Radiation Therapy and Treatment Planning for Carbon Ions

Radiation Dosimetry I

Text: H.E Johns and J.R. Cunningham, The physics of radiology, 4th ed.
http://www.utoledo.edu/med/depts/radther

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Introduction

- Hadron therapy makes use of fast hadrons: non-elementary particles made of quarks and antiquarks
- There are two kinds of hadrons, classified according to their spins: baryons (half spin) and mesons (integer spin). Thus, the hadrons are baryons (proton [p], neutron [n]) and mesons (pion $\pi+$, $\pi-$ and π^o)
- Also - stripped nuclei of He (alpha-particles), C, N
- Often called “particle therapy”

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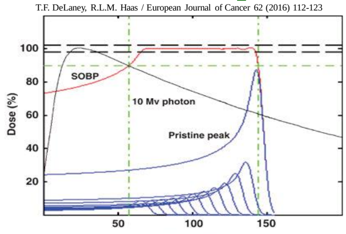
Relative Dose vs Depth: Protons

T.F. DeLaney, R.L.M. Haas / European Journal of Cancer 62 (2016) 112-123



- SOBP – spread out Bragg peak for coverage of extended target
- Range straggling – FWHM at the peak position is ~10mm
- No skin sparing in proton therapy (electron build-up region is <<1mm)

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Physics of proton transport

- Primarily Coulomb interactions with the orbital electrons of the target atoms
  - Direct excitation and ionizations of atoms
  - Energy loss per interaction is small → CSDA up until the very end of track (Bragg peak)
  - Max energy transferred W_m ~4 (m_ec^2/m_pc^2) T = 0.35 MeV at T=160 MeV; secondary electron range <1mm → dose is absorbed locally
  - Does not contribute to deflections of protons (p/e mass ratio is ~2000)
  - Leads to range straggling: Bragg peak will have some minimum width even if the incident beam has zero energy spread

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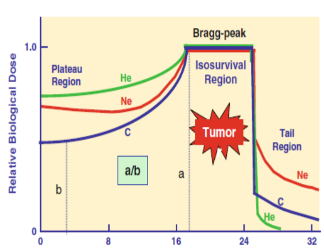
Ion Beam PDD



- Most important for RT property of hadrons – Bragg peak (‘spot’) at the end of the particle range
- For the same biological endpoint carbon ion beams have the largest peak to plateau ratio

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Physics of C-ion Transport

- The energy transferred to the atomic electrons during collisions with ions is very small (as for protons); the average energy loss is ~1 keV, max ~1MeV
- Due to *nuclear* interactions, a considerable part of the C-ions undergo fragmentation reactions, leading to a pronounced tail of light particles beyond the Bragg peak
  - There are also small amounts of gammas and neutrons
  - Target fragments are less important, due to the relatively low energy transferred by the recoil and the resulting very small ranges
- Nuclear fragmentation leads to a significant loss of primaries, ~4% per cm, i.e., at a depth of 15 cm, nearly half of the primaries are lost (plateau to peak ratio)

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Carbon Ion vs. Proton Beams

- A stripped nucleus of carbon (6p+6n) produces a sharper Bragg peak than the one produced by protons: the "spot" due to a mono-energetic C-ion beam has a FWHM of 3–4mm instead of 10mm
- To reach a 28 cm depth a C-ion must have initially about 4800 MeV (400 MeV/nucleon) instead of the 210 MeV of a proton. LET ratio: 4800/210=23 – leads to much higher RBE of C-ions

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Carbon Ion vs. Proton Beams

- Stopping power is $\sim z^2$, therefore the energy loss rate for C-ions is 36:1 compared to protons (25:1 when adjusted for the velocity for the same range)
- The increased mass of heavier ions as compared to protons leads to a significant reduction of the lateral penumbra of treatment beams (smaller deflection of a single ion due to its higher momentum as compared to protons)

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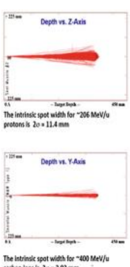
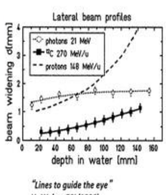
Carbon Ion vs. Proton Beams





- Comparison of intrinsic spot width for protons and carbon ions
- Lateral beam spread increases with depth

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Carbon Ion Sources

- Carbon ions are obtained from carbon dioxide (CO2) gas
  - First, subjected to impacts of highly accelerated electron beam, molecules dissociate and C^{+4} ions are extracted with applied electric field
  - Beam of C^{+4} ions is accelerated to 10% of *c*; the remaining two electrons are removed after beam passes through a sheet of carbon
- **Cyclotrons** (D's with accelerating E-field) and **synchrotrons** (circular accelerator ring with a set of bending magnets, synchronization between the applied electric field and the frequency of revolution of the particle, require larger space)

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Ion Beam Treatment Facilities

- The cost to build an ion beam facility is >$100 million, annual maintenance is ~$25 million
- There are 7 facilities in operation or 6 under construction for carbon-ion RT in the world (2016):
  - Operational: three in Japan, two in Germany, one in Italy, one in China (In Japan NIRS and HIT (1994), Hyogo Ion Beam Medical Center, (2002), and Gunma University Heavy Ion Medical Center, (2010); Institute of Modern Physics (IMP), Lanzhou, China (2006); National Center of Oncological Hadrontherapy (CNAO), Pavia, Italy (2011))
  - Under construction: two in Japan, one in Austria, two in China, one in Korea
- In the USA, *only proton facilities* are in operation or under construction
  - The technology has originated in the US, at Lawrence Berkeley National Lab (radiotherapy applications of neutrons, protons, and heavy ions 1938-1992)

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Ion Beam Treatment Facilities

- Interest in C-ion RT has recently emerged in US with the recent award of four grants, from two federal agencies
- DOE awarded $2 million grant to LBNL to design a much smaller superconducting beam-bending magnet
  - Varian Particle Therapy, which builds proton therapy systems, is contributing an $850 000 cryostat for testing the magnet
- DOE grant, $820 000, awarded to MIT and ProNova Solutions, a proton-beam supplier, for the design of an iron-free superconducting cyclotron (would weigh 1/6 of current cyclotrons)
- NCI awarded grants to UTSW and to the Univ. of California, San Francisco, to develop plans for heavy-ion-beam research centers (the primary focus of the NCI)

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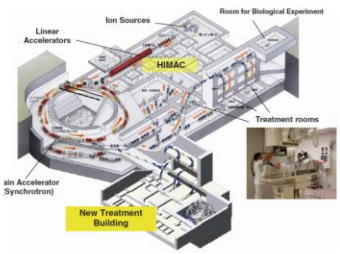
Ion Beam Treatment Facilities



- HIMAC (Heavy-Ion Medical Accelerator in Chiba) was built in 1993 at NIRS (the National Institute of Radiological Sciences)
- Started clinical application of carbon ions in 1994

HIMAC in Chiba (Japan): the world's first accelerator complex dedicated to cancer therapy

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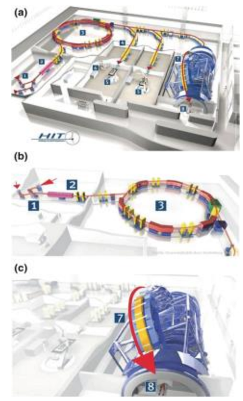

Ion Beam Treatment Facility

a) Synchrotron at the HIT in Heidelberg;
b) Schematic of the synchrotron;
c) Schematic drawing of the HIT gantry.

(1) The ion source accelerator: ion beams composed of positively charged atoms are produced. For protons, hydrogen gas is used. For carbon ions, dioxide is used
(2) A 2-stage linear accelerator: Ions are accelerated at high frequency up to 10 % of the speed of light
(3) The synchrotron: Six 60° magnets bend the ions into a circular path. After 10^6 orbits, ions are accelerated to 75 % of the speed of light
(4) The treatment room beam lines: Magnets guide and focus the beam of ions in vacuum tubes
(5) The treatment room: The beam enters through a window; the patient is positioned on a treatment table
(6) Position control: Digital images are obtained before irradiation to adjusts the position of the patient
(7) The gantry: weighs about 670 tons—600 tons of which can be rotated with submillimeter accuracy
(8) The treatment room in the gantry

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Ion Beam Treatment Facility

Radiation treatment room in the Heidelberg Ion-Beam Therapy Center HIT. The beam exits the gantry (weighs ~670 tons, RT room on top). Two rotation systems and digital X-rays are used to optimize the position of the patient guided by the images taken before irradiation.

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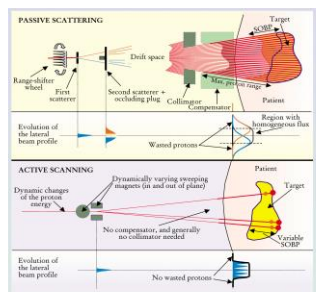
Treatment Implementation



- Spread-Out Bragg Peak (SOBP) principle is the same for all charged particles
- In active scanning the scan may be performed in discrete steps (spot scanning) or continuously (raster scanning)
- By changing the scanning speed or beam intensity, the dose delivered at each point in the target is controlled
- Challenge is to increase the speed of scanning

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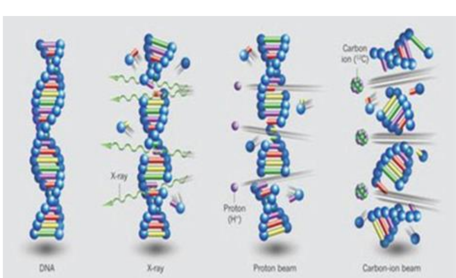
Ion Beam Treatment



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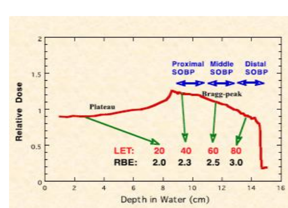
Characteristics of Carbon Ion Beam



LET and RBE of carbon-ion beams (290MeV, SOBP=60mm). For comparison, protons RBE~1.21

- Ionization density increases with depth
- Carbon ions offer enhanced radiobiological effects, which can be beneficial in the treatment of tumors resistant to conventional radiation

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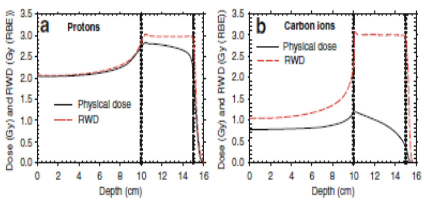
Carbon Ion vs. Proton Beams



Physical doses for proton and carbon ion SOBP required to yield a constant RBE-weighted dose (RWD) of 3 Gy (RBE) are shown. Each SOBP consists of pristine Bragg peaks with fluences optimized to yield a constant RWD

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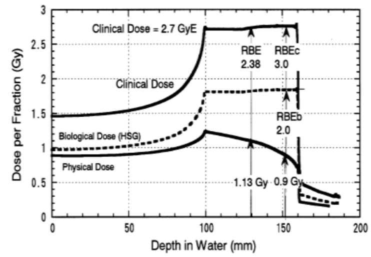
Characteristics of Carbon Ion Beam



Schematic method used to determine the RBE at the center of the SOBP for the clinical situation

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Carbon Ion Beam Dosimetry

- Basics of reference dosimetry are very similar to those of photon/electron TG-51 protocol
- Ionization chamber is the main dosimetric device
- IAEA TRS 398 protocol (calibration factor for ion chamber is obtained, the dose is obtained through a set of correction factors, including beam quality correction factor)
- No additional perturbation factors are used

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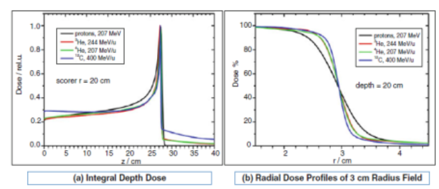
Carbon Ion Beam Dosimetry



Comparison of dose distribution characteristics of scanned monoenergetic beams of range ~28 cm each of ^{3}He , ^{4}He , protons, and ^{12}C ions. (**a**) Carbon ions have a fragmentation tail, which can add up to a significant distal dose when a sequence of energies is used to irradiate a fi nite-sized volume. Panel (**b**) shows that protons have a large penumbra and carbon ions have the smallest penumbra but that the sharpening of penumbra from ^{3}He to ^{12}C is very small.

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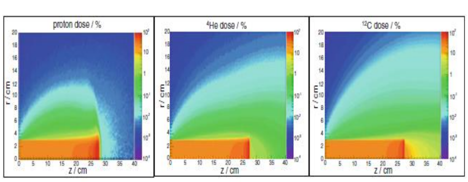
Carbon Ion Beam Dosimetry



Comparison of dose distribution characteristics of scanned monoenergetic beams of range ~28 cm each of ^{3}He , ^{4}He , protons, and ^{12}C ions. (c) The increase in lateral and distal low-dose halo for heavier ions.

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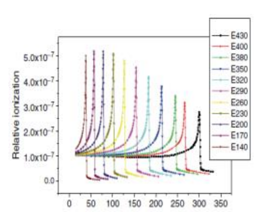
Carbon Ion Beam TPS



Measured integral percentage depth dose as an example of large plane-parallel ionization-chamber dosimetry

- For TPS commissioning a set of measured beam properties is obtained in water: PDD's, profiles, output factors

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Proton TPS Summary

- Proton beams stop - no exit dose
  - Although we don't know exactly where they stop
- Proton beams are more sensitive to
  - CT Hounsfield number/Stopping Power accuracy
  - Complex inhomogeneities
  - Organ motion and anatomy changes
- Proton plans are difficult to evaluate due to uncertainties
- Protons demonstrate excellent low dose sparing

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Treatment Planning for C-ions

- Radiotherapy treatment planning for heavier ions is very similar to proton therapy planning from the physical point of view
- Typically pencil beam models are used, which describe the three-dimensional dose arising from a single mono-energetic beam in water
- For the lateral dose distribution, typically a superposition of Gaussians is used, which exhibit widths which are varying with depth

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Ion Beam Properties

- The larger mass of the carbon ion makes it attractive than protons for therapy
- The extent of beam blurring (straggling) is inversely proportional to the square of the mass number
  - For the same range the Bragg peak is narrower with carbon ions at the end of the range
- Lower lateral beam spreading

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Ion Beam Treatments

- For CIRT increasing the dose per fraction tends to lower the RBE for both tumor and normal tissues, with slower RBE decrease for normal tissues
- This leads to significant reduction in overall treatment time and number of fractions with minor toxicities (in particular, CIRT can be performed more efficiently than PBT)
  - Practically implemented: single-fraction RT for early-stage lung cancer, single or two-fraction RT for liver cancer and 12-fraction RT for prostate cancer

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Ion Beam Treatments

- The selection of patients for CIRT is primarily based on the following 4 clinical criteria:
  1) loco-regional tumor growth
  2) tumor with no or low tendency to metastasize
  3) tumor that is highly resistant to conventional radiotherapy
  4) either cure rates are low or side effects with standard therapy are unacceptably high
- Studies show the potential number of cancer patients that could benefit from charged particle therapy ~13% -15% of all irradiated cancer patients

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Ion Beam Treatments

- There are several types of tumors which cannot be well treated with standard radiotherapy: pancreatic cancer, non-squamous cell head&neck cancer, rectal-pelvis cancer; carbon ion therapy is very effective
- Hirohito Tsujii (Chiba, Japan) treated inoperable pancreatic cancer with carbon ions: 50% of these patients survive for two years, which is double the survival rate seen for other treatments

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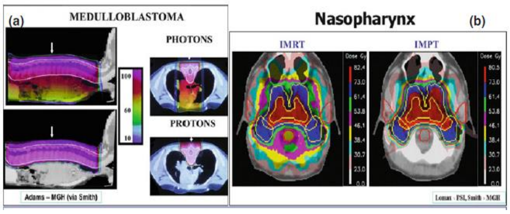
Treatment Planning



Photons vs. protons treatments examples: (**a**) Passively scattered proton therapy vs. 3D conformal therapy of medulloblastoma (courtesy of MGH). (**b**) IMRT vs. IMPT of nasopharynx (courtesy of Tony Lomax, PSI)

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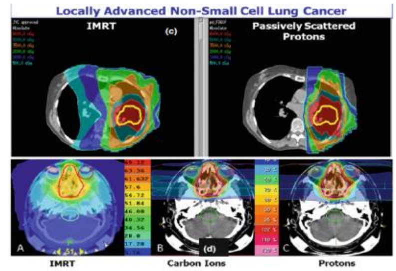
Treatment Planning



(**c**) IMRT vs. PSPT of locally advanced NSCLC
(**d**) IMRT vs. protons vs. carbon ions for base of skull

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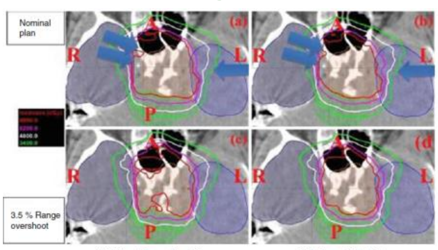
Treatment Planning: Motion Management



Motion management is often implemented with robust optimization

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Future of C-ions in RT

- More advances are needed to make treatment facilities easier to implement (superconducting magnets, advanced acceleration approaches, etc.)
- High cost will remain the main deterrent for wide acceptance of ion beam therapies – government funding is necessary at least in the US

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References

- “Carbon-Ion Radiotherapy”, Eds. H. Tsujii, T. Kamada, et al., Springer Japan, 2014
- “Particle Radiotherapy”, Eds. A. K. Rath, N. Sahoo, Springer India, 2016
- Overview of Carbon-ion Radiotherapy, Hirohiko Tsujii, J. Phys.: Conf. Ser. 777 (2017) 012032

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