HIGH PRECISION DOSE DELIVERY FROM ELECTRON AND X-RAY BEAM LINES

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Abstract

In this paper the challenge of high precision dose delivery from electron and X-ray beam lines is analyzed. At first, dose delivery is discussed from general microbiological and normative principles. Following, the electron beam process is presented and the topics surface dose, product dose and reference dose are discussed in depth. Special emphasis is on the qualification effort and its implications to precise dose delivery. In the third chapter industrial X-ray processing is discussed and preliminary modeling results for a high- precision X-ray research system at Mediscan, Austria are presented.

1. INTRODUCTION

The sterilisation of medical products with ionizing radiation is an established and in many cases the only available method. Besides gamma technology, which is using photons from the decay of the radioactive isotope Co-60, electron beam sterilisation has been around for more than 50 years with an impressive track record. Irradiation using X-rays is finally entering the industrial word.

New applications are characterized by the requirement to deliver doses with very high precision and particularly the need for exact low dose delivery is emerging. In this paper the methodology of dose delivery in electron beam and X-ray technology is analyzed and discussed in depth. Whereas the focus is on medical devices and pharmaceutical applications, the results are applicable to any field in industrial irradiation.

2. DOSE DELIVERY

Rendering a medical device "sterile" is a complex multi-tier process:

(1) The term "sterility" which is generally regarded as "free from harmful micro organisms" has to defined in a scientific and statistical context. This is accomplished by the SAL (sterility assurance level) which is set to 10^{-6} for medical devices, this means only one sample out of one millions may be still contaminated after the irradiation process.

(2) Knowledge of the microbiolocal population together with their D_{10} (the dose which is needed to decrease the population by a factor of 10) levels leads to the sterilisation dose necessary to kill viable microorganisms. This process is formalized for different dose setting methods which are described in depth in the ISO 11137 – Part 2 [1].

Among these the methods VD_{max} 25 and VD_{max} 15 have gained wide acceptance in the last years, however they demand a very low bioburden.

(3) Applying the dose to any part of the product which has to sterile, guarantees that - in a statistical context - no microorganism will survive. However, the maximum dose that the product can tolerate must no be exceeded by the irradiation process. The use of special formulations and additives which minimize chain scission and stabilize the polymer has become a standard procedure, however special product ingredients like bio-active substances still limit the maximum tolerable dose. So typically for modern products, is an extremely small dose window, between the minimum dose D_{min}, which is necessary to sterilize the product and D_{max}, which must no be exceeded in order not to degrade the properties and function of the product.

There are two types of radiation doses which are to delivered:

(1) the routine dose or sterilisation dose. This is the dose which actually is set to kill viable micro organisms.

(2) the dose necessary for dose verification audits. The meaning of this dose needs a little further explanation. Due to the statistical approach taken for the definition of sterility, it is not possible to actually verify that the routine dose sterilizes all but one, from a million product samples. The verification of the sterilisation dose is accomplished by using a lower dose which is tabulated for different bio burden numbers. Since the verification dose is much lower and has to be delivered within a maximum ten percent uncertainty [1], verification dose experiments are more demanding on the process than the routine sterilisation.

Summarizing, radiation sterilisation puts requirements to the process which become more stringent for nowadays applications

(1) The irradiation process must guarantee that the doses in the product are within the window $[D_{min}, D_{max}]$ where D_{min} is the minimum sterilisation dose and D_{max} is the maximum tolerable dose for the product. For demanding products this window is sometimes only 10 percent wide, meaning that the dose uniformity ratio (DUR = D_{max}/D_{min}) has to be below 1.1.

(2) Very low doses must be applied with a low uncertainty, which is typically less that 10 %. For a verification dose of 2.3 kGy, this means that no dose in the verification experiment shall be above 2.56 kGy. This is not only demanding for the process, but also for the dose measuring system.

3. THE ELECTRON BEAM PROCESS

The sterilisation process using electron beam is described using the process specifications of Mediscan GmbH&COKG, based in Kremsmunster, Austria. Mediscan is using two 10 MeV accelerators to provide high quality irradiation services and consulting in process development. Both machines are Rhodotron TT-100 systems, where the second unit installed

in 2009 is featuring two beam lines: a 10 MeV electron beam line and a 6.6 MeV x-ray line for research, process development and small scale irradiations of special products. This paragraph deals with the electron beam process, the next one will discuss the possibilities of the new x-ray beam line.

3.1 SURFACE DOSE

When discussing high precision dose delivery there are two items to consider: the first is the precise, uniform and repeatable delivery of the surface dose. This dose depends, for a fixed energy and surface material, solely on the beam parameters.

$$D = k\frac{I}{s.v}$$

where D is the dose in kGy, I the average beam current (for pulsed beams), s the scan width and v the process speed. The factor k depends on the stopping power of the surface material and has a beam utilisation factor folded in. This equation must be strictly linear and plotting the dose versus the term I/sv is a very good way to test the irradiator performance.

Fig.1 shows the dose against the process variable I/vs, recently measured at the Mediscan TT-100 system for the annual system requalification exercise. Requalification tests like this one, together with scan width, energy and beam current qualifications are a very good way to assure proper performance of the equipment and precise dose delivery [2].
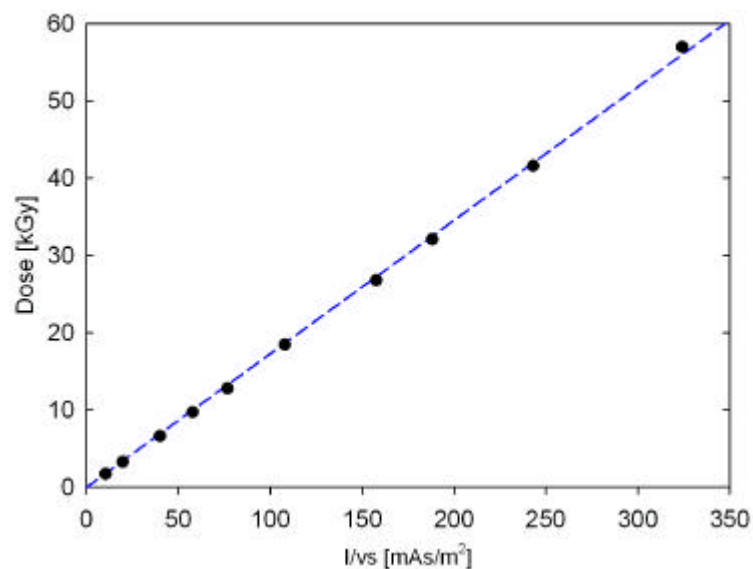

FIG. 1. Linearity check of dose delivery for electron beam lines

3.2 DOSE IN PRODUCT

The process requirement is to deliver precise and repeatable doses to any volume element in the product. As matter of fact, the electron beam depth dose curves shows the typical energy loss behaviour of charged particles.

Following the surface dose a build-up up region with a flat top is visible, following a steep decrease (see Fig.2)
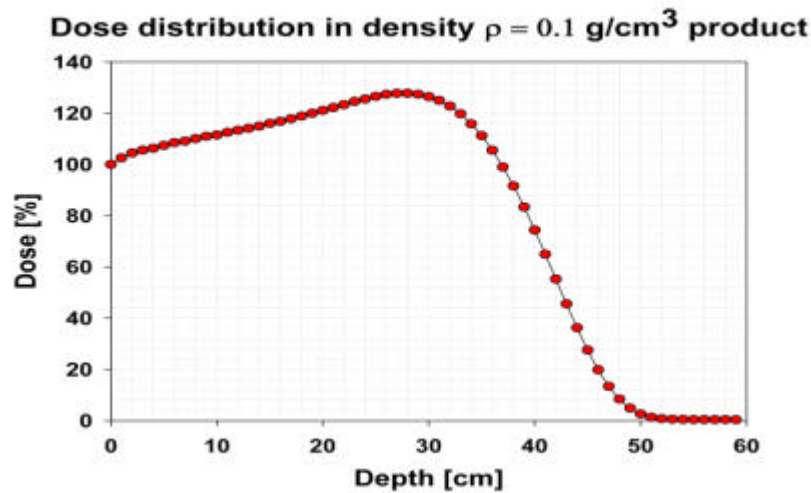

FIG.2 Depth Dose Distribution of a 10 MeV Electron Beam

In order to minimize the dose uniformity ratio in the product the position where the product sits along the depth dose curve must be carefully chosen. Use of build-up plates may be beneficial to bring the product to a certain point on the curve. Never, should a product depth extend over the top, because slight variations in the material or process can result in a dramatical dose decrease.

Finding the minimum and maximum dose is part of the PQ process (Performance Qualification) and is accomplished by dose mapping experiments, where the product is loaded with dosimeters to assess the dose distribution in the product. Details on the dose mapping procedure are given in [3]. Mathematical modelling can help to study the dose distribution in the product and locate the position and variability of the minimum and maximum dose. In addition, mathematical modelling can help to design the irradiation process and optimize build-up materials.

3.3 REFERENCE POSITION

Product release is specified on the outcome of Performance Qualification and the relation between the minimum dose, maximum dose and the reference dose is defined. The reference dosimeter is usually attached to the shipping carton, but the appropriate standard also allows off-product reference positions.

Picking a suitable reference position is important to the overall process uncertainty, because any variation of the reference dosimeter reading is translated to an uncertainty of the minimum and maximum dose, which again accounts to the total uncertainty of the process. For practical reasons the reference dosimeter should be in a place where little variations from backscattering, product inhomogenities and placing biases is expected.

4. X-RAY PROCESSING MODE

Industrial X-ray irradiations was proposed and theoretically described already long ago, but only recently powerful enough accelerators are available that have a chance to render the X-ray irradiation process economically feasible.

The theory behind X-ray processing is simple and meets in some aspects medical X-ray imaging: an electron beam impinges on a heavy nuclei target (e.g. tantalum, tungsten or gold) and through the bremsstrahlung process a beam of photons is generated. The conversion rate is strongly energy dependant and about 8 % for a 6.6 MeV primary electron beam. In contrast to medical imaging where only a small beam spot is used the X-ray beam is generally not focused by virtue of collimators, but directed towards the product which is conveyed through the irradiation field. Due to the sandwich structure of the target consisting of tantalum, cooling water and steel a little bit of beam hardening is achieved, but in general, there is a continuous energy spectrum which starts at about 150 keV and tops at the primary beam energy. The calculated spectrum for the Mediscan beam line is shown in Fig. 3. Valuable information on X-ray beams is given in [4].

The result of the fact that the majority of the photons have low energy below 1 MeV is the high surface dose, which is common to all X-ray applications. Fig.4 shows the the calculated 3D dose distribution for a 60 cm wide electron beam hitting a tantalum target. The size of the cube which defines the simulation region is 1m x 1 m x 1m. Clearly the dose hot spot where the electron beam is hitting the target can be seen. A iso-dose calculation of the X-ray field is presented in Fig.5.
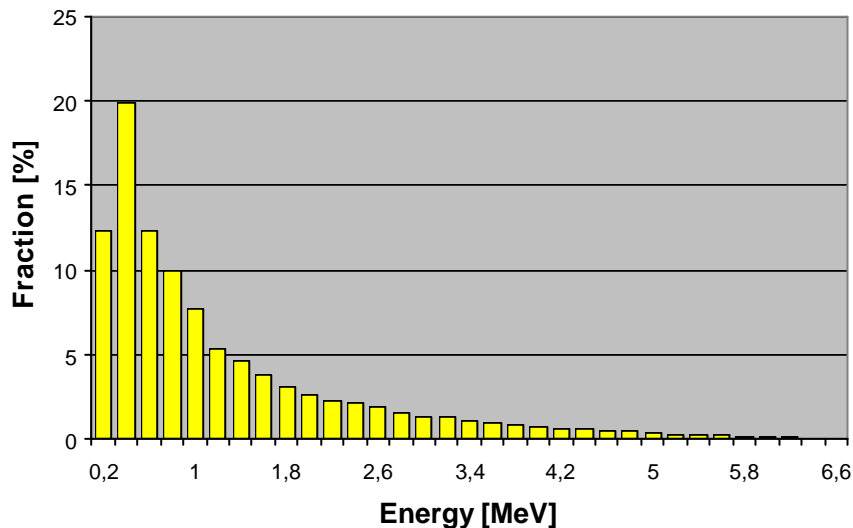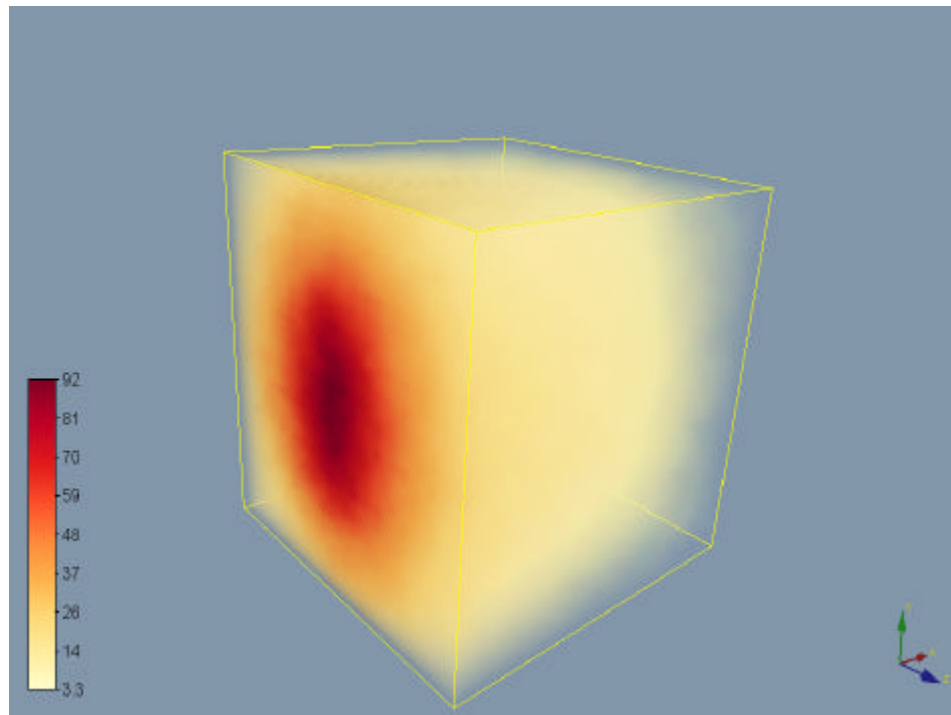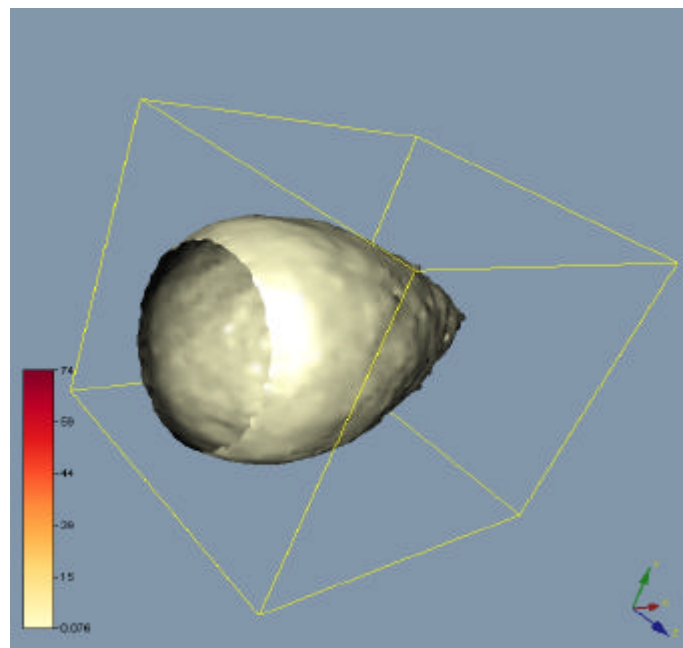

FIG.3 Calculated X-ray spectrum

FIG.4 3D Monte Carlo Calculation of the X-ray dose

FIG.5 3D Monte Carlo Iso-dose Calculation of the X-ray radiation field

To achieve a suitable dose distribution in a product various scheme have been proposed. Some use rotating turn-tables to irradiate at pallet of products other designs work with 4-passes to irradiate a pallet from all sides.

For its research accelerator Mediscan uses a different approach: the used radiation field is limited in space, so that only boxes can be used. However the dose uniformity in the products is calculated to be excellent, because double sided irradiation overcomes the drawback of the exponential doses drop which is typical for a photon source (Fig. 6).
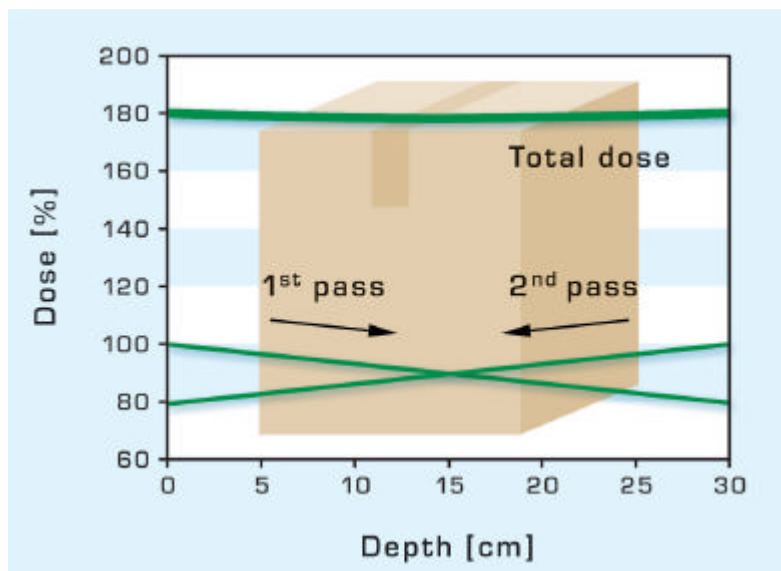

FIG.6 Dose distribution for double sided X-ray treatment

5. DOSIMETRY

Designing, qualifying and maintaining an optimal process is the key to precise dose delivery and we have seen, that mathematical modelling can help in the design, optimization and qualification process. However, an excellent irradiation process is in vain without a proper measurement tool, in our case a dosimetry system. Mediscan is using a Bruker escan dosimetry system with Alanine films and pellets, when accurate dose measurements are needed. The dose uncertainty of typically 3% (2 sigma) fulfils the requirements to fully exploit the process capabilities.

6. CONCLUSION

Summarizing, the "art of precise dose delivery" with electron and X-ray beams depends on reliable and well qualified radiation sources, which operate perfectly within specifications. Even more important is the deep understanding of the processes involved in radiation processing which are assisted by mathematical modelling and high quality dosimetry. Precise dose delivery is challenging, but extremely important to satisfy the needs of the medical device and pharmaceutical industry.

REFERENCES

[1]   ISO 11137 (2006) "Sterilization of health care products — Radiation — Part 2 Establishing the sterilization dose"

[2]   ISO/ASTM 51649 "Standard Practice for Dosimetry in an Electron Beam Facility for Radiation Processing at Energies Between 300 keV and 25 MeV", ASTM, 100 Barr Harbor Dr., Conshohocken, PA 19428.

[3]   ASTM 2303 (2003) "Standard guide for Absorbed –Dose Mapping in Radiation Processing facilities "

[4]   "X-ray dosimetry – Comparing Monte Carlo simulations to experimental results", F. Stichelbaut et.al, Radiation Physics and Chemistry, volume 71 (2004)