ACCELERATORS FOR CHARGED PARTICLE THERAPY: PERFORMANCE CRITERIA FROM THE USER POINT OF VIEW

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ABSTRACT

The introduction of charged particle therapy in the hospitals could provide substantial improvements to external radiation therapy for cancer treatment. Many different types of accelerators have been proposed for installation in the hospitals, all with their own merits and disadvantages. In this report we discuss the requirements posed by charged particle therapy on the quality of the beam delivered by the accelerator (variable or fixed energy, beam duty factor, beam intensity, etc.). **Special emphasis is given to items** like dynamic beam scanning, gantry design and proton radiography and tomography, **which are not well established yet** in this field but **which could eventually have a strong impact on the choice of the accelerator** for charged particle therapy in the future.

1. INTRODUCTION

About 2/3 of all cancer patients receive radiation therapy in the course of the disease (alone or in combination with other therapy modalities, with curative intent or for palliation only). Radiation therapy continues therefore to be one of the most used weapons in the fight against cancer, a disease which nowadays statistically hits (over lifetime) about one individual out of four of the population of the industrial countries.
It is the opinion of many experts working in the field, that improvements in the techniques of radiation therapy, especially concerning **treatment precision**, is needed to improve local control of the primary tumour. Better radiation therapy with curative, instead of palliative intent, will be also probably needed in a rather immediate future in combination and as a complement to new systemic treatments, like immunotherapy and chemotherapy, which hopefully will be able to cope with the problem of the spread of microscopic distant metastasis.
A possible significant improvement in external radiation therapy can be expected from the use of **heavy charged particle beams** (heavier than electrons).

Despite the size and costs of the accelerators and beam transport systems involved, the interest for the introduction of protons (and eventually of heavier ions) in the clinics is steadily increasing in the oncological community. This is certainly also a consequence of the very remarkable event, that in 1991 the first **hospital-based proton facility** of the world has been successfully put into operation in **Loma Linda**, California.
The commitment to further develop radiation therapy with charged particles is also a tradition of PSI, where this goal is being actively pursued since about 10 years, first by the introduction of pion therapy in 1981 and second with the introduction in Europe of the treatment of uveal melanomas with a 70 MeV proton beam. A new beam line dedicated to proton therapy has been assembled this year at PSI. Next year we will install at PSI a compact gantry in the new beam line and we expect to be able to start patient treatments of deep seated tumours with the gantry in 1994.
The experience gained at PSI with proton treatments should encourage the introduction of hospital-based proton machines in our country. This is the reason for our interest in all questions regarding the choice of the accelerator type to be used in a hospital environment.
In this report we focus our attention mainly on the different factors affecting charged particle radiation therapy, with special emphasis on their relationship with the properties of the different proposed accelerators.

2. CHARGED PARTICLES FOR RADIATION THERAPY

We discuss briefly the utilization of **protons, neutrons, pions and heavy ions** as possible alternatives to conventional therapy with **electrons and photons**.

2.1. Comparison of Charged Particles: Classification Criteria

2.1.1. Dose distribution precision

The precision of the dose distribution continues to be a major key for improvements in radiation therapy.

This has been undoubtedly demonstrated in the past by the successes of the introduction of high energy photon machines in the hospitals (megavoltage therapy). This is also documented by the numerous present activities to improve conventional therapy, like the development of 3D treatment planning, dose conformation techniques with multileaf collimators and "inverse" dose algorithms for treatment planning.
The goal to confine the dose to the target volume is the basic requirement of radiation therapy. The therapist is very often faced with contradictory requirements, dictated by practical technical limitations of the dose application system. On one side one needs to increase the dose in the target volume (in order to improve the probability of tumour control) and on the other side it is necessary to reduce the radiation burden on healthy sensitive organs surrounding the tumour (in order to avoid treatment complications). The utilization of the **superior ballistic properties of protons and heavier ions** is expected to be very helpful in all situations, where a better confinement of the dose to the target volume is required.

2.1.2. High and low LET radiation

The Linear Energy Transfer (LET) is a physical quantity describing the density of ionisation events at a microscopic level. Depending on the amount of LET the radiobiological effect of radiation on living cells can be quite different.
a) With **low LET radiation** at low dose rate (factors dose and time) a significant portion of the radiation damages can be repaired by the cells themselves (mainly single DNA strand break repairs). The repair mechanisms are important in the context of fractionated treatments. The fractionation of the dose is used to enhance the differential cell sensitivity between healthy and malignant cells. Most successes of radiation therapy are based on the fact that malignant cells are usually more sensitive to radiation than healthy cells ("positive" therapeutic ratio). **Fractionated low LET radiation** is therefore especially successfull for the treatment of **radiosensitive tumours**.
b) With **high LET** the capability of the cells to repair radiation damages is strongly depleted (the densely ionising radiation produces multiple DNA strand breaks, which are difficult to repair or which are repaired with a high probability of errors). A general reduction of any differential cell sensitivity is usually observed with high LET radiation. This should be an advantage in the case of very **radioresistant tumours** (the reduction, due to the high LET, of the "negative" therapeutic ratio between healthy and cancer cells could provide an improvement of the chances of cure in this case).
High LET radiation is, in other words, a more efficient (with higher relative biological efficiency, RBE), but also less selective method to provide cell killing. Late complications are observed unfortunately more often with this kind of radiation than with low LET.
A very important feature of high LET, which has paved the way to the introduction of neutron and pion therapy in many research centers around the world in the seventies, is the reduction, due to high LET, of the so called Oxygen Enhancement Ratio (OER). Living cells with poor content of oxygen are usually more resistant to radiation than cells in contact with intact blood supply. Since tumours generally have a rather poor vascularization, the oxygen effect is considered to be a possible cause of treatment failure in conventional therapy (cells close to necrotic regions, are poorly oxygenated, are more radioresistant and are therefore likely candidates for tumour regrowth). With high LET the cells at risk should be more efficiently destroyed.
The results of the experience with high LET gained in the last 15 years from neutron, heavy ions and pion treatments seem to indicate that high LET radiation could be advantageous for at most 10 to 15% of all patients. For all the other patients low LET radiation seems to be more appropriate.

2.1.3. The costs for charged particle therapy

The costs for a treatment course of conventional radiation therapy (around 5000$ depending on the country) are usually less than for comparable techniques, like surgery or chemotherapy. Compared with very advanced techniques like heart or bone marrow transplantations, the costs are indeed very low.
If we perform a very rough estimate and we assume the extra investments necessary for installing a proton facility to be about 25 M$ (the money exceeding the costs of an equivalent conventional facility), to be amortized over a period of 10 years and financed with an interest rate of 10%, we end up with additional expenses in the order of 5 M$ per year. If the facility is optimized to treat around 1000 patients per year, the additional costs distributed over individual patients should be in the order of 5000$ per patient. If the proton treatments could be limited only to those cases, where better clinical results are expected, for example in the form of avoiding additional surgical interventions or medical care or to permit the reinsertion of the patient into the work cycle, this amount of money would be immediately justified also from an economical point of view.
In other words: if the results are sufficiently promising and the treatment technique is sufficiently efficient, any of the proposed particle therapy facilities can be justified in the industrial countries also from the economical point of view.
The facility costs clearly remain an important parameter for the comparison of particle accelerators for therapy.

2.2. Comparison of Particles for External Radiation Therapy

Figure 1 shows in a very qualitative picture a personal judgement on the merits of the different particles:

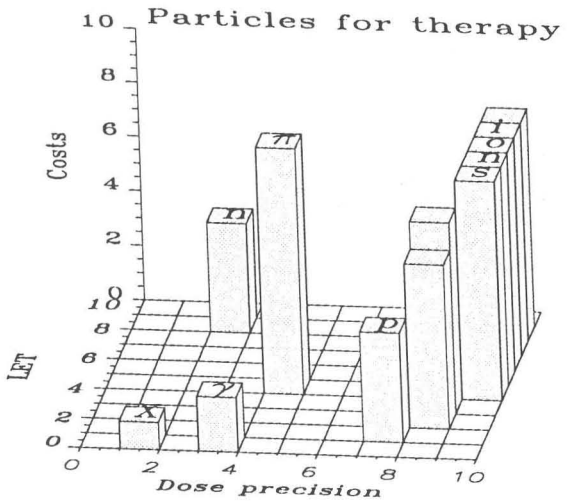

Fig. 1. Qualitative comparison of the different types of particles used for external radiation therapy. The discussion of the judgement criteria is given in the text. The numbers on the scales are arbitrary units.

a) **Photons**

The merits of megavoltage photons in providing a cheap, quite precise low LET radiation source are undiscutable. Photons and electrons will continue to cover the needs of the majority of the cancer patients.

b) **Neutrons**

Neutrons are the cheapest in the class of particles with high LET and are already available since a decade at few selected therapy centers. From the point of view of dose precision they are similar to X-rays and MeV photons. Concerning dose shaping capability they are less precise than pions and heavier ions. Because of their more immediate availability neutrons will continue to be the major source of high LET radiation. The practical impact of neutrons in the hospital environment seems however to be less important than anticipated and hoped for in the seventies.

c) **Pions**

Pions are very expensive, have less precision than ions and have, as secondary particles, very stringent practical dose rate limitations. Pions are probably nowadays the particles which have the least chances for introduction in a hospital environment (heavy ions are probably a better choice in the same range of costs).

d) **Light and heavier ions (from Helium to Neon)**

A very appealing feature of ion accelerators is the flexibility to produce beams of different ion types. In this way it is possible to provide low and high LET with the same radiation source. This flexibility is extremely attractive for facilities planned with strong **research interests**.

Another appealing feature is given by the possibility to use radioactive beams.

Concerning the precision of treatment heavier ions have, at least in theory, the best ballistic properties. In practice the advantages of ions over protons are partly destroyed by the **fragmentation of the ions** and by the complications given by the **variation of RBE and LET** with position inside the dose field.

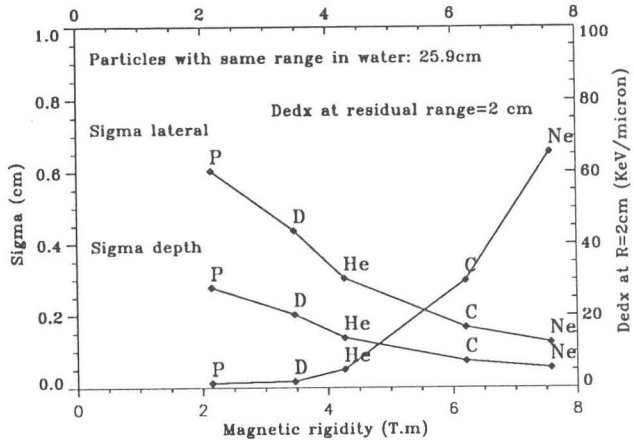

Fig. 2. Dedx, lateral and distal beam width as a function of the magnetic rigidity for different ion types (for the same range of penetration).

Figure 2 shows the calculated lateral (multiple scattering) and distal (range straggling) beam width σ of the dose of a pencil beam for different types of ions (see also section 3.1). The heavier the ion, the better the sharpness of the beam and the higher the LET. The beam width is plotted as a function of the magnetic rigidity of the particles, with the beam energy chosen to provide the same range of penetration of the particles into the patient. The factor of 3 higher magnetic rigidity of the carbon ions compared with protons scales linearly into the dimensions of the accelerator and beam transport system and therefore more than linearly into the costs needed for a facility for ion therapy. Ion therapy is expected to be much more expensive than proton therapy, as it can be argued from a comparison of the costs of the Himac facility in Japan (300 M$) with the costs of the Loma Linda proton facility (60 M$) in the USA.

The higher costs of ion therapy can be justified only in two ways: I) by the need of high LET together with good dose precision (a subclass of the neutron indications?) or II) by the need of extreme dose precision (a subclass of the proton indications?).

How does the extreme precision of the ions compare with other sources of errors, like variations of patient anatomy, organ movements and similar uncertainties?

It is the task of the new ion facility in Chiba, the first in the world dedicated exclusively to ion therapy (and expected to become operational in 1994), to provide the answers to these questions.

Berkeley is at the moment the only place in the world, where ion therapy is performed on patients.

e)**Protons**

Proton therapy is expected to bring significant improvements concerning the quality of the dose distribution at

relatively moderate costs (a doubling of the costs over conventional therapy is a generally accepted estimate). From the radiobiological point of view, protons can be considered to be a low LET radiation. Since for most of the patients low LET seems to be a better choice, protons represent the next immediate alternative to photons for introduction in the hospitals on a large scale.
In the following we will follow our preferences and we will discuss only proton therapy.

3. PROTON THERAPY

3.1. Physical Characteristics Relevant for Therapy

Figure 3 shows, as an example, the dose distribution of a proton pencil beam, measured with a degraded beam at PSI.

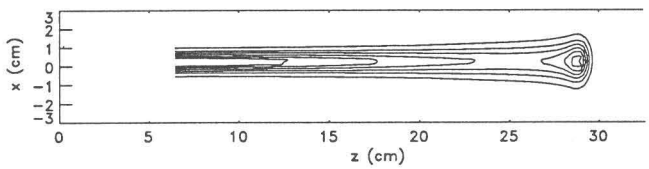

Fig. 3. Dose distribution of a proton pencil beam.

Charged particles, when they penetrate matter, lose energy by collision with atomic electrons. The range of penetration of protons is extremely well defined with a range straggling of about 1% (standard deviation). As the particles approach the position where they stop, they lose more and more energy giving rise to the well known characteristic **Bragg peak**. The dose precision at the distal edge of the field is governed by the range straggling process.
The other major factor affecting the precision of the dose distribution is **multiple Coulomb scattering** (collisions of the projectile with the charge of the nuclei). This affects the precision of the dose in the direction transverse to the beam. Nuclear collisions represent an additional nuisance, since they produce some degree of attenuation of the beam (10-30% depending on the range).
The phase space of the beam delivered by a dedicated proton accelerator should be chosen to be smaller than the contributions from range straggling and multiple scattering at the Bragg peak position.
The precision of the dose fall-off at the edge of the field depends directly on the choice of the **beam energy**. To a good approximation the dose fall-off can be considered to vary linearly with the energy of the beam. The possibility to choose a variable beam energy in the range between 70 and 220 MeV (270 MeV if proton radiography must be supported) is a generally accepted requirement for proton therapy machines for the hospitals.
An ultimate precision in the order of few mm for the confinement of the dose at the edge of the dose distribution and a dose homogeneity of few % inside a 3D shaped target volume is a performance achievable with proton therapy.

3.2. Indications for Proton Therapy

The main strategies to be used to exploit the possible advantages of proton therapy over conventional photon therapy, can be summarized in the following way:
a) **The dose beyond the Bragg peak is essentially zero**. This should be used in all situations, where the tumour is surrounded by sentivitive structures and where stopping the beam exactly in front of healthy, very sensitive structures behind the target volume, brings a significant reduction of treatment complications. This is actually the speciality developed mainly at Harvard, with the treatments of tumours close to the base of the skull (chordomas and chondrosarcomas) or close to the spinal chord. Together with the eye treatments, these very impressive indications represent now the **"classical" proton indications**, those which have attracted the interest of the oncologists on proton therapy worldwide.

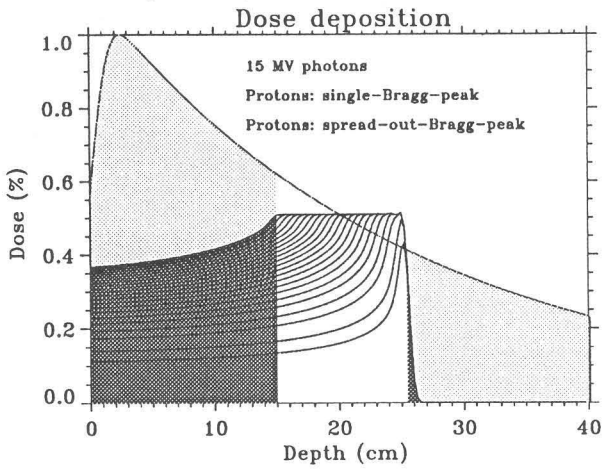

Fig. 4. Depth dose distribution comparison of photons and protons. The shaded areas represent the amount of undesired dose outside a 10 cm target volume located on the axis of a "patient" of 40 cm diameter.

b) **Low integral dose outside of the target volume**. This can be seen from Fig. 4, where the dose distribution of photons and of Spread-Out-Bragg-Peak (SOBP) protons are compared. The light and dark+light shaded area in the picture represent the undesired dose deposited outside the target volume for protons and photons respectively. The situation in the picture is more favourable to protons by about a factor of 3. This advantage is maintained for multiple fields, provided that the same number of fields can be used with protons as with photons (Fig. 5). The reduction of integral dose could prove to be very effective for the treatment of **large target volumes**, where the dose outside the target volume is the limiting factor. These indications require however the installation of **isocentric gantries for proton**

therapy, similar to those used in conventional therapy. Up to now protons have been used only on horizontal beam lines, without isocentric gantries (and sometime with other limitations like insufficient beam energy). This is probably the reason, why up to now protons have been used mainly for treatments of rather small target volumes. Since fall 1991 the door for a completely new class of indications, namely **large target volumes**, has been opened in Loma Linda with the installation of the first proton therapy facility of the world with isocentric gantries.

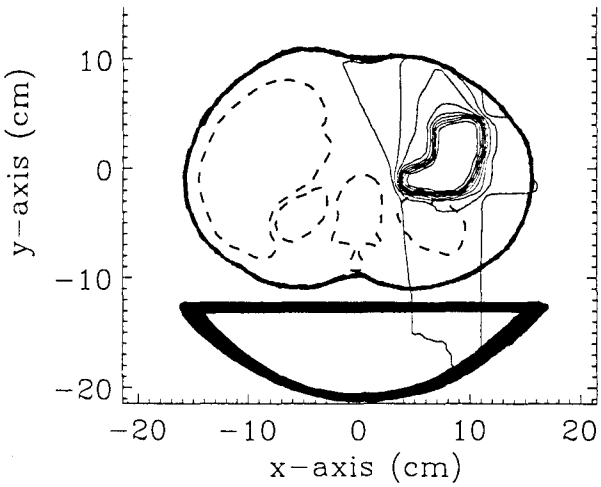

Fig.5. Example of a dose distribution to be achieved using the spot scanning technique: the isodose lines are 10%, 20%, 30%, ..., 90% respectively.

c) **Protons are ideal particles for dose conformation.**
This for two reasons. The first reason is that protons are **charged particles**. They can be transported, focussed and deflected at wish with magnetic devices, giving unpaired flexibility to manipulate the distribution of the dose under **complete computer control**, the rationale for the introduction of the so called **spot scanning technique**.
The second reason is, that protons are **well localized in all three dimensions already as an elementary pencil beam**, as opposed to the photons, which acquire 3D dose localisation only through the overlapping of convergent collimated beams. For these reasons **dose conformation** is expected to be **more precise and easier** to perform **with protons** than with photons.
A true 3D dose conformation with protons, using a spot scanning method is still a novelty to be realized in this field. This is together with the design of a compact gantry dedicated to beam scanning, one of the key points of the developments for proton therapy at PSI. These developments should open the door to a third class of indications for proton therapy, namely **tumours with complex shape** to be treated with a routine automated conformal method.

3.3. Proton Therapy: Factors Affecting the Accelerator Choice

3.3.1. Proton application techniques: scatter foil technique and spot scan technique

The traditional technique used up to now for proton therapy, is based on the spreading of the beam in the transversal direction using **scatter foils** (or similar devices). The lateral shaping of the dose field is performed using **collimators**. The spreading of the beam in depth is performed using **rotating wheels** with variable thickness or **ridge filter systems**. The SOBP function is chosen to produce a dose flat top with constant length equal to the maximal thickness of the target volume in depth. The dose conformation to the target volume is not performed in depth, only the position of the distal edge of the dose field is usually adjusted in depth using **compensator** boluses. Through overlapping of multiple fields excellent 3D-shaped dose distributions can be however achieved with this technique. The advantages of the scatter foil technique are given by its reliability and safety.
An alternative technique is to use the undisturbed focussed beam and to scan the beam in three dimensions. **Magnetic deflections** (and/or patient translations) are used for the positioning of the spot in the lateral direction. For positioning the Bragg peak in depth **range shifting material** is inserted in front of the patient or the **energy of the beam** is changed directly in the accelerator, if this option is available. At PSI we are developing a **discrete spot scanning** technique. The dose is applied statically at each spot position by switching on and off the beam with a **kicker magnet** and by measuring the spot dose with a fast beam monitor system. This simplifies the control system at the expenses of some dead time for the application method.
The spot scanning technique is expected to be superior to the scatter foil method, because of its full flexibility, since it allows a true 3D conformation of the dose (4D conformation -non homogeneous dose distributions- is in principle also readily available) and permits complete computer control with minimal patient individualized hardware. The full beam is dumped (most of the time and in a controlled way) in the patient and is not lost in the equipment, reducing the requirements on beam intensity for the accelerator and reducing the activation problems of all components of the facility.
The spot scanning can be integrated in the optics of the beam transport system of the isocentric gantry, thus permitting a reduction of the gantry diameter.
A possible problem faced by the spot scanning technique is the problem of organ movements during scanning, with possible interferences between scanning of the beam and motion of the patients.
Since the flexibility of the scanning method is achieved by performing dose spot applications sequentially as a function of time, a good **beam duty factor** is required in this case from the accelerator.

We assume here, as a typical example of scanning performance, the irradiation in 2 minutes of a 1 liter (complex shaped) target volume, with scanning on a regular mesh with 5mm distance from spot to spot (positioning of the dose field edge better than ± 2.5mm). This requires about 10000 spot applications in 2 minutes, with a mean spot irradiation time of about 10 ms (100Hz). We don't assume here any particular **stability of the beam**. The PSI scanning method is supposed to be able to cope with beam fluctuations in the order of 100% of the mean intensity. The spot dose is chosen individually for each spot in the treatment planning system. If the dose of each spot has to be controlled with a precison of 1% of its mean value, we must measure it and, when the required amount of dose has been deposited, immediately switch off the beam with a typical reaction time of 100μs (10KHz). These are typical requirements for a fast spot scanning with a DC-like beam (beam of a cyclotron or slow extraction from a synchrotron). Other similar schemes of dynamic scanning have been proposed for example by IBA(Belgium), ITEP Moscow(Russia), Uppsala(Sweden) or under development in Berkeley(USA) and Darmstadt(Germany).[1)]

3.3.2. Isocentric gantries for proton therapy

The major problem encountered in the construction of an isocentric gantry for proton therapy is the high magnetic rigidity of the protons used for therapy (with conventional bending magnets the bending radius can not be chosen smaller than about 1.3 m) For this reason an isocentric gantry for proton therapy is larger and more massive than a conventional gantry for photons.
The only existing gantries of the world are the three "cork-screw" gantries of Loma Linda, which span a diameter of 12 m and have a weight of about 90 tons each. In the "cork-screw" design (first proposed at Harvard) the beam is bent first by 90^0 away from the axis and then is bent back on axis by a 270^0 bending in the plane transverse to the axis of the gantry. The Loma Linda gantry is designed to support both application methods, the spot scan method and the scatter foil technique (the last requiring a large distance between last bending magnet and patient).
The proton gantry to be realized next in the world, should be the gantry for PSI, commissioned for installation in 1993. The diameter of the PSI gantry has been reduced down below 4 m in diameter, by combining the spot scanning technique into the optics of the beam transport system and by mounting the patient transporter excentrically on the gantry. In this way the space in the radial direction is occupied only by the 90^0 magnet and by the patient transporter system respectively. The PSI gantry does not support the scatter foil technique. If the Loma Linda gantry looks like a large disk, the PSI gantry looks like a smaller but longer cylinder. Since the beam used at PSI is a degraded beam (energy degradation from 590 MeV down to 100-260 MeV) the phase space of the beam used at PSI is large and the magnets are correspondingly very massive. The gantry of PSI is heavier (120 tons) than the Loma Linda gantries despite the facts, that less total bending is applied on the beam. This is not a problem of the gantry design itself, but is a problem related to the proton source used at PSI (fixed beam energy and degradation of the beam). A PSI gantry design adapted to a dedicated accelerator with a beam with small phase space and variable energy, would be much less massive than the present prototype. For other gantry designs (IBA (Belgium), Uppsala (Sweden), Moscow (Russia), MSU East Lansing (USA), ACCTEK (USA)) or other solutions with combined fixed horizontal and vertical beams (Tsukuba and Chiba (Japan)) we have to refer here to the literature.[1)]
The performance of isocentric gantries does not depend much on the accelerator type, except for the two factors already mentioned:
a)Depending on the quality of the beam delivered by the accelerator (degraded or direct beam) the gantry magnets can be very massive or not.
b)The gantry dimensions depend partly on the application technique chosen for the gantry, and consequently the feasibility of the gantry depends indirectly on the duty factor of the beam delivered by the accelerator.

3.3.3. Proton radiography and Proton Tomography

The intensity of the proton beam must be attenuated down to a proton rate which permits the use of Multiwire Proportional Chambers (MWPC). The energy is chosen such that the protons barely pierce through the patient and exit on the other side with low energy. The entrance and exit coordinates of each proton are measured with MWPC and the residual energy is measured with a scintillating crystal (or the residual range with a stack of plastic scintillators). The measurement in coincidence of entrance and exit proton coordinates permits to reduce the position resolution error due to multiple Coulomb scattering by about a factor of 4 (position resolution in the order of few mm instead of around 1 cm). Since protons have a well defined penetration range, very few protons give already a very precise information on the integral electron density of the patient along the proton path. Proton radiography is therefore very sensitive to small density variations.
Proton radiography realized in the context of proton therapy could prove to be very appealing for the following reasons:
a) Proton radiography could be used to control the positioning of the patient in the beam directly on the gantry (substitution of the position verification usually performed by X-rays projections).
b) "Absolutely calibrated" proton radiography images contain precious additional information on the exact penetration depth of protons into the patient. Penetration errors due to organ misalignments or wrong calibration of CT data used for treatment planning, could be directly detected with digitized proton radiography images taken

directly **on line** before starting treatment. The quantitative verification by means of absolute **proton radiography** measurements, of the correctness of the residual range values calculated by the treatment planning system for the **passing-through particles**, should give confidence in the correctness of the corresponding calculations for the **stopping protons** for **therapy**. Proton radiography is therefore a very interesting tool to check the penetration depth of the beam into the patient together with the control of the correct positioning of the patient in the beam.
c) Proton radiography has excellent density resolution characteristics. A factor of 10 or 20 less dose is necessary for proton radiography to provide the same density resolution as with X-rays. Proton radiography could eventually prove to be a new interesting diagnostics tool, more sensitive to soft tissue differences.
e)Proton tomography, if possible to realize in practice on the gantry, should give access in theory to the ideal data base for treatment planning, since it would provide directly electron densities without the need of doubtful calibrations of Hounsfield numbers (without beam hardening artefacts like for X-rays).
We plan at PSI to test these ideas in the new beam line dedicated to proton therapy, in order to learn about their practical importance.
For the point of view of the requirements on the accelerator type, proton radiography and tomography require a very high rate of data taking, with individual events resolved by coincidence measurements in time. The duty factor of the beam is a crucial parameter for the acquisition time of the radiographic images.

3.3.4. Synchronisation with breathing

If dynamic scanning with conformation of the dose and/or proton radiography are performed together with the synchronization of breathing of the patient, the requirements on beam duty factor are even more important.

4. ACCELERATOR REQUIREMENTS

In this section we summarize the requirements on accelerators for proton therapy in the prospective of the future developments described in the previous sections:
a) **Maximum beam energy**.
For therapy 220 MeV energy seems to be adequate, but 260-280 MeV energy (40-45 cm range) is necessary for the feasibility of proton radiography in the body.
b) **Fixed beam energy and beam degradation**.
A fixed energy of the beam (cyclotron and synchrocyclotron) could prove to be an acceptable solution for the hospital, for reasons of simplicity and reliability.
The option to choose a variable energy (in steps or continously) is however the solution preferred by most of the proton therapy experts. A possible compromise for fixed energy machines is to use degraded beams, realized with variable thickness absorbers placed in the beam line possibly at an intermediate double focus . The scattered beam must be analyzed in momentum and phase space in the subsequent beam line, which could be the gantry itself. If the degradation of the beam is performed from 260 MeV (needed for proton radiography) down to 70 MeV, the intensity of the analyzed beam is expected to change with energy as much as a factor of 20.
The disadvantges of the degradation are given by the large variation (with all related safety problems) of beam intensity (needed in the accelerator to obtain a constant intensity of the degraded beam), by the increased activation of beam line elements in the region around and before the degrader and by the large phase space of the extracted beam, which requires massive magnets on the gantry.
c) **Variable energy**
directly from the accelerator (continuously from the synchrotron and in steps from a proton linac) is certainly a better solution, if available.
In the case of the synchrotron, the possibility to change beam energy from pulse to pulse is very appealing, since it should permit to control the deposition of the beam without range shifter systems (only the patient body contributes to the scattering of the beam), which is a necessary condition to achieve the ultimate precision possible with proton therapy. This requires however the simultaneous tuning, pulse by pulse, of all magnetic elements in the beam transport system, which could prove to be very difficult to obtain with sufficient beam position stability.
d)**Beam intensity**.
The required beam intensity depends on the application technique used. For tumours treatments with the spot scanning method a few nA proton current should be sufficient. For the scatter foil technique the generally accepted requirement is 10-20 nA.
e) **The duty factor of the beam**.
A good duty factor could prove to be, in the long range, equally important for proton therapy as it has been in the past for physics experiments in the same energy range.
The cyclotron provides the best possible time structure of the beam. This is indicated for beam dynamic scanning and for the data taking for proton radiography and tomography.
The slow extraction from a synchrotron is an acceptable alternative solution, which is however often criticized as a technical complex solution (?).
The other pulsed machines (linac and synchrocyclotron) should provide at least 100 Hz together with some method of control of the beam intensity from pulse to pulse at the ion source (or a 10kHz pulsed beam) in order to remain competitive for dynamic scanning methods (see section 3.3.1). For coincidence measurements with MWPCs for proton radiography a pulsed machine is always less efficient.
f) A **fast beam shutter**, to switch quickly the beam on and off, is a necessary device for the **discrete beam scanning technique**, which is more interesting than a

continuous scan, because of its simplicity and reliability. The switching can be realized with a **kicker magnet** mounted in the high energy proton beam line. For accelerators without ramping of the magnetic field (with sufficiently short transport time from the ion source to the patient) the switching of the beam should be performed more easily at the **ion source**.

g) **Superconducting accelerators and superconducting beam transport systems.**

These developments are very important, since they should provide a true miniaturisation of the proton facility, down to sizes comparable with those used for conventional therapy, up to the point even to envisage the rotation of the accelerator system itself around the patient (proposed MSU facility, East Lansing, USA).[1)]

Superconducting technology should also help to reduce the dimensions of gantries. The problems still to solve are the reliability (long repair time for the cooling down of the cryogenic parts) and the complexity (design, beam optics and wiring) of superconducting bending magnets with small bending radius.

h) **Acceleration of H^- ions.**

This solution can be used to provide a very simple and very reliable slow extraction of the beam from a synchrotron (charge exchange extraction with stripping foils). The phase space of the beam can be chosen to be very small, thus permitting to construct gantry systems with very small magnets (Moscow gantry).[1)] The price to pay for this solution is given by the large dimensions of the accelerator ring (around 15 m diameter) and by the need of ultrahigh vacuum (both requirements are necessary to avoid ion stripping). The large size of the accelerator ring can be compensated by designing the facility to be very compact, with short beam lines connecting the ring with the treatment rooms, aligned on a circle around the accelerator.

i)The **reliability and simplicity of operation** (which does not exclude a priori very advanced technologies, if they are well automatized) of the proposed solutions is probably the most important parameter for the success of the introduction of proton accelerators in the hospital environment.

5. CONCLUSIONS

What we need just now are more hospital-based proton therapy facilities in the world, in order to improve our clinical and technical experience on this subject.

Which is the most optimal technical solution for the clinics is not completely clear yet. The Loma Linda synchrotron represents a well optimized solution, which satisfies the needs of the techniques presently available (scatter foil method on a cork screw gantry) and at the same time permits future developments (slow extraction, variation of the energy pulse by pulse, dynamic scanning, etc.). The practical relative importance of the different performance parameters (like size, costs, patients throughput, simplicity of operation, safety) and the future development of new technical issues (like automated spot scanning, proton radiography and tomography, superconducting accelerators and gantries) could however change the conclusions in favour of other accelerator solutions.

6. ACKNOWLEDGMENTS

In this report we have discussed, for reasons of space, mainly those items, like dynamic scanning, compact gantries, proton radiography and tomography, which are now not well established in the field of charged particles, but which have good chances to become more popular in the case of the spreading of proton therapy facilities. This should not in any case diminish the importance of the more traditional techniques developed in the last decades by the centers pioneering charged particle therapy like Berkeley, Uppsala, Harvard, Dubna, Moscow , Leningrad, Chiba, Triumf, PSI, Tsukuba, Clatterbridge, Loma Linda, Louvain, Nice, Orsay, ...

Many of the ideas discussed in this paper refer indirectly to propositions originating from and presented and discussed in more details at PTCOG (Proton Therapy Co-Operative Group) meetings. I would like to thank all members of the PTCOG community for their help and for the very open and friendly atmosphere, which is much profitable for the promotion of charged particle therapy.

7. REFERENCES

1) The list of contributions of relevance in the context of this paper would be too long to be presented here without important omissions. We refer therefore to the specialized literature. The different charged particle facilities discussed in this paper have been presented at several conferences and the contributions are collected in several proceedings, for example in:

A)Proceedings of the NIRS International Workshop on Heavy Charged Particle Therapy and related subjects, (NIRS-M-81, Chiba, JAPAN, 1991).

B)Proceedings of the Proton Radiotherapy Workshop held at PSI, (Paul Scherrer Institute, CH-5232 Villigen, 1991).

C)Proceedings of the International Heavy Particle Therapy Workshop (PTCOG/EORTC/ECNEU) held at PSI, (Paul Scherrer Institute, CH-5232 Villigen, 1989).

D)Proceedings of the 2nd European Particle Accelerator Conference in Nice, (Ed. Frontieres, 91192 Gif-sur-Yvette Cedex, France, 1990).

E)Extended Abstracts of The fourth Workshop on Heavy Charged Particles in Biology and Medicine in Darmstadt, (GSI-91-29, D-6100 Darmstadt, 1991).

F)Proceedings of the Twelfth International Conference on Cyclotrons and their Applications in Berlin (World Scientific, Singapore, 1989).