Accelerators for Ion-Beam Therapy

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Christoph-Schmelzer Summer School

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Outline

Beam requirements



Cyclotron vs. synchrotron

Overview of some facilities

Recent developments and alternative concepts

Latest synchrotron R&D







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Beam requirements: p or ¹²C⁶⁺



De-facto, p <u>and</u> ¹²C⁶⁺ have their place in ion beam therapy ...

... and they impose very different requirements on the accelerator system.

Beam requirements: Energy

Energy: Defined by required penetration depth.

For 30 cm: **220 MeV** for p **430 MeV/u** for ¹²C⁶⁺



Requirements from dose distribution techniques



Logitudinal distribution (along beam axis):

- 1) **stacking** of a sequence of beams of different energy, or
- 2) use of a single beam of "matching" broad **energy distribution**, or
- 3) a combination of the two.

Accelerator system must provide a wide spectrum of ion energies for each ion species (p, ${}^{12}C^{6+}$, ...)

Requirements from dose distribution techniques

Lateral distribution (transverse to beam):

Durante and Paganetti, Rep. Prog. Phys. 79 (2016)



Pencil-beam scanning

"Paint" iso-energetic slice of the target volume.

Requires beam size, energy, and intensity to be **stable** over several **seconds**!

Required beam intensity

Rule of thumb:

$$D[Gy] \approx 0.1602 \times \phi \left[\frac{10^9}{cm^2}\right] \times \frac{S}{\rho} \left[\frac{MeV}{g/cm^2}\right]$$

with

- D applied dose in Gy = J/kg
- ϕ particle fluence in billions per cm²

 S/ρ density-normalised stopping force $dE/ds \cdot \rho$ at Bragg peak in MeV cm² / g

Typical dose for therapy: ~ 1 Gy per fraction

Typical S/ρ (for protons): ~ 5 MeV cm²/g

 \rightarrow Need ~ 10⁹ protons per cm² of tumor cross-section (\leftarrow Simplified 2D picture!)

 \rightarrow An (average) proton rate of few 10⁹ s⁻¹ (0.1 ... 1 nA) looks reasonable.

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Remarks

- (1) If the beam transport is lossy (e.g. due to energy degraders, collimators, ...) the intensity at the accelerator may need to be much higher.
- (2) Also much lower intensities should be available, e.g. for the fore-most pristine Bragg peak.



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Key requirements for a therapy ion beam

Energy: Defined by required penetration depth.

For 30 cm: **220 MeV** for p **430 MeV/u** for ¹²C⁶⁺

Intensity: few ~ 10⁹ protons/s

few ~ 10^{8 12}C⁶⁺/s

Time structure (raster scanning):

Quasi DC beam pulses of **1** ... **10** s duration

Stable emittance and energy.

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Use electric charge q = Qe of particles:

Electric potential difference \rightarrow Acceleration to kinetic energy E = qU





www.mpi-hd.mpg.de



Original realisation: Wideroe drift tube linac (1928)

Encyclopedia Britannica (2007)

cavity

beam

Radiofrequency Linacs

- (1) Instead of one large proton electrostatic field, use oscillating E fields,
- (2) synchronise particle motion with "accelerating" phase of E-field.

 \rightarrow continuous acceleration.

Alvarez structure of GSI's UNILAC

drift tubes

radio-frequency

power source

Later improved into **resonant** accelerator structures (*Alvarez*-type linacs). \rightarrow *Higher rf power, higher frequencies*.



Cyclotrons

Idea: Re-use the same HF acceleration gap over-and-over again.



E. Lawrence's original concept of the cyclotron (1934 patent):

D-shaped RF electrodes ("*Dees*") placed in a disk-like vacuum chamber and embedded in a large (near-homogeneous) static magnetic field.

 \rightarrow Radius of particle trajectory increases at each passage through the gap.

Classical cyclotron

E. Laurence (1934):

Radial acceleration:

$$\frac{F_{\perp}}{m} = \omega^2 \rho = \frac{q \, \omega \, \rho \, B}{m}$$

 \rightarrow constant (!) cyclotron-frequency:

$$\omega_c = \frac{q B}{m}$$



Kinetic energy after n turns:

 $E = 2 n q U_{RF}$

From $E = m \omega_c^2 \rho^2 / 2 \rightarrow \text{"cyclotron radius"}$ $\rho(n) = \frac{\sqrt{2Em}}{aB} = \frac{\sqrt{4nqU_{RF}m}}{qB}$ Classical case: machine size ~ $E^{1/2}$ Lawrence's first devices (Berkeley) had 1932: $\rho = 35 \text{ cm} \rightarrow p (4.8 \text{ MeV})$ 1937: $\rho = 47 \text{ cm} \rightarrow p (8.0 \text{ MeV})$ 1939: $\rho = 76 \text{ cm} \rightarrow p (16 \text{ MeV})$

Classical cyclotron: Stability of transverse motion



Vertical direction:

In the classical cyclotron, the magnetic field *B* decreases (slowly) with *r*.



"Automatic" focussing in the axial direction.

Relativistic cyclotron

For therapy, we need 220 MeV p (γ = 1.25) or 430 MeV/u ${}^{12}C^{6+}$ (γ = 1.46)

→ Relativistic corrections are not negligible!

 $\omega_c = \frac{qB}{m} \rightarrow \omega_{c,rel} = \frac{\omega_c}{\gamma} = \frac{qB}{\gamma m} \rightarrow \text{Breaks synchronicity with RF. Solutions?}$

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(1) Synchrocyclotron

(2) Isochronous cyclotron

Keep **constant B**, **tune RF** frequency.



CERN Synchrocyclotron: 600 MeV p (1957)

/ikipedia.org

Drawback: Only a short train of particles is in sync with RF ramp.

→ pulsed operation, lower average current. Keep **RF** frequency **constant**, **increase** *B* with *r*.



Most modern cyclotrons are isochronous.

→ cw operation

Relativistic cyclotrons

However, with positive gradient in *B*, there is no axial focussing "for free" anymore ...



Introduce "alternating gradients" (L. Thomas, 1938): Shape magnet faces to have "hills" and "valleys"

> Craddock, Rev. Accel. Sci. Technol. (2008)



 \rightarrow "Strong focussing" at sector edges.



Cyclotrons for ion-beam therapy

The cyclotron is *the most used* accelerator for medical purposes.

Neutron therapy: *(Lawrence & Livingston*)

 $p + {}^{9}Be \rightarrow {}^{9}B + n$ around 1936 @ 8 MeV $d + {}^{9}Be \rightarrow {}^{10}B + n$ cyclotron in Berkeley)

- Proton-beam therapy: Proposed by R. Wilson in 1946 First applied 1954 in Berkely (J. Lawrence & C. Tobias, at the 184"-cyclotron, Berkeley)
- Radioisotope factories for nuclear medicine.

Cyclotrons for ion-beam therapy

Isochronous cyclotron C230 by IBA

Designed for proton therapy.

Installed at 16 facilities.

Mass: 220 t

E = 230 MeV

I_{max} = 300 nA

$$\begin{array}{rl} B &= 2.2 \ \text{T} & \rightarrow \rho \sim 1.1 \ \text{m} \\ & (D_{\text{outer}} \sim 4.5 \ \text{m}) \end{array}$$



Cyclotrons for ion-beam therapy



COMET superconducting cyclotron

Developed by ACCEL / PSI (later Varian Medical) for proton therapy

Mass: 80 t

E = 250 MeV

I = 1 ... 850 nA

$$B_{\text{max}} = 3.8 \text{ T} \rightarrow \rho \sim 0.8 \text{ m}$$
$$(D_{\text{outer}} = 3.1 \text{ m})$$

www.psi.ch

Cyclotrons for ion-beam therapy: Energy selection

A cyclotron is a fixed energy machine ...



Cyclotrons for ion-beam therapy: ¹²C⁶⁺?

Cyclotron frequency:
$$\omega_c = \frac{q B}{\gamma m} \Leftrightarrow \frac{v}{\rho} \gamma m = q B \Leftrightarrow \frac{p}{q} = B \rho$$

Protons (220 MeV): $B\rho = 2.3 \text{ Tm}$
¹²C⁶⁺ (430 MeV/u): $B\rho = 6.6 \text{ Tm}$

"magnetic rigidity":

Relates <u>particle momentum and</u> <u>charge</u> to <u>magnetic field and</u> <u>bending radius</u>.

Arguably the most important quantity in accelerator science!

I.e. to go from protons to carbon ions, one needs to increase either the **magnetic field** or the **size** of the machine by a factor ~3.

Although they are very successful in proton therapy, there is no cyclotron for carbon-ion therapy yet.

Cyclotrons for ion-beam therapy: ¹²C⁶⁺?

There was a project ("ARCHADE") to install a carbon-treatment facility in Caen (France).

Should have been based on a superconducting cyclotron ("C400") developed by IBA.



In 2014, it was decided to build a proton facility first and the C400 project has been postponed ...





All carbon ion-beam therapy centres in operation use synchrotrons as main acceleration stages.



Advantage:







Today, most machines use a "separate function" layout, with individually specialised magnets.

Dipole \rightarrow bending







Quadrupole \rightarrow (de-)focussing







Synchrotrons: Stability of transverse motion



Synchrotrons: Stability of transverse motion
Synchrotrons: Stability of transverse motion

Not all tunes lead to stable transverse motion!

E.g. for an **integer tune**, particle coordinates repeat identically at every turn.

Bending errors dx' due to dipole imperfections accumulate, amplitudes grow beyond *acceptance*.





Half-integer tune: bending errors cancel every 2nd turn.

Synchrotrons: Stability of transverse motion



Synchrotrons: Stability of transverse motion



"Slow extraction"

Exploit instability of horizontal betatron motion at resonance conditions: $n f_{\text{Beta}} \approx m f_{\text{Rev}}$



Exploit instability of horizontal betatron motion at resonance conditions: $n f_{\text{Beta}} \approx m f_{\text{Rev}}$

The "art" of slow extraction:

Make sure particles enter resonance "one-by-one".

 \rightarrow if successful: Quasi-DC emitted beam of several s duration ("spill")

General approach:

Take advantage of the fact that f_{Beta} is not the same for every particle!

E.g. Betatron frequency depends on betatron amplitude if one considers higher field orders!





Example 1: Loma Linda University Medical Center (USA)

250-MeV *p*-synchrotron for ion-beam therapy.







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250-MeV *p*-synchrotron for ion-beam therapy.





Example 2: GSI experimental ¹²C⁶⁺ program

Slow extraction from SIS18 synchrotron via 3rd order (sextupole) resonance.



SIS18, GSI (Darmstadt)









Cyclotron beam vs. Synchrotron beam





- <u>cw-operation</u>: continuous train of short particle bunches.
- High intensity (high dose rates).
- <u>Ion intensity easily variable</u> (modulation of ion source current).

Cons

- <u>Fixed energy</u>: needs degraders (particle loss, radiation safety issues).
- <u>Heavy ions</u> (¹²C⁶⁺) would require very large magnet and chamber.







- Scalable to arbitrary *Bp*, can deliver <u>heavy ions</u>.
- <u>Variable energy</u>, (almost) no particle losses.

Cons

- Control of <u>beam intensity</u> is difficult.
- Pulsed operation, breaks between cycles
- Very high dose rates hard to achieve.
 - \rightarrow see advanced topics chapter!

Synchrotron ion-beam therapy facilities

Loma Linda, USA





1st hospital-based proton therapy centre
(since 1990)
Proton synchrotron designed by Fermilab
> 20000 patients treated

Synchrotron ion-beam therapy facilities



Chiba, Japan:

HIMAC (Heavy-Ion Medical Accelerator in Chiba, NIRS, 1994)

Two 800 MeV/u synchrotrons, for ions up to ${}^{40}Ar^{18+}$, mostly ${}^{12}C^{6+}$.

> 10000 patients treated with ${}^{12}C^{6+}$ (2015)

cern.ch

Synchrotron ion-beam therapy facilities



First hospital-based p/C centre in Europe.

> 7000 patients (2022)

First isocentric ¹²C⁶⁺ gantry.

Today, 3 more facilities in Europe, closely following the HIT design:

> CNAO (Pavia, Italy) MIT (Marburg, Germany) MedAustron (Wiener Neustadt, Austria)

Heidelberg, Germany

Heidelberg Ion-Beam Therapy Centre (HIT), from 2009, based on GSI experiments.



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Single-room solutions

Many efforts to down-size proton accelerators.

Many newly-installed systems are single-room solutions.

S2C2 superconducting synchrocyclotron (IBA) 2.5 m diameter.





Alonso and Antaya, Rev. Accel. Science Technol. 5 (2012) 227

C. Krantz Therapy Accelerators - Schmelzer Summer School - 27 July 2023

"Proteus ONE" single-room solution by IBA: 40 installations world-wide

Single-room solutions





Alonso and Antaya, Rev. Accel. Science Technol. 5 (2012) 227

mevion.com

S250 system by Mevion

Gantry-mounted superconducting synchrocyclotron. Installed at 15 sites.

2022: Development of a fixed-beamline variant ("S250-Fit") that fits into existing linac-cave.

Single-room solutions

Hitachi ProBeat V System

Compact p-synchrotron (250 MeV) with single-room solution





Umezava et al., Hitachi Rev. 64 (2015) 508



ca. 5 m

Gantries



Hitachi ProBeat proton gantry

hitachi, Itd.





 Key element to provide all the DoF in application one is used to from photons ...

Gantries

Heidelberg ¹²C⁶⁺ Gantry (HIT)

 $B\rho$ = 6.6 Tm

Overall weight 600 tons

In operation since 2012.





www.uniklinikum-heidelberg.de

Gantries

Superconducting ¹²C⁶⁺ gantry at HIMAC (2016)

Now produced commercially by Toshiba.





Raster-scanning pencil beam.

Lighter and smaller than normal-conducting gantry for heavy ions (\sim 300 t).

Iwata et al., NIM A 834 (2016)

Industrial ¹²C⁶⁺ machines ...



Toshiba Heavy Ion (¹²C⁶⁺) Therapy System

Installed at multiple sites in Japan and South Korea.

global.toshiba









Alternative accelerator concepts

Amaldi, Proc. of LINAC 2014

Linacs for proton therapy

Partly superconducting to obtain shorter machines.

Can vary energy in accelerator by (de-)activating individual cavities.



↑ AVO LIGHT Linac-only proton accelerator. (London, UK)

First medical trials scheduled for 2023.



Alternative accelerator concepts

Laser acceleration

Beam pulses of high intensity and broad energy distribution

- \rightarrow Energy selecting beam line
- \rightarrow No accelerator: compact
- \rightarrow High power (~ 100 TW) Laser required

Proposed 230 MeV proton gantry for patient treatment using laser acceleration.



Set-up for irradiation of mice using 25 MeV laser-accelerated protons from Dresden DRACO system. Kroll et al., Nature Physics 18 (2022) 316



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Synchrotron R&D

Cyclotron





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- <u>Ion intensity easily (and quickly) variable</u> (modulation of ion source current).

Cons

- <u>Fixed energy</u>: needs degraders (particle loss, radiation safety issues).
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Synchrotron





- Scalable to arbitrary *Bρ*, can deliver <u>heavy ions</u>.
- <u>Variable energy</u>, (almost) no particle losses.

Cons

Trying to

fix these

- Control of <u>beam intensity</u> is difficult.
- <u>Pulsed operation</u>, breaks between cycles
- Very <u>high dose rates hard</u> to achieve.
 - \rightarrow see advanced topics chapter!

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Remember: Slow extraction

Emitted beam is formed by slowly "feeding" particles to a betatron resonance.



Extracted SIS18 "spill"



There are two methods of slowly "feeding" the resonance:



Change betatron tune of the low-amplitude particles. Examples: Slow quadrupole ramp → changes linear focussing.

Slow acceleration (using cavities, induction cores, stochastic noise)

- \rightarrow changes particle momenta.
- → changes particle tunes via chromaticity.

There are two methods for slowly "feeding" the resonance:

(2) Excite horizontal betatron motion of stable particles

Horizontal RF-kicker electrode ~ in sync with horizontal particle tune.



"Transverse RF-Knock-Out" (RF-KO) technique.



Albrecht, PhD, 1996

- → First implemented at HIMAC. A. Noda, NIM A 492 (2002) pp. 253
- \rightarrow <u>Faster</u> and more direct control of destabilization rate.



RF-KO allows for fast (~ms) control of the average spill rate.





Krantz et al., Proc. of IPAC 2018

Major source of < 1 kHz spill ripple:

Instability of power converters

 \rightarrow Tune ripple

iumf.ca

"Pulsing" of separatrix sep. - X



Figure 3: Transfer function for focusing quadrupoles (blue), extraction sextupoles (orange) and main bends (green).



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Solution 1: Active tune stabilisation

Experimental Air Core Quad system at MIT, Marburg.





MIT: ¹²C⁶⁺ @ 167 MeV/u

Solution 2: Control of phase-space population

Use an elaborate RF-KO excitation spectrum to keep the "ripple region" of phase space free of particles.

A. Noda, NIM A 492 (2002) pp. 253







Recently realised at HIT, Heidelberg.





Cortés García, Feldmeier et al., NIM A 1022 (2022) Feldmeier et al., Proc. of IPAC 2022

Synchrotron R&D: Multi-flattop extraction


Synchrotron R&D: Multi-flattop extraction



Multiple extraction flats: Irradiate several energy slices in one cycle. Being implemented at HIT.





Synchrotron R&D: Multi-flattop extraction

Experimental (?) support by

Hitachi ProBeat system





Umezava et al., Hitachi Rev. 64 (2015) 508





Synchrotrons and Flash irradiation

HIT, Heidelberg

Experimental RF-KO extraction at FLASH dose rates > 40 Gy/s.

e.g.

M. Durante, W. Tinganelli, U. Weber, Physica Medica 94 (2022)

Weber, Scifoni, and Durante, Medical Physics. 49 (2022) 1974





Table 2: Intensities reached for FLASH conditions at HIT. Each number is the result of an optimisation for a particular experiment session. They do not show the technical limitation.

Ion	particles per spill	spill duration	intensity
		(ms)	(ions/s)
Protons	$1\cdot 10^{10}$	200	$5\cdot 10^{10}$
4 Helium $^{2+}$	$3.5 \cdot 10^9$	90	$3.9\cdot10^{10}$
12 Carbon ⁶⁺	$4.2 \cdot 10^8$	200	$2.1 \cdot 10^9$
16 Oxygen ⁸⁺	$2 \cdot 10^8$	180	$1.1 \cdot 10^9$

Synchrotrons and Flash irradiation



Take-home messages

Different accelerators serve different purposes.

Proton therapy accelerators and their R&D are almost fully industrialized by now.

Carbon therapy is still more closely tied to research facilities (Europe) ...

... but commercial ¹²C⁶⁺ solutions are getting more common (Japan).

Therapy accelerators *will* change as new technologies become available.