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Laser-Generated Air Contaminants from Medical Laser Applications: A State-of-the-Science Review of Exposure Characterization, Health Effects, and Control

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The clinical use of lasers in surgery began in 1973 with applications of the carbon dioxide laser in otolaryngology, and since then the use of lasers has become commonplace in many medical and surgical specialties. Nonetheless, when biological tissue is subjected to laser radiation, the target cells can be vaporized, resulting in the aerosolization of their contents and the subsequent exposure of health care workers to laser-generated air contaminants (LGACs). The purpose of our analysis was to summarize and present all of the published literature pertaining to the laser-induced plume chemical and physical composition, health effects, and methods of control. The objective was to identify knowledge gaps within exposure science to set a research agenda for the protection of health care personnel exposed to LGACs. A literature search was performed using the PubMed database using a variety of search strategies and keyword combinations. To locate additional studies, we systematically searched the reference lists of all studies identified by our search, as well as key review papers. To date, researchers have identified roughly 150 chemical constituents of plume, as well as fine and ultrafine particulate matter, which has been shown to include viable cellular material, viruses, and bacteria. However, very few studies have attempted to characterize the effects of laser system type, power, and tissue treated, as it relates to LGAC exposure. Furthermore, current control strategies do not appear to be adequate in preventing occupational exposure to LGACs.

Keywords laser-generated air contaminants, laser plume, medical laser

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INTRODUCTION

According to the Occupational Safety and Health Administration (OSHA), each year an estimated 500,000 workers, including surgeons, nurses, anesthesiologists, and surgical technologists, are exposed to laser-generated air contaminants (LGACs) or electrosurgical smoke.[1] The laser surgical smoke or plume is generated as the result of target cells being heated to the point of boiling, causing the membranes to rupture, as well as pyrolysis and combustion of the target material.[2] This cellular vaporization releases steam and cell contents,[3] and the quantity and characteristics of the cellular matter aerosolized are determined by the type of laser being used, its irradiance, and the type of tissue being treated.[3–6]

Although surgeons' exposure to LGACs may be transient, they are considered the most at risk population with respect to health effects due to higher exposures incurred as the result of their proximity to the operative site.[7] The proposed health effects resulting from exposure to LGACs include acute and chronic inflammatory respiratory changes (e.g., emphysema, asthma, chronic bronchitis); hypoxia/dizziness; eye irritation; nausea/vomiting; headache; sneezing; weakness; lightheadedness; carcinoma; dermatitis; cardiovascular dysfunction; throat irritation; lacrimation; colic; anxiety; anemia; leukemia; nasopharyngeal lesions; human immunodeficiency virus, and hepatitis.[2]

Nonetheless, the extent to which these hazards actually exist remain highly debated and not well characterized. Numerous researchers have sought to determine the composition of the laser surgical plume, with specific emphasis on its chemical constituents and particulate matter (PM), including infectious agents. Here we present a review of the literature to date concerning laser-induced surgical plume chemical and physical composition, health effects, and methods of control. The objective was to identify knowledge gaps within exposure science to set a research agenda for the protection of health care personnel exposed to LGACs.

METHODS

A literature search was performed using the U.S. National Library of Medicine and the National Institutes of

Health's PubMed database with combinations of search terms that included but were not limited to laser, medical, surgery, therapy, plume, smoke, aerosol, and hazard. To locate additional studies, reference lists of all publications identified by our search were systematically evaluated, as well as key laser safety review papers. Papers relevant to the medical laser-induced plume, including clinical case reports and laboratory experiments, were identified and reviewed. This review was limited in scope to laser plume-related occupational hazards for health care professionals; manuscripts specifically addressing patient safety were not included.

RESULTS

Chemical Composition

Similar to electrosurgical units, lasers produce high heat (i.e., 100°C to 1000°C), which results in tissue pyrolysis, and the generation of LGACs. Nearly 150 chemicals belonging to the following chemical classes have been identified in the laser plume: alkanes, alkenes, aldehydes, ketones, alkyl aromatics, pyrrols, furans, pyridines, thioles, thiocyanates, pyrimidines, and nitriles.[8,9] However, it has been estimated that there are more than 600 compounds yet to be identified in laser surgical smoke.[10]

Chemical Concentrations

While the constituents of the plume are believed to be the same for nearly all laser devices that generate plume, the concentrations of individual contaminants in the laser plume have been shown to differ with respect to the power density utilized, the irradiation time and resulting temperature in the tissue, and the type and moisture content of the treated tissue.[11–14] Nonetheless, only three studies have been conducted to determine the airborne concentrations of chemicals in the surgical plume.[6,9,15] The methods employed in these studies and their results are presented in Table I.

In 1987, the National Institute for Occupational Safety and Health (NIOSH) performed the first exposure assessment evaluating occupational exposure to chemicals in the laser plume.[6] Results from the air sampling documented detectable but low levels of ethanol, isopropanol, anthracene, C_8-C_{12} aliphatic hydrocarbons, and cyanide. Peak concentrations of formaldehyde were also reported that, according to NIOSH, might cause irritation in some sensitive individuals. In addition, solvent extracts of airborne particles—generated during laser procedures—that were collected by area samplers were found to be mutagenic. In a preliminary analysis of laser irradiation of processed meat (pork) using a 30 W CO_2 laser and a 38 to 84 W Nd:YAG laser, which is not summarized in Table I, Draeger tubes (Draeger, Pittsburgh, Pa.) revealed the presence of hydrogen cyanide at the laser irradiation site at a concentration of 100 ppm.

In addition, detectable but low levels of the following chemicals were reported by Albrecht et al.[15] and Weber[9] during the use of a CO_2 laser: CO, NO, benzene, toluene, styrene, ethylbenzene, benzaldehyde, 2-butanone, butylaldehyde, 2-methylbutylaldehyde, isovaleraldehyde, pyrrole/pyridine, 1-methylpyrrol, methylpyrazine, 2-methylbutyronitrile, and 3-methylbytyronitrile.

Particulate Matter (PM)

The laser plume also consists of PM that has been shown to include viable viruses and bacteria. A brief summary of the literature related to particle size, concentration, and the presence of viruses and bacteria is presented below. In addition, Table II presents a detailed description of the studies that have assessed particle size distribution and PM concentration during laser use, and Table III presents an overview of all of the studies that have investigated the presence of cellular matter, viruses, and bacteria in the laser plume.

Particle Size Distribution

The deposition of and health effects resulting from exposure to airborne particles have been shown to be related to their aerodynamic diameter. Smaller particles travel farther in ambient air relative to larger-sized particles; therefore, exposure, particularly to nonscrubbed surgical staff (circulating nurse, anesthesia care provider), may be largely dependent on particle size.[3,16] Four investigations have assessed the size distribution of the PM in the plume, two of which indicated that the size ranged from 0.1 to 1 μm,[5,17] while the third reported particles up to 27 μm in diameter.[18] The fourth investigation reported only the mass median aerodynamic diameter (0.54 μm).[19] Although two of these studies were performed during CO_2 laser use, there was no internal consistency with respect to the size distributions measured.[5,18]

PM Concentration

Only three studies have investigated the concentration of PM in the plume. Freitag et al.[19] collected PM samples during Nd:YAG vaporization of sheep bronchial tissue and reported a concentration of 0.92 mg/L. Subsequent studies revealed PM concentrations several orders of magnitude lower. Specifically, Albrecht et al.[15] collected plume samples during the CO_2 laser irradiation of porcine liver and reported that the average breathing zone concentration of respirable particles ranged from 0.59 mg/m^3 to 1.69 mg/m^3. Tanpowpong and Koytong[20] reported that the highest measured $PM_{2.5}$ concentration (227.7 $\pm$ 14.8 μg/m^3) during CO_2 laser tissue ablation was over 3-fold and 100-fold higher than the concentration measured in the operating room pre-surgery (69 $\pm$ 13.4 μg/m^3) and in an adjacent office (2.1 $\pm$ 0.3 μg/m^3), respectively. Similar results were reported by Tanpowpong and Koytong for PM_{10} and PM_{15}.

Cellular Matter

The first evidence of the presence of viable cellular matter within the laser plume was reported in 1967 by Hoye and colleagues[21] following experiments using an excimer laser. The analysis was conducted in part because previous investigations had noted that there was a considerable amount of splatter of tumor tissue in all directions in the air as far away

TABLE I. Summary of the Investigations of Chemical Concentrations Resulting from Laser Ablation

Methods Description	Type of Lasers (Operational Parameters)	Agent	Sampling Method	Analytical Technique	Number of Samples	Sample Duration (min)	Concentration Range (Number of Samples Above the LOD)[A]
NIOSH (1990)							
Air sampling was performed in operating rooms and laser clinics during laser use on humans and, experimentally, on mice	CO_2 (P = 4 and 5 W, CM); Nd:YAG (P = 15–30 W, CM); Argon (P = 2.5 and 4 W, CM)	Formaldehyde	Collected using a midget impinger containing 1% sodium bisulfite at 0.5 L/min	Visible absorption spectro-photometry (NIOSH Method 3500)	*Area* (Human) = 3; *BZ* (Human) = 5	*Area* = 7 – 318; *BZ* = 9 – 54	*Area* = trace – 0.013 ppm (N = 3); *BZ* = trace – 0.12 ppm (N = 5)
	CO_2 (NA), Nd:YAG (P = 50 W, CM); Nd:YAG (PE = 60–78 mJ, PD = 8–10 ns, PRR = 10 Hz); Erbium (PE = 30 mJ, PD = 250 ns, PRR = 8 Hz)				*Area* (Mouse) = 4; *BZ* (Mouse) = 2	*Area* = 1.75 – 5; *BZ* = 3 – 4	*Area* = trace (N = 4); *BZ* = trace – 0.44 ppm (N = 2)
	CO_2 (P = 4 W, CM); Nd:YAG (P = 15–30 W, CM)	Ethanol, Isopropanol, Total Other Hydrocar-bons	Collected using a glass tube containing activated charcoal at 1 L/min (qualitative) and 0.2 L/min (quantitative)	Qualitative samples: desorbed with carbon disulfide and analyzed by GC/FD; Quantitative samples: analyzed by GC-MS	*Area* (Human) = 1; *BZ* (Human) = 2	*Area* = 427; *BZ* = 17 – 54	*Area:* Ethanol = ND (N = 0); Isopropanol = 0.5 ppm (N = 1); Total Other Hydrocarbons = trace (N = 1); *BZ:* Ethanol = ND – 4.7 ppm (N = 1); Isopropanol = ND – 16.4 ppm (N = 1); Total Other Hydrocarbons = ND – trace (N = 1)
	CO_2 (P = 4 W, CM); Nd:YAG (P = 15–30 W; CM)	Cyanide	Collected using a MCE filter followed by a glass midget bubbler containing 0.1 ml N potassium hydroxide at 0.5 L/min	Visible absorption spectroscopy	*Area* (Human) = 2; *BZ* (Human) = 3	*Area* = 318 – 427; *BZ* = 11 – 54	*Area* = ND (N = 0); *BZ* = ND – 0.4 mg/m^3 (N = 1)
	CO_2 (NA), Nd:YAG (P = 50 W, CM); Nd:YAG (PE = 60–78 mJ, PD = 8–10 ns, PRR = 10 Hz); Erbium (PE = 30 mJ, PD = 250 ns, PRR = 8 Hz)				*Area* (Mouse) = 4; *BZ* (Mouse) = 2	*Area* = 1.75 – 5; *BZ* = 3 – 4	*Area* = ND (N = 0); *BZ* = 1.05 –1.53 mg/m^3 (N = 2)

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TABLE I. Summary of the Investigations of Chemical Concentrations Resulting from Laser Ablation (Continued)

Methods Description	Type of Lasers (Operational Parameters)	Agent	Sampling Method	Analytical Technique	Number of Samples	Sample Duration (min)	Concentration Range (Number of Samples Above the LOD)[A]
	CO_2 (P = 4 and 5 W, CM); Nd:YAG (P = 15–30 W, CM); Argon (P = 2.5 and 4 W, CM)	Anthracene and Other PNAs	Collected using a Zefluor 2-μm pore size filter and a cellulose acetate O-ring in a cassette, followed by a 7-mm glass tube containing 2 sections of prewashed XAD-2 resin at 2 L/min	Filter and tube samples were analyzed using HPLC and GC/MS	*Area* (Human) = 3; *BZ* (Human) = 5	*Area* = 9 – 427; *BZ* = 9 – 54	*Area:* Anthracene = trace – ND (N = 2), Other PNAs = ND (N = 0); *BZ:* Anthracene = ND (N = 0), Other PNAs = ND (N = 0)
	CO_2 (NA), Nd:YAG (P = 50 W, CM); Nd:YAG (PE = 60 – 78 mJ, PD = 8 – 10 ns, PRR = 10 Hz); Erbium (PE = 30 mJ, PD = 250 ns, PRR = 8 Hz)				*Area* (Mouse) = 4; *BZ* (Mouse) = 2	*Area* = 1.75 – 5; *BZ* = 3 – 4	*Area:* Anthracene = ND (N = 0), Other PNAs = ND (N = 0); *BZ:* Anthracene = trace (N = 1), Other PNAs = ND (N = 0)
Albrecht et al. (1995)							
Plume samples were collected during the laser irradiation of porcine liver	CO_2 (P = 20 W, SD = < 0.8 mm (focused), ~3 mm (nonfocused), CM)	Butylaldehyde, 2-Butanone, Isovaleraldehyde, 2-Methylbutylaldehyde, Pyrrole/Pyridine, Toluene, Ethylbenzene, Styrene, Benzaldehyde	Collected using a Drager tube	Analyzed using GC	*BZ* = 1 (focused), 1 (nonfocused)	NA	Butylaldehyde = 64–83 ng/m^3, 2-Butanone = 10–17 ng/m^3, Isovaleraldehyde = 117–198 ng/m^3, 2-Methylbutylaldehyde = 87–138 ng/m^3, Pyrrole/Pyridine = 36–57 ng/m^3, Toluene = 26–52 ng/m^3, Ethylbenzene = 6–7 ng/m^3, Styrene = 1 ng/m^3, Benzaldehyde = 7–13 ng/m^3

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TABLE I. Summary of the Investigations of Chemical Concentrations Resulting from Laser Ablation (Continued)

Methods Description	Type of Lasers (Operational Parameters)	Agent	Sampling Method	Analytical Technique	Number of Samples	Sample Duration (min)	Concentration Range (Number of Samples Above the LOD)[A]
Weber and Spleiss (1995)							
Plume samples were collected during the laser irradiation of evaporated porcine liver	*Phase 1: Focused*: CO_2 (P = 10 W, SD = 1.1 mm) *Defocused*: (P = 30 W, D = 0.07 kW/cm^2, SD = 7.4 mm);	*Phase 1*: Benzene, Toluene, Ethylbenzene, Styrene, Pyrrol, 1-Methylpyrrol, Methylpyrazine, 2-Methylbutyronitrile, 3-Methylbytyronitrile;	*Phase 1*: VOCs were collected on adsorbents (no additional information was provided);	*Phase 1*: VOCs were analyzed using GC-MS	*Phase 1*: NA;	NA	*Phase 1:*[B] Benzene = 5–44 μg/m^3, Toluene = 67–319 μg/m^3, Ethylbenzene = 4–56 μg/m^3, Styrene = 6–49 μg/m^3, Pyrrol = 30 μg/m^3, 1-Methylpyrrol = 3 μg/m^3, Methylpyrazine = 44–58 μg/m^3, 2-Methylbutyronitrile = 40–50 μg/m^3, 3-Methylbytyronitrile = 100–130 μg/m^3; *Phase 2*: NO = 0–2 ppm, CO = 0–15 ppm
	Phase 2: CO_2 (P = 10 W)	*Phase 2*: NO and CO	*Phase 2*: NO and CO were sampled using direct reading devices		*Phase 2*: 15		

Notes: NA = Not available; P = Power (Watts); CM = Continuous Mode; PE = Pulse Energy (mJoules); PD = Pulse Duration (ns); PRR = Pulse Repetition Rate (Hz); SD = Spot Diameter (mm); Power Density = D (kW/cm^2); Breathing Zone (BZ); Mixed Cellulose Ester (MCE).

[A]Includes samples for which the concentrations were between the Limit of Detection and the Limit of Quantification; these concentrations were reported as "trace."

[B]Reported by the authors as μg of VOC per g of tissue irradiated; for purposes of calculating an airborne concentration the authors assume the "dilution of 1 g of sample tissue in 1 m^3 of air."

TABLE II. Summary of the Investigations of PM Size Distribution and Concentration in the Laser Plume

Methods Description (Study Design)	Type of Laser (Operational Parameters)	Sampling Methodology	Analytical Technique	Results
		PM Size Distribution		
Nezhat et al. (1987)				
Sampling was conducted during laser laparoscopic treatment for endometriosis and/or adhesions; a suction probe was used to control exposure to the plume. (Clinical)	CO_2 (P = 15–30W, D = 6–12 kW/cm^2, SD = 0.5 mm, pulsed)	*Method 1:* Samples (N = 26) were collected from aerosol that had accumulated within the pelvic region and had been vented into a plastic bag. A cascade impactor with mylar substrates was inserted into the bag, and air was drawn through the device at a rate of 2 L/min for 3 min. *Methods 2 and 3*: Air samples were collected in the surgical field (N = 4), and from the abdomen of the patient (N = 2) at a rate of 2 L/min through a cascade impactor with mylar substrates.	Substrates were desiccated (24 hr) and weighed before sampling, and then reweighed after sampling to determine the size distribution	MMD (Geometric SD) = 0.36 μm (1.71 μm); Median aerodynamic diameter: 0.31 μm; Range = 0.10–0.80 μm; Arithmetic mean (STD) = 0.35 μm (0.16 μm) (Results not reported separately for the three methods)
Freitag et al. (1987)				
Sampling was conducted during the laser irradiation of sheep bronchial tissue. (Laboratory)	Nd:YAG (P = 15–20 W) (mode not reported)	Sheep were intubated nasopharyngeally and exposed in an exposure chamber to the laser plume. An air sample was collected using a cascade impactor at the port of the endotracheal tube.	Impaction plates and backup filters were weighed	MMD = 0.54 μm
Kunachak et al. (1998)				
Sampling was conducted during laser irradiation of 10 fresh specimens of human laryngeal papillomatous tissue. (Laboratory)	CO_2 (P = 10 W, CM)	*Method 1*: Samples (N = 10) were collected using a microfilter attached to the tip of the hose of a smoke evacuator that operated at 940 L/min	Scanning electron microscopy (SEM)	Range = 0.5–27 μm, of which 70% were approximately 0.8 μm; Average particle density = 6 particles per mm^2
		Methods 2 and 3: Samples (N = 10 for both) were collected using two layers of filters (Method 2: microfilter and cotton cloth surgical mask; Method 3: Microfilter and paper surgical mask) attached to the tip of the hose of a smoke evacuator that operated at 940 L/min		Range = 1.6–27 μm, of which 65% were approximately 3.7 μm; Average particle density = 2.7 particles per mm^2
Taravella et al. (2001)				
Sampling was conducted while two eye bank eyes were irradiated using a laser set for a phototherapeutic ablation. (Laboratory)	Excimer (EF = 160 mJ/cm^2, PRR = 6 Hz, SD = 6 mm)	Samples (N = 2) were collected using a smoke evacuator (set at level 6; the flow rate was not provided) affixed with a 25 mm methylcellulose filter that was held between 1 and 2 cm from the corneal surface. Prior to the ablations, a control filter affixed to the smoke evacuator was used to sample room air.	The filters were desiccated (5 days) and then coated with gold and analyzed using SEM	Range = 0.13 to 0.42 μm; mean diameter = 0.22 μm; 98 particles were analyzed from the two experimental filters and no particles were found on the control filter
		PM Concentration		
Freitag et al. (1987)				
Plume samples were collected during the laser irradiation of sheep bronchial tissue. (Laboratory)	Nd:YAG (P = 15–20 W) (mode not reported)	Sheep were intubated nasopharyngeally and exposed in an exposure chamber to the laser plume. An air sample was collected using a cascade impactor at the port of the endotracheal tube.	Impaction plates and backup filters were weighed	Total PM = 0.92 mg/L

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TABLE II. Summary of the Investigations of PM Size Distribution and Concentration in the Laser Plume (Continued)

Methods Description (Study Design)	Type of Laser (Operational Parameters)	Sampling Methodology	Analytical Technique	Results
		PM Concentration		
Albrecht et al. (1995)				
Plume samples were collected during the laser irradiation of porcine liver. (Laboratory)	CO_2 (P = 20 W, SD = 0.6–1.2 mm, CM)	Measurements of respirable PM were made using a Ströhlein particle collector (flow rate = 22.5 m^3/hr) in the worker's breathing zone (2 locations, 20–25 cm above operative site), directly behind the surgeon (1 location), near the air outlet (two locations) and near the air inlet (two locations).	NA	*Breathing zone*: Range = 0.59 to 1.69 mg/m^3; *Behind surgeon* = 0.34 mg/m^3; *Near outlet*: Range = 0.16 to 0.19 mg/m^3; *Near inlet*: Range = 0.17 to 0.31 mg/m^3
Tanpowpong et al. (2002)				
Samples were taken in the Otolaryngology Department during laser ablation techniques on unknown specimens. (Laboratory)	CO_2 (NA)	Suspended particulate matter (PM_{15}, PM_{10}, and $PM_{2.5}$) in an office in the morning and afternoon, and in a laser operative room before, during and after laser use were measured continuously for 1 hr using a laser diode portable dust monitor. The operating room was equipped with one fan.	NA	During laser use the highest measured $PM_{2.5}$ concentration (227.7 ±14.8 μg/m^3) was over 3-fold and 100-fold higher than the concentration measured in the OR pre-surgery (69 ± 13.4 μg/m^3) and in the office (2.1 ± 0.3 μg/m^3), respectively. Similar results were reported for PM_{10} and PM_{15}.

Notes: P = Power; D = Power density; SD = Spot Diameter (mm); CM = Continuous Mode; EF = Energy Fluence (mJoules/cm^2); PRR = Pulse Repetition Rate (Hz); MMD = Mass Median Diameter; STD = Standard Deviation; NA = Not Available.

as 6 to 8 ft from the laser impact site. The presence of viable tumor cells in the laser plume has not been confirmed by three subsequent analyses, all of which employed continuous mode CO_2 lasers.[21–24]

Viruses

The presence of viral matter has arguably garnered the most attention with respect to LGAC research. In 1988, Garden and colleagues[25] were the first to demonstrate that the presence of intact viral DNA in the laser plume, reporting that CO_2 laser treatment of bovine and human papillomavirus verruca resulted in the liberation of intact viral DNA. While several subsequent studies on the papillomavirus have confirmed these findings,[26–28] others have not.[29,30] Notably, all of these studies have employed the CO_2 laser. An additional five studies have evaluated the presence of various other viruses/retroviruses, using different experimental methodologies, laser devices (CO_2, excimer, Er:YAG), and operational parameters; the results of these investigations were mixed.[31–35]

Bacteria

A total of six studies were reviewed that assessed the presence of bacteria in the plume. Experiments were conducted in various environments (laboratory and clinical) during different procedures/applications (i.e., tattoo removal, simulated treatment of the vaginal vault, simulated root canal, laser skin resurfacing). Five of the studies employed the CO_2 laser,[36–40] and one used the argon laser,[41] both of which were used at various power settings. All of these studies demonstrated the presence of intact bacterial cells in the plume, particularly when lasers were used at low irradiances. Furthermore, two studies demonstrated the greater resistance of *S. aureus,* relative to *E. coli*, to the thermal effects of lasing.[36,38]

Health Effects Associated with Exposure to LGACs

Numerous studies have been conducted to determine the potential health effects associated with exposure to the laser plume. A review of these studies is presented below and is summarized in Table IV.

Laboratory/Animal Studies: Mutagenicity, Genotoxicity, and Cytotoxicity

When it was learned that smoke condensates from broiling fish and meat exhibited mutagenicity, Tomita and colleagues[42] hypothesized that smoke condensates from laser-irradiated tissue may also be mutagenic. Following their analysis of smoke condensates generated as the result CO_2

TABLE III. Summary of the Investigations of the Presence of Cellular Matter, Viruses, and Bacteria in the Laser Plume

Methods Description (Study Design)	Infectious Agent[A]	Type of Laser (Operational Parameters)[B]	Results
		Cellular Matter	
Hoye et al. (1967)			
Mouse S-91 melanomas were lased, and the resulting splatter was recovered using a glass cone that was positioned above the irradiation site and implanted into the open axilla of a recipient mouse. (Laboratory)	NA	Neodymium: *Laser 1*: PE = 984–1,035 J, PD = 2 ms, SD = 7–8 mm; *Laser 2*: PE – 511–800 J, PD = 2.5 ms, SD = 6 mm	Tumor growth was reported in 5 of 11 recipient mice, and secondary tumors were similar to the parent tumors with respect to the growth rate, gross appearance, and histological characteristics. This provides evidence of viable tumor dissemination.
Oosterhuis et al. (1982)			
Mouse S-91 melanomas were irradiated, and the resulting debris was collected examined via cytologic smears, and viability was tested using the trypan blue test, by in vitro culture, and intraperitoneal and intramuscular inoculations in mice. (Laboratory)	NA	CO_2 (P = 20 W, CM)	Cytologic smears showed carbonized particles, damaged cells, as well as morphologically intact cells; however, viability was not observed in any of the experiments.
Bellina et al. (1982)			
Condylomata acuminate lesions were irradiated, and the plume was collected using an inline filter trap containing a Millipore filter (vacuum maintained at 25 psi). Enzymatic function and the occurrence of DNA replication and RNA transcription was assessed. (Laboratory)	NA	CO_2 (D = 705 W/cm^2, CM)	No metabolic, replication, or transcription activity was observed, and cytologic analyses revealed the presence of dehydrated but morphologically intact cells. The authors concluded that the plume is likely biologically inactive.
Voorhies et al. (1984)			
C-6 rat brain tumors were irradiated, and the plume was collected on adjacently placed Petri dishes. Contents of the Petri dishes were pooled into one tissue culture flask for each brain and incubated for 14 days. (Laboratory)	NA	CO_2 (P = 20 W, CM)	No growth was observed, and based on a microscopic examination of the flask contents, cellular fragments, charred debris, and occasional ballooned, nonviable cells were observed. There was no evidence of cell viability in the plume.
		Viruses	
Garden et al. (1988)			
Cutaneous fibropapillomas (bovine) plantar or mosaic lesions (human) were irradiated and the plume was collected in a phosphate-buffered saline (PBS) bubble chamber in line with a vacuum system (50 mm Hg), and analyzed using DNA hybridization. (Laboratory)	BPV and HPV	CO_2 (*Laser 1*: P = 12 W, PD = 0.1 s, SD = 0.2 mm, D = 38,200 W/cm^2; *Laser 2*: P = 12 W, SD = 2.0 mm, D = 380 W/cm^2; *Laser 3*: P = 4 W, PD = 0.1 s, SD = 0.2 mm, D = 12,700 W/cm^2; *Laser 4*: P = 4 W, SD = 2.0 mm, D = 130 W/cm^2; CM and pulsed)	Intact viral DNA was found in all analyses using BPV, and from 2 to 7 analyses of HPV.

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TABLE III. Summary of the Investigations of the Presence of Cellular Matter, Viruses, and Bacteria in the Laser Plume (Continued)

Methods Description (Study Design)	Infectious Agent[A]	Type of Laser (Operational Parameters)[B]	Results
		Viruses	
Sawchuk et al. (1989)			
Human plantar warts were irradiated and the plume was collected with a dry filter vacuum apparatus set at a flow rate of 42 L/min and analyzed using DNA hybridization. (Clinical)	HPV	CO_2 (P = 10 W, SD = 1 mm, PI = 1270 W/cm^2, CM)	Viral DNA was found in the plume of 5 of 8 irradiations, and surgical masks were effective in stopping the passage of the viral DNA.
Andre et al. (1990)			
Specimens of genital condylomata were irradiated and the plume was collected in a buffered saline bubble chamber in line with a vacuum system (flow rate NR), and analyzed using DNA hybridization. (Clinical)	HPV	CO_2 (D = 3200 W/cm^2, CM)	Viral DNA was found in the plume of 2 of 3 patients; an analysis of the original specimen for the third patient revealed the absence of HPV DNA.
Ferenczy et al. (1990)			
Genital lesions (60% of which were HPV DNA +) were irradiated, and the plume was collected using a standard smoke evacuator; samples were taken from the in-flow end of the disposable prefilter canister (65 patients) and from the inner surface of the distal end of the disposable vacuum tube (45 patients). DNA hybridization was performed. The operating room contained a wall mounted exhaust system. (Clinical)	HPV	CO_2 (D = 500–2000 W/cm^2, CM and pulsed)	Viral DNA was found in 1 of the 5 (20%) canisters, and in none of the vacuum tubes.
Baggish et al. (1991)			
Tissue culture pellets infected with HIV were irradiated, and the plume was evacuated through sterile tubing, then bubbled through sterile culture medium (Roswell Park Memorial Institute [RPMI] medium) positioned in series with a commercial smoke evacuator (flow rate NR). Tissue culture and polymerase chain reaction (PCR) studies were performed on the debris. (Laboratory)	HIV	CO_2 (P = 20 W, D = 500 W/cm^2, SD = 1.5–2.5 cm, CM)	No HIV DNA was detected in the culture medium flask, PCR analysis of particulate debris obtained from the silastic collection tubing was positive from proviral HIV DNA
Starr et al. (1992)			
Culture mediums containing SIV were irradiated, the plume was evacuated through sterile tubing, and bubbled through a sterile culture RPMI medium positioned in series with a commercial smoke evacuator (flow rate NR), and the resulting plume was cultured. (Laboratory)	SIV	CO_2 (D = 400 W/cm^2 and 1600 W/cm^2, CM)	All test cultures remained negative over an 8-week incubation period.
Kunachak et al. (1996)			
Recurrent laryngeal papilloma specimens were irradiated and the plume was collected on a filter attached to a tube connected to a vacuum source (flow rate NR). Samples were cultured, and assessed for infectivity. (Laboratory)	HPV	CO_2 (P = 10 W, SD = 0.5 mm, D = 1667 W/cm^2, CM)	No cell growth was observed in the cultures over the 45-day incubation period, and viral infectivity was not demonstrated.

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TABLE III. Summary of the Investigations of the Presence of Cellular Matter, Viruses, and Bacteria in the Laser Plume (Continued)

Methods Description (Study Design)	Infectious Agent[A]	Type of Laser (Operational Parameters)[B]	Results
		Viruses	
Taravella et al. (1997)			
Embryonic lung fibroblasts infected with attenuated varicella-zoster virus were irradiated, and the plume was collected using a smoke evacuator (set between 1 and 2, flow rate NR) and bubbled through viral culture media. PCR and viral culture analyses were performed on the liquid from the bubble trap and on a swab from the inlet tube from the smoke evacuator. (Laboratory)	Varicella-zoster virus	Excimer (EF = 180 mJ/cm^2, PRR = 10 Hz, SD = 6.5 mm, pulsed)	Viral DNA was detected in the plume and from the swab samples, but live virus could not be demonstrated to have survived ablation.
Ziegler et al. (1998)			
Retrovirus supernatant was placed in a single well in the middle of a 96 well plate and irradiated, surrounding wells were then assayed for the presence of the viral marker genes using reverse transcription-polymerase chain reaction (RT-PCR) and the aerosols were analyzed for infectious viral particles. (Laboratory)	Retrovirus	Erbium:YAG (PE = 60 mJ, SD = 1.2 mm, PD = 250 μs, PRR = 7 Hz)	The laser plume contained viable cells and infectious retroviruses that remained infectious and capable of integrating into the genome of susceptible cells.
Hughes and Hughes (1998)			
Human warts were irradiated and a wipe sample was taken from the laser hand piece and analyzed by PCR. The use of a smoke evacuation system was noted. (Laboratory)	HPV	Erbium:YAG (PE = 175 mJ, SD = 2 mm, PRR = 5 Hz)	No viral DNA was found in any of the samples.
Taravella et al. (1999)			
Embryonic lung fibroblasts infected with the oral polio vaccine virus were irradiated, and the plume was collected using a smoke evacuator (set at 1.5, flow rate NR) and bubbled through viral culture media. The inlet tube from the smoke evacuator was swabbed and cultured for virus, as was liquid from the bubble trap. (Laboratory)	Sabin poliomyelitis (oral polio vaccine virus)	Excimer (EF = 160 mJ/cm^2, SD = 6.0 mm, pulsed)	Cultures from the swab taken from the inlet tube leading to the bubble chamber, and from the liquid in the bubble chamber were positive for live virus.
		Bacteria	
Mullarky et al. (1985)			
Porcine skin inoculated with known quantities of *Staphylococcus aureus* and *Escherichia coli* was irradiated, and the plume was bubbled through sterile saline via a vacuum source (flow rate NR) and cultured. The bacterial population on the skin surface following irradiation was also assessed. (Laboratory)	*S. aureus, E. coli*	CO_2 (*Laser 1*: P = 25 W, SD = 0.2 mm, (focused), D = 79,618 W/cm^2, CM; *Laser 2*: P = 25 W, SD = 3.0 mm (defocused), D = 354 W/cm^2, CM)	Irradiation reduced the bacterial population on the skin surface by several orders of magnitude. No *E. coli* was found, but a small number of *S. aureus* cells were isolated in both laser plumes. Nonetheless, the authors reported that the potential for spread of bacteria by the plume was negligible.
Matthews et al. (1985)			
Trial 1: Plume and splatter were sampled during the laser removal of tattoos and		CO_2 (*CM Laser*: D = 249–746 W/cm^2;	*Trial 1:* Red cells were found in the splatter and increased with

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TABLE III. Summary of the Investigations of the Presence of Cellular Matter, Viruses, and Bacteria in the Laser Plume (Continued)

Methods Description (Study Design)	Infectious Agent[B]	Type of Laser (Operational Parameters)[B]	Results
		Bacteria	
rodent ulcers using a Porton raised-capillary impinger (flow rate = 12 L/min). Following the procedures the medium was passed through a 5-μm nucleopore membrane that was placed on a slide, fixed, and stained for evaluation. (Clinical) *Trial 2*: Post-mortem human skin was inoculated with *Bacillus subtilis var. globigii* spores, placed in a perpex box and irradiated. The plume was sampled using an impinger (flow rate = 12 L/min) and slit sampler (flow rate = 30 L/min), and the impinger fluid was passed through a membrane filter which was placed on a blood agar plate. (Laboratory)	*Bacillus subtilis var. globigii*	*Pulsed Laser*: D = 249–7,073 W/cm^2, PD = 0.05–0.2 s)	increasing power; squames were also reported, but there was no relationship between the number of cells found and the laser power. Red cells were found in the laser plume at all power settings, and the presence of squames were also reported, but to a much lesser extent. *Trial 2:* No spores were detected in any of the slit sampler samples. A few colonies were found with low levels of irradiation (249 W/cm^2) in both the splatter and the plume, and no colonies were present in samples collected when the irradiance > 750 W/cm^2.
Walker et al. (1986)			
Fresh post-mortem skin was injected with *B. subtilis* spores and vaporized in a Perspex box. Samples of the plume and the splatter were collected using impingers (flow rate = 15 L/min), and cultured on a blood agar plate. (Laboratory)	*Bacillus subtilis var. globigii*	CO_2 (*CM Laser*: D = 249–7073 W/cm^2; *Pulsed Laser*: D = 249–746 W/cm^2, PD = 0.05–0.2 s)	Viable spores were found following the vaporization of 5 of 13 specimens treated at an irradiance of <500 W/cm^2; no spores were found in the specimens treated at an irradiance >997 W/cm^2.
Byrne et al. (1987)			
S. aureus and *E. coli* seeded agar roll tubes that were designed to simulate the vaginal vault were irradiated. Plume samples were collected using a slit sampler (flow rate = 30 L/min), and the resulting debris in the tubing for the sampler and on the walls of the roll tubes was collected and cultured. (Laboratory)	*S. aureus, E. coli*	CO_2 (*CM Laser*: P = 6–43 W; *Pulsed Laser*: P = 6–30 W, PD = 0.05–2s, PRR = 4 Hz (maximum))	Irradiation at most power settings resulted in the dispersion of *S. aureus* and *E. coli* colonies <10 mm from the target. Dispersion was also observed at more distant sites in the tube and was much more frequent for *S. aureus* than *E. coli*. Viable bacteria were detected in the plume in all instances, and *S. aureus* was found to be more resistant to the thermal effects of lasing than *E. coli.*
McKinley et al. (1994)			
Extracted teeth were inoculated with *E. coli*, and during irradiation an agar plate was inverted over the target site to collect the plume. (Laboratory)	*E. coli*	Argon (P = 2 W, PD = 0.1 s, CM and pulsed)	Following an incubation period, all of the plates were positive for *E. coli.*
Capizzi et al. (1998)			
Plume samples were collected during laser resurfacing of the periorbital, perioral and full-face regions, using HEPA filters affixed to a smoke evacuator (flow rate NR); both bacterial and viral cultures were obtained per filter. (Clinical)	*Staphylococcus, Corynecacterium, Neisseria*	CO_2 (D = 500 mJ/cm^2, pulsed)	Coagulase-negative *Staphylococcus* was detected in 5 of 13 bacterial cultures, one exhibited simultaneous growth of *Corynebacterium* and another with *Neisseria.* No growth was observed in any of the viral cultures.

[A:] HPV = Human Papillomavirus; BPV = Bovine Papillomavirus; HIV = Human Immunodeficiency Virus; SIV = Simian Immunodeficiency Virus.
[B:] Operational parameter abbreviations: PE = Pulse energy (mJ, J); PD = Pulse Duration (μs, ms, s); SD = Spot Diameter (mm, cm); CM = Continuous Mode; P = Power; D = Power Density (W/cm^2); PI = Peak intensity (W/cm^2); EF = Energy Fluence (mJ/cm^2); PRR = Pulse Repetition Rate (Hz); NA = Not Applicable.

TABLE IV. Summary of the Investigations of the Health Effects Associated with Exposure to the Laser Plume

Methods Description	Type of Laser (Operational Parameters)[A]	Results
	Mutagenicity, Genotoxicity, and Cytotoxicity	
Tomita et al. (1981)		
An excised canine tongue was irradiated in a closed box for 60 sec; the smoke condensates were collected and mutation assays were performed using *Salmonella typhimurium* TAl00 and TA98 in the presence and absence of an S9 mix.	CO_2 (P = 15 W, CM)	The laser induced condensates showed mutagenicity on TA98 in the presence of the S9 mix in a dose-dependent manner. On the contrary, TAl00 was roughly 10-fold less sensitive to the laser condensates.
Stocker et al. (1998)		
Four types of porcine tissue (adipose (A), skin (S), striated muscle (SM) and liver (L)) were irradiated in a sampling chamber. Aerosols were evacuated through a glass fiber filter, and then passed through adsorbers. Human leukocytes were incubated with the laser pyrolysis products (LPP), and assessed using the comet assay genotoxicity, cytotoxicity, mutagenicity, and viability.	CO_2 (P = 10 W, D = 1 kW/cm^2, SD = 1.1 mm, CM)	The particulate fraction (PF) of the aerosols emerging from SM and L resulted in an elevation in DNA strand breaks ($p < 0.001$). The low volatile and highly volatile aerosol fractions of the L induced significantly elevated strand break frequencies in 3 of 4 experiments. The PF of the liver LPP was minimally cytotoxic; viability was not significantly affected by exposure to other fractions of the liver LPP or by LPP from other tissues. The PF of the S, SM, and L were mutagenic, and effects were most pronounced with pyrolysates liberated from liver tissue.
Plappert et al. (1999)		
Four types of porcine tissue (A, S, SM, and L) were irradiated in a sampling chamber. Aerosols were evacuated through a glass fiber filter. Genotoxicity and clastogenicity were assessed using the in vitro sister chromatid exchange (SCE) test and the micronucleus test. Cell viability was assessed using the flourochrome-mediated viability assay, and using the hypoxanthine phosphoribosyl-transferase (HPRT) test, and mutagenicity in mammalian cell cultures was assessed.	CO_2 (P = 10 W, D = 1 kW/cm^2, SD = 1.1 mm, CM)	The particulate fraction of the laser plume was a strong inducer of cytotoxic effects, and induced positive test results in the SCE, micronucleus and HPRT tests, indicating genotoxicity, clastogenicity, and mutagenicity. In general, the liver pyrolysates had the most pronounced effects, and in all systems the effects were dose-dependent.
	Laboratory/Animal Studies: Respiratory Effects and Behavioral Changes	
Baggish and Elbakry (1987)		
Rats were exposed in an exposure chamber to the plume produced by ablation of porcine skin at various intervals. Lungs of animals were analyzed post-mortem for pathologic changes, and animals were observed for behavioral changes.	CO_2 (P = 20 W, SD = 1.5–2.0 mm, CM)	Fine particulate matter was deposited in the alveoli and caused pathologic changes consistent with interstitial pneumonia, bronchiolitis and emphysema. Severity was proportional to exposure duration. Experimental animals became sluggish and stopped active movement.
Freitag et al. (1987)		
Sheep were intubated nasopharyngeally and exposed in a chamber to smoke from the vaporization of sheep bronchial tissue. Mucocilliary clearance and airway mechanics measurements were performed as well as a bronchoalveolar lavage. In addition, the concentration of carbon monoxide in the plume was measured using a URAS device, and PM concentration and mass median diameter in the plume was determined using a cascade impactor.	Nd:YAG (P = 15 to 75 W, mode not reported)	Sampling revealed a carbon monoxide concentration of 0.04%, and a particulate concentration of 0.92 mg/L with a mass median aerodynamic diameter of 0.54 μm. Mucociliary clearance was significantly depressed in a dose-dependent manner ($p < 0.05$), and plume exposure was associated with transient hypoxia. Smoke inhalation also induced a severe inflammation with dramatic increases of inflammatory cells in the lung.

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TABLE IV. Summary of the Investigations of the Health Effects Associated with Exposure to the Laser Plume (Continued)

Methods Description	Type of Laser (Operational Parameters)[A]	Results
Laboratory/Animal Studies: Respiratory Effects and Behavioral Changes		
Baggish et al. (1988)		
The experimental design was similar to that employed by Baggish et al. (1987), except the plume was filtered prior to being introduced to the exposure chamber. Rats were exposed to the filtered plume produced by ablation of porcine skin intermittently for 2 weeks. Two sets of filtration devices were affixed to the standard exhaust system and tested using 6 rats each: a cartridge filter, and a cartridge filter plus an ultra-low penetration air (ULPA) filter. Lungs of animals were analyzed for pathologic changes, and animals were observed for behavioral changes.	CO_2 (P = 20 W, SD = 1.5–2 mm, CM)	Animals exposed to the cartridge filtered air experienced pathologic changes that were similar but to a lesser extent than those seen by Baggish et al. (1987) in animals exposed to the unfiltered plume. Interstitial pneumonia and congestion were identified, but emphysema was diminished, and both terminal bronchiolar hyperplasia and peribronchiolar monocytic infiltration were observed. No pathologic changes were observed in the animals exposed to the dual-filtered air, or the control animals. No behavioral changes were observed in any of the study animals.
Wenig et al. (1993)		
Rats were exposed in an exposure chamber to the plume generated by irradiating porcine skin in the following manner: 2-min intervals 4 times a day for 4 days, 4-min intervals 4 times a day for 7 days, 4-min intervals 4 times a day for 14 days. Lungs of animals were analyzed for pathologic changes, and animals were observed for behavioral changes.	Nd:YAG (P = 15–20 W, contact and noncontact modes, CM)	Histologic analysis revealed alveolar congestion and emphysematous changes that were not dependent on the duration of plume exposure; similar changes in control animals were seen, but to a lesser extent. Within 1 to 1.5 minutes of smoke inhalation, the study animals became sluggish and active movement ceased. Activity resumed during rest periods. However, when exposure resumed, activity stopped completely.
Laboratory/Animal Studies: Viral Transmission		
Wisniewski et al. (1990)		
Phase 1: Vulvar condylomata was irradiated through a cylinder, and the deposited ejecta was collected, fixed, stained and examined using electron microscopy and Southern Blot viral hybridization. Cervical intraepithelial neoplasias were also irradiated, and ejecta that had deposited a speculum was collected, and analyzed in the same manner. In both cases a standard smoke evacuator was employed. *Phase 2:* BVP infected tissue was irradiated through a cylinder; the ejecta was collected and the plume was collected using a saline bubble trap. The ejecta washings were mixed with the plume concentrate and injected into subcuticular tissue in susceptible animals.	CO_2 (*Laser 1*: P = 15W, SD = 1.5 mm, D = 666 W/cm^2, CM [Phase 1 and 2]; *Laser 2*: P = 13 W, superpulse [Phase 1 only])	*Phase 1:* Electron microscopy of the vulvar ejecta revealed only anucleate keratinized squamous epithelial cells, and no intact viral or bacterial organisms. (In one instance deposition of the laser ejecta was observed on the eyeglasses of a surgeon 1 m from the site of laser impact). Electron microscopic examination of the cervical debris revealed similar cells, with vaporization of intracellular water and condensation of cellular carbon. Intact viral or bacterial organisms were also absent. In all instances Southern Blot analysis of the laser ejecta revealed insufficient quantities of DNA for testing. *Phase 2:* Following 70 days of observations, viral transmission was not observed.
Nahhas et al. (1991)		
Hamsters were exposed to the plume generated during laser therapy for intraepithelial neoplasia or condylomata acuminate at irregular intervals over 47 separate days, for a total exposure duration of 34 hours. Animals were sacrificed, autopsied, and samples of grossly abnormal tissue were obtained. When grossly abnormal findings were not observed,	CO_2 (mode and parameters not reported)	Interstitial pneumonitis was observed in 1 of 5 experimental and 3 of 5 control animals, thus was assumed to be unrelated to plume exposure. Light microscopic changes of HPV infection were not observed in any of the animals, and none of the viral DNA probes used hybridized to nuclear DNA in the epithelial cells.

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TABLE IV. Summary of the Investigations of the Health Effects Associated with Exposure to the Laser Plume (Continued)

Methods Description	Type of Laser (Operational Parameters)[A]	Results
	Laboratory/Animal Studies: Viral Transmission	
the cheek pouches and entire respiratory tract were removed. In addition, paraffin blocks of all tissue were submitted for virologic studies.		
Hagen et al. (1997)		
Pseudorabies virus-inoculated tissue culture plates were ablated; an uninoculated tissue plate was positioned in an inverted position over the inoculated plate. The un-inoculated plate was observed for 96 hours to determine if transmission had occurred.	Excimer (EF = 150 and 180 mJ/cm^2, SD = 4 mm, pulsed)	None of the 20 uninoculated cell culture plates provided evidence of transmission.
Garden et al. (2002)		
BVP-induced cutaneous fibropapillomas were irradiated, and the plume was collected in a phosphate-buffered saline (PBS) bubble chamber in line with a vacuum system (500 mm Hg), analyzed for the presence of BVP DNA using DNA extraction and electrophoresis, and reinoculated into the skin of susceptible calves.	CO_2 (*Laser 1*: P = 12 W, SD = 2 mm, D, 380 W/cm^2; EF = 400 J/cm^2, CM; *Laser 2*: P = 4 W, SD = 2 mm, D = 130 W/cm^2, EF, 130 J/cm^2, CM; *Laser 3*: P = 8 W, SD = 0.2 mm, PD = 0.1 s, D = 25,400 W/cm^2, EF = 2540 J/cm^2, pulsed)	The plume was shown to contain BVP DNA. In addition, tumors developed at inoculated sites for all of the laser settings tested, and histological and biochemical analyses revealed that these tumors were infected with the same virus type present in the laser plume.
	Human Health Studies: General Acute and Chronic Health Effects	
Moss et al. (1990)		
As part of a health hazard evaluation that took place at a university health sciences center, NIOSH investigators interviewed 11 workers to determine the type and extent of health complaints experienced by medical personnel involved in laser procedures.	NA	None of the respondents indicated that they had experienced any health effects resulting from plume exposure; however, all the respondents had smoke evacuators available for use. Most of the complaints voiced at the test facility focused on odor and vision impairment; many of these complaints occurred when CO_2 and argon lasers were used to irradiate external body parts.
Gates et al. (2007)		
A prospective population-based epidemiological investigation of 86,747 women in the Nurses' Health Study was conducted to determine if duration of employment as an operating room nurse (a proxy measure for surgical smoke exposure) was associated with increased lung cancer risk. Information on the duration of prior operating room employment was collected in 1984, and participants were followed for incident, confirmed lung cancer, or until June 2000.	NA	A total of 859 incident cases of lung cancer occurred during the study period. Long-term exposure to surgical smoke, as measured by duration of operating room employment was not associated with an increased risk of lung cancer. Notably, nurses in the highest exposure category ($\geq$15 years of operating room employment) had a significantly lower rate of lung cancer than nurses with no prior operating room employment (RR 0.58, 95% CI 0.37–0.91).

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TABLE IV. Summary of the Investigations of the Health Effects Associated with Exposure to the Laser Plume (Continued)

Methods Description	Type of Laser (Operational Parameters)[A]	Results
	Human Health Studies: Viral Transmission	
Lobraico et al. (1988)		
A retrospective analysis was conducted to determine the incidence of acquired HPV lesions among medical laser users and factors that are associated with an increased incidence of such lesions. Questionnaires (N = 4500) were distributed to a multispecialty group of physicians and nurses. Responses were received from 824 individuals representing 11 specialty groups, and of these individuals, 30 were excluded due to their involvement in laser procedures other than verrucae ablation.	CO_2 (NA)	Of the 794 respondents who reported treating verrucae, 26 lesions were reported (incidence = 3.2%). The highest incidence was observed in dermatologists (15.2%), followed by gynecologists (1.7%) and podiatrists (1.6%). An association between the use of the CO_2 laser for the treatment of verrucous lesions and the development of such lesions by physicians was observed, but it was concluded that this was likely due to direct contact with lesions rather than plume exposure (i.e., no lesions were reported in the buccal mucosa or larynx).
Hallmo and Naess (1991)		
Case study examining the association between laryngeal lesions in a laser surgeon and occupational exposure to the laser plume using DNA hybridization.	Nd:YAG (NA)	In situ DNA hybridization of the tissue from the surgeon's tumors revealed HPV DNA types 6 and 11, which are commonly harbored in anogenital condylomas. The case had no known source of infection other than the surgeon's own patients, thus it was concluded that the transmission was more likely than not occupationally related.
Gloster and Roenigk (1995)		
A comparative study was conducted between CO_2 laser surgeons and population-based controls (Olmsted County, and patients treated for warts at Mayo Clinic) to determine if surgeons were at increased risk of acquiring HPV as a result of exposure to the plume produced during the treatment of warts. Questionnaires were sent to 4200 members of two professional societies, regarding the length of time and frequency of CO_2 laser treatment of warts, the precautions taken, the anatomical sites of treated warts, and whether the surgeon had developed warts since the use of the CO_2 laser, and if applicable the anatomical sites of the warts. The survey response rate was 14% (N = 570).	CO_2 (NA)	The overall incidence of warts (all anatomic sites) among the laser surgeons was found to be no different than the incidence in Olmsted County. Statistically significant decreased incidences of plantar and genital/perianal were reported in laser surgeons when compared with the Mayo Clinic control group. An increased incidence of nasopharyngeal lesions was found in laser surgeons relative to the Mayo Clinic controls, thus it was concluded CO_2 laser surgeons are at increased risk of acquiring nasopharyngeal warts through inhalation of the HPV containing laser plume. No difference in the rate of precautionary measure usage was observed between surgeons with and without warts, and no relationship was observed between the cumulative exposure to the laser plume and the incidence of acquired warts among laser surgeons.
Calero et al. (2003)		
Case study examining the association between laryngeal papillomatosis in a gynecological operating room nurse and occupational exposure to the laser plume.	CO_2 (NA)	A virologic analysis confirmed a high probability of correlation between the occupational exposure to HPV DNA and the laryngeal papillomatosis; thus it was concluded that the transmission was occupationally related.

[A]Operational parameter abbreviations: P = Power (Watts); D = Power Density (W/cm^2, kW/cm^2); SD = Spot Diameter (mm), CM = Continuous Mode, EF = Energy Fluence (mJ/cm^2, J/cm^2), PD = Pulse Duration (s); NA = Not Available.

irradiation of excised canine tongue, the authors concluded that the mutagenic potency observed was comparable to that of cigarette smoke, and that irradiation of 1 gram of tissue with a CO_2 laser had the same hazard potential as smoking three unfiltered cigarettes. In subsequent analyses, laser pyrolysis products (LPP) resulting from CO_2 laser irradiation of various tissue types have been shown to be mutagenic, clastogenic, cytotoxic, and genotoxic.[43,44] In addition, the toxicity of the pyrolysates was found to be largely dependent on the type of tissue irradiated.[43,44]

Laboratory/Animal Studies: Respiratory Effects and Behavioral Changes

Four studies were reviewed that examined respiratory effects and behavioral changes experienced in animals following exposure to the laser plume.[45–47] Specifically, two types of lasers (CO_2 and Nd:YAG) and two irradiated tissue types (pig skin and sheep tongue) have been evaluated. Two studies have reported pathological changes in animals following plume exposure that were consistent with interstitial pneumonia, bronchiolitis, and emphysema, similar to what is observed after long-term inhalation of other PM;[45,47] only one of these studies reported that severity of these changes increased proportionately as a function of the duration of exposure. In a subsequent analysis of the effects of plume filtration, animals exposed to the cartridge filtered air experienced pathological changes that were similar, but to a lesser extent, than those seen following exposure to the unfiltered plume, and no pathologic changes were observed in the animals exposed to the dual-filtered (a cartridge filter plus an ultra-low penetration air [ULPA] filter) plume.[46] Impaired mucocilliary clearance, transient hypoxia, and increases in inflammatory cells in the lungs of experimental animals have also been reported.[19] Two studies reported that almost immediately upon the initiation of unfiltered plume exposure, experimental animals became sluggish and stopped active movement.[45,47]

Laboratory/Animal Studies: Viral Transmission

Four animal studies (five separate analyses) have evaluated the possibility of viral transmission due to exposure to the laser plume. Two analyses have been conducted using a CO_2 laser to irradiate human papillomavirus (HPV)-infected tissue,[48,49] one using an excimer laser to irradiate pseudorabies virus-inoculated tissue culture plates,[50] and two using a CO_2 laser to irradiate bovine papillomavirus (BPV) lesions.[49,51] The experimental methodologies employed in these investigations differed drastically; thus, the results are somewhat difficult to compare. Nonetheless, three of these studies (four separate analyses) found no evidence of viral transmission,[48–50] but one reported transmission.[51]

Human Health Studies: General Acute and Chronic Health Effects

Two studies have evaluated general acute and chronic health effects in medical personnel involved in laser procedures. A small survey was conducted by NIOSH on 11 workers involved in laser procedures. The questionnaire administered by NIOSH specifically requested information about the occurrence of the following health effects (and included a section for "other symptoms"): changes in sense of smell, blurred vision, watery eyes, sore throat, headaches, dizziness, skin rashes, lung problems, allergies, coughing, and facial/nasopharyngeal warts. None of the respondents indicated that they had experienced any health effects from plume exposure.[6] However, several complaints were noted related to smells, odors, and vision impairment. To date, only one epidemiological investigation has been conducted to assess the health effects related to exposure to the surgical plume.[52] The study examined lung cancer risk in registered nurses and concluded that their risk was not elevated compared with the referent population; however, no exposure data were collected during this investigation.

Human Health Studies: Viral Transmission

Two studies have examined the risk of acquiring lesions due to viral transmission in health care personnel involved in laser procedures,[53,54] only one of which supported viral infection via inhalation of the laser plume. In addition, two clinical case reports have suggested the occurrence of viral transmission as the result of medical laser use, both of which described laryngeal papillomatosis in health care workers who performed laser therapy on patients with anogenital condylomas. In both cases, virologic analyses confirmed or suggested a causative link between occupational exposure to HPV DNA in the laser plume and the laryngeal papillomatosis.[55,56]

Control and Prevention

Engineering Controls

To reduce exposure to the surgical plume, the recommended air exchange rate provided by dilution ventilation is a minimum of 15 air changes per hour, and all rooms should be maintained at positive pressures.[3,57,58] However, it is generally recognized that dilution ventilation is insufficient to effectively control smoke generated at the surgical site.[10]

Local smoke evacuation systems have been recommended by many consensus organizations (ACGIH®, Association of Operating Room Nurses, American Society for Laser Medicine and Surgery, ECRI, and NIOSH) and may improve the quality of the operating field and the work environment.[3,59,60] Nonetheless, smoke evacuation devices have not been used on a routine and consistent basis in many operating rooms. A recent web-based survey was conducted to assess the frequency of local exhaust ventilation (LEV) and respiratory protection use during laser procedures among Association of Operating Room Nurses members.[61] Researchers found that the frequency of smoke evacuator use was largely dependent on the procedure being performed. Specifically, smoke evacuators were "always or often" used regularly by respondents during condyloma or dysplasia ablation (83%), and other CO_2 laser procedures (75%), and the reports of "never or seldom use" for the two procedures were 10% and 14%, respectively. On the contrary, smoke evacuators were "always

or often" used by less than 20% of the respondents during endoscopy/bronchoscopy, laparoscopy/arthroscopy, and laser-assisted in situ keratomileusis (LASIK), and "never or seldom" use during these procedures was reported for greater than 70% of the respondents. The authors reported that overall, effective engineering controls (i.e., LEV) were being used in fewer than half of the facilities represented by the survey respondents for most laser procedures.

An additional survey in the U.K. revealed that only 3 of 98 surgeons used dedicated smoke extractors, although 72% of surgeons felt that inadequate precautions were taken to protect staff and patients from surgical smoke.[16,62] The lack of integration of LEV is believed to be due to the resistance on the part of health care organizations, surgeons, and perioperative personnel.[7,63] This resistance has been attributed to the lack of knowledge about the potential health hazards associated with exposure to the surgical plume, and desensitization to the offensive odor that accompanies laser procedures.[7] In addition, although OSHA does regulate a wide range of substances found within surgical plumes (e.g., benzene, formaldehyde, hydrogen cyanide), OSHA does not specifically require the use of smoke evacuation and filtering systems.[2,3,64]

The following three components of an efficient evacuation system have been proposed in the literature: (1) a capture device that does not interfere with the surgeon's activities, (2) a vacuum source that has strong enough suction to remove the smoke properly, and (3) a filtration system that is capable of filtering the smoke and making the environment safer.[2,65] To effectively capture airborne contaminants, the suction tip must be placed as close to laser impact as possible. Specifically, NIOSH recommends that the suction nozzle of a local smoke evacuator be kept within 2 inches of the surgical site, and others have reported that the nozzle inlet must be within 1 cm of the surgical site to effectively remove the plume.[10,66] Under both scenarios, it is unlikely that the device is not an impediment to surgical activity, at least to some degree. Karoo et al.[67] designed and tested a simple and reportedly effective method for removing surgical plume. A standard piece of silicone suction tubing was secured to the probe of a hand-held laser unit, roughly 5 cm from the laser tip. At a suction pressure of 30 kPa, the authors reported that the apparatus provided uptake of virtually the entire plume with no adverse effects on cutting or coagulation. This conclusion was based on observation and not confirmed by air monitoring.

NIOSH also recommends the use of systems with capture velocities of 100–150 ft/min that are equipped with a high-efficiency particulate air (HEPA) filter or an equivalent filter. However, it has been suggested that the most effective portable smoke evacuation system is the triple filter system equipped with an ultra-low particulate air (ULPA) filter. These systems include a pre-filter, designed to capture large PM; a charcoal filter; and an ULPA filter.[3] The ULPA filters are capable of capturing 0.01 μm particles at an efficiency rating of 99.9999%, while HEPA filters have capture efficiencies of 99.97% at 0.3 μm.[10,63]

Personal Protective Equipment

It is generally accepted that standard surgical masks provide inadequate protection against exposure to LGACs.[2,3,5,18,63,68] Although surgical masks are relatively efficient at capturing particles with diameters of 5 μm and larger, the laser surgical plume consists of PM that is on average over an order of magnitude smaller, making them highly penetrable. High filtration masks, also known as laser or submicron masks, reportedly filter particles to about 0.1 μm in size.[3,63] However, viral particles can be much smaller than 0.1 μm, and like standard surgical masks, poor fit can severely compromise filter performance. In addition, while N95 respirators provide $>$ 95% filter efficiency when tested with $\sim$0.3 μm sodium chloride aerosol, and grade 100 provide $>$ 99.97% efficiency, various studies have demonstrated that respirators are still insufficient at completely preventing plume exposure.[2,16]

In 2006, an assessment was performed with eight volunteers to compare the particle filtration efficiency of the surgical mask and a laser mask with that of a full-facepiece 2 (FFP2) respirator (minimum filtration efficiency of 94% for particles of 0.3 μm aerodynamic diameter, with a maximum total inward leakage of 8%).[69] The hypothesis was that when a mask of standard surgical design is worn, most of the particles enter the wearer's breathing zone through leaks at the sides of the mask rather than by penetrating the filter material.

To test this hypothesis, the surgical and laser masks were tested when worn normally and when they were taped to the face. Submicron particle counts (0.02 to 1 μm diameter) inside and outside the three protective devices were measured using a standard in vivo respirator performance testing protocol. The mean reductions in particle counts were 3.0-fold for the untaped surgical mask, 3.8-fold for the untaped laser mask, 7.5-fold for the taped surgical mask, 15.6-fold for the taped laser mask, and 102.6-fold for the FFP2 respirator. Statistical comparison between the following five groups was made: surgical mask vs. laser mask, ($p = 0.05$); surgical mask vs. taped surgical mask ($p = 0.01$); laser mask vs. taped laser mask ($p = 0.01$); laser mask vs. FFP2 respirator ($p = 0.02$); and taped laser mask vs. FFP2 respirator ($p = 0.025$). Based on these results, the authors concluded that a substantial fraction of the submicron-sized particles penetrate filter material itself, even with the improved filter material used in the laser mask, and that taping masks to the face provided only a small improvement in protection. Furthermore, the authors opined that laser masks, although marginally more protective than standard surgical masks, provide significantly less protection than the FFP2 respirator in filtering submicron-sized particles.

In the previously described investigation by Edwards and Reiman,[61] the authors also found that while the frequency of smoke evacuator use was low, even lower use rates were observed for respiratory protection equipment. Specifically, the highest frequency of "always or often" N95 respirator use was reported for condyloma or dysplasia ablation at 21%; however, 75% of respondents reported "never or seldom" use

of N95 respirators during this procedure. Likewise, the highest frequency of "always or often" laser mask use was also reported for condyloma or dysplasia ablation (73%), but 20% of respondents reported "never or seldom" using laser masks. On the contrary, 12% or less of the respondents reported "always or often" use of N95 respirators during all other procedures analyzed (including various CO_2 and Nd:YAG procedures; cosmetic and plastic surgery; malignant, benign, and vascular skin lesion removal; hair removal; endoscopy/bronchoscopy; laparoscopy/arthroscopy, and LASIK). Laser mask "always or often" use was reported by 72% of respondents during CO_2 laser tissue resection and other procedures; however, "always or often" use was reported by less than 50% of respondents during Nd:YAG procedures; cosmetic and plastic surgery; malignant, benign, and vascular skin lesion removal; hair removal; endoscopy/bronchoscopy; laparoscopy/arthroscopy, and LASIK.

DISCUSSION

Chemical Composition and Concentrations in the Laser Plume

The dependence of the chemical composition of the laser plume on laser type and operational parameters is to date poorly understood,[10] and only three studies have attempted to quantify the airborne concentration of the chemical constituents in the surgical or laboratory setting.[6,9,15] Nonetheless, these analyses lacked sufficient information on the laser operational parameters, sampled different chemicals in different settings and exposure scenarios, and the results were not stratified by the laser device or application. Therefore, although they provide a starting point for investigation, not much information by way of actual concentrations and the factors that influence exposure can be gleaned from these manuscripts.

Particulate Matter (PM) Concentration and Size Distribution

There have been too few studies, each accounting for different tissue types, laser devices, and operational parameters, to draw any definitive conclusions with respect to the true range of PM diameter. Furthermore, several of these studies sampled at locations that were within centimeters of the operative site; thus, it is not clear how the size distributions measured correspond to those experienced in the breathing zone of laser operators. The generation of a more comprehensive data set that is representative of the various possible exposure scenarios is imperative for designing adequate control strategies.

Although the results reported from two of the three investigations are fairly consistent with respect to the respirable PM concentrations in the laser plume, there are too few data points to make an informed approximation as to the actual PM exposure experienced by health care personnel. In addition, Tanpowpong and Koytong[20] measured $PM_{2.5}$, and the actual size fraction measured by Albrecht et al.[15] was not reported (only reported as respirable). Measured concentrations do not exceed the current OSHA permissible exposure limits (PELs) or the ACGIH threshold limit values (TLVs®) for total or respirable PM. However, the results of the study conducted by Tanpowpong and Koytong[20] are not comparable, and the results from Albrecht et al.[15] may not be comparable to these OELs due to the size fraction of the PM measured, and due to the fact that the aforementioned standards do not apply to biologically active PM. Nonetheless, there is no current enforceable or recommended exposure guideline that applies to the PM fraction of the laser plume. Freitag et al.[19] reported a PM concentration of 0.92 mg/L (920 mg/m^3), which is roughly 60-fold the current OSHA standard for total particulates not otherwise regulated (PNOR). It is not clear whether the results reported by Freitag et al. were an accurate representation of the measured concentration; however, this discrepancy has yet to be discussed in the published literature.

Contaminant concentrations reported in each of these studies were likely critically dependent on local ventilation conditions, yet this information was rarely noted in the literature. Furthermore, in many instances the researchers incorporated the LEV into their sampling flow train; thus, even when LEV was utilized, its efficiency may have been compromised. Nonetheless, ventilation system characteristics were summarized in the corresponding tables as reported by the authors of the original publications.

The Presence of Cellular Matter, Viruses, and Bacteria in the Laser Plume

There are numerous factors that have been hypothesized to influence the presence of viable cellular and viral matter in the laser plume, mainly, laser type, laser procedure/application, and irradiance or output power; thus, it is not surprising that the results presented herein are not entirely consistent. It has been suggested that viral size and the presence of a lipid envelope may also impact the ability of a virus to survive ablation.[33] Although the results of all the studies examining the presence of bacteria in the plume were consistent in that each reported dissemination of bacterial cells when the laser devices were used at low irradiances, only two laser types were tested, and it is not clear if there is a threshold level of irradiance that applies to all laser types above which bacterial dissemination does not occur.

Health Effects Associated with Exposure to LGACs

Although, collectively, there have been numerous animal and laboratory studies that have assessed the health effects resulting from LGACs exposure, there are still significant gaps in the literature that need to be addressed. As described herein, pyrolysates resulting from CO_2 laser irradiation of various tissue types have repeatedly been shown to be mutagenic, cytotoxic, and genotoxic.[42–44] Nonetheless, several researchers have demonstrated that the toxicity of the plume is largely dependent on tissue type; thus, more research is necessary to determine the actual risk posed to health care personnel during various procedures.

Excluding case reports of viral transmission in laser operators, which are suggestive at best, only four studies have been conducted to assess health effects experienced by health care personnel involved in laser procedures. Differing methodologies among these very few studies generated inconsistent results regarding virus transmission.

No epidemiologic studies have been conducted to assess the presence of bacterial infection in medical staff exposed to the laser plume. Epidemiologic investigations, in conjunction with exposure assessment, are necessary to assess the presence of LGAC-related effects in laser operators and ancillary personnel.

Control and Prevention

A series of systematic analyses must be conducted to determine the factors that are associated with exposure and consequently health risk (i.e., operational parameters, laser, and tissue types). By way of the precautionary principle, it would be prudent for the occupational health and safety community to ensure the adequate protection of health care personnel operating and assisting in medical laser applications. As described previously, LEV is not consistently used during laser applications, and its use is often dependent on the procedure performed.[61] The human factors aspects that result in the lack of use of LEV warrant exploration so that an effective and acceptable control solution may be attained. In the interim, it is recommended that the use of PPE be implemented and enforced. Targeted health and safety training to communicate the poorly understood risks to health care professionals should also be implemented, while a more definitive assessment of possible health outcomes may be determined. It is the hope of the authors that the evidence gathered in this article may help the occupational hygiene community convey the critical gaps in knowledge that likely influence exposure and affect risk.

CONCLUSIONS

Very few studies have attempted to characterize exposure to laser-generated air contaminants resulting from medical applications, and the effects of laser system type, operational parameters, and tissue treated, as they relate to exposure, are largely unknown. These unknowns continue to grow as new devices and new clinical applications are developed. There is a need for a fundamental laboratory study to systematically account for the array of variables that influence exposure, followed by a broader assessment of exposure to LGACs in the clinical setting. This improved characterization of exposure is important in the determination of an appropriate exposure guidance value. Control technology and intervention effectiveness research is greatly needed in this arena, and epidemiologic study of health care providers exposed to LGACs may be warranted.

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