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Safety and Efficacy of Hydrogen Peroxide Plasma Sterilization for Repeated Use of Electrophysiology Catheters

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Objectives. **The purpose of this study was to evaluate a new technique for sterilizing nonlumen electrophysiology catheters that uses hydrogen peroxide gas plasma.**

Background. **The reuse of electrophysiology catheters may potentially result in a significant cost savings. While ethylene oxide sterilization appears to be safe and effective from a clinical standpoint, toxic ethylene oxide residuals, which exceed Food and Drug Administration standards, have been reported.**

Methods. **Ten nonlumen electrophysiology catheters were extensively evaluated. Each catheter was used five times and resterilized after each use with hydrogen peroxide gas plasma. Tests for sterility, mechanical and electrical integrity, chemical residuals and standard and electron microscopic inspection were performed.**

Results. **Loss of electrical integrity or mechanical integrity was not observed in any catheter. No evidence of microbial contamination was found. Surface integrity was preserved except for one ablation catheter that exhibited fraying of the insulation at the insulation-electrode interface. Surface inspection using standard magnification and electron microscopy revealed no significant change in surface characteristics associated with the sterilization process. Hydrogen peroxide was the only chemical residual noted, with an average concentration of 0.22% by weight, which is within accepted American Association for the Advancement of Medical Instrumentation limits. The cost for a standard electrophysiology catheter ranges from $200 to $800, and one sterilization cycle costs $10. If electrophysiology catheters are used five times, resterilization could potentially result in a savings of $2,000 per catheter, or $9,000 for five ablation procedures.**

Conclusions. **Hydrogen peroxide gas plasma sterilization may provide a cost-effective means of sterilizing nonlumen electrophysiology catheters without the problem of potentially harmful chemical residuals. However, careful visual inspection of catheters, particularly at the insulation–electrode interface, is required if catheter reuse is performed.**

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Radiofrequency catheter ablation has emerged as an important and therapeutic option for patients suffering from a variety of arrhythmias (1–5). While extremely effective, radiofrequency catheter ablation is an invasive procedure that costs $5,000 to $16,000 (6–8). A significant portion of the cost of an ablation procedure is the cost of the multielectrode diagnostic and ablation electrophysiology catheters. Several studies have addressed the issue of repeated use of electrophysiology catheters using ethylene oxide gas as the sterilizing agent (9–11). While catheter reuse appears to be safe and effective from a clinical standpoint and can lead to a significant cost savings, the quantity of ethylene oxide residuals after sterilization exceeds Food and Drug Administration (FDA) standards (11). In addition, the potentially toxic levels of ethylene oxide remained even after 48 h of aeration (11).

A recently introduced sterilization technique that uses hydrogen peroxide gas plasma as the sterilizing agent has been approved by the FDA. We prospectively evaluated the safety and efficacy of hydrogen peroxide plasma sterilization for nonlumen electrophysiology catheters.

Methods

Materials. Ten electrophysiology catheters, five quadripolar diagnostic catheters (Daig, St. Jude Co., Minnesota) and five deflectable thermistor-tipped ablation catheters (EPT, Sunnyvale, California) were used five times each and sterilized after each use with hydrogen peroxide plasma sterilization. In addition to the 10 catheters used in actual electrophysiology studies, three additional ablation catheters were sterilized a total of 20 times with aggressive manipulation of each catheter between cycles to simulate clinical use.

Sterilization procedure. Each catheter was washed and cleaned of debris with soap and warm tap water for 5 min, rinsed under running tap water and dried with a towel. The catheter was then placed in a commercially available steriliza-

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tion pouch (Baxter Inc., Inglewood, California) in preparation for the hydrogen peroxide gas plasma sterilization procedure (STERRAD System, Advanced Sterilization Products, Irvine California).

Hydrogen peroxide plasma sterilization uses low temperature, low moisture and gas plasma. Gas plasma is defined as a fourth state of matter consisting of clouds of ions, neutrons and electrons created by the application of an electric or magnetic field. The sterilization procedure is divided into two phases: a diffusion phase and a plasma phase. The diffusion phase allows the hydrogen peroxide to come into close proximity with the items to be sterilized. The plasma phase of the cycle creates free radicals, such as hydroperoxyl and hydroxyl radicals, that are known to be reactive with almost all of the molecules essential for normal metabolism of living cells.

The sterilization procedure begins by placing the object to be sterilized in a vacuum chamber into which hydrogen peroxide, at a minimum concentration of 6 mg/L, is injected and vaporized. The hydrogen peroxide gas is then allowed to diffuse throughout the sterilizer load for 50 min. Radiofrequency energy of 400 watts is then applied to create hydrogen peroxide gas plasma. Hydrogen peroxide plasma is then broken apart into reactive species that collide with and kill microorganisms. At the end of the plasma phase, the reactive species lose their high energy and recombine to form oxygen, water and other nontoxic byproducts. The plasma is maintained for a long enough period to ensure complete sterilization, with a standard plasma phase lasting 15 min. The total sterilization procedure takes approximately 1 h.

Analysis of sterilization effects. Mechanical integrity evaluation consisted of examining each catheter for torque capability by confirming one-to-one torque with manipulation. The positive and negative curve of deflectable tip ablation catheters was also measured. Electrical integrity was evaluated by measuring resistance and signal quality for each use. Visual and microscopic inspection of each catheter was performed by looking for gross visual defects and for changes in surface characteristics by both light microscopy (30× and 150× magnification) and scanning electron microscopy (750× magnification).

Sterility testing included evaluation of the sterilization technique against resistant bacterial and viral organisms, as well as assessing sterility of the catheters used in this study. Bacterial testing consisted of Sterility Assurance Level (SAL) testing and Association of Official Analytical Chemists (AOAC) sporicidal testing. The SAL testing was performed by first selecting bacteria that are highly resistant to the sterilization technique and then measuring the amount of sterilization time and/or sterilant required to sterilize a large number (10^6) of the resistant organism to less than 10^{-6}. Sterilization is a probability function, and a SAL value of 10^{-6} means that the probability of an organism surviving after sterilization is less than 10^{-6}. Organism number was measured using two accepted Association for the Advancement of Medical Instrumentation (AAMI) standards: survivor-curve analysis and fraction negative analysis. The AOAC sporicidal testing was performed by attempting to sterilize a large number of carriers contaminated with high numbers of both aerobic and anaerobic bacterial spores. The tips and connector ends of the catheters used in this study were plated on agar plates and incubated at 37° for 5 days to measure for growth of any organisms.

Viral testing included evaluating the sterilization technique against both hydrophilic (polio) and lipophilic (herpes) viruses. Viral loads of at least 3 Log 10 were subjected to an abbreviated sterilization cycle of 30 min, and infectivity was measured. In addition, specific testing was performed against human immunodeficiency virus (HIV). Four petri dishes containing a total of 6.5 Log 10 HIV-1 virus suspended in cell culture media was sterilized for a 25-min (half normal) cycle and residual HIV-1 activity was measured.

For the evaluation of chemical residuals immediately after the sterilization procedure, catheters were placed in deionized water and extraction of chemical residuals was allowed for 4 h. The type and amount of chemical residuals in the extract were then measured using gas chromatography.

Cost analysis. Actual costs for each catheter were obtained and are expressed in terms of 1996 dollars. The cost for the sterilization procedure was estimated by adding the per procedure cost of the sterilization system (by calculating the initial cost of the sterilization system, depreciation on capital equipment and the percentage of use for electrophysiology catheters) and the cost of chemicals necessary for each sterilization cycle. Cost of the sterilization procedure is also expressed in 1996 dollars. At our institution, three quadripolar diagnostic catheters, one decapolar catheter and one quadripolar ablation catheter are typically used for each ablation procedure.

Statistical analysis. Change in radii for the deflectable catheters and resistance values were analyzed using repeated measures and analysis of variance (ANOVA).

Results

Mechanical and electrical integrity. Catheter torque capability remained one to one after 5 uses in all 10 catheters and in the 3 additional ablation catheters sterilized 20 times. The total change in both positive and negative tip deflection of the ablation catheters was less than 2 mm (positive direction: 1.9 ± 0.2 mm; negative direction: 1.6 ± 0.3 mm). Once maximally deflected, all catheters exhibited stable curvature retention. Electrical integrity of all catheters was also maintained with no significant change in resistance or loss of signal quality noted with up to 20 sterilization cycles.

Visual inspection. One ablation catheter in the study exhibited insulation fraying at the insulation–electrode interface after the fifth use (Fig. 1). Insulation fraying was only detected when 30× magnification or greater was used. In addition, glue separation on the electrode surface was observed in this catheter. No other examples of glue separation were identified by microscopy in the other ablation catheters. No loss of surface integrity was observed in any of the diagnostic catheters. Both light microscopy and scanning electron microscopy

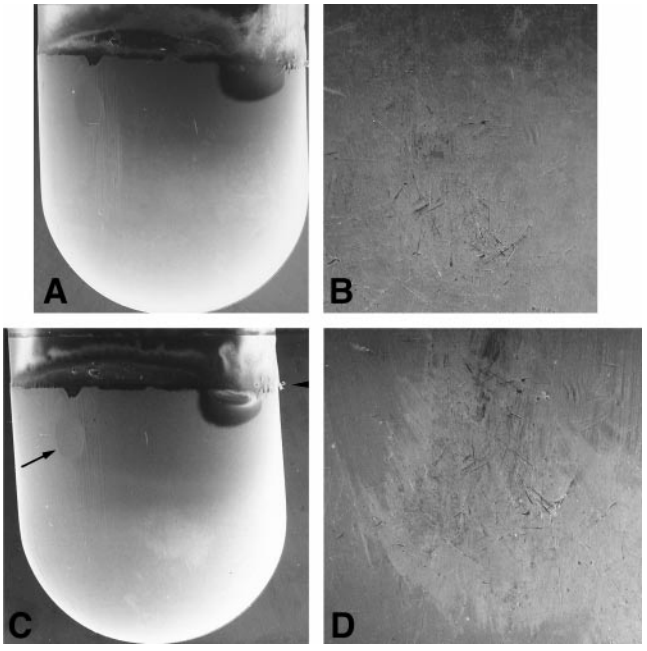

Figure 1. Electrophysiology catheter tip before (**A** and **B**) and after (**C** and **D**) sterilization at 30× (top row) and 150× (bottom row) magnification. The slight decrease in the degree of black residue that can be observed after sterilization on electron microscopy is thought to be a cleansing effect. Fraying of the catheter insulation can be observed in the upper right of the 30× photographs (**arrowhead**). The oval defect in the upper left portion of the electrode is loss of surface glue (**arrow**).

revealed no significant changes in surface characteristics associated with the sterilization process (Fig. 1). The slight decrease in the degree of black residue that can be observed after sterilization on electron microscopy is thought to be a cleansing effect.

Sterility. The bacterial organism most resistant to the sterilization technique was *Bacillus stearothermophilus* ATCC 7953 (Fig. 2). The organism was then used in SAL testing and was effectively sterilized to a level of $<10^{-6}$ with 30 min of diffusion time using both survivor curve and fraction negative analysis (Fig. 3). Both methods of analysis provided similar values. With AOAC sporicidal testing, no failures to achieve complete sterilization were observed. Finally, no growth was noted from any catheter tip or connector after 5 days of incubation.

Viral testing demonstrated no remaining infectivity with either the lipophilic herpes or hydrophilic polio virus after a 20-min diffusion cycle of sterilization. HIV-1 was completely inactivated with half cycle sterilization of 25 min.

Chemical residuals. The only chemical residual found immediately after sterilization was hydrogen peroxide at a concentration of 0.22%. If the catheters were left at room air, the rate of aeration of the residual was rapid at a few minutes. If the catheters were left in the sterilization bags, a common practice, a 65% aeration of hydrogen peroxide residual was recorded in 24 h.

Cost. The average cost of an electrophysiology catheter was $200 to $800 (average $500). The average cost of one hydrogen peroxide sterilization cycle was approximately $10. The reuse of each catheter five times would lead to a cost savings of $2,000 per catheter. With three to five catheters used for the average ablation procedure, a cost savings of $6,000 to $10,000 could be realized for every five ablation procedures performed.

Discussion

The results of this study suggest that hydrogen peroxide plasma sterilization can provide a safe and cost-effective means of reusing electrophysiology catheters. This is the first study to include extensive testing of a catheter sterilization technique against resistant bacterial and viral contaminants. Specific organisms that are highly resistant to the sterilization procedure were chosen for bacterial testing. Viral testing included

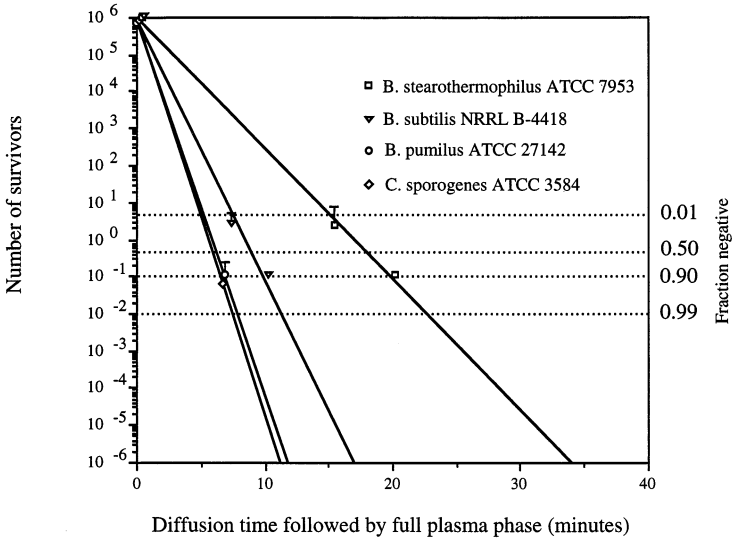

Figure 2. Amount of sterilization time required to achieve organism levels of $<10^{-6}$ for several common, highly resistant bacterial spores (*B. stearothermophilus*, *B. subtilis*, *B. pumilus* and *C. sporogenes*). The fraction of negative samples is plotted to the right. *B. stearothermophilus* spores were the most resistant of the tested spores.

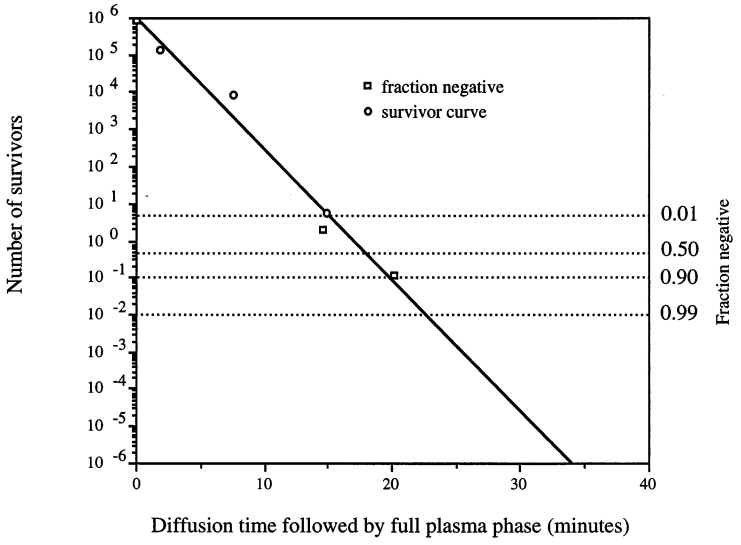

Figure 3. Amount of sterilization time required to achieve *B. stearothermophilus* spore levels of $<10^{-6}$ using both survivor curve analysis and fraction negative analysis. The results yielded a similar linear regression relationship.

common viruses as well as testing against HIV. While testing against hepatitis B virus was not part of this study, other investigators have reported that hydrogen peroxide plasma sterilization is effective against hepatitis B virus (12).

Previous studies. The significant cost of electrophysiology catheters has led to widespread interest in the reuse and sterilization of these devices. Dunnigan et al (9) compared the cost of single use of electrophysiology catheters with catheter reuse. Catheters were reused an average of eight times each. The billing cost for a reused catheter was $30 versus $635 for a new catheter, leading to an estimated cost savings of $257,395 over a 5-year period. Similarly, Avitall et al. (10) reported a significant cost savings of $129,024 over 336 ablation procedures when catheters were reused an average of five times.

The safety of reusing electrophysiology catheters after sterilization with ethylene oxide has also been the subject of several studies. Dunnigan et al. (9) retrospectively analyzed catheter reuse over a 5-year period at their institution. No complications directly attributed to catheter reuse were observed and adequate sterility was maintained. In a prospective study, Avitall et al. (10) evaluated 69 ablation catheters used in 336 ablation procedures over a 1-year period. With an average of five uses, no major catheter failures or adverse clinical events were observed. More recently, Aton et al. (11) randomly examined 12 catheters with extensive electrical, chemical and microbiological testing. While no electrical or microbiological problems were identified, elevated concentrations of ethylene oxide, ethylene chlorohydrin and ethylene glycol which exceeded FDA standards were detected; excessive chemical residuals were still detected even after extended periods of aeration (48 h). On the basis of this finding, the authors recommended that electrophysiologic catheters should only be used once.

Cost analysis. The potential cost savings with catheter reuse in this study is similar to that found in the previous studies. The average cumulative cost of an ablation procedure is $7,000 to $10,000 (8). Material costs account for 25 to 30% of the total expenditure, with catheters accounting for a majority of that cost. Reuse of each diagnostic and ablation catheter five times could potentially lead to a significant cost savings.

Chemical residuals. Although catheter reuse can lead to significant cost savings, the potential hazard of chemical residuals has led to concern regarding the safety of this practice with standard ethylene oxide sterilization (11). In the current study, low concentrations of hydrogen peroxide residuals (0.22%) were detected after the sterilization procedure. The AAMI lists hydrogen peroxide residuals as nontoxic and negligible (13). For comparison, hydrogen peroxide used as a topical antiseptic is a 3% solution; despite the common use of topical hydrogen peroxide as a disinfectant, there is no epidemiologic evidence to suggest that hydrogen peroxide has significant harmful effects.

Catheter integrity. The mechanical and electrical integrity of nonlumen electrophysiology catheters was preserved after 5 uses and after as many as 20 sterilization cycles. In this study, surface integrity was maintained in all but one catheter. Insulation fraying at the insulation–electrode interface and glue separation were observed in one ablation catheter after the fifth use, but no other evidence of glue separation could be identified in the other ablation catheters. These findings are similar to a previous study that evaluated reuse of ablation catheters with ethylene oxide sterilization; the investigators observed tip electrode glue separation in 25% of ablation catheters after an average of four uses (10). While no adverse clinical outcomes were associated with glue separation, weakening of catheter integrity could not be ruled out; the investigators speculated that electrode temperatures >100° during the ablation procedure were responsible for glue separation (10). In our single example of glue separation, the average ablation temperature was 50 to 60°, which suggests that glue

separation can occur with temperatures that are commonly used during ablation procedures. As previously reported, application of radiofrequency energy was associated with shallow pitting in the tip electrode (Fig. 1) (10). We were unable to identify any mechanical or electrical integrity or sterility problems associated with pitting.

No diagnostic catheters exhibited any problems associated with repeated use. It may be that costly specialized multielectrode diagnostic catheters are most appropriate for repeated use since glue separation and shallow pitting are probably due to the transmission of radiofrequency energy through the electrode surface. Hydrogen peroxide plasma sterilization may be particularly suitable for sterilizing heat- and moisture-sensitive materials, such as electrophysiology catheters, since a low-temperature and low-moisture environment is used.

Limitations. First, while hydrogen peroxide plasma sterilization appears to be a promising technique that could be applied to electrophysiology catheters, this study was not designed to examine clinical end points. Larger studies that address clinical outcomes will be necessary to evaluate the complete safety of this technique. Second, although sterility testing was performed against many common bacterial and viral organisms, many less common organisms that may cause infections were not specifically tested. Unusual organisms, such as fungi, may be resistant to hydrogen peroxide plasma sterilization. Finally, selected catheters from a limited number of manufacturers were evaluated in this study. It is possible that the effectiveness and safety of hydrogen peroxide plasma sterilization may differ among catheters from different manufacturers, and that mechanical stability may also differ among manufacturers.

Clinical implications. The practice of catheter resterilization can potentially result in significant cost savings. The results of this study suggest that hydrogen peroxide plasma sterilization may provide an alternative to ethylene oxide gas sterilization that is equal in efficacy but free of the potential hazards of toxic chemical residuals. In particular, specialized multielectrode diagnostic catheters may be most appropriate for catheter reuse. However, if catheter reuse is considered, careful inspection of all catheters, particularly at the insulation–electrode interface, is required.

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