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Report from the fourth annual meeting of the ESTRO European Particle Therapy Network (EPTN) task force

28 June 2018 London, UK



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The fourth annual meeting of the ESTRO European Particle Therapy Network (EPTN) task force was held at University College London (UCL), UK, in June. There were 38 participants from 19 institutions in ten European countries. These numbers reflect the steady increase in the number of new particle therapy facilities operating in Europe, with at least three new centres coming into operation in 2018. The first EPTN meeting, held in 2015, was used to define the roles and tasks of the EPTN work parties. Since then much has been achieved, including the development of questionnaires relating to quality assurance (QA) as well as new guidelines.

This year culminated in eight scientific articles on EPTN work being published in *Radiotherapy & Oncology* in a special issue on proton therapy [1-8]. The accompanying editorial argues that with the combined efforts of the dedicated working groups and institutions, European particle therapy is well placed to move to the next level.

In the report below, you can read about our progress across our seven working parties (WP).

WP1: Clinical

The WP1 clinical group is focused on establishing the content of prospective data registries and assessing methodological strategies for performing clinical research at a European level. At present, there are proposals for a generic assessment and six tumour-specific databases, including central nervous system (CNS), head and neck, lung, oesophagus, breast and prostate. A WP1 consensus meeting took place at Schiphol Airport, Amsterdam, The Netherlands,

on 5 September 2018 . The main purpose of the meeting was to reach consensus on the content of these prospective data registries. This endeavour, named ParticleCARE, is a subproject of the umbrella project conducted by ESTRO and the European Organisation for Research and Treatment of Cancer (EORTC) (E2-RADIaTE). EORTC will set up the IT database infrastructure and will manage the data, while EPTN will set up the governance structures.

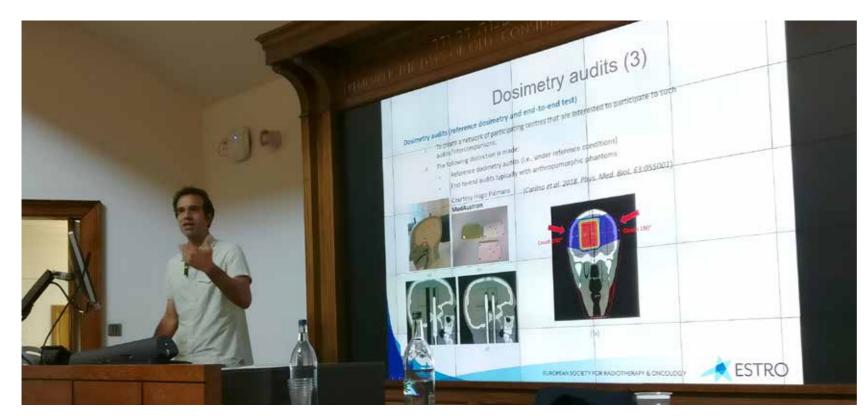
We have published a paper on the background and general aims of the project [5]. In the USA, data registries for adults and children already exist. As far as possible, we plan to link to these registries to facilitate data merging between the US and Europe for future joint research projects. This is crucial given the low incidence and wide variety of tumour types.

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

In total, 27 participants from 21 centres based in ten countries have contributed to the activities of WP2 (as of June 2018).

The second general WP2 workshop was held on 8 May 2018 in Frankfurt, Germany. The workshop focused on the activities of three of the six working groups: (i) the QA / equipment survey, (ii) reference dosimetry, and (iii) audits.

i) QA / equipment survey: the survey was distributed at the end of 2017, with an 88% completion rate. The questionnaire collects information about the dosimetry QA tests



Sairos Safai presenting work of WP2

performed and equipment used in centres across Europe, including: type of test and ▼ procedure, frequency and duration, tolerance levels, equipment used, level of satisfaction and critical assessment of equipment and procedures. One of the main goals is to verify if a consensus exists among the centres in Europe with respect to the QA programme.

A selection of preliminary results were presented at ESTRO 37 in Barcelona, Spain, in April 2018. We compared results on how different centres conduct daily QA of scanning proton treatment units, observing large variation in the tolerance levels used for similar types of tests. For example, some centres performed range/energy checks on a daily basis while

others did not. The full analysis of the questionnaire is ongoing. However, these preliminary results seem to indicate that there is currently no consensus in Europe. The lack of clear recommendations in the particle therapy community and the variety of beam delivery systems may be the source of this heterogeneity. In this context, WP2 can play an important role in encouraging moves to harmonise the QA programme for particle facilities.

- ii) **Reference dosimetry**. We are working on three projects in this area:
 - 1. **Dose-area product (DAP) dosimetry:** to explore an alternative to standard reference dosimetry, using large-area plane-parallel ionisation chambers.
 - 2. SOBP-based dosimetry validation:

dosimetry performed under reference conditions for a representative set of clinically relevant geometrical fields (SOBP) for comparison between predicted and measured dose. It includes the definition of a standard set of fields and comparison between centres.

- 3. Absolute dosimetry with a portable graphite calorimeter: calibration of ionisation chambers directly in the user beam quality via graphite calorimeter. The UK's National Physical Laboratory (NPL), which contributes to the work of WP2, is introducing this concept for particle facilities in the UK. WP2 plans to expand this collaboration with the rest of Europe.
- centres interested in dosimetry audits and end-to-end intercomparison tests. We are working on the following project:

 4. End-to-end audits with anthropomorphic phantoms: the MedAustron (Wiener Neustadt) group has developed an end-to-end test with a head anthropomorphic phantom, which can accommodate ionisation chambers and alanine detectors. This phantom and the related dosimetry approach will be used for comparing end-to-end results among centres.

Projects 1, 3 and 4 require on-site visits and networking between institutes. We believe that these projects could be partially supported by the translational access of the EU grant INSPIRE, and therefore we are preparing grant proposals. ▼



Morten Høyer presenting work of WP3

WP3: Education and training

We have conducted a survey of particle centres in Europe designed to map the needs for a particle therapy education and training programme. In total, 18 centres, nine of which already exist and nine of which are being planned or constructed, have responded. The survey results suggest that hiring experienced staff from existing particle centres occurs relatively infrequently, with centres educating and training their own staff instead. Most new centres need to employ and educate a large number of physicians, physicists and radiation technologists during the first years of operation. Established centres have an ongoing need for employing new staff as well as educating existing staff members. The survey showed that all centres send their staff for training at experienced centres prior

to the start of operation, but the percentage of staff members and the duration of their stay varied considerably. In total, 45 per cent of physicists stayed for a median of 45 weeks; 31% of physicians for a median of 20 weeks; and 26% of radiation therapists (RTTs) for a median of two weeks.

All new centres are willing to send their staff on application training provided by vendors, ESTRO or the PSI Winter School, whereas established centres are more reluctant to do so.

A first meeting for those interested in contributing to WP3 was held during ESTRO 37 in Barcelona. The meeting was well attended. We discussed the survey results, and decided to work on three educational initiatives: i) to integrate particle therapy into the ESTRO core

curriculum, including integrating particle therapy topics into existing ESTRO teaching courses, ii) to establish a masterclass in particle therapy, including a continuous training programme consisting of online teaching courses, workshops and homework, and iii) establishing an inter-centre staff exchange programme.

WP4: Image guidance in particle therapy (IGPT)

WP4 focuses on the importance of imaging and image guidance in particle therapy. We have described the current status of the 19 European particle therapy centres (PTCs) regarding image guidance, including available technologies and clinical procedures, based on the results of a questionnaire sent out in 2016. This survey has been analysed in detail with the support of the sub-WG coordinators, with a focus on image guidance for the different body sites (head and neck, brain, thorax, abdomen and pelvis). The findings have been published [6].

In February 2018, the WP4 coordinators organised a second workshop at the Proton Therapy Centre Czech, Prague, Czech Republic, which brought together 25 participants from 13 centres around Europe. We discussed the following items:

- Specific aims of WP4
- Achievements so far
- Update of the participants in the sub-WG
- Preparation for the next questionnaire
- Definition of the next steps towards establishing a target-specific code of practice and consensus guidelines for IGPT in the clinic. ▼

A literature review of the image-guidance results in particle therapy for each body site has been initiated in each of the sub-WG, considering different aspects, such as patient immobilisation, optimisation of imaging techniques, margins versus robustness, imaging matching methods, and current and new imaging technologies.

This review will form the basis for the new survey and for the clinical guidelines, which will be prepared, taking into account the peculiarities of image guidance for each body site. The next meeting of WP4 will be organised in early 2019 at the Proton Therapy Centre, Azienda Provinciale per I Servizi Sanitari (APSS) in Trento, Italy.

WP5: Treatment planning systems (TPS) in particle therapy

Progress has been made in a number of the sub-tasks being pursued as part of WP5. A collective list of TPS specifications has been published on the **ESTRO website** as a 'reference' document for future proton centres wishing to tender for treatment planning systems. In the 'planning standards' task, and driven by the IPACS consortium, we are developing planning inter-comparisons for head and neck cases between proton centres (a first paper has been submitted). We have also prepared a questionnaire, which will be distributed this autumn to all European proton centres on their policy of patient-specific verifications.

The CT calibration task group has been particularly active and has completed its survey of CT calibration procedures across Europe, the results of which have been published

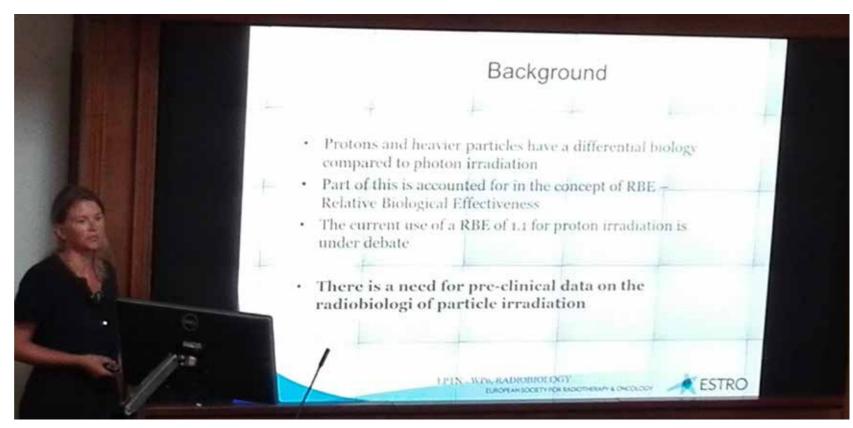
as a poster at ESTRO 37. In addition, a CT calibration inter-comparison phantom has been developed, which is currently travelling around the European proton therapy centres as part of a comprehensive comparison of CT calibration. We will have the results towards the end of 2018 or the start of 2019.

Finally, the task group on robustness has been reviewing and comparing robustness metrics on standard cases in order to move towards a recommended standard for evaluating and reporting plan robustness. In addition, we are initiating a number of new tasks, including LET in TPS, 4D planning and automated planning, the details of which will be discussed at the next meeting of the working group scheduled for November 2018.

WP6: Radiobiology

Protons and heavier particles have a different biology compared to photon irradiation. Part of this is accounted for in the concept of relative biological effectiveness (RBE). The current use of an RBE of 1.1 for proton irradiation is under debate and there is a need for preclinical data on the radiobiology of particle irradiation to support the clinic. The aim of WP6 is to form a network of clinical facilities with radiobiological research in order to facilitate research collaborations, standardisation of radiobiological experiments and to coordinate research in order to obtain the data.

To get an overview of existing and planned clinical facilities that use experimental radiobiology, a questionnaire was sent out ▼



Brita S. Sørensen presenting work of WP6

in 2017 to all centres that showed an interest in participation in WP6. Information was supplied from 13 centres and has been summarised in a publication [7].

WP6 had its first network meeting as a workshop at GSI in February 2018. Dr Michael Scholz was the local organiser. The two-day meeting was open to everyone with an interest in experimental particle radiobiology. In total, there were 28 participants from ten centres at the meeting. The intention was to bring people together to discuss points of shared interest, methodological issues and the future work of WP6. The meeting will be an annual event.

At ESTRO 37, as part of the EPTN session, WP6 gave a presentation on the aims and activities of their work.

WP7: Health economics

WP leader Yolande Lievens presented the work of this WP, the aim of which is to develop a knowledge base for the health economics of proton therapy (PT) and to support discussions on resource allocation, reimbursement and access to PT across Europe. In 2016 a survey was developed to collect basic economic data from PT centres. Unfortunately, the response rate was low, which resulted in too few data to be used for detailed modelling of costs.

Last year, Ulrike Kliebsch initiated a critical review of this survey, examining how easy it was to understand and the level of detail included. A recommendation of this review is to approach centres currently in operation, which can provide

stable and reliable cost and resource data, with a revised survey. Centres still in the planning or preparatory phase may need to correct and adapt their figures as part of their implementation phase. Another important aspect is to align the work to other initiatives within ESTRO (e.g. the health economics in radiation oncology (HERO) project) and EORTC (e.g. E2-RADIatE platform). To avoid redundant data collection and strengthen collaboration across work parties (specifically WP1), Yolande Lievens attended the WP1 meeting in September to discuss data capture strategies within the context of a clinical data registry to be set up by WP1 using EORTC infrastructure.

WP7 has published a paper on economic data registration needs [8]. It describes the background and characteristics of data collection for two modelling concepts which are necessary for a full economic assessment of particle therapy. The cost-effectiveness analysis shows the relative value of a new intervention compared to the standard of care. In addition, the affordability for the Society is evaluated via the budget impact analyses.

We will continue our efforts to redefine economic data capture. We believed that more involvement of administrative and/or financial staff from particle centres will better represent the users' perspective in this work party. ▼

Collaborative efforts

PTCOG

ESTRO and EPTN have signed a memorandum of understanding with the Particle Therapy Co-Operative Group (PTCOG) to collaborate on education, meetings and scientific exchange. Though largely based in the USA, PTCOG has sub-committees in a number of European countries.

EORTC

EORTC and ESTRO have recently launched a new initiative mentioned earlier in this report, E2-RADIatE (EORTC-ESTRO Radiation Infrastructure for Europe), a platform aimed at generating robust data that can be shared to improve clinical research and ultimately cancer treatment. E2-RADIatE has started off with two projects, Oligocare and ParticleCARE, the latter being named during the meeting in London.

ENLIGHT

The similarity of work between the EPTN and the European Network for Light Ion Hadron Therapy (ENLIGHT) originally launched by ESTRO in 2000 was highlighted. It was decided to explore and draw up a collaborative agreement that would benefit both networks.

INSPIRE

INfraStructure in Proton International Research (INSPIRE) is funded by the European Commission and was launched this year. INSPIRE complements EPTN activities and so has room for collaboration on the following activities: networking, transnational access and joint research activities. WPs (e.g. WP2, 5 and 6) are encouraged to explore collaborations with INSPIRE.

General discussion

The broader aim of EPTN, to integrate PT in radiation oncology, was reiterated. The network would benefit from better visibility on the ESTRO website, which will soon be addressed on the Society's new website. Participation of PT centres in the work of the WPs should be encouraged and be more inclusive. The annual meeting of the network is open to all PT centres in Europe. The col-

laboration with ENLIGHT should be clarified.

Due to the amount of physics input to EPTN, a physicist co-chair of the network has been recommended by ESTRO's scientific council. A broad consensus was quickly reached Dietmar Georg, medical physicist from Vienna, Austria, was later in September confirmed by the Board of ESTRO as co-chair of EPTN.

The next meeting of the EPTN will be in April or May 2019 at the ESTRO office in Brussels, Belgium.

On behalf of EPTN: Damien C Weber (Villigen, Switzerland) and Cai Grau (Aarhus, Denmark), EPTN organisers.

EPTN work parties

WP	Title	Coordinators
1	Clinical	Hans Langendijk (Groningen, The Netherlands) – Leader Roberto Orecchia (Milan, Italy), Karin Haustermans (Leuven, Belgium), Daniel Zips (Tübingen, Germany) Jacques Balosso (Grenoble, France), Esther Troost (Dresden, Germany)
2	Dose assessment, quality assurance, dummy runs, technology inventory	Oliver Jäckel (Heidelberg, Germany), Sairos Safai (Villigen, Switzerland), Stefan Menkel (Dresden, Germany)
3	Education	Morten Høyer (Aarhus, Denmark), Marco Schwarz (Trento, Italy)
4	Image guidance in particle therapy	Aswin Hoffmann (Dresden, Germany), Alessandra Bolsi (Villigen, Switzerland)
5	Treatment planning systems in particle therapy	Håkan Nyström (Uppsala, Sweden), Tony Lomax (Villigen, Switzerland)
6	Radiobiology	Manjit Dosanjh (Geneva, Switzerland), Bleddyn Jones (Oxford, UK), Jörg Pawelke (Dresden, Germany) Martin Prutschy (Zurich, Switzerland), Brita S. Sørensen (Aarhus, Denmark)
7	Health economics	Yolande Lievens (Ghent, Belgium), Klaus Nagels (Bayreuth, Germany), Ulrike L. Kliebsch (Villigen, Switzerland)

For more information on EPTN, visit: www.estro.org/about-us/governance-organisation/scientific-council/task-forces/european-particle-therapy-network
Or email Evelyn Chimfwembe@estro.org

REFERENCES

Publications in: *Radiotherapy & Oncology* Vol 128, July 2018 (special issue on proton therapy):

- Optimizing clinical research and generating prospective high-quality data in particle therapy in Europe: Introducing the European Particle Therapy Network (EPTN).
 Grau C, Baumann M, Weber DC DOI: https://doi.org/10.1016/j.radonc.2018.06.021
- [2] The EPTN consensus-based atlas for CT- and MR-based contouring in neuro-oncology.

 Eekers DBP, Ven L, Roelofs E, Postma A, Alapetite C, Burnet NG, Calugaru V, Compter I, Coremans IEM, Høyer M, Lambrecht M, Nyström PW, Romero AM, Paulsen F, Perpar A, de Ruysscher D, Renard L, Timmermann B, Vitek P, Weber DC, van der Weide HL, Whitfield GA, Wiggenraad R, Troost EGC on behalf of the taskforce "European Particle Therapy Network" of ESTRO DOI: https://doi.org/10.1016/j.radonc.2017.12.013
- [3] Radiation dose constraints for organs at risk in neuro-oncology; the European Particle Therapy Network consensus.

 Lambrecht M, Eekers DBP, Alapetite C, Burnet NG, Calugaru V, Coremans IEM, Fossati P, Høyer M, Langendijk JA, Romero AM, Paulsen F, Perpar A, Renard L, de Ruysscher D, Timmermann D, Vitek P, Weber DC, van der Weide HL, Whitfield GA, Wiggenraad R, Roelofs E, Nyström PW, Troost EGC on behalf of work package 1 of the taskforce "European Particle Therapy Network" of ESTRO DOI: https://doi.org/10.1016/j.radonc.2018.05.001
- [4] Proton therapy for paediatric malignancies: fact, figures and costs. A joint consensus statement from the paediatric subcommittee of PTCOG, PROS and EPTN.

 Weber DC, Habrand JH, Hoppe BS, Kayser CH, Laack NN, Langendijk JA, MacDonald SM, McGovern SL, Pater L, Perentesis JP, Thariat J, Timmerman B, Yock TI, Mahajan A

 DOI: https://doi.org/10.1016/j.radonc.2018.05.020

- [5] Prospective data registration and clinical trials for particle therapy in Europe. Langendijk JA, Orecchia R, Haustermans K, Zips D, Balosso J, Lacombe D, Lievens Y, Weber DC, Grau C, Troost EGC DOI: https://doi.org/10.1016/j.radonc.2018.06.001
- [6] Practice patterns of image guided particle therapy in Europe: A 2016 survey of the European Particle Therapy Network (EPTN).
 Bolsi A, Peroni M, Amelio D, Dasu A, Stock M, Toma-Dasu I, Nyström PW, Hoffmann A
 DOI: https://doi.org/10.1016/j.radonc.2018.03.017
- [7] Overview of research and therapy facilities for radiobiological experimental work in particle therapy. Report from the European Particle Therapy Network radiobiology group.