The Characterization of the Bacterial Transmission Network in an ICU and the Impact on the Network of the Strategic Use of Continuous, Self-Cleaning Surfaces.

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INTRODUCTION

Although hospitals and other healthcare associated facilities serve as a place of healing and safety for sick patients, they can place these patients seeking care at risk of acquiring other infections with antibiotic resistant and multidrug resistant organisms (MDROs). Within a hospital setting, the environment surrounding patients often serves as a potential source of contamination as pathogens spread to the areas in close proximity to their hosts. Many factors influence the number and variety of microorganisms in the areas surrounding patients including air humidity, composition of nearby surfaces, degree of activity, and number of people caring for the patient[1]. Healthcare workers often come into contact with many of these surfaces surrounding patients in addition to the patients themselves. Surfaces which are touched most frequently by hands, also known as high-touch surfaces- such as doorknobs, light switches, bedrails, and over-the-bed tables- carry the greatest risk of pathogen transmission[1–3]. In fact, studies have shown that patients occupying rooms previously occupied by patients infected with MDROs have a 73% increased risk of becoming colonized themselves[2].

Hospital acquired infections (HAIs) carry severe risk of additional patient morbidity and mortality in addition to prolonged hospital stays and subsequently increased costs[1]. In a 2011 study of acute-care hospitals in the US, it was estimated that there were approximately 722,000 cases of HAI, of which 75,000 resulted in deaths[4,5]. This is equivalent to 1 patient in every 25 acquiring an HAI[5]. New occupants of rooms previously housing patients infected with pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), *Clostridioides difficile* (formerly *Clostridium difficile or C. diff*), multi-drug resistant *Acinetobacter*, and *Pseudomonas* species are three times more likely to become colonized or infected by the same organisms due to surface contamination and ineffective terminal cleaning methods[6]. A 2015 meta-analysis by Mitchell et al. found patients had a pooled odds ratio (OR) of 2.14 (95% CI 1.65-2.77) for acquiring the same infective organisms as a previously discharged occupant of the same room[7].

It has been documented that up to 40% of HAIs are caused by persistent surface contamination[1]. Studies have demonstrated that up to 52% of ICU surfaces were found to contain MDROs within biofilm despite terminal cleaning after patient discharge[6]. To combat the threat of HAIs as well as to stem the rapidly growing rates of MDROs, hospitals have employed various methods of surface decontamination. Cleaning can take place at different time points during patient care, and varies from routine daily surface cleanings to terminal room cleaning after patients are discharged[3]. However, studies have found that surfaces cleaned in this manner are not adequately disinfected or become re-contaminated within minutes more than one-half the time[3]. Other studies have found commonly used disinfecting chemicals (e.g. chlorine, hydrogen peroxide, etc.) do not remain on surfaces and provide no long-term sanitation properties. Additionally, it has been shown that the cloths used to apply these chemicals to surfaces decrease the disinfectants below their minimum effective concentration[3].

Newer methods that aim to overcome the flaws of surface chemical decontamination have also become common place in many hospitals. The most popular of these use ultraviolet (UV) light or aerosolized hydrogen peroxide for terminal room disinfection following patients with MDRO[4]. Although these innovative methods have been shown to decrease the rate of HAI throughout entire facilities, they have their own limitations[4]. UV light and hydrogen peroxide devices require patient rooms to be evacuated and therefore can only be used for terminal room cleaning purposes. This leaves a wide gap in room cleanings forcing facilities to revert to routine chemical surface cleaning as described previously with its own set of flaws. An emerging area of interest is the study of continuously disinfecting materials and surfaces. Substances such as transition metals and quaternary ammonium compounds have been reported in the literature as having potential application to continuously reduce bacterial colonization of various surfaces[3,8]. Specifically, a 2016 study by Garza-Cervantes et al. found a synergistic mechanism by combining silver and other transition metals (i.e. copper, nickel, zinc) in their antimicrobial properties pointing to a potential use within a clinic setting[8].

Although much emphasis is placed on understanding the infective organisms themselves as well as the means to most effectively disinfect healthcare facilities, another area of study that is equally as important is the movement and contact patterns of healthcare workers[9]. English et al. studied hospital staff movements and interactions at three urban Canadian hospitals and found a great amount of heterogeneity in regard to contact patterns and movements throughout facilities by various professions[9]. Their study was able to create a healthcare worker network showing interactions amongst various professions and points of contact. By identifying networks such as these, more specific interventions can be implemented to interrupt the nodal transmission from one part of the network to another thereby decreasing disease transmission[10].

Based on the current needs as described above and in the current literature, we feel that the continuous self-cleaning surface technology, known as CleanSurface™ (Aionx, Hershey, PA), will reduce microbial contamination, preventing recontamination on the high touch surfaces where it is applied, consistently. By employing this technology at known high-touch surfaces in an ICU setting, we hypothesize that we can cause nodal disruption in the disease transmission and contamination when compared to standard cleaning methods alone in a prospective manner.

METHODS

Study Design

This study was conducted in a prospective, controlled manner at Geisinger Lewistown Hospital (GLH). This investigation serves as a pre-validation investigation to evaluate the usability and safety of the products in their intended use. The study design consisted of two phases. Phase I consisted of an assessment of the normal transmission network prior to the intervention with CleanSurfaces™. After discussion and surveying of healthcare workers in the intensive care unit (ICU) of GLH, high-touch surfaces were identified and selected for monitoring. Samples were taken from a total of 23 surfaces at eight different timepoints (see Table 1 for explanation of surfaces sampled). Phase I occurred between July-August 2018

Phase II of the study assessed the hospital transmission network after installation of the CleanSurfaces™. Study personnel installed CleanSurfaces™ in each of five patient rooms and in the nurses station. Figures 1-3 are pictures showing CleanSurfaces™ in use during the study. Table 1 sets forth the surfaces samples during Phase I and Phase II and the surfaces covered with CleanSurfaces™ during Phase II.

Personnel Training and Monitoring

Prior to initiation of Phase I, all Aionx marketing/clinical personnel received in-service training with GLH staff. Additionally, all study personnel were supervised by trained members of GLH staff while working in patient areas throughout the course of the study so as to comply with all GLH policies and procedures. A separate training course

Fig. 1. A patient room in the study with CleanSurfaces™ covering the bed rails, flat area of the WOW, and nurse table.

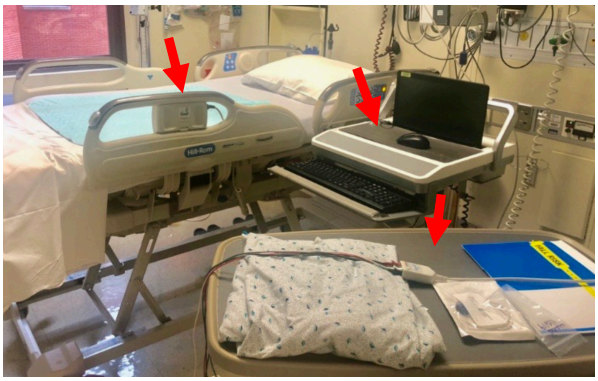


Fig. 2. Close up image of a CleanSurface™ on a bed rail.

Fig. 3. The central nurse station in the study with CleanSurfaces™ covering the WOW flat area and the nurse desk/work area.

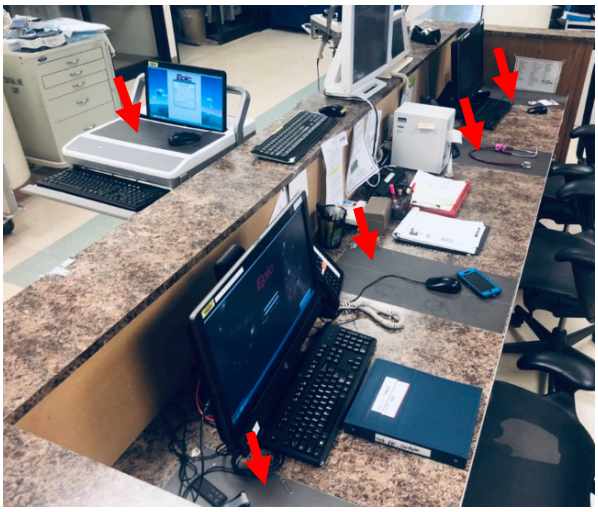


Table 1. Sampled and Covered Surfaces

	Sampled (Phase I and II)	*Covered with CleanSurfaces™ (Phase II)*
Patient Rooms (each of 4 rooms)	Bed rails (x4) Nurse table Patient table IV pump WOW keyboard WOW mouse Supply scanner	Bed rails (x4) Nurse table Patient table Flat area of WOW
Central Nurse Station	Desk/work area Door push plate Landline phone ID badge Keyboard Mouse Desk chair rail Cellphone Stethoscope Glucometer Nurse monitor WOW keyboard WOW mouse	Desk/work area Door push plate Flat area of WOW

was held for all ICU staff members and environmental services (EVS) personnel throughout the length of the study. During this separate training course the ICU staff and EVS were instructed on methods to record their activities and cleaning protocols respectively. They were also instructed not to change any of their protocols for the duration of the study in order to maintain study integrity.

Throughout the study period ICU staff and EVS were asked to monitor the CleanSurfaces™ for major defects or problems. Weekly product evaluations were also conducted by study personnel to ensure the products were functioning.

Sample Collection

Swabbing techniques were standardized before initiation of the study and closely followed sampling methodologies set forth in the CDC's "Procedures for Collecting Surface Environmental Samples for Culturing *Bacillus anthracis*". Samples were collected using Becton Dickinson BBL™ sterile swabs moistened with phosphate buffered saline solution. The techniques were specifically calibrated for each individual surface to be swabbed and then applied throughout the course of the study regardless of phase. Detailed notes were taken at all points during swabbing to record any deviations or other notes of interest.

During Phase I sampling, 43 surfaces were swabbed in total. Specifically, in each of three occupied patient rooms 10 pre-selected surfaces were sampled and an additional 13 surfaces were sampled from the ICU nurses station (see Table 1). Surfaces were sampled between July 25-August 31 2018. On sampling days, each of the pre-established surfaces were sampled at two separate time points per day with a time lapse of 4 hours between samplings.

Phase II followed the same swabbing protocol for each given surface sampled in Phase I. CleanSurfaces™ were placed on 4 objects within each patient room; however, not all surfaces covered with the interventional technology were sampled (see Table 1). After CleanSurfaces™ were installed, the products were left in place and functioning for 12 days before swabbing occurred. On day 13 after installation, swabbing of the same surfaces as was done in Phase I was carried out at two time points separated by a four-hour time lapse on 4 consecutive days.

Microbial Metagenomic Sample Analysis

Bacterial community profiling of the collected samples in both phases was carried out by Contamination Source Identification (Huntingdon, Pennsylvania). Contamination Source Identification (CSI) performed metagenomic analysis of the samples using 16S rRNA amplicon sequencing techniques[11] in addition to their proprietary bioinformatic data pipeline. Results of this analysis yielded all bacteria taxa present in the sent samples as well as each taxon's relative abundance. Further analysis from CSI also provided alpha-diversity information for all samples provided.

Data Analysis

Statistical analysis on the results of the CSI data was performed. Principle coordinate analysis (PCoA) was performed on the data set to compare the two phases of the study and analysis of similarities (ANOSIM) test was used to detect statistical significance. When comparing species richness and abundance between the two study phases, a non-parametric two-sample t-test was utilized for 999 Monte Carlo permutations. Kruskal-Wallis and Bonferroni corrections were added to the data analysis as well where appropriate to assess statistical significance.

RESULTS

Both phases of the study had similar patient profiles with respect to number of patients, length of stay (in both the studied unit and the total hospital), and patients using central lines, urinary catheters and

Table 2. Patient profile

	Before intervention	*After intervention*
Dates of swabbing	Aug 28 – 31	Dec 18 – 21
Patients during swab period	13	14
Dates of entire phase	Jun 31-Aug 31	Oct 21-Dec 21
Patients during phase*	213	212
Avg length of stay ICU/total*	2.03/4.58	2.27/5.00
Patients with central line(s)*	58	78
Patients with urinary catheter*	120	141
Patients on ventilator*	53	41

** Data relates to entire phase, rather than just the four days of swabbing.*

ventilators. There were no documented changes in cleaning protocols between the time points. A summary of ICU profile can be found in Table 2.

Overall a statistically significant decrease in observed species richness was seen after application of the CleanSurfaces™ technology within GLH ICU ($p=0.001$). In fact, a decrease in observed species richness within patient rooms between the study phases was found to be statistically significant ($p<0.05$) (Figure 5). PCoA analysis demonstrated distinct clustering of pre-CleanSurfaces™ and post- CleanSurfaces™ samples ($p=0.001$) (Figure 4). In the post-intervention phase, the signal of 283 unique bacterial species was also found to be significantly reduced (Bonferroni corrected-P <0.01). When assessing the specific areas swabbed (i.e. patient rooms and nursing station) the Phase II swabs were observed to have less bacterial species richness by 20% compared to Phase I swabs without an intervention. Additionally, the decreased species richness was found to be statistically significant within each patient room ($p<0.05$). Further analysis was able to demonstrate notable reductions in multiple bacteria between the two interventions. A specific subset of these bacteria, which are known pathogenic organisms, showed a statistically significant reduction after application of the study intervention (Bonferroni corrected $p<0.05$). Grouping the bacterial species that showed a statistically significant change between study phases by swabbing site revealed that on average 85% of these bacterial species were reduced or eliminated on the sampled surfaces not covered with CleanSurface™ (Table 3).

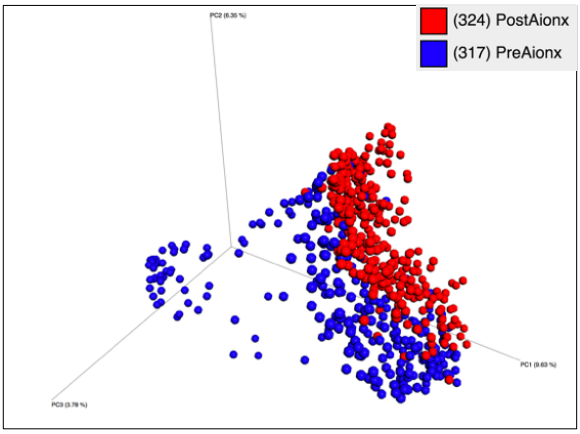
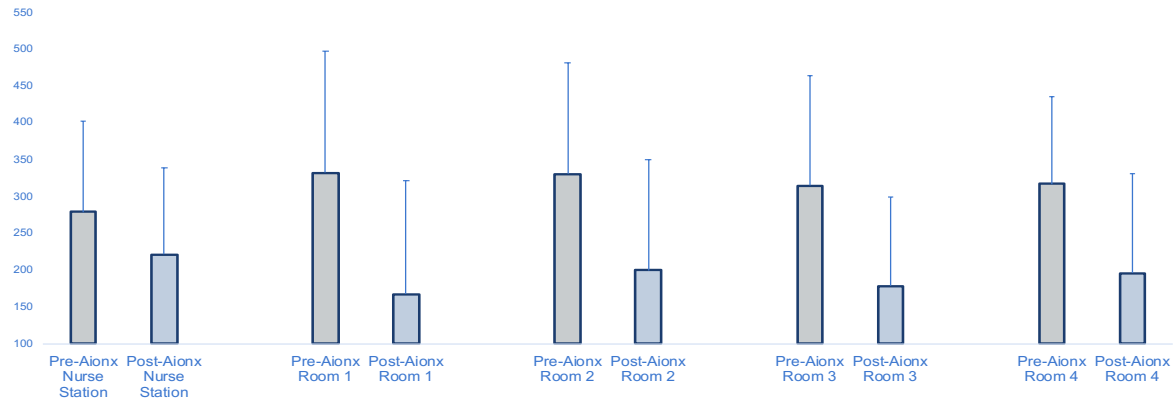


Fig. 4: PCoA plot of samples taken PreAionx (blue) and PostAionx (Red). The clustering pattern observed in the plot area shows a statistically significant difference between the two time points of sampling ($p=0.001$).

DISCUSSION

Although the purpose of this study was to evaluate the safety and usability of CleanSurfaces™ technology within an ICU setting, the results demonstrate significant findings that exceed the objectives previously set forth. Overall application of CleanSurfaces™ to some areas of an ICU resulted in a decrease in bacterial species richness. However, this does not fully encompass what can be gained from further evaluation of the data. The decrease in bacterial species richness did not happen only on the CleanSurfaces™ themselves- this decrease occurred on other surfaces as well, which points to a nodal interruption of bacterial transmission from a contamination source to another site. Of utmost importance is the data presented in Table 3. The data seen here represents the uncovered surfaces that were sampled and contains all bacterial species that had a statistically significant change between the two phases of the study. Of these 12 uncovered surfaces with no CleanSurfaces™ on them, half of them had a 95% or greater reduction in mean bacterial abundance. Furthermore, these percentages are not only reductions but are predominantly eliminations of specific bacterial species. Of the 182 specific bacterial species that were found to have a meaningful difference between the two study time points on the room keyboards, 14 (8%) of the species showed a significant decrease and 162 (89%)

Fig. 5: Species richness pre-Aionx and post-Aionx grouped by specific patient rooms and nurses station. Differences between all patient rooms and nurses station between the two phases were found to be statistically significant ($p<0.05$).



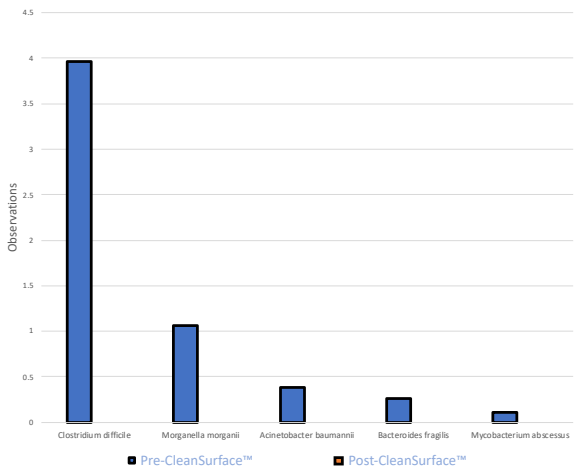


Fig. 6: CDC defined pathogenic bacteria of concern that were detected during the pre-Clean Surfaces™ Phase I but not during the post-Clean Surfaces™ Phse II of the study. All bacterial levels represented here were statistically significant.

were eliminated after application of CleanSurfaces™ in the ICU.

These reductions and eliminations were not limited to trivial bacterial species. Figure 6 depicts five organisms identified by the Centers for Disease Control and Prevention (CDC) as pathogenic bacteria of concern- such as *C. diff*- that were identified prior to installation of CleanSurface™ technology within the ICU. After installation, however, these same bacteria were undetectable after sampling. Although the absence of these bacteria can be explained potentially due to the different time points during which the sampling took place, exposure to these organisms was unchanged between the two phases.

C. diff is a well-known organism within hospitals and can significantly prolong patients' length of stay. During Phase I, *C. diff* was detected in all sampling areas including patient rooms and nurses station. However, there were no patients with known *C. diff* infections on the floor during this time frame. The floor had cared for a patient with a documented *C. diff* infection until August 22 which was 6 days prior to the first sampling day. This data and the timing of the terminal cleaning points to the ineffectiveness of current disinfection methods. Not only was the bacteria still detected 6 days after terminal cleaning but it was also detected throughout other areas of the ICU. Specifically, swabbing revealed *C. diff* signal in all sampled rooms in addition to the nurses station. *C. diff* exposure was not lower during the second phase of the study however. During sampling in Phase II, there were documented cases of active *C. diff* infection within the ICU and within rooms where samples were taken. In fact, one of the patient rooms housed a *C. diff* patient up until approximately 24 hours before the first sampling day of Phase II took place. Despite the extreme proximity of active *C. diff* infections to sampling times in Phase II as well as the extended length of stay that the *C. diff* patient had (11 days total during Phase II), the pathogen was not detected after swabbing.

While the findings of this study point to promising ways that disinfection protocols can be improved in hospital settings, it is not without its limitations. Additionally, throughout the sampling period in Phase II several issues were encountered. Several beds that had CleanSurfaces™ applied to the bedrails were removed from the rooms in order to bring in specialized

Table 3. Bacterial species that had a statistically significant change in mean abundance between Phase I and Phase II were classified by surface ($p<0.1$). Data indicates the number of specific bacterial species that were eliminated, reduced, and the sum of reduced and eliminated species.

	Species with change in mean abundance	Species eliminated		Species reduced		Total species reduced or eliminated	
Keyboard, pt room	182	162	(89%)	14	(8%)	176	(97%)
Mouse, pt room	270	236	(87%)	27	(10%)	263	(97%)
IV pump, pt room	196	176	(90%)	14	(7%)	190	(97%)
Supply scanner, pt room	253	214	(85%)	28	(11%)	242	(96%)
Nurse ID badge	114	101	(89%)	8	(7%)	109	(96%)
Keyboard, nurse station	172	130	(76%)	34	(20%)	164	(95%)
Phone, nurse station	144	84	(58%)	35	(24%)	119	(83%)
Mouse, nurse station	49	18	(37%)	4	(8%)	22	(45%)
Cellphone	33	0	(0%)	13	(39%)	13	(39%)
Glucometer, nurse station	39	13	(33%)	2	(5%)	15	(38%)
Stethoscope	49	0	(0%)	15	(31%)	15	(31%)
Chair rails, nurse station	91	17	(19%)	1	(1%)	18	(20%)

rental beds to meet certain patient needs. There were also several issues with functionality and damage to the CleanSurfaces™ technologies rendering several pieces nonfunctional. Despite these deviations from the protocol and less than ideal circumstances with functionality and damage to the products, the overall study results still demonstrated significant reductions in bacteria compared with Phase I.

Overall this study effectively was able to demonstrate the safety and usability of CleanSurfaces™ technology in an ICU setting. Moreover, the data collected also points to its efficaciousness in reducing bacterial contamination and transmission throughout an ICU. As more research and thought is aimed toward infection prevention, this technology and the means through which it can be applied show great promise. By continuing to understand the intricacies of healthcare worker movements and interactions and employing continuously cleaning surface technologies, such as CleanSurfaces™, at key points within hospitals, the growing issues of HAI and antibiotic resistance may be able to be slowed.

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