Advanced European Medical Facilities

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Abstract

An overview of existing and planned applications of accelerators in medicine.

1. INTRODUCTION

Particle accelerators were first applied in medicine 99 years ago, by a man who was awarded the Nobel prize for his pains. William Konrad Roentgen inadvertently accelerated electrons and discovered X-rays. Now we take it all for granted, but please remember, next time you go to the dentist, that your treatment depends on fundamental research in particle physics, undertaken for no purpose other than the quest for fundamental knowledge. Where would we be, in the modern world without the electron? Yet it is sobering to realise that 97 years ago it did not even exist - in the minds of men.

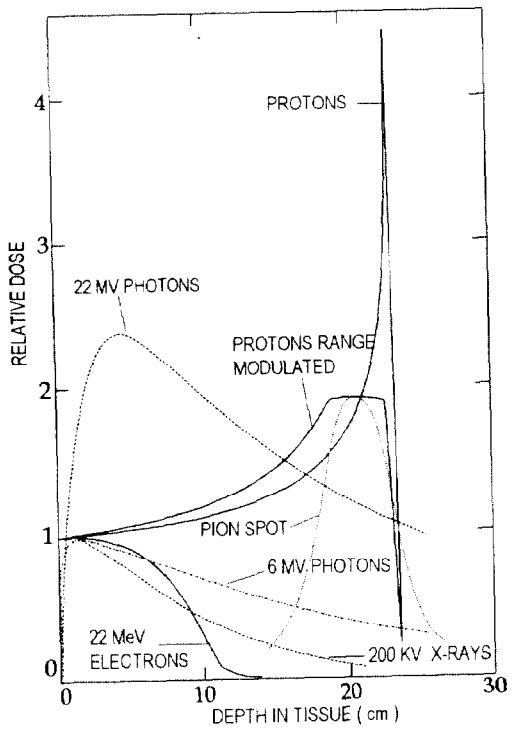

Figure 1. Dose-depth curves for X-rays and protons

2. ELECTRONS AND X-RAYS

Since the beginning of time the medicine men have latched on to any new phenomenon as a possible cure for human mortality. And so in the early days X-rays (as also radioactivity) were recommended for your health. That is now largely discredited - they did more harm than good. But they remain in wide spread use, in small doses for diagnosis, and in larger doses for cancer therapy.

X-ray sources have been continuously improved. In the 1950's betatrons were installed in hospitals for therapy, but these have since been replaced by the travelling wave linacs, invented by Fry in England, and sold in large numbers by foreign manufacturers. I illustrate for example with the French 35 MeV linac, which is in regular use in Nice[1]. Some tumours are better treated directly with the electron beams, others with the secondary X-rays. The radiation length in water is 30 cm, so the electrons and X-rays give different dose distributions, see fig. 1.

The advantage of using high energy X-rays or electrons is that the maximum dose is not at the skin, but some centimetres inside the body, (fig 1). But the beam spreads laterally inside the patient, and there is no well defined end point in range. A better dose concentration at depth is achieved[2] by rotating the beam around the target so as to get a maximum dose at the isocentre, fig. 2. This leads to the so called 'gamma knife', in which many pencil beams

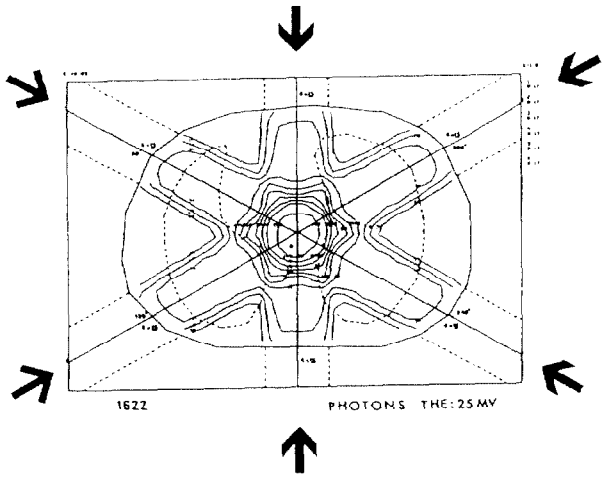

Figure 2. Convergent X-ray beams improve dose distribution for deep seated tumours[2]

are successively aimed at a central point. This is used for treating tumours and also very successfully for cauterising vascular anomalies in the head which can be the precursors of a stroke.

3. ISOTOPE PRODUCTION

Another by-product of particle physics, radioactive isotopes, are widely used in medicine; in small doses for diagnosis and in large doses for treatment. Some elements are specifically concentrated into particular organs; for example iodine into the thyroid gland, and technetium into rapidly growing points in the bones. So tracer quantities of isotopes can reveal anomalies in these tissues, and larger doses can be used to remove them.

Neutron rich isotopes, beta and gamma emitters, are conveniently produced in nuclear reactors. But the neutron deficient, positron emitters required for PET tomography can only come from an accelerator. Some live long enough to be distributed by fast courier, but for others such as C^{11}, N^{13}, O^{15}, F^{18}, and I^{123} it is essential to have an accelerator on site. Thus there is a growing need in hospitals for small isotope production units. Oxford Instruments[3], for example, offer a 12 MeV superconducting H^- cyclotron, fig. 3, delivering 100 μA, while IBA[4] can supply 'Cyclone 10/5' for 10 MeV protons and 5 MeV deuterons. Their 'Cyclone 30' gives at least 350 μA of 30 MeV protons. In each case a more-or-less automatic chemistry kit is supplied, to turn the irradiated product into the chemical compounds most useful to the doctors. These machines can also be used for neutron therapy, or as injectors into larger accelerators (see below).

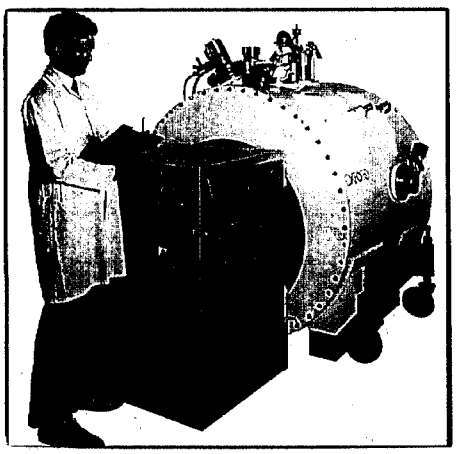

Figure 3. 12 MeV superconducting H^- cyclotron [3]

4. PROTON THERAPY

Fig. 1 shows the variation of dose with depth for a proton beam (the Bragg curve), compared to the dose distribution for various X-rays. To treat a tumour of finite extent the Bragg curve must be spread out by modulating the beam energy, but even then the dose at the surface is much reduced for the same dose at depth, see fig. 1. More significantly the dose drops to zero beyond the end of the range, whereas the dose from X-rays peters out gradually. Therefore proton beams can be fired into tumours in the eye (ocular melanomas) with no "fear it might injure the brain" [5]. Moreover the lateral spread of a proton beam inside the body is small compared with X-rays. The biological effects of protons and X-rays on living cells are however similar. Therefore proton therapy can be more precise than X-rays, and logically is to be preferred. Unfortunately the equipment needed to deliver these improvements costs more, and therefore it has so far been applied only on a limited scale. Current installations in Europe and those coming on line in the immediate future are shown in Table 1.

Table 1
Proton and light ion therapy centres in Europe

	Accelerator	Energy (MeV)	patients (start date)
Clatterbridge	cyclotron	62	470
Louvain-la Neuve	cyclotron	90	25
Moscow ITEP	synchrotron	1000	2600
Nice	cyclotron	65	270
Orsay	SC	200	300
St. Petersburg	SC	1000	800
Uppsala	SC	185	45
PSI Villigen	cyclotron	250 +	1370
TRITRON Munich	booster cyclotron	150	(1995)
COSY Julich	synchrotron	60-250	(1997)
" "	" "	light ions	(1999?)
GSI Darmstadt	synchrotron	light ions	(1996)

The most successful application is to ocular melanoma for which no other treatment is available other than surgical excision of the whole eye. Proton therapy on the other hand achieves a success rate of order 90% with nearly all these patients keeping their vision. A range of 3 cm in tissue is sufficient, corresponding to 65 MeV protons. To treat deeper sites the energy required is typically 185 MeV (range 20 cm), but it is useful to have a margin which can be used for spreading the beam by a system of scattering foils; 230-250 MeV is then recommended. If however the beam is spread out over the tumour by some magnetic system, either static or dynamic, then 185 MeV is sufficient. To treat large tumours in a reasonable time a current of 20 nA is desirable.

This energy range can be easily accessed by cyclotrons, synchrocyclotrons, linacs and synchrotrons. The choice of accelerator is vigorously debated, and they each have their advantages and disadvantages. The synchrotron offers variable energy from 70 to 250 MeV or more, useful for reaching tumours of different depth, but can be low on current. The cyclotron on the other hand has plenty of intensity, and the continuous beam is well suited to

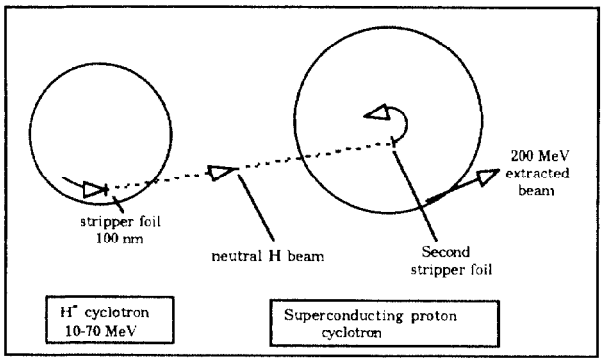

Figure 4. Booster cyclotron with neutral beam transfer

dynamic scanning systems for spreading the beam. But it has fixed energy, so degraders must be used in the beam line, which imply scattering and extra radiation. The synchrocyclotron probably combines the disadvantages of both, and the proton linac may be rather expensive. It is notable that while the Loma Linda hospital in California has installed a synchrotron, a cyclotron is to be preferred in Massachusetts.

A number of projects for the future are under construction or discussed. IBA in Belgium are making a 235 MeV spiral ridge cyclotron which will be installed in the Massachusetts General Hospital, Boston. At PSI in Villigen a new medical beam is being developed by slowing down the protons from the large accelerator, and will soon be operational. (This is described in detail by Pedroni [6] at this conference). The ambitious TERA project in Italy has two proposals [7]; they have taken up the ITEP design of a large H^- synchrotron with low magnetic field and circumference 60 m, cycling at 2 Hz, giving 250 MeV protons, easily extracted by charge exchange. It has been shown that this gives a very low beam emittance so the magnet apertures in the beam delivery system can be quite small, and several independent beams can be extracted. Because of its large radius this machine can later be upgraded for therapy with oxygen ions at 400 MeV per nucleon. They have also proposed a 'compact' synchrotron ('STAC') with 4 Tesla magnets only 2.5 m in diameter for 80-200 MeV protons. H^- cannot be used in this case, because the extra electron would be stripped off by the high magnetic field long before the final energy was reached. A third alternative, to be studied by TERA in collaboration with the Nice group and LASA, Milano, is a compact superconducting cyclotron[8].

Hospitals with existing proton accelerators are looking for supplementary accelerators to boost the energy to about 200 MeV. For this purpose a proton linac is studied as a booster for the 62 MeV Liverpool cyclotron. At Garching near Munich a booster cyclotron TRITRON is in operation, taking the beam from the 28 MeV tandem to 150 MeV, and proton therapy will soon be in place[9]. The Nice group are suggesting an interesting upgrade for H^- cyclotrons, fig. 4. By reducing the thickness of the stripping foil used for extraction it is easy to obtain a good yield of well collimated neutral hydrogen, which exits the magnet tangentially. This can be directed towards the centre of a new high field cyclotron[8], where a second stripper foil converts the beam to protons ready to be accelerated. The spreading of the neutral beam due to scattering in the first stripper is very small. Ideally the two RF frequencies will be locked in phase, so that the bunches from the first machine are picked up efficiently by the second. This scheme greatly simplifies the centre of the second cyclotron, which has no gas sources or cumbersome electrodes; so higher RF voltages can be used, making extraction easier.

5. FAST NEUTRON THERAPY

X-rays and protons kill cancer cells more than normal tissue, because cells are most sensitive during meitosis (cell division), and cancer cells divide frequently. This selective action gives the therapist some margin of safety. On the other hand slowly-growing tumours, and poorly-vasculated oxygen-deficient tumours do not respond well to radiation. For these it is advantageous to treat with particles which give tracks of high linear ionisation density ('high LET'). It has been found that in this case all cells hit by a track are killed, whether slowly growing or not, whether anoxic or not. In a fast neutron beam the ionisation comes largely from proton recoils of very low energy, and these have the desired high LET. Similar results are obtained with beams of fully stripped ions, such as carbon and oxygen (see below). So fast neutron, and ion therapy have a role in cancer treatment, and can give excellent results in appropriate cases. However, these beams are equally lethal to normal tissue: the differential advantage has

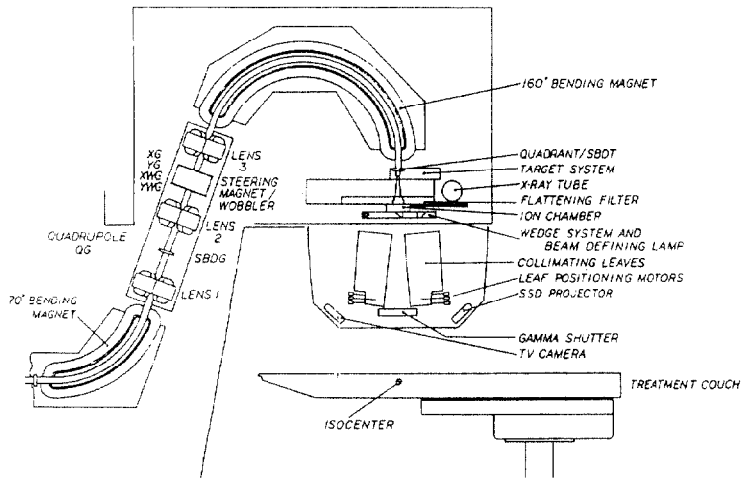

Figure 5. Gantry for fast neutron therapy [10]

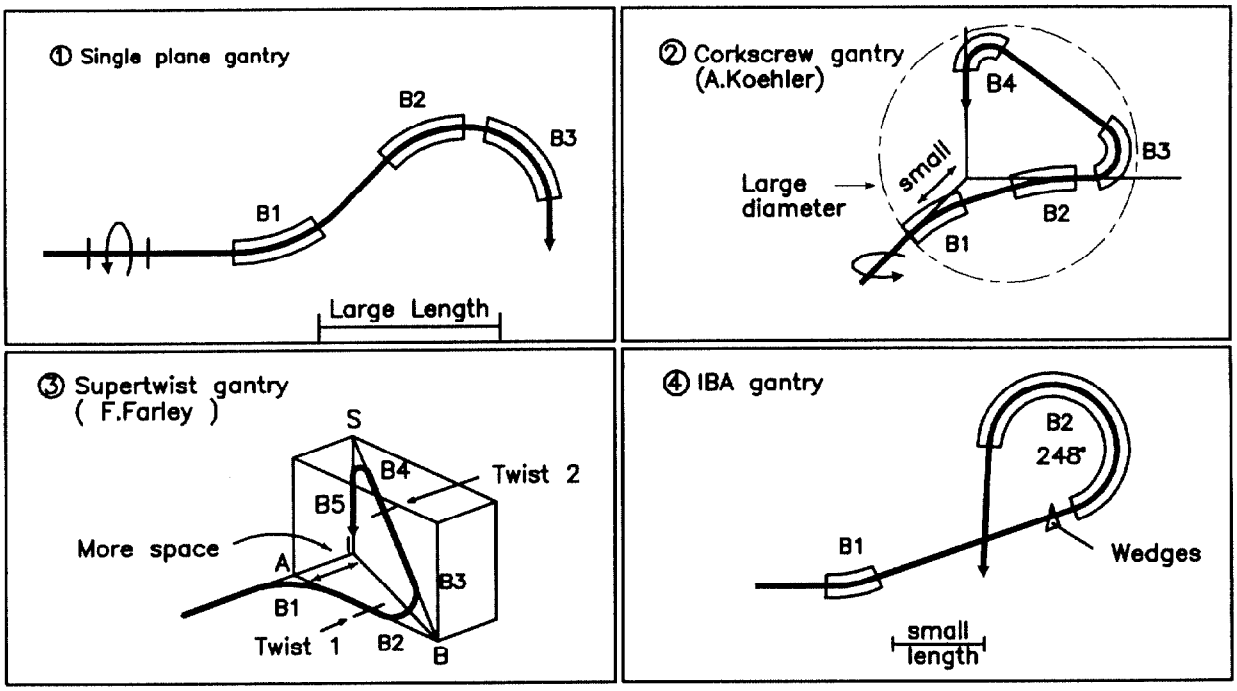

Figure 6. Various rotating gantries, to bring the beam to the patient from a variable direction

been lost; so the therapist has to be doubly careful to put the beam in the right place, and some undesirable effects have sometimes surfaced, many years after the treatment.

Fast neutron therapy is currently practised in Orleans with a 35 MeV cyclotron, in Louvain-la-Neuve and Nice (with 90 and 65 MeV cyclotrons). A typical rotating gantry is shown in fig. 5.

6. NEUTRON CAPTURE THERAPY

The reaction $B^{10}(n,\alpha)Li^7$ has a high cross section for slow neutrons releasing energy into two high LET tracks of short range. If the boron could be concentrated into tumours, irradiation with slow neutrons would destroy them without affecting normal cells. The problems are to find a non-toxic boron compound which goes to the tumour, and to produce a neutron beam of the optimum energy. The diffusion length of thermal neutrons in the body is only about 1 cm, so they will not penetrate far enough. Epithermal neutrons reach further, but as the energy is raised the boron cross section falls as 1/v; a judicious compromise is needed.

In Brookhaven (U.S.A.) the favoured compound is p-boronophenylalanine (BPA) which is concentrated in tumours. The ratio of boron inside the tumour to outside is at least 3:1 with over 20 ppm boron inside, and they can cure over 90% of brain tumours in rats. Treatment of human glioblastoma is planned for 1995. A 'Concerted Action' of the European Community will soon be starting trials on human patients with mercapto-undexahydrododecaborate (BSH) using an epithermal beam from the reactor at the Joint Research Centre in Petten. So far efforts to load boron into tumours using monoclonal antibodies have not been conclusive. The interest for this conference is that the neutrons could alternatively be generated by a high current proton or deuteron accelerator, and this could make the treatment more widely available. The total dose of epithermal neutrons required at the tumour is about 10^{13} neutrons/cm^2 [11].

7. LIGHT ION THERAPY

As mentioned above, ions such as carbon and oxygen with high LET are effective against 'radiation resistant' and anoxic tumours, which are difficult to treat with protons or X-rays. Light ion therapy has been used successfully on the Bevalac at LBL, Berkeley, for many years but this accelerator has now been decommissioned. A feasibility study was carried out under the framework of a European Community 'Concerted Action' to examine the need for ion therapy in Europe, and the machines to deliver it[12]. This study contributed some motivation for the medical beam now being set up at GSI, Darmstadt, where experimental treatments with light ions are planned to start in 1996. On the COSY accelerator at Julich another medical beam is being prepared. Initially planned with protons, it will later be used also for ion therapy[13]. Finally the AUSTRON project in Austria for a spallation neutron source involves a 1.6 GeV synchroton cycling at an impressive 25 Hz, with 100 kW on the target. The

complex will include proton and ion therapy, and is planned for the year 2000[14].

8. BEAM DELIVERY

In all these methods the source of particles is only a part of the total system. It is also important to position the patient precisely, to bring the beam to him from the ideal direction, to spread it uniformly over the target volume, laterally and in range, and to monitor the action. In all these fields there is scope for innovation. In Cape Town, for example, the patient support system is fitted with a number of small white dots which are observed by a set of digitising TV cameras. From this information the software calculates the patient position and automatically moves the table to correct the alignment, using all six degrees of freedom. Just behind the white dots there are small heavy metal fiducials which show on the preparatory X-ray and CT scans, so the whole system is tied together, and the saving of time in the treatment room is significant.

The rotating gantry, required to bring the beam to the patient from the optimum direction, requires major mechanical components, and tends to be costly. The corresponding beam optics should produce a non-dispersed image in the target plane, and leave room for the appropriate range modulation and beam spreading after the final bend. Some alternative designs are shown in fig. 6. In all cases the equipment rotates about the original beam direction as axis. The classic gantry fig. 6(1) has the advantage of simplicity, but has been criticised for its long length which implies a large shielded volume. In the design of PSI [6] the overall diameter is reduced by placing the patient off the main axis on the opposite side from the magnet, and moving him as the beam rotates. In the corkscrew gantry[15] fig. 6(2) the beam is first bent through 90° by B1 and B2, then through 270° in the plane perpendicular to the axis by the coplanar bends B3 and B4, before arriving at the isocentre, I. A variant of the corkscrew which gives more room for the patient is achieved by spiralling the beam along the main axis. This leads to the 'Supertwist' gantry[16] shown in fig. 6(3). The spiral structure introduces some coupling between the transverse planes, but this can be corrected by adding small skew quadrupoles, leading to a good final image, with no dispersion in position or direction in both planes. Fig. 6(4) shows another design put forward by IBA, with a wedge at the dispersed intermediate image to compress the momentum spread in the beam and thus give a more precise end point in range.

9. SUMMARY

Starting from 1895, accelerators have being used with increasing success in medicine. The technology exists and is being continually improved. Medical results are encouraging. The applications will continue to widen as more investment becomes available.

10. ACKNOWLEDGEMENTS

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