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Nanosilver/DCOIT-containing surface coating effectively and constantly reduces microbial load in emergency room surfaces

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SUMMARY

Background: Colonization of near-patient surfaces in hospitals plays an important role as a source of healthcare-associated infections. Routine disinfection methods only result in short-term elimination of pathogens.

Aim: To investigate the efficiency of a newly developed antimicrobial coating containing nanosilver in long-term reduction of bacterial burden in hospital surfaces to close the gap between routine disinfection cycles.

Methods: In this prospective, double-blinded trial, frequently touched surfaces of a routinely used treatment room in an emergency unit of a level-I hospital were treated with a surface coating (nanosilver/DCOIT-coated surface, NCS) containing nanosilver particles and another organic biocidal agent (4,5-dichloro-2-octyl-4-isothiazolin-3-one, DCOIT), whereas surfaces of another room were treated with a coating missing both the nanosilver- and DCOIT-containing ingredient and served as control. Bacterial contamination of the surfaces was examined using contact plates and liquid-based swabs daily for a total trial duration of 90 days. After incubation, total microbial counts and species were assessed.

Findings: In a total of 2880 antimicrobial samples, a significant reduction of the overall bacterial load was observed in the NCS room (median: 0.31 cfu/cm^2; interquartile range: 0.00–1.13) compared with the control coated surfaces (0.69 cfu/cm^2; 0.06–2.00; $P < 0.001$). The nanosilver- and DCOIT-containing surface coating reduced the relative risk of a critical bacterial load (defined as >5 cfu/cm^2) by 60% (odds ratio 0.38, $P < 0.001$). No significant difference in species distribution was detected between NCS and control group.

Conclusion: Nanosilver-/DCOIT-containing surface coating has shown efficiency for sustainable reduction of bacterial load of frequently touched surfaces in a clinical setting.

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Introduction

Increasing numbers of infections due to multidrug-resistant bacteria globally have become one of the biggest challenges in modern medicine [1—3]. Besides the cost burden for the healthcare system, infections with difficult-to-treat micro-organisms are devastating for every patient, not only in orthopaedic surgery. Thus, management of nosocomial infections and their prevention play a crucial role in daily clinical life [4,5]. Furthermore, the ongoing coronavirus pandemic highlights the importance of developing new approaches and strategies to reduce harmful pathogens in nosocomial environments.

Besides pathogen transmission by personnel as well as contaminated medical products, contamination of surface areas with pathogens has been identified as an important source of infection [6]. Therefore, various national and international guidelines and recommendations have been developed over the past decades, in order to reduce antimicrobial burden in a clinical setting [7—9]. Especially for surface emphasis, newly developed agents and strategies have been implemented in clinical routine.

While research has focused on optimizing treatment guidelines — e.g. antibiotic treatment, improving sterility and hygiene concepts for medical staff — there has been comparatively little effort to improve surface disinfection [10]. In a recent review, Otter *et al.* showed that contaminated surfaces in medical facilities contribute to the transmission of several nosocomial pathogens [11]. Besides interventions to optimize surface disinfection, new technologies and concepts such as the integration of hydrogen peroxide fumigation, ultraviolet irradiation or antimicrobial surface coating with silver or copper and photodynamic coatings have been introduced [12—16]. The latter are still in early stages of development and many of them lack evidence to demonstrate their practical feasibility and effectiveness.

However, silver-coating is already used in medical devices such as central venous catheters, urinary tract catheters and orthopaedic implants and has been shown to significantly reduce implant-associated infections [17—19]. Especially in orthopaedic implants, initial data show promising results for silver coating to prevent infections, and silver coating is gradually being integrated into routine clinical practice for large prostheses [20,21].

Silver itself mediates its antimicrobial effects in various ways: by destabilizing bacterial membranes, by inhibiting growth via ionically mediated impairment of protein and enzyme metabolism, by inactivating or denaturing specific molecules as well as by directly damaging DNA molecules [22].

To follow up on these results, the objective of this study was to test a newly developed silver-containing antimicrobial surface coating for its efficacy in reducing bacterial load and diversity in a clinical application on frequently touched surfaces in an emergency department in order to close the gap between routine disinfection cycles.

Methods

Study design

This prospective study was designed to compare microbial load in two equally equipped rooms, one of which was treated with a surface coating containing antimicrobial agents and in the other room was treated with a coating missing the antimicrobial agents (nanosilver/DCOIT-containing coating versus control coating; see Figure 1). The study was performed from August 2018 to January 2019, including a 90-day data sampling period. Data collection and analyses were performed observer-blinded. The study was reported to the local ethics committee. No formal vote was necessary because no personalized data were processed in the context of this research.

Selection of the study site

The study was conducted at the interdisciplinary emergency unit of a German university medical centre (level-I hospital). Within the emergency unit, two identically equipped treatment rooms were selected for study conduction to minimize construction-dependent variations (room size, light conditions, equipment). Moreover, the treatment rooms were comparable with regard to frequency of occupancy, occupancy time and number of treated patients per day. Since only trauma patients and other patients assigned to surgical care were treated in the selected rooms, microbial load bias due to highly variable patient cases was minimized.

Pre-study observational and field-testing

For selection of the surfaces to be examined, field-testing of the microbial load of all objects and surfaces within the selected treatment rooms was conducted to identify highly contaminated surface areas. For this purpose, agar—contact plate testing for plane surfaces and swab testing for curved or small objects was performed. Sample collection was conducted every 2 h from 06:00 to 22:00 for seven consecutive days. Therefore, 63 samples were gathered from every test object and surface.

Evaluation of the field-testing results showed that microbial load and pathogen spectrum of most of the tested surfaces were comparable, so that four frequently used surfaces (surface of working desk, personal computer keyboard, countertop, and drawer of the bandage trolley) were selected for the main investigation.

Moreover, four time-points during daytime of highest occupancy of the emergency room were chosen for the final investigation, since there were only marginal daytime-dependent differences in the field-testing results. As a result of the field-testing, a standard operating protocol for sample collection was prepared including standardized application of pressure with the contact plates and swabs (see 'Sampling and microbiological analysis of samples').

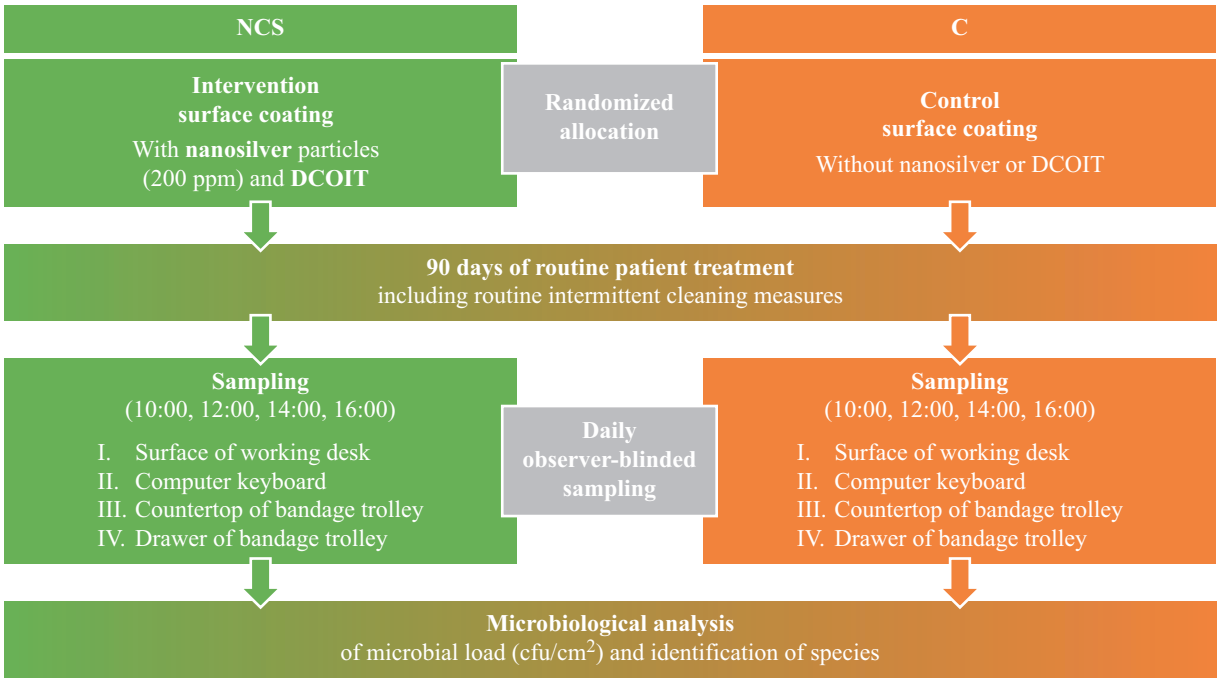

Figure 1. Study flow chart. Both the intervention room (nanosilver/DCOIT-containing surfaces, NCS) and the control room (C) were used in daily routine emergency patient care, whereas samples from four objects and surfaces were collected daily at four fixed times during the working day for a total trial duration of 90 days.

Surface coating method and surface disinfection

At the beginning of the trial period, one of the selected rooms was treated with an antimicrobial surface coating whereas the other room was coated with a control coating without the antimicrobial agents.

For coating of the surfaces in the intervention room (nanosilver/DCOIT-coated surface, NCS), a transparent acid siloxane-based sol—gel containing silver nanoparticles (200 particles per million, ppm) and DCOIT (4,5-dichloro-2-octyl-4-isothiazolin-3-one) as an additive biocide was used (SanPure® K130; RAS AG, Regensburg, Germany; BAUA registry number N-79342). The additive active agent is an organic biocide and is frequently used in antifouling paints, wood preservatives, and coating protectants. The product had already been approved by laboratory tests for effectiveness and skin tolerance (ISO 10993-1: 2009, ISO 10993-10: 2009, OECD TG 439) by the manufacturer prior to the present trial. The coating was sprayed on to the surfaces to be tested by the provider. According to the manufacturer's specifications, the coating thickness is about 1500 nm and coating is resistant to abrasion and scratching as well as chemically resistant to conventional cleaners and disinfectants. According to the manufacturer's data, the bacterial load on the coated surface is reduced by 75% after 1 h, 90% after 3 h, and 99.9% after 12 h.

In contrast to the NCS room, the test surfaces of the control room (C) were coated with the same base of the experimental coating (acid siloxane-based sol-gel) but without any nanosilver or DCOIT being added to the coating.

Routine disinfection processes of all point-of-care as well as all infection-relevant devices and surfaces were maintained throughout the study period. Intermediate routine cleanings, which are performed immediately after each patient treatment, could not be standardized, but were performed as per daily routine. The schedule for comprehensive basic cleaning of the emergency department was not changed during the conduct of the study and was performed in all emergency department treatment rooms 1 h before sampling began. Integrity of the antimicrobial coating was controlled once weekly via fluorescence examination by independent technicians using fluorescent particles added to the coating by the manufacturer.

Sampling and microbiological analysis of samples

Collection and analysis of the samples were performed observer-blinded, since differences between the coated and uncoated rooms were not apparent by visual inspection. According to the field-testing results, samples from four different objects and surfaces (surface of working desk, personal computer keyboard, countertop and drawer of the bandage trolley) were taken every 2 h from 10:00 to 16:00 (four samples per object or surface per day) from Monday to Friday in both the intervention room and the control room.

Samples were taken by two trained study nurses and analysed according to standard protocols (DIN EN ISO 18593, 14698, 13697). TSA with Disinhibitor Plus Contact Plates (diameter: 55 mm; Oxoid Germany GmbH, Wesel, Germany) were applied on the surfaces using the APP Count-Tact applicator 3P® (bioMérieux Germany GmbH, Nürtingen, Germany). The applicator was used according to the manufacturer guidelines. It allows standardized sampling of surfaces in terms of times and pressure (500 $\pm$ 50 g during 10 $\pm$ 1 s). Surfaces not suitable for contact plates (e.g. rough or non-plane surfaces) were sampled using a liquid-based collection and transport System (Copan eSwab® regular; Mast Diagnostica GmbH, Reinfeld, Germany).

After samples were taken in both study rooms, all samples were marked with an ID number and processed for microbiological testing. Contact plates were incubated for 48 h at 36 ± 1 °C. For swab samples 100 µL of the transport medium were plated on Columbia Agar containing 5% sheep blood and McConkey Agar (both Oxoid Germany GmbH, Wesel, Germany) for 48 h at 36 ± 1 °C, respectively.

Total microbial counts were assessed and converted to colony-forming units (cfu)/cm^2 and cfu/mL, respectively. Cultured micro-organisms were identified using matrix-assisted laser desorption/ionization time-of-flight spectrometry (MALDI-TOF; Bruker MicroFlex LT, Bruker Daltonik, Bremen, Germany and MALDI Biotyper Compass 4.1 software with database version 7854). Score values calculated by the software were interpreted according to a cut-off of 1.7 for reliable identification to the species level. In case of clinically relevant pathogenic bacteria, antibiotic susceptibility testing was performed using the EUCAST disc diffusion method (www.eucast.org).

Statistical analysis

In order to compare microbial counts between the NCS and the control group, the non-parametric Mann–Whitney *U*-test was used.

For further analyses, bacterial load was also dichotomized using reference values of >5 and >2.5 cfu/cm^2 as these values have previously been used as margins in the food processing industry and have also been suggested as reference values in a hospital environment [23]. Dichotomized data were presented using absolute and relative frequencies. Both groups were compared using the χ^2-test of independence. Absolute risk reduction (ARR), relative risk reduction (RRR) and, odds ratios (OR) are presented as further effect estimates. Statistical analysis was performed using SPSS software, version 26.0 (SPSS Inc., Chicago, IL, USA).

Results

During the entire study period of 90 days, the surface of the tested areas was always completely coated with the product during the weekly fluorescence examination. At no time was there any sign of coating decline or the need for recoating.

In all, 2880 single samples were collected from the four defined, frequently touched surfaces.

Total microbial load of all tested surfaces at all time-points was approximately half as high on nanosilver/DCOIT-coated surfaces (NCS; median: 0.31 cfu/cm^2; IQR: 0.00–1.13) compared with the control surfaces (median: 0.69 cfu/cm^2; IQR: 0.06–2.00; $P < 0.001$). Analysing only agar contact-plated samples of plane surfaces ($N = 1080$ for each group) and excluding curved surfaces such as handle bars, median bacterial loads were higher but the difference between the groups was also highly significant; median microbial loads could also be nearly halved by nanosilver/DCOIT-containing surface coating compared with the control surfaces (NCS: median: 0.56 cfu/cm^2; IQR: 0.19–1.50 vs control: median: 1.03 cfu/cm^2; IQR: 0.44–2.63; $P < 0.001$).

Analysing the different test surfaces, a significant reduction of microbial load on NCS was detected at all surfaces that were tested by agar-plate sampling (see Figure 2). Moreover, microbial loads were higher with surfaces that were frequently touched (e.g. personal working desk, computer keyboard surfaces) versus infrequently touched surfaces (e.g. bandage trolley).

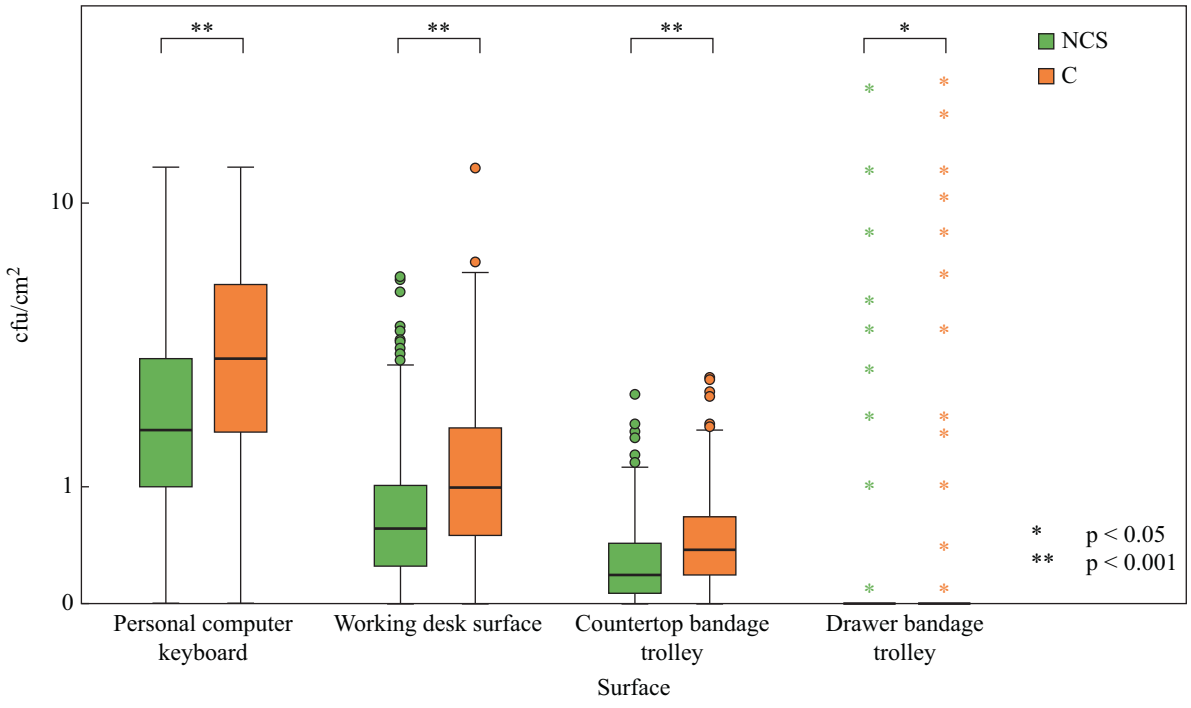

Figure 2. Box plots with logarithmic scale on the *y*-axis showing bacterial loads (in colony-forming units per cm^2) of the different tested surfaces in an emergency treatment cabin with nanosilver/DCOIT-coated surfaces (NCS) compared with a treatment room where the surfaces were treated with a control coating without antimicrobial agents (C).

The reduction of microbial load on the nanosilver/DCOIT-coated surfaces was independently observed at all time-points throughout a work day. Whereas total number of colony-forming units slightly though not significantly increased in both groups over the course of a day, a significant reduction of microbial burden in the nanosilver/DCOIT-coated surface (NCS) group was detected at every time-point compared with control coated surface group (see Table I).

The rate of bacterial counts of >5 cfu/cm^2 was significantly lower on NCS (53 out of 1440, 3.7%) compared with control (131 out of 1440, 9.1%; χ^2-test, $P < 0.001$). Therefore, NCS led to an absolute risk reduction (ARR) of 5.4% and a relative risk reduction (RRR) of 60% (OR: 0.38). When the reference value was set to >2.5 cfu/cm^2, the rate of high bacterial loads was again significantly lower in the NCS group (164 out of 1440, 11.4%) than in the control group (300 out of 1440, 20.8%; χ^2-test, $P < 0.001$) with ARR of 9.4%, RRR of 45%, and OR of 0.49.

In 102 samples, a confluent growth of bacteria on sample plates was detected at different surfaces, especially in samples that had been taken from the personal computer keyboard (94 out of 102 cases, 92.2%). Out of these samples with confluent growth from the personal computer keyboards, only 25 originated from the NCS group compared with 69 samples from the control coated group. Overall, the rate of these peak values was significantly higher in the control group (73/1440, 5.1%) compared with the NCS group (29 out of 1440, 2.0%; $P < 0.001$).

Bacterial and fungal isolates were identified to the species level. There was no significant difference concerning the relative abundance of species between the two groups (see Table II). The four most frequently detected bacterial genera were (in descending order): *Staphylococcus* spp., *Micrococcus* spp., *Bacillus* spp., and *Corynebacterium* spp. Within the staphylococci, *Staphylococcus epidermidis* and *Staphylococcus hominis* were the two most common species. *Staphylococcus aureus* was only detected in 30 out of 2880 samples (1.04%) with a non-significant lower frequency in the NCS group (11 out of 1440, 0.76%) compared with the control group (19 out of 1440, 1.32%) (χ^2, $P = 0.14$). Susceptibility testing showed no multidrug resistance among all cultured bacteria. Of the bacterial isolates, 97.2% were Gram-positive whereas only 2.8% were Gram-negative, with *Moraxella* spp. being the most common genus. In 19 out of 2880 samples *Aspergillus* spp. was detected (NCS: 10 out of 1440, 0.69% vs control: 9 out of 1440, 0.63%; $P > 0.05$). No other moulds or yeasts were cultivated.

Table II
Distribution of micro-organisms in samples taken from nanosilver/DCOIT-coated surfaces (NCS) and control surfaces

Micro-organisms	No. of samples		
	NCS	Control	Total
Acinetobacter spp.	3	3	6
Actinomyces spp.	0	1	1
Arthrobacter spp.	2	0	2
Bacillus spp.	299	281	580
Brevibacterium spp.	1	0	1
Brevundimonas spp.	0	2	2
Corynebacterium spp.	134	142	276
Curtobacterium spp.	1	1	2
Enterobacter spp.	0	1	1
Enterococcus spp.	2	2	4
Escherichia spp.	1	0	1
Exiguobacterium spp.	1	1	2
Jeotgalicoccus spp.	1	0	1
Kocuria spp.	14	14	28
Lactobacillus spp.	5	0	5
Lysinobacillus spp.	2	2	4
Micrococcus spp.	344	455	799
Moraxella spp.	38	38	76
Neisseria spp.	1	6	7
Paenibacillus spp.	12	9	21
Pantoea spp.	1	1	2
Paracoccus spp.	2	3	5
Pseudomonas spp.	3	3	6
Rhizobium spp.	0	2	2
Rothia spp.	1	3	4
Solibacter spp.	0	1	1
Staphylococcus spp.	997	1084	2081
Streptococcus spp.	5	10	15
Streptomyces spp.	1	0	1
Xantomonas spp.	1	0	1
Aspergillus spp.	10	9	19
Total	1882	2074	3956

DCOIT, 4,5-dichloro-2-octyl-4-isothiazolin-3-one.

Discussion

It is well known that routine disinfection procedures reduce the bacterial load of near-patient surfaces only for a certain period of time. In order to close the gap between routine disinfection procedures the additional integration of a nanosilver-

Table I
Time-dependent, selected bacterial load (cfu per cm^2) of nanosilver/DCOIT-coated and control coated surfaces at different time-points within the course of the day[a]

Time-point (no. of tests per group)	Microbial load (cfu/cm^2), median (IQR)		*P*-value
	Nanosilver/DCOIT-coated surface	Control coated surface	
10:00 ($N = 364$)	0.25 (0.00—1.13)	0.50 (0.06—1.98)	<0.001
12:00 ($N = 364$)	0.38 (0.00—1.06)	0.56 (0.06—2.00)	<0.001
14:00 ($N = 356$)	0.31 (0.00—1.25)	0.69 (0.06—2.06)	<0.001
16:00 ($N = 356$)	0.38 (0.00—1.13)	0.75 (0.00—2.05)	<0.001

DCOIT, 4,5-dichloro-2-octyl-4-isothiazolin-3-one; IQR, interquartile range.
[a] Due to technical problems, testing in the afternoon of one study day was not possible, so the total number of afternoon tests is lower.

and DCOIT-containing antimicrobial surface coating on frequently used surfaces in an emergency department treatment room was investigated and revealed the following key results.

- Microbial burden (cfu/cm^2) at all test sites and at all timepoints could significantly be reduced by nanosilver/DCOIT-containing surface (NCS) coating compared with non-antimicrobial-coated control (C) surfaces in an equally constructed treatment room.
- There was a significantly lower incidence of high bacterial burden in the NCS room compared with the control room (using both reference values of >5 and >2.5 cfu/cm^2).
- The use of nanosilver/DCOIT-containing surface coatings resulted in changes in the abundance of bacterial species and no multidrug-resistant pathogens were detected in cultured bacteria.

Hitherto, stainless steel has been the most commonly used surface material in hospital settings because of its appearance, durability, and ease of cleaning [24]. Unfortunately, this material has no antimicrobial properties, and difficult-to-treat bacteria (e.g. meticillin-resistant *Staphylococcus aureus* (MRSA), *Clostridioides difficile*) have been shown to survive on its surface for months [25]. Therefore, new surface materials have been developed, investigated and discussed in recent years. Although copper-containing surface coatings have shown promising results, integration in daily clinical routine is difficult and expensive [26,27]. Therefore, new technologies such as self-sanitizing antimicrobial coatings are needed to overcome the limitations of traditional cleaning and disinfection procedures.

In recent years, promising results have been reported from silver as an antimicrobial agent and silver-coated products have been established in medical applications in recent years, since silver is one of only a few materials approved by the US Food and Drug Administration (FDA). Experiments have demonstrated the antibacterial and antifungal effects of silver nanoparticles on various classes of pathogenic bacteria, viruses and fungi [11,24,28—31].

Therefore, silver has already made its way to clinical use in silver-coated central vein catheters with significant inhibitory effects against bacterial biofilms [32]. Nanosilver coatings have demonstrated antimicrobial efficacy in laboratory and clinical tests and are currently used for dental applications as well as antimicrobial coating for orthopaedic implants [17,33—37].

Although prospective randomized controlled trials are still missing in the latter case, nanosilver-coated implants can be considered a valuable option in high-risk patients with need for revision surgeries or oncologic background as existing studies with more than 500 patients demonstrate promising results [21,37]. As surface contamination with pathogens has been identified as a major source of nosocomial infections and evidence of the antimicrobial activity of nanosilver has increased, nanosilver-containing surface coatings have been developed for clinical use, but have not yet found their way into clinical application [6].

To our knowledge this is the first prospective randomized trial to investigate nanotechnology-based silver-containing surface coating in the clinical application in an emergency unit.

The comparison of two identically built treatment rooms that have been used side-by-side in a clinical real-time setting in an emergency department of a level-I hospital showed significantly lower mean values of bacterial counts at all times at all tested surfaces (see Figure 2). Since cleaning routines have not been altered during study duration and the control room was sprayed with the same surface coating product only lacking the two antimicrobial agents, the reduction of mean bacterial burden and lower total bacterial counts can be concluded as mediated by the tested nanosilver and DCOIT coating. The antimicrobial effect was detected both at different times of day and in a stable manner during the whole study period, since the integrity of the coating surface was maintained throughout the entire trial period, as observed in weekly fluorescence checks.

When excluding curved surfaces and only analysing agar contact-plate samples of plane surfaces, about 50% reduction of microbial burden was observed. Difficulties in cleaning processes as well as coating instabilities on curved surfaces or abstinence of activating humidity may be possible explanations for the reduced antimicrobial effects on nanosilver-coated handlebars.

Reference values of 5 and 2.5 cfu/cm^2 for aerobic bacterial counts were used, since these values are widely accepted as signs of hygiene failure and, moreover, higher levels of bacterial counts are more likely to be associated with the presence of virulent *S. aureus* and MRSA [23,38,39]. Compared with the control group, relative risk reductions of 60% and 45% by nanosilver/DCOIT-containing surface coating were observed using these reference values of 5 and 2.5 cfu/cm^2, respectively ($P < 0.001$).

Comparing these findings to other related trials, relative risk reduction seems to be similar in photodynamic coatings based on singlet oxygen at comparable surfaces (PC desk, PC keyboard, PC mouse, handlebar) [16]. Other photodynamic coatings were tested at different test surfaces (hospital beds, intensive care units) and showed conflicting results [40].

Concerning surface-coatings such as silver, copper or organosilane, the biggest meta-analysis conducted by Muller *et al.* has yet not shown substantial evidence for the reduction of antimicrobial burden [41].

Bacterial identification at species level showed that there was no significant difference in the bacterial spectrum between the experimental coating and the control coating group. Whereas most of the cultured bacteria display physiological skin and environmental micro-organisms, more virulent pathogens such as *S. aureus* were only detected in 1% of all samples. Instead, facultative pathogens such as coagulase-negative staphylococci (e.g. *S. hominis* and *S. epidermidis*) were more frequently found. These coagulase-negative staphylococci, however, play an important role in chronic surgical wound infections and chronic periprosthetic joint infections [42].

Besides demonstrating the antimicrobial effects of the experimental surface coating, the present study has some limitations. First, the experimental surface coating, by contrast with the control coating, contained two additional known antimicrobial agents (both nanosilver and DCOIT), so that the effect on the microbial load of the surfaces cannot be attributed to the silver content alone. The additive organic biocide 4,5-dichloro-2-n-octyl-4-isothiazolin-3-one (DCOIT) is known as an antimicrobial agent in coatings for plastic, metal, and wood surfaces, e.g. wood-preserving and antifouling paints. The biocidal effect is mediated by the formation of free radicals [43]. Recently, the biocidal effects of isothiazolones have prompted

experimental research for clinical application, due to their inhibition of biofilm formation [44]. To enhance the antimicrobial effect of the product, the manufacturing company combined both nanosilver particles and DCOIT in the coating used during the current study, which leads to some uncertainty about the agent causing the main antimicrobial effect.

Even though the effect of the tested product in reduction of microbial colonization was observed a few hours after the coating process and remained unchanged for the entire duration of data collection (90 days) without the need to renew the coating, the results can only be considered as short- to medium-term results. The overall durability of the coating and the duration of the antimicrobial effects are still unknown and will, thus, have to be investigated in further studies.

Furthermore, the present study results remain unclear, if the reduction of bacterial load (colonization) of emergency room surfaces also leads to a noticeable reduction of nosocomial infections. As nosocomial infections cause great costs for healthcare systems, the cost-effectiveness of nanosilver-containing surface coating depends on its ability to reduce nosocomial infections and not only surface contamination [45]. Therefore, the effect of reducing the levels of these pathogens on the incidence of hospital-acquired infections should be part of further studies on the efficacy of antimicrobial coatings.

In conclusion, the present study demonstrated for the first time the antimicrobial effect of a newly developed antimicrobial nanosilver- and DCOIT-containing surface coating in addition to routine cleaning in a clinical application in an emergency unit of a level-I hospital.

A significant reduction of the bacterial burden on all nanosilver/DCOIT-coated surfaces was achieved and the risk of high contamination could significantly be reduced by the coating. Further clinical investigations are needed to clarify the effect of nanosilver/DCOIT-coating-associated germ reduction on the occurrence of nosocomial infections.

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Conflict of interest statement
None declared.

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