

## Particle therapy masterclass

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With the aim to highlight the impact of fundamental research on the broader society, the new Particle Therapy MasterClass (PTMC) package was developed and recently integrated into the International MasterClass 2021 online programme, attracting some 37 institutes from 20 countries and more than 1500 students. The PTMC is focusing on the topic of cancer treatment, a particular sensitive topic. The main idea is to show that (a) fundamental properties of particle interactions with matter, which are used to detect them in physics experiments, are also the basis for treating cancer tumours; and (b) the same accelerator technologies are used in both research laboratories and therapy centres. For the hands-on session, the open source professional Treatment Planning software matRad is used, developed for research and training by DKFZ, the German cancer research institute, Heidelberg. Ultimately students are shown “what physics has to do with medicine” and what are the various possibilities that physics and STEM studies may open up for job opportunities in fields that there is lack of expert personnel.

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## 1. Introduction

The new Particle Therapy MasterClass, PTMC, developed in 2019 and presented in this paper, aims at highlighting applications of fundamental research for the benefit of society. While the mission and mandate of research institutes, such as CERN, GSI and others, is fundamental research, the developed technologies and acquired knowledge find applications in many different domains. The aim of the PTMC is to enhance awareness of such contributions focusing on the particularly sensitive societal topic of cancer therapy, while also enhancing awareness on advanced possibilities of cancer tumour treatment using particles such as protons and heavier ions.

The concept of the PTMC combines different pedagogical elements (Section 2) giving the opportunity to participants to become scientists for a day. Elaborating on the theme “*from particle physics to particle therapy*” it was initially developed targeting high-school students within the International MasterClasses, IMC [1], the flagship project of the International Particle Physics Outreach Group IPPOG [2]. Additionally, it can easily be tailored to different needs and education levels. The developed concept and available material via the PTMC web page [3] were already used to complement training of university students, as basis for a full week specialised school and also for events such as the CERN Open Days and the Science Days of Montenegro.

Within the IMC project, masterclasses are usually organised as full day events, with a typical agenda, followed by the participating institutes. During 6 weeks before the Easter vacations, 3-5 institutes participate every day, inviting high-school students to immerse in the world of particle physics giving them a taste on “what scientists do”. Adapting to an online mode due to the covid pandemic, students were invited by the institutes to join a zoom session, instead of being invited at the institutes. The PTMC specifically shows to students “what physics has to do with medicine”, and triggers questions on how particles can be used for cancer therapy.

The PTMC, coordinated by GSI, was included for the first time in the IMC2020 schedule after a first local test at GSI and a pilot, in early 2019, with the participation of GSI, CERN and DKFZ Heidelberg. This core team represents the world leading research institutes in their domains that also provided tangible applications for health: at GSI the first 450 patients in Europe were treated with carbon ions, at CERN the Proton-Ion Medical Machine Study (PIMMS) design team was hosted and DKFZ is the German Cancer research institute next to the HIT Heidelberg ion therapy facility. The first PTMC session in IMC2020 was performed in Mexico, attracting about 200 students, while the rest of the sessions had to be cancelled. In the IMC2021 season, the PTMC sessions were performed online, and with no limitation on registrations, they attracted more than 1500 students around the world. During the 6 PTMC sessions a total of 37 institutes from 20 countries participated, with about 6 institutes performing the PTMC in the same day. In several cases, students from the whole country could join the online sessions.

## 2. Particle Therapy MasterClass pedagogical elements

The PTMC agenda integrated and expanded the basic elements of the IMC that include, in the morning, introductory lectures and a visit to an experiment or lab, while in the afternoon, a hands-on session followed by a common video-conference among all participating institutes. Each PTMC online session started with a video, showing a particle therapy procedure in a virtual therapy centre. This triggered curiosity and interest. But it also gave an overall visual impression, so that students could relate the specific presentations that followed to the broader image and

procedures. The lectures covered a wide range of topics and supported by videos kept the interest of students. They include introductory presentations, provided by DKFZ experts, but also lectures related to radiation in general spanning from its use in microwave ovens to discoveries studying cosmic radiation. Because this is a multidisciplinary topic, they are complemented by lectures on the expertise of the different institutes, including, for example, detector or software developments that are used in medicine. Imaging, diagnostics, dosimetry, are a critical part of the treatment procedures where the impact of breakthrough developments on detectors for physics experiments is clear. The importance of computing and software developments is also highlighted including machine learning techniques and their possible applications in radiotherapy. The message is always that: **technologies developed for fundamental research find applications for medicine.**

Highlighting the use of accelerators for society, students were surprised to learn that from about 30 000 accelerators that are in operation world-wide, about 6% is used for research, while 1/3 is used for medicine and the rest for different industrial applications. Adapting technologies and methods developed for fundamental particle physics research, sophisticated medical accelerators can deliver particle beams at a desired depth targeting a tumour. Students are also shown that fundamental properties of particle interactions with matter, which are used to detect them in physics experiments, are also the basis for treating cancer tumours. Figure 1A shows, as an example, the Bethe Bloch energy loss used for particle identification in the TPC detector of the ALICE experiment at the CERN LHC, while the middle plot presents the energy deposition as function of depth in water. Here, protons and carbon ions reveal their characteristics, the Bragg peak, which is the basis for Hadron Therapy. It is clearly seen that photons lose most of their energy entering the tissue and they still deposit energy in healthy tissues behind the tumour while ions deposit most of their energy at the end of their trajectory before they come to a full stop. By tuning the energy of the accelerator, one can scan the whole target, what is known as spread-out Bragg peak, shown on the right plot.

Real-time online visits were offered at the end of the morning lectures, at the ALICE heavy-ion experiment. They were complemented with online visits during the afternoon common video-conferencing at the GSI experimental room where carbon ion therapy was pioneered in Europe, and in the CNAO ion therapy centre, close to Milano (Figure 1B). Experts from these institutes provided an excellent interactive help, discussing with the students their results. These online visits further highlighted the connection between heavy-ion physics and heavy-ion therapy.

In general, the PTMC highlighted that technology and knowledge transfer “*from physics to clinics*” resulted in the four carbon-ion therapy centres in Europe. Following the PIMMS initiative, accelerator experts of the CERN NIMMS group work currently on the design of components for a next generation ion therapy machine adapting hi-tech technologies for medical accelerators. As an example, Figure 1C shows the accelerating structures and architect’s concepts (courtesy Kaprinis architects) for a heavy-ion therapy facility which is proposed to be built in South East Europe. The PTMC was performed by several SEE institutes that provided material in several local languages, supporting capacity building in the area.

The PTMC hands-on session is based on the matRad professional open-source treatment planning toolkit developed by DKFZ for research and training (Figure 1D) [4]. It is used to simulate and optimize the “prescription” of the therapeutic intensity-modulated dose distribution that the accelerating structures have to deliver to the cancer tumours using photons, protons or carbon ions. Hence, students can appreciate the differences of these radiation modalities and use them

optimally according to different cases. While matRad gives comparable results with commercial treatment planning software actually used for therapies, it is not licensed for treatment, but lightweight, flexible, accessible and provides results quite fast.

The data provided are a “water phantom” and computer tomography (CT) scans of head and liver tumour cases. matRad presents the data in 3D, provides possibilities to rotate interactively and present slices in 2D projections. It provides graphical tools to visualize the beam directions and volumes to be irradiated. Notably, a particular exercise is planned to demonstrate the importance of accurate patient alignment. Once the volumes to maximise and minimise the dose are selected one can choose the type of radiation (photons, protons or carbon ions) and different angles for irradiation.

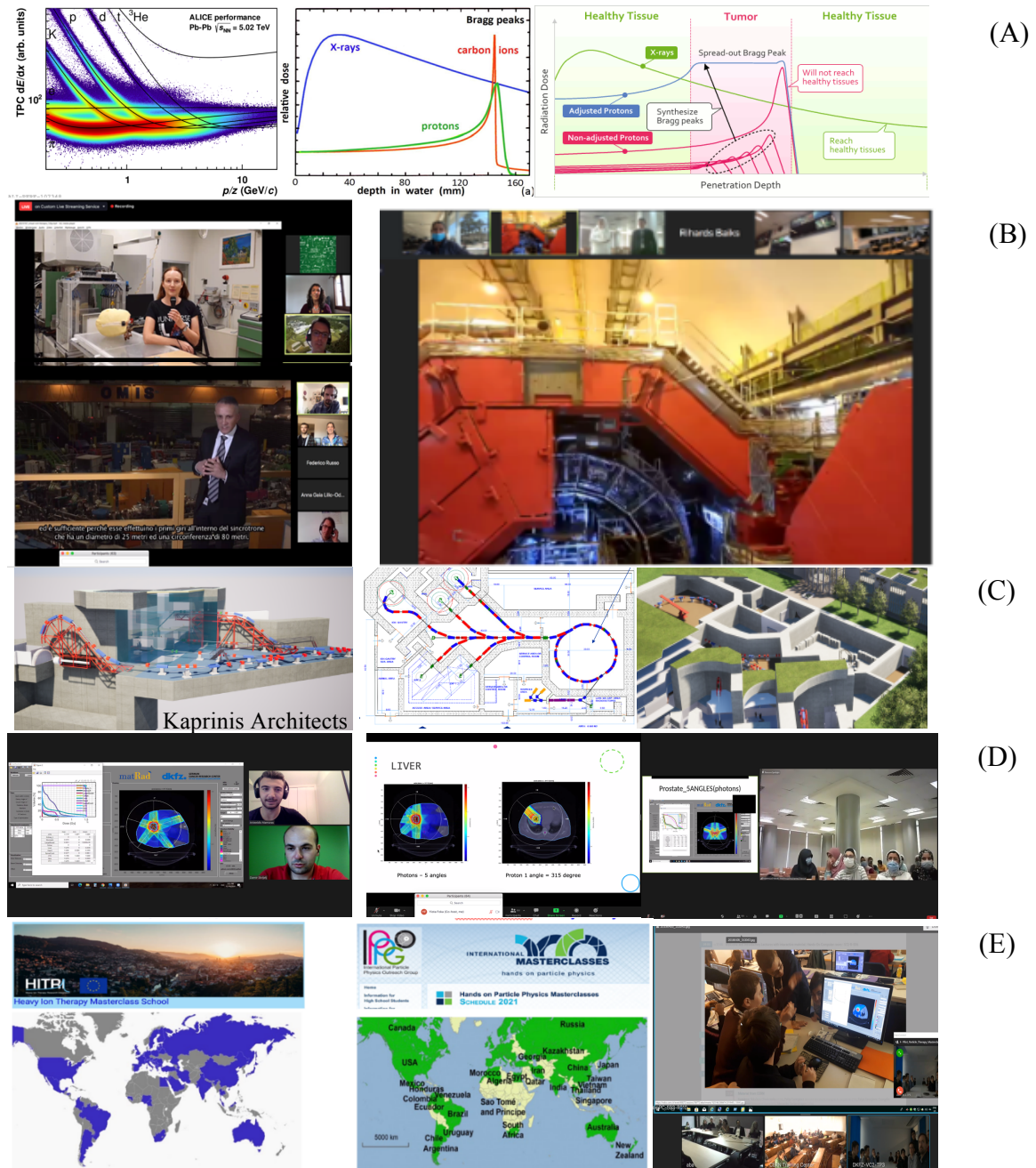
For the dose optimisation, one can use constraints and define a minimum and/or maximum dose value. The visual result on the display, based on a colour scale, is very intuitive to comprehend and easy to associate with the resulting histograms of the delivered dose to the target tumour and organs at risk to avoid. Students can select different angles for irradiation to minimize the deposited dose in each trajectory while accumulating the required dose in the target volume. They can witness the different characteristics of protons and carbon ions, that, in contrast to photons, deposit very little energy in the tissues before and practically none after the tumour (Figure 1D).

Instructions for installing matRad specific software, prepared by the DKFZ colleagues, are available via the PTMC web pages, including recordings and are sent to participants in advance although installation can be handled even during the session. In order to prepare the tutors, moderators and support organisers of the different institutes, weekly dedicated tutorials were offered during the IMC2021 season but also training sessions at request. The PTMC web pages [3] provide a large variety of material in several languages, including links to the “PTMC in a kit” google drive which contains the necessary material needed to perform the PTMC, including recordings with instructions. In addition, it links to the indico agendas of institutes that performed already the PTMC, including their presentations in their local languages.

### 3. Heavy Ion Therapy MasterClass School

Motivated by the received feedback, the format of the PTMC and its pedagogical elements were employed for the full week Heavy Ion Therapy MasterClass school [5], which was organised within the framework of the HITRIplus EU-funded project, from 17-21 May 2021, online, with the support of the PTMC core team of volunteers (Figure 1D, left). It was attended by over 1000 participants, from all over the world, that ranged from undergraduate students to Masters, PhDs, early stage researchers but also professional practitioners, and involved a total of 36 speakers. Participants greatly appreciated the multidisciplinary approach of the school and the presentations from top experts that started from basics and covered most recent developments and future plans in heavy-ion therapy. Recordings are available via the HITM school web page [5].

The worldwide reach of the HITM school demonstrates the increasing interest in heavy-ion therapy but also the power of networks; the participation to the IMC and the HITM school match almost one-to-one (Figure 1E), since the school was also announced through the IPPOG network. An IPPOG colleague from Benha University in Egypt contributed with an interesting initiative organising the participation of some 100 students as part of the University curriculum, joining the sessions from an auditorium and ensuring the presence of the dean for the opening session. Figure 1D right, shows the discussion of their PTMC results for a liver tumour case.



**Figure 1:** (A) Bethe Bloch energy loss used for particle identification, energy deposition as function of depth for photons, protons and carbon ions used for Hadron Therapy and spread-out Bragg peak (B) online visits at GSI heavy-ion research centre, CNAO ion therapy centre and the ALICE heavy-ion experiment (C) accelerating and beam delivery components of a next generation ion medical machine (D) matRAD treatment planning application (E) world-wide reach of HITM school and IMC; first PTMC pilot in 2019.

#### 4. Summary

The PTMC addressing high-school students and the HITM school addressing university students make the young generation aware of the various possibilities that physics, and STEM studies in general, open up for career opportunities in emerging fields where often there is lack of specialised personnel. They also enhance awareness about modern methods for cancer therapy and new research avenues, that are expanding world-wide; and where clearly the development of technology and expertise of research laboratories is important. Participants are impressed

performing a treatment planning like professionals and motivated to contribute to the further advancements of this multidisciplinary field, that opens new horizons. They also come to appreciate the power of networks and importance of international collaborations working on common goals but also the different challenges and approaches of different disciplines (starting from the relative characterisation of “heavy” ions by physicians and physicists) and the importance of finding common grounds. Overall, the opportunities for properly trained scientists is a take-home message.

### Acknowledgements

I am indebted to many of my colleagues at GSI and CERN and my respective bosses for their continuous support. It cannot be just a coincidence that the PTMC was developed with the support of both; of GSI, my home institute, where carbon-ion therapy was pioneered in Europe, and CERN, where the PIMMS designs for ion-therapy machines emerged, and where I was delegated as part of their close collaboration. Which also highlights the importance of close collaboration among research institutes and their coordinated contributions to this multidisciplinary field.

Special thanks go to C. Graeff from GSI for introducing me to this field and the DKFZ colleagues, at the time that I did not know yet what a “treatment planning” is; to the DKFZ and LMU colleagues for providing the matRad treatment planning tools and eagerly supporting the PTMC and HITM school with their expertise (in particular Mark Bangert, Niklas Wahl, Hans-Peter Wieser, Joao Seco); to the ENLIGHT coordinator, Manjit Dosanjh, for guiding me in a new territory, bringing me in contact with relevant people, and providing material; to the students of the Uni of Sarajevo UNSA, and Uni of Thessaloniki AUTH, that contributed setting up the PTMC web pages, dedicated trainings, material in local languages etc; to the students of UNAM, Mexico, for setting up the “PTMC in a kit” first in Spanish and then in English; to ALICE, GSI, CNAO colleagues for being eager to offer real-time online visits and moderate video-conferences.

As a heavy-ion physicist, I was motivated to develop the PTMC, after the ALICE MasterClasses [1, 6], wishing to pass the message that heavy-ions and the tools we develop for our research, can also be used for cancer therapy. It is indeed a great satisfaction to see the impact of such messages and to experience the feedback of students at all levels; from the dedication of the core team volunteers, that help to set up and organise the PTMC sessions, to the interest of high-school students. I would like to acknowledge the help and support of all colleagues that contributed to this endeavour and the taking off of the PTMC; also, the dedication of the core team of volunteers from AUTH and UNSA for keeping up with the work and challenges that came with the growing interest for the PTMC. Last but not least the ARIES EU-funded project and the private "Three Physicists Foundation" for supporting the PTMC development and dissemination.

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