Towards Efficient Low-Temperature Ozone Gas Sterilization of Medical Devices

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1 Purpose

Sterilization is a process intended to render medical devices free of viable micro-organisms thus reducing the risk of patient exposure to pathogens.

SteriLux has patented and developed an ozone-based sterilization device (Figure 1). The process relies on the use of 172 nm V- UV lamps to transform oxygen (O_2) from ambient air into ozone (O_3). Ozone further reacts with water (H_2O) to form hydroxyl radicals which are responsible for the inactivation of micro-organisms. At the end of the sterilization process, a 254 nm V-UV lamp transforms the remaining ozone back into oxygen.

Figure 1: The device and the sterilization containers developed.

The aim of the study was to characterize and validate a new ozone-based low-temperature sterilization process requiring minimal amounts of water and low power consumption for terminal sterilization of metal and heat-sensitive medical devices (MDs).

2 Methods and Materials

Tests were performed in accordance with ISO 11138-7:2019 and ISO 14937:2009. The ozone concentration was measured throughout the process with a non-invasive optical measurement system based on the Beer-Lambert Law. The overkill method was used to prove 12 log reduction (LR) of the most resistant microorganism, *G. stearothermophilus* spores [1, 2, 3, 4]. Both Survivor Curve Method (SCM) & Fraction Negative Method (FNM) tests were performed.

Series of tests were performed at different temperatures (15, 20 and 30°C) and constant ozone concentration (550 ppm). A first series of tests was performed with a validation load consisting in 7.5 kg of stainless steel MDs placed in a stainless steel sterilization basket. Afterwards, another series of tests was done with a validation load consisting in various heat-sensitive MDs wrapped in Tyvek®-plastic sterilization pouches. This second series of tests was done to verify that no alterations of the chemical and physical properties of the polymers nor generation of any toxic by-products would be observed.

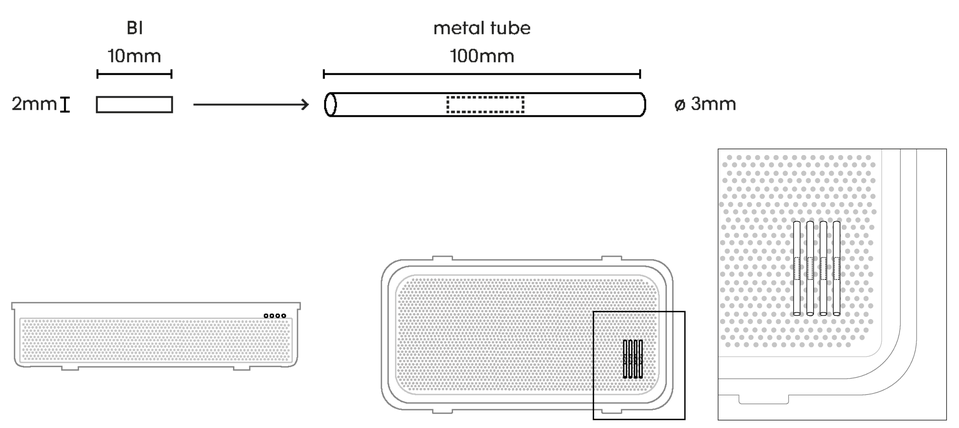
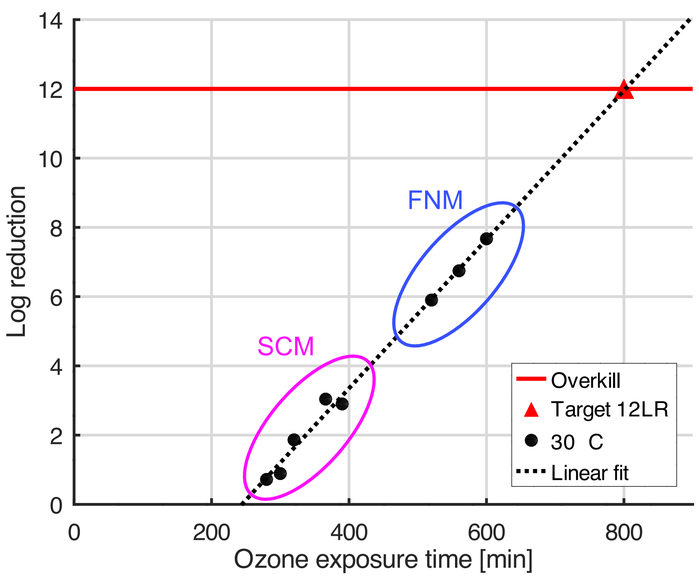


Figure 2: Scheme of the PCD and the most difficult site to sterilize in the container (top corner)

For the first validation load, BIs inoculated with at least 10^6 spores/carrier were placed in the middle of PCDs, consisting in 10 cm-long metal tubes of 3 mm internal diameter, at the most difficult site to sterilize (Figure 2).

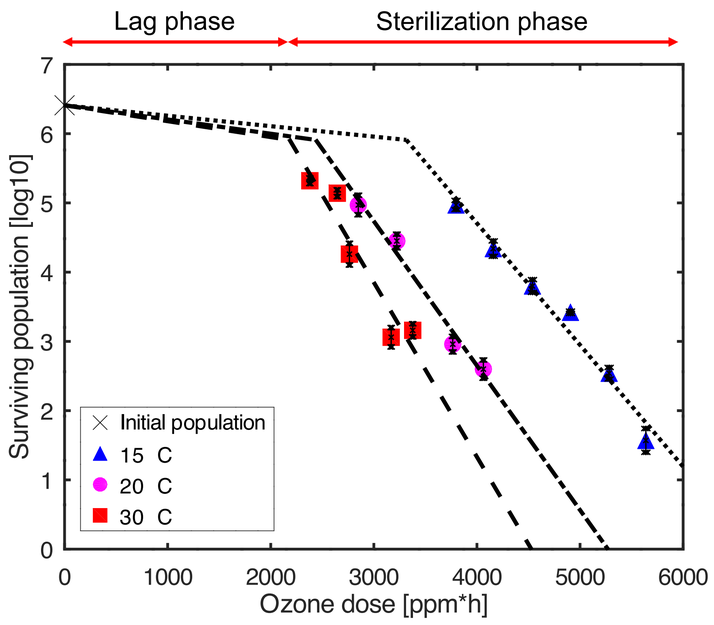
For the second validation load, the same BIs were placed at the most difficult site to sterilize of each MDs wrapped in sterilization pouches.

3 Results



A medical device can be categorized sterile, according to the European Standard EN 556, if a minimum sterility assurance level (SAL) of 10^{-6} CFU/part is reached. The overkill method consists in starting at an initial population of at least 10^6 spores/BI and proving a 12 log reduction (LR) to reach a SAL of 10^{-6}.

With the SCM, the BIs were evaluated by performing enumerations of each exposed BIs, showing 0.5 - 4 LR. With the FNM, the final stages of microbial inactivation were captured (6 - 8 LR). The coefficient of determination (R^2) of the linear fit of both SCM and FNM results is equal to 0.9924 (>0.8) thus allowing extrapolation of the results to 12 LR.



Other series of SCM tests were done in order to determine the influence of the temperature on the process. The ozone dose was plotted in respect to the surviving population (initial population N_0 = $2x10^6$ spores/carrier). The R^2 values were 0.975, 0.981 and 0.901 for the 15°C, 20°C and 30°C curves, respectively. Each data point and its error bar represents the mean of 4 replicates used per test.

A latency between the beginning of the sterilization process and the decrease of bacteria was observed[5, 6], here defined as the lag phase. This phase corresponds to the time it takes to reach humidity saturation in the container.

Polymeric material	Ozone compatibility
PTFE, POM, PEEK, PMMA, PC, PE, PP, PA, PVDF	✓
Nitrile, Natural rubber	✗

Preliminary tests showed no alterations of the chemical and physical properties of many polymers nor generation of any toxic by-products.

4 Conclusions

The results demonstrated the feasibility to sterilize both metal and heat-sensitive medical devices with ozone at ambient temperatures. The developed low-temperature ozone-based sterilization process is a safe, cost-effective and eco-friendly alternative to existing sterilization methods . This new technology can and will ensure that hospitals, health care providers and patients have access to medical devices that are safely and effectively sterilized.

The tests showed that low concentrations of ozone used in the process ensure good compatibility with a large cross-section of materials used to manufacture or fabricate medical devices as well as packaging materials of sterile barrier systems. This ozone-based sterilization process does not generate any toxic by-products and leaves no toxic residues on MDs.

The next steps in the development of the process will be to finalize the compatibility testing with a large cross-section of medical grade materials and to optimize the sterilization cycle by improving the cycle duration and controlling each parameter critical to the effectiveness of the sterilization process. For example, reducing the time it takes to reach humidity saturation in the container would lead to a shorter lag phase and a faster sterilization cycle. Efforts will be put into such considerations and developments.

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