Radiotherapy and Oncology 128 (2018) 1–3

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Editorial

Optimizing clinical research and generating prospective high-quality data in particle therapy in Europe: Introducing the European Particle Therapy Network (EPTN)

Cai Grau [a,*], Michael Baumann [b], Damien Charles Weber [c]

[a] The Danish Center for Particle Therapy, Aarhus University Hospital, Aarhus C, Denmark; [b] The German Cancer Research Center, Heidelberg, Germany; [c] The Paul Scherrer Institute, Villigen, Switzerland

The current issue of Radiotherapy and Oncology includes a series of scientific papers on the use of particle therapy (PT) for cancer treatment, including the first reports from the working groups of The European Particle Therapy Network (EPTN), a Task Force under the Scientific Committee of ESTRO [1–8]. The EPTN reports add to a significant amount of recent papers published in Radiotherapy & Oncology within the field of particle therapy [9–27].

Particle therapy (PT) offers both new opportunities for improvements in cancer care and new opportunities for high-quality research. The need to generate clinical evidence for PT is extremely important for the radiation oncology community. With high initial capital investment and personal costs, with the costs of servicing the hardware, the introduction of PT has been slow and difficult on the old continent. Most European countries have a high degree of public coverage of health care, and thus have also a regulated evidence-based system for investments in new and costly technology. Collaboration between PT centers for generation of scientific and clinical evidence is thus of critical importance.

There have been several European networks working in the field of PT, including ULICE, ENLIGHT and EPTN. The two former were funded by EU grants and have contributed significantly to the science and early clinical development of PT in Europe. ULICE was a 4-year project set up by 20 leading European research organizations, including 2 leading European industrial partners, to respond to the need for greater access to hadron-therapy facilities for particle therapy research. The ULICE project ended in 2014, leaving a substantial contribution of reports and white papers in the public domain. The ENLIGHT scientific network was established in 2002 to coordinate European efforts in hadron therapy research and continues to meet annually for a plenary meeting and educational sessions, focusing primarily on basic and translational research issues within ion beam therapy [8].

The EPTN was established in 2015 in response to the increase in number of clinical PT centers in Europe. The need to cooperate among centers and integrate PT in the framework of existing clinical radiation oncology research networks was identified as being of paramount importance. Especially the integration of PT into radiation oncology was a unique key aim of EPTN. 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. Therefore, ESTRO was asked to collaborate with EPTN and agreed to facilitate the group, and in 2017, EPTN was adopted as an official Task Force of ESTRO, reporting to the Scientific Committee.

The first meeting of the EPTN was hosted by ESTRO in Brussels in May 2015 and included a brainstorm on which areas of PT it might be interesting and suitable to work together. All major European centers interested in particle therapy were invited, with 28 centers and two research organizations (the European Organisation for Nuclear Research (CERN) and the European Organisation for Research and Treatment of Cancer (EORTC)) represented. Smaller working parties (WPs) with experts for different topics to further elaborate PT discussions in Europe were formed (Table 1). It was emphasized that the initiative should be fully inclusive and integrative, and all centers invited to participate in the WPs.

The second meeting in May 2016 was again held at the ESTRO headquarters in Brussels. This meeting saw 27 centers 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. Some key aims, deliverables and milestones were discussed, including the surveys and other work presented in the current issue of Radiotherapy & Oncology [3–7].

During the third meeting in April 2017, it was decided to use the platform of EORTC for a prospective data registration and potentially also for future multicenter clinical PT trials. It was strongly felt that using the EORTC network and clinical trial tools (1), not limited to but including databases that could handle information from multiple clinical, diagnostic and molecular sources and using the Quality Assurance digital platform [2] could benefit substantially the foreseen research performed by the members of EPTN. It was also decided to further integrate the activities of ENLIGHT and EPTN, in the first place by having back-to-back annual meetings, which will happen for the first time in London 2018. EPTN will also actively collaborate with the Particle Therapy Co-Operative Group (PTCOG), founded in 1985 with the mission of promote science, technology and clinical application of particles

* Corresponding author.
E-mail address: caigrau@dadlnet.dk (C. Grau).

https://doi.org/10.1016/j.radonc.2018.06.021
0167-8140/© 2018 Published by Elsevier B.V.

Table 1
Members of the seven work packages (WP) of the European Particle Therapy Network (EPTN).

WP	Title	Coordinators
1	Clinical	Hans Langendijk (Groningen, NL) Roberto Orecchia (Milano, IT) Karin Hausterman (Leuven, BE) Daniel Zips (Tuebingen, DE) Jacques Balosso (Grenoble, FR) Esther Troost (Dresden, DE)
2	Dose assessment and quality assurance	Oliver Jäckel (Heidelberg, DE) Sairos Safai (Villigen, CH) Stefan Menkel (Dresden, DE)
3	Education	Morten Høyer (Aarhus, DK) Marco Schwarz (Trento, IT)
4	Image guidance	Aswin Hoffmann (Dresden, DE) Alessandra Bolsi (Villigen, CH)
5	Treatment planning systems	Håkan Nyström (Uppsala, SE) Tony Lomax (Villigen, CH)
6	Radiobiology	Manjit Dosanjh (Geneva, CH) Bleddyn Jones (Oxford, UK) Jörg Pawelke (Dresden, DE) Martin Pruschy (Zurich, CH) Brita S. Sørensen (Aarhus, DK)
7	Health economy	Yolande Lievens (Ghent, BE) Klaus Nagels (Bayreuth, DE)

for cancer care. In 2013, PTCOG North America was additionally created as a non-profit professional society to foster collaboration between US centers and to develop education and training initiatives for PT to name a few aims. The key difference is that EPTN will interact with health care politics, the various European health care systems and professional societies as an integrated part of radiation oncology, utilizing the interdisciplinary structure of ESTRO.

EPTN will promote clinical research and generate prospective data that are key for the appropriate clinical application of this costly technology. It is interesting to note that although approximately 180,000 patients have been treated with ion beam therapy, most of them with protons, no conclusive data have emerged from these remarkable multi-institutional/international cohorts. The main reasons for this disheartening observation is that PT was usually delivered in the past in remote physics' research facilities with no clear connection with clinics and that the low number of such facilities using various beam delivery technologies hampered severally high-quality clinical research in PT. Importantly, the lack of networking between PT centers and the absence of astute trial methodology at that time additionally prohibited the generation of data in the field of particles. This will definitively change with the construction of a substantial number of PT centers in Europe and elsewhere embedded in hospital campuses using more or less homogeneous industry-generated hard-, firm- and software. Although these developments could foster data generation, a key to achieve this goal is the collaboration between members and the generation of prospective databases as proposed by Langendijk et al. in this issue of Radiotherapy and Oncology [7]. The EPTN network will also tackle some of the perceived limitations of PT, such as image-guidance, as decried by Hoffmann et al. in the same issue [3]. With the combined efforts of all these dedicated working groups and institutions, there is no doubt that European PT is ready for prime time.

References

[1] Weber DC, Abrunhosa-Branquinho A, Bolsi A, et al. Profile of European proton and carbon ion therapy centers assessed by the EORTC facility questionnaire. Radiother Oncol 2017;124:185–9.
[2] Fairchild A, Aird E, Fenton PA, et al. EORTC Radiation Oncology Group quality assurance platform: establishment of a digital central review facility. Radiother Oncol 2012;103:279–86.
[3] Hoffmann AL et al. Practice patterns of image guided particle therapy in Europe: a 2016 survey of the European Particle Therapy Network (EPTN). Radiother Oncol 2018;128:4–8.
[4] Lievens et al. Economic data for particle therapy: dealing with different needs in a heterogeneous landscape. Radiother Oncol 2018;128:19–25.
[5] Lambrecht M et al. Radiation dose constraints for organs at risk in neurooncology; the European Particle Therapy Network consensus. Radiother Oncol 2018;128:26–36.
[6] Sørensen BS et al. Overview of research and therapy facilities for radiobiological experimental work in particle therapy. Report from the European Particle Therapy Network Radiobiology group. Radiother Oncol 2018;128:14–8.
[7] Langendijk HA et al. Prospective data registration and clinical trials for particle therapy in Europe. Radiother Oncol 2018;128:9–13.
[8] Dosanjih et al. ENLIGHT: European Network for Light Ion Hadron Therapy. Radiother Oncol 2018;128:76–82.
[9] Adeberg S, Bernhardt D, Harrabi SB, Uhl M, Paul A, Bougatf N, et al. Sequential proton boost after standard chemoradiation for high-grade glioma. Radiother Oncol 2017;125:266–72.
[10] Arts T, Breedveld S, de Jong MA, Astreinidou E, Tans L, Keskin-Cambay F, et al. The impact of treatment accuracy on proton therapy patient selection for oropharyngeal cancer patients. Radiother Oncol 2017;125:520–5.
[11] Bauer J, Chen W, Nischwitz S, Liebl J, Rieken S, Welzel T, et al. Improving the modelling of irradiation-induced brain activation for in vivo PET verification of proton therapy. Radiother Oncol 2018;128:101–8.
[12] Belosi MF, van der Meer R, de Acilu Garcia, Laa P, Bolsi A, Weber DC, et al. Treatment log files as a tool to identify treatment plan sensitivity to inaccuracies in scanned proton beam delivery. Radiother Oncol 2017;125:514–9.
[13] Fung V, Calugaru V, Bolle S, Mammar H, Alapetite C, Maingon P, et al. Proton beam therapy for skull base chordomas in 106 patients: a dose adaptive radiation protocol. Radiother Oncol 2018;128:198–202.
[14] Gillmann C, Lomax AJ, Weber DC, Jäkel O, Karger CP. Dose response curves for MRI-detected radiation-induced temporal lobe reactions in patients after proton and carbon ion therapy: does the same RBE-weighted dose lead to the same biological effect? Radiother Oncol 2018;128:109–14.
[15] Lühr A, von Neubeck C, Pawelke J, Seidlitz A, Peitzsch C, Bentzen SM, et al. Radiobiology of proton therapy: results of an international expert workshop. Radiother Oncol 2018;128:56–67.
[16] Michiels S, Barragán AM, Souris K, Poels K, Crijns W, Lee JA, et al. Patient-specific bolus for range shifter air gap reduction in intensity-modulated proton therapy of head-and-neck cancer studied with Monte Carlo based plan optimization. Radiother Oncol 2018;128:161–6.
[17] Nenoff L, Priegnitz M, Janssens G, Petzoldt J, Wohlfahrt P, Trezza A, et al. Sensitivity of a prompt-gamma slit-camera to detect range shifts for proton treatment verification. Radiother Oncol 2017;125:534–40.
[18] Paulino AC, Mahajan A, Ye R, Grosshans DR, Fatih Okcu M, Su J, et al. Ototoxicity and cochlear sparing in children with medulloblastoma: proton vs. photon radiotherapy. Radiother Oncol 2018;128:128–32.
[19] Petr J, Platzek I, Hofheinz F, Mutsaerts HJMM, Asllani I, van Osch MJP, et al. Photon vs. proton radiochemotherapy: effects on brain tissue volume and perfusion. Radiother Oncol 2018;128:121–7.
[20] Rechner LA, Maraldo MV, Vogelius IR, Zhu XR, Dabaja BS, Brodin NP, et al. Life years lost attributable to late effects after radiotherapy for early stage Hodgkin

lymphoma: the impact of proton therapy and/or deep inspiration breath hold. Radiother Oncol 2017;125:41–7.

[21] Ribeiro CO, Knopf A, Langendijk JA, Weber DC, Lomax AJ, Zhang Y. Assessment of dosimetric errors induced by deformable image registration methods in 4D pencil beam scanned proton treatment planning for liver tumours. Radiother Oncol 2018;128:174–81.

[22] Shusharina N, Liao Z, Mohan R, Liu A, Niemierko A, Choi N, et al. Differences in lung injury after IMRT or proton therapy assessed by 18FDG PET imaging. Radiother Oncol 2018;128:147–53.

[23] Saager M, Peschke P, Brons S, Debus J, Karger CP. Determination of the proton RBE in the rat spinal cord: is there an increase towards the end of the spread-out Bragg peak? Radiother Oncol 2018;128:115–20.

[24] Unkelbach J, Bangert M, De Amorim Bernstein K, Andratschke N, Guckenberger M. Optimization of combined proton–photon treatments. Radiother Oncol 2018;128:133–8.

[25] Verma V, Rwigema J-CM, Malyapa RS, Regine WF, Simone II CB. Systematic assessment of clinical outcomes and toxicities of proton radiotherapy for reirradiation. Radiother Oncol 2017;125:21–30.

[26] Wohlfahrt P, Möhler C, Stützer K, Greilich S, Richter C. Dual-energy CT based proton range prediction in head and pelvic tumor patients. Radiother Oncol 2017;125:526–33.

[27] Zhang Y, Huth I, Weber DC, Lomax AJ. A statistical comparison of motion mitigation performances and robustness of various pencil beam scanned proton systems for liver tumour treatments. Radiother Oncol 2018;128:182–8.