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Regulatory Control of the Safety of Ion Radiotherapy Facilities

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REGULATORY CONTROL OF THE SAFETY OF ION RADIOTHERAPY FACILITIES

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REGULATORY CONTROL OF THE SAFETY OF ION RADIOTHERAPY FACILITIES

INTERNATIONAL ATOMIC ENERGY AGENCY
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FOREWORD

Ion radiotherapy, which involves discharging high energy ions into cancer cells usually located deep under the skin, has generated significant interest, and several institutions around the world are in the process of implementing, or are considering introducing, this treatment method. Specifically, beams of heavy particles, such as ions of selected isotopes, are particularly suitable for deep seated cancers because of their high dose delivery properties and biological effect in Bragg peak regions. Clinical results of ion radiotherapy have demonstrated benefits to patients from this treatment modality.

At present, there are around 80 operating ion radiotherapy facilities worldwide, and several new facilities are under construction or being planned. As this treatment modality develops, knowledge of ion radiotherapy is growing and is being exchanged within the radiotherapy community, including regulatory bodies, radiotherapy professionals, standards organizations, equipment manufacturers and suppliers. This exchange has contributed to the establishment of good practices for the safety of ion therapy treatment facilities worldwide.

In response to Member State interest, the IAEA prepared this publication summarizing the current best practices in the field of ion radiotherapy safety based on IAEA safety standards. The information included here covers the design of the equipment and facility as well as aspects of their operation.

The IAEA wishes to thank all the experts involved in the development of this publication for their contributions. The IAEA officer responsible for this publication was D. Mroz of the Division of Radiation, Transport and Waste Safety.

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CONTENTS

1. INTRODUCTION

1.1. BACKGROUND

Ion radiotherapy is a method of discharging high energy ions into cancer cells usually located deep under the skin [1]. Most currently existing ion radiotherapy facilities use protons or carbon ions accelerated in cyclotrons or synchrotrons. Radiotherapy using other ions lighter than carbon, such as helium, is also considered for future applications

The International Basic Safety Standards [2] provides basic requirements for the protection of people against exposure to ionizing radiation and for the safety of radiation sources for medical exposure, occupationally exposed personnel, the public and the environment. As new technologies are introduced, risks are assessed, and new safety standards may need to be adopted.

The specific design features of an ion radiotherapy facility and the properties of ion interactions with matter mean that there are corresponding unique safety aspects. These aspects include structural shielding design, and occupational, environmental and medical exposure control. Other aspects requiring special attention are radiation dosimetry and radiation survey of high intensity particle beams and a variety of types of secondary radiation, mainly prompt neutron radiation and induced residual radioactivity. The high energy and intensity of radiation are likely to cause physical and chemical effects in materials and electrical components. The radiation generated by equipment also induces radioactivity in solids, liquids and dust. This radioactivity can aggravate the consequences of floods, fire and earthquakes and is considered in the safety assessment of an ion radiotherapy facility. All the above factors affect the protection of workers, patients, public and the environment.

The major issue for the radiation protection of an ion radiotherapy facility is the massive production of neutron radiation. Ionizing radiation results from prompt neutrons, as well as from the radioactivity induced in exposed materials. Radioactivity is produced in accelerator structures and their beam delivery/shaping components as well as in the structural components and materials integrated into the facility. Induced radioactivity in treated patients may also be high enough to warrant attention.

In addition to the accelerator system for radiotherapy, an ion radiotherapy facility also houses auxiliary equipment producing ionizing radiation for patient imaging. These devices may include computed tomography (CT) X ray scanners, used for dose planning purposes and imaging devices (onboard X ray imaging) integrated into the ion accelerator gantry for verification of patient position. The latter imaging systems can be used for projection radiography or for generating volumetric anatomy information from tomographic imaging (CBCT).

Other imaging devices not generating but only detecting ionizing radiation, include classical positron emission tomography (PET) systems used for target definition and treatment response follow-up. Some facilities utilize ‘passive PET detecting positron emission’ from patient induced radiation (^{11}C) to verify the irradiation area after treatment. New imaging techniques, such as prompt gamma ray camera, proton radiography or proton CT, to verify the range of particle beams in patients are still under development.

Since ion radiotherapy is a relatively new technology, national regulatory authorities are not always equipped with the expertise and tools to exercise effective regulatory control. As a

result, the use of external experts by a regulatory body is often considered when authorizing and inspecting ion radiotherapy facilities [3].

1.2. OBJECTIVE

The objective of this report is to describe the best practices in the regulatory control of ion radiotherapy facilities and to provide guidance on the methodology for facility authorization and inspections. It is addressed mainly to regulatory bodies for radiation safety control, though it can also be used by equipment vendors and organizations operating or planning to construct such facilities.

A practice specific methodology is described, including an example of an applicable form. Technical safety aspects specific to this new technology are described. Another goal is to assist in technical reviews and assessments to demonstrate the safety of facilities using ions for radiotherapy and/or research.

1.3. SCOPE

This publication describes the best international practice related to the regulatory control of radiotherapy facilities using ion accelerators (such as those using protons as well as carbon and helium ions). It also provides guidance on facility authorization and inspection, as well as technical safety aspects that are typical and significant for ion accelerators. The guidance is based on Functions and Processes of the Regulatory Body for Safety (IAEA Safety Standards Series No. GSG-13) [4].

The clinical benefits of ion radiotherapy facilities are not covered in this report, nor are practical design and engineering aspects or the medical performance of the equipment beyond the safe delivery of prescribed doses of ionizing radiation. The safety of the engineering design of the equipment is covered in separate specialized technical standards.

This report covers the approach and procedures specific to safety of ion radiotherapy facilities and activities. The procedures described incorporate the ‘graded approach’. The focus of this document is on the regulatory oversight of radiation safety in planned exposure situations towards minimizing unplanned exposure situations as defined in IAEA Safety Standards Series No. GSR Part 3 [2]. Testing of the equipment installed at medical facilities for the commissioning and routine operation is included in the scope of this publication.

Authorization for manufacturing and testing of the equipment at the equipment production and assembly sites is not discussed in this publication. Also, outside the scope of this report are issues related to the nuclear security and physical protection of radiation sources. The ion radiotherapy equipment constitutes ionizing radiation generators, as opposed to devices based on sealed radioactive sources. Levels of radioactivity induced by ion radiotherapy equipment radiation beams are not significant enough to warrant physical protection measures.

1.4. STRUCTURE

An overview of the technique and theory behind the use of ion beam therapy in medicine is given in Section 2. Section 3 discusses the national system of regulatory control, while Section 4 focuses on the authorization needed for the operation of an ion radiotherapy facility and activities. Section 5 discusses the reviews and assessments of the various documents and applications required for the facility, while Section 6 focuses on planned and announced inspections as part of the regulatory body’s inspection plan. Section 7 discusses the regulatory

decisions required for the control of facilities and activities, including authorization, inspection and enforcement.

Appendix I contains an example of the various forms required, while Appendix II discusses topics related to the licence application, review and assessment. Appendix III describes the risks and hazards involved.

Annex I contains a list of current ion radiotherapy facilities.

2. INTRODUCTION TO ION RADIOTHERAPY

The number of ion beam facilities is increasing worldwide. For example, in the USA in 2018, there were 25 proton therapy facilities in operation, and ten more facilities are under construction. Other States are following this trend, constructing, or planning to construct, proton and ion therapy facilities. Worldwide, about 80 facilities are in operation and more than 35 facilities are under construction.

The main advantage of ion particle therapy is the concentration of the dose to the tumour and the sparing of healthy tissues in the body. The technical basis and the safety issues are different from conventional radiotherapy units based on electron accelerators.

An example of a typical setup of a proton therapy facility is given in Fig. 1. A cyclotron type accelerator and the energy selection system are positioned in a well shielded area (right). The beam is delivered to the treatment bunkers through a beam transportation system equipped with beam guiding deflection magnets.

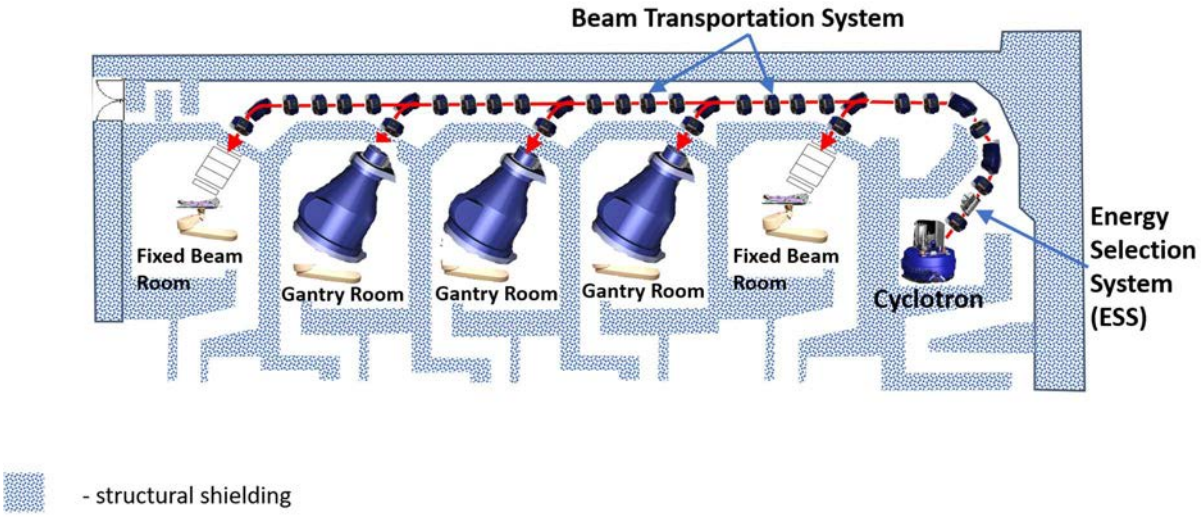
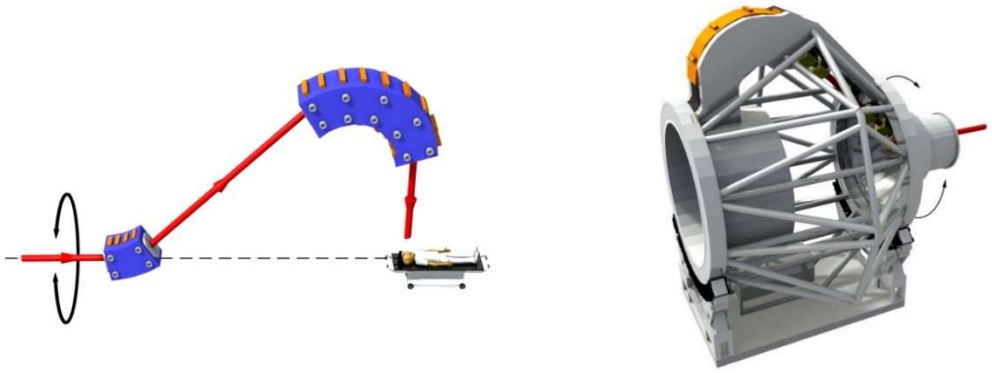


FIG. 1. An example of a proton therapy facility with the accelerator (cyclotron), the energy selection system (ESS), and the treatment bunkers (three gantries and two fixed beam bunkers).

An example of a gantry is given in Fig. 2. Figure 2(a) shows the principle of a rotating gantry with the beam guide and the deflection magnets visible. Figure 2(b) shows the rotating gantry. The overall weight of a proton gantry is well over 100 t. The precision of the beam delivery at the isocentre needs to be in the range of 1 mm.

Ion beam production is associated with expected beam loss in the energy selection system and in the treatment bunkers, thus requiring shielding measures to protect the hospital area and the facility. Accidental beam losses can occur along the beam transportation system and cause radiation, which needs to be shielded as well.



(a) (b)

FIG. 2. (a) Principle of a rotating gantry (here 360°) with the beam guide and the deflection magnets. (b) The gantry construction for proton beams.

The main radiation component affecting shielding measures is neutron radiation. Because of the high velocity of the particles (e.g. two-thirds of the speed of light for protons), the major part of the neutrons generated in the path of the particle beam is high energy radiation. The high neutron energy has two implications. The first is the increased effort for the shielding design, as the attenuation in common shielding materials is lowered at high neutron energies, and the shielding thicknesses need to be adapted accordingly. The second is the production of radioactivity by high energy interactions.

Figure 1 is an example of a facility concept and its shielding design. There are three treatment bunkers with rotating gantries. The gantry rotation is required to provide improved dose distribution for the patient. The two bunkers are used for fixed (horizontally oriented) beam treatments when the medical objectives do not require gantry rotation.

The main radiation production goes in the direction of the primary beam. Scattered radiation occurs everywhere in the treatment bunker and therefore the access paths for people to the bunkers are designed as mazes.

Ion radiotherapy facilities make use of two major types of particle accelerators: cyclotrons and synchrotrons. Cyclotrons are compact accelerators producing beams with a fixed extraction energy. The desired maximum range of ions is usually 30 cm in soft tissue, requiring 220 MeV of kinetic energy.

Cyclotrons are normally used to produce proton beams, though their use for generating ion beams heavier than protons is still under development. The desired energy of the proton beam in cyclotrons is obtained by the application of a degrader that reduces the accelerated particle energy. The degrader represents the strongest radiation source in the facility. Recently, a ‘synchrocyclotron’ machine has become available as a compact version of a cyclotron with variable frequency for particle acceleration. However, this machine still requires an energy degrader.

Synchrotrons produce ion beams with variable energy. Therefore, a degrader is not needed in synchrotron-based radiotherapy facilities. In synchrotrons, protons or ions heavier than protons can be accelerated to a desired energy. The magnetic rigidity (see Section 5.2.5.1 for the

definition of this term) of the synchrotron gives the maximum energy of the accelerated particles.

The accelerator produces a pencil-like beam. Since, in clinical treatments, the tumour target volume is significantly wider than the lateral extent of a single pencil beam, techniques are used to increase the treatment beam lateral coverage. There are two methods to spread the beam to treat a larger target, passive and scanning method.

The passive method is based on beam widening using scattering techniques (single or double scattering). In combination with absorber elements and collimators, an arbitrary shape of the particle distribution is generated. Further elements are applied to increase or decrease the range of particles in tissue.

The scanning method is based on magnets for deflection of the beam to follow the shape of the tumour. An 'energy stacking' method is usually used to deliver the ion beam to the specific depth in a layer by layer fashion. In principle, the scanning method manages tumour irradiation without passive elements, which greatly reduces neutron contamination and particle loss in the scatter devices. The scanning of a narrow pencil beam allows for precise lateral shaping of the treatment beam. Thus, most scanning pencil beam nozzles do not use any lateral beam collimation system, which further reduces the beam loss.

Both accelerator types can be combined with the passive scattering and active scanning methods. Recently, active scanning systems are receiving greater consideration in newer installations. The passive beam forming causes additional radiation to be produced because the beam undergoes nuclear reactions (fragmentation and/or spallation) during transport in the passive elements. From a radiation protection point of view, the active scanning method has advantages compared with the passive beam forming technique.

Beam loss and energy deposition distribution determine the shielding design of an ion beam facility. Beam loss estimations of both cyclotron and synchrotron facilities are given in Section 5.2.5.3. Knowledge of beam losses and shielding data from, say, line of sight models gives a first approach for the shielding design of the facility. Depending on the type of irradiation bunker (for the rotating gantry or for a fixed beam), an annual dose can be derived for the areas adjacent to the treatment bunker.

Further shielding details need to be considered, such as for the bunker entrance and the maze layout to attenuate the radiation coming from patient treatment to the outside of the bunker. Ducts in the treatment bunker shielding barriers need to be designed to keep radiation transport to neighbouring rooms at acceptable levels.

Calculation methods to determine the activation of different materials, based on estimations of the neutron production in combination with the application of activation cross-sections for specific nuclides, are explained in Section 5.2.11. Activation of the air, cooling water, or the soil below the floor also needs to be considered.

Radiation surveys, and the associated necessary instrumentation, are described in Section 5.2.17 for the measurement of high energy neutron radiation.

Examples are given, with the focus on applicable methods of shielding design or activation estimations rather than exact values not directly transferable to other facilities.

3. NATIONAL SYSTEM OF REGULATORY CONTROL

The Fundamental Safety Principles [5] set out the underlying principles for safety upon which the body of safety standards are built:

- Principle 1: Responsibility for safety;
- Principle 2: Role of government;
- Principle 3: Leadership and management for safety;
- Principle 4: Justification of facilities and activities;
- Principle 5: Optimization of protection;
- Principle 6: Limitation of risks to individuals;
- Principle 7: Protection of present and future generations;
- Principle 8: Prevention of accidents;
- Principle 9: Emergency preparedness and response;
- Principle 10: Protective actions to reduce existing or unregulated radiation risks.

Principle 2 states, "An effective legal and governmental framework for safety, including an independent regulatory body, must be established and sustained" [5]. This principle is translated into safety requirements directed towards the government in IAEA Safety Standards Series No. GSR Part 1 (Rev. 1), Governmental, Legal and Regulatory Framework for Safety [6], wherein Requirement 2 states, "The government shall establish and maintain an appropriate governmental, legal and regulatory framework for safety within which responsibilities are clearly allocated".

Thus, the governmental responsibility for safety is at a national level while Safety Fundamentals clearly put the prime responsibility for safety on the person or organization, the authorized party or licensee, responsible for facilities and activities that give rise to radiation risks [5]. This prime responsibility is retained throughout the lifetime of the facility or activity and means that the authorized party is responsible for:

- Establishing and maintaining the necessary competences;
- Providing adequate training and information;
- Establishing procedures and arrangements to maintain safety under all conditions;
- Verifying appropriate design and the adequate quality of facilities and activities and of their associated equipment;
- Ensuring the safe control of all radioactive material that is used, produced, stored or transported;
- Ensuring the safe control of all radioactive waste that is generated.

Requirements for the establishment, upholding and management of protection and safety are specified in paragraphs 2.39–2.52 of GSR Part 3 [2], along with specifications of the responsible parties.

3.1. CONSTITUTION AND ORGANIZATION OF THE REGULATORY BODY

Based on Principle 2 in SF-1 [5], in each Member State:

> "The government, through the legal system, shall establish and maintain a regulatory body, and shall confer on it the legal authority and provide it with the competence and the resources necessary to fulfil its statutory obligation for the regulatory control of facilities and activities".

Furthermore,

> "The government shall ensure that the regulatory body is effectively independent in its safety related decision making and that it has functional separation from entities having responsibilities or interests that could unduly influence its decision making". (Requirement 4 of GSR Part 1 (Rev. 1) [6].)

Specifically, independence requires the regulatory body to:

> "be free from any pressures associated with political circumstances or economic conditions, or pressures from government departments, authorized parties or other organizations". (Paragraph 2.8(d), GSR Part 1 (Rev. 1) [6].)

The constitution of a regulatory body varies from State to State. In some States the legal authority for regulatory control of facilities and activities is assigned to one single institution (authority), while other governments divide the responsibilities of the regulatory body between two or several institutions, each corresponding to different sectors or aspects of safety (e.g. nuclear and radiation safety, security, medical exposures, emergency preparedness and response, occupational exposure or public exposure).

Regardless of the constitution of the regulatory body, the responsibilities and authority of each institution and the interfaces and cooperation between these institutions are supposed to be clearly governed by the regulatory system for safety.

Paragraph 4.1 of GSR Part 1 (Rev. 1) [6] sets out requirements for the regulatory body referring

> "to the organization of the regulatory body: its structure, allocation of resources, coordination with other authorities, management system, staffing, and relationship with advisory bodies and support organizations. This section also establishes general requirements for performing the functions of the regulatory body — in an effectively independent manner — to preserve the consistency and stability of operations and constructive liaison with authorized parties".

The regulatory body´s organization, staffing and allocation of resources will differ significantly between Member States depending on the number, complexity and risk implications of facilities and activities in each State. Nuclear reactor facilities pose a potential high risk from a radiation point of view and require large regulatory resources and staff allocation by the regulatory body. Other activities, e.g. dental X rays, may be conducted on a relatively large scale but add up to an overall risk low enough to require limited regulatory control, thus requiring limited resources from the regulatory body. When necessary, the regulatory body may seek expert advice and support from external resources in executing its regulatory functions. This is done in a manner compatible with the requirement for effective independency in regulatory control. The use of external experts or advisory boards does not relieve the regulatory body of its responsibilities and its obligations to house adequate core competence to make informed decisions.

The regulatory body needs to perform its regulatory control according to established processes incorporated into a management system, where each process:

"[…] shall ensure the stability and consistency of regulatory control and shall prevent subjectivity in decision making by individual staff members of the regulatory body. The regulatory body shall be able to justify its decisions if they are challenged. In connection with its reviews and assessments and its inspections, the regulatory body shall inform applicants of the objectives, principles and associated criteria for safety on which its requirements, judgements and decisions are based". (Paragraph 4.26 of GSR Part 1 (Rev. 1) [6].)

Coordination with other authorities will depend on the constitution of the regulatory bodies in different States and on the nature of the regulated facility or activity. In the case of facilities for ion radiotherapy, such cooperation will in many cases include separate authorities with regulatory responsibilities for medical devices and health care.

Further guidance on the organization, management and staffing of the regulatory body is given in IAEA Safety Standards Series No. GSG-12 [3].

3.2. RESPONSIBILITIES AND FUNCTIONS OF THE REGULATORY BODY

The IAEA publication Functions and Processes of the Regulatory Body for Safety [4] offers in- depth coverage of the regulatory body's responsibilities, processes and functions for authorization, inspections, review and assessment and regulatory enforcement. Sections 3.2.1–3.2.4 summarize the core responsibilities and functions of the regulatory body.

Requirement 3 of GSR Part 3 [2], requires the regulatory body to:

"establish or adopt regulations and guides for protection and safety and shall establish a system to ensure their implementation".

These regulations and guides are aimed at applying the Fundamental Safety Principles, and their implementation is achieved through a regulatory system, applied using a graded approach, which includes:

- Notification and authorization;
- Review and assessment of facilities and activities;
- Inspection of facilities and activities;
- Enforcement of regulatory requirements;
- The regulatory functions relevant to emergency exposure situations and existing exposure situations;
- Provision of information to, and consultation with, parties affected by its decisions and, as appropriate, the public and other interested parties.

GSR Part 1 (Rev. 1) [6] requires the regulatory body to record

(a) "the basis for its decision on the authorization of a facility or an activity, or on its amendment, renewal, suspension or revocation, and shall inform the applicant, in a timely manner, of its decision, and provide the applicant with reasons and a justification for the decision" (paragraph 4.39).
(b) "the results and decisions deriving from reviews and assessments, and shall take appropriate action (including enforcement action) as necessary. The results of reviews

and assessments shall be used as feedback information for the regulatory process" (paragraph 4.48).

(c) "the results of inspections and shall take appropriate action (including enforcement actions as necessary). Results of inspections shall be used as feedback information for the regulatory process and shall be provided to the authorized party" (paragraph 4.51).

The regulatory body is also required to establish a process allowing the authorized parties to appeal against regulatory decisions (paragraph 4.32 of GSR Part 1 (Rev. 1) [6]). Further requirements for the regulatory body related to planned exposure situations are given in GSR Part 1 (Rev. 1) [6], Section 4, divided into:

— Requirements 8, 10, 11, 12, 13 on exemption and clearance, justification, dose limits, optimization and safety assessment;
— Requirements 19 and 20 on optimization, dose limits, exposure monitoring and record-keeping;
— Requirements 29 and 32 on optimization, dose limits, source and environmental monitoring and public exposure assessment;
— Requirement 35 on education, training and competence of health professionals.

3.2.1. Notification

The term 'notification' is defined in GSR Part 3 [2] as:

> "A document submitted to the regulatory body by a person or organization to notify an intention to carry out a practice or other use of a source".

Furthermore, Requirement 7 of GSR Part 3 [2] states that:

> "Any person or organization intending to operate a facility or to conduct an activity shall submit to the regulatory body a notification and, as appropriate, an application for authorization".

Thus, a person or organization intending to introduce a practice for ion radiotherapy is required to notify the regulatory body of the intention. At this stage, a notification may suffice to trigger the regulatory body's established authorization process for licensing, a process being mandatory due to the possible radiation risks imposed by the stages of establishment, operations and decommissioning of such a practice.

The IAEA standard Establishing the Infrastructure for Radiation Safety (IAEA Safety Standards Series No. SSG-44 [7]), states that:

> "The regulatory body should establish requirements for notification and should implement mechanisms to facilitate the submission of information through the notification process" (paragraph 4.19).

> "The requirements for notification should specify the information to be provided to the regulatory body and the prescribed timeframe. The regulatory body should make arrangements for communicating the notification requirements to users and potential users of ionizing radiation" (paragraph 4.20).

Currently, a natural communication channel is through a public authority website. Other pathways for communicating regulatory requirements to potential stakeholders might be through professional organizations or magazines and, in the case of a limited number of potential stakeholders, through direct communication.

Furthermore,

> "The regulatory body should record the information submitted in an appropriate registry system". (Paragraph 4.22 of SSG-44 [7].)

Such a system needs to be part of a transparent and open management system within the regulatory body's area of responsibility.

The authorized party is always supposed to notify the regulatory body of all installations and disposal of sources within the authorized practice. An ion radiotherapy facility will house different sources, apart from the particle accelerator, for dose planning, treatment verification and quality assurance.

3.2.2. Authorization

The IAEA Safety Glossary [8] defines authorization as:

> "the granting by a regulatory body or other governmental body of written permission for a person or organization (the operator) to conduct specified activities".

According to Requirement 23 of GSR Part 1 (Rev. 1) [6],

> "Authorization by the regulatory body, including specification of the conditions necessary for safety, shall be a prerequisite for all those facilities and activities that are not either explicitly exempted or approved by means of a notification process".

Authorization comes in two principal forms: registration and licensing. Registration is "a form of authorization for practices of low or moderate risks" [8], and as such is not applicable for authorization of an ion radiotherapy facility due to its complexity and potential radiation risks for patients, staff and, to a lesser extent, the general public and the environment.

In accordance with paragraph 3.115 of GSG-13 [4], the authorization of complex facilities, as ion radiotherapy facilities, is usually a multistep process including all stages of the facility lifetime, from site planning to decommissioning and facility demolition.

Requirement 24 of GSR Part 1 (Rev. 1) [6] states that:

> "The applicant shall be required to submit an adequate demonstration of safety in support of an application for the authorization of a facility or an activity".

The regulatory body's review and assessment of this demonstration of safety constitutes the basis for the decision on granting a licence or declining the application. To ensure legal certainty in the decision making, the regulatory body needs to house rigid internal routines and processes for all authorization steps. The process needs to be open and transparent and means for the applicant to appeal against decisions need to be established.

Further information on authorization, and on the related responsibilities and requirements for the regulatory body can be found in: paragraphs 4.29–4.48 of GSR Part 1 (Rev. 1) [6] and Action 16 (including paragraphs 4.36–4.42) of SSG-44 [7]. GSG-13 [4] gives comprehensive guidance on the authorization process as well as the review and assessment of information from the applicant in the licensing of facilities and activities.

3.2.3. Inspection

In accordance with Requirement 27 of GSR Part 1 (Rev. 1) [6], the regulatory body

> "shall carry out inspections of facilities and activities to verify that the authorized party is in compliance with the regulatory requirements and with the conditions specified in the authorization".

Inspections can be planned or reactive and announced or unannounced. Regulatory compliance needs to be verified throughout the entire lifetime of a facility or activity. In the case of a complex facility, such as an ion radiotherapy, the authorization process will include multiple licensing steps with the need for inspections necessary to:

- Verify the contents of applicant submitted documents (paragraph 3.151 of GSG-13 [4]);
- Assess compliance with stipulated conditions for the authorization to proceed to the next step.

Paragraphs 4.50 and 4.52 of GSR Part 1 (Rev. 1) [6] state:

> "The regulatory body shall develop and implement a programme of inspection of facilities and activities, to confirm compliance with regulatory requirements and with any conditions specified in the authorization. In this programme, it shall specify the types of regulatory inspection (including scheduled inspections and unannounced inspections), and shall stipulate the frequency of inspections and the areas and programmes to be inspected, in accordance with a graded approach".
>
> "Provision shall be made for free access by regulatory inspectors to any facility or activity, at any time, within the constraints of ensuring operational safety at all times and other constraints associated with the potential for harmful consequences."

In accordance with paragraphs 4.46 and 4.48 of SSG-44 [7], the inspection programme is to be included in a system for regulatory inspections, developed and implemented by the regulatory body and covering the powers, qualifications and training of inspectors and guidance to inspectors, including:

- The legal basis for inspection and the inspectors' authority.
- Use of regulatory requirements, regulations, guides and industrial standards.
- Implementation of the inspection programme, including guidance on the identification of persons to be interviewed, documents to be reviewed, measurements to be made, equipment and checklists to be used, and technical information to be considered;
- Reporting requirements and practices for inspectors;
- Standards of conduct for inspectors;
- The enforcement policy, procedures and practices.

Regulatory inspections need not be limited to the actual authorized facility or activity. This is apparent from paragraph 2.13 of GSR Part 1 (Rev. 1) [6], which states that

> "The regulatory body shall be conferred with the legal authority to require an authorized party or an applicant, whether a person or an organization, to make arrangements to provide:
>
> (a) All necessary safety related information, including information from suppliers, even if this information is proprietary;
> (b) Access, solely or together with the authorized party or applicant, for making inspections on the premises of any designer, supplier, manufacturer, constructor, contractor or operating organization associated with the authorized party."

3.2.4. Enforcement

GSR Part 1 (Rev. 1) [6] requires the regulatory body to:

> "establish and implement an enforcement policy within the legal framework for responding to non-compliance by authorized parties with regulatory requirements or with any conditions specified in the authorization". (Requirement 30.)
>
> "In the event that risks are identified, including risks unforeseen in the authorization process, the regulatory body shall require corrective actions to be taken by authorized parties". (Requirement 31.)

Furthermore, paragraphs 4.55, 4.56 and 4.58 of GSR Part 1 (Rev. 1) [6] state that:

(a) "Enforcement actions by the regulatory body may include recorded verbal notification, written notification, imposition of additional regulatory requirements and conditions, written warnings, penalties and, ultimately, revocation of the authorization. Regulatory enforcement may also entail prosecution, especially in cases where the authorized party does not cooperate satisfactorily in the remediation or resolution of the non-compliance".
(b) "At each significant step in the enforcement process, the regulatory body shall identify and document the nature of non-compliances and the period of time allowed for correcting them, and shall communicate this information in writing to the authorized party".
(c) "The regulatory body shall establish criteria for corrective actions, including enforcing the cessation of activities or the shutting down of a facility where necessary. On-site inspectors, if any, shall be authorized to take corrective action if there is an imminent likelihood of safety significant events".

Paragraph 3.302 of GSG-13 [4] describes the main purpose of enforcement as:

> "to ensure safety by deterring non-compliance, encouraging prompt identification of non-compliances, and ensuring that appropriate corrective actions are taken. Enforcement actions should be chosen to achieve this end."

The criteria and process for choosing the appropriate enforcement method are typically documented in the regulatory body's enforcement policy.

3.3. GRADED APPROACH

The IAEA Safety Glossary [8] defines a graded approach as follows:

> "For a system of control, such as a regulatory system or a safety system, a process or method in which the stringency of the control measures and conditions to be applied is commensurate, to the extent practicable, with the likelihood and possible consequences of, and the level of risk associated with, a loss of control."

This approach is used in the IAEA safety standards with respect to the regulatory control of facilities and activities. It is applied to safety assessment, authorization of facilities and activities, inspections and enforcement measures. It is also used in equipment and facility design and operation with respect to safety measures and risk mitigation. For example, the extent of assessment and review in regulatory control is expected to be commensurate with the safety risk associated with the facility or activity.

The same risk informed principle applies to the strictness of regulatory decisions on compliance with safety requirements, the frequency of inspections, and the choice of enforcement actions in the case of non-compliance with safety requirements.

4. AUTHORIZATION

Authorization of facilities and activities, which is when a regulatory body grants written permission to conduct specified activities using sources of radiation, is a core task for each regulatory body established and maintained by the government through the national legal system.

The authorization of an ion radiotherapy facility covers several safety areas, including radiation protection of patients, workers and the general public. Authorization can also be connected to the certification of newly developed devices. The constitution of the regulatory body for safety may differ between States, meaning that one or several authorities and organizations can be responsible for the authorization of an ion radiotherapy facility. In the latter case, ways of effective coordinating the authorization process need to be well established between the different regulatory parties.

4.1. NOTIFICATION

Any person or organization intending to carry out any of the actions specified in paragraph 3.5 of GSR Part 3 [2], is required to notify the regulatory body for safety of this intention. Such actions include, for example introducing a practice or hire, receive, site, locate, commission, possess, use, operate, maintain, repair and store a source within a practice. The notification is done in writing, preferably by submitting a predefined form, either a web form or a printout available from the regulatory body's official website. An example of a notification form is given in Appendix I.

For ion radiotherapy facilities clearly qualified for authorization, an application for authorization may serve as a notification. In the case of establishing such a facility it is recommended that the regulatory body be notified in the early planning phase, well before any construction work has been initiated. Such a notification would lead to a prompt meeting between the notifying party and the regulatory body where the establishment project plans are presented and discussed. The outcome of this meeting would ideally generate a clear plan for the authorization process.

It is recommended that all relevant authorizations and approvals be obtained before facility construction. Sometimes, preparation of long lead time items begins before authorization for construction is granted. Long lead time items are part of the planned construction and could also be subject to regulatory approvals. Such items are important to identify and account for at an early stage in the authorization process It is the licensee's responsibility to verify that such items meet the appropriate technical standards. Safety related quality issues are usually resolved prior to construction. Long lead time items are discussed in Ref. [9].

4.2. EXCHANGE OF PRELIMINARY INFORMATION

Regardless of whether the authorization process is initiated by a simple notification or a more elaborate licence application for the intended establishment of an ion radiotherapy facility, an initial meeting between the applicant/notifying party is needed as soon as possible. The purpose of this meeting is to exchange preliminary information on the intended facility and its planned operation, but also on the regulatory requirements associated with complex facilities for medical exposures.

The meeting is to identify enough details about the planned facility and its operations to allow the regulatory body to determine the safety requirements relevant for specifying conditions for licence permission.

The information exchanged during this meeting should, at a minimum, include:

- Radiation sources to be used: type and characteristics;
- Intended use of radiation sources;
- Facility siting;
- Available expertise in radiation safety;
- Contractors for facility construction;
- Contractors for source installation and commissioning;
- Contactors for source and facility service and maintenance;
- Contractors for other relevant services;
- Staffing;
- Time schedule for facility establishment.

4.3. AUTHORIZATION STAGES

As pointed out in Section 3.2.2, the authorization of a complex facility, such as an ion radiotherapy facility, usually contains separate phases during facility planning and establishment.

The authorization process during the establishment of an ion radiotherapy facility typically includes the following phases:

- Site approval.
- Design approval and authorization to construct the facility.
- Authorization to acquire ion radiotherapy equipment (accelerator system).
- Test operation of the ion radiotherapy system and commissioning of the facility (usually divided into sub-steps with the beam current ‘ramp up’ and continuous facility commissioning).
- Authorization to operate the ion radiotherapy system for clinical treatments (review and assessment of final safety demonstration including patient safety).
- Licence to service and maintain radiation sources in the facility (one or more service providers).

The authorization may require separate applications for different phases, or a single application can be used and updated with additional or revised information relevant for each phase. Often, each step in the authorization chain includes conditions that must be met before continuing to the next phase.

The regulatory expectations for each phase are documented in the authorization plan. Great care must be taken to ensure that the plan and the conditions for licensing are clear to all parties involved in the licencing process (paragraph 3.116 of Ref. [4]).

The final licences for clinical operations and for service and maintenance have usually limited validity; five years may be considered appropriate, subject to local laws and regulations. When

the licences is close to its expiry date and the facility continues to operate a process for re-licencing is triggered.

Apart from the authorization steps listed above, authorization is required for facility closure and decommissioning and its subsequent release from regulatory control.

5. REVIEW AND ASSESSMENT

5.1. CHECKING THE APPLICATION FOR COMPLETENESS

As soon as an application for authorization (licencing in the case of ion radiotherapy) is received by the regulatory body, the legal process for authorization is triggered. Once an officer, or a team of officers, has been assigned to the authorization task, the first step is to check the application for completeness in relation to the relevant licensing phase in question. At this stage the application does not have to be reviewed in detail, but the need to request additional information is assessed.

If the information in the application is considered insufficient, a written request for additional information is normally sent to the applicant. The request states clearly what additional information is needed and when this information is to be submitted to the regulatory body for further processing of the application. The decision and the basis for the request is sent to the applicant. Information on how to appeal against the regulatory decisions is made available to applicants.

Suggested review and assessment topics to be covered in the licencing of an ion radiotherapy facility are given in Appendix II. The list of relevant topics listed may need to be adapted to the specific parameters of the planned facility and practice.

5.2. TECHNICAL REVIEW OF THE SAFETY ANALYSIS REPORT

According to Requirement 13 of IAEA Safety Standards Series No. GSR Part 3 [2], the application for authorization of a facility or activity must always include a demonstration of a safety assessment. This demonstration comes in the form of a safety analysis report (SAR), which would be reviewed by the regulatory body during the authorization process. The purpose of a safety analysis is to evaluate to what extent safety and regulatory requirements pertinent to the facility or activity are met (paragraph 4.49 of Ref. [10]). The safety assessment must be conducted continuously, and the SAR revised accordingly and presented to the regulatory body during the different phases of the authorization process.

Regardless of whether the submitted SAR is complete, the assigned regulatory officer(s) must initiate the review of the report immediately. Review topics still awaiting additional information are kept on hold until enough information is available for proper review and assessment.

This section provides guidance on the review and assessment of SARs submitted to the regulatory body for authorization to establish, operate and maintain an ion radiotherapy facility. The guidance assumes there is an SAR covering the topics specified in Appendix II.

Technical data to support the review of the SAR report are found in Section 5.2. The guidance focuses mainly on specifics for ion radiotherapy. The complete safety review of a facility also includes assessment of the safety information regarding the use of other medical devices integrated in the radiotherapy process, such as:

- Imaging devices for patient positioning and treatment planning (onboard X ray imaging, CT simulator, PET/CT simulator);
- Treatment planning systems (TPSs);
- Oncology information system (OIS).

5.2.1. Site selection for the facility

The facility location selected is expected to provide adequate safety for workers, the general public and the environment. Natural phenomena, such as volcanic eruptions, earthquakes, wind storms, floods and other phenomena must be considered. The level of urban development and the population density of the surrounding areas must be taken into consideration. Social acceptance of this type of facility is usually high in the local community. Nevertheless, residents and local authorities must be consulted by the regulatory body and the licence applicant during the early phase of facility planning. The reliable supply of power and water must also be ensured.

5.2.2. Facility architecture

The architectural layout of a facility depends on many factors. The choice of accelerator type defines the footprint, size and structure of the accelerator vault, treatment bunkers and other auxiliary premises. Occupancy factors in premises close to the accelerator and treatment bunkers need to be estimated in the planning of each facility architectural design.

The annual number of patients to be treated with specific fractionation schemes determines the number of treatment bunkers. So far, particle therapy facilities have one accelerator delivering the beam to various treatment bunkers. Therefore, the number of treatment bunkers is typically limited to three–five, complemented possibly by a bunker for fixed beam irradiation as well as for eye tumour treatments. Constructing more than five treatment bunkers is not reasonable because the corresponding workload of the accelerator would not allow beam delivery to more bunkers in a quasi-parallel operation. Another bunker, say for research and development, usually supplements the facility.

5.2.3. Accelerator and beam transport system

5.2.3.1. Ion accelerator types

The choice of the accelerator type is influenced by the choice of particles, which are applied for the therapy and the maximum depth of the particles in tissue. Currently, cyclotrons and synchrotrons are the most frequently used accelerator types for particle therapy. The cyclotron is used mainly for proton beams. For maximum dose delivery at a soft tissue depth of 30 cm, a beam energy of 220 MeV is necessary. This beam energy means a magnetic rigidity of about 2.3 Tm.

There are also proton therapy facilities with a synchrotron type accelerator. Examples are the Loma Linda proton therapy center in the USA, where the first hospital based particle therapy centre was built [11], and the Proton Medical Research Center in Tsukuba, Japan.

Beams of particles heavier than protons are usually produced in synchrotrons.

From a radiation protection point of view there is a significant difference in the production of particle therapy beams between the two accelerator types. In a cyclotron the extracted beam energy is non-variable and equal to a maximum acceleration capacity of the cyclotron. If, during the actual treatment process, an energy lower than the maximum energy is required, the particle beam is slowed down to the energy requested by the therapy control system through an energy degrading process inevitably producing a considerable amount of high energy neutron radiation.

In the synchrotron the particle beam is accelerated to the energy which is actual needed in the treatment process. No beam energy degrading in synchrotrons is necessary, and consequently the neutron production in a synchrotron is substantially lower in comparison with a cyclotron.

A synchrotron facility takes up more space, and consequently there are naturally more shielding structures in a facility containing a synchrotron. A cyclotron facility needs less space in comparison to a synchrotron facility, but the beam losses are higher and therefore the shielding thicknesses of the walls and roofs are larger. These two properties (shield thickness versus larger space) offset to certain degree the efforts required to build shielding for either type of accelerator.

An example of a degrader, specifically a wedge-like degrader containing a stationary and moving wedges, is shown in Fig. 3. Because the wedges move against each other, the particle beam passes a layer of carbon material with a given thickness. The particle beam loses energy in the layer.

The positions of the wedges determine the thickness of the layer, which in turn regulates the amount of energy reduction of the beam. This is associated with scattering processes of the particle beam, which result in particle deflections and beam losses. The larger the actual degrader layer thickness the higher the losses (see below). The degrader here is a rapid moving wedge, which allows for quick adaptation of the beam energy. Such rapid energy adjustments are required, for example, for the irradiation of a large treatment volume.

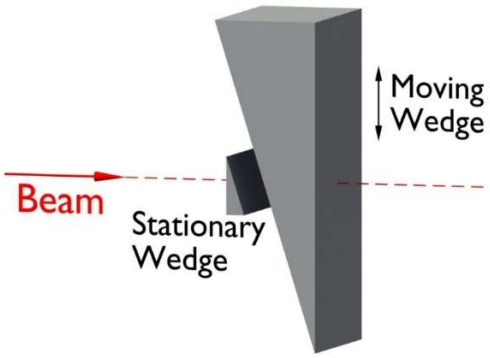


FIG. 3. Example of a degrader consisting of a stationary wedge and a rapid moving wedge. The wedges adjust the particle energy to the actual value to be used during treatment.

5.2.4. Beam delivery options

5.2.4.1. Beam spreading and shaping techniques

The accelerator produces narrowly focused particle beams (pencil beams) for transportation though the beamline. Tumours can have larger lateral extensions. Consequently, the focused pencil beam needs to be spread to a broader beam at the tumour site. Three major methods can be applied: passive scattering, uniform scanning, and pencil beam scanning (spot scanning or raster scanning).

The scattering method is based on the use of scattering foils. If a pencil beam passes a scattering foil the beam is broadened to a gaussian-like profile (Fig. 4(a)). If a collimator is used, a quasi-

homogeneous beam distribution around a small space of the central line is formed. This is the basis of a single scatter system.

A more effective method to widen a pencil beam is the use of a double scattering method (Fig. 4(b)). A beam passes through a first scatterer and a gaussian shaped beam profile is produced. The broadened beam next hits a cylindrical absorber and a ring distribution is generated. This new particle distribution passes a second scattering foil and a further broadening is caused. The in-scatter from the ring shaped flux usually fills in the shadow caused by the cylindrical absorber; therefore, the overall superposition is a uniformly distributed particle flux, which will be collimated laterally by the collimator. The resulting lateral extension is higher than in the first case (see also Ref. [12]).

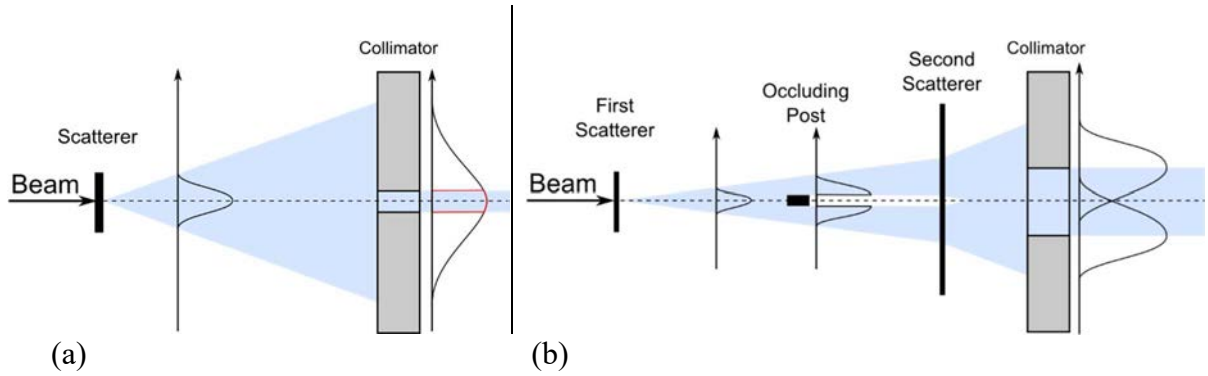


FIG. 4. (a) Forming a pencil beam for a small rectangular shaped particle beam using a scattering foil and a collimator; (b) forming a broader rectangular particle beam using an absorber (occluding post), a second scattering foil and a collimator.

Scanning methods were initially developed at PSI, Switzerland (spot scanning [13]), at the HIMAC, Japan (pixel scanning [14]) and at GSI, Germany (raster scanning [15]). For a more detailed explanation, see Refs [12] [16]. The example described here is the raster scan method. The ion beam is produced in a synchrotron and delivered to the treatment bunker.

The scanning system is upstream of the treatment bunker. The beam is deflected by magnets in two perpendicular directions (Fig. 5). The tumour volume is subdivided consecutively in a series of planes (or layers). The beam energy determines the location of the plane or the depth of penetration. Each plane is irradiated by the ions by applying lateral and vertical deflection. Changing the plane to be irradiated leads to a change of the beam energy. For spot or pixel scanning, the irradiation is interrupted when the spot moves from one location to another. In the raster scan method, the irradiation is continued during a change in the beam position. The homogeneity of the irradiation is ensured by a suitable choice of the spacing of the spot or pixel considering the spatial width distribution of the ions in the spot/pixel. The result is a high conformal irradiation of the tumour volume.

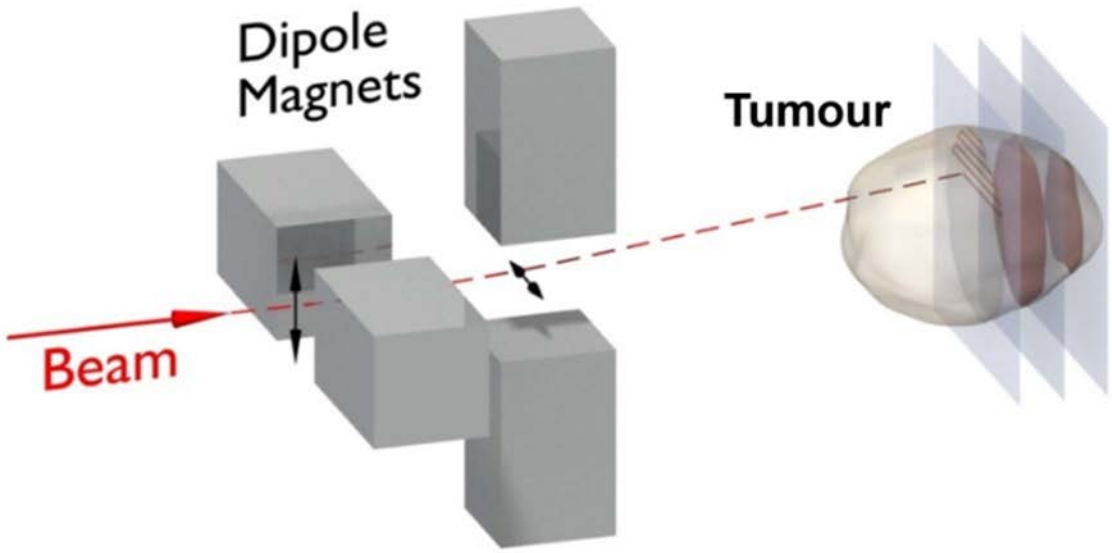


FIG. 5. The raster scan method, developed at GSI, Germany, and used in various facilities (e.g. the HIT facility [17]).

Beam shaping can be accomplished by using an adjustable collimator or a field specific aperture fitted to the tumour shape. The collimation system is similar or identical to the passive scatter system. Depth modulation can be achieved by range shifters/modulators and tumour specific compensators.

If the passive beam forming method is applied, more beam shaping elements than those shown in Fig. 4 are used. For optimized lateral distribution, an occluding post and a ring are applied (see upper part of the figure). The range modulator produces a broader energy distribution of the beam, which is necessary to ensure that the tumour is irradiated throughout its entire depth. The range shifter reduces the beam energy to treat the most shallow or proximal surface of the target. For a conformal irradiation of the tumour, a compensator is necessary. The compensator is individually prepared, and its layout fits the distal shape of the tumour volume and needs to have the effect that critical structures distal to the tumour are spared (Fig. 6).

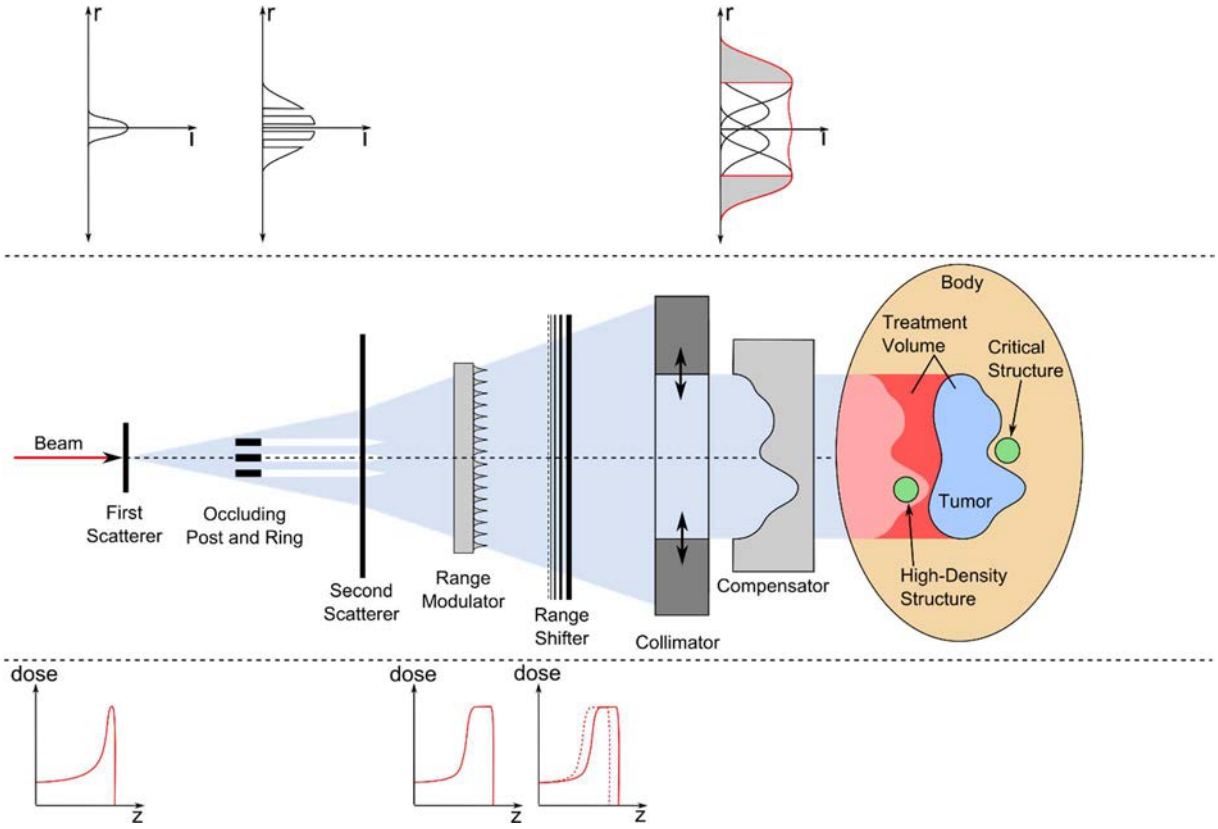


FIG. 6. A passive beam shaping system using the two scatterer method, a range modulator, a range shifter, a collimator and a compensator. Upper panel: Influence of the elements on the beam shape; lower panel: Influence of the elements on the energy distribution. Figure based on Ref. [12].

An overview of the composition and the combination of active and passive beam forming elements is given in Fig. 7. Beam widening is carried out first. Either the scattering method or the scanning or wobbling method can be used.

The energy of the particle beam is adjusted by the features of the accelerator (such as cyclotron degrader setting or synchrotron beam extraction energy selection). Ridge filters, or range modulators, inserted into the gantry nozzle downstream of a scatterer are used to modify particle energy ranges to certain desired ranges (a ridge filter consists of many parallel ridges). Particle range extension and additional scattering processes in the ridge filter cause homogenization of the dose in tissue.

The last step of beam shaping involves a collimator and a compensation bolus to form a particle range distribution focusing the dose on the tumour while minimizing the dose around the tumour as much as possible. Active scan procedures obviate the need for the last step because the narrow pencil beam scanning itself accomplishes a precise beam shaping based on the volume and contour of the tumour.

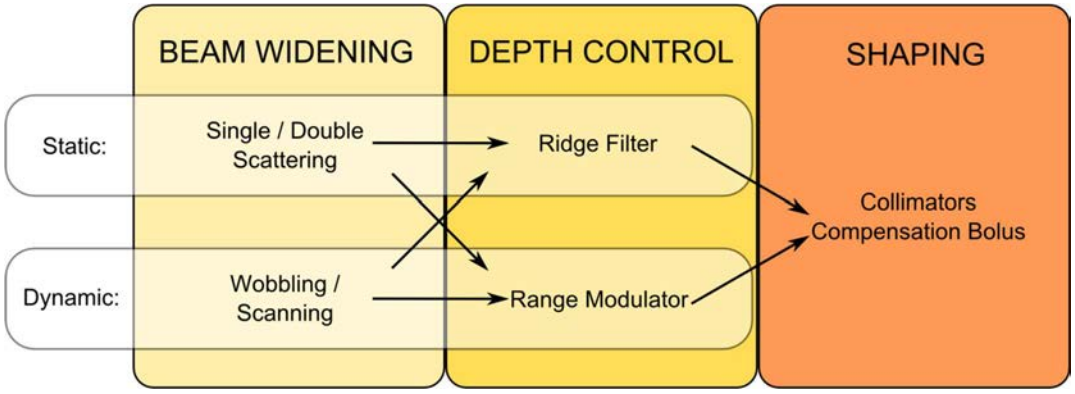


FIG. 7. Scheme for static and dynamic beam forming procedures for beam widening, depth control and shaping.

A list of gantry and treatment parameters, submitted by the applicant to the regulatory body, usually includes the following elements:

- Treatment nozzle specifications;
- Lateral spread modes: double-scatter; uniform scanning; pencil beam scanning;
- Maximum field size at isocentre;
- Maximum and minimum energies of the beam at the nozzle;
- Maximum dose rate by delivering 2 Gy uniform dose to 10 cm ×10 cm × 10 cm cubic volume;
- Virtual source to axis (SAD) distance;
- Specifications for applicator carriage (snout) and accessories, including travel range and movement resolution, and the maximum stopping distance when the emergency stop button is pressed;
- Dose delivery accuracy;
- In pencil bean scanning mode: in-air spot size at the isocentre for every 10 MeV in both lateral directions; range adjustment mode (continuous or discrete); range accuracy; energy layer switching time; spot position accuracy; spot size variations from different gantry angles; spot size variation from different treatment bunkers in multi-bunker configuration.

5.2.5. Beam characteristics

Proton therapy is currently the most common type of ion beam therapy. Until recently, small scale therapy with ions heavier than protons has been performed in research facilities. For example, treatments with carbon ions were carried out at the HIMAC facility (Japan) and at GSI (Germany). The justification for the treatment with heavier ions (such as carbon ions) is the improved physical dose distribution (less particle scattering) and the theory that heavier ions have increased biological effectiveness in comparison to proton beams. In contrast to proton beams, for heavier ions the fragmentation of the projectile nuclei and the additional contributions of dose of the projectile fragments generated must be considered.

A disadvantage of heavier ion therapy facilities is the greater ‘technical effort’ required for the accelerator and the beam delivery system. To obtain particle ranges of 30 cm, higher energies for the particle beams are required. While for proton beams a magnetic rigidity of 2.3 Tm is

enough, a value of 6.6 Tm is necessary for carbon ion beams (see below), which requires a substantially greater technical effort, particularly for the gantry.

Nevertheless, some carbon ion installations are now operating in hospitals or in other facilities dedicated to ion beam therapy. Examples are the: HIT facility in Heidelberg, Germany; the Gunma University Heavy Ion Medical Center, in Maebashi, Japan; the CNAO Center (National Center of Oncological Hadron therapy) in Pavia, Italy; and the MedAustron project in Wiener Neustadt, Austria.

5.2.5.1. Maximum energy

The energy of the particle determines its range in the tissue. The deeper a tumour is in the tissue the higher the particle energy required for the treatment. Radiation therapy with particle beams is often planned for maximum particle ranges in tissue of 30 cm. For the calculation of the relation range and particle energy, water is used as a standard for comparison.

A summary of energy–range relations of light ions is given in Fig. 8. Protons (H), helium (He), carbon (C), nitrogen (N), oxygen (O) and neon (Ne) ions are considered acceptable for particle therapy applications. By applying the Bethe–Bloch formula, the range of ions in water can be estimated.

For example, beams with a range of 30 cm require proton or He beams with an energy of about 220 MeV/nucleon, while Ne beams require a rather high energy of 600 MeV/nucleon.

Accelerator developers commonly use the quantity magnetic rigidity in describing beam energy as a beam characteristic parameter. The magnetic rigidity is defined as [18]:

$$B \cdot \rho = \frac{1}{e \cdot c} \cdot \sqrt{E_k^2 + 2 \cdot E_k \cdot E_0}\,,$$

with ρ the radius of the curvature of the particle path, B the induction of the magnetic field bending the particle trajectory, E_k the kinetic energy and E_0 the rest energy of the particle (with e the charge of the particle and c the velocity of light in a vacuum).

The maximum magnetic rigidity gives decisive information on the type of accelerator to be chosen and the technical effort (magnet type and size of accelerator) which is necessary to construct an accelerator. The range of the particles in tissue (or water) and the ion type are the key parameters for the determination of the maximum magnetic rigidity. This relationship is illustrated in Fig. 9. Beams with a 30 cm range in water can be achieved with the following parameters:

- Proton: 2.3 Tm;
- Carbon ion: 6.6 Tm;
- Neon ion: 8 Tm.

Figure 10 gives the relationship of the kinetic energy of protons and ions (charge mass ratio ½) and the magnetic rigidity.

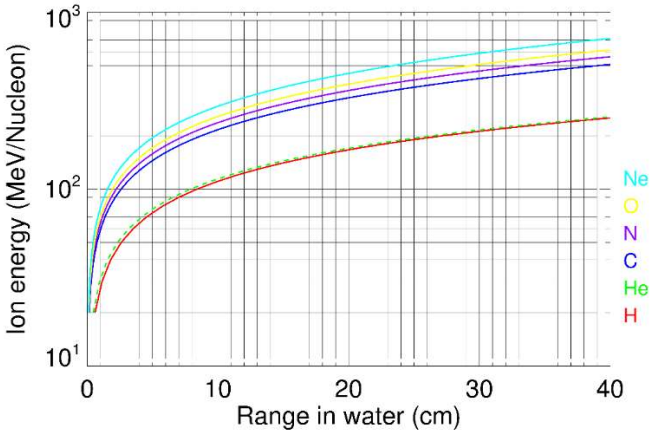


FIG. 8. Relationship of ion energy and range in water for protons (H), He, C, N, O and Ne ions. The ion energy is given in MeV per nucleon.

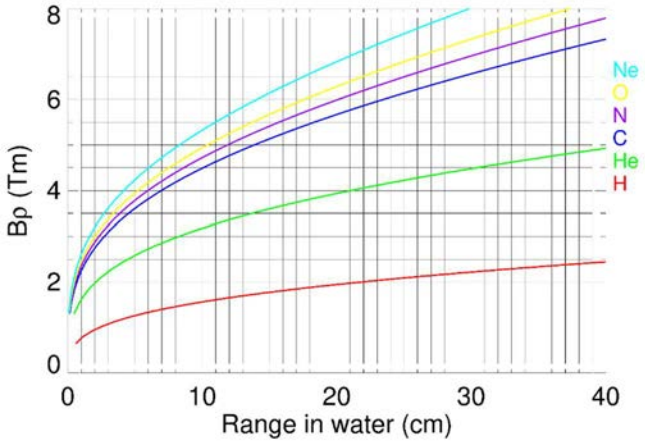


FIG. 9. Magnetic rigidity for protons (H), He, C, N, O and Ne ions for a certain range in water.

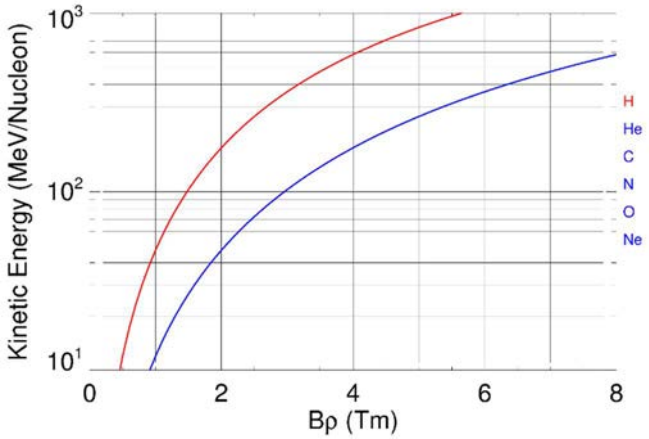


FIG. 10. Relationship between kinetic energy and magnetic rigidity for protons (H) and ions with a charge to mass ratio of ½ as He, C, N, O, and Ne.

5.2.5.2. *Maximum current of the beam*

The maximum beam current is adapted to the desired patient treatment. The full patient treatment dose is usually delivered in smaller dose fractions in the course of days or weeks; about 20–30 fractions with dose values in the range of 2–3 Gy per fraction (a few minutes of irradiation time for each beam delivery). These constraints give the number of particles per second to be delivered to the patient. If one considers the whole chain of beam production, the beam losses along the chain need to be considered. This means that the beam production and the beam losses within the accelerator, the beam losses during the extraction and transport to the irradiation nozzle, and the beam losses in the beam delivery system must be considered.

Figure 11 is an example of the relationship between the pre-degrading beam intensity, as a function of beam energy, required to produce an output beam intensity of 1.3×10^{10} protons/s. For low output energies the major part of the original beam is lost in the degrader. A substantial part of the lost proton beam undergoes nuclear reactions and consequently the degrader is a strong source of prompt neutron and gamma radiation.

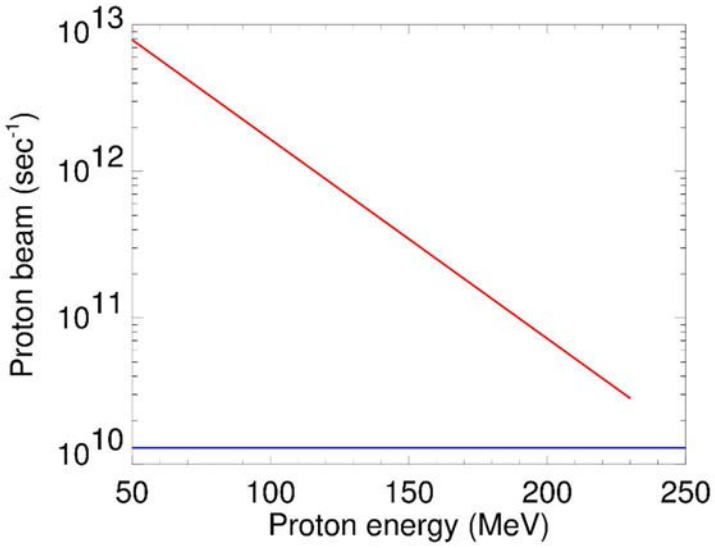


FIG. 11. Example of the relationship of the required starting beam intensity to the desired beam intensity of 1.3×10^{10} protons/s (blue line) as a function of the output proton energy.

Typical values for beam intensities in radiation therapy are a few 10^{10} protons/s or a few 10^{8} C-ions/s. Heavier ions, like carbon ions, deposit a higher physical dose in the tissue and a higher LET (linear energy transfer). Heavier ions can have higher biological effectiveness than protons. Therefore, lower beam intensities are required for heavier ions.

5.2.5.3. *Beam losses and depositions*

Beam production and forming are associated with several beam loss steps. During acceleration in the cyclotron, about 50–65% of the beam is lost in various energy ranges. In beam extraction from the cyclotron, 20–80% of the beam is gone. Depending on the actual required energy, 55–99% of the beam is lost in the degrader. The transport of the beam from the degrader to the nozzle results in a low loss level (1–5% in the magnets). Ultimately, large beam losses can occur in the beam delivery system if the passive beam forming method is used. In the patient,

100% of the remaining beam is deposited. Lower beam losses occur in the beam delivery system when active scanning techniques are applied (a few per cent).

In fact, less than 1% of the initially produced ions are used for treatment. The remaining 99% of the ions produced are lost in the treatment beam production process and pose significant radiation protection issues. An overview of the beam loss processes in a cyclotron therapy facility is given in Fig. 12.

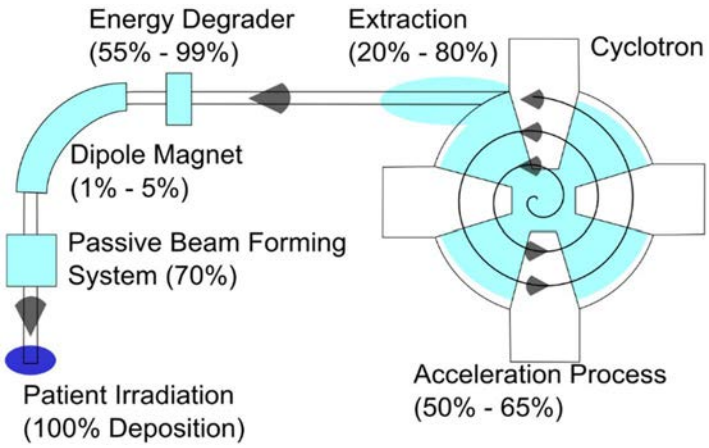


FIG. 12. Beam loss processes for various steps of beam production, beam forming and beam delivery in a cyclotron/synchrotron based particle therapy facility. From Ref. [19].

The situation is different for synchrotron-based therapy facilities. Synchrotrons are fed with pre-accelerated ions from a linear accelerator. Major beam losses occur in the transition area between the linear accelerator and the synchrotron at lower energies (e.g. 7 MeV/nucleon). In the synchrotron, 5–36% of the beam is lost. At the extraction step, 5–10% of the beam is lost and a further 5–10% of the beam is lost in the high energy beam transfer (HEBF). Analogous to the case of cyclotrons, about 70% of the beam is lost in the passive beam forming system. The residual beam is deposited in the patient tissue. An overview of beam losses in a synchrotron-based ion therapy facility is given in Fig. 13. Comparing Figs 12 and 13, it is clear that the overall beam losses in a synchrotron-based particle therapy facility are lower than in a cyclotron-based particle therapy facility.

The radiation generated by beam losses and the beam deposition distributions determine the shielding layout of the facility. The higher the particle energy and the beam loss rate, the higher the magnitude of the produced strayed radiation (here mainly neutron radiation) and dose rates. The higher the level of produced radiation, the higher the effort for the shielding near the beam loss area. The energy of the produced radiation also influences the amount of the necessary shielding.

In particular, high energy neutron radiation requires large shielding thicknesses because the attenuation of this energetic radiation is lowered in common shielding materials like concrete (the higher λ values in Eqs (1) and (2)). Therefore, in areas with high levels of high energy beam depositions, such as the patient treatment bunkers or the energy selection system near the cyclotron, comparatively thick shielding barriers (several metres of high density concrete) are necessary.

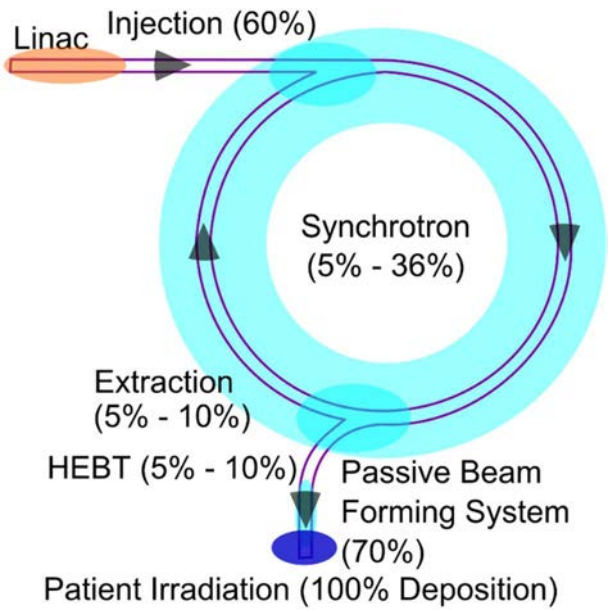


FIG. 13. Beam loss distributions in a synchrotron-based particle therapy facility. From Ref. [19].

Due to the large size of the premises needed to house the beam transportation lines, low beam losses between the accelerator and the treatment bunkers are advantageous from an architectural shielding designing point of view.

A further important aspect the facility planning in a hospital environment is the necessary overall footprint. It can be advantageous to use a compact accelerator, e.g. a cyclotron, which requires a smaller footprint although the shielding effort is higher because of the increased beam losses in the cyclotron and in the energy selection system.

5.2.6. Beam steering and control systems

The beam monitoring system is complex and needs to be comprehensive. If an active beam scanning technique is used a series of functions is controlled. If certain tolerance levels are exceeded an interlock is triggered. The main emphasis of the therapy control system is continuous beam quality control.

The criteria for the beam quality control system include, in particular:

- Deviation of the beam energy from the actual set energy.
- Aberration of the detected number of particles by the various detectors (e.g. ionization chambers) which are operated in parallel and installed one behind the other (providing redundancy). Furthermore, the deviation of the detected particle numbers from the set particle numbers will be monitored.
- Beam position in the detectors (e.g. multi wire proportional chamber). If the beam does not have the exact set position within certain limits, an interlock is triggered.
- Width of the beam with respect to the detector size: confirmation that the width of the beam is within the given tolerance limits.
- Observation of detector functionalities.

Other elements and systems which are used for therapy are integrated in the interlock system. These systems are accelerator elements such as radio frequency generating units, deflection magnets, the magnets of the beam scanner, the electronics of the therapy control unit as well as the personnel access system to the accelerator areas and treatment bunkers.

5.2.7. Structural shielding design

A wide range of radiation fields may exist at particle therapy facilities. The following scenarios may be expected:

- The primary particle beam produced appears as free ions in the air only in the treatment bunker, no direct exposure of the personnel is likely. Furthermore, all areas, where the primary particle beam is transported are defined as access prohibited areas during accelerator operation.
- The ion source and the pre-acceleration units produce X rays with considerable dose rates which need to be controlled.
- As the primary particle beam interacts with matter (therapy beam attenuation in patient tissue during treatment, unwanted beam losses in the accelerator or beam line structure) a considerable amount of secondary radiation is produced. The main radiation component in terms of equivalent dose rate is neutron radiation (>90%) and prompt gamma radiation. These radiation fields require the highest effort for structural shielding. An example of the neutron radiation produced is given in Fig. 14. The neutron energy distribution caused by a 400 MeV/u carbon ion beam, which impinges on a graphite target, is given for the angular range from 0° to 90°. The data are obtained by experiment [20] and by Monte Carlo (MC) calculations using the FLUKA MC simulation package [21].
- Radioactive nuclei are produced if the accelerated particle beam interacts with the accelerator parts and beam line structure. They are created by target fragmentation and, in the case of heavier particles such as carbon ions, also by projectile fragmentation. The resulting remnant dose rates vary for different accelerator types. For cyclotrons the highest dose rates occur at the energy selection system (production of ^{11}C in the graphite degrader), where protons are slowed down to the desired energy. Remnant dose rates up to the Sv/h range can be found.

  Synchrotrons have lower levels of beam losses, and consequently significantly lower remnant dose rate levels which are essentially lower than 1 mSv/h.

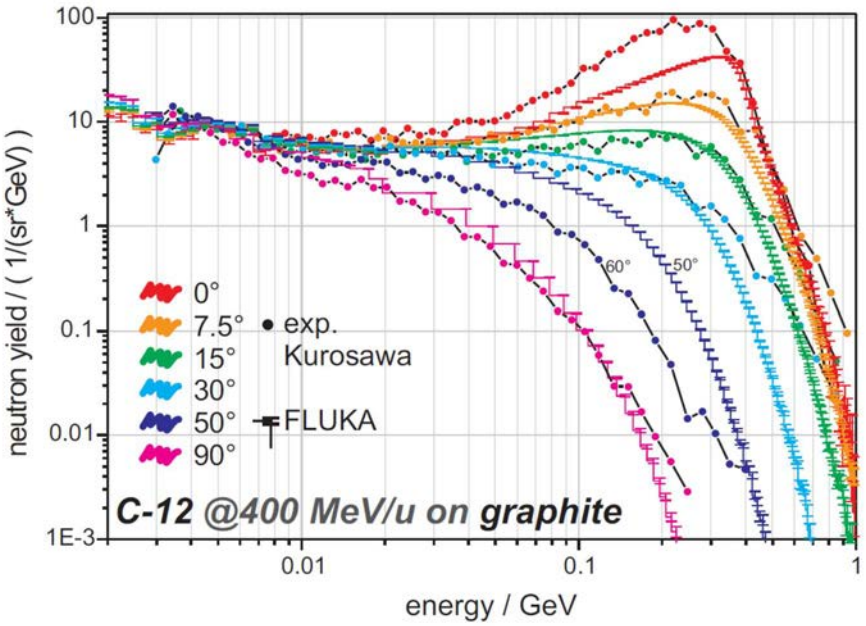


FIG. 14. Neutron spectra for carbon ion beams impinging on a graphite target for the angular range 0° to 90°. The data are based on measurements [20] and FLUKA calculations [21].

Facility structural shielding design requirements depend on several factors, including:

- Accelerator type;
- Equipment location (surface or underground);
- Particle type and maximum energy;
- Beam spreading and shaping technique;
- Beam orientation;
- Operational workload;
- Occupancy factors in the surrounding premises;
- Treatment bunker maze design;
- Skyshine and groundshine (depending on surrounding environment);
- Ducts and pipes for cables, ventilation, and water supply/drainage;
- Alignment of the beamline;
- Beam guide openings between the beamline vault and treatment bunkers.

5.2.7.1. Beam orientation (barrier use factors)

The category (type of radiological area or public area) and occupancy factor of the area outside the shielding barrier influences the required thickness of the barrier. Secondary neutrons are mainly emitted in the original particle beam direction. Thus, in a treatment bunker with a rotating gantry, so-called barrier use factors can be used to take the different orientations of the gantry into account in the calculation of the necessary barrier thicknesses.

5.2.7.2. Beam intensity estimate

The particle beam intensity at the gantry treatment nozzles is adapted to clinical treatment requirements. The production and delivery of particle beams is a multistep process. At each step beam losses occur and the resulting beam intensity at the nozzle in the treatment bunker matches the requirements for the specific patient treatments.

The following statements relate to clinical treatment beam intensities in radiotherapy treatment bunkers. Usually the overall treatment is delivered in 20–30 fractions. The doses per fraction are a few gray in the target volume. This fractionation results, for example, in some 10^{10} protons/s or some 10^{8} ions/s in the case of carbon ions, considering the increased physical dose and possibly increased relative biological effectiveness (RBE) (3–5 for carbon ions).

There are facilities where hypo-fractionation is applied. Consequently, the beam intensity is increased when the overall dose is the same. For radiation protection considerations one can, in the case of proton beams, assume an increase in beam intensity inversely scaled with the number of applied sessions. In the case of heavier ions, the lowering of RBE with increasing doses per fraction needs to be considered and the scaling of the number of ions per second is a much more complex calculation.

Recently, there has been interest in conducting ultra-high dose rate radiotherapy using ion beams, commonly referred to as FLASH irradiation [21] [22]. Experiments in mice showed a unique sparing effect for normal tissues without affecting the killing ability of radiation against tumour cells. Cyclotron based proton therapy systems can deliver such high dose rates, over 40 Gy/s at the patient location inside a treatment room [23]. While the delivered absolute dose might be similar to what is prescribed for typical hypo-fractionated treatment (5–15 Gy per fraction), this ultra-high dose rate may present some challenges because of its high instantaneous neutron flux and short-life activation radiation in the treatment room. Proton PBS has an inherently high instantaneous dose rate due to its small spot size. Nevertheless, FLASH has not been used in human treatment yet; room shielding, and personnel radiation protection strategies may require special consideration.

5.2.7.3. Workloads

For the personnel of the facility, one can assume a maximum presence in the facility of 2000 hours. For estimations of the annual ambient dose at certain positions it is not necessary to calculate a full year of remaining at these positions. The workload of each treatment bunker is the fundamental quantity for the layout. The workload can be estimated by the intended number of patient treatments per week and the administered dose to the patient. The dose fractionation results in an applied dose of about 4 Gy per patient and day. The dose per week can then be derived from the number per patients in one day, the average dose per patient and the number of therapy days. For example, 50 patients per day with 4 Gy dose results in a workload of 1000 Gy per week (five days). The workload is used as an input for the estimation of the number of delivered particles per week for the treatments. The number of particles and their energy distributions form the basis of the shielding calculations. The workload and occupancy factors are applied in dose estimations for areas surrounding the treatment bunker. The calculation just described is valid for areas within the facility.

The situation is different if there are public areas outside the facility. A permanent presence is partially to be assumed (8760 hours). Furthermore, the dose limits for the exposure of individuals of the general public are lower in comparison to the dose occupational limits within

the facility, 1 mSv effective dose per year in most States. In addition, many States stipulate the application of a dose constraint of about 0.1–0.3 mSv annual effective dose to an individual of the general public resulting from the operation of a facility. The dose rates of the prompt radiation are managed using appropriate shielding.

5.2.7.4. Beam energy levels planned

The use of particle beams for the irradiation of tumours requires precisely adapted beam energies. The facilities are prepared to deposit beams in a depth of the patient body up to about 30 cm. Depending on the particle type, the maximum energy is about 230 MeV for proton beams or 430 MeV per nucleon for carbon ion beams.

The site and size of the tumour and the anatomical structures in front of the tumour determine the range of particle energies to be applied for the irradiation of the whole tumour. The typical energy range of proton beams in a cyclotron therapy facility (without additional range shifters) is from 60 to 230 MeV. These values correspond to a range in tissue from about 3 to 30 cm.

5.2.7.5. Layout of structural shielding

The architectural shielding layout is adjusted according to the beam loss and beam deposition distributions in a particle therapy facility. This means increased shielding effort near the accelerator and, if applicable, near the beam degrader. The planned beam depositions in the treatment bunker result in adapted shielding structures considering the different orientation of the gantry or, in the case of a fixed beam geometry, permanent irradiation in one direction. The choice of the beam forming system (active, passive) can also influence the shielding layout.

The use of passive forming techniques causes higher beam deposition rates and needs to be considered in the shielding layout. The facility shielding with wall and roof shielding barriers along the beam lines and floor shielding at specific positions (e.g. the cyclotron/degrader area) to prevent soil activation give the general structure of the facility. Using marble based structural shielding structures near the ESS is believed to reduce the induced radioactivity in the architectural components of a facility [24].

Proper shielding of access routes to the treatment areas and to the accelerator is achieved by maze structures. Mazes help to attenuate scattered radiation efficiently. The extent of the maze, the number of legs in the maze, and the wall thicknesses determine the attenuation of the radiation produced.

Some typical examples of facility layouts can be represented by the following sites:

- Heidelberg Ion Therapy (HIT) facility, in Heidelberg, Germany;
- Skandion Clinic, in Uppsala, Sweden;
- MedAustron, in Wiener Neustadt, Austria;
- OGZ facility, in Dresden, Germany.

The HIT facility was developed at GSI Helmholtz Centre in Darmstadt, Germany, in cooperation with the University Hospital in Heidelberg, the German Cancer Research Centre in Heidelberg, and the Research Centre Rossendorf (now HZDR Dresden-Rossendorf) [17].

The facility is based on a synchrotron accelerator which uses a linear accelerator for pre-acceleration. The facility has two treatment bunkers for fixed beam geometry, a gantry installation (Fig. 15) and a bunker for quality assurance and research. The facility is designed

for carbon ion beams with a maximum energy of 430 MeV/u. Ion beams ranging from proton to oxygen ions can be produced. Patients have been treated since 2009.

The shielding layout was developed at GSI [25]. The specific feature of the facility is the access maze for the I/II treatment bunkers. The main neutron cone in I/II affects the maze, and therefore efficient shielding measures need to be taken. There are three cross walls. Each cross wall is reinforced with steel layers. At the maze entrance a shielding door (made of polyethylene material) is installed. The corresponding spatial dose distributions are given in Fig. 20 for carbon ion beams and proton beams (left, right). The dose distributions were obtained using the FLUKA code [25].

The shielding design goal was to keep the dose rate levels below 3 µSv/h in accessible areas in front of the treatment bunker, even when the high beam parameters (energy, intensity) are applied. The resulting dose rates are in the range of 1 µSv/h.

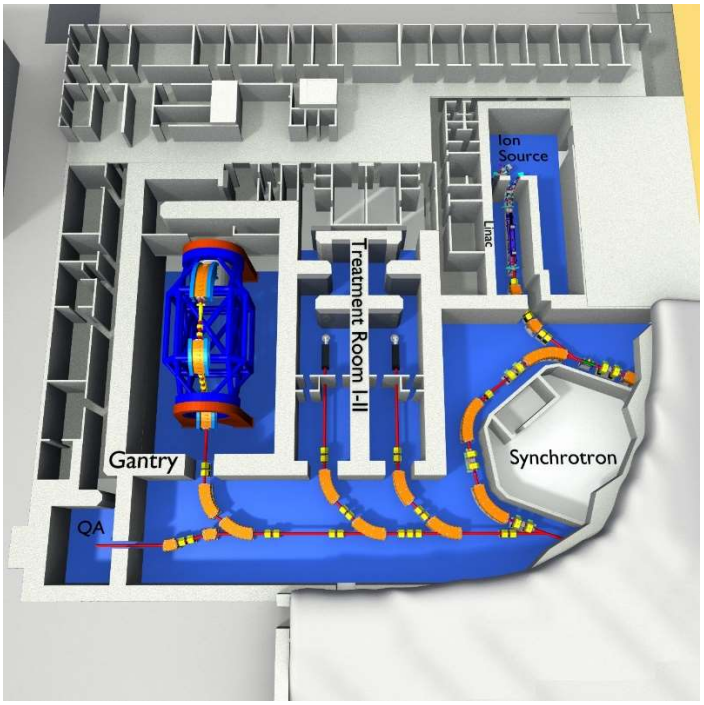


FIG. 15. Layout of the HIT facility in Heidelberg, Germany. The facility consists of the ion source and a linear accelerator for pre-acceleration (upper right), a synchrotron (bottom right), the high energy beam transfer line to the treatment bunkers, the quality assurance bunker, the treatment bunkers I/II and the gantry bunker (adapted from Ref. [11]).

5.2.7.6. Human activities in the rooms in the immediate vicinity of the equipment

A further aspect of the shielding design is dose rate levels in the treatment and work areas adjacent to the treatment bunker which is in operation. In Fig. 20, one can see that the dose rate in the neighbouring treatment bunker is in the range of 1–10 µSv/h.

The areas in the vicinity of the active treatment bunkers are often defined as controlled areas to which only authorized personnel (or those under the supervision of authorized personnel) can enter. Dose rates in the range of 1–10 µSv/h are compatible with common shielding concepts in linear accelerator based therapy facilities.

5.2.7.7. Secondary radiation (e.g. patient scatter)

The shielding layout is governed by the amount of beam losses during beam production and beam transfer to the treatment bunker, the beam forming system to produce a highly conforming therapy beam, and beam deposition in the tissue of the patient. In all beam loss situations, (secondary) radiation is produced.

The main radiation component in ion radiotherapy facilities is neutron radiation. Examples of neutron energy distributions are given in the measurements of Kurosawa et al. [20]. Here the neutron distribution of a carbon ion beam with 400 MeV per nucleon impinging on a graphite target ($20 \times 20 \times 20$ cm^3) is shown. The neutron energy measurements are based on the time of flight method for an angular range from 0° to 90°. Also, neutron spectra obtained by using the FLUKA code are given in the angular range from 0° to 90° for comparison with the measurements [21]. Considerable deviations between the measurements and FLUKA calculations were recorded for the 0° direction (Fig. 14).

High energetic particles are necessary to treat deep seated tumours in the tissue of the patient. For example, particle ranges of about 30 cm require proton beams with 250 MeV or carbon ion beams with 430 MeV/u. If high energetic particles impinge on matter (the target), they interact with the target nuclei. The projectile nuclei undergo nuclear and spallation reactions. Protons, neutrons and nuclei fragments (target fragments and projectile fragments if particles heavier than protons are used) are produced and released. They have roughly the same energy range as the energy of the impinging particle beam (expressed in MeV/nucleon), which means they have energies of several hundred MeV. For 430 MeV/nucleon, carbon ion beams neutrons can have energies up to 1 GeV (Fig. 14).

In conventional radiotherapy with X rays, neutron radiation in the energy range from 1 to 10 MeV is produced. Particle therapy results in neutron energy distributions which can be one to two orders of magnitude higher than the neutron energy distribution in conventional radiotherapy. Particle therapy installations are considered as high energy facilities.

5.2.7.8. Maze geometry

Avoiding excessive exposure outside access routes to accelerator or treatment bunkers using doors as shielding barriers requires massive, heavy doors that are inherently cumbersome and time consuming to maneuver. This is acceptable in the case of entrances to the accelerator bunker but not for treatment bunkers.

To allow for quick access to treatment bunkers, entrance shielding barriers are designed by means of mazes. The layout of mazes prohibits the direct propagation of the source radiation to the protected area outside the entrance. Only multiple scattering of the radiation with repeated change of the direction of the scattered radiation will result in the transport of radiation from the source to the maze entrance.

An example of mazes for a proton therapy facility is shown in Fig. 16. The left part represents a fix beam orientation, while the right shows a lateral orientation of the gantry. A steel layer is added for the reinforcement of the downstream shielding wall. The characteristics of a maze are the single leg length (r_1 …. r_4) and the cross-section of the maze. Methods for the estimation of dose (rate) levels along the maze and near the maze entrance are given, for example in Refs [26] [27].

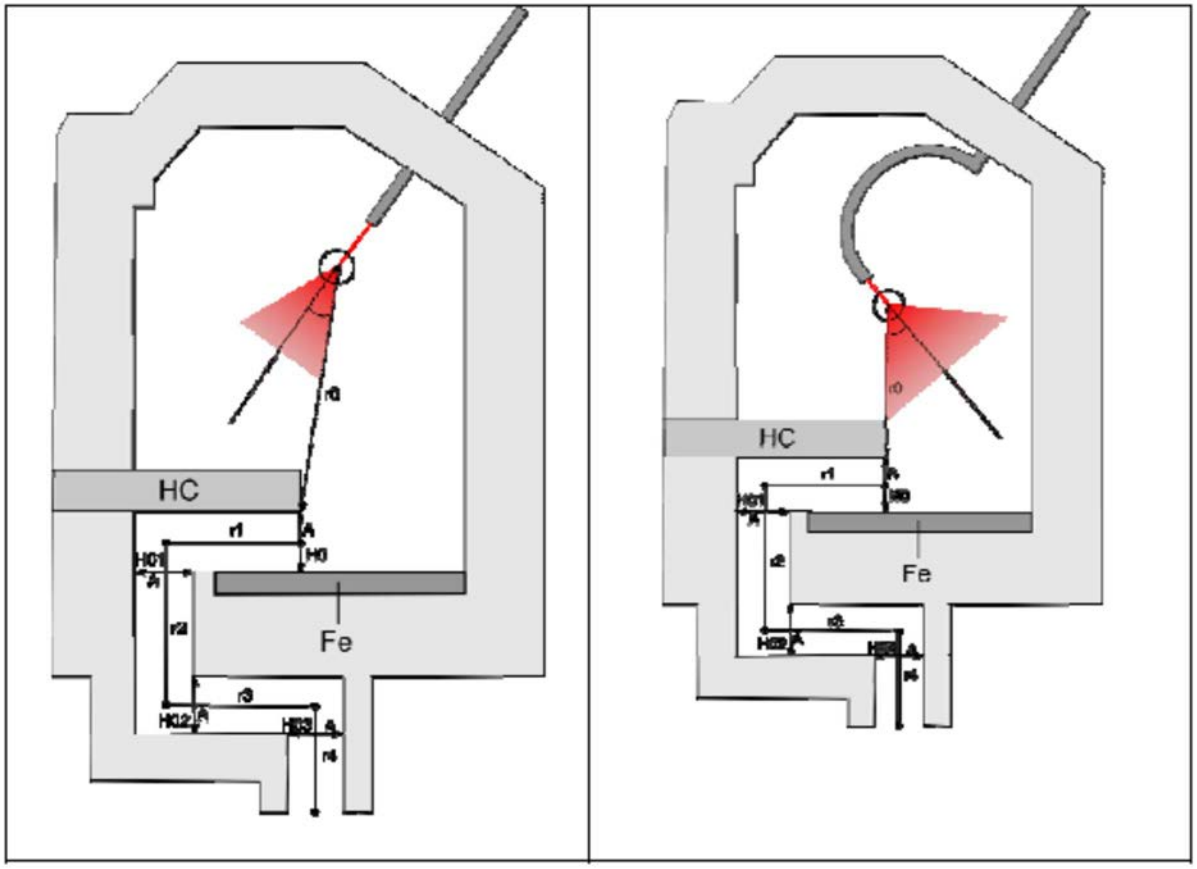


FIG. 16. Example of mazes in treatment bunkers with fix beam geometry (left), and with a rotating gantry (right). Typical for mazes is the right-angled layout of the single maze legs (HC: heavy concrete). Figure adapted from Ref. [11].

During treatment, comparatively high dose rates can occur near the patient. Dose rates ranging from 10 to 100 mSv/h can be recorded for beams with a particle range in tissue of about 27 cm and delivered therapeutic dose rates with a magnitude of Gy/min (Fig. 20). Treatment bunkers are usually not accessible to personnel during beam operation.

5.2.7.9. Shielding materials used (walls, roof, doors)

Architectural shielding structures are usually built using normal concrete with adequate thicknesses to attenuate the radiation produced, particularly high energy neutron radiation. In the case of limited shielding barrier space, shielding materials with more effective attenuation properties are used. Examples are the use of steel blocks or steel layers. Alternatively, high density concrete enriched with special aggregates like hematite can be applied.

Another approach for assembling shielding structures is the sandwich technique where bulk material with enough density and attenuation behaviour is inserted between prefabricated concrete structures (walls, roofs). An example of this technique is the MedAustron facility in Austria. A thorough activation analysis is always carried out for all shielding materials as they (as well as trace elements) can cause unwanted activation by neutron radiation (high energy as well as low energy neutron radiation) and higher energy gamma radiation. The requirements for the shielding of walls are in principle the same as for roofs except that the areas above the roof constitutes exclusion areas during beam operation whereby the amount of necessary

shielding is lower in comparison to the walls. Evaluation of skyshine effects is considered below.

Many particle therapy facilities have layouts using optimized designs based on mazes which avoids shielding access doors. Nevertheless, if shielding properties are necessary for the entrance door to the maze, typical layouts are applied which are well known from linear accelerator facilities. Usually shielding is made up of polyethylene or borated (^{10}B) polyethylene for the shielding of neutron radiation, positioned in between lead layers which results in an attenuation effect of the gamma radiation produced (see also Ref. [28]).

5.2.7.10. Skyshine evaluation

The radiation which is produced during the particle acceleration process — the beam transport from the accelerator to the treatment bunkers, in the beam forming system and/or within the patient in a correctly designed facility — is absorbed or attenuated in the architectural structural shielding.

A certain amount of the radiation produced is directed towards the upper structures of the building. This is affected, for example, by the gantry rotational angle where the bottom–top gantry position causes a neutron radiation cone towards the top of the bunker. Other reasons for an orientation of the main direction of radiation to the upper parts of the building are beam losses in beam lines transporting the ion beams to a higher location in the facility or generally scattered radiation in the treatment bunker. This radiation, or a part of it, can affect radiation levels at the roof of the facility. The roof itself has a shielding function. Usually roof areas are exclusion areas during beam operation and one can assume the roof shielding has a minor importance because there is nobody present on the roof needing exposure protection.

From experience with conventional electron accelerator facilities it is known that radiation emerging from the roof of the accelerator or experimental area can propagate in the environment and can cause measurable dose rates at certain distances to the installation or even in the public area. Figure 17 illustrates the situation where skyshine from a radiation source is produced. Radiation is transmitted through the roof and scattered in the atmosphere down to the ground. A careful analysis by applying a suitable calculation model for the estimation of the radiation levels near the facility is needed (see Ref. [26]). Appropriate roof shielding is necessary to keep the dose rates around the installation below certain limits. An analogous groundshine effect could appear by source radiation, escaping through the facility floor to the ground soil, being scattered towards and through the ground surface and giving rise to increased dose rates in accessible areas.

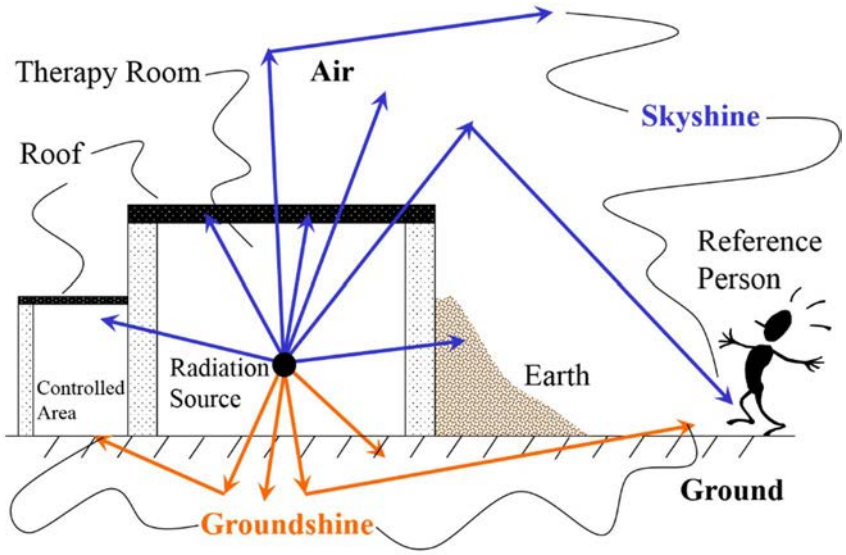


FIG. 17. Illustration of the production of skyshine and groundshine from a radiation source by scattering of the primary radiation in the atmosphere and in the ground.

5.2.7.11. Shielding layout planning and mathematical models used for the barrier thickness and maze geometry

Depending on the planning stage of the facility construction project, different methods of estimating shielding barrier (including floor and roof) thicknesses are used. In early stages so called line of sight models are often used to give a rough estimate on the shielding masses.

In a later phase of the design more sophisticated calculation methods are applied, particularly radiation transport modeling using the Monte Carlo method. Geometrical models of the planned accelerator areas are used for the simulation of beam loss distributions and beam deposition distributions. Various shielding materials can be considered. Realistic assumptions on applied beam intensities and beam energies can easily be implemented in the computation procedure. Figure 18 illustrates the steps which influence or determine the shielding layout.

The choice of the particle type used for patient treatments is key for subsequent radiation protection considerations. For instance, proton beams can be produced by cyclotrons as well as by synchrotrons. Heavier particle beams like carbon ion beams are usually produced by synchrotrons. Both accelerator types have specific advantages and drawbacks.

Cyclotron based facilities have compact accelerator bunkers but need massive shielding structures near the degrader. The degrader reduces the maximum beam energy to the actual needed beam energy. During the slowing down process of the particles, neutron radiation is produced. The degrader in a cyclotron-based facility represents a strong source of neutron radiation.

Synchrotron facilities have generally lower beam losses and produce fewer neutrons — in contrast to cyclotron facilities — but need more space for the accelerator itself which can result in a higher total amount of necessary shielding barrier volumes. The arrangement of the

FIG. 18. Scheme for the shielding layout planning of a particle therapy facility.

accelerator and the treatment bunkers, each equipped with a fixed beam geometry nozzle or a gantry, gives the rough structure of the facility.

The choice of the type of the beam forming system influences the shielding layout of the treatment bunker or the area in front of the treatment bunker. A passive beam forming system requires additional shielding because of greater beam losses in comparison with an active beam forming system. The beam parameter distributions (intensity, particles per year, energy) reflect the clinical use of the treatments (depth and size of tumours to be treated) and serve as a basis for the shielding calculations.

The first generation of particle therapy facilities were often planned based on particle beams with rigorous parameters covering intensity and energy) because of lack of knowledge of shielding data and beam parameter distributions which are needed for the treatments.

Finally, radiation protection legislation in the corresponding State and the application of internal guidelines on dose constraints for optimization of radiation protection (according to

ICRP Publication 103 [29]) provide further inputs for planning the layout of shielding. The entire process of shielding planning is an iterative procedure where parts of the planning sequence usually are repeated.

A first approach for detailed planning of the shielding barrier can use a line of sight model. An upper estimation for the necessary shielding is obtained when the line of sight model uses upper values for the beam parameters. Examples are 230 MeV for a proton beam or 430 MeV/nucleon for a carbon ion beam. The corresponding beam currents are 10^{10} protons/s and 3×10^{8} ions/s, respectively.

Line of sight models use a shielding barrier where the ambient dose (rate) equivalent int a reference point, at a certain distance outside the barrier, can be calculated. In these models the following quantities are used:

— The source strength of the beam loss/deposition point expressed as dose per particle ($H_0(\vartheta)$) at 1 m distance from the interaction point. The dose value depends on the type of the incident particle (proton or heavier ion), the energy of the particle and the azimuthal angle ϑ relative to the beam line and the target type (elemental composition).
— Distance from the interaction point to the reference position.
— Attenuation of the radiation produced in the shielding, involving the projected length in the shielding (d, see Fig. 19), the energy distribution of the radiation produced (e.g. Fig. 13 for 400 MeV/u carbon ion beams) and the resulting attenuation factor in the exponential term, which depends upon the azimuthal angle ($\lambda(\vartheta)$). For larger azimuthal angles (ϑ>50°), a sum of two exponentials is used for a more precise estimation of the attenuation.

The basis of the computation is an assumption of the beam loss in the beam line, the thickness of the shielding barrier and the angle of the reference point relative to the beam line (Fig. 19).

The following formula gives this relation:

$$H(\vartheta) = \frac{H_0(\vartheta)}{r^2} \cdot \exp\left(-\frac{d \cdot \rho}{\lambda(\vartheta)}\right) \quad (1)$$

with H_0 the dose per primary particle (angular dependent), r the distance reference point to beam loss point, d the effective barrier shielding thickness ($d = d_0/\sin(\vartheta)$) and $\lambda(\vartheta)$ the angular dependent attenuation parameter. The angular dependency of λ reflects the different neutron energy distributions for various angles ϑ (the higher ϑ the lower the mean neutron energy).

$H_0(\vartheta)$ considers different neutron fluences and various energy distributions with altered angles ϑ. The values of these parameters need to be calculated for each beam type considering the particle type (proton, carbon ion, etc.) and particle energy (see Fig. 19).

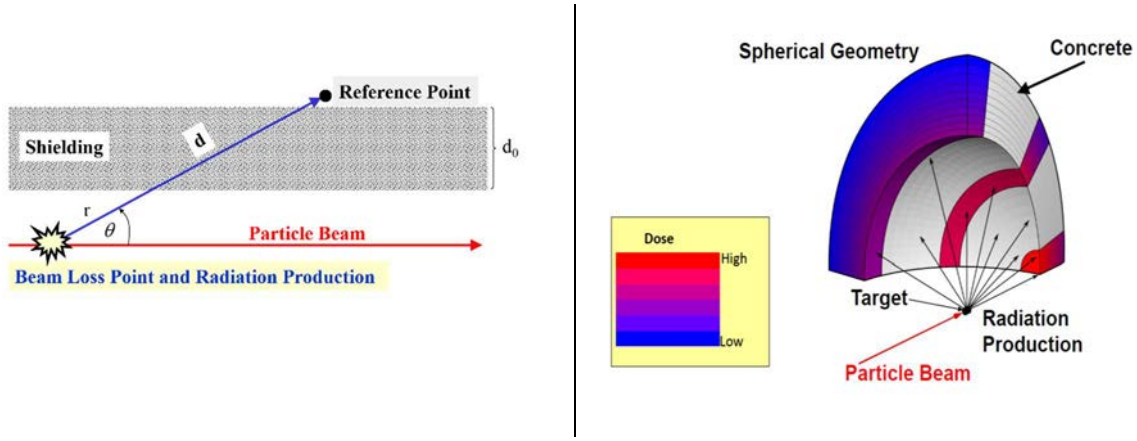


FIG. 19. Principle of the line of sight models considering a beam loss point in the beam line, the barrier thickness and the angle ϑ of the reference point relative to the beam line (left). The creation of line of sight models is often based in radiation transport calculations on a spherical geometry (right).

The calculations are performed in a spherical geometry by means of Monte Carlo radiation transport calculations. Calculation examples of the parameters are given in Refs [30]–[34]. The first generation of these types of calculations was carried out by applying measured double differential neutron spectra (angle, energy) [30].

For more precise calculation of dose values outside the shielding barrier, an additional expression in Eq. (1) is introduced. For angles $\vartheta > 50°$, the following equation is applied:

$$H\left(E_p, \vartheta, d, \lambda_{1,\vartheta}, \lambda_{2,\vartheta}\right) = \frac{H_1\left(E_p, \vartheta\right)}{r^2} \cdot exp\left[-\frac{d}{\lambda_{1,\vartheta}}\right] + \frac{H_2\left(E_p, \vartheta\right)}{r^2} \cdot exp\left[-\frac{d}{\lambda_{2,\vartheta}}\right] \quad (2)$$

The equation includes two exponential summands to account for the two main origins of neutron source contributors in need of shielding, cascade high energy neutrons and evaporation neutrons from the remaining target nuclei. Each summand has its own parameter for the dose H_1, H_2 and λ_1, λ_2. The parameters depend upon the particle energy E_p and the angle ϑ. Line-of-sight models can be applied also by authorities for first rough assessments of the shielding layout of the facility which is applied for by the applicant of the facility. A disadvantage of this method is the fact that the calculation can be carried out only for one beam energy. Additional estimations and approximations are necessary if various beam energies are considered. In practice the calculations are often performed for the highest beam energy and the resulting shielding thicknesses are an upper estimation.

After the first planning phase, where a proposal layout is derived by application of line of sight models or the layout is transferred from existing facilities of the accelerator provider, an additional approval of the shielding layout is necessary. In this situation Monte Carlo based radiation transport calculations are used. A geometrical model of the facility or parts of the facility is created.

Beam losses or beam depositions of the primary beam in the accelerator structure are simulated. The collisions of the incoming projectile hadrons or nuclei with the target nuclei are computed and the released radiation is transported from the radiation source through the shielding layers to the (virtual) detector positions inside and outside the shielding. At these detector points the

spectral fluence of the radiation occurring (essential neutron and gamma radiation) is converted into dose values (ambient dose equivalent or effective dose).

Sampling techniques with so-called biasing are applied. They are useful for specialists carrying out the detailed calculations. For this purpose, the geometrical model of the shielding barriers is subdivided in further layers to introduce the possibility to initiate the simulation of additional particle life histories from one geometrical region to the next, based on already existing particle parameters.

The statistical weight of the artificially created particles needs to be simultaneously reduced (adapted). If particles from the primary source are rejected, the statistical weight of the remaining particles is increased. Using this method, comparatively comprehensive geometries can be modelled and calculated in a reasonable time period. Suitable Monte Carlo codes for radiation transport calculations are:

— FLUKA (http://www.fluka.org/fluka.php);
— MCNPX (https://mcnp.lanl.gov/);
— PHITS (https://phits.jaea.go.jp/);
— GEANT4 (https://geant4.web.cern.ch/).

An example of dose distributions calculated with FLUKA is given in Fig. 20 for the fixed beam treatment bunkers in the HIT Facility in Heidelberg, Germany, for proton and carbon ion beams.

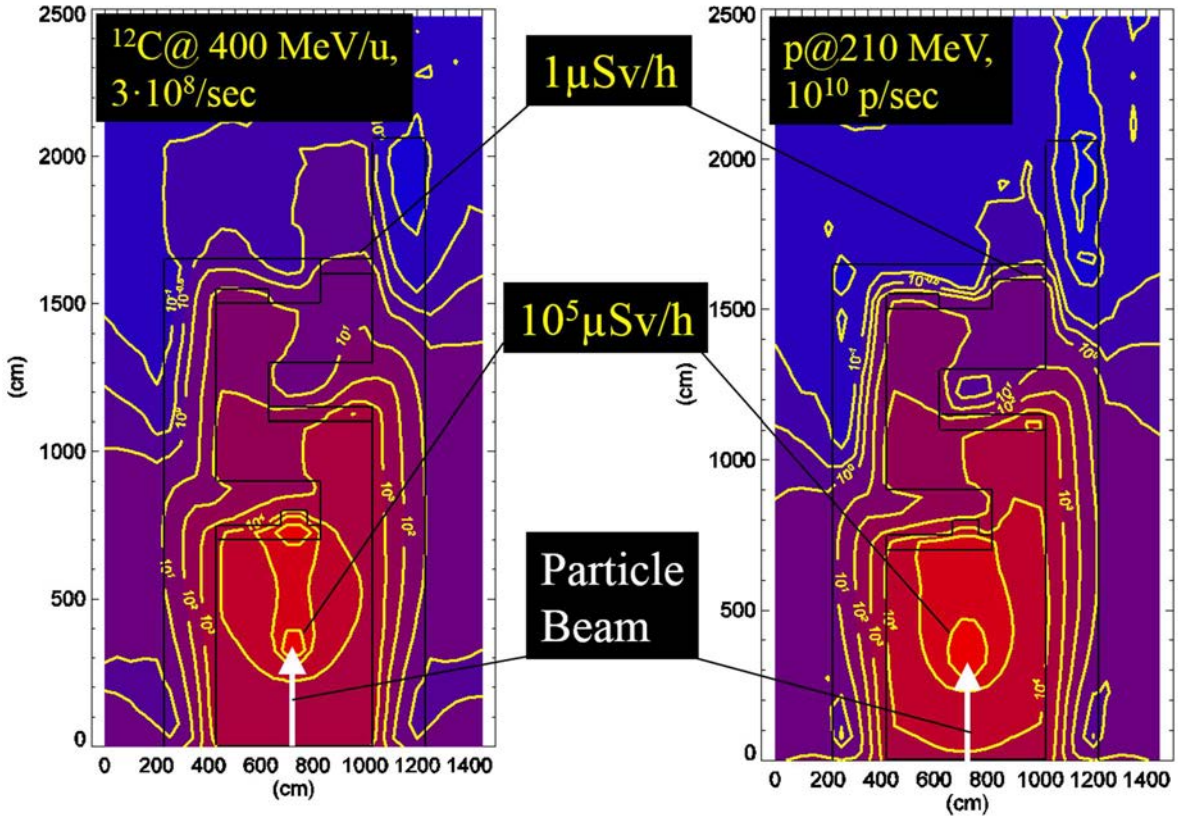


FIG. 20. The layout of the HIT facility with a linear accelerator, synchrotron, a rotating gantry and two horizontal beam lines as shown in Fig. 15. The dose distribution for carbon ion beams and proton beams (white arrows) are deposited in a graphite target (20 cm in length), computed with FLUKA, and the numbers at the isodose curves are given in µSv/h. The concrete and steel shielding are indicated with black lines. The access to the treatment bunker is in the upper part of the isodose drawing (a PE shielding door is installed at the entrance). Left: Carbon ions with an energy of 400 MeV/u and an intensity of 3 × 10^{8}/s. Right: Proton beams with an energy of 210 MeV and an intensity of 10^{10}/s. Figure adapted from Ref. [19] [25].

Accelerator areas, as well as the treatment bunkers, need an access area for the personnel or the patient and technical equipment. These parts of the facility are radiation areas where simple entry in most cases is not possible. Usually at least a shielding door or an entrance maze, or a combination of both, is necessary (Fig. 16).

The computation of the radiation attenuation in a maze can be smartly done using the Monte Carlo based radiation transport method. For the shielding simulation a careful choice of the beam losses (position, percentage of beam intensity) in the beamline is important to ensure that the maze is suitable to protect accessible areas also against beam losses. The radiation attenuation in mazes can also be computed using approximation formulas. Examples and approximation formulas are given in Refs [26], [27], [33], [35].[1] A similar formalism is applied for the planning of ducts in the thick shielding walls, which are used for the feedthrough for cables and pipes for ventilation air and cooling water.

[1] For additional information, see: TESCH, K., The attenuation of the neutron dose equivalent in a labyrinth through an accelerator shield, Part. Accel. **12** 3 (1982) 169–175.

5.2.7.12. Ducts for pipes, electrical wires, cables

The shielding properties of barriers in a particle accelerator facility are in most cases compromised to some degree by ducts for the necessary supply systems. In particular, electrical supplies and cables for the focusing and deflection magnets, ducts for the air exchange in the radiation areas, guides for the transport of the HF to the particle acceleration cavities, or pipes for the cooling of the magnets in the beamline, for the accelerator itself or the magnets in the beam transfer lines, need to be guided through the shielding barriers.

Supply systems can be driven through the shielding barrier using the same shielding method as for the mazes. For instance, the subdivision of the guide path into single legs where the single segments are set in certain angles to each other (e.g. 90°) results in an optimization of the radiation attenuation effect, allowing a shielding effect comparable to that of the unimpaired barrier. Examples are given in Fig. 21. The calculations of the shielding effect of ducts are carried out in the same manner as for mazes (see above).

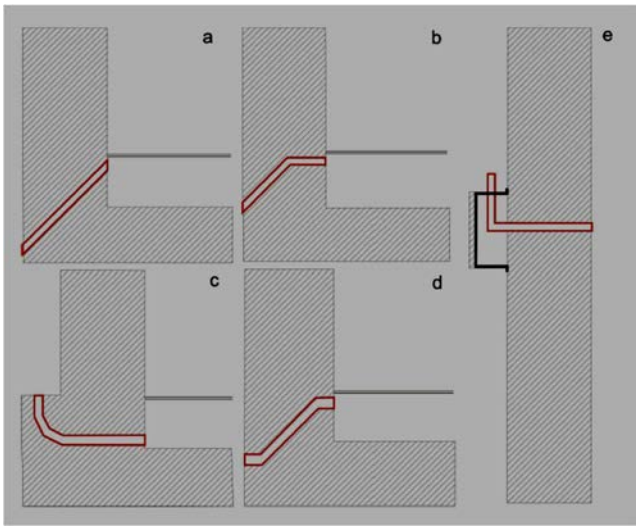


FIG. 21. Examples of ducts: (a) linear extension of a duct; (b), (c) use of a bend; (d) use of two bends; and (e) application of a shielding cover with suitable material. Figure adapted from Ref. [11].

5.2.7.13. Beam guide opening in the shielding wall

A built-in beam pipe in the shielding barrier represents a duct where radiation produced in the accelerator or in the beam transfer line can be transported to the treatment bunker or to areas where personnel stay during beam operation. Although the beam pipe structure itself consists of metal and has a good shielding effect related to high energy (neutron) radiation, detailed procedures are necessary for the installation of the beam pipe as well as the commissioning of the beamline later.

A typical method for the installation phase of the beam pipe is the creation of a comparatively large aperture for the pipe. After positioning of the pipe, including all connections (electrical, cooling) the remaining aperture spacing is filled with small shielding elements (e.g. concrete elements). Dose rate measurements during the commissioning period ensure that the dose rate values are below certain limits, otherwise the shielding around the beam pipe is modified.

5.2.8. Risk identification, mitigation and prevention

Registrants and licensees are expected to incorporate good engineering practices into the establishment of a facility and into safety related activities and processes throughout the lifetime of the facility. Good engineering and manufacturing practice include adherence to applicable technical standards and safety margins in the design and construction of the facility and in facility related operations. All practical measures are to be taken towards preventing accidents and mitigating the effects of accidents that may occur, as stated in Requirement 15 of GSR Part 3 [2].

In accordance with paragraph 3.3.1 of GSR Part 3 [2], authorization applicants and authorized parties conduct safety assessments at different stages in the establishment and lifetime of a facility or activity. Part of the assessment is the identification of potential safety risks arising from the activity practice or through the impact of outside factors. Safety assessment addresses both normal operational conditions and anticipated unwanted events or accidents. Identified risks may be mitigated by suitable preventive measures according to an established time schedule.

Care must be taken to ensure that team members have adequate competence in conducting the safety assessment and setting up the plan for risk mitigation measures. Another vital part in the mitigation of identified risks is to incorporate risk awareness in people involved in risk affected processes. Fostering a sound safety culture in the organization is one of the major contributions to mitigating safety risks and preventing accidents in activities using radiation sources. The management system and structure of such organizations promote a culture of high safety awareness (paragraph 2.47(e) of GSR Part 3 [2]).

Risk analysis and risk mitigation can be performed according to several different formalized systematic methods.

5.2.8.1. Failure mode analysis

One of the commonly applied risk analysis and mitigation methods is the failure mode and effects analysis (FMEA). This analysis prospectively, and in a systematic manner, analyses planned or existing systems, processes and construction designs for weaknesses, failure risks and corresponding unwanted effects. It scores the risk levels of possible presumed failure modes in process steps or system parts according to their assumed probability of occurrence, effect severity and detectability. Sorting the failure associated risks according to their scoring generates an action priority list.

In the case of construction and operation of an ion radiotherapy facility, an FMEA would include systems, processes and functions relating to radiation safety, including protection of workers, patients, environment and the general public. The complexity of setting up an ion radiotherapy facility leads inevitably to the need to conduct several sub-FMEAs with differing scopes and team compositions.

The FMEA is a natural step in setting up a new ion radiotherapy facility. It is also a tool that can be used to ensure the safe introduction of new or modified systems or processes in an already operating facility, as stated in Requirement 15 of GSR Part 3 [2].

The FMEA conducted in setting up an ion radiotherapy facility is expected to cover foreseeable accident scenarios resulting from malfunctions in systems or processes involved in facility operations. However, there are scenarios depending on human factors and possibly external

influences that may not be covered by these FMEAs. Examples of such scenarios include sabotage, natural disasters, incorrect use of equipment and software, power failures and data corruption. These potential scenarios are identified in a safety assessment of the facility and its operation. The identified accident scenarios are taken into account in software and hardware design (redundancy, defence in depth, user interfaces) and maintenance, but also in access control to premises and sensitive data.

In accordance with Requirement 12 of GSR Part 2 [36], measures to reduce the risk of accidents leading to unintended exposure also include establishing a robust safety culture at all levels within the organization(s) involved in the management and operation of the facility.

5.2.8.2. Incident/accident recording, investigation and prevention

Accidents, misses and near misses are eventually likely to occur. Routines to record and investigate such events and to develop proper actions to prevent such events from reoccurring are integrated in the facility management system.

Commercial software systems for recording and follow-up of unwanted events within the medical sector often cover all operational activities, not only activities with ionizing radiation. In procurement of medical systems care is taken to ensure that a system is designed to handle radiation related events.

Dissemination of information about the reported events is vital for accident prevention. Lessons learned from events needs to be fed back to manufacturers, regulatory authorities, other operators/licensees and stakeholders, as stated in Requirement 16 of GSR Part 3 [2].

5.2.9. Management of unplanned exposures

"Registrants and licensees, for sources under their responsibility, shall establish, implement and maintain: […]

(a) Emergency plans, emergency procedures and emergency arrangements, in accordance with the nature and magnitude of the radiation risks associated" (paragraph 3.127, GSR Part 3 [2]).

An ion radiotherapy facility is usually not likely to pose a significant threat to workers, the environment or the general public as a result of an accident. One possible effect could be the spread of activated material in the surrounding due to an earthquake. Another plausible effect on the environment could be drainage of activated cooling water into the ground. The latter is normally prevented by constructing low level drainage pools in the facility to hold water escaping from a breakage in the internal closed cooling system. The extent of emergency preparedness in the licensee's organization is decided ultimately on the results of a safety assessment of the facility and its operation.

The types of possible emergencies concerning ion radiotherapy facilities include:

- Fire;
- Explosion;
- Uncontrolled release of radionuclides in air and/or water;
- Earthquake;
- Flooding;

— Exposure to materials used in the design of the equipment (beam scatterer material);
— Airborne particles and gases;
— Power loss.

5.2.10. Irradiation effects on material properties

Large fluences of high energy ions are known to induce alterations in the chemical structure of the irradiated material. In metals, the predominant radiation damage is caused by atomic displacement in the lattice structure, leading to decreased ductility, thus making the material more prone to cracking. Plastics suffer bond breakages and cross-linking in and between polymer chains, leading to the formation of new polymers with properties differing from the original material.

Extensive irradiation of concrete from high energy photons or fast neutrons can cause heating, leading to water in the concrete being driven out. This in turn results in two effects degrading the shielding properties of the concrete: cracking formation and loss of waterbound hydrogen, resulting in diminished slowing down and subsequent absorption of neutrons.

The extent of mechanical stress and property changes on shielding materials and accelerator components is proportional to the total high energy particle or photon fluence impinging on the material, but also on factors such as the material temperature. In an ion radiotherapy facility, fluences are likely to be well below the levels of significance for structural shielding barriers but high enough to induce significant mechanical stress in components in the accelerator, beam transportation system and treatment nozzle.

Periodic inspections of such components during the entire facility lifetime are of great importance to allow for early detection of material stress that could compromise beam performance or radiation protection of patients, workers and the general public.

5.2.10.1. Irradiation effect on electronic components

Photons and high energy particles are capable of inducing radiation effects in electronic devices such as transistor based microelectronic circuits and optoelectronic components. These effects can be either:

— Dependent on the accumulated dose, leading to a gradual deterioration in device characteristics and ultimately to functional failure;
— Stochastic and resulting from single radiation interaction events, causing damage that can be of both transient and destructive character.

Care needs to be taken to mitigate these effects potentially induced by radiation in electronic devices in an ion transport radiotherapy system. This can be accomplished by careful choice of devices, designed and fabricated to be less sensitive to both single event and total dose effects.

Other measures to reduce the risks of malfunction due to radiation effects are circuit redundancy, device shielding and close monitoring of device and system performance.

5.2.11. Activation

The magnitude of radioactive activation of matter depends on the rate of beam depositions in the component (number of deposited particles per second), the overall period of irradiation (beam depositions), and the type and energy of the particles.

One component of particle therapy facilities which is highly irradiated is the degrader in cyclotron-based therapy facilities.

A cyclotron accelerates protons to a maximum energy (230 MeV for most machines) and the necessary energy of the actual treatment is adjusted in the degrader, where the proton beam is partially slowed down to the desired energy. During the slowing down process nuclear interactions, particularly proton–nucleus collisions, occur in which radioactive nuclei are produced.

The degrader is usually made of graphite. One type of wedge was shown in Fig. 3. The particle beam needs first to pass a stationary wedge and second a moving wedge. The higher the penetration length in the wedge the lower is the transmitted particle energy. The movable wedge adjusts the actual necessary particle energy for the treatment and can be moved rapidly.

Radionuclides produced in the graphite include ^{7}Be, ^{11}C and ^{3}H. The neutron radiation released causes further activation in the metal structure of the degrader. The dose rates soon after beam operation are in the range of some ten mSv/h near the degrader. The main activity is caused by ^{11}C and decays quickly a few hours after operation.

In a particle therapy facility neutron radiation is the main secondary radiation component. The neutron energies occurring range from thermal up to several hundred MeV. A series of different physical processes cause activation. These are neutron capture reactions (n, γ), (n, particle), neutron induced nuclear reactions and spallation reactions. The variability of isotopes produced increases with increasing Z (or mass) of the target nucleus.

Accelerator components are activated and can occasionally be contaminated. Removed components are stored in specific rooms for storage of radioactive material. The storage rooms are controlled rooms or at least surveyed and supervised rooms.

Activated metals have longer lived radioisotopes like ^{7}Be, $^{22, 24}$Na, $^{52, 54}$Mn, ^{48}V, $^{46, 48}$Sc, ^{51}Cr, ^{65}Zn and $^{56, 60}$Co with half-lives ranging from 15 h to 5.3 years (nuclides with shorter half-lives are not listed here).

Accessories consisting of plastic and other low Z materials have short lived radioactivity like ^{11}C (half-life, 20 min) as well as activity with longer half-lives as ^{7}Be (half-life, 53 d).

Upon authorization the licence applicants present routines for proper handling of activated accelerator system components. Such routines include methods for activation quantification, proper marking, secure and shielded storage and ways of disposal in accordance with regulatory requirements.

If components are to be used as spare parts, the licence applicant is expected to establish safety routines and precautionary measures that ensure safe handling when the component is to be repaired or reinstalled.

Accelerator components and treatment accessories are not the only things that can be activated. Activation could also occur in shielding structures, such as in the case of concrete barriers in which the additives of the concrete can become activated. Typical radionuclides identified are ^{22}Na, ^{45}Ca and ^{3}H. The concrete enforcement iron can have comparable activation nuclides as the steel in the accelerator structures. This structural activation poses a challenging task in the decommissioning and closure of an ion beam therapy facility.

Further information on the management of radioactive material, waste management and decommissioning is found in Sections 5.2.13 and 5.2.23. The maintenance work at activated accelerator structures or the handling of passive beam forming elements (e.g. the bolus) are associated with the radiation exposure of personnel.

An overview of radiation exposures occurring at Japanese facilities is given in Ref. [37]. Annual dose values between 0.5 and 5.6 mSv were recorded, depending on the type of accelerated particles (protons or carbon ions), accelerator type and the type of the beam forming system (in Japan at that time the passive forming system).

Equipment maintenance and service work at a proton synchrotron is associated with comparatively low exposures. Typical radionuclides which contribute to the radiation exposure are ^{56,57,58,60}Co, ^{52,54,56}Mn, ^{44,46}Sc and ^{48}V. Annual occupational doses for the Loma Linda University Medical Center (LLUMC) of a few hundred µSv were recorded.[2]

The activation of a probe with a length D by an ion beam can be formulated as:

$$P_i = N_{Ion} \cdot \sigma_i \cdot n_{Target} \cdot D \tag{3}$$

with P_i the saturation production rate of radionuclide i, N_{Ion} the ion current and σ_i the production cross-section of radionuclide i from the target with a density n_{Target}.

If the time dependent buildup of the activity of the nuclide i and the radioactive decay is considered, the activation equation is described as follows:

$$A_i = \left(1 - e^{-ln(2)\cdot\frac{t_{Irradiation}}{t_{HL}^i}}\right) \cdot N_{Ion} \cdot \sigma_i \cdot n_{Target} \cdot D \cdot e^{-ln(2)\cdot\frac{t_{Decay}}{t_{HL}^i}} \tag{4}$$

with $t_{Irradiation}$ the irradiation time, t_{HL} the half-life time and T_{Decay} the decay time after irradiation.

The cross-section σ_i is energy dependent. For radiation protection purposes and for ease of evaluation, an energy independent cross-section is often assumed. In the following example the activation of human tissue is estimated for irradiation with a carbon ion beam with 330 MeV/nucleon.

[2] MOYERS, M.F., LESYNA, D.A., Exposure from residual radiation after synchrotron shutdown, Radiat. Meas. **44** (2009) 176–181.

The cross-sections are taken from the EPAX formula [38] which considers heavy ion interactions with target nuclei. The irradiation duration was 10 min with 10^8 carbon ions/s. The decay time was 1 min.

The activity produced is converted into dose rate values using nuclide specific dose conversion factors [39]. The main contributors to the dose rate are ^{7}Be, ^{10}C, ^{11}C, ^{13}N, ^{14}O and ^{15}O (Fig. 22). The dose rate one minute after irradiation is about 1 µSv/h at 0.5 m distance from the patient, but it decays very rapidly. Substantial radiation exposure of personnel is not expected, but for a therapy facility with a large number of therapy procedures in a year, one can estimate that the occupational radiation exposure can be more than 1 mSv for an individual.

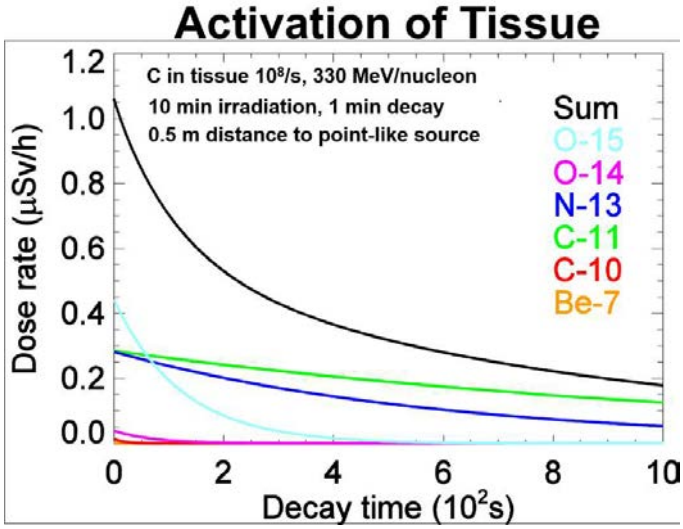


FIG. 22. Dose rate near a patient (0.5 m distance) after 10 min of irradiation with 10^8 carbon ions/s and 330 MeV/nucleon. A decay time of 1 min was considered.

The radioactivity produced for single radionuclides (heavier than ^{7}Be) can be estimated from Eq. (4) and by inserting the parameters of the results from the last example for values in the range from kBq to MBq (^{15}O).

The same formalism can be applied for estimation of the air activity based on Eq. (4). The major part of air activation is caused by the neutron radiation released in the accelerator and in the patient. Ions contribute less to air activation, because the path lengths of ions in air are low (≈ 1 m). The radionuclides produced are ^{7}Be, ^{11}C, ^{13}N, ^{14}O, ^{15}O and ^{41}Ar. The majority of radionuclides are produced by high energy neutrons in nuclear reactions and spallation reactions.

Neutron radiation in a treatment bunker has a wide energy range, including thermalized neutrons. Thermal neutrons undergo capture reactions which is the production process for ^{41}Ar. Argon-41 has a comparatively long half-life of 1.8 h and is emitted from the ventilation system into the environment. Therefore, an estimation, or alternatively a measurement, of the annual emitted activity for all radionuclides is considered.

The focus of planning for heavy ion accelerators with regard to radiation protection issues is on aspects of the shielding of the prompt produced secondary radiation (neutron and gamma rays) and on aspects of potential activations. These are essentially activations of the structure of the accelerator and activation of substances, which are connected to the primary and secondary

radiation sources, e.g. cooling water and air. During heavy ion beam operation, cooling water activation can be caused by two processes:

(a) Fragmentation processes of the carbon ion beam respectively the target nuclei;
(b) Spallation reactions with the mentioned above nuclei, caused by high energy neutrons which are generated during the slowing down process of the heavy ions.

For the reaction products of processes (a) and (b), radionuclides with half-lives in the range of minutes to months need to be considered. Short lived radionuclides decay rapidly, and the buildup of the long lived radioactivity is a slowly growing process. Therefore, only the radionuclides ^{7}Be, ^{11}C, ^{13}N, ^{14}O and ^{15}O are considered for water activation. Process (a) will not be investigated further because the path length of carbon ions in water can be ignored. The carbon ion beam is usually slowed down before it reaches the cooling water. Therefore, only reaction (b), with the production of neutron radiation, will contribute substantially to water activation.

A calculation example using activation cross-sections σ from the literature is given here. The activation of water by neutrons can be estimated by application of the spallation reaction cross-sections [27] [35].

The calculation of the saturation buildup rate P is made according to Eq. (3). For the length D, a value of 2 m was assumed. Table 1 gives an overview of potential production processes for the above mentioned radionuclides, the saturation activity $A_{saturation}$ and the resulting dose rates. As a heavy ion beam, a carbon beam with an intensity of 3×10^{8} ions/s was used, while 10% of the beam was considered as beam loss. Five high energetic neutrons are produced per carbon ion on average. The saturation activity of the nuclei of interest is in the range between 1 and 40 MBq. These values are used for conversion into dose rates by using the dose rate constants K_{γ} [39]. A point-like source geometry is used.

At maximum beam intensities, the activation of cooling water results in dose rates up to 9 µSv/h (1 m distance), if the radiation source is assumed to be point-like (in reality the activity is distributed over the entire cooling system so that the dose rates to be expected are substantially lower). Since the integral dose rate consists of contributions of nuclides with short half-lives, the dose rate decreases comparatively quickly.

TABLE 1. PRODUCTION OF RADIONUCLIDES IN THE COOLING WATER OF THE HEAVY ION SYNCHROTRON BY SPALLATION REACTIONS OF THE HIGH ENERGY NEUTRONS PRODUCED

Nuclide	Half-life ($T_{½}$)	σ (mbarn)	$A_{saturation}$ (MBq)	K_{γ} (mSv·m^2/h·GBq)	Dose rate (mSv/h)
H-3	12.3 a	30	30	—	—
Be-7	53 d	5	5	7.72E-3	3.86E-5
C-11	20 min	5	5	1.59E-1	7.95E-4
N-13	10 min	9	9	1.6E-1	1.44E-3
O-14	1.2 min	1	1	0.45	4.5E-4
O-15	2.1 min	40	40	1.59E-1	6.36E-3
Sum					9.1E-3

In the event of cooling water leakage, it is necessary to drain the activated water to a catchment tank. If water activity measurements conclude that the activity levels are below the clearance limits, an official clearance procedure can be initiated. Otherwise the activated water is stored until the activity levels are below the clearance levels.

There is a possibility that activated accelerator components, in contact with the cooling system, can contaminate the cooling water with long lived radionuclides. It might be necessary to analyse the cooling water for such radionuclides.

Activation of dust is generally of minor importance in a particle therapy accelerator facility. Nevertheless, there are some areas where dust activation needs to be monitored. Areas around the degrader can be assumed to be contaminated. Dust on accelerator surfaces and the building in accelerator areas (floor, walls, ceiling) originates from dust (also sand and earth) transported by the ventilation system, from accelerator component abrasion, rust from accelerator components, or from the deposit of the air (without dust) activation itself. Dust will be activated due to irradiation by neutrons during accelerator operation. Nuclides identified in the dust are ^{54}Mn, ^{7}Be, ^{51}Cr, ^{59}Fe and ^{48}V [40] [41]. For longer lived radioactivity, nuclides such as ^{60}Co also need to be considered.

From Refs [40] [41], one can derive a relation between the contamination of an area and the measured dose rate (several years of operation of a high energy accelerator and a few hours between the end of machine operation and measurements). The relation is given in Fig. 23 for a dose rate range of from 1 to 10 Sv/h. In the area near a degrader dose rates of some ten mSv/h to 0.1 Sv/h have been measured. Therefore, contamination values of about 10 Bq/cm^2 to some hundreds of Bq/cm^2 are expected, if the relation of Fig. 23 is used. For the protective measures one can propose, in addition to an improved filtering of the ventilation air (air inlet, outgoing air), periodic dust removal through the use of suitable cleaning procedures for the accelerator components and the building surfaces.

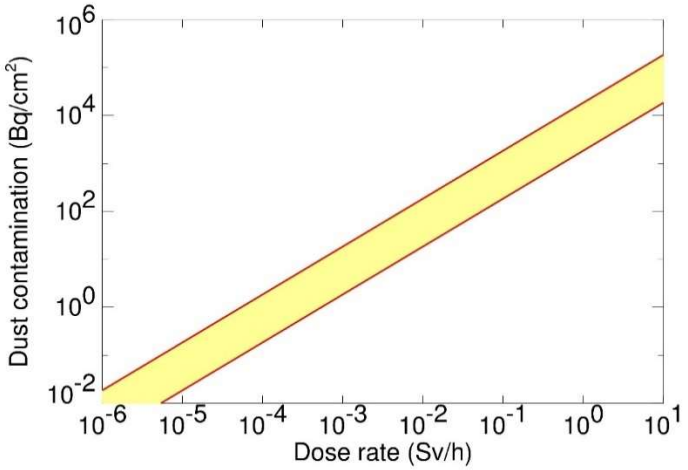


FIG. 23. Relationship between the measured dose rates for an activated area and the estimated contamination level in this area. The data are derived from Refs [40] [41] and are indicated in yellow.

Activation of soil around particle therapy facilities is generally negligible. The thicknesses of underground building structures are enough to attenuate the radiation to a low level of soil activation. Nevertheless, for approval procedures it may be necessary that target areas and the degrader area be investigated for soil activation. The first step in the activation assessment is

the analysis of the soil element composition, including trace elements. In the second step a computational method for the activation estimation is applied. Monte Carlo programs like FLUKA can be used. If they are not available, computations based on cross-sections are possible. Activation cross-sections are given in the literature [27] [35]. Computer software programs for the calculation of cross-sections from the formation of radionuclides [38] [42] are adapted from nuclear astrophysics applications. In the third step, an estimation of the neutron production is carried out. For heavier ions the approximation of Kurosawa can be applied [20]. The neutron yield (E_n > 5 MeV) is:

$$Y = \frac{1.5 \cdot 10^{-6}}{N_T^{1/3}} \cdot E_p^2 \cdot \left(A_p^{1/3} + A_T^{1/3}\right)^2 \cdot N_p \cdot \frac{A_p}{Z_p^2} \tag{5}$$

with N_P and N_T representing the number of neutrons in the projectile nucleus and target nucleus, respectively, A_P and A_T are the overall number of nucleons of the projectile and the target, Z_P is the atomic number of the projectile, and E_P is the projectile energy in MeV/nucleon.

For a proton beam, neutron yield data are taken from IAEA Technical Reports Series No. 283 [27]. The data were originally evaluated by Tesch et al. [33]. In the particle energy range considered here, the neutron production yield is proportional to E_P^2. Figure 24 illustrates that for 250 MeV/nucleon the neutron production yield varies from 0.3 neutrons/p to 2.6 neutrons/per neon ion. For 450 MeV/nucleon, the neutron production yield varies from 0.8 neutrons/p to 8.4 neutrons/neon ion.

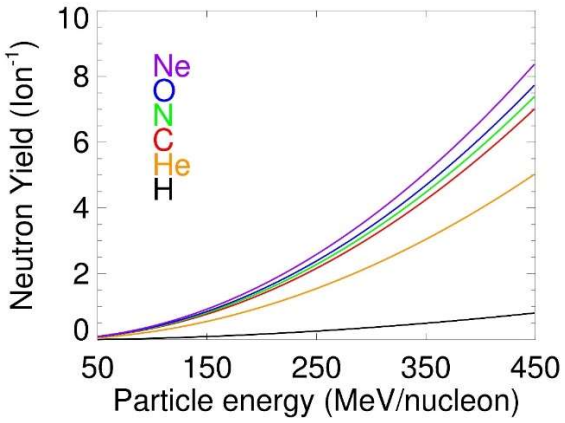


FIG. 24. Neutron production yield for heavy ions slowed down in a carbon target as a function of the ion energy. The yield for He, C, N, O and Ne ions was calculated using the Kurosawa approximation formula [20]. The neutron production yield for protons are taken from Refs [27] [33].

The following calculation gives an example of ground soil activation estimation for a location of a carbon ion treatment facility. The calculation was carried out for a spherical geometry with a carbon target in the centre surrounded by concrete shielding (50 cm thickness) and a ground soil layer (2 m thickness), which represents a simulation of the situation when a carbon beam is directed from the top towards the floor in a treatment bunker. Table 2 shows the distribution for the elemental composition of the ground soil. The activation calculation is based on the corresponding production cross-sections. A specific nuclide can originate from different mother nuclides. All of the radionuclides and production cross-sections considered are listed in Table 3.

TABLE 2. ACTIVATION CALCULATION OF GROUND SOIL FOLLOWING ELEMENTAL COMPOSITION ACCORDING TO THE MASS PROPORTION (DENSITY OF THE GROUND SOIL, 2.4 g/cm^3)

Element	Si	Al	O	K	F	Mg	Fe	Mn	Zr	Others
Content (%)	42.4	1.3	51.2	1.6	0.2	0.2	0.4	0.4	2.0	0.3

TABLE 3. RADIONUCLIDES PRODUCED BY ENERGETIC NEUTRONS
(the production cross-sections are derived from the formulas in Refs [27] [42])

Product radionuclide	Half-life $T_{1/2}$ (s)	Mother nuclide(s)	Cross-section(s) (mb)
Be-7	4.6E6	O-16	0.73E1
Ca-45	1.41E7	Fe-56, Mn-55	0.22E1, 0.19E1
Ca-47	3.92E5	Fe-56, Mn-55	0.11E0, 0.9E-1
Co-60	1.66E8	Zr-94	0.19E0
Fe-55	8.61E7	Fe-56	0.59E2
Fe-59	3.85E6	Zr-94	0.39E-1
H-3	3.89E8	O-16	0.30E2
Mn-54	9.85E5	Fe-56, Mn-55	0.77E2, 0.56E2
Na-22	8.20E7	Mg-24, Al-27, Si-28	0.44E2, 0.15E2, 0.18E2
P-32	1.23E6	K-39	0.22E2
Sc-46	7.24E6	Fe-56, Mn-55	0.94E1, 0.1E2
Sc-47	2.89E5	Fe-56, Mn-55	0.35E1, 0.38E1
Sr-90	9.03E8	Zr-94	0.75E1
V-48	1.38E6	Fe-56, Mn-55	0.11E2, 0.16E2
V-49	2.85E7	Fe-56, Mn-55	0.29E2, 0.43E2
Y-88	9.21E6	Zr-94	0.38E2
Zn-65	2.11E7	Zr-94	0.12E1

Note: In some cases, different mother nuclides are activated to the same product nuclide.
b: barn (= 10^{-28} m^2).

For the activation calculation, a carbon ion beam with an energy of 400 MeV/nucleon and a beam intensity of 10^7 ions/s was chosen. The target material is carbon. These data are used to compute the neutron production. The activation shown in Eq. (4) was used. The decay time was not considered. The buildup of radioactivity is presented in Fig. 25 for these radionuclides. Most nuclides reach a saturation activity after irradiation for 10^8 s (≈ 3 years) and the longer lived radioactivity after 10^9 s (except ^{90}Sr).

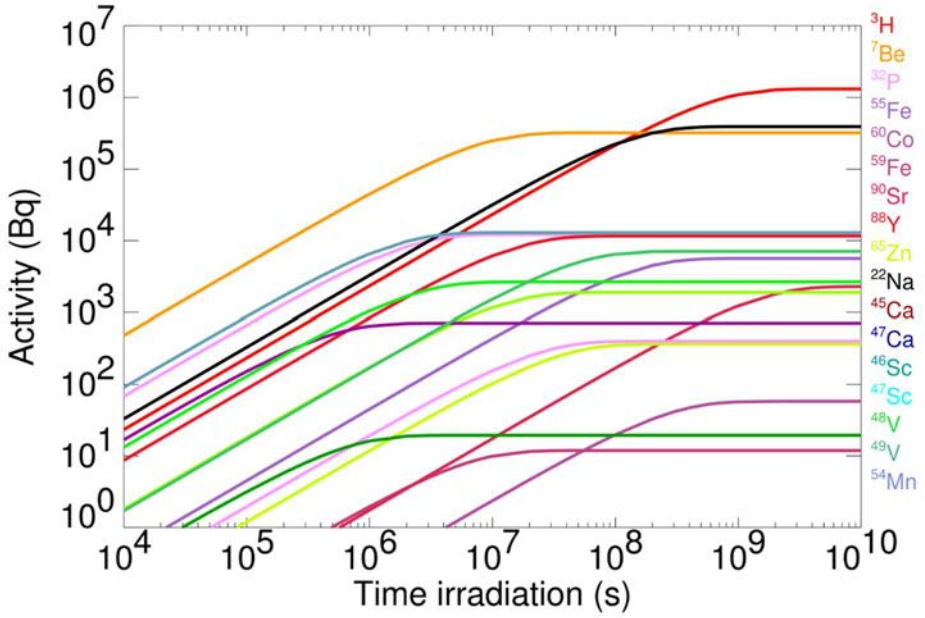


FIG. 25. Activation of ground soil by energetic neutron radiation. The ground soil composition in Table 2 was used (details of model assumptions are mentioned in the text).

In a further step the activity per nuclide and per mass can be evaluated and the nuclide specific exhaustion of the limits of the radiation protection legislation can be analyzed. Factors such as shielding thicknesses, beam energies and mean beam intensities can be studied with respect to the influence on the exhaustion of the given limits, based on the activation model.

A part of the produced activity is dissolved in, and possibly transported by, groundwater. The activity distribution is calculated for energetic neutrons. Thermal neutrons are also transported to the ground soil and can cause additional activation by neutron capture reactions (n, γ). An example is the activation of ^{59}Co to ^{60}Co. The cross-section for thermal neutron capture is 16.5 b. This type of activation also needs to be considered if trace elements with a substantial neutron capture cross-section are present.

If Monte Carlo codes, comprising nucleon–nucleus interactions (e.g. FLUKA), are available to the applicant of the facility or to the radiation protection expert who is commissioned by the authority, the activation can be estimated for a realistic geometry including thermal neutron activation.

5.2.12. Environmental impact and emissions

The operation of a particle therapy facility can cause environmental impacts. These impacts include: direct radiation coming from accelerator areas; skyshine (see Section 5.2.7.10); emission of activated air; and possible activation of the ground soil and groundwater. While direct radiation and ground soil activation can be controlled by shielding, the activation of air is unavoidable above a certain level. Internal shielding of accelerator areas, e.g. the energy selection system of the cyclotron, helps to keep the extent of air activation low. Nevertheless, air activation occurs in the treatment bunkers and thus there is a need to estimate it. An overview of all environmental impacts is given in Fig. 26.

In the context of regulatory control, all environmental paths of emissions and radiation effects on the environment need to be clarified. Dose assessment is carried out for each exposure path.

The annual effective dose limit for public exposure, resulting from the sum of activities with ionizing radiation, is set at 1 mSv in most States. An annual effective dose restriction of 0.1−0.3 mSv is commonly used for public exposure from a single activity (facility) with ionizing radiation. Monitors can be installed for the control of the emissions of airborne radioactivity.

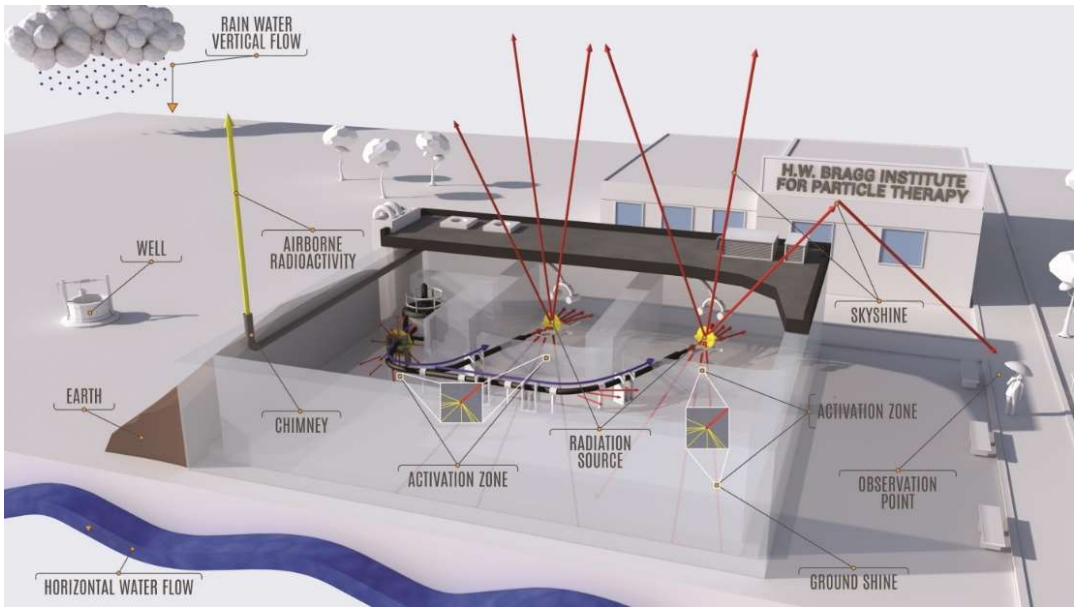


FIG. 26: Overview of relevant environmental impacts of the operation of a particle therapy facility: direct radiation and skyshine, air activation and airborne radioactivity, and ground activation.

5.2.13. Handling of radioactive material

The application for authorization of an ion beam therapy facility includes a plan and routines for the management of radioactive waste, both for regular operation and for future facility decommissioning. The applicant presents routines for assessing the activity in waste, accelerator components and building structures. Routines for exemption clearance and radioactive waste disposal must be included in the application and assessed by the regulatory body during the authorization process.

The waste management plan must be established early in the planning of the facility to allow for waste reduction to be included in the optimization of the facility design and the features of the accelerator system. This plan is not meant to be static, but rather as something requiring continuous revision to adapt to operational changes throughout the facility's lifetime.

During the lifetime of the facility, activated accelerator components will be replaced due to malfunction or in accordance with the manufacturer's preventive maintenance schedule. The facility needs to include proper storage areas for such components to allow for safe storage pending disposal in accordance with the operator's waste management plan. It is advisable to position the storage areas inside the accelerator bunker so as to not introduce additional separate controlled areas in the facility.

5.2.14. Maintenance and servicing

Maintenance and servicing of the accelerator system inevitably include work close to or in direct contact with activated system components. Some repairs could also be conducted on-site involving components from the accelerator system.

Regulatory control, during authorization and inspections, needs to include assessment of routines for safe handling of activated material, both with respect to occupational external exposure and the risk of external or internal contamination. Such routines are to be assessed by both the facility operator and the maintenance/service provider, and independently verified by the regulatory body.

Servicing of certain components or system modules will require a delay time after last 'beam on' to allow for activation decay to acceptable levels. Repair and handling of components removed from the accelerator system need to be conducted in a workspace designed to avoid spreading activated material within and outside the facility.

5.2.15. Transport

The transport of radioactive material is commonly covered in other State or government regulations. Europe utilizes a mutual regulatory framework (the European Agreement concerning the International Carriage of Dangerous Goods by Road (ADR)) for the transport of dangerous goods, including radioactive material. The IAEA Regulations for the Safe Transport of Radioactive Material [43] establish standards of safety which provide an acceptable level of control of radiation, criticality and thermal hazard to people, property and the environment associated with the transport of radioactive material.

In the establishment and operation of ion radiotherapy facilities, the transport of radioactive material is likely to occur during the delivery of accelerator components or modules to and from the facility. Factory tested accelerators may contain certain levels of radiation due to activation generated in the testing process. During the facility's routine operation, activated accelerator components may require transport from the facility to the manufacturer, or for disposal. In the course of the authorization process for the facility, the regulatory body needs to confirm that the applicant, and other parties involved in transporting components and material to and from the facility present transport routines in compliance with regulatory requirements.

5.2.16. Organizational structure and operational management

The organizational structure of a licensee is meant to provide the proper conditions for upholding safety expertise and maintaining sufficient and adequately trained staff (paragraph 5.60 of GS-G-3.1 [44]).

Requirements and guidance on the management of safety are found in GSR Part 2 [36] and in GS-G-3.1 [44]. These publications state that:

(a) "The organizational structures, processes, responsibilities, accountabilities, levels of authority and interfaces within the organization and with external organizations shall be clearly specified in the management system" (paragraph 4.11 [36]).

(b) "An integrated management system should provide a single framework for the arrangements and processes necessary to address all the goals of the organization.

These goals include safety, health, environmental, security, quality and economic elements and other considerations such as social responsibility" (paragraph 2.1 [44]).

(c) "A robust and effective management system should support the enhancement and improvement of safety culture and the achievement of high levels of safety performance. The management system should therefore be designed with these purposes in mind and should be implemented in such a way that it is known, understood and followed by all individuals" (paragraph 2.7 [44]).

In a medical establishment the management of safety must be an integral part of the caregiver's general management system, not a standalone system. Such a system also needs to cover knowledge management, i.e. the gathering, organizing, storing, searching and sharing of information within the organization, the information constituting the collective knowledge of the organization.

International standards for management systems are issued by the International Organization for Standardization (ISO) in the standards family ISO 9000. The standard ISO 9001:2015– Quality management systems–Requirements [45] specifies generic requirements for quality management systems applicable to any type of organization. Standard ISO 13485:2016– Medical devices — Quality management systems — Requirements for regulatory purposes [46] specifies requirements for the medical device sector (design, development, production, storage and distribution, installation, or servicing).

A management system in practices using radiation sources requires expertise to maintain and develop safety for workers, the general public and the environment. In practices with medical exposures, the safety of patients is an additional area to be covered by the management system and adding the need for further expertise.

An organization performing radiotherapy with ions requires as a minimum the following experts:

- Radiation protection officer;
- Medical physicists;
- Chief technical officer;
- Service engineers;
- Medical (radiation) oncologists;
- Radiation therapy technicians (or radiotherapy oncology nurses);
- Facility manager;
- Training and education officer;
- Regulatory affairs officer (interface with the regulatory body).

5.2.17. Radiation measurements and monitoring

5.2.17.1. Radiation survey of new ion radiotherapy facilities

Managing radiation risk is the key responsibility of the facility's radiation protection officer. Prior to authorization, the radiation protection officer ensures that radiation safety measures are applied, verified and documented throughout the entire machine installation, testing, commissioning and application of clinical processes.

The following radiation safety measurements are recommended during the machine installation and testing phase:

— *Initial construction site survey.* The radiation protection officer performs an initial background survey for the construction site. This will serve as the necessary baseline radiation level prior to the installation.
— *Receiving survey.* Some of components of ion radiotherapy equipment, such as the cyclotron, may have gone through extensive radiation testing in the factory. The component may emit considerable residual activation radiation on arrival at the facility site after shipment from the factory. It will be useful to perform an arrival radiation survey to verify that there is no unexpected contamination requiring measures to protect installation workers.
— *Radiation survey since the accelerator RF unit generates X rays.* A radiation survey needs to be performed during first powering on of the unit.
— *Initial radiation survey when beam-on accelerator testing starts.* To protect construction workers and avoid unexpected shielding issues, the radiation protection officer must perform an initial survey to verify no unexpected radiation leakage in the accelerator shielding construction. The officer also ensures that proper radiation signage and access control are established to protect nearby construction workers. A radiation survey also needs to be performed for each treatment bunker shielding when the particle beam is first delivered to a treatment bunker.
— *Radiation protection training:* The radiation safety officer gives basic radiation protection training to construction workers and facility workers so that they can understand the risks associated with radiation exposure, the meaning of radiation signs, and access control policy. This will create a safe radiation environment for the construction site.
— *Comprehensive facility room shielding survey:* The radiation protection officer's duties include assisting the regulator in performing a comprehensive shielding survey when the facility is ready for acceptance testing. Successful validation of facility shielding design is required before the facility is authorized for patient treatment. In multi-treatment bunker configurations, one or two treatment bunkers may be released earlier than the rest. A radiation survey needs to be performed prior to acceptance testing for each new treatment bunker. Special attention must be paid when patients are treated in one or more bunkers while other nearby rooms are still under construction or undergoing beam commissioning.

5.2.17.2. Survey meters

In ion radiotherapy facilities, both photon (activation gamma rays) and neutron radiation exist and are subject to the evaluation. Appropriate survey meters have been designed for various types of radiation and ranges of energies. For photon radiation surveys, pressurized ion chamber survey meters are most commonly used. These are like those used for radiation surveys in photon radiotherapy facilities.

Neutron dose surveys are complicated by the higher energy spectrum of neutrons compared with what is found in high energy photon therapy facilities. Depending on the highest ion beam energy and particle loss in the materials, neutron energy spectrums could be different for different particle beams or shielding designs.

Bonner sphere type survey instruments have been widely used for detecting thermal neutrons. However, the energy response of this type of detector falls off when neutron energies are higher than 10 MeV. Andersson–Braun type monitors use a heavy metal layer (tungsten or lead) to provide additional slowing down of the fast neutrons. This extends the useful range to the GeV region [47]. The Wide Energy Neutron Detector Instrument (WENDI) detector (Thermo Fischer Scientific, Waltham, MA; Model: FHT 762 Wendi-2) is of this type.

The above listed detectors are typically large and heavy. Another option for a portable survey meter is a device based on recoil proton detection. The PRESCILA detector [48] uses an array of ZnS(Ag) scintillators coupled to a side view bi-alkali photomultiplier tube. This device is much smaller and lighter than the WENDI-2, but its upper energy response is limited to ∼100 MeV. This energy response is considered enough for most proton therapy facilities where the maximum beam energy is usually limited to 250 MeV or lower. However, neutron production above 100 MeV may be substantial in facilities accelerating heavy ions to typical energies of 400 MeV per nucleon.

While ionization chamber calibration can be easily done in calibration laboratories, the calibration of neutron survey meters may not be so easy. Energy calibration of neutron survey meters is usually performed at lower energies. In practice, an ^{241}Am–Be or a ^{252}Cf source producing neutrons with a mean energy of ∼4 MeV is often used for calibration. The sensitivity of the WENDI detector is ∼0.84 counts/s μSv^{-1} h^{-1} measured with a ^{252}Cf source. The PRESCILA detector has a sensitivity of ∼0.58 counts/s μSv^{-1} h^{-1} measured with an ^{241}Am–Be source. There is no easy calibration method at high energies. The manufacturer's recommendation of energy response of the neutron survey meter is usually assumed.

5.2.17.3. Personal dose monitoring

Radiation workers, such as therapists and sometimes radiation oncologists in immediate contact with patients, will be inevitably exposed to radiation arising from a small amount of residual tissue activation in the patient's body immediately after the completion of a fraction of ion therapy treatment. Therapists are usually near the patient and assist the patient to get off the treatment couch. When beam apertures are used in scatter or uniform scanning based treatment modes, therapists or physicists who perform patient quality assurance measurements may touch the brass aperture after irradiation. Brass apertures used for beam collimation typically produce activation radiation. After their use, brass apertures are moved to a storage location for approximately four months or longer before shipping out for disposal. Radiation survey is performed for these used brass apertures. If the residual radiation is still high, the device is stored longer. Handling of low level radiation activated materials, such as brass aperture or patients, will require facility workers to wear personal dose monitoring devices.

Other treatment accessories, such as the range shifter, will emit some residual activation radiation as well. Physicists working on quality assurance measurements or service engineers performing maintenance around the beamline, accelerator, nozzle, ion sources and other components susceptible to emit radiation need to wear their own personal dosimeters to monitor radiation exposure.

Typical personal dosimeters may be enough for most proton radiotherapy facilities. Films or thermoluminescent dosimeters (TLDs), or optically stimulated luminescent dosimeters (OSLD) are commonly used in the form of a radiation badge.

To monitor neutron dose, CR39 track etch detectors are commonly used as a component of a radiation badge. Versions of the CR39 are available to detect a range of thermal, intermediate and fast neutrons across the 0.25 eV–40 MeV energy range, with a dose measurement range from 200 μSv to 250 mSv. The drawback of CR39 track etch detectors is that they may be sensitive to radon.

Other methods to monitor neutron dose are discussed in ICRU Report 66 [49]. Albedo dosimeters (neutron measurement and equipment specific calibration are needed) are examples. monitoring personal neutron dose is generally recommended for light ion radiotherapy facilities. Personal dosimeters are usually pre-calibrated and normalized with a control badge that defines the background radiation.

5.2.17.4. Facility radiation monitoring

Personal dosimeters could be used for long term radiation monitoring of selected areas in the facility. Several facility monitoring badges can be placed in public waiting areas, treatment consoles, hallways, exit venting areas, or engineering work areas to provide additional environmental radiation dose monitoring.

Some facilities also install neutron monitors or gamma monitors in common treatment areas, which can provide additional information in high radiation areas. Several years of facility radiation monitoring data may be required as per the regulatory body in some States to ensure that the facility shielding design meets its protection specifications over time.

5.2.18. Radiation safety features

5.2.18.1. General

Comprehensive guidelines on radiation safety features in a radiotherapy facility can be found in Ref. [28]. This section covers some of important features applicable to an ion beam radiotherapy facility.

The establishment and operation of an ion beam radiotherapy facility require extensive measures for the protection of staff, patients, the general public and the environment from the harmful effects of ionizing radiation. An obvious measure is structural shielding barriers to limit exposure levels outside accelerator and treatment bunkers.

In addition to structural shielding, safe facility operation will require introduction of several safeguard systems, devices and routines to prevent unintentional exposure or unauthorized access to radiation sources.

The arrangements and operational routines for safety are built into the facility operator’s quality management system and need to undergo regular revision and quality assurance verification in accordance with an established programme.

5.2.18.2. Access control

This section covers essential, legally obligatory, safety features to be included in an ion radiotherapy facility before an operational licence can be issued.

Apart from protection of patient privacy and medical records, safe operation of an ion radiotherapy facility requires access control to prevent unintended exposure and to uphold the safekeeping for the equipment and the facility.

From a radiation protection point of view, access to supervised and controlled areas is limited to staff with enough knowledge of the risks and safety rules associated with entering the area. For areas such as the interior of the accelerator bunker, access is controlled preferably by a locking mechanism requiring keys, codes, cards or identification check system to grant access. Locking systems are usually not practical for access control to treatment bunkers as expeditious processing of patients is required to cope with the patient workload. The access policy and rules are usually well established and known to all personnel, including external workers.

The radiotherapy system and other radiation generating devices are predominantly controlled by software applications, and unauthorized operation is prevented by password protected user accounts.

Systems for access control are usually well documented and the personnel are trained on how to use them and on how to respond to unauthorized intrusion attempts. Access control methods, controlled areas and devices are specified, documented and included in the staff training. Requirements for granting authorization to persons are well defined. Identity control of authorized personnel can be achieved through such techniques as magnetic cards, passwords, retina, or fingerprint verification.

5.2.18.3. Beam interlock system

A beam interlock system has the purpose of limiting, preventing or interrupting the ion beam if one or more undesirable system conditions occur. These conditions are monitored by a series of control and steering devices, each triggering a beam interlock if monitored conditions are outside specified limits. Depending on the conditions that trigger an interlock, the beam generation may be interlocked completely, or it may only necessitate an interlock preventing the beam to be fed to a single treatment bunker.

Some interlock states can be overridden through acknowledgment by an authorized person, generally a medical physicist or a service engineer. Others may need remedial actions to be taken to enable continued operation. The measures needed to override an interlock depends on the potential consequences of operation under the conditions triggering the interlock in the first place. Regardless, documentation of overridden interlocks is a good practice. A checklist could be used to ensure no overridden interlocks exist during normal patient treatment mode.

Examples of what is normally included in a beam interlock system and conditions that would trigger an interlock are as follows:

- Pressing an emergency stop button;
- Dose rate monitor levels exceeding tolerance levels;
- Violation of environmental conditions that are signaled by the building management system (e.g. unstable power supply, temperature fluctuation);
- Open doors to treatment or accelerator bunkers;
- Visual bunker inspection (last man out) has not been acknowledged;
- Beam monitoring parameters out of tolerance ranges;

— Beam stop settings from treatment plan are reached (monitored dose, number of delivered monitor units, beam on time).

Guidance on the design of interlock systems can be found in Ref. [50].

5.2.18.4. Door interlocks

The purpose of a door interlock is to prevent entry to accelerator and treatment bunkers, or other supervised and controlled areas, during exposure. If the entrance door to a bunker is a shielding barrier, a door interlock will also prevent a possibility of radiation straying to unrestricted areas during active beam generation.

If physical doors are used at bunker entrances, door status is normally monitored by magnetic or optical sensors that trigger a beam delivery interlock. Depending on national legislation, a physical bunker entrance door may not be required if adequate shielding is maintained by shielding mazes. In this case a 'door interlock' can be designed as an entrance 'light curtain', with optical sensors triggering an interlock if the curtain light is intercepted.

Activation of a door interlock does not affect the entire beam generating system, unless necessary. Door interlocks only affect relevant parts of the system, e.g. beam delivery to a single treatment room.

5.2.18.5. Emergency stop and last person out buttons

An adequate number of emergency stop buttons are needed at strategic positions in treatment bunkers, control rooms and in accelerator and beamline areas. The placement of buttons allows quick and easy access from all positions in the rooms and bunkers. The button placement needs to be clearly marked with signs, which are visible in the dark. With the door interlock system, emergency breaker activation usually only affects the relevant beam generating circuits (not the entire system), unless necessary.

It is important to ensure that no person is unintentionally left behind in an elevated dose rate area during beam generation or delivery. Cameras can be used to monitor areas, but they are prone to damage from extensive neutron exposure. Also, full camera coverage of all relevant areas is often impossible.

'Last person out' buttons are used to ensure the treatment room is clear before the radiation is turned on. The last person out action means that an assigned person, being the last one leaving the area, performs a visual inspection of the area before exiting it. Upon leaving the area, the last person out button (or its equivalent) is activated to acknowledge completion of visual inspection and to deactivate the last person out interlock. A good routine is to connect the last person out to an optical and/or acoustic alarm, indicating that exposure is imminent. The last person out inspection is primarily intended to ensure that no person is left in the area, except for the patient in a treatment bunker, before exposure commences.

During the inspection it is also a good practice to pay attention to any abnormalities in the area, such as unexpected odours and noises that could indicate system faults. The inspection is conducted in accordance with an established strict protocol, including well defined check points. One or more acknowledgement buttons may be necessary depending on the complexity of the area to cover.

The access protection can be implemented by optical interlocks, by doors, or shielding doors in combination with electrical contacts and safety circuits. Motion detectors can also be used to ensure that no one except the patient is left in the treatment room or to monitor other sensitive areas of the facility.

Specific safety features that are required (on the equipment and in the facility) are often specified in local regulations.

5.2.18.6. Optical warning signals

Entrance points to the supervised and controlled areas are equipped with warning lights indicating ongoing or imminent exposure. For controlled areas, a three step ramp light is recommended, with the steps indicating [28]:

- *Status 1 (green):* Indicates that there is power to the accelerator system and that the area can be access by authorized persons without restrictions.
- *Status 2 (yellow):* Indicates that beam generation is pending and imminent, and area restricted access is permitted for authorized persons only.
- *Status 3 (red or flashing red):* Indicates that access is prohibited due to ongoing beam generation.

5.2.18.7. Warning signs

Entrance points to controlled areas is clearly marked with signs displaying the area classification (restricted, controlled or supervised). The radiation sources in the area and access limitations are marked with approved appropriate symbols of radiation warning. Supervised area entrance points display an approved sign corresponding to the risks associated with the area.

5.2.18.8. Radiation monitoring

At least initial monitoring of radiation levels is required when the facility starts operations. If it is mandatory in national regulations a continuous monitoring may be required. The following means of monitoring are usually applied:

- Neutron radiation monitors, as needed.
- Radioactive emission monitors/sampling.
- Constant monitoring of radiation in the cyclotron/synchrotron room.
- Constant monitoring of radiation in the vicinity of the energy degrader.
- Required sampling measurements over selected time using passive dosimeters placed at selected locations.
- Monitoring of devices producing X rays (RFQ, linac structures, septa for injection and extraction of proton or ion beam).
- Monitoring of X ray production at the ion source (pre-acceleration area).

5.2.18.9. Patient surveillance and position monitoring

Reference [28] (Section 3.7. Patient Observation and Communication) states that when radiotherapy is performed, it should be possible for the operator to observe the patient from the operating station. Cameras are normally installed in patient treatment room to monitor patients

during treatment. A voice communication system facilitates communications between patients and therapy operators.

Correct patient positioning must be verified before treatment is commenced. This can be accomplished by using gantry integrated onboard X ray imaging systems or patient surface scanning systems. The latter is an example of a system that can be used for continuous monitoring of patient movements during treatment, allowing for automatic beam halt if deviation from a preset position occurs. Internal organ or target structure movements can be monitored during treatment by various tracking methods, including implanted RF transmitters, or controlled by using respiratory gating systems.

5.2.18.10. Occupational dose monitoring

There is usually a requirement for active (direct reading) personal dosimeters for the medical personnel working in the treatment room, for service personnel, and any other staff working in the vicinity of the equipment.

For occupationally exposed persons, individual dose needs to be ascertained. The individual dose determination can be carried out by means of passive dosimeters, for example with a combination of ^{6}Li and ^{7}Li TLDs. Medical personnel can work in an irradiation room only if a stationary dose monitoring system has been installed and does not detect any increased dose values in the room.

Another option for individual dose determination is that the medical staff wear active, directly readable, dosimeters when working in a treatment room and its vicinity. Any higher dose levels that occur are duly recorded and documented, even if they are below the dose limits.

In addition to the passive dosimeters, it is recommended that service or maintenance personnel wear active, directly readable, personal dosimeters for activities in the vicinity of the accelerator system. Locally high dose rates may occur near certain parts of the system that are usually defined and marked with caution/warning signs.

These parts, for example, include devices producing X ray radiation (RFQ, linac structures, septa for injection and extraction of proton, or ion beam). X rays are also produced at the ion sources (pre-acceleration before the linac).

5.2.19. Equipment design safety

5.2.19.1. Sagging of the gantry

Although ion beam gantries are extremely well engineered by the manufacturer, as a gantry rotates, the mechanical isocentre may change due to the design of the gantry. Therefore, the mechanical isocentre may be dependent on the gantry angle, and a lookup table is typically used to correct for the angle dependency to minimize the total isocentre deviation. Acceptance testing includes the requirement to confirm that the error corrections were properly applied so that true isocentric accuracy can be maintained within the specifications (typically < 1 mm in diameter).

5.2.19.2. Mechanical accuracy of patient positioning

Mechanical accuracy of the treatment is usually ensured through various types of patient positioning systems. The factors to be considered are: the maximum supporting weight of the treatment couch; gantry and couch rotation ranges; translational movement ranges of the couch;

gantry movement and rotation resolutions; the maximum speed, pitch and roll correction angle range; and accuracies of all related movements and accessories. These factors are usually subject to safety review. They may need to be reported to the regulatory body.

The operating environment for each subsystem is subject to analysis. The parameters commonly considered are the supply power conditions, ambient temperature, humidity and pressure range. The operating environment is ensured in accordance with the manufacturer's requirements. The external environmental and power conditions are taken into consideration when selecting and installing the equipment and designing the facility.

5.2.19.3. Applicable technical standards

A number of electrical medical devices are likely to be found in an ion radiotherapy clinic. Apart from equipment for therapy, examples of such equipment are a CT simulator, PET/CT, MRI, imaging devices for patient positioning, dose planning software, oncological information systems, and instrumentation for dosimetric measurements.

International standards applicable to such electrical medical equipment in an ion radiotherapy facility are issued by the International Electrotechnical Commission (IEC), Committee TC 62 and subcommittees SC62A, SC62B and SC62C. The following IEC standards are directly applicable to light ion therapy equipment:

- *IEC 60601-2-64:2014.* Requirements for the basic safety and essential performance of light ion beam medical electrical equipment [51];
- *IEC 60601-2-68:2014.* Particular requirements for the basic safety and essential performance of X ray based image guided radiotherapy equipment for use with electron accelerators, light ion beam therapy equipment and radionuclide beam therapy equipment [52];
- *IEC 62667:2017.* Medical light ion beam equipment — Performance characteristics [53].

International standards on quality management systems for organizations in general can be found in the ISO's standard, ISO 9001. ISO 13485 [46] is the international standard applicable specifically for organizations in the medical devices industry.

In addition to the international standards there are applicable regional and national standards. These standards are in some cases developed in cooperation with the IEC. An example are EN-IEC standards developed in collaboration between the European Standard Committee CENELEC and IEC.

5.2.19.4. National certification of the equipment

Most States have a regulatory framework for approval or certification of a medical device for it to enter the national healthcare market. For example, in Europe such an approval, in the form of a CE marking, grants the product access to the entire European Economic Area trade market by complying with regulations based on Council Directive 93/42/EEC [54]. Some States apply a two step certification process of certain medical equipment: equipment general design technical safety and subsequently its suitability for medical applications.

Some practical information can be found on the web sites of the: US Food and Drug Administration (FDA), specifically the Medical Device Section[3]; Health Canada Medical Devices[4]; and the Canadian Nuclear Safety Commission's Certification Requirements of Class II Prescribed Equipment as an example of the approach[5].

5.2.20. Acceptance of the ion radiotherapy system

Acceptance testing is a process to confirm that the vendor's equipment performance meets the original specifications defined in the purchase contract. Acceptance testing procedures are generally defined in the purchase contract well in advance of equipment installation. This allows for early mutual agreement on the protocol to be used for the acceptance testing and avoidance of delaying negotiations late in the installation process. Therefore, the goal of acceptance testing is to validate contractual specifications. Nevertheless, specifications are usually designed to ensure treatment accuracy and functionalities to ensure safe treatment. During the licensing process for an ion radiotherapy facility, regulatory review of acceptance testing results may be beneficial to understand the performance of the system. If certain parameters did not fully meet the original specification, conditional approval may be needed until conditions are resolved. Acceptance testing also demonstrates the functionalities of various components and works as an important stage for medical physicists and engineers to become familiar with the new therapy system.

Acceptance testing is normally conducted in cooperation with local medical physicists and vendor representatives (engineers) to ensure that both contract parties agree on proper test execution and test results. Also, certain tests require vendor's assistance (for example, using special tools). Another option, in order to maintain objectivity in the testing, is to contract an external third party to conduct the actual tests and review the test results against acceptance specifications. In all cases, physicist participation in the acceptance testing is to be viewed as mandatory to ensure proper competence in assessment of system functionality before commencing clinical commissioning.

It is recommended to begin the acceptance test when the equipment installation is at an 'advanced' stage to avoid re-testing due to succeeding equipment performance changes. Successful acceptance testing implies that the equipment and facility meet the original specification and can be handed over to the operator's technical staff (such as physicists) for further validation and for starting the clinical commissioning process.

Every vendor may have a different set of acceptance testing items. The following acceptance tests are considered core requirements for an ion radiotherapy facility:

— *Beam energies.* The maximum beam energy is verified in water phantom ionization measurements according to a previously agreed beam penetration definition. This is usually a Bragg peak curve measurement, where the distance from the water surface to the distal falloff range (80 or 90% from the Bragg peak) is usually defined as the (penetrating) beam energy. Similarly, the minimum beam energy is to be verified along with intermediate beam energies.

[3] https://www.fda.gov/medicaldevices/default.htm.
[4] https://www.canada.ca/en/health-canada/services/drugs-health-products/medical-devices.html.
[5] http://nuclearsafety.gc.ca/eng/nuclear-substances/licensing-class-II-nuclear-facilities-and-prescribed-equipment/certification-requirements-class-II-prescribed-equipment/index.cfm.

— *Adjustable beam energy.* The vendor demonstrates that the beam energy adjustment can be achieved either continuously or in discrete energy steps. The tolerance of the measured range could be different for different energies because sharper falloff is expected at lower energies than at high energies.

— *Energy spread of incoming pristine beam energy.* This parameter can be indirectly measured by the distal penumbra (80 to 20%) of a 'monoenergetic' beam. The typical energy spread is less than 1%.

— *Beam profile measurements.* This can be a predefined uniform treatment volume (Spread-out Bragg Peak, or SOBP) or a single pencil beam spot profile. The shape of the beam profile meets the specification for its uniformity (SOBP) or spot size (pencil beam). The measurement could be in water (for SOBP) or in air (for pencil beam spot size). For pencil beam spot, both spot size and shape, will be evaluated at both the central axis and selected off-axis locations.

— *Beam alignment or positioning accuracy.* The accuracy of beam alignment with the isocentre is measured. The beam alignment is demonstrated in a treatment gantry for selected beam energies. The gantry dependence is less than what is specified in the beam parameter specification. Subsequently, the imaging centre and beam centre alignment are evaluated.

— *Dose rate.* The dose delivery time is measured for treatment of a hypothetical volume with a 2 Gy uniform dose. A typically 10 cm × 10 cm × 10 cm target located approximately 15 cm in depth is used. A faster delivery implies a more efficient beam delivery design, which will improve treatment efficiency.

— *Monitor ion chamber linearity.* The monitor ion chamber controls the accuracy of dose delivery. It is important to use an independent ion chamber to evaluate monitor chamber linearity at different dose levels. The test needs to be repeated in two or more different gantry angles if possible.

— *Maximum field size.* The maximum treatable field size is demonstrated.

— *Beam stability.* Vendors need to demonstrate that the beam is stable over a period of time. This includes the output of the beam as well as the shape of the treatment field, none of which deviate from set specifications over time.

— *Dynamic treatment delivery.* If the ion radiotherapy system is provided with a gating feature, its function is tested under a known condition. Beam lagging is measured to understand the limitation of the gating function.

— *Effective source to axis distance.* An effective 'point' source location that can be used to approximate the inverse square law for output measurement.

— *Range shifter.* Range shifters are used to treat shallow tumours when the lowest energy cannot cover the proximal side of the tumour. Range shifters are evaluated for their mechanical integrity and measured for their nominal water equivalent thickness.

— *Gantry rotation assessment.* This includes the accuracy of the gantry angle indicator, the maximum speed of gantry rotation, the range of gantry rotation, as well as braking distance when an emergency stop button is pushed. The isocentre of the gantry rotation is evaluated. Sometimes the specification is to compare the radiation isocentre alignment at different gantry angles. Gantry sag may be compensated for by the treatment couch or the radiation beam at various gantry angles.

— *Patient positioning system and/or the robotic treatment couch.* These are evaluated for their accuracy of movement and rotation. The speed of the couch's movement is evaluated according to the IEC maximum allowed speed. The couch rotation isocentre

is aligned with the gantry rotation isocentre within the specified tolerance. In addition, couch weight tolerance is carefully evaluated without risking breakage due to stressing the system to its critical limits. Sometimes a weight compensation algorithm is implemented for the treatment couch, which could correct for sag or couch extension. The function of weight compensation is evaluated.

— *Imaging functions.* Imaging functions for patient positioning are tested. This includes various modes of imaging options: orthogonal X ray imaging, cone beam CT imaging, or any special software that can perform automatic image registration. Couch repositioning is tested for correcting setup errors, which includes both translational errors and rotational errors.
— *Laser alignment system.* Lasers are evaluated for their alignment with the beam isocentre and imaging isocentre. The level, or alignment, of the lasers at off-axis distance is evaluated (typically 20 cm from the isocentre).
— *Display of treatment status.* The function of hand pendants and displays is evaluated against the presented information, particularly when treatment accessories are inserted.
— *Safety interlocks.* Collision sensors are tested, laser guards are evaluated for their functions, door interlocks, 'last man out' inspection interlocks, and emergency stop buttons are tested for their functions. In addition, if a motion monitoring mechanism is installed, it is tested.
— *Video/audio communication.* These are evaluated and tested.
— *Treatment console functions.* Various treatment buttons are tested for their functions.
— *Signage.* Room status, radiation warning light, beam-on light, imaging in progress status, and similar function features are evaluated. Warning lights are installed in restricted areas.
— *Connectivity tests.* The treatment planning system (TPS) can send a Digital Imaging and Communications in Medicine–Radiotherapy (DICOM-RT) ion plan to the treatment management system to execute the planned treatment delivery.
— *Room switching time.* In multi-room configurations, the switching time from one room to the other is specified. This switching time demonstrates the efficiency of a multi-room system in sharing the same particle beam from a single accelerator.

Test results indicate that the machine is ready to perform specified functions within the defined tolerances. Acceptance testing represents a major milestone in facility handover to clinical operation. Successful clinical commissioning and facility acceptance will allow for patient treatment.

Unlike acceptance testing, which demonstrates the performance of therapy systems against preset specifications, clinical commissioning includes the preparation and validation of the treatment workflow, performance of the delivery system and the treatment planning system, etc. Staff training and competence will be established to ensure delivery of safe and effective patient treatment. A vital part of the clinical commissioning is the meticulous measurement of treatment beam characteristics and its integration in the TPS. The general definition of clinical commissioning is broad in nature, which reflects the 'readiness' for patient treatment. In general, clinical commissioning includes the categories detailed in Sections 5.2.20.1–5.2.20.7.

5.2.20.1. Workflow preparation for patient treatment

Workflow includes all steps to prepare patients for treatment, from referral justification to accurate delivery of the prescribed dose distribution to the patient. Radiation oncologists, and

possibly other referring physicians, need to learn how to identify patients who can benefit most from ion radiotherapy compared with the standard practice of photon therapy. Guidelines and routines for dose prescription and fractionation schemes (including the RBE in the ion beam) need to be prepared.

Appropriate immobilization devices are selected for ion radiotherapy to minimize the impact of setup errors and range uncertainties in the treatment plan. Dosimetrists and physicists need to learn how to design robust treatment plans that can achieve the prescribed target dose in the presence of uncertainties while minimizing doses to organs at risk. Staff education and training are essential for safe and effective ion radiotherapy. The regulatory body needs to assess that adequate competence is present within the clinical organization by reviewing credentials and training records for all personnel involved in the patient treatment process.

5.2.20.2. Equipment commissioning

Commissioning of equipment used for beam measurement or patient simulation is conducted primarily by medical physicists and generally includes the following tasks:

- *Simulation CT scanner.* The Hounsfield Unit (HU) is calibrated against the particle's stopping power ratio relative to water. Unfortunately for ion beams, the stopping power is not linearly proportional to the electron density. Additional tissue composition may be considered. A standard method is to use a stoichiometric calibration method described by Schneider et al. [55], which uses tissue substitute phantoms of known composition to derive the stopping power of real human tissues, based on human tissue composition published in ICRP Publication 23 [56] and ICRU Report 44 [57]. Peer review of this calibration result is important as there is no commercial software that can be easily used for this conversion.
- *Ion chambers that can be validated for ion beam measurement.* Several types of ion chambers can be used for absolute dose measurements. The recommended thimble or parallel plate chambers for absolute dose measurement are listed in Ref. [58]. In addition, there is a special large parallel chamber with a diameter exceeding 8 cm. This chamber is usually used for integral depth dose measurement in pencil beam scanning systems. Sometimes the TPS requires the measurement of total dose delivered to a plane at a depth. The large parallel plate chamber (a Bragg Peak chamber) is needed for this task. Chambers are validated before their first use. If the Bragg Peak chamber is still too small to measure the entire integral dose, correction factors are considered. Ionization chambers used for calibration are calibrated by accredited national labs for dosimetry services. Examples of instruments and equipment for beam dosimetry measurements can be found in Fig. 27.
- *Beam profile measurements.* Small ion chambers can be used in water to measure beam profiles for SOBP plans for a variety of field sizes. However, the latest pencil beam scanning techniques require in-air beam profile measurements of much higher spatial resolution. Considering that the smallest pencil beam could be as small as 2 mm, a scintillation/film based high resolution (2-D) detector is preferred. The resolution for pencil beam profile measurement is recommended to be at least 0.5 mm to maintain adequate special accuracy. Because the dose rate could be quite high, a high dynamic range detector/electrometer is preferred.
- *Patient dose measurement detectors.* Two dimensional dose measurement is frequently required for patient specific quality assurance as well as in the validation of treatment

planning dose calculation. Due to the high dose rate and large dynamic range, a 2-D ionization array detector is preferred.

— *Electrometers.* Electrometers are tested and calibrated. They are sent for calibration in accordance with local regulatory requirements and/or manufacturer's recommendations.

FIG. 27: Examples of equipment for ion beam dosimetry measurements: (a) water tank; (b) 2-D scintillation detector for high resolution measurement; (c) multi-layer ion chamber array for real-time central-axis depth dose measurement; (d) multi-layer large parallel plate chamber array for real-time integrated pencil beam dose measurement; (e) thimble ion chamber for dose calibration; (f) parallel plate chamber for dose calibration; (g) large parallel plate chamber for pencil beam scanning commissioning.

5.2.20.3. Dose calibration

The purpose of treatment beam dose calibration is to establish the relationship between beam-on time, as measured by the monitor unit (MU), and the dose determined in a reference point and under reference conditions (Gy/MU). Most centres use the protocol in Ref. [58] for absolute dose calibration for the reference point.

The selection of reference point is typically the centre of an SOBP plan (uniform dose delivered to a cubic target with a 10 cm × 10 cm × 10 cm volume). Some scatter or uniform scanning systems can directly produce the SOBP plan without going through a TPS.

However, for a pencil beam scanning system, the TPS needs to be commissioned before generating a SOBP plan for calibration. One convenient reference condition is to use a planar uniformly scanned monoenergetic pencil beam with fixed spot spacing. The reference

measurement point can be selected near the entrance region (at least 1 cm deeper in water) to minimize the uncertainties related to chamber calibration [58].

The absolute dose is a product of a chamber specific factor *(k_{Q,Q_0})*, a calibration factor *(N_{D,w,Q_0})* and the corrected measurement *(M_Q)* of dose in the reference point under reference conditions:

$$D_{w,Q} = M_Q \cdot N_{D,w,Q_0} \cdot k_{Q,Q_0}$$

The raw measurement is corrected for temperature and pressure ($k_{t,p}$), ionic recombination (k_s), polarity effect (k_{pol}) and the electrometer factor (k_{elec}) to yield the corrected measurement M_Q.

The calculated dose by the TPS in the reference point is set identical to the measured dose. To be able to repeat the calibration reference conditions, all measurement equipment is listed in the calibration report along with their calibration records. The calibration factors for carbon ion beams are adapted to the higher stopping power of carbon ions in comparison to protons.

Although the equipment for both ion types can be the same, it is taken into account that beside the ion type specific calibration factors the lateral scattering of protons, particularly with lower energies, is higher than for heavier particles; the proton beam is altered by the dosimetry system (lateral width is higher).

5.2.20.4. Commissioning of the TPS

Commissioning of a TPS is a major effort in commissioning. This task is usually done by the medical physicist and requires several weeks or several months of effort.

Each TPS vendor gives an introduction on what data measurements are required for beam modelling in the TPS. The users follow the instructions for beam measurement. For example, a pencil beam algorithm requires the measurement of

- Integral depth dose curve for every 10 MeV monoenergetic beam;
- Relative dose output at a fixed depth for the same number of MUs for a large uniformly scanned beam pattern;
- In-air spot profile at isocentre and two other distances away from the isocentre;
- For each range shifter, additional in-air spot profiles are measured at the isocentre and two additional distances away from the isocentre.

There are specific instructions and training for adjusting the parameters used in pencil beam dose calculation algorithms. The training for commissioning of the treatment planning algorithm is usually specific to the vendor and the technology implemented (such as scatter or pencil beam scanning). Vendors will provide clear instruction for the configuration of parameters in the TPS. When fitting parameters, it is usually a semi-automatic process to find the best set of parameters that will match with the measurement data.

Additional measurements can be acquired to supplement the parameter tuning process or to provide independent validation of the TPS calculation. Eventually, the performance of the TPS commissioning is compared between the dose measurement and TPS dose calculation for a number of test plans that may resemble the real patient treatment plans.

The average dose agreement is better than 1%, with variations not exceeding 2% for measurements conducted in uniform phantoms or a water tank. Dose distributions can be measured using 2-D detectors. The results are generally better than passing a gamma indicator of 3 mm/3% over 95% of the measurement points.

The test plans are generated based on clinical situations that cover a number of realistic patient treatment cases.

5.2.20.5. Relative biological effectiveness

The RBE is a unique parameter for ion radiotherapy. Charged particle beams such as carbon ions have a relatively high linear energy transfer (LET) when interacting with human tissue (relative to X rays). The concept of relative biological effectiveness is introduced to account for the increased efficiency of high LET radiation in eradicating tumour cells. RBE is defined as being relative to absorbed dose measurement (using, for example, ^{60}Co gamma ray irradiation). The clinical use of an RBE of 1.1 for proton beams has been well supported by a number of clinical studies [59] [60].

For heavy ion radiotherapy, the RBE is quite complex and requires a model based approach. For example, for carbon radiotherapy the modeling is integrated into the TPS. The validation of the RBE model is usually done in hypothetical test cases.

5.2.20.6. End to end tests

The last step of commissioning is to evaluate the entire treatment process. An end to end test is performed by scanning a phantom through the CT simulator, perform treatment planning using imaging tools to set up the phantom for treatment, and finally deliver the treatment plan to the phantom. This type of end to end test has the purpose of validating the entire treatment process, including data transfer and imaging for patient setup. Use Case (a methodology to identify, clarify, and organize system requirements) is designed for different clinical situations, for example a couch-kick is designed to check if image guidance can work effectively with the treatment couch rotated. End to end tests also help to familiarize therapists with the machine setup process.

5.2.20.7. Independent validation

Because dose calibration is the most critical part of the commissioning process, it is strongly recommended that an independent physicist performs a measurement. This will further support the validation of dose calibration.

The final clinical commissioning report is reviewed by the regulator to evaluate the performance of the TPS, as well as the important dose calibration result. The regulator can request explanation if any significant discrepancies in the beam data are noticed.

5.2.21. Equipment quality assurance

The last step in commissioning and before the first patient treatment is to establish a machine quality assurance programme. This programme is best established immediately after the commissioning of the TPS because baseline performance metrics can be established to simplify subsequent quality assurance measurements. In most situations, a repeat of baseline measurements is a simple way to verify there is no change from the status when the machine was initially commissioned. A repeat of the commissioning measurements would significantly

increase the workload. A quality assurance programme needs to be designed based on potential risks of changes in beam characteristics as well as the potential clinical impact.

A typical radiotherapy programme requires daily quality assurance for evaluating common dosimetric parameters. Daily quality assurance is typically performed by therapists as the first task in the morning before treating the first patient. Alternatively, medical physicists or physicist assistants under the supervision of a qualified medical physicist can also perform the daily quality assurance measurement. Weekly or monthly quality assurance programmes will evaluate additional aspects of machine performance to ensure it has not changed since its initial commissioning.

A quality assurance programme typically includes, but need not be limited to, the following checks:

- Dose output measurement;
- Beam energy or beam penetration evaluation;
- Uniformity of dose delivery;
- Beam delivery accuracy (field edge accuracy or spot position accuracy);
- Radiation to imaging isocentre coincidence;
- Radiation isocentre to laser line coincidence;
- Door interlock;
- Accessory interlocks;
- Emergency stop button or/and collision sensor interlocks;
- Audiovisual functionality assessment;
- Backup dose monitor functionality (if equipped).

An essential part of a daily quality assurance procedure is equipment handover from the vendor's on-site service team to the clinical treatment personnel before patient treatments commence. Due to late shift service and maintenance, there may be many changes during the previous night. It is a good practice to have a checklist to restore the normal clinical treatment mode, confirm that no interlocks have been bypassed due to service intervention, and give the medical physicist a list of serviced items completed during the last shift. This will help troubleshooting when unexpected events occur during regular operation. The morning handover checklist is prepared by the vendor's service team and signed by both the service team and the early shift medical physicist after mutual approval.

Written routines for the quality assurance procedure must be established by the operator, preferably in collaboration with the equipment vendor(s), and at least state:

- Equipment (e.g. measuring devices, evaluation software) used for measurement;
- Parameters to be measured or checked, together with corresponding acceptable tolerances (examples are given in Tables 4–7);
- Measurement/check intervals;
- Methods for ensuring proper calibration and functionality of measuring devices prior to performing the measurements;
- Personnel qualified to perform the daily quality assurance measurement;
- Procedures for reporting deviant quality assurance results;

— Personnel qualified to evaluate the results of the daily quality assurance measurements and decide on actions in case of deviant results.

Tables 4–7 list recommended check parameters and associated tolerance levels for safe operation.

TABLE 4. DAILY QUALITY ASSURANCE: EXAMPLE OF CHECK PARAMETERS AND ASSOCIATED TOLERANCE VALUES

Category	Quality assurance item	Tolerances
Dosimetry	Proton output constancy	3%
	Proton range	1.0 mm
Mechanical/imaging	Laser localization	1.5 mm
	Imaging treatment coincidence	1 mm
	Robotic couch positioning	1 mm
	Collision interlocks	Functional
Safety	Door interlock	Functional
	Beam-on/X-ray-on indicators	Functional
	Audiovisual monitors	Functional
	Bunker clearance procedure	Functional

TABLE 5. WEEKLY QUALITY ASSURANCE: EXAMPLE OF CHECK PARAMETERS AND ASSOCIATED TOLERANCE VALUES

Category	Quality assurance item	Tolerances
Proton spot constancy	Proton spot size	1 mm
	Proton spot position	1 mm
	Proton spot shape	10% of spot sigma
	Gantry dependency	10% of baseline

TABLE 6. MONTHLY QUALITY ASSURANCE: EXAMPLE OF CHECK PARAMETERS AND ASSOCIATED TOLERANCE VALUES

Category	Quality assurance item	Tolerances
Dosimetry	Proton output constancy	2%
	Backup monitor constancy	2%
	Proton profile constancy	2% or 1 mm

	Proton range constancy	1 mm
Mechanical	Lasers coincident at isocentre	1.5 mm
	Laser coincident at 20 cm from isocentre	2 mm
	Gantry indicators at cardinal angles	0.5°
	Treatment couch position accuracy	1 mm/0.5°
	Latch/interlock for range shifter	Functional
Safety	Door interlock	Functional
	Door closing safety	Functional
	Audiovisual monitors	Functional
	Radiation area monitor	Functional
	Beam-on/X-ray-on indicators	Functional
Imaging	Imaging and radiation coincidence	1 mm
	Scaling	1 mm
	Spatial resolution	Baseline
	Contrast	Baseline
	Uniformity and noise	Baseline
	Dead pixels, artifacts, etc.	Baseline

TABLE 7. ANNUAL QUALITY ASSURANCE: EXAMPLE OF CHECK PARAMETERS AND ASSOCIATED TOLERANCE VALUES [57]

Category	Quality assurance item	Tolerances
Dosimetry	Dose calibration from Ref. [58]	1%
	Gantry dependency of dose output	2%
	Relative dose output for the same MU at different beam energies	1% from baseline
	Beam penetration and distal penumbra measurements in water tank	1% or 1 mm
	Spot size measurement	5% from baseline
	Spot position accuracy (both at isocentre and off-axis)	1 mm
	Accuracy of SOBP for passive scatter beamline	1 mm/2%

	External audit of dose output	5%
Mechanical	Gantry star shot	1 mm
	Couch star shot	1 mm
	Gantry indicators at cardinal angles	0.5°
	Treatment couch positioning accuracy	1 mm/0.5°
	Couch rotation accuracies	0.5°
	Snout travel accuracy	2 mm
	Mechanical integrity of range shifters	No change
Cross-validation of daily quality assurance and monthly quality assurance	Repeat daily quality assurance	1% of baseline
	Repeat safety checks	Functional
	Trend analysis for daily quality assurance	No suspicious changes
	Trend analysis for monthly quality assurance	No suspicious changes
Imaging	kV image quality measurement	Match baseline
	CBCT image quality measurement	Match baseline
	End to end test of CT imaging of materials with known proton stopping power in TPS	Match expected results
	Contrast	baseline

5.2.22. Equipment maintenance

Ion radiotherapy facilities house technically complex equipment producing, transporting and delivering particle beams for cancer treatment. Such facilities normally also include imaging modalities such as CT and MRI and possibly even multimodality equipment, e.g. PET/CT.

Service and maintenance of the imaging modality equipment is often supplied via vendor contracts included in the equipment procurement process. Contracts usually include one or more preventive maintenance visits a year and remedial service within an agreed response time. Some clinics might also have employed service engineers capable of performing first line service on the equipment.

Due to the complexity of an accelerator system for ion radiotherapy, system performance monitoring and steering require a team of engineers with a high degree of system specific competence. Performance checks and planned maintenance are often performed during evenings and nights to not interfere with clinical operation. Maintaining this kind of around the clock competence is usually not feasible for most authorized parties. Instead, the most common solution is to contract the vendor or other dedicated service organization to station a service team at the facility. Apart from contracted service providers, some providers of ion radiotherapy

will likely have employed local service engineers involved in the maintenance and servicing of parts of the ion therapy system to some extent. In general, ion radiotherapy facilities are likely to have equipment for medical exposures from several suppliers/manufacturers and several service organizations will maintain and service this equipment.

To ensure proper equipment operation and timely delivery of service, great effort needs to be devoted to the clarification of the accountability for and between the parties involved. This is clear from signed contracts with the service organizations and from the authorized party's management system for safety. Strict handover routines need to be in place for returning equipment and software systems from maintenance and service to clinical operation.

The service provider and the facility operator agree on performance tests to be conducted after servicing. The facility operators assign responsibility to staff with enough competence to decide, based on the results of performance tests, whether the equipment is ready for clinical use.

5.2.22.1. Service staff qualification

Staff authorized to perform maintenance and service on radiotherapy equipment and related systems are usually trained by the equipment manufacturer. The minimum education and skills requirements are determined by the complexity of the activities that a service person is authorized to undertake. Ion therapy equipment involves mechanical components, electronic circuits, RF components, vacuum, imaging devices, radiation detectors, etc. Staff with a wide range of technical experience are preferred, in addition to interpersonal communication skills with on-site, non-technical medical staff. Modern equipment often uses microcomputer controllers, so familiarity with control systems, testing equipment, and testing procedures are preferred. Because there are only a few ion radiotherapy equipment manufacturers in the world, standardization in training, credentialing, and licensing of service staff are currently lacking. The curriculum of the service personnel knowledge and experience is usually developed by the specific manufacturers. The credentials of service personnel include manufacturer's training certificates in specific areas of expertise and prior working experience, among other things.

5.2.23. Decommissioning and facility closure

In the early stages of authorization for the establishment of a facility, applicants present a decommissioning plan to the regulator for review and assessment. Some States may require non-publicly financed facility operators to present, to the regulatory body, measures to secure financial guarantees for future decommissioning.

The planning and design for the construction of the facility is accomplished without compromising the radiation protection of people and the environment, while seeking to ease the effort needed for future decommissioning of the facility. This can be done by carefully choosing shielding materials that reduce activation, especially at depth. If activation induced radioactive matter is limited mainly to removable superficial construction layers, demolition and exemption clearance procedures can be greatly simplified. The decommissioning plan is not a static document, but rather should be revised during the authorization process and clinical operations to reflect the consequences of facility operations on the future decommissioning (paragraph 7.5 of Ref. [61]). The plan also needs to be adaptable whether the facility is demolished or used for other activities after decommissioning.

The decommissioning of an ion beam therapy facility, or parts of it, is a subject of yet another regulatory authorization step, requiring the facility operator to apply for authorization to start

the decommissioning. Decommissioning is normally planned and conducted in close cooperation between the licensee and the regulatory body. It will in most cases include regular on-site inspections by the regulator to assess compliance with the licensee's decommissioning plan. The plan must make clear the methods for exemption clearance, as well as how material with activity levels exceeding the exemption limits is to be handled, transported and deposited.

6. INSPECTIONS

This section focuses mainly on planned and announced inspections as part of the regulatory body's inspection plan. Inspections can also be reactive in response to an event. In reactive inspections, the possibility of planning and preparing the inspection is limited and they usually have to be adapted to the situation.

In the early stage, and throughout the authorization of facilities and activities, especially for complex facilitates for ion radiotherapy, focused pre-authorization inspections are a natural and necessary element of the regulatory safety assessment. The extent of such inspections can vary depending on the phase of the authorization. The frequency may also vary depending on the facility's complexity and the speed with which the project progresses. Such pre-authorization inspections include radiation surveys at significant phases of equipment installation and test operation. The surveys are conducted in cooperation with the applicant, equipment vendors and, if necessary, the facility constructors. What is described in this section is broadly applicable to pre-authorization inspection. Certain parts of the planning, preparation, performance and follow-up of inspections may not be possible or even necessary during pre-authorization inspections.

6.1. PLANNING INSPECTIONS

The frequency and extent of regulatory inspections are included in the management system of the regulatory body. A time schedule for planned inspections need to be in place and cover at least the next 12 months, preferably longer. The frequency of inspections is decided in relation to the complexity and safety risk from operation of an ion radiotherapy facility. In some States the frequency of inspections could be regulated in national legislation.

Planned, announced inspections can be publicized in time to allow for the authorized party to compile the information requested for review and assessment. The announcement can be in writing and addressed to the signatory of the authorized party. It would specify what and when safety related information need to be submitted to the regulatory body. It also informs the authorized party regarding the officers, managers and employees to be interviewed during the on-site inspection visit. The names of the persons to be interviewed must be submitted to the regulatory body at least a few days in advance of the on-site visit.

If external expertise is needed for the inspection, the regulatory body may recruit an external expert in advance of the announcement. Depending on the extent of the inspection, the requested information is submitted well in time for the assigned regulatory officer(s) to conduct a proper review and assessment of the safety related information received.

Planning of inspections includes the establishment of a documented plan for each inspection, including the topics for review and assessment as well as relevant regulatory requirements commensurate with the extent and scope of the inspection. Examples of topics and items for review and assessment are given in Refs [4] [62].

6.2. PREPARING FOR AN INSPECTION

In preparation for an inspection, the regulatory officers assigned for the task closely review and assess the requested safety information submitted by the authorized party. Observations and preliminary findings are documented in a report or in a checklist and the observations are used to help draft questions for interviews during the on-site inspection visit.

It is recommended that the inspectors prepare a checklist (if one has not already been prepared) for the on-site inspection. This allows for the systematic and effective conduct of the inspection, eliminating the risk of overseeing important features to be checked [62]. Such a checklist can also be a part of a general inspection checklist covering all the topics and inspection items being included for review and assessment.

Preparation also includes instruments and items to bring to the on-site inspection. These may include [4]:

- Personal dosimeters;
- Appropriate survey meters or other necessary measuring equipment;
- Safety equipment, such as high visibility clothing, safety shoes and hard hats;
- A camera for documentation.

At least two regulatory officers are recommended to attend the inspection. This will allow for one officer to ask question during interviews and the other to take notes. It is encouraged to include regulatory officers with different expertise in the inspection, e.g. behavioural scientists for safety culture and human, technological and organizational factors. If necessary, external experts might be engaged in the inspections [4].

Before the on-site visit to the ion radiotherapy facility, the inspection officers make sure that the authorized party reserve suitable rooms for interviews as well as privacy for the officers to discuss and document their observations. Other actions for preparation include [4] [62]:

- Reviewing the licence and radiation protection programme;
- Examining previous inspection reports;
- Reviewing past correspondence between the regulatory body and the authorized party relating to the inspection area;
- Noting the status of any allegations or incidents;
- Analyzing the response to previous items of non-compliance, noting items marked for follow-up during this inspection and looking at past violations;
- Identifying unresolved issues from the last inspection.
- Reviewing feedback relating to the inspection.

6.3. PERFORMING AN INSPECTION

Each regulatory officer attending an on-site inspection needs to be able to prove to the authorized party his or her identity and position as a regulatory officer. IAEA Member States have agreed on the requirements for inspections, including making provision for free access to facilities for inspection purposes (paragraph 4.52 [6]).

An inspection includes an entrance meeting where the authorized party is informed of the inspection objectives and the practical matters of the on-site inspection. It is usually emphasized that the inspection team will, to the extent consistent with the objectives of the inspection, guard the integrity of individual workers in the resulting inspection report. The inspection ends with an exit meeting where the authorized party is briefed on the preliminary findings of the visit, and informed on how the inspection process proceeds and on the process for any enforcement actions as a result of the inspection.

On-site inspections incorporate one or more of the following methods [4]:

- Monitoring and direct observation (such as of working practices and equipment);
- Discussions and interviews with personnel of the authorized party and of the contractor, if necessary;
- Examination of procedures, records and documentation;
- Confirmatory tests and measurements.

Discussions and interviews need not be limited to the pre-announced persons. They can include any worker present during the inspection, if it is found necessary and suitable for the purpose of assessing compliance with regulatory requirements and with the authorized party's internal routines. Examples of procedures, records and documentation for assessment during inspections include spot checks of [4]:

- Procedures and schedules for maintenance and testing;
- Quality assurance records;
- Test results and data;
- Operational and maintenance records, and results of workplace monitoring;
- Records of deficiencies and incidents;
- Modification records, including records of modifications to management and operating procedures;
- Training records;
- Dose records.

6.4. RECORDING INSPECTION FINDINGS

Inspection observations and findings are documented and compiled by the inspection team in a report which refers to documents received from the authorized party and clearly state and describe assessed non-compliance with regulatory requirements and conditions related to the authorization of the inspected activity. Approval of the report is performed in accordance with routines in the regulatory body's management system. Care must be taken to avoid exposing individual workers in the report. An example of the typical contents of a report is found in paragraph 3.286 of Ref. [4].

All documents (paper and electronic) received from the authorized party during the inspection are stored by the regulatory body in a document management system allowing easy access. Relevant verbal communication between inspectors and the authorized party are documented in writing and stored in the document management system.

6.5. COMMUNICATION OF INSPECTION RESULTS

A good practice is to forward the report with the observations of the inspectors to the authorized party for review before the conclusion on findings. This will prevent misunderstandings and factual errors and increase the acceptance of any enforcement decisions resulting from legal non-compliances identified in the inspection. The actual findings are usually not included for review.

The final, approved inspection report is shared with the authorized party and be accompanied by any decisions on enforcement actions in response to non-compliance findings from the inspection. In some Member States, documents become legally public as soon as they are received or dispatched by the regulatory body, except for information classified in accordance with national confidentiality regulation.

6.6. INSPECTION FOLLOW-UP

Regulatory injunctions on actions in response to findings of non-compliances are followed up by the regulatory body. Once the actions are conducted in a satisfactory manner, the inspection case can be closed. The follow-up can differ significantly depending on the type of corrective action enforced on the authorized party. Some findings might result in a straightforward petition to submit missing documentation and can easily be closed on approval of the submitted material. Other findings may lead to the regulatory body requesting the authorized party to perform and present a root cause analysis and establish a plan for corrective measures. The implementation of such measures can be confirmed preferably through focused follow-up inspections.

It is recommended that inspection results and experiences are compiled on a regular basis to allow for improvement of the inspection process and to identify non-compliance with regulatory requirements. Such trends can function as useful input in the establishment of plans for upcoming inspections.

7. REGULATORY DECISIONS

Regulatory control of facilities and activities includes authorization, inspection and enforcement. These regulatory tasks inevitably lead to regulatory decisions on, for example, issuing a licence, refusal of the application, or enforcement actions.

The power to make such decisions is expected to be clear from the management system of the regulatory body. All decisions related to the tasks above are sent in writing to the signatory of the authorized party. The decision needs to be accompanied by an acknowledgement form for receipt. The signed form must be returned to the regulatory body without delay upon receipt of the decision. For every decision, the authorized party is informed on how to appeal against the decision. Such information needs to be enclosed when the decision is sent to the authorized party.

Appendix I
FORMS

I.1. EXAMPLE OF A NOTIFICATION FORM

This form is for completion and submission to the regulatory body by any person or organization intending to use radiation sources.

1. Details on the organization/legal person making the notification

Name and address	
Organizational or personal identification number (as applicable)	Name and position of legal signatory
Telephone	E-mail address

2. Intended use of radiation sources

Description of the intended use of radiation sources and its purpose
References to the justification of the intended use of radiation sources

3. Current license or registration

Are you currently holding a license for the notified practice or is the practice registered by [the regulatory body]?

□ Yes, license number: _____

□ Yes, registration reference number: _____

□ No, this is a new practice and an authorization application form is included with the notification.

4. Notified practice facility (e.g. hospital)

Main address (if unknown, attach a map indicating the intended location)	
	Location (e.g. department) name
A	
B	
C	
D	

5. Details on radioactive sources related to the notification

Fill out the information known at the time of notification

Radionuclide (e.g. ^{131}I)	**Source type designation**	**Individual source ID** (if applicable)	**Location** (e.g. A)	**Activity** (MBq)	**Activity date**	**Physical form** (e.g. sealed, un-sealed, solid, liquid, gas)

6. Details on technical devices producing ionizing radiation

Fill out the information known at the time of notification

Device type (e.g. cyclotron, linear accelerator, CT, C-arm)	**Manufacturer**	**Model**	**Serial number**	**Location** (e.g. A)	**Radiation type** (e.g. X-ray, protons, electrons)	**Maximum radiation beam energy and current**[1]

[1] *Specify beam energy in keV or MeV as applicable. Beam current in mA.*

Return the completed and signed form to:

[Regulatory body]
[Postal address]
[Zip code/post code]
[City]

_____ _____

Date Signature, legal signatory

Appendix II
LICENCE APPLICATION REVIEW AND ASSESSMENT TOPICS

II.1. APPLICANT INFORMATION

- Applicant details (name, address, telephone, e-mail, organization identification number, signatory's name and position);
- Organization structure description and schematics;
- Expertise resources for safety.

II.2. GENERAL INFORMATION

- Schematic layout of facility;
- Identification of relevant national regulatory requirements;
- Phases in facility establishment (from siting to clinical operation);
- Description of the organization for safety including management functions, expertise functions, responsibilities, cooperation and intercommunication.

II.3. SAFETY ANALYSIS REPORT TOPICS

The safety analysis report contains a risk analysis of the activities within the scope of the relevant authorization phase. A plan for mitigation of identified risks is included. The safety analysis report usually covers safety aspects, descriptions and specifications regarding the topics below. Other topics that might be relevant, depending on national legislation and special circumstances, are listed below:

- Description of the types and extent of the activities included in the licence application;
- Facility location and surroundings;
- Radiation sources (technical devices and sealed radioactive sources);
- Accelerator;
- Beam transport system;
- Beam delivery technique (beam spreading and shaping);
- Control and steering system (accelerator, beam transport and beam delivery);
- Structural shielding;
- Patient positioning system (couch, positioning verification systems);
- Power supply;
- Accelerator cooling system;
- Ventilation system;
- Fire protection;
- Radiation waste management;
- Water and drainage system;
- Sources and expected levels of radiation;
- Activation of equipment components, air and water (expected nuclides and activity concentrations);
- Release of activated water and air to the environment;

— Management system (focus on promotion of safety and safety culture);
— Competence and training;
— Radiation monitoring of the facility and its surroundings;
— Categorization of premises;
— Access limitation to sources and premises;
— Safety measures to avoid unintentional occupational or public exposure;
— Local dose constraints during establishment phases and clinical operation;
— Management of accidents, unplanned events and conditions with relevance to radiation safety;
— Emergency preparedness;
— Measures for occupational radiation protection;
— Occupational personal dosimetry;
— Medical examinations and health controls of staff;
— Quality assurance and calibration programme for equipment and radiation measurement instruments;
— Quality assurance programme for safety systems;
— Arrangements for service and maintenance of equipment and facility;
— Handover routines for equipment after service and maintenance;
— Decommissioning.

While this report does not provide explicit guidance on the review and assessment of topics related to treatment related patient safety, the topics below are usually mandatory in the review and assessment of an application for clinical operation of an ion therapy facility.

— Routines for justification and optimization of medical exposures;
— Safety measures to avoid unintentional patient exposure;
— Methods to verify that the delivered treatment dose agrees with the planned treatment dose;
— Quality assurance programme for software systems for patient treatment (e.g. TPS).

Appendix III
RISKS AND HAZARDS

III.1. FORESEEABLE RISKS AND HAZARDS

Certain risks and hazards are related to the equipment and facility design as well as to the patient treatment workflow. It is important to understand potential risks in the system and prepare mitigation strategies to minimize their impact to patients and staff. To evaluate potential hazards, it is recommended separating the treatment system into different subsystems or functions of a modern ion therapy system, as shown in Table 8. The table also includes a generic patient treatment workflow to identify steps in the patient treatment process. Finally, the table lists the facility services essential for normal facility operation.

TABLE 8. ION BEAM TREATMENT SUBSYSTEMS, GENERIC PATIENT TREATMENT WORKFLOW STEPS AND FACLILITY/EQUIPMENT SERVICES

	Subsystems
1A	Beam generation/accelerator system
1B	Beam transport and energy selection systems
1C	Motion control of gantry, patient positioning system, imaging system and accessories
1D	Beam monitoring system (dose, beam position detection)
1E	Therapy control (treatment delivery, interlock monitoring, beam control, etc.)
1F	Patient positioning system
1G	Safety interlock systems
1H	Data communication and status monitoring
1I	Treatment setting and display
1J	Site specific configuration of operating parameters
	Treatment workflow
2A	Patient preparation
2B	Imaging and patient positioning
2C	Position verification
2D	Treatment implementation — beam delivery to patients
2E	Dynamic Delivery and motion management (gating, motion tracking)
2F	Basic data management of ion beam (treatment log, record and verification)
	Facility and equipment services
3A	Facility water (cooling and heating water)
3B	Facility power management
3C	Facility IT support (networking and remote services)
3D	Facility emergency response management
3E	Goods disposal and radioactive material management
3F	Facility security and monitoring systems
3G	Transportation (installation, delivery, services)
3H	Service and maintenance

Risk and hazards can be separated into categories. Table 9 includes typical hazards in different categories. The focus of this report, though, is on radiation related hazards.

TABLE 9. RISK AND HAZARDS IN ION BEAM THERAPY

	Possible causes, consequences, and mitigation strategies
Electromagnetic hazards	
High electric current (1A, 1B, 1C, 1D, 3B, 3H)	High electric current (~1000 A) is often used in electromagnetic coils to create static or dynamic magnetic fields. Unstable current could create magnetic field fluctuations which will affect the acceleration of particles as well as the positional inaccuracy of the scanned particle beams in the patient. Proper cooling for high current carrying cables is important, as well as heat insulation.
Line voltage (3B, 1A)	Stability of line voltage is critical for the stable operation of high power consumption systems, such as accelerators, electromagnets, etc. Manufacturers recommend a line voltage conditioner if needed so that stable operation can be guaranteed.
Electromagnetic influence (EMC) (1H, 2A, 2D)	High field EMC could cause interference of signals or patient devices, such as pacemakers, etc.
Strong magnetic field (3A, 3B, 3D)	A magnetic field could change the path of particle beams and magnetize storage units and affect many measurement devices. High field magnetic field could also cause mechanical/collision damage if a nearby ferromagnetic metal becomes loose.
Radiation hazards	
Ionizing radiation (1A, 1B, 1D, 1E, 1F, 2B, 2D, 2E, 3A, 3H)	The biggest concern is the activation radiation from exposure of ion beams to materials, such as beam collimation system, aperture, ESS, extraction unit of accelerator, and materials used to stop the beam. Therapists operate the ion therapy unit. There are also concerns related to low level airborne and cooling water activations. Ventilation of air in the facility and groundwater handling need to be reviewed.
Prompt neutron radiation (1A, 1B, 1D, 2D, 2E, 3H)	When ion particle beams interact with materials, the biggest concern is neutron production, which causes a cascade of induced radiations. Proper shielding design is essential, as well as the handling of residual radiation from materials in the beam path.
Treatment beam (particle beam) (1A, 1B, 1D, 1E, 1F, 2B, 2D, 2E, 3A, 3H)	Improper treatment plans or malfunction of the dosimetry system or beam control system could cause the wrong dose to be delivered to patients.
Patient radioactivity (2D, 2E)	Due to activation radiation by particle beams, patients receiving ion therapy will have short term radioactivity in their body. The activation radiation will decay very quickly within 30 s of treatment. Nevertheless, it is still a concern for therapists who handle patient treatment on a daily basis.
Heat hazards	
High temperature (3H)	High current magnetic field coils could introduce heat hazards.

Mechanical hazards	
Ceiling-mounted unit (2A)	Improper securing of ceiling mounted devices could cause fall hazards
Unstable rupture, vibration, moving parts (1C)	Moving parts, such as the gantry, robotic couch, and imaging devices could cause either inaccurate operation or mechanical risks to patients or operators
Acoustic noise (1D, 2A)	Large dose monitors installed in the treatment nozzle could be sensitive to acoustic noise in the treatment bunker, which can interfere with the primary dose monitor in the nozzle. In addition, acoustic noise could affect communication with the patient either inside a bunker or remotely through a speaker.
High pressure (3A, 1A, 1B)	High pressure water cooling or heating could affect many functions in the beam control system or power supplies. Air pressure is also used in some mechanical movements/motions or brakes.
Vacuum (1A, 1B)	Vacuum sealing is important for proper transport of particles to the treatment bunker. High vacuum exists inside the accelerator as well as in the beamline. Rotational joints and insertion of devices into the beamline may need proper vacuum sealing in the design.
Gantry rotation (1C)	Potential collision with patient, treatment couch, imaging devices, or other accessories that may be in the path of the movement/motion,
Fluid spills (1A, 1B)	Cooling water, gear oil, bearings could create electrical shorts or loss of functions.
Metal dust (1F, 2E)	Metal dust from gantry rotation could introduce a patient hazard, and create unfavourable operating conditions for robust, imaging devices, etc.
Earthquake hazards	
Earthquakes (1A, 1B, 3A, 3B, 3C)	Earthquakes can cause beam operation interruption, cracks in shielding, activate fluid spill, liquid helium cooling magnets, laser misalignment. Proper building code and emergency plans to minimize earthquake impacts.
Biological hazards	
Infection (2D)	Policy for treating patients with infectious disease is established. Communication with people performing late shift activities contain the information if cleaning procedure has not been completed.
Chemical hazards	
Toxic chemical composition	
Biological incompatibility	

Toxic or flammable gas leakage Explosive substances	
Environmental hazards	
Water activation (1A, 1B, 3A)	Cooling water may be near the high radiation area (degrader or accelerator extraction channel, etc.) and become (radiation) activated. Handling of activated water is considered in a holding area until the activity is below a certain level.
Air activation (3)	Neutrons and other activation particles can also create airborne radioactive particles. Careful design of ventilation system is needed.
Improper disposal (3)	Materials that are directly or indirectly activated by particle beams or secondary neutron emissions are handled properly. Patient specific apertures for beam collimations are stored for at least four months and surveyed to ensure low residual activity before disposal or shipping to another location. Proper documentation of radioactive materials is recommended.
Functional hazards	
Inadequate signs and zone demarcation (2A)	Radiation signage needs to be appropriate to avoid accidental radiation or treatment interruption when patients or staff enter a secure location. The 'beam-on' indicator needs to be clear, and the 'clear-out' procedure needs to be well defined.
Patient data collection, evaluation and display (1E, 1G, 2B, 2C)	Correct patients are identified and properly displayed on a computer screen for confirmation.
Data transmission (1H, 1I, 2F, 3C)	Transmission verification protocols are used to ensure proper transmission of treatment parameters.
Dynamic treatment (1C, 2D, 2E)	When dynamic beam delivery is used, proper commissioning and validation are needed. Improper calibration or training may significantly reduce the treatment effectiveness, with increased risk due to high dose rate delivery
Service and maintenance	
Staffing level of service personnel and skill sets (1J, 3H)	Service personnel need to be properly trained in the required skill sets. In addition, the staffing level must be adequate to support additional shifts for service and maintenance to keep the centre at the required 'up-time'.
Handover procedure (3H)	A handover procedure is needed to ensure smooth transition and communication. Overnight service and maintenance and communicated with on-site physics staff.

Hazards in use	
Inadequate fail-safe design (1G, 2D)	Certain devices, such as a beam-stopper, need to be designed to be fail-safe during power loss.
Inadvertent disabling of safety interlocks (1G, 1E, 3D)	An interlock bypass protocol is implemented to avoid using unproven parameters in patient treatment mode. During maintenance or upgrade, the configuration may be changed. It is important to verify changes to ensure safe and accurate treatment.
Calibration of imaging devices (2B)	Regular geometrical calibration and imaging quality calibration are necessary to ensure accurate imaging for patient positioning.
User interface (1I, 1J, 2A, 2B, 2C, 2D, 2E)	The user interface design contains the necessary information to make treatment decisions.
Malice software (1H, 2F, 3C)	Proper installation of a firewall against cyber-attacks or unauthorized access.
Treatment interruption and resume (1D, 1E, 1G, 2A, 2D, 2E)	Treatment could be interrupted by other factors. A procedure is needed to resume treatment, considering the radiation dose already delivered. Independent verification of partial delivery is strongly recommended.
Error in use (all)	Error messages must be clear and self-explanatory. Communication with service staff needs to be defined to ensure good understanding of beam delivery interruptions.
Untrained user (all)	Proper training of users to perform their role is critical.
Unsuitable accessories (1C, 1D, 2A, 2D, 2E)	Treatment accessories must be checked regularly to ensure that they are functioning.
Inadequate maintenance/ quality assurance (1D, 2B)	Since treatment parameters may be changed over time, a routine quality assurance schedule is an important part of the quality management programme.
Workflow and configuration (2A, 2B, 2C, 2D, 2E, 2F)	Workflow, policy and procedures are established so that patients can be prepared adequately and have adequate expectations/information for any changes in the schedule. For example, a machine downtime policy is needed to handle the situation when the machine is unexpectedly down for one day, two days, three days, or more.
Hazard relevant to labels and instructions	
Improper identification (2A)	Patient specific treatment devices or immobilization devices must have proper identification to ensure that the correct devices are used for patient treatment.
Inadequate installation, repair and maintenance practices (1J, 3H)	Service signature, interlock bypass records, communication of changes to facility physicists or other relevant personnel.

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LIST OF DEFINITIONS

albedo dosimeter. Neutron dosimeter which measure indirect neutrons, scattered by an object, creating a neutron flux of thermal and albedo neutrons at the surface of the scatterer. Dosimeter which measure neutrons doses over the whole range of energies.

Andersson–Braun type monitor. Instrument in which a detector with a high sensitivity to thermal neutrons is placed inside a moderator–attenuator. The response function of the rem counter reproduces the curve of the conversion coefficient from neutron fluence to dose equivalent on a wide energy range.

Bonner sphere system. Consists of, for example, a europium doped lithium iodide (LiI(Eu)) scintillator detector in conjunction with polyethylene spherical moderators.

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.

Committee TC 62. International Electrotechnical Commission (IEC) committee to prepare international standards for electrical equipment in medical practice.

Council Directive 93/42/EEG. European Council Directive of 14 June 1993 concerning medical devices.

CR39 track etch detector. Columbia Resin #39, a thermosetting plastic and plastic polymer. Tracks resulting from energetic charged particles coming from interactions of the neutrons with a CR39 are visible with an optical microscope after chemical etching.

cyclotron. Device that accelerates charged atomic and subatomic particles to a given fixed kinetic energy in an alternating electromagnetic field along a spiral or circular path.

DICOM-RT. Digital Imaging and Communications in Medicine–Radiotherapy. A standard used in radiation therapy which supports the transfer of radiotherapy-related data between devices.

energy selection system (ESS). Part of a cyclotron beam transport system that lowers the beam energy to a clinically desired level.

fragmentation. Nuclear decay mechanism in which at least three intermediate mass fragments are produced.

Hounsfield Unit (HU). Dimensionless unit universally used in computed tomography for standardization and convenience.

klystron. Electron vacuum tube to generate or amplify microwaves.

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: $L = dE/dl$. The unit of L is J/m or keV/μm.

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[*] Definitions based on: YONEKURA, Y., et al., Radiological Protection in Ion Beam Radiotherapy, ICRP Publication 127, Ann. ICRP **43** 4 (2014).

long lead time items. Items identified at the earliest stage of a project to have a delivery time long enough to directly affect the overall project lead time. Construction projects are to be fully integrated with manufacturing and procurement programmes with emphasis on items with a long lead time.

occupancy factor. A typical estimated fraction of the time which a location is occupied by an individual or group.

oncology information system (OIS). Information system designed to connect different oncology activities and cancer patient information for patient care.

PRESCILA detector. Model of a lightweight neutron rem meter.

relative biological effect (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 end point considered.

spallation. Process in which a heavy nucleus emits many nucleons when impacted by a high energy particle.

Subcommittees SC 62A (SC 62A). IEC subcommittee to prepare international standards concerning the common aspects of the manufacture, installation and application of electrical equipment used in medical practice.

Subcommittees SC 62B (SC 62B). IEC subcommittee to prepare international publications for safety and performance for all types of medical diagnostic imaging equipment, including associated equipment and accessories as well as quality procedures to be applied during the lifetime of the imaging equipment.

Subcommittees SC 62C (SC 62C). IEC subcommittee to prepare standards for the safe operation of medical equipment and systems using ionizing radiation for the treatment of disease; associated equipment and software used in planning, delivering and monitoring such treatments; instruments measuring ionizing radiation used in the diagnosis and treatment of disease as well as radiation conditions for testing them; and nuclear medicine equipment used for imaging the distribution of radioactive substances within the human body for both diagnostic purposes and radionuclide therapies.

synchrocyclotron. Special type of cyclotron in which the frequency of the driving electromagnetic field is varied to compensate for relativistic effects at very high speed of the accelerated particle.

synchrotron. A particle accelerator in which the accelerating particle beam travels around a circular spiral path. An outside oscillating magnetic field, synchronized with the particle movement and its kinetic energy level, bends the particle path while the particles are being accelerated by alternating electrical fields. The final particle energy can be variable depending on the selected parameters of operation of the synchrotron.

treatment planning system (TPS). The process by which an appropriate external or internal radiotherapy technique for a patient with cancer is devised. Modern particle therapy planning systems use the patient's computed tomography images to model radiation transport through the patient to ensure that adequate target dose is achieved while minimizing normal organ doses.

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[*] Definitions based on: YONEKURA, Y., et al., Radiological Protection in Ion Beam Radiotherapy, ICRP Publication 127, Ann. ICRP **43** 4 (2014).

Use Case modelling. Conceptual modelling to study behaviour in different treatment scenarios.

ABBREVIATIONS

2-D/3-D	two dimensional/three dimensional
ADCL	Accredited Dosimetry Calibration Laboratory
ADR	European Agreement on the International Carriage of Dangerous Goods by Road
CBCT	cone beam computed tomography
CNAO	National Centre of Oncological Hadron Therapy, Pavia, Italy
CPU	central processing unit (central processor of a computer)
CT	computed tomography
EMC	electromagnetic compatibility
EN-IEC	Adoption of international standard as a European Standard through the parallel procedure
EPAX	Formula used to describe the fragmentation of medium to heavy mass projectiles
ESS	energy selection system
FLUKA	Monte Carlo code for the transport of hadrons, heavy ions, and electromagnetic particles
FMEA	failure mode and effects analysis
GEANT4	Software for the simulation of the particle transport used in accelerator physics
GSI	GSI Helmholtzzentrum für Schwerionenforschung, Darmstadt, Germany
Gy	gray: unit of ionizing radiation dose
HEBT	high energy beam transfer
HF	high frequency
HIMAC	Heavy Ion Medical Accelerator Chiba, Japan
HIT	Heidelberg Ion-Beam Therapy Centre, Germany
HZDR	Helmholtz-Zentrum Dresden-Rossendorf, Germany
ICRP	International Commission on Radiological Protection
IEC	International Electrotechnical Commission
ISO	International Organization for Standardization
linac	linear accelerator
LLUMC	Loma Linda University Medical Center, USA
MC	Monte Carlo
MCNP	Monte Carlo N-particle transport software package for simulating nuclear processes
eV	electronvolt, unit of energy in high energy physics
MRI	magnetic resonance imaging
MU	monitoring unit, a measure of output from a clinical accelerator for radiation therapy
OIS	oncological information system
OSLD	optically stimulated luminescence dosimeter
PBS	pencil beam scanning

PET	positron emission tomography
PHITS	Particle and Heavy Ion Transport Code System: A Monte Carlo simulation code
PRESCILA	Proton Recoil Scintillator Los Alamos, USA
PSI	Paul Scherrer Institute, Switzerland
RF	radio frequency
RFQ	radio frequency quadrupole: a type of linear accelerator
RP	radiation protection
S/C/SC	synchrotron (S)/cyclotron (C)/synchrocyclotron (SC)
SAD	source axis distance
SOBP	Spread out Bragg peak
Sv	Sievert: unit of dose equivalent
TLD	thermoluminescent dosimeter
Tm	Tesla-meter; a unit of magnetic rigidity
TPS	treatment planning system
WENDI	wide energy neutron detector instrument
Z	atomic number

Annex
EXISTING ION RADIOTHERAPY FACILITIES

TABLE A–1. ION RADIOTHERAPY FACILITIES IN CLINICAL OPERATION
(p: proton; C-ion: carbon ion; horiz.: horizontal)

Country	Name and location	Type of ion	Accelerator type (S/C/SC*) Max. energy (MeV)	Beam direction	Date of first patient treatment
Austria	MedAustron, Wiener Neustadt	p	S 253	2 horiz., 1 vertical fixed beam**, 1 gantry** (under construction)	2016
Austria	MedAustron, Wiener Neustadt	C ion	S 403/u	2 horiz., 1 vertical fixed beam**	2019
Canada	TRIUMF, Vancouver	p	C 72	1 horiz. fixed beam	1995
Czech Republic	PTC Czech r.s.o., Prague	p	C 230	3 gantries**, 1 horiz. fixed beam	2012
China	WPTC, Wanjie, Zi-Bo	p	C 230	2 gantries, 1 horiz. fixed beam	2004
China	IMP-CAS, Lanzhou	C-ion	S 400/u	1 horiz. fixed beam	2006
China	SPHIC, Shanghai	p	S 250	3 horiz. fixed beams**	2014
China	SPHIC, Shanghai	C ion	S 430/u	3 horiz. fixed beams**	2014
China	SPHIC, Shanghai	P&C ion	S 250 and S 430/u	3 horiz. fixed beams**	2014
China	Heavy Ion Cancer Treatment Centre, Wuwei, Gansu	C ion	S 400/u	4 horiz. fixed beams**	2019
Denmark	Dansk Centre for Partikelterapi, Aarhus	P	C 250	3 gantries**, 1 horiz. fixed beam**	2019
France	CAL/IMPT, Nice	p	C165, SC 235	1 horiz.fixed beam, 1 gantry	1991, 2016

France	CPO, Orsay	p	C 230	1 gantry, 2 horiz. fixed beams	1991, 2014
France	CYCLHAD, Caen	p	C 230	1 gantry**	2018
Germany	HZB, Berlin	p	C 250	1 horiz. fixed beams	1998
Germany	RPTC, Munich	p	C 250	4 gantries**, 1 horiz. fixed beams	2009
Germany	HIT, Heidelberg	p	S 250	2 horiz. fixed beams, 1 gantry**	2009, 2012
Germany	HIT, Heidelberg	C ion	S 430/u	2 horiz. fixed beams, 1 gantry**	2009, 2012
Germany	WPE, Essen	p	C 230	4 gantries***, 1 horiz. fixed beams	2013
Germany	UPTD, Dresden	p	C 230	1 gantry***	2014
Germany	MIT, Marburg	p	S 250	3 horiz., 1 45° fixed beams**	2015
Germany	MIT, Marburg	C ion	S 430/u	3 horiz., 1 45° fixed beams**	2015
India	Apollo Hospitals PTC, Chennai	p	C 230	2 gantries, 1 horiz. fixed beam**	2019
Italy	INFN-LNS, Catania	p	C 60	1 horiz. fixed beam	2002
Italy	CNAO, Pavia	p	S 250	3 horiz., 1 vertical, fixed beams	2011
Italy	CNAO, Pavia	C ion	S 480/u	3 horiz., 1 vertical, fixed beams	2012
Italy	APSS, Trento	p	C 230	2 gantries**, 1 horiz. fixed beam	2014
Japan	HIMAC, Chiba	C ion	S 800/u	Horiz.***, vertical***, fixed beams, 1 gantry	1994, 2017
Japan	NCC, Kashiwa	p	C 235	2 gantries***	1998
Japan	HIBMC, Hyogo	p	S 230	1 gantry	2001

Japan	HIBMC, Hyogo	C-ion	S 320/u	horiz., vertical, fixed beams	2002
Japan	PMRC 2, Tsukuba	p	S 250	2 gantries***	2001
Japan	Shizuoka Cancer Center	p	S 235	3 gantries, 1 horiz. fixed beam	2003
Japan	STPTC, Koriyama-City	p	S 235	2 gantries**, 1 horiz. fixed beam	2008
Japan	GHMC, Gunma	C-ion	S 400/u	3 horiz., 1 vertical, fixed beams	2010
Japan	MPTRC, Ibusuki	p	S 250	3 gantries***	2011
Japan	Fukui Prefectural Hospital PTC, Fukui City	p	S 235	2 gantries***, 1 horiz. fixed beam	2011
Japan	Nagoya PTC, Nagoya City, Aichi	p	S 250	2 gantries***, 1 horiz. fixed beam	2013
Japan	SAGA-HIMAT, Tosu	C-ion	S 400/u	3 horiz., vertical, 45°, fixed beams	2013
Japan	Hokkaido Univ. Hospital PBTC, Hokkaido	p	S 220	1 gantry	2014
Japan	Aizawa Hospital PTC, Nagano	p	C 235	1 gantry	2014
Japan	i-Rock Kanagawa Cancer Center, Yokohama	C-ion	S 430/u	4 horiz., 2 vertical, fixed beams	2015
Japan	Tsuyama Chuo Hospital, Okayama	p	S 235	1 gantry	2016
Japan	Hakuhokai Group Osaka PT Clinic, Osaka	p	S 235	1 gantry	2017
Japan	Kobe Proton Center, Kobe	p	S 235	1 gantry	2017
Japan	Narita Memorial Proton Center, Toyohashi	p	C 235	1 gantry**	2018

Japan	Osaka Heavy Ion Therapy Center	C ion	S 430/u	3 rooms, 6 fixed beams	2018
Korea, Republic of	KNCC, IIsan	p	C 230	2 gantries, 1 horiz. fixed beam	2007
Korea, Republic of	Samsung PTC, Seoul	p	C 230	2 gantries	2016
Netherlands	UMC PTC, Groningen	p	C 230	2 gantries**	2018
Netherlands	Holland PTC, Delft	p	C 250	2 gantries**, 1 horiz. fixed beam	2018
Netherlands	ZON PTC, Maastricht	p	SC 250	1 gantry**	2019
Poland	IFJ PAN, Krakow	p	C 230	1 horiz. fixed beam, 2 gantries	2011, 2016
Russian Federation	ITEP, Moscow	p	S 250	1 horiz. fixed beam	1969
Russian Federation	JINR 2, Dubna	p	C 200****	1 horiz. fixed beam	1999
Russian Federation	MIBS, Saint-Petersburg	p	C 250	2 gantries**	2018
Russian Federation	MRRC, Obninsk	p	S 250	1 fixed beam	2016
South Africa	NRF - iThemba Labs	p	C 200	1 horiz. fixed beam	1993
Sweden	The Skandion Clinic, Uppsala	p	C 230	2 gantries**	2015
Switzerland	CPT, PSI, Villigen	p	C 250	1 horiz. fixed beam, 3 gantries**	1984, 1996, 2013, 2018
Taiwan, China	Chang Gung Memorial Hospital, Taipei	p	C 230	4 gantries***, 1 horiz. fixed beam exp.	2015
United Kingdom	Clatterbridge	p	C 62	1 horiz. fixed beam	1989
United Kingdom	Proton Partners Rutherford CC, Newport	p	C 230	1 gantry**	2018
United Kingdom	Christie Proton Therapy Centre, Manchester	p	C 250	3 gantries**	2018

USA	J. Slater PTC, Loma Linda, CA	p	S 250	3 gantries, 1 horiz. fixed beam	1990
USA	UCSF-CNL, San Francisco, CA	p	C 60	1 horiz. fixed beam	1994
USA,	MGH Francis H. Burr PTC, Boston, MA	p	C 235	2 gantries***, 1 horiz. fixed beam	2001
USA	MD Anderson Cancer Center, Houston, TX	p	S 250	3 gantries***, 1 horiz. fixed beam	2006
USA	UFHPTI, Jacksonville, FL	p	C 230	3 gantries***, 1 horiz. fixed beam	2006
USA	ProCure PTC, Oklahoma City, OK	p	C 230	1 gantry, 1 horiz, 2 horiz and 60°, fixed beams	2009
USA	Roberts PTC, UPenn, Philadelphia, PA	p	C 230	4 gantries***, 1 horiz. fixed beam	2010
USA	Chicago Proton Center, Warrenville, IL	p	C 230	1 gantry**, 1 horiz, 2 horiz and 60°, fixed beams	2010
USA	HUPTI, Hampton, VA	p	C 230	4 gantries, 1 horiz. fixed beam	2010
USA	ProCure Proton Therapy Center, Somerset, NJ	p	C 230	4 gantries***	2012
USA	SCCA ProCure Proton Therapy Center, Seattle, WA	p	C 230	4 gantries***	2013
USA	S. Lee Kling PTC, Barnes Jewish Hospital, St. Louis, MO	p	SC 250	1 gantry	2013
USA	ProVision Cancer Cares Proton Therapy Center, Knoxville, TN	p	C 230	3 gantries**	2014
USA	California Protons Cancer Therapy Center, San Diego, CA	p	C 250	3 gantries**, 2 horiz. fixed beams**	2014

USA	Willis Knighton Proton Therapy Cancer Center, Shreveport, LA	p	C 230	1 gantry**	2014
USA	Ackerman Cancer Center, Jacksonville, FL	p	SC 250	1 gantry	2015
USA	Mayo Clinic Proton Beam Therapy Center, Rochester, NY	p	S 220	4 gantries**	2015
USA	Laurie Proton Center of Robert Wood Johnson Univ. Hospital, New Brunswick, NJ	p	SC 250	1 gantry	2015
USA	Texas Center for Proton Therapy, Irving, TX	p	C 230	2 gantries**, 1 horiz. fixed beam	2015
USA	St. Jude Red Frog Events Proton Therapy Center, Memphis, TN	p	S 220	2 gantries**, 1 horiz. fixed beam	2015
USA	Mayo Clinic Proton Therapy Center, Phoenix, AZ	p	S 220	4 gantries**	2016
USA	Maryland Proton Treatment Center, Baltimore, MD	p	C 250	4 gantries**, 1 horiz. fixed beam**	2016
USA	Orlando Health PTC, Orlando, FL	p	SC 250	1 gantry	2016
USA	UH Sideman CC, Cleveland, OH	p	SC 250	1 gantry	2016
USA	Cincinnati Children's Proton Therapy Center, Cincinnati, OH	p	C 250	3 gantries**	2016
USA	Beaumont Health Proton Therapy Center, Royal Oak, Detroit, MI	p	C 230	1 gantry**	2017
USA	Baptist Hospital’s Cancer Institute PTC, Miami, FL	p	C 230	3 gantries**	2017

USA	Medstar Georgetown University Hospital PTC, Washington, DC	p	SC 250	1 gantry**	2018
USA	Provision CARES, Nashville, TN	p	C 230	2 gantries**	2018
USA	Emory Proton Therapy Center, Atlanta, GA	p	C 250	3 gantries**, 2 horiz. fixed beams**	2018
USA	Stephenson Cancer Center, Oklahoma City, OK	p	SC 250	1 gantry**	2019

* S/C/SC: synchrotron/cyclotron/synchrocyclotron.

** With pencil beam scanning.

*** With spread beam and pencil beam scanning.

**** Degraded beam.

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