ISBN: 978-3-95450-168-7 doi:10.18429/JACoW-IPAC2015-THXC2

ION BEAM THERAPY WITH IONS HEAVIER THAN PROTONS: PERFORMANCE AND PROSPECTS

U. Linz, Forschungszentrum Jülich, D-52425 Jülich, Germany

Abstract

This presentation focuses on two aspects of the therapy with ions heavier than protons: technical equipment and rationale for the choice of ion. The part on equipment concentrates on accelerator and gantry. Biophysical, medical, and economical considerations will be discussed in the part featuring the choice of the proper ion.

INTRODUCTION

Whereas all ions have Bragg peak and magnetic deflectability in common, ions heavier than protons are characterized by a narrower dose peak, less lateral scattering, and an increased biological effectiveness. All of these properties render them interesting as ions for therapy. However, with increasing atomic mass ions tend to fragment after nuclear collision. The resulting lighter ions and neutrons cause tailing of the Bragg peak with a higher dose in the exit zone. The increasing number of neutrons per projectile are also a reason for increased cost due to shielding requirements. Another cost factor is the size of the accelerator and the gantry. Both are directly correlated with the choice of the ion. The question *which is the optimum ion* or *which ions do we need* is therefore one that influences future facility design.

ACCELERATORS FOR ION BEAM THERAPY

An accelerator system for ion beam therapy (IBT) has to be highly reliable, easy to operate and to maintain. In order to be competitive with other clinical treatment systems, the cost for operation, maintenance, and follow-up should be low.

All active IBT centers that utilize ions heavier than protons have opted for carbon ions and all these centers have a normal-conducting slow-cycling synchrotron (SCS) as accelerator. They value the established slow extraction method and the high beam stability of this accelerator type. A first design study of a compact (ø 6-10 m), superconducting SCS has been published by Noda et al. of NIRS [1]. A superconducting isochronous cyclotron is under development by IBA and intended for ARCHADE in France [2]. Plans for other accelerators such as the rapid-cycling synchrotron were presented in the past [3] but have not yet been put into action in any therapy center.

NECESSITY OF A GANTRY

State-of-the art for proton therapy, a gantry should also be conceived for an IBT center using ions heavier than protons, even though it is a significant cost factor. From a clinical point of view, external irradiation should be carried out from the optimum angle to reduce unnecessary radiation exposure, and the radiation beam should be directed to the target not the target to the beam.

The first IBT center with a rotating gantry for carbon ions has been HIT in Heidelberg, Germany. The gantry is 25 meters long, has a diameter of 13 meters, weighs 600 tons, moves with an accuracy of ±0.3º, and has a braking distance of only 1º. It is an engineering masterpiece but as a standard for IBT it is prohibitive.

A superconducting gantry is under development at NIRS which provides the same ion range but has only half the length and weight of the HIT gantry. The aperture size will be somewhat smaller than at HIT, but with 20x20 cm^2 it should be compatible with 3D scanning [4].

The non-scaling fixed-field alternating gradient gantry claims a reduction of the weight of the beam line by approx. 2 orders of magnitude (1.5 t vs. 135 t) [5]. Unfortunately, a working prototype of such a slimmed-down gantry has not yet been put into practice.

THE OPTIMUM ION

From a clinical point of view, a therapeutic ion beam should display as little as possible (low-LET) radiation in the entrance channel or plateau region to spare normal tissue. In the Bragg peak or target area the radiation quality should preferably be high-LET and of high relative biological effectiveness (RBE). Minimum fragmentation, a low neutron dose, and a high benefit-cost ratio are further requirements that the optimum therapeutic ion should meet. Despite decades of clinical experience with protons and carbon ions in particular, or helium and neon ions on a smaller scale, systematic experimental studies to find the optimum ion are lacking.

Simulation experiments illustrate that only ions up to boron (Z=5) stay significantly below an ionization density of 20 keV/µm in the entrance channel of a spread-out Bragg peak (SOBP) [6]. This is considered the lower limit of high-LET radiation. Carbon is borderline and oxygen and all heavier ions show definite unwanted high-LET behavior in this area with healthy tissue that should not be damaged.

Beyond the SOBP, ions up to boron show an insignificant dose tail of low-LET fragments. Carbon exhibits a short high-LET dose tail of 2-3 centimeters. For heavier ions, this unwanted fragmentation tail is further pronounced.

ISBN: 978-3-95450-168-7 doi:10.18429/JACoW-IPAC2015-THXC2

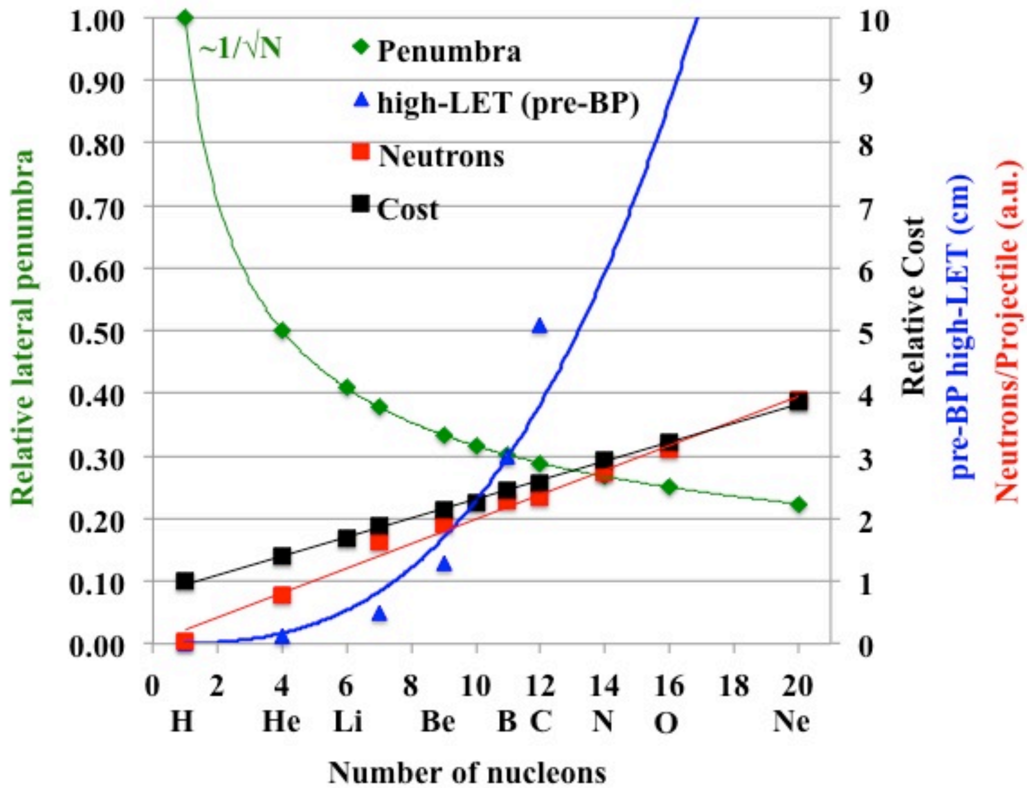

Figure 1: Therapy-relevant ion properties and cost as function of the number of nucleons (mass number). Lateral penumbra refers to the fall-off of absorbed dose from 80% to 20%. Pre-BP high-LET refers to the distance in front of the Bragg peak that receives high-LET radiation (≥20 keV/µm). Neutrons per projectile describe the production of neutrons in tissue for an ion beam of 26 cm range. Relative cost refers to the cost of an IBT facility with a normal-conducting synchrotron and one treatment room with gantry.

Figure 1 outlines how various therapy-relevant parameters vary with ion type. Lateral penumbra or range straggling decrease with the square root of the number of nucleons. The steepest gradient is from hydrogen to helium. The four times higher mass of He leads to only half the range straggling or lateral scattering as compared to H. This improves the therapeutic value of the respective ions but is opposed by their tendency to fragment after nuclear collision. The number of neutrons produced per projectile increases approx. linearly with the number of nucleons. This leads to unwanted dose to the patient and requires shielding to protect staff and environment. Relative to hydrogen, the number of neutrons produced in tissue increases by about a factor of four per additional nucleon. This means a 16-fold higher neutron production for He as compared to H. In addition, high-LET effects do not only occur as unwanted tailing beyond the Bragg peak. The higher ionization energy of the heavier ions extends the high-LET zone also in the pre-Bragg peak region. This increases the risk for damage to normal tissue in the entrance channel of the ion trajectory.

Cost for the accelerator and beam line scale with the magnetic rigidity of the ions, cost for shielding with their specific kinetic energy. The total facility cost shows a linear dependency on the mass number (cf. Table 1).

Table 1: First-order cost estimate for a basic ion beam therapy facility equipped with one treatment room with gantry (modified according to [7]).

Ion Type	Fixed Costs	Accelerator Costs	Shielding Costs	Total Costs
1H	1	1	1	1
4He	1	1.6	1.6	1.4
7Li	1	2.0	2.7	1.9
9Be	1	2.1	3.4	2.1
11B	1	2.2	4.2	2.4
12C	1	2.1	4.6	2.6
14N	1	2.2	5.5	2.9
16O	1	2.3	6.3	3.2
20Ne	1	2.5	8.1	3.9

CLINICAL TRIALS

Not the least due to its considerable cost, IBT has to prove its benefit in clinical trials. These should be prospective randomized controlled trials, as retrospective

ISBN: 978-3-95450-168-7 doi:10.18429/JACoW-IPAC2015-THXC2

cohort or case-control studies are more bias-prone and provide less compelling evidence. The huge number of possible variables, among them tumor type, tumor stage, study endpoint, and treatment alternative require perseverance. Trials can easily last a decade just for one parameter. This necessitates resources, continuity, and sustained compliance to master the numerous challenges.

CONCLUSION

Considering pros and cons of the various ions, a lithium or beryllium facility might be a worthwhile goal. In comparison to a carbon ion facility, the beam penumbra would only be about 15% larger. The high-LET region in front of the Bragg peak could be restricted to <2 cm or less than half the distance in the case of carbon, the neutron production would be approximately one third and the cost 20% lower. However, these differences would only be relevant with optimized technical and medical procedures in place, a situation which is far from being implemented. To enter the field of new, probably more favorable ions would take at least another two to three decades to carry out the clinical trials necessary for comparison with protons, carbon ions or any other competing treatment. Therefore, on the short run, it might be more meaningful to jointly focus on finding those areas where carbon ion therapy demonstrates its superiority and justifies the extra cost. Efforts should also include technical developments and treatment routines that reduce cost.

ACKNOWLEDGMENT

The author is indebted to many colleagues of the IBT community. Special thanks go to T. Kamada and K. Noda of NIRS, Chiba, Japan, T. Ohno of GHMC, Maebashi, Japan, M. Pullia of CNAO, Pavia, Italy, and J. Alonso of LBL, Berkeley, USA.

REFERENCES

[1] K. Noda et al., Recent Progress and Future Plan of Heavy-Ion Radiotherapy Facility, HIMAC, THOAB01, Proc. IPAC'14, Dresden, Germany (2014).

[2] Y.Yongen et al., Compact Superconducting Cyclotron C400 for Hadron Therapy, Nucl. Instr. Meth. Phys. Res. A 624, 47-53 (2010).

[3] D. Trbojevic et al., Lattice Design of a Rapid Cycling Medical Synchrotron for Carbon/Proton Therapy, WEPS028, Proc. IPAC'11, San Sebastián, Spain (2011).

[4] Y. Iwata et al., Development of a Compact Superconducting Rotating Gantry for Heavy-Ion Therapy, J. Rad. Res. 55, i24-25 (2014).

[5] D. Trbojevic et al., Superconducting Non-Scaling FFAG Gantry for Carbon/Proton Cancer Therapy, Proc PAC'07, IEEE, 3199-3201, Albuquerque, NM, USA (2007)

[6] I. Kantemiris et al., Dose and Dose Averaged LET Comparison of 1H, 4He, 6Li, 9Be, 10B, 12C, 14N, and 16O Ion Beams Forming a Spread-Out Bragg Peak, Med. Phys. 38, 6585 (2011).

[7] U.Linz, Physical and Biological Rationale of Using Ions in Therapy, in *Ion Beam Therapy*, U. Linz (ed.) Springer Verlag Heidelberg, p. 45 (2012).