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Salahaddin University-Erbil

Research Project

Acceleration for Protontherapy

Submitted to the department of Physics in partial fulfillment of the requirements for the degree of BSc. in Physics

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بِسْمِ اللهِ الرَّحْمنِ الرَّحِيمِ

قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة الاية32

Supervisor Certificate

This research project has been written under my supervision and has been submitted for the award of the degree of BSc. in (Physics).

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Date 4/04/2023

I confirm that all requirements have been completed.

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Name: Dr. Rashad Hasan Mahmud
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Date: 4 /04/2023

This project is dedicated to:

This thesis is dedicated to: Allah Almighty, my Creator and my Master, My great teacher and messenger, Mohammed (May Allah bless and grant him), who taught us the purpose of life, My homeland Kurdistan, the warmest womb, The University of Salahaddin-Erbil; my second magnificent home; My great parents, who never stop giving of themselves in countless ways, My beloved brothers and sisters; To all my family, the symbol of love and giving, My friends who encourage and support me, All the people in my life who touch my heart.

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LIST OF SYMBOLS AND ABBREVIATIONS

Symbol	Description
MGH	Massachusetts General Hospital
ZGS	zero-gradient synchrotron
PTF	proton therapy facility
RFQ	radiofrequency quadrupole
CERN	Conseil européen pour la Recherche Nucléaire
BNCT	Boron neutron capture therapy
TOP	Terapia Oncologica con Protoni
HIBT	Heidelberg Ion-beam Therapy
QNAO	Centro Nazionale di Adroterapia Oncologica
PIMMS	Proton-Ion Medical Machine Study
RBE	Radio-Biological Efficiency

CHAPTER ONE

INTRODUCTION

1.1 INTRODUCTION

Cancer is the 2nd cause of death after heart disease contributing to ~ 23% of all deaths in developed countries. Nowadays cure from cancer is achieved for 45% of all cancer patients using the currently available therapeutic strategies: surgery, radiation therapy and chemotherapy (Southworth, B., 1989). With the tumor detected in its early stages and still well localized the use of local therapies such as surgery and radiation therapy offer the patient a reasonably good chance of survival and cure (Eickhoff, 2003). About 50% of all cancer patients receive radiation therapies during the course of their treatment mostly by external beam therapies. Experience showed that radiotherapy is the modality of choice for localized inoperable tumors. In palliative care radiation therapy can be used to shrink tumors and reduce pressure, pain and other symptoms of cancer. Many cancer patients find that they have a better quality of life when radiation is used for this purpose Proton therapy is a modality for treating cancer cells through localized deposition of controlled amount of radiation energy within tumor region. The method uses the distinct feature of heavy charged particle interaction with matter, namely that they have a well-defined penetration range and concentrated deposition of energy at the end of this range. This gave rise to the so-called Bragg peak (Klein, H. U., 2002). Superiority to photon energy deposition is evident, as the later has a nearly exponential fall off with depth. With a single proton beam, it is possible to tailor the energy deposition (dose) not only in the lateral direction but also as a function of the depth in the patient (Chao, A.,2004).

1.2 PROTON THERAPY FACILITY

A typical proton-therapy facility includes three main components: an accelerator with an energy selection system, a beam transport system, and a treatment delivery system (COUTRAKON,1999).

An illustration of a typical proton-therapy facility , and the layout of proton-therapy facility at Massachusetts General Hospital (MGH) is shown in Figure 1.1.

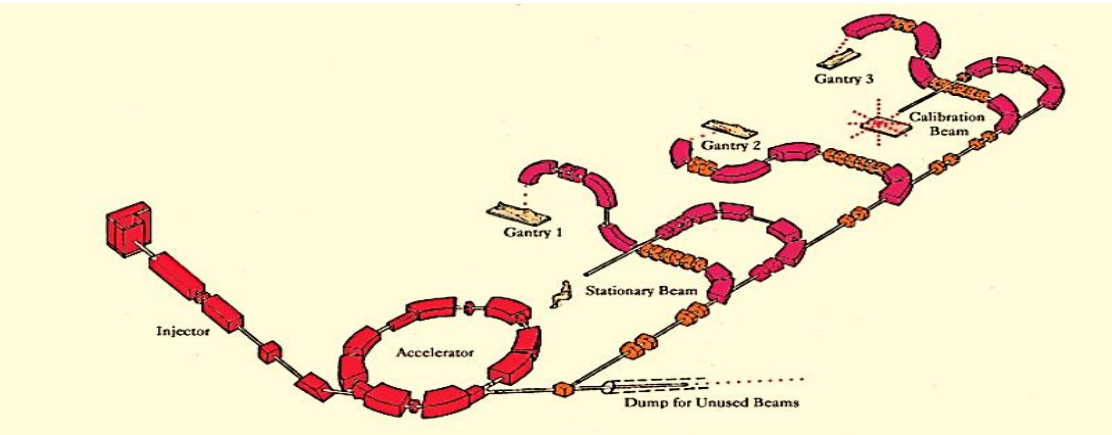


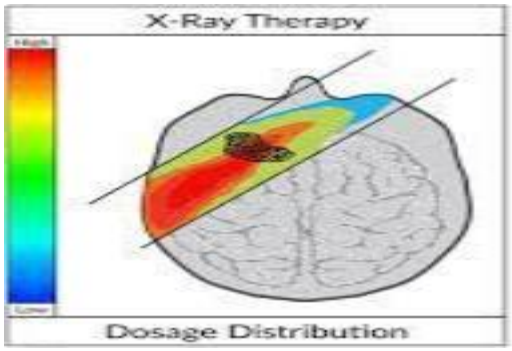
Figure 1.1 A typical layout of proton therapy facility (Guan, F., 2010).

1.3 COMPARISIO N OF EFFECTS X-RAY AND PARTICLE BEAM RADIATION THERAPIES

X-rays are used in conventional radiation therapies, and they have a characteristic ability to powerfully penetrate our body. They are also used in diagnostic radiography. When X-rays pass through our bodies, they weaken as they release energy in their path and produce the treatment effects.

The energy of X-rays is distributed in such a way that it reaches its peak in the subcutaneous tissue, which is one to two centimeters under the skin; then they wane gradually. Although this effect depends upon the thickness of the body, X-rays still release 30% to 60% of their energy when they reach the other side of the body. This means that, when we try to irradiate the focus area, healthy tissues that exist above the focus area in the X-ray path absorb a higher radiation dose than the focus area does. X-rays also continue to give off radiation to tissues beyond the focus point.

To perform X-ray therapy, we must always consider the maximum dose that healthy tissues in the X-ray path can withstand. To minimize side effects, we need to moderate the radiation dose. There are many cases in which the dose turns out to be insufficient to eliminate the cancer completely.



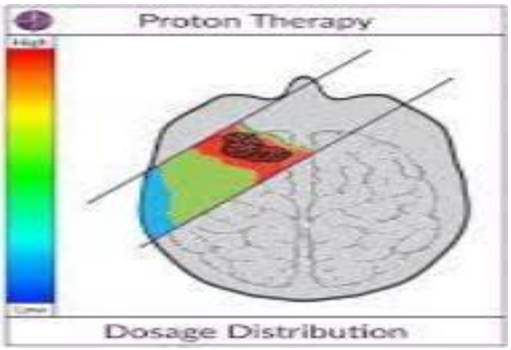


Figure 1.2 x-ray therapy beam vs proton therapy beam. Proton Therapy Treatment | Precise Radiation Therapy | ProTom (protominternational.com)

Unlike X-rays, a particle beam penetrates the body to a certain depth, where it suddenly gives off high energy to the surroundings and then extinguishes. Using this characteristic, we can adjust the beam to release the most powerful energy in the focus area and little energy in the rest of its path (Claude, L., 2004). We can use a higher dose of radiation on the cancerous focus area and achieve better results in the treatment with particle beam radiation as compared to X-ray therapy. It is also known that the same dose of radiation will cause more severe side effects if the field of irradiation is wider, and milder side effects if it is narrower. Particle beam radiation therapy allows us to narrow the field of irradiation in which a high dose is given to the cancerous focus area.

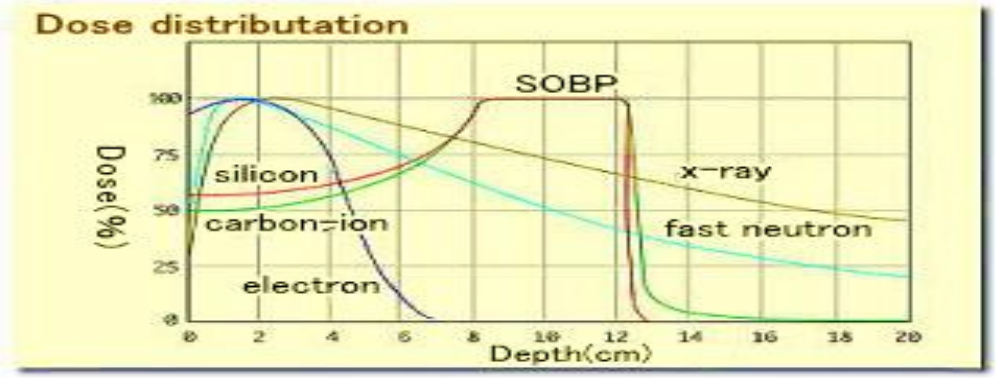


Figure (1.3) Dose distribution of X-Ray and Particle Beam Radiation Therapies (Kim, H.,2019).

As a result, side effects are minimized. It has been reported that when particle beams are compared to the same physical dose of X-rays in biological testing, the proton beam is only slightly more effective than X-rays (approximately 1.1 times more), but the carbon-ion beam is 3 times more effective. (In the actual therapy, the carbon-ion dose needs to be set lower than the X-ray or proton dose to reduce side effects.) The carbon-ion beam exhibits strong effectiveness in treatment, especially against cancers with properties that are resistant to X-rays.

CHAPTER TWO

THEORY

2.1 TYPICAL STRUCTURE OF A HOSPITAL-BASED PROTON THERAPY FACILITY

The typical proton therapy facility (PTF) structure is presented below:

- Accelerator,
- Beam transport lines to treatment rooms,
- A number of treatment rooms with patient positioners and alignment systems,
- Beam delivery systems,
- Treatment planning systems,
- Integrated accelerator and treatment control system,
- Dosimetry systems,
- Quality assurance and patient safety systems,
- Ancillary medical equipment.

2.2ACCELERATOR

Basically, proton accelerator of any type (cyclotron, synchrotron, linac) can be used for PTF. Generally, it is desirable to have a small medical accelerator, but one should take into account that accelerator hall area does not considerably contribute to the total PTF footprint provided 3-5 treatment rooms and beam transport lines are used (Peggs, S. G., 2002). Accelerator types are including: The beam requirements for cancer treatment, as listed in the above table, must be translated into detailed technical specifications of the proton therapy equipment. The technical specifications are strongly related to the choices of accelerator type and beam delivery systems. Various types of proton accelerators (up to the proton energy of 280 MeV) have been either used or proposed for dedicated medical accelerator facilities.

2.2.1 SYNCHROTRON

A 250 MeV zero-gradient synchrotron (ZGS), constructed at the Loma Linda Medical Center, is compact (20meter circumference), and its weak-focusing and large momentum dispersion characteristics allow a high space-charge limit (10" protons per pulse) producing a maximum intensity per unit circumference of the ring. Proton beams are extracted at any desired energy between 70 and 250 MeV. An ion source delivers 37-keV protons to a short (1.6 m) radiofrequency quadrupole (RFQ) accelerator, which accelerates the protons to 2 MeV and injectinto the synchrotron. The typical intensity of the extracted beam is 3 $x10^{10}$ protons per pulse at 27 pulses per minute.

2.2.2 ISOCHRONOUS CYCLOTRON

Isochronous cyclotron (constructed at the Higashi Hospital in Kashiwa, Japan and the NPTC in Boston, Massachusetts, USA) is compact machine (4 m diameter) which accelerates H* beam to 235 MeV, and the proton beam is extracted at the full energy. The extracted proton energy is degraded using a carbon absorber to provide proton beams, at energies between 70 MeV and the full energy. The energy can be changed by 10% in less than 2 seconds. The resulting energy spread straggling is reduced by magnetic momentum analysis and collimators. The extracted beam is of a continuous nature, and its intensity is controlled within 15 microseconds. Such a beam characteristic is suitable for both passive and active beam delivery methods.

2.2.3 SUPERCONDUCTING CYCLOTRON

A 238-MeV three-sector superconducting cyclotron, as proposed by the Centre Antoine Lacassagne in Nice, France and Siemens, Germany, is very compact (the cyclotron outer radius is 1.6 m and the height 2 m), inherently stable, and easy to operate. The proposed neutral beam injection line makes it simple to switch the beam on and off within microseconds. Combined with the cyclotron's high beam intensity, this capability naturally accommodates beam scanning. In a similar vein, a 3-Tesla isochronous superconducting cyclotron was designed by the National Cyclotron Laboratory in East Lansing, Michigan, USA. A new type of superconducting ring cyclotron with split sector magnets has been proposed by the National Accelerator Center in Faure (South Africa).

2.2.4 $H2^+$ CYCLOTRON

The novel superconducting cyclotron injector developed in the energy amplifier project at Conseil européen pour la Recherche Nucléaire CERN could be used for proton therapy. A simple and efficient extraction is possible with such a $H2^+$ cyclotron, and also simultaneous multiple beam extractions at different energies are possible. As the binding energy of H2+ (16 eV) is relatively large, ~2.9 Tesla magnetic field may be employed, allowing the use of superconducting technology for designing such an accelerator to keep it very compact.

2.2.5 H^- SYNCHROTRON

H^- synchrotron concept (proposed by ACCTEK in Illinois, USA; the ITEP in Moscow, Russia, and the ADROTERAPIA collaboration in Italy) is

chosen for various clinical reasons: namely, the extraction (by thin stripping foil) is simple, several extraction channels can be provided for independent extractions at different energies enabling simultaneous multi-room operations, the very small emittance (~0.1 n mm-mrad) will provide a small beam spot, which would allow designing lighter and more economical rotating gantries using smaller aperture magnets, and the extracted beam intensity is readily controllable by feedback. To reduce the Lorenz force stripping of H ions, a comparatively low magnetic field (0.54 Tesla maximum) is used, making the accelerator circumference larger (~60 meters). However, the larger circumference would present a possibility of a future upgrading of the proton accelerator to accelerate fully stripped light ionsof masses up to O^{16} to a final energy per nucleon in the range of 120-400 MeV with minor basis to be useful for beam scanning. Many have discussed the alternative uses of a proton therapy accelerator for other purposes, such as isotope productions or neutron production for fast neutron therapy or boron neutron capture therapy (BNCT). Very general observations in this regard are presented here. To be useful in isotope production, the beam with the energy of 7-12 MeV and the current of approximately 50 uA from the injector in case of a synchrotron or from the initial part of a linac should be available. For producing more exotic isotopes, higher proton energies (>70 MeV) may become useful. For fast neutron therapy one needs to have either proton or deuteron beams of the energy of approximately 50 MeV, and a time-averaged beam current of >10 uA. To produce clinically significant epithermal neutrons, either proton beams of the energy of approximately 2.5 MeV with a time-averaged current of >25 mA, or deuteron beams of the energy of about 4-20 MeV with a time-averaged current of >2mA, are needed.

2.2.6 LINACS

Linac is proposed by the Terapia Oncologica con Protoni (TOP) project in Rome, Italy. A 3 GHz variable energy linac may be used for proton therapy. The extracted proton beam pulse duration is 5 microseconds at a repetition rate of 400 Hz. Such an accelerator will provide the proton with energy from 75 to 250 MeV at a proton current of 0.1 - 20 nA (Owen, H., 2016)

2.2.7 ACCELERATORS FOR CARBON IONS

A beam of carbon ions is by its nature a very different radiation compared to X-rays and protons. Firstly, a fully stripped carbon ion e i.e. a nucleus of carbon made of six protons and six neutrons e produces a sharper Bragg peak than the one produced by protons so that the “spot” due to a mono-

energetic carbon ion beam has a FWHM of 3e4 mm instead than 10 mm. This implies that with carbon ions one can deliver a dose that is macroscopically more conformal to the tumour target than the doses due to protons and X-rays. Secondly, to reach a 28 cm depth a carbon ion must have initially about 4800 MeV (400MeV/nucleon) instead than the 210 MeV of a proton. This is due to the fact that carbon ions, with an electric charge six times larger than protons, slow down more rapidly. In this process they leave more energy per unit length than a proton in the ratio of the energy needed to reach the same depth: 4800/210 ~ 23. This is the average ratio of the LET of the two beams and is also the ratio between the numbers of ionizations left in the nucleus of each traversed cell. The consequence is that, even if a beam of carbon ions deposits the same dose in a tumour tissue, at the molecular level the biological effects are different from those of protons (and of X-rays) because they have a larger "Radio-Biological Efficiency" (RBE). Carbon ions at the end of their range can have, in some types of cells, three times higher RBE than protons. This makes them more effective in killing radioresistant cells than protons and X-rays, similarly to what happens with fast neutron beams but with the advantage that the macroscopic distribution of the dose can be made very conformal to the tumour target because of the small dimensions of the spot [Ankenbrandt, C., 2022]. Thus, the high LET difference makes carbon ions capable of treating radioresistant and hypoxic tumours which represent about 5% of the 2000 tumours irradiated each year with X-rays, in a population of one million inhabitants, where all the medical and technical competence accumulated in Darmstadt has been applied. The HIT was a joint endeavour of the GSI and the Siemens Medical company. HIT, with its 25 m long rotating gantry [Caporaso, G.J.,2007] that can be used both for protons and carbon ions, has been the first hadron therapy center able to compare clinical results obtained with protons and carbon ions with beams coming from the optimal directions. After HIT, CNAO (Centro Nazionale di Adroterapia Oncologica) in Pavia was the second institution in the world to offer e outside Japan e radiotherapy treatment with carbon ions. The CNAO design is based on a study carried out at CERN between 1996 and 2000, the so-called PIMMS (Proton-Ion Medical Machine Study). The TERA Foundation contributed, together with the Austrian MedAustron group, the group Oncology 2000 (Czech Republic) and many CERN scientists and engineers, under the leadership of Phil Bryant. The outcome of PIMMS [Peggs, S.,2007] was conceived as a toolkit from which any European user could select and adapt the parts best suited to their own goals. The PIMMS design was then modified by TERA into the PIMMS- TERA design eventually adopted for the CNAO centre.

CHAPTER THREE

3.1FROM PHYSICS LABORATORIES TO CLINICAL CENTRES

From the 50's both cyclotrons and synchrotrons and built for fundamental research e have been used for hadron therapy treatments and radiobiology. Certainly the facility that made the largest impact on the development of proton therapy was the 160 MeV [Geisler, A.,]2004. This was the cyclotron at which Bob Wilson was working in 1946 and was undoubtedly the best place to start proton therapy.In 1961 Raymond Kjellberg, a young neurosurgeon at Massachusetts General Hospital (MGH) in Boston, became the first to use the Harvard beam to treat a malignant brain tumour. By the mid1970s at the Harvard Cyclotron Laboratory the physicists Andy Koehler, Bernard Gottschalk and their colleagues e working with radiation oncologists guided by Herman Suit e had developed methods to treat large brain tumours, while Michael Goitein had written very sophisticated codes for quantifying the related treatment plans.

Overall three groups of radiation oncologists worked for many decades with Harvard physicists on three clinical studies: neurosurgery for intracranial lesions (3687 patients), eye tumours (2979 patients) and head-neck tumours (2449 patients). The results obtained convinced many radiation oncologists of the superiority of protons with respect to X-rays to treat tumours that are close toorgans at risk. From the fifties to the mid-eighties particle radiotherapy was based exclusively on accelerator facilities developed for nuclear physics research, with easy-to-build horizontal beam lines used for
proton therapy (Table 1). Significant numbers of patients were treated at the Harvard Cyclotron Laboratory and also, even if with smaller numbers, at the Gustav Werner Institute in Uppsala, the Institute of Theoretical and Experimental Physics in Moscow, the Joint Institute of Nuclear Research in Dubna, the Leningrad Institute of Nuclear Physics in Gatchina, the National Institute of Radiological Sciences in Chiba, the University of Tsukuba and
the Paul Scherrer Institute in Villigen, that started a program
devoted in particular to paediatric tumours.It was frequently stated that the field would not develop without dedicated facilities. However this step took almost thirty years, a much longer time compared to X-ray therapy. The reasons
are easy to explain. For X-ray therapy of deep tumours, it is enough to accelerate electrons up to 10 MeV; instead protons must be taken to at least 200 MeV, an energy that is twenty times larger. More-over, the proton mass (938 MeV/c2) is about two thousand times larger than that of the electron; medical proton accelerators e cy-clotrons or synchrotrons e are therefore much larger and more expensive than the electron linacs producing X-rays. For these

reasons, until the beginning of the nineties accelerators built for nuclear and particle physics experiments were used for proton therapy; a fraction of the machine time was dedicated to the treatment of a few patients, the rest to research activities.

Table 3.1 The pioneers of proton therapy; these facilities are now no longer in operation except for PSI and the centers in Moscow and St. Petersburg.

Facility	Country	Years of operation
Lawrence Berkeley Laboratory	USA	1954–1957
Uppsala	Sweden	1957–1976
Harvard Cyclotron Laboratory	USA	1961–2002
Dubna	Russia	1967–1996
Moscow	Russia	1969–now
St. Petersburg	Russia	1975–now
Chiba	Japan	1979–2002
Tsukuba University	Japan	1983–2000
Paul Scherrer Institute (PSI)	Switzerland	1984–now

3.2 RECENT TRENDS IN ACCELERATORS AND GANTRIES

In 2014 only cyclotrons or synchrotrons are used clinically for hadron-therapy treatments, but in the last years, novel ideas and approaches have been proposed and studied to improve the beam quality and/orreduce the overall size and cost [Schippers, J.M.,2011]. Recent developments include: i) fast extraction synchrotrons with fast varying energy, ii) novel commercial solutions for proton therapy single room facilities, iii) new accelerating schemes (FFAG and linacs) and other accelerating techniques (DWA, laser-driven accelerators), iv) proton and carbon ion gantries with novel superconducting solutions.

3.3 NEW SYNCHROTRONS

For a synchrotron, typically one has to wait 1e2 s until the next spill reaches a different beam energy. Ideas for rapid cycling synchrotrons are based on fast extraction schemes, as opposite to slow extraction scheme adopted by the existing medical synchrotrons. The beam is fully extracted in one turn and at a repetition rate as high as 30 Hz, allowing energy variation in the energy range from 70 to 250 MeV [Peggs, S.,2002]. Small beams are obtained by strong focusing optics. With a high repetition rate (spills with variable energy at 30 Hz) and strong focussing, a high dose rate of 20 Gy per litre per minute can be obtained. The design exists also for a dual machine for both protons and carbon ions up to 400 MeV/u, which consists of a racetrack lattice of 60 m, with two parallel zero dispersion straight sections and an injector which is placed inside the ring, as in CNAO [Trbojevic, D.,2011]. The design of this “ion Rapidly Cycling Medical Synchrotron” (iRCMS) has been adopted by Best Medical

International (USA), with a collaboration agreement signed with Brookhaven National Laboratory at the beginning of 2012. Fast changes of the energy of a conventional synchrotron have been studied at HIMAC [KATAGIRI, K.,2011] and carbon-ion beams with various energies have been used for scanned particle therapy at NIRS [Mizushima, K.,2014]. By carefully changing the magnets current and simultaneously decelerating the beam during the slow extraction process, the energy of the extracted beam can be varied within a spill. Energy variation times of about $10e^{20}$ ms have been achieved. This makes such synchrotrons more suitable for rapid scanning techniques than the ones of traditional designs.

3.4BEAM PARAMETER

Beam parameter requirements depend upon the treatment sites and modalities chosen by the physicians and medical physicists [Chu, W.T.,1993, Coutrakon, G.B., 2001]. Basic Passive Scattering puts variable thickness material in the nozzle at the end of the gantry, to adjust the range of a broad beam to match the distal edge of the target volume and to scatter the beam.Higher beam currents and energies are required to compensate for this upstream material and also to compensate for cyclotron energy degraders. In pencil beam scanning the beam is dynamically steered transversely with magnets, and its range is adjusted by modulating the energy. Intensity Modulated Particle Therapy is pencil beam scanning with controlled beam intensity variation. IMPT enables the most conformal dose delivery [Peggs, S.,2007].

3.4.1 PENETRATION DEPTH

The penetration depth of about 38 cm in water. An equivalent carbon ion beam has an energy of about 410 MeV/u per nucleon. Required rigidities are therefore about 2.46 Tm and 6.50Tm, 2.64 times higher for carbon.

3.4.2 DOSE RATE

The daily dose of typically around 2 Gray (J/kg) must be delivered in 1 or 2 minutes. A large 1 liter more thus requires delivery of a modest average beam power of order 0.02 W and an average current of about 0.08 nA, if the tumor is 25 cm deep. Delivery is not 100% efficient!

3.4.3 CONFORMITY

The integrated dose must conform at the 1% or 2% level to the treatment plan within the treatment volume, and should decrease sharply across the tumor surface.

3.5 SCANNING PARAMETERS

A continuous beam from a cyclotron or slowly extracted from a synchrotron may pause at a sequence of control points during “point-and-shoot” 3D tumor scanning. Or, discrete beam pulses may be delivered to each of many voxels in sequence. “How few independent control points are needed to deliver the sharpest possible dose distribution, limited only by the physics of multiple scattering and energy straggling?” The practical answer depends on treatment planning details and hadron specie, but under some assumptions an approximate scaling for protons is

$$N_{TOT} \sim 2600\, f V^{\frac{2}{3}} \qquad (1.1)$$

where f is a geometric form factor bigger than 1, and V is the treatment volume in liters [Peggs, S., 2003].

3.6 BEAM DELIVERY SYSTEMS

Different beam delivery techniques can be used for distributing the protons to cover the target volume with a uniform dose. The primary goal is to provide a homogeneity of the dose of typically ±2-3% inside the target volume. The secondary goal is to deposit as little dose as possible in the surrounding healthy tissues in order to avoid unnecessary treatment complications. This second goal is especially important when the target volume is surrounded byradiation sensitivee healthy structures, which is the typical indication for protons therapy.

The goal to spare healthy tissues can be achieved by tailoring precisely the dose in all 3 dimensions to the target volume (three-dimensional dose conformation), by using multiple beam ports and by a careful selection of the angles of beam incidence onto the patient (to avoid organs at risk in the beam path and to avoid complex density heterogeneities in the body). Here is where the different beam delivery technologies show their different merits. Here we find the rationale for the development of dynamic beam delivery techniques and for the utilization of proton gantries. The quality of dose distribution will depend finally on the achieved degree of conformity of the dose in all 3 dimensions including the sharpness of the fall-off of the dose in both the lateral and distal directions. In the comparison of the merits of the different beam delivery methods, we should not neglect other practical aspects like complexity and costs of the system, reliability, safety, and how efficiently a method can be used.

3.7 DYNAMIC BEAM DELIVERY - BEAM SCANNING METHODS

The idea common to all different developed or proposed dynamic methods is to scan pencil beams of protons directly into the patient (Wang, K. D.,2020). The proton pencil beam deposits its dose along a line with a maximum at the end where the protons stop in the Bragg peak region. The dose maximum is well localized in space in all 3 dimensions and resembles to a hot spot of dose (the technique is therefore called sometime spot scanning technique). Each dose spot can be individually adjusted in position (lateral positions and depth) and dosage adjustment by computer control (Wang, K. D.,2022). The fast magnetic scanning (applied at least in one transverse direction) allows to delivery under computer control of a very large number of pencil beam in a reasonably short time. Through the superposition of these beams, it is possible to construct a complex-shape dose distribution. The advantages expected from this method are the following:The methods allows to working with variable range modulation (as opposed to the fixed modulation of the passive scattering system). In this way it is possible to provide the best possible conformation of the dose very close to the physical limits. The additional dose sparing provided by the spot scanning method compared to passive scattering can be quite significant for the treatment of large irregular volumes. With the exception of the immobilization mold this method does not require individually shaped hardware, since everything is done by computer. For the treatment of sequential beam ports in the same session (without interruption between gantry angles) this is expected to improve the treatment efficiency and patient throughput (Herrod, A. T.,2021).

In combination with a proton gantry the scanning of the beam can be realized within the beam optic. The spot scanning method is well suited also for the treatment of very large tumors. From the conceptual point of view, the method is simpler than the passive scattering system, and requires only few elements (one device for each scanning axis). The development of the software is however more involved and is the real challenging part of the development.
The spot scanning method can deliver homogenous, but also planned non-homogeneous dose distributions. The flexibility of the delivery allows to work with simultaneously optimized distributions of the dose from many beam angles, which allows to parallel with protons the future IMRT developments of photon therapy, but with the additional degrees of freedom to control the dose also in depth. The possible disadvantages are: the method is new, technologically more complex to develop, and less well established. Because it

is a dynamic method, special attention must be paid to the safety aspects, requiring double computers (one for dose delivery and the other for dose monitoring) and other redundant methods of control One should also not forget a higher sensitivity of this method concerning the effect on the dose of organ motion during scanning (Kacperek, A.,2009). To reduce this disadvantage, as one of the intermediate steps, a combination of computer controlled collimator and range modulating system using wobbled broad beam is under development at NIRS (Dougherty, J.M.,2022). Is must be remembered that this method requires a convenient time structure and/or tunable intensity of the beam such that the target volume can be scanned with a fine granularity within the specified treatment time.

3.8CLINICAL REQUIREMENTS OF MEDICAL BEAMS

The clinical requirements of medical beams include specifications of such physical quantities as the residual range of the beam in patient, the extent of range modulation to cover the thickness of targets, the maximum dose rate, as well as the minimum dose rate that can be precisely controlled, the beam spill structure, the maximum attainable port size, the dose uniformity across the ports, the effective source-to-axis distance (SAD), the allowable degradation in distal dose falloffs and lateral penumbrae, which affect normal tissue sparing, and the attainable precision in delivered dose.These clinical requirements with many competing specifications drive the designs of medical beams. For example, clinicians may ask for a large treatment field, up to 40 cm x 40 cm, which may be provided using a scattering method, necessarily degrading the beam emittance. Another clinical requirement is the sharp lateral dose falloff (penumbra) required at the boundary of the treatment field. One may try to achieve it by increasing the apparent source-to-axis distance (SAD), which is not easily achievable on a treatment beam line mounted on a rotating gantry.
Achieving it using heavy collimation may not be allowed either because it may unacceptably reduce the beam utilization efficiency. Instrumentation must be constructed weighing the many pros and cons of competing designs and implementations, and finding the optimal solution that satisfies all of the clinical requirements.

3.9 CLINICALLY COMPARISON TRADITIONAL AND HADRON THERAPY FOR IDIOPATHIC PULMONARY FIBROSIS (IPF)

From January 2010 to October 2017, Idiopathic pulmonary is associated with fatal complications after radiotherapy for lung cancer patients. they retrospectively reviewed the medical records of 264 patients with stage I-II non-small cell lung cancer treated with definitive RT alone. Ultimately, 30 patients (11.4%) who had underlying IPF were analyzed. Among these, X-ray and proton RT were delivered to 22 and 8 patients, respectively. Treatment-related complications and survival outcomes were compared between X-ray and proton therapy. The median follow-up duration was 11 months (range, 2 to 51 months). All living patients were followed-up at least 9 months. Treatment-related death occurred in four patients (18.2%) treated with X-ray but none with proton therapy. Most patients died within one month after the onset of pulmonary symptoms in spite of aggressive treatment. In addition, the 1-year overall survival (OS) rate in patients treated with X-ray and proton was 46.4 and 66.7%, respectively, and patients treated with proton therapy showed a tendency of better survival compared to X-ray (p = 0.081). Especially, in GAP stage II and III subgroups, patients treated with proton therapy showed significantly increased survival outcomes compared to X-ray (1-year OS rate; 50.0% versus 26.4%, p = 0.036) in univariate analysis.

Figure (3.1) Overall survival curves according to treatment; 1-year OS rate in patients of X-ray and proton groups were 46.4 and 66.7%, respectively (Kim, H.,2019).

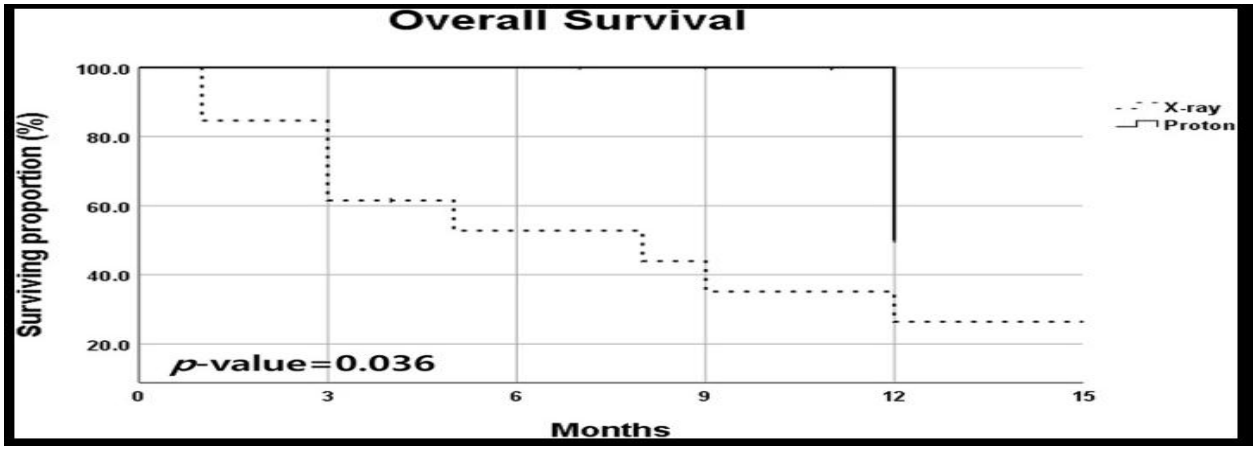


Figure (3.2) Overall survival curves according to treatment in GAP stage II and III subgroups; 1- year OS rate in patients of X-ray and proton groups were 26.4 and 50.0%, respectively (Kim, H.,2019).

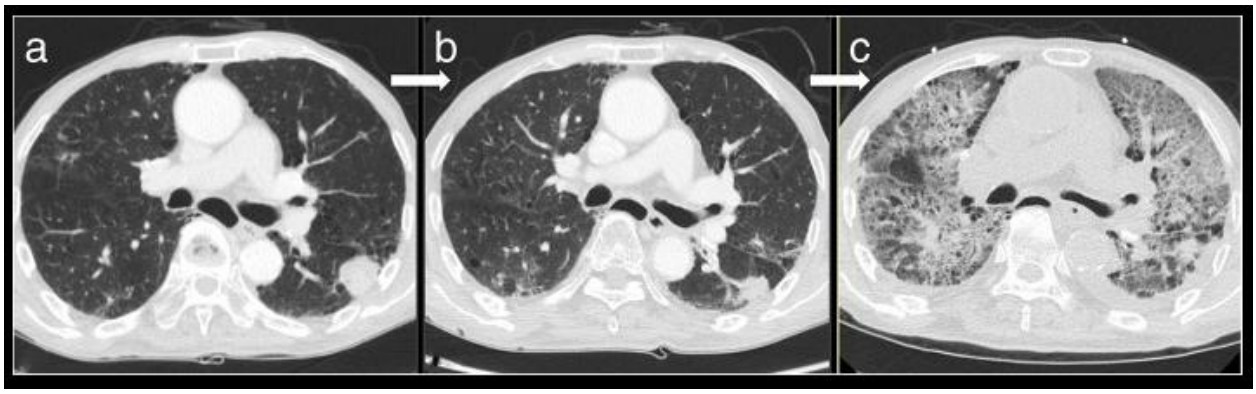


Figure (3.3) Chest CT axial imaging of the patient who showed grade 5 radiation pneumonitis after radiotherapy; (3a) Pretreatment chest CT image, (3b) At 1month follow-up, and (3c) At 2 months follow-up (Kim, H.,2019).

3.10COMPARISON OF EFFECTS X-RAY AND HADRON THERAPY FOR ESOPHAGEAL CANCER

Surgery is the standard treatment for esophageal cancer, but concurrent hadron therapy has benefits with regard to prognosis, mortality and quality of life after treatment. Immediately after the start of radiotherapy, all patients received the first cycle of chemotherapy. This consisted of an intravenous infusion of cisplatin (70 mg/m^2 body surface area) over 3 h followed by fluorouracil (2800 mg/m^2) over 96 h. Therefore, concurrent chemotherapy was administered during Days 1 to 5 of radiotherapy. Additional cycles of chemotherapy were scheduled at 3-week intervals. Thus, patients received two cycles of chemotherapy during fractionated radiotherapy. Patients in the X-ray group were treated with only X-rays and chemotherapy, and those in the proton

group were treated with only protons and the same chemotherapy regimen. Thus, no patient received a combination of X-rays and proton beams. For X-ray planning, a two-field anteroposterior and posteroanterior (AP/PA) beam arrangement was used for CTV1 up to 40 Gy, and then a two-field right anterior oblique (RAO) and left posterior oblique (LPO) arrangement was used for the boost to CTV2. Field-in-field techniques and wedge compensators were sometimes used to maintain dose distribution uniformity. A total dose of 40 gray (Gy) or gray equivalent (GyE), with relative biological effectiveness (RBE) set to 1.1 for the proton beam, was given to clinical target volume (CTV1) using conventional fractionation with a fractional dose of 2 Gy. An additional dose of 20 Gy or GyE in 10 fractions was given to CTV2. The planning target volume (PTV) was made by adding adequate margins to the CTVs.

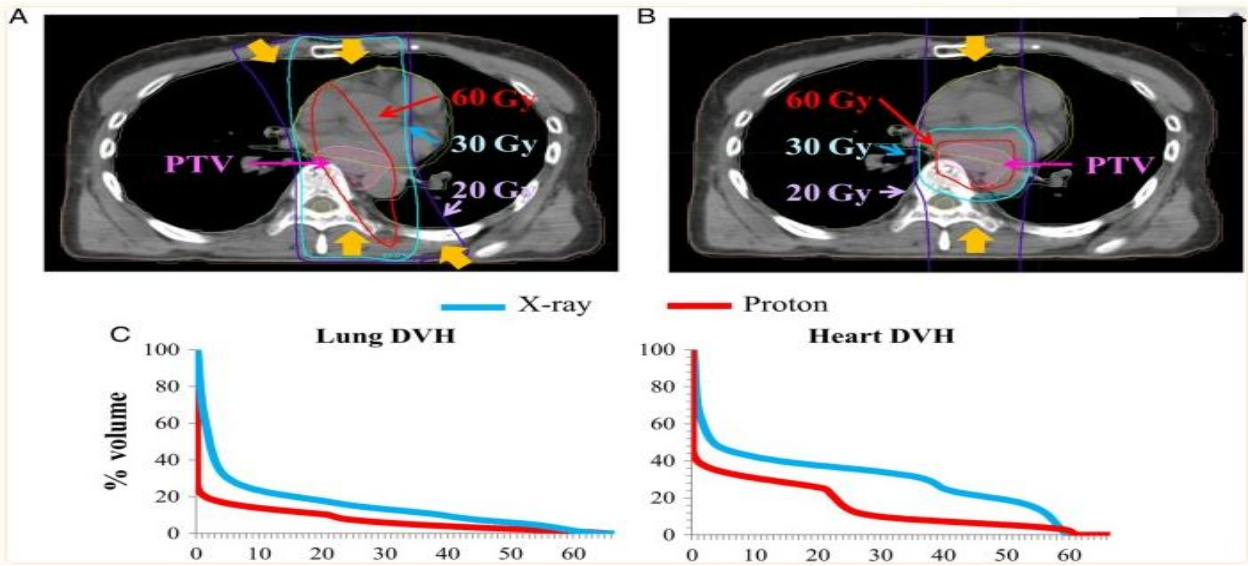


Figure (3.4) Typical dose distributions and dose–volume histograms in treatment of esophageal cancer in (**A**) X-ray 3D-CRT and (**B**) PBT. In 3D-CRT, 20 Gy is delivered widely to the lung, 30 Gy is delivered to most of the heart, and 60 Gy is also delivered widely to the heart. (**C**) Typical dose–volume histograms of the lung and heart. PBT results in lower irradiation doses in both OARs.

3.11 CONCLUSIONS ABOUT ACCELERATOR TYPES

As already mentioned, a cyclotron produces continuous beams, and if their intensities are rapidly controllable, they are suitable for beam scanning. On the other hand, a synchrotron is a pulsed machine, and to use synchrotron beams for beam scanning, a method of producing slow beam extraction (with a duty factor probably >0.5) should be developed. In case of a linac, with a very low duty factor, the extracted beam intensity must be accurately controlled on a

pulse-to-pulse machined profile of the disc is rotated into the beam and is used to change the range of the beam as a function of time in order to produce a layer of uniform dose (which must correspond at least to the maximal thickness of the target volume in depth).

An improved dose distribution is usually achieved by using a compensator bolus in front of the patient. This element is a spatially variable absorber block fabricated on a computer-controlled milling machine. The programmed variable the thickness of the compensator is used to shift the range of the beam to correspond exactly with the distal surface of the target volume. Concerning the advantages of the passive scattering method, we mention the reliability and the safety inherent in the use of passive methods and the fact that most of the experience in proton therapy has been achieved with this method (a well-established method). There are however also some disadvantages. The methods require the use of a lot of individually shaped hardware, which must be adjusted for each gantry angle. This could be a factor affecting the efficiency of utilization of the beam on a gantry (Aminov, B.,2005). The method is well suited only for small to medium size fields. For a very large field, it is difficult to be realized on a gantry with a short drift space.

The dose produced by a passive scattering method is not truly 3-dimensionally conformed, since the modulation of the range is constant over the whole target volume. The importance of the goal to achieve a good 3-dimensional conformation of the dose using advanced sophisticated beam delivery methods is being more and more recognized by the radiation therapy community and a large effort for the development of new beam delivery techniques can be observed also in conventional therapy (Chen, Y.,2009).

The physical advantages of the protons could soon be challenged by the technological progress achieved with dynamic beam delivery techniques in photon therapy. However, any new technique which can be delivered with photons can be applied by protons as well, and this with the additional freedom to control the dose in depth. From the physics point of view and using equivalent techniques, protons are always capable of producing superior dose distributions. It is therefore important for the proton therapy community to follow this development in order to remain competitive also in the future. The fact that protons are charged particles makes them ideal for dynamic beam delivery techniques, since it offers the possibility to scan the beam directly in the patient by magnetic scanning under computer control. This could be another practical important advantage for the protons in this competition.

CHAPTER FOUR

4.1 CONCLUSION

Sixt years after the first treatments performed in Berkley, more than 110,000 patients have been treated with protons and 11,000 with carbon ions. More than 95% of these patients have been treated with “passive” spreading systems, i.e. by using a wide hadron beam covering the whole transverse dimensions of the tumour. The “active” methods (spot scanning and raster scanning) are entering in the clinics, with their improved dose distributions. Only very recently moving tumours (because of the inspiration cycle, for instance) have been irradiated with a technique, already in use for X-rays, which can be called “Image Guided Particle Therapy”. The advantages of hadron beams will be fully exploited only when this technique will become common practice.

Despite of the fact that the numbers of treated patients are increasing, they are still very small compared to all the cases that would benefit from proton or carbon ion therapy, and that are nowadays treated with conventional X-ray therapy. While carbon ions are indicated for particular types of tumours (the so called radioresistant tumours) representing up to 5% of the total number of patients treated with X-rays, protons would be indicated in more than 12e15% of the cases, that is in about 240e300 cases every year per 1 million inhabitants. In terms of size, hadron therapy centres are much bigger than conventional radiotherapy machines.

In fact accelerating proton beams to the energy of 230 MeV needed for treatments or carbon ions up to 400 MeV/u in small spaces is still a technological challenge. The accelerators used for proton therapy are mainly cyclotrons, while for carbon ion therapy only synchrotrons have been used up to now. Such machines have been proved to be reliable and efficient, but more compact and more adapted designs have been investigated. In particular high frequency RF linacs are now commercially available for proton therapy and in the future possibly also for carbon ions. FFAG have also been prototyped.
Further in the future laser accelerators, potentially smaller than cyclotrons, synchrotrons or linacs, would allow to reduce the di- mensions of hadron therapy facilities; but certainly time is needed to bring such a technology to a mature stage.

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