

## **Report from the Fifth Annual Meeting of the ESTRO European Particle Therapy Network Task Force**

9 April 2019, Brussels, Belgium

The fifth annual meeting of the European Particle Therapy Network (EPTN), a task force of the European Society for Radiotherapy and Oncology (ESTRO), took place at the ESTRO office in Brussels, Belgium. It enjoyed wide representation, as there were 44 participants from 33 institutions in 13 European countries. Dietmar Georg was introduced as an additional co-chair of the network. Dr Georg is head of the Division of Medical Radiation Physics in the Department of Radiation Oncology at the Medical University of Vienna.

Three more new particle therapy facilities have begun operating since the last meeting of the EPTN in London on 28 June. One is in Denmark, another in The Netherlands and the third in the UK.

The network was informed of the meeting of the European Commission's subgroup of the Steering Group on Proton Therapy, held in October last year to define the future of proton therapy and its access for European cancer patients. Formation of this subgroup/task force was initiated by the EU Commission-DG Santé and the European Investment Bank (EIB), which receives many requests for financial support from EU members to set up proton therapy centres. The subgroup will draw up a draft of a white paper on proton therapy, which should be available by the end of 2019, and will be disbanded once it has completed its allocated tasks.

The EPTN took part in the scientific programme of ESTRO 38, in Milan, Italy, 26-30 April 2019. It was also invited to present at the Particle Therapy Co-operative Group (PTCOG) meeting in Manchester in June 2019.



*EPTN meeting in progress at the ESTRO office in Brussels*

### **Collaborative efforts**

#### *PTCOG*

ESTRO and EPTN have held a memorandum of understanding with the Particle Therapy Co-Operative Group (PTCOG) since 2018, to collaborate on education, meetings and scientific exchange. During this meeting, it was felt that a closer collaboration with

PTCOG was not necessary at this time. EPTN this year was represented at the PTCOG 58 meeting, which was held between 10 June and 15 June in Manchester, UK.

### *INSPIRE*

NfraStructure in Proton International Research (INSPIRE) is funded by the European Commission. It was launched in 2017 and is made up of three components: networking, transnational access and joint research activities. These activities complement those of EPTN, which enables collaboration. WPs are encouraged to take advantage of these opportunities and collaborate with INSPIRE.

### *FUTURE OF EPTN*

EPTN was created in 2014. The network has expanded steadily and collaborates with other partners. It is well established in ESTRO as a task force and its particle therapy activities are integrated into ESTRO and EORTC. At this meeting, there was a discussion about whether there was a need to change EPTN's structure in ESTRO and perhaps become a committee. It was decided that EPTN should remain an ESTRO task force for as long as possible, since particle therapy is one of the many treatment options in radiotherapy and its proponents should aim to be completely integrated in the radiotherapy community. The way forward would be to extend EPTN's activities in the areas of clinical trials and education. It was thought that the network should work towards finding ways to standardise methodology and technology in particle therapy in order to be able to show the technology's benefits. This would also ease collaboration and networking.

Ways to boost EPTN's profile in ESTRO and externally should be explored, e.g. through the use of more communications channels of ESTRO and its European Cancer Foundation (ECF), to reach a wider audience of stakeholders than there is currently. Another possibility would be to create a communication working party to take care of such activities.

The next meeting of the EPTN will be on 25 March 2020 at the ESTRO office in Brussels. In the report below, you can read about our progress across our seven working parties.

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## **Report on the activities of Working Parties**

### **WP1: Clinical**

The main activities of working party 1 (WP1) are directed towards establishing the content of prospective data registries at a European level. A WP1 consensus meeting took place at Schiphol Airport on 5 September 2019. The content was agreed for a number of prospective data registries, including the generic assessment and tumour-specific registries for central nervous system, head and neck, breast, lung, oesophageal and prostate cancers.

A paper that explains the background and general aims has been published by the GREEN JOURNAL.

In the USA, a prospective data registry for paediatric patients has been launched. The proposal is that the EPTN should link as much as possible to this registry to prevent redundancy and to facilitate data sharing between the USA and Europe for future common projects. This is crucial given the low incidence and wide variety of different tumours. From EPTN, Beate Timmermann is leading this sub-task.

The European Organisation for Research and Treatment of Cancer (EORTC) and ESTRO are to set up a collaborative venture, to be called EORTC-ESTRO Radiation Infrastructure for Europe or, more interestingly, E<sup>2</sup>-RADIatE. It will comprise two projects: OligoCare and ParticleCare, which will form the EPTN prospective data registry. EORTC will set up the infrastructure for the IT database and will be the custodian of the data, while ESTRO is responsible for setting up the governance structure.

Under the auspices of EORTC, there are currently three proposals for a head-and-neck cancer trial to test the hypothesis that proton therapy results in less radiation-induced toxicity than photon therapy. Two of the planned randomised controlled trials will use an enrichment paradigm with or without a Dutch model-based approach. Other emerging international trials in oesophageal and breast cancer are also utilising the platform of EPTN.

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

As of May 2019, 30 participants in 22 centres based in 10 countries were contributing to WP2.

The 3<sup>rd</sup> WP2 workshop was held on 27 March 2019 at the ESTRO office in Brussels. The focus of the workshop was on (i) quality analysis (QA)/equipment survey, (ii) reference and absolute dosimetry and (iii) dosimetry audits. In the following, the main outcome of the workshop is summarised.

#### **i) QA/equipment Survey:**

The current analysis of the survey data collected in 2018 shows a significant variability among the responses, not only regarding the methods used for QA but also in the tolerances and types of tests. Before publication of the

outcome, WP2 has decided to investigate further the possible reasons for such diversity, in order to identify and remove possible biases. Some of the information that was collected is incomplete or of difficult interpretation, so it was decided that the centres that participated in the survey should be contacted again for a re-assessment of the data. In addition, some centres have recently started clinical operations and will be included in the survey as well.

WP2 will initiate a discussion and exchange among centres through the organisation of the first dedicated QA workshop in autumn 2019. All centres in the network are welcome to participate and contribute. Each centre will have time to explain their QA concept and experience in the form of a presentation. The workshop will be held over one or two days. It will provide a unique opportunity for interested parties to benefit from one another's experience and to understand the variability of the processes and methods used among the facilities. We are confident that the workshop will also help in drawing up robust and meaningful conclusions from the results of the survey.

ii) ***Reference and absolute dosimetry:***

The National Physical Laboratory (NPL) is working on a new UK code of practice for the use of absolute dosimetry in particle therapy. This is a UK initiative, which among other things proposes to calibrate ionisation chamber user beam quality directly, using a graphite calorimeter. NPL is to perform measurements at different centres to redefine the protocol and provide data for the update of Dosimetry in Radiotherapy (TRS) 398.

WP2 hopes to obtain funding and resources to expand the activities of NPL to the rest of Europe. In this regard, a first project proposal was submitted to the European Commission initiative, INfraStructure in Proton International Research (INSPIRE) for support through INSPIRE's transnational access (TNA) infrastructure. So far, two access providers have joined the project: the Paul Scherrer Institute (Villigen, Switzerland) and the Danish Centre for Particle Therapy (Aarhus, Denmark). NPL acts as the user group. The basic idea is that NPL would travel to these centres with its own equipment, which includes a graphite calorimeter, to perform measurements.

iii) ***Audits:***

The aim is to create a network of centres interested in participation in dosimetry audits and end-to-end inter-comparison tests.

A MedAustron (Austria) initiative in collaboration with NPL offers to the proton therapy community a dosimetry audit based on end-to-end testing. A few facilities in Europe could make use of this initiative.

As with the NPL initiative, WP2 hopes to be awarded funding to collect data from other centres. In this regard, MedAustron is also preparing a project

proposal to submit to INSPIRE TNA, in order to be able to visit and audit centres within the network.

WP2 recognises that some particle centres in Europe are not yet participating in its activities, and efforts will be made to contact these centres to encourage them to join the network.

### **WP3: Education and training**

The primary task of the latest work package was to survey staff at European proton centres to discover their needs for education and training. The survey revealed requirements for training in upcoming as well as in existing centres.

A second task was to seek the incorporation of particle therapy into the ESTRO core curriculum and the ESTRO School teaching courses. The ESTRO School has agreed to integrate proton therapy into courses where it is relevant. However, the School's overall strategy is to teach radiation therapy in general and not to add sections and teachers from the different radiation modalities such as MRI-linac, brachytherapy or proton therapy to each of the teaching courses. As an alternative, it was suggested that workshops could be established in, for example, planning of proton-therapy treatment to supplement the ESTRO School teaching course in particle therapy.

A third agenda item in the work package was to pave the way for a staff exchange programme between the European proton centres. The WP3 will organise a second survey, this time on the need and capacity for exchange between the centres. Staff can apply for ESTRO mobility grants, but there is no funding available for the host institutions. The WP3 will look into the possibilities of establishing generic training programmes and e-learning that will reduce the teaching load at the host centres.

### **WP4: Image Guidance in Particle Therapy**

Image guidance is critical to achieve high-precision particle therapy. However, imaging equipment, procedures and clinical workflows vary substantially between particletherapy centres. Currently, there is a lack of standardisation for image-guided proton therapy (IGPT).

The aim of this working party is to gain insight into the current practice parameters of IGPT and to drive harmonisation through the establishment of body-site specific consensus guidelines.

Within WP4, five sub-working groups are currently active:

1. Brain and head-and-neck (H&N) (Dante Amelio, Iuliana Toma-Dasu)
2. Thorax (Alexandru Dasu, Petra Witt-Nyström)
3. Abdomen and pelvis (Markus Stock, Christoph Fussl)
4. Extremities (Alessandra Bolsi, Juliette Thariat)
5. Cranio-spinal irradiation (CSI) (Petra Trnkova)

Within these sub-working groups, about 40 collaborators from almost all European particle therapy centres are represented. All imaging workflow stages are covered by a multidisciplinary team of radiation oncologists, medical physicists and radiation therapists. Recently, a radiologist joined the brain and H&N working group.

So far, three annual workshops have been organised. The most recent meeting took place over 21-22 February 2019 in Trento, Italy, and 21 colleagues from 10 European countries actively participated. Ten particle centres were represented; eight of which were in the process of treating patients. Nine participants were newcomers. The aims of the workshop were: (1) to work on the finalisation of a body-site specific survey to be sent out before the end of the year, and (2) to discuss ideas for future WP4-specific projects.

For the brain and H&N, and abdomen and pelvis, sub-working groups, all questions of the survey were reviewed and prioritised. The thorax group finalised its list of questions and worked on the restructuring and harmonisation of the format. The questions for the CSI sub-group require a careful last review by the collaborators. The part of the survey that concerns the extremities sub-group is in active progress.

Agreement was reached on how to proceed with the consensus guideline. Literature regarding IGPT for brain, breast and prostate treatment will be reviewed in the coming months. In parallel, the new survey will be sent out to all European particle therapy centres before the end of the year.

Several ideas were discussed for future WP4-specific projects. Among them were: the advantages and disadvantages of external and in-room patient positioning; the role of on-line imaging versus prior 4D-CT information; a comprehensive overview of setup accuracies for immobilisation tools; and end-to-end testing of imaging procedures. Agreement on a first WP4-specific project should be reached during the next workshop in 2020.

Furthermore, a need was identified to put together a wish list for vendors to be able to start a dialogue on solutions for body-site specific bottlenecks in current IGPT procedures and workflow steps.

The next WP4 workshop will take place on 5-6 March 2020 at MedAustron in Wiener Neustadt, Austria.

### **WP5: Treatment planning systems in particle therapy**

The WP5 is working on several sub-tasks in order to cover the most important aspects. For the sub-group that considers treatment planning system (TPS) specifications, a collective list of specifications has been published on the ESTRO website to aid and inspire future proton centre managers in their procurement processes. In addition, a dialogue with relevant vendors has been initiated to highlight and share ideas regarding future needs. The very active CT calibration sub-group has completed an inter-comparison with delivery of a CT phantom to the European proton sites. Results from this inter-comparison were reported at the ESTRO conference. A planning standards sub-group is working in close collaboration with the IPACS consortium. A first publication on H&N has been submitted, work on base of the skull is ongoing and publications on more body sites are to come. A TPS commissioning and validation sub-

group is focused on validation of MC-based algorithms and the particle specific aspects thereof, since that is presently lacking. Within the frame of the patient-specific QA sub-group, a workshop is planned, with the aim of considering improvements to efficiency without compromising safety. Finally, a new sub-group on 4D planning has been formed as well a LET sub-group to deal with the handling and incorporation of LET into the optimisation and plan calculations.

During active discussions in the WP5 group, new topics/areas of importance and interest are continually identified and as a result, a brainstorming session/senior-level discussion with doctors on artificial intelligence/deep learning and automation will be organised.

To conclude, the WP5 group is increasingly active and welcomes new members with an interest in the topics covered. It would in particular welcome non-physicist members to the group.

### **WP6: Radiobiology**

Irradiation with protons and heavier particles shows different biological effects compared with photon irradiation. This is partly accounted for in the concept of relative biological effectiveness (RBE). The current setting of RBE at 1.1 for proton irradiation is under debate, and there is a need for pre-clinical data regarding the radiobiology of particle irradiation to support the clinic. The aim of WP6 is to form a network of clinical with radiobiological research facilities in order to facilitate research collaboration and standardisation of radiobiological experiments and to coordinate the research in order to obtain the needed data.

In February 2019 WP6 held a workshop in Groningen with Peter van Luijk as local organiser. It was an open meeting for anybody with an interest in experimental particle radiobiology and 43 participants from 11 countries and 23 centres were present at the two-day meeting. The intention of the meeting was to get people together to network, and to discuss primary points of interest, methodological issues and future directions for WP6. The sessions were centred around the topics identified to be of primary interest at the first WP6 workshop: differential RBE, dose volume effects, normal tissue response, combination therapy, modelling, basic mechanisms, and new techniques. The programme included two presentations from participants, as well as discussions on the data that was needed and future directions to fill the gaps in the current knowledge. The presentations offered an update on the European INSPIRE and ENLIGHT projects, and on recent developments in the Dutch particle community with the establishment of a European facility for particle radiobiology research, IMPACT. There were also tours of the clinical facilities at University Medical Center Groningen (UMCG) and the experimental facilities at the KVI Center for Advanced Radiation Technology (KVI-CART).





*Participants at the WP6 workshop in Groningen*

### **WP7: Health economics**

Activities regarding health economics (HE) in proton therapy were presented by Yolande Lievens and Klaus Nagels.

Yolande Lievens discussed the current status of WP7. It is a very small working group that has more difficulties to develop activities than other WPs within EPTN. The relevance of cost-effectiveness and costing data remains unquestionable, but collecting real-world data is a big challenge. In collaboration with WP1, a simple form of collecting health-economic data during and after proton therapy will be implemented in the core data set for the OlicoCare and ParticleCare projects using the E2-RADlatE platform within EORTC.

Klaus Nagels presented results of some HE activities outside EPTN. A top-down approach was used based on published data from different sources (PTCOG, Mevion, etc.) regarding the budgetary impact of current treatment costs in the EU, current technologies and treatment changes (e.g. FLASH, hypofractionation) that may change and improve the health economic performance profile of particle therapy in the context of competing radiation modalities.



**EPTN WP Coordinators**

<b>WP</b>	<b>Title</b>	<b>Coordinators</b>
1	Clinical	Hans Langendijk ( <i>Groningen, NL</i> )-Leader Roberto Orecchia ( <i>Milano, IT</i> ) Karin Hausterman ( <i>Leuven, BE</i> ) Daniel Zips ( <i>Tuebingen, DE</i> ) Jacques Balosso ( <i>Grenoble, FR</i> ) Esther Troost ( <i>Dresden, DE</i> )
2	Dose assessment, quality assurance, dummy runs, technology inventory	Oliver Jäckel ( <i>Heidelberg, DE</i> ) Sairos Safai ( <i>Villigen, CH</i> ) Stefan Menkel ( <i>Dresden, DE</i> )
3	Education	Morten Høyer ( <i>Aarhus, DK</i> ) Marco Schwarz ( <i>Trento, IT</i> )
4	Image guidance in particle therapy	Aswin Hoffmann ( <i>Dresden, DE</i> ) Alessandra Bolsi ( <i>Villigen, CH</i> )
5	TPS in particle therapy	Håkan Nyström ( <i>Uppsala, SE</i> ) Tony Lomax ( <i>Villigen, CH</i> )
6	Radiobiology, RBE	Manjit Dosanjh ( <i>Geneva, CH</i> ) Bleddyn Jones ( <i>Oxford, UK</i> ) Jörg Pawelke ( <i>Dresden, DE</i> ) Martin Prutschy ( <i>Zurich, CH</i> ) Brita S. Sørensen ( <i>Aarhus, DK</i> )
7	Health Economics	Yolande Lievens ( <i>Ghent, BE</i> ) Klaus Nagels ( <i>Bayreuth, DE</i> ) Ulrike L. Kliebsch ( <i>Villigen, CH</i> )