South East European International Institute for Sustainable Technologies (SEEIIST)

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Abstract

In November 2016 the South East European International Institute for Sustainable Technologies (SEEIIST) was proposed by Herwig Schopper at the World Academy of Art and Sciences. Soon after it was brought to the political level by Sanja Damjanovic, Minister of Science of Montenegro. The core of SEEIIST is a 'Facility for Tumour Therapy and Biomedical Research with Protons and Heavier Ions". The initiative was presented in January 2018 at the 'Forum on New International Research Facilities for South East Europe' at the ICTP in Trieste. The political support to SEEIIST was first based on a Declaration of Intent signed by eight SEE Ministers responsible for science in October 2017 at CERN, Geneva. More recently, in July 2019, six Prime Ministers signed a Memorandum of Cooperation at the occasion of the Summit of the Berlin Process in Poznan.

SEEIIST will be a platform for internationally competitive state-of-the-art research in the spirit of 'Science for Peace', following the models of CERN and SESAME. It will offer the world-class research needed to reduce or even to revert the brain drain that is causing a shortage of talent and major economic losses in South-East Europe. The aim of SEEIIST is to create a local community of experts, provide them with powerful instruments for first-class research and thus retain and increase the number of specialists and doctors within the region. No such a centre currently exists in South-East Europe in spite of a growing number of tumours being diagnosed. The SEEIIST beam time will be shared 50:50 between treating patients and performing research with a wide spectrum of different ions beyond the presently used protons and carbon ions, making the facility unique in the world.

Thanks to the first financial support from the European Commission (DG RTD), the SEEIIST Project has recently moved from a Conceptual to a Design Phase which, thanks to their generous support, is hosted in the renowned research centres, CERN in Geneva and GSI in Darmstadt. The next phase of the realization of the project includes a final technical design for the facility, a structure and a business plan for the organization and the definition of conditions for the selection of the site. If all proceeds as planned the construction could start in 2023, with first patients to be treated in 2028.

Birth of SEEIIST

In 2016, at a Workshop of the World Academy of Art and Science held in Dubrovnik, Professor Herwig Schopper proposed the creation in South East Europe of an International Institute devoted to sustainable technologies. The SEE region is comprised of countries that are EC member states (Slovenia, Croatia, Bulgaria and Greece) but also from countries that are aspiring for the membership in the near future.

The project has two main objectives. The first objective is to promote collaboration between science, technology and industry. In addition, as well as providing a platform to educate talented young people and engineers on the basis of knowledge and technology transfer from European centres such as CERN and others. The second important objective is to bring together people from different countries in the region, not only scientist but also engineers and administration.

Establishment of a large, new institute, based on new technologies that would allow so-called "first class research" is the only way to achieve the primary mission of "Science for Peace" as has been illustrated by the successful example of CERN's model which was recently followed by the SESAME synchrotron light infrastructure for the countries of the Middle East .

The Government of Montenegro was the first to officially support this initiative for establishment of SEEIIST in the SEE (Balkans) region with the mission of "Science for Peace." Minister of Science Sanja Darmanović believes that such a project, which is unique in the region, would significantly impact on economic development, improvement of living standards, reducing unemployment and would represent a certain type of 'industrialisation' of the region on the basis of sustainable technologies.

Dr Damjanovic, , brought the Initiative to the political level by contacting the relevant Ministers of the South East Europe (SEE) countries and convincing them to participate in launching this project. Given the positive reactions, in Spring 2017 two Editorial Committee aiming at the preparation of the conceptual design report of a **'Facility for Tumour Hadron Therapy and Biomedical Research'** lead by Ugo Amaldi and the **"4th Generation Synchrotron Light Source for Science and Technology"** lead by Dr Dieter Einfeld were established.

During the drafting of the conceptual designs of the two facilities, a meeting of the Ministers of Science or their representative took place at CERN on 25 October, 2017and a Declaration of Intent for future collaboration was signed Albania, Bosnia and Herzegovina, Bulgaria, Kosovo*, the FYR Macedonia, Montenegro, Serbia, and Slovenia where Croatia agreed 'ad referendum', while Greece participated as an observer. The declaration stated that the Parties have a common vision and that the Institute shall operate with the mission of "Science for Peace".

Following this, an Intergovernmental Steering Committee was created, and Dr Damjanovic was elected as the chairperson and in this framework on January 25−26 a Forum on "New International Research Facilities for South East Europe" was organized at ICTP (Trieste).

On 5th of July, 2019 in Poznan, Poland, the governments of six [1] states in South-Eastern Europe signed a Memorandum of Cooperation - Framework (MoC) to jointly build a new Research Infrastructure (RI) facility in the SEE region, focussed on the most advanced radio-oncological technology for cancer treatment. This MoC was a direct response to the Sofia Declaration in which h the Western Balkan states recommitted to the European perspective as their firm strategic choice and to reinforce mutual support. In return, the EU confirmed that in order to bring "…*our citizens and economies closer together (…) it is determined to strengthen and intensify its engagement at all levels to support the region's political, economic and social transformation, including through increased assistance.*" The statement underlined the ongoing efforts by the European Commission (EC) to bring the SEE States closer to the EU in terms of its shared values, social cohesion and economic prosperity. Both outgoing EC President Juncker in his 2018 State of the Union as well as the incoming EC President Von der Leyen have stressed the need for intensive cooperation, and Von der Leyen has stated that this will be one of her priorities during the next five years. The Sofia-sentiment was also reinforced by the European Council in June 2019 when it presented its conclusions on the Enlargement of the EU and the Association Process related to – inter alia – the Western Balkans.

The creation of a new RI is meant to show tangible, visible and sustained international cooperation in the SEE region after a period of regional conflict. The RI will gather scientists, engineers, medical doctors, young people and technicians within this joint infrastructure with the mission to deliver "Science for Peace".

The **South East European International Institute for Sustainable Technologies (SEEIIST)** will focus on Hadron Cancer Therapy and Biomedical Research with Protons and Heavy Ions. SEEIIST will thus enable scientists from different countries to work together in the fight against cancer. This particular initiative has been chosen in part because it binds people together against a 'common enemy' and is an example of what people in the SEE can do when they work together. In that sense, SEEIIST's mission is aligned with the basic concept behind other big RIs like CERN: Science for Peace, Science for Diplomacy and Science for Society. A second reason for putting a hadron facility in the SEE area is the fact that in contrast to western Europe no technical provision exists anywhere in SEE to treat patients with certain malignant types of tumours. The choice for a hadron facility over other types of Radio Therapy (RT) like a proton-centre or other non-radiological treatment modalities (like for example: immunotherapy) is the fact that a hadron therapy centre is urgently needed to achieve breakthrough research advances in pre-clinical physics, pre-clinical radiobiology and medical physics related to cancer treatment as well as a means to retain research talent in the region.

SEEIIST state-of-the-art Facility has now moved from a conceptual to a design phase, thanks to the first financial support from the European Commission. The Status of the Project was presented to the public at a SEEIIST Kick-off meeting 'Start of the SEEIIST Design Phase' on 18 September 2019 in Budva, Montenegro. The next steps are underway for preparing a definite technical design for the facility, to propose a structure and business plan for the organization and to define the conditions for the selection of the site.

[2] Including but not limited to dedicated workshops like the "Forum on New International Research Facilities for South East Europe 2018" (Trieste Italy; http://indico.ictp.it/event/8506/) and the workshop on "Ideas and Technologies for Next Generation Facility for Medical Research and Therapy with Ions 2018" (Archamps France; https://indico.cern.ch/event/682210/).

Scientific case for SEEIIST facility in SEE

Cancer in the SEE Region & the need for a hadron therapy & research facility in SEE.

Every sixth death in the world is caused by cancer, making it the second leading cause of death second only to cardiovascular diseases [R1]. Demographic drivers of increasing population size, life expectancy and - particularly in higher-income countries - aging populations, as well as progress against many other causes of deaths, mean that the total number of cancer deaths continues to increase. This is a very personal issue to many: nearly everyone knows or has lost someone dear to them from cancer. In Europe, over 3.7 million new cases are diagnosed per year. Cancer not only has a negative impact on an individual's health but also comes at a very high cost to the economy. Cancer costs the EU circa €126 billion with health care accounting for €51 billion, productivity losses due to early death estimated at €43 billion, lost working days estimated at €9 billion and informal care estimated at €23 billion [ref].

It is for this reason that the European Commission invested €1.6 billion in FP7 and, so far, €1.2 billion in H2020 on cancer research [R2]. H2020 policy prioritises health and wellbeing to be a societal challenge under which cancer research is categorised [R3]. In Horizon Europe, the commission gives the fight against cancer even more priority by considering it to be one of the greatest world challenges and specifically placing the mission against cancer as a top priority in its mission-oriented policy [R4].

Figure 3: Cancer statistics – mortality/incidence ration (all cancers, excl. non-melanoma skin cancers). Source: Vesna Gershan, Institute of Physics, Skopje.

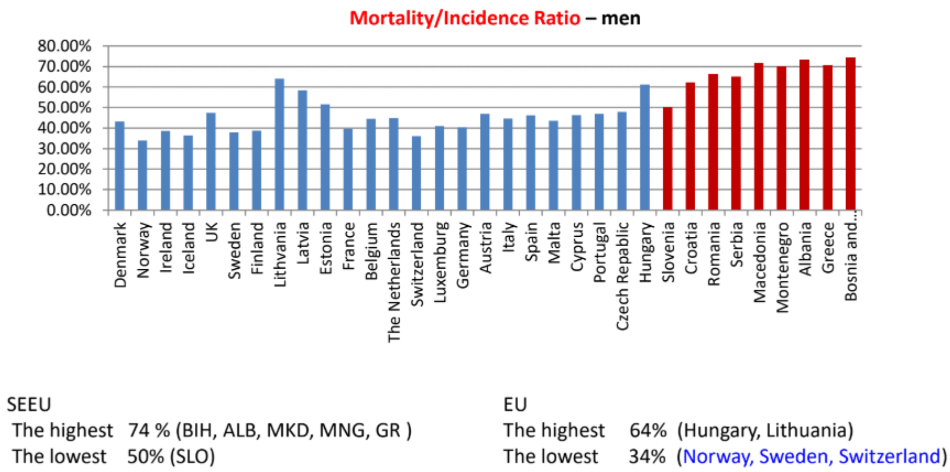

Figure 3 shows the most recent age standardised death rates from all cancer types measured as the number of deaths per 100,000 across Europe. The image highlights a higher death rate concentration in the SEE region (shown in darker orange) compared to most of the EU. One factor in the higher mortality rate in the SEE countries is the lack of imaging and treatment equipment.

Radiotherapy (RT), in which ionizing radiation is used to control or kill malignant cells, is a fundamental component of effective cancer treatment benefiting around half of the cancer patients (treatment, local control or palliative). The main goal of radiotherapy is to maximise the damage to the tumour while causing minimum damage to the surrounding healthy tissue and critical organs, thereby reducing the toxicity as well as acute and late side effects which positively affects the patient's quality of life. As will be described in more detail below, conventional X-ray RT has made significant progress, but the maximum dose deposition profile of X-rays does not make it suitable for around 5% of cancer patients who have deeper lying tumours, or tumours on moving organs due to the fact that X-rays deposition a substantial part of their energy at distances beyond the cancer target.

State- of-the-art Hadron therapy facilities (Maurizio, Elena and Mariusz) SEEIIST going beyond the state of the art

1.4 Overall concept underpinning the project and progress beyond-the-state-of-the-art

The overall conceptual design has three main innovation pillars which centre on significantly improved access to joint research activities, targeted medical treatment, smaller physical size and reduced cost of the infrastructure. The pillars are:

1. novel subsystems technology: accelerator, gantry and magnet;
2. innovative precision treatment: beam delivery, patient positioning, in-room imaging, control and safety;
3. industrialisation of the novel technology and distributed RI.

State of the art research in the hardon therapy (Manjit and Durante)

Beyond the stare-of the art research at the SEEIIST infrastructure

Project aim and specific objectives

Over the past 2 years, the SEEIIST SC developed the objectives for the SEEIIST RI through a range of activities, among which:

- in-depth studies of academic papers and articles,
- reviews of the results from clinical trials,
- discussions with oncologists and medical practitioners,
- discussion with specialists working in operational particle therapy facilities,
- discussions with scientists and engineers specialised in accelerator technology, biophysics, medical physics etc;
- discussions in thematic workshops[2] and network meetings including the European Network for Light Ion Hadron Therapy (ENLIGHT) and the Particle Therapy Co-Operative Group (PTCOG), attended by hundreds of members of the global, European and SEE user community,
- The "Advancing the Design of the South-East European International Institute for Sustainable Technologies (SEEIIST)" Service Facility in Support of the Strategic Development of International Cooperation in Research and Innovation N°30-CE-0838742/00-87 [PP-04341-2016]. The related €1 Million contract, signed by the EC on 4 July 2019, is covering a preliminary comparison of accelerator options, the definition of some initial biophysics cases for the facility, and a first analysis of business, location, and sustainability issues.

Throughout this scoping activities, the SEEIIST SC has continuously emphasised its user-oriented approach as the critical starting point in designing an effective RI with long-term exploitation goals. Needs of the user communities (specifically: clinicians and researchers) take clear precedence over what technology can offer. Europe's leading accelerator physicists, scientists and engineers, advised by senior oncologists from the operational heavy ion therapy facilities in Germany, Italy, Austria and France have subsequently taken the SEEIIST objectives and turned them into the following main aim for the HITRI project:

HITRI's overall aim is to design a **world-class**, **innovative, compact, flexible, expandable, next generation, pan-European RI** which can be **built in the SEE region** and which produces the world's **most intense heavy ion therapy beam** with **simpler operation** and **lower cost**. In future,

[2] Including but not limited to dedicated workshops like the "Forum on New International Research Facilities for South East Europe 2018" (Trieste Italy; http://indico.ictp.it/event/8506/) and the workshop on "Ideas and Technologies for Next Generation Facility for Medical Research and Therapy with Ions 2018" (Archamps France; https://indico.cern.ch/event/682210/).

this should allow the clinical and scientific user community to fully exploit the advantages of heavy ion therapy, enable applied and clinical R&D and provide an innovation and training platform.

From the above, the following 8 Specific Objectives (SO) were derived for this project whose overall ambition is to allow Europe to remain at the forefront of the advancement of research in this field and to be able to support European industry to strengthen its base of knowledge and its technical knowhow. Each of these SOs will significantly move beyond the current state-of-the-art technology used at the operational facilities in the EU. SO1 and SO4 will also lead to a technical advancement beyond current state-of-the-art in Japan (which is globally seen as the most advanced in this field from a technological point of view). With regard to SO3 and SO7, the envisaged technological improvement will allow Europe to compete with Japan and will further increase its lead over developments in the US.

SO1 – Outstanding Beam Intensity and Dose Delivery

Activity: Design a synchrotron-based heavy ion therapy RI capable of delivering an intense beam of carbon ions at 430 MeV/u – and other heavy ions having the capability of treating deep seated tumours – by addressing related technical challenges: higher injection energy (with the related design of an innovative 10 MeV/u linac), multiturn injection, extraction of particles at different energies in a single acceleration cycle, improved optics of the beamlines, and fast dose delivery with 2D and 3D painting. ***KPIs*:** Achieving carbon intensities up to 2×10^{10} accelerated ions per pulse (pp). This corresponds to 20 times more than the current European centres and is the present record intensity realised in Japan in the 4-times larger HIMAC synchrotron (i.e. with 4-times smaller particle density). Achieving dose rates of >50Gy/s for research purposes and small tumours. Achieve a time for energy change on the flat-top below 250 ms. ***Expected Impacts:*** The increased intensity will enable superior treatment of moving targets such as lung and liver cancers. The increased dose rate will allow faster treatment times and the study, with different ion species, of new treatment modalities like FLASH therapy[3]. The improved multiple energy extraction will result in more effective patient treatment and a reduction of the number of particles dumped after acceleration with a positive impact on radiation protection.

SO2 - Flexibility

Activity: Design a synchrotron-based heavy ion therapy RI characterized by a flexible beam operation with a large variety of ions, to support a wide experimental programme covering any of the new treatment modalities under study. ***KPIs:*** Provide different ion species from protons to argon as required by research projects, allowing for a change of ion species in less than 1s. Provide carbon ion intensities from 10^3 to 2×10^{10} ions per pulse at the exit of the synchrotron, and equivalent intensities for other ions. Provide fast extraction in a single turn i.e. about 0.1 µs for research, and slow beam extraction from about 100 ms to about 30 s for therapy. ***Expected impacts*:** The flexibility of the machine will enable therapy-related research under controlled conditions with fast translation to clinical reality. A user-friendly machine maintained to the highest clinical standards for stable working conditions will streamline basic joint research activities in physics and biology. The study of ion therapy treatments with different particle types will allow exploring combined treatments with multiple ions, which will possibly open new scenarios in personalised cancer therapy. The combination of using lighter ions (e.g. protons or helium) for imaging and heavier ions for treatment may provide crucial beam range information on the patient in the treatment position.

[3] FLASH Therapy: delivery of high dose protons in less than 0.5 s to allow therapy on moving organs (like lungs) & spare normal tissue from toxic radiation.

SO3 - Compactness

Activity: Develop the design of the most compact heavy ion therapy synchrotron and gantry in the world. ***KPIs:*** The innovative design will reduce the footprint of the heavy ion therapy accelerator by about 50% with respect to existing facilities, i.e. from about 2000 m^2 to about 1000 m^2. The innovative gantry system for beam delivery will aim at reducing its size by 30% with respect to the most advanced existing design, down to about 10 m in length. ***Expected impacts:*** Reducing the size and footprint will reduce the investment required for land and building and make it easier to install the facility in areas with space restrictions e.g. in proximity of hospitals.

SO4 - Lower Construction and Operation Cost

Activity: Design a synchrotron-based heavy ion therapy RI at a lower construction cost than the state-of-the-art thanks to improved accelerator designs, the introduction of superconductivity, and a new light-weight gantry design. Design it for lower operation cost than state-of-the-art thanks to reduced maintenance costs because of a lower number of components with higher reliability, and thanks to the use of superconductivity (SC) to reduce electrical power consumption. ***KPIs:*** Reducing the cost of current heavy ion therapy accelerators by >30% with respect to existing facilities, from an estimated €43 Million[4] to less than €30 Million. Cost reduction of a carbon-ion gantry to less than €25 Million. Additionally, the reduced gantry weight to less than 150 tonnes, will drastically reduce the infrastructure costs. Reduction of the power requirements for the accelerator and the beam lines by a factor of nearly 3, and reduction in the electrical consumption by 30% thanks to the use of superconducting magnet technology since the magnet power consumption of the accelerator and the beam lines will be reduced from several MW to about 1 MW. Reduction of maintenance costs with respect to present therapy facilities from about 5% of capital cost per year to less than 4% of capital cost per year. ***Expected impacts:*** Reducing cost of the heavy ion therapy machines will make them more affordable and will hence increase market penetration and improve European citizens' access to heavy ion therapy. Reducing the cost of the gantry will make it affordable to increase the number of treatment rooms equipped with such systems making high-quality treatment accessible to a larger number of patients. Wider availability of gantry systems will allow faster treatments with improved quality because of better optimization of dose distribution, increased reproducibility of patient's set-up, introduction of dynamic techniques such as arc therapy, etc.

SO5 - Sustainability

Activity: Incorporate sustainability in all aspects of the machine and facility design, in line with the ESFRI long-term sustainability working group recommendations: financial sustainability, environmental sustainability, the sustainability of excellence, the sustainability of human resources and their skills, the convergence of the RI operation with other RIs. ***KPIs***: A detailed sustainability plan will be drawn up to ensure that sustainability is incorporated with every aspect of HITRI and eventually in the SEEIIST RI. In particular: (a) the facility will be designed not only for research but also for patient treatment with the goal of ensuring the full financial sustainability of the facility. The production of isotopes with the injector linac, in particular for PET imaging which can be delivered to hospitals in the region, will also contribute to this financial sustainability. (b) environmental sustainability is guaranteed by the complete offsetting of the facility power consumption by a solar panel photovoltaic farm or a wind farm (the Environmental Sustainability Hub of SEEIIST) hence keeping the facility 100% carbon neutral. ***Expected impacts***: Financial and environmental sustainability will ensure that the RI is exploited to its maximum potential through its entire lifecycle.

[4] Cost excluding beamlines from U. Amaldi (ed.), "A Facility for Tumour Therapy and Biomedical Research in South-Eastern Europe", CERN-2019-002.

SO6 - Expandability ***Activity:*** The RI layout and machine parameters will be designed with sufficient flexibility and space reserved to enable possible expansions and upgrades including: (a) additional beamlines for experiment and treatment; (b) additional gantries; (c) a facility for isotope production using the beam from the injector linac on the pulses not needed for synchrotron injection; (d) the inclusion of organ motion therapy and on-line monitoring of the dose delivered to the patient. ***KPIs:*** The machine will be designed such that it can expand from the initial 3 irradiation rooms (1 for research, 2 for treatment – one with a horizontal beam and one with a gantry) to 6 irradiation rooms (2 for research, 4 for treatment, 2 of which with a gantry). At the exit of the injector linac, space will be reserved for the isotope facility. Space will be reserved in each room for additional diagnostics (in-room CT in the gantry room, vertical CT and online PET in the other room). ***Expected impacts:*** The machine's expandability will enable a smooth growth of the facility according to the medical and experimental requirements. This will enable the RI to remain for many years at the forefront of the advancement of research.
SO7 - Innovation and Industrialisation ***Activity:*** Develop a novel synchrotron-based heavy ion therapy accelerator equipped with a cutting-edge gantry and make the related technologies available to industry in the EU and SEE. In particular, the innovative superconducting magnet technologies required for the synchrotron and for the gantry will be transferred to the industri(es) in charge of production. They have many possible applications in other fields and the potential to become the key components for a new generation of compact low-energy accelerators to be used for basic and applied research and related applications. ***KPIs:*** To have a group of companies (at least 2) in a position to manufacture the key components (superconducting magnets, accelerating system, instrumentation, etc.) for a new heavy ion therapy accelerator and its gantry. ***Expected impacts:*** Make new advanced technologies available to European industry. Increase market penetration of heavy ion therapy, making it more accessible to European citizens. The HITRI technologies will give to the involved European companies a competitive advantage, in particular to challenge the Japanese monopoly in the rapidly growing cancer treatment markets in Asia.
SO8 - Build Scientific and Technological Capacity in South East Europe ***Activity:*** Close collaboration and knowledge transfer to/with the universities and research centres based in SEE, with the goal of building a training-needs portfolio and helping them acquire and retain the competences required to build and operate a research and therapy accelerator centre. Create a network of medical centres in the SEE countries that will participate in the operation of the facility, in the joint research activities and in providing patients. Identify industries in the SEE region that can contribute to the construction of the facility. ***KPIs:*** Participation of SEE institutes to the work packages (WPs) and deliverables of HITRI, exchange of staff between Western European and SEE centres, training of SEE experts. Establishment of a local network of hospitals interested in using heavy ion therapy. Organisation of industry events, to present the HITRI technologies and opportunities to local industry. ***Expected impacts:*** Capacity building in the region to design, construct and operate the facility successfully and contributing to the reversal of the brain drain from the area. Improving connections and cooperation between countries that were at war in the recent past, thus contributing to the restoration of a peaceful collaborative environment through science, technology, research, and innovation.

New subtitle here – Building the Medical treatment case

Alternative RTs to X-ray photons include protons and heavier charged ion particles (e.g. hadron). At this time, RT technology used for treatment of cancer patients in SEE is mainly X-ray based (incl. XXXX and IMRT). **In the entire SEE region covering about 40 million inhabitants, there is no medical treatment facility using either proton or hadron therapy (HT)**. If patients from SEE countries need this type of specialised treatment, their only option – at high cost to the national health system – is to travel to one of the 70 proton centres or 3 hadron centres in operation in western Europe (see figure 4).

Setting aside the high cost and the stress for patients from SEE needing to travel hundreds or thousands of km to undergo proton or hadron RT, one might argue that the building of a new HT facility is only warranted if first the awareness of clinicians about its potential is increased, so that they will consider HT a serious treatment option, and secondly a sufficiently large fraction of potential SEE patients can be treated. It has also been argued that part of the reason why the number of patients that could benefit from HT is lower than should be expected on purely medical grounds, has to do with a reluctance of clinicians and/or health insurance providers to refer patients outside their own hospital/region because of financial reasons. These arguments disregard the fact that: (1) awareness will only rise is there is the potential to refer patients in the first place, (2) the only way to give the possibility on the long term to all SEE patients to access now unavailable cures is to start with the construction in the Region of an excellence centre that can check in practice costs and benefits, and (3) a similar situation existed in the past for proton centres, but thanks to continuing and concerted efforts by researchers and companies and the reduction in side-effects of radiation therapy, the treatment costs per patient have come down sufficiently to make these affordable more widely.

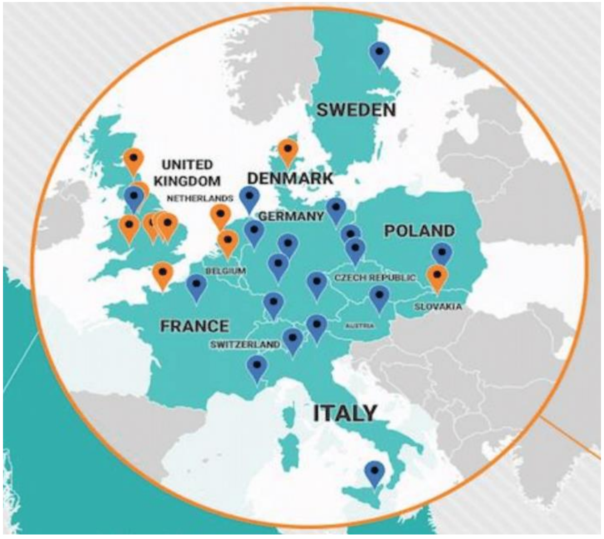

Figure 4: Particle therapy centres in Europe (June 2018). Blue denotes functional centres, orange denotes centres under construction. Source: ENLIGHT network.

The reduction of side effects has also enabled treatment of tumours in patients, which could not get RT because of its too high risk of side effects. For this reason, it has been accepted to treat children preferably with hadron therapy. In order to obtain a broad support in the clinical community, it is important to involve the referring clinicians and institutes in the preparation of the treatment. Various models for such a collaboration exist in several EU countries and it will be discussed with the SEE participants what collaboration-model will be used in the here proposed facility.

An equally strong argument in favour of creating new hadron RI in the SEE region is that the demand for beam-time for biomedical and bio-physics research purposes surpasses current availability across Europe by a factor of X. **The SEEIIST facility will be the first of the European hadron RIs whose business case will be based on a 50-50% split of the beamtime available during day-time dedicated to medical treatment and to research.** Also night time and weekends will be devoted to research, as it happens in all existing HT centres. This will allow research communities in SEE and the rest of Europe highly needed access to work in comfortable conditions and ample time on biological breakthroughs related to cancer stem cells, hypofractionation, FLASH, combined treatments, radio genomics, biomarkers, intra-tumoural heterogeneity (hypoxia), noncancer diseases, treatments of second cancers, particle-immunotherapy. Thanks to the SEEIIST hadron facility, major advancements are also expected in pre-clinical physics including: imaging in radiotherapy, adaptive treatment planning, LET optimised strategies, 4D optimisation and delivery, benign diseases. The RI will also provide beamtime for research in radiobiology, and other non-cancer applications as cardiac arrhythmias and renal denervation, nanoparticles as well as non-clinical research including space radiation protection, plant breeding, materials research & detector calibration. In many of these areas, the EU has the ambition to be global leaders. Without the construction of the SEEIIST RI, this ambition will be difficult to achieve.

Herein we can project the number of the potential patients from each country who will need a hadron therapy, calculated from the population and the incidence.

Distributed research in SEEIST HUBs (Sanja and Hans)

Additional Benefits of SEEIIST

Before the Yugoslav wars, the region had a long history of excellence in science. Before CERN was established in Geneva in 1954, and the International Centre for Theoretical Physics in Trieste and the European Molecular Biology Organization in Heidelberg were set up in 1964, former Yugoslavia already had three older international research institutes. The Vinča Institute of Nuclear Science in Belgrade was founded in 1948, the Jožef Stefan Institute in Ljubljana in 1949 and the Ruđer Bošković Institute in Zagreb in 1950. Yugoslavia was also one of the founding countries of CERN.

But that scientific progress began to crumble in 1991, along with Yugoslavia's dissolution and the 1991 - 2001 wars in former Yugoslavia diminished the economies and science capacity of all countries in the area. An entire young generation of scientists was brain-drained to the Western countries even in the after-crisis period. Looking to the political will of neighbouring countries and of the EU, "To bring back the tradition in science and technology that we had in the past."

A new large-scale research infrastructure will revive the scientific and technological potential of the Balkans, whilst helping its economy and bringing people together around a shared endeavour. A vision of a world-leading research institute, built to the same collaborative model as CERN. A €200 million investment in an international research facility in the Balkans could heal the wounds left by years of ethnic conflicts, help to stop the brain drain and lead to the region regaining its former scientific glory. The countries involved in SEEIIST hope it will help the region overcome economic difficulties and bring them closer to EU membership.

A technical design for the facility and organization to define the conditions for the selection of the site are underway. To carry out these tasks several working groups are being set up at CERN and at GSI-FAIR in Darmstadt, Germany. If all goes well, construction is expected to start in 2023, with first patient treatments in 2028.

Inclusion of SEEIIST on the EU's next roadmap for research infrastructures being drawn up by the European Strategy Forum on Research Infrastructures (ESFRI) in 2021 will really help to put the project on the "scientific and political map".