D.JRA 2.6 – Implementation, testing and evaluation of the structure with typical “cases” for research and development

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WP n° and title: WP 2 – Concepts and terms for dose volume parameters and for outcome assessment in hadron-therapy integrating applied biology, medical physics and clinical medicine in ULICE

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LIST OF ABBREVIATIONS AND DEFINITIONS

ARCHADE  Advance Research Centre for HADron therapy in Europe located at Caen, France.
CNAO  Centro Nazionale di Adroterapia Oncologica – Italian National Centre for Hadron Therapy located at Pavia, Italy.
ETOILE  Espace de Traitement Oncologique par Ions Légers Européen – French National Hadron-therapy Centre located at Lyon, France.
HIT  Heidelberger Ionenstrahl-Therapiezentrum – Heidelberg Ion-Beam Therapy Centre located at the Heidelberg University Hospital, Germany.
JRA  Joint Research Activities.
ULICE  Union of Light-Ion Centres in Europe.
WP  Work-Package.
PUBLISHABLE SUMMARY

The overall frame for coordinated clinical and translational research as set up in deliverable 2.3 is and has to be extensive (paragraph 3) defining the various disciplines and research representatives which are mandatory to coordinate high quality research on the European level as a European Hadron Therapy Research Board. As a first step a Core Group (“Executive Committee”) is implemented based on the existing members of work-package two and the centres in operation and in preparation. This Core Group will then be transformed and expanded into the European Hadron Research Board in the period following ULICE. 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 hadron and advanced photon radiotherapy research.


CONTENTS AND SPECIFIC DOCUMENT STRUCTURE

1 Background and Introduction

Following the deliverable of WP 2.3 in February 2011 (deliverable 2.3) a systematic discussion was performed in WP 2 in order to clarify the objectives of the projected research, the clinical and translational research methodology and the various scenarios applicable for hadron therapy in the current situation of new centres in Europe.

In parallel, a transnational trial design was set up by the French radiotherapy group including ETOILE and ARCHADE for a phase III clinical trial together with HIT. This trial investigates the additional benefit of carbon ions compared to advanced photons in adenoidcystic carcinoma of the salivary glands in the head and neck region. This model may serve as a test case for transnational access within the frame of prospective clinical trials.

The overall frame for coordinated clinical and translational research as set up in deliverable 2.3 has been extensive (paragraph 3) defining the various disciplines and research representatives which are mandatory to coordinate high quality research on the European level. Finally, the decision was taken to take first pragmatic steps towards a Core Group (“Executive Committee”), in contrast to start with setting up a comprehensive frame which was considered as not appropriate for the current situation in hadron therapy with limited resources. This comprehensive frame is still valid, but has to be regarded as (ultimate) goal to be aimed at for coordinated European research in hadron therapy. Therefore, the implementation is only being started now and the evaluation of the first steps will only become possible at the end of ULICE in August 2013 and adaptations will be developed for the phase following ULICE.

2 Implementation of the European Hadron Research Board and the Core Group (Executive Committee)

In order to enable the design, implementation and the operation of coordinated research during the present phase of the early operation of two centres for carbon ion and proton radiotherapy in Heidelberg and Pavia, the implementation of MedAustron in Wiener Neustadt (start 2015) and the preparation of ETOILE and ARCHADE in France, a European Hadron Research Board is implemented in the last year of ULICE via a Core Group (“Executive Committee”) with a continuously expanding structure beyond ULICE. Other carbon-ion centres outside Europe and specific proton centres will also have to be considered.

2.1 Tasks of the Hadron Therapy Research Board

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, imaging (including anatomical mapping), treatment, morbidity, quality of life and disease outcome characteristics are prospectively collected. General considerations on infrastructure, organisation and specific responsibilities for such coordinated research needs to be defined.
This European Hadron Therapy Research Board will have the following specific tasks:

- to guide the design, implementation, operation and continuous evaluation of the prospective multi-centre database for patients treated in a defined consortium of centres with carbon ions, protons, advanced photons;
- to guide the design, performance and results of database orientated research;
- to design, to decide and to follow up on multi-centre phase I, II, and III clinical studies performed in the carbon-ion centres alone or in combination with photon and/or proton facilities;
- to link translational research from various areas of interest (e.g. hypoxia) and research groups to ongoing and projected clinical trial and database orientated research.

2.2 Stepwise Procedure for the Implementation Process

In a first step a Core Group for the research board is set up and put into operation within the frame of ULICE. This Core Group comprises in any case the major representatives of the different facilities in operation and the related loco-regional research structures (e.g. universities). This Core Group should in the beginning have at least one radiation oncologist from each centre and at least overall one medical physicist and one clinical radiation biologist. A clinical methodologist and a statistician should be involved as appropriate. Representatives from major cancer related research disciplines and groups/networks are to be involved as appropriate: e.g. oncologic imaging including bio-imaging, cancer pathology, organ oncology specialists (e.g. neuro-oncology), medical oncology.

In a second step this Core Group is transformed into a structure which fulfils the needs of the European hadron therapy research board consortium following ULICE (after August 2013).

2.3 Practical Steps

After thorough discussion within the frame of ULICE during 2011 and 2012 in various work-packages, in particular WP 2, WP 3, WP 11, WP 13, in the JRA network, and at the annual meetings in Marburg 2011 and in Pavia 2012, a formal decision was taken at the last Technical Board on September 14 to implement such European Hadron Therapy Research Board as soon as possible, preferably still in 2012 (see minutes of the Technical Board and Figure 1).

The first physical meeting of such Core Group is planned as a one day meeting in January 2013, where the roadmap for the time within ULICE (eight months) and beyond ULICE will be decided. During this first meeting and a second consecutive meeting (during ULICE) the following tasks have to be initiated and completed as feasible:

- The structure and the mechanisms of operation are decided for a first period of three years. This group is focused on the existing centres in operation and those in concrete planning and should be called “Core Group”.
- Pathways for the build up of a mid- and long-term structure will be defined. These structures will also comprise specific task orientated research groups, various research disciplines, and organ orientated research groups which will altogether form the comprehensive European Hadron Research Board with a limited size executive committee.
Figure 1: European Hadron Therapy Research Board and the corresponding hadron facilities.

- A check of existing trial protocols is performed as proof of principle in regard to deliverables as provided within WP 2 (2.1 – 2.8). These protocols are those which were developed in the operating centres (HIT and CNAO). At least two protocols are to be finalised.
- A check procedure is prepared for the phase III trial protocol between the French group and HIT.
- “Catalogues” with assessment scales are developed for these trial protocol checking procedures. To achieve this aim the deliverables have to be translated into an operational form for handling efficiently the different concepts and terms.
- A roadmap is established for building up the projected international multi-centre joint database research infrastructure with prospectively collected comprehensive parameters on patient, tumour, treatment, morbidity, quality of life and disease outcome characteristics.
- Concepts and specific plans are provided how to integrate the research plans of the individual centres, in particular from HIT and CNAO, for the following three year period into a joint European approach, which is then represented by the European Hadron Therapy Research Board. The role of the upcoming centres is defined, in particular for MedAustron (operational in 2015).
- A mechanism is defined on the link and the mutual responsibilities between this European Hadron Therapy Research Board on the one hand and the hadron facilities.

Such Core Group (“Executive Committee”) will be implemented in January on the occasion of the first physical meeting with a clear structure (coordinator, secretary) appointed by its members for time period which is then responsible for the regular and continuous operative activities in regard to the coordinated research efforts.

The activities of this European Hadron Therapy Research Board will be linked to relevant clinical radiotherapy research organisations and networks on the international/national/regional level in European member states and regions which focus on hadron and advanced photon radiotherapy research.
CONCLUSIONS

Following the deliverable of WP 2.3 in February 2011 (deliverable 2.3) a systematic discussion was performed in WP 2 in order to clarify the objectives of the projected research, the clinical and translational research methodology and the various scenarios applicable for hadron therapy in the current situation of new centres in Europe. A Core Group for the European Hadron Therapy Research Board is implemented in the last year of ULICE to enable the design, implementation and the operation of coordinated research. This Core Group comprises the major representatives of the different facilities in operation, work-package two and the related loco-regional research structures. The first meeting of the Core Group of the European Hadron Therapy Research Board is planned in January 2013, where the structure, organisation and the roadmap for the period within ULICE and beyond will be decided upon.