Medtronic Engineering the extraordinary

Evidence compendium
Surgical smoke

Medtronic Engineering the extraordinary

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1. Disclaimer and scope

1.1. Content

This document presents a compendium of data regarding the subject of smoke or plume generated during operative procedures (including surgeries, physician's office, and others). Data include primary sources, reviews, surveys, and opinion pieces. The focus of the dossier is on the production, content, and associated potential risks of surgical smoke or plume. It does not include an overview of legal frameworks or governmental or society guidelines, except where these have been reported in the studies contributing to the dossier, for example in reference to chemical exposure limits for compounds that have been detected in surgical plume. To remain concise, although results returned through the literature search described later in this document were reviewed, not all studies are presented or fully expounded to reduce duplication among overlapping results.

Note on terminology: in the dossier as often occurs in the literature, surgical smoke and plume are sometimes used interchangeably in reference to the aerosolized byproduct of surgical procedures where tissue is vaporized or mechanically reduced. More specifically, "smoke" may be taken to refer to the byproducts specific to combustion of tissue, while "plume" consists of all aerosol components (including smoke from combustion).

1.2. Data sources

Data regarding surgical smoke/plume informing this document consist of published data identified through a publicly available database (PubMed). Search strings used and article screening results are presented in Section 6. Searches were conducted to identify literature in English, German, or French, published in the last 10 years (2010 onwards) to reflect recent data on the subject. Pre-2010 data were considered for inclusion for background sections, or from reference lists of captured articles if those references represented the most recent knowledge on the corresponding subject. All relevant publication types were considered, including reports on data obtained from clinical settings, survey and experiential reports from practitioners, reports of chemical analyses, and results from preclinical or animal tissue studies where corresponding human data were not available. Note that publication details (including year of publication) are indicated according to the PubMed record at the time of article capture, which defaults to the print publication date. Publication year may therefore differ according to first online availability or other changes or updates to the PubMed database.

1.3. Analysis method and disclaimers

Clinical results from individual studies are presented as reported (including indication of statistical significance where determined). Where results from multiple studies are presented in an amalgamated plot or table, units may have been converted for consistency of presentation; individual studies will vary in terms of design, protocol, other methodological details and, patient population (where applicable), which may limit conclusions drawn from direct comparison

and interpretation of analysis of statistical significance. Determination of statistical significance does not assume clinical significance, which should be determined based on local practice. Results determined in experimental or animal models may not directly translate into equivalent outcomes in human patients. Plots are generated from data sources and, unless otherwise indicated, are not images reproduced from source material. Images have similarly been created for the dossier from cited materials unless otherwise noted as reproductions with appropriate citation.

2. Executive summary

Medical devices to dissect, seal, or otherwise manipulate tissues are an essential component of surgical and operative procedures. Broad classes include energy-based (laser, electrosurgical or diathermy, and ultrasonic) and mechanical devices and each has the potential to interact with tissue to create small particles released into the air.[1-5] This byproduct constitutes surgical smoke or plume.

Surgical plume is a complex mixture of substances, consisting of chemical, particulate, and biological materials present at varying levels.[6-8] The type of device producing the plume will determine the sizes of the particles produced (ranging from 15 µm to smaller than 0.1 µm),[1,3,5,9-11] and in turn, the particle size will determine the extent of their penetration into the respiratory tract of individuals exposed.[12,13] The chemical component of surgical smoke includes toxins, carcinogens, and irritants present at levels sufficient to impact human health.[13-18] The biological component of plume represents an infectious risk, as demonstrated by the detection of hepatitis B virus[19] and human papilloma virus, [20-24] the latter of which has been demonstrated to be transmitted to healthcare staff.[21-23]

Both patients and providers are at risk from surgical smoke. As one example, the chemical benzene, a known carcinogen, has been detected in the operating room at levels that could pose a risk to surgeons,[25] and it has also been demonstrated to have been absorbed by patients.[26] Even when chemical constituents of smoke are below exposure limit levels, the long-term effects of chronic exposure are unknown.[27] Perioperative staff can experience multiple sessions of surgical smoke exposure per week totaling hours of exposure spanning multi-year careers.[28] These individuals have been shown to have a higher prevalence of respiratory ailments including asthma and bronchitis, although a causative link to surgical smoke exposure has not been established,[15] possibly due to factors such as the time lag between exposure and development of health effects or confounding effects of variable study designs and results.[17]

In the management of risks posed by surgical smoke, room ventilation alone is insufficient to protect staff.[14,17,25,29] Instead, local exhaust ventilation at the surgical site has been shown to remove 44-60% of particulate matter[30] and 60% of total volatile organic compounds.[31] Similarly for biological smoke contaminants, a study conducted during gynecological procedures reported a decrease in the detection of viral DNA, from 54% to 9% of samples, as the smoke evacuation system was moved closer to the electrosurgical operative site.[20]

The emergence of a novel coronavirus (Severe Acute Respiratory Syndrome coronavirus-2 [SARS-CoV-2]) and its associated respiratory disease COVID-19 have spurred a refocusing of attention on workplace hazards faced by healthcare staff, including that from surgical smoke. Healthcare workers have comprised 10-29% of all reported positive infections,[32,33] and they experience non-negligible mortality.[34-36] The impact of surgical smoke on COVID-19 risk is still unknown, but authors consider it a risk that cannot be eliminated due to demonstrated detection in smoke of other viruses.[37-39] That risk does not appear to be affected by the access type of surgery, as reviews[37-39] and individual studies[40,41] have shown there is no indication of increased SARS-CoV-2 infection risk with laparoscopic versus open procedures. As such, risk from delayed surgery and disease progression,[39] may outweigh potential for SARS-CoV-2 infection given the available recommendations of modifications to procedures to minimize this risk.[39,41,42] Authors note the benefits of laparoscopic surgery in containment of any aerosolized virus while also allowing the patient to benefit from the advantages of minimally invasive surgery.[42]

Surgical smoke and plume represent a hazard to both healthcare staff and patients, but they are a hazard that can be managed with appropriate controls.[20,30,31,39,41,42] Such modification requires awareness of the issue and successful implementation of protocols to manage this health hazard.[14,43]

3. Introduction to surgical smoke

3.1. Summary and key messages

- **Smoke or plume is a byproduct of commonly used medical devices:** Both energy-based (laser, electrosurgical, ultrasonic) and mechanical have the potential to create aerosolized particles in the form of smoke or plume.[1-5]
- **Plume is a complex mixture of substances:** Surgical plume consists of chemical, particulate, and biological materials present at varying levels.[6-8]
- **Constituents of plume depend on device:** Electrosurgical devices produce the smallest particulate matter debris, followed by laser, ultrasonic, and mechanical; the different operational temperatures of these devices will influence the chemical and biological material content of the plume generated.[1,3,5,9-11]
- **Particulate matter (PM) size will determine its penetration into the respiratory system:** In the absence of protective equipment or filters, larger particles will be deposited in the upper respiratory tract, but smaller particles penetrate deeper where they can reach the functional units of the lung and be taken into the bloodstream.[a,12,13]
- **A variety of impacts on health can result from exposure:** Components detected in surgical smoke include toxins, carcinogens, and irritants present at levels sufficient to potentially impact human health.[13-17]
- **Biological material in surgical plume is potentially infectious:** Cases have been identified of human papillomavirus (HPV) DNA detection or infection in healthcare staff where the most probable etiology was occupational exposure to surgical smoke during gynecological electrosurgery.[20-23]
- **Smoke production can impair visibility:** Transient decreases in visualization of the surgical field due to smoke generation can lengthen procedures and increase risks to patients due to prolonged anesthesia or delayed identification of origin of intraoperative bleeding.[29,44]

3.2. Sources of surgical smoke

Operative procedures, whether during surgery in an operating room or during a less invasive procedure in a physician's office, can involve the separation or dissection of tissues and subsequent resealing, for example to prevent blood

[a] World Health Organization, Air Pollution information page https://www.who.int/airpollution/household/pollutants/combustion/en/ ; accessed: 15 Sep 2020

loss or promote healing. These processes of tissue modification may be aided by technologies that heat or mechanically destroy tissues and thereby have the potential to produce particulate matter and chemical or biological materials that can be inhaled by healthcare staff or patients during a procedure. General categories of technologies that have been associated with the production of surgical plume are depicted in Figure 3-1. On average, the smallest particles are generated by electrosurgical or electrocautery devices followed by laser, ultrasonic, and finally mechanical devices with the largest average particle sizes. Note that even within categories, the extent of smoke production may differ depending on operative parameters. Energy devices such as ultrasonic or monopolar devices can be operated in different modes depending on the desired effect on tissue. These modes can include cutting, where tissue dissection is the aim, versus coagulation, in which a broader cauterization of tissue is desired. The type of device and mode of operation can have different effects on the surgical smoke produced (see example, Figure 3-11). In ultrasonic devices, these differing modes of operation have been demonstrated to generate different amounts of smoke-caused obstruction of the visual field in experiments on animal tissue.[45]

Figure 3-1 Potential sources of surgical smoke

	Electrosurgical (mono/bipolar)	Laser (ablative)	Ultrasonic (scalpel/shears)	Mechanical (drill/saw)
Typical particle size	0.07-0.42µm	0.1-0.8µm	0.35-6.5µm	0.5-15µm
Active temperature	100-200°C	100-1,000°C	50-100°C	45-100°C

Operative procedure technologies that have been associated with production of surgical smoke or plume. Typical particle sizes for electrosurgical, laser and ultrasonic as reported by Limchantra et al.[1] and Zakka et al.[9] Mechanical particle size as reported for orthopedic saw in the review of Sobti et al.[10] Laser temperature as reported in Pierce et al.,[3] ultrasonic temperature as reported in Mayo-Yánez et al.,[5] and orthopedic saw as reported in Larsen et al.[11]

3.2.1. Laser

Often used in dermatological procedures. Can be ablative, where tissue is vaporized or nonablative where the outer surface of the tissue is undamaged and the target for energy absorption is deeper. The former case, where tissues are vaporized, is that which will produce surgical plume.[46] The high temperatures associated with laser procedures result in tissue pyrolysis to generate smoke.

3.2.2. Ultrasonic

Surgical technologies that use high-frequency mechanical vibration to dissect and seal tissues, that can sometimes be operationalized as scalpels or shears. The ultrasonic energy results in partial heating of the tissue to generate plume,[47] but due to the lower associated temperatures compared to laser or electrosurgery, the product is often referenced as low-temperature vaporization, generating an aerosol or plume.[5]

3.2.3. Electrosurgical

Electrosurgical devices can include any using electrical energy where tissue is heated, with the aim of dissection or sealing or both. These may include monopolar[47] and bipolar[48] electrosurgical technologies, and electrocautery[30] technologies. The latter devices heat tissue via a different mechanism than typical mono- or bipolar devices, but similarly result in the generation of smoke or plume from the heating and vaporization of tissue.

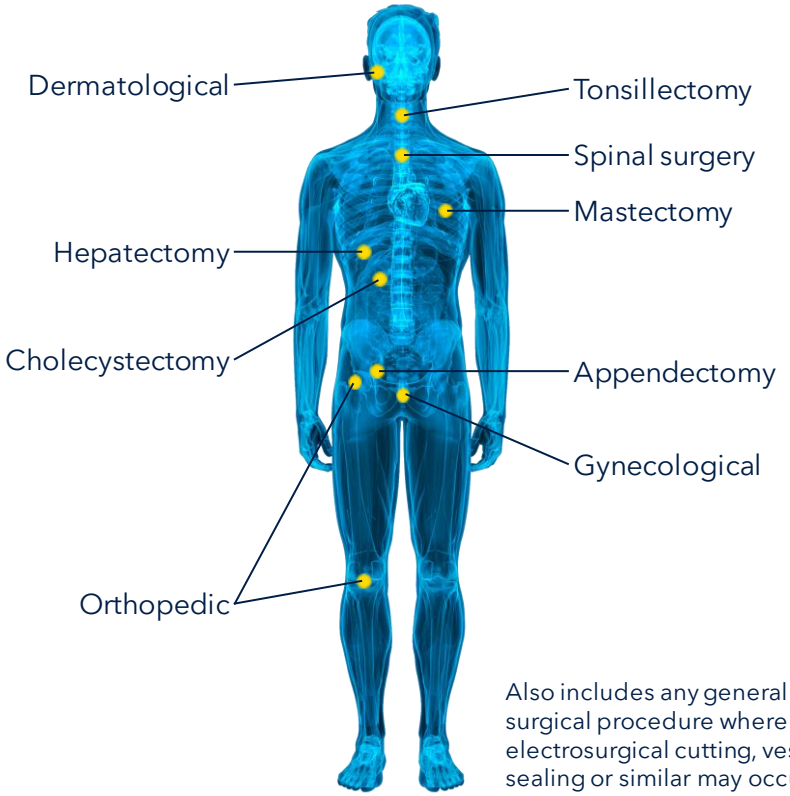
3.2.4. Mechanical

Technologies that mechanically cut or grind hard tissues such as bone or teeth include saws and drills, and may be applied in the context of orthopedic, bone remodeling, or dental procedures. The grinding of tissue generates fine particles that can become airborne and inhaled by staff[4,49] or pose a potential risk to patients.[50] The particles generated can additionally impact the procedure by obscuring the visual field.[51]

3.3. Procedures in which surgical smoke may be generated

In principle, surgical smoke or plume can affect any surgical procedure where tissue is heated resulting in boiling or vaporization of (usually soft) tissue, or mechanical drilling or sawing of hard tissue. Body systems involved in example procedures are depicted in Figure 3-2. This depiction is a nonexhaustive list, as dermatological procedures can be performed on any region of the skin and those on internal organs that use electrosurgical or ultrasonic energy, for example, to dissect tissue or seal blood vessels may also result in production of surgical plume.

Figure 3-2 Select procedures where surgical smoke is generated



Shown are sample surgeries where issues around the production or management of surgical smoke have been reported. Procedures include tonsillectomy,[52] those involving multiple abdominal organs,[26,53] mastectomy,[31] dermatology,[46] gynecological,[20] and orthopedic procedures.[54] The list is not exhaustive, as many other surgical procedures where, for example, electrosurgical vessel sealing may be employed, are not shown.

3.4. Variability of reporting on surgical smoke

The following sections (3.5, 3.6) provide details on components that have been detected in surgical smoke, from chemical to biological. Issues regarding the potential hazards of surgical smoke have been reported for decades, and during that time, vast differences have been observed in components, where, for example, one study may detect a chemical and a subsequent study does not.[53]

There are likely many reasons for these differences. For example, studies will use different methods of sample collection for analysis (that is, in how the air is collected or chemicals extracted from the air using adsorption)[3] and different technologies to quantify concentrations of chemicals (including gas chromatography and high performance liquid chromatography).[3]

The type of device used in surgery that generates smoke will also play a role in reported differences. One study presented a comparative analysis of ultrasonic and electrosurgical smoke generation in laparoscopic surgery.[16] That study collected 200 mL of air on deflation of the pneumoperitoneum at the end of surgery (unknown time interval after the energy device was used). Of the compounds tested in the collected air samples, some of these were at or below

detection thresholds.[16] This procedure contrasts with other studies that, for example, collect liters of gas during the laparoscopic procedure while the energy device is in use to obtain a better sense of chemical concentrations before leakage or diffusion can dilute them.[25]

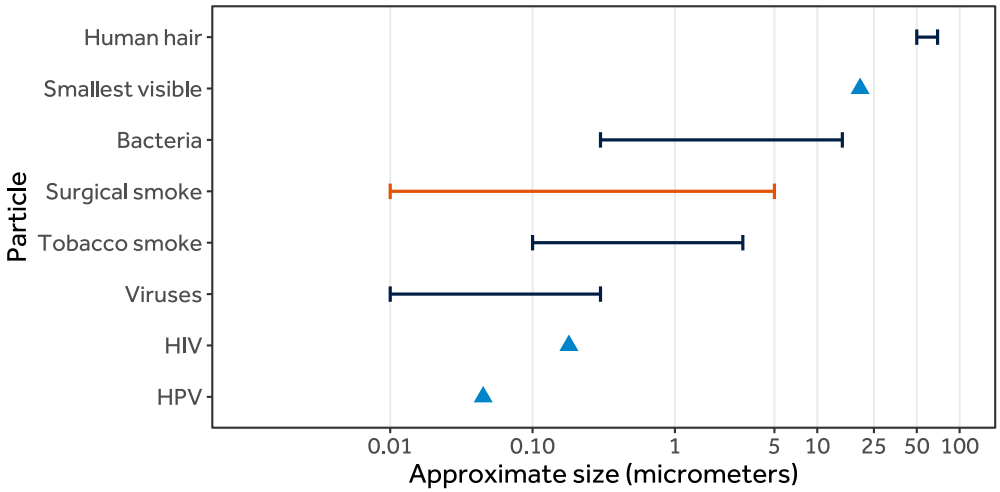
Additionally, differences in collection location (position in a procedure room, type or size of room)[25] will affect detectable concentrations, as will the use of air conditioning versus ventilation.[55,56] These collection and situational parameters are not always consistently reported. The type of tissue being targeted will also affect the chemicals produced.

As a result of these varied factors, conflicting study results may complicate assessment of the available evidence regarding whether surgical smoke and its associated components pose a risk to patients or staff. Individual study results should therefore be considered keeping in mind the details of how the analyses were performed. The effects of long-term, chronic exposure to chemicals or other hazardous compounds, even if below a defined exposure threshold, are unknown and therefore may still represent a risk to human health.[31,55,56]

3.5. Content of surgical smoke

Surgical plume is primarily produced by the generation of heat in tissues, resulting in both the incomplete combustion of cellular materials and the heating of fluids in tissues to boiling.[52] The resulting aerosol is a complex mixture consisting of approximately 95% water vapor and 5% other materials that can include organic chemicals, blood, cellular debris, viable cells from targeted tissue, bacteria, viral particles, and genetic material from viruses (for which infectivity is unknown).[14] Relevant sizes are depicted in Figure 3-3.

Figure 3-3 Relevant size scale of surgical smoke particles

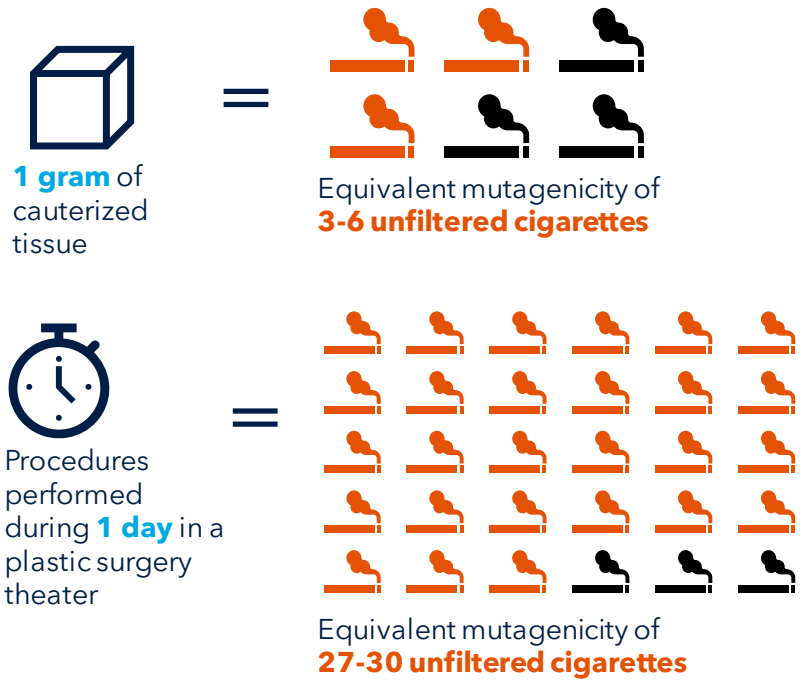


Relative particle sizes[57,58] are shown (approximate sizes and typical ranges) as reported by de Boorder et al, 2007 and updated for minimal surgical smoke particle size as reported by Brüske-Hohlfeld, 2008. Ranges are indicated by bars while triangles denote single values. The highlighted bar (orange) corresponds to surgical smoke. Typical size of human hair taken from United States Environmental Protection Agency information page on air pollution.[b] Note that the horizontal axis (particle size) is displayed using a logarithmic scale. HIV, human immunodeficiency virus; HPV, human papillomavirus.

In recognition of the toxic components that have been identified in surgical smoke (see sections 3.6.1 and 3.6.2), the production of surgical smoke and the exposure to surgical smoke of those who may inhale it have been expressed in terms of tobacco smoke, a known smoke product with hazardous health effects (Figure 3-4).[17,18]

[b] United States Environmental Protection Agency, https://www.epa.gov/pmcourse/what-particle-pollution

Figure 3-4 Estimated comparative mutagenicity of surgical and tobacco smoke



Pictographic representation of data from studies, where the mutagenic content of 1 gram of tissue ablated during laser surgery was found comparable to 3-6 unfiltered cigarettes (Tomita et al., 1981)[18] and extrapolation to tissue ablated during procedures occurring over 1 day in a plastic surgery operating theater of 27-30 cigarettes.[17]

3.6. Potential hazards of surgical smoke

3.6.1. Chemicals and toxins

As described above, when surgical plume is generated, a wide array of chemical compounds is released including volatile organic compounds (VOCs). These compounds include monocyclic chemicals such as benzene and polycyclic aromatic hydrocarbons (PAHs) so named since they consist of multiple stable aromatic carbon rings. Across multiple clinical and benchtop experimental studies, numerous chemicals falling within these categories have been qualitatively identified, with some differences noted according to the class of device that generated the surgical plume (Table 3-1).[3,16,25,59,60]

Table 3-1 Examples of chemicals detected in surgical smoke

Laser	Electrosurgical	Ultrasonic
Acetonitrile Acrolein Ammonia Benzaldehyde Carbon monoxide Benzene Ethylene Ethylbenzene Formaldehyde Styrene Toluene	Acrylonitrile Benzaldehyde Benzonitrile Decene Ethylbenzene Ethynyl benzene Furfural Hexadecanoic acid Indole Methyl pyrazine Pyrrole Toluene	Methylpropene Toluene Benzene Ethylbenzene Heptene Styrene

Examples of chemicals that have been identified in laser and electrosurgical plume are listed from the studies of Searle[59] et al., 2020 and review of Pierce[3] et al., 2011. Note that the list is nonexhaustive; data for ultrasonic devices were as reported in a study that quantitatively targeted a selection of compounds, rather than a qualitative assessment of all compounds generated.[16] The number of chemicals appearing under each type of device should therefore not be taken as a comparative indication of toxicity or variety of chemicals generated by each device.

The chemicals produced during laser, electrosurgical, or ultrasonic dissection or remodeling of tissue vary according to the device used and the target tissue, but some common chemicals have been observed, including toluene and benzene derivatives.[16,25,59,60] Additionally, independently of the specific chemical identified, those agents produced fall into common general categories including irritants of the eyes or respiratory tract, toxic substances, and agents classified as having carcinogenic properties (Table 3-2).[13] Though, the reported effects may not occur at exposure levels relevant to surgical smokee, but in addition, the effect of chronic exposure to lower doses is unknown.

Some studies have compared the concentrations of chemicals detected in surgical smoke with corresponding exposure limits that have been established by regulatory or advisory bodies. In the United States, for example, bodies such as the National Institute for Occupational Safety and Health (NIOSH) or the Department of Labor Occupational Safety and Health Administration (OSHA) publish data regarding occupational exposures for various chemicals according to method of exposure (such as skin contact or inhalation) and method of measurement (such as a volume concentration as a time weighted average over a fixed period).[c] In one example of smoke collected 2 cm from electrosurgical reduction mammoplasty, the components of smoke were measured and compared to occupational exposure limits (OEL).[57,61] The report found several of the compounds (propanenitrile, furfural, and 1-decene) to be at concentrations well above allowable limits (Figure 3-5). Note that the results represent a sampling during a procedure and indicate concentrations of gases

[c] Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH), https://www.cdc.gov/niosh/npg/default.html

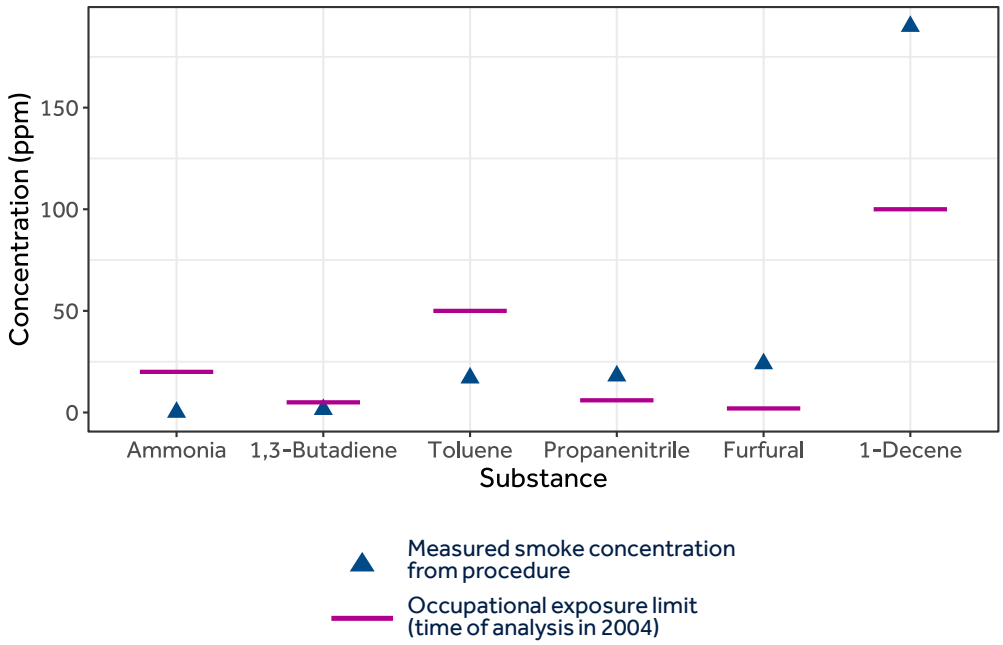
collected at the source of smoke generation, which are likely lower than those that will be inhaled by operating room staff. Depending on the specification, OEL values may be defined according to a mean concentration over an 8 hour period. In contrast, study data regarding surgical smoke exposure are usually over the course of a procedure that represents a shorter time interval. Appropriate exposure level limits for this acute exposure case are thus unknown.[61]

Table 3-2 Effects on human health of example chemicals detected in surgical smoke

Agent	Potential effect	Carcinogenic potential
Acetaldehyde	Eye, skin, respiratory tract irritation	2B
Acetylene	Headache, dizziness, reduced visual acuity, weakness	NR
Acrolein	Eye, skin, upper respiratory tract irritation	3
Acetonitrile	Nasal irritation, damage to liver and kidney in animal models	NR
Acrylonitrile	Eye irritation, nausea, vomiting, headache, weakness	2B
Benzene	Headache, weakness, injury to blood-forming tissues from chronic low-level exposure	1
Cyclohexanone	Potent respiratory irritation, suspected neurotoxin	3
Formaldehyde	Eye, nose, throat, respiratory system irritation, cough, bronchospasms	1
Furfural	Eye, skin, upper respiratory irritation, headache, shortness of breath, vomiting	3
Polycyclic aromatic hydrocarbons [PAH] (including naphthalene)	Eye, respiratory irritation, "effects noted at very low doses"	2B
Styrene	Respiratory irritant	2A
Toluene	Eye, respiratory tract irritation, effects on nervous system observed in animal models	3

A select portion of chemicals reported in the review of Okoshi et al., 2015 listing chemicals detected in surgical smoke and their potential effects on human health.[13] Carcinogenic classifications are according to the most recent version reported by the International Agency for Research on Cancer (IARC) https://monographs.iarc.fr/list-of-classifications, accessed 28 September 2020. Group I, carcinogenic to humans; 2A, probably carcinogenic to humans; 2B possibly carcinogenic to humans; 3 not classifiable as to its carcinogenicity in humans. NR, not reported. While the Agents may be present in surgical smoke, the level may not be sufficient to pose a hazard.

Figure 3-5 Select electrosurgical smoke compounds from reduction mammoplasty



Data[61] from the study of Hollman et al, 2004, reviewed in de Boorder et al.[57] Monopolar electrosurgical reduction mammoplasty was performed, and the gases collected 2 cm from the source for qualitative and quantitative analysis.[57] Triangles represent the concentration measured from smoke collection during the procedure while lines correspond to occupational exposure limits (OEL), time weighted averages over 8 hours. OELs are as reported in the source publication, with the exception of limits for 1-decene, which were obtained from a vendor chemical safety data sheet,[d] and for propionitrile (synonym of propanenitrile), for which reference exposure limits were obtained from the United States Centers for Disease Control and Prevention National Institute for Occupational Safety and Health (NIOSH).[e] Ethylene was another compound reported but not shown, as its measured concentration (0.065 ppm) was many orders of magnitude below the OEL (10,000 ppm). Other reported compounds for which no exposure limits at the time of publishing in 2004 were omitted. ppm, parts per million.

3.6.2. Particulate matter

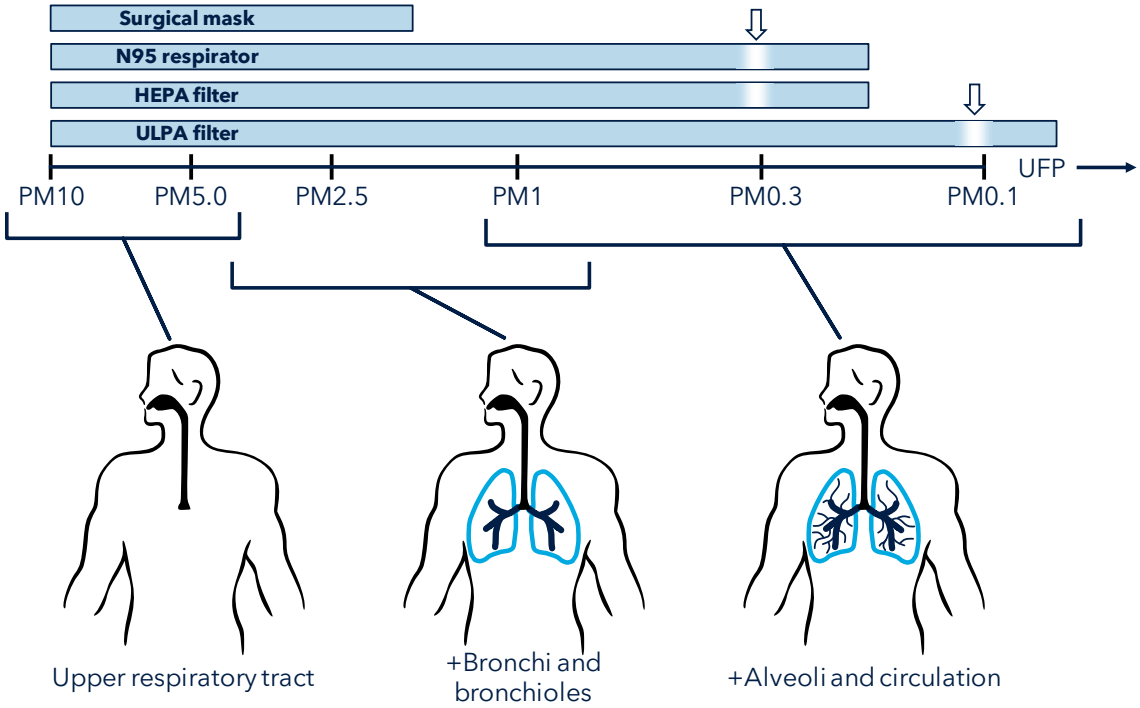
The solid materials that contribute to making plume visible consist of particles of varying size. The size distribution will depend on the means by which they are generated; particles generated by electrosurgical devices, for example, are on average smaller than those generated by ultrasonic devices (see also Figure 3-1).[9] Particle size is typically characterized according to the aerodynamic diameter of the average constituent. Coarse particles are those with a diameter of ~10 micrometers (also known as microns), indicated by particulate matter size 10 (PM10 or PM_{10}). Small particles are considered PM5, fine particles PM2.5, very fine particles PM1.0 and ultrafine particles (UFP) less than PM0.1. The size of the particles generated in part determines their depth of penetration into the human respiratory system, as defense and structural features will

[d] Gelest, Inc., standards per American Industrial Hygiene Association (AIHA) http://www.gelest.com/wp-content/uploads/ENED0720_1-DECENE_GHS-US_English-US.pdf

[e] Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health (NIOSH), pocket guide reference for Propionitrile (synonym for propanenitrile), https://www.cdc.gov/niosh/npg/npgd0530.html

prevent larger particles from progression (Figure 3-6). The larger, PM10 and up, particles are trapped in the upper respiratory tract and can be removed by mucus lining the airways. As particle size decreases, the depth the particles can penetrate the respiratory tract increases, such that they can be deposited in the functional units of the lung (alveoli) where they may be taken up into the bloodstream. The fine particulate content of surgical smoke therefore has the potential to breach the natural defenses of the body, allowing transmission of particles or any material on them into the body's systems and presenting a hazard to health.[12]

Figure 3-6 Particulate size and human airway penetration



Shown is a schematic of particulate matter (PM) sizes and approximate penetration into the human respiratory tract (compiled from various sources[f,12,13,62]). Larger particles (PM5.0 and larger) are trapped in the upper tract, while smaller particles can travel deeper to the bronchi (PM2.5) and the alveoli, ultimately reaching the bloodstream (PM0.1 and smaller). Above the chart are common protective filtration methods.[46] Note the paler bands in the N95, HEPA, and ULPA filter size ranges correspond to particle sizes for which the minimum efficiency (95% or higher) is defined; these filters will also trap particles larger and smaller than this rated size. See section 4.5.4 for further details. HEPA, high efficiency particulate air (filter); UFP, ultrafine particles; ULPA, ultra-low particulate or penetration air (filter).[g,12,13] Note that size scale is logarithmic.

The particulate matter diameter (PM10, PM2.5, etc.) refers only to the average aerodynamic diameter (size) of the constituent particles. These particles can

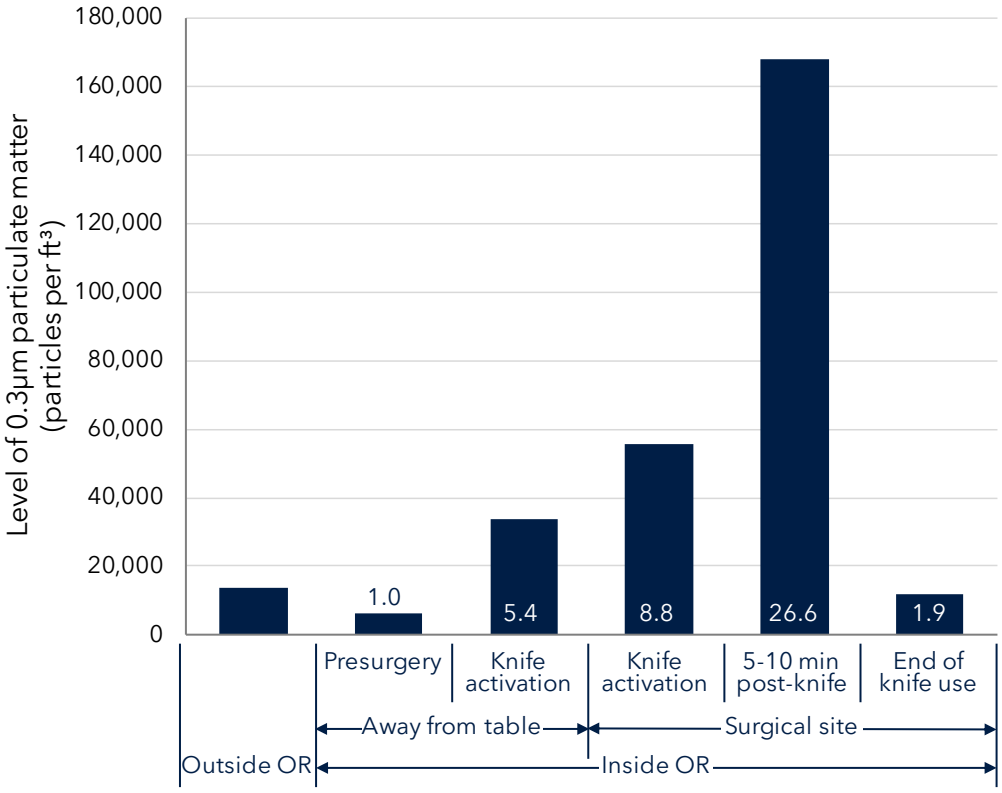
[f] World Health Organization, Air Pollution information page https://www.who.int/airpollution/household/pollutants/combustion/en/ ; accessed: 15 Sep 2020

[g] World Health Organization, Air Pollution information page https://www.who.int/airpollution/household/pollutants/combustion/en/ ; accessed: 15 Sep 2020

therefore themselves be composed of various materials or serve as carriers of other substances (chemical or biological in origin). PM2.5 particles have been of special research interest due to their penetrative ability in the human respiratory system, particularly in the context of environmental science and outdoor air pollution, where they may consist of heavy metals or other inorganic compounds.[12] The same principle applies to the delivery of toxic chemicals in the nongaseous phase or other debris resulting from surgical smoke that can be transported deep into the respiratory tract.

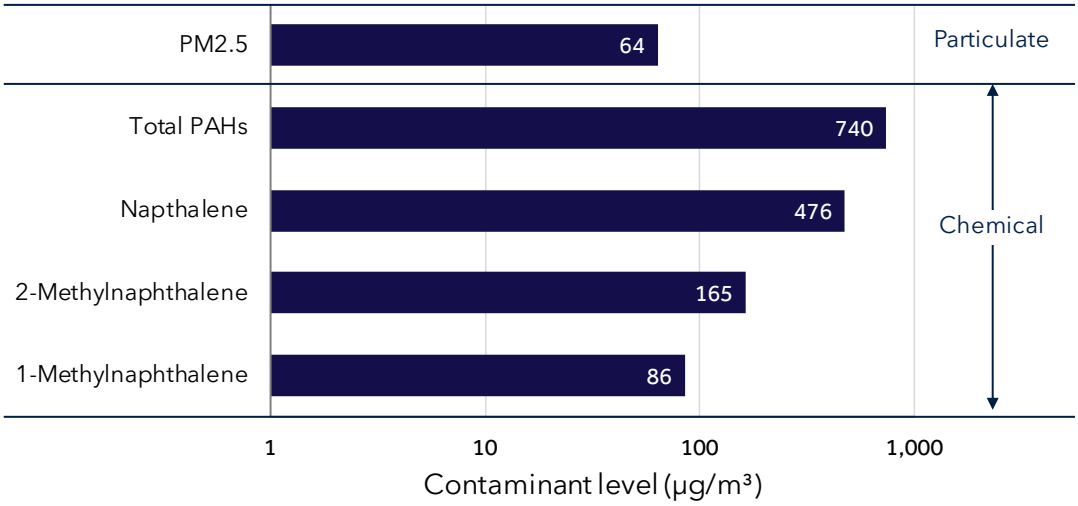
Fine particulate matter, with sizes ranging from 0.3 µm to 5 µm, has been characterized in association with mono- and bipolar electrosurgical device use in gynecological procedures.[6] Measurements during 30 procedures were taken outside and at different locations inside the operating room. The study also considered the factor of time in relation to surgery, with measurements recorded: prior to the start of the procedure to establish a background or baseline value, at electrosurgical knife activation, at a time point after knife use, and at the end of knife use (Figure 3-7). The largest increases were observed for particles in the 0.3 µm range, corresponding to the particulate matter typically generated by electrosurgical devices. On activation of the electrosurgical knife, clear increases in PM0.3 above background presurgical levels were observed both at the surgical site and away from the surgical table, within the operating room.[6] At the surgical table, smoke particulate levels increase by 9- and 27-fold above baseline levels during knife activation and 5-10 minutes after activation respectively. Even after the end of knife use, levels are still approximately twice as high as before surgery. In the same study, a concurrent analysis was also performed of average PM2.5 levels and polycyclic aromatic hydrocarbons (Figure 3-8).[6]

Figure 3-7 Particulate matter inside and outside of operating rooms during electrosurgical device use



Data from the study of 2020 study of Li et al. are shown comparing concentrations of particulate matter inside and outside of the operating room at various points during surgery.[6] Numbers on the bars indicate the relative fold-change increase in particle density compared to presurgical levels. Duration of exposure not reported. OR, operating room.

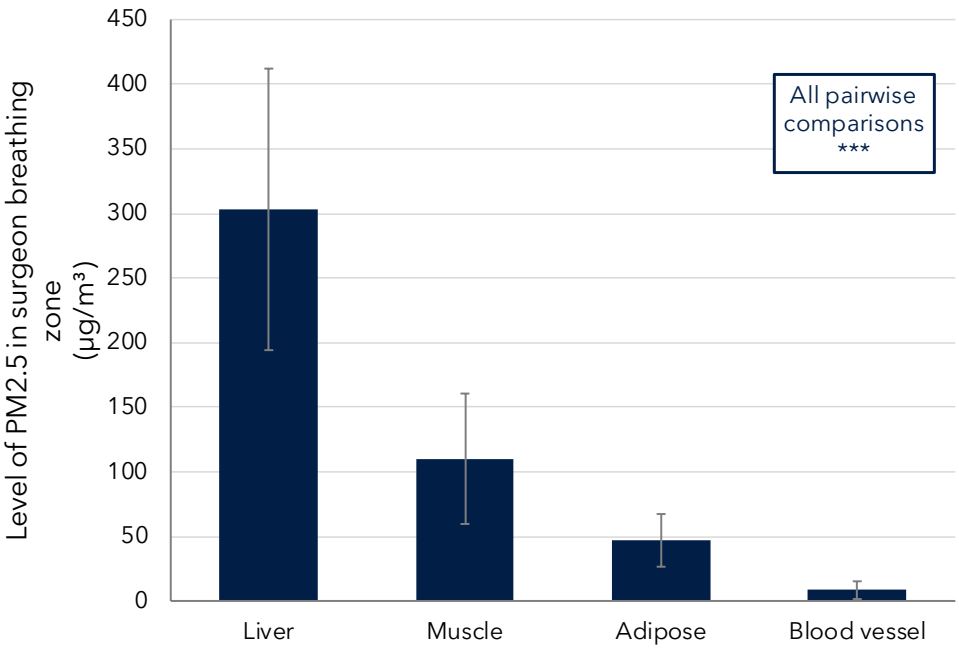
Figure 3-8 Average particulate matter and chemical composition of surgical smoke



In the study of Li et al., 2020, average concentrations of PM2.5 were measured, as well as polycyclic aromatic hydrocarbons (PAHs) at the main knife range, outside the operating table, and outside the operating room.[6] The major constituents of the PAHs detected were various species of naphthalene, identified as an eye and respiratory tract irritant for which effects have been noted at low doses, and also identified as a potential carcinogen (see Table 3-2). Note horizontal scale is logarithmic.

Investigations performed during surgeries have also identified different particle size distributions dependent on the type of tissue involved (Figure 3-9). During 50 hemihepatectomies performed with an electrosurgical knife, a measurement device was placed in the breathing zone of the chief surgeon (5 cm away, around the level of the mouth and nose) to measure the PM2.5 concentrations. Large differences in the level of debris were seen, with the highest concentrations observed for liver tissue and the lowest for blood vessels. Because the measurements were taken during surgeries, the PM2.5 levels recorded are not directly comparable with air quality index ranges established by the United States Environmental Protection Agency (EPA) as reported in the study of Tan et al.[7] EPA measures refer to pollution exposure over a 24 hour period, and the composition of that pollution (outdoor air or other everyday exposure) is likely different from that of surgical smoke. Instead, the proposed EPA air quality ranges reported by Wang et al., 2015 who also investigated surgical smoke may be a better comparison.[8] By this scale, exposure of ~ 300 µg/m³ corresponds to a potentially hazardous concentration of PM2.5, but the comparison must again be made with caution due to the influence of time weighting and duration of exposure, which is unknown in the study of Tan et al.[7,8]

Figure 3-9 Particulate matter generation according to tissue type



Particulate matter (PM2.5) concentrations were recorded in the surgeon's breathing zone (5 cm around and at the same height as mouth and nose of chief surgeon) for different tissue types during hemihepatectomy on 50 patients.[7] Asterisks indicate statistical significance of the differences: *** $p < 0.001$.

3.6.3. Pathogens and infectious material

Although high temperatures are generated when electrosurgical and laser devices are used during surgery, not all biological material aerosolized in plume will be destroyed.[63] Cells and tissue adjacent to the operating zone of the knife may be heated to boiling causing ruptures in tissues still farther removed from the knife, thus allowing biologically intact material to be released that has not been directly subjected to the heat produced by the energy device. Ultrasonic devices, with their generally lower temperatures, also release an aerosol that may increase the chance of transportation of more infectious and viable material than in higher temperature aerosols.[5]

Surgical plume has been evaluated for the presence of evidence of biologically infectious materials. Infectivity has not been clinically demonstrated beyond all doubt, but studies have shown likely evidence of transmission of infectious material (human papillomavirus or HPV) from patients to healthcare providers via surgical plume (Table 3-3). Note, however, that as with chemical components found in surgical plume, results of pathogen analyses vary by report and surgical device. A review that compiled results from laser surgeries listed studies where no HPV DNA or cultured cells were recovered,[2] in contrast to reports from electrosurgery where transmission of HPV from patient to healthcare worker was concluded.[21-23] A 2021 systematic review by Robertson-More and Wu summarizing 21 studies reporting on viral transmission in surgical smoke concluded that the "transmission of viable viral particles in surgical smoke is possible and can produce clinically important infections".[64]

Table 3-3 Pathogens that have been studied in the content of surgical smoke

Agent or pathogen	Evidence
Human papillomavirus	▪HPV DNA detected in surgical smoke, throat swabs from two surgeons matched genotypes of operated patients[20] ▪High-risk HPV DNA detected in surgical smoke during LEEP of high-grade squamous intraepithelial lesions[24] ▪Two cases of HPV positive tonsillar cancer in which the primary risk factor was occupational exposure to laser plume during gynecological procedures[21] ▪Surgeon with laryngeal papillomatosis positive for HPV DNA genotypes consistent with those found in lesions subjected to laser treatment during career[22] ▪Recurrent laryngeal papillomatosis in an operating room nurse recognized as an occupational disease due to correlation with exposure to electrosurgical and laser treatment of gynecological lesions[23]
Hepatitis B virus	▪HBV DNA detected in surgical smoke of 10 of 11 HBV antigen positive patients[19]
Human immunodeficiency virus	▪Detection of proviral HIV DNA in inner lining of tubing to remove laser-generated smoke from infected tissue culture sample[65]
Bacteria	▪Cultures raised from 5 of 13 samples derived from patients treated with laser resurfacing positive for staphylococci bacteria[66]

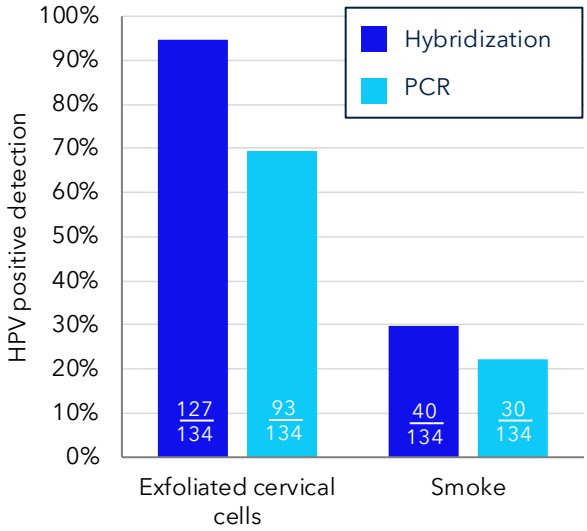
A summary is shown from the reviews of Addley et al.,[14] Mowbray et al.,[67] and Searle et al.[59] listing viruses and bacteria that have been detected, cultured, or from which genetic material has been recovered where infectivity was unknown. HBV, hepatitis B virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; LEEP, loop electrosurgical excision procedures.

The presence of HPV has been assessed using different methods in the context of gynecological surgery for the removal of cervical lesions at high risk of HPV infection.[20] In one study, 134 women underwent operations by 31 surgeons performing loop electrosurgical excision procedures (LEEP).[20] The presence of HPV DNA was tested both in cervical cells and in surgical smoke sampled 2 cm from the operational site using fluorescence hybridization and polymerase chain reaction (PCR) assays (Figure 3-10).[20] By fluorescence hybridization assay, more samples were found to be positive than according to polymerase chain reaction (PCR) assay. Also, more samples of patient cells were positive for HPV (although not all patients were) compared to surgical smoke. Regardless of method, at least 20% of smoke sampled 2 cm from the site of operation appeared to be positive for HPV.[20]

In this study, operating surgeons were also subjected to throat swabs to detect whether they may have been contaminated with HPV.[20] Samples for all surgeons

taken before the operations were negative for HPV, but in postoperative testing, 2 of the 31 surgeons tested positive. These 2 surgeons were among those who performed the 70% (94/134) of procedures during which ordinary face masks as opposed to special N95 surgical masks were worn.[20] Smoke evacuation devices were used during all procedures at varying distances from the surgical site, but the distances for these two surgeons was not reported (see Figure 4-11 for relevance of proximity of smoke evacuation). Genotyping of the surgeon samples revealed their HPV subtypes matched the subtype of the patients on whom the surgeons operated.[20] In both cases, the contamination resolved (no HPV was further detected) within 3 to 6 months of the initial detection.[20]

Figure 3-10 Detection of HPV DNA in patient and surgical smoke samples during gynecological procedures



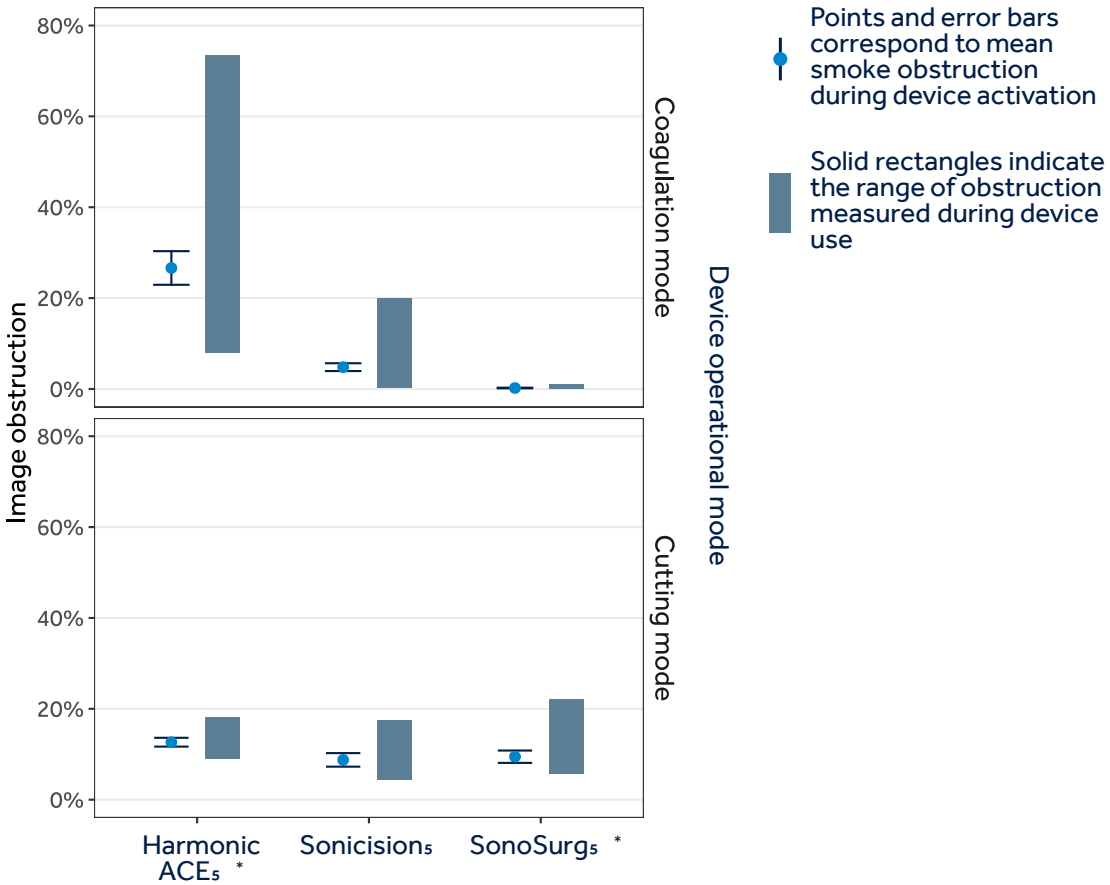
Data are shown from the 2019 study of Zhou et al.[20] to detect human papillomavirus (HPV) DNA in samples collected from patients and surgical smoke. More samples were found to be positive according to fluorescence hybridization compared to PCR assay and not all patient lesions were found to be HPV-positive. HPV, human papillomavirus; PCR, polymerase chain reaction assay.

3.6.4. Visibility reduction

Surgical smoke presents an operative risk not just due to its chemical and pathogen content, but also due to its impact on visualizing the operative area.[29,48] Impairment of the surgeon's field of view has the potential to lengthen surgeries and increase the risk of patients' experiencing negative effects of extended anesthesia.[29] During laparoscopy, smoke can contribute to lens fogging, described as a major impediment to a clear visual field.[68] Decreased smoke production, according to one study that compared ultrasonic to monopolar diathermy, resulted in surgical time savings as lenses did not require repeated cleaning.[44] This result of decreased smoke production according to electrosurgical device is consistent with that of another study that reported a ultrasonic device to produce significantly less smoke than a monopolar according to independent observers using a 5-point scale.[47]

Even among members of a single class of smoke-producing surgical devices, differences may occur in the amount of smoke generated and the accompanying visual impairment. One study performed experiments to quantify how much of the operative field was obstructed by smoke using animal tissue in a simulation of laparoscopic surgery.[45] All devices used ultrasonic energy, but the effects varied in terms of how much the smoke produced may interfere with visualization during an operative procedure (Figure 3-11). The mode of operation of the device, cutting versus coagulation, also played a role with the latter mode generally producing more smoke.[45] It should be noted that the results of this quantification, performed in a simulated setting on animal tissue, may not directly translate to the exact values that would occur with human patients in a real operative setting. Nevertheless, the issue of visual field impairment in relation to surgical smoke has been observed in real patients, indicating the potential for increasing adverse event risks or resource burden in increased duration of operations.[44]

Figure 3-11 Comparison of visual field obstruction by ultrasonic device



The study of Kim et al., 2012 represents an example quantifying the difference in smoke production (according to percentage of the visual field obscured) by three different devices within the same class of smoke-producing surgical energy devices (ultrasonic).[45] Experiments were performed using bovine liver in a simulation of laparoscopic surgery with the devices in coagulation mode (top) or cutting mode (bottom). Points indicate means and error bars are standard errors of the mean as reported in the source publication. Experimental results on animal tissue, or in controlled benchtop test settings will not necessarily directly translate to humans in surgical context.

4. Staff and patients

4.1. Summary and key messages

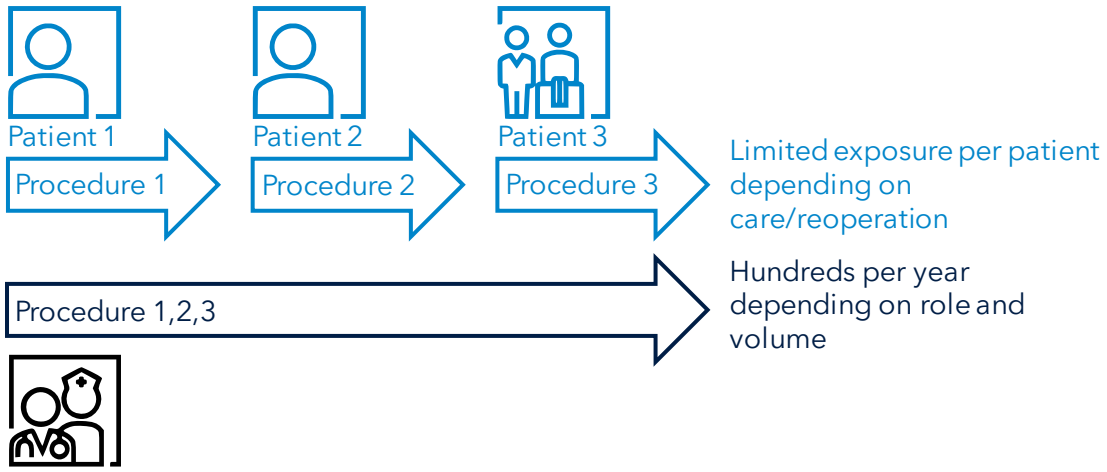
- **Both patients and providers are at risk from surgical smoke:** Despite differing degrees of exposure for patients (acute) versus healthcare staff (chronic), both groups may be adversely affected by surgical smoke given the presence of chemicals such as benzene that are a carcinogen and can reach levels that could pose a risk to surgeons[25] and have been shown to be absorbed by patients.[26]
- **Healthcare staff endure chronic exposure to surgical smoke:** Perioperative staff across disciplines can experience multiple sessions of surgical smoke exposure per week totaling hours of exposure spanning multi-year careers.[28]
- **Viral transmission via surgical plume has been observed in clinical practice:** Case reports have been published of gynecological surgeons who have developed throat carcinoma positive for human papillomavirus (HPV), whose primary risk factor was occupational exposure to surgical smoke during loop electrosurgical excision procedures (LEEP).[21]
- **Matching viral genotypes between surgeon throat and patient lesions:** Studies have confirmed genotype matches between HPV found in gynecological patient cells and lesions swabbed from throats of surgeons who subsequently tested positive for HPV.[20]
- **Room ventilation is insufficient to manage smoke:** Smooth, layered air flow in an operating room will assist in some diffusion of contaminants and maintenance of sterility but will not adequately reduce levels of surgical smoke produced.[14,17,25,29]
- **Local exhaust ventilation removes contaminants of surgical smoke:** Local exhaust ventilation technologies have been shown to remove 44-60% of particulate matter[30] and 60% of total volatile organic compounds.[31]
- **Proximity to source of smoke can remove more pathogenic material:** A study of human papillomavirus detection from air samples during gynecological procedures found detection of viral DNA to decrease (54% of samples to 9% of samples) as the local exhaust device was used closer to the electrosurgical operative site.[20]

4.2. Chronic versus acute exposure

As described previously (chapter 3), the smoke or plume generated during surgical procedures contains toxic substances (chemical, particulate, and pathogenic) that potentially pose a risk to individuals who consume them. Staff may inspire these compounds and recommendations have been made

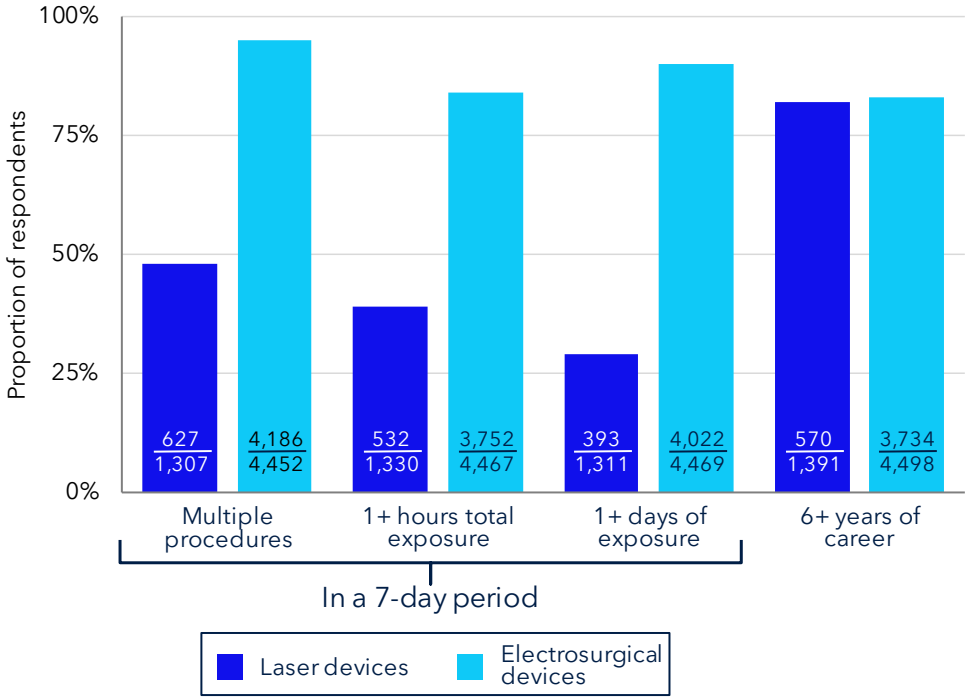
regarding measures that can be adopted to reduce staff exposure.[14,59]
Depending on the procedure, patients, who may be connected to closed ventilation systems for anesthesia, are less likely to inhale smoke products, but instead may absorb them directly into the bloodstream through the peritoneal wall during laparoscopic procedures.[26] Patient exposure is similar to that of providers, though, in procedures where only local anesthesia is used, patients are not ventilated, and patients thus breathe the same air as the healthcare workers.[69] The nature of the smoke generation results in potentially differing periods of exposure, where for an individual patient, exposure is acute during an individual procedure, whereas healthcare staff, performing multiple procedures have a longer duration of exposure to byproducts generated during procedures (Figure 4-1).[27]
These multiple exposures are not uncommon, as suggested by a survey of 4,533 healthcare professionals who reported being exposed to surgical smoke.[28] Survey responses differed between those involved in laser procedures that generated smoke versus those in electrosurgical device procedures, but in both cases, large proportions, over a single week, were involved in more than one procedure where they were within 5 feet of surgical smoke production (48% laser and 95% electrosurgical device respondents), had exposures over multiple days (29% laser, 90% electrosurgical device) and for a total duration of at least 1 hour (39% laser, 84% electrosurgical device).[28] These exposures also extend over years for each practitioner, as 82% of those exposed to smoke from laser and 83% of those exposed to smoke from electrosurgical devices reported 6 or more years of their careers working in areas where surgical smoke is generated (Figure 4-2).[28]
While patient exposure is clearly episodic, it is unknown to what degree accumulation of exposure may or may not occur in healthcare staff. Authors have remarked, however, that even when low levels of toxic compounds are reported in studies, in the long term for practitioners, there is the potential for cumulative or additive effects in interactions among the various components of surgical smoke that could present a hazard to health that has not yet been demonstrated by a sufficiently large and controlled study.[27,31,55,56]

Figure 4-1 Schematic of patient versus healthcare staff exposure to aerosol surgical procedure byproducts



A depiction of exposure to smoke byproducts generated during surgical or other procedures. Patient exposure is likely limited to one, or few procedures depending on the nature of the treatment or need for reoperation. Healthcare staff face repeated procedures with associated exposure. Note, data are a depiction only and not intended to infer a strictly cumulative or additive effect for healthcare staff, as such accumulation of smoke byproducts is unknown.

Figure 4-2 Healthcare professional survey responses regarding exposure to surgical smoke



Data are shown from the study of Steege et al., 2016 of responses from 4,533 healthcare professionals, including nurses, technicians, physicians and surgical assistants.[28]

4.3. Personnel risks

Personnel involved in the care of patients can participate in multiple procedures per day. Surgeons, nurses, and various support staff who may be present for an operation or other procedure have the potential to undergo multiple independent exposures to surgical smoke or plume generated during procedures that produce it. Still, despite the demonstration that surgical plume contains toxic chemical, particulate, and biological material that can prove hazardous to human health, there remains debate whether long-term exposure to these toxins, some at low doses, poses a danger. Authors have noted that, in the comparative example of illustration of the dangerous effects of tobacco smoke, many individuals over a number of years were required to conclusively demonstrate the link between smoking and negative health effects.[17] In contrast, there is a relatively smaller proportion of operating or procedure room staff. These individuals may also have confounding variables such as smoking status or exposure to local outdoor air pollution. Further, there is a time lag between exposure and development of disease. These factors together make demonstrating a statistically significant link between surgical smoke exposure and deleterious health effects more challenging.[17] Some of these considerations are summarized in Table 4-1.

Table 4-1 Challenges to studying link between surgical smoke and health effects

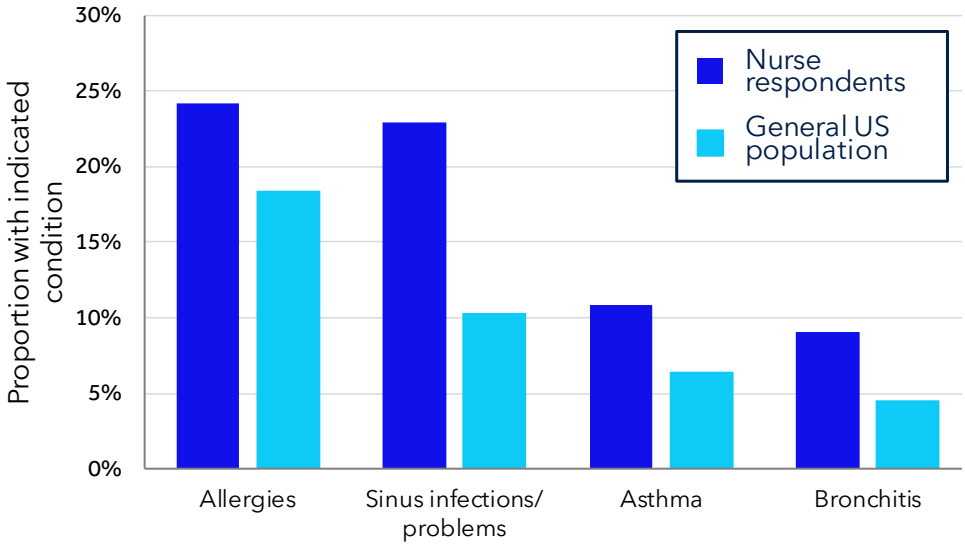
Consideration	Detail
Time	Some acute effects may only occur at high exposure Long time lag between exposure and development of some health effects
Dose	Components may be at low dose Findings of genetic material of infectious agents, but no demonstration of clinical infectivity
Population	Study population sizes represent relatively small numbers of at-risk staff
Characteristics	Variable reporting of clinical detail
Demographics	Potentially confounding parameters such as smoking status or exposure to local air pollution

The concepts listed were collected from Hill et al.[17]

As a partial illustration of issues relevant to healthcare workers, a survey of perioperative nursing staff was conducted to assess prevalence of respiratory issues.[15] The results comprised 777 participants who completed the survey and they reported notably higher prevalence of respiratory issues compared to the general population (Figure 4-3). Due to study design, causation cannot be inferred. With differences in operating room practices, procedures performed, and unknown contributions of factors outside of the workplace, the higher prevalence may result from other factors not controlled by the study design.[15] Whether the higher prevalence of respiratory issues has resulted from occupational exposures to surgical smoke or plume, however, the data indicate that perioperative nurses are associated with higher levels of conditions

affecting the respiratory system. This observation may make this population more sensitive to the components of surgical smoke or plume.[15]

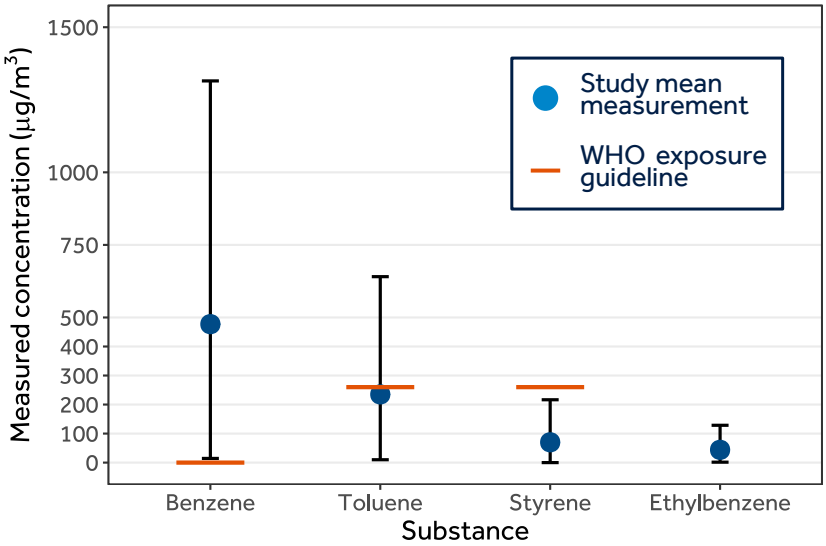
Figure 4-3 Prevalence of conditions affecting respiratory system: perioperative nurses and the general US population



Results from Ball, 2010 are shown for a survey of 777 perioperative nurses in the United States.[15]

In the domain of laparoscopic surgery, the pneumoperitoneum created to allow movement in the operating field can serve as a reservoir where products of surgical plume can accumulate.[25] During conventional and robotic operations, samples of surgical smoke were collected from the patients' abdomens, from a point behind the surgeon (to reduce interference during the procedure) and at an exhaust vent. Low concentrations of potentially hazardous chemicals were detected near the surgeon and at the vent, as expected due to dilution effects, but the measurements from within the patient abdomen indicated high levels, in some cases greater than or comparable to World Health Organization (WHO) continuous exposure limits (Figure 4-4).[25] Benzene was of particular note, as WHO guidelines indicate no safe level of exposure. The authors further note that although concentrations were diluted farther away from the operative site, associated risks remain.[25] There is the potential for leakage from trocars and the collected gas must be managed to prevent simple release into the operating room air on deflation of the pneumoperitoneum at the end of the surgery. It is also noteworthy that in the pneumoperitoneum, patient tissues are also exposed to these elevated concentrations of chemicals. Although chemical absorption by the patient was not assessed in this study, such absorption has been observed in other studies where smoke-associated chemicals in urine have been measured in patients before and after surgery (see Figure 4-5).

Figure 4-4 Concentrations of compounds in laparoscopic surgical patients

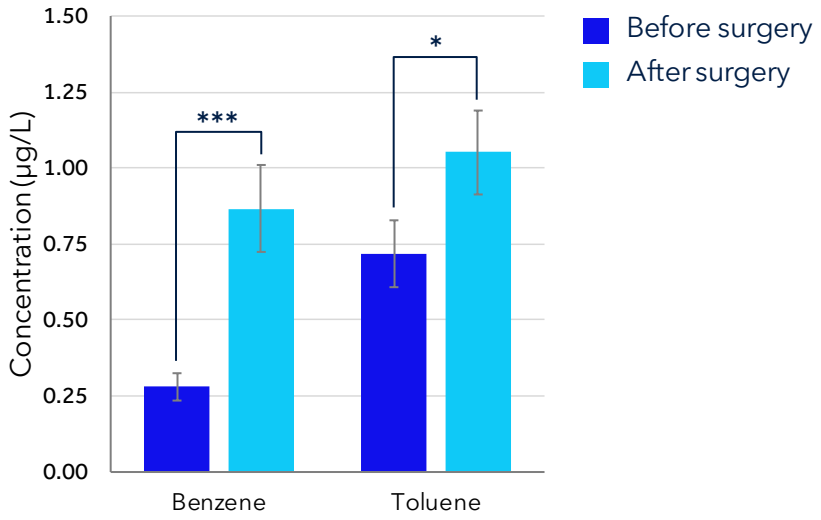


Data are shown from Choi et al, 2017 where multiple samples were collected from patient abdomens during conventional and robotic surgery for analysis of constituent gases.[25] The points indicate the mean concentration measured across all surgeries, while error bars indicate the range of levels detected across individual surgeries. Orange lines indicate World Health Organization continuous exposure limits (as reported in the study); the bar at 0 for benzene indicates no acceptable level and the missing bar for ethylbenzene indicates no data. WHO, World Health Organization.

4.4. Patient risks

Although patient exposure to surgical smoke is acute and limited to the duration of the procedure, there remains potential risk associated with the generation of surgical smoke. Analyses have been performed to assess patient levels of chemicals that have been detected as components of surgery before and after exposure.[26] In an example of laparoscopic cholecystectomy, measurements of chemicals that have been identified in smoke from electrosurgical device use were taken before and after surgery to detect any increase above baseline environmental exposure associated with the surgery. Numerous chemical compounds were identified in the smoke generated during the laparoscopic procedure, including aldehydes (formaldehyde, acetaldehyde), aromatic hydrocarbons (including benzene, ethylbenzene, and toluene), and dioxins.[26] Analysis of a subset of these chemicals identified significant increases in benzene and toluene in patient urine, indicating that the chemicals were absorbed and processed by the patients' bodies (Figure 4-5).[26] The measurements indicate increases of 300% and 46% above baseline for benzene and toluene respectively.

Figure 4-5 Detection of benzene and toluene in patient urine samples before and after laparoscopic electrosurgical procedures



Data from the study of Dobrogowski et al. were recorded from 82 patients who underwent laparoscopic cholecystectomy.[26] A compositional analysis first analyzed what chemicals were detectable in the smoke produced and subsequently a subset of these chemicals were analyzed in patient urine samples before and after surgery. Of the four chemicals that were reported in the urine analysis, only the two which demonstrated significant differences between before and after levels are shown. The heights of the bars indicate means and error bars correspond to standard errors of the mean. Asterisks indicate statistical significance of the differences: *** $p<0.001$, * $p<0.05$.

As well as the direct effect of exposure to surgical smoke, there is also an indirect increase in risk to patients due to the production of smoke and its effect on the procedure. The production of smoke can make the operative field appear "hazy" and has been reported as an impediment to finding the source of bleeding during laparoscopic cholecystectomy,[44] and for surgical procedures in general with potentially deadly consequences.[48] The smoke produced also necessitates cleaning of lenses used to visualize the field in laparoscopic surgery,[44] and together, these effects of smoke may increase patient risk by lengthening surgical procedures and increasing the risk of negative effects of extended anesthesia on patients.[29]

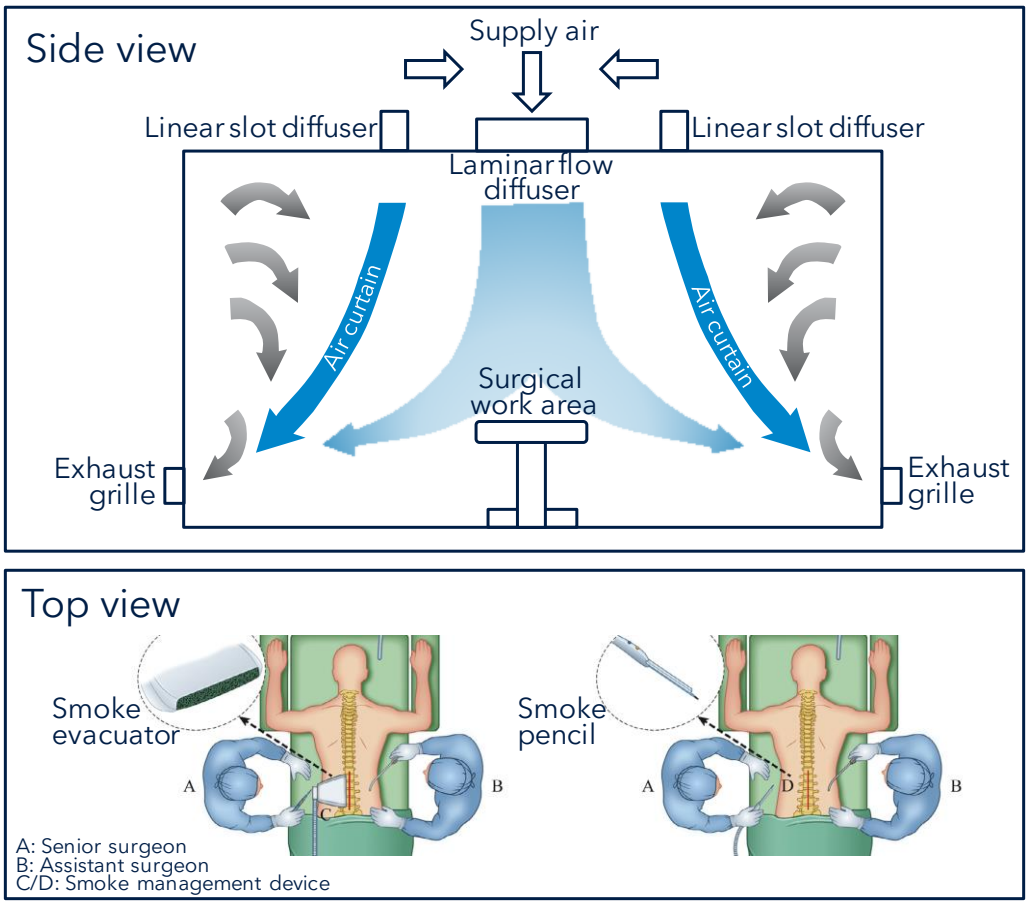
4.5. Management of smoke to mitigate risks

One consideration for smoke management is to reduce the amount of smoke initially produced. In that respect, different surgical technologies have been investigated comparing the amount of smoke they generate.[44,45,47] Complete elimination of smoke producing devices is not, however, feasible as these have increased in usage due to their effectiveness in procedures. For internal dissection and wound closure, electrosurgical devices have been associated with a reduction in operative time[70-73] and blood loss[70-74] compared to suture. Another example is seen in the improved wound healing results that have been observed with lasers compared to nonlaser methods.[75]

Given that smoke production is an expected component of many operative procedures, the next consideration in minimizing risk to those exposed is the

dissipation or removal of smoke by capture and disposal. Levels of air flow control span general room ventilation to more localized technologies to manage plume production (Figure 4-6).
Personal protective equipment, in the form of surgical masks versus respirators (N95) constitute another method of management of staff exposure to surgical plume, but the details of these are not examined in the present document.

Figure 4-6 Ventilation and surgical smoke management in the operating room



Schematics are shown of an example operating room with downward laminar flow in cross-section (top).[76] The air currents generated maintain a clean supply of air in the surgical working space while directing contaminated air to exhaust vents. In an example of spine surgery,[30] local smoke management is performed using a smoke evacuator with a broader intake profile for comparison with a smoke pencil, which is more localized to the point of smoke generation. Image shown for the top view of spinal surgery[30] is from Liu et al., 2020.

4.5.1. General room ventilation

Room ventilation is a form of background air management that aids in maintain procedure room sterility and diluting potential contaminants.[76] Ventilation function is often expressed in terms of the number of total room air changes per hour (ACH), ranging from a minimum of 5 to over 20 times per hour.[25,31,76] Ventilation via downward laminar flow aids in maintaining operating room sterility but room ventilation alone is insufficient to deal with smoke produced during operations[13,14,29] and may still leave staff such as surgeons at risk by

insufficiently diluting select surgical smoke components.[25] Procedures that generate smoke outside of the operating room (such as dentistry or dermatology) may occur in locations without dedicated laminar flow and therefore lack any background air-flow management to assist in smoke removal.

4.5.2. Smoke evacuation devices

Smoke evacuation devices serve as local exhaust ventilation (LEV) technologies and work over an area that is localized to the site of smoke generation, in contrast to overall room ventilation.[30,31] Evacuation devices may be several inches from the actual site of smoke production as they remain largely fixed and cover a local area of the surgical field.[30] As they are positioned independently of the smoke-generating device, they can be used with a variety of laser or electrosurgical tools.

4.5.3. Smoke evacuation pencils

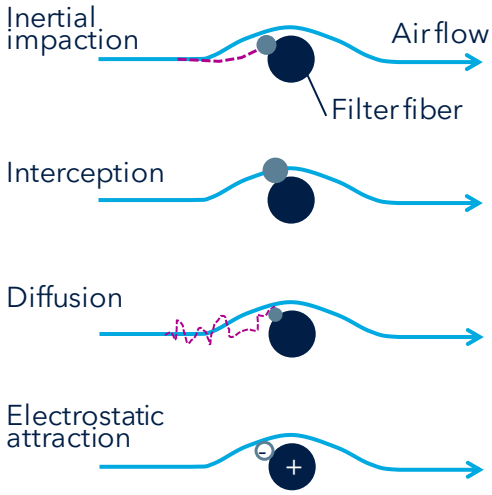
Smoke evacuation pencils are a form of LEV that can be positioned close to the source of smoke generation. A difference between evacuators and pencils, is that smoke evacuation pencils may be attached within 1 or 2 inches (2-5cm) of the functional tip of an electrosurgical device and integrated into a single unit.[30] With these devices, depending on specific features, plume is aspirated directly into a receptacle equipped with filters and a collection chamber contemporaneously with its generation thereby limiting opportunity to spread beyond the tip of the device. A consequence of this highly localized collection is that it may not be compatible for use with all types of electrosurgical or laser devices, for example bipolar sealing devices that require maneuvering of jaws around and clamping onto tissues before activation.

4.5.4. Filtration systems

Systems designed to collect surgical smoke work not just to remove plume from the air, but they must also capture and retain its constituents to prevent their further diffusion or other contamination of the working environment. Different types of filters are designed to capture different types of substances according to regulatory standards.

Filters are commonly composed of dense meshes of fibers through which air is passed. Filtration is achieved by different mechanisms that remove particles from the air; the size of particle will in part determine the possible mechanism by which it can be trapped (Figure 4-7). By these mechanisms, particles falling between 0.1 and 0.5 μm are less effectively trapped, thereby indicating that filter performance is defined according to the minimum, or worst-performing particle capture. Activated carbon (or activated charcoal) filters are not fiber-based and function via different mechanisms to adsorb organic compounds for removal from air.

Figure 4-7 Mechanisms of particle capture



Four mechanisms by which particles are captured by fibrous filters. Each mechanism works with different efficiency dependent on particle size. Schematics reproduced from the United States Centers for Disease Control and Prevention.[h]

Two types of fiber-based filters useful for removing contaminants from the air are the high-efficiency particulate air (HEPA) filter and the ultra-low particulate (or penetration) air (ULPA) filter. HEPA filters remove most small particles of around 0.3 µm aerodynamic diameter, although the exact definition differs between United States and European standards (Table 4-2). According to the United States definition, set by the Department of Energy,[i] a HEPA filter should capture at least 99.97% of particles 0.3 µm and above, but it should be noted that this particle size is not necessarily the smallest particle size that can be captured by the filter. A typical HEPA performance plot, showing efficiency versus particle size is shown in Figure 4-8. Note that the HEPA-standard definition of 0.3 µm is slightly larger than the most penetrating particle size (MPPS). In contrast, the European standard EN1822[j] is defined according to efficiency of capture of the MPPS. By either definition, however, the filter will remove particles both above and below the rated value, as the defined particle size corresponds to the size most poorly captured by the filter.

[h] https://blogs.cdc.gov/niosh-science-blog/2009/10/14/n95/
[i] https://www.standards.doe.gov/
[j] https://weerhuisje.eu/pdf/EN1822-1-2009_Highefficiencyairfilters_EPA_HEPA_ULPA_Part1_Classification_performance.pdf

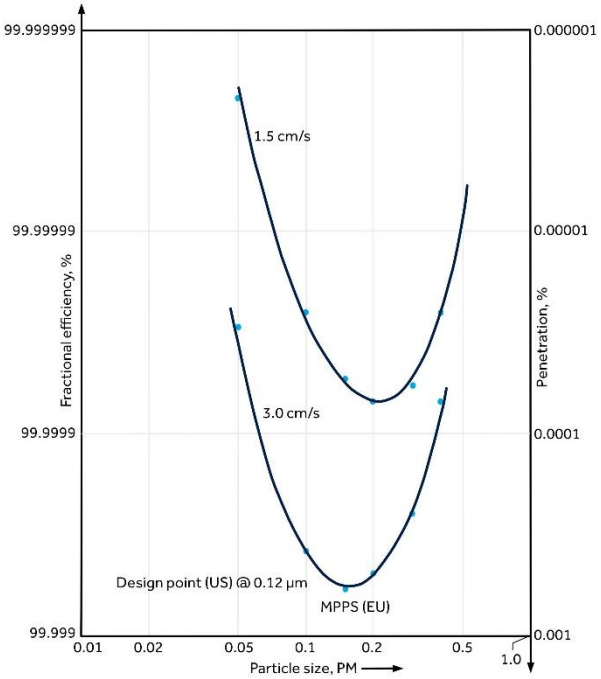
Table 4-2 United States and European Union definitions of filter standards

Region	Filter (class)	Definition
US	HEPA	99.97% removal of particles 0.3 μm diameter
	ULPA	99.9995% removal of particles 0.12 μm diameter
Europe	HEPA (H13)	≥ 99.95% MPPS
	HEPA (H14)	≥ 99.995% MPPS
	ULPA (U15)	≥ 99.999 5% MPPS
	ULPA (U16)	≥ 99.999 95% MPPS
	ULPA (U17)	≥ 99.999 995% MPPS

HEPA, high-efficiency particulate air (filter); MPPS, most penetrating particle size; ULPA, ultra-low particulate air (filter).

ULPA filters are comprised of similar fibrous materials as HEPA filters but are designed to remove still more material from the air. At minimum, these filters remove 99.9995% of material (particles of 0.12 μm diameter by the United States standard, or of the MPPS by European standard).
Whatever design of filter is used, design and performance must also include consideration of air flow. The filters will be attached to a vacuum system, and air must be able to flow through these filters to function. As depicted by capture schemes (Figure 4-7, Figure 4-8) captured particles adhere to the fibers of the filter and over time, these will impede air flow and reach capacity for capturing new material as the surface of the fibers becomes occupied with particles. HEPA and ULPA filters must therefore be regularly changed according to manufacturer specifications to maintain effectiveness.

Figure 4-8 ULPA performance example versus particle size



A typical performance graph of a ULPA filter is shown for efficiency of capture versus particle size. According to the United States standard, the ULPA design point required 99.97% capture efficiency of particles 0.3 µm and larger, although smaller particles will also be captured with high efficiency. In contrast, the European standard is defined according to efficiency of capture of the most penetrating particle (MPPS) and particles larger and smaller will be captured will still higher efficiency. Figure reproduced from DIN EN 1822-1:2019 specification example, edited to highlight MPPS and design point.[k]

4.6. Impact of smoke management

Although insufficient on its own to fully address the potential hazards of surgical smoke, operating setting properties (notably ventilation) play an important role. Overall airflow management can vary from air conditioning systems to ventilation systems capable of multiple complete air exchanges per hour.[25,31,55,56,76]

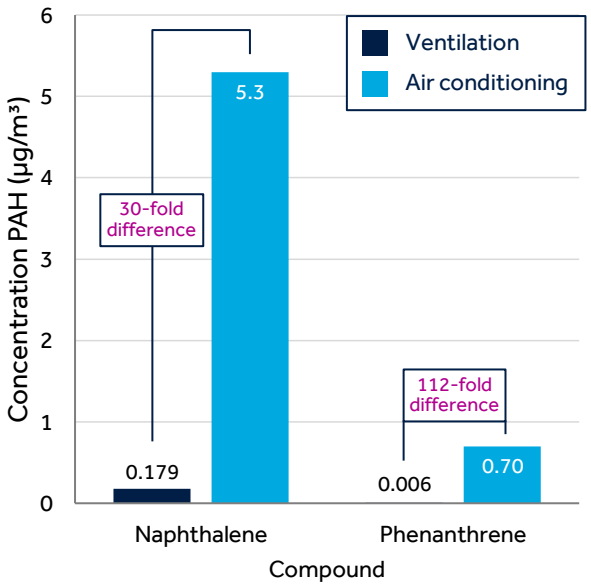
Airflow can be one of the factors as mentioned earlier (section 3.4), that may influence levels of chemicals measured in an operative setting. An example can be seen in comparison of the 2012 study of Naslund et al.[56] and the 2017 study of Claudio et al.[55] Both sought to characterize 16 polycyclic aromatic hydrocarbons (PAH) in surgical smoke produced during abdominal surgical procedures. The study of Naslund et al. included only peritonectomy and collected surgical smoke generated during 40 surgeries using both a personal collector and a smoke evacuation device adapted to include a collection cartridge located 5 cm from the site of the device use.[56] In contrast, the study of Claudio et al. presented a mixture of abdominal surgeries (including cholecystectomy and appendectomy), 27% of which were open, and surgical smoke was collected using a stationary device located 7 cm from the surgical site.[55] A further key difference between the two reports is that ventilation was

[k] https://www.din.de/en/getting-involved/standards-committees/nam/publications/wdc-beuth:din21:297837528?destinationLanguage=&sourceLanguage=

used in the Naslund et al., study of 20 air changes per hour, while the Claudio et al. study consisted of two air conditioning units and no exhaust fan.[55,56] The Naslund et al. study also included use of smoke evacuation technology during a latter phase of the surgery.

A stark difference is noted in the levels of the two most abundant (according to the Naslund et al. study) PAHs detected in surgical smoke: naphthalene and phenanthrene (Figure 4-9).[56] These were also the only two compounds reported in the Claudio et al. study, although the protocol indicated detection of 16 PAHs.[55] The study in which room ventilation with exhaust was employed reported levels of naphthalene 30-fold lower and of phenanthrene 112-fold lower than where only air conditioning without exhaust was used. Due to differences in surgical parameters, the large discrepancy cannot be solely attributed to the difference in ventilation strategy; authors of the more recent study specifically note, however, that the lack of ventilation with exhaust contributes to poor air quality and puts intraoperative staff at risk.[55] The distinction may be relevant for procedures, such as in dermatology, that can occur outside of hospital operating theaters.

Figure 4-9 Detection of polycyclic aromatic hydrocarbons during abdominal surgery



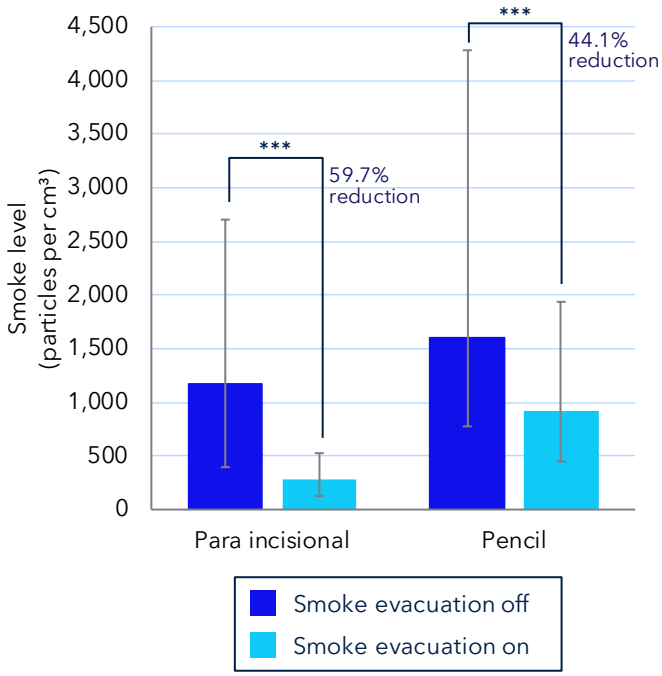
Two studies characterized 16 polycyclic aromatic hydrocarbons in abdominal surgeries: that of Naslund et al., 2012 of open peritonectomies[56] and Claudio et al, 2017 that consisted of a mixture of open and laparoscopic abdominal procedures.[55] A key difference in operative setting noted by the authors of the more recent study is the lack of a ventilation system with exhaust, resulting in poorer environmental air quality, posing "risks to the health of the intraoperative team."[55]

Local evacuation systems can be employed during surgery (or other operative procedures) to manage the risks posed by exposure of staff or patients to smoke or plume. As noted above (section 4.5), different strategies are available to deal with surgical smoke. Since surgical plume is comprised of chemical, particulate and biological substances, example studies have investigated the

removal of these components according to type of management employed and how it was used.

The removal of small and ultrafine particulate matter is one aspect of surgical plume management that has been investigated according to the type of LEV used during surgical procedure.[30] During spinal surgery, both a smoke evacuation system (para incisional, with intake approximately 9 inches/23 cm wide positioned 5 cm from the incision) and a smoke evacuation pencil (intake mounted directly above the electrosurgical tip) were compared for particulate smoke levels when the evacuators were off and on (Figure 4-10).[30] Both devices achieved significant reductions in the levels of smoke detected around the operative site when activated. In this study, greater variability was observed in the surgeries for which the smoke evacuation pencil was used, potentially contributing to a lesser decrease in smoke levels on activation of the device. The authors state that the study aim was not to identify a "better" smoke removal device, as surgical parameters (open versus laparoscopic, interference with reaching the surgical field, or electrosurgical device) will influence which is most appropriate for different surgeries.[30]

Figure 4-10 Local exhaust ventilation with para incisional evacuation and a smoke evacuation pencil

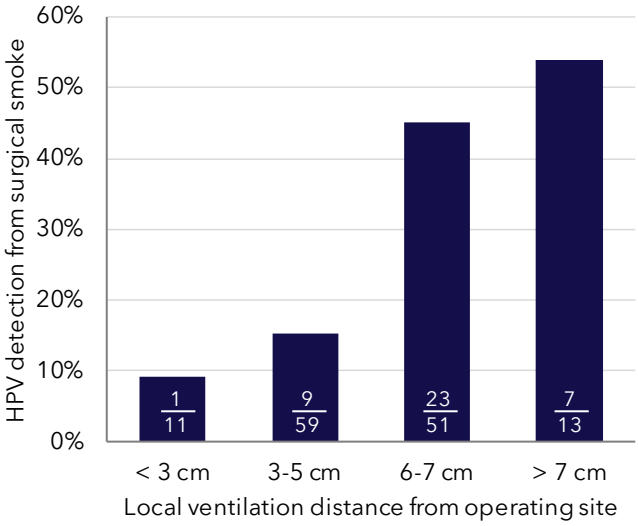


Data are shown from Liu et al., 2020 for spinal surgeries conducted with two forms of local smoke management (para incisional and a smoke pencil).[30] Levels of smoke were compared between the evacuators in the on and off modes. Asterisks indicate statistical significance of the differences: *** $p < 0.001$.

A further illustration of the impact of proximity of the smoke evacuation system to the site of smoke generation is seen in a study of detection of HPV DNA in surgical smoke samples taken during loop electrosurgical excision procedures (LEEP) in patients with lesions at high risk of HPV infection.[20] During operations

by 31 surgeons on 134 patients, the distance of the smoke evacuation system from the site of smoke generation varied and was recorded while the smoke near the site was sampled at a constant distance of 2 cm. Results showed that less HPV DNA was detected in the air the closer the smoke evacuation system was brought to the site of smoke generation (Figure 4-11).[20]

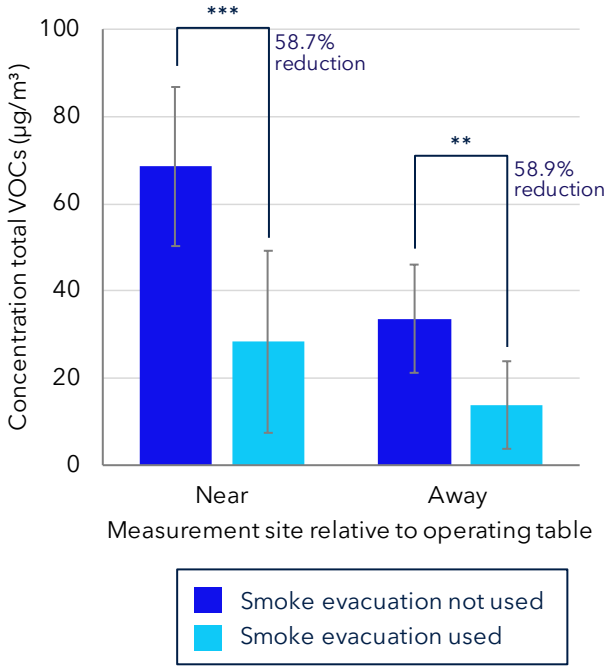
Figure 4-11 Position of local smoke evacuation system and HPV detection



Data are shown from Zhou et al., 2019 reporting the percentage of samples in which human papillomavirus (HPV) DNA was detected.[20] The position of a smoke evacuation system was recorded during treatment of 134 patients with cervical lesions at high risk for HPV infection. Samples for testing were taken 2 cm from the surgical site by aseptic swab and the proportion of those positive for HPV DNA was noted. Values on the bars indicate the number of positive samples over the number of procedures in which the evacuation system was located according to the indicated distance.

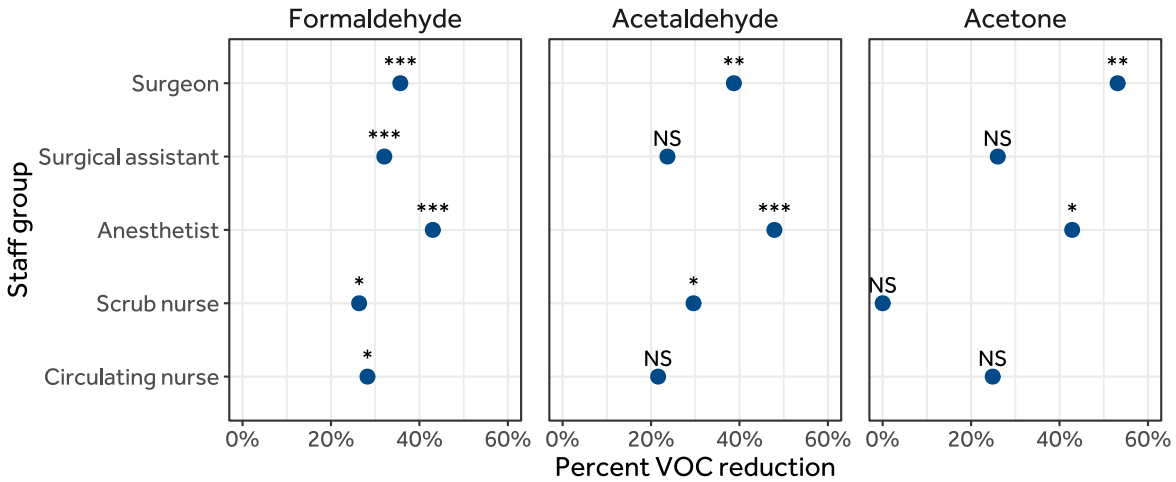
To more clearly demonstrate the effect of local smoke evacuation, one study randomized use and non-use of a smoke evacuation device and measured concentrations of volatile organic compounds (VOCs).[31] The procedures performed were breast-conserving surgeries and mastectomies and measurements were taken from fixed points within the operating room, and from recording devices worn by medical personnel.
When measuring total VOCs, use of the device was associated with significant reductions in levels both at and away from the surgical table (Figure 4-12).[31] Measurements recorded from detectors worn by staff to assess personal exposure levels were all below local exposure limits (Japan Ministry of Health, Labor, and Welfare) whether the smoke evacuation system was active or not. Nevertheless, significant reductions were observed for formaldehyde, acetaldehyde, and acetone for surgeons and anesthetists, while reductions were both significant and nonsignificant for surgical assistants, scrub nurses, and circulating nurses.[31] With the exception of scrub nurse exposure to acetone, where no change was observed, other percentage reductions (Figure 4-13) across the three compounds ranged from 22% to 53% (geometric mean of 33% reduction).

Figure 4-12 Effect of smoke evacuator use on volatile organic compound concentrations



Data are shown from the study of Tokuda et al., 2020 in which concentrations of total volatile organic compounds were measured according to the randomized use or non-use of a smoke evacuator.[31] Measurements were taken at the surgical table and removed from the table. VOCs, volatile organic compounds. Asterisks indicate the statistical significance of the differences: *** p < 0.001; ** p < 0.01.

Figure 4-13 Reduction of volatile organic compounds measured by detectors on staff



Data are shown from the study of Tokuda et al., 2020 in which concentrations of total volatile organic compounds were measured according detectors worn by surgical staff members during surgeries for breast cancer.[31] The indicated percent reduction in the amount (µg/m³) of three volatile organic compounds was calculated from reported values as (level no evacuation – level with evacuation)/(level no evacuation). Asterisks indicate statistical significance of the differences * p < 0.05; ** p < 0.01; *** p < 0.001; NS, nonsignificant.

5. Surgical smoke and COVID-19

5.1. Summary and key messages

- **SARS-CoV-2 and COVID-19 represent a global health emergency:** The Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) virus and its associated disease COVID-19 have been declared a pandemic by the World Health Organization,[l] causing infections in over 38 million people with over one million deaths.[m]
- **A considerable proportion of transmission is via individuals with no symptoms:** Estimates from mass testing in defined settings suggest 18% to 75% of individuals positive for SARS-CoV-2 may not show symptoms.[77]
- **The virus may be present in multiple organs:** Genetic material of the virus is predominantly found in samples from the lungs, but evidence suggests it may be present in other organs.[78-80]
- **Impact of surgical smoke on COVID-19 risk is unknown[32,33]:** In the absence of clinical data, authors describe only the theoretical risk of surgical smoke as a vector of transmission given evidence of viral genetic material detection in non-SARS-CoV-2 studies.[37-39]
- **No suggestion of increased risk of COVID19 from laparoscopic surgery:** Reviews[37-39] and individual studies[40,41] of minimally-invasive surgery suggest no increased risk of healthcare-staff infection by SARS-CoV-2 from laparoscopic procedures, in contrast to early recommendations from surgical societies.[81]
- **The COVID-19 pandemic has refocused attention on dangers of surgical smoke:** Although no documented cases via surgical smoke have been identified, authors have noted that increased awareness of the potential for transmission of SARS-CoV-2 has encouraged evaluation of infection control measures and risks to healthcare staff, including the dangers posed by surgical smoke.[81,82]

[l] https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
[m] Johns Hopkins University COVID-19 tracker, https://www.covidtracker.com/

5.2. Brief introduction to COVID-19

In late 2019, a new respiratory illness emerged and began spreading rapidly throughout the world. The causative agent was later identified to be a novel member of the coronavirus family, receiving the designation severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated disease was named COVID-19.[83] At the end of January 2020, the World Health Organization declared the disease a "public health emergency of international concern"[n] and by March 2020, the disease was declared a pandemic due to its rampant spread.[o] The need for data regarding the virus and characteristics of the accompanying disease has sparked an explosion of research into the topic. The PubMed literature database listed 1,843 articles to the end of January 2020 and this number had increased to 60,192 by the end of September 2020 (see Table 6-3). The information presented in the dossier therefore represents a snapshot, with a focus on characteristics relevant for the context of surgical smoke but is not intended to be a comprehensive review on the topic, especially given the rapid development of understanding regarding the virus and the disease.

5.2.1. Viral infection and disease course

The SARS-CoV-2 virus is an enveloped, single-stranded RNA virus.[83,84] Research has found that a primary means of entry into human cells is via the angiotensin converting enzyme 2 (ACE2) receptor. The ACE2 receptor is broadly expressed in numerous tissues, including the lung, gastrointestinal tract, kidney, and blood vessels, thereby increasing the number of tissues that can potentially be infected.[80] Another protein believed to be important in the viral entry to cells is the transmembrane serine protease 2 (TMPRSS2) enzyme, also found on the surface of human cells.[78] Proteins on the surface of the virus bind to the ACE2 receptor and the TMPRSS2 cleaves a portion of the protein (the protein spike) facilitating entry of the virus to cells.[78]

Research has found that the genetic material of the virus is predominantly found in naso- oropharyngeal swabs of the upper respiratory tract and expectorate sputum and bronchoalveolar lavage of the lower respiratory tract.[79,84] Considerably lower rates of detection have been found in blood and urine.[79] There is keen interest in potential tissue targets of SARS-CoV-2 because in the most severe cases, multiple organs demonstrate injury, despite the lungs' being the focus of viral entry.[78,79]

Common symptoms of COVID-19 are similar to influenza and include dry cough, fever, body aches and chills.[83,84] Other symptoms include dysfunction in taste or smell or both.[85] More severe cases suffer respiratory complications and

[n] https://www.who.int/publications/m/item/covid-19-public-health-emergency-of-international-concern-(pheic)-global-research-and-innovation-forum

[o] https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020

dysfunction or failure in multiple organs. A progression of symptoms according to disease severity is shown in Table 5-1.[84]

Table 5-1 COVID-19 disease severity and symptomatology

Classification	Presentation
Uncomplicated (mild) illness	Mild fever, dry cough, sore throat, nasal congestion, malaise, headache, muscle pain, new loss of taste or smell
Moderate pneumonia	Cough or shortness of breath, but without signs of severe pneumonia
Severe pneumonia	Fever with severe dyspnea, respiratory distress, tachypnea (> 30 breaths/min), hypoxia (SpO_2 < 90%)
Acute respiratory distress syndrome (ARDS)	Indicative of serious new-onset respiratory failure
Extrapulmonary manifestations	Sepsis including: Severe dyspnea and hypoxemia, renal impairment, tachycardia, altered mental state, liver dysfunction Septic shock Increased mortality, circulatory and cellular or metabolic abnormalities

Data are summarized in the review of Cascella et al.[84]

5.2.2. Diagnosis

Testing for SARS-CoV-2 generally falls into two categories: genetic material or antibody identification. Tests performed on samples from the throat or nose of suspect cases are submitted for analysis by real-time polymerase chain reaction (RT-PCR) assay to detect the genetic material of the virus. These tests will identify active cases of disease. In contrast, serological testing will look for signs of infection through detection of antibodies to viral proteins as evidence of an adaptive immune response to SARS-CoV-2.[83,84] Given the time lag of approximately 2 weeks to develop a detectable immune response, the latter serological tests identify previous infections and are less informative in acute diagnosis.[83] At the time of writing, a wide variety of antibody tests is available and they still suffer some degree of limited sensitivity (ability to correctly identify a positive antibody response) and specificity (ability to correctly identify a negative antibody response).[84]

Imaging also plays a role in diagnosis of COVID-19, although which modalities are useful depends on the stage of disease.[84] X-Ray is not expected to show changes in lung appearance in the early stages of disease consistently, whereas computed tomography does. Lung ultrasound can also be used to monitor changes in lung tissue during and after the course of disease.[84]

5.2.3. Transmission

Some individuals with COVID-19 present as asymptomatic (no symptoms) or (few, very mild symptoms that may not be identified as associated with an illness).[77,84,86] Studies from various settings, including a town in Italy and marine vessels, have estimated proportions of 18% to 75% of patients who test positive for SARS-CoV-2 not to have presented with symptoms of disease, with more studies tending towards higher percentages.[77] These individuals, along with pre-symptomatic cases (people who will go on to develop symptoms, but initially show none after the infection has taken hold) therefore represent a large pool of cases that can transmit the virus unbeknownst to others.[77] Testing regimes vary by country and resources, but many focus on those already displaying symptoms leaving others who may be transmitting the disease unidentified.[77] One study from the UK among healthcare workers found on screening of 1,032 asymptomatic healthcare workers that 30 (3%) were positive for SARS-CoV-2 on throat swab.[86] Of the positive cases, 17 of 30 (57%) were truly asymptomatic, while 12 (40%) had experienced symptoms consistent with COVID-19 more than a week prior to the test.[86] The study concluded that screening among healthcare workers not currently displaying symptoms was therefore needed, given the confirmed presence of virus and the associated risk of transmission.[86]

The primary means of transmission is thought to be via inhaled droplets containing viral particles of size 5-10 μm as may be generated by coughing and release of sputum.[84] Aerosols of smaller diameter (see relative sizes and respiratory tract penetration Figure 3-6) are also considered a possible means of transmission during prolonged exposure in confined spaces.[84] Contact transmission with contaminated surfaces cannot be excluded, as studies on other infectious human coronaviruses have shown such contact as a means of transmission.[87] In aerosol form as small droplets, the particles may be suspended in the air for longer, enabling their inhalation and providing access to the lining of the upper respiratory tract where there is also abundant expression of ACE2.

5.3. COVID-19 and the provision of healthcare

Based on available data, the SARS-CoV-2 virus can be present in individuals who do not have signs or symptoms of the disease at the time of presentation. These may be asymptomatic, paucisymptomatic, or pre-symptomatic patients (see 5.2.3 above). Patients receiving care for conditions other than COVID-19 such as elective surgeries must therefore be assessed for the risk of transmission of SARS-CoV-2.

The risk to healthcare staff has been demonstrated in high rates of infection. A study in Los Angeles county in the United states found that by May 31, 2020, there were 5,500 healthcare workers with positive COVID-19 diagnoses, representing 9.6% of all reported cases.[32] These workers had both clinical and non-clinical roles and almost half were nurses (49.4%).[32] A similarly great impact was seen in other countries, where in the early stages of their respective crises,

29% in China and 20% in Italy of all registered SARS-CoV-2 cases were healthcare workers, decreasing to 4.4% and 10% respectively at later stages.[33] The risk of infection may be affected by specialty and procedure, with some expected to be higher risk than others. The risk ratio of infection for personnel who manage patients with diseases of the aerodigestive tract has been estimated to be 2.1.[5] An international study identified 361 otolaryngologists and of 325 with data for analysis, half were under 44 years of age, 54% were believed to have acquired the infection through clinical activity and 24 (7.4%) had died.[35] The presence of virus in the respiratory system, gastrointestinal tract, and genitourinary system makes aerosol-generating procedures on these tissues a relevant consideration in the context of the highly-contagious SARS-CoV-2.[82]

The result of infection in healthcare workers can be the same as for the general populace, with both ranging from seemingly paucisymptomatic cases to the need for hospitalization. There is also a non-negligible associated risk of death,[34,35] suggested to be particularly high depending on ethnicity.[36] Some differences have been noted in the mortality risks among healthcare workers; a study reporting the first 100 healthcare worker deaths in Italy, an epicenter of infection at one phase of the crisis, found 95 of them to be men, far exceeding typical ratios in the general populace.[34] Differences in infection control awareness and age were hypothesized to contribute to the difference, and the authors also noted the potential for a dosing impact, whereby greater exposure to the virus may impact on infection.[34]

5.4. Surgical plume and COVID-19

At the time of writing (Oct 2020), the risk of transmission of SARS-CoV-2 by surgical smoke has not yet been demonstrated. Active discussions are taking place in the medical literature regarding the degree of infection hazard that may be posed by exposure to surgical smoke[42,81,88] in part fueled by questions of whether tissues under dissection contain appreciable amounts of virus.[88]

5.4.1. General risks due to biological material

As noted earlier (section 3.6.3), viral material has been identified in smoke plume[19,20,65] and cases of morbidity in healthcare workers have been linked to occupational exposure to plume as the mostly likely risk factor.[21-23] Should infectious material be present in tissues being dissected or remodeled during surgeries, then, the high temperatures generated by laser or electrosurgical devices, for example, cannot be expected to eliminate all potentially-infectious genetic material. In the case of SARS-CoV-2, full elucidation of the extent of viral infection in all tissues is not known.

In the absence of direct clinical evidence, research studies investigating tissue expression of the virus become relevant in terms of assessing potential risk. Surgical smoke and plume are generated from the manipulation of tissues, whether through electrosurgical, laser, ultrasonic, or mechanical devices (see section 3.2). As a result, tissues that contain the virus serve as potential sources of biological material that can enter the plume and contain SARS-CoV-2

material or components when these tissues are dissected, sealed, or otherwise manipulated.

5.4.2. Case study of SARS-CoV-2 transmission in otolaryngology

One case of apparent transmission to a surgeon occurred in the emergency treatment of a patient suffering epistaxis.[35] The bleeding was controlled by cautery and ligation, and at the time of presentation, the results of the patient's SARS-CoV-2 test were unknown, but results later showed the patient to have been positive. Risks to healthcare staff regarding COVID-19 were known and the surgeon used an N95 respirator as a precaution in the absence of the test result, but nevertheless tested positive for SARS-CoV-2 requiring hospitalization and intensive care unit treatment.[35] Cautery was used in the treatment, but the study did not directly report on the potential for surgical smoke as a vector of transmission. Other cases from the discipline, even where patients tested negative prior to the procedure, have resulted in surgeon death, leading to the suggestion that precautions must be taken for all patients.[35] This study is, though, a case study and may not be necessarily representative for SARS-CoV-2 transmission over surgical smoke.

5.4.3. SARS-CoV-2 and minimally-invasive surgery

Although high-quality evidence is still lacking, the need to address the risks to healthcare staff posed by the novel coronavirus has led to recommendations for managing that risk. One report by surgeons addressing the issue of laparoscopy versus laparotomy noted the potential for high concentrations of the dangerous contents of surgical smoke in the pneumoperitoneum generated during laparoscopic procedures and the potential for leakage.[89] Among recommendations proposed was "[l]iberal use of suction devices to remove smoke and aerosol during operations, and especially, before converting from laparoscopy to open surgery or any extra-peritoneal maneuver" and to "[a]void untimely and unfiltered release of pneumoperitoneum".[89] A number of societies went further, based on available information at the time, and advocated against the use of minimally-invasive procedures.[81,90]

Recommendations and guidance are in constant review, particularly in the context of the rapidly evolving understanding of SARS-CoV-2. In patients with confirmed SARS-CoV-2 infection, studies reporting on samples taken during laparoscopic surgeries have not detected SARS-CoV-2 virus in the peritoneal fluid,[40,91] omentum,[91] or subcutaneous fat,[91] but did find the virus in rectal swabs,[91] consistent with earlier findings of the virus in feces.[83] It should be noted that these studies did not collect aerosols for analysis, and one used smoke evacuation during appendectomy and evacuated the pneumoperitoneum via closed suction system, so the presence or absence of infectious content could not be determined from aerosolized material.[40]

A review was performed of the best available evidence regarding the potential for contamination with SARS-CoV-2 around laparoscopic surgery.[39] The authors described five hypothetical transmission routes for SARS-CoV-2 to infect staff: during intubation/extubation, smoke and air evacuation during surgery, extraction of tissue during surgery, desufflation of the pneumoperitoneum after

surgery, and the use of positive pressure systems in the operating room that could push contaminated air to other locations (Table 5-2).[39] Despite the extent of the review, the available evidence was minimal to not available (Table 5-2). Of potential means of transmission, intubation and extubation are suggested to present the highest risk to staff, with an odds ratio of 30 for becoming infected during the first SARS outbreak in 2003-2004 compared to healthcare workers who did not perform intubations.[92] Nevertheless, despite a lack of data specific to the more recent SARS-CoV-2, in consideration of the theoretical risks posed and data from other studies about infectious materials, surgical smoke, and laparoscopic surgery, they propose suggestions to reduce risk of contamination for staff.

Table 5-2 Recommendations to reduce SARS-CoV-2 risks to staff around laparoscopic surgery

Transmission route	Evidence	Advice
Positive pressure OR	Minimal	Turn off positive pressure, prepare several negative pressure ORs
Intubation/extubation	Minimal	Level III protection, should not be performed in a positive pressure OR
Smoke evacuation	Minimal	Use a proper filter in a closed vacuum system
Tissue extraction	None	Use masks and screens/goggle at minimum.
Desufflation or abdomen	None	Use a proper filter and a closed system

Statements are as reproduced from Table 4 of de Leeuw et al.[39] OR, Operating room.

A common consensus presented by studies investigating laparoscopy is that laparoscopic surgery is not likely to pose any additional risk to healthcare staff in comparison to open surgery,[37,38,42] and delaying surgery may cause more harm to the patient due to disease progression.[39] Experience from high-volume centers in Italy conducting minimally-invasive urologic surgery served as an illustration of the possibility to still perform these procedures during the COVID-19 pandemic. The authors concluded that renouncing the benefits of this surgery would be counterproductive in the scenario of long-lasting cohabitation with the virus.[41] Suggestions for mitigation strategies are available, and it has further been suggested that laparoscopic surgery may be beneficial not only in providing containment of any potential aerosolized virus, but also allowing the patient to benefit from the advantages of minimally invasive surgery.[42]

6. Structured literature search details

Structured searches were performed (August 2020) to identify literature reporting on surgical smoke or plume (Table 6-1). The dossier mandate included consideration for the novel coronavirus SARS-CoV-2 and the associated COVID-19 disease. As available data were subject to change, the searches were executed again towards the end of the dossier development process. Database metainformation, especially around the evolving COVID-19/SARS-CoV-2 information space, are subject to change as updates are managed by the National Center for Biotechnology Information (NCBI) in the United States, as the curators of the PubMed database. These changes are not expected to affect large swathes of results, but individual records may be impacted. As a result, future execution of the presented search strings may yield different results.

Table 6-1 Structured searches in PubMed to identify data on surgical smoke/plume

Index	Aim	Search string	Hits
#1	surgical smoke	("surgical procedures, operative"[MeSH] OR "surgery"[tiab] OR "operative"[tiab] OR "operative surgical procedures"[tiab] OR laparoscopic[tiab] OR laparoscopy[tiab]) AND ("smoke"[MeSH] OR "smoke"[tiab] OR "plume"[tiab] OR "air quality"[tiab] OR "particulate matter"[tiab] OR "particulate matter"[MeSH] OR "PM2.5"[tiab]) OR "surgical smoke"[all] OR "surgical plume"[all]	3,044
#2	limit to 10 years	"2010/01/01":"2020/08/24"[pdat]	11,468,203
#3	useable languages	english[la] OR french[la] OR german[la]	28,236,927
#4	tobacco-related smoke†	("smoked"[All] OR "smokes"[All] OR "smoking"[MeSH] OR "smoking"[All] OR "smokings"[All] OR "smoking s"[All] OR "tobacco"[MeSH] OR "tobacco"[All] OR "tobacco products"[MeSH] OR "tobacco products"[All] OR "tobaccos"[All] OR "tobacco s"[All] OR "tobacco smoke"[All] OR "cigarett"[All] OR "cigarette s"[All] OR "cigaretts"[All] OR "cigarette"[All] OR "cigarettes"[All] OR cigar[All] OR cigars[All] OR "vaped"[All] OR "vaping"[MeSH] OR "vaping"[All] OR "vapes"[All] OR "E-cigarettes"[All] OR "E-cigarette"[All]) NOT ("surgical smoke"[All] OR "surgical plume"[All])	363,583
#5	core search of relevant surgical smoke literature	#1 AND #2 AND #3 NOT #4	803

†Articles referencing smoking in the context of tobacco products were only excluded if there was not also direct reference to surgical smoke.

Table 6-2 Article screening results

Criterion	Notes	Excluded	Count
All articles		--	803
No abstract	Items with neither abstract, nor title that suggests relevant data	62	741
Tobacco smoke	Tobacco products with no link to surgical smoke	94	647
Smoke inhalation injury	Burn patients and smoke inhalation	55	592
No relevant data	Incidental mention of smoke	131	461
Not surgical smoke	General operating room hygiene, outdoor air pollution, Moya Moya disease	276	185

A search was additionally performed to generate article counts related to Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) and COVID-19 publications (Table 6-3). The search was performed 15 October 2020. As noted previously (section 1.2), exact counts may change due to updates to the PubMed database.

Table 6-3 Article counts for SARS-CoV-2/COVID-19 literature

Index	Aim	Search string	Hits
#1	COVID-19	"severe acute respiratory syndrome coronavirus 2"[Supplementary Concept] OR "severe acute respiratory syndrome coronavirus 2"[All Fields] OR "ncov"[All Fields] OR "2019 ncov"[All Fields] OR "covid 19"[All Fields] OR "sars cov 2"[All Fields] OR (("coronavirus"[All Fields] OR "cov"[All Fields]) AND 2019/11/01:3000/12/31[Date - Publication])	63,481
#2	Date range: Dec 2019 – Jan 2020	#1 AND "2019/11/01":"2020/01/31"[pdat]	1,843
#3	Date range Dec 2019 – Sep 2020	#1 AND "2019/11/01":"2020/09/30"[pdat]	60,194

7. References

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