotron and radioisotope centre (CYRIC), Tohoku University.

3. Current research: What projects are you working on? Are they part of your current education? What are the challenges for you?

I'm engaged in the “tan-Q” project which supports learning for high school students in co-operation with college students and researchers. As part of the project, we're studying polymer gel dosimeters for radiotherapy which change their colour depending on the absorbed dose because the high school student (She) was very interested in radiotherapy. I help her make gels, simulate and analyze the absorbed dose. We conducted an irradiation experiment with X-rays and gamma-rays at CYRIC and UVSOR Synchrotron Facility.

We also tried to team up with the students in Argentina and Mexico online for Beamline for Schools 2021 and our research has been selected to the short-list. The experience makes me grow a lot. Accordingly, my purpose is to share with other people the accurate information and the versatility of radiation that has been achieved through the project.

The high school student and I, making polymer gels at CYRIC, Tohoku University

The project members, conducting irradiating the gel with gamma-ray at UVSOR

4. What was the most interesting thing you learned during the HITRIplus Heavy Ion Therapy Masterclass school?

The Hands-On Treatment Planning using MatRad was the most interesting class for me during this school. I have studied the technology and method for irradiating and measuring protons but never experienced simulating treatment plan. The simulation data of MatRad is easy to perceive visually. In my opinion, radiotherapy in Japan in the cancer field has not sufficiently spread in comparison with surgery, anticancer drugs. I think it includes the problem that lack of correct knowledge and recognition of radiotherapy and radiation, not just a matter of cost, technique.

5. Which is/are your dream(s) for future research and future career? Where do you see yourself in 10 years from today?

I think particle therapy plays an important role in cancer treatment because of the physical characteristics such as Bragg peak, plateau, and SOBP. Hence, this will make it possible to treat cancers that cannot be treated with surgery or drugs while maintaining a good quality of life. In this course, I was able to learn more about the effects of particle therapy on the human body and its therapeutic effects.

6. What do you think of radiation therapy for cancer and particle therapy?

The project members, in front of the AVF Cyclotron at CYRIC

After completing my master's course, I want to use my expertise to get a job as an engineer.

If the opportunity arises, I would like to be involved in radiotherapy or medical engineering. (I'm still struggling.) I will always be conscious of understanding and communicating correctly in my future life.

KOUROUMIDIS IOANNIS

Aristotle University of Thessaloniki (AUTh) and my MSc in Theoretical Physics at the University of Edinburgh (UoE)

My name is Kouroumidis Ioannis (Yiannis) and I am a Greek theoretical physicist. I obtained my bachelor degree in physics, at the Aristotle University of Thessaloniki (AUTh) and my MSc in Theoretical Physics at the University of Edinburgh (UoE).

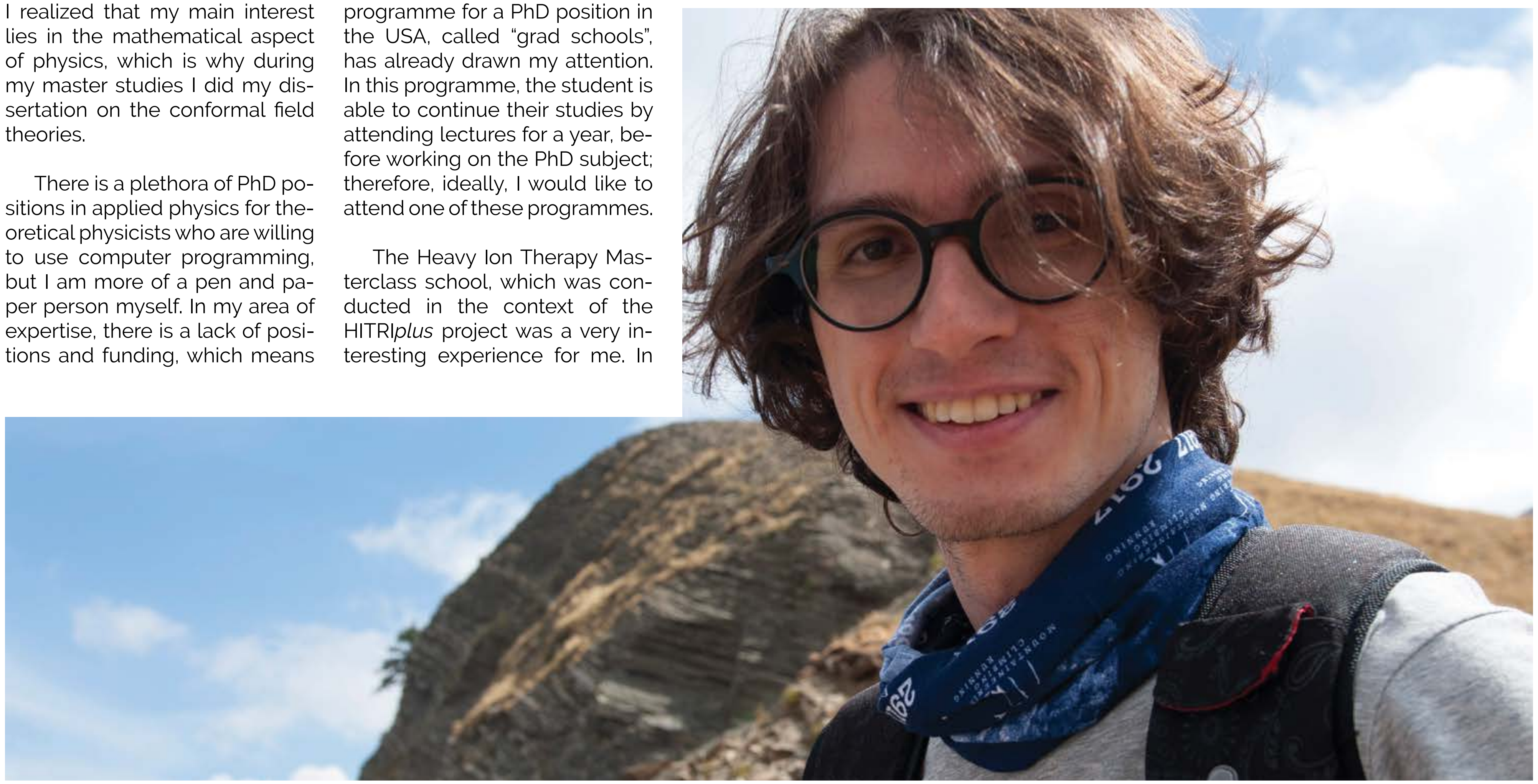
During my educational career, I realized that my main interest lies in the mathematical aspect of physics, which is why during my master studies I did my dissertation on the conformal field theories.

There is a plethora of PhD positions in applied physics for theoretical physicists who are willing to use computer programming, but I am more of a pen and paper person myself. In my area of expertise, there is a lack of positions and funding, which means that the competition is quite stiff and a small percentage of scientists/researchers is being "absorbed".

My main aim is to continue my studies and enhance my knowledge in theoretical physics, while also starting a PhD in the near future. An interesting programme for a PhD position in the USA, called "grad schools", has already drawn my attention. In this programme, the student is able to continue their studies by attending lectures for a year, before working on the PhD subject; therefore, ideally, I would like to attend one of these programmes.

The Heavy Ion Therapy Masterclass school, which was conducted in the context of the HITRI*plus* project was a very interesting experience for me. In particular, the hands-on activity offered me the opportunity to wear the shoes of a real-life medical physicist, understand the treatment planning and how one, can deal with a tumour using gamma radiation and ions. The most interesting part was trying to avoid radiating important organs, known as organs at risk, while also dealing with the cancerous tumour. In figure 1, one can see the dose distribution of a 5-angle photon beam irradiation (on the left) and single-angle irradiation with carbon ions (on the right) for a cancer tumour in the liver. In figures 2 and 3, the Dose-Volume Histograms (DVH) for both cases are given, where one can notice that the target areas (PTV, CTV, GTV) have received similar mean dose, in both cases; whereas in the case of photons, Organs At Risk (OAR), like heart, have received some "collateral damage".

Ioannis just started this last October his obligatory service in the army.



A synopsis including some of the OARs and a comparison of the dose that they have absorbed in the previous cases, signifying the differences between the radiation treatment methods, is provided in the table below.

Currently, the resources in Greece are inadequate and thus, there is little to no research in medical physics, making it difficult for medical physicists to find a job here. This sets a limit in the capabilities of upcoming researchers and future medical physicists, causing a minimization of the country's brain drain. Another burden is posed by the lack of information on specialized applied physics subjects, such as the cancer treatment with ion beams. Hence, initiatives and projects such as the Heavy Ion Therapy MasterClass project play a significant role and contribute to the deterioration of this knowledge gap by offering the ability to discover the applications of physics in a variety of scientific fields, for free.

Visualizing myself 10 years from today, I would like to have completed my PhD and perhaps post-doc studies, and working by applying my physics knowledge for the good of society. After the HITM school experience, I am also examining a possible future synergy in the medical physics field because I firmly believe that

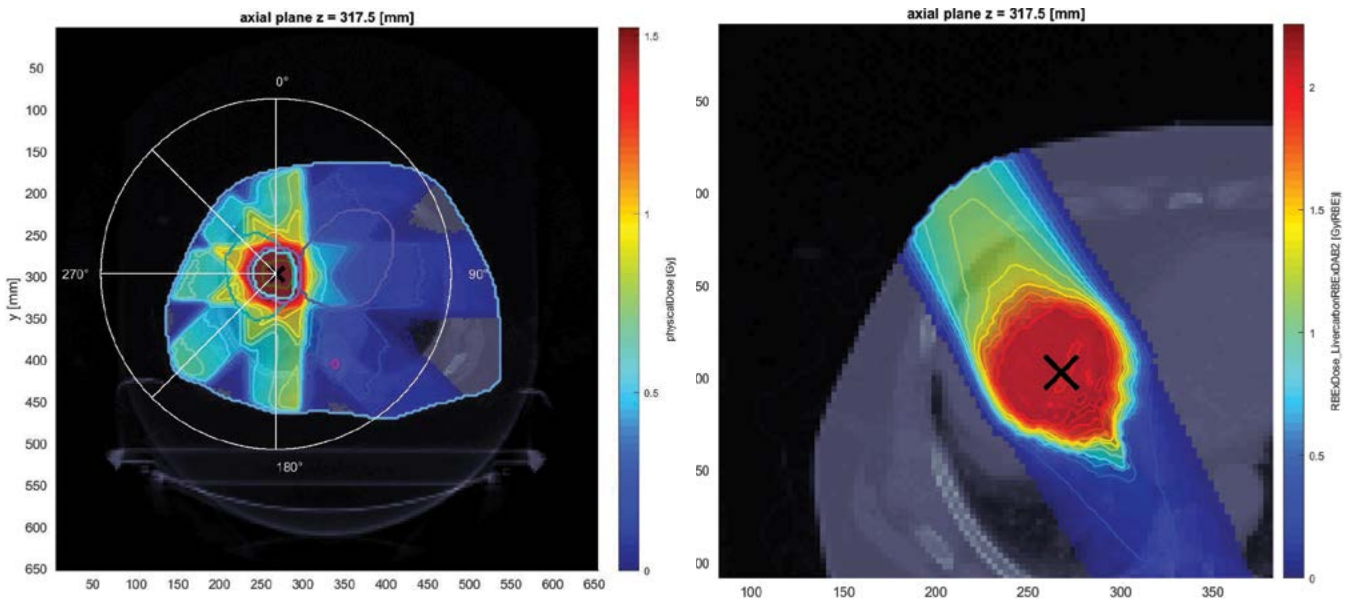


Figure 1: *Cancer treatment of a liver case with photons (on the left hand side) and carbons (on the right hand side).*

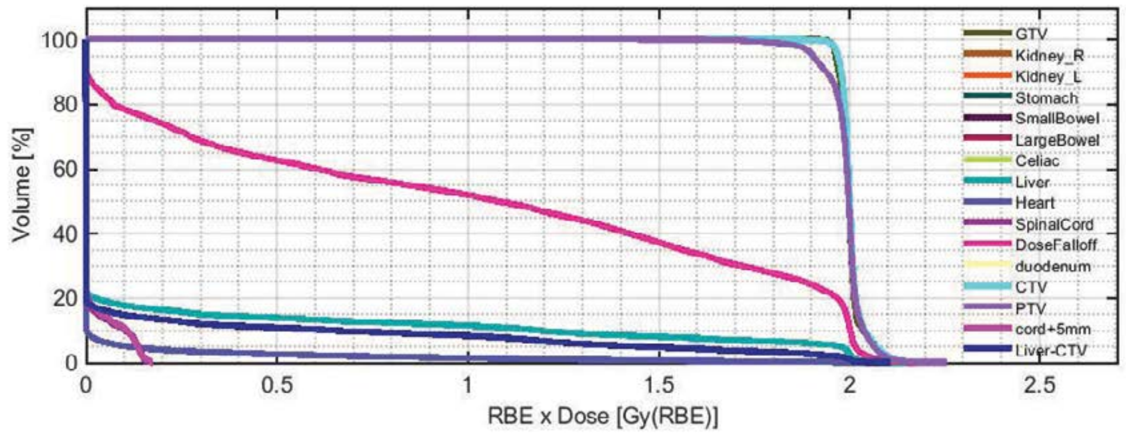
Table: Comparison of mean dose between photon and carbon treatment techniques for the liver case.

Organs	Photons	Carbons
Heart	0.22	0.03
Stomach	0.02	0.00
Spinal cord	0.03	0.01

particle therapy will contribute significantly to the extinguishing of numerous cases of cancer.

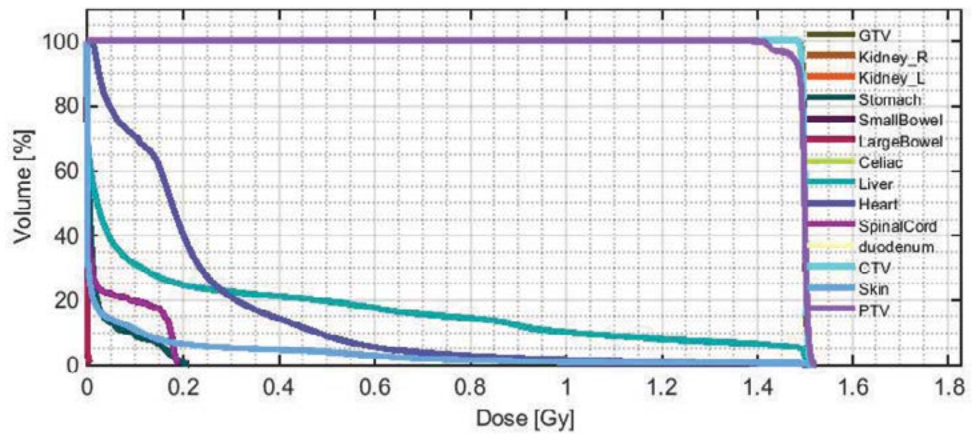
However, my career is currently at a pause. As all men of Greece, I must serve in the army for 9 months. While the main purpose of the army is to familiarize us with the life of a soldier, it often degenerates into a lesson about following commands without asking questions. Nevertheless, I find myself enjoying some aspects of the army. I got to interact with people that I would otherwise avoid conversing with, which gave me a perspective of the world that was foreign to me. There is also plenty of time to read books, which provides an escape for the mind. Picture 1 depicts my brother, myself and my cousin and (from left to right), back when we were fond of the idea of being soldiers.

At this point, I would like to express my gratitude to the organizers of such a fruitful school and for giving me the chance to express my personal opinion through this document. I am looking forward to taking part in similar events in the future.



	max	min	mean	std
GTV	2.1432	1.9224	2.0024	0.0288
Kidney_R	0	0	0	0
Kidney_L	0	0	0	0
Stomach	0	0	0	0
SmallBowel	0	0	0	0
LargeBowel	0	0	0	0
Celiac	0	0	0	0
Liver	2.1974	0	0.2230	0.5589
Heart	2.0906	0	0.0349	0.1872
SpinalCord	0.1616	0	0.0174	0.0426
DoseFalloff	2.2566	0	1.0162	0.7880
duodenum	0	0	0	0
CTV	2.1974	1.8464	2.0062	0.0304
PTV	2.2566	1.4470	1.9931	0.0519
cord+5mm	0.1788	0	0.0182	0.0430

Figure 3: *Dose volume histogram for a carbon treatment.*



	max	min	mean	std
GTV	1.5128	1.4852	1.4999	0.0040
Kidney_R	0	0	0	0
Kidney_L	0	0	0	0
Stomach	0.2159	0	0.0233	0.0471
SmallBowel	0	0	0	0
LargeBowel	0.0091	0	1.3170e-04	7.1326e-04
Celiac	0	0	0	0
Liver	1.5233	0	0.2464	0.4419
Heart	1.5053	0.0089	0.2201	0.2137
SpinalCord	0.1916	0	0.0371	0.0671
duodenum	0	0	0	0
CTV	1.5213	1.4847	1.5001	0.0046
Skin	1.5247	0	0.0501	0.1735
PTV	1.5247	1.3885	1.4967	0.0154

Figure 2: *Dose volume histogram for 5-angles photon treatment.*

KICK-OFF MEETING

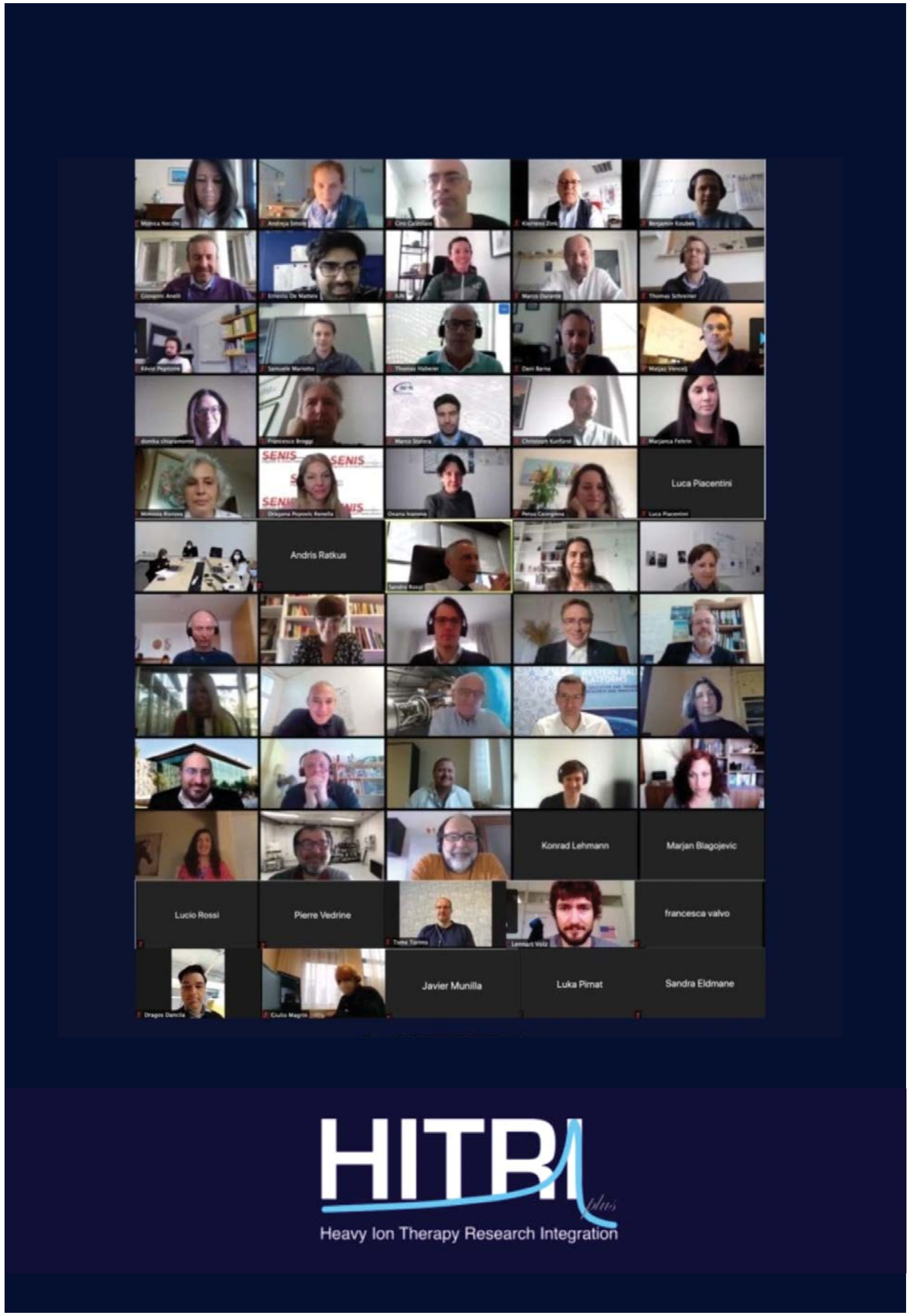
HITRIplus

The HITRIplus project formally started on 1st April 2021 and its kick off meeting was held on 13th April, from 9:30 a.m. to 4:00 p.m..

This meeting, attended by more than 80 people, was the opportunity to introduce the team of the project and to highlight the project's background, goals and requirements, to get the project team aligned and on the same page. With this purpose the meeting started with the welcome and opening of the Coordinator and the introduction of the EU Project Officer. Afterwards, each pillar coordinator introduced its own pillar, underlining aims, milestones and critical points. The details of the activities were then deepened by the individual WP leaders who, in addition to having presented their objectives, also introduced their team and the individual responsibilities. Finally, the coordination team has summarized the Administrative and Financial issues related to HITRI*plus*.

Unfortunately, due to the pandemic restrictions, it was not possible to organize the meeting in person, but nevertheless this was an invaluable opportunity to get all the people to communicate key project information and to discuss everything that will guide the project to success.

Author:
Angelica Facoetti, CNAO



GENERAL ASSEMBLY MEETING

HITRIplus

The General Assembly (GA) is the highest decision-making body of the Project. The GA consists of one senior level representative for each beneficiary. Coordinator (Sandro Rossi) and Deputy Coordinator (Maurizio Vretenar) are ex-officio members, without voting rights. Each Party has one vote, and decisions are taken by a majority vote. The GA is regularly updated by the Project Coordinator about overall Project progress and other matters that may have an impact on the goals and/or deliverables of the Project. The GA is managed by a Chairperson, appointed within its members. For the first year of the project, the Chairperson was appointed by the SEEIIST Association, for each of the following years a new Chairperson will be elected by the GA members. The GA will meet least twice a year (one in person, if possible, and one by videoconferencing). The GA is regularly informed by the Coordinator about overall project progress and other matters that may have a structural impact on the goals and/or deliverables of the project.

A pre-GA meeting was held on March 18, 2021 during which the composition of the GA was formalized and Sanja Damjanovic was appointed as the chairperson of the GA representing the SEEIIST Association. The members of the External Scientific Advisory Board (ESAB) and the Advisory Board for Ethical/Legal/Industrial Issues (ABELII), upon proposal of the Project Coordinator, have been appointed as well. The first GA meeting has been held online on June 21, 2021 and the following one is foreseen for the beginning of December 2021 with the appointment of the new GA chairperson that will chair for the second year of the project.

SEMINARS

HITRIplus

One of the objectives of the Networking and dissemination, communication and outreach Work Package is to promote awareness and understanding of heavy ion therapy needs of particle therapy in the community at large, which includes industrial beneficiaries, academics in other related fields and projects. Organising outreach events such as the HITRI*plus* monthly seminars will increase widely the social engagement of the project and promote the research activities, both of TA and JRA, among the HITRI*plus* WPs and to external communities.

Since the kick-off of HITRI*plus*, four seminars have taken place virtually with nearly 100-150 participants for each of the sessions. The interest in these outreach events has increased progressively and researchers from all over Europe and abroad have now started to register regularly.

Opening Seminar of HITRI*plus* – CNAO: Sandro Rossi, General Director of CNAO and Ester Orlandi, chief of the Clinical Department, CNAO
Topics:
- Importance of Transnational Access, status and perspectives of CNAO
- Clinical aspects - the use of carbon ions for the treatment of complex tumours: CNAO experience

2nd Seminar of HITRI*plus* - INSPIRE project: Karen Kirkby leads research in PBT and FLASH between the University of Manchester and the Christie

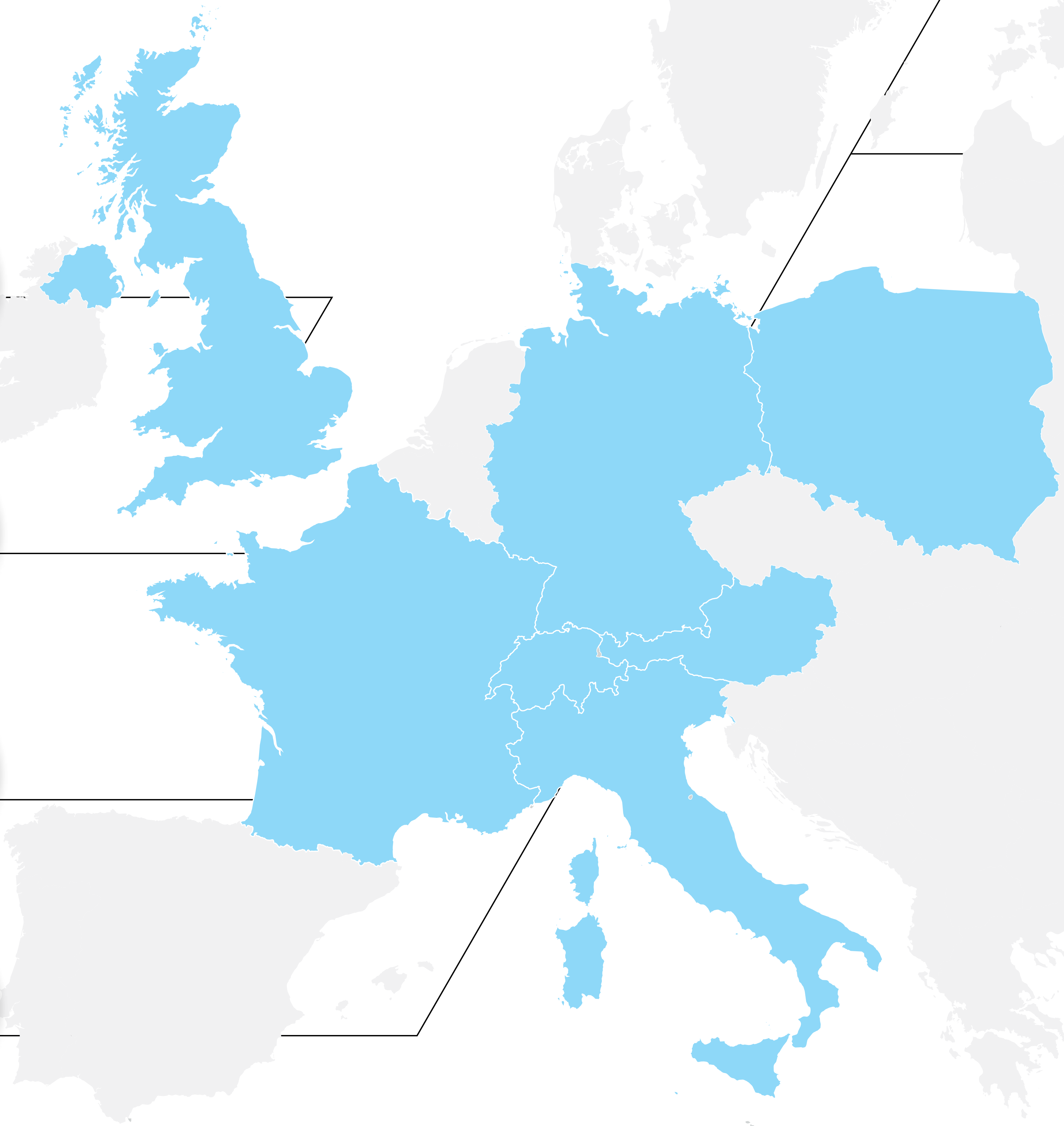
3rd Seminar of HITRI*plus* - Ion Beam Therapy at HIT: Options for Multi-Ion Treatment and Research, Heidelberg University Hospital.
Thomas Haberer, Scientific & Technical Director at the Heidelberg Ion Beam Therapy Center

4th Seminar of HITRI*plus* - CIRT at MedAustron: the first 200 patients - Piero Fossati, Scientific Director, Carbon Ions Program Director

Future Events

NAME OF THE EVENT	DATE OF EVENT	PLACE OF EVENT
1-3 December 2021	FLASH and particle therapy - FRPT 2021	Vienna, Austria
7 December 2021	HITRI*plus* General Assembly and Project Meeting	Online
06 - 10 May 2022	ESTRO 41 Annual Meeting	Copenhagen, Denmark
27 June - 1 July 2022	PTCOG 60 Annual Meeting	Miami, FL, USA
22 -26 October 2022	ASTRO's 64th Annual Meeting	San Antonio, Texas
5 – 12 November 2022	2022 IEEE Nuclear Science Symposium and Medical Imaging Conference	Milano, Italy

ENLIGHT advisory COMMITTEE



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THE EUROPEAN NETWORK FOR LIGHT ION HADRON THERAPY

A multidisciplinary platform aimed at a coordinated effort towards ion beam research in Europe.

The European Network for Light Ion Hadron Therapy (ENLIGHT), which had its inaugural meeting at the European Organization for Nuclear Research (CERN) in February 2002, today has more than 600 participants from nearly 25 European countries. Harnessing the full potential of particle therapy requires the expertise and ability of physicists, physicians, radiobiologists, engineers, and information technology experts, as well as collaboration between academic, research, and industrial partners.

The ENLIGHT network has been instrumental in bringing together different European centres to promote hadron therapy and to help establish international discussions comparing the respective advantages of intensity modulated radiation proton and carbon therapies. A major success of ENLIGHT has been the creation of a multidisciplinary platform bringing together communities that were traditionally separated, so that clinicians, physicists, biologists, and engineers work side-by-side. Special attention is also given to the training of young researchers and professionals of oncologic radiotherapy.

For more information and contact details please visit the **ENLIGHT website at cern.ch/enlight**
Join the ENLIGHT network.
Register to become a member here.
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Together, we can do even greater things!