Alesi Surgical Technologies INC
1539 Orchard Park Drive,
Houston,
TX 77077
www.alesi-surgical.com

September 30, 2025

Millicent Barajas, Executive Officer
Department of Industrial Relations
Division of Occupational Health and Safety
1515 Clay St., Suite 1901
Oakland, California 94612

Subject: Alesi Surgical Ltd.'s Comments on Cal/OSHA Rulemaking to Implement AB1007 Concerning Occupational Exposure to Plume in Health Care

Dear Ms. Barajas,

Alesi Surgical Ltd. ("Alesi") appreciates the opportunity to provide comments on Cal/OSHA's discussion draft to implement Assembly Bill 1007 (2023–2024) concerning occupational exposure to surgical plume in general acute care hospitals and ambulatory surgical centers. Alesi supports Cal/OSHA's objective of protecting healthcare workers from the hazards of surgical smoke. To achieve this goal, the final regulation should remain performance-based and technology-neutral, allowing healthcare facilities to select from all validated, FDA-cleared options, whether suction-based evacuators, electrostatic precipitators, or future innovations, so that each facility can adopt the approach that best integrates with its surgical practices and patient care models while protecting the health and safety of surgical personnel. To that end, Alesi recommends revising the definition of "plume evacuation system" to the more inclusive "plume control system," so that the definition will encompass validated non-evacuation-based technologies, such as electrostatic precipitation.

About Alesi and Electrostatic Precipitation Technology

Alesi is an international medical device company dedicated to enhancing the safety and efficacy of advanced surgical procedures. The company is particularly committed to protecting hospital personnel from surgical plume by serving as a member of the Association of periOperative Registered Nurses ("AORN") Smoke Policy Council.

In 2016, Alesi received U.S. Food and Drug Administration ("FDA") de novo authorization to market a novel medical device known as the Ultravision System, which is indicated for the

clearance of smoke and other particulate matter that is created during surgery, including laparoscopic surgery.[1]

The Ultravision System utilizes an electrode as a source of low-energy electrons – the Ionwand – which is introduced into the patient's body and remains in place during the surgical procedure. The emitted electrons create negative ions that transiently electrostatically charge the surgical smoke and turn it into precipitate, which is not released into the surgical environment.

In brief, electrostatic precipitation of surgical smoke prevents aerosolization into the operating room, which protects healthcare personnel from harmful exposure. To further illustrate how this technology functions in practice, we direct you to a video demonstration of the Ultravision™ system in laparoscopic surgery. *See* Ultravision™ in laparoscopic surgery.[2]

In addition to addressing the hazards of surgical plume, other benefits of electrostatic precipitation technology include an improved visual field, less gas volume needed for insufflation (i.e., introduction of gas to create additional working space for the surgeon), and fewer surgical interruptions to clean the camera lens or vent accumulated debris and gas.

Safety & Efficacy of Electrostatic Precipitators

Prior to approving the Ultravision System, FDA required extensive testing to maintain safety for both patients and healthcare personnel. This included chemical characterization and a toxicological risk assessment of the treated surgical smoke. These tests used both monopolar and ultrasonic surgical tools and measured chemical changes to surgical smoke after treatment. Additional studies compared the risk of retaining precipitated smoke versus smoke from standard dilution and purging methods. Results showed no additional patient risk beyond the current standard of care.[3]

Ultimately, FDA authorized the Ultravision System as the first electrostatic precipitator for surgical use, confirming that it clears smoke and other particulate matter that is created during surgery (thereby protecting healthcare personnel), without introducing new risks to patients.

Since introduction, the Ultravision System has been used in over 40,000 procedures across multiple countries including the USA, with no patient or operator adverse events reported.

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[1] See DEN150022. FDA's De Novo Classification Order is provided as **Attachment A** and is additionally available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN150022 (Last Visited September 26, 2025). The FDA has subsequently cleared other devices, and the 510(k) summaries are provided as **Attachment B** - FDA 510(k) Summary of Ultravision Visual Field Clearing System (K200035) and **Attachment C** - FDA 510(k) Summary of Ultravision2 (K240868).

[2] The video can be viewed at the following URL, which is also listed in **Attachment D:** https://www.alesi-surgical.com/ultravision-in-use/ Last Visited September 26, 2025).

[3] See **Attachment A** - FDA De Novo Decision Summary of Ultravision Visual Field Clearing System (DEN150022)

The Current State of Electrostatic Precipitators & Required Testing

FDA's authorization of the Ultravision System in 2016 established FDA Product Code PQM, thereby allowing other surgical smoke precipitators to gain FDA clearance by demonstrating that they (1) are substantially equivalent to another legally marketed (i.e., FDA cleared or approved) surgical smoke precipitator; and (2) satisfy FDA's special controls applicable to surgical smoke precipitators set forth in 21 CFR 878.5050.

Since that time, other surgical smoke precipitators have been developed and cleared by FDA for use in surgery. Pursuant to 21 CFR 878.5050, all FDA-cleared electrostatic precipitators must undergo extensive testing including chemical characterization and toxicological risk assessment of the treated surgical smoke, as well as animal simulated-use testing to demonstrate the device performs as intended under anticipated conditions of use.

In sum, electrostatic precipitators are thoroughly tested and evaluated by FDA prior to obtaining 510(k) clearance, and the technology is widely used, including in California, for its ability to address issues caused by intraoperative plume, including reducing the associated exposure risks for healthcare personnel.

How Electrostatic Precipitation Differs from Other Surgical Smoke Management Technologies

Electrostatic precipitation electrically charges surgical smoke such that it precipitates out of the air **at the surgical site**, thereby protecting healthcare works from harmful aerosols.

By contrast, a number of other surgical smoke management technologies such as passive filtering, active filtering, and circular filtration rely on a combination of aerosol evacuation and filtration. Generally, these technologies manage surgical plume by suctioning air or carbon dioxide (in laparoscopic and robotic surgeries) through an ultra-low particulate air ("ULPA") filter. Some technologies also utilize carbon filters. The effectiveness of these systems depends on nozzle placement, air/carbon dioxide flow rate, filter quality, operator settings, and a number of other factors. As a result, there is no standardized performance specification attributed to filter-based smoke evacuation technologies other than the specification of the ULPA filter.

Given these differences, electrostatic precipitation technology is widely used and can be preferred by surgeons due to its ability to improve visibility during laparoscopic surgery and reduce interruptions caused by the need to clean smoke from the intraoperative camera.[4,5]

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[4] See **Attachment E** - J. Answell, et. al., Electrostatic precipitation is a novel way of maintaining visual field clarity during laparoscopic surgery: a prospective double-blind randomized controlled pilot study. Surg Endosc (2014) 28:2057–2065.

[5] See **Attachment F** - D. Levine et. al., Electrostatic Precipitation in Low Pressure Laparoscopic Hysterectomy and Myomectomy. JSLS. 2020 Oct-Dec;24(4):e2020.00051.

With respect to the safety of healthcare personnel, electrostatic precipitation efficiently reduces the risk of bioaerosol exposure,[6] and can more effectively control surgical smoke when compared to traditional evacuation and filtration systems.[7] Moreover, electrostatic precipitation can provide much-needed protection for healthcare personnel by capturing *and inactivating* viral particles within aerosols that are generated during surgery.[8]

Given that electrostatic precipitation can significantly reduce occupational exposure to surgical plume,[9] an increasing number of surgical facilities, including in California, protect healthcare personnel from the hazardous effects of surgical plume by utilizing FDA-cleared electrostatic precipitation devices, which have undergone rigorous testing and therefore satisfy the protective objectives of AB 1007.

Alesi therefore believes that the draft language should be modified so it does not inadvertently exclude electrostatic precipitation or, indeed, any other technologies that are well-studied, FDA-cleared, and currently in use.

Need for Inclusive Draft Language

Alesi agrees with Cal/OSHA's proposal to require employers to "*establish a written surgical plume exposure plan, implement controls to prevent exposure to surgical plume to the greatest extent possible, and provide accompanying training.*" However, the current draft may be interpreted to exclude electrostatic precipitation devices among the various types of surgical plume control technologies that could be employed to manage risks associated with surgical smoke plumes.

Specifically, the draft could be read to require the use of evacuation and filtering systems to the exclusion of electrostatic precipitation or other FDA-cleared devices, even in situations where healthcare personnel choose to employ such alternatives for important safety reasons (e.g., to reduce the infectious potential of viruses; to address concerns about excessive carbon dioxide exposure to patients; or to minimize bioaerosol exposure associated with traditional evacuation and filter systems).

The draft rule currently defines a "plume **evacuation** system" to include smoke evacuators, plume scavengers, and local exhaust ventilators. While this list references both evacuators and scavengers, framing the regulatory definition under the heading "**evacuation** system" is

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[6] See **Attachment G** - J.R. Buggisch et. al., Experimental Model to Test Electrostatic Precipitation Technology in the COVID-19 Era: A Pilot Study, J Am Coll Surg. 2020 Dec;231(6):704-712.

[7] See **Attachment H** - D. Gohler et al., Performance of intraoperative surgical smoke management technologies for laparoscopic surgery: A comparative in-vivo pig study. Journal of Aerosol Science 177 (2024) 106309.

[8] See **Attachment I** - H.E. Preston et. al., Capture and inactivation of viral particles from bioaerosols by electrostatic precipitation. iScience. 2023 Aug 9;26(9):107567.

[9] See Alesi Surgical Performance Data: https://www.alesi-surgical.com/performance-data/ (Last Visited September 29, 2025).

unnecessarily narrow. Moreover, because the draft rule does not define "plume scavenger," it leaves ambiguity as to whether non-evacuation-based technologies such as electrostatic precipitation fall within the scope of compliance.

AB 1007 directs Cal/OSHA to establish standards "to protect nurses and other health care workers from noxious airborne contaminants or plume generated as byproducts during a variety of surgical, diagnostic, or therapeutic procedures in acute care settings."[10] It requires health facilities to use a "plume **scavenging** system," defined broadly to encompass technologies that, "when used in concert with other engineering controls and equipment, and to the extent technologically feasible, capture and neutralize plume at the site of origin and before plume can make ocular contact or contact with the respiratory tract of employees."[11]

Electrostatic precipitators are consistent with this statutory definition because they capture and neutralize plume at the site of origin. At the same time, because the draft regulation frames the requirement under the narrower title "plume **evacuation** system" and leaves "plume **scavenger**" undefined, there remains a risk that newer or alternative technologies could be excluded or overlooked. To avoid this confusion and ensure alignment with the statute's protective purpose, the regulation should adopt a broader, performance-based term such as "plume control system."

AB 1007 further requires Cal/OSHA to benchmark ISO 16571 and CSA Z305.13-13 and to consider OSHA and NIOSH recommendations. These standards are performance-based, focusing on outcomes rather than mandating any single method of control. Electrostatic precipitators align with this performance-based approach, even though their mechanism differs from suction and filtration.

Preservation of Rights and Objections on Statutory Scope

While electrostatic precipitation can reasonably be interpreted as a "plume scavenger" under AB 1007, Alesi is concerned that the combination of the statutory list and the draft regulation's heading ("plume **evacuation** system") could be read narrowly in the future, unintentionally excluding newer or alternative technologies. To the extent Cal/OSHA or others interpret the statutory or regulatory definition to exclude electrostatic precipitators, Alesi preserves its objection that such an interpretation would be inconsistent with AB 1007's protective purpose and with Cal/OSHA's obligation to adopt performance-based standards.

To avoid ambiguity and to ensure consistency with the statute's purpose, Alesi recommends revising the definition to use broader, neutral terminology such as "plume control system." This approach focuses on outcomes, i.e., the effective capture or neutralization of plume, rather than privileging one method (evacuation) over another, and ensures that healthcare facilities can adopt any validated technology that achieves the protective objective of AB 1007.

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[10] Cal. Assemb. B. 1007, § 1 (2023).

[11] Cal. Lab. Code § 144.9(a)(8)(2024).

Proposed Revisions

Alesi recommends revising the draft definition as follows:

> (12) ~~"Plume evacuation system (PES)" means smoke evacuators, laser plume evacuators, plume scavengers, and local exhaust ventilators~~ "Plume control system (PCS)" means any system, device, or technology that, when used in concert with other engineering controls and equipment, and to the extent technologically feasible, effectively captures, ~~and~~ removes, or neutralizes plume at the site of origin and before plume can make contact with the eyes or contact with the respiratory tract. Such systems may include smoke evacuators, laser plume evacuators, plume scavengers, local exhaust ventilators, electrostatic precipitators, or other FDA-cleared or ISO/CSA-validated technologies.

This definition maintains recognition of existing suction-based systems while expressly including electrostatic precipitators and other validated approaches.

Additional redlines to the regulation, reflecting this definitional change, are included in Appendix B.

Conclusion

Alesi respectfully submits these comments for the record and reserves the right to supplement them as the rulemaking proceeds. Alesi preserves all objections to any definitions or requirements that are unduly prescriptive or that exclude FDA-cleared or otherwise validated technologies that achieve equivalent or superior worker protection.

We commend Cal/OSHA for addressing the health hazards of surgical smoke and urge adoption of inclusive, performance-based language that ensures healthcare facilities have access to all validated protective technologies. We would welcome the opportunity to discuss these comments further with Cal/OSHA staff.

For Cal/OSHA's reference, Alesi has attached FDA marketing authorizations and supporting documents[12] that describe electrostatic precipitator technology in more detail.

Dr. Dominic Griffiths
CEO, Alesi Surgical

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[12] For additional information regarding the Ultravision System's use in laparoscopic, robitic, and open surgery, please see **Attachment J** - Alesi Ultravision US Brochure (Laparoscopic & Robotic Surgery) and **Attachment K** - Alesi Ultravision US Brochure (Open Surgery).

ENCLOSED:

Attachment A - FDA De Novo Decision Summary of Ultravision Visual Field Clearing System (DEN150022)

Attachment B - FDA 510(k) Summary of Ultravision Visual Field Clearing System (K200035)

Attachment C - FDA 510(k) Summary of Ultravision2 (K240868)

Attachment D – See https://www.alesi-surgical.com/ultravision-in-use/

Attachment E - Ansell J et al 2014

Attachment F - Levine et al, 2020

Attachment G - Buggisch et al, 2020

Attachment H - Gohler et al 2024

Attachment I - Preston et al 2023

Attachment J - Alesi Ultravision US Brochure (Laparoscopic & Robotic Surgery)

Attachment K - Alesi Ultravision US Brochure (OpenSurgery)

Attachment A

DE NOVO CLASSIFICATION REQUEST FOR ULTRAVISION™ VISUAL FIELD CLEARING SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Surgical smoke precipitator: A surgical smoke precipitator is a prescription device intended for clearance of the visual field by precipitation of surgical smoke and other aerosolized particulate matter created during laparoscopic surgery.

NEW REGULATION NUMBER: 21 CFR 878.5050

CLASSIFICATION: CLASS II

PRODUCT CODE: PQM

BACKGROUND

DEVICE NAME: ULTRAVISION™ VISUAL FIELD CLEARING SYSTEM

SUBMISSION NUMBER: DEN150022

DATE OF DE NOVO: May 26, 2015

CONTACT: Alesi Surgical
Suite 18, Cardiff Medicentre
Health Park, Cardiff
CF14 4UJ
United Kingdom

INDICATIONS FOR USE

The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during laparoscopic surgery.

LIMITATIONS

The sale, distribution, and use of the device are restricted to prescription use in accordance with 21 CFR §801.109.

The Ultravision™ Visual Field Clearing System is not intended for non-laparoscopic surgeries. The provided nonclinical and clinical studies did not address open surgeries of any kind.

The Ultravision™ Visual Field Clearing System should only be used by appropriately trained medical personnel.

PLEASE REFER TO THE LABELING FOR A MORE COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Ultravision™ Visual Field Clearing System is a device that precipitates surgical smoke generated during laparoscopic procedures to clear the visual field. The device components are summarized briefly in Table 1, below.

Table 1 – Device Components

Components of the Ultravision™ Visual Field Clearing System		
Model #	***Component Description***	***Purpose***
DAD-001-010	Standalone, battery-operated generator	Generation of energy source
DAD-001-024	Battery recharging station	Recharging of the reusable battery
DAD-001-003	Ionwand™ Sterile Pack consisting of Stainless steel active cable; the Ionwand™, Catheter and Trocar	Ionwand™: Delivery of the energy from the generator to the abdominal cavity. Catheter: Holds Ionwand™ in place during surgery Trocar: Introduction of the catheter into the abdominal cavity
DAD-001-006 (Solid) DAD-001-007 (Split)	Patient return adaptor	Provides common return path with electrosurgical generator

The standalone battery-operated generator unit is used to generate the energy source that is responsible for the electrostatic precipitation of smoke particles.

The Ionwand™ (Figure 1) is an active cable that terminates in filaments of medical grade stainless steel. The Ionwand™ is introduced into the abdomen of the patient and provides the source of the electrons that create the negative ions that transiently charge the surgical smoke particles. The Ionwand™ is held in place during the surgical procedure using a catheter. The catheter is introduced into the abdominal cavity using a laparoscopic trocar (Figure 2). The Ionwand™ and the preassembled catheter and trocar are supplied sterile together in one single-use disposable package (Figure 3). The catheter, trocar and Ionwand™ constitute the only tissue contacting components of the device.

Figure 1 – Ultravision™ Visual Field Clearing System Component: Ionwand™

Figure 2 – Ultravision™ Visual Field Clearing System Components: Catheter and Trocar.

Figure 3 – Packaged Sterile Ultravision™ Visual Field Clearing System Components: Ionwand™, Catheter and Trocar.

Reusable patient return adaptor ("PRA"). The Ultravision™ Visual Field Clearing System has been designed to operate with both instruments that require a patient return electrode (i.e., monopolar instruments) and those that do not (i.e., bipolar and ultrasonic instruments). To function, the Ultravision™ Visual Field Clearing System requires the use of a patient return electrode (not supplied). The PRA is only required when using a monopolar instrument. The PRA connects the Ultravision™ generator to the electrosurgical unit with which it is used, allowing both generators to share a common patient return pad. There are two variants of the

PRA; one to receive a "solid" patient return electrode connector and a second that receives a "split" patient return electrode connector.

BIOCOMPATIBILITY/MATERIALS

Biocompatibility testing was conducted on the Ultravision™ Visual Field Clearing System's patient-contacting components, as described in Table 3, below.

Table 2 – Biocompatibility Testing

Test	Purpose	Method	Result
In vitro Cytotoxicity	Determine if the Ionwand™, catheter, and trocar elicit cytotoxic responses	ISO 10993-5:2009 Biological Evaluation of Medical Devices: Tests for Cytotoxicity: in Vitro b(4) CCI :	Negative control b(4) : 0 Positive control b(4) : 4 Test article: Grade 1 (mild reactivity). PASS
Sensitization	Evaluate the potential for delayed dermal contact sensitization of the Ionwand™, catheter, and trocar	ISO 10993-10:2010 Biological Evaluation of Medical Devices- Part 10 (2010): Tests for Irritation and Skin Sensitization: Maximization test.	Scores of 0 for all negative control and test samples. (PASS)
Intracutaneous Reactivity	Determine whether extracts from the Ionwand™, catheter, and trocar will be irritating to the dermal tissue of the rabbit	ISO 10993-10:2010 Biological Evaluation of Medical Devices- Part 10 (2010): Tests for Irritation and Skin Sensitization: Maximization test.	Pass
Acute Systemic Toxicity	Evaluate acute systemic toxicity of the test article extract following a single intravenous or intraperitoneal injection in mouse	ISO 10993 standard- Part 11 (2006): Tests for Systemic Toxicity	Pass: No mortality during the study in mice injected with the test article extracts. All animals appeared clinically normal at the beginning and throughout the study
Endotoxin Levels	Detect and quantify bacterial endotoxin in the Ionwand™, catheter and trocar	ANSI/AAMI ST72:2011: Bacterial endotoxin -Test methods, routine monitoring and alternatives to batch testing	b(4) EU/device PASS

CHEMICAL CHARACTERIZATION OF TREATED SMOKE/RISK ASSESSMENT:

The purpose of this study was to assess potential chemical modifications and new chemical species resulting from Ultravision™ Visual Field Clearing System treatment of surgical smoke with the intention to identify and quantify any newly generated chemical species or confirm a lack of observable modifications to surgical smoke. Surgical smoke was generated in a simulated pneumoperitoneum using monopolar and ultrasonic tools. Surgical smoke was characterized using b(4) CCI Mass Spectrometry, b(4) CCI Mass Spectrometry, b(4) CCI X-ray and b(4) CCI b(4) CCI Spectroscopy. No measureable chemical modifications to surgical smoke were observed following treatment of surgical smoke.

A risk assessment was conducted to address the effects of the use of the Ultravision ™ Visual Field Clearing System on surgical smoke. As the chemical characterization did not result in identified chemical changes, the risk assessment addressed the precipitation of surgical smoke against the amount of surgical smoke that would be retained in the surgical

site with the current practices of dilution and purging of surgical smoke. The risk assessment addresses acute irritancy and tolerance; system acute toxicity, local chronic tolerances; distributed chronic toxicity; and distributed and local carcinogenicity and mutagenicity. The risk assessment concludes that the additional amount of surgical smoke (1-40%) that is likely to remain in the patient does not introduce any new risk to the patient beyond the current standard of care.

The provided chemical characterization and risk assessment support the conclusion that the use of the Ultravision™ Visual Field Clearing System does not create new safety concerns in the precipitation of surgical smoke.

SHELF LIFE/STERILITY

The sterilization process for the Ultravision™ Ionwand™ sterile package, which includes the Ionwand™, Catheter, and Trocar, has been validated in accordance with the requirements of the standard ISO 11135-1:2007, "Sterilization of health care products -- Ethylene oxide -- Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices." The b(4) CCI method was used, and the sterility assurance level was 1×10^{-6}.

The ethylene oxide and ethylene chlorohydrin residuals remaining on the device after sterilization and 7 days of aeration are below the limits described in the ANSI AAMI ISO 10993-7:2008(R)2012 for a limited exposure device.

The sterile components of the Ultravision™ Visual Field Clearing System (the Ionwand™, catheter and trocar) are packaged in custom designed b(4) blister trays with b(4) lids under ISO b(4) CCI conditions. b(4) CCI The Ultravision™ Generator (x1), Battery (x2), Recharging Station (x1), Patient Return Adaptor (SOLID, x1) and Patient Return Adaptor (SPLIT, x1) are provided non-sterile in a shipper.

Shelf Life: The applicant provided accelerated aging test reports for a three year sterile packaging claim and supporting real time test reports conducted over one year. Package inspections and product performance evaluations were conducted both at baseline and after aging and simulated shipping conditions.

The shelf life testing consisted of the following packaging and functional testing.

Packaging testing:

- Visual inspection of the package for obvious damage, deterioration, or defects
- Package seal strength Dye Penetration Testing

Functional product testing:

- Visual inspection of the product for obvious degradation or damage
- Plug secure connection test

The packaging and functional product testing is sufficient to support the three-year shelf life.

ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The submission contained test reports for:

- IEC 60601-1:2005 + C:109 + A2:10, Medical electrical equipment - Part 1: General requirements for basic safety and essential performance

- IEC 60601-1-2:2007: Medical Electrical Equipment - Part 2: General requirements for basic safety and essential performance - Collateral standard: Electromagnetic disturbances - Requirements and Tests

The report utilized a Risk Management process in accordance with: ISO 14971: - Application of risk management to medical devices, to determine the appropriate and applicable test clauses.

IEC 60601-1:
The sponsor addressed the differences in the tests performed versus the US requirements; the subject device passed all applicable requirements for AAMI/ANSI ES60601-1.

- The following tests were completed on the device as a system:
    - Power Input (IEC 60601-1 §4.11)
    - Humidity and Preconditioning (§5.7)
    - Determination of accessible parts (§7.1.2)
    - Markings:
        - Legibility (§7.1.2)
        - Durability (§7.1.3)
    - Voltage limitation (§8.4.4)
    - Means of Protection (§8.5.1)
        - Means of Patient protection (§8.5.1.2)
        - Means of Operator protection (§8.5.1.3)
        - Separation of Patient Connections (§8.5.2)
        - Working voltage measurement (§8.5.4)
        - Defibrillation proof applied parts (§8.5.5)
        - Energy reduction test (§8.5.5.2)
    - Leakage Current test (§8.7)
    - Dielectric Voltage withstand (§8.8.3)
    - Ball pressure (§8.8.4.1)
    - Thermal cycling test for spaces filled by insulating compound (§8.9.3)
    - Stability and Transportability (§9.4.2)
    - Acoustic Energy Measurement (§9.6.2.1)
    - Temperature test (§11)
    - Overflow, Spillage, Leakage, Cleaning, Sterilization and Disinfection, Harmful Ingress of Liquids (§11.6)
    - Abnormal Operation and Single Fault Conditions (§13)
    - Enclosure Mechanical Strength (§15.3)

    - Drop test (§15.3.4)
    - Mould stress relief (§15.3.6)
    - Reverse Battery connection / overcharging (§15.4.3)
- All tests passed.

IEC 60601-2-2:

- The following tests were completed on the device
    - Compatibility with third party Active Electrodes
        - Neutral Electrode cord attachment (§201.15.101.2)
        - Neutral Electrode cord connector, no conductive parts on Patient (§201.15.101.3)
- All tests passed.

IEC 60601-1-2:

- The test report confirms that there were no modifications made to the devices in order to achieve compliance.

- The system encompasses two components that require separate types of testing (battery charging station and the generator unit).
    - These two components work independently of each other and do not need to be tested as a system.

- The following tests were completed of the generator unit:
    - Electromagnetic radiation disturbance(§6.1.1.1)
    - Electrostatic Discharge (ESD) (§6.2.2.1)
    - Radiated RF Electromagnetic Fields (§6.2.3.1)
    - Conducted Disturbances, Induced by RF fields (§6.2.6.1)
    - Power Frequency magnetic fields (§6.2.8.1)
    - All tests passed.

- The following tests were completed of the battery charging station:
    - Electromagnetic radiation disturbance (§6.1.1.1)
        - Mains terminal disturbance
    - Harmonic Distortion (§6.1.3.1.1)
    - Voltage fluctuation and flicker (§6.1.3.1.2)
    - Electrostatic Discharge (ESD) (§6.2.2.1)
    - Radiated RF Electromagnetic Fields (§6.2.3.1)
    - Electrical fast transients and bursts (§6.2.4.1)
    - Surges (§6.2.5.1)
    - Conducted Disturbances, Induced by RF fields (§6.2.6.1)
    - Voltage Dips, short interruptions and voltage variations on power supply input lines (§6.2.7.1)
    - Power Frequency magnetic fields (§6.2.8.1)
    - All tests passed.

SOFTWARE

The first function of the software in the Ultravision™ generator is to generate the audible alerts through the speaker that indicate when the system is in 'proximity alarm' mode – i.e., in contact with tissue or another conductive surface and hence not able to operate at full smoke-clearing efficiency. This is a parallel alert to the visual indicators alongside the Ionwand™ and return sockets on the front of the generator, which are not under software control.

The second function of the software is to illuminate the fault light on the generator upper membrane in the situation where the speaker becomes accidentally disconnected from the main processor board of the generator.

The software is considered to have a moderate level of concern (LOC) because:

1) The software does not control the high potential voltage source. The hardware has built in back-off control.
2) The software only controls audible alarms as detected by the hardware.
3) The audible alarms are additional signals and risk controls to those implemented in hardware.
4) Under any condition where the hardware backs off the high potential source, this would reduce the effectiveness of the device clearing smoke and thus give a clear visual indication of under-performance to the user. This can be diagnosed independent of the audio alarm and resolved by the user.

It appears that the only harm failure the software could cause is ineffective clearing of the surgical smoke.

The applicant has provided adequate software documentation per FDA's "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices."

The sponsor has tested its specifications of the alarm both under fault and normal conditions and the software functioned according to specification. Therefore, based on the traceability analysis, all identified hazards are properly mitigated.

PERFORMANCE TESTING – ANIMAL

A safety and simulated use performance validation of the Ultravision™ Visual Field Clearing System was conducted in a GLP animal study. Simulated laparoscopic surgeries (50-100 minutes in duration) were performed on porcine omentum using monopolar, bipolar and ultrasonic electrosurgical instruments, followed by 28 day recovery period. Histology, coagulation and clinical chemistry were evaluated for preoperative, immediate post-operative and 28 day post-operative conditions.

The study had the following objectives:

- Demonstration of the functionality of the Ultravision™ Ionwand™ trocar/ introducer assembly

- Demonstration of the ability of Ultravision™ Visual Field Clearing System to maintain a smoke free laparoscopic surgical field during normal use of monopolar, bipolar and ultrasonic electrosurgical cutting and ablation devices.
- Evaluation on anesthetic control of the subject device.
- Evaluation of effects on pneumoperitoneum
- Verification of alarm if Ionwand™ touches tissue/organs
- Evaluation of effect of device on hematology, clinical chemistry and coagulation

Acceptance criteria for the study were qualitative verification of performance and usability, through observed clearance of the visual field and an absence of observed clinical chemistry or histology concerns.

The results of the study indicated that the device functions as intended without usability concerns and that there were no identified clinical chemistry concerns.

The study was concluded to be adequate to demonstrate performance of the device and supports safe use of the device.

SUMMARY OF CLINICAL INFORMATION

The applicant completed a randomized, double-blinded, controlled, prospective trial consisting of 30 patients with six weeks of follow-up on 25/30 enrolled patients. The 30 patients underwent elective cholecystectomy at a single site with an active device and a de-activated control device to blind the surgeon. The primary endpoint of the study was the maintenance of a clear visual field during surgery. Secondary endpoints included patient safety (based on details of adverse events and bloodstream measurement of carboxyhemoglobin before and after surgery), pain score at discharge, and number of times a procedure was interrupted due to impairment of visual field by presence of particulates or smoke. Additional secondary endpoints were included in the study as potential metrics of device effectiveness, but these metrics were not considered necessary to support granting of this *de novo* request.

All patients in the study had a single-use sterile Ionwand™ placed percutaneously by the surgeon. The Ultravision™ generator was switched on throughout surgery. All surgical procedures were video-recorded using a direct output link from the laparoscopic camera in use to a digital video recorder. Relevant events of note and any problems associated with the use of the Ultravision™ Visual Field Clearing System that occurred during surgery were recorded by an independent member of the research team present.

All patients had a 6-week postoperative visit and assessment by their surgeon. At this visit patients were asked about postoperative pain, nausea, infection and medications taken. Each patient indicated their pain on a 100mm visual analog scale (VAS).

The following results were provided:

Primary Endpoint: The Ultravision™ Visual Field Clearing System was determined to be effective at maintaining a clear visual field during the surgeries. The surgeons and

reviewing panel rated the treatment group to have a higher mean proportion of procedures with effective visibility than the control group.

Secondary Endpoints: There were no adverse events that could be attributed to the device. There was no detectable difference in either Carbon Monoxide (CO) or Methemogloblin (MetHb) levels between the two groups of patients both pre- and post-surgery. Pain scores were similar between treatment and control groups.

Treatment and control groups both had procedure interruptions, but in the treatment group there were eight procedures that had no interruptions. In the control group, no cases were completed without interruptions resulting from impairment of the visual field. The frequency with which the surgeon needed to remove the laparoscopic camera for cleaning was also different between the two groups of patients. In 85% of the procedures during which Ultravision™ Visual Field Clearing System was active, there was no requirement to remove the camera for cleaning. However, in the control group, only 35% of the procedures could be completed without camera cleaning.

This study confirmed safe performance of the device in a clinical setting as demonstrated by the controlled clinical trial, and contributed to the benefit/risk assessment.

Pediatric Extrapolation

In this *de novo* request, existing data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The labeling is sufficient and meets the requirements of 21 CFR 801.109. The user manual contains the indications for use, summary device description, warnings and precautions, instructions for use, instructions for device maintenance, troubleshooting instructions, shelf life, and information related to electromagnetic compatibility.

RISKS TO HEALTH

Table 4 below identifies the risks to health that may be associated with use of the Surgical smoke precipitator and the measures necessary to mitigate these risks.

Table 4 – Identified Risks to Health and Mitigation Measures

Identified Risk	**Mitigation Measures**
Electrical shock	Electrical safety testing Labeling
Electromagnetic interference with other devices	Electromagnetic compatibility testing Labeling
Infection	Sterilization validation Shelf-life validation Labeling
Adverse tissue reaction	Biocompatibility evaluation

Tissue injury **S**	Animal testing Software verification, validation, and hazard analysis Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the Surgical smoke precipitator is subject to the following special controls:

1. Adverse tissue reaction must be mitigated through the following:
   a. Chemical characterization and toxicological risk assessment of the treated surgical smoke.
   b. Demonstration that the elements of the device that may contact the patient are biocompatible.
2. Electrical safety and electromagnetic compatibility testing must demonstrate that the device performs as intended.
3. Software verification, validation, and hazard analysis must be performed.
4. Performance data must demonstrate the sterility of the patient contacting components of the device.
5. Performance data must support the shelf life of the sterile components of the device by demonstrating continued functionality, sterility and package integrity over the identified shelf life.
6. Animal simulated-use testing must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
   a. Device must be demonstrated to be effectively inserted, positioned and removed from the site of use.
   b. Device must be demonstrated to precipitate surgical smoke particulates to clear the visual field for laparoscopic surgeries.
   c. Device must be demonstrated to be non-damaging to the site of use and animal subject.
7. Labeling must identify the following:
   a. Detailed instructions for use.
   b. Electrical safety and electromagnetic compatibility information.
   c. A shelf life.

BENEFIT/RISK DETERMINATION

The risks of the device are based on nonclinical laboratory, animal studies, and the clinical study described above. There were no device-related adverse events during the clinical study. Additionally, there was no detectable difference in either CO or MetHb levels between the two groups of patients both pre- and post-surgery despite greater volume of gas administered in the control group for the 30 patient trial.

The probable benefits of the device are also based on the nonclinical laboratory, animal, and clinical study described above. The probable benefits are:

1. Improved visual field

2. Less gas volume needed for insufflation
3. Less frequent need to stop procedures to clean the camera lens or vent accumulated debris and gas.

The subject device does not directly benefit the patient. However, the device appears to benefit surgeons performing laparoscopic procedures through maintenance of a clear visual field. The use of this device may allow the surgeon to proceed without having to stop procedures to clean the camera lens and/or vent the accumulated debris.

Patient Perspectives

Patient-reported pain scores were recorded for both treatment and control groups in the clinical trial. Pain scores were based on the VAS scale and were similar between both groups.

Benefit/Risk Conclusion

Maintaining a clear visual field is critical during laparoscopic procedures. Use of this device may allow the surgeon to proceed without having to stop procedures to clean the camera lens and/or vent the accumulated debris. No adverse events were attributed to the device in the clinical study.

In conclusion, given the available information above, the data support that for precipitation of surgical smoke for laparoscopic procedures, the probable benefits outweigh the probable risks for the Ultravision™ Visual Field Clearing System. The device provides benefits and the risks can be mitigated by the use of general and the identified special controls.

CONCLUSION

The de novo request for the Ultravision™ Visual Field Clearing System is granted and the device is classified under the following:

Product Code: PQM
Device Type: Surgical smoke precipitator
Class: Class II
Regulation: 21 CFR 878.5050

Attachment B

May 4, 2020

Alesi Surgical Ltd.
℅ Michele Lucey
Regulatory Affairs Advisor
Lakeshore Medical Device Consulting LLC
128 Blye Hill Landing
Newbury, New Hampshire 03255

Re: K200035
Trade/Device Name: Ultravision Visual Field Clearing System
Regulation Number: 21 CFR 878.5050
Regulation Name: Surgical Smoke Precipitator
Regulatory Class: Class II
Product Code: PQM
Dated: January 31, 2020
Received: February 4, 2020

Dear Michele Lucey:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

CAPT Elizabeth F. Claverie, MS
Assistant Director
DHT4B: Division of Infection Control
and Plastic Surgery Devices
OHT4: Office of Surgical
and Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

K200035

Device Name

Ultravision™ Visual Field Clearing System

Indications for Use *(Describe)*

The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during surgery, including laparoscopic surgery.

The Ultravision™ 5mm Trocar component establishes a path of entry for instruments used in laparoscopic surgery.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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K200035 510(K)
SUMMARY
TRADITIONAL
As required by 21 CFR 807.92

Submitter Information:

Submitter's Name:	Alesi Surgical Ltd
Address:	Cardiff Medicentre Heath Park Cardiff CF14 4UJ UK
Telephone: Fax:	+44 (0) 2920291022 +44 (0) 2920750239
Contact Person:	Michele Lucey Lakeshore Medical Device Consulting LLC. 128 Blye Hill Landing. Newbury, New Hampshire 03255
Telephone:	603-748-1374

Date Prepared:	4th May 2020
Device Trade Name:	Ultravision™ Visual Field Clearing System
Common Name	Surgical Smoke Precipitator
Classification Name:	21CFR 878.5050
Regulatory Class:	Class II
Product Code(s):	PQM
Predicate Device:	Ultravision™ Visual Field Clearing System (K182053)
Reference Devices:	1. Smoke Evacuator pencil system comprising of Valley Lab Button switch pencil E2516H (K914400) fitted with a Buffalo Penadapt tubing set (PA 2010) (K000904) and Medtronic Rapidvac smoke evacuation generator (K142335) 2. Medcare Yankauer Suction device (K954869)

Indications for Use:

The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during surgery, including laparoscopic surgery. The Ultravision™ 5mm Trocar component establishes a path of entry for instruments used in laparoscopic surgery.

Device Description:

The Ultravision™ Visual Clearing System removes surgical smoke and particulates from the visual field by means of electrostatic precipitation.

The System consists of the Ultravision Generator, the Ionwand Sterile Pack, and the Ultravision 5mm Trocar. The Ionwand is connected to the energy source and is then introduced into the body cavity near the smoke generating electrosurgical device. The Ultravision™ 5mm Trocar is intended for use only with the Ultravision™ Visual Field Clearing System to introduce the Ionwand while providing a pathway for laparoscopic instruments through one 5 mm trocar incision. The trocar may be used with or without the Ionwand component of the system. The system is powered using a rechargeable battery or through mains power. Accessories include the rechargeable battery, battery recharging station, mains converter power supply, mains converter, power supply unit, and patient return adaptor.

The purpose of this submission is to add a new indication for use in open surgical procedures.

Technological Characteristics Comparison Table:

Shown below is a comparison of the subject device with the predicate device.

Comparison Chart			
Feature/ Specification	**DEVICE NAME** Ultravision™ Visual Field Clearing System	**PREDICATE DEVICE** Ultravision™ Visual Field Clearing System	**Comparison**
Regulatory Clearance/ Approval Reference	K200035	K182053	N/A
Product Code	PQM	PQM	Same
Regulation Number	21 CFR 878.5050	21 CFR 878.5050	Same
Regulation Name	Surgical Smoke Precipitator	Surgical Smoke Precipitator	Same
Mechanism of Action	Electrostatic precipitation	Electrostatic precipitation	Same
Where used (environment)	Operating Room	Operating Room	Same
Anatomical Sites	General and laparoscopic procedures	Abdominal sites - laparoscopic procedures	Similar

Comparison Chart			
Feature/ Specification	**DEVICE NAME** Ultravision™ Visual Field Clearing System	**PREDICATE DEVICE** Ultravision™ Visual Field Clearing System	**Comparison**
Intended Use	The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during surgery, including laparoscopic surgery The Ultravision™ 5mm Trocar component establishes a path of entry for instruments used in laparoscopic surgery.	The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during laparoscopic surgery. The Ultravision™ 5mm Trocar component establishes a path of entry for instruments used in laparoscopic surgery.	Similar
Software	Yes – identical to predicate	Yes	Same
Alarms	Yes – identical to predicate	Yes	Same
Accessories	Yes, identical to predicate	Yes	Same
Dimensions	Identical	Identical	Same
Materials	Identical	Identical	Same
Generator Output	9.8KV dc (No Change)	9.8KV dc (No Change)	Same
How Supplied	Non-sterile generator. Sterile Consumable (Ionwand) Non-sterile accessories. Identical	Non-sterile generator. Sterile Consumable (Ionwand) Non-sterile accessories. Identical	Same
Biocompatibility	Meets ISO 10993 Part 5,10 and 11	Meets ISO 10993 Part 5,10 and 11	Same
Sterilization	Ethylene Oxide	Ethylene Oxide	Same
Sterility Assurance Level	10^{-6}	10^{-6}	Same

Summary of Non-clinical Testing:

The system has been previously updated for mains power (K182053) and accordingly new electrical safety and electromagnetic compatibility tests have been successfully completed.

There are no changes to the materials and processing of patient contact materials from the submissions in DEN150022 and K170178, consequently no additional biocompatibility testing is required.

Tests carried out to support the added indication for use in open surgical procedures includes the following:

Name of the Test	Purpose	Acceptance Criteria	Results
Cytotoxicity ISO 10993-5	To analyze the potential of the test article to induce a cytotoxic effect	Must not cause cell lysis or toxicity greater than a grade of 2 (mild reactivity)	Reactivity of grade 1 was observed – Pass
Intracutaneous Irritation ISO 10993-10	To analyze the potential of the test article to induce a local irritation response	No evidence of significant intracutaneous irritation	No evidence of intracutaneous irritation - Pass
Systemic Toxicity ISO 10993-11	To analyze the potential of the test article to induce a systemic response	No evidence of significant systemic toxicity or mortality after test article extracts injection	No evidence of systemic toxicity – Pass
Maximization Sensitization ISO 10993-10	To analyze the potential of the test article to induce a sensitization or allergic response	No evidence of induced delayed sensitization	Not a sensitizer - Pass
Performance Test 1 Simulated Use	Comparison of smoke clearing characteristics of Ultravision versus other smoke clearing devices	Must be considered at least equivalent to comparators	Results of the evaluation demonstrated that Ultravision was at least equivalent to the comparator devices - Pass
Performance Test 2 Risk Assessment comparing the risks associated with open procedure use versus laparoscopic use	Evaluation of device use in an oxygen rich (open) environment considering ozone generation, and tissue damage, includes empirical testing on ozone generation	The risks associated with the use of Ultravision in an open procedure must not be greater than those for a laparoscopic procedure. Ozone generation must comply with 21 CFR Part 801.415.	There were no new risks associated with the use of Ultravision in an open procedure; risks were found to be lower. The time weighted average for ozone production was below acceptable limits - Pass

Performance Test 1

A comparison study was conducted under simulated use conditions to demonstrate that the Ultravision Visual Field Clearing System when used in open procedures provides equivalent performance when compared to the reference device. To support this, a human factors evaluation was also conducted during simulated surgery by actual users (surgeons). The users compared the Ultravision device to an electrosurgical pencil equipped with suction tubing and provided feedback comparing the Ultravision to a hand-held suction device (reference devices).

It was concluded from this feedback that in terms of surgical workflow, ease of use and risks, that the Ultravision system was considered equivalent to the reference device.

Performance Test 2

It was recognized that a potential risk of the system being used in an oxygen rich (open) environment might be the production of ozone. Accordingly, the level of ozone generation in a worst-case model was analyzed. Risk assessment was performed to address the expected relative levels of tissue damage and injury when moving from the original cleared laparoscopic environment to the proposed open environment. This was assessed over six attributes namely, principle of operation, Ultravision Settings, Ultravision components to be utilized to clear surgical smoke, surgical technique, principal electrosurgical modalities used with Ultravision and finally the volumes and composition of smoke produced by electrosurgical devices to be used with Ultravision. This concluded that the risk from open surgery was lower than that associated with the use of Ultravision in its current cleared laparoscopic indication.

Conclusion

Based on a review of bench top assessments, comparison of the device classification, intended use, operating principle, technological characteristics, sterility, and biocompatibility the subject device is as safe, as effective, and performs as well as or better than the legally marketed predicate device, K182053.

Attachment C

August 12, 2024

Alesi Surgical Limited
Pravin Patel
Regulatory & Quality Manager
Cardiff Medicentre, Heath Park, Cardiff, CF14 4UJ
Cardiff,
United Kingdom

Re: K240868
Trade/Device Name: Ultravision2™ IonPencil
Regulation Number: 21 CFR 878.5050
Regulation Name: Surgical Smoke Precipitator
Regulatory Class: Class II
Product Code: PQM, GEI
Dated: March 28, 2024
Received: March 29, 2024

Dear Pravin Patel:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Stephen A. Anisko -S

Digitally signed by Stephen A. Anisko -S
Date: 2024.08.12 14:11:51 -04'00'

for: Christopher Dugard
Assistant Director
DHT4C: Division of Infection Control
and Plastic and Reconstructive Surgery Devices
OHT4: Office of Surgical
and Infection Control Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K240868

Device Name
Ultravision2™ IonPencil

Indications for Use *(Describe)*

The Ultravision2™ System is indicated for use in surgery including laparoscopic surgery.

- The Ultravision2™ Generator is intended to interface directly with the electrosurgical generator and serve as a pass-through for HF energy to HF electrosurgical instruments, to manage surgical smoke produced by energy-based instruments, and is indicated for use in surgery including laparoscopic surgery.

- The Ionwand™ Pack is intended to be used to manage surgical smoke and is indicated for use in surgery including laparoscopic surgery.

- The Ultravision™ 5mm Trocar is intended to be used to establish a path of entry for instruments and includes an Ionwand to manage surgical smoke, and is indicated for laparoscopic surgery.

- The Integrated Monopolar L-Hook (H/S)™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during laparoscopic surgical procedures, and is indicated for use in laparoscopic surgery.

- The IonPencil™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during general surgical procedures, and is indicated for use in surgery.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

K240868

510(K) SUMMARY
TRADITIONAL
As required by 21 CFR 807.92

Submitter Information:	
Submitter's Name:	Alesi Surgical Ltd
Address:	Cardiff Medicentre Heath Park Cardiff CF14 4UJ UK
Telephone:	+44 (0) 2920291022
Contact Person:	Pravin Patel
Date Prepared:	**August 9th, 2024**
Device Proprietary Name:	Ultravision2™ IonPencil
Common Name:	Surgical Smoke Precipitator
Classification Name:	Surgical Smoke Precipitator
Classification Regulation:	21 CFR 878.5050
Product Code:	PQM
Common Name:	Electrosurgical accessory
Classification Regulation:	21 CFR 878.4400
Product Code:	GEI
Regulatory Class:	Class II
Predicate Device:	Ultravision 2 System including Integrated Monopolar L-Hook (H/S) (K231298) Ultravision™ Visual Field Clearing System (K200035) Megadyne Pencil (K965054) and Megadyne EZ Clean Electrosurgical Electrode (K081791)

Indications for Use:

The Ultravision2™ System is indicated for use in surgery including laparoscopic surgery.

• The Ultravision2™ Generator is intended to interface directly with the electrosurgical generator and serve as a pass-through for HF energy to HF electrosurgical instruments, to manage surgical smoke produced by energy-based instruments, and is indicated for use in surgery including laparoscopic surgery.

• The Ionwand™ Pack is intended to be used to manage surgical smoke and is indicated for use in surgery including laparoscopic surgery.

• The Ultravision™ 5mm Trocar is intended to be used to establish a path of entry for instruments and includes an Ionwand to manage surgical smoke, and is indicated for laparoscopic surgery.

• The Integrated Monopolar L-Hook (H/S)™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during laparoscopic surgical procedures, and is indicated for use in laparoscopic surgery.

• The IonPencil™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during general surgical procedures, and is indicated for use in surgery.

Device Description/Technological Characteristics:

The Ultravision2™ System is a multifunctional system that synchronizes visual field clearing with the activation of smoke-producing electrosurgical devices. The system interfaces with commercially available electrosurgical instruments. The Ultravision2™ Generator connects directly to a commercially available electrosurgical generator (ESU) and passes the RF energy through to the desired electrosurgical instrument connected to the Utravision2™ Generator. The Ultravison2™ System is able to automate the activation of the Ionwand for visual field clearing to the activation of the electrosurgical device to synchronize visual field clearing with the generation of smoke.

The components of the overall system will be:

- Ultravision2™ system comprising:
    - Ultravision2™ generator
    - Link cables (x4)
    - Power cable
    - Equipotential cable
- IonPencil™ accessory
- Integrated Monopolar L-Hook(H/S)™ accessory
- Ionwand™ accessory
- Ultravision™ 5mm Trocar accessory

The IonPencil™ is a bifunctional open surgery device that combines proprietary smoke management (via visual field clearing) and monopolar HF tissue cutting and coagulation in a single device. It's addition to the Ultravision 2 System adds the general open procedure capability to the Ultravision2™ indications of use along with the new single use accessory.

The IonPencil™ can only interface with the Ultravision2 generator which connects directly to a commercially available electrosurgical generator (ESU) for its HF monopolar energy source. The IonPencil™ provides two smoke clearing emitters that are automatically activated to clear the visual field when the device cutting function (HF) is activated. The mode of action of smoke management (visual field clearing) is electrostatic precipitation as per the predicate Ultravision system. When the tissue cutting or coagulation is ceased, the visual field clearing signal is automatically switched off after a short delay period that is settable on the Ultravision2™ generator user interface.

Activation of the HF function of the IonPencil™ is via a yellow (Cut) or blue (Coag) button located on the handpiece, or via a footswitch if this connected to the parent electrosurgical generator which is connected to the Ultravision2™ system. The IonPencil™ itself is incompatible with the connectors of third-party electrosurgical generators. The IonPencil™ is provided with a 69mm long PTFE coated blade.

The following cleared accessories have not changed:

• The Integrated Monopolar L-Hook(H/S)™ is a bifunctional laparoscopic device that combines proprietary smoke management (via visual field clearing) and monopolar HF tissue cutting and coagulation in a single device.

• The Ionwand™ pack comprises a dedicated percutaneous 3mm trocar/catheter which accommodates the Ionwand™ cable that delivers low energy from the generator to the patient for smoke management.

• The Ultravision™ 5mm Trocar includes a dedicated Ionwand™ cable.

Technological Characteristics Comparison:

The comparison table below provides the similarities and differences between the predicate and subject devices. The modifications made to the subject device do not raise any risk to safety or effectiveness.

Technical Characteristics Comparison Table					
Feature/ Specification	**Ultravision2™ System with IonPencil™**	**Ultravision2™ System Integrated Monopolar L-Hook (H/S)™ Predicate 1**	**Ultravision Visual Field Clearing System Predicate 2**	**Megadyne Pencil with Megadyne EZ Clean Electrosurgical Electrode Predicate 3,4**	**Comparison**
Regulatory Clearance/ Approval Reference	K240868	K231298	K200035	K965054 K081791	N/A
Product Code(s)	PQM GEI	PQM GEI	PQM	GEI	Equivalent
Regulation Number(s)	878.5050 878.4400	878.5050 878.4400	878.5050	878.4400	Equivalent
Regulation Name(s)	Surgical Smoke Precipitator AND	Surgical Smoke Precipitator AND	Surgical Smoke Precipitator	Electrosurgical Cutting &Coagulation &	Same

Technical Characteristics Comparison Table					
Feature/ Specification	**Ultravision2™ System with IonPencil™**	**Ultravision2™ System Integrated Monopolar L-Hook (H/S)™ Predicate 1**	**Ultravision Visual Field Clearing System Predicate 2**	**Megadyne Pencil with Megadyne EZ Clean Electrosurgical Electrode Predicate 3,4**	**Comparison**
	Electrosurgical Cutting & Coagulation & Accessories	Electrosurgical Cutting & Coagulation & Accessories		Accessories	
Intended Use and Indications	The Ultravision2™ System is indicated for use in surgery including laparoscopic surgery. • The Ultravision2™ Generator is intended to interface directly with the electrosurgical generator and serve as a pass-through for HF energy to HF electrosurgical instruments, to manage surgical smoke produced by energy-based instruments, and is indicated for use in surgery including laparoscopic surgery. • The Ionwand™ Pack is intended to be used to manage surgical smoke and is indicated for use in surgery including laparoscopic surgery. • The Ultravision™ 5mm Trocar is intended to be used to establish a path of entry for instruments and includes an Ionwand to manage surgical smoke,	The Ultravision 2™ Integrated Monopolar L-Hook (H/S)™ is intended to be used with applications in surgical procedures to facilitate cutting, coagulating of tissue, in combination with the clearance of smoke and other particulate matter that is created during laparoscopic surgery.	The Ultravision™ Visual Field Clearing System is indicated for the clearance of smoke and other particulate matter that is created during surgery, including laparoscopic surgery. The Ultravision™ 5mm Trocar component establishes a path of entry for instruments used in laparoscopic surgery.	E-Z Clean electrosurgical electrodes are intended to conduct radio frequency (RF) current for cutting and coagulation from the RE electrosurgical generator to target soft tissue in a broad range of surgical procedures requiring the use of electrosurgery for cutting and cauterization. Some tip configurations have a specific geometry that minimizes blanching and thermal damage in skin incisions when used in conjunction with the generator's Advanced Cutting Effect (ACE) mode.	Similar The predicate devices include integration of smoke management with electrosurgical function and cover laparoscopic and general surgery indications for both functions

Technical Characteristics Comparison Table					
Feature/ Specification	**Ultravision2™ System with IonPencil™**	**Ultravision2™ System Integrated Monopolar L-Hook (H/S)™ Predicate 1**	**Ultravision Visual Field Clearing System Predicate 2**	**Megadyne Pencil with Megadyne EZ Clean Electrosurgical Electrode Predicate 3,4**	**Comparison**
	and is indicated for laparoscopic surgery. • The Integrated Monopolar L-Hook (H/S)™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during laparoscopic surgical procedures, and is indicated for use in laparoscopic surgery • The IonPencil™ is intended to be used to facilitate the cutting and coagulation of soft tissue, to manage surgical smoke during general surgical procedures, and is indicated for use in surgery.				
Where used (environment)	General Surgery(open), including laparoscopic surgery	Laparoscopic surgery	General Surgery (open), including laparoscopic surgery	General Surgery (open)	Similar
Anatomical Sites	Soft tissue in a broad range of surgical procedures	Abdominal and pelvic cavity.	Abdominal and pelvic cavity.	Soft tissue in a broad range of surgical procedures	Similar
Target population	General patients requiring electrosurgery in a hospital setting	General patients requiring electrosurgery in a hospital setting	General patients requiring electrosurgery in a hospital setting	General patients requiring electrosurgery in a hospital setting	Same
Current	Ionwand- intermittent max 20µA Integrated L-Hook instrument & IonPencil- 2	Ionwand- intermittent max 20µA Integrated L-Hook instrument- 2 x 20µA (40µA total)	Continuous max 10µA	N/A	Similar

Technical Characteristics Comparison Table					
Feature/ Specification	**Ultravision2™ System with IonPencil™**	**Ultravision2™ System Integrated Monopolar L-Hook (H/S)™ Predicate 1**	**Ultravision Visual Field Clearing System Predicate 2**	**Megadyne Pencil with Megadyne EZ Clean Electrosurgical Electrode Predicate 3,4**	**Comparison**
	emitters (40μA total) intermittent max	intermittent max			
Visual field clearing mechanism of action	Electrostatic Precipitation	Electrostatic Precipitation	Electrostatic Precipitation	NA	Same
Ultravision2 Software Category	Basic Documentation	Basic Documentation	Basic Documentation	NA	Same
Ionwand tip material	Implant grade Stainless steel, annealed	Implant grade Stainless steel, annealed	Implant grade Stainless steel, annealed	N/A	Same
Ionwand energy modality	HVDC	HVDC	HVDC	N/A	Same
Ionwand working length	N/A- integrated into instrument - refer to electrode working length	N/A- integrated into instrument - refer to electrode working length	109mm	N/A	Similar feature but different dimension
Handpiece electrosurgical energy modality	Monopolar	Monopolar	N/A	Monopolar	Same
Handpiece Operation Principle	Colored and segregated finger switches for a) Cutting (yellow) b) Coagulation (blue)	Colored and segregated finger switches for a) Cutting (yellow) b) Coagulation (blue) c) Manual Smoke precipitation (grey)	NA	Colored segregated finger switches a) Cutting (yellow) b) Coagulation (blue)	Same
Handpiece physical and dimensional characteristics	Includes electrode and handpiece in an integrated form	Includes electrode and handpiece in an integrated form	N/A	Comprises separate handpiece and electrode	Similar
Handpiece shaft and shaft insulation materials	Stainless steel shaft, fluoropolymer shaft insulation	Stainless steel shaft, fluoropolymer shaft insulation	NA	Stainless steel shaft, polyolefin shaft insulation	Similar
Handpiece total electrode resistance (tip to	5Ω max	5Ω max	N/A	Unknown	Similar

Technical Characteristics Comparison Table					
Feature/ Specification	**Ultravision2™ System with IonPencil™**	**Ultravision2™ System Integrated Monopolar L-Hook (H/S)™ Predicate 1**	**Ultravision Visual Field Clearing System Predicate 2**	**Megadyne Pencil with Megadyne EZ Clean Electrosurgical Electrode Predicate 3,4**	**Comparison**
plug)					
Electrode tip insulation	PTFE electrode tip insulation PTFE coated electrode	PTFE electrode tip insulation PTFE coated electrode	N/A	PTFE electrode tip insulation, non-coated electrode, and PTFE coated electrode	Similar
Electrode tip design	Stainless steel	L- wire, stainless steel	N/A	stainless steel	Similar
Handpiece performance	Performs cut and coagulation in electrosurgical procedures AND Visual field clearing	Performs cut and coagulation in electrosurgical procedures AND Visual field clearing	Visual field clearing	Performs cut and coagulation in electrosurgical procedures	Similar
Handpiece compatibility	Compatible with the Ultravision2™ Generator	Compatible with 5mm cannular or larger Compatible with the Ultravision2™ Generator	N/A	Compatible with Megadyne Generator	Similar. The difference in generator compatibility does not raise new questions of safety and effectiveness
How Supplied (single use)	IonPencil -supplied sterile in single blister pack or pouch	Integrated handpiece -supplied sterile in single blister pack or pouch	Ionwand, trocar - supplied sterile in single blister or pouch	Supplied sterile in single pouches	Same
Biocompatibility	Meets ISO 10993 Part 5,10 and 11	Meets ISO 10993 Part 5,10 and 11	Meets ISO 10993 Part 5,10 and 11	Biocompatible	Same
Sterilization	EtO	EtO	EtO	Gamma Irradiation	Similar. All use standard sterilization modalities
Sterility Assurance Level	10^{-6}	10^{-6}	10^{-6}	10^{-6}	Same

Summary of Non-clinical Testing:

Testing demonstrated acceptable device performance for the device's intended use. System verification and validation activities were successfully completed as follows:

Test Performed	Standard/Specification Followed	Acceptance Criteria	Results
Electrical safety and electromagnetic compatibility in accordance with IEC 60601-1,	IEC 60601-1 Medical Electrical Equipment, Edition 3.1, which is Edition 3.0 (2005-12) as modified by AM1 (2012-07) evaluation.	Device must meet the requirements of the applicable clauses in the standards	Pass
IEC 60601-2-2, IEC 60601-1-2 including capacitive coupling assessment.	IEC 60601-2-2 High Frequency Surgical Equipment (2017-03) evaluation EN 60601-1-2:2015 + A1:2021 Medical electrical equipment General requirements for basic safety and essential performance. Collateral Standard: Electromagnetic disturbances	Device must meet the requirements of the applicable clauses in the standards	Pass
Shelf Life	ASTM F1980-16 Standard Guide for Accelerated Aging of Sterile Medical Device Packages ASTM 2096 Standard Test Method for Detecting Gross Leaks in Packaging by Internal Pressurization ASTM F88/F88M -15 Standard Test Method for Seal Strength of Flexible Barrier Materials	Product and package must demonstrate stability for the claimed shelf life of six months.	Pass
Mechanical robustness of device	Internal Specification	Device must meet mechanical specification per internal standards.	Pass
General, visual, dimensional and electrical verification of instrument	Internal Specification	Device must meet dimensional, electrical, and physical specifications per internal standards.	Pass
Visual field clearing (surgical smoke removal)	Internal Specification	Device must meet performance specifications per the internal standards.	Pass
Electrical bench tests	Internal Specification	Device must meet electrical performance and safety specifications per the internal standards.	Pass

Test Performed	Standard/Specification Followed	Acceptance Criteria	Results
Assessment of thermal depth of margin	Internal Specification	The thermal margin must be substantially equivalent to the predicate device in terms of its potential for tissue damage	Pass
Design validation under simulated use conditions	Internal Specification	Device must achieve its intended use when used by end users and that performance is at least equivalent to the predicate device	Pass

Biocompatibility

The tissue contacting components of the Ultravision2™ IonPencil are similar to the materials of the predicate devices. Biocompatibility testing was performed to demonstrate that the device is biocompatible. The following testing was completed with acceptable results:

Test Name	Standard	Acceptance Criteria	Pass/Fail
Cytotoxicity	ISO 10993-5: 2009	Under the condition of the test, the test article must be non-cytotoxic	Pass
Skin Irritation Study in Rabbits	ISO10993-23: 2021	Under the condition of the test, the test article must be non-irritating.	Pass
Systemic Toxicity in Mice	ISO 10993-11: 2017	Under the condition of the test, the test article must not elicit evidence of systemic toxicity.	Pass
Guinea Pig Maximization Sensitization Test	ISO 10993-10: 2021	Under the condition of the test, the test article must be non-sensitizing.	Pass
Hemolysis	ISO 10993-4: 2017	Under the condition of the test, the test article must be non-hemolytic.	Pass
Material Mediated Pyrogens	USP General Chapter <151>	Under the condition of the test, the test article must be non-pyrogenic	Pass

Conclusion

The conclusion drawn from the nonclinical tests demonstrates that the subject device in this 510(k) submission, K240868 is as safe, as effective, and performs as well as or better than the legally marketed predicate devices cleared under K231298, K200035, Class II (21 CFR 878.5050), product code PQM, and K965054, K081791, Class II (21 CFR 878.4400), product code GEI.

Attachment D

Attachment C:

A video demonstrating use of the Ultravision electrostatic precipitation system in laparoscopic surgery is available at the following URL:

https://www.alesi-surgical.com/ultravision-in-use/

Attachment E

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Electrostatic precipitation is a novel way of maintaining visual field clarity during laparoscopic surgery: a prospective double-blind randomized controlled pilot study

James Ansell · Neil Warren · Pete Wall · Kim Cocks · Stuart Goddard · Richard Whiston · Michael Stechman · David Scott-Coombes · Jared Torkington

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Abstract
Background Ultravision^{TM} is a new device that utilizes electrostatic precipitation to clear surgical smoke. The aim was to evaluate its performance during laparoscopic cholecystectomy.
Methods Patients undergoing laparoscopic cholecystectomy were randomized into "active (device on)" or "control (device off)." Three operating surgeons scored the percentage effective visibility and three reviewers scored the percentage of the procedure where smoke was present. All assessors also used a 5-point scale (1 = imperceptible/excellent and 5 = very annoying/bad) to rate visual impairment. Secondary outcomes were the number of smoke-related pauses, camera cleaning, and pneumoperitoneum reductions. Mean results are presented with 95 % confidence intervals (CI).
Results In 30 patients (active 13, control 17), the effective visibility was 89.2 % (83.3–95.0) for active cases and 71.2 % (65.7–76.7) for controls. The proportion of the procedure where smoke was present was 41.1 % (33.8–48.3) for active cases and 61.5 % (49.0–74.1) for controls. Operating surgeons rated the visual impairment as 2.2 (1.7–2.6) for active cases and 3.2 (2.8–3.5) for controls. Reviewers rated the visual impairment as 2.3 (2.0–2.5) for active cases and 3.2 (2.8–3.7) for controls. In the active group, 23 % of procedures were paused to allow smoke clearance compared to 94 % of control cases. Camera cleaning was not needed in 85 % of active procedures and 35 % of controls. The pneumoperitoneum was reduced in 0 % of active cases and 88 % of controls.
Conclusions Ultravision^{TM} improves visibility during laparoscopic surgery and reduces delays in surgery for smoke clearance and camera cleaning.

Keywords Abdominal · Quality control · Instruments · Technical · Clinical papers/trials/research · Surgical

J. Ansell (✉) · N. Warren · S. Goddard
Welsh Institute for Minimal Access Therapy (WIMAT), Cardiff CF14 4UJ, Wales, UK
e-mail: ansellj@cardiff.ac.uk

P. Wall
Isca Healthcare Research, Newport, UK

K. Cocks
KCStats Consultancy, Leeds, UK

R. Whiston
Department of Vascular Surgery, University Hospital of Wales, Cardiff, UK

M. Stechman · D. Scott-Coombes
Department of Endocrine and General Surgery, University Hospital of Wales, Cardiff, UK

J. Torkington
Department of Colorectal Surgery, University Hospital of Wales, Cardiff, UK

Surgical smoke is generated as a by-product of electrosurgical dissection during laparoscopic surgery. It can obscure the operative view, which has safety implications [1–4]. Smoke is frequently vented into the operating theater and the immediate surrounding environment. Carcinogenic molecules have been identified within diathermy, ultrasonic, and laser smoke. These include toluene, ethyl benzene, styrene, hydrogen cyanide, acetylene, and butadiene [5–7]. Viruses, bacteria, and malignant cells have also been isolated [8–10]. There is widespread acceptance that chronic exposure of theater staff to surgical smoke may be

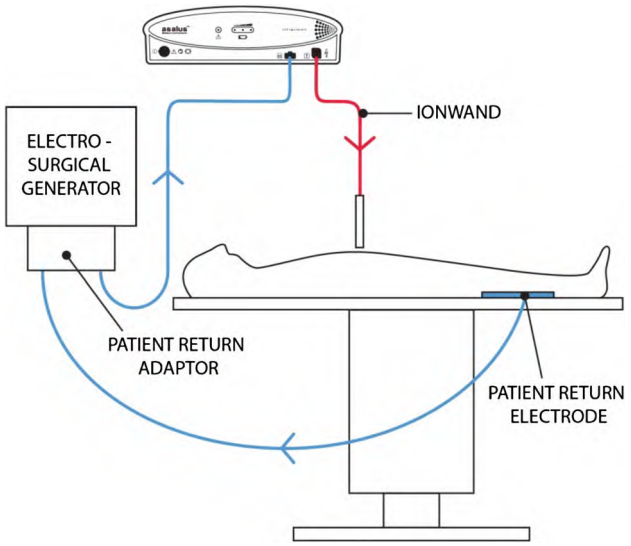

Fig. 1 Ultravision™ theater setup

hazardous, but there is no clear evidence to support a cause-and-effect relationship [11].

Most commercially available devices for the removal of smoke from the abdominal cavity use vacuum filtering systems. These have a number of disadvantages; they are typically large and cumbersome, noisy in the operating environment, expensive, may require a dedicated access port, and require several disposable or semidisposable components [12]. In addition, there may be pathophysiological issues. These include prolonged replacement of carbon dioxide during surgery leading to drying of the internal organs and tissues, increased risk of postsurgical adhesions, and reduction in core body temperature [13, 14]. The use of smoke extraction systems is therefore limited, and feedback on current systems has been described as universally negative [12].

The Ultravision™ system is a novel way of removing smoke from the operative field by the principle of electrostatic precipitation. The device can be connected to any standard electrosurgical system (Fig. 1). A 15 cm Ionwand™ is inserted percutaneously through a hollow needle, adjacent to the operative site. The Ionwand™ is a stainless steel microfilament brush equivalent in size to a Veress needle. The device is placed into the abdomen under direct vision after the insertion of the laparoscopic camera. The Ionwand™ does not interfere with the operation itself, and the puncture site does not require any additional closure methods. A DC voltage (9 kV) is applied to the wand, which leads to the release of ions, which in turn collide with particles of surgical smoke, transferring a negative charge. These negatively charged smoke particles are then attracted to the nearest grounded or positively charged surface, which in laparoscopic surgery is the internal abdominal cavity. This process clears smoke away from the operative field in an efficient manner.

The aim of this pilot study was to evaluate the performance of the Ultravision™ system during laparoscopic cholecystectomy. We aimed to establish any change in the operative field when the device was used, test novel end points for assessing the visual field, and highlight the feasibility of blinding the surgeon to treatment group allocation. Results will be used to learn the sample size required for subsequent research in this field.

Materials and methods

A single-center randomized double-blind prospective pilot study was conducted between May and October 2012 (Trials Database Registration NCT01534832). The study protocol was approved by the UK Competent Authority, Medicines and Healthcare products Regulatory Agency (MHRA) (CI/2012/0007), the research ethics committee for Wales (protocol AMIL/2011/INV01), and the Research and Development Office, Cardiff and Vale University Heath Board.

Inclusion and exclusion criteria

Patients scheduled for elective laparoscopic cholecystectomy for gallstone disease who were ≥18 years old with the capacity to provide informed consent were included. Exclusion criteria were age less than 18 years old; lactating or pregnant; evidence of previous extensive abdominal surgery; or currently recruited into another drug or device study. Laparoscopic procedures that were converted to an open technique were excluded from analysis, as were procedures where the video capture failed. All enrolled patients were chronologically allocated an ID number from a specified series on an enrollment log specific to the investigational site.

Randomization

Enrolled patients were randomized at the time of their operation to either surgery with the Ultravision™ system active or surgery with Ultravision™ inactive in a 1:1 ratio via an independent centralized telephone-based randomization service. This was undertaken by an independent surgical research fellow to ensure that the operating surgeon remained blinded to group allocation throughout surgery. Patients were replaced in the study if the procedure was converted to an open procedure or if the patient was unable to be safely anesthetized. The Ultravision™ return connector was covered during each procedure to

ensure that the operating surgeons remained blinded to the patient group throughout the surgery.

Operative intervention

Three experienced laparoscopic surgeons performed the procedures at the University Hospital Llandough, Wales. Each operation was performed using the same high-definition (HD) laparoscopic camera system (Olympus, Japan). These were videorecorded (using the camera output) onto a standard HD recording device and subsequently transferred to individual HD memory cards, labeled with the participant's ID number. Each video was then edited to include only the gallbladder removal from the gallbladder fossa. This was chosen as the most likely stage of the procedure where surgical smoke would be generated.

Primary outcomes

The primary outcome was based on the visual clarity during each procedure. This was measured by the operating surgeon on completion of the surgery and by an independent panel of surgeons via video analysis.

Operating surgeon

The operating surgeon was asked to give an overall rating of visibility using a 5-point scale [15] and to provide a percentage of the procedure performed with effective visibility (0–100 %) (Table 1).

Independent panel

Three senior experienced laparoscopic surgeons blinded to group allocation were asked to assess each procedure via the digital recordings. Independent reviewers recorded their overall rating of visibility using the same 5-point scale as the surgeons (Table 2). They also recorded the percentage of time with smoke present and visibility rating for each 60-second segment of the video. An average proportion of time with smoke present was calculated for each procedure, and this was then averaged across the three reviewers to obtain a mean opinion score for each procedure. Videos began with the start of diathermy and monopolar hook dissection of the gallbladder, and they finished when the gallbladder was completely free.

Table 1 Overall rating of visibility proforma for operating surgeon

Score	Impairment scale	Quality
1	Imperceptible	Excellent
2	Perceptible (but not annoying)	Good
3	Slightly annoying	Fair
4	Annoying	Poor
5	Very annoying	Bad
Please provide an overall rating of visibility throughout the procedure.		
Please indicate the % of the procedure with effective visibility.		
Do you think this patient was in the Ultravision™ On group?		Yes No
If you answered Yes or No, what influenced your decision?		

Secondary outcomes

Secondary outcomes were recorded by a research fellow during the operative stage. These included the number of times during the procedure that surgery was paused as a result of impairment of the visual field by the presence of particulates and/or smoke; the number of times during the procedure that the pneumoperitoneum was reduced to dissipate particulates and/or smoke obscuring the visual field; and the number of times during the procedure that the laparoscopic camera was removed to enable cleaning of contamination resulting from smoke and/or particulates. Total volume of insufflation gas (CO_2) used, duration of the procedure, and investigator opinion on whether blinding was successful were also recorded. A Masimo RAD 87 Pulse Co-Oximetry device (Masimo Corp., USA) was used to measure pre- and postoperative carboxyhemoglobin (SpCO) levels.

Follow-up

Patients were followed up at 6 weeks after surgery. Details of any nausea, pain, or wound complications experienced during this time period were recorded. Patients were asked to assess their current level of pain on a visual analog scale. If patients did not attend an outpatient appointment, they were contacted by telephone a total of three times on three separate occasions. If there was no response, they were deemed lost to follow-up.

Statistical analysis

There is no previous information for this medical device upon which to base a sample size calculation. A previous randomized comparative study of surgical smoke clearance (suction vs. standard clearance of diathermy in open procedures) included 15 per group [16]. A total of 30 patients (15 per arm) was deemed sufficient to fulfill the aims of this study based on this and recommendations for pilot study sample sizes [17]. Randomization was used to gain concurrent data on a control arm rather than to formally compare the arms.

Table 2 Proportion of procedure where smoke was present proforma for independent panel

ASSESSMENT OF VISUAL FIELD

Score	Impairment Scale (Impairments are:)	Quality
1	Imperceptible	Excellent
2	Perceptible (but not annoying)	Good
3	Slightly annoying	Fair
4	Annoying	Poor
5	Very annoying	Bad

DVD Filename:

For each 60 second segment of the DVD recording, please record on the form below:

1. the percentage of the recording for which smoke was present
2. your overall rating of the visibility throughout the 60s (using scale above)

Segment 1: Smoke Present	%	Segment 1: Visibility Rating	
Segment 2: Smoke Present	%	Segment 2: Visibility Rating	
Segment 3: Smoke Present	%	Segment 3: Visibility Rating	
Segment 4: Smoke Present	%	Segment 4: Visibility Rating	
Segment 5: Smoke Present	%	Segment 5: Visibility Rating	
Segment 6: Smoke Present	%	Segment 6: Visibility Rating	
Segment 7: Smoke Present	%	Segment 7: Visibility Rating	
Segment 8: Smoke Present	%	Segment 8: Visibility Rating	
Segment 9: Smoke Present	%	Segment 9: Visibility Rating	
Segment 10: Smoke Present	%	Segment 10: Visibility Rating	
Segment 11: Smoke Present	%	Segment 11: Visibility Rating	
Segment 12: Smoke Present	%	Segment 12: Visibility Rating	

Statistical analyses were undertaken by SAS for Windows software (SAS Institute, USA) and followed the study statistical analysis plan, which was approved before commencing the study. No formal statistical testing was planned for this pilot study because of the small sample size. Descriptive statistics were used, and estimates were reported with 95 % confidence intervals (CI) for all patients who were not replaced in the study (according to the prespecified criteria). An intracluster correlation coefficient was used as a measure of the level of agreement between assessors.

Results

Thirty-five patients were entered into the study and randomized (Fig. 2). Two patients were converted to open procedures, two did not have primary end point data

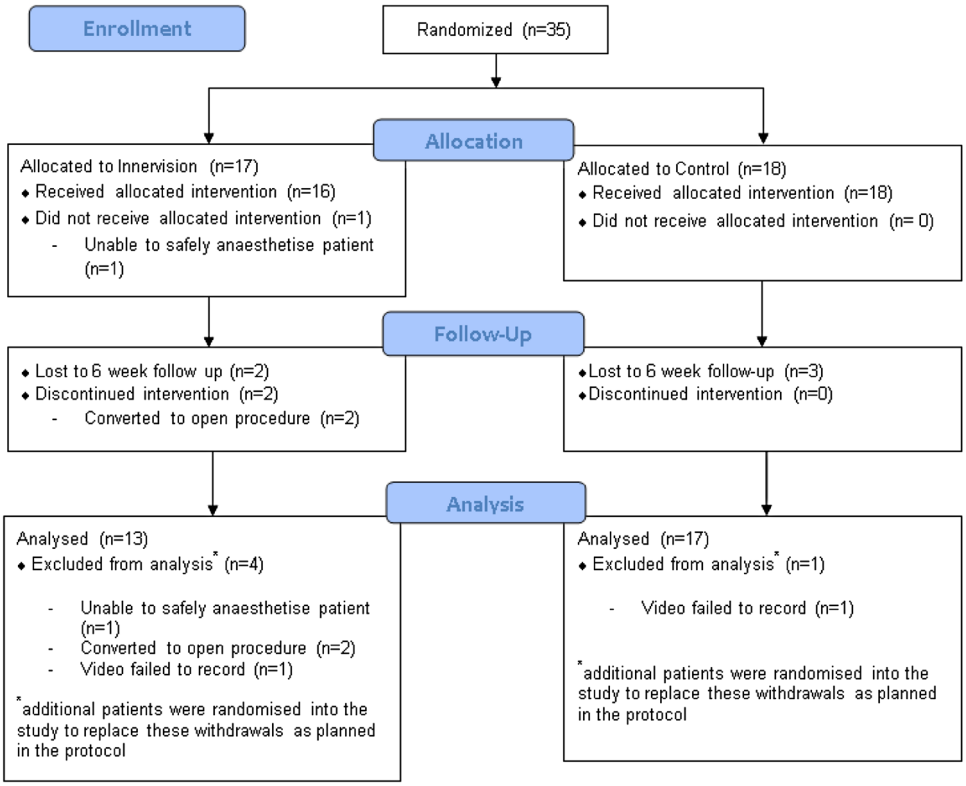

Fig. 2 Trial CONSORT diagram

available because the video failed to record, and one patient could not be safely anesthetized. These patients were replaced in the study, and all analyses exclude these patients. Baseline demographics of patients within each group were similar (Table 3). In the majority of cases (87 %), the Valleylab diathermy system (Covidien, USA) was connected to the Ultravision^{TM} system. A mean power of 30 W (range, 25–35 W) was used. The gallbladder dissection was performed using a laparoscopic hook diathermy in all procedures. There were no side effects as a result of the Ionwand^{TM} insertion.

Primary analysis

Operating surgeon

Operating surgeons rated the mean visibility rating as 2.2 (1.7–2.6) for active cases and 3.2 (2.8–3.5) for controls. Figure 3 shows the frequency of each visibility rating. The active group also demonstrated a higher mean proportion of procedures with effective visibility, 89.2 % (83.3–95.0) compared to the control value of 71.2 % (65.7–76.7) (Fig. 4).

Independent panel

The mean visibility rating when smoke was present was 2.3 (2.0–2.5) for active and 3.2 (2.8–3.7) for control groups. Figure 5 shows the frequency of each visibility rating. The active group demonstrated a lower percentage of time when smoke was present, 41.1 % (33.8–48.3) compared to the control group, 61.5 % (49.0–74.1) (Fig. 6). The intracluster correlation coefficient was 0.67, indicating moderate to strong agreement between reviewers.

Comparison between operating surgeon and independent panel

Figure 7 shows the percentage effective visibility rated by the operative surgeons versus the average independent panels' assessment of the percentage of gallbladder dissection that had smoke present. A trend can be seen whereby the percentage effective visibility decreases as the percentage of smoke present during the resection increases.

Secondary analysis

Twenty-two (73 %) procedures required at least one or more than one interruption (pause, reduction of pneumoperitoneum, or camera removal). In eight (27 %) procedures, all in the active group, there were no recorded interruptions. Surgery was paused as a result of impairment of visual field between 0 and 11 times in the procedures. Ultravision^{TM} procedures were not paused more than three times whereas the control group had 7 of 17 (41 %)

Table 3 Baseline demographics of active and control groups

Demographic	Treatment group	
	Active ($n = 13$)	Control ($n = 17$)
Male gender, *n* (%)	5 (38 %)	3 (18 %)
Age, years	44.6 (SE 3.5)	48.6 (SE 3.2)
Weight, kg	86.8 (SE 9.0)	82.1 (SE 5.9)
Preoperative findings		
Bilirubin, μmol L^{-1}	7.6 (SE 1.3)	8.8 (SE 0.8)
AP, IU L^{-1}	88.7 (SE 4.3)	99.4 (SE 17)
ALT, IU L^{-1}	28.0 (SE 4.6)	55.7 (SE 23.5)
Albumin, g L^{-1}	37.8 (SE 0.8)	39.5 (SE1.0)
Sodium, mmol L^{-1}	138.2 (SE 0.6)	138.9 (SE 0.5)
Potassium, mmol L^{-1}	4.1 (SE 0.1)	4.2 (SE 0.1)
Urea, mmol L^{-1}	3.4 (SE 0.5)	4.3 (SE 0.6)
Creatinine, mmol L^{-1}	68.3 (SE 4.2)	64.0 (SE 4.2)
Arterial $Paco_2$, kPa	4.8 (SE 0.2)	4.8 (SE 0.2)
Hemoglobin, g L^{-1}	13.4 (SE 0.3)	13.2 (SE 0.3)
Platelets, $\times 10^9$ L^{-1}	295 (SE 24.0)	246 (SE 22.1)
Hematocrit, %	0.4 (SE 0.0)	0.4 (SE 0.0)
No. of comorbidities for each body system		
Blood/lymphatic	1	0
Cardiovascular	0	1
Endocrine	1	0
Gastrointestinal	2	3
Musculoskeletal	0	1
Respiratory	0	1

ALT alanine aminotransferase, *SE* standard error, *AP* alkaline phosphatase

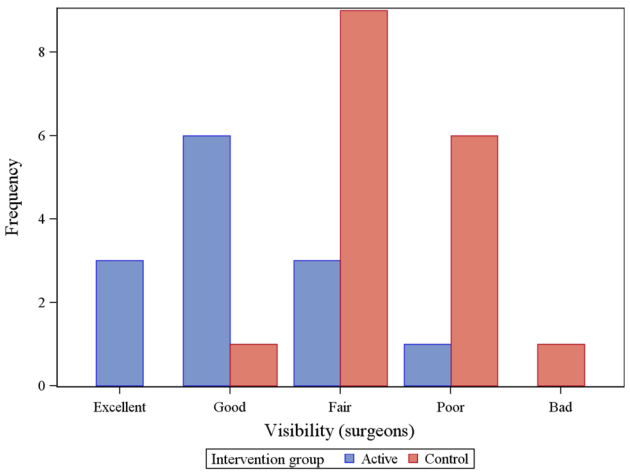

Fig. 3 Bar chart showing frequency of visibility rating categories (surgeons)

procedures paused more than three times (Fig. 8). The majority of the Ultravision™ procedures (10 of 13, 77 %) did not have any pauses. The pneumoperitoneum was

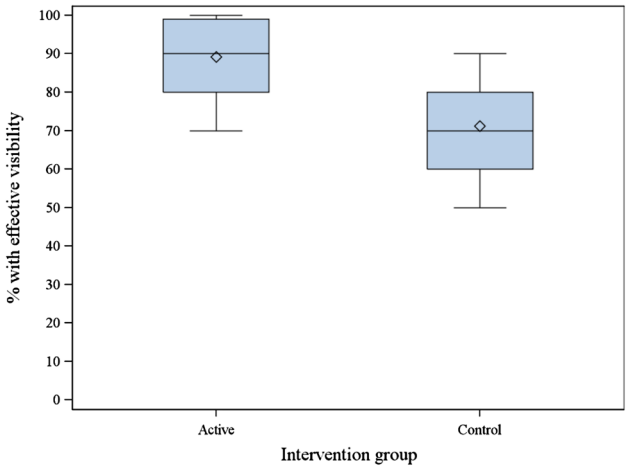

Fig. 4 Surgeon assessment of proportion of procedure with effective visibility. *Diamond* mean score, *line* median

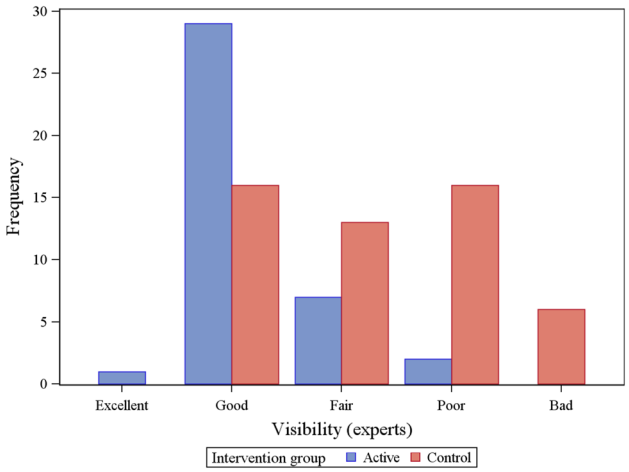

Fig. 5 Bar chart showing frequency of visibility rating categories (reviewers)

reduced to dissipate particulates and smoke in 15 of 17 (88 %) control procedures. None of the active procedures required the pneumoperitoneum to be reduced (Fig. 9). The majority of the Ultravision™ procedures (11 of 13, 85 %) did not need the camera to be removed for cleaning (Fig. 10) compared to 6 of 17 (35 %) in the control group. In the active cases, the mean volume of CO_2 (L) used was 37.7 (26.5–48.9) compared with 57.6 (32.4–82.9) for controls. The mean duration (minutes) of procedures was 47.8 (32.1–63.4) for active cases and 58.0 (46.6–69.4) for controls. The median change in baseline levels of SpCO in both study groups was 0 %. Surgeons believed that they knew the intervention group in all 30 procedures. Their guesses were correct in 28 of 30 (93 %) of procedures, with several reasons provided (Table 4). The operating surgeon

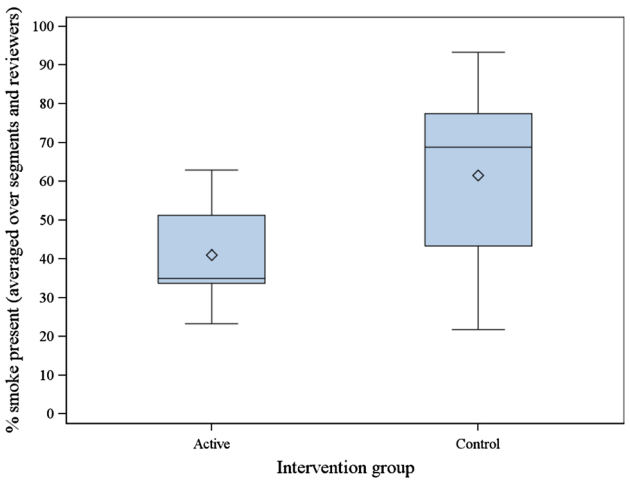

Fig. 6 Percentage of gallbladder removal where smoke present, reviewer assessment. *Diamond* mean score, *line* median

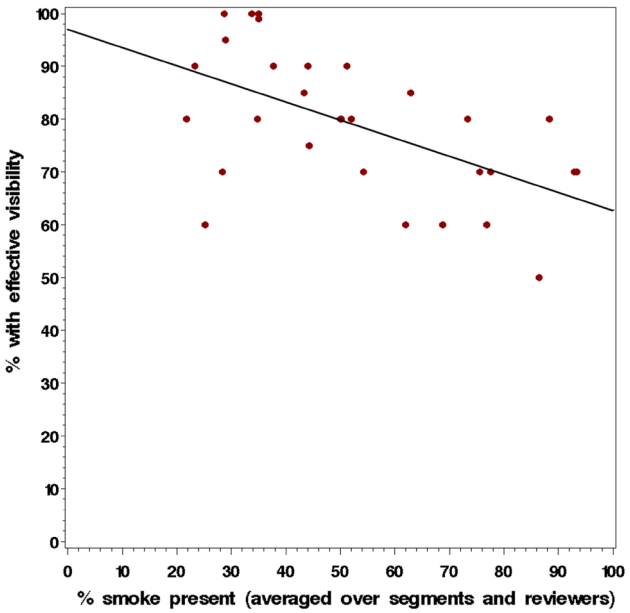

Fig. 7 Scatter plot of surgeon percentage effective visibility versus overall reviewer percentage smoke present

correctly identified whether Ultravision™ was on or off in all of the control patients and in 85 % of the active patients. In two active cases, the surgeon thought that the instrument was not connected and incorrectly thought the patient was in the control group.

Follow-up

There were no adverse events or complications as a result of using Ultravision™. Five patients were lost to follow-up by failing to attend outpatient clinics and respond to

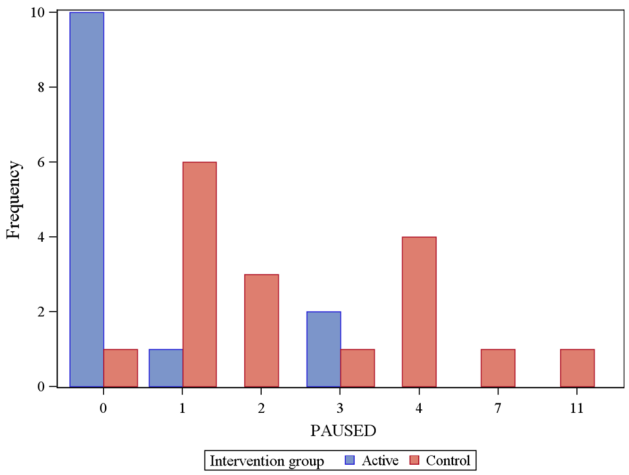

Fig. 8 Number of times surgery paused as a result of impairment of visual field

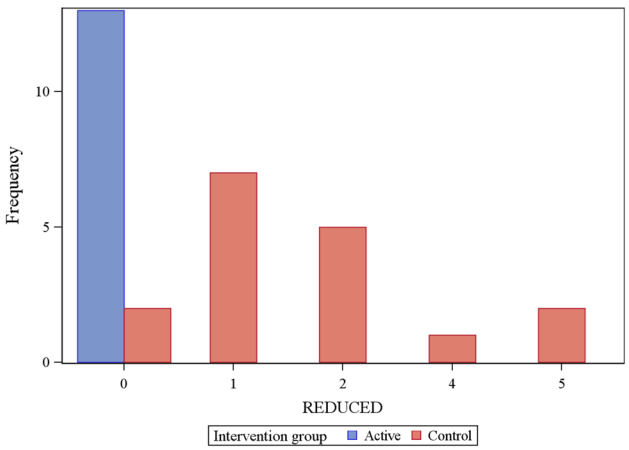

Fig. 9 Number of times pneumoperitoneum was reduced to dissipate particulates/smoke

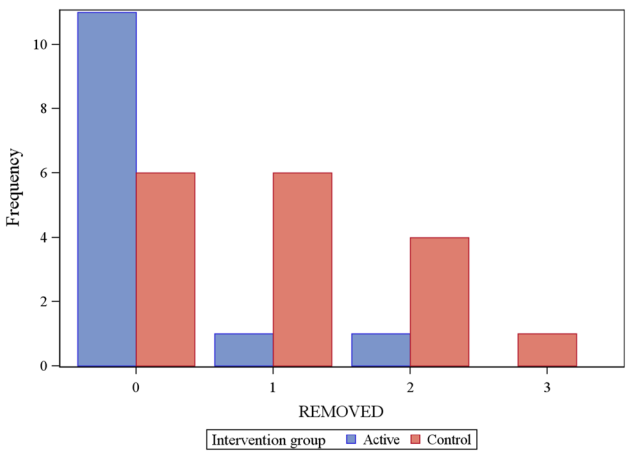

Fig. 10 Number of times laparoscopic camera was removed to enable cleaning of contamination resulting from smoke and/or particulates

Table 4 Success of blinding operative surgeons and summary of free-text comments by blinded operative surgeons to justify their reasons for why they thought the patient was in the active or control group

Intervention group	Do you think the patient was in the Innervision on group?	*n* (%)	Reasons
Active	Yes[a]	11 (85 %)	Smoke disappeared ($n = 7$)
			Appeared to be working intermittently ($n = 2$)
			No reason given ($n = 2$)
	No	2 (15 %)	Fog/smoke ($n = 1$)
			Smoke hung around ($n = 1$)
Control	Yes	0	
	No[a]	17 (100 %)	Smoke hung around ($n = 6$)
			Fog/smoke ($n = 5$)
			Needed to vent/clear smoke ($n = 3$)
			Device came out during procedure ($n = 1$)
			Smoke buildup ($n = 1$)
			No reason given ($n = 1$)

[a] Correct guess

telephone calls. One patient (in the control group) was readmitted with a symptomatic gallbladder fossa collection that was managed conservatively with antibiotic therapy. The majority of patients reported no pain, measured on a 100 mm visual analog scale. Seven patients (three active, four controls) reported a nonzero pain score. None of the reported pain was attributable, directly or indirectly, to the use of the Ultravision^{TM} system. There was one superficial port site wound infection (control group), and nausea was apparent in two active and one control patients.

Conclusions

Surgical smoke is generated by the use of energy-based instruments in the operating theater. Concerns have been raised regarding the infectivity, mutagenicity, and cytotoxicity of surgical smoke [8–10]. In addition, surgical smoke reduces the view of the operative field, especially during laparoscopic procedures [18].

This is the first clinical trial to demonstrate the principle of electrostatic precipitation for the clearance of surgical smoke. The Ultravision^{TM} device provides enhanced laparoscopic visibility, which leads to a reduction in operative duration times and volume of CO_2 used. This suggests that Ultravision^{TM} may have a significant economic impact for laparoscopic surgery by reducing the delays caused by camera cleaning and surgical smoke clearance. This will be further investigated now that the product as received CE marking. Ultravision^{TM} also provides a feasible alternative to current vacuum smoke removal systems. The device has the advantage of being minimally invasive, operator independent, and nondesufflating. This study demonstrates its application in laparoscopic cholecystectomy using monopolar diathermy at a single institution. It would be desirable to repeat the study in other centers to confirm the findings presented.

There are currently no validated forms of assessment that can be used to evaluate the effect of surgical smoke on visual clarity during laparoscopic surgery. We have tested the use of an impairment rating scale previously used to rate the quality of television pictures. Both operating surgeons and independent reviewers used this scale successfully alongside a simple percentage scale to indicate effective visibility (surgeons) and the presence of smoke (reviewers). These outcome measures have been successful in showing enhanced effective visibility and a reduction in the percentage of smoke present with the Ultravision^{TM} system. There is a correlation for effective visibility (assessed by the operating surgeon) to decrease as the percentage of smoke present (assessed by the independent review of digital recordings) increases (Fig. 7). This may imply that the use of two different assessors and methods leads to a valid assessment of the operative field. It also suggests that the presence of surgical smoke has a significant impact on the surgeon's laparoscopic operative view.

Results for secondary outcome measures in this trial also favored the Ultravision^{TM} active group. There was a trend toward reduced operative time in the Ultravision^{TM} system. Use of the Ultravision^{TM} system led to fewer pauses while waiting for smoke to clear, and it also led to a reduction in the number of times the laparoscopic camera was removed for cleaning. There was a lower volume of CO_2 insufflation in the active group.

There was no release of smoke into the theater environment when the Ultravision^{TM} was active. This suggests that the device is protective against chronic exposure to smoke. Smoke pollution was not measured during this trial

but should be considered in future work. More information is required to evaluate the constituents of surgical smoke and the impact of chronic exposure to them.

This study was a pilot study of 30 patients. A double-blind trial design was used to test whether blinding of the surgeons was feasible during the procedure. Although the physical masking of whether the Ultravision™ system was on or off was successful, the surgeons indicated that they could guess intervention group allocation from changes in their visual field (smoke hanging around or clearing quickly). The two cases where they guessed incorrectly that Ultravision™ was switched off may have been the result of placement of the Ionwand™ at an inappropriate distance from the operative site. It may also have been the case that the tip of the Ionwand™ was in contact with abdominal wall or an adjacent laparoscopic port, reducing its efficacy to clear smoke. Although it is intuitive to believe that the results from a 6-week follow-up would be comparable in a long-term analysis, it would be prudent to confirm this. Finally, this study focuses on the surgical smoke generated from diathermy dissection. In order to fully assess the use of Ultravision™, it would be useful to measure its effect with other modalities such as ultrasonic dissectors. This concept has been tested with good effect in a GLP preclinical animal study before this trial [19]. The Ultravision™ was tested on live porcine models using monopolar, bipolar, and ultrasonic dissection of mesenteric fat. Postmortem examination at 28 days after surgery showed no pathological findings of note at either macroscopic or microscopic levels. Clinical biochemistry, hematology, and cellular histology were normal in all cases.

The Ultravision™ smoke clearance system uses electrostatic precipitation to provide enhanced visual clarity during laparoscopic surgery and is safe to use. This technology has the potential to be used across a range of laparoscopic procedures. It may improve patient safety, reduce operative time, and limit chronic exposure to the potentially harmful effects of surgical smoke.

Acknowledgments James Ansell is supported by a Royal College of Surgeons Research Fellowship. Asalus Medical Instruments Ltd. provided the medical equipment required to conduct the trial.

Disclosures Neil Warren is the inventor of the Ultravision™ instrument but has received no funds for this trial. Pete Wall and Kim Cocks have received consulting fees from Asalus Medical Instruments Ltd. Jared Torkington is a consultant to Asalus Medical Instruments Ltd. James Ansell, Stuart Goddard, David Scott-Coombes, Richard Whiston, and Michael Stechman have no conflicts of interest or financial ties to disclose.

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Attachment F

RESEARCH ARTICLE JSLS

Electrostatic Precipitation in Low Pressure Laparoscopic Hysterectomy and Myomectomy

David Levine, MD, Gregory F. Petroski, PhD, Tracy Haertling, DO, MS, Teresa Beaudoin, RN, BSN

ABSTRACT

Background and Objective: The purpose of this study was to evaluate the impact of using electrostatic precipitation to manage the surgical plume during low pressure laparoscopic gynecologic procedures.

Methods: This was a prospective, blinded, randomized controlled study of women with a clinical indication for laparoscopic hysterectomy (n = 30) or myomectomy (n = 5). Patients were randomized to either use electrostatic precipitation (EP) during the procedure, or not (No EP, hysterectomy group only).

Results: Low pressure surgery could be undertaken in 87% of hysterectomy cases (13/15) when using EP to manage the surgical plume, compared to only 53% (8/15) in the No EP group. Overall average rating of the visual field was excellent with EP vs fair for No EP. Average CO_2 consumption was reduced by 29% when using EP (16.7L vs 23.5L, p = 0.152). The average number of procedural pauses to vent smoke was lower with EP than the No EP group (1.5 per case vs. 3.7 per case, p = 0.005). Average procedure duration for the EP vs No EP group was 40.5 min vs. 46.9 min (p = 0.987). There were no measurable differences between groups for body temperature, end-tidal CO_2, and discharge pain scores. In myomectomy, all five cases could be performed at low pressure, with an excellent visual field rating.

Conclusion: Electrostatic precipitation enhances low pressure laparoscopic hysterectomy and myomectomy. This was achieved by minimizing interruptions to surgery and exchange of CO_2; providing a clear visual field throughout the procedure; and eliminating surgical smoke at the site of origin.

Key Words: Laparoscopic, Low pressure, Visualization.

INTRODUCTION

Advances in laparoscopic surgery have significantly decreased recovery time, infection, and inpatient days.[1] Laparoscopic instrumentation has improved efficiency and safety by creating power sources that minimize spread to adjacent tissues. Cauterization is an effective surgical tool, but the smoke generated fills the abdomen partially or totally obscuring the surgeon's view which has safety implications. Smoke clearing strategies vary from releasing the smoke to using CO_2 exchangers. Studies have evaluated potential dangers associated with surgical smoke in the operating suite.[2] Approaches to improve visibility and prevent smoke release rely on dilution of the smoke-containing CO_2 with fresh CO_2 from the insufflator. Attempts have been made to quantify the clinical effects of high pressure and CO_2 volumes. Studies have shown that maintaining pneumoperitoneal pressure at no more than 10 mmHg may improve patient outcomes.[3] A recent prospective randomized controlled study in 178 patients who underwent total laparoscopic hysterectomy reported that low pressure laparoscopy is an effective and safe technique for the reduction of postoperative pain and laparoscopy-induced metabolic and vegetative alterations following laparoscopic hysterectomy for benign indications.[4]

Electrostatic precipitation (Ultravision™ Visual Field Clearing System, Alesi Surgical Ltd) offers a new technique to improve visualization and smoke management during laparoscopic surgery. The Ultravision™ System is an FDA approved device indicated for the clearance of smoke and other particulate matter created during

Department of Obstetrics and Gynecology, Mercy Hospital, 621 S. New Ballas Rd, St. Louis, Missouri (Dr. Levine).

Biostatistics & Research Design Unit, University of Missouri – Columbia School of Medicine, 182C Galena Hall, Columbia, Missouri (Dr. Petroski).

Mercy Research, 3231 S. National Ave., Ste 210, Springfield, Missouri (Ms Haertling).

Mercy Research, 615 S. New Ballas Rd, Ste 2010, St. Louis, Missouri (Ms Beaudoin).

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Conflicts of Interest: The authors declare no conflict of interest.

Informed consent: Dr. David Levine declares that written informed consent was obtained from the patient/s for publication of this study/report and any accompanying images.

Address correspondence to: Dr. David Levine, Department of Obstetrics and Gynecology Mercy Hospital St. Louis, 621 S. New Ballas Road, St. Louis, Missouri 63141. Telephone: 314-251-7650, Fax: 314 251-7651, E-mail: David.Levine@Mercy.net.

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laparoscopic surgery. Electrostatic precipitation is unique in that it eliminates smoke particles without CO_2 exchange within the abdomen. It has been shown previously in laparoscopic cholecystectomy to minimize CO_2 exposure and provide a more stable pneumoperitoneum.[5]

Although consistent with the labeled indications for use, electrostatic precipitation use during laparoscopic gynecologic procedures has not been reported in the literature. Laparoscopic hysterectomy and myomectomy generate considerable smoke and present an appropriate setting for further evaluation.

This study aimed to determine if electrostatic precipitation can maintain visual field clearance under low pressure laparoscopic conditions using a standard insufflator, thereby facilitating low pressure surgery whilst reducing patient CO_2 exposure.

MATERIALS AND METHODS

Study Design

This is a prospective blinded, randomized controlled study comparing laparoscopic hysterectomy, the most common laparoscopic gynecological procedure, with electrostatic precipitation (EP), Arm 1, versus laparoscopic hysterectomy without electrostatic precipitation (No EP), Arm 2. Study Arm 3 included patients undergoing laparoscopic myomectomy with electrostatic precipitation. Arm 3 was included because, although less frequently performed, myomectomy is a procedure that often creates large amounts of surgical plume and hence (a) generates data from an additional procedure; and (b) was considered to present at least as significant a challenge as hysterectomy for the device under evaluation.

Subjects

Inclusion criteria for the study were: $\geq$ 21 years of age, clinically indicated to undergo laparoscopic hysterectomy (with or without unilateral or bilateral oophorectomy or salpingo-oophorectomy) or myomectomy; willingness to attend all follow-up assessments; and ability to provide written informed consent. **Table 1** summarizes the clinical indications that presented during the study.

Exclusion criteria included: pregnancy and existing comorbidities that would be contraindications for laparoscopic surgery, such as inability to tolerate general anesthesia or multiple previous abdominal surgeries.

Informed consent was obtained from all patients.

Outcomes

The study outcomes assessed both performance and safety of electrostatic precipitation during laparoscopic hysterectomy and myomectomy. The primary outcome measures were quality of surgical field visualization as assessed by the investigator and the amount of carbon dioxide consumed from the time of placement of all surgical ports to colpotomy (hysterectomy) or closure of last uterine defect (myomectomy). Secondary outcomes included the number of ventilating and lens cleaning episodes and other pauses during the procedure; loss of pneumoperitoneum due to smoke evacuation, maximum intra-abdominal pressure, and duration at maximum pressure; number of changes or increases in pressure during the procedure and reason for change; body temperature and end-tidal CO_2 measured during the procedure; procedure duration; duration of postoperative hospital care; postoperative pain assessments; and medication utilization for pain and adverse events.

Randomization

For eligible patients undergoing laparoscopic hysterectomy, randomization was performed after obtaining informed consent. Patients were enrolled consecutively. The study was designed to compare 30 laparoscopic hysterectomies using a 1:1 randomization with 15 subjects allocated to the EP group and 15 subjects to the No EP group. Randomization was achieved using an envelope system, with each envelope containing either an "Ultravision" or a "Non-Ultravision" card. The study coordinator opened one envelope immediately prior to surgery and allocated the patient to Arm 1 or Arm 2, according to the text on the card. The investigator was blinded to the group assignment until the subject was transferred to recovery and the intra-operative and immediately postoperative data collection (i.e. that involving surgeon feedback) was complete. A third nonrandomized group of five patients undergoing myomectomy with electrostatic precipitation (Arm 3) was also evaluated.

Intervention

Pre-operative evaluations were obtained according to the current standard of care.

Table 1.
Patient Characteristics

	EP (n = 15)	No EP (n = 15)	Myomectomy (n = 5)
Age (years)	45.5 (± 10.2)	46.1 (± 8.5)	37.2 (± 9.7)
Ethnicity			
White/Caucasian	11 (73.33%)	12 (80%)	2 (40%)
Black/African-American	4 (26.67%)	2 (13.33%)	3 (60%)
Hispanic/Latino	0 (0%)	1 (6.67%)	0 (0%)
BMI (kg/m^2)	30.4 (± 7.2)	33.3 (± 10.5)	32.7 (± 9.7)
Diagnosis (procedure indication)			
Uterine fibroids	4	10	5
Abnormal Uterine Bleeding	3	0	0
Pelvic pain	7	4	0
Ovarian mass	1	0	0
Uterine prolapse	0	1	0
Abdominal Ultrasound findings			
Adenomyosis	2	0	0
Fibroids	5	8	5
Ovarian mass/cyst	1	1	0
Other*	2	3	0
Normal	1	0	0
Not done	4	3	0

EP, electrostatic precipitation; BMI, body mass index.
Age and BMI – Mean (Standard Deviation); Ethnicity – frequency (%).
*Other ultrasound findings included enlarged heterogenous uterus, heterogenous uterus with fluid-filled cavity, thickened endometrial canal and isthmocele.

The Ultravision System consists of a standalone battery-operated generator unit and the Ionwand™ electrode, which is introduced into the abdomen through either the Ultravision™ 5 mm Trocar or a 2.5 mm percutaneous catheter. The electrode provides the source of electrons that create the negative ions that transiently charge the surgical smoke particles and accelerate their sedimentation.

Electrostatic precipitation was set up for all procedures. The electrode was introduced as described per the Instructions for Use. Investigator blinding was created for the EP and No EP groups by placing the generator behind the surgeon and covering the system such that the electronic display, indicating whether the system was on or off, was not visible to the investigator. Device set up was conducted by supporting personnel such that the surgeon was not aware if the system was on or off. The speaker was turned down to minimize any audible indicators. The system was turned off for all procedures for subjects in the No EP group.

All surgical procedures were performed by the same surgeon, the study principal investigator.

A starting pneumoperitoneal pressure of 10 mmHg was used, delivered from a conventional insufflator. A total hysterectomy with or without adnexectomy by laparoscopy at 10 mmHg was performed using standard technique. All abdominal entry was performed using a 3 mm port at Palmer's point, as advised by the manufacturer and to provide consistency between patients. Once the abdominal cavity was clearly visualized, a 5 mm umbilical port and three additional 5 mm ports were placed lateral to the inferior epigastric vessels. The electrostatic precipitation electrode was placed in the left upper quadrant through the previous port site. All procedures were undertaken in steep Trendelenburg. After the uterus and adnexa were delivered vaginally, the cuff was closed using 3 figure-of-eight sutures of polydioxanone. Cutaneous closure was performed with skin glue for all 5 mm ports. The lateral myomectomy 10 mm port was

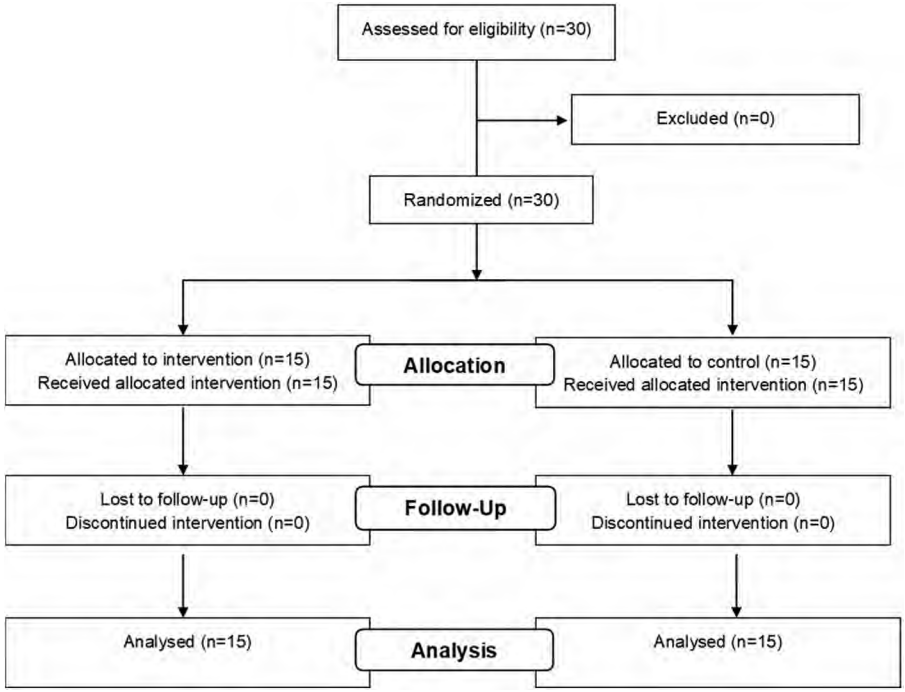


Figure 1. Study flow diagram.

closed using the Carter Thomason closure device and a 4-O subcutaneous suture.

Outcomes related to the procedure and intra-operative period were collected in real-time during the procedure by the study coordinator. The procedure duration was defined as the time all ports were in place to completion of colpotomy for hysterectomy and to closure of last uterine defect for myomectomy. Overall procedure duration was defined as the time all ports were in place to completion of the procedure.

Immediately following each procedure, the investigator answered the following questions:1) the proportion of operating time with effective visibility on a 1 to 100 numerical rating scale, and 2) the overall rating of visibility on a scale from 1 to 5 where 1 = Excellent, 2 = Good, 3 = Fair, 4 = Poor and 5 = Bad.

Post-Operative Period

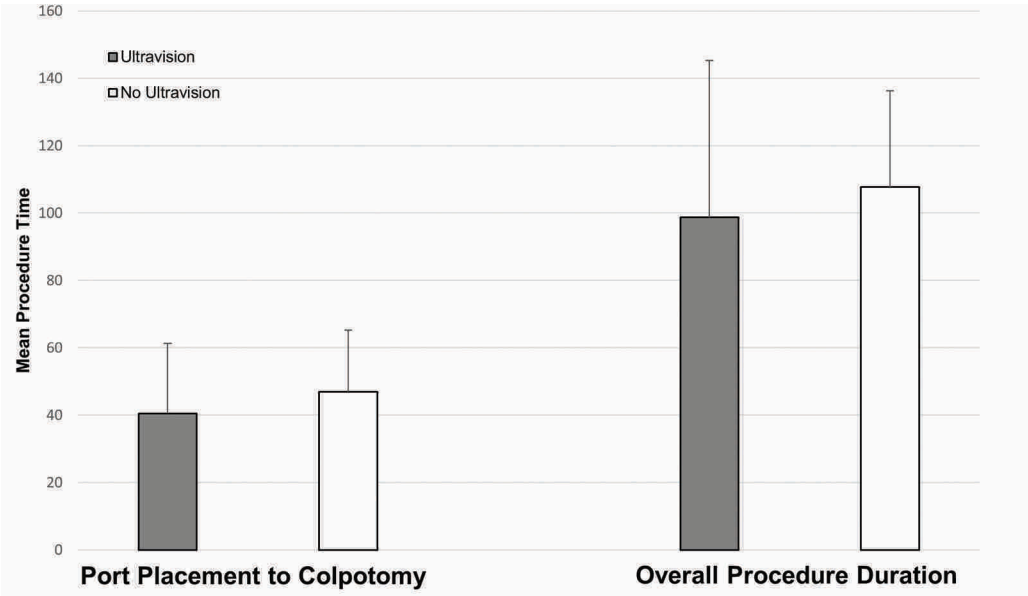
Postoperative care was provided and subjects were seen for a two-week follow up clinic visit, which is the current standard of care. Postoperative outcomes included duration of postoperative care, pain medication utilization, and pain assessments. The duration of postoperative hospital care was defined as time of entry to postoperative recovery to discharge. Pain score and pain location documented in the medical record during postoperative recovery, prior to discharge and at the two-week follow-up visit was collected.

Data Collection

Data were collected on a prospective basis. Collection points occurred at baseline (to assess eligibility for inclusion, 1 to 3 months prior to date of surgery); pre-operatively (to confirm eligibility, within 24 h of surgery); during the procedure (performance data); in recovery (time in recovery, pain medications, and score); immediately prior to discharge (pain medication and score) from the hospital; and two weeks post-discharge, per standard of care (pain score).

Statistical Analysis

Significance testing was used to compare outcomes for the EP and No EP groups. Summary statistics for the myomectomy group are included for descriptive purposes. Fisher's Exact Test was used for group comparisons on categorical variables and the two-sample t test or Wilcoxon Rank Sum Test for continuous variables. Body temperature and end-tidal CO_2 were measured at 15-min intervals. A two-way repeated measures analysis of variance with group by time interaction was used to test if there were group differences



Group	Variable	N	Mean	Std Dev	Median	Min	Max	p Value
No Ultravision	Port to Colpotomy	15	46.9	18.3	51	19	97	
	Overall	15	107.7	28.6	108	62	158	
Ultravision	Port to Colpotomy	15	40.5	20.8	34	22	95	0.097
	Overall	15	98.7	46.6	80	57	236	0.152

Figure 2. The average procedure time in minutes. Error bars are standard deviation and a p-value ≤ 0.05 was considered significant.

in these outcomes over the first 60 min of the procedure. All p values are for two-sided alternatives, and those ≤ 0.05 were considered to indicate statistical significance.

RESULTS

During the study period, 30 patients with clinical indication for laparoscopic hysterectomy were evaluated for eligibility, randomized, and all were included in the final analysis (**Figure 1**). Five patients were eligible for Arm 3, laparoscopic myomectomy. All five patients underwent the procedure using electrostatic precipitation and completed follow up. Data for all five patients were analyzed. Characteristics of the included patients are listed in **Table 1**.

Procedural Characteristics

There were 14 subjects in the EP group and 12 in the No EP group who underwent hysterectomy with bilateral salpingo-oophorectomy, and one patient in the EP group and three in the No EP group who underwent hysterectomy with unilateral oophorectomy and unilateral salpingo-oophorectomy. The same electrostatic precipitation system set up, generator (serial number 2014-A00195) and (Ionwand™, batch number 17161827), was used for all procedures (n = 35). The Covidien VLFT10GEN diathermy system was used for all procedures (n = 35) with Covidien harmonic and Storz bipolar tools used for all procedures.

Procedure Duration

Procedure time and overall procedure duration, as defined above, for the EP (Arm 1) and No EP (Arm 2) groups is summarized in **Figure 2**. For Arm 3, the average time from insertion of all ports to closure of last uterine defect was 56.8 min (± 31.5 min).The average overall procedure duration for the myomectomy group was 92.4 min (± 29.5 min) for (data not shown).

CO_2 Utilization

The mean volume of CO_2 consumption during the procedure, measured during the period between all trocars being inserted to the completion of the colpotomy, for the EP and No EP groups (p = .125) is shown in **Figure 3**. Average CO_2 consumption was reduced by 29% when using electrostatic precipitation (16.7L vs 23.5L, p = .152). See **Figure 3**. The mean volume of CO_2 consumption

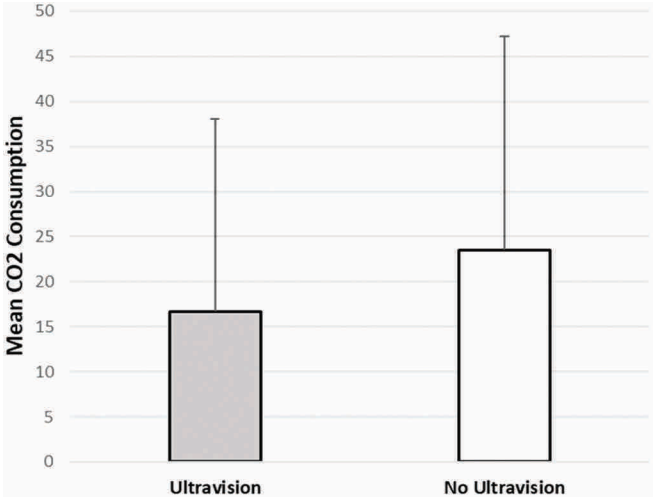


Figure 3. Average procedural CO_2 consumption in liters. N = 15, Error bars are standard deviation and a p-value ≤ 0.05 was considered significant.

during the procedure for the myomectomy group was 25.7L (± 25.3).

Procedural Pauses

Figure 4 summarizes the number of pauses during the procedure and the reason for the pause for the EP and No EP groups. Comparing EP to No EP, there was a 42% improvement in visibility (p = .043), a 56% reduction in smoke (p = .011), and a 59.5% reduction in venting (p = .005). There was a significant difference in the average number of pauses to clear the smoke, 1.5 per case for EP vs 3.7 for No EP (p = .005).

Of the four subjects in the myomectomy group where pauses occurred, three subjects had one pause and one subject had three pauses. Reasons for pauses included temporary poor visibility and camera cleaning.

Intra-Abdominal Pressure

An initial intra-abdominal pressure of 10 mmHg was confirmed for all subject procedures (n = 35). When intra-abdominal pressure was increased, all increases were to 15 mmHg and due to insufficient working space. There were two increases in the EP group and seven increases in the No EP group. The mean duration of the pressure increase was 31.5 minutes (± 6.4) for the EP group and 59.8 minutes (± 37.4) for the No EP group. No more than one pressure increase was noted. Using a standard insufflator, low pressure surgery could be undertaken in 87% of cases (13/15) when using electrostatic precipitation compared to only 53% (8/15) when electrostatic precipitation was not used. No increases in pressure were noted for the five subjects in the myomectomy group.

Clinical Outcomes

All subjects (n = 35) were discharged on the same day as the procedure (within 24 h of procedure).

Pain Assessments

The mean discharge pain score was 2.7 out of 10 (± 2.4) for the EP group and 2.7 out of 10 (± 1.8) for the No EP group (p = .832). The mean discharge pain score for the myomectomy group was 2.8 (± 1.9). No patients reported shoulder pain at discharge.

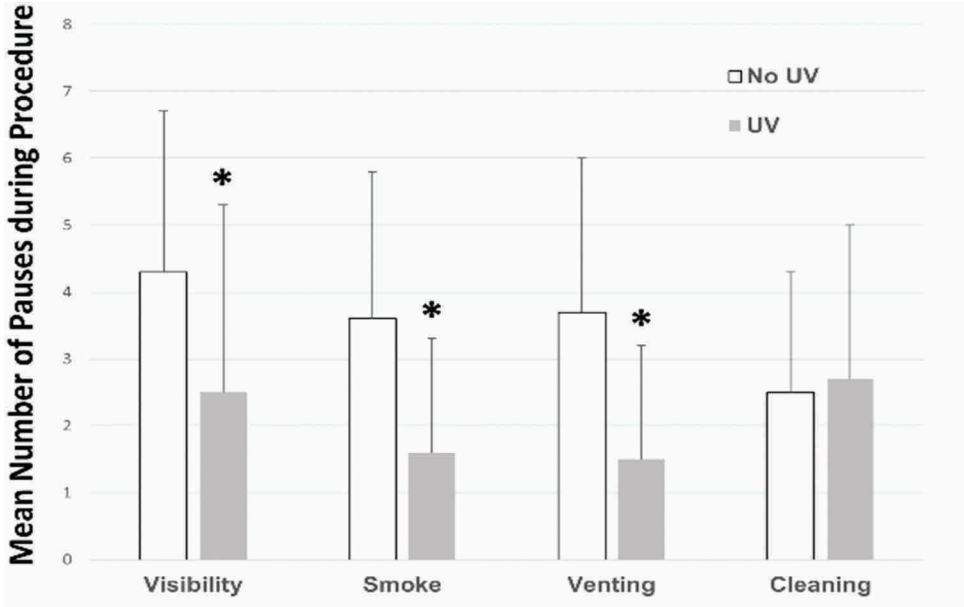
At the two-week follow up, two patients in the EP group reported pain, with ratings of 2/10 and 9/10 respectively. Neither patient reported shoulder pain. Two patients in the EP group rated their pain 0/10 but reported shoulder pain. One patient in the No EP group reported pain (2/10). Of the 15 patients in the No EP group, four rated their pain 0/10 but reported shoulder pain. All five patients in the myomectomy group reported 0/10 pain and none reported shoulder pain.

Pain Medication Utilization

Table 2 summarizes pain medication utilization for all three study groups across study time points by medication type. Immediately postoperatively, a prescription for a narcotic was written for the first 2 to 3 days, to be used as needed, until the patient felt able to convert to an NSAID non-narcotic medication. For both the EP and No EP groups, 12/15 (80%) subjects received postoperative opioid pain medication (p = 1.0). The discharge medication list of all 15 patients in both the EP and No EP groups included an oral opioid medication. At the two-week postoperative visit, 10/15 (67%) subjects in the EP group and 7/15 (47%) in the No EP group reported taking opioid pain medication (p = .462). One patient in the EP group and the No EP group used pyridium postoperatively and post-discharge. One patient in the No EP group received gabapentin postoperatively.

Body Temperature and End-Tidal CO_2

Body temperature and end-tidal CO_2 levels were recorded at 15-min increments throughout the procedure. Captured



Group	Variable	N	Mean	Std Dev	Median	Min	Max	*p* value
No UV	Visibility	15	4.3	2.4	4	1	8	
	Smoke	15	3.6	2.2	3	1	8	
	Venting	15	3.7	2.3	3	1	8	
	Cleaning	15	2.5	1.8	2	0	6	
	Total Pauses	15	5.6	2.8	5	1	10	
UV	Visibility	15	2.5	2.8	2	0	8	**0.043**
	Smoke	15	1.6	1.7	1	0	5	**0.011**
	Venting	15	1.5	1.7	1	0	5	**0.005**
	Cleaning	15	2.7	2.3	2	0	7	0.926
	Total Pauses	15	4.2	3.6	3	0	10	0.203

Figure 4. Procedural pauses for the electrostatic precipitation versus no electrostatic precipitation groups. Summary of the number of pauses and reasons for pauses. Error bars are standard deviation and a *p*-value ≤ 0.05 was considered significant (*and bold font).

Table 2.
Post-Operative Pain Medication Utilization

Study Time Point	Post-Operative Hospitalization		Discharge Medications		2-Week Follow-up	
Medication Type	Opioid[1]	Nonopioid[2]	Opioid	Nonopioid	Opioid	Nonopioid
EP (n = 15)	12	14	15	5	10	10
No EP (n = 15)	12	14	15	8	7	9
Myomectomy (n = 5)	5	5	5	1	5	1

EP, electrostatic precipitation.
[1]Postoperative opioid medications included intravenous and/or oral opioids.
[2]Nonopioid medications included acetaminophen and/or nonsteroidal anti-inflammatory medications.

Table 3.
Average Intra-Operative Body Temperature and End-Tidal CO_2 Levels

Group	n	0 Min	15 Min	30 Min	45 Min	60 Min
Body Temp (°C)						
EP	15*	35.93 (0.49)	35.93 (0.44)	35.99 (0.48)	36.03 (0.51)	36.19 (0.52)
No EP	15	35.75 (0.51)	35.87 (0.30)	35.93 (0.29)	36.09 (0.36)	36.05 (0.30)
Myomectomy	5	35.96 (0.48)	36.14 (0.39)	36.18 (0.33)	36.42 (0.22)	36.20 (0.40)
End-Tidal CO_2 Level						
EP	15*	35.4 (3.0)	35.7 (3.7)	35.1 (4.2)	35.9 (2.8)	36.1 (3.1)
No EP	15	35.1 (2.6)	36.1 (2.4)	35.8 (3.4)	35.4 (3.5)	35.0 (2.8)
Myomectomy	5	33.6 (2.0)	34.2 (1.3)	34.0 (1.0)	35.4 (1.7)	35.8 (1.6)

EP, electrostatic precipitation.
Mean and (Standard Deviation).
*At the 60 min timepoint, n = 14 for the EP group.

data points became limited after 60 min due to variance in procedure duration. Therefore, analysis was performed on data up to 60 min. **Table 3** summarizes average temperature and end-tidal CO_2 levels across timepoints for the three study groups. Effects from the analysis of variance for body temperature (p = .092) and end-tidal CO_2 (p = .328) were not statistically significant. Only the time effect for body temperature was statistically significant (p = .012) reflecting slight warming in both groups over the 60-min period of analysis.

Adverse Events

There were no reports of device-related adverse events.

Visualization and Surgeon Satisfaction

Immediately following each procedure, the investigator answered the following questions:1) what was the proportion of operating time with effective visibility on a 1 to 100 numerical rating scale? 2) what was the overall rating of visibility on a scale from 1 to 5 where 1 = Excellent, 2 = Good, 3 = Fair, 4 = Poor and 5 = Bad?

Table 4.
Surgeon Overall Rating of Visibility

	Excellent	Good	Fair	Poor	Bad
EP	9	2	3	1	0
No EP	1	2	7	4	1
Myomectomy	5	0	0	0	0

EP, electrostatic precipitation.

For the surgeon assessment of the proportion of operating time with effective visibility on a scale from 1 – 100, the average was 90.7% (± 10.2) of the time for the EP group versus 74.3% (± 12.1) for the No EP group (p = .0006). For the myomectomy group, the proportion of operating time with effective visibility was 100% for all five subjects.

The overall rating of visibility during the procedure on a scale from 1 to 5 is summarized for each subject procedure in **Table 4**.

DISCUSSION

Laparoscopic hysterectomy is typically performed using an intra-abdominal pressure of 15 mmHg. However, studies have shown that maintaining pneumoperitoneal pressure, at no more than 10 mmHg, may improve patient outcomes.[3,4] Although there are modern, advanced insufflators that offer the potential to operate at low pressure, there has been a recent report that use of such high flow insufflators results in operating room air becoming entrained into the abdomen, increasing the potential for gas embolism with poorly absorbed oxygen and nitrogen.[6] The present study was initiated to evaluate electrostatic precipitation when laparoscopic hysterectomy is performed under low intra-abdominal pressures using a conventional insufflator.

When hysterectomy was attempted at low pressure (10 mmHg) it could only be completed in 53% of cases without electrostatic precipitation, as compared to 87%

with electrostatic precipitation (p = .109). This study demonstrates that low pressure (10 mmHg) laparoscopic hysterectomy can be performed more easily with fewer interruptions using electrostatic precipitation as compared to traditional valve-venting techniques alone.

The potential additional advantages of a low and constant intra-abdominal pressure environment include maintenance of a constant core body temperature and the protective effect to the peritoneal tissues. The negative effects of cold, dry CO_2 have been shown in rat models demonstrating extensive mesothelial desquamation and disruption of underlying connective tissue.[7] Those findings and others have suggested a benefit of humidified CO_2.[8] However, a 2016 Cochran review concluded that there is no clear clinical benefit to humidified and warmed CO_2 in laparoscopic abdominal surgery.[9] Because extraction of smoke-containing CO_2 is not required in order to maintain a clear operative field of view, the use of electrostatic precipitation reduced CO_2 consumption by 29% (p = .125). The present study did not look at the difference between cold, dry CO_2 to humidified and warmed CO_2 which has been evaluated in the past.

The annoyance of smoke plume created by desiccation and coagulation of tissues causes the surgeon to stop and purge the abdominal cavity of smoke. The present study clearly showed a significant decrease in the number of times the surgery was halted because of poor visibility (p = .043), waiting for smoke to clear (p = .011), and venting of smoke into the operating room because of poor visibility (p = .05). This not only decreased the operating time, but also enhanced the surgical experience by preventing multiple pauses in the surgery.

An additional danger associated with purging the smoke into the operating room is the potential effect on the surgeon and other operating room personnel. Studies have demonstrated an association between smoke plumes from electrosurgery and acute headaches, eye, nose and throat irritation; dermatitis, and acute and chronic pulmonary conditions.[10] Purging of smoke was no longer required when using electrostatic precipitation, due to its mode of action in clearing the visual field without requiring CO_2 removal and replenishment.

The system tested in this study is different to other reported means of facilitating low pressure surgery in that, rather than utilizing a high flow of carbon dioxide to rapidly extract smoke-containing CO_2 and dilute remaining smoke with fresh CO_2, its mode of action utilizes electrostatic precipitation. This technique requires a generator that supplies a low power (80mW maximum output) DC energy supply to the pneumoperitoneum via an electrode, introduced via a percutaneous catheter. In use, this creates a constant flow of negatively charged, low-energy gas ions that migrate towards the patient tissue due to the patient return electrode ("ground pad") on the patient, which is also connected to the generator. As they migrate, the ions collide and temporarily associate with particulates and water vapor, which accelerates the natural sedimentation that otherwise occurs to the mass of the combusted matter. As the charged particles land, the charge is released back to the generator via the patient return electrode. Uniquely, this electrostatic interaction requires no gas exchange and therefore allows for low CO_2 use, a stable pneumoperitoneum and, as evidenced by these data, facilitates the ability to perform surgery at low abdominal pressure.

It is noteworthy that, unlike alternative approaches, the mode of action results in the retention of organic particulate matter within the abdomen. Although it would be possible to remove this using postsurgical lavage, this is not included in the instructions for use and was not performed during the study. As reported in the previous study,[5] there were no reports of any patient-related adverse events relating to this during surgery, in recovery or post discharge. Examination of the Manufacturer and User Facility Device Experience adverse event database using the product brand name yielded no adverse event reports in the USA to date.

An attempt was made to demonstrate a difference in pain scores and pain medication utilization postoperatively. There was no significant difference between the two groups even though the CO_2 consumption was significantly less in the electrostatic precipitation group. Given that 70% of the procedures (21 out of 30 patients) were successfully carried out at 10 mmHg, this result is unsurprising. Having established the feasibility of this technique, a recommended follow-up study would be to compare the clinical outcomes from a cohort of patients where electrostatic precipitation is used at low pressure compared to one that used electrostatic precipitation at conventional, 15 mmHg pressure.

LIMITATIONS

There are several limitations to this study. The sample size included in the study does not provide statistical power. As a result, this small sample size may overestimate the magnitude of associations seen between the group where electrostatic precipitation was used and where it was not

used, and the myomectomy group was too small to draw any conclusions. With the small sample size, the ability to adjust for potential confounding variables may be limited. Furthermore, variables that may impact the surgical procedure including uterine size, parity, and surgical findings such as pelvic adhesions, were not collected. While there may be benefits to having a single surgeon perform all procedures in terms of less variability in surgical technique, overall patient management, and consistency in perception of visual field quality, there may also be limitations. The ratings of the visual field are based on a single surgeon's perspective, who was also the Principal Investigator, which may be limited by bias. Findings with other surgeons may vary on the surgeon's level of experience with the procedure, surgical techniques, and use of the smoke clearing device.

CONCLUSION

In this feasibility study, the use of electrostatic precipitation was found to facilitate low pressure laparoscopic hysterectomy using a standard insufflator. This was also demonstrated in myomectomy, although without a comparator. This was achieved by minimizing interruptions to surgery and exchange of CO_2, providing a clear visual field throughout the procedure, and eliminating surgical smoke at the site of origin.

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Attachment G

Experimental Model to Test Electrostatic Precipitation Technology in the COVID-19 Era: A Pilot Study

Jonathan R Buggisch, Daniel Göhler, Dipl Ing, Alain Le Pape, PhD, PharmD, DSc, Sébastien Roger, PhD, Mehdi Ouaissi, MD, PhD, Michael Stintz, Dr Ing habil, Andreas Rudolph, Dr Ing, Urs Giger-Pabst, MD

BACKGROUND: In the COVID-19 crisis, laparoscopic surgery is in focus as a relevant source of bioaerosol release. The efficacy of electrostatic aerosol precipitation (EAP) and continuous aerosol evacuation (CAE) to eliminate bioaerosols during laparoscopic surgery was verified.

STUDY DESIGN: Ex-vivo laparoscopic cholecystectomies (LCs) were simulated ± EAP or CAE in Pelvitrainer equipped with swine gallbladders. Release of bioaerosols was initiated by performing high-frequency electrosurgery with a monopolar electro hook (MP-HOOK) force at 40 watts (MP-HOOK40) and 60 watts (MP-HOOK60), as well as by ultrasonic cutting (USC). Particle number concentrations (PNC) of arising aerosols were analyzed with a condensation particle counter (CPC). Aerosol samples were taken within the Pelvitrainer close to the source, outside the Pelvitrainer at the working trocar, and in the breathing zone of the surgeon.

RESULTS: Within the Pelvitrainer, MP-HOOK40 (6.4×10^5 cm^{-3}) and MP-HOOK60 (7.3×10^5 cm^{-3}) showed significantly higher median PNCs compared to USC (4.4×10^5 cm^{-3}) ($p = 0.001$). EAP led to a significant decrease of the median PNCs in all 3 groups. A high linear correlation with Pearson correlation coefficients of 0.852, 0.825, and 0.759 were observed by comparing MP-HOOK40 (± EAP), MP-HOOK60 (± EAP), and USC (± EAP), respectively. During ex-vivo LC and CAE, significant bioaerosol contaminations of the operating room occurred. Ex-vivo LC with EAP led to a considerable reduction of the bioaerosol concentration.

CONCLUSIONS: EAP was found to be efficient for intraoperative bioaerosol elimination and reducing the risk of bioaerosol exposure for surgical staff. (J Am Coll Surg 2020;231:704–712. © 2020 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Exposure of surgical staff in operating room facilities to surgically induced aerosols, which are released during surgical procedures such as high-frequency electrosurgery and ultrasonic cutting (USC), represents a potential health risk.[1,2] Fractions of released aerosols can reach the breathing zone of healthcare workers,[3] especially when they are close to the surgical field. In a survey among operating room facility healthcare workers in the US, 99% of the responders reported being within 5 feet (1.52 m) from the aerosol source.[4,5] Furthermore, health authorities report that about 500,000 healthcare workers are exposed regularly to surgical-induced aerosols annually in the US.[6]

Authors Buggisch and Göhler contributed equally to this work.

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From CNRS UPS44, CIPA, PHENOMIN-TAAM, Orléans, (Buggisch, Le Pape), EA4245 Transplantation, Immunologie, Inflammation, Université de Tours, Tours (Roger, Ouaissi), Institut Universitaire de France, Paris (Roger), Department of Digestive, Oncological, Endocrine, Hepato-Biliary, Pancreatic and Liver Transplant Surgery, University Hospital of Tours (Ouaissi), Tours, France; and Technologie-orientierte Partikel-, Analysen- und Sensortechnik, Topas GmbH (Göhler, Rudolph), Research Group Mechanical Process Engineering, Institute of Process Engineering and Environmental Technology, Technische Universität Dresden (Stintz), Dresden, and Chirurgische Klinik I, Mathias-Spital Rheine (Giger-Pabst), Germany.

Correspondence address: Jonathan R Buggisch, University of Münster, Albert-Schweitzer-Straße 21, 48149 Münster, Germany. email: j_bugg01@uni-muenster.de

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Abbreviations and Acronyms

CAE = continuous aerosol evacuation
COVID-19 = Coronavirus disease 2019
CPC = condensation particle counter
EAP = electrostatic aerosol precipitation
LC = laparoscopic cholecystectomy
MP HOOK = monopolar electrocautery endo-hook
PNC = particle number concentration in air ($1/cm^3$)
USC = ultrasonic cutting

Surgically induced aerosols can contain viral DNA (HPV, HIV, Hep B), but also viable tumor cells, therefore questioning the general protection of surgical teams when operating on such patients.[7-10] In the course of the COVID-19 pandemic, it is therefore reasonable to assume that such bioaerosols might harbor a relevant risk of infecting surgical staff by the coronavirus SARS-CoV-2.[11-14] Currently, some experts tend to assume that laparoscopic surgery could increase the surgeon's risk of exposure to aerosolized coronaviruses because the capnoperitoneum itself is a potential source of aerosols.[15] Moreover, a recently performed study reports higher levels of SARS-CoV-2 RNA concentrations in the peritoneal fluid than in the respiratory tract.[16] Although there is no societal consensus on limiting or restricting laparoscopic surgery, there is expert consensus to minimize any risk of coronavirus transmission by a restrictive use of high-frequency electrosurgery and ultrasonic cutting (USC) devices and the use of active aerosol evacuation or passive filter systems during laparoscopic surgery.[17,18]

Electrostatic aerosol precipitation (EAP) technology is widely used in industry as a filtration device that removes fine particles, like dust and smoke, from exhaust gases using the force of an induced electrostatic charge. More recently, EAP technology is now also available as a commercial and medically approved system. Its efficiency has been demonstrated to maintain visual surgical field clarity by bioaerosol clearance in the abdominal cavity during laparoscopic surgery.[19] Although EAP is not widely known in the community of laparoscopic surgeons, this technology has a potential to considerably minimize the exposure risk of surgical-induced aerosols for surgical staff. Therefore, this ex-vivo pilot study focuses on the efficacy of EAP to eliminate surgically induced bioaerosols. Its efficacy is furthermore compared to the intraoperative use of continuous aerosol elimination (CAE) by active filtering of the capnoperitoneum, which is currently one of the most widely used technologies for bioaerosol elimination during laparoscopic surgery.

METHODS

Legal background

Authorization from the Health Department of Bochum, Germany, was obtained to experiment with fresh post-mortal animal tissue. The tissue specimens were disposed of after the experiments in accordance with German law (Tierische Nebenprodukte-Beseitigungsgesetz). Experiments were performed in compliance with German coronavirus containment rules at the Aesculap Akademie GmbH in Bochum, Germany.

Operation room facility and experimental setup

Ex-vivo laparoscopic cholecystectomy (LC) simulations were performed in an operating room facility (6 m × 9 m × 3 m = 162 m^3) in the Aesculap Akademie GmbH in Bochum, Germany. The operating room facility contained a downward displacement airflow ventilation system with an air flow rate of 326.63 m^3/h. The operating table was located in the center of the room and set to a typical operation height of 1 m.

Ex-vivo LCs took place within an airtight Pelvitrainer (Kessler Kunststoffverarbeitung GmbH & Co. KG, and Gotthold Müller Schaumstoffe GmbH & Co.KG) that was modified to a total volume of 9 L CO_2 at a capnoperitoneal pressure of 12 mmHg. The modified Pelvitrainer was equipped with fresh liver and attached gallbladder of a German land race pig (volumetry by water displacement analyses at room temperature revealed a median liver volume of 2.0 [1.7 to 2.1] L). Accordingly, the capnoperitoneal volume within the Pelvitrainer was about 7L—approximately 2 times higher than the one for humans. The specimen was placed on the return electrode plate attached to an electrosurgical generator in the right upper quadrant of the Pelvitrainer. To mimic more realistic conditions within the Pelvitrainer, the inner surface of the Pelvitrainer was coated with a fine layer (1.5 m^2 surface area) of nitrocellulose membrane, which was previously soaked with an aqueous 0.9 wt.-% NaCl solution (Braun). The operative and technical setup was implemented in French position. To obtain maximum tightness of the capnoperitoneum, 4 balloon trocars (Kii Fios First Entry, Applied Medical) were placed by means of puncturing as follows: one 12-mm trocar below the umbilicus for the endoscope and a further 12-mm trocar in the left middle abdomen as the main working trocar, one 5-mm trocar subxyphoidal, and a further 5-mm trocar in the right middle abdomen. Airtightness of the Pelvitrainer was confirmed for each experiment by applying a capnoperitoneum with a capnoperitoneal pressure of

12 mmHg for 10 minutes with a maximum tolerated carbon dioxide leakage volume of 100 mL.

During the experiments, the research team wore standard surgical protective clothing including FFP3 breathing masks (3M Aura 1863+). The Pelvitrainer and the surrounding working place were covered with single use sterile surgical drapes. The following technical equipment was operated: a radiance G2 26" HB/Monitor (NDS Surgical Imaging), a 12-mm CMOS Full HD camera system (Aesculap), an LED light source (OP 940, Aesculap), an insufflator flow system (40/PG080, Aesculap), an electrosurgical generator for monopolar electrocautery endo-hook (MP-HOOK) surgery (GN 640, Aesculap), an ultrasonic scalpel system (Lotus, BOWA-electronic GmbH), and a smoke evacuation system (SHE SHA, BOWA-electronic GmbH).

Generation of surgical-induced bioaerosols by ex-vivo laparoscopic cholecystectomy

To generate typical surgical-induced bioaerosols, particle release was initiated by the simulation of ex-vivo LCs. Standardized incisions of the gallbladder peritoneum in the sulcus between the gallbladder fundus and the Glisson's capsule were performed for 3 seconds by means of high frequency electrosurgery (HFE) using a monopolar electrocautery endo-hook (MP-HOOK) and ultrasonic cutting (USC) device.

The operated devices and parameters to perform ex-vivo LCs were used as follows: monopolar electrocautery endo-hook (MP-HOOK), forced coagulation at 40 watts (MP-HOOK40); monopolar electrocautery endo-hook (MP-HOOK), forced coagulation at 60 watts (MP-HOOK60); and ultrasonic scalpel (USC) in standard cutting mode.

Electrostatic aerosol precipitation for elimination of surgical-induced bioaerosols

To characterize the efficacy of electrostatic aerosol precipitation (EAP) a commercial and medically approved EAP system (Ultravision, Alesi Surgical) was used to eliminate surgically induced bioaerosols during performed laparoscopic cholecystectomies. The operated EAP system is composed of a generator unit (high voltage of 7500−9500 V, current of $\leq$10 μA), a stainless-steel brush electrode (Ionwand, Alesi Surgical), and a return electrode connected to the return plate. The brush electrode produces electrons, which ionize present gas molecules.[20] The formed electrical field between brush electrode and grounded surface lead to unipolar field charging of the aerosol particles (efficient particle charging down to approximately some tenth of nanometers[21]) by the gas ions and to transportation of the particles on the field lines to the grounded surface (called electrostatic deposition). Also, charged particles that escape the electrical field will be deposed more efficiently than noncharged particles. This is due to the induction of image charges on present dipole water molecules on wet surfaces that lead to increased attractive forces.[22] Accordingly, the inner surface of the Pelvitrainer was moistened as described above.

In this study, the brush electrode was introduced into the Pelvitrainer cavity by subcostal puncture via a needle (diameter of 3 mm). The tip was pushed forward to the surgical field as close as possible without interfering with the following surgical manipulations. For all experiments, the positions of the brush electrode and the trocars were kept constant because the distance between brush electrode and bioaerosol source affects the deposition efficiency. For the purpose of comparison, all laparoscopic cholecystectomies experiments were performed with and without electrostatic aerosol precipitation (EAP).

Aerosol-analytical characterization of surgical-induced aerosols

Previous studies have shown that surgical-induced aerosols can span over a considerably wide size range, from a few nanometers to several micrometers, but the largest particle number quantities were found to be between 40 nm and 200 nm.[5] To characterize the surgical-induced bioaerosols in this study, a water-based condensation particle counter (CPC Model 3789, TSI Inc) was operated at a flow rate of 0.6 L/min to determine the total particle number concentration (PNC) in a size range from 7 nm to 1,000 nm. The CPC operation parameters were kept constant over all experiments.

Bioaerosol characterization was performed at 3 relevant locations with different states of aerosol dispersion: near the source within the Pelvitrainer (primary release from the agitated tissue), outside the Pelvitrainer immediately at the working trocar (secondary release from the capnoperitoneum), and in the breathing zone of the surgeon (nearfield exposure of surgical staff). The 3 sampling locations as well as the experimental setup at the Pelvitrainer are shown in Fig. 1.

To keep particles losses by electrostatic effects[23] constant, a conductive tube (Tygon), 60 cm long, was used for aerosol sampling. In the case of primary release characterization from the agitated tissue, the sample tube was connected to the Luer side tap of the subxyphoidal trocar by pushing the tube over the Luer outlet. In case of secondary release from the capnoperitoneum, the inlet of the aerosol sampling tube was fixed with a tripod in a static position 2 cm laterally from the inlet of the 12-mm working trocar. Aerosol sampling in the breathing zone of the surgeon (for exposure characterization) was

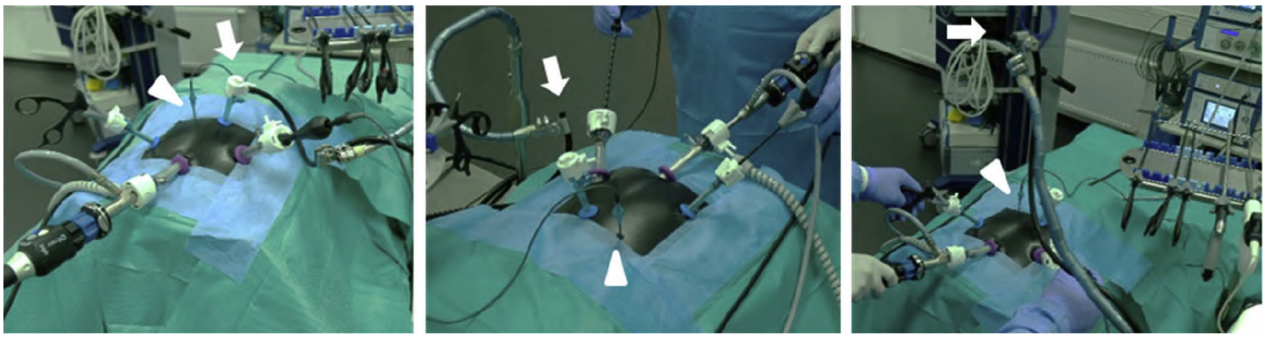

Figure 1. Photographs of the experimental setup: Pelvitrainer with trocar positions and aerosol sampling locations within the Pelvitrainer at the source (left panel), outside the Pelvitrainer at the working trocar (middle panel), and in the surgeon's breathing zone (right panel). Legend: White arrows indicate the position of the inlet of the aerosol sampling tube (left panel: at the Luer valve of the subxyphoidal 5-mm trocar for source sampling in the Pelvitrainer, middle panel: 12-mm working trocar, right panel: breathing zone of surgeon). White triangles show the trocar with inserted brush electrode.

realized via a tripod centered at a height of 70 cm above the 12-mm trocar for the endoscope (umbilicus).

Beside the differences in the sampling locations, there were also some differences in the experimental procedures. Primary release characterization within the Pelvitrainer was performed over a time frame of 100 seconds, with ambient air instead of carbon dioxide. Analyses were performed for monopolar electrocautery endohook at 40 watts (MP-HOOK40), 60 watts (MP-HOOK60), and ultrasonic scalpel (USC) with and without EAP. Between each experiment, the Pelvitrainer was restored by purging it with particle-free air (based on a high efficiency particulate air filter). Both secondary release characterization at the main working trocar and exposure characterization in the surgeon's breathing zone were performed over a time frame of 12 minutes for MP-HOOK60 in an established capnoperitoneum at a capnoperitoneal pressure of 12 mmHg. In contrast to EAP, continuous aerosol/smoke evacuation (CAE) is a well-known and suggested procedure to reduce surgical-induced aerosols during laparoscopic surgery.[18] In addition to analyses with and without EAP, the efficacy of CAE at a carbon dioxide flow rate of 12 L/minute (SHE SHA Level 2) was studied for MP-HOOK60 outside the Pelvitrainer immediately at the working trocar.

Statistical analysis

All experiments were performed in triplicate. Data analysis was performed by means of professional statistics software (SPSS V26.0, IBM Corp). Data are presented as median (minimum/maximum range) and boxplots (median and interquartile range [IQR] = Q3 − Q1) of particle number concentrations in number of particles per cm^3 of air ($1/cm^3$). For aerosol source characterization, each test was performed over 100 seconds at a time resolution of 1 second. Aerosol sampling during simulated ex-vivo LC was continuously performed over 12 minutes, with a time resolution of 1 second.

Quantitative variables were compared using the Mann-Whitney test. A value of $p < 0.05$ represented a significant difference. The Pearson correlation coefficient r was calculated for characterizing the impact of EAP on the formed bioaerosol within the Pelvitrainer; $r > 0.5$ is considered as high degree of linear correlation.

RESULTS

Bioaerosol concentration within the Pelvitrainer near the release source (primary release)

The concentration data of the bioaerosols within the Pelvitrainer have to be doubled when approximating the measured data of this study to typical human capnoperitonea, since the capnoperitoneal volume for humans is approx. 3.5 L, which is the half of the volume of the used Pelvitrainer (ie Pelvitrainer volume of 9 L minus 2 L liver volume). In Figure 2, the arising particle number concentrations (PNCs) of the performed laparoscopic cholecystectomies (ie MP-HOOK40, MP-HOOK60, and USC) with and without EAP are summarized.

According to Fig. 2, the highest median particle number concentrations (PNCs) were determined for laparoscopic cholecystectomies without EAP. With a median PNC of 7.3×10^5 ($7.4 \times 10^4 - 1.0 \times 10^6$) cm^{-3}, MP-HOOK60 showed the highest bioaerosol concentration, followed by MP-HOOK40 with 6.4×10^5 ($1.8 \times 10^4 - 1 \times 10^6$) cm^{-3} and USC with 4.4×10^5 ($1.3 \times 10^5 - 9.8 \times 10^5$) cm^{-3} ($p < 0.01$). In all 3 experiments, the continuous use of EAP decreased the prevailing bioaerosol significantly during the performed laparoscopic cholecystectomies.

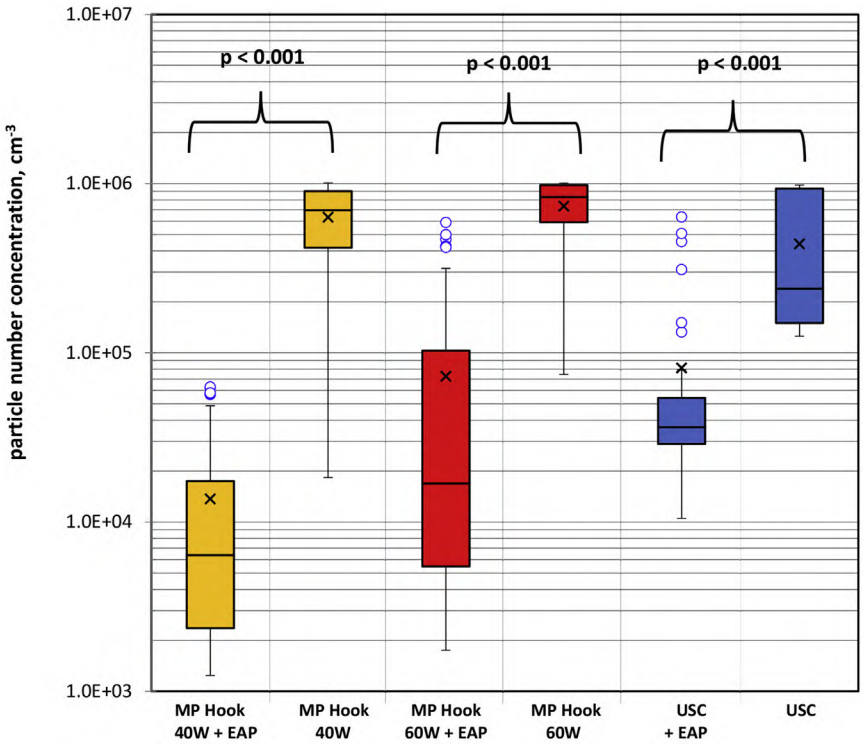

Figure 2. Bioaerosol concentration within the Pelvitrainer: Effect of ex-vivo laparoscopic cholecystectomy (LC) type (ie, MP-HOOK40, MP-HOOK60, ultrasonic cutting [USC]) with and without electrostatic aerosol precipitation (EAP) on the particle number concentration of the surgical-induced bioaerosols. MP-HOOK40, ex-vivo laparoscopic cholecystectomy based on monopolar electrocautery endo-hook forced coagulation at 40 watts; MP-HOOK60, ex-vivo LC based on monopolar electrocautery endo-hook forced coagulation at 60 watts.

The lowest median PNC with 1.4×10^4 ($1.2 \times 10^3 - 3.1 \times 10^4$) cm^{-3} was measured for MP-HOOK40 + EAP, followed by 7.2×10^4 ($1 \times 10^4 - 6 \times 10^5$) cm^{-3} for USC + EAP and 7.5×10^4 ($1.8 \times 10^3 - 5.9 \times 10^5$) cm^{-3} for MP-HOOK60 + EAP. A high linear correlation (Pearson correlation coefficients of 0.852, 0.825, and 0.759) was observed by comparing MP-HOOK40 with and without EAP, MP-HOOK60 with and without EAP, and USC with and without EAP, respectively. The lowest median PNC over all experiments was determined for MP-HOOK40 + EAP ($p < 0.01$).

Bioaerosol concentration outside the Pelvitrainer at the working trocar (secondary release)

Representative measurement data of the PNC over time of the surgical-induced bioaerosols based on MP-HOOK60 and MP-HOOK60 + EAP and each initial operating room facility background aerosol are provided in Figure 3.

Measurements of the background aerosol, which prevailed in the operation room facility at the Pelvitrainer, showed a median PNC of 9.4×10^2 ($8.3 \times 10^2 - 1.0 \times 10^3$) cm^{-3}. According to Figure 3, considerable PNC were measured in the aerosol cloud outside the Pelvitrainer near the working trocar during MP-HOOK60 without EAP. With a median PNC of 2.6×10^5 ($2.6 \times 10^3 - 9.9 \times 10^5$) cm^{-3}, laparoscopic cholecystectomy based on MP-HOOK60 led to an approximately 274 times higher median PNC, as determined for the operating room facility background aerosol ($p < 0.0001$). Performing MP-HOOK60 in combination with EAP significantly reduced the particle number concentration (PNC) in the aerosol cloud at the working trocar by a factor of approximately 152, to a median PNC of 1.7×10^3 ($9.0 \times 10^2 - 7.7 \times 10^4$) cm^{-3}. The slight increase of the PNC based on MP-HOOK60 + EAP in comparison to the background aerosol (factor 1.8) can possibly attributed to amounts of ultrafine particles < 30 nm in the bioaerosol, for which the charging probability becomes lower than 100% and decreases with decreasing particle size. To get an impression of the efficacy of bioaerosol evacuation by continuous

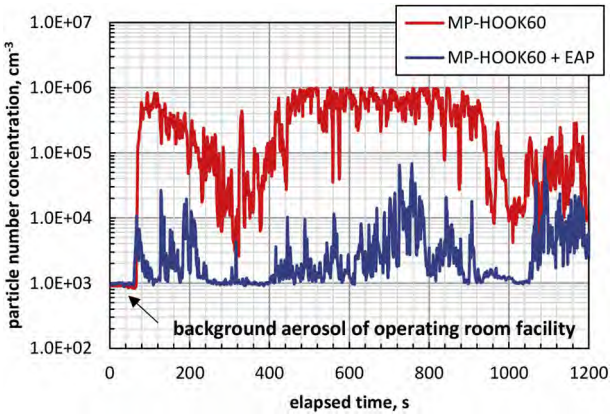

Figure 3. Bioaerosol concentration in the released aerosol cloud outside the Pelvitrainer near the working trocar: particle number concentration over time of the background aerosol and the surgical-induced bioaerosols based on ex-vivo laparoscopic cholecystectomy based on monopolar electrocautery endo-hook forced coagulation at 60 watts (MP-HOOK60) and MP-HOOK60 + electrostatic aerosol precipitation (EAP).

aerosol elimination (CAE) technology and EAP, Figure 4 depicts the PNC over time at the working trocar during a laparoscopic cholecystectomy with the monopolar electrocautery endo-hook at 60 watts (MP-HOOK60).

As can be deduced from Fig. 4, continuous aerosol evacuation (CAE) at a carbon dioxide flow rate of 12 L/minute (SHE SHA Level 2) leads during MP-HOOK60 operation to a considerable high steady state PNC level, with a median PNC of 9.4×10^5 ($9.1 \times 10^5 - 9.6 \times 10^5$) cm^{-3} that decreases gradually after switching off

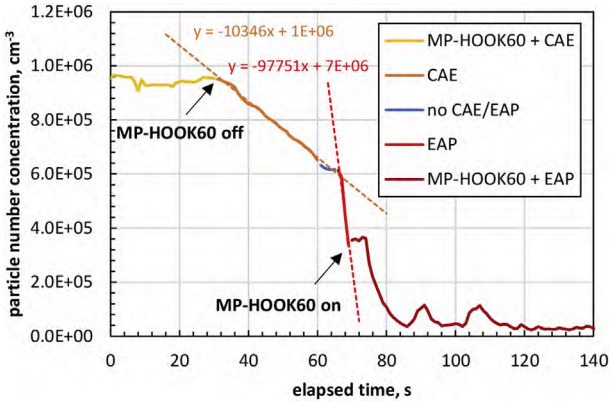

Figure 4. Representative bioaerosol concentrations in the released aerosol cloud outside the Pelvitrainer near the working trocar: effect of continuous aerosol evacuation (CAE) and electrostatic aerosol precipitation (EAP) on the particle number concentration (PNC) over time for a bioaerosol induced during an experimental laparoscopic cholecystectomy with ex-vivo laparoscopic cholecystectomy based on monopolar electrocautery endo-hook forced coagulation at 60 watts (MP-HOOK60).

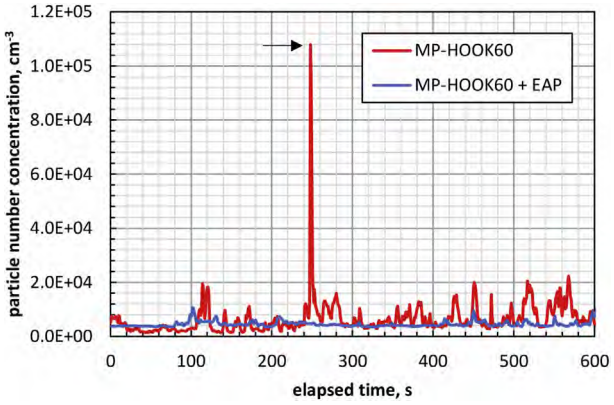

Figure 5. Bioaerosol concentration in the surgeons breathing zone during an experimental ex-vivo laparoscopic cholecystectomy: particle number concentration over time of the background aerosol and the surgical-induced bioaerosols based on ex-vivo laparoscopic cholecystectomy based on monopolar electrocautery endo-hook forced coagulation at 60 watts (MP-HOOK60) and MP-HOOK60 + electrostatic aerosol precipitation (EAP). Black arrow, high short-term bioaerosol concentration during manipulations with a 10-mm clip forceps via the working trocar.

MP-HOOK60. In contrast, switching on EAP (without MP-HOOK60) results in an even more rapid decrease of the PNC. After switching MP-HOOK60 on during continuous EAP operation, the PNC further decreases and leads finally to a median PNC of 4.1×10^4 ($1.5 \times 10^4 - 1.1 \times 10^5$) cm^{-3} ($p < 0.0001$), which is 23 times lower than during the CAE operation with MP-HOOK60 at a carbon dioxide flow rate of 12 L/minute (SHE SHA Level 2).

Bioaerosol concentrations in the breathing zone of the surgeon

Figure 5 compares intrinsically measured PNC courses over time, as received from the breathing zone sampling point during MP-HOOK60 operation with and without EAP. The median PNC of the represented time course of MP-HOOK60 without EAP in Figure 5 (time frame of 600 seconds) was determined to be 4.7×10^3 ($1.4 \times 10^3 - 1.1 \times 10^5$) cm^{-3}. Indeed, MHE60 with EAP shows with a median PNC of 4.2×10^3 ($3.4 \times 10^3 - 1.1 \times 10^4$) cm^{-3} only a slightly lower median PNC. But in contrast to MP-HOOK60 without EAP, MP-HOOK60 with EAP does not show considerably high short-term PNC peak events.

DISCUSSION

There is a major lack of interest and knowledge among surgeons that the exposure to surgical-induced aerosols represents a potential health risk.[24,25] For economic reasons, hospital administrations urge surgeons to minimize

intervention times. Accordingly, surgical techniques like systems for high frequency electrosurgery (HSF) and ultrasound cutting (USC) are operated at high energy levels to achieve faster tissue transection and sealing. This is accompanied by the formation of highly concentrated and sometimes toxic bioaerosols. To further reduce costs, the use of aerosol elimination systems is often avoided. But in the course of the COVID-19 pandemic, the potential risk to acquire COVID-19 by exposure with coronavirus-laden surgical aerosols has raised major concern and uncertainty among surgeons. In the meantime, national and international expert committees and professional societies have published their recommendations for avoiding unnecessary bioaerosol generation and guidelines for exposure protection.[15,17,18,26] However, unknown to most surgeons, electrostatic aerosol precipitation (EAP), as used, for example, to improve drug deposition during pressurized intraperitoneal aerosol chemotherapy,[20,22] is a cost-efficient and effective method to eliminate surgical-induced aerosols during laparoscopic surgery.

In this study, the efficacy of EAP was analyzed by ex-vivo simulations on a clinically relevant experimental setup with a phantom for laparoscopic procedures by characterizing the particle number concentration of surgically induced bioaerosols within the laparoscopic cavity (primary release from tissue), outside the laparoscopic cavity near the working trocar (secondary release from the cavity), and in the breathing zone (exposure) of the surgeon. During incision on the used swine gallbladder peritoneum by high-frequency electrosurgery with a monopolar electro hook (MP-HOOK) force at 40 watts (MP-HOOK40) respectively, 60 watts (MP-HOOK60), and by ultrasonic cutting (USC), a considerable release of particles was determined within the laparoscopic cavity.

In daily practice, the energy settings for laparoscopic cholecystectomy with monopolar electrosurgery in the US are generally in the 25 to 30 watt range.[27] Because such low energy settings did not allow adequate tissue transection of cadaveric swine gall bladders in our ex-vivo Pelvitrainer model, higher energy settings of 40 and 60 watts were used for this study. Additionally, to our very best knowledge, power settings for monopolar cholecystectomy in many German hospitals and German surgical training centers, such as the Aesculap Academy in Bochum, are generally between 40 to 60 watts.

The highest PNC was observed for MP-HOOK60. A trend toward a lower PNC was determined for MP-HOOK40. However, this difference was not statistically significant. A significant lower PNC occurred for USC in standard cutting mode as well as power settings. These findings are in line with the results of previous work, which showed higher particle release rates for monopolar-based instruments than for USC.[11,28,29] Although USC has been shown to produce fewer aerosol particles than mono- and bipolar cutting devices, the COVID-19 pandemic has raised new concerns about the use of USC. This is due to the generation of aerosols composed of tissue, blood, and blood degradation products that could be identified up to 40 cm from the source.[11]

The results of this study show that a continuous operation of EAP significantly lowers the PNC within the abdominal cavity of the phantom, irrespective of the operated tissue dissection technique. Despite the fact that released particles become airborne at the site of surgery, the largest amount is immediately deposited on the tissue in close proximity. Therefore, only small quantities of released particles can distribute in the entire capnoperitoneum. Besides improving the endoscopic view, the reduced quantity of airborne particles also lowers potential release quantities from the laparoscopic cavity via the access ports (ie trocars) into the environment of the operating room facility.

To study bioaerosol release into the operating room facility at the site of the working trocar and in the breathing zone of the surgeon, clinical conditions were simulated as realistically as possible. Therefore, the instruments were operated similar to typical clinical use, with various lengths of application. To compare environment contaminations, all ex-vivo LCs were performed according to a strict protocol. In contrast to MP-HOOK40 without EAP, MP-HOOK60 without EAP led to significant particle number concentrations at the access port (trocar) outside the laparoscopic cavity. Considerable PNCs, which were about 274 times higher than the background aerosol of the operating room facility, were monitored during the exchange, and the use of laparoscopic instruments (mainly for clip forceps and laparoscopic swaps). In contrast, continuous operation of EAP during MP-HOOK60 led to a concentration level 152 times lower at the access port, which was only 1.8 times higher than the level of the background aerosol of the operating room facility. Additionally, the performance of EAP was compared with that of the currently suggested safety measure for continuous aerosol/smoke evacuation (CAE). Therefore, MP-HOOK60 was also performed in combination with CAE at a continuous carbon dioxide flow rate of 12 L/minute (SHE SHA Level 2). During MP-HOOK60, CAE operation showed significant contaminations at working trocars that were 23 times higher than for EAP operation.

Besides the high aerosol elimination efficacy, EAP also has other important advantages over carbon dioxide-

driven active and passive aerosol evacuation and filter systems. First, the efficiency of passive filter systems correlates with the level of the capnoperitoneal pressure. Therefore, surgery at lower pressure is even more difficult because the endoscopic view at the surgical site can be hampered by intraperitoneal aerosol accumulation and worse exposure of the surgical field. Second, the efficacy of active and passive aerosol evacuation and filter systems depends on a high carbon dioxide flow rate. This makes it more difficult for the surgical staff to recognize and prevent unintended carbon dioxide and bioaerosol leaking into the environment. Especially active aerosol evacuation systems, which are operated at high carbon dioxide flow rates, lead to fluctuations in the capnoperitoneal pressure that is accompanied by movements of the abdominal wall, trocars, and the camera position with a changing view of the surgical site. Therefore, such movements complicate surgical procedures and can harm the patient.

The authors are aware that the current data reflect only the clinical situation with some limitations. Foremost, the generation of surgical smoke on non-vital/non-perfused tissue in a Pelvitrainer at room temperature is certainly a major limiting factor of this study. Moreover, this pilot study includes neither in-vivo analyses nor a detailed characterization of the generated surgical aerosol in terms of size distributions. Due to the temporal lack of aerosol sizing technologies as well as the national restrictions in the course of the COVID-19 pandemic, only a condensation particle counter was operated. Therefore, the considerable release of particles during ex-vivo LC limited the incision time for release characterization to 3 seconds to avoid a passing of the concentration limit of the operated device. For studying particle release and exposure of surgical-induced bioaerosols for long-term or repeated LCs in future work, besides size-selective aerosol-analytical instruments, appropriate aerosol dilution measures[30,31] should be used. However, with regard to the coronavirus, released particles/droplets equal to or larger than the virus (65 to 125 nm) are relevant.[32] The determined particle number concentrations alone can only serve as an indicator for a lowered risk of becoming infected by aerosolized virus particles encountered during laparoscopic surgery. It is therefore necessary to carry out follow-up studies on in-vivo laparoscopic animal models with a detailed characterization of generated bioaerosols.

CONCLUSIONS

EAP is an efficient method to eliminate generated bioaerosols already at the surgical site and minimize potential bioaerosol exposure to surgical staff. EAP is currently the most efficient method for aerosol evacuation and elimination. A previous study reported the efficient capture of viruses and its concomitant deactivation using electrostatic precipitation technology,[33] so EAP should become even more promising in the future.

Author Contributions

Study conception and design: Giger-Pabst, Buggisch, Göhler
Acquisition of data: Giger-Pabst, Buggisch
Analysis and interpretation of data: Giger-Pabst, Buggisch, Göhler
Drafting of manuscript: Giger-Pabst, Buggisch, Göhler
Critical revision: Roger, Ouaissi, Stintz, Rudolph, Le Pape

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Attachment H

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Performance of intraoperative surgical smoke management technologies for laparoscopic surgery: A comparative *in-vivo* pig study

Daniel Göhler [a,b,1,*], Levon Aslanyan [c,1], Kathrin Oelschlägel [a], Petru Bucur [d], Jonathan Buggisch [e], Nadia Azhari [f], Andreas Rudolph [a], Sébastien Roger [f], Michael Stintz [b], Dirk Bausch [g], Cédric Demtröder [h], Mehdi Ouaissi [d,f,2], Urs Giger-Pabst [f,i,2]

[a] *Topas GmbH, Dresden, Germany*
[b] *Research Group Mechanical Process Engineering, Institute of Process Engineering and Environmental Technology, Technische Universität Dresden, Dresden, Germany*
[c] *Ruhr University Bochum, Bochum, Germany*
[d] *Department of Digestive, Oncological, Endocrine, Hepato-Biliary, Pancreatic and Liver Transplant Surgery, University Hospital of Tours, France*
[e] *Westphalian Wilhelms University Münster, Münster, Germany*
[f] *EA4245 Transplantation, Immunologie, Inflammation, Université de Tours, France*
[g] *Chirurgische Klinik, Marienhospital Herne, Klinikum der Ruhr Universität Bochum, Bochum, Germany*
[h] *Martinus-Krankenhaus, Department of Surgery, Düsseldorf, Germany*
[i] *Fliedner Fachhochschule, University of Applied Science Düsseldorf, Düsseldorf, Germany*

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ABSTRACT

Background: Various technologies exist to remove surgical smoke. Despite high significance in surgical practice, comparative *in-vivo* performance data are missing.
Study design: The performance of five smoke management technologies (venting, passive filtering, active filtering, circular filtration, electrostatic precipitation) was analysed in-vivo by three different laparoscopic interventions (cholecystectomy, atypic liver resection, colon surgery) with high-energy surgical instruments. Surgical smoke formation/evacuation was characterised by various aerosol-analytical instruments. In addition, operational parameters like CO_2 consumption and capnoperitoneal pressure were determined.
Results: The half-life of particle concentration was found to be a suitable parameter to describe smoke elimination efficacy and varied between (10 - 45) s. It is shown that the efficacy of smoke elimination technologies based on particle removal by evacuation can also be predicted by simple equations. Furthermore, it was found that the combination of surgical cutter and tissue defines charge and polarity of surgical smoke that influences especially the efficacy of electrostatic precipitation. Depending on the smoke elimination technology, the CO_2 consumption varied between (0.5 - 16) L/min, the capnoperitoneal stability between (2 - 17) %.
Conclusions: Each smoke elimination technology showed advantages and disadvantages. Simple charcoal filters rapidly degrade and should be exchanged regularly during surgery. Active

* Corresponding author. Topas GmbH, Gasanstaltstraße 47, 01237, Dresden, Germany.
E-mail address: dgoehler@topas-gmbh.de (D. Göhler).
[1] Both authors contributed equally and each should be considered as first author.
[2] Both authors contributed equally and each should be considered as senior author.

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filtering is efficient for smoke management, but the unstable capnoperitoneum interferes with surgery. Circular filtration forms a stable capnoperitoneum, but the valveless trocar promotes relevant levels of smoke release into the environment. Electrostatic precipitation was found to be most efficient for smoke management with minimal CO_2 consumption and highly-stable capnoperitoneum.

Abbreviations

APS	Aerodynamic particle sizer
CPC	Condensation particle counter
EAD	Electrical aerosol detector
HEPA	High efficiency particulate air (filter)
LALR	Laparoscopic atypic liver resection
LAP	Laser aerosol particle size spectrometer
LCHE	Laparoscopic cholecystectomy
LCS	Laparoscopic colon surgery
MEH	Monopolar endo-hook
OPS	Optical particle sizer
SLI	Standard laparoscopic insufflator
USC	Ultrasonic cutting

1. Introduction

Laparoscopic surgery is a since 1980s established sub-speciality of surgery that deals with minimal-invasive, endoscopic interventions in the abdominal cavity under general anaesthetic. The number of annually performed laparoscopic interventions increases steadily and reached already in 2018 more than 15 million (Boberg et al., 2022). The most frequent laparoscopic interventions are the removal of the appendix (appendectomy), the gallbladder (cholecystectomy) or diseased tissue of the liver (atypic liver resection). Prior a laparoscopic intervention, a muscle relaxant is administrated and the abdominal cavity is inflated via an insufflator (i.e., a device for pressure-controlled gas supply) with carbon dioxide to create a sufficient working space (called capnoperitoneum) for the intervention. Afterwards special tubular passages with integrated closure seals (called trocars) are set to get access to the surgical field for laparoscopic instruments like endoscopes, scissors, scalpels or forceps.

In the last decades, classical surgical cutting instruments were widely replaced by modern energy-driven instruments like monopolar endo-hooks (MEH) or ultrasonic cutters (USC) for precise and fast laparoscopic surgery. Common to them is combustion, vaporisation, coagulation and/or mechanical disintegration of tissue and body fluids (Ott et al., 1998; Qaiser et al., 2020). Thus, their use is accompanied with the formation of surgical smoke that contains i.a. water vapour, particulate matter, cell debris, bacteria, viruses and malignant cells (Steege et al., 2016; Limchantra et al., 2019; Van Gestel et al., 2020; AORN 2021; Vortman et al., 2021), which are potentially harmful to exposed healthcare workers.

Surgical smoke leaves the pressurised capnoperitoneum into the operating room in form of aerosol jets through the trocars, especially when laparoscopic instruments are moved. Intra-operative smoke simulation showed that modern overpressure ventilation systems used in operating rooms are not sufficient to eliminate adequately surgical smoke (Elmashae et al., 2018; Hardy et al., 2021). The health risk posed by surgical smoke is underlined by published data from public health authorities that indicate that approximatively 500′000 US healthcare workers are regularly exposed each year (Steege et al., 2016).

The potential risk of intra-operative transmission of severe acute respiratory syndrome coronavirus through surgically induced smoke led to intensive debates on the safety of laparoscopic surgery. To minimize intra-operative smoke generation and excessive escape into the operating room, expert panels recommend operating energy-driven surgical devices at the lowest possible energy settings, decreasing capnoperitoneal pressure, and minimising or avoiding CO_2 flow/consumption and unintended capnoperitoneal leaks through trocars. Much attention has been paid on technologies for intra-operative surgical smoke management (Buggisch et al., 2020; Francis et al., 2020; Mowbray et al., 2020; Pryor, 2020) that serve to lower the concentration level within the capnoperitoneum. Currently, different technologies for surgical smoke management are promoted. The most common methods are passive or active filtration of the capnoperitoneum and more recently electrostatic precipitation.

Although all guidelines recommend the use of intra-operative surgical smoke management technologies, only limited data on the efficacy of these technologies exist, and relevant comparative *in-vivo* data are still missing (Francis et al., 2020; Mowbray et al., 2020; Pryor, 2020). The present study focuses on the comparative performance characterisation of different surgical smoke management technologies in a clinically relevant setting.

2. Methods

2.1. Animals and anaesthesia

A total of 20 pigs (Large White) with a female/male sex ratio of 4/16, a body weight of (40.3 ± 3.2) kg and an age of (90.4 ± 8.2) days were used. Anaesthesia was induced by intramuscular injection of ketamine 20 mg/kg, xylazine 2 mg/kg, subcutaneous atropine 0.02 mg/kg and followed by endotracheal intubation. Animals were maintained under anaesthesia by isoflurane 3 %, intravenous sufentanil, and cisatracurium. Finally, animals were euthanised by intravenous pentobarbital.

2.2. Operating room characteristics

Surgery and analyses took place in a non-technical-ventilated operating room (volume $V_{OR} = 82.3\ m^3$) at a temperature of $\vartheta_{OR} = (25.3 \pm 1.3)\ °C$, a relative humidity of $\varphi_{OR} = (35.2 \pm 3.7)$ % and a pressure of $p_{OR} = (101.6 \pm 3.3)$ kPa.

2.3. Surgical interventions

Animals (in supine position) were connected to the return plate of an electro-surgery generator (GN 640, Aesculap, Germany) and fixed at the operation table. Access to the abdomen was achieved by Veress needle puncture at Palmer's point. Afterwards, a capnoperitoneum at 10 mmHg (1.3 kPa) was established by a standard insufflator (40/PG080, Aesculap, Germany) and trocars (Kii Shielded Bladed Access System; Applied Medical, USA) were positioned as follows: in the centre of the abdomen a 12 mm trocar (T5), under visual control with a 10 mm zero-degree camera (CMOS Full HD, Aesculap, Germany) one 5 mm trocar (T1) each subxyphoidal, mid-abdomen laterally left (T2) and right (T3), and another 12 mm trocar (T3) in the middle lower abdomen. Laparoscopic cholecystectomy (LCHE), laparoscopic atypical liver resection (LALR) and laparoscopic colon surgery (LCS) were performed in sequence for each animal as follows:

- **LCHE**: Monopolar electrocautery endo-hook (MEH, GK384R, Aesculap, Germany) operated on forced coagulation at 30 W. Clipping of cystic duct/artery with a 10 mm clip applicator (Titan Challenger®, Aesculap, Germany) and transection with 5 mm scissors (PO004R, Aesculap, Germany).
- **LALR**: Ultrasonic cutter (USC, Lotus LG4 5.5 × 394 mm, BOWA MEDICAL, Germany) operated at low energy settings. Liver parenchyma cut of 15 cm (left lateral lobe).
- **LCS**: Caecal mobilisation by close dissection along the colon to the first colonic coil using USC. Five minutes after the end, a left transverse 20 cm mid-abdomen laparotomy was performed to eventerise the caecum.

2.4. Surgical smoke management technologies

Five surgical smoke management technologies were examined during the surgical interventions for four pigs each:

- **A**: continuous passive venting (i.e., simple purging) of the capnoperitoneum via the side valve of trocar T3.
- **B**: continuous passive filtration via trocar T3 and an activated charcoal filter (HEPA-14, LSES 3604, Purple Surgical, UK).
- **C**: continuous active filtration with an aerosol evacuation system (SHE SHA, BOWA MEDICAL, Germany) equipped with a multistage filter system (composed pre-filter, ULPA-15 filter, charcoal filter, post-filter) and operated at intermediate intensity level at the side valve of trocar T3.
- **D**: circular filtration (AirSeal® iFS CONMED, USA) via a tri-lumen (for pressure-controlled supply and removal of carbon dioxide by capnoperitoneal pressure monitoring) filtered tube set (ULPA filter) connected to the AirSeal® access port in T3 position operated at high smoke evacuation mode.
- **E**: continuous electrostatic aerosol precipitation based on an ion generation system (Ultravision™, Alesi Surgical Ltd., UK) that operates a negative-polarised brush electrode (operated at 9 kV, positioned in the right upper quadrant for LCHE/LALR and in the

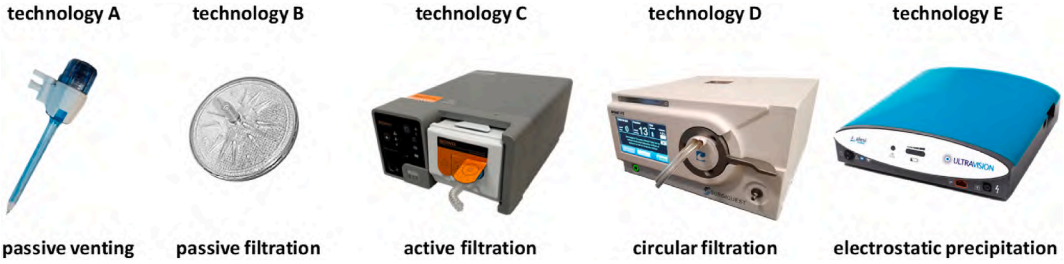

Fig. 1. Photographic images of the examined surgical smoke management technologies.

left lower quadrant for LCS) and forms in combination with an electro-surgery setup an electrical field between brush electrode and peritoneum for particle removal (Ansell, Warren, & Wall, 2014).

In summary, the examined surgical smoke management technologies as shown in Fig. 1 make use of two mechanisms for surgical smoke removal, i.e., by particle evacuation via steady carbon dioxide exchange (A/B/C/D) at specific flow rates and by intra-abdominal particle deposition by electrostatic precipitation (E).

Excepting for technology D, the standard insufflator was operated. Surgery was briefly interrupted if intra-operative visibility was inadequate. Unusual events and observations during surgery were recorded. Details on the implementation of the surgical smoke management technologies are shown in Fig. 2.

2.5. *Monitoring of capnoperitoneal volume, capnoperitoneal pressure and carbon dioxide flow rate as well as carbon dioxide leak quantification of the AirSeal® access port*

The capnoperitoneal volume as well as the carbon dioxide flow rate were determined using the displayed values for total carbon dioxide consumption from the operated insufflators. To calculate the carbon dioxide flow rate, carbon dioxide consumption data were recorded at (2, 4, 6, 7, 8) min after start of each intervention.

The capnoperitoneal pressure was monitored at 0.1 Hz by a precision pressure probe (Almemo 2590-4AS data logger with FDA612SR sensor, Ahlborn, Germany) via the side valve of trocar T4.

Previous work showed significant carbon dioxide leakage via the 12 mm AirSeal® access port (Dalli et al., 2020). Accordingly, CO_2 leakage quantification was performed in additional analyses by means of a bubble flowmeter (Gilibrator 2, Sensidyne, USA) connected airtight to the trocar at capnoperitoneal pressures of (10, 12, 15) mmHg that corresponds to (1.3, 1.6, 2.0) kPa.

2.6. *Surgical smoke characterisation*

Modern energy-driven surgical instruments lead to the formation of smoke particles in a size range of (0.01–10) µm (Ott et al., 1998; Elmashae et al., 2018; Dalli et al., 2020; Francis et al., 2020; Mowbray et al., 2020). Performed preliminary laboratory analyses (Göhler et al., 2021) by simulating smoke formation from fresh post-mortem swine livers due to LCHE and LALR within a training dummy for surgeons (Pelvitrainer, Kessler Kunststoffverarbeitung GmbH & Co. KG, and Gotthold Müller Schaumstoffe GmbH & Co. KG) have shown two important facts for the current *in-vivo* study. First, the number-weighted size distribution based on LCHE (geometric mean diameter $x_{m,geo,LCHE} = 136$ nm, geometric standard deviation $\sigma_{ln,LCHE} = 1.52$) is slightly finer than the size distribution for LALR ($x_{m,geo,LALR} = 143$ nm, $\sigma_{ln,LALR} = 1.52$). Second, smoke formation during surgical interventions is highly unsteady, i.e., characterisation of smoke formation requires a sufficient high time resolution.

A two-sectional aerosol-analytical setup for simultaneous intra- and extra-abdominal surgical smoke analyses was arranged on a

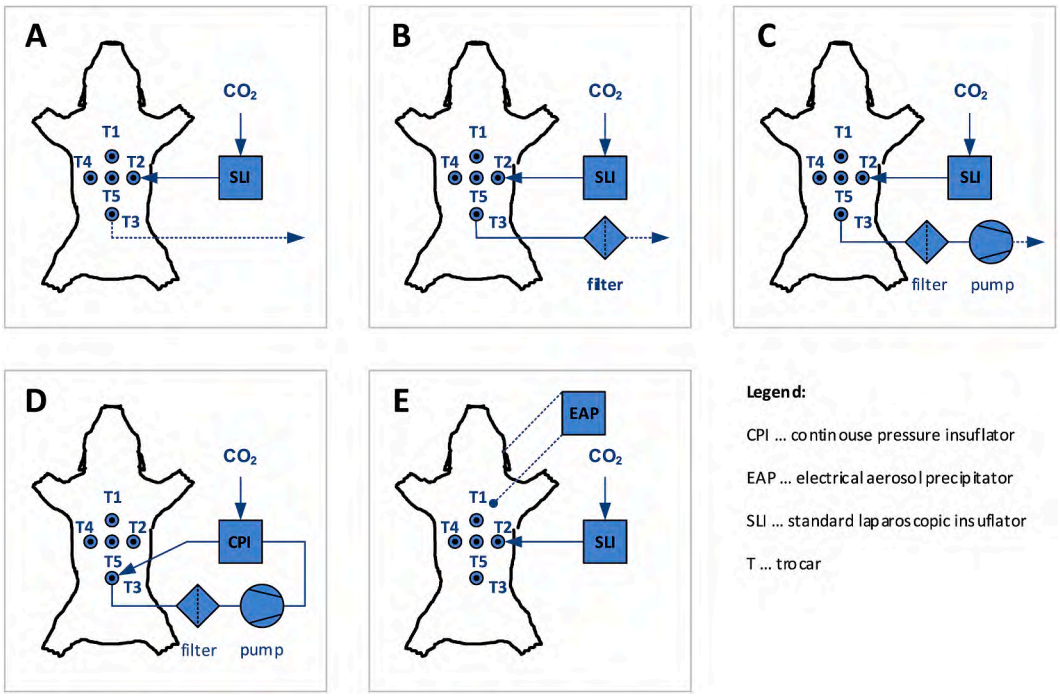

Fig. 2. Implementation of examined surgical smoke management technologies.

transport trolley. One section served for intra-abdominal smoke sampling via the side valve of trocar T4, while the other section was used for extra-abdominal smoke characterisation via a sampling hood in close proximity to trocar T3. A schematic representation of the two-sectional setup is given in Fig. 3, a photographic image is provided in the supplement.

In order to obtain reliable data over the entire size range and specific size fractions, different aerosol-analytical instruments were operated. Surgical smoke was characterised by means of two condensation particle counters (CPC, Model 3772, TSI Inc., USA; size range of (0.01 - 10) µm, time resolution of 1 s) (Sem, 2002), two laser aerosol particle size spectrometers (LAP, Model LAP 323, Topas GmbH, Germany; size range of (0.15 - 5) µm, time resolution of 2 s; ISO 2009), an optical particle sizer (OPS, Model 3330, TSI Inc., USA; size range of (0.3 - 10) µm, time resolution of 10 s; ISO 2009), a time-of-flight spectrometer (APS, Model 3321, TSI Inc., USA; size range of (0.5 - 20) µm, time resolution of 10 s) (Holm et al., 1997; Wilson & Liu, 1980) and an electrical aerosol detector (EAD, Model 3070A, TSI Inc., USA) (Li, & ChenTsai, 2009).

Beside aerosol analytical instruments, the two-sectional setup was equipped also with various components to enable proper operation of the instruments and to avoid analytical artefacts. The following aerosol sampling and aerosol conditioning measures were realised in both sections of the aerosol-analytical setup:

- Sampling of the intra-abdominal aerosol in setup section S1 was realised on the side valve of trocar T4, while trocar T3 was equipped with a self-made sampling hood to improve repeatability of measurements of setup section S2.
- To counteract time-depended particle losses in the sampling lines to the measurement devices, conductive hose-lines and conductive connection elements were used for all aerosol-bearing regions of both setups.
- To ensure accurate operation of the aerosol-analytical instruments that are designed for the use for aerosols made of air, the carbon dioxide-based aerosol sample flow rate of (0.17 ± 0.03) L/min was mixed with a sufficient high particle-free air flow rate of (2.79 ± 0.05) L/min prior further conditioning and analyses.
- Three types of measures for defined aerosol dilution were realised within the two aerosol-analytical setups to enable proper operation of the aerosol-analytical instruments. The already mentioned primary mixture of sample flow with particle-free air in setup section S1 served also for a primary aerosol dilution (dilution factor 18.02 ± 5.77). In both setups, the exhaust air of selected instruments was HEPA filtered and remixed with the main aerosol sampling flow (dilution factor of 1.75 in setup S1, dilution factor of 9 in setup S2). Furthermore, section S1 was equipped with an additional dynamic dilution system (DDS 560, Topas GmbH, Dresden, Germany) to decrease the particle number concentration situational by a further dilution factor of 20 - 300. The realised overall dilution in setup S1 varied in dependence of the surgical interventions and the prevailing conditions between 293 and 15'593.

In addition, analyses were performed to characterise electrical charge and polarity of smoke released from different tissues (i.e., liver, colon, small intestine, stomach, and spleen). Repetitive tissue cuts were made for 3 s by use of MEH and USC. Surgical smoke was sampled and characterised via the side valve of trocar T4 by the EAD.

2.6.1. *Calculation formula for particle concentration decrease and concentration half-life*

Exponential particle number concentration decrease can be described by Eq. (1):

$$c_0(t_2) = c_0(t_1) \bullet \exp(\lambda \bullet (t_2 - t_1)) \tag{1}$$

The particle number concentration half-life $T_{1/2}$ for exponential concentration decrease can be determined by means of Eq. (2):

$$T_{1/2} = \frac{\ln(2)}{\lambda} = \frac{\ln(2) \bullet (t_2 - t_1)}{\ln\left(\frac{c_0(t_2)}{c_0(t_1)}\right)} \tag{2}$$

In the case of evacuation-based surgical smoke management technologies (A/B/C/D), the intra-abdominal concentration half-life can also be estimated on the base of the capnoperitoneal volume $V_C(p_C)$ and the CO_2 flow rate $Q_{C,CO2}$ by Eq. (3), which was derived from

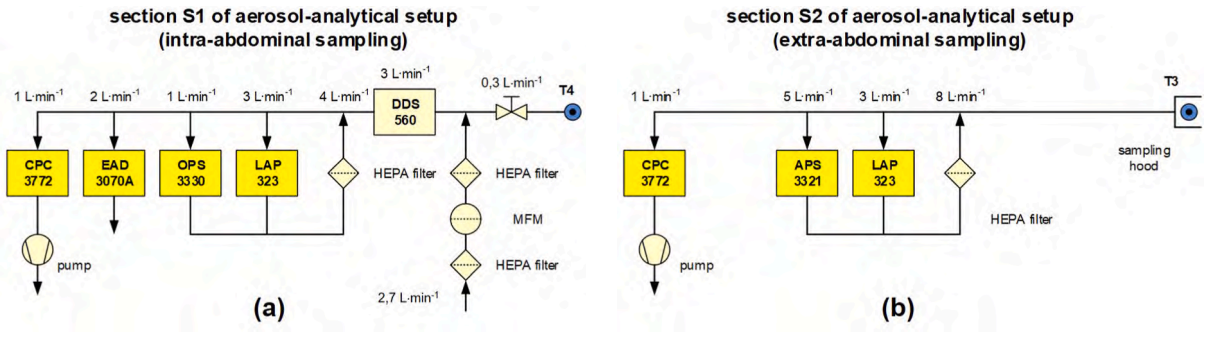

Fig. 3. Schematic representation of operated two-sectional aerosol-analytical setup.

the standard one-box steady state model for the decay phase as typically used in the area of occupational hygiene to describe the concentration decrease in well-ventilated rooms (Hewett & Ganser, 2017).

$$T^{*}_{1/2} = \ln(1/2) \bullet -\frac{V_C(p_C)}{Q_{C,CO2}} \tag{3}$$

It should be noted that Eq. (3) is not suitable for estimating the concentration half-life of surgical smoke management technology E, since electrostatic precipitation is not covered by the model.

2.7. Statistical analyses

Data are presented as mean values with standard deviation and as boxplots (median values with interquartile range (IQR) = Q3 – Q1). Statistical data assessment (i.e., testing whether there aresignificant differences in the obtained data) based on the Kruskal-Wallis H test (Kruskal & Wallis, 1952) (see Tab. S1) for group evaluation and the Mann-Whitney test (Mann & Whitney, 1947; Wilcoxon, 1945) for paired comparisons. A p-value of < 0.05 represents for each of the mentioned tests a significant difference.

3. Results

3.1. Capnoperitoneal volume/pressure, CO_2 flow rate and duration of surgery

Prior the surgical interventions, a mean capnoperitoneal volume of $V_C = (3.9 \pm 0.5)$ L was determined for a nominal capnoperitoneal pressure of 10 mmHg (1.3 kPa). The determined total CO_2 flow rates are shown in Fig. 4.

According to Fig. 4, the CO_2 flow rate does not depend on the intervention, but on the smoke management technology and the following ranking applies:

$$Q_{C,CO2}(E) < Q_{C,CO2}(B) < Q_{C,CO2}(D) < Q_{C,CO2}(A) < Q_{C,CO2}(C)$$

For passive filtering (B), the flow rate decreased continuously over time due to increasing wetting of the charcoal filter. Although the continuous insufflation system (D) is described as a closed circulating system, a significant CO_2 flow rate of (4.9 ± 0.5) L/min was observed from the Airseal® trocar at a capnoperitoneal pressure of 10 mmHg, if no surgical instrument was inserted. It is assumed that this leak flow rate originates rather from the particle-free carbon dioxide supply flow than from the capnoperitoneum. Additional data for that trocar are provided in the supplement (Fig. S2).

The prevailing capnoperitoneal pressure for each intervention and smoke management technology is shown in Fig. 5.

As shown in Fig. 5, the capnoperitoneal pressure is highly influenced by the used smoke management technology and the following ranking applies:

$$p_C(C) < p_C(D) < p_C(B) < p_C(E) < p_C(A)$$

The stability of the capnoperitoneal pressure can be defined by the coefficient of variation between the set pressure of 10 mmHg and pressure deviations from it. This results in the following order:

$$c_{v,p}(E) = 1.71\ \% < c_{v,p}(D) = 5.27\ \% < c_{v,p}(A) = 5.34\ \% < c_{v,p}(B) = 11.2\ \% < c_{v,p}(C) = 17.1\ \%$$

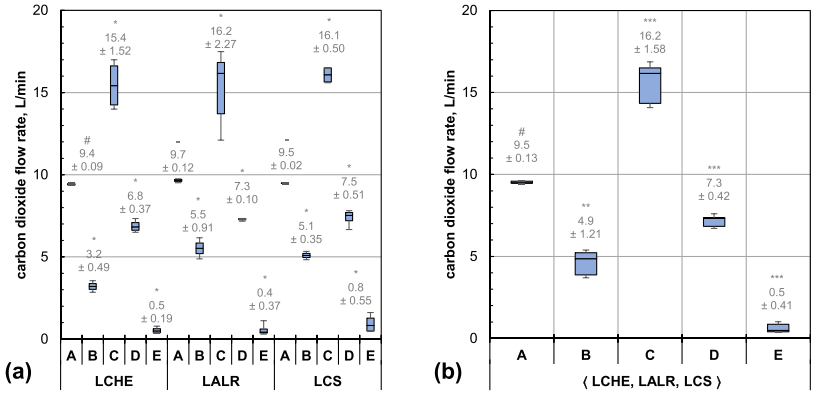

Fig. 4. Total carbon dioxide consumption flow rate (i.e., sum of leakage flow rate, sample flow rate of (0.17 ± 0.03) L/min and flow rate of smoke management technology) for each surgical intervention and smoke management technology (a) and for each smoke management technology over all surgical interventions (b). Represented values = median values ± standard deviation; # = reference, * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

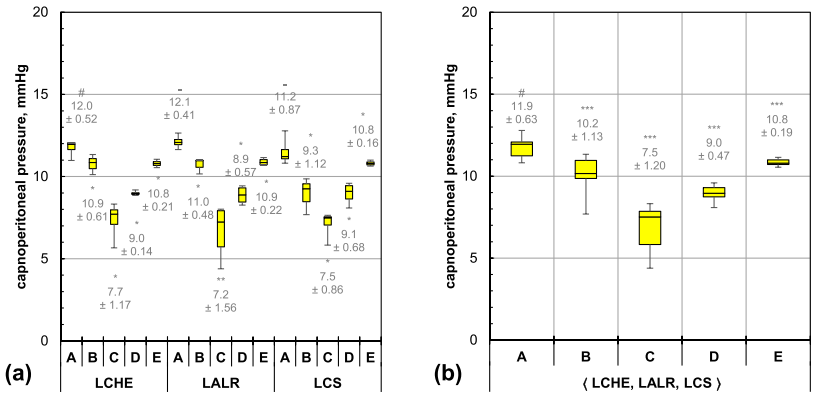

Fig. 5. Capnoperitoneal pressure (p_c) for each combination of surgical intervention and smoke management technology (a) and for each smoke management technology over all surgical interventions (b). Represented values = median values ± standard deviation; # = reference, - = not significant, * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$.

Accordingly, the highest stability of the capnoperitoneal pressure was found for electrostatic precipitation (E) and the worst for active filtration (C). In the case of technology C, the standard insufflator was not able to maintain a capnoperitoneal pressure of 10 mmHg (1.3 kPa) due to intensive intra-abdominal aspiration for surgical smoke elimination.

The surgical intervention time is affected by both the intervention and the smoke management technology (see Fig. S3). The median intervention time of LCHE, LALR and LCS over all smoke management technologies were determined to be (12.7 ± 2.7) min, (10.9 ± 3.0) min and (16.3 ± 3.7) min, respectively. Within the individual interventions, the highest spreading of the duration was observed for active filtration (C), especially during LCS due to aspiration of small bowel loops into the trocar which required interruptions of surgery.

3.2. *Particle number concentration of surgical smoke particles*

Typical time courses of intra- and extra-abdominal measured particle number concentrations are shown in Fig. 6a. The repetitive concentration drop downs in the time courses are typically and are mainly caused by unintentional performed surgery pauses due to poor visibility. Exponentially concentration decrease after the end of intervention was observed for each combination of intervention and surgical smoke management technology.

Fig. 6b shows the mean intra-abdominal smoke concentration values for each combination of intervention and smoke management technology. From an overarching perspective (Fig. 6b), the highest intra-abdominal particle number concentrations based on CPC were determined for intervention LCHE, followed by LALR ($p_{LCHE/LALR} < 0.001$) and LCS ($p_{LALR/LCS} < 0.05$). In the case of LAP and OPS, the

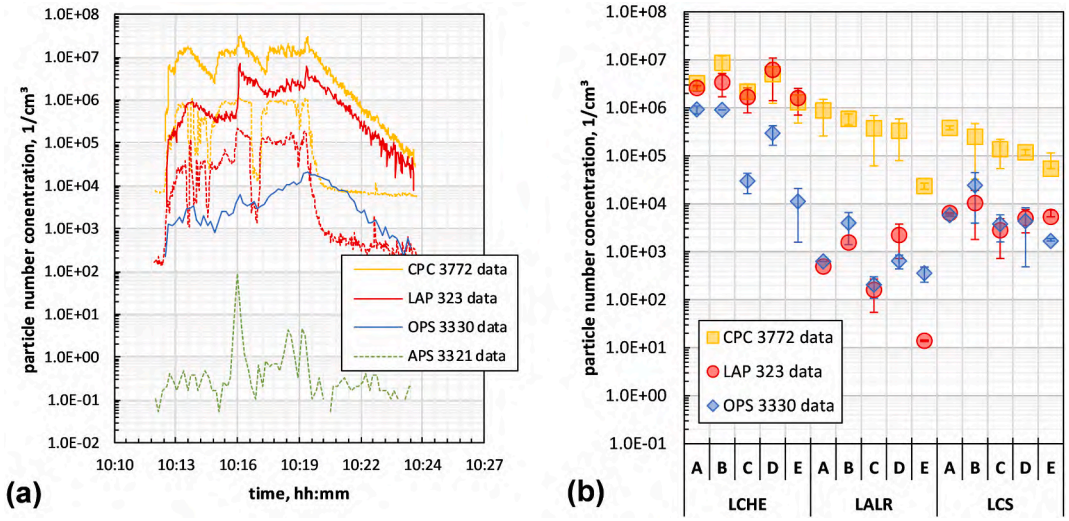

Fig. 6. Typical time courses of intra-abdominal (solid lines) and extra-abdominal (dashed lines) measured particle number concentration of surgical smoke based on intervention LCHE in combination with management technology B - passive filtering (a) and mean intra-abdominal particle number concentrations (b).

concentration ranking changes to LCHE > LCS ($p_{LCHE/LCS} < 0.001$) > LALR ($p_{LCS/LAR} < 0.001$). This indicates that LCS releases higher quantities of coarser particles than LALR. With regard to all smoke management technologies, electrostatic precipitation technology (E) shows statistically significant lower mean intra-abdominal particle number concentrations based on CPC data for LCHE ($p_{E/A,B,D} < 0.05$), LALR ($p_{E/B,D} < 0.05$) and LCS ($p_{E/D} < 0.05$).

Due to multiple external effects, extra-abdominal concentration data caused by accidental leaks demonstrated considerable scatter (see Fig. S4). Accordingly, no common conclusion for the smoke management technologies could be deduced. On the other hand, the observation of significant extra-abdominal concentrations shows that surgical smoke management technologies can lower but not fully eliminate the risk of exposure.

3.3. Half-life of particle number concentration for assessing smoke elimination efficacy

Fig. 7 shows the determined $T_{1/2}$ values for the smoke management technologies based on the data of the different aerosol-analytical instruments.

Despite different measurement principles and measuring ranges, the half-live values based on the different aerosol-analytical instruments are very similar for each smoke management technology. Moreover, significant differences between smoke management technologies can be observed and the following ranking applies:

$$T_{1/2}(C) \approx T_{1/2}(E) < T_{1/2}(A) \approx T_{1/2}(D) < T_{1/2}(B)$$

The lower $T_{1/2}$, the more effective is smoke elimination. Accordingly, active filtering (C) and electrostatic smoke precipitation (E) show the best performance, while passive filtering (B) the poorest due to the lowest CO_2 flow rate. In addition, the computed value ranges for $T_{1/2}$ of the evacuation-based technologies (A/B/C/D) approximate well with experimental data.

Next to the determined intra-abdominal concentration half-live values based on the measurement data of the aerosol-analytical instruments, Fig. 7 shows also the computed one-sigma concentration half-life value range on the basis of Eq. (3) and the pure measured values for the capnoperitoneal volume and the total carbon dioxide flow rates (as shown in Fig. 4b). The lower half-life limits ($T_{1/2,lower}$) were determined by using the upper capnoperitoneal volume ($V_{C,upper} = V_{C,mean} + \sigma_{VC} = 4.4$ L) and the lower carbon dioxide flow rate ($Q_{C,CO2,lower} = Q_{C,CO2} - \sigma_{QC}$) of the corresponding technology. In the case of the upper half-life limits ($T_{1/2,upper}$), the lower capnoperitoneal volume ($V_{C,upper} = V_{C,mean} - \sigma_{VC} = 3.3$ L) and the upper carbon dioxide flow rate ($Q_{C,CO2,lower} = Q_{C,CO2} + \sigma_{QC}$) were used. Accordingly, the computed one-sigma concentration half-life values based on the following ranges for the carbon dioxide exchange rate ($r_i = V_{C,i}/Q_{C,CO2,i}$):

$$r(B) = (0.8 - 1.7)\ min^{-1} < r(D) = (1.5 - 2.3)\ min^{-1} < r(A) = (2.1 - 2.9)\ min^{-1} < r(C) = (3.2 - 5.2)\ min^{-1}$$

The computed one-sigma concentration half-life value ranges do not fit fully all, but cover well most data of the aerosol-analytical instruments. Deviations are attributed to the limitations of the chosen calculation model given in Eq. (3) that assumes ideal conditions like well mixing without recirculation.

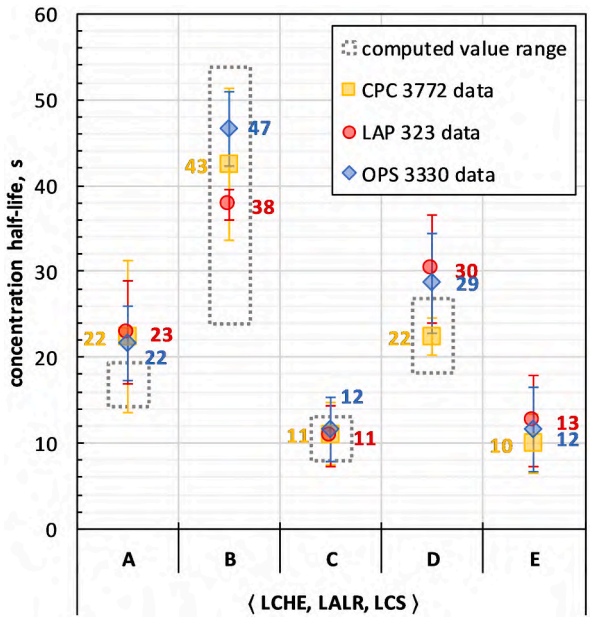

Fig. 7. Mean intra-abdominal half-life of smoke particle number concentration with computed one-sigma concentration half-life value range based on CO_2 flow range and capnoperitoneal volume.

The reciprocal of the carbon dioxide exchange rate gives the mean carbon dioxide residence time within the capnoperitoneum:

$t(C) = (12 - 19)\ s < t(A) = (21 - 28)\ s < t(D) = (26 - 39)\ s < t(B) = (34 - 78)\ s$

Assuming that the surgical smoke particle residence time correlates directly with the mean carbon dioxide residence time, also the impact of particle-particle (i.e., concentration decrease and size increase due to agglomeration/coagulation) and particle-wall (i.e., concentration decrease by intra-abdominal particle losses) interactions on the reliability of the efficacy evaluation of the evacuation-based surgical smoke management technologies can be assessed. The higher the particle residence time in the capnoperitoneum, the higher the concentration reduction by agglomeration/coagulation and particle losses. This implies that the worse the particle removal of an evacuation-based surgical smoke management technology the more the measured concentration data are affected and thus technologies are evaluated more positive than they actual are.

Fig. 8 a shows exemplarily the decrease of the surgical smoke particle number concentration over time as calculated by using Eq. (1), the determined mean half-life concentration values and an initial concentration of $c_0(t_1) = 1 \times 10^7\ cm^{-3}$ for all examined surgical smoke management technologies. A visual comparison between calculated and measured particle number concentration decrease over time is represented in normalised form for selected surgical smoke management technologies in Fig. 8 b.

The visual comparison in Fig. 8 b indicates that calculations based on Eq. (1) and the determined mean half-life concentration values fit well with the measured particle number concentration decay. Thus, surgeons can simply estimate the follow-up operational time of surgical smoke management technologies after finishing the surgical intervention before draining the capnoperitoneum to avoid unintentional surgical smoke particle release and exposure.

3.4. Intra-abdominal smoke particle formation/release rates

Intra-abdominal smoke particle formation/release rates as shown in Fig. 9 were deduced in analogy to Göhler et al. (2013) by means of monitored particle number concentrations, total CO_2 consumption during surgery and adjusted analytical settings.

Fig. 9a shows that the smoke particle formation/release rates of the evacuation-based smoke management technologies (A/B/C/D) are very similar and are orders of magnitude higher than the release data of the electrostatic aerosol precipitation technology (E). Thus, evacuation-based smoke management technologies do not affect smoke particle release. For the CPC data (0.01 - 10) µm, LCHE shows the highest particle release rate, followed by LALR ($p_{LALR/LCHE} < 0.001$) and LCS ($p_{LCS/LALR} < 0.05$). In the case of LAP (0.15 - 5) µm and OPS (0.3 - 10) µm, the particle release rate ranking changes in analogy to the concentration ranking to LCHE > LCS ($p_{LCHE/LCS} < 0.001$) > LALR ($p_{LCS/LAR} < 0.001$). This indicates that LCS releases higher quantities of coarser particles than LALR. The application of continuous electrostatic smoke particle precipitation technology (E) decreases smoke particle release into the capnoperitoneum. Thus, the use of technology (E) reduces the particle release rate determined by CPC for LCHE by a factor 46 ($p_{E/LCHE} < 0.01$), for LALR by 225 ($p_{E/LALR} < 0.05$) and for LCS by 78 ($p_{E/LCS} < 0.05$). The factor variation is attributed on charge state, quantity and size of surgical smoke particles.

3.5. Electric charge state of surgical smoke

The electrical charge of surgical smoke particles was characterised for MEH and USC on different tissues. Surgical smoke based on MEH was found to be strongly positively charged regardless of tissue type. In the case of USC, surgical smoke aerosols are only slightly negatively, neutrally, or even positively charged, depending on the tissue type. Details are summarized in the Appendix (Tab. S2).

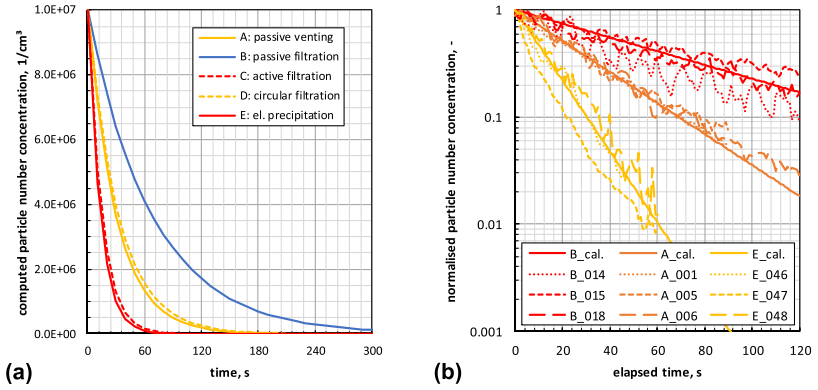

Fig. 8. Calculated decrease of surgical smoke particle number concentration over time using determined mean half-life concentration values and an initial particle number concentration of 1×10^7 particles per cm^3 (a) comparison of calculated concentration decrease based on mean half-life values with arbitrary-selected normalised CPC measurement data (b).

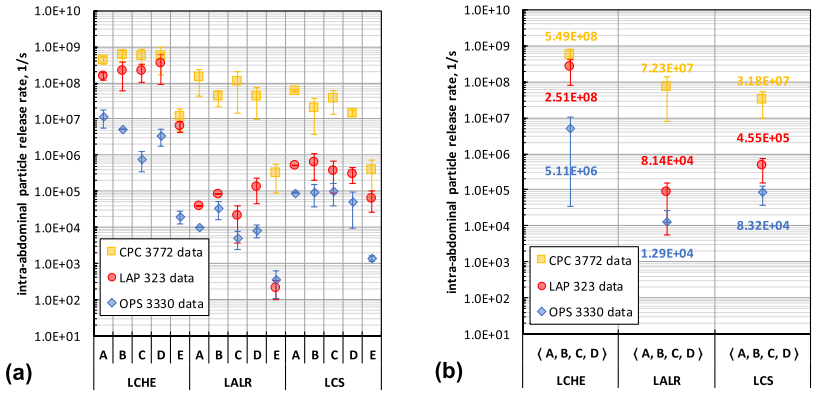

Fig. 9. Mean intra-abdominal smoke particle release rates for each combination of surgical intervention and smoke management technology (a) and for each surgical intervention over the evacuation-based smoke management technologies (b).

4. Discussion

The performance of five smoke management technologies (A: passive venting, B: passive filtration, C: active filtration, D: circular filtration, E: electrostatic precipitation) was characterised by performing three laparoscopic interventions (LCHE: cholecystectomy, LARL: atypical liver resection, LCS: colon surgery) using two energy-driven surgical instruments (MEH: monopolar endo-hook, USC: ultrasonic cutter) in a clinically relevant setting. Following expert guidelines on surgical smoke avoidance and exposure control, surgical instruments were operated at low power settings and reduced capnoperitoneal pressure of 10 mmHg (Phillips et al., 1999; Francis et al., 2020; Pryor, 2020). Animals with a human-like capnoperitoneal volume were handled, while the speed of tissue transection was surgeons-specific and therefore analogous to clinical practice.

Performance assessment (summarized in Table 1) was deduced by aerosol characteristics (particle number concentration, concentration half-life, particle formation/release rates) and physical parameters (CO_2 consumption, capnoperitoneal pressure). The basis for assessing surgical smoke management was the intra-abdominal intervention-induced formation/release rate of surgical smoke. In the size range of (0.01 - 10) µm, LCHE shows the highest formation/release rate with $(549 \pm 261) \times 10^6\ s^{-1}$, followed by LALR with $(72 \pm 64) \times 10^6\ s^{-1}$ ($p_{LALR/LCHE} < 0.001$) and LCS with $(31 \pm 22) \times 10^6\ s^{-1}$ ($p_{LCS/LALR} < 0.05$). This is consistent with previous work, were electrosurgical devices like MEH result in higher release quantities compared to USC (Ott et al., 1998; Weld et al., 2007; Karjalainen et al., 2018; Elmashae 2020).

The examined smoke management technologies make use of two mechanisms for smoke particles removal, i.e., particle evacuation via steady CO_2 exchange (A/B/C/D) and intra-abdominal particle deposition by electrostatic precipitation (E). Theoretically, the efficacy of evacuation-based technologies should increase with increasing flow rate. This could be partly confirmed for LCHE by the

Table 1
Summary of the most important characteristics of the individual smoke management technologies. Legend:=not relevant/observed, + = acceptable, ++ = good, +++ = very good, ++++ = best.

Property	unit	surgical smoke management technology				
		A	B	C	D	E
principle	–	Passive venting	Passive filtration	Active filtration	Circular filtration	Electrostatic precipitation
carbon dioxide flow rate (consumption)	L/min	9.5 ± 0.1	4.9 ± 1.2	16.2 ± 1.6	7.3 ± 1.6	0.5 ± 0.4
coefficient of variation of carbon dioxide flow rate	%	1.4	26.2	10.1	5.9	60.2
capnoperitoneal pressure	mmHg	11.9 ± 0.6	10.2 ± 1.1	7.5 ± 1.2	9.0 ± 0.5	10.8 ± 0.2
coefficient of variation of capnoperitoneal pressure	%	5.3	11.2	17.1	5.3	1.7
half-life of particle number concentration	s	22.3	42.7	11.3	27.7	11.7
freedom of surgery	–	+++	++	+	++++	++++
interruption of surgery	–	–	–	+	–	–
adverse due to smoke management	–	–	–	small bowel aspiration	–	–
interruption of smoke management	–	–	progredient filter degradation	clogging due to small bowel aspiration	–	short circuits
others	–	strong odour nuisance, eye irritation and cough	minimal odour nuisance	noise disturbance	minimal odour nuisance	–

determined mean intra-abdominal particle number concentration but not for LALR and LCS due high scatter in recorded data, which were affected by frequently but not regular interruptions in surgery due to poor intraoperative visibility and other surgical complications accompanied with the use of high-flow smoke management technologies (e.g.: aspiration of tissue, loss of capnoperitoneal volume).

To bridge this drawback, the concentration decrease at the end of each intervention was considered. It was found that the exponential slope in the concentration decrease is specific for each smoke management technology. Accordingly, the concentration half-life ($T_{1/2}$), i.e., the time span to decrease the concentration by half, was determined to assess the efficacy of all smoke management technologies. Conveniently, similar $T_{1/2}$-values yielded for each of the operated aerosol-analytical instruments. The lowest $T_{1/2}$-values of (10 - 13) s and thus the highest efficacies were observed for C (15.6 $\pm$ 1.6 L/min) and E. $T_{1/2}$-values of (20 - 30) s was determined for A (9.5 $\pm$ 0.1 L/min) and D (7.2 $\pm$ 0.4 L/min), while highest $T_{1/2}$-values of (38 - 47) s were found for B (4.6 $\pm$ 1.2 L/min). To verify the empirical data, additional calculations were performed for the evacuation technologies (A/B/C/D) based on an approach to describe concentration decrease in well-ventilated rooms (Hewett & Ganser, 2017). Pleasingly, calculated value ranges for $T_{1/2}$ fit well with experimental data. Thus, calculations can replace future experiments on evacuation technologies. Moreover, surgeons can now estimate how long a smoke management technology should be operated to avoid unintentional smoke leakage before capnoperitoneal draining.

The current design of trocars and laparoscopic instruments result in significant leakage of smoke (Cahill et al., 2020; Dalli et al., 2021; Elmashae et al., 2018; Hardy et al., 2021; Robertson et al., 2022; Uecker et al., 2021). Thus, the best safety measure is to minimize the rate of smoke formation and intra-abdominal release within the capnoperitoneum. A previous *ex-vivo* study observed that electrostatic precipitation significantly decreases smoke release within the capnoperitoneum (Buggisch et al., 2020). The present study confirms this finding and identifies that electrostatic precipitation was most effective and significantly reduced the intra-abdominal smoke particle release rate by factors of 47 for LCHE, 225 for LALR and 78 for LCS. These efficacy differences may be attributed to differences of the electrical charge state of surgical smoke particles. Additional performed analyses confirmed that MEH operation led to highly positively charged surgical smoke, whereas USC causes weakly charged smoke with sometimes positively, neutral or negatively charge character. Technology E produces a defined and therefore limited quantity of negative ions, which are rapidly depleted if highly positively charged smoke (cf. LCHE) or higher quantities of coarser particles with neutral or slight unipolar character (cf. USC) are present. These findings are important for future research and technological improvements.

Extra-abdominal particle number concentrations in close proximity to the working trocar were found to be between 1.8 and 66.8 times lower than the intra-abdominal concentrations. However, the high scatter in these values, attributed to temporary leakage flows based on instrument movement within the trocar and multiple external effects on aerosol propagation (Clark et al., 2012; Göhler et al., 2017; Göhler et al., 2018), make extra-abdominal concentrations less suitable for efficacy assessment. Accordingly, it is recommended to focus on particle source/capnoperitoneum characterisation in future research to obtain robust and reliable data.

Despite legal requirements on safe handling of surgical smoke in some countries, mandatory regulations are usually missing (CSA 2020). Many surgeons are not aware that surgical smoke poses a health issue (Steege et al., 2016; Michaelis et al., 2020). Thus, **passive venting** is a widely used simple and cost-effective method. Beside release of harmful surgical smoke, venting is also accompanied by a considerable CO_2 consumption. Even at reduced capnoperitoneal pressure of 10 mmHg, 9 L/min are consumed. Furthermore, the insufflator-based pulsatile administration of CO_2 into the abdominal cavity cause pressure fluctuations and reduces freedom of surgery. Finally, the efficiency of smoke elimination/intra-operative view was intermediate.

Passive filtration with charcoal filters is promoted as a cheap and highly-effective method to eliminate smoke and gases. The capnoperitoneum was stable with a high freedom for surgery. But the filter performance rapidly decreases due to wetting. As a result, the intra-abdominal smoke concentrations and leakage increased and visibility became poorer over time. Thus, filters need to be replaced intra-operatively that increases costs and workload for the surgical team. The smoke elimination efficacy observed in this study was the lowest. One possible improvement of this technology could be an additional upstream moisture separation.

Active filtration at intermediate intensity shows a high smoke elimination efficiency but is accompanied by a considerable CO_2 consumption (16 L/min), which causes high pressure fluctuations that limit freedom of surgery by poor tissue exposure at the surgical site and repetitive aspiration of small bowel loops into the evacuation trocar. In addition, the operation noise was perceived as disruptive. Thus, it is recommended to operate such devices at low aspiration rate and/or only intermittently. With regard on the high CO_2 consumption, one should also keep in mind that there is still a debate whether cold and/or non-humidified CO_2 promotes postoperative pain (Sammour et al., 2008; Binda, 2015; Birch et al., 2016; Balayssac et al., 2017; Cheong et al., 2018).

Circular filtration showed a CO_2 consumption of 7 L/min with a stable capnoperitoneal pressure and a very high degree of surgical freedom. Previous data indicate that the valve-less trocar leaks (1 - 2) L/min (Dalli et al., 2020). In this study a leak rate of 5 L/min was observed at 10 mmHg, if no surgical instrument was inserted. The leak rate was found to be inversely proportional to the capnoperitoneal pressure and is assumed to originate rather from the particle-free carbon dioxide supply flow than from the capnoperitoneum. Smoke elimination effectiveness was inferior compared to active filtration or electrostatic precipitation.

Electrostatic precipitation does not require CO_2 exchange. Thus, the observed CO_2 flow rate of 0.5 L/min is attributed to trocar leaks. During colon resection, intermittent brief interruptions of smoke elimination occurred due to short circuits between small bowel and the ion electrode. Despite intra-abdominal retention of surgical smoke particles, no patient-related adverse effects of that technology are known so far (Levine et al., 2020). Nevertheless, with the highest efficacy for smoke elimination and a stable capnoperitoneum a high freedom of surgery prevailed.

5. Conclusion

Simple charcoal filters rapidly degrade and should be exchanged several times during surgical interventions. Active filtering is efficient for smoke elimination, but the unstable capnoperitoneum interferes with surgery. Circular filtration forms a stable capnoperitoneum, but the valve-less trocar promotes relevant smoke release into the environment. Electrostatic precipitation is most efficient for smoke elimination with minimal CO_2 consumption at a highly-stable capnoperitoneum.

Endnotes

Within the manuscript, the unit "mmHg" for the pressure is used instead of standard international (SI) unit "Pa" since most surgical instruments are adjusted via that classical unit and surgeons are more familiar with.

Author contributions

Levon Aslanyan and Daniel Göhler: study design, experiments, data acquisition, data interpretation and drafting of manuscript.
Petru Bucur, Jonathan Buggisch: ethics request and surgery.
Katrin Oelschlägel: experiments, data acquisition, data interpretation and drafting of manuscript.
Nadja Azhari: experiments and data acquisition.
Andreas Rudolph, Sébastien Roger, Michael Stintz, Dirk Bausch and Cédric Demtröder: technical support, critical revision for important content of the manuscript according to their field of research.
Mehdi Ouaissi and Urs Giger-Pabst: study design, coordination of study, experiments, surgery, data acquisition, data interpretation, logistics, drafting of manuscript and critical revision for important content of the manuscript.

Ethical approval

In-vivo analyses were approved by the French Ministry of Higher Education, Research and Innovation (Ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation, France) under registration #32547–20211117072337 v3. Animals were handled and cared in accordance with national and institutional guidelines. Protocols were conducted by authorized investigators. All methods are reported in accordance with ARRIVE guidelines (Percie du Sert, 2020).

Declaration of competing interest

The study with the number #32547–20211117072337 v3 was approved by the French Ministry of Higher Education and Research (Ministère de l'enseignement supérieur et de la recherche). Animals were handled and cared according to all guidelines by authorized investigators. The study was supported by the Association Tourangelle de Recherche en Oncologie du Val de Loire (AT-ROVL), Chambray les Tours, France. All authors have no conflicts of interest or financial ties to declare. We explicitly emphasize, that all authors declare no financial ties or any other conflicts of interest with Aesculap Akademie GmbH (Bochum, Germany), BOWA-electronic GmbH & Co. KG (Gomaringen, Germany), Alesi Surgical Ltd. (Cardiff, United Kingdom), CONMED Corp. (New York, USA), Technomedics GmbH (Illertissen, Germany) and Topas GmbH (Dresden, Germany).

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaerosci.2023.106309.

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Attachment I

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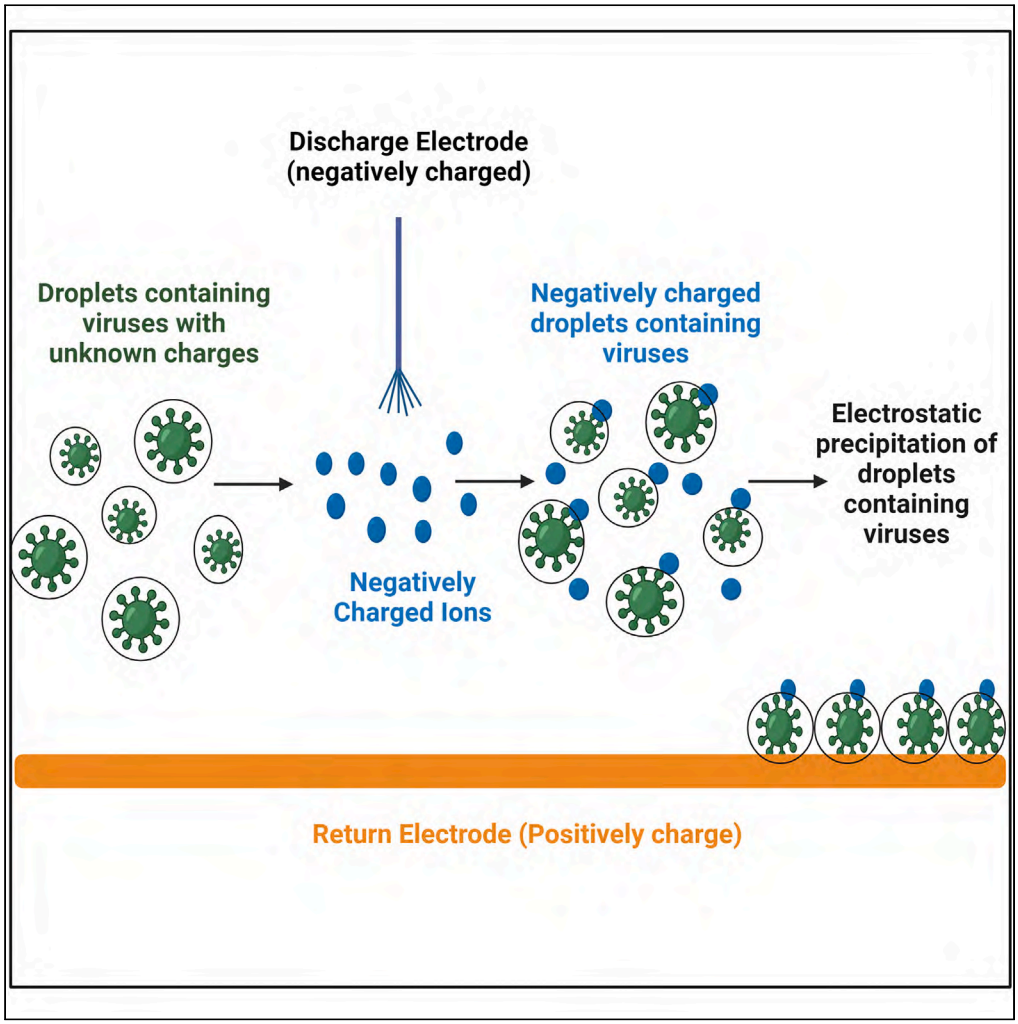
Capture and inactivation of viral particles from bioaerosols by electrostatic precipitation



Hannah E. Preston, Rebecca Bayliss, Nigel Temperton, Martin Mayora Neto, Jason Brewer, Alan L. Parker

parkeral@cardiff.ac.uk

Highlights

Bioaerosols released from patients during surgery can facilitate viral spread

Electrostatic precipitation captures and inactivates viral particles preventing spread

Electrostatic precipitation is effective against enveloped and non-enveloped viruses

Electrostatic precipitation represents a viable means to reduce nosocomial infections

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Article

Capture and inactivation of viral particles from bioaerosols by electrostatic precipitation

Hannah E. Preston,[1] Rebecca Bayliss,[1] Nigel Temperton,[2] Martin Mayora Neto,[2] Jason Brewer,[3] and Alan L. Parker[1,4,5,*]

SUMMARY

Infectious viral particles in bioaerosols generated during laparoscopic surgery place staff and patients at significant risk of infection and contributed to the postponement of countless surgical procedures during the COVID-19 pandemic causing excess deaths. The implementation of devices that inactivate viral particles from bioaerosols aid in preventing nosocomial viral spread. We evaluated whether electrostatic precipitation (EP) is effective in capturing and inactivating aerosolized enveloped and non-enveloped viruses. Using a closed-system model mimicking release of bioaerosols during laparoscopic surgery, known concentrations of each virus were aerosolized, exposed to EP and collected for analysis. We demonstrate that both enveloped and non-enveloped viral particles were efficiently captured and inactivated by EP, which was enhanced by increasing the voltage to 10 kV or using two discharge electrodes together at 8 kV. This study highlights EP as an effective means for capturing and inactivating viral particles in bioaerosols, which may enable continued surgical procedures during future pandemics.

INTRODUCTION

Acute respiratory viruses are the fourth leading cause of mortality worldwide.[1] Although respiratory viruses can be spread by physical contact, contaminated fomites, and large droplets, key transmission occurs via the dispersion of bioaerosols from an infectious individual.[2] Additionally, previous studies have shown that wild-type non-respiratory viruses, such as human immunodeficiency virus (HIV) and human papillomavirus (HPV) can also be released in bioaerosols, during aerosol-generating medical procedures, enabling viral transmission.[3,4]

With particular focus on the 2019 SARS-CoV-2 pandemic, >640 million cases and >6.5 million directly related deaths were reported worldwide in December 2022.[5] Regarding the indirect consequences of the pandemic, it is estimated that hundreds of thousands of surgeries were delayed or canceled as a result. Bioaerosol-generating procedures, including laparoscopy, tracheostomy, open suctioning, and administration of nebulized treatments were at the highest risk of cancelation, due to the likelihood of airborne transmission to staff and other patients.[6] This has left patients untreated and undiagnosed, creating enormous backlogs of waitlisted surgeries, thereby increasing the demand for private healthcare.[7]

Mitigation strategies such as mask wearing, personal protective equipment (PPE), social distancing, isolation of infected patients, and mass vaccinations were enforced and encouraged by the health authorities to reduce the spread of SARS-CoV-2.[8] However, cases of SARS-CoV-2 infection continued to fluctuate at high levels, due to the evolution of new viral strains, easing of government-enforced restrictions and a lack in vaccine confidence by the general public.[9,10] Therefore, the population remains at risk, emphasizing the need for novel non-pharmaceutical interventions (NPIs).

Commonly used NPIs for reducing the spread of disease in hospitals are ultra-low or high-efficiency particulate air filters (ULPA or HEPA), ultraviolet (UV) light sterilization, and aerosolized hydrogen peroxide (AHP) sprays.[11,12] Although these NPIs are somewhat capable of purifying indoor air and decontaminating surfaces, each system is hindered by limitations. ULPA/HEPA filters are non-economical and labor intensive, as they use high levels of energy to run and require regular filter changes. Viruses that are trapped via a filter can remain live and active, adding an additional risk to their use within hospitals and requiring appropriate treatment as a biohazard during disposal.[13] UV light is capable of inactivating viruses; however, its efficiency is limited to its alignment with and distance from the virus itself.[14] As well as this, the exposure time and irradiance doses of UV light used to decontaminate indoor environments has not been well standardized, and incorrect usage of UV light can be hazardous.[14] AHP sprays consist of 6% hydrogen peroxide mixed with 50 ppm silver ions and have been shown to eliminate SARS CoV-2 in nosocomial environments.[12] Although AHP sprays are cost effective and have displayed efficacy as dry aerosol disinfectants, hydrogen peroxide is an irritant to the human skin and eyes, and if inhaled can be toxic.[15]

[1]Division of Cancer and Genetics, Cardiff University School of Medicine, Heath Park, Cardiff CF14 4XN, UK
[2]Viral Pseudotype Unit, Medway School of Pharmacy, University of Kent, Central Avenue, Chatham ME4 4BF, UK
[3]Alesi Surgical Ltd, Medicentre, Heath Park Way, Cardiff CF14 4UJ, UK
[4]Systems Immunity University Research Institute, Cardiff University School of Medicine, Heath Park, Cardiff CF14 4XN, UK
[5]Lead contact
*Correspondence: parkeral@cardiff.ac.uk
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As nosocomial virus transmission occurs most commonly by the release of bioaerosols from infectious patients, it would be beneficial to develop an NPI that efficiently captures and inactivates viral particles from bioaerosols in hospital environments. Electrostatic precipitation (EP) technology has been developed to be used during key-hole surgeries, such as abdominal laparoscopies, to eliminate surgical smoke.[16,17] Surgical smoke is produced by the thermal destruction of tissue by electrosurgical instruments during medical procedures and can obstruct the surgeons field of vision, resulting in safety implications.[18] Surgical smoke consists of 95% water vapor and 5% cellular debris, of which can contain live bacterial and viral particles.[18] EP clears surgical smoke via the generation of an electric field which precipitates particles out of aerosolized dispersion and onto a charged collection surface.[19] This occurs by a discharge electrode emitting negatively charged ions into a neutrally charged space, creating a corona discharge.[20] The current produced from a negatively charged discharge electrode results in the creation of low-energy gas ions and subsequent transient electrostatic charging of aerosolized matter within a local atmosphere. A return electrode carrying a positive charge is connected to a collector plate and located at a distance from the discharge electrode enabling the precipitation of negatively charged particles onto the positively charged collector plate via electrostatic attraction. This mechanism is exploited during key-hole surgery to clear surgical smoke, whereby aerosolized particles are ionized by a discharge electrode and precipitated onto the patient's abdominal tissue, which is connected to a positively charged return electrode pad.[21] Therefore, it was rational to assume that EP could also eliminate virus particles from surgical smoke, as bioaerosols released from patients consist of micrometer sized droplets, which can contain virus particles if the patient is infected. Subjecting virally contaminated aerosolized droplets to the negative charge emitted from the discharge electrode would thereby precipitate virus particles onto the positively charged return electrode, resulting in viral capture. Additionally, it was likely that EP could also inactivate virus particles from bioaerosols following contact with negatively charged air ions and formed radicals, as this has been previously suggested in other studies.[22–25]

It has been suggested that EP could be used in point-of-care systems as a method of aerosol sampling, to diagnose patients rapidly and accurately for respiratory viral infections, reducing the need to perform invasive and uncomfortable diagnostic procedures such as bronchoscopy.[26] Furthermore, EP has been incorporated into a microfluidic lab-on-chip device, for immediate pathogenic detection from aerosol droplets released in the exhaled breath of patients.[26] Custom bioaerosol samplers, employing EP mechanisms have also been developed and demonstrated to detect airborne influenza virus particles; of which studies have claimed may reduce sampling times down from hours to minutes, thus inhibiting viral transmission faster than currently existing approaches.[27] EP is thereby capable of efficiently capturing airborne virus particles. Besides medical applications, EP has been used for decades in aerosol science to collect aerosol particles onto substrates for subsequent morphological analysis by scanning electron microscopy (SEM) and total reflection x-ray fluorescence (TXRF).[28,29]

Since EP is capable of efficiently clearing surgical smoke and has the capacity to capture airborne virus particles, it was rational to evaluate the ability of EP to capture and inactivate aerosolized viral particles from bioaerosols. Furthermore, EP has already been cleared by regulators as safe and effective in use,[16,30] thereby serving as a practical, multi-modal device to use during medical procedures to prevent the spread of aerosolized viral particles. In addition, EP is capable of precipitating particles at a minimum diameter of 7 nm,[17] thus improving the efficiency of particle capture and filtration compared to other established and commonly used ventilation and filtration systems, providing an alternative NPI for reducing disease transmission in hospitals.

The objective of our study was to evaluate the capture and inactivation of bioaerosol-containing viral particles by EP. Non-enveloped (Ad5) and enveloped (SARS-CoV-2 pseudotyped lentivirus) viral particles were aerosolized into a closed-system model, that was representative of key-hole surgery, and exposed to EP. Recovered samples were analyzed for viral presence by real-time quantitative polymerase chain reaction (qPCR) of viral genomes and for biological activity by transduction and plaque assays in target cell lines. We hypothesized that viral exposure to EP would result in significant viral capture and inactivation.

Reducing viral transmission is not limited to SARS-CoV-2, but accounts for all viral outbreaks that may lead to future pandemics. It is therefore important that novel NPIs are evaluated and developed, to increase our preparation, improve safety within hospitals, and prevent the need to cancel surgeries and medical procedures in the case of future pandemics.

RESULTS

Ad5 particles were successfully captured and inactivated by electrostatic precipitation when aerosolized at 37°C

First, we sought to evaluate whether EP could capture and inactivate aerosolized non-enveloped Ad5 particles using our standard closed-system model (shown schematically in Figure 1). The number of recovered Ad5 genomes significantly decreased following Ad5 exposure to inactive EP as gauged by qPCR for viral genomes, indicating viral loss as a result of sample aerosolization alone (Figure 2). A significant 6.8-fold reduction in the number of recovered Ad5 genomes was observed following Ad5 exposure to active EP (Figure 2A). Ad5 viability was not affected following exposure to inactive EP, as displayed by transduction and plaque assays (Figures 2B and 2C), indicating that sample aerosolization at 37°C was not detrimental to Ad5. The transduction assay demonstrated a 13.6-fold reduction in the percentage of transduction, in cells that were treated with Ad5 that had been exposed to active EP (Figure 2B). Mirroring this, the plaque assay displayed a $4x10^3$-fold reduction in active Ad5 particles, in the sample exposed to active EP (Figures 2C and 2D). These results indicated that EP successfully captured and inactivated aerosolized Ad5 particles within our standard closed-system model.

Capture and inactivation of Ad5.GFP was most efficient when exposing viral particles to 10kV

Multiple parameters may impact the efficiency of EP. We assessed the impact of increasing voltages on the ability of EP to capture and inactivate aerosolized Ad5. EP is currently used at 8 kV to clear surgical smoke during laparoscopies. We exposed aerosolized samples of Ad5 to EP active at 6 kV, 8 kV, and 10 kV, to determine whether decreasing or increasing the standard voltage impacted its ability to capture and

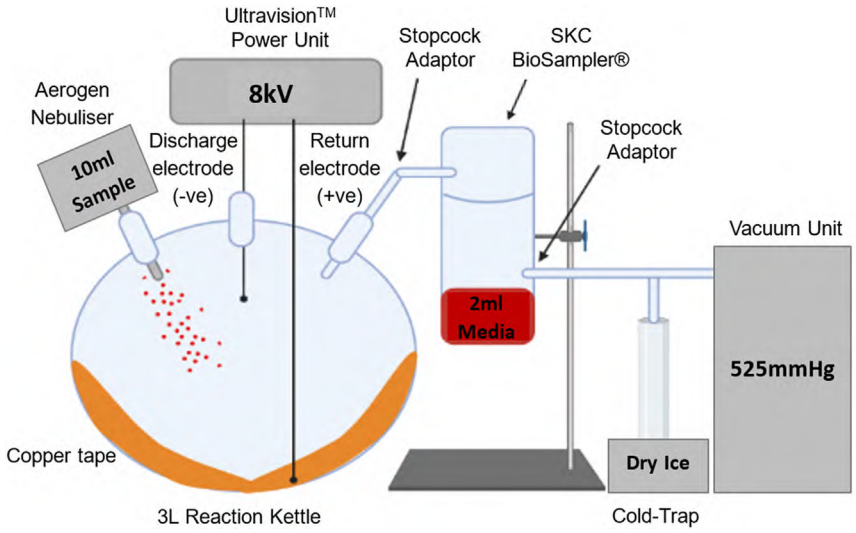


Figure 1. Schematic of the experimental setup of the refined closed-system model

All samples were aerosolized into the air-tight reaction kettle, exposed to EP (active/inactive) and suctioned into the BioSampler for recovery and collection. Collected samples were stored at −80°C immediately after each experimental run, prior to experimental analysis.

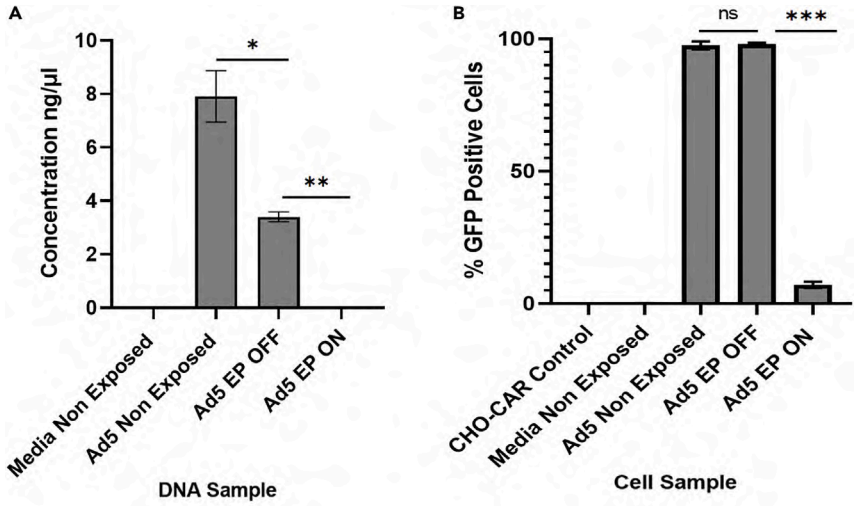
inactivate viral particles. By increasing the voltage of EP, the region of corona discharge was expanded, thus reaching a larger surface area and contacting more aerosolized virus particles. As 10 kV is the maximum voltage that is medically approved for EP use during surgery, voltages above this were not evaluated.

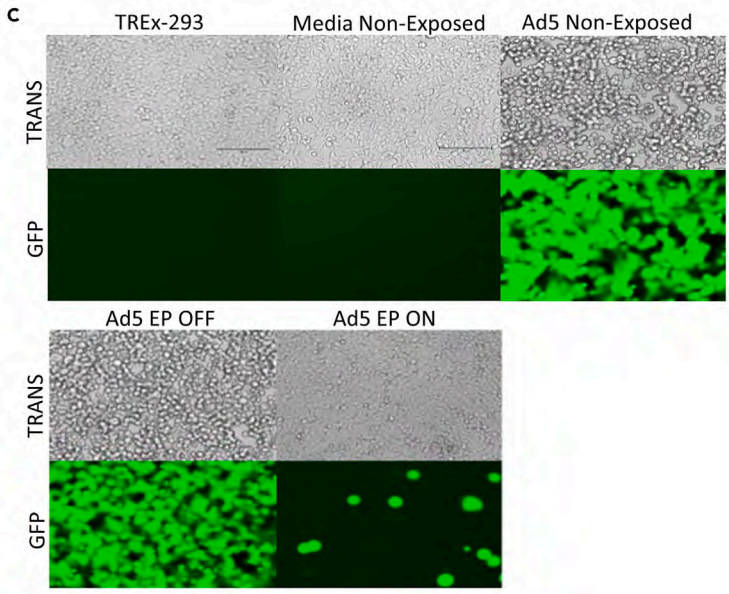
qPCR analysis of treated samples indicated significant viral capture by EP, following sample exposure to 6 kV, 8 kV, and 10 kV (Figure 3A). The number of viral genomes was reduced by 21.8-fold and 16.8-fold, following Ad5 exposure to 6 kV and 8 kV, respectively. However, Ad5 capture was enhanced when exposing the viral particles to 10 kV, as shown by a $7.4x10^3$-fold reduction in the number of viral genomes (Figure 3A). Increasing the voltage to 10 kV also improved viral inactivation, demonstrated by transduction and plaque assay (Figures 3B and 3C). The percentage of transduced cells infected with Ad5 samples that had been exposed to 6 kV and 8 kV was significantly reduced by 6.6-fold and 25.6-fold, respectively (Figure 3B). Cells treated with Ad5 that had been exposed to 10 kV displayed a 529.4-fold reduction in viral transduction (Figure 3B). Mirroring this, plaque assays of treated samples demonstrated a significant decrease in the number of viable Ad5 particles in samples that were exposed to 6 kV, 8 kV, and 10kV (Figure 3C and D). Imagining of GFP highlighted a complete absence of viable Ad5 particles in cells infected with Ad5 samples that had been exposed to 10 kV, indicating that 10 kV is the optimal voltage to elicit efficient EP of bioaerosols during surgery, to completely prevent the transmission of infectious aerosolized virus particles (Figure 3C). While 6 kV significantly reduced the number of viable virus particles, EP by 8 kV and 10 kV resulted in log reductions of >3.5, suggesting a decrease within a clinically significant range.

Using 2 discharge electrodes enhanced adenoviral capture and inactivation

We next evaluated whether enhanced viral inactivation was possible when exposing aerosolized Ad5 particles to 2, rather than a single discharge electrode. Both discharge electrodes were used at 8 kV, maintaining the voltage setting that is currently used during laparoscopic surgery. Separate Ad5 samples were exposed to either 1 or 2 discharge electrodes, to evaluate whether combining 2 discharge electrodes improved viral capture and inactivation.

qPCR results displayed a significant decrease in the number of viral genomes in Ad5 samples that were exposed to either 1 or 2 active discharge electrodes. A 125-fold reduction in the number of Ad5 genomes was observed in the sample exposed to 1 active discharge electrode, whereas exposure of Ad5 to 2 discharge electrodes resulted in an increased $1.25x10^3$-fold reduction in the number of Ad5 genomes detected (Figure 4A). This indicated that using 2 discharge electrodes, both active at 8 kV, enhanced viral capture by a further 10-fold. Similarly, Ad5 samples exposed to 1 or 2 discharge electrodes were both significantly inactivated. Cells treated with the Ad5 sample that had been exposed to a single active discharge electrode displayed a 31.6-fold reduction in the percentage of virally transduced cells (Figure 4B). In comparison, cells treated with the Ad5 sample that had been exposed to 2 active discharge electrodes displayed a 215.2-fold reduction in the percentage of transduced cells, indicating that using 2 discharge electrodes enhanced viral capture (Figure 4B). Plaque assay confirmed these findings, as shown by an 800-fold decrease in the number of active Ad5 particles, post exposure to a single discharge electrode, in comparison to a complete elimination of active Ad5 particles, post exposure to 2 discharge electrodes (Figures 4C and 4D). This experimental run highlighted that using 2 discharge electrodes enhanced viral capture and inactivation in a synergistic manner.





D

Sample	Functional Titre
Ad5 Non-Exposed	4.46 x 10^8 pfu/ml
Ad5 EP OFF	2.7 x 10^8 pfu/ml
Ad5 EP ON	6.83 x 10^3pfu/ml

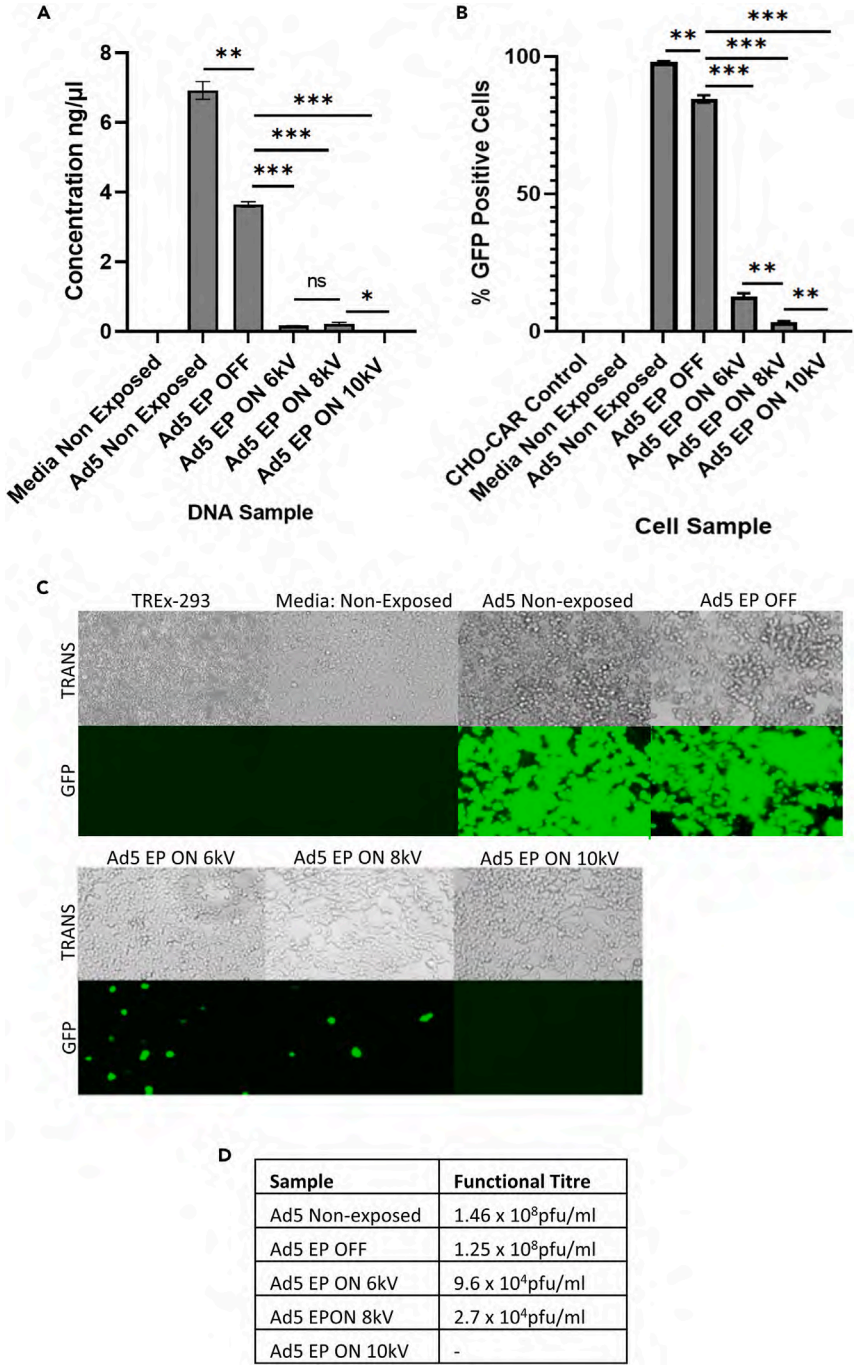
Figure 2. Capture and inactivation of Ad5 by electrostatic precipitation

"EP OFF" signifies sample exposure to inactive EP and "EP ON" signifies sample exposure to active EP. "Non-Exposed" signifies samples that were not aerosolized through the model system, nor exposed to EP.

(A) Viral capture quantified by qPCR.

(B) Viral inactivation demonstrated by transduction assay.

(C and D) Viral inactivation displayed by plaque assay in TREx-293 cells. TREx-293 cells treated with samples and analyzed for GFP fluorescence. TRANS = Brightfield transmitted light, GFP = GFP light source. Error bars represent the ±SD (n = 3). Plaque assay functional titers represent the mean (n = 5). Significance values represent *$p < 0.05$, **$p < 0.005$, ***$p < 0.0005$.



D

Sample	Functional Titre
Ad5 Non-exposed	1.46 x 10^8pfu/ml
Ad5 EP OFF	1.25 x 10^8pfu/ml
Ad5 EP ON 6kV	9.6 x 10^4pfu/ml
Ad5 EPON 8kV	2.7 x 10^4pfu/ml
Ad5 EP ON 10kV	-

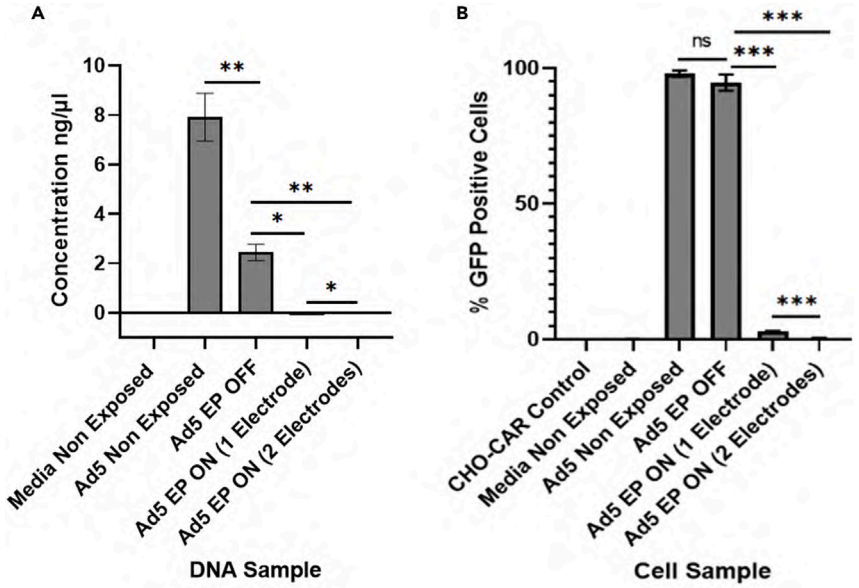
Figure 3. Increasing the voltage of EP to 10 kV enhances viral capture and inactivation

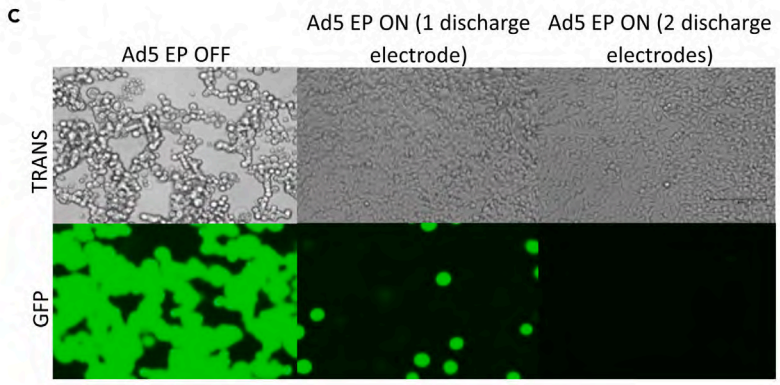
"EP OFF" signifies sample exposure to inactive EP and "EP ON" signifies sample exposure to active EP. "Non-Exposed" signifies samples that were not aerosolized through the model system, nor exposed to EP.

(A) Viral capture demonstrated by qPCR.

(B) Viral inactivation determined by transduction assay.

(C and D) Viral inactivation displayed by plaque assay in TREx-293 cells. TREx-293 cells treated with samples and analyzed for GFP fluorescence. TRANS = Brightfield transmitted light, GFP = GFP light source. Error bars represent the ±SD (n = 3). Plaque assay functional titers represent the mean (n = 5). Significance values represent *$p < 0.05$, **$p < 0.005$, ***$p < 0.0005$.





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Sample	Functional Titre
Ad5 EP OFF	1.2 x 10^7vp/ml
Ad5 EP ON (1 discharge electrode)	1.5 x 10^4vp/ml
Ad5 EP ON (2 discharge electrodes)	-

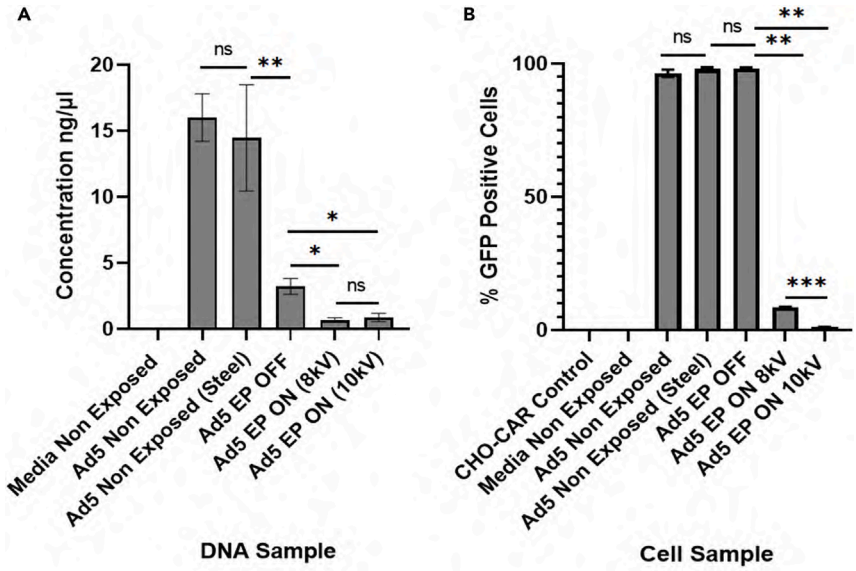
Figure 4. Exposing Ad5 particles to 2 discharge electrodes, opposed to 1, enhances viral capture and inactivation

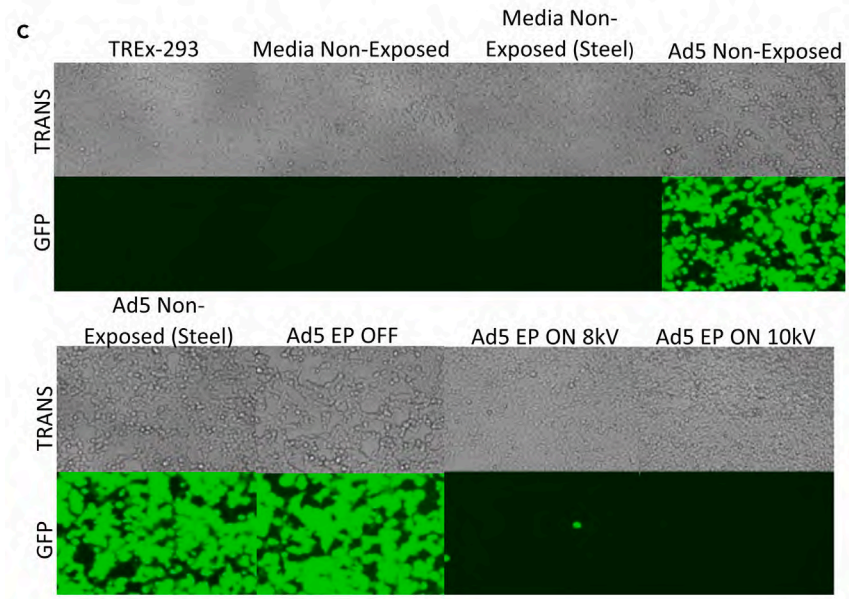
"EP OFF" signifies sample exposure to inactive EP and "EP ON" signifies sample exposure to active EP. "Non-Exposed" signifies samples that were not aerosolized through the model system, nor exposed to EP.

(A) Viral capture demonstrated by qPCR.

(B) Viral inactivation determined by transduction assay.

(C and D) Viral inactivation displayed by plaque assay in TREx-293 cells. TREx-293 cells treated with samples and analyzed for GFP fluorescence. TRANS = Brightfield transmitted light, GFP = GFP light source. Error bars represent the ±SD (n = 3). Plaque assay functional titers represent the mean (n = 5).. Significance values represent *p < 0.05, **p < 0.005, ***p < 0.0005.





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Sample	Functional Titre
Ad5 Non-Exposed	1.2 x 10^8pfu/ml
Ad5 Non-Exposed (Steel)	1.1 x 10^8pfu/ml
Ad5 EP OFF	9.5 x 10^7pfu/ml
Ad5 EP ON 8kV	1.1 x 10^3pfu/ml
Ad5 EP ON 10kV	-

Figure 5. Evidencing EP as the sole cause of viral inactivation

"EP OFF" signifies sample exposure to inactive EP and "EP ON" signifies sample exposure to active EP. "Non-Exposed" signifies samples that were not aerosolized through the model system, nor exposed to EP. "Steel" signifies samples that were exposed (direct contact) to stainless-steel for 2 min.

(A) Viral capture demonstrated by qPCR.

Figure 5. *Continued*

(B) Viral inactivation determined by transduction assay.

(C and D) Viral inactivation displayed by plaque assay in TREx-293 cells. TREx-293 cells treated with samples and analyzed for GFP fluorescence. TRANS = Brightfield transmitted light, GFP = GFP light source. Error bars represent the ±SD (n = 3). Plaque assay functional titers represent the mean (n = 5). Significance values represent *p < 0.05, **p < 0.005, ***p < 0.0005.

Replacing the copper return electrode with a stainless-steel electrode indicated that electrostatic precipitation was the sole cause of viral inactivation

In previous runs, copper tape was attached to the positively charged return electrode, functioning as a collector plate for the precipitation of ionized virus particles. However, copper is a naturally virucidal metal and studies have shown direct contact between copper and viral particles resulting in viral inactivation.[31] Therefore, we hypothesized that direct contact between the aerosolized viral particles and the copper tape may have been causing the viral inactivation observed in previous runs. To determine whether EP or the copper tape was causing viral inactivation, stainless-steel sheets were used to replace the copper tape. Stainless-steel is a biologically inert, non-toxic metal,[32] and should not inactivate Ad5 particles upon direct contact. Ad5 samples that were not aerosolized, nor exposed to EP, were exposed to the stainless-steel sheets (direct contact for 2 min) and analyzed for viral activity in the same way as the collected experimental samples.

There was no significant difference between the number of Ad5 viral genomes in the non-exposed Ad5 sample and the Ad5 sample that was exposed to stainless-steel (Figure 5A). This indicated that stainless-steel did not alter the integrity of the viral DNA. The number of Ad5 genomes was significantly decreased in the Ad5 sample exposed to inactive EP, indicating that aerosolization alone resulted in a reduction in viral DNA collected within the sampling system, or potentially highlighting a size-specific particle loss phenomenon. However, the number of viral genomes was further significantly reduced in Ad5 samples following exposure to active EP at 8 kV and 10 kV (Figure 5A). This indicated that EP successfully captured the aerosolized Ad5 particles. Cells treated with non-exposed Ad5 and the Ad5 sample that was non-exposed to the closed-system but exposed to stainless-steel showed no significant difference in the percentage of virally transduced cells (Figure 5B). Plaque assay results mirrored this result, showing no visible differences between TREx-293T cells infected with either sample (Figure 5C). This indicated that direct contact between Ad5 particles and stainless-steel did not affect viral viability. In addition, CHO-CAR cells infected with Ad5 samples exposed to active EP at 8 kV and 10 kV displayed 11.32-fold and 86.9-fold reductions in the percentage of virally transduced cells, indicating successful inactivation of Ad5 particles by EP (Figure 5B). Confirming this, TREx-293T cells infected with Ad5 samples that had been exposed to active EP at 8 kV and 10 kV showed visibly reduced levels of fluorescence, indicating successful inactivation (Figure 5C).

Electrostatic precipitation successfully captured and inactivated enveloped viral particles (SARS-2 PV)

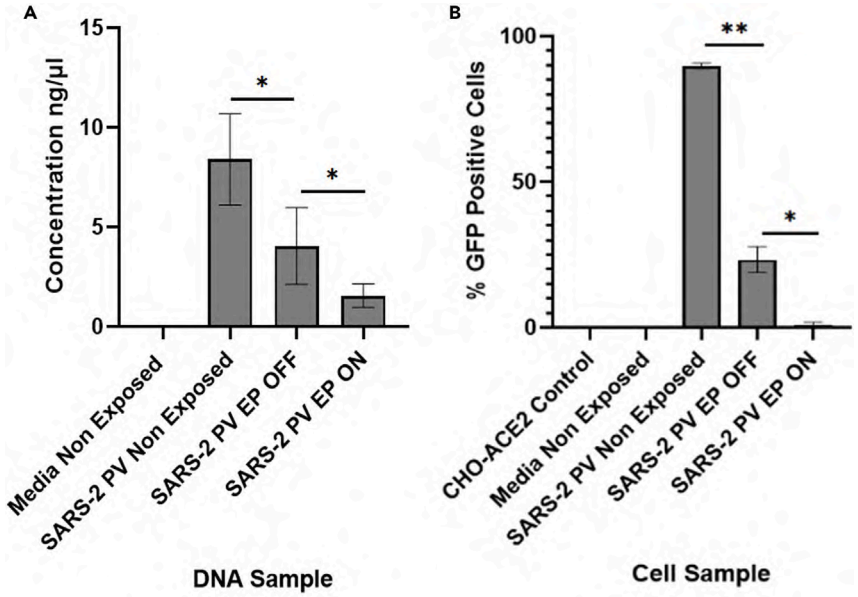
Finally, we sought to evaluate the ability of EP to capture and inactivate enveloped viral particles, such as SARS-CoV-2. As Ad5 is a non-enveloped virus, we used a SARS-CoV-2 pseudotyped lentivirus (SARS-2 PV), as its core and genetic material is enclosed by a lipid envelope which expresses the Wuhan Spike protein on its surface, thereby resembling the external structure of wild-type SARS-CoV-2. Neat samples of SARS-2 PV were aerosolized and exposed to EP in the same way as Ad5 in Figure 1.

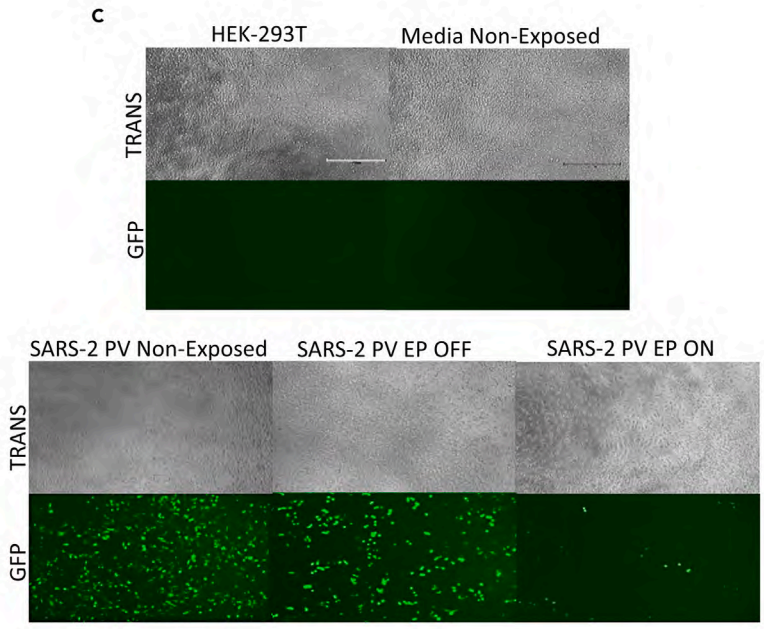
SARS-2 PV was significantly captured by EP, as quantified by qPCR (Figure 6A). A 2.6-fold reduction in the number of viral genomes was observed in the SARS-2 PV sample that had been exposed to active EP, indicating successful virus capture (Figure 6A). In addition, transduction and plaque assays using the collected samples showed that EP significantly inactivated aerosolized SARS-2 PV particles (Figures 6B–6D). CHO-ACE2-TMPRSS2 cells infected with the SARS-2 PV sample that had been exposed to active EP displayed a 27.7-fold reduction in the percentage of viral transduction (Figure 6B). Likewise, HEK-293T cells infected with SARS-2 PV that had been exposed to active EP displayed a visually decreased number of fluorescent cells, compared to the non-exposed sample and the SARS-2 PV sample exposed to inactive EP (Figure 6C). However, the number of viral genomes, as well as viral viability, was significantly reduced in the SARS-2 PV samples that were aerosolized and exposed to inactive EP (Figure 6). This indicated that aerosolized SARS-2 PV was less stable than aerosolized Ad5, and that the sample was more susceptible to inactivation or degradation by aerosolization alone.

DISCUSSION

Existing methods of purifying indoor air are limited by their inability to capture aerosolized particles smaller than 0.15 μm and failure to inactivate live pathogens upon successful capture.[13] These limitations facilitate disease transmission. During periods of viral outbreaks, such as the 2019 SARS-CoV-2 pandemic, bioaerosol-generating medical procedures are at risk of cancellation and delay, due to the likelihood of viral spread.[6] It is therefore crucial that novel NPIs are developed to prevent airborne viral transmission in hospital settings, enabling medical procedures to continue safely and as normal. Established EP systems are currently used to sample and filter indoor air, as well as to clear surgical smoke during key-hole surgeries. Here we have demonstrated additional modalities of EP, in its ability to efficiently capture and inactivate aerosolized viral particles.

Significant capture and inactivation of aerosolized Ad5 and SARS-2 PV particles by EP was observed in our standardized closed-system model. Viral capture was displayed by a reduction in the number of viral genomes collected within the sampling system, following sample exposure to active EP, compared to recovered samples exposed to inactive EP. Similarly, viral inactivation was shown by a reduction in biological activity of viral particles, as gauged by the percentage of transduced cells that were treated with recovered samples post exposure to active EP, compared to samples exposed to inactive EP. Interestingly, it appeared that viral inactivation by EP was more successful than viral capture. Although the copper collector plate used within our closed-system model was naturally virucidal, our findings show that EP was the





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Sample	Functional Titre
SARS-2 PV Non-Exposed	3 x 10^7 pfu/ml
SARS-2 PV EP OFF	2.2 x 10^4 pfu/ml
SARS-2 PV EP ON	5.3 x 10^3 pfu/ml

Figure 6. Capture and inactivation of SARS-2 PV by EP

"EP OFF" signifies sample exposure to inactive EP and "EP ON" signifies sample exposure to active EP. "Non-Exposed" signifies samples that were not aerosolized through the model system, nor exposed to EP.

(A) Viral capture determined by qPCR.

Figure 6. *Continued*

(B) Viral inactivation demonstrated by transduction assay.

(C and D) Viral inactivation displayed by plaque assay in HEK-293T cells. HEK-293T cells treated with samples and analyzed for GFP fluorescence. TRANS = Brightfield transmitted light, GFP = GFP light source. Error bars represent the ±SD (n = 3). Plaque assay functional titers represent the mean (n = 5). Significance values represent *p < 0.05, **p < 0.005.

major cause of viral inactivation. However, using a virucidal collector plate, such as copper, may provide additional safety benefits for the removal of viable pathogens from bioaerosols by EP, thereby outperforming existing devices like HEPA filters.

Viral inactivation by EP was highly efficient, at approximately 90–95% efficiency when using EP at 8 kV, and at >99% efficiency when using EP at 10 kV or when using 2 discharge electrodes (both at 8 kV). Arguably, viral inactivation is more important than viral capture, as this can prevent the spread of disease. Previous studies evaluating the ability of EP to inactivate viruses suggest that the corona discharge, produced by the discharge electrode, generates air ions and reactive species (O_3 and various radicals, such as O·, N·, OH·, and HO_2·) capable of degrading and inactivating viral particles.[22–25] Although this mechanism has not been explicitly investigated here, our results indicate that this could be the cause of viral inactivation. In agreement, degradation of viral particles would result in the release of viral DNA/RNA, explaining the collection of viral genomes in the sampling system following sample exposure to active EP. As isolated viral DNA is biochemically inert and requires an intact capsid to bind and enter target cells, the degradation of aerosolized viral particles seems a practical way of inactivating viruses and reducing their transmission.[33,34]

We have demonstrated that EP can efficiently capture and inactivate both non-enveloped (Ad5) and enveloped (SARS-2 PV) viral particles. However, aerosolization alone significantly reduced SARS-2 PV viability and the integrity of its capsid, causing the release of its viral genome. This was not surprising as SARS-2 PV is not a respiratory virus and is therefore not transmissible via airborne routes. However, other non-respiratory viruses, such as wild-type HIV and HPV, have been identified in surgical bioaerosols with the ability to infect healthcare staff. Therefore, it is important that EP can capture and inactivate a variety of viral particles.[3,4] Future studies will focus on evaluating the ability of EP to capture and inactivate respiratory enveloped viruses, as well as non-respiratory non-enveloped viruses. In addition, other physical parameters govern viral spread and stability, including temperature, humidity, droplet size, and air-space volume.[35] Evaluating changes to viral capture and inactivation, following the alteration of such parameters, as well as parameters effecting the efficiency of EP, such as voltage, flow rate, geometric design of the EP system, and size and concentration of the ionized particles,[36] will be important to optimize in future studies, prior to implementing EP in hospitals as a method of reducing viral spread.

In addition, EP may play a role beyond clearing surgical smoke and eliminating viral particles during key-hole surgery. Due to recent advances in EP technology, it is likely that EP will be employed during open surgeries in the near future to clear surgical smoke. It is therefore possible that EP could be manipulated to capture and inactivate viral particles in "open" systems. For example, EP could be used to filter the release of CO_2 upon patient deflation following laparoscopic surgery, as well as during open surgery, to filter bioaerosols released into the surgical environment in an attempt to protect healthcare professionals within close proximity. This could provide an alternative and intriguing means of replacing HEPA filters, which are currently used to filter bioaerosols in open environments. However, this would of course require adaptations to the device itself to enable sufficient exposure of the corona discharge to bioaerosols covering a much larger surface area succeeding release from the patient. As well as this, EP could be implemented when delivering aerosolized medications or advanced therapy medicinal products (ATMPs) to patients. For example, pressurized intraperitoneal aerosol chemotherapy (PIPAC) has recently been developed as a method of treating unresectable metastatic peritoneal tumors.[37,38] PIPAC is an emerging technology and may be useful for more novel therapeutic deliveries, such as oncolytic virotherapies. Moving forwards, use of these technologies will require efficient means of controlling their emission during delivery. EP could be implemented during this type of therapeutic delivery to prevent the escape of oncolytic viruses into operating theaters, while simultaneously ensuring and directing efficient delivery of drugs to the tumor site. PIPAC has been developed for use during key-hole closed surgery; therefore, EP could be placed within the patient's abdomen for the duration of drug delivery, as it already is during abdominal laparoscopies that use EP to clear surgical smoke.

In summary, our findings indicate that EP could be used during surgery to capture and inactivate viral particles released in bioaerosols, as well as potentially during other medical procedures, to enhance efficacy and safety. Employing EP as an NPI to reduce viral spread in hospitals may resolve issues experienced with existing air-purification systems, which in turn could reduce pressures on the NHS by preventing indirect morbidities and mortalities. For example, recent outbreaks of the highly pathogenic avian influenza A (H5N1) in wild birds and poultry has the capacity to spread to human hosts, which if unprevented, could result in the next human global pandemic.[39] Using data obtained from this study, we predict that it is possible to use EP to minimize viral spread thus preventing future viral pandemics.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead contact
  - Materials availability
  - Data and code availability
- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2023.107567.

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AUTHOR CONTRIBUTIONS

Conceptualization, R.B., J.B., and A.L.P. Methodology, H.E.P, R.B, J.B., and A.L.P. Investigation, H.E.P. with input from R.B., J.B., and A.L.P. Formal analysis, H.E.P., R.B., and A.L.P. Resources, M.M.N. and N.T. Writing – original draft H.E.P. with input from R.B. and A.L.P. Writing – review and editing – H.E.P, R.B., N.T., M.M.N., J.B., and A.L.P. Supervision and funding acquisition, A.L.P.

DECLARATION OF INTERESTS

J.B. is an employee of Alesi Surgical Ltd. A.L.P. is Chief Scientific Officer of Trocept Therapeutics Ltd.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Bacterial and virus strains		
Ad5.GFP	In-house (Stanton et al.[40])	N/A
SARS-2 PV	(Di Genova et al.[41])	N/A
Chemicals, peptides, and recombinant proteins		
Caesium Chloride	Invitrogen™	15507-023
0.45 µm acetate cellulose filter	StarLab	E4780-1453
FuGene® HD Transfection reagent	Promega	E2311
Critical commercial assays		
Micro BCA™ Protein Assay Kit	Thermo Fisher	23235
QIAamp MinElute Virus Kit	Qiagen	57704
PowerUp SYBR Green Master Mix	Thermo Fisher	A25741
Deposited data		
Raw and analyzed data	Mendeley Data Repository	Access numbers required
Experimental models: Cell lines		
Human T-REx-293	Invitrogen™	R71007
Human HEK-293T/17 cells	ATCC	CRL-1573
Hamster CHO	ATCC	
Hamster CHO-CAR	(Uusi-Kerttula et al.[42])	N/A
Hamster CHO-ACE2-TMPRSS2	(Rebendenne et al.[43])	N/A
Oligonucleotides		
Primers Ad5 Hexon - Forward: CCTGCTTACCCCCAACGAGTTTGA. Reverse: GGAGTACATGCGGTCCTTGTAGCTC.	Thermo Fisher	N/A
Primers P24 Capsid – Forward: GGCTTTCAGCCCAGAAGTGATACC. Reverse: GGGTCCTCCTACTCCCTGACATG.	Thermo Fisher	N/A
Recombinant DNA		
Spike SARS2 (D614G)-pCAGGS	NIBSC	CFAR100985
pCSGW encoding Green Fluorescent Protein	(Carnell et al.[44])	N/A
Lentiviral Core p8.91	(Carnell et al.[44])	N/A
MT126 pRRL- SFFV-ACE2-IRES plasmid	AddGene	145839
MT131 pRRL- SFFV-TMPRSS2.v1-IRES plasmid	AddGene	145843
Software and algorithms		
QuantStudio™ 5 Real-Time PCR	Thermo Fisher	https://www.thermofisher.com/uk/en/home/global/forms/life-science/quantstudio-3-5-software.html
FlowJo™v10	BD Biosciences	https://www.flowjo.com/solutions/flowjo/downloads
Prism v4.03	GraphPad	https://www.graphpad.com/scientific-software/prism
Other		
Aerogen® Solo Nebuliser	Aerogen Ltd	AG-A53000-XX
QuickFit™ Wide Neck Flask Reaction 3L	Scientific Laboratory Supplies Ltd	QFR3LF
QuickFit™ Borosilicate Glass Flange Lid	Fisher Scientific	MAF3/52

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REAGENT or RESOURCE	SOURCE	IDENTIFIER
Ultravision™ Generator	BOWA Medial UK	DAD-001-015
Ionwand™	BOWA Medial UK	DAD-001-003
Suba-Seal®	Sigma-Aldrich	Z124621
QuickFit™ Borosilicate Glass Stopcock Adaptors	Fisher Scientific	MF14/3/SC
Duet Flat- Back Aspirator	SSCOR	2314B
BioSampler®	SKC Ltd	225-9595
QuickFit™ Cold-trap	VWR	201-3052
NanoSight NS300	Malvern Panalytical	N/A
EVOS M7000	Invitrogen™	AMF7000
Accuri C6 v.1.0.264.21	BD Biosciences	N/A

RESOURCE AVAILABILITY

Lead contact

Further information and any related requests should be directed to and will be fulfilled by the lead contact, Professor Alan Parker (ParkerAL@cardiff.ac.uk).

Materials availability

This study did not generate new unique reagents.

Data and code availability

- All flow cytometry data presented in this study are deposited in the Mendeley data repository (FCS files) and are publicly available as of the date of publication. All qPCR data presented in this study are deposited in the Mendeley data repository (EDS/EDT files) and are publicly available as of the date of publication. Accession numbers are listed in the key resources table.
- This paper does not report original code.
- Any additional information required to reanalyse the data reported in this paper is available from the lead contact upon request.

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Cell lines

T-REx-293 (Tetracycline Repressor Protein expression cells, Invitrogen™, R71007) and HEK-293T cells (Human Embryonic Kidney cells, ATCC, CRL-1573) were used to produce Ad5 and SARS-2 PV virus stocks, respectively. Original CHO cell lines were obtained from ATCC (CCL-61). The CHO-CAR (Chinese Hamster Ovarian cells, transfected to express Human CAR)[42] and CHO-ACE2-TMPRSS2 (Chinese Hamster Ovarian cells, expressing Human ACE2 and TMPRSS2)stable cell lines were used in transduction assays with Ad5.GFP and SARS-2 PV, respectively. The CHO-ACE2-TMPRSS2 stable cell line was generated using the MT126 pRRL- SFFV-ACE2-IRES (AddGene, 145839) and MT131 pRRL- SFFV-TMPRSS2.v1-IRES (AddGene, 145843) plasmids.[43] T-REx-293 and HEK-293T cells were cultured in DMEM media (Dulbecco's Modified Eagle's Medium; Sigma-Aldrich, Gillingham, UK #D5796), whilst CHO-CAR and CHO-ACE2-TMPRSS2 cells were cultured in DMEM-F12 media (Dulbecco's Modified Eagle's Medium/Nutrient Mixture F-12 Ham; Sigma-Aldrich, Gillingham, UK #D0697). All media were supplemented with 10% FBS (Foetal Bovine Serum; Gibco, Paisley, UK #10500-064), 2% Penicillin and Streptomycin (Gibco, Paisley, UK #15070-063) and 1% L-Glutamine (stock 200 mM; Gibco, Paisley, UK #25030-024). CHO-ACE2-TMPRSS2 cells were also passaged with 2μg/mL Puromycin and 100μg/mL Hygromycin once a week. Cells were grown at 37°C with 5% CO_2. Dulbecco's Phosphate Buffered Saline (PBS, Gibco™, #10010023) and 0.05% Trypsin (Gibco™, #11590626) were used for subculture.

METHOD DETAILS

Virus production

Ad5 was modified to express Green Fluorescent Protein (GFP)[40] and was propagated in T-REx-293 cells expressing E1 gene products and purified using Caesium Chloride gradient ultracentrifugation as previously described.[45] Stock titres were determined by Micro-BCA assay (Pierce, Thermo Fisher, Loughborough, #23235), assuming that 1μg protein was equal to 4 x 10^9 virus particles (vp) and monodispersity was confirmed by Nanoparticle Tracking Analysis (NanoSight NS300, Malvern, UK), which identified the mean diameter of particles in the stock solutions. Infectious titres were quantified by end-point dilution plaque assay, performed in T-REx-293 cells, determining plaque forming units per millilitre (PFU/ml).

The SARS-CoV-2 Pseudotyped Lentivirus (SARS-2 PV) contained a HIV core and expressed Wuhan strain SARS-CoV-2 Spike Proteins (GenBank accession: 43740568) on their viral envelope. SARS-2 PV are replication deficient and express GFP under the control of a spleen focus-forming virus (SFFV) promoter post transduction.[46,47] SARS-2 PV were produced in HEK-293T/17 cells (ATCC CRL11268) that were pre-seeded in a T175 flask (Thermo) with approximately 5 x10^6 cells the day before transfection. Cells were then co-transfected with 2 μg of packaging lentiviral core p8.91,[44] 3 μg of pCSGW encoding Green Fluorescent Protein,[44] and 2 μg of the spike SARS2 (D614G)-pCAGGS (Medicines & Healthcare Products Regulatory Agency, #CFAR100985) using FuGENE HD (Promega, UK, #E2311) transfection reagent at a ratio of 1:3 DNA:Fugene in optiMEM (Gibco, Thermo, UK, #31985062). SARS-2 PV were harvested at 48h post transfection and supernatant filtered through a 0.45 μm acetate cellulose filter (Starlab, Milton Keynes, #E4780-1453).[41,48] Functional titres were determined by plaque assay.

Experimental setup of the closed-system model

The standard closed-system model (Figure 1) was optimised and altered for some experiments, however the general setup remained consistent in each run. A medical grade nebuliser (Aerogen® Solo Starter Kit, Aerogen Ltd, Galway, AG-A53000-XX) was used to aerosolise 10ml of each sample into a 3L reaction kettle (QuickFit™ Wide Neck Flask Reaction 3L, Scientific Laboratory Supplies Ltd, UK, QFR3LF). The nebuliser emitted droplet sizes of 4.47 $\pm$ 0.05 μm, at an aerosol output rate of 0.536 $\pm$ 0.01 ml/min, as determined by laser diffraction (Spraytec; Malvern Panalytical Instruments).[49] Aerosolised samples containing virus therefore consisted of 4.47 $\pm$ 0.05 μm sized media droplets, each containing a dispersion of virus particles (each approximately 90-100nm in diameter).The reaction kettle was fitted with a lid containing multiple culture vessels (QuickFit™ Borosilicate Glass Flange Lid, Fisher Scientific, Leicestershire, MAF3/52), enabling the insertion of samples and materials, whilst maintaining an air-tight system. Ultravision™ technology was used to induce electrostatic precipitation. The power supply (Ultravision™ Generator, BOWA Medial UK, Newton Abbot, DAD-001-015) was stationed outside of the closed system. The discharge electrode (Ionwand™, BOWA Medial UK, Newton Abbot, DAD-001-003) was inserted into the reaction kettle through a Suba-Seal®, 15cm from the bottom of the reaction kettle and 7cm from either side of the reaction kettle. The power supply was attached to copper tape that covered the inside of the reaction kettle via a modified patient return electrode cable, functioning as a positively charged collector-plate. It is important to note that copper ions are virucidal, and therefore may affect viral viability. As a countercheck, an experimental run was performed using biologically inert stainless-steel as the positively charged collector-plate, to determine whether copper affected the viability of electrostatically precipitated viral particles. Stopcock adapters (QuickFit™ Borosilicate Glass Stopcock Adaptors with Sockets, Fisher Scientific, Leicestershire, MF14/3/SC) were placed throughout the system, ensuring unidirectional flow of the aerosol. A vacuum unit (Duet Flat- Back Aspirator, SSCOR, US, 2314B) was used, at maximum flow rate (>30LPM), to suction the aerosol through the reaction kettle and into a sampling system (BioSampler®, SKC Ltd, Dorset, 225-9595). The sampling system (assembled as per manufacturer's instructions) contained 2ml sterile serum-free media (DMEM) to recover the captured aerosol samples. To prevent viral contamination, a cold-trap (QuickFit™ Cold-trap, VWR, Pennsylvania, 201-3052) was fitted between the sampling system and the vacuum unit. All experimentation was conducted in a Class II laminar flow hood, and all materials were autoclaved or sterilised with 70% Industrialised Methylated Spirit (IMS) (Thermo Fisher, #15950957, Leicestershire) before and after use.

Experimental procedure

To mimic the release of bioaerosols that occurs during key-hole surgery, we developed a closed-system model representing laparoscopy within a peritoneal cavity. A 3L reaction kettle was used to resemble the peritoneal cavity, which is sufflated to approximately 3L with CO_2 during laparoscopy.[42] The discharge electrode was positioned within the reaction kettle, directly above the region of bioaerosol release, as it would be during laparoscopy. Quick-fit® glassware was used to ensure that the entire model was air-tight, preventing the release of virally contaminated aerosols.

In each experimental run, 10ml samples were aerosolised into the reaction kettle, which was heated to 37°C to avoid sample condensation and to resemble the average Human body temperature. Closed surgeries using electrocautery devices produce particle sizes of 0.07μm, whilst Ultrasonic scalpels produce particle sizes between 0.35-6.5μm.[50,51] Particles produced by the nebuliser were approximately 4.5μm in size, and virus particles (90-100nm diameter) were dispersed within each particle, thus resembling aerosol particles that are released during surgery. The samples were exposed to inactivate/active EP, until the entire sample had been completely aerosolised (1 hour/sample). Samples aerosolised through the system included: Serum-free media (negative control), Ad5.GFP diluted to 1 x 10^{10}vp/ml in media and SARS-2 PV diluted to 1 x 10^7pfu/ml in media. Both viruses expressed GFP for detection in experimental assays. Additionally, 2ml of each sample was not aerosolised through the system ('non-exposed') and was immediately stored at -80°C to be used as 'untreated' controls. A vacuum unit was employed to suction the aerosol through the closed-system model in a unidirectional flow into the sampling system for sample recovery, to assess viral presence within the aerosol following exposure to EP. Recovered samples were analysed for viral presence by qPCR and for viral activity via transduction and plaque assays. Immediately after complete sample aerosolisation, the collected samples were stored at -80°C. Physical parameters thought to affect the efficiency of EP were altered, in an attempt to determine optimal EP settings. Such parameters included temperature, voltage, the number of discharge electrodes within the reaction kettle and the material of the collector plate attached to the positively charged return electrode.

Quantification of viral genomes by qPCR

DNA was extracted using the QIAamp MinElute Virus Kit (Qiagen, USA, #57704). Purified DNA was eluted in 50µl of Ultra-Pure Water (UltraPure™ DNase/RNase-Free Distilled Water, Invitrogen™, Thermo Fisher, #11538646) and stored at -20°C. DNA extracted from the virus stocks were used as standards (Serial dilution: undiluted (200ng/µl), 10^{-1}, 10^{-2}, 10^{-3}, 10^{-4}, 10^{-5} and 10^{-6}). DNA extracted from experimental samples remained undiluted. Primers (Ad5 Hexon Forward: CCTGCTTACCCCCAACGAGTTTGA, Ad5 Hexon Reverse: GGAGTACATGC GGTCCTTGTAGCTC; P24 Capsid: Forward: GGCTTTCAGCCCAGAAGTGATACC, P24 Capsid Reverse: GGGTCCTCCTACTCCCTG ACATG) were used at 10Mm. qPCR for viral DNA was performed using the SYBR Green Master Mix (PowerUp™ SYBR™ Green Master Mix, Applied Biosystems™, Thermo Fisher, #A25741) (per reaction: 15µl Master Mix and 5µl DNA). Reactions were performed in triplicate (for both samples and standards). QuantStudio™ software was used to set the thermal cycling conditions of the qPCR (Pharmaceutical Analytics QuantStudio™ 5 Real-Time PCR System, Applied Biosystems™, Thermo Fisher, #A31670). Samples were held at 50°C for 2 min, followed by 95°C for 2 min. Samples were then cycled at 95°C for 15 sec and 60°C for 1 min for 40 cycles.

Transduction assays

CHO-CAR/CHO-ACE2-TMPRSS2 cells were seeded into a 96-well plate at a density of $2x10^4$ cells/well in 200µl complete media and cultured overnight. The following day, complete media was removed, cells were washed briefly in PBS, and experimental samples were added to the cells (100µl, undiluted) and incubated at 37°C for 3 hours. The media was then removed and discarded, and the cells were washed twice with 100µl PBS, prior to replenishing the cells with 200µl total media and culturing for an additional 48 hours. Cells were visualised for GFP expression using a microscopic imaging system (EVOS M7000, Invitrogen™, Thermo Fisher Scientific, #AMF7000), then harvested in FACS buffer and fixed with 4% Paraformaldehyde. Flow Cytometry was performed, using the Accuri (Accuri C6 v.1.0.264.21, BD Biosciences) and the FL1-A channel, to detect virally transduced cells. FlowJo™v10 software was used to analyse all Flow Cytometry data.

Plaque assays

T-REx-293/HEK-293T cells were seeded in 12-well plates in complete media, at a density of $1x10^5$ cells/well in triplicate. Cells were cultured for 24 hours, prior to the experiments. Medium was removed, and the cells were washed with 1ml PBS. Experimental samples were added to the wells (1ml, undiluted) in duplicate. The cells were incubated at 37°C for 2 hours, then the medium was removed and replaced with 1ml complete media. The cells were cultured for a further 48 hours, before analysis. Microscopy (EVOS M7000, Invitrogen™, Thermo Fisher Scientific, #AMF7000) was used to image the cells (Objective Lens X20). Transduced cells fluoresced green light under the GFP light source, enabling manual counting of infected cells. The PFU/ml of each sample was calculated using the formula:

$$\left(\frac{\left(\text{Average number of florescent } \frac{\text{cells}}{\text{well}} \times 594\left(\frac{\text{Fields}}{\text{well}}\right)\right)}{(\text{Volume of viral sample } \mu \times \text{dilution factor})}\right) \times 1000 = \frac{\text{PFU}}{\text{ml}}$$

QUANTIFICATION AND STATISTICAL ANALYSIS

All data presented show the mean ± SD. GraphPad Prism v4.03 (GraphPad Software Inc., La Jolla, CA) was used to produce all bar chart figures. The GraphPad Quickcalcs t-test calculator was used to perform the two-tailed paired t-test. p-Values of * = $p<0.05$, ** = $p<0.005$, *** = $p<0.0005$, ns = not statistically significant, $p>0.05$. All statistical details of the experiments can be found in the figures and figure legends of the results section. The n value is equal to the number of technical repeats.

Attachment J

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ULTRAVISION™

ULTRAVISION2

Solving surgical smoke problems in *laparoscopic* and *robotic surgery*

Smoke **Management**
Enhanced **Visualization**
Stable **Pneumoperitoneum**
Workflow **Optimization**

alesi surgical

ULTRAVISION™

Revolutionising laparoscopic and robotic surgery.

Ultravision™ is the world's only advanced surgical smoke management technology that provides class-leading visualization and minimizes patient CO_2 exposure.

A revolutionary new system that filters surgical smoke using the proven process of electrostatic precipitation, providing surgical smoke control at the point of origin. The Ultravision technology's unique mode of action delivers unparalleled bioaerosol control [1], advanced visualization, stable pneumoperitoneum in standard and low pressure surgery, and minimizes workflow disruptions caused by surgical smoke.

Scan for 'Ultravision2™ Mode of Action'

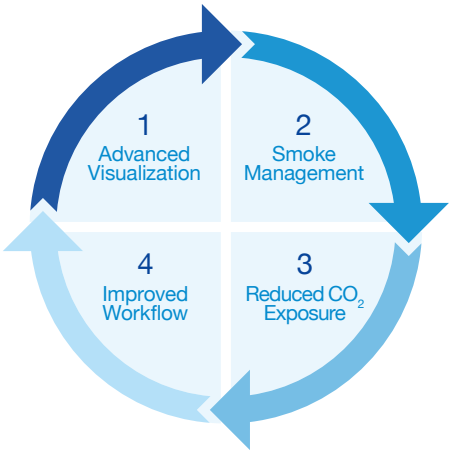
Scan for 'Ultravision2™ in Action'

Features + key benefits

alesi surgical

ULTRAVISION™

Ultravision performance



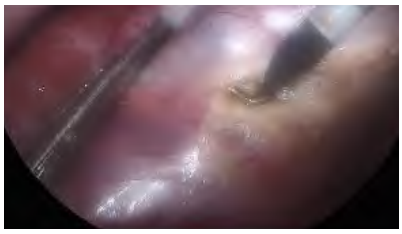
The Ultravision technology has undergone a variety of rigorous independent tests, achieving outstanding results.*

*All data generated using the Ultravision system.

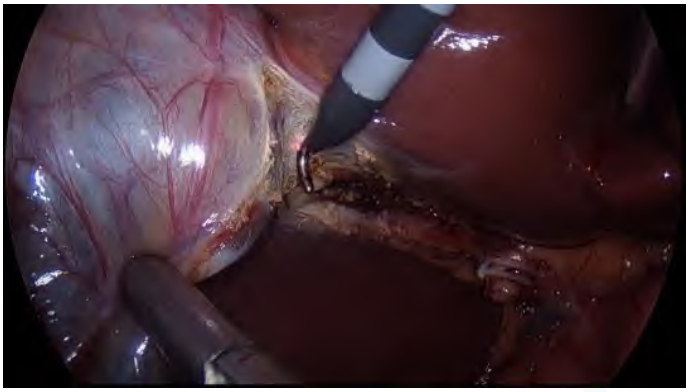
Visualization performance

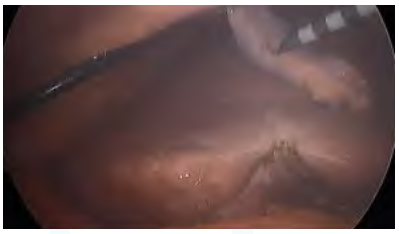
1

Ultravision consistently delivers advanced visualization, optimising procedural performance.



Venting through port





Advanced insufflator

Ultravision | Advanced visualization

Images courtesy Dr. Jin S. Yoo, Duke University Hospital, US.

In independent tests Ultravision delivered surgeon visualization scores of Excellent or Good in 80% of cases, compared to only 20% when venting.[3]

The surgeon's view

When we're doing laparoscopic surgery visualization is just about everything.

We need to be able see very clearly what we are doing and anatomically what we are trying to accomplish.

Dr. Richard Rosenfield, MD
Executive Medical Director, Pearl Women's Center, US

Further studies available on alesi-surgical.com

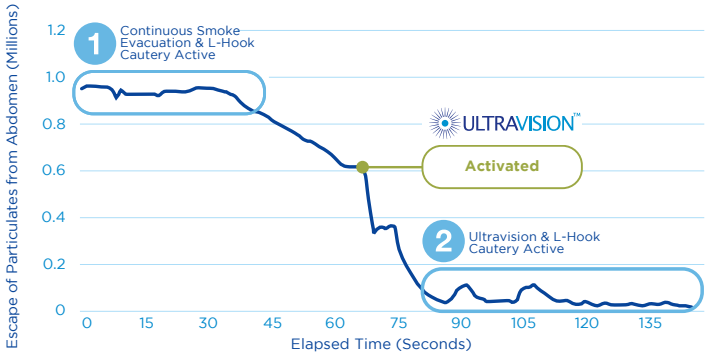
Smoke management performance

2

Ultravision technology proven to be faster and more efficient than traditional smoke evacuation systems.

Study

Measuring unintentional release of smoke into the operating room.
Ultravision versus continuous smoke evacuation system. [4]



1) Continuous smoke evacuation experiences additional escape of smoke particulates through leaks in trocars and during instrument exchanges.

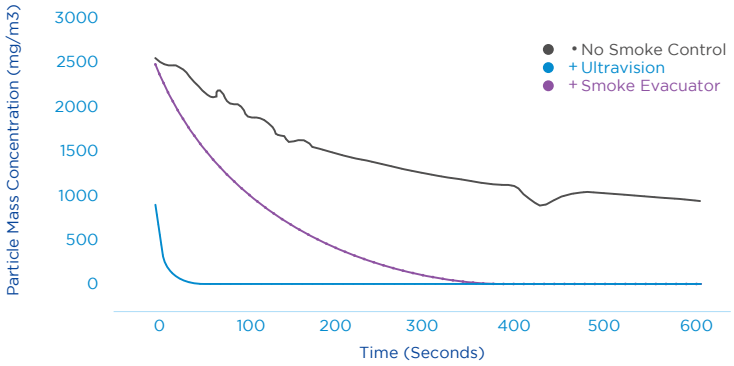
2) Ultravision suppresses smoke and bioaerosols at the point of creation which reduces the likelihood of release in the operating room.

Result

In simulated surgery, the use of Ultravision was 23-times more effective in reducing the amount of surgical smoke aerosol that escaped into the OR due to accidental leaks during the procedure.

Study

Measuring speed & effectiveness.
Ultravision versus filter-based smoke evacuation system.[5]



Result

Ultravision minimizes surgical smoke, providing two levels of risk reduction:

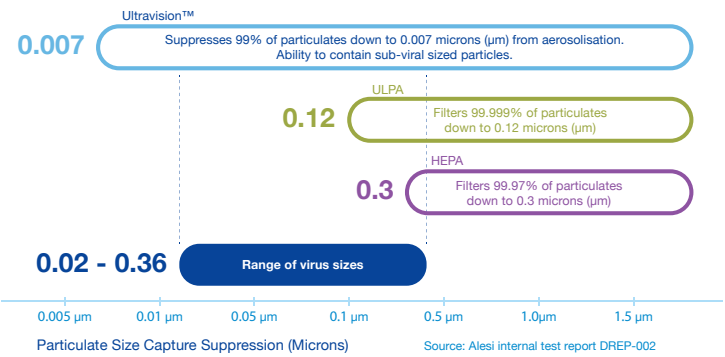
1. Particle suppression at the point of creation.

2. More rapid elimination of smoke compared to smoke evacuators.

After 60 seconds Ultravision removes 99.9% of particles from the atmosphere, versus 30.2% with a smoke evacuator.

Study

Removal efficiency test for sub-viral particulates.
Suppression of particulate by size.[5]



Source: Alesi internal test report DREP-002

Result

1. Suppresses 99% of particulates down to 0.007 microns (µm) from aerosolization. [1]

2. The only technology verified to be effective at sub-viral particle sizes.

alesi surgical

ULTRAVISION™

CO_2 **management** performance

3

Ultravision's unique system provides stable pneumoperitoneum in standard and low-pressure surgery, enables low-CO_2 surgery, and reduces CO_2 usage.

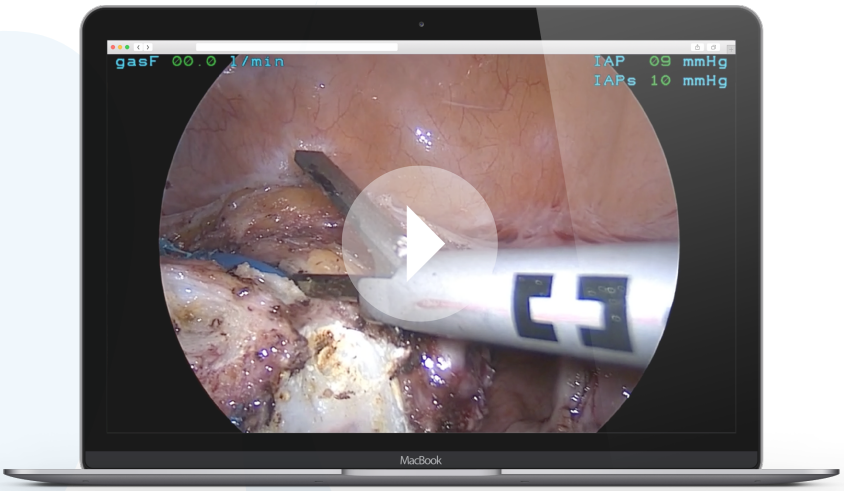
Watch full video at www.alesi-surgical.com

Study

A test to explore the use of Ultravision in facilitating low pressure surgery in total laparoscopic hysterectomy (TLH) and myomectomy.[6]

Result

Ultravision enhances low pressure laparoscopic hysterectomy and myomectomy. This was achieved by minimizing interruptions to surgery and exchange of CO_2, providing stable pneumoperitoneum, a clear visual field throughout the procedure, and eliminating surgical smoke at the site of origin.



Improving OR efficiency

Ultravision enables a more efficient OR through time savings and reduced CO_2 usage.

Study

Evaluate Ultravision performance during laparoscopic cholecystectomy.[3]

Result

1. 8 minutes per case saved.
2. Zero pauses in 77% of procedures.
3. No camera cleaning required in 95% of cases.

Visit alesi-surgical.com to read full study

alesi surgical

ULTRAVISION™

Order Number	Item Description	
DPD-006-001	Ultravision2™ Generator	
DAD-001-003	Ionwand™ Sterile Pack (x10)	
DPD-006-201	Ultravision2™ Integrated Monopolar L Hook (H/S)™ (x5)	
DAD-003-014	Ultravision™ 5mm Trocar (x6)	
DPD-007-002	Ultravision2™ IonPencil™ (x40)	

What the surgeons say

"I have used Ultravision for the last two years in most of my laparoscopic cases. The advancements in Ultravision2 have vastly improved overall performance and ease of use. The new integrated monopolar instrument is a game-changer for the technology."

Dr. Urs Pabst-Giger, Senior Consultant Surgeon,
University Hospital Münster, Germany

*1 Gohler D et al, Journal of Aerosol Science (accepted)

*2 Based on Ultravision2 maximum consumption of 62VA versus representative smoke evacuator of 1000VA.

*3 Ansell et al, Electrostatic precipitation is a novel way of maintaining visual field clarity during laparoscopic surgery: a prospective double-blind randomized controlled pilot study Surgical Endoscopy (2014) 28: 2057-2065

*4 Buggisch et al, Experimental Model to Test Electrostatic Precipitation Technology in the COVID-19 Era: A Pilot Study Journal of American College of Surgeons, (2020), 231 (6) 704-712

*5 Alesi internal reports DVER-006-015 and DREP-002

*6 Levine, D et al, "Electrostatic Precipitation in Low Pressure Laparoscopic Hysterectomy and Myomectomy" (2020), JSLS, Volume 24, Issue 4.

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ULTRAVISION™

Solving surgical smoke problems

Tel: +44 (0) 29 2029 1022
Email: info@alesi-surgical.com

Alesi Surgical Limited, Cardiff Medicentre, Cardiff, U.K.

www.alesi-surgical.com

DLU-006-005v4US

Attachment K

alesi surgical

ULTRAVISION™

ULTRAVISION2

See your smoke management problems disappear

New!

Effective **Smoke Management**
Slimline, **Easy To Use**
Silent, **No Distractions**
Environmentally **Friendly**

alesi surgical

ULTRAVISION™

Why Choose Ultravision **For Open Surgery?**

Ultravision2™ provides advanced smoke management for OR staff with the new IonPencil™ for use in open surgery.

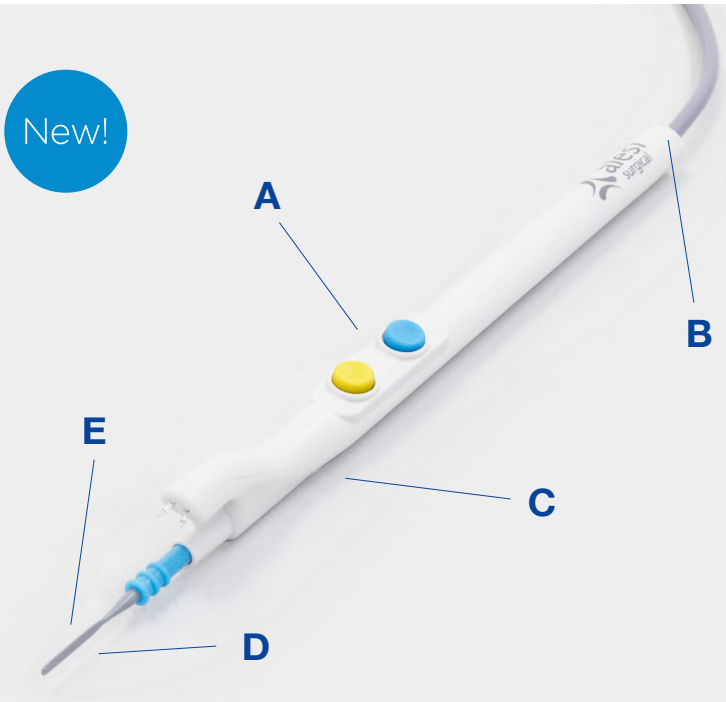
The IonPencil suppresses aerosolization of the surgical smoke at the source, using the proven process of electrostatic precipitation, thereby minimizing its release into the operating room. The slimline ergonomic design provides an unshrouded electrode tip, enabling excellent operative site access, and the lack of tubing ensures minimal torque and drag.

The silent Ultravision2 generator helps ensure OR staff can concentrate on the patient, with minimal distractions. The efficient design also improves sustainability with reduced packaging, reduced single use plastics, reduced energy consumption, and no disposable filters.

Scan for 'Ultravision2™ Mode of Action'

Scan for 'Ultravision2™ in Action'

New!



The IonPencil™

The IonPencil has been developed to provide excellent smoke management performance but without any of the bulk associated with conventional "smoke pencils" that can compromise surgical performance.

A - Slimline handle.
B - No tubing.
C - Reduced weight compared to smoke pencil.
D - Unshrouded electrode tip.
E - Easy to handle, greater tissue access.

alesi surgical

ULTRAVISION™

Key features & benefits

Lightweight ergonomic 'slimline design'
Easy to handle, greater tissue access

Silent in operation
Less distraction, more focus

Efficient smoke management
Reduced exposure to potentially hazardous surgical smoke

Reduced waste versus smoke pencil
No disposable filters, less packaging, less single use plastic

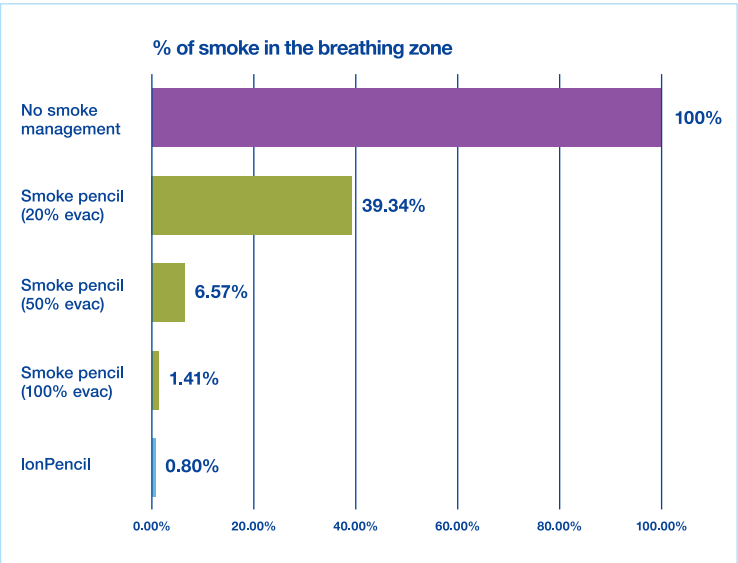
Ultravision Performance Comparison...

	IonPencil	Telescopic Smoke Pencil	Non-Telescopic Smoke Pencil
Best-in-class operative site access	●	◔	◑
High maneuverability	●	◑	◔
Silent in operation	●	◔	◔
High energy efficiency	●	◔	◔
Low environmental impact	●	◔	◔

IonPencil delivers excellent smoke management performance

Smoke management performance was assessed in simulated testing against a representative smoke pencil. The IonPencil demonstrated consistent and excellent performance in suppressing smoke released into the atmosphere, whereas the smoke pencil performance was highly dependent upon the vacuum setting of the smoke evacuator*.

In simulated surgery to assess volatile organic chemicals (VOCs), even without room ventilation, only five of 64 VOCs assessed were elevated in room air samples when using the IonPencil. Quantifying these five VOCs confirmed a large margin of safety for both fifteen-minute, short-term (STEL) and eight-hour daily average (TWA) exposure limits**.



** Source: Alesi Surgical report MCR-007-3 Rev 1*
*** Using the Environmental Protection Agency (EPA) TO-15 test method, margins of safety ranges were STEL: 26-28,000; TWA: 17-75,000.*
Source – Alesi Surgical report DVER-007-012 Rev 1.

alesi surgical

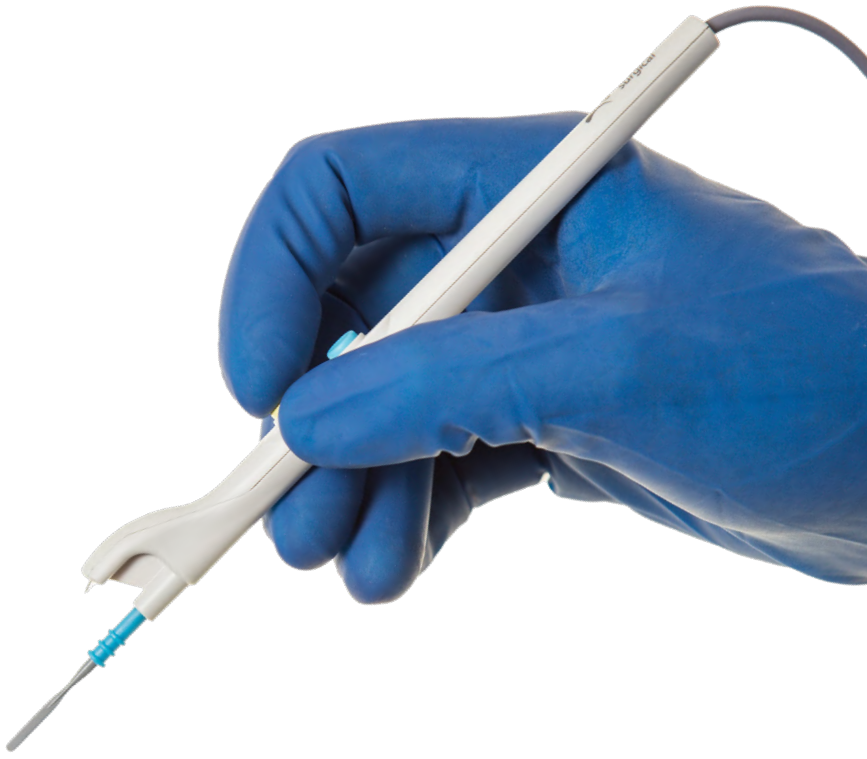
ULTRAVISION™

Order Number	Item Description	
DPD-006-001	Ultravision2™ Generator	
DPD-007-002	Ultravision2™ IonPencil™ (x40)	
DPD-006-201	Ultravision2™ Integrated Monopolar L Hook (H/S)™ (x5)	
DAD-003-014	Ultravision™ 5mm Trocar (x6)	
DAD-001-003	Ionwand™ Sterile Pack (x10)	

What the surgeons say

"My experience with the IonPencil has been excellent. It feels very similar to a standard pencil but generates *no smoke!*"

Colorectal surgeon, UK.



Tel: +44 (0) 29 2029 1022
Email: info@alesi-surgical.com

Alesi Surgical Limited, Cardiff Medicentre, Cardiff, U.K.

www.alesi-surgical.com

Alesi Surgical Inc. Suggested Changes to Proposed Rule

Add new Section 51XX to read:

§ 51XX. Occupational Exposure to Plume in Health Care

(a) Scope and Application. This section applies to occupational exposure to plume in general acute care hospitals and ambulatory surgical centers.

(1) Exposures to plume in other health care settings and exposures to similar smoke, particulates, vapors, and gases in other settings are covered under Title 8, Group 16—Control of Hazardous Substances, and other applicable substance-specific standards.

(2) This section does not preclude the application of sections 3203, 5141, 5143, 5144, 5155, 5193, 5199 or other title 8 safety orders to occupational exposure to plume.

(b) Definitions.

(1) "Administrative control" means a method to limit exposure to a hazard by adjustment of work procedures, practices, or schedules.

(2) "Ambulatory surgical center or ASC" means any surgical clinic as defined in the California Health and Safety Code Section 1204, subdivision (b)(1), any ambulatory surgical center that is certified to participate in the Medicare program under Title XVIII (42 U.S.C. SEC. 1395 et seq.) of the federal Social Security Act, or any surgical clinic accredited by an accrediting agency as approved by the Licensing Division of the Medical Board of California pursuant to Health and Safety Code Sections 1248.15 and 1248.4 to use anesthesia, except local anesthesia or peripheral nerve blocks, or both, in compliance with the community standard of practice, in doses that, when administered have the probability of placing a patient at risk for loss of the patient's life-preserving protective reflexes.

(3) "Authorized employee representative" for purposes of this section only, means an organization that has a collective bargaining relationship with an employer or an organization acknowledged by a public agency as representing its employees.

(4) "Designated employee representative" for purposes of this section only, means any individual or organization to whom an employee gives written authorization to exercise their right to access records required by this section.

(5) "Electrocautery device" means a device that is electrically heated to cut, ablate, or coagulate human tissue.

(6) "Electrosurgical device" means a device that uses a radio frequency electric current that passes through human tissue to cut, ablate, or coagulate.

(7) "Energy-based device" means a device that uses energy to ablate, cauterize, or mechanically manipulate human tissue, including lasers, electrosurgical generators, broadband light sources, ultrasonic instruments, plasma generators, bone saws, and drills.

This is a draft of possible language regarding AB 1007. This draft is for discussion purposes only and is not a final rulemaking proposal.

(8) "Gas phase filter" (e.g., activated carbon filter) means a filter that effectively removes gaseous air contaminants, which are too small to be filtered by particulate filters, through adsorption, absorption, or other chemical reaction.

(9) "General acute care hospital" means a hospital licensed by the California Department of Public Health as such meeting the definition provided in Health and Safety Code Section 1250(a) or California Code of Regulations, Title 22, Section 70005, and all services within the hospital's license.

(10) High efficiency particulate air (HEPA) filter means a filter that is at least 99.97% efficient in removing monodisperse particles of 0.3 micrometers in diameter.

(11) "Plume" means airborne contaminants generated from the use of energy-based devices, electrosurgical devices, electrocautery devices, or mechanical tools during surgical, diagnostic, or therapeutic procedures.

(12) ~~"Plume evacuation system (PES)" means smoke evacuators, laser plume evacuators, plume scavengers, and local exhaust ventilators.~~ "Plume control system (PCS)" means any system, device, or technology that, when used in concert with other engineering controls and equipment, and to the extent technologically feasible, effectively captures, ~~and~~ removes, or neutralizes plume at the site of origin and before plume can make contact with the eyes or contact with the respiratory tract. Such systems may include smoke evacuators, laser plume evacuators, plume scavengers, local exhaust ventilators, electrostatic precipitators, or other FDA-cleared or ISO/CSA-validated technologies.

(13) "Plume scavenger" means a technology, system, or component designed to capture or neutralize plume at or near the site-of-origin, including but not limited to suction-based devices and non-suction-based technologies such as electrostatic precipitators.

(14~~3~~) "Site-of-origin" means the location where tissue is being altered, worked on, or destroyed by a medical device or devices.

(15~~4~~) "Ultra-low particulate air (ULPA) filter" means a filter that removes particles as small as 0.12 micrometers with a filtration efficiency of not less than 99.999%.

(c) Written Exposure Control Plan.

(1) Employers shall establish, implement, and maintain a written exposure control plan that provides clear instructions for the effective use of plume ~~evacuation~~ control systems to minimize employee exposure to plume and that contains all the elements in subsection (c)(2).

(2) The plan shall contain all of the following elements:

(A) The name(s) or title(s) of the person(s) responsible for implementing the plan.

Commented [1]: Language mirroring the Bill text.

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(B) A list of all job classifications that have occupational exposure to plume.

(C) Effective procedures for identifying and evaluating occupational exposure to plume in accordance with Section 3203(a)(4).

(D) Effective procedures to control employee exposure to plume. The procedures shall contain clear instructions for whenever energy-based devices, electrosurgical devices, electrocautery devices, or mechanical tools are in use.

(E) Effective procedures for reviewing, at least annually, the effectiveness of the plan.

(F) Effective procedures for obtaining the active involvement of employees and authorized employee representatives in all elements of the exposure control plan including, but not limited to:

1. Identifying and evaluating exposures to plume;
2. Controlling exposures to plume including administrative controls, and selection and use of plume ~~evacuation~~ control systems;
3. Selection and use of personal protective equipment;
4. Selection and use of respirators;
5. Reviewing and updating the plan; and
6. Training.

(3) The exposure control plan shall be reviewed, evaluated, and updated:

(A) At least annually,

(B) When new processes, procedures, and equipment are introduced to the workplace, and

(C) Whenever a new or previously unrecognized hazard is identified.

(d) Control Measures.

(1) Engineering Controls.

(A) Plume ~~Evacuation~~ Control Systems. Exposure to plume shall be prevented ~~by plume evacuation systems~~ to the greatest extent feasible through plume control systems. Plume ~~evacuation~~ control systems shall:

1. Be in operation continually whenever plume is generated; and~~.~~

2. Be designed, located, integrated, or otherwise configured to effectively capture, remove, or neutralize plume at or near ~~as close as possible to~~ the site-of-origin, consistent with the technology's mode of action; and~~.~~

This is a draft of possible language regarding AB 1007. This draft is for discussion purposes only and is not a final rulemaking proposal.

3. Plume control systems shall either:

i. When relying on exhaust or filtration:

Exhaust in accordance with section 5143 and by one or a combination of the following:

~~i.~~ Directly outdoors at least 25 feet from any doors, window, air intakes, other openings in buildings, or places where persons are may be present; and/or

~~ii.~~ Indoors through an ULPA filter and gas phase filter.

~~4.~~ Be used, constructed, installed, inspected, tested, and maintained in accordance with section 5143 and in accordance with the manufacturer's instructions.

ii. When relying on another FDA-cleared or ISO/CSA-validated mode of action: Demonstrate that the system, when installed, operated, and maintained in accordance with the manufacturer's instructions, provides effective reduction of plume consistent with its mode of action and in accordance with recognized performance benchmarks as applicable (e.g., ISO 16571, CSA Z305.13-13), such that worker protection is at least equivalent in effectiveness to conventional smoke evacuation methods in controlling particulate plume.

(B) General Ventilation. The minimum total air exchange rate for the room or area where surgical plume is generated shall be at least 20 air changes per hour and shall be used in addition to plume ~~evacuation~~ control systems and other local exhaust ventilation systems. The room air shall be exhausted directly to the outdoors or returned to the air circulation system through a HEPA filter.

(2) Administrative controls shall be used to minimize employee exposure to plume to the greatest extent feasible.

(3) Respirators that provide protection against particulates and organic vapors shall be used in accordance with section 5144 when the engineering controls and administrative controls do not prevent plume from contacting the respiratory tract of employees.

NOTE: Surgical masks are not respirators pursuant to section 5144.

(4) The employer shall provide and ensure employees use appropriate eye protection where plume may contact the eyes of an employee.

Commented [2]: Note to Cal/OSHA: It is important to clarify how performance equivalence should be understood in this context. Conventional smoke evacuators generally specify only the efficiency of their particulate filters (e.g., ULPA filtration of 99.999% at 0.12 µm). They do not typically make claims or provide specifications for overall plume capture performance, nor do they provide data on reduction of volatile organic compounds (VOCs).
By contrast, electrostatic precipitators have been tested against conventional smoke evacuation systems using smoke particle meters, which represent the standard and accepted method for comparing particulate plume reduction. These studies show that electrostatic precipitation achieves at least equivalent particulate control.
Because conventional systems make no performance claims for VOC reduction, it is not possible to demonstrate equivalence in that area. Instead, equivalence should be framed in terms of **recognized benchmarks and modes of action**: particulate capture for suction-based systems, and neutralization/precipitation for electrostatic systems. This approach aligns with AB 1007's requirement that Cal/OSHA benchmark ISO 16571 and CSA Z305.13-13, which are performance-based standards focused on outcomes rather than prescribing a single method of control.

This is a draft of possible language regarding AB 1007. This draft is for discussion purposes only and is not a final rulemaking proposal.

(e) Training. The employer shall provide effective training to all employees who have occupational exposure to plume, including new employees and to exposed employees' supervisors. The initial training shall be provided when the written procedures are first established and annually thereafter. Training shall include at least the following elements as applicable to the employee's assignment:

(1) General education on the contents of plume;

(2) The circumstances in which plume is generated;

(3) Procedures, diagnostics, and techniques used at the worksite that generate plume;

(4) The safety and health hazards associated with exposure to plume;

(5) The appropriate use of the plume ~~evacuation~~ control systems utilized by the employer, including the employer's written exposure control plan and procedures required by subsection (c);

(6) The employer's procedures to ensure proper use, inspection, and maintenance of engineering controls and personal protective equipment, as applicable;

(7) Administrative controls to minimize exposure to plume, as applicable;

(8) An opportunity for interactive questions and answers with a person knowledgeable about occupational exposure to plume and the specific plume control equipment utilized by the employer; ~~to scavenge plume;~~ and~~;~~

(9) The contents of this section.

(f) Recordkeeping. The employer shall make available for examination and provide copies of records required by this subsection to employees, authorized employee representatives, designated employee representatives, and representatives of the Division upon request.

(1) The written exposure control plan required by subsection (c) shall be available at the worksite at all times.

(2) Training records. These records shall be maintained for at least three years.

(A) Training records shall include the following information:

1. The date(s) of the training session(s);

2. The contents or a summary of the training session(s);

3. The names and qualifications of people conducting the training or who are designated to respond to interactive questions; and

4. The names and job titles of all persons attending the training sessions.

This is a draft of possible language regarding AB 1007. This draft is for discussion purposes only and is not a final rulemaking proposal.

(3) Plume ~~evacuation~~ control systems.

(A) The employer shall maintain records that the plume ~~evacuation~~ control system conforms to the minimum requirements in section (d)(1)(A) and which demonstrate that it is installed, operated, and maintained in accordance with the manufacturer's instructions. These records shall be retained for at least 5 years.

(B) For systems that rely on exhaust or filtration, ~~R~~records of testing ~~of plume evacuation systems~~ shall be maintained in accordance with section 5143. For other validated technologies, the employer shall maintain documentation showing that the system is installed, operated, and maintained in accordance with manufacturer's instructions and provides effective protection consistent with this section. Records of the testing shall be retained for at least 5 years.

This is a draft of possible language regarding AB 1007. This draft is for discussion purposes only and is not a final rulemaking proposal.

Appendix A (Non-Mandatory)

The following are examples of professional occupational safety guidelines for the protection of health care workers exposed to plume:

2022 AORN Guideline for Surgical Smoke Safety.

CSA Z305.1313, (reaffirmed 2020) *Plume scavenging in surgical, diagnostic, therapeutic, and aesthetic settings.*

CSA Z7001:24 National Standard of Canada. *Safe use of energy-based medical and surgical devices in health care.*

ISO 16571: Second edition 2024-03, *Systems for evacuation of plume generated by medical devices*.

NIOSH Control of Smoke from Laser/Electric Surgical Procedures, DHHS (NIOSH) Publication No. 96-128

Note: This appendix is non-exhaustive. Employers may also rely on FDA authorizations, ISO/CSA benchmarks, and other validated evidence to demonstrate compliance, provided the technology achieves equivalent or superior worker protection.

Note: Authority cited: Sections 142.3 and 144.6, Labor Code. Reference: Section 142.3, 144.6 and 6308, Labor Code.