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FACILITIES FOR RADIOTHERAPY WITH ION BEAMS STATUS AND WORLDWIDE DEVELOPMENTS

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Forty-five years after the first ion beam therapy in Berkeley around 25,000 cancer patients worldwide have been treated successfully. Ion accelerators, designed for nuclear research, delivered most of this treatment. The first hospital-based facility started operation in 1998 at Loma Linda California, the first for heavier ions at Chiba, Japan in 1994 and the first commercially delivered facilities started operation in 1998 at Kashiwa, Japan. In 2000, the Harvard Medical Centre, Boston, US, will commence operation and several new facilities are planned or under construction worldwide, although none in Australia.

This paper will discuss the physical and biological advantages of ion beams over x-rays and electrons. In the treatment of cancer patients ion beam therapy is especially suited for localised tumours in radiation sensitive areas like skull or spine. Heavier ions are also effective in anoxic tumour cells (found around the normally oxygenated cell population). An additional advantage of the heavier carbon or oxygen ions is the possibility of using in situ 'Positron imaging' of the ion range in the patient during the treatment. With modern spot scanning techniques a 3-dimensional target-conform treatment is possible, a technique which minimises radiation exposure to healthy tissue. The available accelerator and beam delivering systems will be discussed in respect of flexibility and simplicity for routine patient treatment in a hospital environment.

In conclusion, a possible scheme for an Australian Ion Therapy facility for the 21st century will be outlined.

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1. INTRODUCTION

About 100 years ago William Bragg discovered that charged particles, when passing through matter, deposit most of their energy at the end of their path. In 1946 Robert Wilson from the Lawrence Berkeley Laboratory proposed the use of proton beams for tumour therapy and in 1954 the first patient was treated in Berkeley with protons [1]. Since that time more than 25,000 patients have received treatment with protons or heavier ions worldwide at around 20 centres. Most of these treatments have been carried out at accelerators planned for and used by nuclear physicists and not designed for routine hospital-based therapy.

Many of these accelerators are limited in energy (below 100 MeV) and thus the possible maximum range of the protons to less than 7.5 cm. Hence the reason why nearly 50% of all patients so far have been treated for eye diseases with remarkably high success rates. Incidentally, it was an Australian ophthalmologist (I. Constable from Perth) who in the late sixties took part in the first studies at the Harvard Cyclotron Laboratory showing that proton beams could be used to treat eye tumours. More details on facilities and numbers of patients are summarised in Table 3 (Appendix 1). In parallel to this experience with patients, huge effort went into radiobiological research of the interaction mechanisms of energetic ions in living material, resulting in a profound knowledge of the processes involved [2] [3]. This information gives the groundwork for advanced biology based treatment planning computer programs.

In 1992 the first hospital-based proton therapy facility started operation at the Loma Linda University in California and the first heavy ion therapy facility at the NIRS (National Institute of Radiological Science) in Chiba, Japan, in 1994. Today, proton therapy facilities are commercially available from several companies and 10 new centres are under construction or funded worldwide, most of them in Japan and the US.

Priority in the progress in radiotherapy was always given firstly to lesser dose to healthy tissue and secondly to better target-conform treatment. For both points ions and spot scanning are the answer for future improvements. Why did it need so long to take advantage of the precision of proton therapy? Mainly because there was no similar precise imaging technique available before CT (Computer Tomography) and MRI (Magnetic Resonance Imaging) were introduced in the 1970's. With the precision in imaging it now makes sense to go for precise target conform treatment of deep-seated tumours.

Six monthly meetings, dedicated to particle therapy are organised by the Proton Therapy Co-Operative Group (PTCOG) based at the Harvard University in Boston, US. An information newsletter on particle beam therapy, 'Particles' is edited twice a year by Janet Sisterson of the Massachusetts General Hospital and is available on the Internet [4]. Several books have been published on the medical, biological and technical aspects of proton and heavy ion therapy [5] [6].

2. PHYSICAL PROPERTIES OF ION BEAMS

Protons and heavier ions have a limited range and deposit the highest dose at the end of their path through matter. This phenomenon is called the Bragg peak. To adjust the narrow peak to the thickness of a tumour the proton energy has to be varied to superimpose several Bragg peaks to a so-called spread out Bragg peak (SOBP) (see Figure 1) [7].

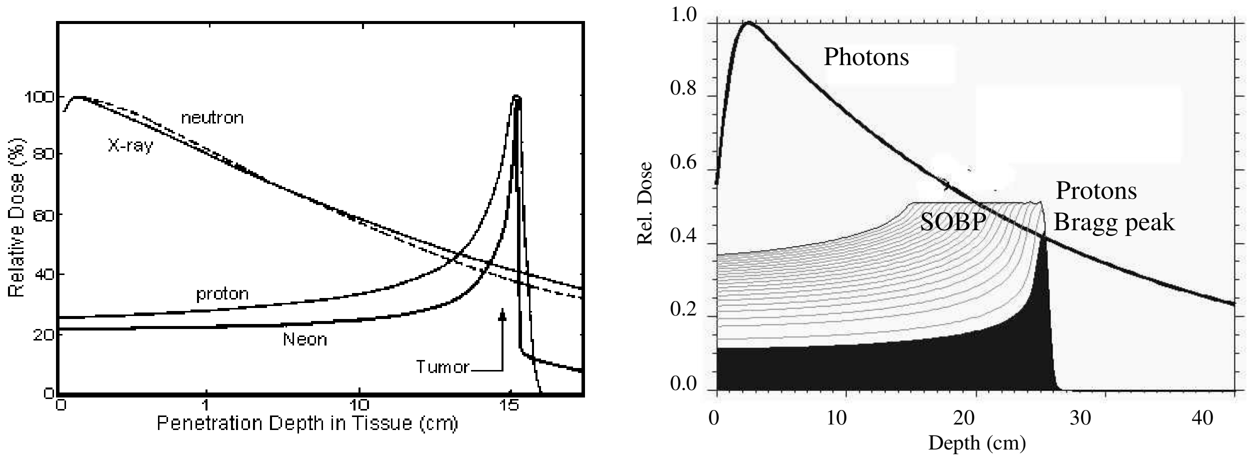

Figure 1 a) Depth dose profile for several types of radiation. Proton and ion energy adjusted to 15 cm range [26]. b) Spread out Bragg peak [7]

This is quite different from photons (x-rays) which have the highest impact at, or short after, the surface (depending on their energy) decaying nearly exponentially inside matter. In regard to dose or damage to a tumour inside the body, photons deliver the highest dose before and also a considerable amount behind the tumour. In contrast, ions deliver a smaller dose to the tissue before, most of their energy inside a tumour and none behind. In addition, there is very little dose delivered besides the planned volume. Thus, particle therapy can be much better target conform than treatment with photons (or neutrons or electrons) and allows the treatment of deep-seated tumours in the vicinity of radiation sensitive tissue like brain stem or spinal cord. These advantages are also valid for multiple field treatment where one can choose to spare healthy tissue by the same factor (reducing the normal tissue complication probability (NTCP)), or one can apply fewer fields for the same dose to the tumour (reducing the cost of the treatment), or one can increase the dose to the tumour while retaining the dose to the healthy tissue (NPTC) thus improving the tumour control probability (TCP) (Figure 2) [8].

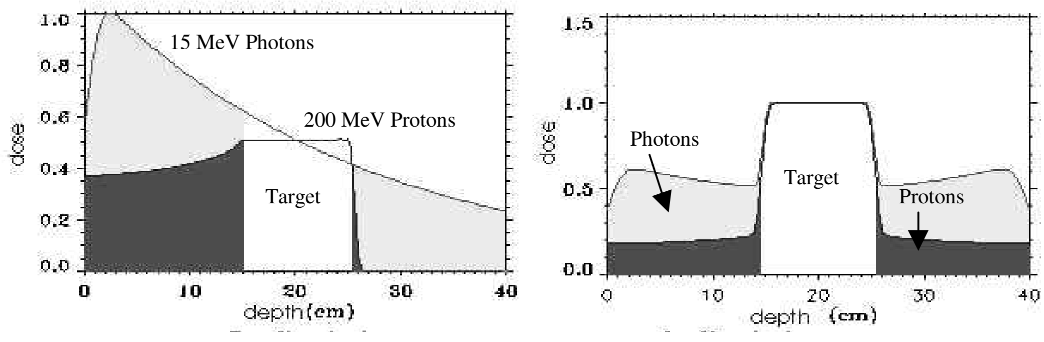

Figure 2. Comparison of proton SOBP and photon dose distribution for one field and four fields [7].

To reach deep-seated tumours a range of 30 cm is agreed to be necessary. This corresponds to a maximum necessary energy for protons of about 230 MeV (about 10% less for variable energy accelerators) and for carbon 430 MeV/u (Figure 3). Charged particles can be guided and focused by magnetic fields. This enables the delivery of the ion beam to various treatment areas and the scanning of a pencil beam over a target volume leading again to an improved

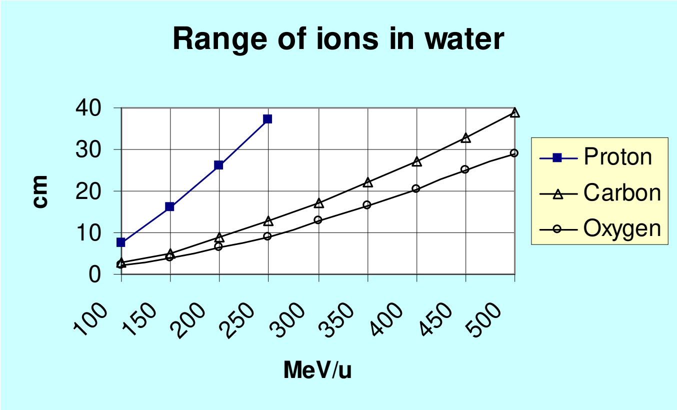

Figure 3. Range of protons and ions depending on the energy.

conform 3D dose delivery to a tumour. Heavy ions such as carbon are even more precise than protons, but need higher energy for the same range and therefore larger (and more expensive) accelerators and beam delivery systems.

3. BIOLOGICAL PROPERTIES OF ION BEAMS

Protons and heavier ions transfer their energy to cell molecules by Coulomb interaction with electrons resulting mostly in ionisation processes affecting all molecules in the cells, but DNA is the most sensitive target. The biological efficiency is related to the energy loss or Linear Energy Transfer (LET).

LET is given in keV/µm and is a function of the particle velocity. The LET is highest in the maximum of the Bragg peak. One distinguishes between low LET particles (protons or Helium) which are similar in effect to photons and high LET particles (ions and neutrons). The physical dose D in (Gy) is given by the following formula [9]:

$$\mathrm{D} = \frac{1.6 \cdot 10^{-7} \cdot LET \cdot F}{\rho}$$

Where LET is in (keV/µm), F the particle fluence in (particles/ mm^2) and ρ is the mass density in (g/cm^3).

To describe the effectiveness of the ion irradiation on biological targets it is not sufficient to know the LET or the physical dose, but also the specific reaction of a specific cell species to the particle beam. This is described by the Relative Biological Effectiveness (RBE) that is defined as:

$$\mathrm{RBE} = \frac{D_{photon}}{D_{ion}} \text{ necessary for the same effect.}$$

Ions show a high RBE in slowly growing tumours, but a low RBE in fast growing ones (see Figure 4) [10]. They are also effective in anoxic cells found quite often around tumours [10]. The varying repair mechanisms of healthy or tumour cells also influence the final value of the RBE [10]. Usually range and dose are defined for water, which is also correct for most of the human tissue, but there are of course, deviations in areas of different density such as bone or air gaps [10].

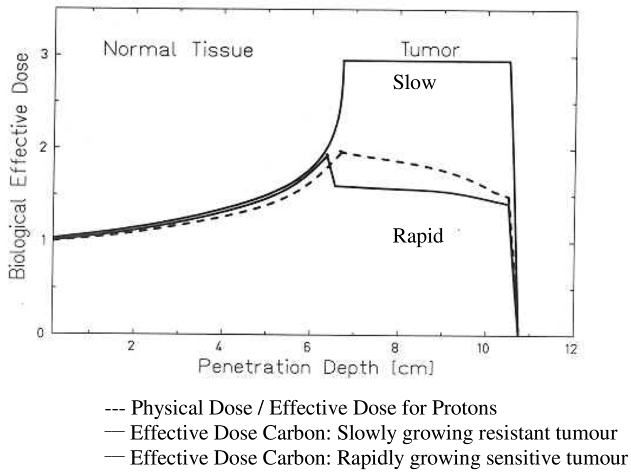

Figure 4. Comparison of physical and biological effective doses profiles [10].

4. ACCELERATOR ARRANGEMENTS

A proton or carbon therapy facility consists of an accelerator to generate the beam of required energy, a beam delivery system to the treatment rooms with gantries or fixed beam lines, nozzles or scanners which shape the beam to the target and a patient positioning system. All should be highly reliable, easy to run and maintain, and highly automated in their operation. Figure 5 shows as a typical arrangement the new proton therapy centre of the Tsukuba University in Japan [11].

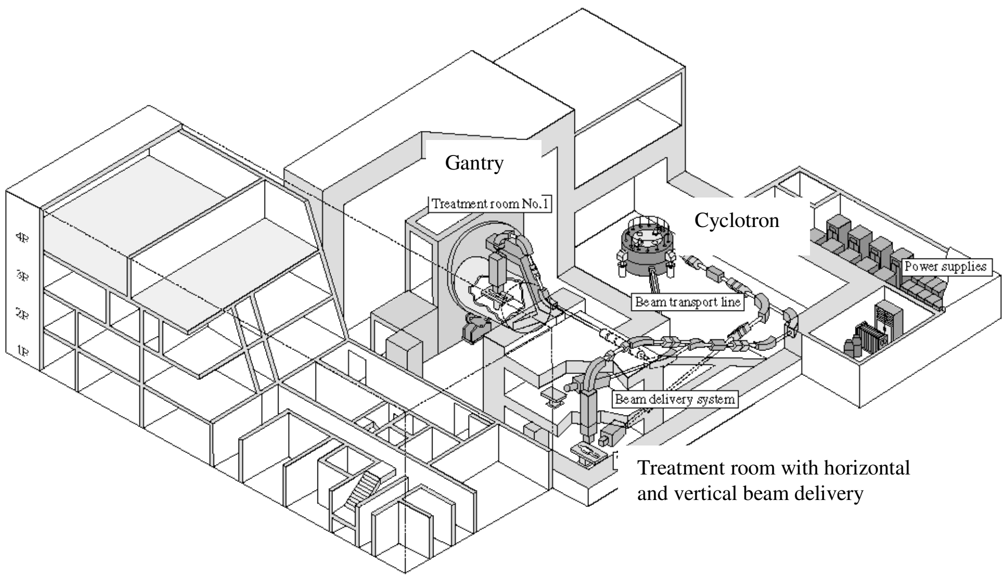

Figure 5. Principle accelerator arrangements with different delivery systems. The heavy shielding necessary for high-energy particles can be seen and also the area for patient preparation, laboratories and administration (about 50% of the building, but less than 30% of costs) [11].

- *Accelerators*

Cyclotrons or synchrotrons are used for acceleration of the ion beams. Cyclotrons accelerate the particles on a spiral path in a constant magnetic field to a fixed energy and deliver a dc beam. Due to their limited energy they can only be used for protons and need a separate energy selection device in which up to 90% of the beam is lost producing high levels of neutron and x-ray radiation. Synchrotrons accelerate a pulsed beam on a constant orbit of a pulsed magnetic ring structure and deliver a pulsed beam the energy of which can be varied in less than a second pulse-to-pulse without additional losses. The flexibility of the synchrotron is ideally matched to spot scanning techniques of the ion beam.
Cyclotrons are easy to control and have a simple rf system, synchrotrons are more sophisticated with their ramped magnets and rf systems, but also easy to operate with standard computer networks.

- *Energy selection*

In the case of a fixed energy accelerator like a cyclotron, the energy selection has to be done separately in an energy selection section. This consists of a carbon degrader of variable thickness which slows the beam down to the right energy followed by a set of slits and a magnet to shape the beam to the precision needed. Due to scattering and energy spread of the particles 50 to 90% of the accelerated beam is lost in this section which is not required for ion beams from synchrotrons with their variable energy.

- *Beam transport and gantries*

After acceleration (and energy definition) the beam is transported to one or more treatment rooms with gantries or fixed beam lines. Proton or heavy ion gantries (see Figure 6) are complex structures that can deliver the beam to the patient from any direction enabling a supine patient position. The final part of a passive delivery system is the nozzle that contains beam spreading, shaping (see below) and dose distribution measurement devices. Beam scanning devices are usually part of the gantry. To control the beam intensity and position for every single Voxel (in case of spot scanning) fast position sensitive detectors are used in front of the patient.

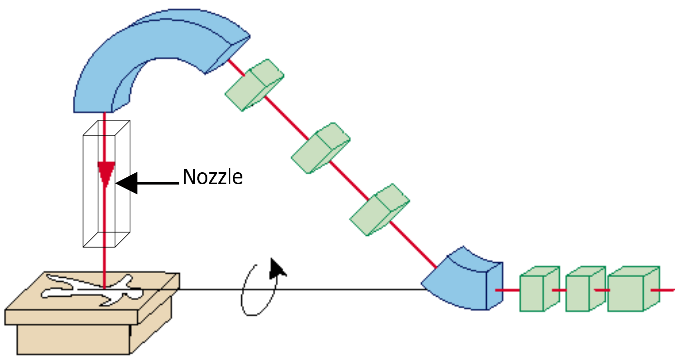

Figure 6. Gantry scheme with magnetic focusing elements (small blocks) and magnets.
The nozzle contains beam spreading, shaping and control devices [11].

- *Patient Positioning System*

The outstanding precision of the proton or carbon beam delivery to the tumour requires the same precision to the patient's positioning. The patient is immobilised in moulds or masks on a table (or chair in case of eye treatment) that can be positioned and controlled, reproducible to better than half a millimetre in all directions.

5. BEAM DELIVERY SYSTEMS

The ion beam is directed from the accelerator or the energy definition system as a monoenergetic small pencil beam. To adjust it to the size or volume of the tumour targeted one has to spread it out transversally and modulate the energy (longitudinal spread). This can be done by different methods and in different areas of the beam line. The two main principles are:

5.1 Scattering of the beam

The principle of a beam scattering system is shown in Figure 7 [12]. The beam, after passing the final beam line or gantry and having an energy high enough to reach the deepest part of the target, is gradually slowed down by a range shifter so that the Bragg peak is spread out over the depths of the target. Afterwards the beam passes one or more scattering foils and is spread out laterally over a circular area, the size of which depends mainly on the distance to the target. This distance is usually limited by the gantry design to about 2 to 3 meters. A patient specific or an adjustable laminated collimator limits the beam to the actual tumour size and a compensator or bolus adjusts the beam to the shape of the back of the tumour. Additional elements might be used to improve the homogeneity of the beam or to improve also the dose distribution in front of the tumour. Usually, the beam scattering devices are located in the nozzle between gantry exit and patient. It is quite similar to the technique used at electron accelerators.

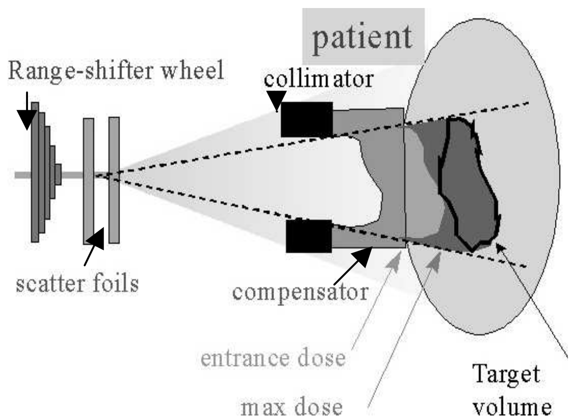

Figure 7. Principle of passive beam scattering and shaping[12].

5.2 Scanning

The principle of a beam scanning system is shown in Figure 8 [13]. The beam coming from the accelerator is scanned in both perpendicular directions by fast scanning magnets conform over the area of the tumour. The magnets can be positioned before or in case of protons also after the last bending magnet of the gantry (influencing its size of course). The energy or depth adjustment can be done also with a range shifter after the last magnet (in case of a fixed energy of the accelerator like a cyclotron) or by changing the energy of the accelerator itself pulse-to-pulse in case of a synchrotron. In the latter case, the dose can be delivered 3D target conform in a tumour specific Voxel-plan. Sensitive parts in the area or vicinity of the tumour can be treated with a reduced dose. i.e spot by spot intensity modulation is possible without extra costs.

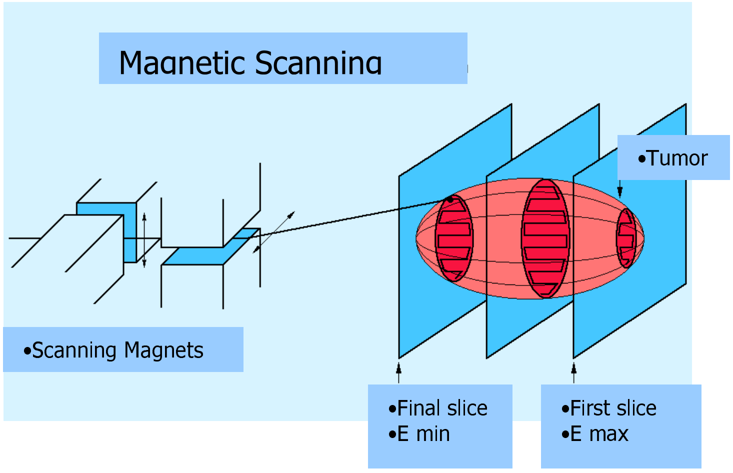

Figure 8. Principle of active beam scanning (spot or raster-scanning) [13] [28].

There have also been hybrid systems used with magnetic wobbling of the beam in one or both directions and mechanical movement of magnets or patient's bench position. A fast kicker magnet can switch a dc beam from the cyclotron accelerator to allow spot scanning delivery of the beam.

6. SPECIAL FEATURES OF IONS AND IN SITU PET IMAGING

Heavier ions are even more precise than protons, mainly because the lateral scattering of the beam in the body becomes smaller (see Figure 9). On the other hand, fragmentation of ions and target atoms can occur, resulting in a longer range of the fragments of lower atomic number, which are also mainly radioisotopes, beyond the Bragg peak. This effect is larger for heavier ions and limits the useful mass range to below 20 (or Ne).

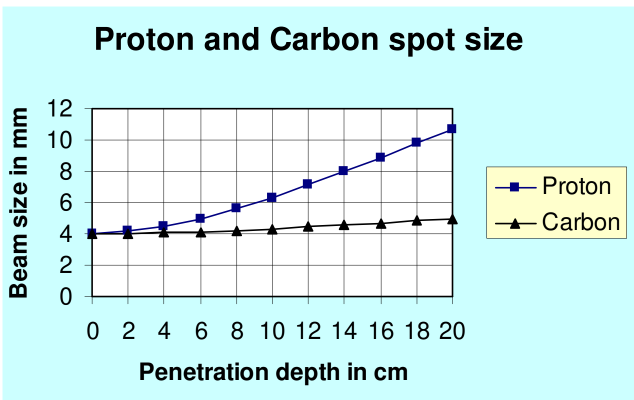

Figure 9. Lateral beam scattering for protons and carbon ions.

The fragmentation however, yields a very positive effect: the production of positron emitting radioisotopes ^{11}C and ^{10}C (see Figure 10). This allows an in situ dose control, or Positron

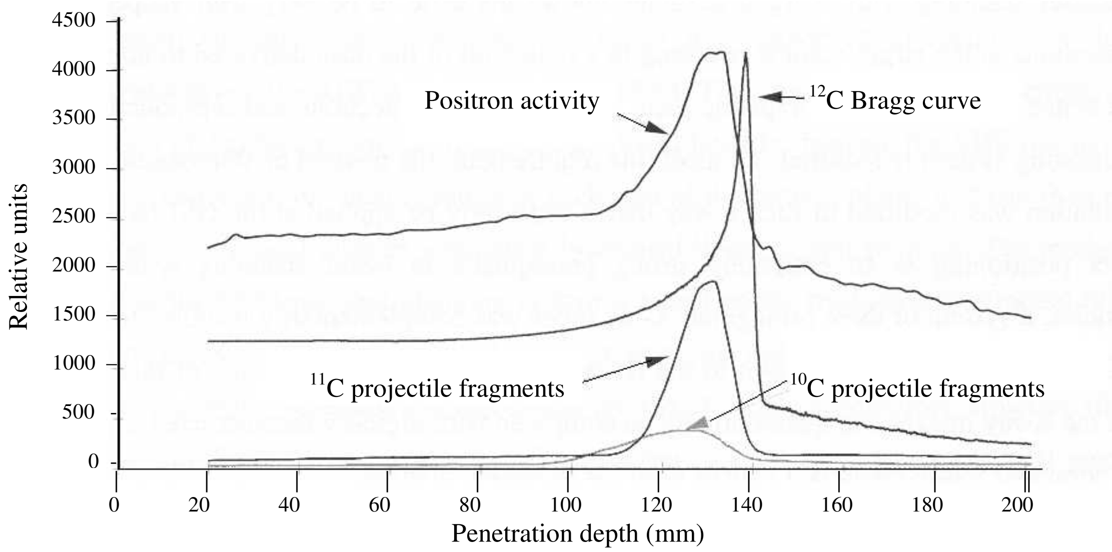

Figure 10. Distribution of C isotopes used for therapy and Positron Emission Tomography control [14] [28].

Emission Tomography (PET), during, and immediately after, a treatment session (when the patient is still in the immobilised position) allowing a fine-tuning of the treatment plan during the session or for the next one [14]. This is a very important tool because of the range uncertainties caused by density variation of the various tissues.

7. MEDICAL SPECIFICATIONS FOR THERAPY FACILITY

Any proposal for a clinical therapy facility has to start with clinical specifications leading to appropriate technical solutions. As an example, the specifications for the NPTC proton facility is given in Table 1. The centre is designed for 3 treatment rooms (2 with gantries) and

Table1: Specifications for a proton therapy facility

Clinical Specifications	
Parameter	**Specification**
Range in Patient	32 g/cm^2 Maximum, 3.5 g/cm^2 Minimum
Range Modulation	Steps of <0.5 g/cm^2
Range Adjustment	Steps of <0.1 g/cm^2
Average Dose Rate	25 cm x 25 cm modulated to 32 g/cm^2: 2 Gy in <1 min.
Spill Structure	Scanning Ready
Field size Fixed Beam Line	>40 cm x 40 cm
Field size Gantry	>40 cm x 30 cm
Dose Uniformity	2.5%
Distal Dose Fall-off	<0.1 g/cm^2
Lateral Penumbra	<2 mm
Effective Source to Axis Distance	~2.5 m

Facility Specifications	
Parameter	**Specification**
Time for start-up from standby	<30 mins.
Cold start-up time	<2 hours
Time for shut-down from standby	<10 mins.
Time for 'manual' set-up in one room	<1 min.
Time for auto set-up in one room	<0.5 min.
System availability	>95%
Time to switch rooms	<1 min.
Time to switch energy	<2 s
Dosimetry reproducibility	1.5% (Daily) 3% (Weekly)
Radiation level	ALARA

one experimental area, a total of 5 beam lines. In addition, there was a specification for the building of about 4,000 m^2 on three levels [15] [16].

Apart from these specifications there are estimates of the capacity needed depending on the region served, the type of tumours targeted, research capacity required and the infrastructure already available within a photon therapy centre. All these points will influence the size of the building necessary to host a proton or ion therapy facility.

8. TREATMENT PLANNING AND QUALITY INSURANCE

Treatment planning for proton is similar to the planning for photons, but is quite different for carbon because the RBE has to be taken into account. The RBE depends on dose, atomic number of the particle, on the proliferation of the tissue under concern and the type of reaction, typical for deactivation or late effects. There has been a Local Effect Model (LEM) developed based on the link to x-ray sensitivity of the tissue and the radial dose distribution within the particle tracks and their dependence on energy and atomic number of the particles [17]. Thus LEM gives a recipe to take into account all these dependencies when switching from photons to ions and for the first time in radiation therapy the treatment planning can be based on biology and not only on the physical dose optimisation.

The delivered dose and beam position is controlled precisely by a double array of detectors in front of the patient. Any intensity deviation is detected and, if larger than 5%, a safety interrupt will occur within less than 1 ms. The same will happen if there is a deviation in the pencil-beam position of more than 30%. Along the accelerator and beam delivery system are various control devices connected to the interlock system to ensure that only the planned beam and dose can reach the patient.

Within the Proton Therapy Co-Ordination Group, a Clinical Protocol Working Group was established [18]. Through this group, the worldwide proton and heavy ion therapy community will be able to learn about the status of all ongoing trials, discuss the objectives of future trials and be able to enter patients into appropriate ongoing clinical trials.

Tables 4 and 5 (Appendix 2) give lists of typical tumours and other diseases treated with protons or ions. It is obvious that different centres concentrate on different indications (depending also on the country). More information on treatment results can be found in [20] [21] [22] [23] and in the web pages given in [24] [25] [26] [27].

9. TYPICAL COSTS AND CAPACITIES OF HOSPITAL-BASED FACILITIES

The following graph Figure 11 compares the costs for two proton and one ion facility [15] [19] [28]. Typical costs for a commercially ordered key-ready proton facility are:

- About 25 M$ US for three treatment areas and a similar amount for the building with patient preparation rooms, laboratories and administration areas.
- Such a facility has a capacity of 1,000 to 1,500 patients per year or 15,000 to 30,000 fractions per year.
- To date it would serve a population of about 10 million people decreasing with more indications treated.

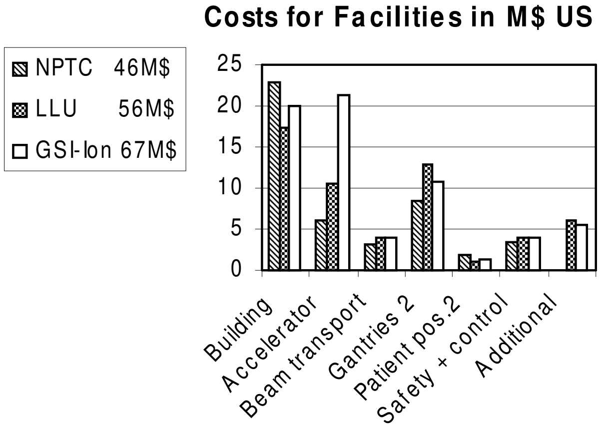

Figure 11. Costs for hospital-based ion beam facilities.
Protons: NPTC (Northeast Proton Therapy Center, US) [15],
LLU (Loma Linda University, US) [19].
Carbon ions: GSI proposal for Heidelberg University, Germany [28].

10. TYPICAL RUNNING COSTS OF HOSPITAL-BASED FACILITIES

The cost for running a proton or ion therapy facility depends highly on the design and capacity chosen. For orientation some typical figures are:

- About 10 M$ US per year for protons, 16 M$ US/year for ions about 40 % of which is capital cost.
- Cost per treatment depends strongly on the patient throughput and the number of fractions per patient. They also vary significantly from country to country, partly due to varying costs, partly due to different hospital financing and organisational structures. As a rough estimate an average of 7,000 $ US/patient can be taken.
- They are comparable with modern conform and intensity modulated photon treatment or surgery and cheaper than chemotherapy.
- There are less material costs and a lower level of secondary radiation for the spot scanning technique.
- In general, one can expect less costs for hospitalisation and rehabilitation during or after ion beam therapy compared to other therapy methods.

In Table 2 the annual operational costs for a typical proton and ion facility are listed for comparison on the base of the treatment of 50 patients/day [19] [28].

Table 2

	LLU proton facility	**Planned GSI ion facility**
Supplies (moulds, boluses, patient needs)	$US 350,000	$US 704,000
Maintenance	1,600,000	1,760,000
Utilities - 24h/day	300,000	1,470,000
Depreciation - equipment	3,100,000	7,110,000
Depreciation - building	700,000	capital 15years, Interest. 6.5%
Personnel 46(LLU) – 75(GSI)	3,500,000	5,900,000
Total annual costs	10,550,000	16,944,000

11. PROPOSAL FOR AN AUSTRALIAN PROTON THERAPY FACILITY

When planning a proton (or ion) therapy for Australia one has to take into account the following points:

- There is no suitable accelerator in the country to start training or clinical trial programs on a small basis;
- limited expertise in accelerator technology;
- very little expertise in radiobiology with ion beams;
- a population of about 20 million living mainly in the south east of the continent;
- a high standard of medical research and photon therapy experience (including up-to-date planning programs).

These facts lead to the need for getting a small group of interested parties together to define the medical needs in Australia, prepare a substantial proposal (including a business plan) for a national ion therapy centre based on the following:

- A commercial ion beam facility with scanning possibility modelled on one of the existing worldwide facilities;
- A facility that is connected to a hospital experienced in photon therapy and with research capacity;
- A facility that might be realised in steps to have the time to develop the expertise necessary to run a full scale commercial facility;
- Advisory committees with Australian and international technical and medical experts to help during the planning stage and to review a proposal, tendering, commissioning and acceptance phases of such a project;
- A plan for international co-operation and training of clinical and technical staff right from the beginning of the project;
- Developing treatment planning procedures based on existing Australian programs;
- Implementation of international safety and dosimetry standards for proton therapy following the ICRU protocols in contact with other PTCOG members.

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APPENDIX

1. Patient statistics

Table 3: Worldwide Charged Particle Patient Totals
July 1999[Particles 24][29]

WHO	WHERE	WHAT	DATE FIRST RX	DATE LAST RX	RECENT PATIENT TOTAL	DATE OF TOTAL
Berkeley 184	CA. USA	p	1954	— 1957	30	
Berkeley	CA. USA	He	1957	— 1992	2054	June-91
Uppsala	Sweden	p	1957	— 1976	73	
Harvard (160 MeV)	MA. USA	p	1961		8160	Jun-99
Dubna	Russia	p	1967	— 1974	84	
Moscow	Russia	p	1969		3100	Dec-98
Los Alamos	NM. USA	π^-	1974	— 1982	230	
St. Petersburg	Russia	p	1975		1029	Jun-98
Berkeley	CA. USA	heavy ion	1975	— 1992	433	June-91
# Chiba (90 MeV)*	Japan	p	1979		96	Oct-96
TRIUMF	Canada	π^-	1979	— 1994	367	Dec-93
PSI (SIN)	Switzerland	π^-	1980	— 1993	503	
PMRC, Tsukuba	Japan	p	1983		606	Mar-99
PSI (72 MeV)*	Switzerland	p	1984		2753	Dec-98
Dubna	Russia	p	1987		41	Jun-99
Uppsala	Sweden	p	1989		147	Feb-98
# Clatterbridge (62 MeV)*	England	p	1989		817	May-98
# Loma Linda	CA. USA	p	1990		4330	May-99
Louvain-la-Neuve (90 MeV)*	Belgium	p	1991	– 1993	21	
# Nice (62 MeV)*	France	p	1991		1350	Jun-99
Orsay	France	p	1991		1219	July-98
N.A.C.	South Africa	p	1993		310	May-99
MPRI	IN USA	p	1993		9	Dec-98
UCSF - CNL	CA USA	p	1994		214	Jun-99
# HIMAC, Chiba	Japan	heavy ion	1994		473	Sept-98
TRIUMF (70 MeV)*	Canada	p	1995		47	Dec-98
PSI (200 MeV)	Switzerland	p	1996		20	Dec-98
G.S.I Darmstadt	Germany	heavy ion	1997		20	Dec-98
Berlin (72 MeV)*	Germany	p	1998		30	Dec-98
# NCC, Kashiwa	Japan	p	1998		8	Jun-98
					1100	**pions**
					2980	**ions**
					24494	**protons**
				TOTAL	**28574**	**all particles**

Hospital based * Low energy (Eye)

2. Cancer types treated with protons or ions

Table 4: Percentage of cancers treated in different centres

	LLU	NPTC	HIMAC	Tsukuba
Prostate	64%	2.50%	12.00%	0
Head & neck	6%	8.50%	27%	15%
Chordoma & Chondrosarcoma	5%	0	0	0
AVM	3%	0	0	6%
Others	22%	11%	20%	26%
Uveal Melanomas	0	34%	0	0
Neurosurgery	0	44%	0	0
Lung	0	0	19%	9%
Liver	0	0	12%	31%
Uterine cervix	0	0	10%	6%
Bladder	0	0	0	7%

[24] [25] [26] [27]

Table 5: Tumors and other diseases treated at LLU [24]

Brain and Spinal Cord	Gliomas (intermediate and low-grade) Isolated brain metastases Pituitary adenomas Arteriovenous malformations
Base of Skull	Meningiomas Acoustic neuromas Chordomas Chondrosarcomas
Eye	Uveal Melanoma Macular degeneration
Head and Neck	Nasopharynx (primary and recurrent) Oropharynx (locally advanced)
Chest and Abdomen	Stage A lung cancer (medically inoperable) Chordomas and chondrosarcomas
Pelvis	Prostate Unresectable pelvic cancers Chordomas and chondrosarcomas
Pediatrics	Brain and spinal cord tumors Orbital and ocular tumors Sarcomas of the base of skull and spine Abdominal and pelvic malignancies

3. Information on the Internet*

PARTICLES

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PROTON THERAPY CO-OPERATIVE GROUP

A Newsletter for those interested in proton, light ion and heavy charged particle radiotherapy.

Number 24 July 1999 Janet Sisterson Ph.D., NPTC

Particles on the Internet: The URL for the Harvard Cyclotron Laboratory is:-

- http://neurosurgery.mgh.harvard.edu/hcl/ or http://brain.mgh.harvard.edu:100/hcl
  This contains links to recent issues of Particles.

Other proton therapy links:

- Northeast Proton Therapy Center: http://www.mgh.harvard.edu/depts/nptc/nptc.htm
- LLUMC, California: http://www.llu.edu/proton
- U of California, Davis: http://crocker.ucdavis.edu/cnl/research/eyet.htm
- Midwest Proton Radiation Institute: http://www.iucf.indiana.edu
- National Association for Proton Therapy: http://www.proton-therapy.org/
- Prolit - database of particle radiation therapy: http://proton.llu.edu
- TRIUMF, Canada protons: http://www.triumf.ca/welcome/proton_thrpy.html
- TRIUMF, Canada pions: http://www.triumf.ca/welcome/pion_trtmt.html
- PSI, Switzerland: http://www.psi.ch/
- Proton Oncological Therapy, Project of the ISS, Italy: http://top.iss.infn.it
- TERA foundation, Italy: http://www.tera.it
- GSI homepage: http://www.gsi.de
- The Svedborg Laboratory, Sweden: http://www.tsl.uu.se/
- Clatterbridge Centre for Oncology: http://synaptic.mvc.mcc.ac.uk/simulators.html
- Tsukuba, Japan: http://www-medical.kek.jp/index.html
- Tsukuba, Japan - new facility plans:
- http://www-medical.kek.jp/devnewfac.html
- HIMAC, Chiba, Japan: http://www.nirs.go.jp/ENG/particl.htm (ENG case sensitive)
- NAC, South Africa: http://www.nac.ac.za/~medrad/

* html file from Bernhard Wolf: b.wolf@tassie.net.au