Final Report Summary - ULICE (Union of Light-Ion Centres in Europe)

Executive Summary:
ULICE is an FP7 project started on 1st September 2009 with the aim to respond to the need for greater access to hadron-therapy facilities for particle therapy research.

The original duration of 4 years has been extended up to 5 years to allow the start of transnational access activities and run with good results, both for the consortium and for external researchers involved in the field.

The project, coordinated by the National Center for Oncologic Hadrontherapy (CNAO), is set up by 20 leading European research organisations, among which two leading European industrial partners and the two existing European Hadron Research Facilities, UKL-HD located in Heidelberg (Germany), and CNAO in Pavia (Italy). Planned facilities like MedAustron (Austria), Etoile and Archade (France), also participate in ULICE to gain experience from running centers and strongly work together in a network integrating several competencies, from clinic to radiobiology, engineering to medical physics.

Full exploitation of all different resources, unrestricted spread of information and the improvement of existing and upcoming facilities are provided by using grid-based data sharing.

The project is built around 3 pillars with measurable outputs.

1. Joint Research Activities (JRA), coordinated by the Medical University of Vienna (MUW), focuses on development of instruments and protocols: new gantry design, improvement of four-dimensional particle beam delivery, adaptive treatment planning, mechanisms for patient selection to the whole European Community and database development for specific tumours which can best be treated using carbon ions.

2. Networking (NA), coordinated by the European Organization for Nuclear Research (CERN), aims at increasing cooperation between facilities and research communities wanting to work with the research infrastructures. The main outputs are to make hadrontherapy well known through the participation of ULICE to the most important congresses in the field (i.e. ESTRO) and to give the possibility to new users to become close confident with hadrontherapy. One product of the activities is a report on recommendations for strategically optimal locations for future RIs throughout Europe, training to new users.

3. Transnational Access (TA), coordinated by the University Hospital of Heidelberg (UKL-HD), through 2-step approach, allowed...
researchers to visit the facility, and radiobiological and physics experiments to take place.

Project Context and Objectives:
The ULICE project focuses on hadrontherapy i.e. the use of particle beams such as protons and carbon ions against tumours. Particle beams can reach the tumour more selectively sparing the surrounding normal tissues. Light ions, as carbon ions, have physical properties similar to those of protons but unique and more favorable radiobiological characteristics. The European scientific community on hadrontherapy has been growing significantly during the last decade. Different forms of co-operation have been established in this multidisciplinary field, e.g. a program called ENLIGHT hadrontherapy was the successful approach towards a systematic Europe wide multi-centre and multi-cultural research community. The highly technical field of hadrontherapy needs urgently large scale research infrastructures characterized by their complexity. Hadrontherapy is supradisciplinary at the outset since it cannot flourish without the active participation of high-level experts coming from a wide range of disciplines ranging from nuclear physics to information and communication technologies to medicine.

One of the major task of the project, in fact, is joining different competencies together and foster cooperation between different specialties providing access to hadrontherapy facilities.

ULICE activities range from research in radiobiology useful to identify tumours that would need the superior physical and radiobiological selectivity provided by particles given their difficult location close to critical normal organs and their scarce sensibility to conventional radiotherapy, to clinical protocols trough which patients are treated having as common basis all the clinical data collected by the participant institutions. The project stands on the great need of joining scientific results obtained by different institutions in different fields of excellence and translate them in a real benefit to the community.

Another important objective of the project is the communication between all the professional expertise involved just to focus the efforts on the same point and to ensure a better communication and understanding of all the data that can be transferred from a facility or a treating center to another.

The consortium is composed by the world class European institutions in radiotherapy and applied research. They are all the existing and planned light ion facilities, University of Heidelberg, CNAO, ETOILE, ARCHADE, University of Marburg, MedAustron. Many University Hospitals are represented above all by Radiotherapy Departments as: Medical University of Vienna, the Catholic University of Louvain, the Medical University Aarhus, St. Radboud University. The contribution of research institutes is nevertheless fundamental as CERN, GSI, Technical University of Dresden, Karolinska Institute, Université Claude Bernard Lyon 1, INFN, Institute of Nuclear Physics Polish Academy of Sciences. Two industries acting in the field are part of the project too, they are IBA and SIEMENS. Another partner of the project is ESTRO, a professional scientific society whose mission is to foster radiation oncology in all its aspects through training of professionals subjects.

Project Results:
Following the organizational structure of the ULICE consortium and organization of the activities, the main outputs in terms of S&T results can be founded above all in the activities of the Joint Research activities, the pillar representing research:
1. Producing a consensus among ULICE members on dose and volume concepts to be used in heavy ion radiotherapy. This agreement can bring to shared clinical protocols to get evidence on hadrontherapy benefits.
2. Testing with software, models, optical tracking systems, organ motion compensator the results come close to match the volume treated by active scanning particle beams closely to the target volume. In order to achieve the best chance of success to control the cancer lesion, the irradiation must always adequately cover the full tumour volume and touch as little as possible the surrounding normal tissues. These results of researches can be the starting points for improving other devices in use in hadrontherapy.
3. Facing the four-dimensional particle-beam delivery through new software and hardware tools to measure and predict organ motion and for tracking the beam. Moving targets and organs during irradiation is actually an important cutting-edge issue in radiotherapy and needs special attention (e.g. respiration). This issue is particularly challenging when scanning beams are used because of the risk of interference between the scanning beam and the moving organs. That is why a dose delivery system able to steer the beam in the right time has been improved and tested.
4. Using adaptive treatment planning, which takes into account any knowledge obtained about dynamic alterations of patient or tumour specific parameters. In particular this can be the variation of the radiosensitivity, time dose fractionation and the variation of anatomy and topography. In addition, combined treatment protocols using different radiation qualities (e.g. photons, protons, carbon ions) are conceivable by including the pre-irradiation data into an adaptive treatment planning system.
5. Designing of a new carbon ion gantry. The benefit related to the superior characteristics of the particle beams (depth dose, penumbra...) can only be fully exploited through the use of multiple, individually shaped fields. Beam delivery is facilitated (patient comfort) and made more accurate by an isocentric rotating gantry. For radio therapy using carbon ions, only fixed beam rooms have been used in clinical routine. However, for certain tumour locations, a carbon ion gantry offers superior dose distributions.
6. Paving the way for a mechanism for patient selection based on the individual biological features of the specific tumour. A
systematic review of the existing literature was conducted.

7. Adopting a biology based computer assisted patient selection program accessible to the whole European community interested in hadron-therapy, which enables a relevant and efficient patient referral to existing facilities and high level clinical research focused on tumours with specific biological characteristics and/or critical location. Such software prototype, taking into account a variety of radiobiological and clinical parameters, can finally allow different centres to decide which radiation quality has the best chance to cure an individual patient.

Potential Impact:

Important results obtained through Networking activities have been to establish contacts and cooperation among European and non-European hadron facilities external to the ULICE consortium. That is really meaningful in a field like that of hadrontherapy where the collecting of data is not easy given the few centers in the world treating patients. Standardized protocols describing specific procedures carried out in operational hadron-therapy facilities were published. They can be considered as starting point and reference for new studies coming along. It was possible to collect data in order to describe financial and epidemiological parameters relevant to existing and planned European hadron facilities, growing in the last years.

The ULICE activities had impact on the training for researchers, scientists and specialists working in running facilities and in facilities close to start their activities with patients. This possibility had a real great impact on improving the experience and acquaintance of mentioned professionals as they enrich their curricula. It has to be underlined that many of them, above all young people, have then been recruited by particle therapy centres. The ULICE project directly contributed to improve access to Hadron facilities by offering a total of 770 hours of “free access” beam time to the European radio-therapy research community. The free access beam time has been dedicated to external researchers for clinical trials and for radiobiology and physical experiments selected among more than 10 proposals. Around 90 patients have been treated with hadrontherapy at the Italian (CNAO) and at the German (UKL-HD) facility thanks to the possibility given by the project to select and receive therapy against the oncological disease they are affected.

The project helped to foster a collaborative culture and to provide the tools, procedures and standards for integrated use and knowledge sharing between the Hadron research facilities the clinical data throughout the European research Radiotherapy community. The overall frame for coordinated clinical and translational research developed in the project, is extensive, defining the various disciplines and research representatives which are mandatory to coordinate high quality research on the European level. For these tasks, ion therapy research boards (IONTREB) has been implemented at the international level. The boards must involve all major (clinical and translational, but also basic) research groups and facilities focused on ion therapy as well as advanced photon therapy research programmes, and must establish a link to relevant international and national scientific associations and networks (e.g. EORTC HPT Group) in clinical radiation oncology, medical physics and translational radiobiology. In addition, at a national level, such boards are essential to coordinate and harmonize patient referral to studies that are to be initiated or ongoing at the ion beam centres. At the international level, this research board is required to structure and guide the design, implementation, operation, and continuous evaluation of database orientated clinical and translational research and multicentre clinical phase I/II/III trials.

As a first step within ULICE, a Core Group (“Executive Research Committee”, ERC) was implemented based on the existing members of clinical work-packages and the centres in operation and in preparation. This ERC will then be transformed and expanded into IONTREB in the period following the termination of the ULICE project under the umbrella and with a strong link to EORTC. The major tasks of this board are related to international prospective multi-centre cooperative phase I, II, and III trials and an international multi-centre joint database research structure, in which comprehensive parameters on patient, tumour, treatment, morbidity, quality of life and disease outcome characteristics are prospectively collected. Structure and roadmap will be decided for the starting phase and as mid- and long-term perspective. The activities of this research board will be linked to relevant clinical radiotherapy research organisations and networks on the international, national, and regional level in European member states and regions which focus on ion and advanced photon radiotherapy research.

The ULICE project was strongly focused on disseminating results and involving the research community in the activities and services provided. A specific workpackage had been taking care of all the dissemination actions. The consortium indeed did recognize that it is fundamental to raise awareness among the research community and cancer patients about the potentiality of research on and treatment with the hadron therapy.

Effective communication actions will help catalyze the collaboration between the different scientific communities (radiation, surgical and medical oncologists in the different fields of cancer, radiologists, physicists, biologists, biomedical engineers, detector experts, computer simulation and modelling). Every year, the networking activities’ pillar organized workshops where hadrontherapy was promoted amongst external stakeholders as vendors, universities, patients society, educational world.

To assure that the results of the project will be disseminated to a broad scientific and non-scientific audience a multi-faceted dissemination and communication plan has been prepared at an early stage in the project. In particular, ULICE’s dissemination policy has been directed towards:
The dissemination strategy of the ULICE consortium has been five-pronged:

1. establishing a dedicated communication tool and network;
2. publicizing the research opportunities to the European research communities and the treatment potentialities to the wider public and cancer patients;
3. training courses on services provided;
4. disseminating project results through workshops, meetings and the Internet;
5. disseminating knowledge through scientific publications.

ULICE scientific workshops have been organized on a yearly basis all along the project’s lifetime with the aim of catalyzing the discussion within the scientific Hadron-therapy community and decision makers. The workshops were held together with ENLIGHT community and ESTRO including other cancer related societies (e.g. ECCO and organ and method specific societies) and ULICE partners to promote the collaboration between the different scientific communities.

Industrial partners participate throughout the year to various specialised meetings and exhibitions in which they most often have a commercial booth. These are visited by a large –specialized- audience, including medical doctors, administrators and people willing to develop/enhance particle therapy centres, as well as delegations from a lot of surrounding markets (computing, dosimetry, imaging...). Providing information about the ULICE community (through brochures, posters,...) made these people aware of the existence and activities of the network, but also this made them interested in joining the network and hence constantly extending it towards a truly pan-European partnership.

A dedicated ULICE Video has been developed to promote Hadron radio-therapy, explaining the emerging technology and the access services provided by the facilities.

The consortium foresaw a relevant and regular publication activity resulting from the scientific research on radio-therapy technologies (improvements in JRA) and from clinical research carried out in the context of the Transnational Access (TA) pillar of the project. Participants in the ULICE project were expected to regularly publish the scientific results obtained by individual institutions and through collaborations, in appropriate scientific journals and conference proceedings. These publications have also been published on the ULICE website.

ULICE partners dealing with the JRA activities and wanting to publish were subject to a specifically organised review procedure and committee to provide scientific feedback on articles that will be explicitly publicised on behalf of the ULICE project. The project has been developing partial products which can be exploited in the relatively short term. This is related to the following 4 major project results:

1. A prototype software “Biologically Based Expert System for Individualized Patient Allocation”
2. Motion models, monitoring and tracking system
3. New protocols and software for optimized tailoring of treatment parameters
4. An optimised (lightweight) carbon ion gantry design.

List of Websites:

The ULICE project coordinator is the Centro Nazionale di Adroterapia Oncologica (CNAO), from Italy.

Coordinator’s contacts are:
Dr. Roberto Orecchia: roberto.orecchia@cnao.it
Mrs. Cristina Bono: cristina.bono@cnao.it

The project’s beneficiaries are:
Centro Nazionale di Adroterapia Oncologica (IT), MUW Medical University of Vienna (AT), UKL-HD University Hospital of Heidelberg (DE), CERN European Organization for Nuclear Research (CH), MEDA MedAustron (AT), UCBL Université Claude Bernard Lyon 1 (FR), UNIMAR Philippus-Universität Marburg (DE), GSI Helmholtzzentrum fuer Schwerionenforschung GmbH (DE), KI Karolinska Institute (SE), UOXF Oxford University (UK), TUD Technical University of Dresden (DE), SAG Siemens AG - MED PT PLM P (DE), ESTRO European Society for Therapeutic Radiology and Oncology (BE), UCL Université Catholique de Louvain (BE), AUH AS Medical University Aarhus (DK), RUNMC Stichting Katholieke Universiteit (NL), IBA Ion Beam Applications SA (BE), INFN Istituto Nazionale di Fisica Nucleare (IT), IFJ PAN Henryk Niewodniczanski Institute of Nuclear Physics Polish Academy of Sciences (PL), ARC Archade (FR).

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