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Radiological Protection in Ion Beam Radiotherapy



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Aims and Scope

The International Commission on Radiological Protection (ICRP) is the primary body in protection against ionising radiation. ICRP is a registered charity and is thus an independent non-governmental organization created by the 1928 International Congress of Radiology to advance for the public benefit the science of radiological protection. ICRP provides recommendations and guidance on protection against the risks associated with ionising radiation from artificial sources widely used in medicine, general industry and nuclear enterprises, and from naturally occurring sources. These reports and recommendations are published approximately four times each year on behalf of ICRP as the journal *Annals of the ICRP*. Each issue provides in-depth coverage of a specific subject area.

Subscribers to the journal receive each new report as soon as it appears so that they are kept up to date on the latest developments in this important field. While many subscribers prefer to acquire a complete set of ICRP reports and recommendations, single issues of the journal are also available separately for those individuals and organizations needing a single report covering their own field of interest. Please order through your bookseller, subscription agent, or direct from the publisher.

ICRP is composed of a Main Commission, a Scientific Secretariat, and five standing Committees on: radiation effects, doses from radiation exposure, protection in medicine, the application of ICRP recommendations, and protection of the environment. The Main Commission consists of a Chair and twelve other members. Committees typically comprise 10–15 members each.

ICRP uses Task Groups to prepare its reports. A Task Group is usually chaired by an ICRP Committee member and usually contains a number of specialists from outside ICRP. Thus, ICRP is an independent international network of specialists in various fields of radiological protection, and, at any one time, about two hundred eminent scientists and policy makers are actively involved in the work of ICRP. The Task Groups are assigned the responsibility for drafting documents on various subjects, which are reviewed and finally approved by the Main Commission. These documents are then published as the *Annals of the ICRP*.

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Annals of the ICRP

ICRP PUBLICATION 127

Radiological Protection in Ion Beam Radiotherapy

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CONTENTS

EDITORIAL	5
ABSTRACT	9
PREFACE	11
MAIN POINTS	13
GLOSSARY.....	15
1. INTRODUCTION.....	23
2. OUTLINE OF ION BEAM RADIOTHERAPY	25
2.1. Clinical target of ion beam radiotherapy	25
2.2. General treatment processes	25
2.3. Introduction of the beam delivery system and irradiation method	28
3. PHYSICAL ISSUES FOR RADIOLOGICAL PROTECTION	37
3.1. Travelling of ions in matter.....	37
3.2. Production of secondary radiation	37
3.3. Spatial distribution of radiation	39
4. RADIOBIOLOGICAL IMPLICATIONS	43
4.1. Interactions of radiation with DNA	43
4.2. Health effects of ionising radiation.....	44
4.3. Effects on embryos, fetuses, and children	47
4.4. Radiobiological factors	48
4.5. Relative biological effectiveness for ion beams and neutrons.....	49
5. RADIATION EXPOSURES IN ION BEAM RADIOTHERAPY	53
5.1. Medical exposure of patients from therapeutic irradiation	53
5.2. Medical exposure of patients from imaging procedures.....	69
5.3. Occupational exposure	77
5.4. Public exposure	82
6. RADIATION SAFETY MANAGEMENT FOR ION BEAM RADIOTHERAPY FACILITIES	83

6.1. Radiation safety management for ion beam radiotherapy facilities..... 83

6.2. Management of exposure due to activation of devices 83

6.3. Management of radioactivity due to activated nuclides 83

6.4. Monitoring system for management of radiological protection..... 86

6.5. Quality assurance in management of radiological protection of ion
beam radiotherapy facilities..... 86

7. PREVENTING ACCIDENTAL EXPOSURES OF PATIENTS FROM
ION BEAM RADIOTHERAPY 87

7.1. Accidental exposures to patients undergoing radiotherapy..... 87

7.2. Potential accidental exposures in ion beam radiotherapy 88

7.3. Quality assurance programme and audit 88

8. CONCLUSIONS AND RECOMMENDATIONS 93

REFERENCES..... 95

ANNEX A. DOSIMETRY AND MODEL 107

A.1. Dosimetry techniques 107

A.2. Application of Monte Carlo simulation codes 110

A.3. Biological response model..... 110

CORRIGENDA..... 114

Editorial

ICRP RECOMMENDATIONS PAST, PRESENT, AND FUTURE: A FOCUS ON RADIOLOGICAL PROTECTION IN MEDICINE

This issue completes the first volume of the *Annals of the ICRP* published with SAGE. The four issues of this volume (which represent 1 year of publications, at least notionally) are a reasonable cross-section of the types of reports published by ICRP. *Publication 124* (ICRP, 2014a) was on protection of the environment, *Publications 125* (ICRP, 2014b) and *126* (ICRP, 2014c) examined the application of the system of radiological protection to specific circumstances, specifically security screening and protection against radon, and the current publication addresses radiological protection in medicine.

An even better appreciation for the number and types of reports published by ICRP can be gained by looking at what has been published since the 2007 Recommendations (ICRP, 2007).

Twenty-six publications (many being multiple issues) have been produced in the past 7 years. Three of these were produced jointly with our sister organisation, the International Commission on Radiological Units and Measurements (ICRU), and one was published by ICRU (2010).

More than one-quarter of these publications, seven of the 26, are in the medical area. This is not surprising given that medicine is where ICRP, originally named the International X-ray and Radium Protection Committee (IXRPC), began in 1928. Radiological protection in medicine continues to be a major focus today.

Six publications are related to calculation of dose. This is perhaps more than average for a collection of 26 ICRP publications. This is a result of the enormous effort that has been made, and remains ongoing, to produce a full new set of dose coefficients for radiological protection purposes. Many more publications in this area will follow in the coming years.

Three publications address radiological protection of the environment, an area that ICRP began to tackle in earnest almost a decade ago with the creation of ICRP Committee 5, although results of earlier efforts are evident [e.g. in *Publication 91* (ICRP, 2003)].

Seven publications support and clarify how the principles of the system of radiological protection apply beyond medicine and the environment, dealing with protection of people in such diverse circumstances as radon in homes, astronauts in space, and post-accident recovery.

Two extensive reports have been reviews of current areas of science, and implications of this new knowledge for the system of radiological protection. Scientific understanding is one of the three pillars that form the foundation of the system, the others being ethical values and experience. The system of radiological protection must continue to evolve to remain solidly based on all three of these pillars.

The one remaining publication since 2007 is the proceedings (ICRP, 2012) of ICRP's First International Symposium. This took place near Washington, DC, USA in October 2011. Our Second International Symposium on the System of Radiological Protection was held 2 years later in Abu Dhabi, United Arab Emirates. The proceedings for this symposium are due to be published shortly, and pre-press articles are already available electronically at the time of writing this editorial. ICRP's Third International Symposium on the System of Radiological Protection will be held in October 2015 in Seoul, Korea, and plans are already underway for future symposia. These biennial ICRP events, attracting many hundreds of radiological protection professionals from around the world, have become a cornerstone in our efforts to be a more open and transparent organisation. Radiological protection in medicine has featured highly in each of the symposia to date, and will continue to do so.

This current publication continues ICRP's nearly 90-year focus on radiological protection in medicine. Since that time, the most basic principle in all circumstances has remained the same: providing protection from the negative effects of exposure to radiation while not unduly limiting the related benefits. However, even at this fundamental level, there are some important differences between the recommendations of 1928 and today. The first recommendations of ICRP (ICRP, 1928) related to safety of medical professionals and researchers through 'the provision of adequate protection and suitable working conditions'. Interestingly, this included providing fresh air and sunshine, and 'not less than one month's holiday a year' for 'whole-time X-ray and radium workers'. However, there were also more recognisable recommendations; for example, 'An X-ray operator should on no account expose himself unnecessarily to a direct beam of X-rays' and 'should place himself as remote as practicable from the X-ray tube'. Perhaps it is a bit of a stretch, but these and other considerations in the 1928 Recommendations are not too far away from the ideas of justification and optimisation used today.

Today, ICRP recommendations extend protection beyond those who work with radiation, to patients and members of the public. Chapter 6 of the current publication deals with protection of workers and the public, considering, for example,

management of activated devices, air in the treatment room and being discharged, management of solid waste, and release of patients. Chapter 7 focuses on protection of patients through prevention of accidental exposures from ion beam therapy. Covering protection of workers, patients, and the public is not a special feature of the current publication. In recent years, ICRP has made an effort to include all of these aspects in publications on radiological protection in medicine.

Of course, protection is not enough. Developments in ion beam radiotherapy have been motivated by the benefits provided by improved treatment of tumours. Although these benefits are not the focus of this publication, these recommendations would not be necessary without the success of ion beam therapy as described in the introduction to this report. While the business of ICRP is protection against negative effects of radiation, developments such as ion beam radiotherapy are very much welcomed as they improve the overall human condition. ICRP will continue to accompany developments of the use of beneficial radiation in medicine and in other areas, to help ensure that these wonderful new technologies and techniques are used safely.

CHRISTOPHER H. CLEMENT
ICRP SCIENTIFIC SECRETARY
EDITOR-IN-CHIEF

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Radiological Protection in Ion Beam Radiotherapy

ICRP PUBLICATION 127

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Abstract—The goal of external-beam radiotherapy is to provide precise dose localisation in the treatment volume of the target with minimal damage to the surrounding normal tissue. Ion beams, such as protons and carbon ions, provide excellent dose distributions due primarily to their finite range, allowing a significant reduction of undesired exposure of normal tissue. Careful treatment planning is required for the given type and localisation of the tumour to be treated in order to maximise treatment efficiency and minimise the dose to normal tissue. Radiation exposure in out-of-field volumes arises from secondary neutrons and photons, particle fragments, and photons from activated materials. These unavoidable doses should be considered from the standpoint of radiological protection of the patient. Radiological protection of medical staff at ion beam radiotherapy facilities requires special attention. Appropriate management and control are required for the therapeutic equipment and the air in the treatment room that can be activated by the particle beam and its secondaries. Radiological protection and safety management should always conform with regulatory requirements. The current regulations for occupational exposures in photon radiotherapy are applicable to ion beam radiotherapy with protons or carbon ions. However, ion beam radiotherapy requires a more complex treatment system than conventional radiotherapy, and appropriate training of staff and suitable quality assurance programmes are recommended to avoid possible accidental exposure of patients, to minimise unnecessary doses to normal tissue, and to minimise radiation exposure of staff.

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Keywords: Radiotherapy; Ion beam; Proton; Carbon ion

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PREFACE

Over the years, the International Commission on Radiological Protection (ICRP) has issued many reports providing advice on radiological protection and safety in medicine. *Publication 105* is a general overview of this area (ICRP, 2007d). These reports summarise the general principles of radiological protection, and provide advice on the application of these principles to the various uses of ionising radiation in medicine.

Most of these reports are of a general nature, and the Commission wishes to address some specific situations where difficulties have been observed. Reports on such problem areas should be written in a style that is accessible to those who may be directly concerned in their daily work, and every effort should be taken to ensure wide circulation of such reports.

Rapid advances in radiotherapy require practical guidance for radiological protection of patients and medical staff. *Publication 86* (ICRP, 2000) dealt with the prevention of accidental exposure of radiotherapy patients, and provided the lessons learned from real case histories of major accidental exposures, and recommendations to prevent such accidental exposure of patients. *Publication 112* (ICRP, 2009) followed the same theme with particular emphasis on new technologies in external radiotherapy.

Ion beam radiotherapy is a recently introduced technique that could potentially offer an improved dose conformation to the target volume with better sparing of the surrounding normal tissue. As ion beam radiotherapy requires a more complex treatment system than conventional radiotherapy, appropriate training of staff and suitable quality assurance programmes are recommended to avoid possible accidental exposure of patients, and to keep radiation exposure of staff to a minimum level. The Commission launched a Task Group on Radiological Protection in Ion Beam Radiotherapy in 2012.

The membership of the Task Group was as follows:

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MAIN POINTS

- External-beam radiotherapy relies on precise dose localisation in the target treatment volume with minimal damage to the surrounding normal tissue. The success of treatment largely depends on the performance and capacity of accelerators, the beam delivery system, and the quality of the treatment planning systems used.
- The clinical use of ion beams, such as protons and carbon ions, provides precise dose distributions due primarily to their finite range in tissue. Such precise deposition of energy in tumour volumes enables a significant reduction in radiation exposure of uninvolved normal tissue.
- The clinical advantage of ion beam radiotherapy results from the manner in which protons and carbon ions lose their energy in tissue. Much of their energy is lost near the end of their range in tissue. This peak of energy loss or stopping power is called the 'Bragg peak'. This physical phenomenon is exploited in ion beam therapy of cancer to achieve a higher absorbed dose within the tumour than in surrounding healthy tissues.
- Relative biological effectiveness (RBE) values for different ions vary for different endpoints but tend to increase with increments of stopping power or linear energy transfer (LET) up to a maximum value before declining. Proton beams in clinical use are low-LET radiations, hence the RBE values are very close to those of high-energy x rays. For a given biological endpoint, carbon ions have higher RBE values than protons. RBE values increase with depth, and have their maximum near the depth where the Bragg peak occurs.
- An ion beam delivery system generally consists of an accelerator, a transport beam line, and an irradiation system, where dose is delivered to the patient as either a narrow beam (pencil beam scanning method) or a broadened beam (broad beam method). When ion beams pass through or hit these beam line structures, secondary radiations including neutrons are produced. Some of the particles in the structures can become radioactive, and form an autoradioactive component of the beam.
- The first step for ion beam radiotherapy, similar to any medical procedure, is justification. The proper selection of the patient should be based on knowledge of radiation oncology, the specific tumour to be treated, and available clinical results to provide the optimal benefit to the patient.
- Careful treatment planning is required for optimisation to maximise the efficiency of treatment and minimise the dose to normal tissue, and depends on the treatment method and the targeted tumour. Theoretically, ion beam radiotherapy delivers radiation dose to the target volume more efficiently than conventional radiotherapy, while minimising undesired exposure of normal tissue. Nonetheless, the treatment planning must be sufficiently precise to avoid damaging the critical organs or tissues within or near the target.
- Doses in the out-of-field volumes arise from the secondary neutrons and photons, particle fragments, and photons from activated materials. These undesired but unavoidable doses should be considered from the standpoint of radiological protection. Secondary neutrons are the major contributor to absorbed dose in areas distant

from the treatment volume. The pencil beam scanning method can minimise this type of radiation exposure.

- Imaging procedures are essential in treatment planning, similar to other modern radiotherapies, and deliver an additional small dose of radiation to the patient.
- Appropriate management is required for the therapeutic equipment and the air in the treatment room which is activated. Management should always conform with regulatory requirements. The current regulations for occupational exposures in photon radiotherapy are applicable to ion beam radiotherapy with protons or carbon ions.
- After treatment with ion beams, the patient will be slightly radioactive for a short time. However, radiation exposure of their family members and caretakers, as well as the public, due to this activation is negligible, and no specific protection procedures are required. Thus, the methods of radiological protection for public exposures in photon radiotherapy facilities are applicable to, and adequate for, ion beam radiotherapy facilities.
- As ion beam radiotherapy requires a more complex treatment system than conventional radiotherapy, appropriate training of staff and suitable quality assurance programmes are essential to avoid possible accidental exposure of patients.

GLOSSARY

Absorbed dose, D

The fundamental dose quantity given by:

$$D = \frac{d\bar{\epsilon}}{dm}$$

where $d\bar{\epsilon}$ is the mean energy imparted to matter of mass dm by ionising radiation. The SI unit for absorbed dose is joule per kilogramme (J kg^{-1}), and its special name is gray (Gy).

Activation

Physical phenomenon in which radioactivity is induced in materials irradiated with radiation such as high-energy photons, neutrons, and ion beams.

Bragg peak

The Bragg peak is a pronounced peak on the Bragg curve that plots the energy loss of ion beams during their passage through matter. For protons and other ions, the peak occurs near the end of their range. In radiation therapy with ions, the term ‘Bragg peak’ is used for the peak in the curve of absorbed dose against depth in the irradiated phantom or patient. Although this is not strictly correct, this usage is applied in this report (see also ‘Spread-out Bragg peak’).

Broad beam

A beam of radiant energy covering the irradiation field entirely in an approximately conical or cylindrical portion of space of relatively large diameter.

Broad beam (algorithm)

One of the dose calculation techniques for radiotherapy treatment planning. It assumes that any beam incidenting the patient travels straight on the incident axis through the patient with no lateral blurring. The dose at any point of interest is given as a function of the corresponding thickness to the point on the beam axis.

Broad beam (irradiation technique)

Incident beam from an accelerator is broadened laterally to cover the target uniformly. The ‘broad beam’ is then shaped using a collimator to match the irradiation field to the cross-section of the target.

Cone beam computed tomography (CBCT)

A form of x-ray computed tomography in which the x rays, in the form of a divergent cone or pyramid, illuminate a two-dimensional detector array for image capture. It can also be referred to as ‘digital volume tomography’.

Deterministic effect

Injury in populations of cells, characterised by a threshold dose and an increase in the severity of the reaction as the dose is increased. It is also termed ‘tissue reaction’. In some cases, deterministic effects are modifiable by post-irradiation procedures including biological response modifiers.

Detriment

The total harm to health experienced by an exposed group and its descendants as a result of the group’s exposure to a radiation source. Detriment is a multi-dimensional concept. Its principal components are the stochastic quantities: probability of attributable fatal cancer, weighted probability of attributable non-fatal cancer, weighted probability of severe heritable effects, and length of life lost if the harm occurs.

Diagnostic reference level

Used in medical imaging with ionising radiation to indicate whether, in routine conditions, the patient dose or administered activity (amount of radioactive material) from a specified procedure is unusually high or low for that procedure.

Dose equivalent, H

The product of D and Q at a point in tissue, where D is the absorbed dose and Q is the quality factor for the specific radiation at this point, thus:

$$H = D \cdot Q$$

The unit of dose equivalent is joule per kilogramme (J kg^{-1}), and its special name is sievert (Sv).

Effective dose, E

The tissue-weighted sum of the equivalent doses in all specified tissues and organs of the body, given by the expression:

$$E = \sum_{\text{T}} w_{\text{T}} \sum_{\text{R}} w_{\text{R}} D_{\text{T,R}}$$

or:

$$E = \sum_T w_T \sum_R H_T$$

where H_T or $w_R D_{T,R}$ is the equivalent dose in a tissue or organ, T, and w_T is the tissue weighting factor. The unit for effective dose is the same as for absorbed dose (J kg^{-1}), and its special name is sievert (Sv).

Equivalent dose, H_T

The dose in a tissue or organ T given by:

$$H_T = \sum_R w_R D_{T,R}$$

where $D_{T,R}$ is the mean absorbed dose from radiation R in a tissue or organ T, and w_R is the radiation weighting factor. As w_R is dimensionless, the unit for equivalent dose is the same as for absorbed dose (J kg^{-1}), and its special name is sievert (Sv).

Fluence, Φ

The quotient of dN by da , where dN is the number of particles incident on a sphere of cross-sectional area da , thus:

$$\Phi = \frac{dN}{da}$$

Intensity-modulated radiotherapy (IMRT)

Advanced mode of high-precision radiotherapy that uses computer-controlled linear accelerators to deliver precise radiation doses to malignant tumour or specific areas within the tumour. IMRT can make appropriate three-dimensional dose distribution by modulating the intensity of the radiation beams from multiple directions.

Lineal energy

The lineal energy, y , is the quotient of ε_s by $\bar{l}$, where ε_s is the energy imparted to the matter in a given volume by a single energy-deposition event, and $\bar{l}$ is the mean chord length of that volume, thus:

$$y = \frac{\varepsilon_s}{\bar{l}}$$

The unit of y is given in J m^{-1} or $\text{keV } \mu\text{m}^{-1}$.

Linear energy transfer (LET)

The average linear rate of energy loss of charged particle radiation in a medium (i.e. the radiation energy lost per unit length of path through a material). That is, the quotient of dE by dl where dE is the mean energy lost by a charged particle owing to collisions with electrons in traversing a distance dl in matter:

$$L = \frac{dE}{dl}$$

The unit of L is J m^{-1} or $\text{keV } \mu\text{m}^{-1}$.

MeV n^{-1}

Kinetic energy of a particle expressed by a unit of mega-electron volt per nucleon (MeV n^{-1}). It reflects the square of the speed v of the particle. Particles sharing the same MeV n^{-1} value have the same $\beta = v/c$ (where c is light speed).

Millibarn (mb)

Barn is a unit of area, originally used in nuclear physics for cross-sectional area of nuclei and defined as 10^{-28}m^2 . 1 mb is equal to 10^{-31}m^2 .

Organ at risk (OAR)

An organ that may be damaged during exposure to radiation. OAR most frequently refers to healthy organs located in the radiation field during radiotherapy.

Oxygen enhancement ratio (OER)

The ratio of the absorbed dose required to cause the same biological endpoint in hypoxic conditions as in normoxic conditions. Hypoxia often occurs in the middle of a rapidly growing tumour. The OER of x rays is approximately 3, while high-LET radiation tends to show smaller OERs down to 1, indicating that high-LET radiation is effective against hypoxic tumours.

Pencil beam

A beam of radiant energy concentrated in an approximately conical or cylindrical portion of space of relatively small diameter.

Pencil beam (algorithm)

One of the dose calculation techniques for radiotherapy treatment planning. It assumes that any beam incidenting the patient is actually a conglomeration of lots of ‘pencil beams’, and the dose at any point of interest is given as the superposition of all the pencil beams.

Pencil beam (in scanning irradiation technique)

Dose is delivered by superposing ‘pencil beams’ from an accelerator on the target by controlling the beam path three-dimensionally.

Quality factor, $Q(L)$

The factor characterising the biological effectiveness of a radiation, based on the ionisation density along the tracks of ion beams in tissue. Q is defined as a function of the unrestricted linear energy transfer, L_∞ (often denoted as L or LET), of ion beams in water:

$$Q(L) = \begin{cases} 1 & L < 10 \text{ keV}/\mu\text{m} \\ 0.32L - 2.2 & 10 \leq L \leq 100 \text{ keV}/\mu\text{m} \\ 300/\sqrt{L} & L > 100 \text{ keV}/\mu\text{m} \end{cases}$$

Q has been replaced by the radiation weighting factor in the definition of equivalent dose, but is still used in calculating the operational dose equivalent quantities for monitoring purposes.

Radiation detriment

A concept used to quantify the harmful health effects of radiation exposure in different parts of the body. It is defined by the Commission as a function of several factors, including incidence of radiation-related cancer or heritable effects, lethality of these conditions, quality of life, and years of life lost due to these conditions.

Radiation-induced second cancer

Ionising radiation has paradoxical aspects in both beneficial effects of curing cancer and the risk of inducing cancer. Induction of cancer by low to high doses of radiation has been demonstrated by the significant increase in the incidence of cancers among workers handling radioactive substances and among atomic bomb survivors, as well as among survivors after radiotherapy.

Radiation weighting factor, w_R

A dimensionless factor by which the organ or tissue absorbed dose is weighted to reflect the higher biological effectiveness of high-LET radiation compared with low-LET radiation. It is used to derive the equivalent dose from the absorbed dose averaged over a tissue or organ.

Relative biological effectiveness (RBE)

The ratio of a dose of a low-LET reference radiation to a dose of the radiation considered that has an identical biological effect. RBE values vary with the dose, dose rate, and biological endpoint considered.

Secondary radiation

Radiation produced by interaction between the primary beam and the matter. In the radiotherapy treatment room, all radiation except for the primary beam is secondary radiation, which is produced by scattering of objects or leakage through the protective shield.

Spread-out Bragg peak (SOBP)

The extended isoeffect region in depth formed by the optimal stacking of multiple depth dose curves of pristine Bragg peaks of different energies.

Stochastic effect

The induction of malignant disease or heritable effects for which the probability of an effect occurring, but not its severity, is regarded, for the purpose of radiological protection, to be increasing with dose without a threshold.

Time-resolved computed tomography (4DCT)

X-ray computed tomography apparatus capable of rapidly acquiring serial three-dimensional volumetric images as a function of time. The image is often associated with breathing or heartbeat phase.

Tissue reaction

See ‘Deterministic effect’.

Tissue weighting factor, w_T

The factor by which the equivalent dose in a tissue or organ T is weighted to represent the relative contribution of that tissue or organ to the total health detriment resulting from uniform irradiation of the body (ICRP, 2007b). It is weighted such that:

$$\sum_T w_T = 1$$

Voxel phantom

Computational anthropomorphic phantom based on medical tomographic images where the anatomy is described by small three-dimensional volume elements (voxels) specifying the density and the atomic composition of the various organs and tissues of the human body.

1. INTRODUCTION

(1) Considerable progress has been made in the treatment of patients with radiation in terms of increased applicability and improved therapeutic outcomes. Most notably, high-precision photon beam radiotherapy, such as intensity-modulated radiotherapy (IMRT) and stereotactic radiotherapy, are used effectively in clinical practice.

(2) The goal of external radiotherapy is precise dose localisation in the treatment volume of the target, with minimal damage to the surrounding normal tissue. The success of treatment largely depends on the performance and capacity of accelerators and the treatment planning system (TPS), in addition to accurate delineation of the targeted tumour volume and patient positioning by the radiation oncologist. This became particularly evident in the 1950s, when it was recognised that high-energy photons contributed significantly to improvement of the treatment outcome. The beginning of modern radiotherapy takes its origins in the 1950s when cobalt therapy units and high-energy accelerators were developed and applied to clinical use.

(3) Cancer therapy with ion beams has a history of more than 50 years (Tobias et al., 1956). Ion beam radiotherapy is characterised by production of the maximum ionisation density at depth in tissue, referred to as the ‘Bragg peak’, and therefore offers an improved dose conformation to the treatment volume with better sparing of the surrounding normal tissue compared with photon beams. Furthermore, protons and heavier ion beams allow a reduction of the total energy deposited in the patient compared with photon techniques. In many cases, this allows dose escalation in the target or a significant reduction in dose to healthy tissue. The latter is of particular importance if the treatment volume is close to critical structures. In addition, ion beams, such as protons and carbon ions, exhibit a strong increase in linear energy transfer (LET) in the Bragg peak compared with the entrance region. In cancer radiotherapy, the physical and biological properties of ion beams are much more favourable than those of photon beams (Castro et al., 1985). Consequently, ion beam radiotherapy with protons and carbon ions has gained increasing interest, and has expanded rapidly in the last decade.

(4) Ion beam radiotherapy with protons is becoming popular in some countries, and carbon ion radiotherapy has also been introduced in medical care. Approximately 10 years ago, there were nearly 20 ion beam radiotherapy facilities in the world.^a At the time of writing, this number has doubled and many new facilities are being built or planned. Potential demand is anticipated to exceed the projected increased number of facilities.

(5) High-energy radiation is necessary for ion beam radiotherapy. The treatment facility generally requires a large-scale accelerator installed in the building with appropriate shielding. There are specific issues in radiological protection to operate such a treatment facility.

^aReferred from Particle Therapy Co-operative Group website: <http://ptcog.web.psi.ch/>

(6) A result of the worldwide development and spread of high-precision radiotherapy has been the increased opportunity to treat benign diseases and malignant cancers in young patients. The therapeutic outcome has also been improved for locally advanced cancers that were not curable with conventional methods. Many of these patients now survive for longer periods, and thus, more attention should be paid to any late-occurring radiation effects.

(7) In the past, radiation oncologists focused mainly on curing cancers with little consideration of second cancers or radiotherapy-related cardiovascular disease. Recently, the situation has changed; while high-precision photon radiotherapy methods are superior in terms of the dose distribution they deliver to a tumour, a large volume of the surrounding normal tissue may be exposed to low and medium levels of dose (NCRP, 2011). Ion beam radiotherapy with protons or carbon ions largely contributes to localised dose to the tumour, and the additional dose received by the surrounding normal tissue is reduced. However, the possible risk of high-LET radiation in the surrounding normal tissue may be of more general concern, despite the fact that the absolute dose level is reduced.

(8) This report reviews the present status and problems associated with the use of ion beam radiotherapy from the viewpoint of radiological protection and safety, and provides practical guidance for the effective and safe use of ion beams for medical treatment of benign and malignant disease.

2. OUTLINE OF ION BEAM RADIOTHERAPY

2.1. Clinical target of ion beam radiotherapy

(9) The introduction of new technologies in radiotherapy aims to improve treatment outcome by means of a dose distribution that conforms more strictly to the tumour volume and treatment volume (ICRP, 2009). Ion beams are considered to have the optimum properties for dose localisation. The selection of patients suitable for ion beam radiotherapy is the first step in the treatment. Benefits of ion beam therapy can be achieved in patients with solid cancer with defined borders. This non-invasive treatment does not require surgery to remove the cancer, making it ideal for inoperable tumours. Proton beam radiotherapy may offer clinical advantages compared with conventional photon radiotherapy for many cancers, mainly as a result of a more favourable distribution of the radiation dose (Lundkvist et al., 2005).

(10) Ion beams that are heavier than protons have the additional advantage of enhanced biological effects; these increase with depth, reaching a maximum at the end of the beam's range. These unique properties have led to the use of heavy ion beams, such as helium, carbon, and neon ions, for cancer radiotherapy. The carbon ions enable the treatment of various tumours that are resistant to conventional photon radiotherapy or chemotherapy (Chauvel, 1995). The clinical benefits of carbon ion radiotherapy have been demonstrated in non-squamous cell tumour types, including sarcoma, malignant melanoma, adenocarcinoma, adenoid cystic carcinoma, and chordoma (Tsuji and Kamada, 2012).

(11) Some studies have suggested that new technology has not yet resulted in a substantial improvement in the long-term outcome for most patients (Soarers et al., 2005), and there is a need for systematic evaluation of the benefits, considering the total cost of the method (Allen et al., 2012; Lievens and Pijls-Johannesma, 2013).

2.2. General treatment processes

2.2.1. Features of ion beams

(12) Ion beams, as indicated above, are characterised by dose concentration at depth in tissue and enhanced biological effectiveness. The clinical advantage results from a steeply rising absorbed dose, or Bragg peak, and a rapid decrease in dose after the peak. Therefore, by targeting the lesion within the Bragg peak, a superior dose concentration is achieved. This superiority is similar for both proton and carbon ion beams.

(13) Relative biological effectiveness (RBE) values vary for different endpoints for most cells and tissues, but tend to increase in parallel with increments of LET up to a maximum value before declining. Proton beams in clinical use are low-LET radiations, hence the RBE values are very close to those of high-energy x rays. The International Commission on Radiation Units and Measurements (ICRU) has recommended 1.1 as a generic RBE for proton beams (ICRU, 2007). This is based on the available evidence indicating that the magnitude of RBE variation with treatment

parameters is relatively small compared with possible realistic RBEs. There is some concern about the use of a generic RBE value due to the limited range of data, particularly given the lack of human cell types, and future clarification is needed. For carbon ions, LET increases with depth in tissue, reaching a maximum at the end of a particle's range. Carbon ions have higher RBE values than protons, but variations with depth in tissue and energy are not well defined.

(14) The available data indicate that the oxygen enhancement ratio (OER, the ratio of the absorbed dose required to cause the same biological endpoint in hypoxic conditions as in normoxic conditions) is reduced using high-LET radiation, and that high-LET radiation has less influence on the variation in radiosensitivity with respect to a phase in the cell division cycle. In order to treat cancers with ion beams, it is essential to have the knowledge and technology to use the characteristic features of the beams.

2.2.2. Imaging

(15) Imaging technology plays a crucial role for precise localisation of the target volume in radiotherapy. In the case of ion beam radiotherapy, state-of-the-art diagnostic imaging with x-ray computed tomography (CT), magnetic resonance imaging, and positron emission tomography (PET) is indispensable in the entire procedure of treatment planning. For example, in treatment planning, CT gives patient density information to calculate dose distribution and design the shape of the spread-out Bragg peak (SOBP) to conform to the target volume. Recently, the PET-CT system has been developed, and this provides valuable diagnostic information for treatment planning. It is common to use x-ray exposures for patient positioning in ion beam radiotherapy.

2.2.3. High-precision beam delivery system

(16) In order to appreciate the advantage of dose distribution, ion beams are spread to conform to the target by passive scattering, pencil beam scanning, and wobbling or uniform scanning. Thus, the high-precision beam delivery system covers the target with the designed spread beam with millimetre accuracy. In the past, the most commonly used method was passive beam scattering, including single and double scattering. For the treatment of a target volume moving with respiration, the respiratory-gated irradiation method has been used in passive scattering.

2.2.4. Procedures for ion beam radiotherapy

(17) Procedures for ion beam radiotherapy are described below. These include patient immobilisation, planning CT, treatment planning, patient positioning, and beam delivery.

Patient immobilisation

(18) Rotating gantries have become available for proton radiotherapy (Slater, 1995), while fixed horizontal or vertical beams are used in most carbon ion therapy facilities. In the case of fixed beam lines, different beam directions can only be achieved by a combination of patient's positions, with or without rotating the patient. Normally, ion beam radiotherapy is fractionated over several weeks. It is crucial for radiotherapy to repeat the beam delivery with high precision over the period. Initially, it is important to examine diagnostic images to determine the treatment sites and available beam directions. Immobilisation must be sufficiently robust to maintain its integrity for the duration of treatment, and fully support a reproducible patient treatment position. In some cases, physiological factors are actively controlled (e.g. bladder filling in patients with prostate cancer). For immobilisation, care should be taken not only for the patient's comfort but also for the possible influence on the beam delivery. Safety and cost should also be included in the consideration. In many facilities, vacuum bags, bite blocks, individual cradles, and thermoplastics are used.

Planning CT

(19) Treatment planning for ion beam radiotherapy is performed using CT images, which must be taken under the same conditions as used for treatment. The patient must be immobilised on the treatment couch under the same breathing conditions as for treatment. This sometimes requires respiratory gating for both CT scanning and subsequent beam delivery. The planning CT images provide patient density information for dose calculation. The use of contrast agents is therefore normally avoided in planning CT scans.

Treatment planning

(20) The clinical target volume and organs at risk (OARs) are first defined on the planning CT images. In practice, additional diagnostic images, such as contrast-enhanced or breath-hold CT, magnetic resonance images, and PET images, are often helpful for delineation of the target if they are taken under treatment conditions (Hosokawa et al., 1995). The planning target volume is then determined, which also considers physiological changes between planning CT and treatment, organ motion (ICRU, 1993b, 1999; Osaka et al., 1997), and setup errors. The ion beams are designed to deliver the prescribed dose uniformly to the planning target volume, and beam parameters are chosen or varied to obtain an optimum dose distribution for the prescription (ICRU, 2007).

Patient positioning

(21) For high-precision ion beam radiotherapy, the patient position is aligned and verified with orthogonal x rays in comparison with digital radiographs reconstructed

from planning CT images for the setup of each patient. The reference planning images can be substituted by the equivalent x-ray images, which are taken prior to the first treatment. Bony structures and fiducial markers, implanted near the site before the planning CT, are often used as reference points in patient positioning.

Beam delivery

(22) After the patient is immobilised and positioned, the ion beams are delivered as planned for a period of seconds or minutes. During beam delivery, the patient and active devices are visually or electrically monitored for interlock in case of any emergency. The beam is stopped when the prescribed dose is administered, for which the dose monitor output has to be calibrated prior to treatment. Due to the complexity of ion beam delivery systems, dose monitor calibration may require specific control measurement on a beam-by-beam basis.

2.3. Introduction of the beam delivery system and irradiation method

(23) An ion beam delivery system generally consists of an accelerator system, a high-energy beam transport system, and an irradiation system. In most cases, a synchrotron, cyclotron, or synchro-cyclotron is used to accelerate particles. A high-energy ion beam is delivered through a beam transport system to an irradiation system. The narrow pristine beam extracted from the accelerator, which is called a 'pencil beam', is not ready for use in treatment except for the beam scanning method. The irradiation system broadens the pencil beam for the target volume. This method is called the 'broad beam method' and is classified as the 'passive method' (Fig. 2.1).

(24) A layer stacking method is a more advanced broad beam method that uses a multileaf collimator (MLC), resulting in higher relative dose being delivered to the target volume than the standard broad beam method (Kanai et al., 1983; Futami et al., 1999). In a scanning method, pencil beams are scanned over a target tumour, three-dimensionally, without expanding the pencil beam, unlike the conventional broad beam method (Fig. 2.2). The layer stacking and scanning methods are classified as 'active methods'.

2.3.1. Broad beam method

(25) In the broad beam method, a narrow pencil beam, extracted from an accelerator, is broadened uniformly in the lateral and depth directions, and part of the expanded uniform beam is clipped to conform to the high-dose region induced by the beam to the target tumour volume in a patient's body. The main methods used to widen the pencil beam uniformly in the lateral direction are double scattering and

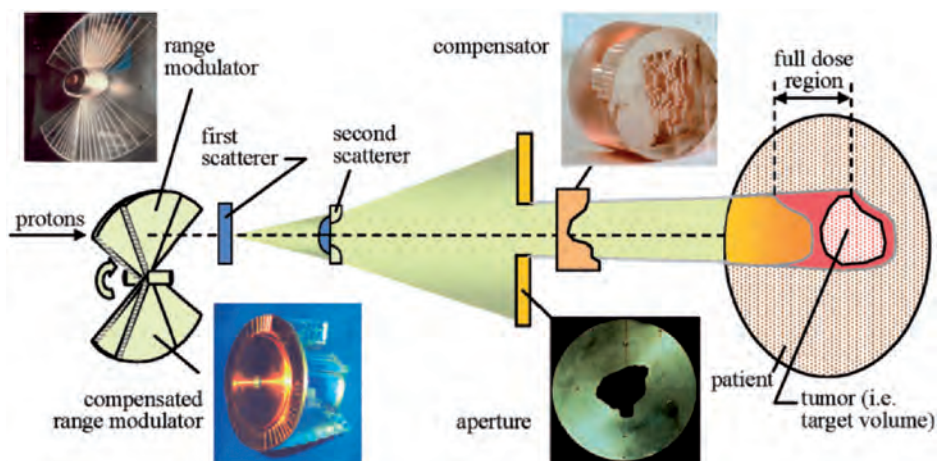


Fig. 2.1. Broad beam system with passive scattering for proton beam therapy. Reprinted from Goitein (2008).

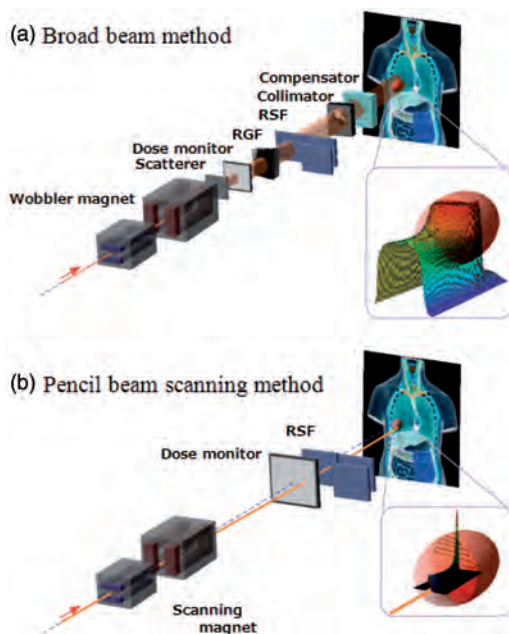


Fig. 2.2. Beam delivery system for carbon ion radiotherapy. (a) Concept of broad beam method. (b) Concept of pencil beam scanning method. RSF, range shift filter; RGF, ridge filter.

wobbler scattering. Single-scattering methods can be applied for small field sizes such as in radiosurgery.

(26) The double-scattering method (Fig. 2.1) makes a uniform irradiation field using two scatterers with different structures (Grusell et al., 1994; Gottschalk, 2008). The first scatterer, installed upstream in the irradiation system, is made of a uniform, heavy material (lead is commonly used), and the pencil beam is broadened by multiple Coulomb scattering. The distribution of the beam takes on a Gaussian-like shape with small tails. The second scatterer, placed downstream from the first scatterer, is made of two materials: a high Z component of decreasing thickness as a function of distance to the beam centre, and a low Z component of increasing thickness with distance to the beam centre.

(27) The wobbler-scattering method (Fig. 2.3) generates a uniform irradiation field using a combination of a wobbler-magnet system and a scattering system (Torikoshi et al., 2007). The wobbler-magnet system is a pair of bending magnets which are installed so that the direction of their magnetic fields is mutually orthogonal. By applying alternating currents to the two magnets, which are out of phase with each other by 90° , the pencil beam delivered from the accelerator is rotated in a circular pattern. The radius of the circle can be changed by varying the effective current supplied to the wobbler-magnet system. The annular beam is broadened by the scattering system placed downstream from the wobbler-magnet system.

(28) Uniform broadening of a beam, in the depth direction, corresponds to producing an SOBP. The SOBP is formed by superimposing many different pristine Bragg peaks. In other words, the SOBP is the response to energy modulation of a mono-energetic beam. There are two main ways of modulating beam energy and superimposing Bragg peaks: one uses a ridge filter device (Larsson, 1961; Kostjuchenko et al., 2001), and the other uses a rotating range modulator (Koehler et al., 1975). The ridge filter device is composed of many uniform bar-ridges, manufactured with highly precise processing technology, that are set parallel to each other on one plane as shown in Fig. 2.4. Ridge filter devices, corresponding to different SOBP widths, are often prepared for both high- and low-energy beams. As the cross-sectional shape of the bar-ridge determines the thickness of the beam, appropriate design of the bar-ridge allows delivery of a homogeneous weighted dose to the target region.

(29) A rotating range modulator is a wheel with a cyclic part of different water-equivalent thickness for different central angle regions. As a beam passes through the cyclic part, its energy is modulated by the thickness in the region where the beam passes. The depth-dose distribution formed using the rotating range modulator has a time structure corresponding to the rotation frequency of the modulator.

(30) After the broadening of a beam in the lateral and depth directions, the beam is shaped to the target tumour, projected in the beam's eye view. A customised patient collimator, an MLC, or a combination is used for two-dimensional shaping of a uniform beam. A customised patient collimator is a block that has a tumour

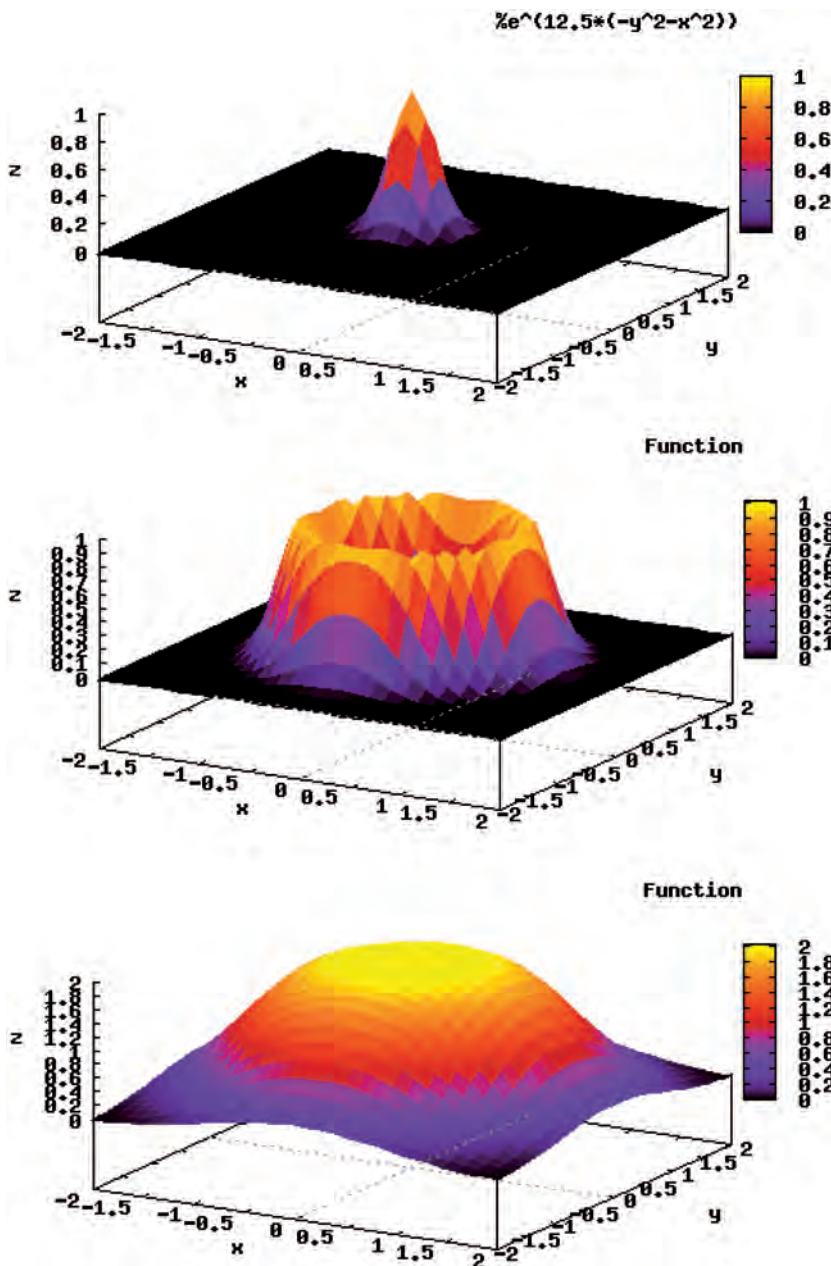


Fig. 2.3. Uniform broad beam generated by the wobbler-scattering method. (Top panel) A pencil beam delivered from an accelerator source. (Middle panel) A beam rotated by wobbler magnets. (Bottom panel) A beam broadened by a scattering system placed downstream from the wobbler-magnet system.

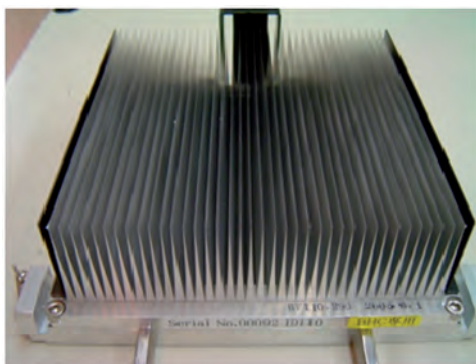


Fig. 2.4. Ridge filter. Ridge filter devices, corresponding to different spread-out Bragg peak widths, are often prepared for high- and low-energy beams.

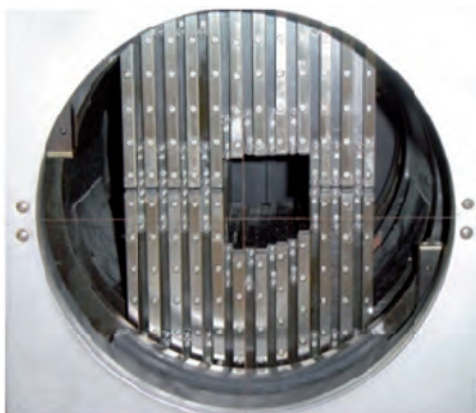


Fig. 2.5. Multileaf collimator.

projection-shaped aperture. The block is thicker than the maximum range of the beam and often made of brass, which is easy to cut with a wire-electrical discharge machine or a milling machine. Although a customised patient collimator needs to be manufactured for each irradiation direction, it reduces blurring of the lateral dose falloff because the patient collimator can be placed near the body surface of the patient.

(31) An MLC has many pairs of thin leaves (Fig. 2.5). These leaves are shifted to suitable positions to make the aperture fit the tumour projected shape. Use of an MLC device has the advantage of increased speed and reduced costs for treatment preparation because no individual patient collimators need to be manufactured. On the other hand, due to mechanical limitations, MLCs often cannot be positioned as

close to the patient's surface as block collimators. The larger gap between the end of the collimator and the patient surface spoils the sharp lateral dose falloff to some extent. Therefore, MLCs are not often used when precise field shaping is required.

(32) A range shifter device is applied for the sake of adjusting the residual range in a patient's body. A range shifter device is composed of several energy absorbers with different thicknesses, and the total thickness of the system can be changed by selecting suitable absorbers. The beam range can be adjusted uniformly by using a range shifter device. Range shifter devices are not commonly used in the treatment head (except for fine tuning), as synchrotrons can deliver the desired energy and cyclotrons typically use energy degraders at the cyclotron exit to send the desired energy into the treatment room.

(33) A patient compensator is a block that has an engraved depression in the shape of the distal surface of the target volume. The block is often made of high-density polyethylene which is easy to engrave and has a low atomic number to reduce scattering of the beam. Patient compensators, like patient collimators, also need to be manufactured for each irradiation direction.

(34) Regarding patient exposure to radiation, the beam efficiency is low for the broad beam method due to the loss of ion particles before reaching the patient. There is a loss of beam intensity with every device used to modulate and shape the beam, and these points can also generate undesired radiation, such as neutrons.

2.3.2. Layer stacking method

(35) In the broad beam method, with a range modulator, a constant SOBP over the field area results in an undesirable dose to the normal tissue proximal to the target (Goitein, 1983; Kanai et al., 1993; Kanematsu et al., 2002). Therefore, in order to avoid unwanted doses, a layer stacking method was developed. The layer stacking method is a way of stacking multiple mini-SOBPs along the depth direction, and changing apertures of the MLC in such a way that the lineation of the cross-sectional surface at the corresponding depth of the target tumour volume is drawn. Regarding patient exposure to radiation, the efficiency of beam usage is also low for the layer stacking method.

2.3.3. Pencil beam scanning method

(36) Pencil beam scanning is a method to achieve a highly conformal field by three-dimensional scanning of a pencil beam, extracted from an accelerator, within the target tumour volume. A conceptual diagram of a pencil beam scanning method is shown in Fig. 2.2 (b).

(37) Historically, the first proton beam scanning was achieved with a low-energy beam (70 MeV) that was not used in patient treatments (Kanai et al., 1980). A new

project for treating deep-seated tumours with a proton pencil beam scanning was started in 1992 at Paul Scherrer Institute (PSI) (Pedroni et al., 1995). Almost in parallel to PSI, Gesellschaft für Schwerionenforschung (GSI) in Germany developed pencil beam scanning for carbon ions using a horizontal, fixed beam line for treating tumours at the base of the skull. The scanning system at GSI is based on a raster scanning technique, which uses a double magnetic scanning system and changes the beam energy dynamically with the synchrotron (Haberer et al., 1993).

(38) The pencil beam is scanned laterally, usually using orthogonal scanning magnets, to form a lateral irradiation field. The scanning speed along one direction is higher than that along the other orthogonal direction. This allows the use of a mechanical shifting system along the slowly scanning axis, instead of a scanning magnet (e.g. as used on Gantry I at PSI). It is then scanned longitudinally by either a range shifter device or a stepwise energy change by the accelerator. The pencil beam scanning method is characterised by a high beam efficiency of almost 100%, and therefore benefits from lower production of neutrons.

2.3.4. Rotating gantry system

(39) The rotating gantry system allows a wide choice of beam orientation compared with a fixed port irradiation system. In clinical practice, in fixed beam delivery systems, the beam is limited to either the horizontal or vertical direction, and thus the patient has to be fixed in a supine, prone, or sitting position. The patient is often rolled into a new position to get a better combination of beams. This often places a burden on the patient, complicates treatment planning, and leads to imprecise positioning. It also limits the accuracy of beam delivery due to the possible movement of internal structures and organs by rolling the patient. The rotating gantry system, which allows 360° rotation around the patient, resolves many of these problems and is the standard for conventional x-ray teletherapy systems. The rotating gantry for ion beam radiotherapy is much larger than that for photons; typically 10 m in diameter in commercial proton radiotherapy systems.

2.3.5. Respiratory gating irradiation

(40) Organ motion during patient positioning and beam delivery degrades the precision in dose delivery. In particular, breathing causes movement of up to a few centimetres in the thoracic and abdominal regions, which may also influence the whole body when the patient is in the prone position. In order to solve the problem, breath holding and active breathing control during the treatment have been proposed (Wong et al., 1999). Respiratory gating of radiation exposures also effectively mitigates such motion effects by synchronising beam extraction with respiration. Breathing motion can be detected with, for example, an infra-red light spot and a position-sensitive charge coupled device camera, which gives a respiration