



# International Symposium on Ion Therapy: Planning the First Hospital-Based Heavy Ion Therapy Center in the United States

Aaron Laine, MD, PhD; Arnold Pompos, PhD; Michael Story, PhD; Steve Jiang, PhD; Robert Timmerman, MD; Hak Choy, MD

Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX, USA

## Abstract

Investigation into the use of heavy ions for therapeutic purposes was initially pioneered at Lawrence Berkeley National Laboratory in the 1970s [1, 2]. More recently, however, significant advances in determining the safety and efficacy of using heavy ions in the hospital setting have been reported in Japan and Germany [3, 4]. These promising results have helped to resurrect interest in the establishment of hospital-based heavy ion therapy in the United States. In line with these efforts, world experts in the field of heavy ion therapy were invited to attend the first annual International Symposium on Ion Therapy, which was held at the University of Texas Southwestern Medical Center, Dallas, Texas, from November 12 to 14, 2014. A brief overview of the results and discussions that took place during the symposium are presented in this article.

**Keywords:** heavy ion therapy; carbon ion therapy; charged particle therapy

## Introduction

Heavy ion therapy offers several theoretical advantages over conventional (photon and proton) radiotherapy, including higher biological effectiveness and a lower integral radiation dose delivered to healthy tissues surrounding the tumor, enabling dose escalation and leading to improved tumor control with less adverse effects [5]. Some of the advantages of heavy ions have already been confirmed, but there are many more expected physical, biological, and clinical promises that need to be confirmed via a thorough scientific approach. Only then will the full potential of heavy ions be uncovered, understood, and ready for clinical use.

In 2015, the National Cancer Institute awarded planning grants to the University of Texas Southwestern and to the University of California, San Francisco, to help develop plans for heavy ion beam research centers in conjunction with their planned heavy ion therapy center. As an initial step in establishing a national particle therapy research center, the first annual International Symposium on Ion Therapy was held at the University of Texas Southwestern Medical Center, Dallas, Texas [6], which was attended by radiobiology, physics, and clinical experts in heavy ion therapy from all over the world, and also by heavy ion vendors, to discuss the current state of the field and to propose future directions for further investigation and development.

## Clinical

Several heavy ion centers in Asia and Europe reviewed the planning, construction, and commissioning of their research and therapeutic facilities, providing insight into their

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### Corresponding author:

Hak Choy  
Department of Radiation  
Oncology  
University of Texas  
Southwestern Medical Center  
5801 Forest Park Rd  
Dallas, TX 75235, USA  
Phone: +1 (214) 645-7620  
hak.choy@utsouthwestern.  
edu

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respective experiences. It was concluded that a dedicated research bunker is essential for the success of any future research center. Current clinical results and outcomes were also presented, reinforcing the importance of the heavy ion therapy methods to be tested via thorough clinical trials.

An extensive discussion was held on the design and development of clinical trials investigating the benefits of heavy ion therapy. It was proposed that all patients treated with carbon ions be enrolled in a clinical trial in some fashion, with the goal of performing primarily translational, evidence-based, scientific research to improve therapeutic outcomes. Four research theme categories were identified in which the strength of heavy ion therapy could be demonstrated: (1) ablative and hypofractionated radiotherapy, (2) rational molecular targeted combination therapy, (3) overcoming therapeutic resistance, and (4) survivorship and quality of life. By narrowing our focus, the potential advantages will include sharing of resources, creating more cohesive grant applications, and exploiting or developing institutional strengths while prioritizing a team approach. The overall aim is to develop therapy that will be personalized, effective, tolerable, and cost-effective.

A few disease sites were discussed that could be initially studied to demonstrate the potential advantage of heavy ion therapy, including pancreatic cancer and oligometastatic disease for which current conventional methods cannot deliver sufficient therapeutic dose without causing significant toxicities.

In addition, with the goal of establishing a national particle therapy resource, ways in which to effectively and efficiently identify patients who may benefit from heavy ion therapy were proposed. Of interest was the current model used by The National Centre of Oncological Hadrontherapy in Italy, which has established external reference (referral) centers where knowledgeable teams evaluate patient suitability for carbon ion therapy. This would help to minimize patients' disappointment if they are unable to be treated with carbon ions.

## Radiation Biology

The establishment of an infrastructure that would facilitate effective biological research was stressed, which would include space for short-term housing of small and large animals, anesthesia, complete tissue culture and biological laboratories, and advanced animal imaging modalities. One of the major outstanding questions in regard to heavy ions is their relative biological effectiveness (RBE) and corresponding reduction of associated uncertainties. Determining a consensus RBE is critical for the development of uniform dose prescriptions among different existing and future centers. Several aspects of RBE were debated including what would be the most important end point to study—tumor or normal tissue, and if *in vitro* RBE measurements truly translate to *in vivo* effects. In addition, the volume effect of tissue irradiated can further complicate true biological outcomes. The potential biological advantages of other charged particles, such as helium and oxygen, were also reviewed. The role of radiogenomics going forward was discussed, and its ability to potentially identify tumors that may benefit from combined modality therapy, to predict normal tissue response, or to estimate risk of secondary malignancies from heavy ion therapy. An area of interest also included the potential for heavy ion therapy to promote a greater antitumor immunogenic state because it is more conducive to dose escalation and because of its higher RBE.

## Physics

Sophisticated image-guided patient setup and range verification techniques and *in vivo* tissue surveillance during heavy ion treatment are critical to facilitate the clinical studies proposed above. Accounting for motion, various techniques that could be used to manage and minimize this motion were proposed, which include breath-hold technique, abdominal compression, respiratory gating combined with fast rescanning or development of fiducial or markerless tracking and dynamic dose delivery. On-board/in-room imaging solutions would also be required for *in vivo* dosimetry, adaptive re-planning, and most importantly, for range verification. The role in developing and using fast and accurate Monte Carlo dose calculations, as well as how to attempt to incorporate uncertainties (range or RBE) into the development of a treatment planning system, was discussed.

## Heavy Ion Technology

Five renowned heavy ion therapy system vendors presented their current technology as well as their plans for short- and medium-term development of accelerators, beam delivery, patient positioning, imaging, and treatment planning systems. It was concluded that technology for future heavy ion facilities must include fast scanning delivery, fast ion switching options, and fast online imaging of both tissue and the delivered dose. In addition, the option to target the tumor from multiple directions was

highlighted as being critical to achieve the proposed clinical goals; hence, the inclusion of an ion gantry was suggested to be an essential part of the heavy ion center.

## Conclusion

Overall, a very lively and productive discussion was held on the above mentioned areas during the symposium. Valuable experience and advice was shared by the different international heavy ion centers, which greatly helped to establish a strong foundation for the development of a national particle therapy research center at the University of Texas Southwestern. Ongoing advances in the field proposed at this symposium will certainly inspire and push developments that will ultimately benefit all centers involved.

## ADDITIONAL INFORMATION AND DECLARATIONS

**Conflicts of Interest:** The authors have no conflicts of interest to disclose.

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