



*Sterilization Methods of
Artificial Joint Prostheses*

Group R2
Richard Kiok
Siddharth Fernandes
Summit Gupta
Andrew James

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INTRODUCTION

Total joint replacement is frequent and costly. An estimated 120,000 total hip replacements and 120,000 total knee replacements are performed in the United States annually. The total hospital and physician cost for each procedure is generally between \$25,000 and \$30,000 (Ward & MacWilliam, 1995). And in Ontario, Canada, (where health care is governmentally subsidized) 6,200 hip and 5,000 knee replacements were performed in 1991. The costs of surgery are covered by hospital budgets including the prostheses, cost of the operation, acute follow-up care and in-hospital rehabilitation. However, joint replacement is considered an elective procedure for most cases. Therefore, some hospitals cap the number of prostheses ordered and limit operating time (Williams, J. I. et al., 1991). Typically, the life expectancy of a replaced joint is 15 years (Candor Technologies, 1996). Because of the high cost of the procedures and the potential waiting times, increasing the life expectancy of the artificial joint prostheses would be beneficial to both hospitals and patients.

There have been documented reports of failure of the UHMWPE implants. In some cases, the implant underwent failure *in vivo* either by fracturing and/or causing dislocation of the prosthetic joint (Wright Medical Technology, 1995). In fact, degradation of the UHMWPE implant is one of the primary factors causing the need for replacement surgeries to be performed (corrosion fatigue of the metal alloy is the other major factor) (Bioengineering Laboratory II Lab Manual, 1997). However, since UHMWPE showed resistance to failure to those types of failure *in vitro*, changes in the mechanical properties of the implant must have occurred either *in vivo* or during the sterilization process that takes place before implantation.

HISTORICAL PERSPECTIVE OF STERILIZATION

Prior to 1950, the sterilization of medical instruments and devices was largely the responsibility of the physician's office or the hospital's central supply department. Medical devices were primarily made of metal (scalpels, forceps, etc.) and were not adversely affected by the universal dry heat, steam (autoclave), or chemical sterilizing solutions. However, individual sterilization practices varied from place to place, and some treatments were not as effective as others. The term "nosocomial infection" was coined to describe patient infections caused by instruments that had not successfully been sterilized. In order to eradicate these infections, a new industry was developed—the disposable medical device industry. Nosocomial infections decreased significantly once this industry became regulated and sterilization processes became standardized. The new disposable products were created from a class of newly developed low cost plastics—polyethylene and UHMWPE. They were produced and packaged to maintain their sterile properties up to the time of use (SteriGenics International).

The disposable plastic devices, such as syringes, blood transfusion kits, and hospital gowns could not be subjected to the traditional sterilization methods of dry heat or steam (autoclave) because they would melt. UHMWPE has a relatively low melting point because, as a hydrocarbon, it has only the weak induced dipole-induced dipole attraction comprising its intermolecular forces (Callister, 1997). New methods of low temperature sterilization had to be developed in order to allow the use of these devices in a sterile environment.

STERILIZATION METHODS

AUTOCLAVE

Autoclaves are vessels, usually made of metal, that are able to withstand very high temperatures and pressures. Instruments are sterilized by being placed in water in an autoclave and heating the water above its boiling point under pressure. Autoclave is the sterilization method used in most hospitals and other institutions that require the removal of microbial organisms from instruments. Autoclave is ideal for metal instruments. However, many of the polyethylene were unable to withstand the high temperature and pressure conditions.

ETHYLENE OXIDE

Initially, ethylene oxide (EtO) was the low temperature sterilization method of choice. Gas chambers of various sizes were designed for use by physicians' offices, hospitals, and device manufacturers. While their capacities were limited, additional chambers could be added as the need arose. The cost of the EtO gas was low, and its effectiveness as a sterilant was better than autoclave sterilization. It appeared to be a viable solution to the problem of low temperature sterilization.

As the use of EtO grew through the industry, its characteristics became better known and defined. Its use as a sterilant was limited.

1. EtO is only useful as a surface sterilant. It is unable to reach blocked-off surfaces, such as those found in hypodermic plunger/barrel interfaces in hypodermic needles.
2. EtO requires careful and simultaneous control of six variable but interdependent parameters: gas concentration, vacuum, pressure, temperature, relative humidity, and time of exposure.

These considerations become secondary when discussing the potential effect of EtO on workers and patients. Initially, it was thought that EtO was so volatile that it was incapable of leaving a residue on treated products. However, it was discovered that EtO reacts with moisture and chloride ions to form ethylene glycol and 2-cholorethanol, a non-volatile toxic residue. Beginning in 1968, studies performed with both human and animal subjects verified EtO's potential to be toxic, carcinogenic, and mutagenic (SteriGenics). For these reasons, EtO is now used on radiation sensitive materials, such as custom procedure kits containing unit dose drugs contained hermetically sealed packages.

GAMMA RADIATION

Gamma rays, high energy, neutrally charged electromagnetic waves, are emitted from a Cobalt 60 or Cesium 137 source encapsulated by a double layer of stainless steel to prevent the escape of radioactivity to the environment. The devices to be sterilized are placed near the emitting source until they have been exposed to the required amount of radiation. No radiation is "absorbed" by the devices (that is, they are not radioactive after sterilization), so they can be used immediately after sterilization.

The use and knowledge of gamma radiation has grown throughout the medical device industry. There is great confidence in its effectiveness as a sterilant and its many advantages:

1. Gamma radiation is a penetrating sterilant. No area of the device or container is left with uncertain sterility. This includes prefilled containers.
2. There is no need for specialized packaging. Since there is no requirement for pressure or vacuum, seals are not stressed.

3. Gamma radiation is highly reliable due to its single variable to control—exposure time.
4. Gamma processing has demonstrated lower overall costs. Both large and small product volumes can be accommodated in a cost-effective manner.

Gamma radiation sterilization is not without its drawbacks. Recently, tests have shown that the gamma radiation provides an environment conducive to the oxidation of the UHMWPE (Wright Medical Technology, 1995 and Naidu et al., 1997). Many researchers have concluded that this oxidation process explains the diminished wear properties of the UHMWPE in the human body by changing the percent crystallinity of the UHMWPE (Naidu et al., 1997).

UHMWPE is comprised of three types of structures: crystalline, amorphous, and the interfacial region between the first two structures. It is the percentages of these three types of structures that distinguish the mechanical and chemical properties between the different types of UHMWPE (BE Lab, 1997). Research has shown that the oxidation in the amorphous regions results in the growth of crystalline regions. It is this effect of the oxidation that has brought about the diminished mechanical properties of the UHMWPE (Naidu et al., 1997).

It would seem that best way to reduce the oxidative effect brought about by gamma radiation treatment would be to treat the UHMWPE without the presence of any *strong* oxidizing agents. One possibility is the use of argon or nitrogen gas as a medium for gamma radiation instead of air because they are both gamma inert. Even though gamma radiation makes the UHMWPE more susceptible to oxidation, the stable nature of the argon and molecular nitrogen may counter this deleterious effect of the gamma radiation (Wright Medical Technology, 1995). A further discussion of the possible oxidation mechanism of UHMWPE is key to the understanding of the studies which may determine whether argon gas as a medium for gamma radiation can prevent the oxidation of UHMWPE.

The proposed oxidation mechanism of UHMWPE is through free radicals. Here the gamma energy is responsible for the splitting of a hydrogen-carbon bond from a UHMWPE chain to form the radical. Oxygen then attacks the radical carbon in the chain and forms a single bond with the carbon. Here, two reactions can occur. In one mechanism, one of the oxygen atoms in the diatomic molecule, may become a carbonyl oxygen bonded to the carbon atom adjacent to the former carbon radical atom. At this point, the carbonyl carbon will have had lost two hydrogen atoms. The other oxygen atom remains attached to the former carbon radical and, with the addition of hydrogen, forms an alcohol group. Here, the former carbon radical likewise receives a hydrogen atom to form a stable species while the carbon atom on the other side of the carbonyl carbon becomes a radical species. In the other mechanism, the chain breaks apart at the initial radical carbon. Each of the oxygen atoms becomes the carbonyl atom in the aldehyde group of each of the chains. Also, the carbon atom next to the carbonyl carbon on one of the broken chains becomes a radical species. The radical species in both of the mechanisms are susceptible to an attack by an oxygen molecule at its radical carbon, where the attack may result in chain excision. It is this shortening of the UHMWPE chains that changes the its properties (Naidu et al., 1997).

The short chains resulting from the free radical breaking mechanism are better able to align themselves in an orderly structure, thus forming a more crystalline structure. Such separation of UHMWPE chains in the amorphous region leads to the growth of crystalline regions. Because of the low energy associated with the bonds in the crystalline regions, greater energy is needed to overcome these bonds in order to produce a phase change. Hence, the melting point and the heat of fusion of the UHMWPE increases (BE Lab Manual, 1997). Also the bonds in the crystalline regions are more apt to break under a high load instead of stretching. This characteristic of the

crystalline regions is indicative of the increase in the brittleness of the UHMWPE. Because of this increased inclination to failure, the UHMWPE has decreased toughness and the ultimate elongation (Wright Medical Technology, 1996). But is there any way an inert environment can protect UHMWPE from oxidation in its role as a medium during gamma radiation treatment?

The purpose of sterilizing in an inert atmosphere would be to isolate the UHMWPE implant from oxygen. However tests have confirmed that the oxygen diffusion in UHMWPE increases with the dosage of gamma radiation (Naidu et al., 1997). So not only does the radiation drive the free radical oxidation forward but also brings the important oxidizing agent closer to the UHMWPE. Packaging the UHMWPE "airtight" will not prevent contact with oxygen because the oxygen will diffuse through packaging (Wright Medical Technology, 1996). Also, dissolved oxygen in vivo would find its way to the implanted UHMWPE.

Free radicals are not necessarily detrimental to the mechanical properties of UHMWPE. Sun et al. have shown that irradiation in an inert environment followed by time in an elevated temperature will crosslink all of the reactive free radicals in a process called STABILIZATION. Oxidation does not occur in UHMWPE when the component is re-exposed to oxygen or other oxidative agents. It also leads to improvements in wear resistance, creep resistance, and other mechanical properties.

<i>Process</i>	Unaged	23 Day/80 degree C Aging
<i>Low Molecular Weight Fraction, %</i>		
<i>Air-Irradiated</i>	28	47
<i>Stabilized</i>	18	8
<i>Ultimate Tensile Strength</i>		
<i>Unirradiated</i>	7760 ± 190	6710 ± 290
<i>Air-Irradiated</i>	6500 ± 480	3190 ± 273
<i>N₂-Irradiated</i>	6875 ± 470	6000 ± 380
<i>Stabilized</i>	6940 ± 350	6900 ± 340
<i>Hip Simulator Wear Rate, mg./million cycles</i>		
<i>Air-Irradiated</i>	27.8	106.7
<i>Stabilized</i>	16.6	16.1

The materials that compromise most prosthetic devices are limited with respect to their biocompatibility. Several steps are taken to modify them in order to make the devices important applications in medicine. In the case of the UHMWPE, it must be sterilized in order to prevent the introduction of pathogens into the body. In terms of its mechanical properties, UHMWPE can function in vivo very well. However from the gamma sterilization treatment one quality of biocompatibility is compromised for another as the treatment makes the UHMWPE more susceptible to mechanical failure. In this way, UHMWPE is distinctive from most materials that make up prosthetic devices. Here, in order to improve the biocompatibility of this material a safer sterilization technique must be developed with the use of argon gas being but one attempt. So for this instrument of technology the common question of "how can we change things to make them better?" has been replaced with "how can we improve the way we make things better?"

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