Bactericidal Drain Tube Attachment for the Prevention of Surgical Site Infections Following Fluid Drainage

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Abstract:

Surgical site infections develop in 12-26% of mastectomy patients who undergo reconstruction with a tissue expander. In an effort to reduce these complications, a surgical drain tube attachment device is described that will curb the aforementioned infection rates. The device consists of a protective platinum-cured silicone cap covering a pair of polyurethane bactericidal sponges. The cap includes two sites for the surgeon to suture the device directly to the skin. The inner sponge in the pair of concentric rings is impregnated with chlorhexidine gluconate (3%), while the outer ring employs silver sulfadiazine (1%), both clinically safe antimicrobial agents. The sponges were tested under a controlled environment over a period of 14 days, and the combined microcidal agents were proven efficacious at inhibiting growth of the four most prevalent surgical site infection microbes: Methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis, and Streptococcus pyrogenes* and *Pseudomonas aeruginosa* for a full 14 day period. The device is not limited to exclusively mastectomies, but can be extended to include any operation involving prolonged use of a drain tube.

Keywords: Mastectomy, Drain Tube, Antimicrobial, Surgical sight infections

Introduction

Surgical site infections (SSI's) represent a significant portion of healthcare associated infections, with 1 - 3 % of all surgeries developing an SSI, totaling between 500,000 and 750,000 per year[1]. Mastectomies, in particular, have a disproportionately high rate of SSI's. Mastectomies are surgical procedures that involve the removal of one or both breasts usually as a treatment for breast cancer. Breast cancer incidence rates are approaching 300,000 cases per year in the United States[2] with Mastectomies being performed on about 38% of those patients[3] equating to around 114,000 mastectomies/year. In addition to this number, an increasing number of patients are undergoing prophylactic mastectomy due to significant family history or the presence of a genetic mutation increasing their personal risk of breast cancer.

Many mastectomy patients undergo breast reconstruction procedures, the most common of which includes placement of a tissue expander at the mastectomy site, which eventually is replaced with a permanent breast implant. Due to the relatively destructive nature of the procedure, excess blood and fluid build up at the surgical site, necessitating the need for post-operative drainage. Between 12 and 26 % of mastectomy patients who undergo reconstruction with tissue expanders develop an infection during the period of drain tube usage, which can last up to two weeks[4]. Additionally, 5% require tissue expander removal due to the severity of the infection. This significantly delays reconstruction. Mayo Clinic conducted a study on infections after breast surgery from 2003 – 2006 and found an overall SSI rates as high as 26%. Furthermore, 24% of patients required both pre- and post-operative antibiotics. Use of prophylactic antibiotics, however, has not shown a reduction in SSI rate after breast surgery[5]. One study has shown mean attributable costs for SSI's of $25,546[6]. Assuming 26% of the 114,000 mastectomy patients will develop an SSI, approximately $757 million will be spent annually to treat mastectomy-related SSI's alone. SSI in breast cancer procedures (among others) increases health care costs, recovery time, and the possibility of additional treatments.

The drainage process involves the use of a surgical drain tube. This device is inserted at the end of the surgery and is pulled through a 5 mm incision. After the drain has been situated, the surgeon places a suture from the nearby skin to the drain tube; this is conventionally utilized to prevent the drain from sliding either into or out of the surgical site. Provisionally, a BioPatch® dressing can be placed followed by a semi-occlusive dressing. The BioPatch® is an antimicrobial dressing used more commonly with catheters, and is designed to last a period of 7 days. Because drain tubes are often in place for up to two weeks, it is usually necessary to replace the BioPatch® frequently, which adds additional time, manipulation of the drain, discomfort, and costs. Avoiding the necessity of replacing the device during the draining period would decrease risk of infection. Thus, a device, pictured in figure 1, has been developed specifically for surgical drain tubes in an effort to circumvent the shortcomings of the BioPatch®.

The drain tube attachment device, or CidalSeal™ is a medical device that that has been specifically designed to integrate with commonly available and utilized surgical drain tubes to prevent surgical site infections. It is composed of a silicone outer casing, seen in Figure 2, that covers two antimicrobial foams pictured in Figure 3. One sponge is impregnated with chlorhexidine gluconate (CHG) and the other with silver sulfadiazine (SSD). CHG is a commonly used antiseptic agent. It is used to clean the skin after an injury, before surgery, or before an injection[7].CHG is most often clinically used with a 2-4% solution, by weight

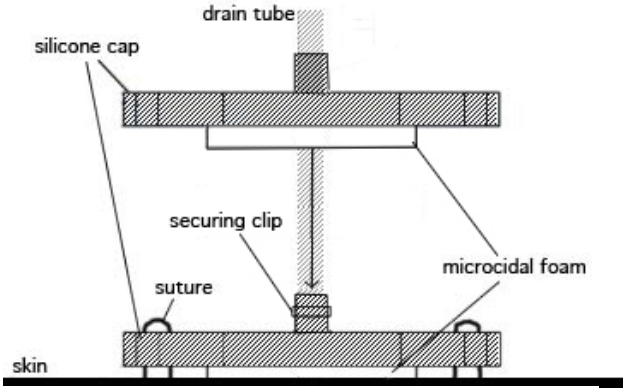


Figure 1: Design of CidalSeal.

The CidalSeal™ utilizes an intermediate value of 3% CHG by weight. CHG works to inhibit a fairly wide array of common skin bacteria seen in SSI, including methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus epidermidis.* CHG, however, has not been shown to work effectively over long periods of time on *Pseudomonas aeruginosa*, which is sometimes encountered with SSI's.

Similarly to CHG, SSD is another clinically used topical medication, most commonly used to treat infections of second- and third-degree burns[8]. This agent is known to kill a wide range of bacteria, including Pseudomonas aeruginosa[10]. The sponge material used to impregnate the SSD was chosen in a similar fashion as the CHG sponge, and is described in the testing section.

Methods

The silicone cap was produced to encase and protect the antimicrobial sponge pieces. Its other main function is to provide suture tabs so that the surgeon may secure the device directly to the skin. The shape of the cap is ovoid, improving the overall mechanical strength and stability. An ABS rapid prototyping machine was used to create molds for the caps. A Platinum Silicone Elastomer was thoroughly mixed in a 10:1 ratio elastomer to curing agent, respectively. It was then poured into the mold, placed in a vacuum for 5 minutes, and let sit in a refrigerator (~35˚F) overnight. It was then set out in room temperature to cure.

Five different open-celled polyurethane foam types were chosen based on their density and porosity. These were sterilized in ethanol, and then soaked in a 3% CHG- water solution for 10 minutes. The impregnated foams were then allowed to dry in a sterile environment. The weight of the foams was taken before and after impregnation to quantify the CHG absorbed by each foam type. The sponge impregnated with CHG was chosen based on its absorptive ability as well as rate of release of antiseptic throughout preliminary tests over a period of 14 days. The six foams tested are shown in Table 1.

Table 1. List of foams tested for release of microcidal agents. Note foams C and D are memory foams, so firmness was important property.

Foam	Density
A	28.8 kg/m^3
B	49.2 kg/m^3
C	92.9 kg/m^3, firmness 4
D	92.9 kg/m^3, firmness 1
E	32.03 kg/m^3
F	23.2 kg/m^3

The CHG impregnated foam with the highest absorptive quality, an open celled polyurethane foam with density of 28.8 kg/m^3 (foam A), was further tested in an in vitro setting to quantify its microcidal action against *Streptococcus pyrogenes, Staphylococcus aureus* (MRSA), *Staphylococcus epidermidis, and Pseudomonas aeruginosa*. Data from these tests demonstrated the expected effective microcidal action of the CHG impregnated foam against *S. pyogenes, S. aureus* (MRSA), and *S. epidermidis,* but was ineffective against *P. aeruginosa,* which is further detailed in the results section.

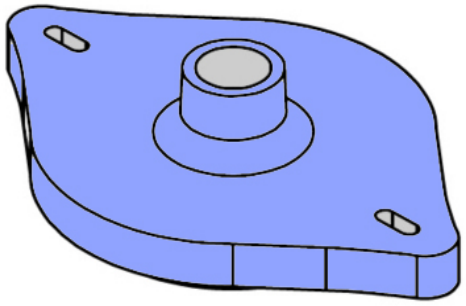


Figure 2: Top isometric view diagram of the CidalSealTM

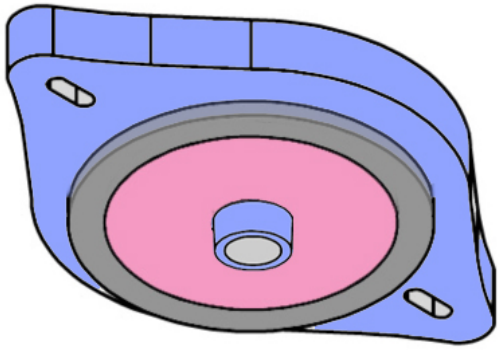


Figure 3: Bottom Isometric view diagram of the CidalSeal™

The foam chosen for impregnation with silver sulfadiazine (open cell polyurethane foam E) was used in the same in vitro testing procedure as the CHG foam, but only against the bacteria *P. aeruginosa.* For in vitro testing, cation-supplemented Mueller-Hinton agar (MHA; REMEL, Lenexa, KS) in 150 mm diameter agar plates was brought to room temperature.

A suspension of the test bacterial organisms were individually prepared in 0.85% sodium chloride to match an 0.5 McFarland barium sulfate turbidity standard, equivalent to 1.5 x 10^8 CFU/mL (colony-forming units per milliliter), and this suspension was used to inoculate the MHA plates using standard methods[9]. Within 15 minutes of inoculation, the foam pieces were placed on the seeded agar. Those containing microcidal agent were placed first followed by a microcidal-free control. Plates were incubated upright at 35 $\pm$ 1°C in ambient air for 18-24 hr. After the 18-24 hour period had passed the foams were moved to a freshly inoculated MHA plate – control foam pieces were moved first and clean forceps (rinsed with deionized water and wiped dry) were used for each of the 5 impregnated foam pieces. After the foam pieces were moved to a freshly inoculated MHA plate, the diameter of the zones of inhibition were measured and recorded. The zone measured includes the diameter of the circular area immediately surrounding the foam samples, where the organisms were inhibited from growth; a sample plate is depicted in Figure 4. The diameters of inhibition were recorded daily over a period of 13 days (in the case of the CHG impregnated foams) or 14 days (in the case of the silver sulfadiazine impregnated foams). The only deviation from this procedure occurred when testing with S. pyogenes In this case MHA containing 5% sheep blood was used for testing; however all other procedural steps remained constant for all tests.

Figure 4. Silver sulfadiazine impregnated sponge samples plated on pseudomonas aeruginosa

For the initial test set the open celled polyurethane foam with a density of 1.8 kg/m^3 (foam A) was used. Five CHG impregnated replicates and one CHG-free control were included in the testing. The inhibitory effects of the foams were tested against four bacterial species (*S. aureus* -MRSA ATCC 33592, *S. epidermidis* ATCC 12228, *S. pyogenes* ATCC 19615, and *P. aeruginosa* ATCC 27853).

A final round of testing was conducted in a manner analogous to the first. This time using open celled polyurethane foam with a density of 32.04 kg/m^3 (foam E), which was impregnated with 1% silver sulfadiazine. In this final found of testing the goal was to determine the inhibitory effects of the silver sulfadiazine foam against growth of *P. aeruginosa.*

Results

The foams that were impregnated with CHG were analyzed to determine which had absorbed the greatest mass of microcidal agent. It was found that open celled polyurethane foam A displayed the greatest CHG absorption at 2.068 [g CHG/mm^3 foam]. Preliminary testing showed successful inhibition of *S. aureus* for the full period of testing (13 days), by this foam, and as such it was used for further

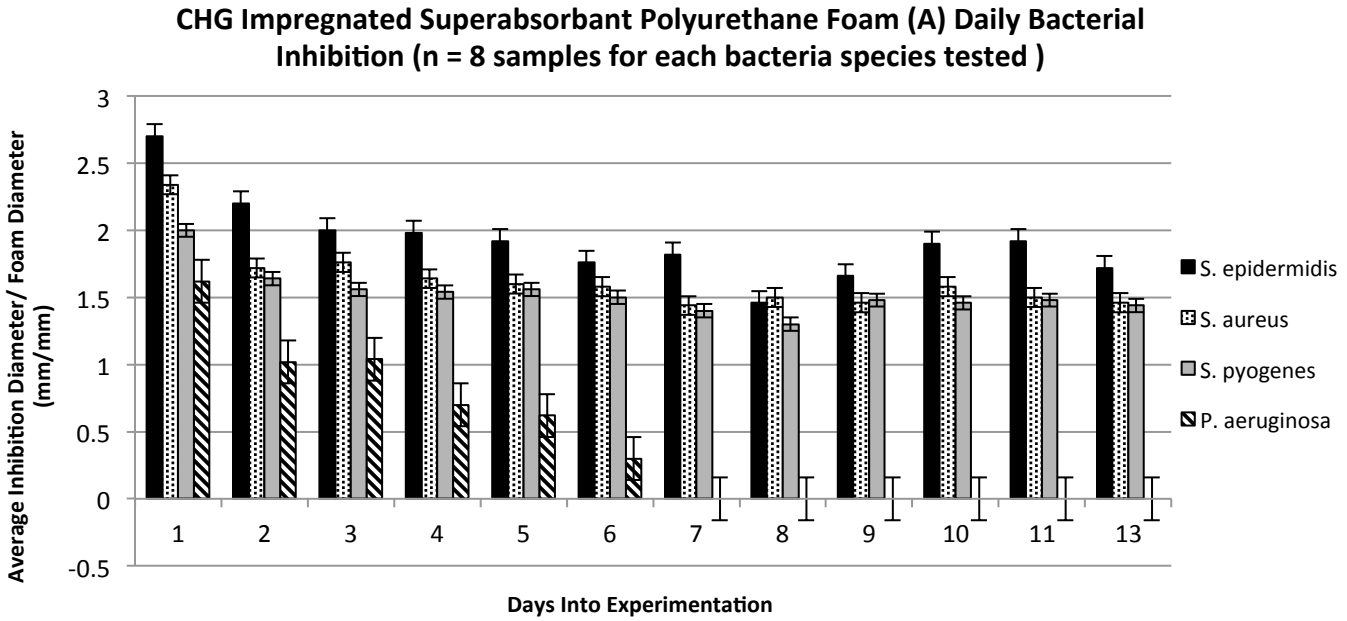
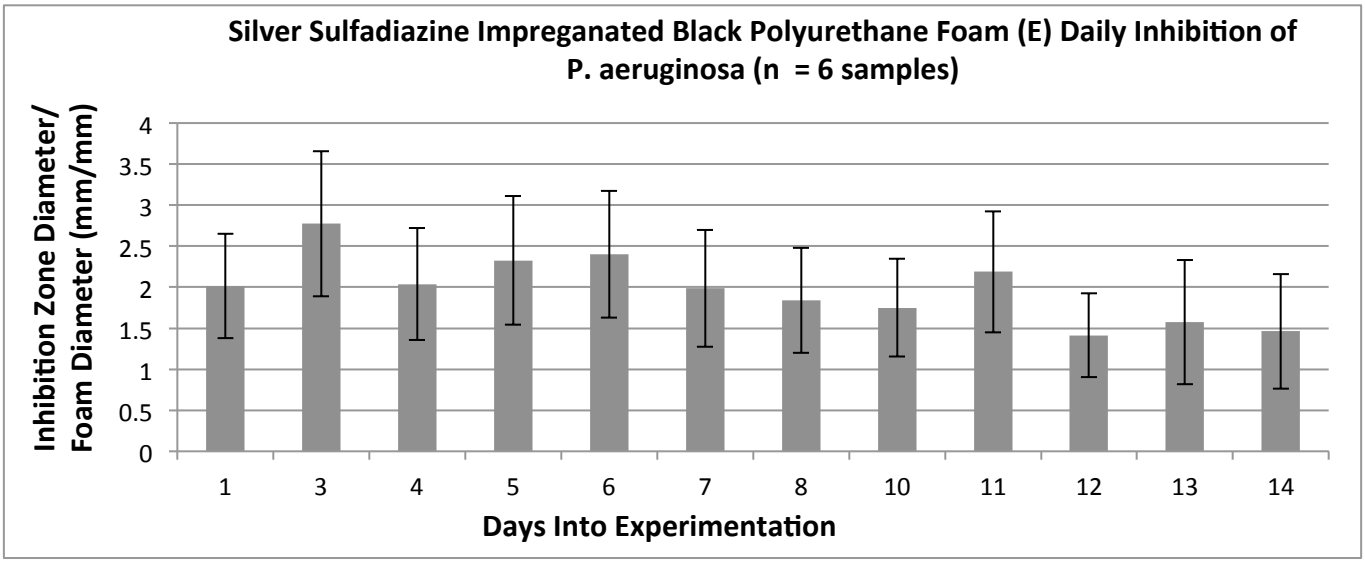


Figure 5: The results of polyurethane foam A on 4 common infection causing skin bacteria over a testing period of 13 days.

The results from the initial set of *in vitro* bacterial testing furthered demonstrated foam A successfully inhibited bacterial growth of *S. pyogenes, S.aureus* (MRSA), and *S. epidermidis*, shown in Figure 5. The data displayed in the chart shows the proportion of the average diameter of the inhibition zone created by microcidal action to the diameter of the foam A. Values which are greater than one indicate that the diameter of inhibition was maintained at a value greater than the diameter of the foam. This is found to be the case over all 13 days of testing for *S. pyogenes, S. aureus*, and *S. epidermidis*. The CHG impregnated foam failed to produce a diameter of inhibition greater than the diameter of the foam after 3 days of testing against *P. aeruginosa*.

The failure of the CHG impregnated sponge against *P. aeruginosa* prompted the testing of an alternative antimicrobial agent that is more effective at preventing growth of *P. aeruginosa,* namely, silver sulfadiazine. Testing set three demonstrated that polyurethane foam E was effective at holding and releasing the silver sulfadiazine compound, and therefore successfully inhibiting growth of *P. aeruginosa* over the testing period of 14 days. Two of the ten samples produced results that appeared to be significantly different as compared to the results from the eight remaining samples. When daily standard deviations were calculated for the in vitro



results it was determined that the results from these two samples were more than two standard deviations from the mean and could be considered outliers. Thus, only the data from the remaining eight samples were included in analysis of the microcidal effectiveness of the impregnated foam. Figure 6 displays ratios of the average zone of inhibition for the samples to the diameter of the samples. As can be seen from the data, the silver sulfadiazine impregnated foam produces an average diameter of inhibition consistently greater than the physical dimensions of the sponge.

Discussion

These two bactericidal efficacy tests were conducted to determine which combination of antimicrobial and specific sponge material would yield the most effective bacterial inhibition. The results from the tests indicate a wide range of inhibition for the device. The CHG impregnated foam component of the device is able to effectively and consistently release the bactericidal agent over a period of 13 days. It was proven efficacious *S.pyogenes, S. aureus* (MRSA), and *S. epidermidis*, of which remain very common infection-causing skin bacteria. The CHG-sponge failed to effectively inhibit growth of *P. aeruginosa* for the intended 13-day period. Trials with the silver sulfadiazine sponge component, however, were able to inhibit growth of *P. aeruginosa* for the expected 14-day testing period. These tests were conducted to determine which combination of antimicrobial and specific sponge material yielded the most effective bacterial inhibition. Surprisingly, the most effective sponge material for the CHG releasing component differed from the most effective sponge material for the silver sulfadiazine releasing component. The CHG component material is therefore polyurethane foam A, whereas the SSD component material is polyurethane foam E. The mechanism governing the difference between the drug and pore size remains unknown. One possibility could be the difference in densities. An equally likely hypothesis for the difference, however, could be in the reticulation of the two foams, as foam E appears to be less reticulated, and has more closed cell windows than foam A. This feature may be more conducive for the retention and release of the SSD compound. More testing would need to be done to conclude the physical mechanism for the difference between these two foam types. Nonetheless, combining these two foam components will give a much wider range of bacterial inhibition than previous devices used in a clinical setting.

Conclusion

The CidalSeal^{TM} is a medical device that has shown *in vitro* to act as an effective means of preventing growth of Methicillin-resistant *S. aureus* (MRSA)*, S. epidermidis, S.pyrogenes, and P. aeruginosa.* The current methods of infection prevention for patients with drain tubes, most notably use of the BioPatch®, are ineffective and unfit for the application for which they are being used. The BioPatch® only protects against bacterial infection for 7 days, and only incorporates one microcidal agent, thus missing the important bacterial species *P. aeruginosa* in its inhibitory effects. In contrast, the CidalSeal^{TM} exhibits protection of a greater variety of bacterial species, and is effective for a full two weeks. Thus, the CidalSeal^{TM} is a promising development for use in post-surgical patients requiring insertion of a drain tube.

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