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NEWSLETTER SEPTEMBER - OCTOBER

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European particle therapy
network



PROJECTS & RESEARCH





EUROPEAN PARTICLE THERAPY NETWORK

Report on a new initiative

First meeting 8 May 2015

The European Particle Therapy Network (EPTN) was established in 2015 in response to the anticipated increase in the number of particle therapy centres in Europe. In addition, the need to cooperate among centres and integrate particles (i.e. protons and carbons) in the framework of clinical research networks was identified as being of paramount importance. ESTRO was asked to collaborate with EPTN and agreed to facilitate the group. The first meeting of the EPTN was on 8 May 2015, hosted by ESTRO in Brussels.

Particle therapy (PT) is only one part of radiation oncology, and needs to be well aligned with other radiation techniques as well as with general developments in cancer research and patient care. PT offers both new opportunities for providing excellence in cancer care, and new opportunities for high-quality research in the framework of European research networks.

The purpose of the first meeting was to brainstorm in which areas of particle therapy it might be interesting and suitable to work together, and how this could be organised. All major European centres interested in particle therapy were invited, with 28 centres and two research organisations (the European Organisation for

Nuclear Research (CERN) and the European Organisation for Research and Treatment of Cancer (EORTC)) represented at this inaugural meeting.

It was agreed unanimously at the meeting to have joint European initiatives and cooperation in PT and to launch smaller working parties (WPs) with experts for different topics to further elaborate particle therapy discussions in Europe. It was emphasised that the initiative be fully inclusive and integrative (i.e. all centres who want to are invited to participate in the WPs) and that collaborators work on particle therapy as one integral component of the radiation oncology research community, and not as a separate field. Seven WPs were formed (see table below for details), and all centres involved or intending to work on particle therapy were invited to participate. The group agreed to meet annually in Brussels.

Second meeting 18 May 2016

Held at the same venue as the first, this meeting saw 27 centres represented including EORTC and CERN. The purpose of the meeting was to receive an update on the activities of the WPs and discuss the way forward. We briefly present the outcomes of the discussions:



MICHAEL BAUMANN



DAMIEN WEBER

WP1: Scoring of normal tissue reactions and tumour response particle / photon radiotherapy

WP1 discussed how to homogenise scoring of normal tissue toxicity. So far, a proposal for a minimum requirement on normal tissue scoring has been set up for prostate cancer that includes standard acute and late toxicity scores and patient quality of life. Inclusion of patient-reported outcomes is under discussion.

It was decided that to avoid duplication, this WP will fuse with the clinical trials group, WP3. Major aims for the future are the generation of an example for joint data evaluation between the centres including the storage of data in a homogeneous manner.

WP2: Dose assessment, quality assurance, dummy runs, technology inventory

This WP is in the process of finalising

collaborating members. As of May, 12 centres from eight different countries confirmed their interest in contributing to WP2, with a total of 15 participants. WP2 has identified the following six areas of interest:

- 1. QA / equipment survey:** preparation of a questionnaire to be sent to interested centres in Europe with the aim of collecting information regarding the dosimetric quality assurance tests performed on particle machines by the different centres, including the type of test, the frequency, the tolerance and the equipment used.
- 2. Absolute dosimetry:** focus on those aspects of absolute and reference dosimetry that, we believe, are not satisfactorily covered by the current standards (code of practice)
- 3. Dosimetry audits:** some countries may require dosimetry audits to be performed to obtain the license to treat patients. Regular dosimetry audits or dosimetric intercomparison between centres could also be part of the regular QA programme. The aim is to create a network of participating centres that could be interested in participating in such audits / intercomparisons.
- 4. End-to-end tests:** the focus will be on the tests and phantoms that could be used for this purpose
- 5. Dosimetry tools:** to create a database of dosimetry equipment in use in particle therapy. The following questions are of interest: does the current (commercial) available dosimetry equipment satisfy all

EPTN work parties:

WP	Title	Coordinators
1	Scoring of normal tissue reactions and tumour response particle/photon radiotherapy; endpoint definitions, outcome database	Hans Langendijk (Groningen, The Netherlands) Mechthild Krause (Dresden, Germany) Roberto Orecchia (Milan, Italy)
2	Dose assessment, quality assurance, dummy runs, technology inventory	Oliver Jäckel (Heidelberg, Germany) Sairos Safai (Villigen, Switzerland) Stefan Menkel (Dresden, Germany)
3	Trials inventory (website); 'Towards joint clinical trials'	Karin Haustermans (Leuven, Belgium) Cai Grau (Aarhus, Denmark) Daniel Zips (Tübingen, Germany) Jacques Balosso (Grenoble, France)
4	Image guidance in particle therapy	Aswin Hoffmann (Dresden, Germany) Alessandra Bolsi (Villigen, Switzerland)
5	TPS in particle therapy	Håkan Nyström (Uppsala, Sweden) Tony Lomax (Villigen, Switzerland)
6	Radiobiology, RBE	Manjit Dosanjh (Geneva, Switzerland) Bleddyn Jones (Oxford, U.K.) Jörg Pawelke (Dresden, Germany) Jan Alsner (Aarhus, Denmark) Martin Prutschy (Zurich, Switzerland)
7	Health Economy	Yolande Lievens (Ghent, Belgium) Klaus Nagels (Bayreuth, Germany)

the requirements of particle dosimetry and QA? If not, what additional specifications should be satisfied, and what additional dosimetric developments are of interest for the community?

6. **Web-based platform for teaching activities:** to explore the feasibility and needs of having a web-based platform for teaching activities.

In the coming months collaborators will be assigned to selected topics. The first priority is the QA survey and the aim is to have the questionnaire defined and sent to interested centres by the end of the year.

The presented topics were well received at the meeting and the audience encouraged the realisation of the survey as presented.

WP3: Towards joint clinical trials

The following vision and scope statements for European clinical trials in particle therapy were presented and generally accepted:

- Emphasis should be on performing high-quality trials with properly selected candidates and using relevant, validated clinical endpoints
- A small number of pivotal randomised controlled trials (RCTs) are urgently needed, but most patients will enter other types of controlled trials, and we need to develop / test / validate the methodologies (e.g. multiple cohort RCTs)
- Model-based selection (as a predictive biomarker) is a useful concept for NTCP

based studies, and this concept should later be extended to incorporate also TCP

- European centres must join forces to create such trials and evidence soon
- Trials involving state-of-the-art photon radiotherapy are welcome, as particle therapy should be seen as an integral component of radiation oncology
- European trials should be open to accredited centres with expertise and relatively high numbers who wish to collaborate
- Prospective collection of high-quality data for proton patients treated outside of clinical trials (using common ontology and data collection forms)
- There is a need to develop a European QA platform for particle therapy trials.

A survey of ongoing clinical trials listed on ClinicalTrials.gov was presented. The experience from the Union of Light-Ion Centres in Europe (ULICE) was also discussed. Several of the documents, which are publicly available, are ready to be used in clinical trials.

WP4: Image guidance in particle therapy

This WP will focus on the importance of imaging and image guidance in advanced particle therapy. The first aim is to understand and investigate the merits and caveats of the use of image guided particle therapy (IGPT) in current practice within European particle therapy centres (PTCs). Secondly WP4 aims to identify current challenges and ongoing as well as future research activities

in this rapidly developing field. WP4 will focus on developing a strategy proposal for IGPT research that would require a European network of PTCs.

Reference persons willing to participate in WP4 have been identified throughout 19 European PTCs. A survey on the current status and future perspective of IGPT has been sent out to these PTCs. All PTCs completed and returned the questionnaire and the data have been preliminarily analysed. Results showing the main features, trends and wishes, were presented during the second meeting of the European Particle Therapy Group in Brussels on 18 May 2016. The next steps are to complete data analysis and to communicate this to the reference persons. This will take place in a future meeting with reference persons, in which the specific goals for subgroups of WP4 will be defined.

WP5: TPS in particle therapy

The treatment planning working party coordinators (WP5) organised a pre-meeting the day before the main meeting (17 May) with all interested parties, which was attended by 19 participants from 14 different centres around Europe. The following agenda points were discussed:

- Collective TPS specifications
- Planning standards and case solutions
- The role of automated planning
- TPS commissioning and validation
- CT calibration
- The role of robust optimisation/evaluation

- Linear energy transfer, relative biologic effectiveness (LET/RBE).

Based on these discussions, seven task groups have been created with defined coordinators to start discussions on each of these points. Future meetings of this WP will be organised in November and also at the ESTRO meeting next year in Vienna.

WP6: Radiobiology, RBE

A working party on radiobiology has been established to consider all aspects of particle radiobiology. Following initial discussions at the meeting in Brussels it was decided to proceed with a questionnaire to determine the current status and detailed specification of the radiobiological studies in the existing, and planned, clinical and research particle therapy centres in Europe. This information will help to guide future collaborative research.



See Radiobiology corner of this newsletter for more details.

WP7: Health economy

Particle beam radiation is one of the most promising advances in radiation oncology, with clear benefits for cancer patients. Intensifying health economic challenges posed by the need for documented comparative effectiveness of particle beam therapy represents a pressing issue that must



European Particle Therapy Network participants at 18 May 2016 meeting in Brussels

be solved, particularly related to national service listings and reimbursement issues. In that respect both clinical and health economic performance parameters need to be collected and translated into value dossiers.

As the required data collection process has not been established in a harmonised way across Europe, the WP7 team aims to initiate this process. As a first step, a survey was performed earlier this year in order to produce a basic data inventory of the participating particle beam therapy centres. However, the return of resent survey forms was unsatisfactory. Therefore, the team is thinking of other ways to make this work since it is in the interests of all particle beam therapy centres to have good arguments with regard to health policy-related resource allocation decisions. It needs to be taken into account that a complex innovation, such as particle beam

therapy will not succeed without these data.

Furthermore, the WP7 has started to establish work interfaces with work packages specialising in clinical aspects of particle beam therapy. Finally, an external contact person with the EUnetHTA organisation (European network for HTA = Health Technology Assessments) has been identified in order to better understand the current EU view on complex technologies with regard to HTA procedures, which are vital since HTA includes health economic evaluation modules.

EORTC potential contributions to EPTN

EORTC presented its interest in developing a new partnership to avoid the duplication of infrastructure for clinical research and network management. Such routes for cooperation are already in place with many societies and

academic organisations, notably with ESTRO and the European Society for Paediatric Oncology (SIOPE), which are certainly relevant to this initiative. At the moment, EORTC remains the only pan-European, multidisciplinary clinical research infrastructure working across tumour types, delivering data sets which are regulatory compliant. EORTC has developed a number of solutions, which could be customised to the service of this initiative:

- Database and IT solutions for network management; clinical trials and data integration (clinical, quality of life (QoL), HE, quality assurance in radiotherapy (QART) etc...) with regulatory compliance and auditable quality ensuring long term follow up of patients
- Methodology expertise for clinical trials design, validation of biomarkers which could rapidly pick up the achievements of ULICE
- International regulatory expertise for the launch and conduct of clinical trials with capacity to act as the sponsor, with regulatory driven innovation (trans-border directive)
- Expertise in new clinical research platforms not limited to prospective randomised trials but integrating real-life cohorts. Links with a number of new key stakeholders in the field, such as regulators and payers to build such initiatives, taking into account all interests and needs

- Multidisciplinarity: link into QoL but also rare tumour networks, link into the new EU ERN (European Research network)
- QART platform which is well known in the field of radiotherapy and which is going to provide services to SIOPE
- Potential support into EU affairs and fundraising with the expertise in place at the EORTC head office.

General remarks

- Education and training issues will need to be addressed across the board.
- Particle therapy is expensive so collaboration is important:
 - We should engage with industry in a way that ensures that participating centres have control over patient data.
 - Joint efforts to source funding from the European Commission. A funded project with clinical aspects is likely to have all centres participate. For technical projects not all partners can participate, but all will be kept informed. For this reason, a dissemination component is essential in keeping the entire network informed.
- We need to map what centres are doing to be able to identify gaps for future work. From this, one or two topics can be identified to start the lobby for funding.
- A subgroup for paediatric tumours is needed.

In terms of operations, at the moment EPTN is facilitated by ESTRO. The group agreed that a more tangible association with ESTRO would be more meaningful for recognition and requested to become a task force of ESTRO. The ESTRO board will consider the request.

The EPTN will next meet in Brussels in 2017.

Michael Baumann (Dresden, Germany) and Damien Weber (Paul Scherrer Institute, Villigen, Switzerland), EPTN organisers

For more information on EPTN, email Evelyn Chimfwembe at echimfwembe@estro.org or Ulrike Koch at Ulrike.Koch@uniklinikum-dresden.de

