# Introduction to the EC's Marie Curie Initial Training Network (MC-ITN) project: Particle Training Network for European Radiotherapy (PARTNER)

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PARTNER (Particle Training Network for European Radiotherapy) is a project funded by the European Commission's Marie Curie-ITN funding scheme through the ENLIGHT Platform for 5.6 million Euro. PARTNER has brought together academic institutes, research centres and leading European companies, focusing in particular on a specialized radiotherapy (RT) called hadron therapy (HT), interchangeably referred to as particle therapy (PT). The ultimate goal of HT is to deliver more effective treatment to cancer patients leading to major improvement in the health of citizens. In Europe, several hundred million Euro have been invested, since the beginning of this century, in PT. In this decade, the use of HT is rapidly growing across Europe, and there is an urgent need for qualified researchers from a range of disciplines to work on its translational research. In response to this need, the European community of HT, and in particular 10 leading academic institutes, research centres, companies and small and medium-sized enterprises, joined together to form the PARTNER consortium. All partners have international reputations in the diverse but complementary fields associated with PT: clinical, radiobiological and technological. Thus the network incorporates a unique set of competencies, expertise, infrastructures and training possibilities. This paper describes the status and needs of PT research in Europe, the importance of and challenges associated with the creation of a training network, the objectives, the initial results, and the expected long-term benefits of the PARTNER initiative.

Keywords: radiation therapy; hadron therapy; cancer; imaging; training

# INTRODUCTION

Every year nearly 3.2 million people in Europe are diagnosed with some form of cancer, making it one of the major societal challenges [1]. Radiotherapy (RT) is a highly potent and cost-effective treatment for tumours, and forms a central part, with surgery, of modern cancer therapy. Conventional X-ray RT accounts for 40% of the cure rate. RT also plays an important role in symptom control and pain relief for incurable patients. RT is by far the most cost-effective modality for cancer treatment, with the added advantage of conserving tissue function.

In recent years, there has been increasing evidence that RT with hadrons—such as protons and carbon ions—has the potential to increase the local control rate for many types of tumours, while improving the survival chances and quality of life of treated patients. Hadrons can overcome the limitations of X-ray beams since they deposit most of their energy at the end of their range, in the target. Such ions thus allow for a more appropriate radiation dose distribution, a lower total energy deposition in the body, and better placement of energy to destroy the cancer cells while sparing more of the surrounding healthy tissues.

Protons are currently used in a number of hospitals around the world. The next step in RT is to exploit beams of ions heavier than protons, since they have additional properties that can be used in cancer therapy. Indeed light ions, like carbon ions, have unique physical properties and more favourable depth dose distributions than protons. Unlike X-rays and protons, light ions have a lower lateral diffusion and above all a superior radio-biological effectiveness (RBE) at the end of their range. This means that they

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can produce severe damage to the tumour while sparing healthy tissues, and are less dependent than X-rays and protons on the presence of oxygen to produce cell death in cancers with low oxygen levels (hypoxia). Hypoxic tumours in fact are known to be very resistant to X-rays. Around 15% of the tumours requiring RT can be defined as radio-resistant and could benefit from the use of high-linear energy transfer particles as carbon ions at lower energies.

With cancer continuing to be an increasing health risk, Europe faces the major challenge of training more competent researchers in the field of RT. This need was of particular urgency in 2008 when PARTNER started, since two PT facilities were becoming operational: the Heidelberg Ion Therapy Centre (HIT, Germany), and the Italian Centro Nazionale di Adroterapia Oncologica (CNAO) in Pavia. In Europe, during the financed life of PARTNER, the first dual centres (i.e. centres which use both proton and carbon-ion beams) began treating patients, two proton therapy clinical facilities treated their first patients (the Rinecker Proton Therapy Center (RPTC) in Munich, Germany, and the Proton Therapy Centre (PTC) in Prague, Czech Republic), while construction began of dual facilities such as MedAustron in Wiener Neustadt, Austria, and the Particle Therapy Center (PTC) in Marburg, Germany, and proton facilities such as the Agenzia Provinciale Per la Protonterapia (ATreP) in Trento, Italy, and Westdeutsches Protonentherapiezentrum (WPE) in Essen, Germany [2]. The long-term plans for advanced accelerator systems in France, Poland, the Slovak Republic, Spain, Sweden, Switzerland and the UK have progressed considerably.

The project offered research and training opportunities to 25 young biologists, engineers, physicians and physicists, and allowed them to actively develop modern techniques for treating cancer. For this purpose PARTNER relied on cutting edge research and technology development, effective networking, and open access to national facilities, as well as providing training by specialists in the field. PARTNER was the first organic attempt of multidisciplinary training of scientists in this rapidly growing field at a pan-European level.

## **Overall objectives**

The unique properties of hadron beams raise new challenges for researchers and exciting training opportunities on novel applications. There is an ever-increasing need for precision when treating cancers in moving organs or very sensitive organs such as the brain-stem. Not only is precision important for accurate delivery but also the dispersion of beam-energy before and after hitting the tumour area is critical for improving the treatment (therapeutic ratio) and the resulting outcome.

The principal objective of PARTNER was to educate and train young researchers in HT for the future, and thus help to integrate and develop clinical, biological and technical knowledge. The training network was inspired by the existing ENLIGHT network, a platform from which scientists and specialists in HT disciplines from more than 100 institutes of over 20 different European countries meet regularly and discuss innovations in the field [3–5].

The scientific objectives of the PARTNER training programme were achieved by carrying out the research activities illustrated in Table 1. The work plan was divided into three main categories: clinical, biological and instrumentation. Each of the institutions in the proposed network already had a scientific programme in one or all of these areas. PARTNER concentrated on the development of new solutions as well as on the continuation of the existing scientific programmes.

The ambitious scientific objectives achieved through PARTNER are:

- enhancement of clinical research by expanding the first cohort of European patients treated with common protocols;
- production of knowledge, through experiments and modelling, about the biological mechanisms and the molecular players that are involved in the response of healthy and tumour tissues to light ions, to better identify which tumours are suitable for proton and carbon ion therapy;
- use of the most recent developments in the field of e-Health to provide a common system of clinical records able to be used by all the European facilities for the recruitment and the follow-up of the patients, including those from far-away hospitals of countries which do not yet have a hadron therapy centre;
- development of synergy and commonality of design for various proposed projects, in particular regarding the delivery system and the Treatment Planning System (TPS), so as to achieve better quality control while giving European industry a lead in the manufacture of crucial components of future hadron therapy facilities;
- development of a second generation of in-beam PET detectors, which can map more precisely the space distribution of the positron-emitting isotopes produced during patient treatment with carbon ions and proton beams, leading to improvement in the quality control of the treatment;
- study and design of carbon-ion rotating gantries based on the experience obtained at HIT with the only ion gantry currently in existence—affordable for other centres because of the lower cost and energy consumption;
- development of the European common demonstration platform, starting with the most advanced facilities, in particular HIT in Heidelberg, and CNAO in Pavia.

Network participant	Researchers and projects
CERN, European Organization for Nuclear Research, Switzerland	<ul><li> 1 researcher in <i>Simulation and Dosimetry</i></li><li> 3 researchers in <i>GRID Hadron Therapy Test Bed</i></li></ul>
Fondazione CNAO, Italy	<ul> <li>1 researcher in <i>Clinical Studies</i></li> <li>1 researcher in <i>Epidemiology and Patient Selection</i></li> <li>1 researcher in <i>Image Guided Hadron Therapy</i></li> <li>1 researcher in <i>Novel Gantry Design</i></li> </ul>
GSI, Gesellschaft für Schwerionenforschung, Germany	• 2 researchers in <i>Radiobiology</i>
HIT, Heidelberg Ion Therapy, Germany	<ul> <li>1 researcher in <i>Clinical Studies</i></li> <li>1 researcher in <i>Epidemiology and Patient Selection</i></li> <li>1 researcher in <i>Simulation and Dosimetry</i></li> </ul>
Karolinska Institutet, Sweden	<ul><li> 2 researchers in <i>Radiobiology</i></li><li> 1 researcher in <i>PET Prototype, in-situ Monitoring</i></li></ul>
Ebg MedAustron, Austria	• 2 researchers in <i>Treatment Planning</i>
University of Surrey, UK	<ul><li> 1 researcher in <i>Radiobiology</i></li><li> 1 researcher in <i>Treatment Planning</i></li></ul>
TERA Foundation, Italy	<ul><li> 1 researcher in <i>In-situ Monitoring</i></li><li> 1 researcher in <i>Novel Accelerator Study</i></li></ul>
Ion Beam Applications, Belgium	• 1 researcher in Treatment Planning
Siemens Medical Solutions, Germany	<ul><li> 1 researcher in <i>Simulation and Dosimetry</i></li><li> 1 researcher in <i>Image Guided Hadron Therapy</i></li></ul>
Associated Partners	
ETOILE Project, France	
IFIMED Project, Spain	

**Table 1.** Research activities hosted at PARTNER's institutes

Additional objectives that complemented the network are equally important, and can be summarized as follows:

- transformation of the existing co-ordinated network, ENLIGHT, into a promoter of R&D and training programs;
- organization of courses and demonstrations for European clinicians and medical physicists;
- creation of bridges between academics and commercial enterprises while maintaining the uniqueness of each institution, thus avoiding antagonism and promoting complementarity and most of all:
- creation of long-term collaborations among the young researchers who will become the leading scientists of tomorrow's HT.

# Development and implementation of the scientific programme

It should be noted that such an extensive collaboration, incorporating as many scientific and technological aspects

and as much expertise as ENLIGHT [6] does, and consequently PARTNER does, is unique in the field of HT, not only in Europe but worldwide.

Europe is playing an emerging role in particle RT, which could put this geographic area in the leading position throughout the coming years. Institutions involved in the network share the responsibility this entails, and are putting considerable effort into designing the training programme.

The result has been to propose a series of activities complementing conventional PhD programmes, including a balanced variety of courses ranging from more general courses through sectorial to subject-specific and hands-on training. The innovation of the research programme was based on close interaction between the numerous and diverse research fields, being practised in parallel by clinical radiation oncologists, radiobiologists, medical physicists, accelerator and detector physicists, and engineers (see Fig. 1).

The originality was in the intrinsic translational character of all the research programmes, which were conceived in such a way as to bring benefits to the cancer patients. Some of the original publications resulting from the research



Fig. 1. Research work packages and interactions implemented in the PARTNER project.

performed in the framework of the project are following in this special issue dedicated to PARTNER.

first researchers were recruited as staff of existing and soon-to-become operational facilities.

#### RESULTS

The PARTNER network provided important outcomes in various aspects: it contributed to important scientific results, it provided valuable and much needed education, and it guaranteed the training of the quality personnel necessary for the new centres.

The PARTNER collaborators made important and crucial contributions to all scientific fields in cancer RT. These significant advances are resulting in optimization of the HT that will be used in the years to come.

In parallel, the network offered a unique opportunity to learn and to solve problems that are of paramount importance to the understanding of the medical use of ionizing radiation. Young researchers, normally specialized and trained in specific backgrounds, learned from clinicians, physicists and engineers how to work, interact and collaborate with a multidisciplinary team and to communicate effectively at all levels.

Finally, the very specific goal of PARTNER was to perform R&D and to train relevant personnel for the various European centres and existing facilities (Heidelberg, Pavia, GSI, CERN, Karolinska and the UK micro-beam facility), in such a manner that the patients will be able to be treated with optimal efficiency and without delay as the new centres become operational. The goal of providing new and experienced personnel to HT centres was successfully achieved even before the conclusion of the project, when the

### **CONCLUSION AND OUTLOOK**

The existing HT centres in Europe are running on less than maximal capacity (both with respect to clinical services and R&D) and they need to increase patient throughput. Many of the facilities are limited by manpower, and recruitment is not easy due to the limited availability of experienced/ trained personnel. Industries in HT are also limited in their capacity for delivery and installation, mainly due to restricted manpower. PARTNER has been a successful initiative that has provided a considerable number of researchers in the field, however the 25 trainees of the first programme alone cannot solve the current problem. The experience gathered through PARTNER should be utilized and become a benchmark for future similar initiatives.

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