Chapter II.14

Applications of low-energy accelerators

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Particle accelerators have been invented and developed almost exclusively as tools for the exploration of the subatomic world. In the wake of these big high-energy facilities, about forty-five thousand small accelerators are at work every day, almost unnoticed. These accelerators, which represent about 95% of all accelerators operating worldwide, have an energy not larger than 50 MeV. They produce beams of particles and photons, and are used in hospitals, in manufacturing plants, in small research laboratories, in sterilisation industry, in ports and on ships at sea, and even in museums. We will discuss these accelerators and their major applications in domains as radiotherapy, radioisotope production, radiation processing and ion implantation.

II.14.1 Particle accelerators and their uses

II.14.1.1 Applications of particle accelerators

Accelerators have been invented to respond to demands of researchers in nuclear and particle physics. They got their greatest visibility in our society thanks to their remarkable contribution to these fields. From the first conception of accelerators about 100 years ago to present-day giant colliders, accelerators have always played a crucial role in progress of these two research fields and they will do it also in the future. However, if we look into numbers, the picture of the accelerator field is completely different. The total number of operational accelerators worldwide is presently estimated to be around 45000. A classification can be made over their different application domains [1]. Figure II.14.1 shows their distribution. It is remarkable to note that only a very small amount, less than 0.5% of all operating accelerators in the world, is running for the two high-energy research fields for which accelerators have been invented and which gave them their greatest visibility and celebrity. The vast majority of present-day accelerators is operating in other domains, to a large extent unknown and unseen by the major part of the general public [2, 3].

About 1/3 of all present-day accelerators are used for health applications. Electron, proton and ion accelerators are used for the radiation therapy of cancer. They are also applied for the production of radioactive isotopes that are used in cancer therapy and as tracers in medical diagnostics. Over 50% of all present accelerators are used in industry, mainly for ion implantation, and for radiation processing of materials. All these accelerators, used in medicine and industry, are spin-off products of the machines that were initially developed for high-energy physics. But the requirements imposed on them substantially differ from those on machines designed for experimental nuclear and particle research. The energies of

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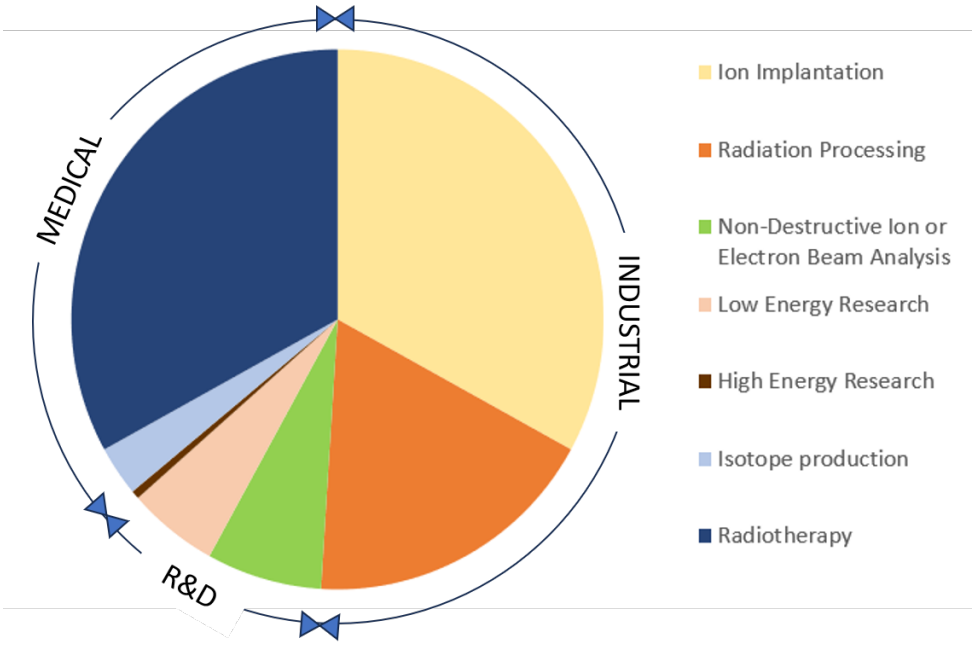

Fig. II.14.1: Estimated share of accelerators in the world over their domains of application.

the present accelerator facilities for nuclear and particle physics have reached the TeV-range, their dimensions are in the km-range and their construction, personnel and operation costs can only be afforded at an international scale. On the contrary, accelerator facilities for applications have to be adapted to constraints of the medical or industrial environment in which they operate which is generally characterised by limited available space, restricted accessibility and severe economic constraints.

II.14.1.2 General features of low-energy accelerators for applications in medicine and industry

In contrast to the well-known research accelerators, low-energy accelerators for medicine and industry:

- have an energy not higher than 50 MeV;
- must easily fit into a production line or in a hospital room, which implies a compact footprint and compact radiation shields. Often they have to be self-shielded;
- have to be simple in construction, operation and maintenance. Usually, they are purpose-built and their configuration is standardised;
- must operate in a competitive environment. They have to run at affordable prices and have to be managed by a small crew of technicians and engineers, not always having a long specialised education and training in the accelerator field. The machines must be highly electrically-efficient, reliable and preferably have a fail-safe (quasi) autonomous running;
- deliver beam currents which are often up to six orders of magnitude higher than in typical research facilities. In contrast, beam quality parameters as momentum resolution or beam emittance, crucial for high-energy physics, are less important.

Steady improvements in accelerator technologies during the last two decades have led to compact, reliable and efficient accelerator designs, often with very high beam intensities. These modern low-energy

machines form now the basis for the use of accelerators in a wide range of medical and industrial domains. Their beams of charged particles (electrons, protons or ions) can be used directly or, alternatively, they can be transformed into secondary beams of photons or neutrons.

II.14.1.2.1 Production of primary beams with low-energy accelerators: charged particles

Beams of electrons, protons or ions for applications are produced in low-energy versions of the standard accelerator types invented for nuclear and particle physics. For information on basic principles of these accelerator types, we refer to several other Chapters of these proceedings, I.11, I.13, II.16 and II.17, and III.1. where particle accelerators for high-energy physics are extensively discussed. Stringent performance requirements demanded for most modern medical and industrial accelerators (compactness, high intensity and beam power, reliability, electrical efficiency ...) have led to additional specific developments in the technology of these machines [4]. Major low-energy accelerators for medical and industrial applications are:

- **Direct voltage accelerators**
  - Dynamitrons^{TM} and Cockcroft Walton accelerators (energies up to 5 MeV),
  - Van de Graaff accelerators (energies up to 10 MeV),
  - Inductive core transformers (ICT) (energies up to 5 MeV);
- **Linear microwave accelerators**
  - Electron linacs (electron energies from 1 to 50 MeV),
  - Ion linacs (ion energies from 1 to 50 MeV), often with a radio frequency quadrupole (RFQ) injector coupled to a drift tube (DTL) or a superconducting linac (SCL);
- **Circular microwave accelerators**
  - Cyclotrons (proton and ion energies from 10 to 50 MeV),
  - Rhodotrons^{TM} and microtrons (electron energies from 5 to 40 MeV).

These low-energy accelerators are also used for the production of beams of photons or neutrons.

II.14.1.2.2 Production of secondary beams with low-energy accelerators: photons and neutrons

High-brightness photon beams can be generated in synchrotron radiation facilities and very intense neutron beams can be produced in spallation sources. But, as these facilities require particle accelerators in the GeV-range, implying a major installation and a big crew at a significant cost, they are not adapted to a hospital or an industrial plant. They are not used in this context, and accordingly also not discussed.

When relativistic electrons from a low-energy accelerator are directed onto a suitable target, they are deflected in the radial Coulomb field of atomic nuclei, thereby losing part of their energy via radiation of photons, called braking radiation or Bremsstrahlung (see Fig.II.14.2, left). Bremsstrahlung is a forward-directed beam of photons whose energy spectrum has an endpoint energy equal to the maximum energy of the incident electrons [5,6]. Bremsstrahlung intensity is proportional to Z^2, Z being the atomic number of the Bremsstrahlung target material, and to E, the kinetic energy of the incident electrons. As

electrons also deposit heat in the Bremsstrahlung targets, targets are usually made of high-Z materials with a high melting point, such as W, Ta or Au. Radioactive sources may also emit photons. In what follows we will label photons as "γ's" or "γ-rays" when they are emitted from a radioactive source, and "X-rays" when they are produced in the Bremsstrahlung process of an accelerator.

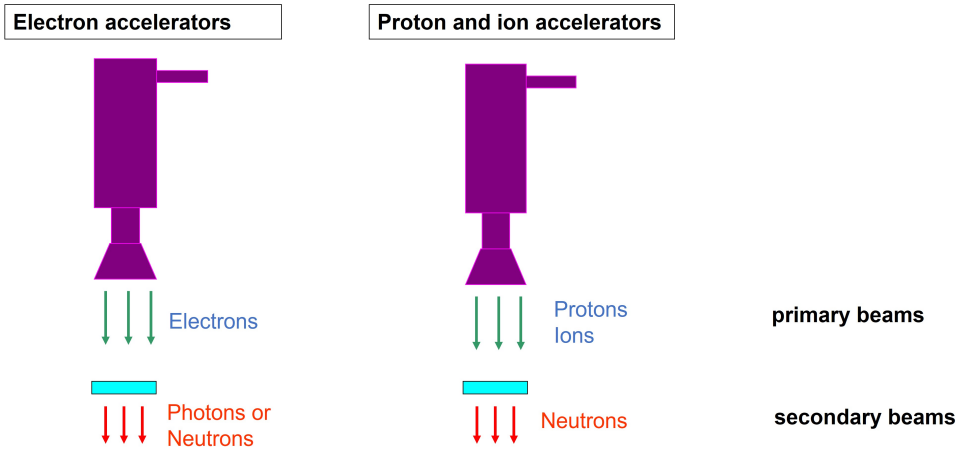

Fig. II.14.2: Accelerator beams for applications.

The most common neutron source reactions for the production of neutron beams in the energy range from 0.1 to 20 MeV are fusion reactions [7]. The d-t reaction (^{3}H (d,n) ^{4}He), which produces 14 MeV neutrons, has by far the largest cross section, even at low deuteron bombarding energy. A large neutron yield can already be obtained with deuteron beams of only 100–300 keV, so that relative intense neutron beams can be produced with simple mobile electrostatic accelerators. The d-d reaction (^{2}H(d,n)^{4}He) produces 2.45 MeV neutrons. Other neutron sources at small accelerators often use proton- or deuteron-induced reactions on light nuclei ^{7}Li or ^{9}B, but also on heavier nuclei ^{10}B, ^{11}B, ^{12}C, ^{13}C and ^{36}Cl.

Neutrons can also be generated with an electron accelerator via photonuclear reactions. Bremsstrahlung photons are directed to a photoneutron target, where photons interact with the nuclei. The cross section for photon-induced reactions is strongly enhanced in the 10–20 MeV range by the presence of giant dipole resonances in heavy nuclei, related with collective oscillations of all protons against all neutrons. These excited nuclei can than de-excite by releasing one or more neutrons [8]. If the neutron production target is made of fissile material, neutrons can also be emitted after photon-induced fission.

II.14.1.3 Ionising radiation and its interactions

In accelerator-based applications, a beam of charged particles, photons or neutrons is directed onto matter. A long and complex chain of phenomena is set in motion by the slowing down and absorption of the projectiles in the medium. A detailed description of basic interaction mechanisms can be found in publications and in textbooks on radiation physics or detectors (see for example Ref. [9]). Within the scope of this chapter, we will limit the discussion to a simplified scheme, highlighting only those basic aspects, which are relevant for the understanding of the great diversity of applications in medicine and

industry. In the energy range covered by low-energy accelerators, two major interactions of the beam with the atoms in the irradiated material are of relevance:

– Coulomb interactions ejecting orbital electrons of the atoms (so called ionisation reactions);
– interactions with nuclei (nuclear reactions).

During irradiation of matter by an accelerator beam in the energy range up to 50 MeV, energy deposition is dominated by collisions of the projectiles with orbital electrons. Such collisions may excite an electron from an occupied orbital into an empty, higher-energy orbital. This process is called excitation, that ends up in creating heat in the irradiated matter. But, more important in this context, the radiation carries enough energy to remove an orbital electron from an atom or molecule and to ionise it. This is valid for all charged particles from accelerators. Charged particles are therefore called directly ionising radiation.

Photons, having no mass, do not collide directly, but have other types of interaction (photo-electric effect and Compton scattering) leading to ejection of orbital electrons. When a neutron collides with a proton in the target nucleus, the proton may recoil and ionise. At the end of its path, a neutron may be captured by a nucleus in an (n,γ)-reaction leading to emission of a photon, which can provoke an ionising reaction. Therefore, photons and neutrons are called indirectly ionising radiation.

II.14.1.3.1 Interactions of ionising radiation with orbital electrons: ionisation reactions

During the passage and slowing down in a medium, charged particles exert Coulomb forces on atomic electrons of nuclei and impart energy to them (see Fig. II.14.3). Although the energy of the particles is transferred in a series of discrete events, the events are of random nature (e.g., ejected electrons having variable amount of energy). The process can best be approximated by a continuous loss of energy. The average rate of collision energy loss of charged particles in a medium, $-dE/dx$, called collision stopping power, is given by the Bethe-Bloch formula

$$-\frac{dE}{dx} = \frac{4\pi N_{\mathrm{A}} z^2 e^4}{m_e c^2 \beta^2} \rho \frac{Z}{A} B \approx (2\mathrm{MeV}\frac{\mathrm{cm}^2}{\mathrm{g}})\rho\frac{z^2}{\beta^2} \quad , \tag{II.14.1}$$

where N_{A} is Avogadro's number, z is the charge of the particle, e the elementary charge, m_e the electron rest mass, β the speed v of the particle divided by speed of light, ρ the density of the irradiated medium, Z and A are the atomic and mass number of the absorbing atom and B is a correction factor depending on the particle type and medium. There are differences between Bethe-Bloch equations for light and heavier particles (e.g., relativistic effects, shell corrections, mean excitation energy, etc.). They are all incorporated in factor B, but have no notable impact on our discussion. For the purpose of a qualitative description, the approximation of Bethe–Bloch equation, given above, is very useful. For all particles, the collision energy has a constant, energy-independent value, when β approaches 1. As can be seen, collision stopping power is proportional to material density and inversely proportional to the square of the velocity. Due to this, for low velocities at the end of the particle trajectories, the deposited energy grows sharply.

Photons from a low-energy electron accelerator with maximum energy of 50 MeV, whether produced via the Bremsstrahlung process during slowing down of electrons in the medium, or produced in an

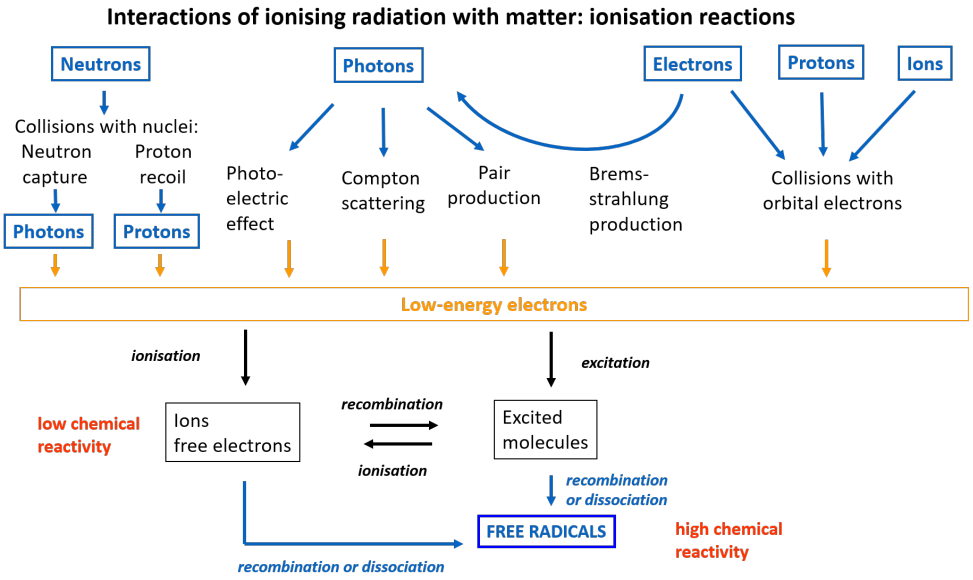

Fig. II.14.3: Simplified scheme of interactions of particles and photons during ionisation slowing down.

external Bremsstrahlung target, interact with target material via three major reactions: the photoelectric effect, Compton scattering and pair production. Compton scattering does not remove the photons, they just lose some energy to electrons when they are diverted. In the two other processes photons disappear and low-energy electrons emerge. The essence is that in all three processes, photon energy is transferred to low-energy electrons, which cause subsequently many ionisations. When a neutron collides with a target nucleus, an ionising proton may be emitted or the neutron may be captured, leading to the emission of a photon which may cause further ionisation reactions.

In the end, the net effect of an irradiation with particles or photons is always the same: incident beam energy is distributed to low-energy electrons in the irradiated sample [10, 11]. As the energy of the incident beam (MeV-range) is much larger than the ionisation energy, the energy needed to eject an orbital electron from an atomic or molecular structure (between 5 and 25 eV), a single particle or photon from an accelerator is capable of producing thousands of ions and free electrons. These ejected electrons may have enough energy to ionise other atoms and molecules, so that a cascade of events is developing.

At some point in the radiation absorption process, nearly all the energy of the initial beam is transferred to low-energy electrons, creating ions and, to lesser extent, also excited molecules or atoms. The chemical reactivity of ions and excited atoms and molecules is not very high, but if they dissociate or recombine with other ions, they can form free radicals. Free radicals are atoms, molecules or ions with an unpaired valence electron in their outer shell. Because of their unpaired electrons, free radicals are highly reactive. For example, when ionising radiation irradiates water, the free radicals formed are among the strongest oxidising agents that can exist in aqueous solutions.

II.14.1.3.1.1 Free radicals

The ability of ionising radiation to produce free radicals, in large quantities and great variety, forms the basis of many applications in medicine and industry. In a particular target material, the type of free

radicals will be, in general, the same, regardless of type and energy of the ionising radiation. Therefore, all ionising radiations will give rise to qualitatively similar chemical or biological effects.

Free radicals (R^0) form the basis of the application of ionising radiation in the medicine and industry:

- Free radicals may damage DNA and kill a human cell, which is used in *radiotherapy*;
- If a free radical is generated in the nucleus of a cell of a microorganism, it may break and disable the DNA, preventing reproduction. This is applied in *food irradiation and sterilisation*;
- If a free radical is reacting with a molecule, the product may be another free radical, provoking a chain reaction, as used in *polymer chemistry*, e.g., in *polymerisation* and *crosslinking*

$$R^0 + AB \rightarrow R - AB^0 \qquad \text{followed by} \qquad R - AB^0 + AB \rightarrow R - AB - AB^0 \quad ...;$$

- Free radicals allow also the induction of chemical reactions not possible in conventional chemistry. This is applied in *radiation synthesis*;
- By choice of appropriate conditions it is also possible to graft a second polymer onto the original polymer material, as applied in *grafting of polymers* and the *synthesis of biomaterials*.

II.14.1.3.1.2 Absorbed dose, depth-dose and range

Because, as described before, the quantity of reactive species (e.g., free radicals) produced is directly related with the energy deposited by the incident beam of ionising radiation, absorbed dose is the primary physical quantity to characterise irradiation processes. Dose is the measure of energy deposited in matter by ionising radiation per unit mass. The SI unit of measure is the Gray (Gy), which is defined as one Joule of energy absorbed per kilogram of matter.

Although all ionising radiations will give in a particular material rise to similar end products (free radicals), there will be substantial quantitative differences in the resulting effects. These differences stem from different spatial distributions of absorbed dose and accordingly of the reactive species, which are produced near the patterns of initial energy deposition. To account for spatial distributions of irradiation effects, depth-dose curves are used. They describe the distribution of the absorbed dose deposited by an ionising radiation beam into a medium as it varies with depth along the axis of the incident beam [12, 13]. Figure II.14.4 shows that there are important differences in the way how the doses are deposited as a function of penetration depth, depending on the type and energy of the incident ionising radiation. These differences form the basis of the large variety of approaches in accelerator applications.

Also important for applications, is the range of a particle. The range is the distance travelled by a particle in the medium. It can be calculated using the reciprocal of the total stopping power (including the stopping power associated with other processes as Bremsstrahlung production, not only collisions). The range (in cm) for a particle with energy E_0 impinging on a material is given by

$$R(E_0) = \int_0^{E_0} \left(\frac{dE}{dx}\right)^{-1} dE \quad . \tag{II.14.2}$$

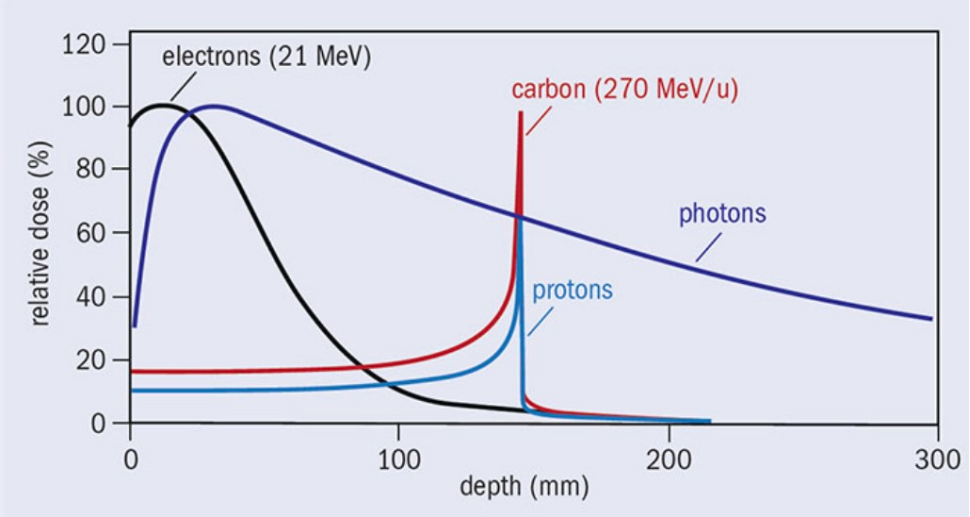

Fig. II.14.4: Examples of depth-dose curves in soft tissue for different types of ionising radiation [13].

The range (in cm) is inversely proportional to the density ρ of the medium (see Eq. II.14.1). Range and penetration depth of a particle are not necessarily equal. Electrons collide with orbital electrons of identical mass. Due to multiple scattering over significant angles, they do not travel along a straight path, but their trajectories are erratically twisted. The energy releases are widely spaced in the medium along tortuous tracks. On the contrary, protons and ions, as they are heavier than atomic electrons, can transfer only a small fraction of their energy in a single collision with atomic electrons and their deflection angle is negligibly small. So, all heavy charged particles travel along rather straight paths in matter and they are slowed down as a result of a large number of small energy losses, leaving a dense track of ionised and excited atoms in their wake. As photons and neutrons travel considerable distances through matter between two interactions and there is an exponentially decreasing transmission probability for their passage through material, it is not useful to apply for single photons or neutrons the concept of range. Instead, a better approximation is to use a sufficiently high number of photons or neutrons and describe transmission of the beam during passage in a medium by means of a simple exponential law, at least after a certain dose build-up zone as shown in Fig. II.14.4.

As we will see further, depth-dose curves and ranges are crucial in understanding applications of low-energy accelerators. They form the basis of the choices that must be made for each particular application (type of radiation, energy, beam power, type of accelerator, irradiation configuration, etc.).

II.14.1.3.2 Interactions of ionising radiation with nuclei: nuclear reactions

As discussed in the previous paragraph, the energy deposition in matter via ionisation collisions and the resulting free radical production is very important for applications in the domain of radiotherapy and radiation processing. By contrast, interactions with nuclei via so called nuclear reactions are especially important in two other domains: radioisotope production and ion implantation. A detailed discussion of how particles or photons interact with a nucleus is beyond the scope of this chapter. We limit the description here to some general aspects of those reactions which are relevant for low-energy accelerator applications. When an incident projectile (charged particle, neutron or photon) interacts with a nucleus

in the target material

- the projectile penetrates the target nucleus and transforms the nature of it. One or more new nuclei and nucleons or photons are produced. The process is referred to as a nuclear absorption reaction, often simply called nuclear reaction;
- or the projectile bounces from the nucleus without changing the nature of the nucleus. The process is referred to as a nuclear scattering reaction.

II.14.1.3.2.1 Particle- or photon-induced nuclear absorption reactions

In a nuclear absorption reaction, the incident projectile penetrates the target nucleus and ejects one or a few nucleons directly, or it combines first with the nucleus, creating for a very short time (10^{-15} s) a compound nucleus. In the latter case, the projectile loses its identity, and the total energy within the compound nucleus is shared among all nuclear constituents, before the compound nucleus decomposes by emission of particles. The two steps are considered to be independent of one another and the decomposition can take place by numerous different paths, called exit channels. So, a nuclear reaction will produce new nuclides and particles along channels which are independent of the way in which the compound nucleus was formed. Nuclear reactions are designated as *A(a,b)B* (the projectile is labelled by "*a*". When *a* enters nucleus *A*, it is transformed into nucleus *B* and a lighter particle *b*, which is emitted).

There is a vast number of possible nuclear reactions which can be triggered by accelerator beams with an energy up to 50 MeV. Transfer reactions, capture reactions and photonuclear reactions are the most important in this context. In a transfer reaction a projectile is absorbed and re-ejected together with one or a cluster of particles. These reactions mainly take place at the surface of the nucleus. In capture reactions, nuclei capture the projectile, become excited and de-excite via emission of photons. Photonuclear reactions occur when a high energy photon is absorbed by the nucleus of an atom, resulting in an emission of a neutron ((γ,n) reaction) or proton ((γ,p) reaction) and a transformation of the nucleus. These reactions may produce radioactive isotopes and are extensively used for *radioisotope production*.

Nuclear reactions often have a threshold energy, defined as the smallest value of a projectile's kinetic energy at which a nuclear reaction can occur. A reaction between a charged particle and a nucleus cannot take place if the centre-of-mass energy of the two bodies is less than the Coulomb barrier (neglecting the rare effects of quantum tunnelling). Neutrons penetrate the nuclei quite easily, because they do not have to overcome a Coulomb barrier. To allow ejection of a nucleon from a target nucleus, the incoming projectile, must have an energy higher than the binding energy of that nucleon in the nucleus, which is of the order of 8 MeV on average. For example, in the range from a few MeV to about 50 MeV, protons can induce different types of reactions, as (p,n), (p,pn), (p,2n), (p,p2n), (p,α)... where each of these reactions begins at a higher threshold energy than the preceding one (rule of the thumb: around 8 to 10 MeV higher energy threshold per additional nucleon expelled).

II.14.1.3.2.2 Nuclear scattering reactions

Nuclear scattering processes have relevance only for accelerator applications in which heavy particles scatter (elastically or inelastically) at target atoms located in a crystal lattice. When an ion collides with nuclei in a crystal lattice, the ion can scatter and transfer part of its energy to the atom in the lattice. In

case of a hard collision, a lattice atom can get enough energy to break free from the lattice, which causes lattice disorder and damage of crystal structure. Displaced atoms can in turn displace others, and the net result is production of a highly disordered region around the ion path. This is used for *nanoscale modification* of materials. The impinging ion can also be stopped, the process being called nuclear stopping, useful for ion implantation. Both techniques are *ion beam applications*.

II.14.1.4 Classification of applications of particles or photons from low-energy accelerators

One of the essential features of the use of accelerator beams for medical or industrial purposes is the fact that exposure of materials to beams of particles or radiation can induce modifications in their physical, chemical and/or biological properties. The goal is to perform an irradiation with ionising radiation in a targeted manner, leading to the expected features and with minimum of side effects. Ionising radiation can be used for medical or industrial purposes in basically two ways: (1) for modification, or (2) for analysis of materials. In the context of our discussion here, the term "materials" must be interpreted in a broad sense. Materials can be industrial products, foodstuff, integrated circuits, tires, etc., but also human tissue, cancer cells, air samples, explosives, gemstones or pieces of art, etc.

II.14.1.4.1 Materials modification

In the area of materials modification, there are four application domains for ionising radiation:

- two application domains are based on the ionisation reactions of ionising radiation. Ionisation leads to the production of free radicals, that induce chemical and/or biological changes, a feature extensively used in radiotherapy applications (see Section II.14.2) and in radiation processing (see Section II.14.4). For reasons explained in Section II.14.2.1, in the energy domain below 50 MeV, only electron accelerators are used for the applications which are based on free radicals;
- two other application domains are based on the nuclear reactions resulting from the direct interaction of the incident radiation with nuclei of the medium, which induces physical changes in the target material. This may result in transformation of the target nucleus into a radioactive isotope, which is used in isotope production for nuclear medicine (see Section II.14.3). Collisions of accelerated ions with target nuclei, may also stop and "bury" the incident ion or displace a target nucleus in its lattice. These features are used in ion beam applications (see Section II.14.5), more in particular for ion implantation and for nanoscale modification.

More than 80% of all accelerators worldwide are operating in these four accelerator application domains.

II.14.1.4.2 Analysis of materials

The wide diversity of reactions induced by energetic particles and photons, can also be used for many powerful analytical and imaging techniques applied to a variety of materials. Particles and photons can penetrate materials and provide via electronic or nuclear reactions a "signature" of the materials present. This offers very effective tools for interrogating objects or characterising materials. Low-energy accelerator-based analysis techniques are: Ion beam analysis (IBA), Accelerator mass spectrometry (AMS) and inspection with photons or neutrons (see Section II.14.6).

Table II.14.1 summarises the interactions of ionising radiation which are most relevant for the different application domains of low-energy accelerators, as well as their key target products, on which different applications are based. In the following we will discuss each of these domains more in detail.

Table II.14.1: Relevant interactions of ionising radiation for low-energy accelerator applications.

Application domain	Projectiles	Main interaction type	Goal: production of
Radiotherapy	X, e^-	Ionisation	Free radicals
Radioisotopes production	p, d, α, X	Nuclear absorption reactions	Radioactive nuclides
Radiation processing	X, e^-	Ionisation	Free radicals
Ion beam applications	Ions	Nuclear scattering reactions	Implanted ions, Impurities, Interstitials, Crystal damage
Analysis of materials	Ions, X, n	Ionisation or nuclear reactions	"Signature" of materials

II.14.2 Radiotherapy

II.14.2.1 Radiotherapy with photons and electrons versus proton or ion therapy

The most direct impact that particle accelerators have on our lives is surely by their applications in radiotherapy, namely treatment of cancer with accelerator beams. Radiotherapy is applied along two lines:

- using *photons or electrons*. Around 16000 medical electron accelerators are in operation;
- using *protons or ions*, also called hadron therapy, with around 110 hadron accelerators.

Presently about 50% of all patients with cancer undergo radiotherapy, often in conjunction with other treatments such as chemotherapy or surgery. The most common form of radiation therapy is external beam radiotherapy where a beam of ionising radiation from an accelerator is fired into the tumour. The goal is to destroy cancer cells by damage created, mainly in the DNA of the cells. Unfortunately, the ionising radiation does not kill cancerous cells only; it also damages healthy cells. This can lead to harmful side effects for the patient. The aim of radiotherapy is to concentrate a high dose of radiation into the tumour whilst reducing the radiation dose in healthy tissue.

In an ideal world one would never use electrons or photons in radiotherapy, as protons and heavier charged particles have several advantages, beneficial for radiation therapy: the presence of a Bragg peak in their depth-dose distributions and the higher radiobiological effectiveness (RBE) because of their better Linear Energy Transfer (LET) [14].

Due to the β^{-2} dependence (see Eq. II.14.1 and Fig. II.14.4) the ionisation energy loss of charged particles increases towards the end of the range, where the energy deposition reaches a maximum and then abruptly drops to zero. In literature, this sharp peak in the dose-depth curves for protons and heavier particles is referred to as "Bragg peak". For electrons this absorbed dose increase is hardly observable, as it is substantial only over the last nanometres of the trajectory, where the electron energy is already very low. For high-energy protons and heavier particles this region extends over a few millimetres. By

successive exposures at increasing proton or ion energies, one can gradually displace the Bragg peak over the volume of the tumour and "paint" a high dose in it, while sparing the surrounding tissue.

In radiotherapy deposition of energy at µm-scale (cell dimensions) is an important parameter. The LET describes the density of ionisation events along tracks, via the average amount of radiation energy deposited per unit length on µm-scale, which is usually expressed in keV/µm. Electrons and photons (X-rays or γ-rays) have low LET, because they are sparsely ionising radiation, with a few discrete ionisations at µm-scale. They destroy DNA, mainly via the production of free radicals. Protons and ions form densely ionising radiation with many discrete ionisations at µm-scale, which gives them a higher probability to hit DNA directly, leading to a higher radiobiological efficiency (RBE) for damaging cells.

Despite the advantages associated with the Bragg peak and the higher RBE for protons and ions, the number of hadron therapy machines in the world represents less than 0,7% of all radiotherapy accelerators. The reason is the following: to reach a tumour in every position of a human body, 230 MeV protons are needed (requiring a large size cyclotron or synchrotron), compared to a beam of 8 MeV photons, which can be produced with a small electron accelerator with an overall length of one to two meters. Simply based on magnetic rigidity, dimensions of hadron therapy machines are about 35 times larger. So, hadron machines do not fulfil the requirements of a low-energy accelerator, as defined in Section II.14.1.2. Photon and electron therapy remains the routine therapy, while hadron therapy is generally reserved for treatment of special tumours near critical organs, of paediatric tumours or tumours resistant to photons.

II.14.2.2 Radiotherapy with photon and electron beams

Electron accelerators can be used in two ways, with electron beams or with Bremsstrahlung photon beams (X-rays). Electron beam therapy is only useful for treating tumours near the surface, because of the limited range of electrons in biological matter. X-ray beams have much higher penetration so that X-ray therapy, is by far the most common form of radiotherapy.

It is the goal of radiotherapy to kill the tumour cells by creating radiation damage in the most sensitive region of the cell, the genetic material DNA [15]. Based on the principles discussed in Section II.14.1.3.1, X-rays or electrons damage DNA, either directly by a direct hit destroying a chemical bond, or indirectly by the action of free radicals, created as a result of ionisation of water in the cell. Damage by free radicals is the dominant mechanism. In DNA, damage of the nitrogenous bases (adenine, thymine, guanine and cytosine) or the hydrogen bonds, as well as chain breaks may alter the genetic code and lead to transformations of the cell (see Fig. II.14.5 (a)) which may finally kill the cell.

However, living species are exposed already for millions of years to terrestrial radioactivity and to cosmic radiation. During evolution, DNA has developed repair mechanisms to radiation damage. Base damage, bond breaks and single chain breaks can often be repaired, but the probability of repair of double chain breaks is much lower. Unfortunately, radiation does not only harm the cancerous cells; it also damages healthy cells at locations in the patient's body that cannot be avoided by the beam. This can lead to harmful side effects for the patient.

The aim of all new techniques in radiotherapy is to deliver a high dose of radiation to the tumour, to get a high cure rate, whilst reducing to a minimum the radiation dose in healthy tissue, in order to limit

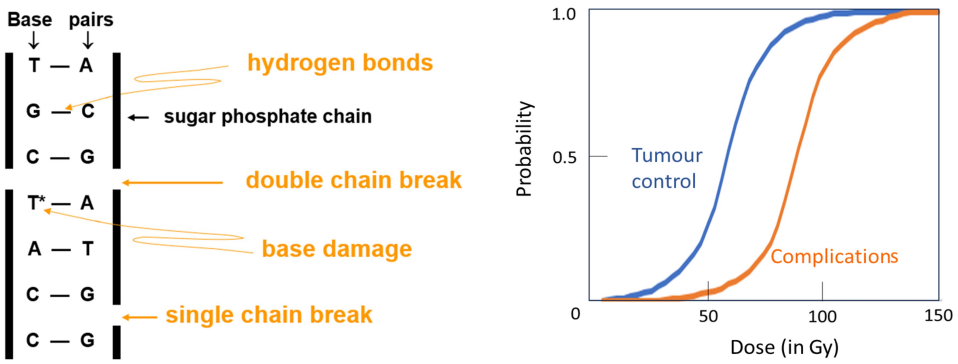

Fig. II.14.5: (a) Radiation damage to DNA and (b) tumour control probability versus probability of complications.

side effects (see Fig. II.14.5 (b)). The optimum choice of the target dose is such that it maximises the tumour control probability and simultaneously minimises the normal tissue complications probability. The proper dose to be delivered to the tumour is very high, typically 60 Gy. To maximise the destroying effects to tumour cells, while minimising the damage to healthy cells, radiotherapists apply a combination of three approaches [16, 17]:

- dose fractionation with dose delivery being spread out over a time of weeks;
- a cross-firing technique;
- advanced treatment techniques.

II.14.2.2.1 Fractionation of the dose delivery

Compared to tumour tissue, normal tissue has a higher survival probability when it is irradiated with low doses. When a dose is not high enough to kill a cell, cell repair is more efficient in normal cells, as cancer cells are generally less differentiated and more stem cell-like. Cancer cells "invest" more in their reproduction than healthy cells, and as a result they have less ability to repair sub-lethal damage. This is one of the reasons why the total dose delivered to the patient is fractionated: the total dose needed to destroy the tumour is not delivered in one session, but spread out over time, typically 2 Gy per session over 30 sessions in 6 weeks. Fractionation gives normal cells time to recover, while not all tumour cells have enough time to repair between fractions. There are two additional reasons for fractionation: (1) It randomises the moment in the cell cycle at which doses are applied. This allows tumour cells that were in a relatively radio-resistant phase of the cell cycle during one treatment, to evolve further into a more sensitive phase of the cycle when the next fraction is given. (2) Cells with higher O_2 content are generally more sensitive to radiation. Cell killing in well oxygenated regions can be up to three times greater as irradiation generates oxygen-derived free radicals which increase DNA damage. During tumour growth, tumour cells may become hypoxic (poor of oxygen) and therefore more radioresistant. When the tumor shrinks after a fraction of irradiation, hypoxic cells may become reoxygenated, improving the tumor cell killing probability at the next irradiation fraction.

II.14.2.2.2 The cross-firing technique

Figure II.14.6 shows the typical layout of the internal structure of an electron accelerator for radiotherapy. Once the electron beam is accelerated to the treatment energy, electromagnets direct the electron beam into the treatment head of the machine and further toward the patient, lying on a couch. Photon beams are by far the most used in radiotherapy machines, as the penetration depth of electrons is rather low. An acceptable dose distribution (high dose in tumour, low dose in surrounding tissue) cannot be obtained when only a single photon beam coming from one direction is directed toward the patient. As is shown in Fig. II.14.4, the depth-dose distribution for photons has roughly an exponential decrease inside water, after a dose build-up in a superficial layer (the same applies for tissue in a patient). Hence, treating a deep-lying tumour (for example at depth around 10 cm) involves significant doses upstream and downstream of the defined tumour volume. High dose levels to surrounding normal tissues can be avoided by using the cross-firing technique, where collimated photon beams are brought in, sequentially, from several directions so that they overlap at the tumour. To allow treatment from any angle, the beams are leaving the treatment head located in a gantry, which is the rotating part of a radiotherapy machine. The fixed part is the stand. The gantry can rotate 360° around a single point, the isocentre, where the photon beams from all directions intersect. The patient on a couch is positioned such that the tumour is at the isocentre.

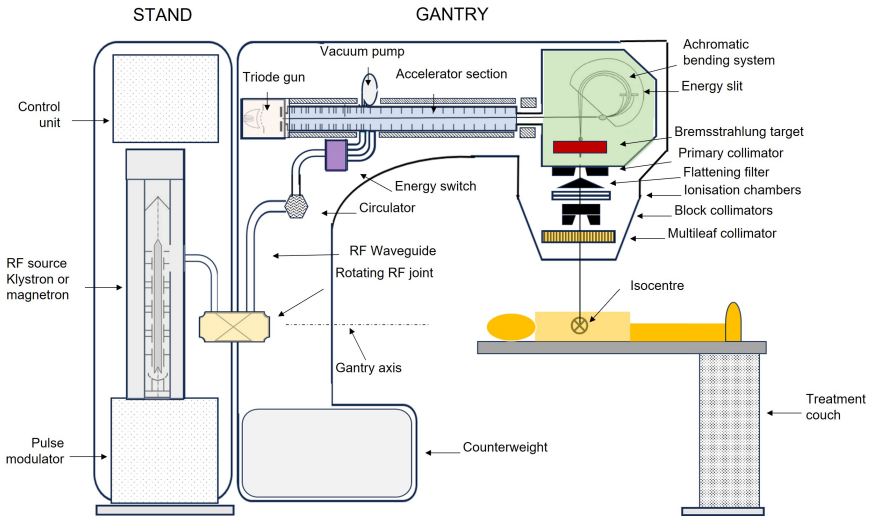

Fig. II.14.6: Schematic layout of the internal structure of a radiotherapy facility in photon mode.

In the treatment head a Bremsstrahlung target is placed in the electron beam path. The photon beam is made laterally uniform using a flattening filter and it is collimated using rectangular collimator blocks, usually made of tungsten, to generate a uniform beam of the appropriate size needed for treatment (typically 40 cm by 40 cm). This approach used to be the classical method in X-ray radiotherapy, extensively applied at the beginning of this century. Development and implementation of several novel advanced treatment techniques during recent years, brought X-ray therapy to unprecedented precision.

II.14.2.2.3 Advanced treatment techniques

II.14.2.2.3.1 Conformal therapy

In conformal therapy [18], the cross section of the radiation beam after the collimator, is not rectangular, but shaped to fit the cross section of the tumour, projected along the beam axis. This can be realised by using a so called multileaf collimator (MLC). In such an MLC about 40 tungsten plates can move independently in and out of the path of a radiotherapy beam. The individual leaves can be positioned to generate, for each beam direction, a custom shape for the collimator opening that blocks dose to areas outside of the intended target volume.

II.14.2.2.3.2 Intensity-modulated radiotherapy (IMRT)

In conformal therapy, it is difficult or sometimes even impossible to create a high-dose zone in three dimensions which fits the shape of a complex tumour, simply by superposition of uniform X-ray fields. When a tumour is not well separated from surrounding healthy organs and/or has a concave or irregular shape, there may be no practical combination of superimposed uniform intensity beams that will safely treat the tumour and spare the healthy organs. This is for example problematic in the case of treating prostate cancer, or when a tumour is wrapped around a critical organ. In IMRT [19], the cross-fire technique is applied with beams having an intensity distribution which is non-uniform over their cross section. For each irradiation direction, an optimised non-uniform intensity distribution is created by superposition of a number of individual beams with different cross section. During irradiation, dynamic adjustments of the leaves of the MLC continually re-shape and move the beam aperture over the planned treatment area, so that one can modulate the absorbed dose in small volumes of the tumour and superimpose them. The dynamic modulation of the beams allows for much tighter conformality of the radiation dose distribution with the tumour volume and better sparing of nearby normal tissues.

II.14.2.2.3.3 Image-guided radiotherapy (IGRT)

The better the dose conformity, the higher the risk for over/underdose due to positional changes of the tumour with respect to the beam (respiration during irradiation, movement of organs, positioning of patient between fractions, shrinkage of tumour over time, etc.). Radiotherapy with integrated imaging allows real-time adjustment of the therapeutic beams. Computerised tomography (CT) imaging with X-rays is used. Recently magnetic resonance imaging (MRI) combined with an electron accelerator was successfully realised [20, 21]. MRI has many advantages (better differentiation of cancerous from healthy tissue, faster real-time imaging during treatment with ability to see the tumor on-line, no ionising radiation used for imaging). But significant technological challenges are related to the integration of a linac (typically 6 MeV) and an MRI magnet (typically 1.5 T) [22, 23]. For example, the linear accelerator has many critical components, as the electron gun, radiofrequency (RF) source, RF circulator and energy switch which do not function properly in a high magnetic field. Magnetic fields also influence the electron beam traveling within the beam transport system and dose distributions in the tumour (e.g., via secondary electrons generated inside patients). Vice versa, RF fields from the accelerator and vibrations of moving machine components may significantly deteriorate MR image quality. The highly innovative technology of direct integration of MRI and linear accelerators is very new (first treatment of patients was in 2017)

and represents an exciting new development [24]. The number of newly installed and operational MRI-linac systems is rapidly increasing worldwide.

II.14.2.2.3.4 Other modern techniques

Additional alternative techniques in photon and electron therapy are [17]:

- *Robotic radiotherapy*: a robotic arm orients a linac which directs a large number of precisely focused radiation beams (pencil beams) from many directions to the tumour;
- *Intra-operative radiotherapy (IORT)*: apart from the standard procedure described above, there are two alternative irradiation approaches: (1) intracorporal, using a small accelerator in the surgery room and (2) extra-corporal, with temporary removal of a bone affected by cancer, irradiation outside the body and re-implantation of the treated bone [25, 26].

II.14.2.3 Accelerators for external radiotherapy

Today, a typical medical accelerator has the following capabilities: dual photon energy (typically 18 and 25 MV) and electrons with multiple electron energies (typically five energies); compact achromatic bending magnet; dual scattering foils or scanned electron pencil beam; full dynamic conformal dose delivery with intensity modulated beams produced with a multi-leaf collimator and if possible, an integrated tumour imaging system. The vast majority of the machines uses microwave S-band electron linacs, with a travelling or standing wave disc-loaded accelerator section (often biperiodic or side-coupled), designed for a high shunt-impedance to realise compactness. Changing power from the radiofrequency source, in combination with an energy switch between buncher and accelerator part of the section, allows easy switching between several energies while maintaining good beam quality.

II.14.3 Production of radioisotopes for nuclear medicine

II.14.3.1 Use of radioisotopes for diagnostics and internal radiotherapy

Nuclear medicine covers all medical uses of radioactive sources, that are introduced into a patient for the purpose of diagnostics or therapy [27]. Radioisotopes are now routinely applied in hospitals worldwide in millions of procedures annually. Roughly 5% of all accelerators worldwide are used for production of radioisotopes. 95% of these medical radionuclides are used for imaging and 5% for cancer treatment. Medical isotopes are produced using nuclear reactions induced by neutrons in a reactor or by beams of protons, ions or photons from an accelerator. When a beam strikes an isotope production target, the number of protons and/or neutrons in the nuclei of the target material alter as a result of nuclear reactions (see Section II.14.1.3.2), transforming them into radioisotopes. This process is called activation. After isolation and purification of the medical isotopes, they can be combined with relevant biomolecules, e.g., glucose, to form a radiopharmaceutical. This radiopharmaceutical can be injected into a patient, where it accumulates in tissues with high metabolic activity, as for example in tumours. The radioisotopes, which are collected in the targeted organ or tumour, emit radiation, which is used either for medical diagnosis or for treatment. Alternatively, after production, the radioisotopes can be encapsulated and placed in or near a tumour for a specific period of time needed for therapy.

A variety of radioisotopes can be produced. Their half-lives cover a wide range and different isotopes emit diverse types of radiation, allowing their flexible and effective use for specific applications. The choice of the "best-suited" radioisotope is based on several parameters. For medical diagnostics penetrating radiation from γ-emitters is needed to allow detection outside the patient's body. In addition, the half-life of an imaging isotope must be long enough to allow transport from the production site to end-use hospitals without excessive loss of activity, and short enough to minimise the unwanted radiation dose to the patient after the procedure. Therapy applications require injection of radioisotopes producing high LET radiation (α or β) having shorter range, to deposit dose locally in the tumour, and with half-lives long enough for the time needed for therapy.

The generator method, which enables on-demand availability of important radionuclides, is often used. A generator with a long half-life parent radionuclide is produced, from which the short-lived radionuclide, to be used in the hospital, is formed continuously as a result of decay. The most important example is the generator combination ^{99}Mo/^{99m}Tc. The longer-lived parent ^{99}Mo (half-life of 2.75 days) decays to its shorter-lived daughter ^{99m}Tc (half-life of 6 hours), so that clinicians can extract ("milk") the ^{99m}Tc daughter from the generator when needed.

II.14.3.1.1 Imaging for medical diagnostics

Isotopes emitting γ-rays or positrons can serve as diagnostic probes, with detectors located outside the patient to image the radiation distribution and thus the biological structures where the radioisotopes have accumulated [27, 28]. They allow to see metabolism (the functioning body), in contrast to X-ray (CT) scans or MRI that are better to visualise the anatomy (the body structure). There are two techniques (see Fig. II.14.7):

– single photon emission computed tomography (SPECT) [29];
– positron emission tomography (PET) [30].

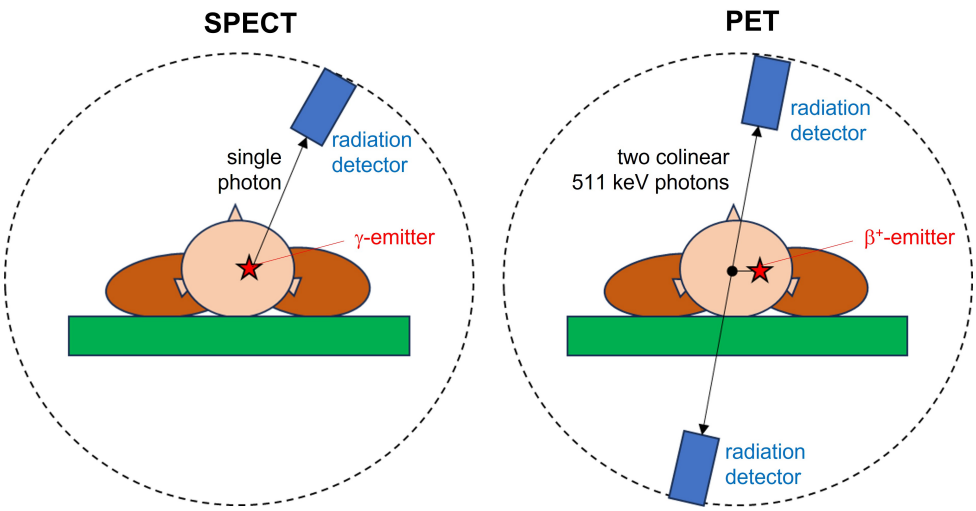

Fig. II.14.7: SPECT and PET.

II.14.3.1.1.1 Single photon emission computed tomography (SPECT)

SPECT uses γ-emitting radioisotopes. Single photons are detected by a gamma camera that can view organs from many different angles. Detected photons designate where bio-molecules labelled with radioisotopes have accumulated (e.g., in a tumour) and are a measure of the level of biological activity. ^{99}Tc (emitting 140 keV photons) is used in about 80% of all SPECT imaging procedures and is thus the workhorse of diagnostic nuclear medicine. Other SPECT radioisotopes are ^{123}I, ^{111}In and ^{201}Tl.

II.14.3.1.1.2 Positron emission tomography (PET)

In PET, radioisotopes emit positrons that annihilate with electrons in a tissue, causing two 511 keV photons, emitted in colinear opposite directions. A PET scanner detects these emissions "coincident" in time, which provides more accurate information on radiation emission localisation and, thus, higher spatial resolution images than SPECT. The positron emitter ^{18}F (1h50' half-life) is the radioisotope of choice for PET. It is attached to a bio-molecule such as FDG (Fluorodeoxy-glucose), with major applications in oncology, neurology and cardiology. Other examples are ^{11}C, ^{13}N, ^{15}O, ^{64}Cu and ^{124}I.

II.14.3.1.2 Internal radiotherapy

Emitters of β-rays and α-particles deposit most of their energy close to the site of the emitting nucleus and serve as therapeutic agents to destroy cancerous tissue. The following three approaches are in use: brachytherapy, targeted therapy and boron-neutron capture therapy.

II.14.3.1.2.1 Brachytherapy

In Brachytherapy [31] metallic capsules containing β-emitting isotopes such as ^{103}Pd are surgically implanted directly into a tumour, a procedure widely used now for prostate, uterus and skin treatments. Irradiation with β's affects only a very localised area, while healthy tissues are spared.

II.14.3.1.2.2 Targeted therapy

In targeted therapy, isotopes with decay products as Auger electrons, α- or β-particles and photons are used. A promising new therapy involves binding the radioisotope (e.g., ^{211}At, ^{213}Bi, ^{225}Ac) to an antibody that specifically targets a tumour cell (radio-immunotherapy). Targeted alpha therapy (TAT) [32] is an excellent way to treat diffuse cancers (e.g., leukaemia) or metastasis. One of the most promising α-emitting isotopes is ^{211}At (Astatine) that can be produced by a deuteron accelerator with energy below 30 MeV. ^{225}Ac is an α- and γ-emitting isotope, so that therapy and diagnostics can be combined in a single procedure, called "theragnostics". ^{67}Cu is another theragnostics isotope.

II.14.3.1.2.3 Boron-neutron capture therapy (BNCT)

An "atypical" but promising form of therapy for difficult-to-treat cancers is BNCT [33]. A pharmaceutical compound which carries ^{10}B and concentrates selectively in the tumour cells is administered to the patient. ^{10}B is a stable non-radioactive isotope, but it has a very large capture cross section for thermal neutrons. When a patient is irradiated with an epithermal neutron beam from a reactor or an accelerator (neutron energy range from 0.5 eV to 100 keV), the neutrons thermalised in the tissue may be captured

by ^{10}B to yield excited ^{11}B. ^{11}B undergoes radioactive decay into an alpha particle and a lithium nucleus, the combined ranges of which are $\sim$ 10 µm, approximately one cell diameter. This damages the cells in which the capture took place. The success of this therapy depends on the availability of a neutron beam with a suitable energy spectrum and sufficient intensity. Delivering neutrons with high flow rate in the epithermal energy range is extremely difficult. A lot of research on accelerator-based BNCT sources is ongoing. Recent technological breakthrough made in compact accelerator-based production of intense beams of epithermal neutrons, suitable for BNCT, allows the application of BNCT in hospitals and cancer research centres [34].

II.14.3.2 Production of radioisotopes

Neutron-rich radioisotopes (^{99m}Tc, ^{131}I, ^{166}Ho, ^{177}Lu, etc.) are generally produced in research reactors. Neutron-deficient radioisotopes (^{18}F, ^{201}Tl, ^{123}I, ^{67}Ga, etc.) are typically produced via charged particle reactions in accelerators. Proton accelerator beams lead to nuclear reactions of the type (p,xn) or (p,α) resulting in short-lived proton-rich β^+-emitting isotopes. Using accelerators, quite often the same radioisotopes can be obtained via different reaction channels, as reaction channels where target and product isotopes are different, are easy to find. In the range from 7 MeV to about 50 MeV, protons can induce different types of reactions, such as (p,n), (p,pn), (p,2n), (p,p2n), (p,α), etc. with increasing threshold energy. Nearly 50 radioisotopes can be routinely produced in this way, including the most common traditional γ-ray emitters (such as ^{201}Th, ^{123}I and ^{111}In), short-lived β^+-emitting isotopes (^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{64}Cu and ^{124}I), as well as β^--emitting isotopes such as ^{103}Pd.

The production rate R of the radioisotope in an accelerator is given by [35]

$$R = NI(1 - e^{-\lambda t}) \int_{E_i}^{E_f} \frac{\sigma(E)}{dE/dx} dE \quad , \tag{II.14.3}$$

where *R* is the number of nuclei formed per second, *N* is the target thickness in nuclei per cm^2, *I* is the incident particle flux per second ($\sim$ beam current), λ is the decay constant equal to $(\ln 2)/T_{1/2}$ (with $T_{1/2}$ being the half-life), t is the irradiation time in seconds, $\sigma(E)$ is the reaction cross-section as a function of particle energy expressed in cm^2 which changes during slowing down of the incident particle in the target. dE/dx is equal to the total stopping power defined earlier in this chapter (see Eq. II.14.1). The integration is from the initial energy E_i to the final energy E_f of the incident particle along its path.

Reactor-produced radionuclides for medical purposes continue to be important because the relative cost of their production is lower. However, accelerators have important advantages:

- Radioisotopes produced with accelerators have higher specific activity (radioactivity/gram), because, in reactors, after neutron capture, the final nuclide often possesses the same chemical properties as the target nuclide. Bombardment with charged particles results in a different element, allowing easier chemical separation of reaction products and starting material;
- Accelerators greatly expand the range of isotopes. Charged particles can easily be accelerated to higher energies than fast neutrons in a reactor. This allows to open more reaction channels, creating new isotopes. To optimise production routes, good knowledge of charged particle induced activation cross-sections as function of energy (also called “the excitation function”), is needed [34];

– A smaller amount of radioactive waste is generated from charged particle reactions;
– The radionuclides obtained in accelerators have higher purity. For a certain radioisotope, the combination of accelerator beam energy and thickness of the radioisotope production target can be optimised, such that the energy of the charged particles within the target remains within well-defined limits, so that competing reactions, that may create impurities, can be limited or even excluded. For example, for the production of ^{201}Tl the reaction is ^{203}Tl(p,3n)^{201}Pb, where ^{201}Pb decays to ^{201}Tl. The cross section for this reaction is important between 20 and 40 MeV proton energy, with a peak at 30 MeV. However there are competing reactions (p,2n), producing of ^{202}Pb, and (p,4n), producing ^{200}Pb, which must be avoided. By choosing 30 MeV as the maximum proton beam energy of the accelerator, the protons remain below the threshold energy for the cross section of the (p,4n) reaction. By limiting the target thickness such that the proton energy in the ^{203}Tl production target never drops below 20 MeV, the energy region, where the cross section for the competing (p,2n) reaction becomes important (< 20 MeV) is avoided (for more details see Ref. [35], page 119).

Thus, by carefully selecting the target nucleus, the bombarding particle and its energy, and the thickness of the target, it is possible to produce a specific radionuclide. In an optimised combination, the incident beam intensity and the irradiation time are the two remaining parameters, defining the production rate *R* of the radioisotope. During irradiation, there is competition between formation and decay of the radioactive isotope. This competition will come to equilibrium at sufficiently long bombardment times. The time dependence of the activity is expressed by the term $(1-\mathrm{e}^{-\lambda t})$ in the formula for the production rate *R*. This term is called saturation function. After 3.5 half-lives the saturation function is at a level of 90% of its maximum. Therefore, except for the shortest-lived radioisotopes, irradiation times in an accelerator will rarely exceed 3.5 half-lives, as no matter how much longer the irradiation is carried out, the extra gain of radioactivity is never above 10%. As a result, the incident particle flux, and not the irradiation time, is the determining factor for obtaining a high final activity. Therefore, accelerators producing high-intensity beams are needed for efficient radioisotope production.

II.14.3.3 Accelerators for the production of radioisotopes

Proton cyclotrons (some of them also accelerating deuterons) are the most widely used accelerators for the production of proton-rich radioisotopes (about 950 medical cyclotrons worldwide) [36]. These are proton accelerators with internal targets, or H^--accelerators with stripping foils for extraction, allowing simple and efficient extraction of intense proton beams. There are four groups of them:

– Hospital-based small, compact cyclotrons with very low proton energy (< 10 MeV), designed for on-site production of a single PET isotope. The smallest cyclotron accelerates deuterons to about 3.4 MeV, i.e., below the break-up threshold of the deuteron (to avoid neutron background). It is used exclusively in a hospital environment to produce ^{15}O via the ^{14}N(d,n)^{15}O reaction. Other low-energy proton cyclotrons produce, for example, ^{18}F in amounts of a single patient dose;
– Cyclotrons with proton energy less than 20 MeV, primarily producing positron emitting radionuclides, in particular the four standard PET radioisotopes (^{11}C, ^{13}N, ^{15}O and ^{18}F). These cyclotrons accelerate protons in the 10 to 20 MeV range, some also deuterons with an energy from 5 to 9 MeV.

The cyclotrons are usually located in a regional centre or hospital. The PET isotopes have short half-lives. Because of considerable yield loss during the delivery time from cyclotron to patient, they must be used on-site. The same accelerators can also produce more novel positron emitters such as ^{64}Cu for PET, ^{123}I for SPECT and ^{103}Pd for therapy. These machines have beam currents less than 100 µA and external targets. Many of the cyclotrons are self-shielded;

– Proton cyclotrons, with proton energy between 20 and 30 MeV, primarily producing gamma-emitting radioisotopes for SPECT, such as ^{123}I, ^{111}In and ^{201}Tl. The SPECT isotopes have medium half-lives which permit isotope delivery to more distant users in a group of hospitals. Production generally takes place in a dedicated production facility with high power targets and larger throughput. The beam intensity is often more than 100 µA with multiple external beam lines and targets. These cyclotrons also produce other isotopes such as ^{124}I (PET) and ^{68}Ge (generator for ^{68}Ga, a SPECT isotope). One of the most promising α-emitters is ^{211}At, obtained by a bombardment of a natural Bismuth target with an α-beam (^{209}Bi(α,2n)^{211}At reaction). The optimum energy is 28 MeV (sufficient yield but below threshold for ^{210}Po production);
– Larger cyclotrons with proton energies greater than 35 MeV are used in the production of a number of the isotopes used for internal radiotherapy, such as ^{125}I and ^{103}Pd. They usually operate at an industrial scale with high beam currents (1 mA) and internal targets. They also deliver several clinically useful longer-lived isotopes for SPECT such as ^{201}Tl, ^{123}I and ^{67}Cu.

Recently, compact proton linac-based radioisotope production facilities became commercially available. They consist of an RFQ with DTL machine producing a 7 MeV, 9 mA, 1% duty cycle proton beam for ^{18}F-FDG production. Besides that, photonuclear reactions are also used for medical radionuclide production using Bremsstrahlung originating from electron beams. Feasibility studies have demonstrated the viability of linear electron accelerators and Rhodotrons to produce radioisotopes with Bremsstrahlung photons. Rhodotrons can deliver high-power electron beams of 120 kW at 40 MeV. This allows efficient production of isotopes such as ^{225}Ac, ^{99}Mo, ^{64}Cu, ^{67}Cu and ^{47}Sc [37].

For BNCT, accelerator-based neutron sources are an attractive alternative to nuclear reactors for providing epithermal neutron beams. Excellent epithermal neutron beams can be produced via the ^{7}Li(p,n)^{7}Be reaction at proton energies of $\sim$2.5 MeV. The primary challenge today is to improve the flux and beam quality of present sources. An electrostatic quadrupole accelerator and a lithium target, which can deliver and handle 2.5 MeV protons at beam currents up to 35 mA, are already commercially available. The first is commissioned at Helsinki University Hospital.

II.14.3.4 The ^{99}Tc crisis: a challenge for the accelerator community

By far the most commonly used radioisotope is ^{99m}Tc, which is applied in SPECT in about 80% of all nuclear medical imaging procedures. Almost all of the used clinical-grade ^{99m}Tc in nuclear medicine is derived from ^{99}Mo/^{99m}Tc generators. The generator isotope ^{99}Mo is a fission product produced in nuclear reactors. Almost the whole ^{99m}Tc demand worldwide is covered by only six reactors which are all about 60 years old. The half-life of 2.75 days of ^{99}Mo is long enough to allow worldwide distribution. In the hospitals clinicians "milk" the ^{99m}Tc daughter (half-life 6 hours) from the generator when needed. In 2009 there was a severe ^{99m}Tc crisis, due to worldwide ^{99}Mo shortage, as several of the ag-

ing production reactors were unexpectedly unavailable at the same time. In addition, since then several reactors have been shut down or are approaching the end of their life cycle in a few years. As a result, the global supply of radioisotopes has become fragile and future secure supply of ^{99m}Tc is becoming at risk. This triggered a worldwide policy-driven demand for research towards alternative production methods using accelerators. Figure II.14.8 summarises major possible accelerator-based routes for the production of ^{99m}Tc, presently under investigation. All these accelerators have an energy not higher than 40 MeV [38].

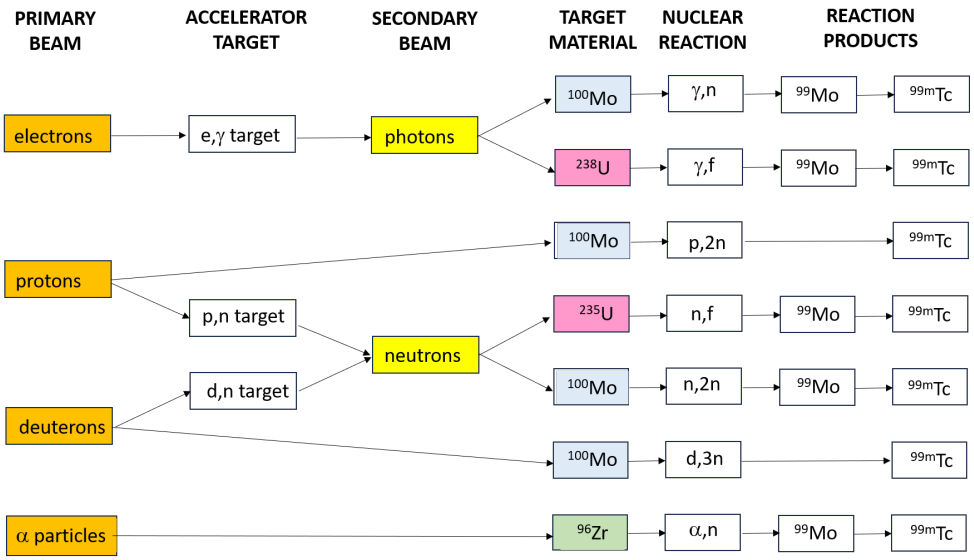

Fig. II.14.8: Accelerator-based methods for production of ^{99m}Tc and its parent isotope ^{99}Mo.

II.14.4 Radiation processing

II.14.4.1 Electron and photon beams for industry

Radiation processing is a means to change physical, chemical or biological characteristics of commercial products and materials by treatment with electrons or photons (see Fig. II.14.9) [39]. It is one of the major applications of accelerators and the fastest growing field both in number of facilities and in power ratings that are used. Electron beams are produced with electron accelerators, while photons for radiation processing are either emitted by radioactive sources (β-rays) or produced by electron accelerators via the Bremsstrahlung process (X-rays), as explained in Section II.14.1.2.2.

In recent years, γ-sources, which were two decades ago the workhorses for radiation applications in industry (as well as in medicine), have been steadily replaced by Bremsstrahlung sources, which offer many advantages (switchable on/off, forward-peaked beams, variable energy, dual mode e^-/X, no nuclear waste). In view of economic efficiency, it is important that conversion of electron beam power into X-ray beam power is maximised. Bremsstrahlung target thickness is an important optimisation parameter, as the target should be thick enough to allow development of the full photon cascade, while it should not be too thick, to avoid internal absorption of the photons in the X-ray target. Calculations reveal that optimum thickness is around 40% of the electrons range in the target material. At this optimum

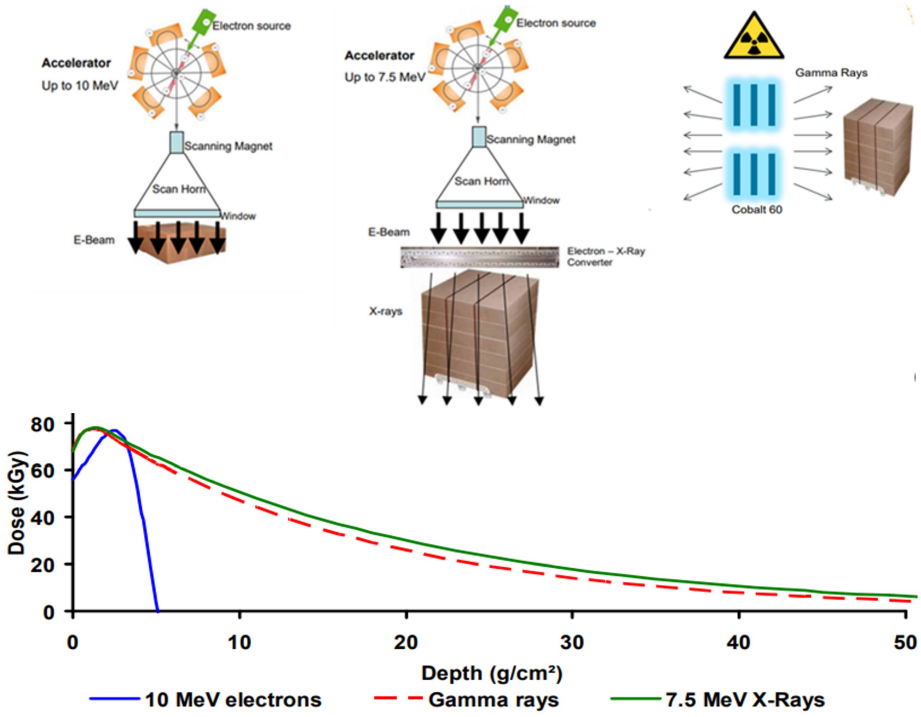

Fig. II.14.9: Sources of ionising radiation for radiation processing (top) and depth-dose curves in water (bottom).

target thickness, Bremsstrahlung efficiency (emitted photon power in forward direction over electron beam power) is about 9,5% for 5 MeV electrons in Ta, 13,3% at 7.5 MeV and 16% at 10 MeV [40].

Bremsstrahlung production increases with the electron kinetic energy. However, there are legal limitations with respect to the maximum energy of electrons and photons applied in industrial applications. It is essential that treatment with ionising radiation of a product for human consumption, does not leave the product radioactive. Therefore, based on scientific arguments and following experimental data collected over several decades, especially in food processing, the energy limits for radiation processing are fixed at 10 MeV for irradiation with electrons. For X-rays the maximum beam energy is fixed at 7.5 MeV in the US, and at 5 MeV in Europe and elsewhere [41, 42].

The relatively low efficiencies, resulting from legally imposed energy limitations, can be compensated by using high-intensity electron accelerators to produce X-ray dose rates sufficiently high for industrial applications. A typical industrial Co-source of 3 MCi emits 45 kW isotropic photon power. To reach a similar Bremsstrahlung beam power, an electron accelerator with an electron beam power of 475 kW at 5 MeV is needed. Only in the last two decades, reliable, compact, easy to operate high-intensity electron accelerators of the required energy and beam power level became available and entered the market at large scale. Almost all γ-sources in industrial plants have been steadily replaced by accelerator-based Bremsstrahlung sources, as it was also the case with γ-sources in hospitals, two decades earlier.

In Section II.14.1.3.1.2 we discussed the importance of depth-dose curves and ranges of different ionising radiations, crucial in understanding applications of low-energy accelerators. The Bethe-Bloch formula (see Eq. II.14.1) shows that particle range in a medium is inversely proportional to its density

ρ. In Fig. II.14.9 it can be seen that photons are much more penetrating than electrons. For example, if an electron accelerator irradiates water with 10 MeV electrons, their useful range is less than 4 cm. If a 7.5 MeV electron beam is transformed into an X-ray beam, about 20 cm of water can reasonably be irradiated. However, at 7.5 MeV the efficiency of transformation of electron beam power into photon beam power in an optimised Bremsstrahlung target is only about 13%. In the same accelerator, electron-beam processing offers a higher throughput then X-rays, but X-rays can better be used to treat or sterilise materials which are too thick or too dense for direct treatment with electrons. The limited penetrating power of electrons and a rather low efficiency of the Bremsstrahlung process means that electron irradiation is best employed when high dose rates are required in thin products and/or low-density materials.

II.14.4.2 Industrial applications of radiation processing

Industrial applications of electron or X-ray radiation are manifold and the number of application fields is rapidly increasing. We can group the majority of the applications in four domains:

- Polymer chemistry;
- Sterilisation;
- Food treatment;
- Environmental treatment.

In Section II.14.1.3.1.1 we already discussed in detail the crucial role played by free radicals in applications of ionising radiation. The ability of photons and electrons to break chemical bonds and to release free radicals has led to a wide range of important industrial applications. Free radicals have the ability to break and disable DNA of microorganisms, trigger a chain reaction in polymers, induce uncommon chemical reactions, break molecules of pollutants, create defects in crystals, etc. Industrial accelerators even enable manufacturing of products and providing treatments that would not be possible with other techniques. Via the production of free radicals, ionising radiation is a unique source of energy which can initiate chemical reactions at any temperature, including ambient, under any pressure, in any phase (gas, liquid or solid), without use of catalysts. A non-exhaustive list of industrial applications is given below. It is impossible to comment them here comprehensively. More details can be found in Refs. [43–45]. More than half of the world capacity of industrial electron accelerators is used for the first three applications in this list. The length of this list is steadily increasing:

- crosslinking of cable insulation;
- polymerisation of films;
- curing of coatings;
- production of heat-shrinkable plastics, processing of foamed plastics;
- vulcanisation of car tyres;
- curing of composites for vehicle components;
- finishing of textile materials;
- grafting acrylic acid on polyethylene;
- production of carbon fibre reinforced epoxies and wood-polymer composites;

- synthesis of biomaterials (biodegradable polymers, hydrogels for burn wound treatment);
- sterilisation of medical disposables and pharmaceutical drug ingredients;
- treatment (disinfection, shelf life extension, sterilisation, etc.) of fruit, vegetables, spices, fish, fresh meats (elimination of food-borne pathogens, as Escherichia coli, Salmonella or Listeria);
- sterilisation of hospital diets, prepared foods, etc.;
- liquid effluents treatment: water, industrial or hospital waste, sewage sludge;
- power plant emitted flue gases purification, treatment of marine diesel exhaust gases;
- reduction of molecular weight of powdered Teflon for lubricants, high quality inks;
- reduction of pollution (chemicals in viscose industry; soils polluted with hydrocarbons);
- improvement of electrical properties of semiconductors;
- colouring of gemstones.

II.14.4.3 Industrial electron accelerators

The range of possible applications of a radiation processing accelerator is defined by the energy of the electrons, the beam current, and the acceleration technique. While medical applications require doses in the Gy-range, typical industrial applications require doses in the kGy and MGy-range. In order to perform the delivery of doses in a reasonable time, the dose rate produced by the beam must be as high as possible. The dose rate is equal to the deposited energy per unit mass and per unit time. It is proportional to the impinging electron beam power, which is equal to the product of accelerator beam intensity and beam energy (strictly speaking, the beam energy must be expressed as the potential difference of an electrostatic electron accelerator that would lead to the same kinetic energy). But beam energy is not the suitable way to increase beam power and dose rate as (1) the maximum energy is fixed by law, and (2) increasing electron energy augments the depth of penetration into a target material but not the deposited energy per unit mass. So, high materials processing rates require high beam current, and accordingly high-intensity electron accelerators are needed [46].

As already mentioned earlier, all industrial accelerators are derived from accelerators which were initially designed for nuclear and particle physics. There is only one exception, the Rhodotron, a powerful 10 MeV electron accelerator, designed from the beginning in view of radiation processing applications. It is the machine with the highest beam power at 10 MeV, up to an order of magnitude higher than other accelerators available on the market.

The radiation processing accelerators have a beam line where the electron beams can be used directly, quite often after passage through a magnet, sweeping the beam over the product to be treated. Depending on the type of applications, this beam line can also be equipped with a removable X-ray target so that the facility can accommodate both electron-beam and X-ray irradiation processes. Alternatively separate electron and X-ray beam lines are used. In order to compensate for non-uniform depth-dose distributions, double-sided irradiation of the products is often applied.

There are different ways to classify radiation processing accelerators. As their energy defines the possible depth of penetration into a target material and accordingly the possible range of applications, we will use electron energy as the parameter to classify radiation processing accelerators.

II.14.4.3.1 Electron accelerators in the energy range from 50 keV to 500 keV

Low-energy high-intensity electron-beam accelerators are single-stage electrostatic accelerators. They are quite simple machines with an electron source at high voltage and the beam exit window foil at mass potential. The cathode is an elongated filament, up to three-meters long, which generates a "curtain" of electrons. Output beam currents can range from 10 to 250 mA. These machines are self-shielded and require no further radiation shielding when operated in uncontrolled areas. They have very low penetration capability and are intended for curing inks, coatings and adhesives; cross-linking polymers in thin plastic films; surface sterilisation of medical devices and food packaging.

II.14.4.3.2 Electron accelerators in the energy range from 500 keV to 5 MeV

Medium-energy electron-beam irradiators are electrostatic accelerators using multi-stage direct-current power supplies and multiple-gap acceleration tubes. There are different types, differing only by the way how the high-voltage is generated. As a large processing rate is needed, high-voltage systems delivering high current are essential. Cockroft-Waltons, Dynamitrons and insulating-core transformers are therefore preferred. These multi-stage accelerators can produce beams up to three meters wide, either with long filaments or beam sweeping magnets. Medium-energy electron beams find their most common uses in cross-linking polymers for wire and cable insulation, heat-shrinkable plastic tubing and films, moulded plastic parts and fibre-reinforced components; production of foamed ethylene; and in the vulcanisation (partial cross-linking) of rubber components in tyres.

II.14.4.3.3 Electron accelerators in the energy range from 5 MeV to 10 MeV

Radiofrequency (RF) linear accelerators with high shunt impedance or Rhodotrons are used. In RF linacs maximum beam power is limited to 50 kW, due to beam loading, as they usually operate at 3 GHz and accordingly RF power stored in the cavities is limited. Rhodotrons typically operate at 200 MHz (leading to cavity dimensions an order of magnitude larger) so that beam loading is not a real issue. Very high electron beam power (up to 700 kW) can be obtained making them ideally suited for radiation processing applications as for example bulk sterilisation of pre-packaged medical devices, food treatment and cross-linking of thicker plastic products including large diameter pipes and moulded parts.

II.14.5 Ion beam applications

II.14.5.1 Ion beams for industry

Ion beam applications are very important accelerator-based industrial processes in which accelerated ions or protons impinge onto the surface of a material to change its physical, chemical, or electrical properties [47, 48]. As already discussed earlier, when an energetic ion penetrates a solid, it undergoes a series of collisions with nuclei and with electrons in the target. In these collisions the incident particle loses energy at a rate dE/dx of a few to 100 eV nm^{-1}, depending on its energy and charge, as well as on atomic and mass number and density of the target material. In the energy domain normally covered by ion implantation (beams from a few hundred eV, up to 10 MeV), the electronic contribution dominates the stopping power at high ion velocity, while the nuclear contribution becomes dominant towards the end of the ion range. This process is used for (1) controlled insertion of ions for doping of semiconductors,

(2) ion implantation in near surface-layers of metals, and also ceramics and glasses, and (3) nanoscale modifications of structural properties of materials.

II.14.5.1.1 Ion implantation for doping of semiconductors

Ion acceleration of dopants and other ions is an essential and widespread tool for the fabrication of semiconductor devices as well as various forms of electronic, photovoltaic and photonic materials. It can be applied to introduce atoms precisely into discrete zones of semiconducting materials to alter their electronic properties such as electron mobility. This process is called doping [49]. In semiconductor device fabrication, B, P or As are introduced into semiconductors in a fully controlled way. After implantation and annealing, each dopant atom can create a charge carrier in the semiconductor: a hole can be created for a p-type dopant, and an electron for an n-type dopant, which modifies the conductivity of the semiconductor in its vicinity. The technique is used, for example, for adjusting the threshold voltage of a MOSFET, one of the basic constituents of modern integrated circuits (ICs). About 30% of all accelerators worldwide are used to dope Si or Ge in order to create ICs for computers.

II.14.5.1.2 Ion implantation into modern functional materials

Implanting high concentrations (1 to 20%) of some selected elements (N, Ti, B) into metals, ceramics or glasses changes dramatically their surface properties by forming new alloys (nitrides, borides, etc.). These modifications to the near-surface microstructure can appear as changes in corrosion behaviour, electronic properties, stiffness, hardness, wear-resistance, friction response, or other surface-region-sensitive mechanical properties such as fatigue and contact fracture toughness [50]. For example:

- Implanting N into low carbon steel increases surface hardness. Structural changes caused by implantation produce a surface compression in the steel, which prevents crack propagation;
- Implanting Ti into steel reduces the coefficient of friction in, for example, ball bearings or engine block cylinders;
- Implants of elements such as Cr, Ta, Pd or B into metals can change their chemical reactivity and make a tool more resistant to corrosion. For example, prosthetics such as artificial joints, must have surfaces very resistant to both chemical corrosion and wear due to friction.

II.14.5.1.3 Nanoscale modification

Ion bombardment can also modify material properties at nanoscale, see Ref. [43], Chapter 17. With fast heavy ions (MeV/atomic mass unit) one can create latent tracks of damage. This is used to fabricate track-etched membranes, with track diameters ranging from 10 to 100 nm, applicable for ultrafiltration, or as membranes with electrical and magnetic properties, with potential uses as chemical detectors and biosensors, see Ref. [43], Chapter 18. Ion track membranes can also be used as templates for making different nanostructures or composites. An example is the electrodeposition of nanowires of metal, of semiconductors and of magnetic materials.

The doses required for ion implantation in metals are usually much higher, of the order of 10^{17} ions/cm^2, than implantation in semiconductors (10^{15} ions/cm^2). They are also applied over wider

surfaces. Therefore high-intensity implanters (“high-current implanters”) are required, but purity and energy dispersion of the beams are less critical than for implanters for electronic devices.

II.14.5.2 Industrial ion beam accelerators

Ion implantation uses a wide variety of accelerator systems [51] and end station designs as well as many special techniques, however, apart from the accelerator, the basic designs are all similar, as shown in Fig. II.14.10. Atoms of the desired element (in principle each element from hydrogen up to uranium) are vaporised and ionised in a plasma ion source. The ions are emitted by the source and separated in an analysing magnet by their mass-to-charge ratios. All this equipment is located on a “hot deck”, which is brought at a high electrostatic voltage. For high-energy ion implantation applications this equipment is placed at the entrance of a tandem or a linear ion accelerator. The ions analysed in the magnet are accelerated and after leaving the accelerator, a uniform beam spot is obtained by focusing with quadrupoles. The ion beam is deflected with a horizontal and vertical scanning magnets, so that the ions are homogeneously distributed in a desired pattern over the surface of the wafer, and implanted in it.

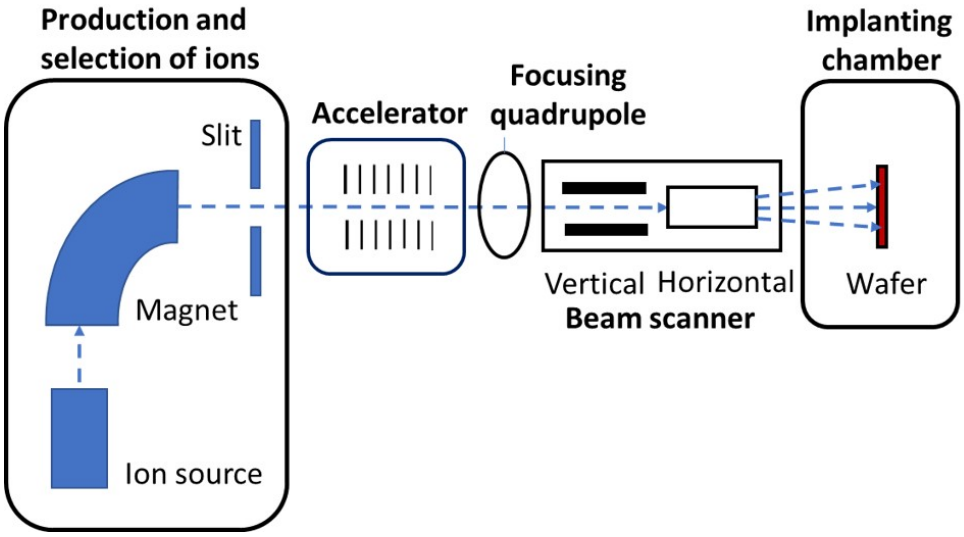

Fig. II.14.10: Typical ion implantation facility.

The accelerator types depend on the application [52]. There are three classes of machines:

- **Low energy/ high current implanter**
  - High current implanters with currents up to 50 mA,
  - Variable ion energies from few hundred eV to tens of keV,
  - Single gap electrostatic accelerators;
- **Medium energy/ medium current implanter**
  - Original ion implanter with currents in the 0.01 to 2 mA range,
  - Variable energies of 50 to 300 keV range,
  - Usually, multi-gap direct voltage units from high-voltage power supplies based on voltage-multiplier systems;

– **High energy/ low current implanter**
  – Implanters for special applications (e.g., nano-structuring) with beam currents up to 100 µA,
  – Variable energies from 1 to 10 MeV,
  – Linacs or tandem charge-exchange columns with high-charge-states for upper energy range.

II.14.6 Analysis of materials

II.14.6.1 Analytical techniques based on ion accelerators

The use of ion beams for analysis of materials is a relatively new application based on electrostatic single-ended and tandem accelerators (one to several MV) [53]. They are used in many fields ranging from materials and environmental sciences to the study of cultural heritage and biological samples. There are two different approaches (see Fig. II.14.11):

– Ion beam analysis (IBA): ion beams probing surface structure and materials behaviour [54];
– Accelerator mass spectrometry (AMS): a sample is vaporised and transformed into an ion beam to perform mass spectrometry of trace elements and long-lived isotopes [55].

Both techniques are very sensitive. They allow analysis of very small samples (pg to µg) with a sensitivity of µg/g and isotopic ratios $1 : 10^{15}$. It is possible to probe atomic layers, even to count individual atoms. Quite often both approaches (IBA and AMS) are linked to the same accelerator facility.

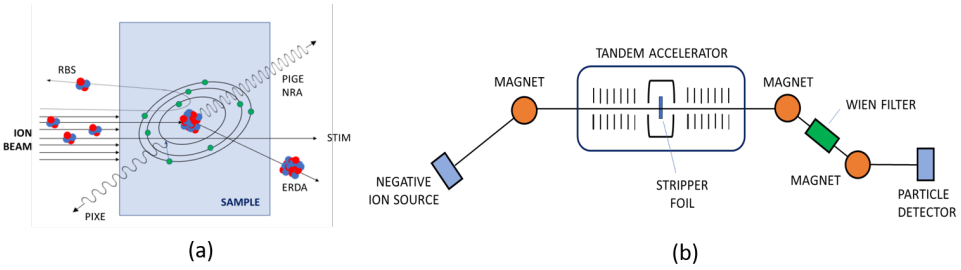

Fig. II.14.11: (a) Ion beam analysis (IBA) and (b) Atomic mass spectrometry (AMS).

II.14.6.1.1 Ion beam analysis (IBA)

Ion beam analysis (IBA) groups a collection of analytical techniques that exploits the interactions of MeV ions with matter. When an energetic ion strikes a target there are a variety of interactions, any (or all) of which can be used (together or separately) to obtain information about the target. IBA probes elemental composition as a function of depth up to several microns. Fig. II.14.11 (a) shows different possible interactions of accelerated ions with matter. Some ion beam analytical techniques rely on stimulating photons or particles to be emitted from the sample: particle-induced X-ray emission (PIXE), particle induced gamma ray emission (PIGE) and nuclear reaction analysis (NRA), which are sensitive to the chemical or isotopic composition of materials. Other techniques utilise scattering or absorption,

as well as recoil of ions from the sample to characterise the chemical and structural composition of materials or to obtain elemental concentration depth profiles. Techniques are Rutherford back scattering (RBS), elastic recoil detection analysis (ERDA) and scanning transmission ion microscopy (STIM). The relevant scientific information is obtained from measured quantities such as the characteristic energy spectra of the resulting photons or charged particles emitted. The integration of all these techniques in a so-called "total-IBA" measurement allows covering almost the whole periodic table (H to U) with high sensitivity and the complete characterisation of all elements in a sample. With special quadrupoles a so-called microprobe can be formed which can focus MeV ion beams into $1 \times 1\,\mu m$ spot sizes, allowing micro-mapping.

Examples of analysis techniques at IBA facilities are: thin film and multilayer analysis; bulk composition analysis; depth distribution of heavy ion implantation; surface damage and contamination; defect depth distribution due to ion implantation damage; lattice location of impurities in single crystal and lattice strain measurement of superlattices. Ion beam methods can also be used to analyse in a non-destructive way cultural heritage items. An interesting example is the AGLAE (Accélérateur Grand Louvre d'Analyse Élémentaire in Paris) accelerator facility in the basement of the Louvre, fully dedicated to the study and investigation of works of art and archeologic artifacts. The 4 MeV proton beam delicately probes a large variety of materials: jewels, ceramics, glass, alloys, coins and statues, as well as paintings and drawings. These investigations provide information on the sources of the materials, the ancient formulas used to produce them, and the optimal ways to preserve these treasures.

II.14.6.1.2 Accelerator mass spectrometry (AMS)

Accelerator mass spectrometry (AMS) is an ultra-sensitive technique of counting individual atoms. It accelerates ions to kinetic energies up to the MeV-range to improve mass analysis sensitivity. In essence, an AMS facility is an ion tandem accelerator between two mass spectrometers (see Fig. II.14.11 (b)). The introduction of the tandem accelerator, followed by several ion-filtering devices reduces the background by a factor of the order of 10^8. The special gain of AMS, compared to other mass spectrometry methods, is its capacity to separate a rare isotope from an abundant neighboring mass. This is extensively applied to separate ^{14}C from ^{12}C, as used for example in the ^{14}C dating method. It makes also possible the detection of naturally occurring, long-lived radio-isotopes such as ^{10}Be, ^{36}Cl and ^{26}Al. AMS is capable of measuring very small isotope ratios in the range from 10^{-10} to 10^{-15}.

In conventional MS, samples are vaporised and ionised, separated by their mass-to-charge ratio, then measured by a detector. Rare isotopes such as ^{14}C present a challenge due to their very low natural abundance and high background levels. Conventional MS suffers from interferences: (1) isobaric interference (interference from equal mass isotopes of different elements such as ^{14}N in ^{14}C analysis), isotopic interference (interference from equal mass to charge isotopes of different elements, e.g., $^{112}Cd^{++}$ and $^{56}Fe^{+}$) and molecular interference (interference from equal mass to charge molecules, such as $^{12}CH_2^-$, ^{12}CD, or CH^- in ^{14}C analysis). By AMS these interferences can be eliminated almost completely (see Fig. II.14.11 (b)) [56]:

– Isobaric interference is already eliminated in the negative ion sputter source. This type of ion source does not form certain negative ions. In the cases of ^{14}C, ^{26}Al and ^{129}I, isobaric interferences

are eliminated because ^{14}N, ^{26}Mg and ^{129}Xe all have negative electron affinity, so that their stable negative ions cannot be formed;

– Molecular interference is eliminated in the stripper foil. The negative ions are mass-analysed in the low-energy magnet and then accelerated to the positive high-voltage terminal of the accelerator where they encounter a stripper foil or gas. In the stripper negative atomic ions are converted into multiply charged positive ions. Multiply charged negative molecular ions are unstable and do not survive, as they dissociate into their component atoms;
– After second acceleration back to ground potential there is a second mass analysis. In the magnetic analysis system, the radius of the trajectory is proportional to the magnetic rigidity of the isotopes (p/q). An additional analysis stage, consisting of a velocity filter (Wien filter) is added, to remove that small fraction of isotopic or molecular fragments which may have acquired the correct momentum, but with another velocity. A Wien filter is a system made of a combination of orthogonal electric field *E* and magnetic field *B*, such that particles with correct speed $(v = E/B)$ will be unaffected, while other particles will be deflected.

The applications of AMS are many:

– It is most often employed to determine the concentration of ^{14}C, e.g., by archaeological studies for radiocarbon dating. It remains the most important isotope in IBA, but much of the ^{14}C research is now directed towards understanding of global climate change via studies of oceanic circulation, atmospheric processes and past climates. Biomedical applications of ^{14}C are also becoming increasingly important;
– Cosmic ray exposure dating, which exploits the build-up of ^{10}Be, ^{26}Al, and ^{36}Cl in surface rocks, is making significant contributions to studies of landscape evolution. ^{10}Be is used in studies of soil processes, deposition of ocean sediments, and sources of volcanic rocks. ^{36}Cl and ^{129}I have been used in hydrology and in tracing the migration of nuclear waste;
– ^{26}Al and ^{41}Ca have found application in biomedicine. In particular, ^{41}Ca has been used to measure bone resorption in postmenopausal women.

Nearly 100 AMS facilities now exist worldwide, one of them is incorporated into the AGLAE facility used by the Louvre museum (see above).

II.14.6.2 Imaging and screening techniques with photons and neutrons

Photons and neutrons can easily penetrate deeply into matter, as they have no charge. Beams of X-rays or neutrons can be applied as very effective tools for nonintrusive inspection of objects of all sizes and composition. Without creating any damage, they allow to interrogate objects by imaging the internal composition or by providing material-specific information on their contents.

Beams of photons or neutrons from accelerators are used in two ways:

– via transmission photon and neutron radiography images of the composition of bulk material;
– via generation of diagnostic signals or materials signatures by photon- or neutron-induced reactions in the object under investigation. By exploiting well-defined interactions within the object, it is possible to deduce physical or chemical properties of the materials of interest.

This makes them important tools in the field of non-destructive testing (inspection of industrial components; quality analysis of constructional elements of buildings, of castings or weldings; safety in aerospace; etc.), as well as in domains of security (cargo inspection; detection of illicit trafficking; etc.). More and more small particle accelerators, providing X-rays and neutrons, are now deployed at national borders, harbours, airports and transport hubs for detection of drugs trafficking, weapons, contraband goods or people smuggling, as well as CBRNE (Chemical, Biological, Radiological, Nuclear materials and Explosives) materials, which are hazardous materials or devices that may be used in a terrorist attack or other emergency situation. To detect the associated materials for a particular threat requires a broad range of detection processes. Photon and neutron-based inspection technologies must be configured to inspect items as small as postal parcels, bottles of liquid, laptop computers, but also devices must be developed to check large items as luggage, trucks, air cargo or shipping containers. Inspection procedures must be applied as rapidly as possible with minimal interference of the stream of goods. Recent advances have made these procedures very sensitive, flexible and automatic.

II.14.6.2.1 X-ray and neutron imaging

Photon or neutron beams can provide an image of an object under investigation using the transmission radiography technique [57]. During passage through matter photon or neutron beams are attenuated because of the various types of interactions that may occur in materials of varying densities. Elements of high atomic number will attenuate X-rays to the greatest extent, whereas neutrons are attenuated mostly by elements of low atomic mass, as neutrons transfer significant amounts of their energy to light elements by inelastic scattering. As a consequence, neutron and X-ray radiography are complementary techniques.

X-ray transmission radiography is the established screening technique in border control. It relies on Bremsstrahlung production by electrons, which are accelerated to several MeV, usually in a commercially available linac. Such X-ray generators are typically around a metre long, and are capable of delivering significant dose rates according to the penetration and regulation requirements for a particular transport method and objects to be scanned. However, in practice this method can only offer the ability to discriminate materials with large differences in densities, such as in metal objects. Typically, dual-energy systems operating at two X-ray energies are utilised in order to better discriminate between different materials. X-ray attenuation is element- and energy-dependent. By comparing photon attenuation in the object at two different energies, it is possible to calculate with sophisticated algorithms densities and approximate atomic numbers of materials in the photon beam.

The images that neutrons produce after passing through an object will mainly reveal substances containing light elements, which are generally invisible with X-rays (e.g., hydrogen, lithium, boron, and carbon). Because neutrons interact with the nucleus rather than with orbital electrons, they can also distinguish between different isotopes of the same element. Fast neutron radiography offers the potential to discriminate between various classes of organic materials. It is particularly attractive for screening cargo for contraband such as narcotics and explosives that have similar densities and shapes to many common substances.

II.14.6.2.2 Photon- and neutron-induced reaction spectroscopy

Accelerator-based active screening methods [58] complement the element-sensitive radiographic scanning of freight, discussed above. "Active" in this context means to expose materials (e.g., in a cargo container) to X-ray or neutron beams to generate a "fingerprint" characteristic for the materials in the beam. These techniques allow determination of the chemical components of the cargo material and identification of potential threats.

In nuclear resonance fluorescence (NRF) [59], Bremsstrahlung photons with a continuous energy distribution (typically covering the energy range from 2 to 8 MeV) excite, in isotopes of the irradiated material, specific energy resonances, which release gamma rays that have a discrete energy distribution, unique to the emitting isotopes. In a similar way, interrogating beams of neutrons can be used to stimulate the emission of characteristic elemental gamma rays resulting from nuclear reactions, primarily via thermal-neutron capture and/or inelastic scattering of fast neutrons.

Other active detection systems utilise Bremsstrahlung X-rays with beam energies high enough to cause photofission in any fissile nuclear materials present in cargo. The fission of nuclear material contained in the cargo generates additional neutrons and gamma-rays that can be detected, and which will have an energy and/or signature which is characteristic of the fission process in the nuclear material present. During the past decade, a number of active neutron-based techniques have been developed to provide detection of highly-shielded nuclear materials (especially highly-enriched uranium) by neutron-induced fission, similar to photofission.

II.14.6.2.3 Accelerators for photon- or neutron-based analytical techniques

The useful photon energy range (e.g., for scanning of bulk cargo or for industrial non-destructive testing) using X-ray radiography or NRF is between 1 and 10 MeV (not higher to limit accidental high dose exposures of humans and to reduce activation of materials). Interrogating photons in this energy range permit making X-ray images through steel with a thickness of several tens of cm. The photon beams are produced by radio frequency electron linear accelerators, similar to the linacs for radiotherapy. Generally, high average beam currents are desirable to improve detection statistics and to speed up the interrogation process. Units are designed to be mobile so that they can be moved around the objects in industrial plants or cargos to be inspected. They permit to locate flaws in large metal castings and welded joints as well as to inspect large solid-fuel rocket engines. In cargo inspection they allow identification of threats such as explosives, fissile materials, toxic materials and weapons of mass destruction. Systems can be designed to involve minimal operator intervention, to minimise dose to the object, and to provide high throughput at commercial seaports, airports and other entry points [60].

The wide variety of accelerator-based neutron sources deployed in neutron radiography or neutron spectroscopy have become known as compact accelerator-based neutron sources (CANS). They are using different accelerator types, described in detail in Refs. [7, 61].

II.14.7 Conclusion

Accelerators play an important role in numerous applications in domains as diverse as nuclear and particle physics, health, industry, security and environment. During the last hundred years, accelerators for

nuclear and particle physics research have been built in great diversity, and they have constantly grown in complexity and dimensions. They are extensively discussed in the other chapters of this book.

In the present, rather short overview, we have focused on the more than 40000 other accelerators that are currently operational and which produce ionising radiations in the form of energetic particles and X-rays to be used for many practical applications in medicine, industry and other domains of our daily life. To illustrate the diversity of this field a few examples of these applications can be mentioned: diagnosis and treatment of diseases, synthesis of intelligent drug-delivery systems, detection of suspicious cargo, implantation of ions in semiconductors, production of better radial tires, cleaning of flue gases or dating of archaeological finds. Countless other examples can be given. The concepts of many of these applications have been proposed, as soon as X-rays and elementary particles were discovered and the accelerators that could produce beams of ionising radiation became available. However, during the following decades, many of the proposed applications never developed to the extent anticipated in the early years, mainly due to a lack of suitable, dependable and affordable machines. Only in the last two decades, the field of accelerator applications in medical and industrial domains came to full maturity, with the advent of compact, reliable and efficient low-energy accelerator designs, often generating very high beam intensities, many orders of magnitude higher than those usually applied for high-energy research. This was made possible thanks to a fruitful synergy of progress in domains as accelerator technology, radiation chemistry and dosimetry, process engineering and automatisation, informatics with computer simulations and 3-D imaging.

It is impossible to discuss, within the boundaries of this chapter, the full extent of this vast and exciting domain of low-energy accelerators, their applications in many domains of human activity and the perspectives that recent progress can offer. For those interested in more details of a particular domain or a specific application, we refer to the following list of references. The cited books, reports and specialised papers and the many references therein, are a good starting point for further reading needed to get additional insight in this challenging field of research and engineering.

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