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Review Article

Evaluation of an Advanced Oxidation System in Controlling Healthcare - Associated Infections in Active Patient Environments

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Abstract

Antimicrobial resistant pathogens pose an ongoing and increasing challenge to hospitals since they cause healthcare-associated infections (HAIs) during clinical treatment of patients. In addition, these pathogens pose a difficult challenge in the prevention of cross-transmission and contamination. Existing methods to address this challenge have included aggressive sanitizers or "bleach" treatment and deployment of UV-C technology. UV-C refers to ultraviolet light with wavelengths between 200 – 280 nanometers. Both solutions have limitations. The effectiveness of sanitizer treatments is limited to the thoroughness of application process, often limited by time constraints between patient room turnover and the effectiveness of the cleaning staff. The effectiveness of UV-C technology is limited to line-of-sight and physical distance from the device, as well as by steady degradation of treatment efficacy with bulb life. In each case, the solution is a one-time treatment without continuous cleaning or ongoing prophylaxis, and neither solution addresses airborne pathogens.

Along with HIAs is the concern that naturally occurring microorganisms that constitute a global catastrophic biological risk (GCBR) are becoming a topic of concern. The recent emergence of severe infectious diseases with pandemic potential has triggered much interest in understanding the broader pandemic threat landscape. A substantial proportion of infectious disease preparedness activities have, to date, focused on a historical list-based approach constructed around biological warfare agents and on recent outbreaks, e.g., severe acute respiratory syndrome (SARS). Nevertheless, such an approach is not proactive or forward-looking and will inherently fail to account for agents not currently known or those without historical precedent. Activities that are solely limited to list-based approaches may foster a static nonative-minded approach to the problem, hamper preparedness, and lessen resilience. This type of approach was adopted by the United States, and many other nations have followed suit. Johns Hopkins Center for Health Security conducted this study to elucidate the characteristics of naturally occurring microorganisms that constitute a GCBR. Biological decontamination using a non-thermal gas discharge at atmospheric pressure in air is the subject of significant research effort at this time. The mechanism for bacterial inactivation undergoes much speculation, particularly with regard to the role of ions and reactive gas species. Two mechanisms have been proposed: electrostatic disruption of cell membranes and lethal oxidation of membrane or cytoplasmic components. Results show that death is accompanied by cell lysis and fragmentation in Gram-negative bacteria but not Gram-positive species, although cytoplasmic leakage is generally observed. Gas discharges can be a source of charged particles, ions, reactive gas species, radicals, and radiation (ultraviolet, infrared, and visible), many of which have documented biocidal properties. The individual roles played by these in decontamination are not well understood or quantified. However, the reactions of some species with biomolecules are documented otherwise in the literature. Oxidative stress is relatively well studied, and it is likely that exposure to gas discharges in air causes extreme oxidative challenge.

This study evaluates the effectiveness of an advanced oxidation technology developed by airPHX Health in addressing airborne and surface HAI organisms in common hospital facilities including stainless steel, plastic and linoleum floors. However, among the various classes of microbes, many possess some or all of the characteristics necessary to be identified as a GCBR. Several features of viruses make this class of microbial agents the most likely to cause

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GCBRs. Viruses possess higher capacity for genetic mutability due to both the structure of their genomes and the generation time for replication in which large numbers of progeny virus are created each day. Additionally, the inability of a virus to be countered with a broad-spectrum antiviral compared with bacteria, fungi, and parasites makes viruses the more likely cause of a GCBR. Within the viral class, RNA viruses merit special concern chiefly because of their higher mutability compared to DNA viruses. Treatment via the airPHX system attacks the virus and bacterial cell wall allowing for complete destruction and no further RNA/DNA resistance mutation. These actions will be further delineated in subsequent publications aimed at GCBRs. It should be noted that airPHX Health technology eliminates airborne pathogens and distributes into the treatment space oxygen-based oxidizing molecules that sanitize ambient air and hospital surfaces. Using airPHX technology, treatment is not limited to line-of-sight or physical distance, can be scaled to any size treatment space without sacrificing treatment efficacy, and is continuous and highly effective.

Key Words: Healthcare-Associated Infections (HAIs); Johns Hopkins Center For Health Security; Severe Acute Respiratory Syndrome (SARS); Global Catastrophic Biological Risk (GCBR); UV-C Technology; Oxygen-Based Oxidizing Molecules

"Tubular Corona" Technology

Tubular corona technology is capable of producing a stable coronal ionic discharge (plasma) using a proprietary electro-mechanical device. The plasma field is created along the inside and outside of a tubular dielectric, which is composed, of pairs of cylindrical wire mesh electrodes (anode and cathode) placed inside and outside of a tubular insulator. When electrical power is applied to these electrodes, a stable, non-thermal corona is produced along the entire extent of the tubular dielectric which generates plasma. The fact that this plasma can be created at varying external temperatures, varying relative humidity, in the absence of a vacuum or a noble gas, and with low and high energy dielectric tubes in the same reaction chamber, are all unique features of airPHX technology [1].

The subject equipment creates a stable, non-collapsing, non-drifting "tubular corona discharge" within its reaction chamber (Figure 1). Alternative systems generate a large amount of heat due to inefficiency in production of the plasma field. This technology does not increase the ambient temperature. Hence, airPHX units create a "non-thermal" plasma.

When air is drawn through the plasma in a reaction chamber, a number of the oxygen molecules present are converted into oxygen based oxidizing molecules that are referred to as reactive oxygen species (ROS). These ROS include oxygen ions, free radicals and peroxides that are highly reactive due to the presence of an unpaired valence shell electrons [2-4].

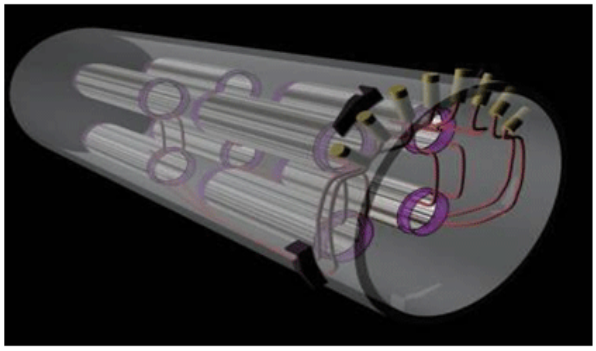


Figure 1: "Tubular Corona" Technology

Measurable levels of gaseous hydrogen peroxide and other ROS are produced within the chamber and, given their half-lives, can be allowed to enter the surrounding environment when this is desired [5-6]. The hydrogen peroxide produced is different than vaporized or aerosolized hydrogen peroxide. Gas-phase hydrogen peroxide has a more acute bond angle and is shorter lived than the more stable liquid or vaporized forms. In addition to gas-phase hydrogen peroxide, the ROS includes hydroxyl radicals, superoxide, singlet oxygen and ozone. When ozone is released from this unit, based on the intended use, it interacts with airborne contamination and is consequently at very low dissolved levels [7].

Adaptive Technology

The technology developed has a wide range of applications because of its ability to produce a highly oxidative environment within its reaction chamber and its ability to discharge molecules that have an oxidizing capacity at levels that are safe for human exposure into the environment.

The range of applications is enhanced because the equipment can be scaled and modified to meet the particular needs by:

1. Varying the size and number of tubular dielectrics within a reaction chamber;

2. Modifying the power supply to change the components of the ROS formed; and,

3. Passing the discharge from the unit through a catalyst or series of catalysts to eliminate or reduce the discharge of an ROS from the unit.

Safety Considerations

The airPHX technology is equipped and regulated through the use of an integrated Aeroqual sensor (Aeroqual Limited, Aukland, New Zealand) monitoring ozone (O_3) as an indicator of ROS production. The low level O_3 byproduct of the clean process that takes place within an airPHX unit is safe according to the OSHA Hazard Communication Standard 29 CFR 1910.1200. The airPHX technology relies on electricity and the oxygen present in ambient air to produce marginal levels of reactive oxygen species where O_3 is stabilized (average less than 0.03 ppm) within a treated area or space. This level is lower than limits established by the Occupational Safety and Health Administration of 0.10 ppm and the Center for Disease Control through The National Institute for Occupational Safety and Health (NIOSH) of 0.10 ppm.

The hydrogen peroxide produced (previously discussed) is different from vaporized or aerosolized hydrogen peroxide (H_2O_2). This by-product is from the clean process that takes place within an airPHX unit is not hazardous according to the OSHA Hazard Communication Standard 29 CFR 1910.1200. The airPHX technology relies on electricity and the oxygen present in ambient air to produce marginal levels of H_2O_2 where it is stabilized (average less than 0.07 ppm) within a treated area or space. Such treated area(s) should have consistent/constant airflow to provide a uniform distribution of the sanitizer. This level is lower than limits established by the Occupational Safety and Health Administration for General Industry: 29 CFR 1910.1000 1 ppm and the Center for Disease Control through The National Institute for Occupational Safety and Health (NIOSH) of 1 ppm.

Mechanism of Action, Lethality

Broad spectrums of microorganisms are susceptible to plasma exposure, including Gram-negative and Gram-positive bacteria, bacterial endospores, yeasts, viruses [8], and biofilms [9]. Reductions in bacteria viability of over 6 log10 are reported from short exposures of less than 30s [10-12], and a total cell fragmentation is seen after longer exposures.

Typical of most sterilization techniques, the rates and magnitudes of cell killing in response to a particular treatment regime differ for various species and strains of bacteria. Spores are generally more resistant than vegetative or actively growing bacteria, while there is no consensus on the relative susceptibility of Gram-negative or Gram-positive bacteria. Bacterial inactivation is accompanied by leakage of proteins, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) from the cellular cytoplasm [13]. These macro molecules are detectible in the supernatant of a cell suspension of Gram-negative *E.coli* treated with atmospheric pressure plasma after 10s, and 15s of treatment for Gram-positive *S. aureus*. Observations of the physical damage inflicted on Gram-negative and Gram-positive bacteria show marked differences. Impairment of some metabolic function, not resulting in cell death, has been reported from sublethal exposures, indicative of changes in enzyme activity [14-15]. There are two main hypotheses for the mechanism of cell death caused by gas discharge, both involving lethal damage to cell membrane structures and ultimately leading to leakage of cytoplasmic contents or lysis. They are electrostatic disruption and oxidation of membrane components. The electrostatic disruption mechanism[16] suggests that the total electric force caused by accumulation of surface charge could exceed the total tensile force on the membrane (Gram-negative), the probability of which is greater where some surface irregularities give regions of higher local curvature. The tensile strength of the membrane is conferred by a murein layer, which is thicker in Gram-positive bacteria (~15–18nm) than Gram-negative bacteria (~2nm), meaning a lower accumulated charge would be required for lysis of Gram-negative bacteria than Gram-positive. In the second mechanism, oxidation and damage of membrane or cellular components are suggested to be caused by the energetic ions, radicals, and reactive species generated by gas discharge. Active radicals are generated directly in plasma and diffuse to the cell surface, while reaction chemistry in a moisture layer on the cell surface can produce secondary radicals. It is well documented that ROS have profoundly damaging effects on cells through reactions with various bio-macromolecules [17-20]. The involvement of superoxide in the bactericidal effects of a corona discharge is alluded to by the protective effects demonstrated by super oxide dismutase (SOD) enzymes [21-22].

Objective

The objective of this study was to evaluate the effectiveness of ROS exposure in reducing bacterial air and surface populations in an active oncology wing of a hospital, the Oncology Wing Test (OW) and the waiting area in a hospital Emergency Room (ER) Waiting Area Test.

Material and Methods

The tests were conducted in a 600 bed hospital in the Mid-Atlantic U.S. The senior executives of the hospital system in the areas of Safety and Industrial Hygiene and Facilities Operations conducted direct oversight of the testing. The Chief Physician Officer of the hospital system reviewed and validated the trial results.

Volumetric Air Sampling

Air sampling entailed drawing 30 liters of air per sample using a MicroBio MB1 volumetric air sampler, Cantium Scientific, Clarendon Gardens, Dartford UK. Scientific Air Solutions is the North American

Distributer for the MB1 and MB2 volumetric air samplers.

Air samples were impinged on 15x100mm potato dextrose agar plates acquired from Hardy Diagnostics, Santa Maria, California. Air sample morphology and enumeration was completed by Scientific Air Solutions, Turlock, California. Recorded results are normalized to colony-forming units per cubic meter of air, CFU/m^3.

Surface Testing

Surface testing included surface swabs acquired from Solar Biologicals, Inc., Ontario, Canada. A uniform six (6) inch (15 cm) surface swabbed for each sample, with swab sponges forwarded to Scientific Air Solutions for enumeration. All swab samples were examined for the number of organisms and recorded as colony forming units per square centimeter, CFU/cm^2.

Treatment

For both the OW Test and the ER Waiting Room Test sample locations were mapped and noted as either air sampling or surface swabbing. Upon completion of pre-treatment sampling, an airPHX PA2400P portable unit was placed in the treatment area and activated. The airPHX unit was allowed to operate continuously for eighteen days in the OW Test and thirty six days in the ER Waiting Room Test. At the end of the treatment period, in-treatment volumetric air samples and surface swabbing were taken in the same locations as the pre-treatment sampling. External air samples were taken to understand the influence of the supplied air to the two test locations. Results are given in Tables 1 and 2.

Table 1: Summary of testing results: OW Test.

Volumetric Air Samples, CFU/m^3				
Sample Location	# Samples	Pre-Treatment	In-Treatment	% Reduction
Oncology Main Hallway	20	767	40	94.8
Nurse Station 1-3 Utility Hallway	5	1,113	80	92.8
Elevator Bay Floor 1-7	7	1,538	62	96.0
Elevator Bay Floor 8	4	1,742	33	98.1
Exterior	2	2,933	2,917	0.5
Surface "Contact" Swabs, CFU/cm^2				
Sample Location	# Samples	Pre-Treatment	In-Treatment	% Reduction
Treatment Area, see "S" samples	13	17	0.21	98.8
Negative control	1	0	0	0

Table 2: Summary of testing results: ER Waiting Room Test.

Volumetric Air Samples, CFU/m^3				
Sample Location	# Samples	Pre-Treatment	In-Treatment	% Reduction
Waiting Room Interior	10	880	77	91.3
Exterior	2	2,417	2,400	0.7
Surface "Contact" Swabs, CFU/cm^2				
Sample Location	# Samples	Pre-Treatment	In-Treatment	% Reduction
Treatment Area, see "S" samples	7	41	1.9	95.4
Negative control	1	0	0	0

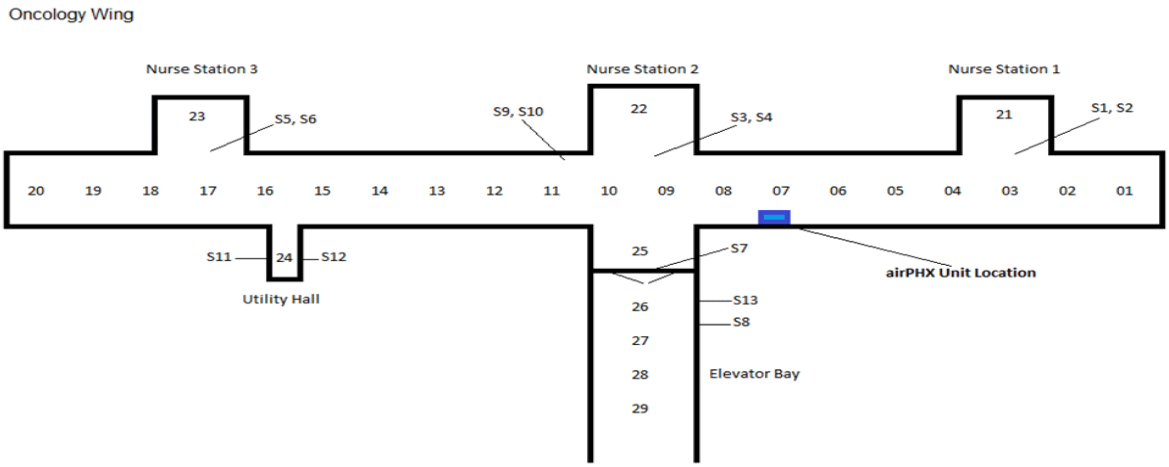
Results and Discussion

Oncology Wing

The OW is on a single floor of the facility, and it includes patient rooms, three nurse stations and a utility hall. Fresh air is required in all patient spaces. Typically, inpatient areas have six (6) total air exchanges per hour with two being fresh or outdoor air.

These figures can increase as most air handling units have an economizer, using 100% outdoor air when outside conditions permit. All air passes through 95% filters in the air handlers, and the patient rooms have HEPA terminal filters at the diffusers. A total of 36 air samples and 13 surface swabs were taken (Figure 2).

Figure 2: Layout of oncology wing with volumetric air and surface sample locations, designated as S1 to S13, noted below.



Volumetric Air Samples

1. Pre-treatment air samples ranged from 767 to 1,742 CFU/m^3
2. In-treatment results ranged from 33 to 80 CFU/m^3, a reduction of 93-98% thus showing the airPHX system reduced the outside air bioburden and further sanitizes the locations examined.
3. Exterior air samples showed relatively high organism counts, approximately 2,933 and 2,917 CFU/m^3 respectively, indicating a very high bioburden being introduced into the OW.
4. Favorable treatment results extended beyond the treatment location, as sampling in the elevator bays on the seven (7) other floors were reduced from 1,538 to 62 CFU/m^3 showing a 96% reduction.

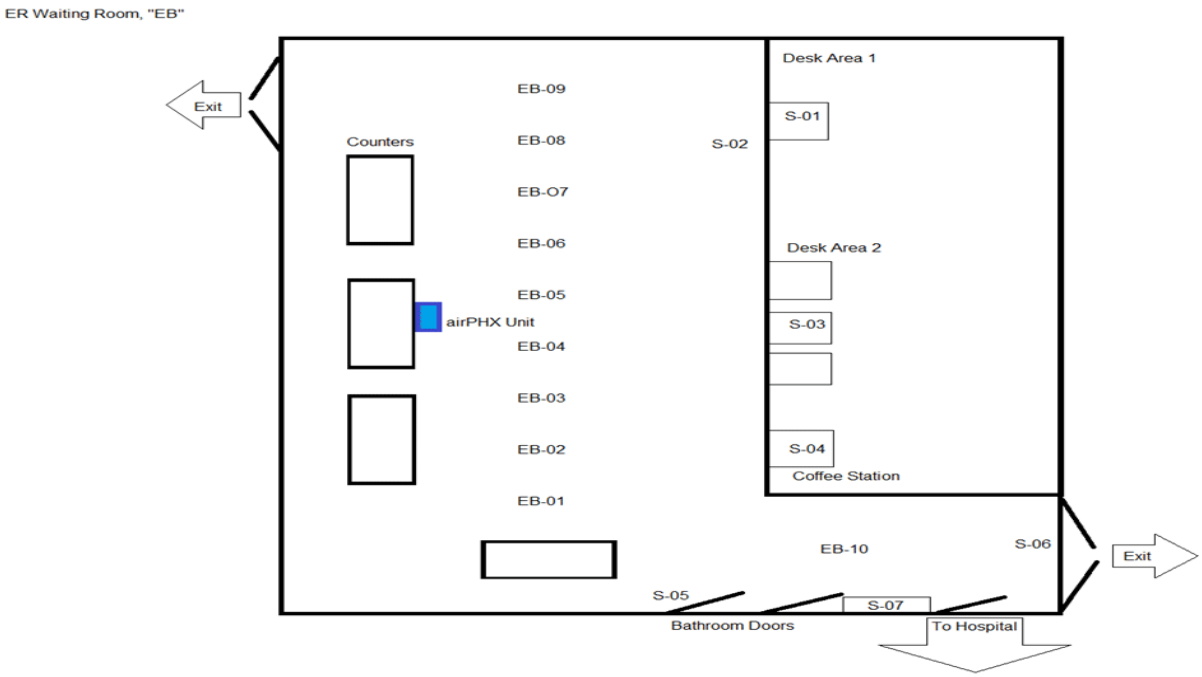
Surface Contact "Swabs"

1. Pre-treatment surface swab results were 17 CFU/cm^2.
2. In-treatment surface testing results revealed 0.21 CFU/cm^2, yielding a 99% reduction.

Emergency Waiting Room

Upon completion of the OW test, the airPHX portable device was moved to the waiting room area of the emergency room. The ER waiting room includes three (3) counters, several administrative desks, and a patient waiting area. The testing was conducted in the midst of flu season, and the foot traffic and turnover of patients was elevated, including frequent exterior door openings and introduction of outside air and contaminants. The airPHX unit ran continuously; however, when conducting the in-treatment tests, it was discovered that the unit had been turned off, so the results may reflect only intermittent activation of the technology. A total of ten (10) air samples and seven (7) surface swabs were taken (Figure 3).

Figure 3: Layout of ER waiting room with volumetric air and surface sample locations designated as S-01 to S-07, noted below.



Volumetric Air Samples

1. Pre-treatment air samples averaged 880 CFU/m^3.
2. In-treatment results averaged 77 CFU/m^3, a 91% reduction.
3. Exterior air samples showed relatively high bioburden, approximately 2,917 and 2,400 CFU/m^3 respectively, indicating a very high bioburden being introduced into the ER waiting room.
4. Favorable treatment results were seen, notwithstanding frequent door openings and high foot traffic in this area.

Surface Contact "Swabs"

1. Pre-treatment surface swab results were 41 CFU/cm^2.
2. In-treatment surface testing results revealed 1.9 CFU/cm^2, yielding a 95% reduction.

Conclusion

The results are consistent in both the Oncology Wing and ER Waiting Room testing, with significant reductions in airborne and surface organisms, respectively. The pre-treatment test results from both spaces show lower colony forming unit (CFU) counts than exterior samples, an indication of the effectiveness of the airPHX treatment in overcoming the existing high bioburden from the outside environment. The in-treatment test results in both spaces showed excellent reductions in counts from both air and surface tests, indicating that the airPHX technology dramatically reduced the bioburden in the existing air and will definitely favorably impact infection control efforts in traditional HAI environments. The scalable and easily deployed nature of the airPHX technology appears to offer a solution to the large and unpredictable risks posed by GCBRs.

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