Facilities for Hadrontherapy- Requirements, Concepts, Status

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Abstract

Especially within the last years a remarkable dynamics can be observed with respect to the realization of new hadrontherapy facilities. The reasons are the development of new treatment modalities like the rasterscan-method, but also commercial aspects, arising from the number of patients that would profit from this treatment and the according demand of such facilities. The interest of industrial firms in constructing and operating 'turn-key' facilities has increased and at present several firms provide such facilities for proton treatment as well as for light ion (and proton) treatments.

This paper gives an overview of basic biophysical properties and the treatment modalities, the status of existing and planned facilities as well as developments on this field.

Biophysical properties and treatment modalities

Biophysical properties

For the treatment of localized tumors both photon- and particle irradiation is in use since many decades.

The concept is to achieve severe cell damages inside the tumor volume by applying a high dose with photon- or particle beams and to minimize the damage in the healthy tissue outside the tumor.

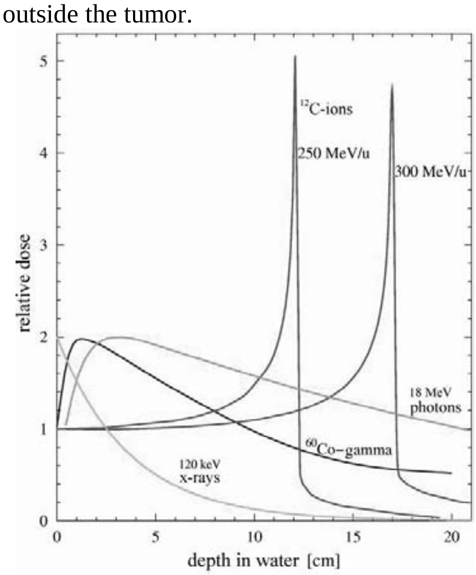

Fig. 1: Depth-dose distribution for photons and ions

Fig. 1. shows the depth-dose distribution for photons and ions: whereas photons have a maximum dose close to the surface, protons and ion beams deposit the dose maximum (Bragg-peak) near the end of their range, which can be adjusted with a proper selection of the particle energy. The 'inverse dose depth-profile' of hadrons gives ideal conditions for the treatment of deeply seated tumors, as the effects on the tissue in the entrance channel can be minimized. To cover a range up to 30 cm in tissue particle energies of about 220 MeV (for protons) or 430 MeV/u (for carbon ions) are requested. The advantage of C-ions in comparison to protons is their enhanced RBE (radiobiological efficiency) and their nearly constant beamsize over long ranges.

Treatment modalities

The treatment modalities can be distinguished between 'passive' and 'active' ones. For the passive modality the

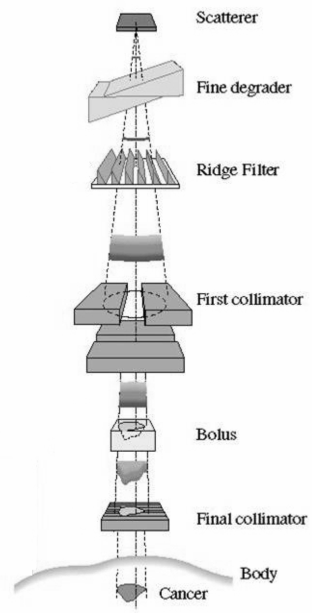

Fig. 2: 'passive' treatment modality

accelerator delivers a beam with nearly constant or only slowly varying properties (eg. energy); by means of various mechanical components (degrader, collimators, individual boli) the beam is shaped both in transverse and in longitudinal direction to achieve an appropriate conformity at the location of the tumor (see Fig. 2).

The concept of the 'active' treatment modality is to avoid all passive beam shaping components and to provide the appropriate beam properties from the accelerator. In Fig. 3 the 'intensity controlled' rasterscan procedure is described, which has been developed at the GSI and applied at GSI to about 400 patients with very good results during the last 10 years.

The principle of this treatment method is that the tumor volume can be composed of slices ('isoenergy-slices') of different depths. These slices are irradiated with ions of specific energies, correlated to the requested penetration depth. By a sequential treatment of such slices with adequate intensities the requested dose profile for the tumor volume is achieved.

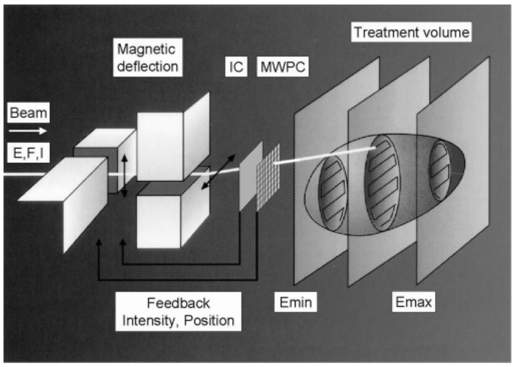

Fig. 3: 'active' treatment modality (intensity controlled rasterscan)

To cover the lateral dimensions of the tumor the ion beam passes two fast scanner magnets that deflect the ions both in horizontal and vertical direction after being accelerated to the requested energy in a synchrotron and slowly extracted.
The rasterscan control system determines the excitation of the scanning magnets to deposit the requested dose profile, measuring the number of ions at a specific irradiation point by means of ionization chambers and the position and beam width at each scanning point by means of fast multiwire proportional counters in front of the patient. When a required dose limit of an isoenergy-slice has been reached the beam extraction is interrupted very quickly (< 0.5 ms).
The requirements of the 'passive' modality to the accelerator-systems are rather low, as nearly constant beam paramneters are requested; the disadvantages of this modality are worse tumor conformity, compared with the 'active' modality and enhanced fragmentation due to scattering processes at the collimators and boli. The 'active' method on the other hand demands fast, active energy-variation to provide different penetration depths. Beside this energy variation also intensity- and beam spot variations at the treatment location on a pulse to pulse basis can be requested to minimize the treatment time.
At present only very few of the existing hadrontherapy facilities are equipped with the rasterscan treatment modality (PSI and GSI), but for the major part of the planned facilities the application of this 'active' modality is foreseen.

Status of Hadrontherapy

Status, Demand

Since around 1955 patient treatments with hadrons were performed with different ion species, mainly protons, but also light ions, like He and preferable carbon ions; in addition treatments with pions were investigated. The major part of treatment facilities are located in Europe, USA and Asia, especially Japan. Until now about 56000 patients were treated with hadrons, the largest fraction, nearly 90 % is attributed to p-treatments, followed by C and He-ions. About 30 facilities are at present in operation, of which most of the patient treatments (11000) have been performed since 1990 at the p-accelerator at the Loma Linda Hospital in USA (see Fig. 4).

	WHERE	WHAT	FIRST PATIENT	PATIENT TOTAL
Canada	Vancouver (TRIUMF)	p	1995	111
China	Wanjie (WPTC)	p	2004	270
England	Clatterbridge	p	1989	1584
France	Nice (CAL)	p	1991	3129
France	Orsay (CPO)	p	1991	3126
France	Orsay (CPO)	p	1991	640
Germany	Darmstadt (GSI)	C ion	1997	316
Germany	Berlin (HMI)	p	1998	829
Italy	Catania (INFN-LNS)	p	2002	114
Japan	Chiba (HIMAC)	C ion	1994	2867
Japan	Kashiwa (NCC)	p	1998	462
Japan	Hyogo (HIBMC)	p	2001	1099
Japan	Hyogo (HIBMC)	C ion	2002	131
Japan	Tsukuba (PMRC, 2)	p	2001	930
Japan	WERC	p	2002	33
Japan	Shizuoka	p	2003	410
Russia	Moscow (ITEP)	p	1969	3858
Russia	St. Petersburg	p	1975	1320
Russia	Dubna (JINR, 2)	p	1999	318
South Africa	iThemba LABS	p	1993	486
Sweden	Uppsala (2)	p	1989	738
Switzerland	Villigen PSI (72 MeV-Optis)	p	1984	4646
Switzerland	Villigen PSI (230 MeV)	p	1996	262
CA., USA	UCSF - CNL	p	1994	920
CA., USA	Loma Linda (LLUMC)	p	1990	11414
IN., USA	Bloomington (MPRI, 2)	p	2004	220
MA., USA	Boston (NPTC)	p	2001	2080
TX, USA	Houston (M.D. Anderson)	p	2006	114
FL, USA	Jacksonville (UFPTI)	p	2006	15

Fig. 4 :Hadron-treatment facilities, presently in operation (status. 2006)

Intensive studies have been performed to determine the tumor entities and the number of patients that could profit from the superior properties of hadrontherapy. These patients belong to the group, where localized tumors have been diagnosed, but where a failure of local control occurs (see Fig. 5). Due to these studies a significant patient number of this category would benefit from such treatments, especially those with tumours in the brain and base of the skull region, sarkoma and prostate carcinoma. This would result for Europe in a total number of about 100 patients per year for each 1 million inhabitants; e. g. for Germany about 8000 patients per year.

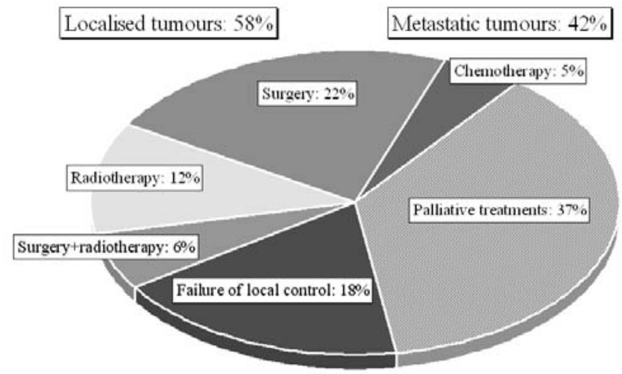

Fig. 5: Present situation of cancer treatment [1, 2]

<u>Facilities (planned or under construction)</u>

The good results of hadrontherapy and the demands led to major activities world-wide in designing and constructing according facilities. Fig. 6 gives a summary of the present situation, indicating that about 15 new facilities will come into operation within the next four years. Nearly all system are integrated into a hospital environment, in contrast to the past, when a great deal were located in nuclear research institutes. Whereas in former times technical developments were dominant aspects, at present a significant focus is put upon the medical aspects of patient treatment and follow-up procedures, that imply hospital based facilities with large patient throughput (> 1000 patients/year).

It should be also emphasized, that a drastically increased commercial interest is seen in such facilities, as the costs per patient treatment is around 20.000 €/patient. At present firms like SIEMENS, IBA and VARIAN are offerimg and constructing turn-key facilities and partly also overtake the operation.

The planned facilities (see Fig. 6) mainly deliver either protons or protons and light ions, preferably C-ions. Although C-ions are in some extend superior to p-beams, for special treatments p-irradiation (‘low LET’) is preferred or combined with ‘high LET’ C-irradiation.

With respect to the accelerator-technical aspects it should be noted, that according to the difference in the maximum ‘magnetic rigidity’ (for proton beams about 2.2 Tm, for C-beams about 6.3 Tm for a range of 30 cm) the application of different technologies has to be considered. Concerning economical aspects for proton beams both cyclotrons and synchrotrons are appropriate for the acceleration to the design energy; for C-beams, however, only synchrotrons are at present a cost-effective solution, because of their larger magnetic rigidity. As the application of the active treatment modality demands many energy-variations during a treatment session, the synchrotron technology is preferred for this case.

At present in Europe two compact, hospital based light ion therapy facilities are in the commissioning phase: in Germany the HIT-facility at the Clinics of Heidelberg [3] and in Italy the CNAO-facility in Pavia [4]. The basic

WHO, WHERE	COUNTRY	PARTICLE	MAX. CLINICAL ENERGY (MeV)	BEAM DIRECTION	NO. OF TREATMENT ROOMS	START OF TREATMENT PLANNED
RPTC, Munich*	Germany	p	250 SC cyclotron	4 gantries, with scanning, 1 horiz.	5	2007
PSI, Villigen*	Switzerland	p	250 SC cyclotron	Additional gantry, 2D parallel scanning, 1 horiz.	3	2007/08 (OPTIS2/ Gantry2)
NCC, Seoul*	Korea	p	230 cyclotron	2 gantries 1 horiz.	3	2007
UPenn	USA	p	230 cyclotron	4 gantries 1 horiz.	5	2009
Med-AUSTRON	Austria	p, ion	synchrotron	2 gantries 1-2 horiz.	3-4	2011?
Trento	Italy	p	? cyclotron	1 gantry 1 horiz.	2	2010?
CNAO, Pavia*	Italy	p, ion	430/u synchrotron	1 gantry? 3 horiz. 1 vert	3-4	2009?
Heidelberg/GSI Darmstadt*	Germany	p, ion	430/u synchrotron	1 gantry, raster scanning, 2 fixed beams	3	2007
iThemba Labs	South Africa	p	230 cyclotron	1 gantry 2 horiz.	3	2009?
RPTC, Koeln	Germany	p	250 SC cyclotron	4 gantries 1 horiz.	5	2009?
WPE, Essen*	Germany	p	230 cyclotron	3 gantries 1 horiz.	4	2009
CPO, Orsay	France	p	230 cyclotron	1 gantry, 4 fixed beams	3	2010?
PTC, Marburg	Germany	p, ion	430/u synchrotron	3 horiz. fixed beams, 1 45 degrees fixed beam	4	2010?
Northern Illinois PT Res.Institute, W. Chicago, IL	USA	p	250 accelerator	2-3 gantries, 1-2 horiz.	4	2011

Fig. 6. Facilities planned or under construction

specifications of HIT may be summarized as follows (the CNAO specifications are similar; for CNAO the installation of a gantry is foreseen as an upgrade) :

- ion-species : p, He, C, O
- ion-range (in water) : 20 - 300 mm
- ion-energy $^{(*)}$: 50 - 430 MeV/u
- extraction-time : 1 - 10 s
- beam-diameter : 4 - 10 mm (h/v)
- intensity (ions/spill)$^{(*)}$: $1*10^{6}$ to $4*10^{10}$

  $^{(*)}$ (dependent upon ion species)
- fast change of ion species
- 3 treatment areas to treat a large number of patients
- integration of an isocentric gantry

Both HIT and CNAO have a nearly identical concept for the source and linac section (double ECR-source, RFQ- and IH-DTL-linac for an acceleration to 7 MeV/u); the layout of the synchrotron is based on the PIMMS [5]-design, whereas for HIT a design developed at GSI has been chosen. The facilities are designed to treat more than thousand patients per year applying 15 to 20 sequential treatment fractions for each patient.

New developments

New technological developments are driven both from the requests of the oncologists to optimize the treatment technique and from the commercial side to design more compact and/or more cost effective solutions for the accelerator systems.
With respect to the patient treatment the following topics are in focus: optimization of quality assurance by improved imaging, the application of 'on-beam PET' ('Positron Emission Tomography') [6], optimizations of treatment planning programmes, treatment of moving organs and optimal 3-dimensional conformation of the tumor volume. Especially the last two topics have direct implications to the technology of accelerator systems.

Concepts of accelerator and beam transport systems
For an optimal 3D conformation of the tumor volume an irradiation with a horizontal beam is not sufficient, even though the additional horizontal degrees of freedom of the patient couch is considered. As most of the physicians avoid a major tilt of the patient, the various vertical irradiation directions are neglected. In part this can be taken into account by additional vertical beamlines, as realized at the HIMAC-facility in Japan and also planned for CNAO or by additional tilted beam lines, a.g. 45 degrees, as realized at the HIBMC facility in Hyoge / Japan. An optimal solution, however, is the installation of an 'isocentric gantry' with 360 degrees rotation perpendicular to the rotation axis of the patient couch.
For proton facilities the installation of such gantries is quite common; e.g. Loma Linda has installed 3 and the Munich Rinecker proton facility 4 gantries.

Light ion Gantry

Although p-gantries (excentric and isocentric) are in operation in many facilities, the world wide first isocentric 360^0-gantry for light ions is presently installed only at the HIT facility [7]. Due to the large maximum magnetic rigidity of 6.6 Tm the magnet components, which are normalconducting, are rather heavy, corresponding to a mechanical structure with a total moving weight of about 200 tons and a total weight of 600 to (including all beam line components and shielding counterweights).

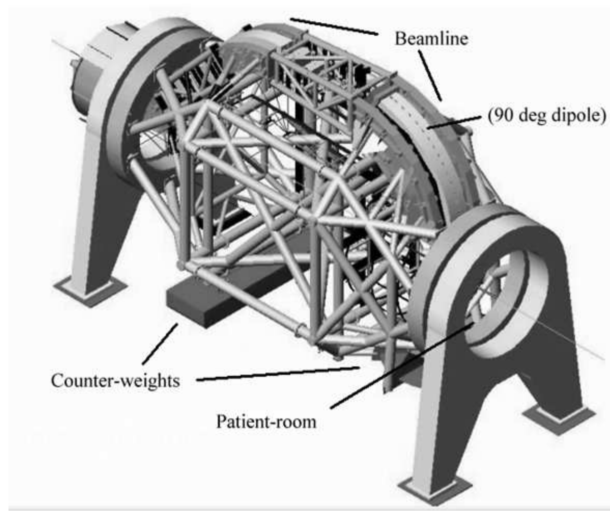

Fig. 7: Light Ion gantry (HIT)

Accelerator structures
At present tumor irradiation of moving organs (e.g due to breathing) is performed at few facilities (e. g. HIMAC) by 'gating' procedures: the actual position of the organ is detected and the beam delivery only takes place, when the position is inside a predefined tolerance, which means that beam extraction is gated with a signal detecting the position of the organ. This respiration gating technique requires fast beam switch on and –off possibilities (e. g. by the transverse knock-out technique for slow extraction out of the synchrotron). For an optimized treatment and an effective usage of the treatment time an active 3D position control of the beam is desirable. The lateral beam adjustment can be performed with the fast scanner magnets, used for the rasterscan irradiation. To cover the longitudinal-/ range deviations due to the movements a fast energy variation in the ms-range of the beam is requested. Tests with a 3D online motion compensator, using for the beam correction the scanner magnets and a dynamic PMMA wedge system to vary the ion range were successful [8]; an active, fast energy variation on a ms-time scale with the accelerator would be desirable. One proposed solution for this demand is the FFAG accelerator concept.

Besides the conventional cyclotron and linac-synchrotron alternative accelerating systems like the FFAG ('Fixed Field Alternating Gradient') synchrotron concept, which was developed about 50 years ago, are considered. In the 'non-scaling' FFAG design fixed field combined function bending magnets are foreseen; this design allows fast beam acceleration with compact machines without ramping the magnets; predesign studies pursue the objective to accelerate carbon beams up to 400 MeV/u, with repetition rate of 200 Hz, with compact and cost effective normal- or superconducting structures. Such

systems would allow a fast energy variation, requested for the treatment of moving organs.
The FFAG concept is also proposed in studies for new generations of Gantries with applications of compact superconducting combined function bending magnets [10].

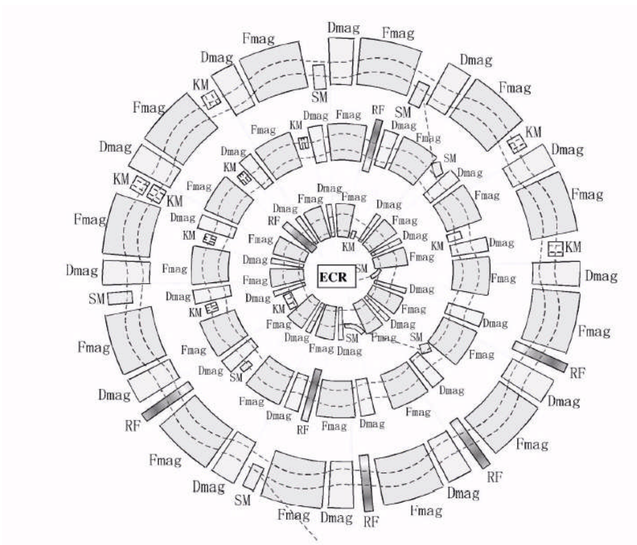

Fig. 8 triple-cascade radial-sector FFAG system (FFAG-design) [9]

One of the initiatives of the TERA foundation in Italy was the design of a linac-booster (LIBO) for proton therapy, operating at the very high operating frequenc of 3 GHz, capable to accelerate protons up to 250 MeV also with the possiblility of fast energy variations [11]. The evolution of this concept CABOTO (Carbon Booster for Therapy in Oncology) is suited to accelerate carbon ions.
As a long term vision towards compact treatment facilities developments of ion acceleration by means of high power lasers is under investigation at different labs. Due to observations that particle acceleration, especially electron and protons, on very short distances by means of high intensity short puled lasers (10- 100 TW, laser pulslength < 1 ps) occurs, investigations were performed to design very compact therapy facilities [12]. As the energy distribution of the particle beams from such a source is not peaked, special RF pahse rotating schemes in combination to beam cooling methods are proposed to form a monoenergetic beam out of this spectrum. [13].

In addition to new accelerator concepts the application of antiprotons were proposed. The arguments are the high RBE-factor. At present this proposal seems to be hardly realistc, also because of the enormous investment cots of such a facility.

Dual use of such a facility is also under discussion, using such systems for isotope production within the time intervals, in which no treatments take place.

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