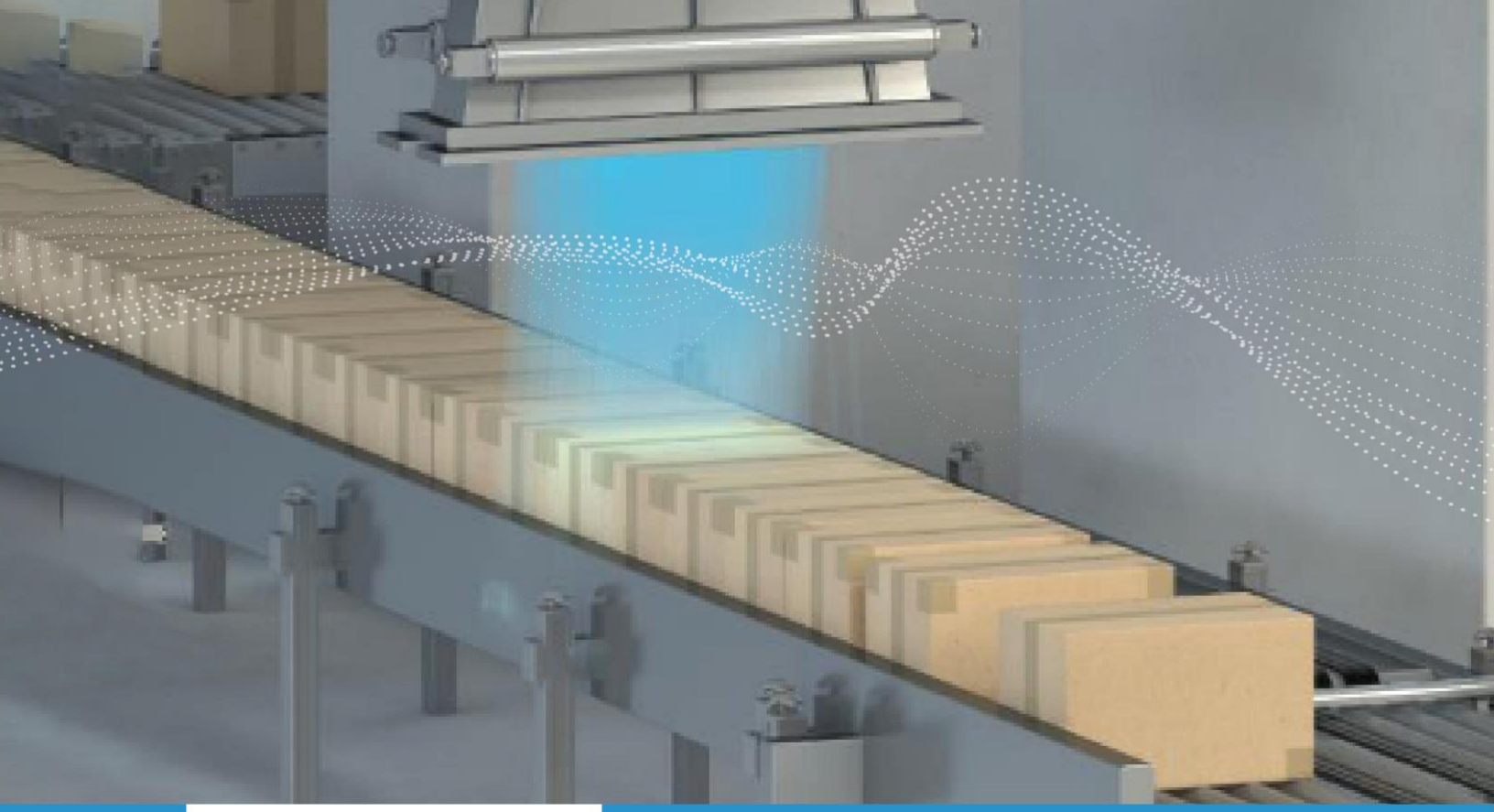

buyer's guide

# Accelerators for Sterilization of Medical Devices

## *A Guide for Prospective Buyers*

EB-X Working Group | May 2021

iia

# TABLE OF CONTENTS

# WHY THIS GUIDE?

The core mission of the Industrial Irradiation Association (iia) is to promote the beneficial use of irradiation, which includes the three types of ionizing radiation used in the industry: gamma rays, electron beams (EB) and X-rays.

After polymer modification, which is almost exclusively the domain of EB, sterilization of healthcare products is the second most important application of irradiation. Until now, ethylene oxide and gamma irradiation are the predominant sterilization modalities. Gamma irradiation has long established itself as a safe, robust, reliable, and affordable technology. Whilst thousands of low or medium energy accelerators are in operation around the world for the modification of polymers, the number of electron accelerators used to sterilize medical devices has remained relatively small. Reliability issues, the complexity of early machines and a limited offer can explain the slow uptake of accelerators for sterilization applications. In the 21st century, these reasons appear to be less valid and the landscape for the different technologies is changing. The design and components of modern accelerators make them more reliable, the offer has expanded and diversified considerably, and though still retaining a degree of complexity, improved interfaces make machines more user-friendly. More medical devices could be treated with accelerators than is currently the case and the option for new products should be considered. Accelerators can be used to produce two types of ionizing radiation: electron beams and X-rays. The choice between them will be guided by the package size, geometry, and density, as well as by the required dose range.

The recent years have already seen an increase in the volumes of healthcare products sterilized by EB and X-rays. In 2020, the number of new EB-X sterilization facilities was greater than the number of new gamma facilities. The share of these modalities against other sterilization modalities will probably keep growing but the perception that electrons do not penetrate enough and that accelerators are too complex is still a deterrent. Low energy electrons are already used by a small number of device or drug companies. The time of X-rays seems to have come and if their cost can be improved their potential is immense.

The International Irradiation Association is technology-neutral and considers that medical device manufacturers need all three irradiation modalities to be and to remain available to meet the growing demand for sterilization. There are many technical books and articles on accelerators but, as far as we know, no publication where the information needed by prospective buyers has been selected and put in the form of a guide. This guide was written with two main categories of readers in mind:

- Medical device manufacturers considering an in-house sterilization solution,
- Sterilization service contractors wishing to diversify the technologies that they offer.

Both are familiar with the regulatory environment of medical device sterilization. Information that can be easily found elsewhere was left out, such as the comparison of the different radiation technologies and non-radiation sterilization technologies, or the descriptions and details of accelerators and their components. The Technical Library at the end of the document includes a list of recent references. The cost that are given are indicative only. These and other figures appearing in the document should be

obtained from or confirmed by potential suppliers. The last appendix of the document includes a list of reputable suppliers who are members of the iia. Their websites are also an excellent source of technical information.

It is hoped that with this document the prospective buyer of an accelerator will have the necessary unbiased information and understanding of what an accelerator project entails in order to facilitate discussions with potential suppliers.

# WHO WHOTE THIS GUIDE?

This document is the collective work of the International Irradiation Association and several of its members.

The iia drafted the document and coordinated the contributions and reviews. The main contributors to the contents were:

- Fermi National Accelerator Laboratory (USA)[1]
- IBA (Belgium)
- Mevex (Canada)
- Sterigenics (USA)

The initial and final drafts were reviewed b

- Aerial (France)
- ITHPP (France)
- STERIS AST (USA)

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## LIST OF MAIN UNITS USED IN ACCELERATOR TECHNOLOGY

| | Unit | Simplified definition | Symbol |
|---|---|---|---|
| Dose | Gray | Energy absorbed per mass unit | Gy<br>1 Gy = 1 $J.kg^{-1}$ |
| Energy | Electron-volt | Kinetic energy gained by a single electron accelerating from rest through an electric potential difference of one volt in vacuum | eV<br>1 eV = $1.602 \times 10^{-19}$ J |
| Power | Watt | Rate of energy transfer | W<br>1 W = 1 $J.s^{-1}$ |
| Current | Ampere | Flow of electricity through a conductor | A |
| Frequency | Hertz | Number of energy waves that pass a fixed point in unit time | Hz<br>1 Hz = 1 per second |
| Equivalent dose | Sievert | Absorbed dose to human body adjusted to account for the effectiveness of the type of radiation | Sv<br>Numerically equivalent to Gray for electrons and X-rays |

# ARE THE PRODUCTS SUITABLE FOR EB OR X-RAY STERILIZATION?

Recent concerns regarding the supply chain flexibility and sustainability regarding the dominant sterilization technologies has resulted in the market considering that novel or multiple sterilization modalities are now more desirable [Ref. 1]. The selection of a sterilization modality requires a full understanding of the intended use and the sterilization process characteristics. The key aspects and decision trees have been described by Jami McLaren in a comprehensive article [Ref. 2].

Suitability essentially means material tolerance. The rate at which the different types of ionizing radiation deposit their energy may result in different effects on the materials of the medical device or the package for the same dose. With gamma radiation, the dose is delivered over several hours, during which oxygen may continuously diffuse within the device and fuel oxidative reactions. With the same dose delivered in a matter of seconds with EB, oxygen is instantly depleted and the time for oxidation is extremely short. Effects will be different if the device is packed under vacuum or in nitrogen. While temperature gently rises with gamma, electrons create an instant temperature spike followed by a quick cooling. The former can excessively heat material with low specific heat[2] while the latter may fracture some products. X-rays have lower dose rates than EBs but higher than gamma.

Some materials exhibit less degradation when processed with electrons or X-rays than with gamma. For example, some polypropylene materials may exhibit less breakdown and long-term aging effects. However, there is no general rule: there are many possible formulations for each type of polymer which means different combinations of additives that may modify radiation tolerance.

Whether dealing with new product or changing sterilization modality, the maximum acceptable dose needs to be (re-)assessed [Ref. 3][Ref. 4]. When treated at this maximum dose, product must meet its specified functional requirements throughout its defined lifetime (ISO 11137-1 8.1.1). Assessment of the sterilization as well as the verification dose are also required when converting from one sterilization modality to another (ISO 11137-1 8.4).

The technical information report AAMI TIR 17: 2018 [Ref. 5] was developed to provide additional guidance on material compatibility, design and testing to reduce cost and time required to perform material qualifications. In the U.S.A., the Team Nablo initiative led by Pacific Northwest National Laboratory and industry players has started publishing data [Ref. 6] [Ref. 7] for polymers used in the manufacturing of single-use medical devices when given sterilization-level radiation doses from e-beam or X-ray. In 2020 the IAEA launched a five-year Coordinated Research Project to investigate radiation effects on polymer materials commonly used in medical devices by comparing gamma, EB, and X-ray irradiation [Ref. 8].

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[2] Temperature increase ΔT (K) = Dose (kGy) / Specific heat ($J \cdot kg^{-1} \cdot K^{-1}$). At 25 kGy the temperature is 6°C for water and 46°C for titanium in adiabatic conditions (which is never the case in reality).

Section 4

# THE STERILIZATION REQUIREMENTS

Future users of an accelerator should write a User Requirements Specifications describing what will be required from the system. The document will be useful for the potential suppliers to have a good understanding of what your needs are: products to be treated, packaging, materials, density, doses, size of batches, possibility to flip the package, etc. The document will also be used during the validation process at the time of User Acceptance Testing or Initial Qualification.

To define the characteristics of the beam that will meet these requirements and the type of machine that would be suitable, three categories of data are essential:

- The product or irradiation container configuration (dimension, weight and density)
- The dose range required for each type of product,
- The volumes of each type of product to be processed annually.

## 4.1 Dose Range

Establishing the minimum dose required for sterilization (Dster) and the maximum dose acceptable by the product (Dmax,acc) is a prerequisite.

The ratio of the maximum dose to the minimum dose (Dmax / Dmin) obtained in an irradiation container during the routine process, called dose uniformity ratio (DUR) is a commonly used value. This ratio must be lower than the ratio of the maximum acceptable dose to the minimum sterilization dose (Dmax,acc / Dster). As undesirable effects increase with dose, a low DUR is favorable in terms of product quality. A low DUR also means that there is less unnecessary energy wasted in the product, which is favorable in terms of throughput. The radiation emitted by accelerators being unidirectional, the thickness that an electron or X-photon must cross and the mass that it meets on its path all influence the DUR. A variety of options are used to improve the DUR:

- Irradiating on multiple sides.
- Modifying the size, number, and orientation of product units within the package.
- Creating empty spaces in the product arrangement.
- Filling selected locations with dummy material.
- Shielding parts of the product with dense material, for example to protect sensitive electronic or biological components from irradiation. Fig.1 shows a creative solution developed for an inline system.
- Optimizing the beam properties i.e., energy, direction, or overscan.
- Adding accessories such as “scattering plates” to scatter the beam.

*Fig. 1: Shielding of some product parts in an inline sterilization system [Ref. 9]*


Product density and packaging characteristics greatly influence the value and the location of the minimum and maximum doses. They differ for gamma, EB and X-rays. Maximum dose seldom being less than twice the minimum dose, it is with EB that reaching an acceptable DUR is the most challenging. The DUR that can realistically be achieved with EB must be discussed at an early stage with potential suppliers and the values should be confirmed by modelling and / or tests using an accelerator capable of simulating the characteristics of the equipment under consideration. The centers listed in Appendix A can perform dose mapping studies to determine dose distribution for specific product characteristics and configurations and can confirm that the accelerator being considered can indeed achieve the required DUR.

## 4.2 Volumes to be Processed

The volumes to be processed, the pace at which they must be processed and how volumes are expected to grow are necessary data. Though it is often difficult to establish, a forecast of the volumes to be processed per day, month or year is necessary as well as the anticipated evolution over 5 to 10 years.

*Table 1: Example of volume forecast presentation.*

| Volumes to be processed | **Year 1** | **Year 5** | **Year 10** |
|---|---|---|---|
| Hours of operation per day | 8 | 12 | 16 |
| Day of operation per year | 250 | 250 | 250 |
| Product 1 | 10,000 m³ | 12,000 m³ | 8,000 m³ |
| Product 2 | 7,000 m³ | 9,000 m³ | 12,000 m³ |
| Product 3 | 5,000 m³ | 6,500 m³ | 8,000 m³ |
| Product 4 | 3,000 m³ | 5,000 m³ | 7,000 m³ |
| Product 5 | 2,000 m³ | 3,000 m³ | 4,000 m³ |
| Product 6 | 1,000 m³ | 2,000 m³ | 4,000 m³ |

These capacity requirements will determine the power needs. With accelerators, a fixed maximum capacity is available from day one. By putting them in stand-by or switching them off, the emission of radiation is paused. During the first years of operation, for example while the market builds-up, the number of shifts can be adapted to demand, *i.e*., utilization is usually the variable used to adjust throughput.

# ENERGY REQUIRED

The energy of accelerators is expressed in megaelectron-volts (MeV) or kiloelectron-volts (keV). Energy determines how far into the product the beam will penetrate. This in turn determines how inhomogeneous the treatment will be (DUR value). Consequently, energy is a key factor of process capability: type and density of product and packaging that can be treated, thin layers, dispensers, boxes, or full pallets.

## 5.1 EB Energy

Selecting the appropriate energy is particularly critical for e-beam systems. Most machines can work at different energy levels but the range within which the energy can be adjusted may be limited.

The concept of area density (or surface density) is used to quantify penetration because it conveniently combines density and thickness.

Area density ($g/cm^2$) = Average density ($g/cm^3$) x Thickness (cm)

**Examples:**
Product 1: Density = 0.10 $g/cm^3$and thickness= 30 cm, area density = 3.0 $g/cm^2$.
Product 2: Density = 0.25 $g/cm^3$and thickness= 20 cm, area density = 5.0 $g/cm^2$.
In a single side process, penetration and DUR will be better in product 1 than in product 2.

The figure below shows that products with different densities may have identical area densities.

*Fig. 2: Area density comparison*

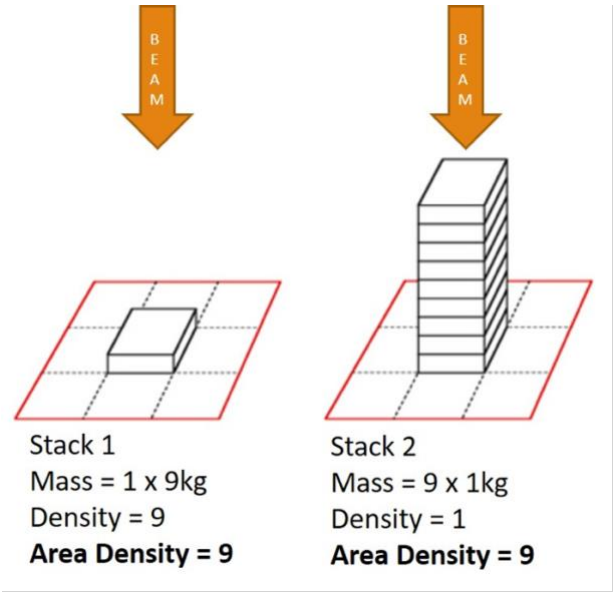
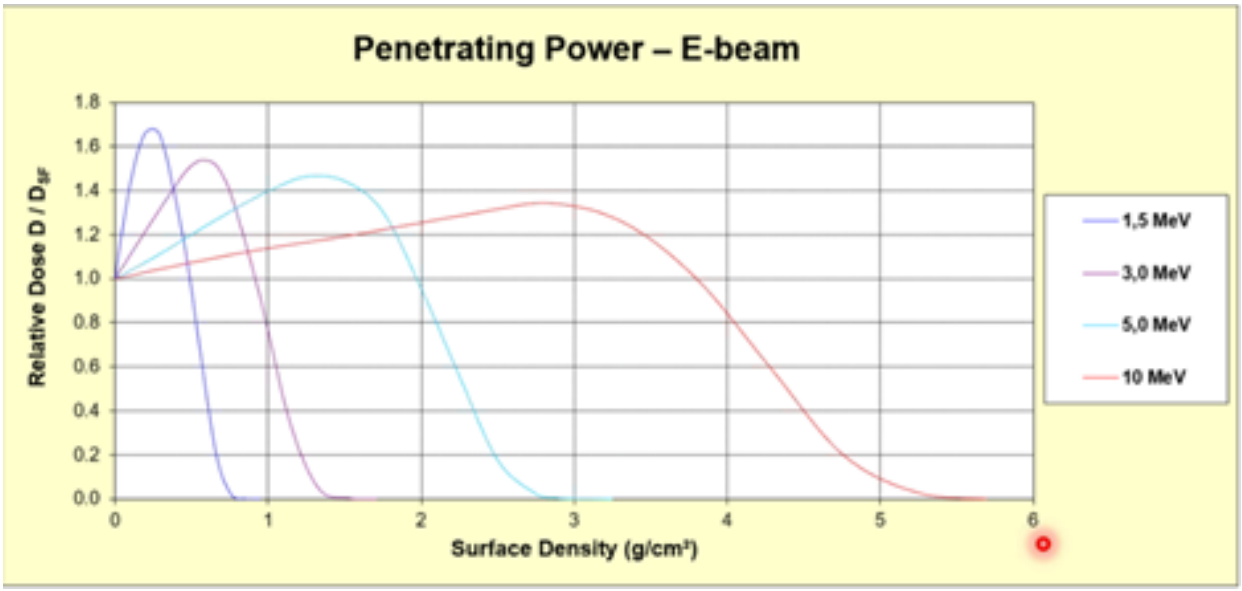


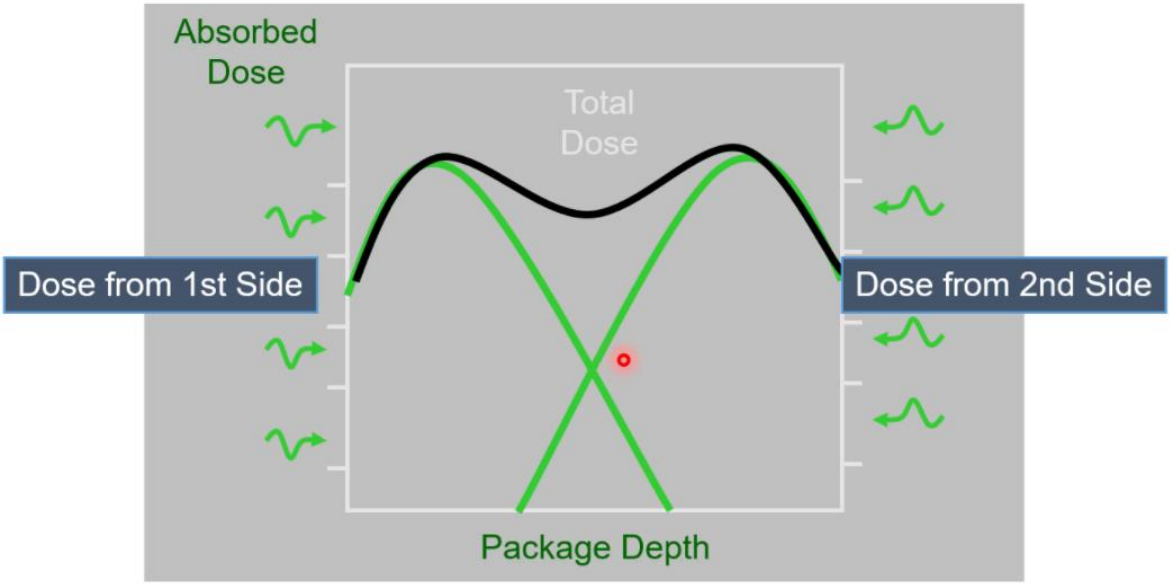
*Fig. 3 below shows that the maximum penetration of an electron beam is a function of its energy. At 10 MeV, the penetration of electrons in water (density 1.0 g/cm$^3$) is only 5.5 cm. At 5 MeV it drops to about 3 cm.*

*Fig. 3: EB depth dose curves*



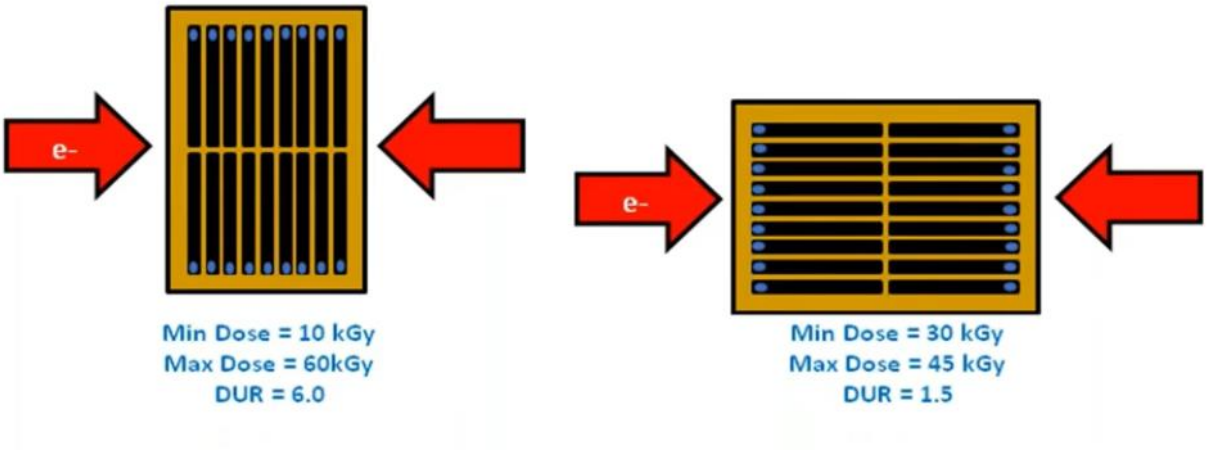

Products are often irradiated on two opposite sides. Fig. 4 shows a simple example of how irradiation on both sides of a package improves the DUR by increasing the lowest dose value after irradiation on a single side. The shape of the black curve representing the sum of doses depends on beam energy and area density.

*Fig. 4: Addition of doses from double sided electron irradiation (10 MeV - density 0.1) Credit STERIS AST*



The dose distribution resulting from EB irradiation is affected by scattering and shadowing. The orientation of product on the conveyor or in the carrier system as well as the orientation of the products within the package affect the DUR.

*Fig. 5: Effects of product orientation within package on DUR (Credit STERIS AST)*




Frequently, the selection of the energy of an e-beam system is a compromise between optimum penetration capabilities and system size and cost.

It must be noted that beyond 10 MeV, accelerated electrons may induce the creation of short-lived radionuclides within the product. This must be evaluated (ISO 11137-1 5.1.1) even if the risk is small.

## SUMMARY

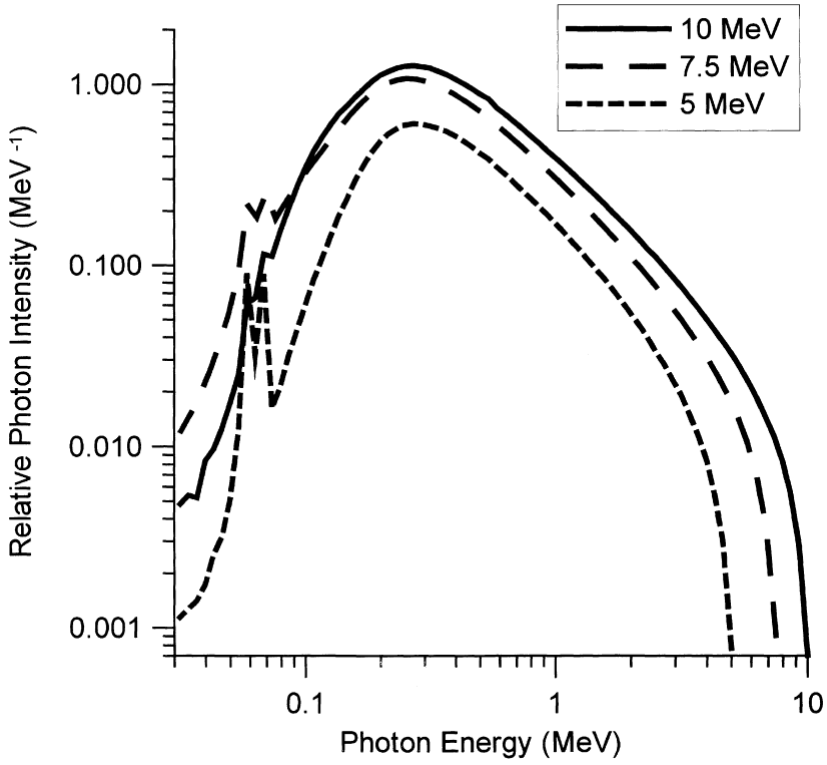
### EB Energy Selection

- Identify the main products that the system will irradiate with packaging size and weight
- Identify minimum doses for sterility
- Identify maximum doses acceptable by products
- Use modeling or simulations to determine achievable DUR at different energies
- Consider modifying package, filling, or orientation to improve DUR
- Confirm the results by performing a dose map in a comparable accelerator facility
- If required DUR cannot be achieved with electrons, consider X-rays

## 5.2 X-Ray Energy

X-ray energy is an output from the input electron beam energy and results from the interaction of the incident electrons with a target of high atomic number. The phenomenon is called *bremsstrahlung*, the German name for braking radiation. The energy spectrum depends on the type of machine and conversion system. The energy spread can range from a minimum of 10keV to several hundred keV and to a maximum that is the maximum e-beam energy, with the average X-ray energy somewhere in the low energy range. Consequently, only a small portion of the spectrum is at the highest energy levels. The exact spectrum is specific to the design and operation of the accelerator and the EB to X-Ray conversion system.

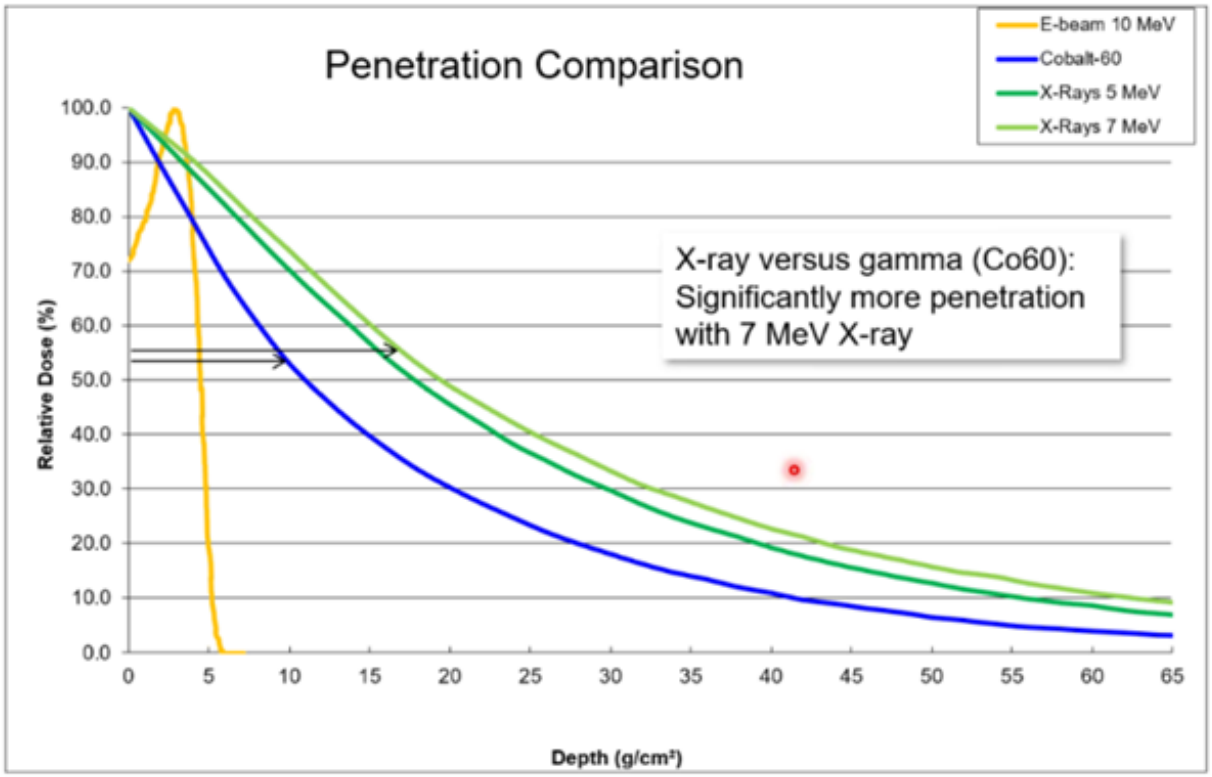
*Fig. 6: Calculated X-ray photon spectra for electrons with 5, 7.5 and 10 MeV incident energies [Ref. 10]*




Unlike for EB, this spectrum cannot be directly measured but it can be precisely calculated using Monte Carlo algorithms, based on the physical properties of the incident EB. By design, some types of machines have a narrower electron energy spectrum than others.

With high energy X-ray irradiation (5-7.5 MeV), dose distribution is as good as or better than with gamma irradiation, making treatment of large packages or full pallets possible [Ref. 9].

*Fig. 7: Depth dose profile for different types of ionizing radiation used for medical sterilization. (Credit STERIS AST)*



# BEAM POWER REQUIRED

Power is expressed in kilowatts (kW) a unit equivalent to kilojoules per second (kJ/s).

For a specific energy and target product, the throughput of an e-beam or X-ray system is proportional to its power. The more power a system has, the less time it takes to deliver a specific dose.

The intensity of the beam current (I) expressed in milliamperes (mA) links the accelerating voltage (V) proportional to the energy (E) and the power(P).

P (kW) = V (MeV) x I (mA)

## 6.1 EB Power

With EBs, power determines the treatment capacity of the EB plant.

Electricity consumption being one of the most important operational cost items, the proportion of consumed electricity transformed into EB power is a major consideration. How a quoted efficiency is defined should be understood by the prospective buyer. Electrical efficiency may cover the efficiency of the accelerator alone or include all ancillary equipment (cooling, vacuum system, ozone extraction, etc.). Depending on the type of machine, electricity efficiency can range from 10% to 80% with highest rates for direct current machines (DC), then recirculation machines and then linacs. However, the energy of DC accelerators usually does not exceed 3 MeV.

Selecting the correct power is a critical decision that must be based on a forecast of the processing capacity initially needed and its anticipated growth over several years, preferably over the first 5 to 10 years.

*Table 2: Example of power needs calculation*

| | **Volumes to be processed m³/hour** | | | **Beam power needed * kW/1,000m³ over 1 y** | **Power needed kW** | | |
|---|---|---|---|---|---|---|---|
| | Year 1 | Year 5 | Year 10 | | Year 1 | Year 5 | Year 10 |
| **Product 1** | 3 | 3 | 3 | 0.8 | 2,4 | 2,4 | 2,4 |
| **Product 2** | 3 | 4 | 5 | 1.3 | 3,9 | 5,2 | 6,5 |
| **Product 3** | 5 | 6 | 8 | 0.9 | 4,5 | 5,4 | 7,2 |
| **Product 4** | 2 | 3 | 4 | 1.0 | 2 | 3 | 4 |
| **Product 5** | 2 | 3 | 4 | 1.1 | 2,2 | 3,3 | 4,4 |
| **Product 6** | 0.5 | 1 | 4 | 1.0 | 0,5 | 1 | 4 |
| | | | | Total : | 15,5 | 20,3 | 28,5 |

*Examples of values based on the density and dose required for each product and exposure configuration. These values are calculated by the potential supplier.*

Insufficient power results in the system not being able to process all the products requiring sterilization over the anticipated period. It will take longer to sterilize them. Overestimating the needed power will result in an over specified system and extra cost, but one merit is that it will allow to process backlogs faster in case of downtime or to absorb peaks in the demand.

Selecting beam power must also be done according to production shift strategy. For the same beam power, the processed volumes increase with the time that the machine is in operation which translates in the number of shifts.

Delivering the required dose can be achieved with one or two accelerators.

- **Using a single accelerator.**
  This is the lower investment option. The risk of having production relying on a single machine must be considered, along with the possibility of occasionally having to outsource sterilization.

- **Using two accelerators.**
  Redundancy comes at an extra investment and operational cost, but its main advantage is that when one machine is down the system can still operate at reduced capacity. Also, when both accelerators are installed on each side of the product, flipping or rotating boxes is not necessary. This option makes validation more complex. Validation is less complex when both accelerators point in the same direction but then boxes must be flipped or rotated for double side treatment. It is possible to start with one e-beam accelerator and add the second one when processing needs have grown.

## 6.2 X-ray power

High energy X-ray generators are basically an e-beam system with an X-ray converter (or X-ray target) placed on the path of the emerging electron beam. This X-ray converter is made of high atomic number metal optimized for a particular EB energy level. While gold and tungsten can in principle be used, tantalum appears to be the best compromise between conversion efficiency, thermal capacity and ductility.

*Fig. 8: X ray system principle (Credit MEVEX)*

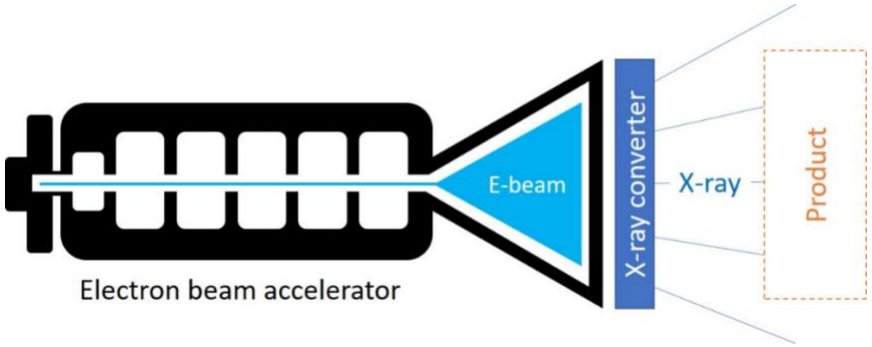
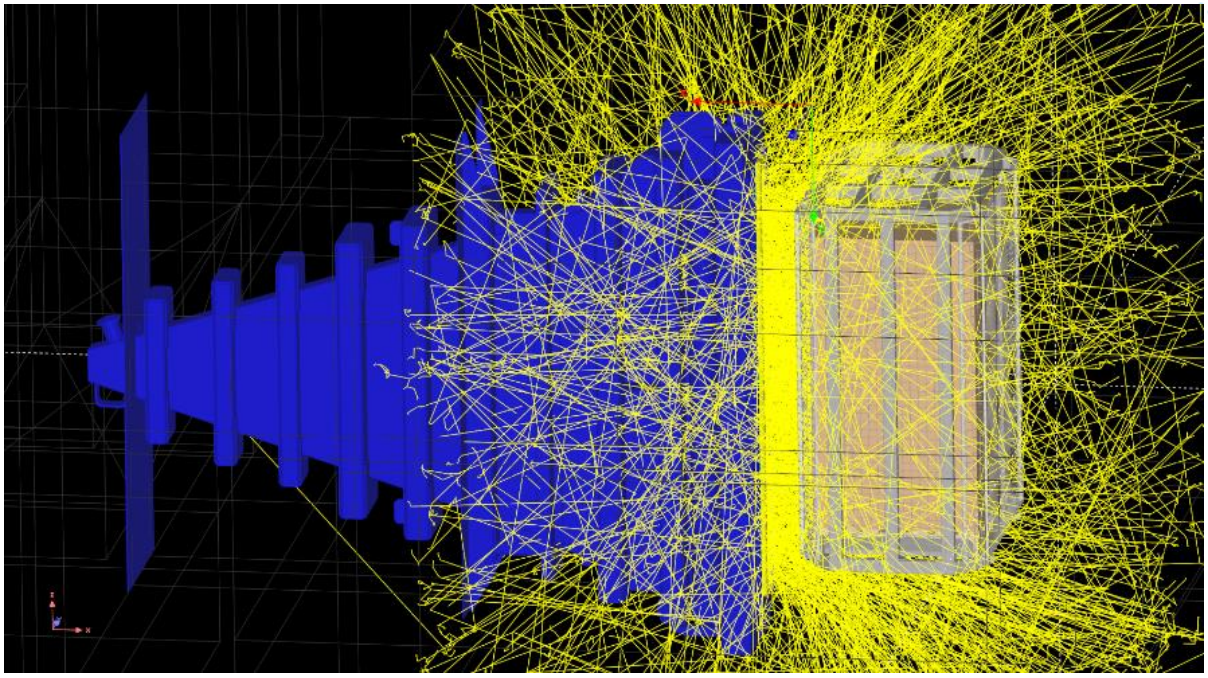


*Fig. 9: X-ray conversion modelling* (Credit IBA and Aerial)



Most of the energy from the electron beam is dissipated in the form of heat in the target. A powerful water-cooling system is needed to evacuate the heat.

Only a small portion of the EB power is transformed into X-ray, which explains why X-rays were not a commercially viable option for medical device sterilization before the advent of very high-current, mid and high-energy accelerators, and why EB is inherently a more efficient technology than X-ray. How much of the electron beam power is transformed into X rays depends on the energy of the incident electron beam on the target.

*Table 3: Indicative conversion efficiency as a function of energy (Credit Mevex)*

| Energy of the electron beam (MeV) | 1 | 5 | 7.5 |
|---|---|---|---|
| X ray power for 100 kW of electron beam power | 1 kW | 8 kW | 10-12 kW |
| Conversion rate to X-ray | 1% | 8% | 10-12% |

To reach maximum efficiency, energies up to 7.5 MeV are used to sterilize medical devices. Beyond 5 MeV, X-rays may induce the creation of short-lived radionuclides within the product. Even if the risk is small, the significance of this induced radioactivity must be assessed (ISO 11137-1 5.1.1).

# SYSTEM OPTIONS

The table shows the main categories of EB and X-ray systems used in industry and their main features based on the type of shielding required.

*Table 4: EB and X-ray systems used in industry.*

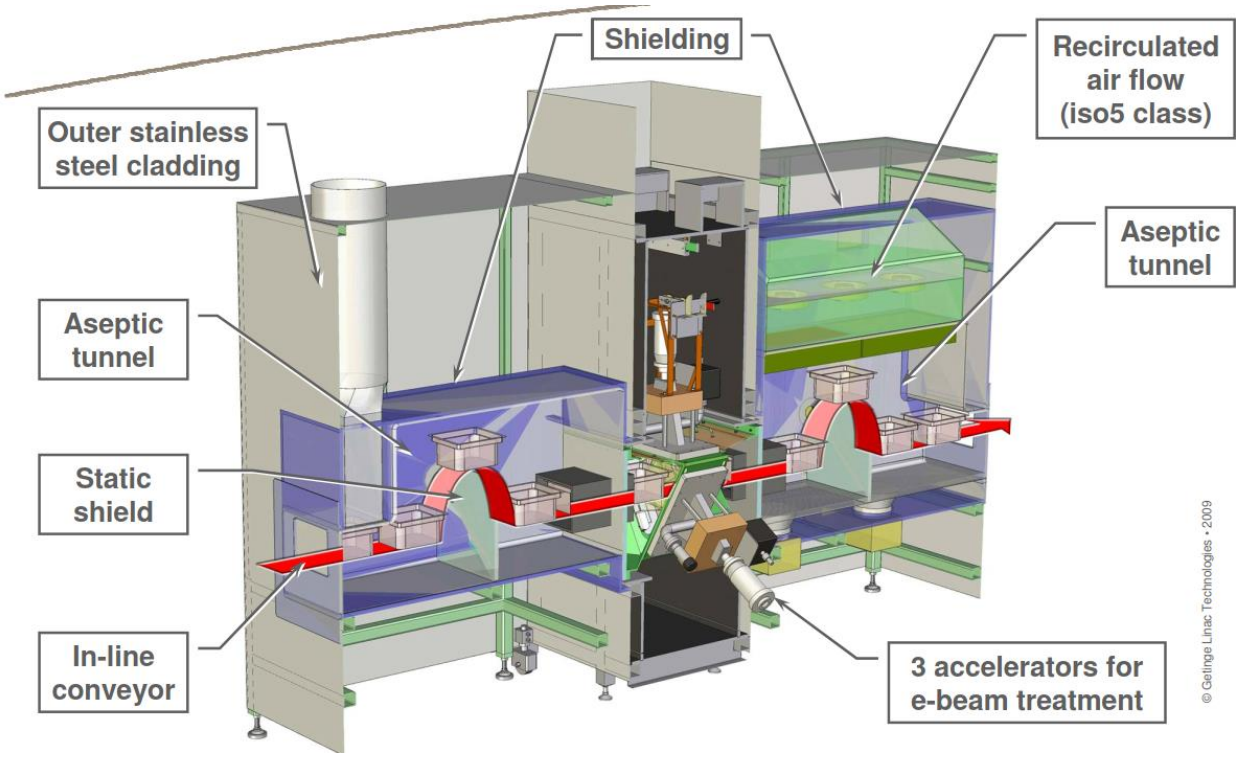
| System | Low energy EB | Medium energy EB | High energy EB | High energy X-ray |
|---|---|---|---|---|
| **Energy range** | < 300 keV | 2 - 8 MeV | 8-12 MeV | 5– 7.5 MeV |
| **Shielding type** | Self-shielded below 3 MeV | Shield or bunker | Large bunker | |
| **Shielding material** | Steel, lead | Steel, lead, concrete | Concrete | |
| **Shielding footprint** | Up to 60 m² | Up to 200 m² | 400-500 m² | 400-500 m² |
| **Mode (typical)** | Surface or thin product treatment<br>In-line processing | In-line processing<br>Terminal sterilization | Terminal sterilization | Terminal sterilization |
| **Product** | Unit product | Low density | Low to medium density | Any density |
| **Package** | None / Individual packs | Individual packs<br>Dispensers<br>Shallow cartons | Shallow cartons | Cartons, pallets |
| **Project cost (order of magnitude)** | X00,000 to X,000,000 USD | X,000,000 USD | X,000,000 USD | > 10,000,000 USD |

As a rule, the higher the energy, the larger the machines, the larger the footprint, the larger the shielding, and the higher the investment costs. The initial cost must be balanced against the cost of irradiating one unit, one box or one pallet. Consequently, the size and density of the packages to be treated will also dictate the technical options.

For in-house projects, where only surface sterilization is required or if thickness and density are low enough (individual packs), in-line sterilization with low-energy electrons may be an option. Fig. 10 shows an example.

Low energy EBs of 500 keV are used, for example, to sterilize entire bag (internal and external part) and EBs of less than 300 keV are used to decontaminate the external surfaces of presterilized tubs for vials or syringes before being filled with a biological product in an aseptic filling area.

*Fig. 10: Ster-Star™ EB tunnel [Ref. 12]*



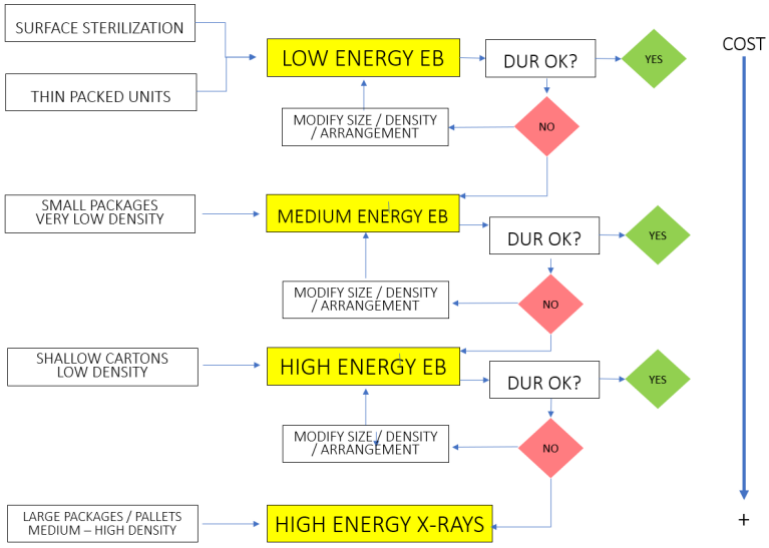

There is currently no industrial low-energy X-ray system to sterilize medical products.

A better electrical efficiency means more kilograys into the product per consumed unit of electricity power. From the point of view of energy efficiency only, EB treatment is probably the first choice, but a choice that will necessarily limit the size and density of the packages that can be treated, which may change the overall economics of the project. EBs can work well with uniformly packaged products of low and medium density such as gauze, drapes, towels, bandages, wound care dressings, lab ware, bottles, caps, containers, tubing sets, procedure trays, catheters. However, with most common medical devices the DUR will be greater or even much greater than two.

When EB is not an option, the only radiation sterilization alternative not involving radioactive material is X-ray. Only electron accelerators with a power of at least 50 kW and energy higher than 5 MeV can produce enough power of high energy X-rays to sterilize large volumes of medical devices.

Dual technology systems (EB and X) are hybrid solutions to accommodate products having different DUR tolerances. The advantage of these dual systems is the flexibility that they offer to treat some products with one technology and the rest with the other. However, they are always optimized for one technology since they are an e-beam system with X-ray capabilities or an X-ray system with e-beam capabilities.

*Fig. 11 presents a simple decision trees based on required DUR and main product characteristics.*




Volumes to be processed are another key factor in the choice of technology. To say that any product that can be treated by EB should be treated by EB might be oversimplistic. The economics of the process makes EB suitable for small as well as large volumes of a limited category of medical devices. X-ray machines can economically process large volumes and a much broader range of products than EB, which explains their growing adoption for service centers. However, X-ray machines are not competitive for small volumes or even medium volumes, with the possible exception of high-value products requiring a low DUR. Figures indicating a volume threshold from which X-ray machines become competitive must be considered with extreme care because there are many factors influencing this threshold.

Though relatively costly, EB-X dual systems offer the best of both technologies but are generally optimized for one or the other. They are an interesting solution in sterilization service where a wide range of products is processed.

Even if recent accelerators reach utilization of 95% during 8,000 hours per year, with the adequate preventive maintenance, accelerators remain complex machines. They can be down for many days while the cause is being identified, the repair takes place, or a spare part reaches the site. Having a back-up system in place, including outsourcing sterilization is therefore recommended as a risk management measure. Where the product to be sterilized can be transported, preparing a backup solution with a contract irradiation facility is also wise.

What precedes has shown that it is important to select the beam that meets the requirements for an application. Having defined the required beam characteristics, the next consideration will be the accelerator that can produce this beam.

# TYPE OF MACHINE

Once the beam energy and power have been defined, the choice of the machine capable of producing it can be made. However, one must bear in mind that the accelerator itself is but one component of a whole system. Decisions regarding shielding design, how to handle products, how to transport them to the irradiation area, how to present them to the beam and how to integrate the irradiation system with other production and storage processes are also critical decisions.

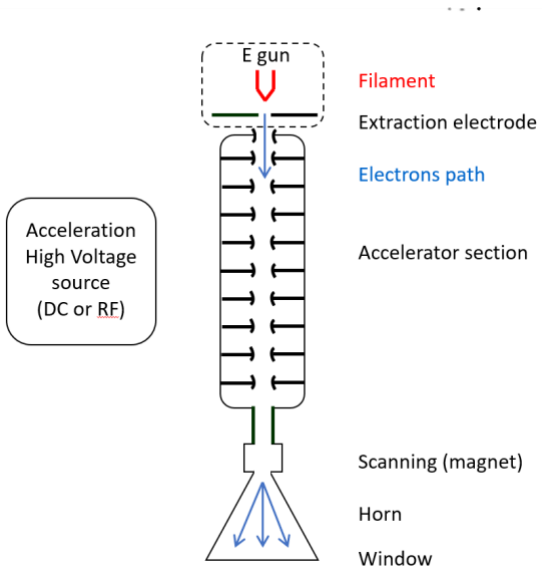
Electron energy ranges are commonly used to categorize accelerators but there is no consensus on the limit of medium and high energy:

- Low-energy, self-shielded units, in the 80-300 keV range according to an ASTM definition.
- Mid-energy, high-current units. The upper limit is sometimes set at 5 MeV and sometimes at 7 MeV.
- High-energy units. The upper limit is usually 10 MeV but 12 MeV can be considered.

Various electrical designs have evolved in each of these categories. Most accelerators above 300 keV are scanned beam systems. Those at or below 300 keV are mostly based on elongated filaments or filament arrays and are all self-shielded.

Industrial accelerators must be able to deliver a beam power of a few kilowatts minimum up to hundreds of kilowatts. Most accelerators above 300 keV use the same concept of a filament generating electrons, a high voltage source (DC or RF) accelerating electrons in a deep vacuum system, and optic coils (focus, steering, scanning).

*Fig. 12: Electron accelerator principle (Credit: Francis Martin)*

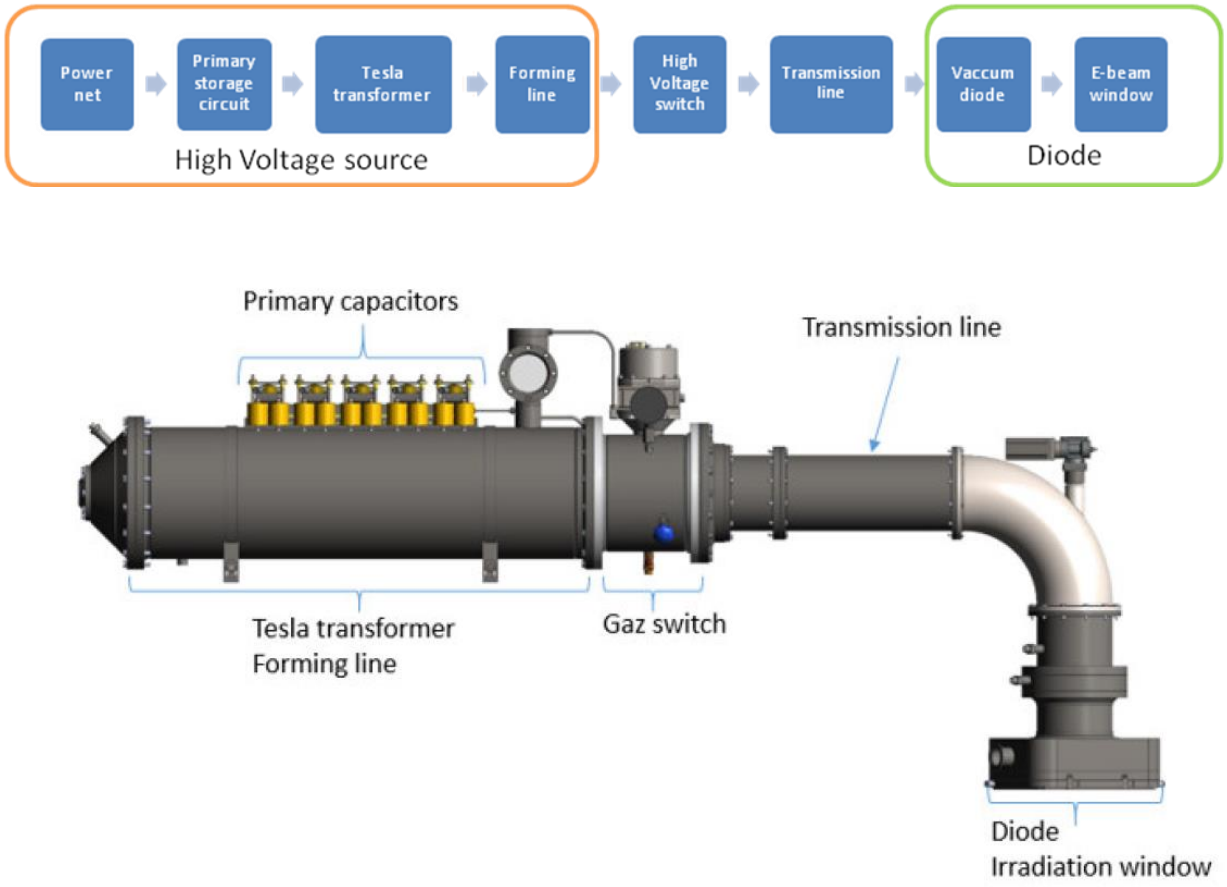


These are the main types of industrial machines used for sterilization of medical products:

- Low energy low power machines (up to 300keV)
  These have high voltage DC power supply with single gap acceleration:
  - Curtain systems in the 150 to 300 keV range relying on linear or multiple cathode concepts. Because the source is a linear source rather than a point source, no scanning is necessary.
  - Sealed tube or maintained vacuum systems in which a stream of electrons seeking ground is directed within the acceleration chamber toward the beam transmission window, often a thin (25 microns or less) titanium foil.

- Low energy High Pulsed Power (HPP) machines (up to 500 keV). The design of these machines allows the EB energy to be adapted to the products in order to obtain the best solution in term of DUR and shielding.

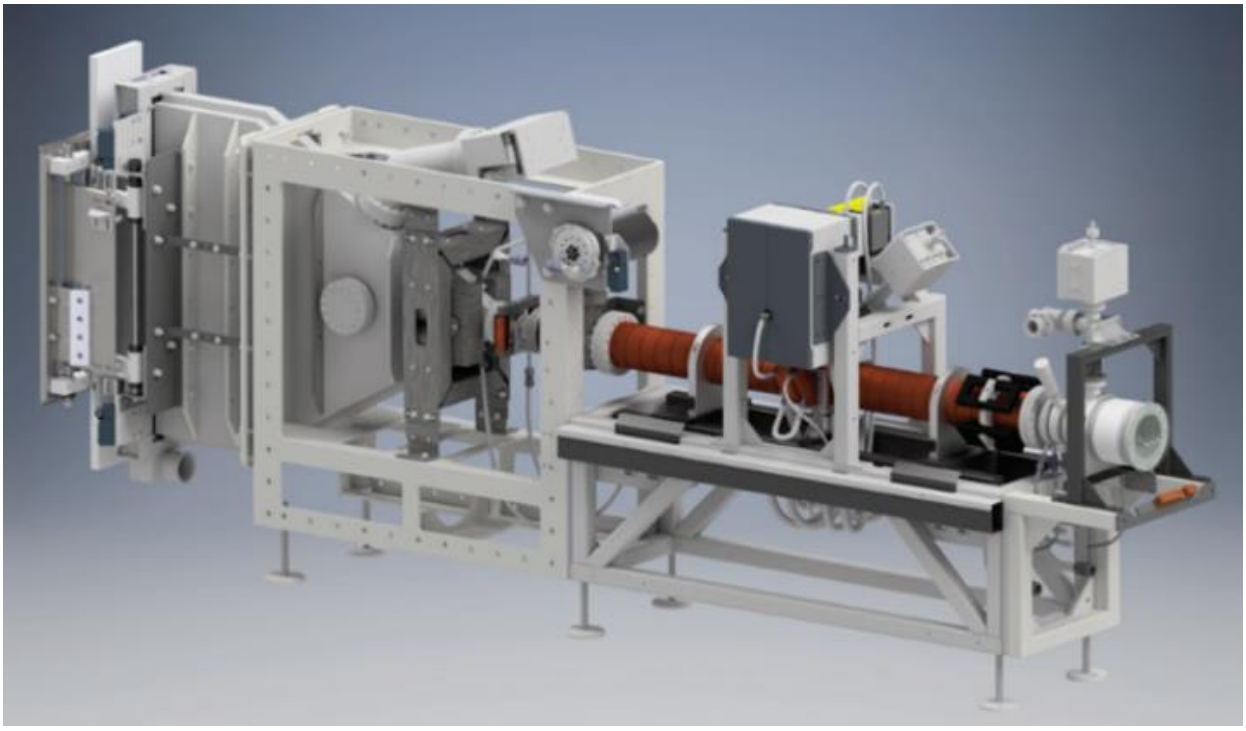
*Fig. 13: Principle of a low energy High Pulsed Power machines (Credit ITHPP)*



- In direct voltage (DC) machines, a high voltage gradient is applied to electrons gun. These machines have an energy up to 5 MeV and beam power up to 500 kW but they are seldom used for medical sterilization.

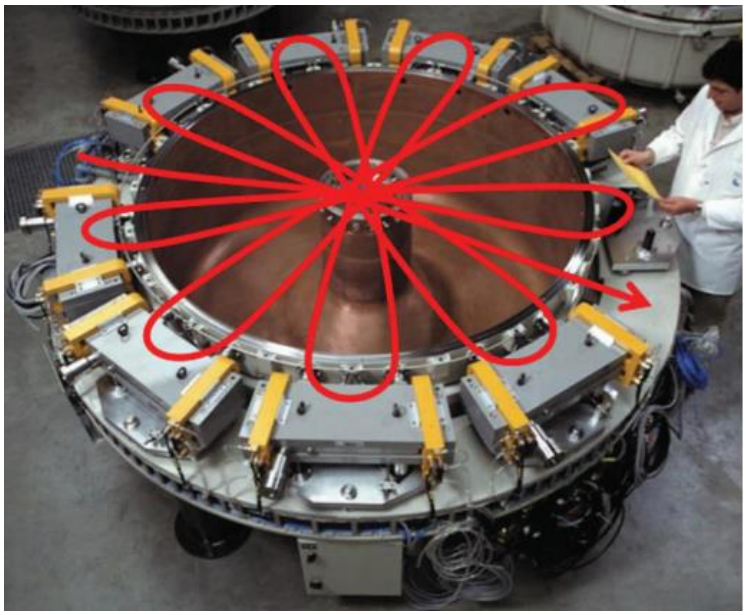
- Linear Accelerators (Linacs) are among the most popular high energy industrial accelerators. Their energy is up to 12 MeV and would be able to reach a beam power of 300 kW. One of the main advantages of Linacs are their compact size and the possibility to adjust energy to the level best suited for each type of product. RF Linacs use radio frequency cavities where the generated voltage gives successive “pushes” to groups of electrons. Standing wave linacs can operate at frequencies which range from 0.8 to 9 GHz and can generate energies from 1 to 12 MeV. In Linacs, the electrons pass through the accelerating cavities once before passing through a beam line to a scanning system that sweeps the beam over the product. This sweeping system can include a removable conversion target to create X-rays.

*Fig. 14: Linear accelerator (Credit Mevex)*



In recirculating machines, magnetic fields are used to recirculate several times the electron beam through an accelerating cavity powered by radio frequency energy. The electrons pass through the accelerating electric field from one to a dozen times depending on the desired energy. The energy is up to 10 MeV and beam power up to 560 kW. Then the beam is sent through a beam line to the scanning horn like in any other system. Technically, a separate beam line can be added to any magnet port and two or three energy levels can be made available at the same beam port.

*Fig.15: Rhodotron®, a recirculation-based accelerator (Credit IBA)*



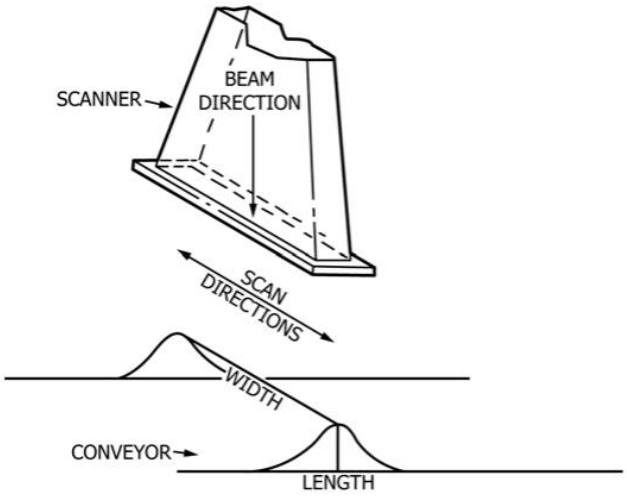
Irradiation dose is controlled by adjusting beam accelerating voltage, beam current and width, and the under-beam conveyor line speed. Being a completely electrical device, the beam current of an electron beam accelerator can be electrically interlocked with the drive systems. An increase in speed triggers an increase in beam current, keeping the dose delivered to the product constant.

Dose delivered is proportional to average beam current (I) and inversely proportional to conveyor speed (V) and to beam width (Wb).

Dose (kGy) = [k x I (mA)] / [conveyor speed (m/min) x beam width (m)]

The "k value" is an empirically derived proportionality constant, which is a function of various beam design features, including geometry and distance to the beam window.

*Fig. 16: Beam scanning parameters*




For high energy systems the “sterilization process width” is usually defined by the maximum scan width, and for low energy system it is defined by the number of filaments or source geometry. If the beam width is larger than the product width, only a portion of the area scanned by the beam is occupied by product. The unused electrons need to be stopped by a beam stop in front of the irradiation horn. As this beam stop absorbs a lot of energy, it needs to be water cooled.

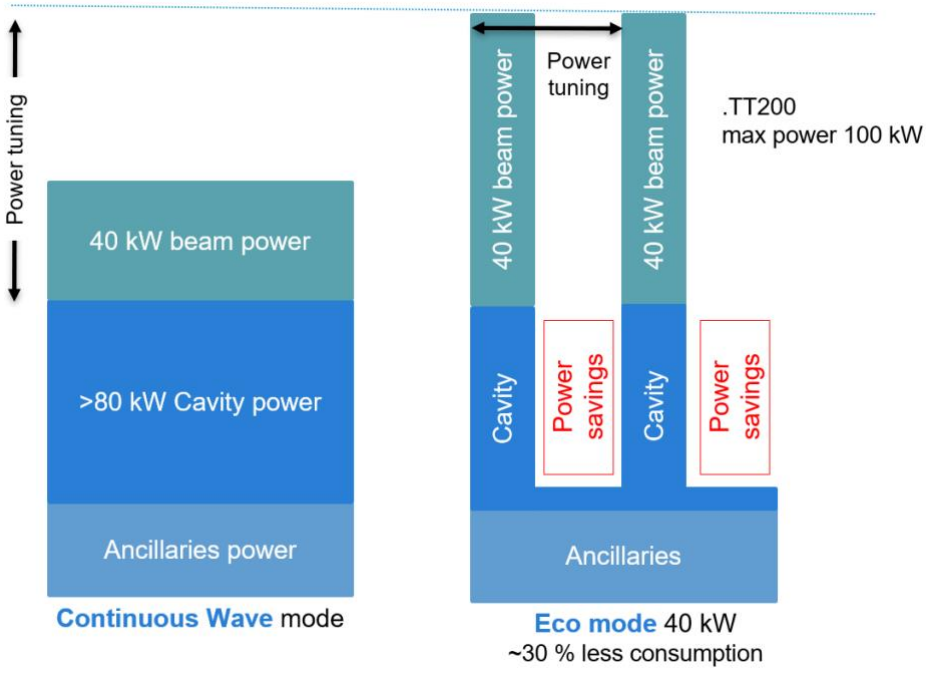
*Fig. 17: Under beam conveyor composed of chains running at a controlled speed over an aluminum water cooled beam stop (Credit IBA)*

Over the years, many features have been introduced to improve the efficiency, the reliability and the flexibility of accelerator systems.

- Pulsed beams:

Today, most high energy electron beam accelerators operate in pulsed beam mode. Instead of being delivered as a continuous wave, electrons can also be delivered in pulse mode, producing the same quantity of electrons over a shorter time, which translates into a higher processing rate. Depending on the type of machine, in energy saving mode the pulsing frequency can range from 10 Hz to 100 Hz. The main advantage is the resulting electrical power saving, which is significant at low to medium power.

*Fig. 18: Continuous wave vs. pulses (Credit IBA)*




- Multi-energy options:

Most accelerators can produce several types of beam and energies, so that a wider range of products can be treated. The performance of these systems can be optimized through desired orientation, scan properties, beam power, etc.

**The common options are:**

- Production of electrons or X-rays in the same beam line and horn, by using a movable conversion target. This option is valid at low power (typically 50 to 80kW).
- Accelerators able to adjust energy to any value within a specified energy range.
- Accelerators with fixed energy and multiple beam lines and targets. Such systems can be used with a single conveyor or multiple ones in separate rooms.
- Fixed X-ray targets for high beam power (up to 560 kW at 7 MeV).

- Some manufacturers offer a “pay as you grow” approach with the possibility to increase the processing capacity at a later stage by adding power modules, thus reducing the initial investment.

*Fig. 19: Example of dual EB-X dual system (Credit IBA / Aerial)*

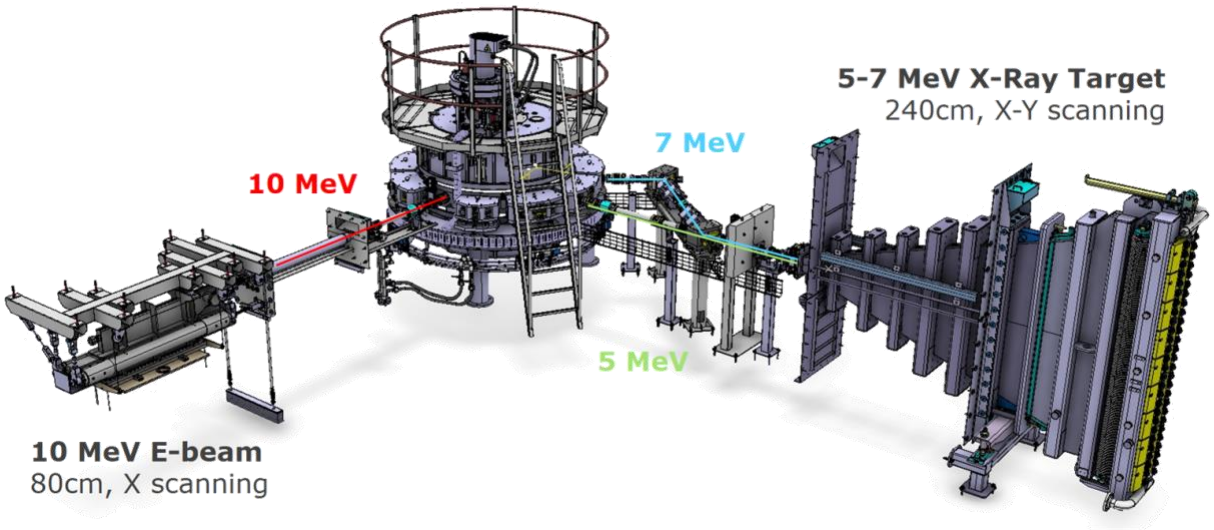
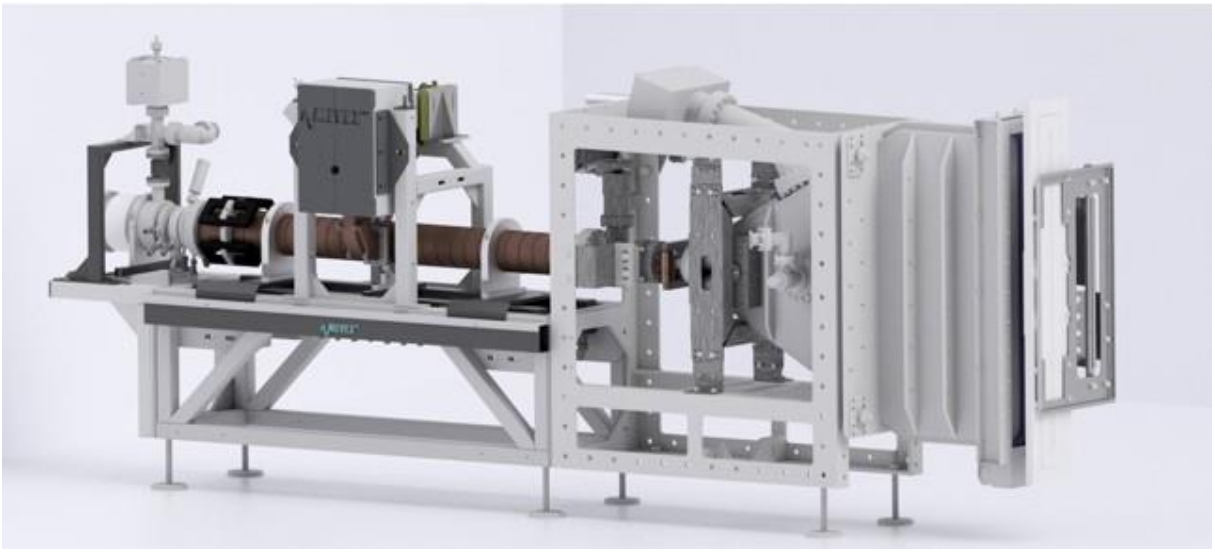



*Fig. 20: Linac with adjustable energy (5-10 MeV) in a single scan horn (Credit Mevex)*



Technological developments have accelerated over the past few years and it now seems that almost any accelerator configuration has become possible. The choice of beam must then be linked to the choice of the conveyor systems to obtain the desired DUR and throughput.

Whatever the choice of machine is, these are important features for the operation of an accelerator:

- Beam energy:
  - Nominal energy
  - Type and range of electron energy adjustment
  - Energy spread
  - Energy stability
  - Energy single selection mode.

- Beam power:
  - Nominal average beam power
  - Type and range of beam power adjustment
  - Nominal average beam current
  - Type and range of beam current setting
  - Beam current instability
  - Beam pulse parameters (frequency, current, duration).

# TAKING PRODUCT TO AND FROM BEAM AREA

The choice of a conveying system is critical. It must first be decided how products will be sent to the irradiation area. There are several options:

- Individually packed units in the case of low-energy accelerators,
- Individually packed units, in bulk before further packaging, or in shallow shipper cartons, directly on the conveyor or in a tray or irradiation container for medium-energy accelerators,
- In shipper cartons in the case of high-energy accelerators or stacked on a pallet in the case of high-energy X-rays.

*Fig. 21: Simple conveyor line for a high energy accelerator (Credit Nuctech)*

The layout of the conveyor must be such that the area where non-sterile products are loaded and the area where sterile products are unloaded are physically segregated. Loading and unloading at dedicated stations can be manual or it can be automated, for example to unstack and restack pallets.

Extensive automation of product handling is possible for example with robots, palletizers and automated guided vehicles (AGV). The extra cost of automation must be weighed against the cost of labor.

*Fig. 22: Loading/unloading area with loading line (right) and box a device ("Tornado") to flip the boxes at each pass (Credit IBA / OCME)*

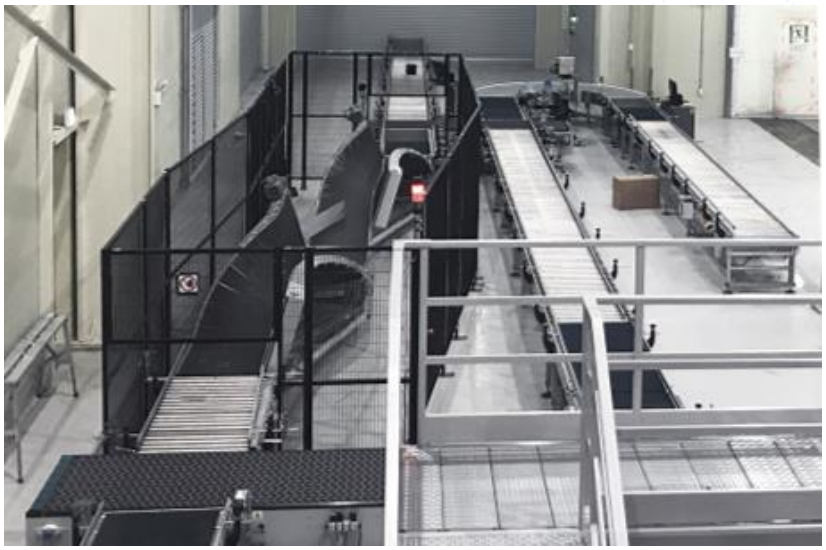


*Fig. 23: Example of palletization robot (Credit Mevex)*

For the facility to work in continuous mode, a maze must be created between the safe area and the irradiation area. The walls of the maze will attenuate radiation and the succession of right angles contains the bouncing of photons outside the irradiation area.

In the maze, using two levels for the conveyor as shown in Fig. 24 reduces the footprint and the amount of shielding.

*Fig. 24: Conveyor over two levels in maze (Credit IBA)*

Product handling can be supplied by the accelerator manufacturer or by other specialized companies. When the accelerator and the product handling are not provided by the same supplier, the integration must be carefully planned.

# PRESENTING PRODUCT TO BEAM

There are many possible ways to present the product to the beam in order obtain the desired result

## 10.1 EB

In most cases the product will have to be treated from two opposite sides to obtain the desired DUR. There are two basic solutions:

- Irradiating the product on one side, flipping or rotating the box 180° via mechanisms to present the opposite side to the beam, and then irradiating this other side. Using two 90° angles and two curves also allows a natural rotation for lateral irradiationof fragile products.

*Fig. 25: Low energy irradiation (generators in blue) of individual products (Credit ITHPP)*

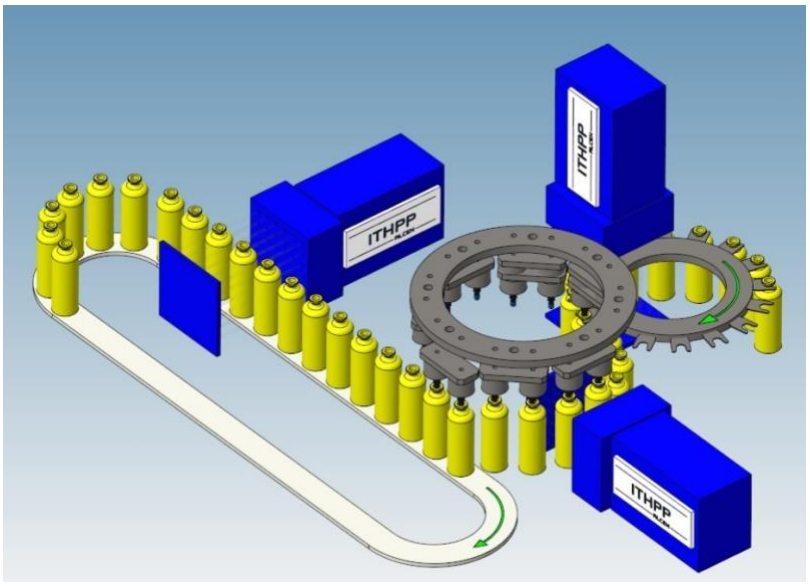
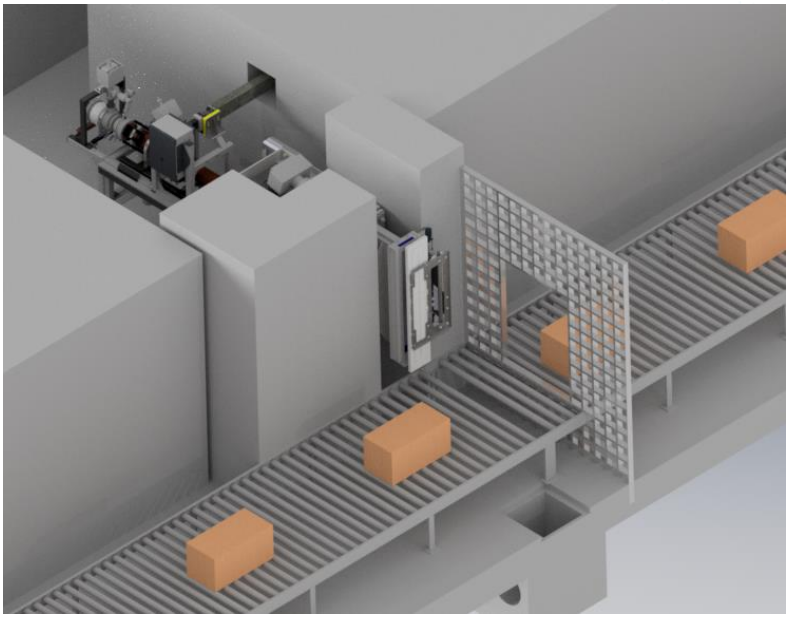
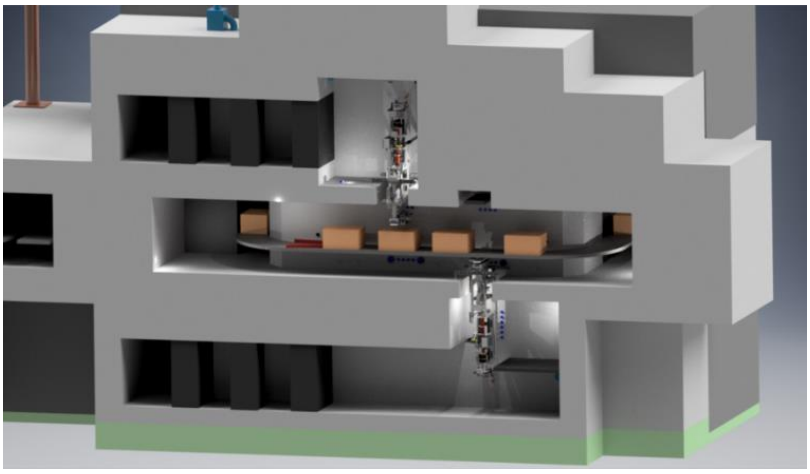


*Fig. 26: Lateral irradiation with a single accelerator* (Credit: Mevex)



- Irradiating the product on one side with a first accelerator and irradiating the product on the opposite side with a second accelerator. The choice of orienting the two accelerators horizontally (lateral irradiation) or vertically (irradiation from top and bottom) will impact the design and shielding requirements of the facility. Because the product does not need to be flipped, vertical irradiation with two accelerators is well suited for fragile products that could be damaged by excessive handling. This will increase the overall height of the bunker.

*Fig. 27: Top and bottom irradiation with two accelerators (Credit: Mevex)*



## 10.2 X-ray

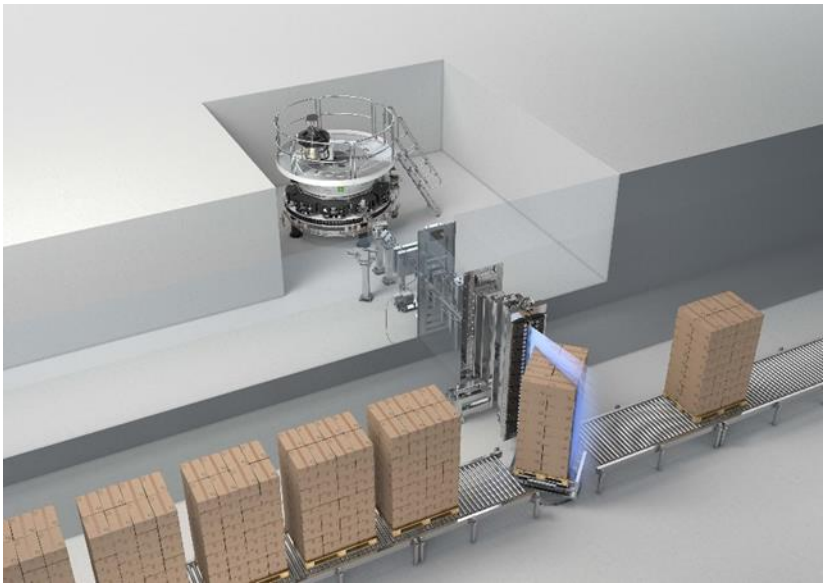
Because dose profiles resulting from X-ray irradiation greatly differ from e-beam irradiation, the way to present product to the beam to optimize throughput and utilization of the generated X-ray is also different.

Typical solutions to convey product to the X-ray beam are:

- Single cartons on a tray or roller conveyor.
- Cartons inside an irradiation container such as a tote or a hanging carrier.
- Cartons stacked on a pallet, which minimizes handling.

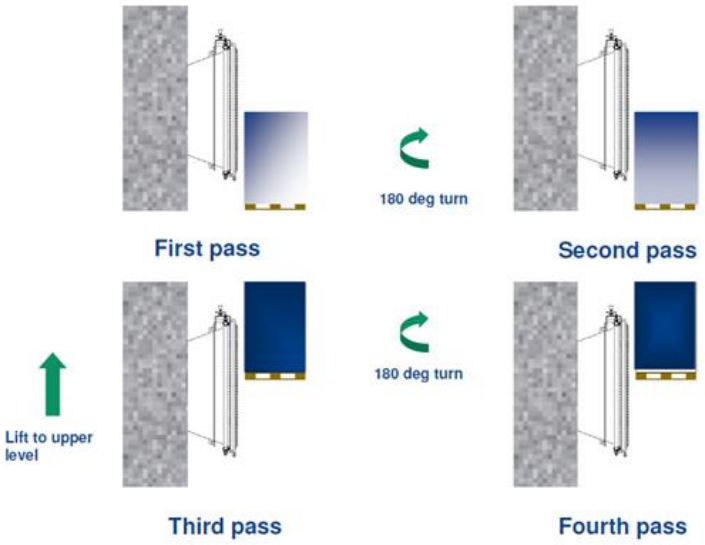
Irradiation of pallets on all sides can be done by rotating them in front of the beam or away from the beam path, possibly in the maze and behind a shielding wall.

*Fig. 28: Pallet rotating in front of X-ray beam (Credit IBA)*



Pallets requiring low DUR can also be exposed from two sides and on two levels as shown in the figure below. The pallet will thus pass at least 4 times in front of the beam to receive the full dose by increments.

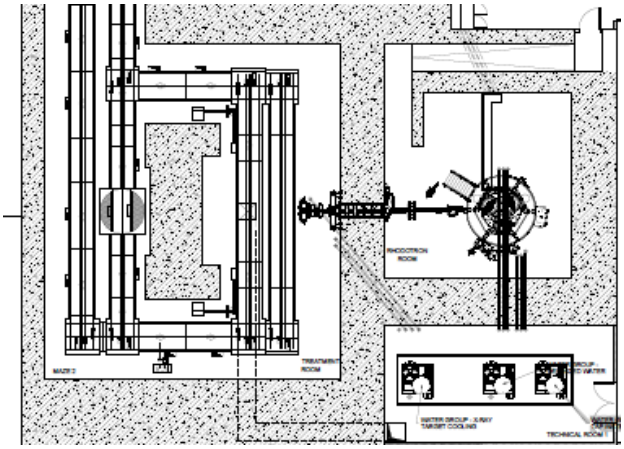
*Fig. 29: Two sides and two levels X-ray exposure (top level represented only) (Credit: STERIS AST)*




The advantage of these systems is that there is no wasted beam at the edges and the X-ray beam is used most efficiently. Also, they offer the flexibility to treat a wide range of product densities while increasing the total throughput of the system.

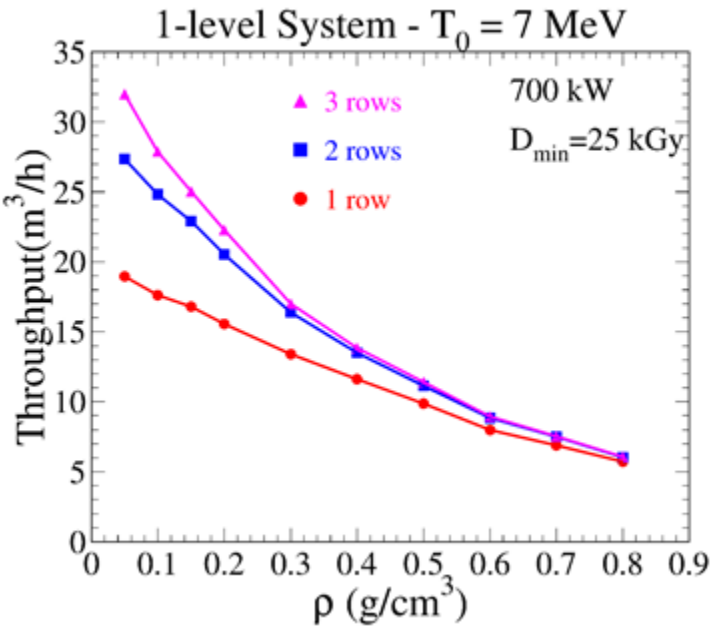
In another approach, pallets travel in parallel rows in front of the beam so that the energy remaining after the row closest to the horn is absorbed in the row(s) behind, like in gamma irradiators for medical products.

*Fig. 30: X-ray irradiator with multiple pass conveyor (Credit IBA)*



By recovering more of the emitted X-ray energy into products the total throughput is significantly increased at low and medium densities. The figure below shows an increase of around 25 % until a density of 0.2 g/cm³. It should be noted however that this pattern seriously complicates validation, especially if products of different densities are being processed. Therefore, this configuration is best suited for large batches of the same product.

*Fig. 31: Comparison of throughputs with multiple passes on 1, 2 or 3 rows patterns (Credit IBA)*

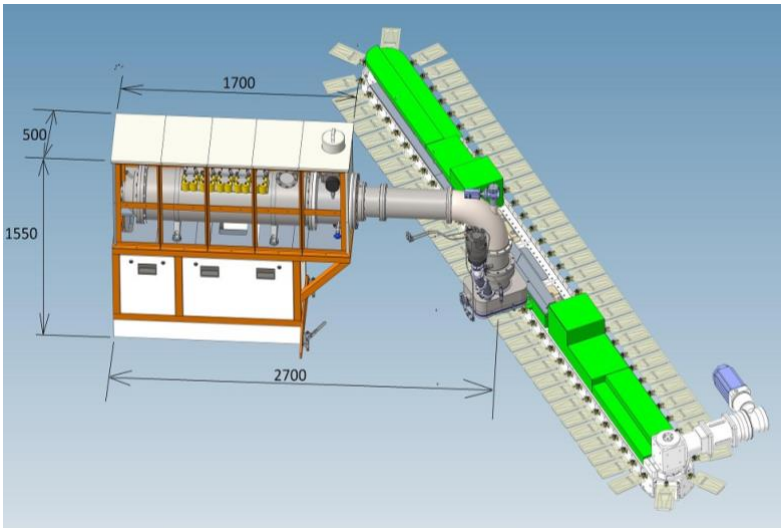


# OTHER COMPONENTS

## 11.1 Integration and Layout

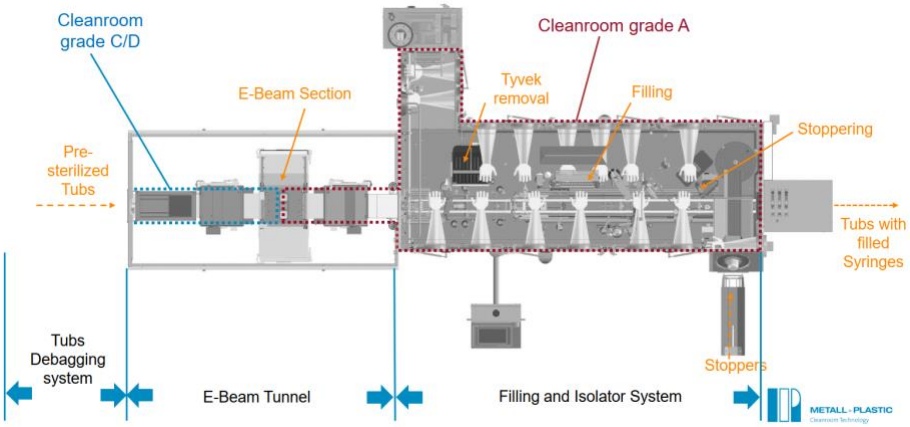
Companies who prefer to conduct sterilization in-house will try to integrate the process into their manufacturing line. Integrating a self-shielded accelerator is the fastest solution.

*Fig.32: Self-shielded system using pulsed electrons beam (Credit ITHPP)*




The system sterilizing tubs containing syringes shown in Fig. 33 is bulkier but can still be part of a manufacturing line.

*Fig. 33: Top view of an EB tunnel, filling and isolator system (Credit Metal+Plastic)*




From an energy of about 1 MeV, the construction of a concrete bunker becomes necessary, which makes integration into an existing site more challenging but possible. In-house systems can service just one manufacturing site or an entire company's products. In the latter case, the in-house sterilization facility will match the size and throughput of a contract facility. The following areas are then required:

- Distinct storage areas to keep processed and unprocessed materials separate
- A material handling system (conveyor). Typically, this passes through a labyrinth instead of doors to maintain a continuous flow of material
- The irradiation chamber itself
- The accelerator enclosure(s) which are typically shielded separately from the irradiation chamber
- A power supply and control electronics room
- Rooms for auxiliary systems.

*Fig. 34: EB multipurpose irradiation center (credit Mevex)*

*x)*

The conventional infrastructure required for an irradiation facility is like any medium industrial setting found in a typical industrial park.

## 11.2 Shielding

Both the accelerator and the irradiation area require shielding to protect workers and the public from the harmful effects of ionizing radiation generated while the products are being treated. Besides the ionizing radiation produced by the accelerator, there are also X-rays generated from interaction with different materials in the irradiation area. These X-rays scatter in every possible direction.

Low-energy electron systems (< 500 keV) can be purchased as complete units where the manufacturer encases the critical areas of their equipment in lead. Typically, 1 cm of lead is sufficient to stop any X-rays generated by a 150 keV accelerator.  Lead shielding is practical up to the 300 keV level.

At acceleration voltages above 500 keV, a shielded space must be created to house the accelerator and the area where the products are processed. The racks of power supplies and control electronics must be located outside of the shielding. It is more the energy of the electron or x-ray beam than their power that determine the amount of shielding required. Because of the directional nature of accelerator produced radiation, it is possible to conform the shielding to the radiation field.

Between the irradiation room and the outside of the bunker, the conveyor runs through a maze where a succession of right angles keeps the amount of irradiation that merge below admissible levels.

All materials have the same shielding effectiveness when scaled by their density. In other words, 6 cm of lead (density 11.3 g/cm$^3$) has the same shielding value as 30 cm of concrete (density 2.35 g/cm$^3$). This

means that one can reduce the volume of necessary shielding, but not its mass. The cost of a potential shielding material is strongly related to its density. Concrete is therefore the most common shielding material. Lead is also sometimes used to shield areas where the equivalent dose rate measured in micro sieverts per hour is above the acceptable level.

The table below gives an idea of the thickness of concrete needed for the walls facing the beam for the X-rays produced by an electron beam at two energies and at four power levels. For each project, these values need to be calculated by experts.

*Table 5: Indicative wall thickness for X-rays*

| Power (kW) | 10 | 50 | 100 | 200 |
|---|---|---|---|---|
| Beam energy (MeV) | Shielding (cm) | | | |
| 5 | 200 | 250 | 275 | 300 |
| 10 | 290 | 355 | 380 | 410 |

Beam energy, power, and orientation as well as conveyor systems have an influence on the shielding requirement which is a significant part of the investment cost. Shielding can be calculated and optimized using simple analytical methods or more complex Monte Carlo algorithms. Specialized software is available to design shielding taking into consideration space constraints. The typical limits to be reached for a public area is 0.5 microsieverts per hour, and 10 microsieverts per hour for controlled areas.

Most manufacturers offer the service of shielding calculation and optimization for their solutions.

## 11.3 Control System

New control systems make operation and control easier than in the past thanks to increasingly intuitive interfaces. It is now common to have systems including advance maintenance and diagnostic tools, autonomous vacuum system, data tracking, trending, and archiving, remote control, and support.

A control system can be divided into four components:

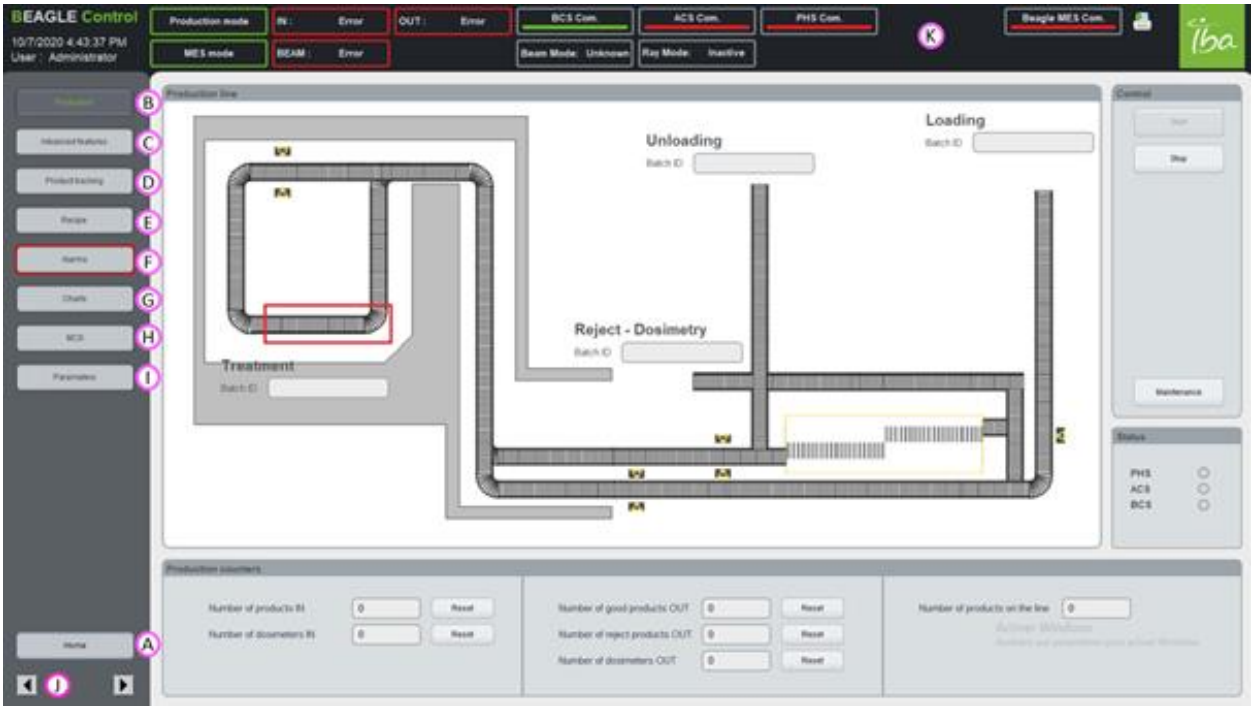
- Accelerator Control System (or ACS)
- Conveyor Control System (CCS)
- Safety control System (SCS)
- Process Control System (PCS)

Process control systems manage the entire production line, ensure traceability of batches or individual packages through bar code identification, store and manage production recipes, generate process data and statistics, and archive them. Some systems can identify which products have received the required dose and which have not when irradiation is interrupted, paused, or resumed. The most advanced systems can seamlessly integrate with existing Enterprise Resource Planning systems (ERPs).

Though generally provided by the accelerator manufacturer, the process control software suite can also be purchased from another specialized supplier. In this case attention should be given to the integration of these systems.

Software used in the process and control of medical device sterilization must be validated. For healthcare products exported to the U.S., compliance with Title 21 CFR Part 11 regarding electronic records and electronic signatures is required.

*Fig. 35: Example of process control display (Credit IBA)*




## 11.4 Safety and Security Systems

Ionizing radiation can be harmful and must therefore be properly controlled. The dose rates produced in industrial irradiation areas are so high that a person accidentally present in the radiation room could receive a lethal dose within minutes or even seconds.

Irradiation facilities are designed to preclude exposure of an individual. Engineered devices called safety interlocks prevent access to the radiation room while the electron beam is energized. Access by personnel to the irradiation cell, securing of the radiation room prior to initiating an irradiation, and irradiation start procedures incorporate a series of sequential safety interlocks and controls. Attempts to preempt the controls or to apply them out of sequence automatically prevent the intended operation and renders the system safe.

Before the irradiation process can begin, the personnel access door to the radiation room must be closed and secured. A “Last Person Out” (LPO) procedure ensures that obscured areas are clear of personnel. Opening this door disables the means of producing radiation.

The safety interlocks for the access door are integrated into the master control system so that violation of the safety interlock system or use of the door will cause irradiation to automatically cease. A violation or failure of the safety interlock for the access door triggers visible and audible alarms.

A person technically competent in radiation protection must be designated by the operating organization to oversee compliance with the requirements of the safety standards. This radiation protection officer should report directly to senior management and should have sufficient authority to have radiation safety requirements take priority over operational imperatives such as meeting production targets.

To assess and control occupational exposure, radiation surveys must be carried out to measure the dose equivalent rates in the various working areas and public areas. The radiation survey instrument must be appropriate for the type of ionizing radiation produced in the facility.

EB accelerators may come equipped with X-ray detection devices, which will read the background level and will be interlocked with the accelerator to shut it down instantly should an increased level of background X-rays be detected.

## 11.5 Electricity Supply

The beam power of low-energy self-contained EB accelerators range from 5 to 20 kW depending on the intended use. High-energy EB systems (5 – 10 MeV) with beam powers of 30 to 80 kW will need to be supplied by 3 to 4 times the beam power. X-ray systems between 200 and 500 kW of EB power will require approximately twice this input power to the power supplies. The primary electrical supply at 400 or 480V can therefore vary from approximately 100 KWh to up to 2 MWh. The cooling needs are also important, requiring primary water cooling by a tower or a chiller, depending on the type of accelerator. The consumption of a cooling tower is about 10% of the total dissipated power, while a chiller will require 25% of extra power. Ancillary supplies and control electronics will consume at minimum another 10%, which may be included when stating the overall system demand.

Stability of the electricity supply is also important. High energy systems using radiofrequency (RF) accelerators are resonant systems operating under high vacuum. Due to the need to maintain the proper frequency and vacuum level, they can be sensitive to instabilities so power conditioning systems may be required. For some machines, the thermal balance between cooling systems and the heat produced in the accelerating cavities affects the resonant frequency of the cavities and can be disrupted by variations in power.

To minimize accelerator downtime after power interruptions, it is wise to have an external Uninterruptible Power Supply (UPS) powering critical subsystems. The objective of the UPS is not to power the entire plant but just to keep the accelerator “awake” so that when power comes back the beam can be generated again very rapidly. As a mere indication, without UPS it takes 2 to 4 hours to restart a system after a power failure.

## 11.6 Cooling

To operate properly, most components of accelerator systems require cooling. Power supplies, RF power sources, the accelerating structure, and the X-ray target all require cooling to collect the dissipated power. This is typically done with chilled water or glycol systems as in many other industrial situations. The coefficient of performance for such cooling systems is typically 4 – 5, meaning one can get 4 – 5 kW of cooling for 1 kW of input power. This value rises to 10 kW for a cooling tower. Almost all the input power will end up as heat in one way or another. Power supplies and power transformers can generally be air cooled. The accelerating structure dissipates much of the input power as heat unless the structure is superconducting as for superconducting accelerators. For industrial uses, these accelerators are only over the horizon.

To conserve energy, the dissipated heat can be recovered with a heat pump or an integrated co-generation system, increasing the overall system efficiency and further reducing the environmental impact of the facility. The hot water from a high-power X-ray system may in theory be used to heat the adjacent building and offices.

Attention must be given to the suitability and quality of the water used in cooling systems.

## 11.7 Ozone Production

Toxic gases are produced in air ionized by radiation. Ozone is at the highest concentration of these gases. The removal of the ozone from the treatment area is required for the health and safety of employees in the facility, and to extend the lifetime of the equipment in the treatment area. The typical method of ozone removal is to pull air from the treatment area and exhaust it outside the building. The ozone extraction system is often interlocked with the building safety system. The volume and concentration of ozone in the work environment and outside the facility must be evaluated to ensure that they are below the regulatory limits. Ozone removal requirements are provided by most manufacturers of accelerators.

Both the high dose rates and the high ozone concentration make the irradiation chamber a very hostile environment that oxidizes metals and damages electronic devices. Stainless steel is preferred in the irradiation area.

## 11.8 Control of Environmental Conditions

Accelerator systems are designed and manufactured in highly developed countries with temperate climates. As these systems are adopted for use in other areas, additional attention to the operating environment is needed. Standard cooling systems may need to be augmented if they are to operate in areas with higher temperatures than that experienced in temperate zones. The ambient air temperature and humidity for machine and utilities may need to be conditioned for best performance and component lifetime.

Areas that experience dusty conditions may need additional filters for air cooled components.

# IMPLEMENTING AN ACCELERATOR PROJECT

An accelerator project has all the features of any other industrial project so this chapter will focus on specific aspects only.

## 12.1 Feasibility

Leaving aside product regulatory approvals, a project of accelerator purchase will start with a feasibility study. The feasibility study is a multidisciplinary exercise that encompasses many different aspects:

- Legal: licensing, applicable laws and regulations, zoning, radiation safety, air quality, permitted land use,
- Economic: cost benefits, market studies, return on investment,
- Technical: review of technical solutions and capabilities of available equipment,
- Operational: to determine how the irradiation facility will be operated to meet market needs and achieve business objectives,
- Scheduling: to determine how long it will take to complete the project through to commissioning and validation.

The study will precisely define the needs, make a preliminary evaluation of the best suited radiation technology (e-beam or/and X-ray), propose a preliminary design of the solution (building, machine, product handling). These first assumptions will make a budgetary estimate of the project possible. Then the business case will be built using iterations. The feasibility study can be done in-house, with the help of a consultant, an external validation center such as an irradiation service provider, or an equipment manufacturer.

If the accelerator is for uses at a service facility, the market study will be the single most important element of decision. The integration of logistics and storage are also critical.

## 12.2 Project management

Once the feasibility study and business case are approved the project plan can be developed. The project scope should be well defined, including all the deliverables for a successful project. The project budget will then be developed in iterations as the costs for each of the deliverables are established.

The project schedule will require careful co-ordination and management of multiple suppliers. The key milestones for the project with typical delivery times shown in brackets are:

- Purchase of accelerator
- Purchase of conveyor
- Shield design complete
- Construction or adaption of building complete (6 to 12 months)
- Construction of shield complete (4 to 6 months)
- Delivery of accelerator (12 months)

- Delivery of conveyor (8 to 12 months)
- Installation and commissioning of irradiator equipment (IQ/OQ) complete (5 to 6 months)

Construction of the shield and building can occur in sequence or concurrently. However, the building and shield should be complete prior to the installation of irradiator equipment. After the rigging, the installation will typically last between 4 and 6 months, depending on the level of complexity and the number of components to be integrated. It is important to have the technical staff who will operate and maintain the system involved in the installation as this is a significant training opportunity.

A license may be required before starting construction. The license review will generally address shielding calculations, safety and security systems, staff training plan, and environmental impact.

## 12.3 Validation

Because the effectiveness of an irradiation process cannot be readily verified by measurement or examination, it is a special process [Ref. 3][Ref. 13] and therefore a process validation is required. Validation provides objective evidence that the irradiation process will consistently produce a result or product meeting predefined requirements.

A Validation Master Plan should be established.

### 12.3.1 Installation Qualification (IQ)

Installation Qualification is the first step to determine that, prior to use, equipment can produce the desired results as defined in the requirements and equipment specifications. IQ includes:

- Safety system performance testing;
- Testing and calibration of Critical Process Parameters (CPPs), the key variables and attributes that affect the production process;
- Calibration of analytical equipment. The importance of having a high-quality dosimetry system, a core equipment for radiation processing, cannot be overemphasized.
- Network security assessment.
- Control systems and manufacturing system software validation.
- Development of procedures for maintenance.

At this stage, a process Failure Mode Effect Analysis (FMEA) should have been carried out. This analysis is a systematic and proactive evaluation of a process to identify how it might fail and what the impact will be. The purpose is to identify where process improvement and risk mitigation are required.

### 12.3.2 Operational Qualification (OQ)

Operational qualification is performed after a successful IQ process to obtain and document evidence that installed equipment operates within predetermined limits. Different tests will be required throughout the range of operation limits and scenarios such as multiple paths, scan widths and energy ranges. The test plan includes dose mapping within homogenous material to determine the dose distribution and variability. Hundreds of calibrated dosimeters will be needed. OQ takes several weeks and may require external expertise for protocol development and data analysis.

### 12.3.3 Performance Qualification (PQ)

Performance Qualification is the process of obtaining and documenting evidence that the equipment consistently performs in accordance with predetermined criteria and yields product meeting its specification. Dose mapping individual product is completed during the performance qualifications Compared to photon irradiation (gamma or X-rays), EB irradiation introduces complexities (larger and localized dose gradients) due to the interactions of electrons. As a result, PQ for EB irradiation requires detailed dosimeter placement planning and potentially more dose map samples. Also, product configuration requires higher control because variations in product mass, geometry and orientation to the beam have a much larger impact.

PQ protocols are usually developed with the customer who will identify the number of product categories and sample size for dose mapping. Once dose mapping results and processing data have been thoroughly analyzed, a detailed process specification is developed.

## 12.4 Accreditation

When validation has been completed, before the commencement of commercial service, a Quality Management System must be implemented. ISO 11137, ISO 13485, ISO 9001 and GMPs are the usual references. A certificate of registration and compliance issued by a third party will be expected by users. Besides obtaining the license to operate, the irradiation facility will also need to be registered with national and foreign regulatory authorities for the products being processed.

# CAPITAL EXPENDITURE BREAKDOWN AND PARAMETERS

The following tables list the cost items of an accelerator project.

*Table 6: Breakdown of cost for an accelerator project*

| **Category** | **Items** | **Options / *comment*** |
|---|---|---|
| Project feasibility study | Product suitability<br>Regulatory approval | If change of sterilization modality |
| | Dose distribution studies | External service |
| | Market study and business case | Consultant |
| Project Management | Selection of process equipment | Internal and external resources<br>Time and travel<br>Meetings with consultant and vendors. |
| Regulatory compliance | Commissioning License Fee<br>Operational License Fee<br>Annual Operations Fees<br>Radiation Safety Officer training | Consultant to guide process if no expertise in the company |
| | Ozone abatement determination<br>Compliance with regulatory bodies requirements for medical products | |
| Land | Real estate fees<br>Taxes | For greenfield facility |
| Building and shielding | Permitting | Creation or modification |
| | Shield / bunker<br>Storage space / Loading and unloading areas / Docks /<br>Offices / Technical rooms (control, dosimetry…) | Design and construction<br>*Fitting a large bunker in an existing building can be more expensive than constructing a new building* |
| EB or X-ray generator | Accelerator | Beam line(s) design |

| Category | Items | Options / *comment* |
|---|---|---|
| Ancillary systems | Water cooling | Tower or chiller |
| | Electrical supply | UPS |
| | Ozone removal fan<br>Compressed air<br>Technical gases | <br><br>Dry air, dry nitrogen, helium |
| Product handling | Under beam conveyor | |
| | Shield and warehouse conveyor<br>Infeed and outfeed conveyors | Box flipping system, palletization robot, Automated Guided Vehicles, automatic storage equipment, forklifts.<br>Cost can be superior to accelerator cost depending on level of complexity and automation |
| Safety and security systems | Accelerator, conveyor, shield / bunker safety<br>Facility/warehouse safety<br>Personnel dosimetry | Access control<br>Video security and process monitoring<br>Fire extinguishing system<br>Radiation dose meters<br>Individual dosimeters |
| IT<br>Process control system<br>Product tracking system | PLCs / PCs - Network<br>Software suite<br>Bar code printer and reader<br>Security software and devices | Integration with inhouse ERP |
| Spare parts | Initial stock | Consumables<br>Electron source<br>RF amplifier tubes<br>Cathodes<br>Belts<br>Chains<br>Bearings<br>Sprockets… |

| Category | Items | Options / *comment* |
|---|---|---|
| Equipment installation | Equipment rigging<br>Connection of specific equipment<br>Training | Installation cost often included in price of the equipment. Client may have to provide cranes, specific tools, and manpower (*e.g.* electrician, plumber, welder) |
| Process validation | IQ-OQ-PQ | Consultancy services |
| Dosimetry | Dosimeters<br>Dosimetry system<br>Calibration | *Many hundreds for EB, less for X*<br>*More than one system for EB and X-ray*<br>External service |
| Other costs | Transport, shipping<br>Import duties<br>Insurance<br>Tools and fixtures specific to process validation and maintenance<br>Maintenance contract after warranty | |

The approximate cost range of the different items for medium or high energy accelerators is given in Table 7. The amounts are indicative only as they can significantly vary depending on the supplier, the technical options, and the local context.

*Table 7: Initial cost*

| Item | Minimum USD | Maximum USD |
|---|---|---|
| Accelerator electron beam | 300,000 | 5,000,000 |
| Accelerator X-ray | 300,000 | 8,000,000 |
| Building | 500,000 | 5,000,000 |
| Shielding | 500,000 | 2,000,000 |
| Product handling | 200,000 | 3,000,000 |
| Ancillary systems | 200,000 | 500,000 |
| IT Process control | 50,000 | 400,000 |
| Safety systems<br>(if not included in accelerator price) | 100,000 | 200,000 |
| Shipping, installation (if not included in accelerator price) | 50,000 | 250,000 |
| Spare parts | 100,000 | 300,000 |
| Feasibility | 8,000 | 50,000 |
| License | 3,000 | 40,000 |
| Validation | 5,000 | 20,000 |
| Dosimetry | 5,000 | 30,000 |

# OPERATING COST

This chapter addresses the cost that are specific to a business operating an accelerator.

## 14.1 Staff

During project initiation through to completion, the business should have a skilled project manager to manage the schedule, budget, and resources. Specific skilled personnel can be outsourced during the project, where internal expertise is not available.

The operation of an electron beam irradiator facility is not very different from most manufacturing or other types of sterilization facilities such as gamma irradiation and ethylene oxide. The technical and validation expertise requirements are essentially the same. Although accelerators involve diverse engineering disciplines in their design, the routine maintenance does not require highly skilled maintenance personnel. This maintenance personnel qualification requirements will depend on the level of support that the equipment supplier will provide through a maintenance contract. Once the machine is operating, personnel with a technical diploma or degree in electrical engineering are needed to carry out routine tasks and diagnosis in case of technical problem. These personnel will be the counterpart of the supplier. Mechanical skills and resources are also required to diagnose and repair the material handling system.

The rest of the staff does not widely differ from what is needed in other types of sterilization facilities.

## 14.2 Utilities

Electricity is a major operating cost and therefore the electrical efficiency of the accelerator and its auxiliaries must be carefully considered at the time of acquisition. The suitability of the local electricity supply, in terms of power and stability must be assessed at an early stage of the project. Depending on the power of the system, local price of electricity and how many hours the facility is used, the yearly cost of electricity will range from approximately 100,000 USD to 1,500,000 USD per year.

The type of cooling systems used to maintain the accelerator and remove excess heat from targets will be selected based on the required operating temperature, environment and efficiency. If an evaporative cooling tower is selected over a chiller system then consideration for water consumption and waste will need to be considered. The primary cooling water supply system must be dimensioned to be compatible and powerful enough for the proper functioning of the secondary cooling systems (*e.g.* cavities, magnets, X target...).

Technical gases such as nitrogen, helium and possibly sulfur hexafluoride are required for accelerator operation and maintenance. High purity nitrogen and helium are used in the maintenance of vacuum systems. Sulfur hexafluoride is used as an electrical insulator in waveguides and electrostatic accelerating cavities such as a Dynamitron. The user must take provisions to have them readily available when topping up is required, for preventive maintenance or in case of breakdown.

## 14.3 Maintenance

Proper maintenance is required to ensure that the machine is available when and as much as it is needed. When properly maintained, accelerators can reach an availability greater than 90% over the year. The difference in machine availability may reflect the quality and the reliability of the machine - which is not unrelated to cost- but also the maintenance policy.

Maintenance schedules must be established and timely both for availability and quality management purposes. Asset management and monitoring systems are used to optimize equipment performance through:

- Life cycle management (design, warranty, disposal)
- Work orders and scheduling management (labor, preventive maintenance)
- Inventory and materials control
- Maintenance data and analytics
- Monitoring predictive maintenance, Independent Operational Test (IOT), sensors.

Remote access and support via internet access are increasingly important. This requires sufficient quality of the internet link and has security implications.

Though this may seem unnecessary right after operation has begun, having a maintenance contract with equipment suppliers is generally wise and may save money in the long term. The supplier's staff will have skills and knowledge that the operator's staff do not have to diagnose the machine, to evaluate the condition of critical components, or to carry out the most difficult maintenance tasks.

The most frequent causes of downtime tend to be related to consumable parts and some sensitive systems such as:

- Mechanical parts for conveyor (bearings, belts, chains)
- Electron gun cathode
- RF Amplifier (klystron, tetrode)
- Vacuum pumps
- Minor components such as power supply or sensors
- Cables and wires exposed to radiation or ozone
- Window foil
- Loss of vacuum (vacuum pump, vacuum gauge, gasket…)

*Table 8: Indicative lifetime and cost of some critical components*

| | Indicative lifetime (hours) | Indicative price (USD) |
|---|---|---|
| **Electron gun** | 8,000 to 20,000 | 2,000 - 20,000 |
| **RF final amplifier** | 24,000 | 75,000 - 120,000 |
| **Vacuum pumps** | 30,000 | 2,000 - 20,000 |
| **Window foil** | 8,000 to 80,000 | 1,000 - 3,000 |

A maintenance strategy should be developed to maximize availability and reduce risk of extended downtime due to lack of critical spares or long delivery times. Best practice is to perform a risk assessment to identify critical spare requirements.

## 14.4 Dosimetry tools, accessories, and consumables

Dosimetry plays a key role in radiation processing and can be used as evidence that the process was properly conducted. It is important to make the necessary investment in a proper dosimetry system, including the readout equipment, dedicated validated software, and calibration tools and accessories. The latter include an aluminum wedge for electron beam energy, an irradiation jig for scan width and length and process interruption, plates and boxes of homogeneous material for depth dose profiles and edge effects. The preparation and reading of some sensitive dosimeters may require a laboratory with specific environmental conditions, such as UV-protected lights, temperature and humidity control.

These are some of the main applicable standards and guidance documents:

- EN ISO 11137-3:2017 Sterilization of health care products. Radiation. Guidance on dosimetric aspects of development, validation and routine control
- ISO/ASTM51707-15 Standard Guide for Estimation of Measurement Uncertainty in Dosimetry for Radiation Processing
- ISO/ASTM51261-13 Standard Practice for Calibration of Routine Dosimetry Systems for Radiation Processing
- ISO/ASTM52628-13 Standard Practice for Dosimetry in Radiation Processing
- ISO/ASTM52701-13 Standard Guide for Performance Characterization of Dosimeters and Dosimetry Systems for Use in Radiation Processing

The selection of a dosimetry system must consider factors such as range of applied dose, radiation energy, and product complexity. For radiation sterilization of medical devices, the use of well-established systems is recommended. These include:

- Film dosimeters such as FWT 60, GEX B3 and CTA. Their absorbance, which is a function of the absorbed dose, is read-out at specific wavelength with spectrophotometers.
- Alanine dosimeters. They are sensitive, accurate and stable. They are readout with an ESR spectrometer to measure the amount of induced free radicals in the irradiated alanine dosimeter.

For medium and high energy electron beam applications, graphite or polystyrene calorimeters ay be used as well.

The cost of dosimeters can be significant. When qualifying a new irradiation plant (IQ/OQ) or requalifying it, thousands of dosimeters and a few rolls of CTAs may be used. PQ also uses many dosimeters as it must be performed for each processed product or product family. Costs are also generated by the necessity to calibrate and verify annually various measuring and maintenance instruments so as to maintain traceability to national or international references.

## ACCELERATOR SELECTION KEY CRITERIA

- **Electron energy**
- **Average beam power**
- **Electrical efficiency**
- **Reliability**
- **Quality of process control system**
- **Price**
- **Balance between size, efficiency, and cost.**

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Association for the Advancement of Medical Instrumentation (AAMI) Arlington, VA, USA

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National Center for Electron Beam Research, Texas A&M University, USA

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Didier Morisseau
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IAEA, Vienna – May 2009
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[13]ISO 9000:2015 Quality management systems — Fundamentals and vocabular

# Technical Library

## iia resources https://iiaglobal.com

Electron beam factsheet

X ray iia factsheet

A Comparison of Gamma, E-beam, X-ray and Ethylene Oxide Technologies for the Industrial Sterilization of Medical Devices and Healthcare Products
iia white paper - August 31, 2017

Database of accelerators installed since 2015

## IAEA resources

Economic Feasibility of Transitioning from Gamma Sterilization to Accelerator-based Sterilization
Report of a consultants meeting, Vienna, Austria 19 – 22 August 2019
International Atomic Energy Agency Vienna, Austria, 2019
Download

Radiation Safety of Gamma, Electron and X Ray Irradiation Facilities : Specific Safety Guide.
IAEA Safety Standards Series no. SSG-8
International Atomic Energy Agency, Vienna, 2010
Download

## Other Resources

Guidance when transferring a product from one irradiator to another within the same modality, or from one modality of radiation to another—for example, from gamma to electron beam or vice versa.
AAMI TIR 104
To be published in early 2021

X-ray: An Effective Photon
Brian McEvoy; Hervé Michel; Daniel Howell; Philip Roxby
Biomedical Instruments Technology (2020) 54 (s1): 23–30.
Download

Change of Irradiation Modalities in Radiation Sterilization of Medical Devices – Normative Requirements and Aspects in EN ISO 11137-1
The Panel on Gamma and Electron Irradiation – 2020
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Guide on the use of low energy electron beams for the decontamination of surfaces
The Panel on Gamma and Electron Irradiation - 2013
Download

IBA Webinar: Project Experience with E-Beam: -Case study
March 25, 2021
Watch presentations

# Appendix A: Reference and experimental institutes for the use of EB and X ray

**Aerial**

Parc d'innovation - 250 rue Laurent Fries
67400 Illkirch – France

Contact: Dr Alain Strasser and Dr Florent Kuntz
T: +33 3 88 19 15 15
E: aerial@aerial-crt.com
W: www.aerial-crt.com/en/

**IAEA collaborating center**

**Equipment:**

- High energy E-beam and X-rays (FEERIX)
- Medium energy E-beam and X-rays
- Low energy E-beam
- Low energy X-rays
- Multiple dosimetry systems (accredited dosimetry laboratory)

**iBA**
Long Island, New York - USA

**Contact:** Rick Galloway
T: +1-631-595-4117
E: rick.galloway@iba-group.com
W: www.iba-industrial.com/services-upgrades

**Equipment:**
E-beam and X-ray testing services. Up to 3 MeV, 1.20 m beam scan, 70 cm under-beam.

**Illinois Accelerator Research Center (IARC)**
Fermi National Accelerator Laboratory
P.O. Box 500, MS 312 Batavia, IL 60510 - USA

**Contact**: Dr Thomas K. Kroc
T: +1 630 840 6955
E: kroc@fnal.gov
W: www.fnal.gov

Equipment: Linear accelerator

**Institute of Nuclear Technology and Chemistry**
ul.Dorodna 16 03-195 Warsaw - Poland

**Contact:** Prof. Andrzej Chmielewski
T: + 4822 5041205
E: a.chmielewski@ichtj.waw.p
W: www.ichtj.waw.pl

**National Center for Electron Beam Research**
400 Discovery Drive College Station, Texas 77845 USA

**Contact:** Dr Suresh Pillai
T: +1 979-458-3229
E: s-pillai@tamu.edu
W: https://ebeam-tamu.org/

**IAEA collaborating center**

**Equipment :**

- Two vertically mounted opposing 10 MeV / 18 kW Electron Beam Linear Accelerators (LINAC) and
- One single horizontally mounted 5 MeV / 15 kW X-Ray Linear Accelerator
- IAEA collaborating center.

# Appendix B: Suppliers of accelerators

**Budker Institute of Nuclear Physics – BINP**
Siberian Branch of the Russian Academy of Science
11 Akademika Lavrentieva Prospect
Novosibirsk 630090 Russia

**Contact:** Aleksandr Bryazgin
E: a.a.bryazgin@inp.nsk.su
T: +7 383 329 43 91
W: http://www.inp.nsk.su/

*Design and manufacture of ELV and ILU electron accelerators. ILU type RF accelerators are for e-beam and X-ray in the 1-10 MeV range and power up to 100 kW. ELV DC accelerators in the 0.5-3 MeV energy range with power up to 500 kW.*

**CGN Dasheng Electron Accelerator Technology**
1288 Shexi Road, Beishe
Fenhu, Wujiang, Jiangsu 21514 PR China

**Contact:** Mr. Wang Ping
T: +86-0512-82859888-8879
E: EBTech@cgndasheng.com
W: http://www.cgndea.com/

*Design and manufacturing of E-Beam systems*

**IBA Industrial Solutions (Ion Beam Applications)**
Chemin du Cyclotron
3 – 1348 Louvain-la-Neuve Belgium

**Contact:** Jeremy Brison
T: +32 474 456 984
E: Jeremy.Brison@iba-group.com
W: http://www.iba-industrial.com/

*Design and manufacturing of Rhodotron® E-Beam accelerators (1 to 40 MeV, 1 to 560 kW) for EB-X systems and service and upgrade of Dynamitron® E-Beam accelerators (0.5 to 5 MeV).*

**ITHPP**
Drèle - 46500 Thégra France

**Contact:** Sébastien Boisne
T: +33 5 65 33 43 30
E: sboisne@ithpp-alcen.fr
W: www.ithpp-alcen.com/en/industry/pulsed-electron-beam-sterilisation

*Pulsed electron beam systems for surface/core decontamination or sterilization purposes.*

**MEVEX**
P.O. Box 1178, 108 Willowlea Road
Stittsville, ON K2S 1B4 Canada

**Contact**: Dave Brown
T: + 1 613 831-2664
E: info@mevex.com
W: www.mevex.com

*Design and manufacturing of EB and X-ray linear accelerators with beam energies from 1 to 40MeV and beam powers from 1kW to 300kW. Concrete and steel shield, Box and pallet conveyors, equipment and process control systems, automation and robotics*

**NUCWAY Co. Ltd.**
7/F, Zi Guang Building , No.1, ZhongGuanCun East Road,
HaiDian District,
Beijing 100084 P.R. CHINA

**Contact:** Mr. Guang Yang
T: 86-13910058021
E: yangguang@nuctech.com
W: eb.nuctech.com

*Design, construction and technical service of integrated, customized and specialized E-beam/X-ray Irradiation Systems covering 1-10MeV Linac-up to 50kW, high power ELV accelerators up to 100kW, electronic curtain accelerators and X-ray biological irradiators, Advanced high energy electron beam irradiation processing quality control key technology equipment.*

**Shanxi Yitaike Electrical Equipment Co. Ltd**
8# Road, Chuangye Street, Huitong Industrial Park, Jinzhong Development Zone
Shanxi Demonstration Region
Jingzhong 030600 PR China

**Contact:** Mr. Zhang Changyou
T: +86 354 399 86 29 or +86 18903512710
E: 2422051579@qq.com
W: http://www.rcelv.com

*Co-manufacturing and design with BINP of CELV electron accelerators with beam energy from 0.5 to 3 MeV, beam current up to 130mA and beam power up to 100kW.*

**Vanform Corporation**
No.2711, Yingxiu Road, High-tech Park,
Jinan, Shandong, 250101 PR China

**Contact:** Mr. Wei PENG
E: pengwei@vanform.com, info@vanform.com
T: +86 0531 81217203
W: www.vanform.com

*Design and manufacturing of linear electron accelerators*

**WuXi El Pont Radiation Technology Co. Ltd.**
No. 8 Weiye Road, Qianqiao,
Wuxi, Jiangsu 214151 PR China

**Contact:** Dr. Yuwei Zhang
E: sales@elpont.net
T: 86 510-837 003 87
W: www.elpont.net/en

*Design and manufacturing of electron accelerators in the 0.5-10 MeV range and conveyors.*

Accelerators for Sterilization of Medical Devices
*A Guide for Prospective Buyers*

iiaglobal.com