

Sterilisation of Bioresorbable Polymer Implants

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Bioresorbable polymer implants are rapidly growing alternatives to traditional implants in many applications. Because of their resorption in the body, it is necessary to sterilise the complete product before application. The suitability of different sterilisation methods for bioresorbable polymers is discussed using polylactic acid implants as an example.

Image: PhotoDisc

This article was first published in *Medical Device Technology*, vol. 18, no. 3, May-June 2007.

The requirements

Traditional metal implants have been used by surgeons in a large variety of applications for many years. Although widely used, an inherent set of problems such as long-term compatibility and possible migration, breakage and material reactions have led to the development of bioresorbable polymer implants and devices. Biodegradable polymers can be natural or synthetic. Synthetic polymers offer greater advantages than natural materials in that they show greater lot uniformity and are free from immunogenic concerns. The most widely used polymers are polyhydroxy acids such as polylactic acid (PLA), poly-D-lactic acid (PDLA) and their copolymers; and polyglycolic acid (PGA) and its copolymer, polylactic coglycolic acid (PLGA). These polymers have excellent mechanical properties. Commercially available biodegradable devices are employed in sutures, orthopaedic fixation devices, dental implants, ligature clips, tissue staples and skin covering devices.

These implants are only required to serve for a certain time period ranging from weeks to months. The functional behaviour of these implants is generally determined by their glass transition temperature, which can be as low as 10°C. In addition, residual stresses may remain in the moulded parts after manufacturing, which can lead to

deformation on heating to, or above, the glass transition temperature. PLA, PGA and their copolymer PLGA are hydrolytically unstable; even presence of small amounts of moisture can degrade them in storage, during processing and after device fabrication.¹ These polymers are sensitive to high temperatures because their molecular weight decreases at higher temperatures, which affects storage and sterilisation of these components. In the context of bioresorbable polymer implants, the suitability of five principal methods of sterilisation is examined below.

Moist and dry heat sterilisation

Sterilisation with moist heat in an autoclave is usually performed at temperatures equal to or higher than 121°C; dry heat sterilisation requires considerably higher temperatures to effectively inactivate bacterial spores. The susceptibility of PLA, PGA and PLGA implants to hydrolysis and their deformation at higher temperatures therefore precludes the use of these sterilisation methods.

Ethylene oxide sterilisation

Ethylene oxide (EtO) sterilisation requires extensive degassing (desorption) procedures after sterilisation. Complete removal of residual traces of gas is difficult to achieve,² especially in products with a large surface such as

mesh, warps or wovens. EtO is chemically highly reactive and could act as a plasticiser for the polymer, which could lead to changes in the polymer structure.³ In addition, EtO sterilisation is performed at temperatures of 50–60°C, which is well above the critical temperatures for changes in molecular weight of the polymers being discussed.

Plasma sterilisation

Plasma sterilisation is usually performed with hydrogen peroxide in the plasma state. It is a surface sterilisation method. Bioresorbable implants need to be sterilised in their entirety to preclude patient infection during their degradation.

Radiation sterilisation

Irradiation, particularly at doses above 35 kGy, may induce degradation of the polymer chain and result in reduced molecular weight and influence mechanical properties and degradation profile.¹ However, because of its physical nature, radiation has definite advantages in that it is penetrating and free of residues. Also, material temperatures are only moderately elevated during sterilisation. For the radiation sterilisation of bioresorbable implants, temperature and dose conditions need to be closely considered. Temperatures must be kept below the temperature at which molecular weight change



→ of the polymer occurs to prevent the part geometry from changing during sterilisation. Because gamma irradiation takes place at room temperatures and product temperature is elevated as a result of gamma ray absorption, cooling of product to 0°C or less during irradiation is advised.¹ This requires the use of cooling agents in the irradiation container to prevent heating to the critical temperature where molecular weight is affected. However, presence of cooling agent in the irradiation container may lead to radiation shading during irradiation with accelerated electrons (e-beams); this is the absorption of radiation because of the high density of the material, which leads to incomplete irradiation of neighbouring product. This effect is not observed with gamma irradiation.

Microbiological validation experiments according to ISO 11137, Sterilisation of Health Care Products, Requirements for Validation and Routine Control, Radiation Sterilisation, have shown that microorganisms are effectively inactivated by gamma irradiation in dry ice at doses of 16 kGy or more. Various combinations of doses and temperatures are employed to achieve product sterility without adversely affecting the product. In practice, the following are used by the author:

- 25–35 kGy at approximately 10°C
- 25–40 kGy in dry ice
- 18–25 kGy at room temperature
- 18–25 kGy in dry ice.

The actual temperature–dose combination used is determined by the radiation sensitivity of the product.

Gamma sterilisation of PLA implants

Based on the above considerations, many producers of bioresorbable implants use gamma irradiation at controlled temperatures as the preferred method for sterilisation. Two processes for gamma sterilisation are described below, one for product in aluminium pouches, and one for finished product in its sales package. The cooling agents used are commercially available cooling packs at a temperature of approxi-

mately 10°C or dry ice (solid carbon dioxide, sublimation point -78°C). Dry ice requires special precautions when handling because it can cause frostbite if handled without special gloves. The advantage of dry ice is its temperature stability⁴ due to sublimation, which ensures that the cooled product will be kept at -78°C, providing sufficient quantities of dry ice are present in the irradiation container. Dry ice is readily obtainable and can be kept in an insulated storage container for several days without significant loss of material.

Aluminium pouches. For gamma sterilisation of aluminium pouches (in this case skin covering devices), a commercially available aluminium transport container with a hinged cover is fitted with 25-mm styrofoam insulation on all the insides. The container is filled with product and 6 to 10 cooling packs are distributed evenly inside; the packs are cooled in advance in a refrigerator to -24°C. Temperature sensitive labels are placed in the container to monitor temperature conditions during transport and irradiation. The container is tightly closed and transported to the irradiation facility for sterilising. In the facility the container is placed in a tote and irradiated at the required dose.

Finished product. Finished product in its final package is irradiated in shipping cartons that are fitted with styrofoam insulation on the insides. Dry ice is added to polyethylene bags placed in the cartons in sufficient amounts to cool the product during the sterilisation cycle. Care should be taken not to close these bags too tightly to allow sublimated carbon dioxide gas to escape from the carton. The bags with residual dry ice are removed after irradiation and before shipping, because packages containing dry ice are not accepted by most transport companies. The shipping cartons should be fitted with temperature-sensitive labels to monitor temperature throughout the complete cycle of transport to and from the

irradiation facility and during irradiation and storage there.

Optimum sterilisation

Bioresorbable polymer implants form a rapidly growing alternative to traditional implants in many applications. Because of their resorption in the body, it is necessary to sterilise the complete product before application. Their sensitivity to hydrolysis and decrease of molecular weight at temperatures slightly higher than body temperature does not allow the use of sterilisation methods that employ gases and/or higher temperatures that affect the shape and structure of the product. Gamma sterilisation at selected doses in combination with sufficient cooling during irradiation allows effective sterilisation of the products without adverse effects.

References

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