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Options for a light ion facility for hadron therapy and research

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Abstract

Several proposals have being prepared for the construction in Australia of a high-performance accelerator complex for radiation therapy and possibly research. In all cases the accelerators on which the facility would have been based required proton beams between 60 and 250 MeV. One of the previous proposals also suggested a more advanced accelerator system capable of producing carbon beams with energies variable from 120 – 430 MeV/amu. This paper summarises some of the physical processes involved in this treatment regime and considers some options for a possible Australian Facility.

Introduction

Cancer is a major burden on the Australian community with more than 100,000 cases reported each year. Cancer is a leading cause of death in Australia with over 36,000 people succumbing each year, in spite of a 30 percent improvement in survival over the last two decades. Cancers most commonly causing death are lung, prostate and colorectal in males and breast, lung and colorectal in women.

Although there are many kinds of cancer affecting different organs in the body, they all are caused by uncontrolled growth of abnormal cells. In a healthy individual, cells grow, divide, and die in a highly regulated fashion. During childhood, healthy cells grow and divide very rapidly until the individual becomes an adult. At this stage, cell growth slows until in most parts of the body, cells only divide to replace worn-out or dying cells and repair injuries. Cancer cells often travel to other parts of the body where they begin to grow and replace normal tissue. This process, called metastasis, occurs when cancer cells find their way into the bloodstream or lymphatic system of our body.

Cancer can be considered in two classes from the viewpoint of attempting to treat the patient:

- Generalized cancer where the cancer has spread from the original infested area to other parts of the body; and
- Localised Tumours.

Based on European Union data, the proportion of generalised cancers, when detected, constitutes about 42% of all cases. Of these, the mortality rate is about 88%. The two treatment regimes are surgery and chemotherapy although radiotherapy has value for palliative care. The remaining 58% comprise localized tumours where a variety of treatment regimes including surgery, chemotherapy and radiation treatment result in prolonging patient life by more than 5 years in 57% of cases. However, the morbidity is still very high and patient outcomes even with survival often leave the patient with some unpleasant physical consequences.

Improvements in radiotherapy over the last 20 years or so have contributed to increased survival but clearly there needs to be a major advance in treatment methods. Hadron Therapy (with protons, carbon ions) fills this gap and a large number of centres have been

built in recent years or are under construction (Jean-Michel Lagniel, PAC-07). Already more than 70,000 patients world-wide have been treated using this new method.

Physics Principles in Hadron Therapy

The physical advantages that ion beams (hadrons) have over X-ray beams (photons) was first pointed out in 1946 by Robert Wilson, 1946, although this had little impact on the medical community at the time. The first application of charged-particle beams took place at Lawrence Berkeley in 1954 and, after a long period of low-level investment, major development of the technique began with the installation of dedicated hospital facilities at Loma Linda and Massachusetts General Hospital.

Interaction Rate

The value of hadron beams in radiation therapy can be readily understood by considering the underlying physics of the interaction of various types of particles with human tissue. The best technology currently available in Australia utilises X-rays (photons). Photons which is the generalized word to describe electromagnetic radiation i.e., X-rays, gamma rays, bremsstrahlung, interact with matter via three processes, the Photoelectric Effect, Compton scattering and Pair production. In principle each photon interacts only once with the components of the body and, accordingly, the intensity of the photon beam decreases as it enters the body. Therefore the dose deposited in the human body has an exponential term of the following form:

$$I = I_o e^{-\mu_x} \qquad (1)$$

Thus, the maximum dose is delivered to the near surface of the body where there are healthy cells, there is no finite range to the dose distribution and the dose continues past the tumour being treated. Furthermore, because of the effective negligible mass of the photon, there is a large angular deviation of the photon beam as it passes through the body. On the contrary, hadrons e.g. protons and carbon ions have a different interaction process, principally coulomb interaction with target electrons in the irradiated body. The dose rate is given by the following expression:

$$\frac{dE}{dx} = \left(\frac{e^4 Z^2_{eff} Z^2 N}{mv^2}\right) * \text{other terms.} \qquad (2)$$

Simply, this means that a specific hadron ion gradually loses energy as it enters the body, slows down and finally stops altogether. At the end of its path it deposits a very large amount of energy as may be seen from the equation 2 above. This effect can readily be seen because of the term mv^2 in the denominator which becomes asymptotically small as the energy or velocity of the particle decreases. This effect which is called the Bragg Peak has been known for more than 100 years and was first pointed out by the two Australian scientists, William Bragg and his son. Furthermore, there is no radiation dose or energy loss after the ion has stopped. The key to the use of hadron beams is to adjust the energy of the hadrons so that they deposit their greatest energy in the tumour being targeted. The results of this difference in interaction are illustrated in Figure 1. The data for two ion beams, protons and carbon ions, and for traditional X-ray beams are shown. The dramatic increase in the radiation dose at the end of the carbon and proton pathways can be readily seen. Note that the doses in the figure are normalised to 1 at entry.

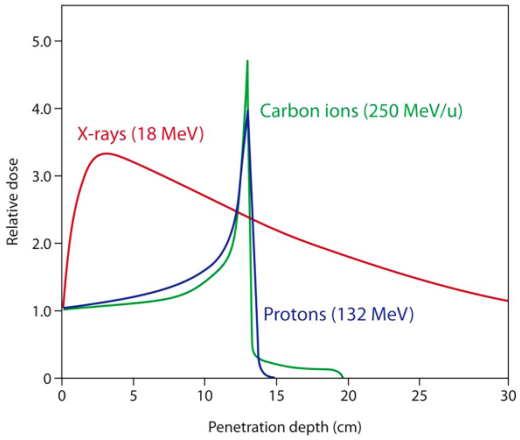

Figure 1: Normalised Relative Dose rates for X-rays, protons and carbon ions.

Linear Energy Transfer

Figure 2 shows the microscopic dose distributions for protons and carbon ions in water and DNA strand breakages for various energy ranges near the end of their tracks, (Haberer (2009)).

The dramatic increase in DNA double strand breakage observed with the carbon ions (right hand side of figure 2) shows that they are particularly useful in the treatment of radiation resistant tumours. With single strand breakage, DNA has the ability to repair itself but with double strand breakage this is no longer possible.

Lateral Deviation of Hadron Beams

A third important characteristic of the interaction of hadrons with human tissue is the lack of deviation of the hadron beam from the original beam direction. Figure 4, from a presentation by Thomas Haberer (2009), shows the lateral scattering of three hadron beams as a function of depth in water. The lateral scattering is much less than that with photons and the degree of lateral scattering diminishes with atomic charge.

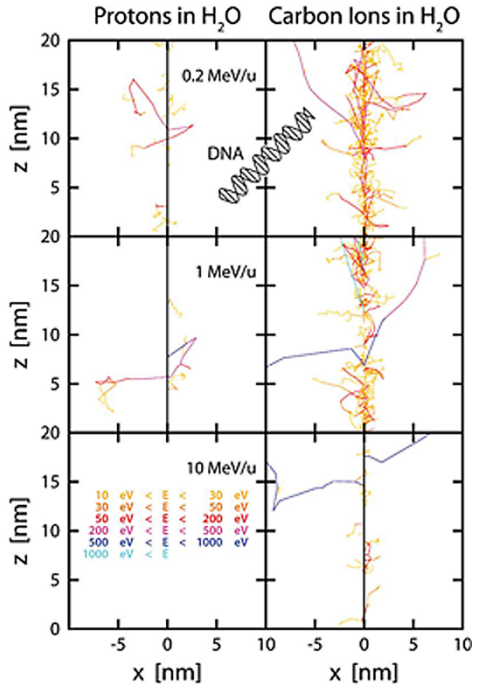

Figure 2: Microscopic Dose Distributions for Protons and Carbon Ions

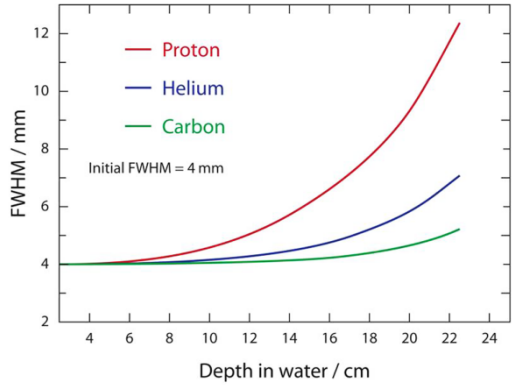

Figure 3: Lateral Deviations of Proton, Helium and Carbon Beams in Water

These properties of hadron beams translate into a far more targeted dose in many cancer cases. There are many examples in the literature of comparisons of dose distributions for hadron beams with those using the latest technology with X-rays (photons). Examples are not

reproduced here, but extensive studies will be found in Haberer (2009) and Boldeman et al. (2010).

Summary

The advantage that hadron therapy has over conventional radiotherapy can be summarized as follows:

- In the treatment process, the dose to healthy cells is reduced by factors between 3 and 10. This is particularly important in the treatment of children who have many years of life before them.
- Because the hadron beams can be controlled by magnets and because of the small deviation of the hadron beam as it enters the human body it is possible to target tumours very close to critical organs.
- It is possible to kill tumours that are resistant to normal electromagnetic radiation.
- Hadron beams are more effective and the number of fractions (i.e., the number of times a patient needs to attend the facility) is reduced.
- Side effects such as nausea are reduced.
- With modern accelerator systems it is possible to use magnetically controlled pencil beams to radiate the detailed shape of the tumour. This is called raster scanning.

Hadron therapy is particularly suitable for the treatment of deep-seated tumours that are located near to critical organs and which respond poorly to conventional X-ray (photon) or electron radiotherapy. Because of the significantly reduced dose to healthy tissues during a typical treatment, it is especially appropriate for tumours in children.

Scientific Applications of a Hadron Therapy Facility

The second possible objective in the installation of a Hadron Therapy and Research Facility follows from the many opportunities that such a facility would provide.

Radiobiological Research

The proposed facility would revolutionise research in many areas particularly in the biological sciences because of its ability to produce a variety of very energetic particles previously unavailable in Australia. These include the following areas of research:

- the study of low-dose effects;
- Radio Biological Effectiveness (late effects, genetic mutation, transformation) of high energy particles;
- determination of radiosensitivity of different tumours and normal tissues and molecular correlates;
- detailed study of chromosome damage;
- the importance of hypoxia;
- interaction of ion therapy and chemotherapeutic agents; and
- integration of biologic data into biological modelling for treatment planning.

Basic Research

In a number of areas of basic research the facility has the capability of extending Australian studies significantly. These areas include:

- proton – neutron production cross-sections;
- proton scattering cross-sections;
- nuclear cross section measurements;
- preliminary studies of ADS systems;
- decay spectroscopy, gamma spectroscopy;
- exotic beams and reactions;
- spectroscopy and atomic properties of relativistic ion systems;
- optical spectroscop;
- Atomic Collision Process;
- dielectric recombination measurements;
- heavy- ion ionisation processes;
- charge-state studies;

- coulomb fragmentation in heavy ion collisions;
- radiative electron capture studies; and
- heavy-ion stopping in matter.

Alternatives for an Australian Hadron Therapy Facility

The requirements for the hadron beams from any facility include:

- maximum penetration depth in the human body of approximately 32 cm;
- minimum penetration depth of 3.5 cm; and
- sufficient current to provide 2 grays of radiation to a targeted tumour in about 2 – 3 minutes.

With these principal requirements the hadron beams must be variable in energy:

- 60 – 250 MeV for protons; and
- 120 – 430 MeV/u for C12 beams.

The accelerator alternatives include:

- commercial cyclotron facility – protons only;
- commercial synchrotron facility – protons only;
- nationally constructed synchrotron facility – protons only; and
- nationally constructed synchrotron facility – protons and carbon beams.

An installation would require, besides the accelerator, a number of shielded treatment rooms plus the appropriate magnets to shape and transfer the beam to these areas. In most evaluations of the costs of the full installation, it is typical to include one treatment area for low energy beams, two places for horizontal treatment and another where the beam can be rotated either through 180° or at least have a vertical beam in addition to a horizontal.

In evaluating the alternatives and costs there is a number of over riding issues. The beamlines are to a large extent independent of the accelerator facility that drives them although the transfer magnets for a carbon beam are slightly more expensive

Cyclotrons, whether conventional or superconducting, require the smallest amount of space for the accelerator. A synchrotron providing protons only would be approximately 22m in circumference while the combined proton carbon beam would be 77 m in circumference. All of the treatment options mentioned above would be required for a commercially-based proton synchrotron and with some modification a cyclotron-based facility. Furthermore, the buildings which comprise a major component of the costs of a facility are not too different depending on the options. However, the footprint of a combined carbon- proton machine is about 20% larger.

A careful evaluation has been made of the costs of a combined proton carbon synchrotron and appropriate supporting facilities at $180 M, Boldeman et al 2010. If a proton only synchrotron were installed, the costs would reduce by approximately $20 M, because of the reduced number of magnets and the smaller area required for the accelerator. The installation of a cyclotron for the accelerator complex would result in an additional reduction of about $5 M.

The layout of the Heidelberg Ion Therapy Facility (HIT) at the University Hospital of Heidelberg is shown in Figure 4 as an example of the type of facility that is proposed for Australia. At this stage the proposed design for a combined proton carbon facility has a slightly different arrangements of the magnets in the accelerator system and the actual configuration of the delivery system to the various treatment rooms would be modified to suit the selected site.

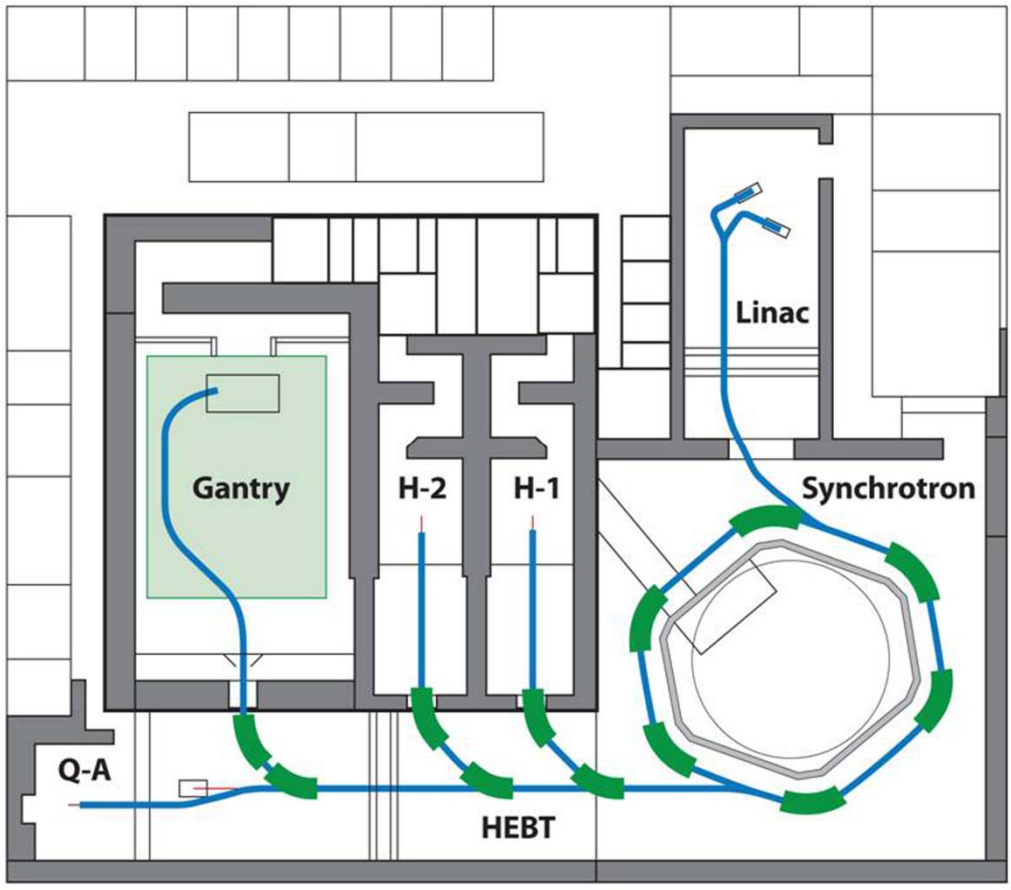

Figure 4: Layout of the Heidelberg Ion Therapy Facility

A preliminary assessment of the pros and cons of the alternative options is given in Tables 1- 4.

PROS	CONS
• Lowest cost option. • Low risk. • Short construction time.	• Slightly inferior performance relative to a synchrotron. • No flexibility. • Very limited research capability. • Very limited technology transfer. • Long term dependence on supplier organization.

Table 1 – Commercial Cyclotron – Protons only – Warm or superconducting

PROS	CONS
• Low cost . • Low risk.	• More control of beam than with a cyclotron. • Some flexibility but limited by the synchrotron. • Limited research capability. • Some technology transfer. • Independence from the supplier.

Table 2 – Commercial Synchrotron – Protons only

PROS	CONS
• Potentially lowest cost of all. • Greater flexibility. • Good technology transfer. • Improved research capability.	• Some risk. • Less options than carbon-proton machine.

Table 3 – Nationally Constructed Synchrotron – Protons only

Summary

A **commercial cyclotron facility** can be purchased from a number of international suppliers. There is limited risk in this operation. However the facility would have very limited value for research, a slightly lower therapy capability and the majority of the funds would be spent overseas. Technology generation in Australia would be at a minimum.

A **Nationally-Constructed High Performance Synchrotron** facility offers the optimum in performance, research and technology development. A high proportion of the funds would be spent in Australia. The physics design of such a facility has been completed and specialist international advisors have committed to providing support. However this is the highest cost facility.

A more modest synchrotron with proton beams only could be designed with limited effort. The transfer beamlines could be adapted with minimum effort from the designs already developed for the higher performance synchrotron.

The construction of the facility will in its own right introduce a great number of new technologies into Australia as has been seen with the construction of two pieces of scientific infrastructure, the OPAL research reactor and the Australian Synchrotron.

References

Jean-Michel Lagniel (2007), *Particle Accelerator Conference (PAC-07)*, Alberqueque, New Mexico, MOZBC02, page 127.

R. R. Wilson (1946) Radiological Use of fast Neutrons, *Radiology*, **47**, 487.

Thomas Harberer (2009) Heidelberg Ion Therapy Center, *Hadron Therapy Workshop*, Erice.

Thomas Haberer (2009) Heidelberg Ion Therapy Center, Particle Beam Production – A Synchrotron-Based System, *Particle Therapy Co-Operative Group (PTCOG).*

J.W. Boldeman, R. Banati, H. Buttner, D. Cohen, R.L. Garrett (2010) *Preliminary Details of a Light Ion Facility for Hadron Therapy and Research*; ANSTO/E-770, Australian Nuclear Science and Technology Organisation, Lucas Heights, NSW, Australia.

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