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Novel photodynamic coating reduces the bioburden on near-patient surfaces thereby reducing the risk for onward pathogen transmission: a field study in two hospitals

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SUMMARY

Background: Near-patient surfaces are recognized as a source for hospital-acquired infections. Such surfaces act as reservoirs for microbial contamination by which pathogens can be transmitted from colonized or infected patients to susceptible patients. Routine disinfection of surfaces only results in a temporal elimination of pathogens, and recontamination inevitably occurs shortly between disinfections.

Aim: A novel antimicrobial coating based on photodynamics was tested under laboratory conditions and subsequently in a field study in two hospitals under real-life conditions.

Methods: Identical surfaces received a photodynamic or control coating. Bacterial counts [colony-forming units (cfu)/cm^2) were assessed regularly for up to 6 months.

Findings: The laboratory study revealed a mean reduction of several human pathogens of up to 4.0 $\pm$ 0.3 $\log_{10}$. The field study in near-patient environments demonstrated mean bacterial values of 6.1 $\pm$ 24.7 cfu/cm^2 on all control coatings. Photodynamic coatings showed a significantly lower mean value of 1.9 $\pm$ 2.8 cfu/cm^2 ($P<0.001$). When considering benchmarks of 2.5 cfu/cm^2 or 5 cfu/cm^2, the relative risk for high bacterial counts on surfaces was reduced by 48% (odds ratio 0.38, $P<0.001$) or 67% (odds ratio 0.27, $P<0.001$), respectively.

Conclusion: Photodynamic coatings provide a significant and lasting reduction of bacterial counts on near-patient surfaces, particularly for high bacterial loads, in addition to routine hygiene. The promising results of this proof-of-concept study highlight the need for further studies to determine how this novel technology is correlated with the frequency of hospital-acquired infections.

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Introduction

In 2015, approximately 63.5% of infections with antibiotic-resistant bacteria were associated with healthcare units, and many of these infections led to death and disability-adjusted life years [1]. Multiple strategies to limit the spread of antibiotic-resistant pathogens in the healthcare setting have been implemented, such as active surveillance to identify and isolate colonized patients, efforts to increase hand hygiene adherence, and antibiotic stewardship [2].

In addition, there has been much debate about the specific contribution of contaminated surfaces as risk factors for healthcare-associated infections, especially in under-developed countries [3]. Environmental screening confirms repeated contamination of items, equipment and general sites in bed spaces and rooms of colonized or infected patients, and often throughout multiple clinical areas in a healthcare institution [4]. Meanwhile, it is generally accepted that the environment may facilitate transmission of several important healthcare-associated pathogens [2,5]. Besides hand hygiene, cleaning and disinfection of surfaces in a healthcare unit is an important step to reduce the transmission of pathogenic micro-organisms and thereby the risk of hospital-acquired infections.

In hospitals, liquid disinfectants are usually applied, which contain various chemical substances to kill most pathogenic micro-organisms. However, disinfectant effects only last for seconds or minutes because cleaned surfaces become recontaminated by contact with staff, patients or other items. In addition, one of the disadvantages of using liquid disinfectants is that their efficacy is very much dependent on the rigour of the cleaning operatives in applying these disinfectants appropriately. This is a human factor that is challenging to improve. To avoid recontamination between two consecutive disinfection procedures, surfaces can be equipped with so-called 'self-sanitizing' coatings which kill micro-organisms automatically [6].

This study investigated a novel antimicrobial coating based on photodynamics. A photodynamic molecule (photosensitizer) absorbs visible light and transfers the light energy to adjacent oxygen molecules, thereby generating reactive oxygen species such as the non-radical gaseous singlet oxygen. The photosensitizer used in the study generates singlet oxygen alone [7,8]. A thin coating contains a photosensitizer which is exposed to visible light. Singlet oxygen is generated and these gaseous molecules can diffuse from the inside coating to the micro-organisms located on the coated surface and kill them via oxidation [9]. Under ambient light conditions, the photosensitizer remains stable in the coating for a few years, and therefore generates singlet oxygen continuously upon light exposure.

First, the photodynamic effect on bacterial killing on inanimate surfaces was investigated under standardized laboratory conditions. The antimicrobial coating was subsequently tested under real-life conditions in near-patient environments by performing a field study of frequently touched surfaces in two hospitals.

Methods

Laboratory study

The photodynamic coating system DYPHOX® (TriOptoTec GmbH, Regensburg, Germany) was applied to glass slides with or without photosensitizer. *Staphylococcus aureus* (ATCC 25923), *Enterococcus faecalis* (ATCC 29212), *Staphylococcus epidermidis* (patient isolate) or *Pseudomonas aeruginosa* (ATCC 27853) was resuspended in Millipore water + 0.1% Tween20. Cells were applied to the coated surface by pipetting a spot of 50 µL corresponding to $\sim 10^5$ cells. The glass samples were kept in the dark until the suspension was visibly dry (~30–60 min). Samples were irradiated homogeneously with blue LED light (customized device, Lumiled LED) at different radiant exposures (J/cm^2) using 18 mW/cm^2 or 18 µW/cm^2.

After irradiation, the bacteria were removed from the surface using a sterile cotton-tipped rod. After serial dilution and incubation on Mueller–Hinton agar at 37 °C for 24 h, the survival of bacteria was determined by counting the number of colony-forming units per mL (cfu/mL). All treated samples (light and coated with photosensitizer), light control (light, no photosensitizer) and dark control (coated with photosensitizer, no light) were compared against the untreated reference control (no light, no photosensitizer). The recovery efficacy of this method was tested previously [10].

Field study

The field study was undertaken at the emergency departments of two hospitals: the University Medical Centre of Regensburg, Germany (Hospital 1) and the Caritas Hospital St. Josef of Regensburg, Germany (Hospital 2). In each emergency department, two treatment rooms with comparable patient occupancy and light conditions were selected. The surfaces with most frequent touches in both rooms of both emergency departments were coated with DYPHOX®: the table surface (PC working station), the PC keyboard, the PC mouse and a frequently used handle of a cabinet door. Inanimate surfaces in one room at each emergency department received photodynamic coatings; in the other room at each emergency department, a control coating without photosensitizer was used. The stability of all coatings was checked regularly during the field study to ensure that all coatings were in place. The duration of this part of the study was 3 months.

The antimicrobial coating was also studied in patient rooms at Hospital 1. Surfaces of a writing desk (room in outpatient department) and a dining table (patient room on the ward) received photodynamic coating, and control coating was used in comparable rooms with comparable light conditions. This part of the study was extended from 3 to 6 months to investigate the long-term efficacy of antimicrobial coatings. As for all other surfaces, Samples 1–50 were taken in the first 3 months of the field study, and Samples 51–98 were taken in the subsequent 3 months.

Routine cleaning and disinfection

Throughout the study, the routine cleaning and disinfection procedures were left unchanged in both participating hospitals to avoid any potential bias on the study results. The two hospitals had similar standard operating procedures (SOPs): after discharge of a patient, all horizontal surfaces in each treatment room with direct patient or staff contact (hand contacts) were cleaned routinely with the same disinfectant containing 1.5% (w/v) hydrogen peroxide (Incidin, oxywipe S, ecolab,

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Monheim am Rhein, Germany). During the study, adherence to the cleaning and disinfection SOPs was audited on a regular basis by members of the infection control teams, and was constantly reported to be in the range of 90–100% in both hospitals.

Measurement of light

The energy of a photon is given by $E = h \bullet c/\lambda$, where h is the Planck constant, c is the speed of light, and λ is the wavelength. Light intensity is the number of photons which reach a surface with an area of 1 cm^2/s. Light intensity at the surfaces with photodynamic and control coatings was measured at different times in all rooms (AvaSpec-ULS2048L-EVO-RS, Avantes, The Netherlands). The mean of all measured values was 89 ± 57 $\mu W/cm^2$. The measured values comprise photons from artificial light sources (e.g. fluorescent tubes or LEDs) and natural sunlight (if windows exist) in each room. The measurement only considers the photons in the spectral range of photosensitizer absorption. In the field study, the rooms used for comparison of antimicrobial coatings and control coatings had comparable light conditions.

Sampling and quantification of bacteria

The bacterial counts on all included surfaces (N = 50 for each surface) of all rooms, were measured up to four times per week at the same time of day, for 3 months. Due to the extension of the study from 3 months to 6 months in the outpatient rooms and ward rooms at Hospital 1, the sample numbers for these rooms increased from 50 to 98.

The evaluation of bacterial counts was based on European standard EN 13697. TSA with Disinhibitor Plus Contact Plates (Ø 55 mm, Oxoid Germany GmbH, Wesel, Germany) were used within the APP Count-Tact applicator 3P for contact plates (bioMérieux Germany GmbH, Nürtingen, Germany). The applicator allows standardization of surface sampling in terms of time and pressure (500 ± 50 g during 10 ± 1 s). The applicator was used in accordance with the manufacturer's guidelines. After sampling, contact plates were incubated at 36 ± 1 °C. All tested surfaces that were not suitable for contact plates were sampled using a liquid-based collection and transport system (eSwab regular, Mast Diagnostica GmbH, Reinfeld, Germany). Counted values were converted into cfu/cm^2 depending on the size of the sampled area.

Bacterial identification

Along with the counting procedure, bacterial colonies on all plates were inspected visually in the microbiological laboratory. A small representative sample (approximately 1%) was used for further identification by matrix-assisted laser desorption/ionization time-of-flight spectrometry (MALDI-TOF, Bruker MicroFlex LT, Bruker Daltonik, Bremen, Germany and MALDI Biotyper Compass 4.1 with Database Version 7854). Score values calculated by the software were interpreted according to a cut-off of 1.7 for reliable identification to species level.

Susceptibility testing

For selected bacterial isolates, antibiotic susceptibility testing was performed using the EUCAST disc diffusion method (www.eucast.org). The colonies were suspended in sterile saline (0.85% NaCl) to the density of a 0.5 McFarland turbidity standard. The suspension was plated on Mueller–Hinton agar (Oxoid Germany GmbH, Wesel, Germany), and antimicrobial disks (BD BBL sensi-disc, BD Germany, Heidelberg, Germany) were applied to the surface. After incubation at 36 ± 1°C in air for 18 ± 2 h (24 h for enterococci and vancomycin), inhibition zones were read and interpreted according to EUCAST Breakpoint Table Version 9.0.

Statistical analysis

All bacterial counts are presented as mean ± standard deviation and were compared between photodynamic and control coatings using the non-parametric Mann–Whitney U-test or Kruskal–Wallis test. Bacterial counts were further dichotomized using the cut-offs >5 cfu/cm^2 and >2.5 cfu/cm^2. Absolute and relative frequencies are presented, and photodynamic and control coatings were compared using logistic regression models. Absolute and relative risk reductions for high bacterial counts on surfaces, as well as odds ratios with corresponding 95% confidence intervals (95% CI), were calculated as effect estimates. $P<0.05$ was considered to indicate statistical significance. All analyses were performed using SAS Version 9.4 (SAS Institute, Cary, NC, USA).

Results

Laboratory study

After drying on the coated surface, bacteria were irradiated with visible light (LED) at different radiant exposures (11–22 J/cm^2). The number of tested bacteria decreased on the photodynamic coating upon light exposure, and the reduction ranged from 2.0 ± 0.3 to 4.0 ± 0.3 log_{10} (Table I). When using ambient light conditions (LED 18 $\mu W/cm^2$), the bacterial count for *S. aureus* was found to reduce by 4.0 ± 0.1 log_{10} after 7 h.

Field study in hospitals: mean reduction of bacterial counts on surfaces

To analyse the antimicrobial potential of photodynamic coating under real-life conditions, comparable rooms were selected within the emergency departments of two hospitals. To avoid systematic bias, the number of patients in the emergency rooms at Hospital 1 were 258 (photodynamic coating) and 238 (control coating), respectively. The number of patients in the emergency rooms at Hospital 2 were 617 (photodynamic coating) and 657 (control coating), respectively.

In Hospital 1, outpatient rooms (dermatology) with and without photodynamic coating were visited by almost the same number of patients (15–18 patients per day) during the 6 months of the study, plus physicians and nurses. Furthermore, both ward rooms were occupied continuously by patients, with a mean stay of 4.8 days per patient. Physicians, nurses and visitors had access to the ward rooms, with comparable frequency for both rooms.

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Table I
Logarithmic reduction (mean ± standard deviation, log_{10}) of human pathogens on antimicrobial coatings in laboratory experiments (LED, 18 mW/cm^2; *N*=3)

Bacterial species	Radiant exposure (J/cm^2)	Recovery	Light control	Dark control	Photodynamic coating
Staphylococcus aureus	11	0.1 ± 0.4	0.2 ± 0.4	0.3 ± 0.4	4.0 ± 0.3
Staphylococcus epidermidis	11	0.0 ± 0.3	0.2 ± 0.0	0.1 ± 0.0	3.9 ± 0.4
Enterococcus faecalis	11	0.2 ± 0.1	0.1 ± 0.1	0.0 ± 0.0	3.0 ± 0.6
Pseudomonas aeruginosa	22	0.5 ± 0.3	0.9 ± 0.1	0.1 ± 0.2	2.0 ± 0.3

The measurement of bacterial counts on all surfaces in the study yielded a total of 1289 samples. For the control coating, the bacterial count ranged from 0 to 480 cfu/cm^2, with a mean value of 6.1 ± 24.7 cfu/cm^2. For the antimicrobial coating, the bacterial count ranged from 0 to 28 cfu/cm^2. The mean value for the antimicrobial coating (1.9 ± 2.8 cfu/cm^2) showed a significant reduction in microbial burden compared with the control coating (P<0.001; Table II).

Emergency rooms in both hospitals showed different bacterial counts for the control coating [4.9 ± 10.8 cfu/cm^2 (Hospital 1) and 9.6 ± 40.9 cfu/cm^2 (Hospital 2)], but the differences almost disappeared for the antimicrobial coating (2.0 ± 3.3 and 2.1 ± 3.2, respectively).

The antimicrobial coating reduced the bacterial count significantly on tested surfaces, with almost no difference between the data after 50 or 98 samples (Tables II and III). A linear regression model was applied for all 98 samples taken from antimicrobial surfaces in the outpatient and ward rooms of Hospital 1 (Table III). The linear regression of data showed a small change in mean cfu/cm^2 (slope a = +0.24% for outpatient rooms; slope a = −0.76% for ward rooms) (P<0.0001).

Field study in hospitals: reduction of bacteria to benchmarks

The frequency of numbers with bacterial counts >5 cfu/cm^2 or >2.5 cfu/cm^2 were significantly lower for antimicrobial surfaces compared with control surfaces. When applying a benchmark of 5 cfu/cm^2, the complete data yield an absolute risk reduction of 15.4% and a relative risk reduction of 67.3% for high bacterial counts on surfaces, with an odds ratio of 0.27 (95% CI 0.19–0.39; P<0.001) (Table IV). Considering a benchmark of 2.5 cfu/cm^2, the complete data yield an absolute risk reduction of 20.9% and a relative risk reduction of 48.0% for high bacterial counts on surfaces, with an odds ratio of 0.38 (95% CI 0.30–0.48; P<0.001) (Table IV).

Identification of bacteria

MALDI-TOF examinations yielded 21 different types of bacteria, including *Micrococcus luteus*, *S. epidermidis*, *Staphylococcus hominis*, *Staphylococcus lugdunensis*, *Staphylococcus warneri*, *Staphylococcus pasteuri*, *Staphylococcus caprae*, *Bacillus* spp, *Paenibacillus* spp. and *Psychrobacter* spp. *S. aureus* and *Enterococcus faecium* were also found, both of which showed standard antibiotic susceptibility. Five of 11 isolates of *S. epidermidis* showed a meticillin-resistant phenotype with sensitivity to rifampicin.

Discusssion

Usual disinfection procedures reduce the number of bacteria and other micro-organisms on inanimate surfaces for a short time. However, the bacterial burden on such surfaces increases again depending on the accuracy of regular surface disinfection, adherence to hand hygiene instructions, and the time interval between disinfection procedures (hours or days). In addition to routine disinfection schedules, self-sanitizing antimicrobial coatings could also be used to close the gap.

Laboratory study

The amount of singlet oxygen which is produced by a photosensitizer correlates with the light energy absorbed by the photosensitizer. The light-activated photodynamic coating produced a sufficient amount of singlet oxygen molecules to kill different bacterial species on its surface (Table I). Gram-negative bacteria need more radiant exposure values and therefore more singlet oxygen molecules, which has been shown previously [8,11]. In all experiments, bacteria were allowed to dry on the surface because relevant surfaces in healthcare units are also dry in cases of normal room humidity. Bacteria were still alive as shown by the recovery experiments even after 24 h. This is not surprising as bacteria may survive on inanimate dry surfaces for days to months [12].

In the case of other antimicrobial coatings, substances like copper, silver or biocidal products (e.g. isothiazolinones) have to be activated to affect the viability of bacteria, which requires fluid (e.g. water) on the surface. This might be the reason why in-vitro tests of other antimicrobial coatings were mainly performed on coated surfaces which were kept wet during testing [13–15]. In contrast, the dryness of an inanimate surface is not a problem for photodynamic coatings because gaseous singlet oxygen can easily diffuse from its generation

Table II
Bacterial counts on all coatings and in emergency rooms (mean number ± standard deviation, colony-forming units/cm^2)

	All coatings[a]	Emergency room hospital 1[b]	Emergency room hospital 2[c]
Photodynamic coating	1.9 ± 2.8 (*N*=694)	2.0 ± 3.3 (*N*=200)	2.1 ± 3.2 (*N*=200)
Control coating	6.1 ± 24.7 (*N*=595)	4.9 ± 10.8 (*N*=200)	9.6 ± 40.9 (*N*=200)

Non-parametric Mann–Whitney U-test: [a]P<0.001, [b]P=0.009, [c]P<0.001.

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Table III
Bacterial counts in other rooms (outpatient rooms and ward rooms) of Hospital 1 (mean ± standard deviation, colony-forming units/cm^2)

		Outpatient room[a]	Ward room[b]
Interim evaluation after 50 samples	Photodynamic coating	2.5 ± 3.0	1.2 ± 1.1
	Control coating	4.6 ± 3.9	3.4 ± 4.2
Final evaluation after 98 samples	Photodynamic coating	2.5 ± 2.7	1.4 ± 1.5
	Control coating	4.2 ± 3.5	3.2 ± 3.6

[a] Mann–Whitney U-test: $P<0.001$.
[b] Kruskal–Wallis test: $P=0.02$.

Table IV
Risk reduction for high bacterial counts on surfaces for benchmarks ≤2.5 and ≤5 colony-forming units (cfu)/cm^2 ($N=1289$)

Benchmark		cfu/cm^2 ≤2.5	Total	cfu/cm^2 ≤5	Total
Antimicrobial coating	Number	537	694	642	694
		77.4%	100.0%	92.5%	100.0%
Control coating	Number	336	595	459	595
		56.5%	100.0%	77.1%	100.0%
Total	Number	873	1289	1101	1289
		67.7%	100.0%	85.4%	100.0%

site in the coating to the bacteria present on the coating. In the case of photocatalytic coatings, substances like titanium dioxide are activated by ultraviolet radiation, with decreasing antimicrobial efficacy for visible light; this is a limitation when used indoors [14]. In contrast, the photodynamic process is very effective using visible light.

Reduction of bacterial counts on near-patient surfaces

Evaluation of bacterial counts on all control surfaces showed a large range from 0 to 480 cfu/cm^2 with a mean of 6.1 ± 24.7 cfu/cm^2 (Table II). On the contrary, on the antimicrobial surfaces, the bacterial count showed a lower mean value of 1.9 ± 2.8 cfu/cm^2, which was statistically significant ($P<0.001$) compared with the control surfaces. The reduced standard deviation correlates with a smaller range of bacterial counts for the antimicrobial surfaces (0–28 cfu/cm^2). As all surfaces were cleaned routinely according to the hospitals' hygiene schedules, the difference between antimicrobial and control coatings can be attributed to the photodynamic effect alone.

Regardless of the origin of the light in the rooms, light photons with an appropriate wavelength are absorbed by the photosensitizer when reaching the antimicrobial coating. The more light photons are absorbed in the photosensitizer, the more singlet oxygen is produced on the coating for bacterial killing.

The antimicrobial effect of the coating is stable for at least 6 months when comparing the results after 50 and 98 samples (Table III). Since the slopes of the linear regression indicate a small change in data of <1%, the change in antimicrobial efficacy should be considered negligible within the study time of 6 months.

The overall reduction in bacterial count seems to be an important indicator regarding transmission of pathogenic and/or multi-drug-resistant (MDR) bacteria. A hospital study showed that patient rooms were often contaminated with MDR bacteria, especially *Acinetobacter baumannii*, and that environmental contamination was the best predictor of MDR bacterial transmission [16].

During the field study, it was noticed that bacterial counts were higher on control surfaces (peak values up to 480 cfu/cm^2). On the antimicrobial surfaces, the peak values were significantly lower and less frequent ($P<0.001$). Aerobic colony counts of 2.5–5 cfu/cm^2 on hand touch sites and 1 cfu/cm^2 for hospital pathogens (e.g. meticillin-resistant *S. aureus*, vancomycin-resistant enterococci, *Clostridium difficile*, etc.) have been proposed and tested as microbiological benchmarks. Hygiene failures were defined as aerobic colony counts of >2.5 cfu/cm^2 and/or the presence of *S. aureus* on hand touch sites [2,17]. According to these proposed values, statistical analysis of study data yielded a relative risk reduction of 67% for high bacterial counts on surfaces when considering a benchmark of 5 cfu/cm^2 (odds ratio 0.27, $P<0.001$) (Table IV). Even for a smaller benchmark of 2.5 cfu/cm^2, the calculated risk reduction was 48% (odds ratio 0.38, $P<0.001$) (Table IV) for high bacterial counts on surfaces. In comparison, the efficacy of other antimicrobial coating technologies was investigated when using a photocatalytic coating with titanium dioxide and silver zeolite. One study showed gradual diminution of bioburden on the treated surfaces according to the benchmark of 2.5 cfu/cm^2 [18], and another study showed almost no effect [19]. A review in 2016 reported on 11 field studies which investigated the effect of copper, silver, metal alloy or organosilane-treated surfaces. The authors found weak and conflicting results with very low quality overall [20].

Bacterial identification

MALDI-TOF identification of a representative sample of bacteria revealed the presence of micrococci, bacilli and various coagulase-negative staphylococci (CoNS). It is well documented in the literature that skin commensals as well as pathogenic bacteria can be found on inanimate surfaces which are in frequent contact with staff or patients [2]. Only a few pathogens like *S. aureus* and *E. faecium* were identified. In

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addition to the well-known pathogenic, even multi-resistant, bacteria, CoNS should be regarded as pathogens of significance, and a recent study reported that the prevalence of multi-resistant CoNS is also increasing, ranging from 50% to 69% for various species [21]. Another study evaluated the involvement of CoNS in periprosthetic joint infections and found bacteria like *S. epidermidis*, *S. lugdunensis*, *S. warneri* and *S. hominis* [22]. *S. epidermidis* has evolved to become a formidable nosocomial pathogen with resistance to rifampicin, and reduced susceptibility to glycopeptide antibiotics, vancomycin and teicoplanin [23]. Thus, antimicrobial coatings should not only be discussed in connection with well-known pathogens causing severe infections (e.g. *S. aureus*), but may also prove beneficial in reducing the number of other potential pathogenic bacteria on surfaces.

Safety of coatings

The photodynamic process is a well-known mechanism that has been used clinically in the treatment of tumours and investigated for the killing of micro-organisms [10,24–26] for many years. In the present application, the photosensitizer inside the very thin coating generates gaseous singlet oxygen. The lifetime of singlet oxygen in air is short, and therefore the range of the biocidal singlet oxygen is <1 mm above the coated surface. Thus, no biocidal substance reaches other environments. Singlet oxygen is also produced along with medical drugs in various clinical applications (e.g. dermatology, ophthalmology), and has proven its safety for more than 20 years [24,25,27]. The production of singlet oxygen is safe for the skin [10] and other tissues such as the retina of the eye [27]. Other antimicrobial coatings continuously release metal ions, nanoparticles (e.g. copper, silver, titanium dioxide) and biocidal substances (e.g. isothiazolinon, chlorhexidine, triclosan, benzalkonium chloride) which might harm humans or accumulate in the environment and hence threaten humans or other animate beings [28–31].

Risk of biocide resistance

In light of possibly large and numerous surfaces in hospitals and other healthcare facilities, various bacteria and other micro-organisms are persistently exposed to the biocidal substances used. Therefore, it is important that the use of antimicrobial coatings does not contribute to the emergence of biocide resistance. In the case of photodynamic coatings, singlet oxygen causes unspecific damage in bacterial cells via peroxidation of many biomolecules like proteins and lipids. Singlet oxygen is not produced inside or taken up by bacterial cells that further prevent any onset of resistance mechanisms. Photodynamic mechanisms of action neither select for photodynamic resistance nor alter sensitivity to conventional antibacterial drugs. Therefore, it is very unlikely that the photodynamic approach will provoke resistance in bacteria [26].

In contrast, a number of well-known biocidal substances like chlorhexidine, triclosan and povidone-iodine have already provoked resistance in certain bacteria [32,33]. In addition, silver is known to provoke resistance in some bacteria [34], and some *Escherichia coli* and *P. aeruginosa* can develop resistance after repeated exposure [35]. Bacteria pre-exposed to sublethal doses of silver exhibited increased resistance to antibiotics (ampicillin and Pen-Strep) [36]. Exposure of *A. baumannii* to sub-inhibitory concentrations of copper allowed them to better adapt to and grow in high concentrations of copper. Genomic analysis revealed numerous putative copper resistance proteins that share amino acid homology with known proteins in *E. coli* and *P. aeruginosa* [37].

In conclusion, the field study demonstrated a reduced bacterial burden on surfaces treated with photodynamic coating that might contribute to patient safety. It supports the concept that a continuous reduction of pathogens, including MDR bacteria, on near-patient surfaces further supplements infection prevention strategies. The field study has some limitations because it was only performed in two hospitals and the antimicrobial activity of the coating was not assessed beyond the field study. As a next step, studies will be undertaken to evaluate the effect of the photodynamic coating on hospital-acquired infections, especially in high-risk areas such as intensive care or haemato-oncology units.

Conflict of interest statement

AE and WB are shareholders in TriOptoTec GmbH. The other authors report no conflict of interests.

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