Proposition:
The more important heavy charged particle radiotherapy of the future is more likely to be with heavy ions rather than protons.

Against the Proposition

Al Smith, Ph.D.
To be Clear:

- I support, without reservation, clinical research using carbon ions.
- I have the greatest respect for my colleagues who are engaged in carbon ion clinical research.

However: The proposition that carbon ions will be more important than protons for cancer therapy in the future is not supportable.
Things you should know about Carbon Ions
Carbon facilities cost more than proton facilities:

- Equipment costs ~ 4 times as much
- Total facility cost 2-3 times as much

\(^{12}\text{C}\) treatment facility: DKFZ Heidelberg, Germany
Heavy Ion Medical Accelerator at Chiba (HIMC)

Ministry of Science and Technology
(Mitsubishi, Sumitomo, Hitachi & Toshiba)

Fig. 1: Bird’s Eye View of HIMAC.
Isocentric gantries for carbon ions are large and expensive: 13 m diameter; 25 m length; **600 ton weight**. Therefore, most patients are treated with fixed beams.

Proton gantries:
- 360 ° proton gantries weigh 120 to 190 tons;
- 180 ° gantries weigh 70 to 90 tons.
RBE depends on
- energy/LET
- dose & fractionation
- tissue
  - late/early responding tissues
  - pO² status
  - position in cell cycle

"Treatment planning for $^{12}\text{C}$ ion beams is substantially more complex than for $^{1}\text{H}$ beams because varying LET and associated RBE values result in large uncertainties in RBE values.

"I think you should be more explicit here in step two."
Design of a 290 MeV 12C ion beam with a 6 cm SOBP for an assumed maximum RBE of 3.0. The impact of an error in selecting the RBE were the true RBE in the range of 2.5–3.5 is represented by the uncertainty bands around the dose in Gy(RBE) across the SOBP. **The RBE for Protons is ~ 1.1.**
Rat Spinal Cord Injury (Late responding normal tissue)

RBE as a function of dose

Higher RBE for OAR (lower doses)

Wilkins and Oelfke:
Carbon ion depth dose distributions have a tail of dose extending beyond the Bragg peak.

The tail develops from fragmentation of the carbon ions in the primary beam, due to nuclear interactions. Some fragments travel beyond the range of the primary beam for distances that depend on the energy of the primary beam. The tails are low physical dose and relatively high RBE with the net result being a non-negligible biologically effective dose in the fragmentation tail of carbon beams.
DIRECT COMPARISON OF BIOLOGICALLY OPTIMIZED SPREAD-OUT BRAGG PEAKS FOR PROTONS AND CARBON IONS : JAN J. WILKENS, PH.D., AND UWE OELFKE, PH.D.
Department of Medical Physics in Radiation Oncology, German Cancer Research Center (DKFZ), Heidelberg, Germany
Proton vs. carbon ion beams in the definitive radiation treatment of cancer patients: Herman Suit, et. al., Radiotherapy and Oncology 95 (2010) 3-22
“Should high LET provide a clinical advantage, one basis could be an inherently higher sensitivity of tumor than normal cells to high LET radiations, i.e. a higher RBE for tumor than normal cell irradiated under identical conditions. **Substantial experimental data do not provide support such a differential sensitivity.**”

The potential gain from high RBE & LET **may** be due primarily to a lower OER for **some** tumor cells.

Proton vs carbon ion beams in the definitive radiation treatment of cancer patients: Herman Suit, et. al., Radiotherapy and Oncology 95 (2010) 3-22
The “theoretical” advantages of carbon ions over protons have not been proven in a clinical setting. Studies performed thus far have shown an approximate clinical equivalence of both modalities.

Proposition: The more important heavy charged particle radiotherapy of the future is more likely to be with heavy ions rather than protons.

No matter how many ways I look at the word “important”, I cannot find a way to support the proposition.
Thank You!

Al Smith
RBE as a function of dose

Higher RBE for OAR (lower doses)

Wilkins and Oelfke:
Present and Future Particle Facilities

• Facilities in operation worldwide:
  – Proton: 36 (93,895 patients treated)
  – Carbon: 6 (10,756 patients treated)

• Facilities in planning stage or under construction worldwide:
  – Proton: 31
  – Carbon: 5

It is not reasonable to expect that the number of carbon ion facilities will even overtake, much less outnumber, proton facilities in the foreseeable future. It has recently been reported that in the US 20 institutions are seriously considering proton therapy. Many more patients will be treated with protons than with carbon ions.
Additional hurdles for Carbon Ions in the United States

• Continued pressure to decrease the costs of medical care will make it very difficult to build expensive carbon ion facilities.

• There is no FDA approval for carbon ion equipment and no predicate facilities as a basis for an FDA 510(k) application.

• There is no established reimbursement for carbon ion therapy, therefore, there is little incentive for investment in carbon ion facilities.
Bottom Line

• Even should carbon ion therapy prove to be a good treatment for some cancers, its expense and complexity will likely prevent the building of many carbon facilities. In such case, carbon ions will not have a major impact on cancer cure, because, to do so, large numbers of patients need to be treated.

• Therefore, carbon therapy will not be a more important treatment modality than proton therapy in the future.
"Particles, particles, particles."
RBE as a function of dose

- RBE decreases with increasing dose
- The lower the LET, the smaller the effect

Weyrather et al., IJRB 1999

Wilkins and Oelfke, IJROBP 2008