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Low-energy electron-beam treatment as alternative for on-site sterilization of highly functionalized medical products – A feasibility study

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ABSTRACT

Over the last decades, the medical device industry has grown significantly. Complex and highly functionalized medical devices and implants are being developed to improve patient treatment and to enhance their health-related quality of life. However, medical devices from this new generation often cannot be sterilized by standard methods such as autoclaving or sterilizing gases, as they are temperature sensitive, containing electronic components like sensors and microchips, or consist of polymers. Gamma irradiation for sterilization of such products is also problematic due to long processing times under highly reactive conditions resulting in material degradation or loss of functionality. Low-energy electron-beam treatment could enable irradiation sterilization of medical surfaces within seconds. This method is very fast in comparison to gamma irradiation because of its high dose rate and therefore degradation processes of polymers can be reduced or even prevented. Additionally, electron penetration depth can be precisely controlled to prevent damage of sensitive components like electronics and semiconductors.

The presented study focuses on two key aspects: 1.) Can new and highly functionalized medical products in future be sterilized using low-energy electron-beam irradiation; and 2.) Is the low-energy electron-beam technology suitable to be set up on-site to speed up sterilization processing or make it available "just-in-time". To address these questions, different test specimens were chosen with complex geometry or electronic functional parts to gather information about the limitations and chances for this new approach. The test specimens were inoculated with clinical relevant test organisms (Pseudomonas aeruginosa) as well as with approved radiation resistant organisms (*Deinococcus radiodurans* and *Bacillus pumilus*) to prove the suitability of low-energy electron-beam treatment for the above-mentioned medical products. The calculation of the D10 value for *B. pumilus* revealed equal efficacy when compared to standard high-energy irradiation sterilization. All of the above-mentioned germs were successfully inactivated by low-energy electron-beam treatment when test specimens were inoculated with a germ load > 10^6 CFU and treated with doses ≥ 10 kGy (for *B. pumilus* and *P. aeruginosa*) and > 300 kGy (for *D. radiodurans*) respectively. As an example, for specialized electronic components to be sterilized, an impedance sensor for cell culture applications was sterilized and unimpaired functionality was demonstrated even after five repeated sterilization cycles to a total dose of 50 kGy. To address the second aspect of on-site suitability of this technology, the product handling for low-energy electron-beam treatment had to be adapted to minimize the size of the electron-beam facility. Therefore, a mini electron-beam source was used and a specialized sample holder and 3D-handling regime were developed to allow reproducible surface treatment for complex product geometries. Inactivation of *B. pumilus* inoculated medical screws (> 10^6 CFU) was successful using the developed handling procedure. In addition, a packaging material (PET12/PE50) for medical products was investigated for its suitability for low-energy irradiation sterilization. Biocompatibility assessment revealed the material to be eligible for this application as even overdoses did not impair the biocompatibility of the material.

With these results, the principal suitability of low-energy electron-beam treatment for sterilization of medical

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products containing electronics like sensors is demonstrated. The low-energy technology and the specialized 3D-handling regime allow the on-site setup of the technology in hospitals, medical practices or any other point of care.

1. Introduction

Health care-associated infections (HAI) are a prominent risk in medical treatment as more than 4 million patients are affected annually already in Europe (Pittet et al., 2005). European surveillance data show 37,000 annual deaths attributable to such infections, 16 million extra days of hospital stay and an economic burden of around €7 billion (WHO). The most common nosocomial infections are surgical site infections and infections of the respiratory and gastrointestinal tracts (Behnke et al., 2013, 2017; Ott et al., 2013). Although the predominant causatives for acquiring HAIs are the spreading of endogenous germs or transmission from hospital staff, medical devices are also one potential source of HAIs. Especially re-usable medical devices that have been in contact with patients, staff and the environment are of concern. To prevent any transmission of infection, thorough cleaning, disinfection and sterilization processes are performed before use with the next patient. These are tightly controlled processes especially in hospital sterilization facilities. However, it has been reported that efforts to reduce costs have led many health systems to start re-using medical devices after reprocessing, even if they are intended single use devices (Shuman and Chenoweth, 2012). The FDA has stated that the risk of acquiring infections from inadequately reprocessed medical devices is relatively low but remains an important public health concern. The US FDA pointed out that the causative association is often not recognized or reported and the prevalence of HAIs due to inadequate reprocessed devices therefore unknown. In 2015, the FDA alerted healthcare providers and facilities about the need to more closely monitor procedures for cleaning, disinfecting and sterilization due to non-compliance posing a critical gap in patient safety (Centers for Disease Control and Prevention, 2015; FDA U.S. Food and Drug Administration). This demonstrates that there remains a large unmet medical need for improved infection control. As re-use has become common practice, presumably more often in outpatient facilities, and is likely to occur with costly high-tech medical devices that cannot be sterilized by standard methods, an easy to use but safe and efficient sterilization applicable for use on-site for such medical devices might be suitable to cover this gap (Wallace, 2016).

There are a number of approved sterilization methods for medical devices. These methods can be divided into three main groups: physical sterilization (e.g. autoclaving), chemical sterilization (e.g. ethylene oxide, chlorine dioxide) and radiation sterilization (e.g. gamma irradiation, high-energy electron-beam irradiation) (Wallhäussers Praxis der Sterilization, 2008; Wilson and Nayak, 2016). However, many of these methods are limited in their applicability, especially for sophisticated medical devices (Huff et al., 2003; Rutala and Weber, 2013; Linke, 2017). For example, thermo-labile medical devices, such as those containing electronic components are extremely sensitive to hot steam and therefore cannot be sterilized by autoclave. Polymeric materials or electronics are thermo-labile and can react with the highly reactive gases present during chemical sterilization. Also, the applied vacuum during these processes poses a risk for the product functionality especially when batteries are embedded (Linke, 2011). This leads to reduced lifetime and/or performance of the sterilized product, thereby posing a risk to the patient. The lack of more suitable sterilization methods and though it is a known carcinogenic agent, ethylene oxide gas sterilization is currently the preferred method for sterilization of temperature-sensitive products like polymers. Some of the associated negative effects of ethylene oxide sterilization are avoidable by using irradiation-based methods like gamma irradiation for sterilization. Nevertheless, this method is associated with long processing times under very reactive conditions, which can induce degradation processes in radiation sensitive polymers and lead to loss of function for electronic components (Linke, 2011). This study demonstrates the low-energy electron-beam treatment is a suitable alternative overcoming all of these drawbacks and giving new and highly functionalized medical products (e.g. so called “intelligent implants”) the possibility to be used within humans as they can be safely sterilized. The low-energy electron-beam technology works with high dose rates and is therefore a very fast process (treatment within some seconds) when compared to traditional autoclaving or gamma irradiation. Another drawback of the commonly used high-energy irradiation based sterilization technology is the emittance of high-energy-X-rays (Wallhäussers Praxis der Sterilization, 2008; Schiller et al., 1995), which leads to complex shielding requirements to protect the environment and staff from radiation. This results in the setup of such facilities in centralized sterilization service units; “small-scale” units for on-site use in health care facilities are typically not available. Outsourced reprocessing of medical devices can be linked with risks due to long process chains, requires stock-keeping of medical products and is time consuming (Hospital Epidemiology and Infection Control, 2012). A big goal in medical device reprocessing is a fast and controllable process chain (Beroule et al., 2016; Dehnavieh et al., 2016). An on-site available sterilization process, that is especially suitable for thermo-labile medical products and highly functionalized ones (e.g. with integrated electronics) could find remedy for these problems (Wallace, 2016).

Using the electron-beam technology that works with low-energy, an on-site setup of a sterilization facility is feasible. Therefore, an assessment was made to investigate if by adaption of the product handling, the low-energy technology can be integrated in a small sterilization unit suitable for set up directly in hospitals, medical practices or care facilities to provide fast and easy on-site sterilization of sophisticated medical devices and products. This demonstrated that for specialized and highly sensitive medical products low-energy electron-beam irradiation is a potential alternative to existing sterilization technologies, which are not applicable for such products. Nevertheless, product specific process validation will be a necessary next step towards practical use of the investigated technology.

A small on-site sterilization unit will have limited space for shielding provisions; for this reason, the focus of the presented research was on low-energy irradiation (acceleration voltages below 300 keV). Within these small-scale dimensions, surface sterilization of medical devices is possible only with a complex 3D-handling process to ensure reliable and complete surface treatment of the products. Accordingly, such an on-site sterilization unit would need to be composed of a miniaturized electron-beam source, a specialized product holder with an adapted handling procedure for free movement of complex objects under the electron-beam, and an easy to handle, radiation resistant packaging. For these reasons, this investigation focused also on suitable packaging materials and solutions for the handling of complex 3D geometries. Although a surgical screw made by stainless steel can traditionally be sterilized by autoclaving, it was used as a test specimen because of its complex geometry. The focus was on the reproducible inactivation of bacterial contaminations applied on the complex geometry of the screw thread. For comparability with conventional radiation based sterilization methods like gamma, the sterilization efficacy and the D_{10} value of known radiation resistant bioindicator spores of *B. pumilus* were determined using low-energy electron-beam irradiation. To exclude any effects caused by geometry or roughness, planar standard surfaces (stainless steel spatulas) were used to address this issue.