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Current status and future trends in particle therapy – lessons from an interdisciplinary workshop

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Abstract

Purpose To provide an introduction to the special issue containing the proceedings of the workshop on cancer therapy using hadrons (proton, carbon ions or boron neutron capture therapy) that was held in Pavia in October 2023 and organized by CNAO and IAEA.

Methods Papers contained in the issue are briefly summarized.

Results This issue contains a collection of papers from the workshop that provide a great opportunity to learn about the status and progress of this technology.

Conclusions Particle therapy is exponentially growing worldwide. While several clinical trials are now providing convincing evidence of the effectiveness of the treatment in tumor control and reduced toxicity, the technology remains expensive and the cost effectiveness is still under debate. The IAEA-CNAO workshop provided a clear picture of the state of the art and future prospective of this technology.

Keywords Particle therapy · BNCT · Proton therapy · Carbon ions · Radiotherapy

Cancer therapy with accelerated charged has a long history (see the paper by Ugo Amaldi in this issue). According to the statistics of the Particle Therapy Co-Operative Group (PTCOG), in 2024 there are 120 proton and 14 carbon ion therapy centers in operation [1], and many more under construction. At the end of 2022, over 300,000 patients had been treated with protons and over 50,000 with C-ions [2]. However, notwithstanding the physical [3] and radiobiological [4] rationale, particle therapy has been often criticized for the high cost/benefit ratio – in particular, lack of level-1 evidence of superiority compared to X-ray therapy, but much higher costs [5–7].

In recent years, with the exponential increase of particle therapy centers worldwide, there is an accumulating clinical evidence that particle therapy can indeed reduce toxicity [8, 9] and improve survival in specific cases [10]. An additional benefit comes from a careful selection of the patients, i.e. identifying those patients that will benefit the most form particles compared to X-rays (see Orlandi et al. in this issue). Yet particle therapy remains more expensive, and an effort to build facilities more compact remains essential to democratize this technology [11, 12]. Moreover, the new facilities should have higher intensity to be able to exploit the FLASH effect [13] and increase conformality to reduce the margins around the target [14].

The workshop organized by CNAO and IAEA in Pavia in October 2023 addressed this issue with a highly interdisciplinary approach. The status of the heavy ion facilities in Pavia (Venchi et al.), Austria (Pivi et al.) and Marburg (Zink et al.) is described in this issue. A special emphasis was dedicated to clinical results for chordomas and chondrosarcomas (Fossati et al.), head and neck (Vischioni et al.), gynecological tumors (Barcellini et al.) and CNS (Harrabi et al.).

About the problem of health effectiveness of particle therapy, important contributions come from Krengli et al. and Livraga et al. and for cost reduction there are disruptive

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ideas about accelerator design (Rossi et al., Vretnar et al.) and beam delivery (Volz et al., Pullia et al.).

It is likely that the next breakthrough in particle therapy will come from biology, as described in the contribution of Story et al. and Scifoni et al., this latter focusing on FLASH with light ions.

Seven papers in the issue discuss status and perspective of boron neutron capture therapy (BNCT), a technology already introduced many years ago [15] but now experiencing an upswing thanks to the introduction of dedicated linear accelerators (see Kreiner et al.). Interestingly, CNAO in Pavia will be the first radiotherapy center able to offer protons, carbon ions, and BNCT (see Rossi et al. and Licitra et al.). The selection of the patients in CNAO will be a very interesting task, as the center can direct the patient to any hadron.

In conclusion, the CNAO-IAEA workshop demonstrated that particle therapy is an effective technology, but also that more research is needed to achieve the full benefit of light ions and neutrons in cancer cure. Part of research goes in physics and technology, with the aim of producing smaller accelerators and faster and more conformal beam delivery, also exploiting AI. Another large part goes in pre-clinical radiobiology, especially important for high-LET ions and neutrons. Biology and physics should then drive clinical research that still needs randomized trials to gather level-1 evidence of superiority. This research is highly interdisciplinary, and physicians, physicists, engineers and biologists are all needed in this effort. There will be soon many more proton, neutron and heavy ion facilities available, and it is essential that a global research effort proceeds in parallel to support these new opportunities. International co-operation is very important for this research and in this context PTCOG and IAEA can play an important role.

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Declarations

Conflicts of interest/Competing interests The author declares no conflict of inetrests.

References

1. PTCOG, Particle therapy facilities in operation. (2024). https://www.ptcog.ch/ (accessed February 16, 2024).
2. PTCOG, Patient statistics. (2022). http://ptcog.ch/ (accessed February 16, 2024).
3. Durante M, Paganetti H. Nuclear physics in particle therapy: a review. Rep Prog Phys. 2016;79:096702. https://doi.org/10.1088/0034-4885/79/9/096702.
4. Durante M. New challenges in high-energy particle radiobiology. Br J Radiol. 2014;87:20130626. https://doi.org/10.1259/bjr.20130626.
5. Lievens Y, Pijls-Johannesma M. Health economic controversy and cost-effectiveness of proton therapy. Semin Radiat Oncol. 2013;23:134–41. https://doi.org/10.1016/j.semradonc.2012.11.005.
6. Mitin T, Zietman AL. Promise and pitfalls of Heavy-Particle Therapy. J Clin Oncol. 2014;32:2855–63. https://doi.org/10.1200/JCO.2014.55.1945.
7. Schulz RJ, Smith AR, Orton CG. Proton therapy is too expensive for the minimal potential improvements in outcome claimed. Med Phys. 2007;34:1135–8. https://doi.org/10.1118/1.2717380.
8. Baumann BC, Mitra N, Harton JG, Xiao Y, Wojcieszynski AP, Gabriel PE, Zhong H, Geng H, Doucette A, Wei J, O'Dwyer PJ, Bekelman JE, Metz JM. Comparative effectiveness of Proton vs Photon Therapy as Part of Concurrent Chemoradiotherapy for locally Advanced Cancer. JAMA Oncol. 2020;6:237. https://doi.org/10.1001/jamaoncol.2019.4889.
9. Youssef I, Yoon J, Mohamed N, Zakeri K, Press RH, Chen L, Gelblum DY, McBride SM, Tsai CJ, Riaz N, Yu Y, Cohen MA, Dunn LA, Ho AL, Wong RJ, Michel LS, Boyle JO, Singh B, Kriplani A, Ganly I, Sherman EJ, Pfister DG, Fetten J, Lee NY. Toxicity profiles and survival outcomes among patients with non-metastatic Oropharyngeal Carcinoma treated with intensity-modulated Proton Therapy vs intensity-modulated Radiation Therapy, JAMA Netw. Open. 2022;5:e2241538. https://doi.org/10.1001/jamanetworkopen.2022.41538.
10. Yang JT, Wijetunga NA, Pentsova E, Wolden S, Young RJ, Correa D, Zhang Z, Zheng J, Steckler A, Bucwinska W, Bernstein A, Betof Warner A, Yu H, Kris MG, Seidman AD, Wilcox JA, Malani R, Lin A, DeAngelis LM, Lee NY, Powell SN, Boire A. Randomized phase II trial of Proton Craniospinal Irradiation Versus Photon involved-field radiotherapy for patients with solid Tumor Leptomeningeal Metastasis. J Clin Oncol. 2022;40:3858–67. https://doi.org/10.1200/JCO.22.01148.
11. Graeff C, Volz L, Durante M. Emerging technologies for cancer therapy using accelerated particles. Prog Part Nucl Phys. 2023;131:104046. https://doi.org/10.1016/j.ppnp.2023.104046.
12. Yan S, Ngoma TA, Ngwa W, Bortfeld TR. Global democratisation of proton radiotherapy. Lancet Oncol. 2023;24:e245–54. https://doi.org/10.1016/S1470-2045(23)00184-5.
13. Vozenin M-C, Bourhis J, Durante M. Towards clinical translation of FLASH radiotherapy. Nat Rev Clin Oncol. 2022;19:791–803. https://doi.org/10.1038/s41571-022-00697-z.

14. Lomax AJ. Myths and realities of range uncertainty. Br J Radiol. 2020;93:20190582. https://doi.org/10.1259/bjr.20190582.
15. Jin WH, Seldon C, Butkus M, Sauerwein W, Giap HB. A review of Boron Neutron capture Therapy: its history and current challenges. Int J Part Ther. 2022;9:71–82. https://doi.org/10.14338/IJPT-22-00002.1.