Ecotoxicology and Environmental Safety 209 (2021) 111855

Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

journal homepage: www.elsevier.com/locate/ecoenv

Sources and components of volatile organic compounds in breast surgery operating rooms

Ming-Huei Cheng[a,b,1], Chun-Hui Chiu[c,d,1], Chi-Tsung Chen[e], Hsu-Huan Chou[e,f], Li-Heng Pao[c,g], Gwo-Hwa Wan[h,i,j,k,*]

[a] Department of Plastic and Reconstruction Surgery, Chang Gung Memorial Hospital, Taoyuan, Taiwan
[b] College of Medicine, Chang Gung University, Taoyuan, Taiwan
[c] Graduate Institute of Health Industry and Technology, Research Center for Chinese Herbal Medicine, Research Center for Food and Cosmetic Safety, College of Human Ecology, Chang Gung University of Science and Technology, Taoyuan, Taiwan
[d] Department of Traditional Chinese Medicine, Keelung Chang Gung Memorial Hospital, Keelung, Taiwan
[e] Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University, Taoyuan, Taiwan
[f] Department of General Surgery, Linkou Chang Gung Memorial Hospital, Taoyuan, Taiwan
[g] Department of Gastroenterology and Hepatology, Linkuo Chang Gung Memorial Hospital, Taoyuan, Taiwan
[h] Department of Respiratory Therapy, College of Medicine, Chang Gung University, Taoyuan, Taiwan
[i] Department of Respiratory Care, Chang Gung University of Science and Technology, Chiayi, Taiwan
[j] Department of Obstetrics and Gynaecology, Taipei Chang Gung Memorial Hospital, Taipei, Taiwan
[k] Center for Environmental Sustainability and Human Health, Ming Chi University of Technology, Taishan, New Taipei, Taiwan

ARTICLE INFO

Edited by: Dr G Liu

Keywords:
Surgical smoke
Breast surgery
Electrosurgical units
Electrocautery power
Volatile organic compounds

ABSTRACT

Objectives: The composition and concentration distribution of volatile organic compounds (VOCs) in surgical smoke had seldomly been reported. This study aimed to investigate the profile of VOCs and their concentration in surgical smoke from breast surgery during electrocautery in different tissues, electrosurgical units, and electrocautery powers.

Methods: Thirty-eight surgical smoke samples from 23 patients performed breast surgery were collected using evacuated stainless steel canisters. The concentrations of 87 VOCs in surgical smoke samples were analyzed by gas chromatography-mass spectrometry. The human tissues, electrosurgical units, and electrocautery power were recorded.

Results: The median level of total VOCs concentrations in surgical smoke samples from mammary glands (total VOCs: 9953.5 ppb; benzene: 222.7 ppb; 1,3-butadiene: 856.2 ppb; vinyl chloride: 3.1 ppb) using conventional electrosurgical knives were significantly higher than that from other tissues (total VOCs: 365.7–4266.8 ppb, $P < 0.05$; benzene: 26.4–112 ppb, $P < 0.05$; 1,3-butadiene: 15.6–384 ppb, $P < 0.05$; vinyl chloride: 0.6–1.8 ppb, $P < 0.05$) using different electrosurgical units. A high methanol concentration was found in surgical smoke generated during breast surgery (641.4–4452.5 ppb) using different electrosurgical units. An electrocautery power of ≥ 27.5 watts used for skin tissues produced a higher VOCs concentration (2905.8 ppb).

Conclusions: The surgical smoke samples collected from mammary glands using conventional electrosurgical knives had high VOCs concentrations. The carcinogens (including benzene, 1,3-butadiene, and vinyl chloride) and methanol were found in the surgical smoke samples from different electrosurgical units. The type of electrosurgical unit and electrocautery power used affected VOCs concentrations in surgical smoke.

1. Introduction

An electrosurgical machine utilizes tissue resistance to the flow of current from the electrode to convert electrical energy into heat. Tissue heating may not completely be achieved during electrosurgical procedures and often accompany by surgical smoke with an unpleasant

* Correspondence to: Department of Respiratory Therapy, College of Medicine, Chang Gung University, Wen-Hwa 1st Road, Kwei-Shan, Taoyuan, Taiwan.
E-mail addresses: minghuei@cgmh.org.tw (M.-H. Cheng), chchiu@mail.cgust.edu.tw (C.-H. Chiu), jackson08036@gmail.com (C.-T. Chen), b9002009@cgmh.org.tw (H.-H. Chou), paolh@mail.cgust.edu.tw (L.-H. Pao), ghwan@mail.cgu.edu.tw (G.-H. Wan).

[1] The author was equally contributed with the first author.

https://doi.org/10.1016/j.ecoenv.2020.111855
Received 30 September 2020; Received in revised form 15 December 2020; Accepted 21 December 2020
Available online 29 December 2020

odor (Massarweh et al., 2006). Surgical smoke is mainly composed of 95% water vapor, 5% suspended particles, bioaerosols, and chemical gases (Ulmer, 2008). Hill et al. (2012) indicated that the average daily diathermy activation time was 12 min and 43 s for surgery, and the surgical smoke production per day is equivalent to smoking 27–30 cigarettes per day.

Three factors such as human tissue, type of surgery, and electrosurgical unit influence the concentration and composition of VOCs. The increase in electrocautery power was not related to the changes in the concentrations of 1,3-butadiene, benzene, and furfural in surgical smoke (Kocher et al., 2019). A Brazil study showed that the components of VOCs in surgical smoke produced when electrocoagulating subcutaneous tissue, pork meat, and liver tissue of pigs were different (Kalil et al., 2016). The concentrations of toluene, ethylbenzene, and xylene produced from verruca extraction surgery were higher than those produced from pilonidal sinus removal surgery and abdominal surgery (Al Sahaf et al., 2007). In addition to styrene, the mean concentrations of benzene, ethylbenzene, toluene, heptane, and methylpropene produced from electrocautery was significantly higher than those from the ultrasonic knife (Fitzgerald et al., 2012). The National Institute for Occupational Safety and Health study indicated that the most common components in surgical smoke were ethanol and isopropyl alcohol; other pollutants, including acetaldehyde, acetone, acetonitrile, benzene, hexane, styrene, and toluene, were also found (Lee et al., 2018). Additionally, the electrocautery time was positively associated with the VOC concentration in the air inside the operating rooms (ORs) (Liang et al., 2020).

The Unites States Occupational Safety and Health Administration (OSHA) estimated that 500,000 health care personnel in ORs were exposed to surgical smoke each year (Occupational Safety and Health Administration OSHA, 2008). A few studies have investigated the health hazards associated with surgical smoke exposure. An *in vitro* study found that surgical smoke exposure can cause apoptosis in 40% of human small airway epithelial cells and 20% of mice macrophages as well as increase the concentration of lactate dehydrogenase in both cell types, causing impairment in the cell membrane structure (Sisler et al., 2018). Moreover, a questionnaire-based study found that the risk of severe persistent asthma in OR nurses was 2.48 times higher than that in the administrative nurse after adjusting for age, body mass index, and smoking history (Le Moual et al., 2013). The risk of lung cancer in OR nurses who worked for over 15 years was 0.58-fold higher than that in nurses who worked in other units of the hospital when adjusted for age, smoking history, secondhand smoke exposure, and fruit and vegetable intake. The working year had no association with the incidence of lung cancer in OR nurses (Gates et al., 2007).

To date, only a few studies have evaluated the composition and change of VOC concentration in surgical smoke under different electrocautery conditions. Therefore, this study aimed to evaluate the profile of VOCs and their concentration distribution in surgical smoke during breast surgery.

2. Materials and methods

2.1. Surgical smoke sampling and analysis

The breast surgery ORs were located on the second floor of an 11-story medical building in Linkuo Chang Gung Memorial Hospital in northern Taiwan. The breast surgery ORs were categorized as ISO 14644–1 class 7 (ISO International Organization for Standardization, 2015) and measured room volumes of 110–140 m^3. Each OR was equipped with high-efficiency particulate air (HEPA) H14 filters, which were changed annually, in the central ceiling of the ORs. The ventilation rate of ORs was 20–22 air changes per hour (ACH) throughout the day and around 85% of the total circulating airflow was returned through four return air vents to the supply air system. The breast surgery ORs were kept at 19–23 °C of set indoor temperature and 55–65% of set relative humidity (RH). Additionally, the OR personnel usually included one surgeon, two scrubbing nurses, one circulating nurse, and one anesthesia nurse.

Altogether, 38 surgical smoke samples from 23 patients were collected during breast surgery (partial mastectomy, simple mastectomy, sentinel lymph node dissection, and breast reconstruction surgery) including breast skin (n = 8), breast adipose tissues (n = 6), mammary glands (n = 10), breast tumors (n = 3), abdominal skin (n = 2), and abdominal adipose tissues (n = 3) using conventional electrosurgical knives as well as breast adipose tissues (n = 3) and mammary glands (n = 3) using pulsed electron avalanche knives (PEAK). Additionally, this study collected 3 air samples during disinfection from patients to evaluate the VOC concentrations in alcohol-based disinfectants.

The surgical smoke samples were collected from the start of cauterization of a particular site. A grab sampling technique was used with a 6 liter of evacuated canister for 30 s followed by the NIOSH sampling method (LeBouf et al., 2012). During the sampling period, the sampling head was placed at 2–3 cm to the surgical site, and the information such as electrosurgical unit, electrocautery power, electrocautery tissue, and indoor thermal–hygrometric conditions of the ORs were recorded. The gas chromatography – mass spectrometry analysis of 87 VOCs in surgical smoke samples was performed using the NIEA A715.15B standard method of Taiwan's Environmental Analysis Laboratory (Environmental Analytical Laboratory (EAL), 2014). The analytical system included an Agilent 6890 series gas chromatograph with HP7673 autosampler, split/splitless injector, MSD detector and DB-1 column (60 m x 0.32 mm x 3.0 μm, Agilent, USA). The parameters were set as follows: oven temperature at 35 °C for 5 min and raised at rates of 10 °C/min to 200 °C, high-purity helium gas flow rate was 2.0 mL/min in constant flow mode, inlet temperature was 125 °C, split ratio was 0.2:1. The temperatures of the interface and the ion source were set at 230 °C and mass scan range was 30–280 *m/z*. All MS data for analytes were collected by ChemStation software. To achieve the quality control and assurance of the analytical data, a standard gas sample (1 ppmv, Linde Spectra Environmental Gases, USA) was prepared and a calibration curve (1–80 ppbv) of 87 VOCs was analyzed for each experiment. All the data of 87 VOCs in standard gas samples and surgical smoke samples from patients were blank-corrected to account for background signal. Additionally, ten percent of the steel canisters were sampled for blank analysis to ensure data quality. The relative difference in duplicate measurements of the samples was below 25%, and the recovery rate of samples ranged between 70% and 130% in this study.

2.2. Statistical methods

This study used the SPSS version 25.0 (SPSS, Chicago, Illinois, USA) for statistical analysis. The figures were graphed using the GraphPad Prism 7.0 software (GraphPad Software, Inc., San Diego, CA, USA). The significance level was set at 0.05. The Kruskal-Wallis test and Mann-Whitney *U* test were used to analyze the changes in VOC concentration in surgical smoke samples in different electrocautery tissues, electrosurgical units, and electrocautery power.

This study combined the VOC data from breast skin with that from abdominal skin and defined as subcutaneous tissues. In addition, VOC data from breast and abdominal adipose tissues were pooled and defined as adipose tissues.

3. Results

During the skin disinfection procedure performed in surgical patients, 23 VOCs were detected in the air samples, indicating that methanol (24.9 ppb) had the highest mean concentration, followed by acetone (12.6 ppb), isopropylbenzene (4.0 ppb), toluene (3.1 ppb), and propane (1.7 ppb) (Fig. 1). Other VOCs included 2-butanone, chloromethane, (*p,m*)-xylene, alpha-methyl styrene, n-undecane, dichlorodifluoromethane, chlorodifluoromethane, n-dodecane, methylene chloride, o-xylene, benzene, trichlorofluoromethane, ethylbenzene, 1,3-

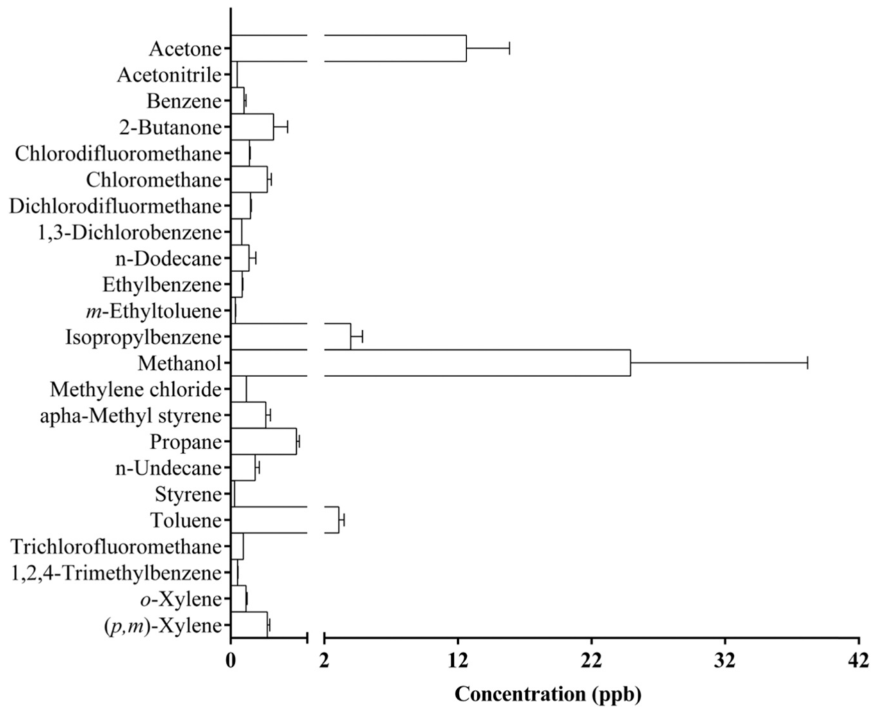

Fig. 1. VOC concentration distribution in background air samples during the skin disinfection procedure. Data were represented as mean and standard error of the mean.

dichlorobenzene, 1,2,4-trimethylbenzene, acetonitrile, m-ethyltoluene, and styrene.

The thermal-hygrometric characteristics of the breast surgery ORs were 18.50–22.95 °C and 41.63–56.46%. The median VOC concentration in surgical smoke samples from mammary glands (9953.5 ppb) was significantly higher than that from breast subcutaneous tissues (2024.4 ppb, $P < 0.001$), breast adipose tissues (1865.9 ppb, $P = 0.001$), and breast tumors (1308.8 ppb, $P = 0.011$) using conventional electrosurgical knives as well as that from breast adipose tissues (365.8 ppb, $P = 0.011$) and mammary glands (4266.8 ppb, $P = 0.011$) using PEAK (Fig. 2).

The mean methanol concentration (1182.9 ppb) in surgical smoke samples from breast subcutaneous tissues using conventional electrosurgical knives was the highest, followed by acetonitrile (264.7 ppb), propane (225.7 ppb), 1,3-butadiene (170.7 ppb), acrolein (82.5 ppb), acrylonitrile (77.4 ppb), acetone (65.69 ppb), 1-hexene (56.7 ppb), and benzene (52.15 ppb) (Table 1). The mean methanol concentration (1088.1 ppb) in surgical smoke samples from breast adipose tissues using conventional electrosurgical knives was the highest, followed by 1,3-butadiene (313.1 ppb), propane (265.5 ppb), acetonitrile (174.1 ppb), acrolein (146.7 ppb), acetone (129.5 ppb), 1-hexene (105.4 ppb), acrylonitrile (77.4 ppb), and benzene (74.1 ppb). Moreover, the mean methanol concentration (4304.6 ppb) in surgical smoke samples from mammary glands using conventional electrosurgical knives was the highest, followed by acetonitrile (1665.4 ppb), propane (1228.2 ppb), 1,3-butadiene (1002.8 ppb), acrylonitrile (549.6 ppb), acrolein (509.4 ppb), acetone (316.1 ppb), 1-hexene (268.4 ppb), benzene (242.5 ppb), and trans-2-butadiene (130.0 ppb). The composition of VOCs in the surgical smoke samples from breast tumor using conventional electrosurgical knives mainly included methanol (736.7 ppb), acetonitrile (258.4 ppb), propane (88.9 ppb), acetone (83.1 ppb), acrylonitrile (68.7 ppb), acrolein (39.7 ppb), benzene (31.6 ppb), 1,3-butadiene (26.8 ppb),

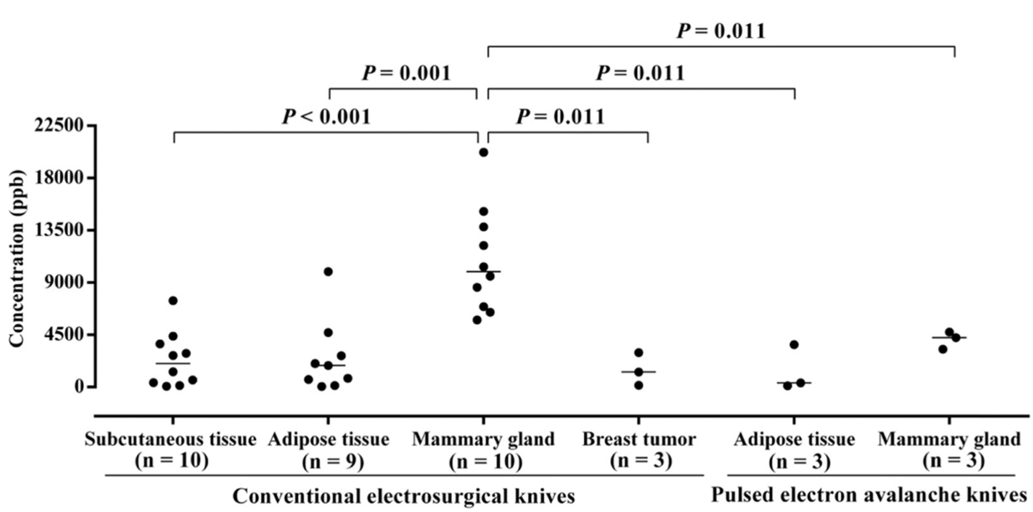

Fig. 2. 87 VOCs concentrations in surgical smoke samples from breast surgeries using electrosurgical knives and PEAK. PEAK: pulsed electron avalanche knives.

Table 1
Concentration distribution of VOCs in surgical smoke samples from different tissues using two electrosurgical units.

IARC group	Compounds (ppb)	Electrosurgical knives								PEAK knives			
		Breast subcutaneous tissue (n = 10)		Breast adipose tissue (n = 9)		Mammary gland (n = 10)		Breast tumor (n = 3)		Breast adipose tissue (n = 3)		Mammary gland (n = 3)	
3	(*p,m*)-Xylene	2.29	(1.27)§	2.29	(0.89)§	4.98	(1.39)	1.82	(1.23)§	2.53	(0.78)§	3.86	(1.93)
3	1,1,1-Trichloroethane	–		–		–		–		–		–	
2B	1,1,2,2-Tetrachloroethane	–		–		–		–		–		–	
	1,1,2-Trichloro-1,2,2-trifluoroethane	–		–		–		–		–		–	
3	1,1,2-Trichloroethane	–		–		–		–		–		–	
	1,1-Dichloroethane	1.32	(a)	–		–		–		–		–	
	1,1-Dichloroethene	0.26	(a)	–		–		–		–		–	
	1,2,3-trimethylbenzene	0.14	(0.01)	0.16	(a)	0.13	(0.02)	0.11	(a)	0.19	(a)	–	
	1,2,4-Trichlorobenzene	–		0.44	(0.02)	0.66	(a)	–		–		–	
	1,2,4-Trimethylbenzene	0.30	(0.09)§	0.26	(0.07)§	0.40	(0.07)	0.23	(0.11)§	0.30	(0.18)§	0.22	(0.04)§
	1,2-Dibromoethane	–		–		–		–		–		–	
	1,2-Dichloro-1,1,2,2,-tetrafluoroethane	–		–		–		–		–		–	
	1,2-Dichlorobenzene	–		–		–		–		–		–	
2B	1,2-Dichloroethane	0.20	(0.08)	0.26	(0.08)	0.42	(0.01)†	0.15	(a)	0.49	(0.44)	0.27	(a)
1	1,2-Dichloropropane	–		–		–		–		–		–	
	1,3,5-Trimethylbenzene	0.23	(0.19)	–		0.28	(0.29)	0.11	(a)	0.13	(a)	–	
1	1,3-Butadiene	170.73	(184.84)§	313.06	(444.81)§	1002.75	(459.69)	26.75	(30.44)§	194.23	(128.84)§	418.27	(172.77)§
	1,3-Dichlorobenzene	–		–		–		–		–		–	
	1,4-Dichlorobenzene	–		–		–		–		0.14	(a)	–	
	1-Hexene	56.70	(64.05)§	105.44	(128.10)§	268.40	(98.66)	23.36	(27.67)§	56.16	(48.62)§	88.82	(25.61)§
	2,2,4-Trimethylpentane	0.19	(0.04)	–		–		–		–		–	
	2,3-Dimethylpentane	0.33	(a)	0.12	(a)	–		–		–		–	
	2,4-Dimethylpentane	–		–		–		–		–		–	
	2-Butanone	12.17	(8.98)§	14.33	(12.74)§	47.31	(20.76)	12.35	(13.74)§	17.47	(20.89)§	28.38	(11.98)§
	2-Methylheptane	1.16	(0.73)§	1.40	(1.69)§	2.93	(1.54)	1.31	(a)	0.17	(0.06)§	1.04	(0.14)§
	2-Methylhexane	2.77	(1.71)§	3.03	(3.31)§	7.87	(1.53)	0.94	(a)	1.29	(0.78)§	3.82	(0.79)§
	2-Methylpentane	0.70	(0.50)§	1.16	(1.18)§	2.23	(0.43)	0.79	(0.50)§	0.93	(0.70)§	1.29	(a)
	3-Chloro-1-Propene	–		–		–		–		0.17	(a)	–	
	3-Methylheptane	0.61	(0.21)§	0.85	(0.61)§	1.34	(0.67)	0.27	(a)	0.64	(a)	–	
	3-Methylpentane	0.56	(0.53)	–		0.28	(a)	–		5.52	(a)	1.26	(a)
	4-Methyl-2-Pentanone	0.37	(a)	0.19	(0.04)§	0.79	(0.52)	0.45	(0.23)§	0.36	(a)	–	
	Acetone	65.69	(66.69)§	129.53	(173.86)§	316.12	(249.58)	83.06	(66.70)§	70.02	(42.24)§	126.43	(49.55)§
	Acetonitrile	264.74	(388.96)§	174.09	(257.86)§	1665.37	(1234.65)	258.42	(281.97)§	162.46	(119.28)§	566.50	(86.53)§
3	Acrolein	82.45	(90.81)§	146.66	(219.74)§	509.39	(218.51)	39.72	(51.42)§	100.24	(63.91)§	156.03	(66.22)§
2B	Acrylonitrile	77.44	(97.11)§	77.41	(84.97)§	549.58	(399.65)	68.72	(72.56)§	48.96	(27.96)§	183.87	(66.60)§
	Apha-Methyl styrene	1.24	(0.35)	1.22	(0.39)	1.14	(0.38)	0.71	(0.11)	0.92	(0.40)	0.41	(0.29)
1	Benzene	52.15	(64.82)§	74.12	(103.03)§	242.53	(95.73)	31.62	(29.10)§	43.60	(24.23)§	120.60	(17.20)†,§
2 A	Benzyl chloride	0.67	(a)	0.14	(a)	0.45	(0.28)	–		–		0.17	(a)
2B	Bromodichloromethane	–		–		–		–		–		–	
	Bromomethane	–		–		0.20	(0.06)	–		–		–	
2B	Carbon tetrachloride	0.11	(a)	–		0.19	((a))	–		–		–	
	Chlorobenzene	1.44	(a)	–		0.32	(0.01)	5.36	(a)	–		–	
3	Chlorodifluoromethane	0.53	(0.14)	0.53	(0.16)	0.49	(0.12)	0.42	(0.20)	0.56	(0.14)	0.68	(0.32)
3	Chloroethane	1.44	(1.01)	1.69	(a)	2.17	(0.79)	0.71	(a)	–		1.28	(0.77)
2B	Chloroform	0.19	(0.13)	0.19	(0.07)	–		0.18	(0.08)	0.59	(a)	0.35	(0.03)
	Chloromethane	18.24	(33.42)§	11.42	(16.28)§	71.55	(47.85)	25.30	(20.21)§	9.46	(6.20)§	28.62	(7.91)§
	cis-1,2-Dichloroethene	0.28	(a)	–		–		–		–		–	
2B	cis-1,3-Dichloropropene	–		–		–		–		–		–	
	cis-2-Butene	26.31	(16.87)§	49.81	(62.18)§	111.19	(38.63)	10.78	(9.33)§	26.30	(19.14)§	32.65	(12.25)§
	cis-2-Pentene	10.65	(9.54)§	15.51	(17.17)§	35.00	(12.11)	2.86	(2.66)§	8.38	(7.20)§	10.47	(3.24)§
	Cyclohexane	0.36	(a)	–		–		–		1.23	(a)	0.76	(a)

(*continued on next page*)

Table 1 (*continued*)

IARC group	Compounds (ppb)	Electrosurgical knives								PEAK knives			
		Breast subcutaneous tissue (n = 10)		Breast adipose tissue (n = 9)		Mammary gland (n = 10)		Breast tumor (n = 3)		Breast adipose tissue (n = 3)		Mammary gland (n = 3)	
	Dibromochloromethane	–		–		–		–		–		–	
	Dichlorodifluormethane	0.51	(0.08)	0.53	(0.13)	0.52	(0.20)	0.50	(0.05)	0.53	(0.30)	0.37	(0.07)
2B	Ethylbenzene	3.78	(4.18)[§]	2.72	(2.62)[§]	13.64	(5.27)	4.37	(4.34)[§]	2.57	(1.29)[§]	7.89	(5.82)[‡]
	Heptane	12.36	(10.03)[§]	14.06	(14.96)[§]	50.63	(23.20)	8.68	(9.13)[§]	9.33	(7.90)[§]	20.26	(9.21)[§]
3	Hexachlorobutadiene	–		–		–		–		–		–	
	Hexane	10.21	(8.97)[§]	14.90	(17.44)[§]	39.30	(9.08)	3.63	(2.98)[§]	10.02	(9.13)[§]	13.50	(1.65)[§]
	Isopentane	1.86	(0.69)[§]	2.05	(1.06)[§]	6.11	(8.27)	–		4.72	(4.20)[§]	4.57	([a])
	Isopropylbenzene	4.78	(3.18)	5.03	(2.00)	3.80	(1.00)	2.91	(1.24)	3.97	(2.29)	2.67	(3.01)
	m-Dienthylbenzene	–		–		–		–		–		–	
	Methanol	1182.94	(1368.91)[§]	1088.06	(1199.92)[§]	4304.60	(2176.35)	736.73	(671.02)[§]	950.26	(936.34)[§]	1806.40	(489.52)[§]
3	Methyl methacrylate	1.38	(0.20)	3.07	(2.29)	–		0.85	([a])	3.03	(1.92)	4.00	(1.29)
	Methylcyclohexane	0.83	(0.55)[§]	1.14	(1.19)[§]	2.76	(0.60)	0.57	(0.30)[§]	1.04	(0.92)[§]	1.18	(0.42)[§]
	Methylcyclopentane	2.30	(1.62)[§]	2.97	(2.74)[§]	6.47	(1.58)	0.73	(0.63)[§]	1.72	(1.41)[§]	2.38	(0.21)[§]
2A	Methylene chloride	0.80	(0.58)	0.62	(0.24)	0.69	(0.29)	3.37	([a])	1.09	(0.22)[‡]	1.31	(0.66)
	m-Ethyltoluene	0.26	(0.12)	0.26	(0.08)	0.50	(0.12)	0.28	(0.13)	0.28	(0.14)	0.26	(0.04)
	n-Dodecane	0.93	(0.48)	0.91	(0.31)	1.54	(0.73)	0.81	(0.64)	0.57	(0.33)	0.47	([a])
	n-Pentane	16.21	(15.33)[§]	29.79	(42.68)[§]	81.18	(29.99)	6.19	(5.59)[§]	18.79	(11.85)[§]	29.60	(9.51)[§]
	n-Propylbenzene	0.43	(0.31)[§]	0.33	(0.21)[§]	1.07	(0.43)	0.34	(0.25)[§]	0.29	(0.11)[§]	0.44	(0.23)[§]
	n-Undecane	1.36	(0.47)[§]	1.46	(0.81)[§]	2.96	(0.68)	0.90	(0.70)[§]	1.29	(0.49)[§]	1.08	(0.39)[§]
	Octane	5.99	(5.33)[§]	10.57	(12.33)[§]	25.90	(5.36)	1.74	(1.38)[§]	6.78	(6.28)[§]	9.81	(0.72)[§]
	o-Ethyltoluene	0.21	(0.11)	0.19	(0.07)	0.34	(0.09)	0.24	([a])	0.21	([a])	–	
3	*o*-Xylene	0.91	(0.51)[§]	0.93	(0.46)[§]	2.13	(0.45)	0.86	(0.52)[§]	1.07	(0.24)[§]	1.35	(0.46)
	p-Dienthylbenzene	–		–		–		–		–		–	
	p-Ethyltoluene	0.21	(0.11)	0.15	(0.02)	0.26	(0.09)	0.12	([a])	0.18	(0.08)	0.14	([a])
	Propane	225.70	(238.45)[§]	265.50	(393.26)[§]	1228.15	(742.82)	88.87	(106.61)[§]	243.25	(241.21)[§]	299.21	(218.26)[§]
2A	Styrene	3.78	(4.71)[§]	3.50	(3.21)[§]	14.48	(5.63)	3.80	(3.73)[§]	2.31	(1.28)[§]	6.47	(4.41)[§]
2A	Tetrachloroethylene	–		–		–		–		0.56	([a])	0.53	([a])
3	Toluene	25.06	(22.22)[§]	23.74	(23.18)[§]	84.41	(42.16)	26.67	(18.94)[§]	23.21	(14.68)[§]	40.61	(11.65)[§]
	trans-1,2-Dichloroethene	–		–		–		–		–		0.26	([a])
2B	trans-1,3-Dichloropropene	–		–		–		–		–		–	
	trans-2-Butadiene	27.57	(20.98)[§]	59.19	(74.74)[§]	130.01	(46.55)	8.93	(9.91)[§]	31.41	(24.34)[§]	38.60	(14.91)[§]
	trans-2-Pentene	14.48	(12.46)[§]	22.93	(26.96)[§]	46.90	(17.26)	4.01	(3.67)[§]	10.29	(7.10)[§]	16.76	(7.39)[§]
1	Trichloroethylene	–		–		–		–		–		–	
	Trichlorofluoromethane	0.23	(0.01)	0.34	(0.08)	0.27	(0.10)	0.23	([a])	0.23	([a])	0.26	(0.06)
2B	Vinyl acetate	5.96	(5.12)[§]	3.11	(0.78)[§]	23.08	(7.92)	4.13	(4.90)[§]	6.78	(4.37)[§]	8.67	(3.34)[‡,§]
1	Vinyl chloride	1.06	(0.99)[§]	1.08	(0.91)[§]	3.32	(1.22)	0.69	(0.44)[§]	0.55	(0.34)[§]	1.62	(0.39)[§]

Data were presented as mean (SD). –: not detected.

[a] only one air sample was detected.

[†] compared to breast subcutaneous tissue using electrosurgical knives, $P < 0.05$;

[‡] compared to breast adipose tissue using electrosurgical knives, $P < 0.05$;

[§] compared to mammary gland using electrosurgical knives, $P < 0.05$.

toluene (26.7 ppb), and chloromethane (25.3 ppb).

The predominant composition of VOCs from breast adipose tissues using PEAK included methanol (950.3 ppb), propane (243.3 ppb), 1,3-butadiene (194.2 ppb), acetonitrile (162.5 ppb), acrolein (100.2 ppb), acetone (70.0 ppb), 1-hexene (56.2 ppb), acrylonitrile (49.0 ppb), and benzene (43.6 ppb) (Table 1). For mammary glands, the mean methanol concentration (1806.4 ppb) was highest, followed by acetonitrile (566.5 ppb), 1,3-butadiene (418.3 ppb), propane (299.2 ppb), acrylonitrile (183.9 ppb), acrolein (156.0 ppb), acetone (126.4 ppb), benzene (120.6 ppb), 1-hexene (88.8 ppb), and toluene (40.6 ppb).

Furthermore, this study evaluated the changes in the concentrations of carcinogenic benzene (IARC group 1) in the surgical smoke samples, indicating that the median concentration of benzene from mammary glands (222.7 ppb) was significantly higher than that from breast subcutaneous tissues (39.1 ppb, $P < 0.01$), breast adipose tissues (39.1 ppb, $P < 0.01$), and breast tumors (26.4 ppb, $P = 0.011$) using conventional electrosurgical knives, as well as that from adipose tissues (45.1 ppb, $P = 0.011$), and mammary glands (112.0 ppb, $P = 0.018$) using PEAK. In addition, the median concentration of benzene in the surgical smoke samples from mammary glands using PEAK was significantly higher than that from breast subcutaneous tissues using conventional electrosurgical knives (39.1 ppb, $P = 0.043$). For 1,3-butadiene (IARC group 1), the median concentration in the surgical smoke samples from mammary glands (856.2 ppb) was significantly higher than that from breast subcutaneous tissues (80.1 ppb, $P < 0.01$), breast adipose tissues (147.3 ppb, $P < 0.01$), and breast tumors (15.6 ppb, $P = 0.011$) using conventional electrosurgical knives as well as that from adipose tissues (210.6 ppb, $P = 0.011$) and mammary glands (384.0 ppb, $P = 0.028$) using PEAK.

With regard to IARC group 2 A, no difference was observed in the median concentrations of benzyl chloride and tetrachloroethylene in the surgical smoke samples from different tissues using conventional electrosurgical knives and PEAK. The median concentrations of IARC group 2B substances, acrylonitrile (440.2 ppb) and vinyl acetate (20.2 ppb) in surgical smoke samples from mammary glands using conventional electrosurgical knives were significantly higher than that from breast subcutaneous tissues (acrylonitrile: 40.3 ppb, $P < 0.01$; vinyl acetate: 5.0 ppb, $P < 0.01$), breast adipose tissues (acrylonitrile: 43.5 ppb, $P < 0.01$; vinyl acetate: 2.9 ppb, $P < 0.01$), and breast tumors (acrylonitrile: 43.2 ppb, $P = 0.011$; vinyl acetate: 2.3 ppb, $P = 0.017$), as well as that from adipose tissues (acrylonitrile: 39.6 ppb, $P = 0.011$; vinyl acetate: 6.8 ppb, $P = 0.04$) and mammary glands (acrylonitrile: 184.0 ppb, $P = 0.018$; vinyl acetate: 8.3 ppb, $P = 0.017$) using PEAK. No differences were observed in the median levels of chloroform and carbon tetrachloride in surgical smoke samples from different breast tissues.

In IARC group 3, the median levels of acrolein (440.2 ppb), toluene (70.2 ppb), and (*p,m*)-xylene (5.1 ppb), and *o*-xylene (2.2 ppb) in surgical smoke samples from mammary glands using conventional electrosurgical knives were significantly higher than that from breast subcutaneous tissues (acrolein: 51.6 ppb, toluene: 20.9 ppb, (*p,m*)-xylene: 1.9 ppb, *o*-xylene: 0.8 ppb, $P < 0.01$), breast adipose tissues (acrolein: 64.7 ppb, toluene: 16.2 ppb, (*p,m*)-xylene: 2.2 ppb, *o*-xylene: 0.8 ppb, $P < 0.01$), and breast tumors (acrolein: 18.2 ppb, $P = 0.011$; toluene: 19.8 ppb, $P = 0.018$; (*p,m*)-xylene: 1.5 ppb, $P = 0.018$; *o*-xylene: 0.7 ppb, $P = 0.018$), as well as that from breast adipose tissues (acrolein: 116.9 ppb, $P = 0.011$; toluene: 19.0 ppb, $P = 0.011$; (*p,m*)-xylene: 2.4 ppb, $P = 0.018$; *o*-xylene: 1.0 ppb, $P = 0.018$) and mammary glands (acrolein: 118.0 ppb, $P = 0.011$; toluene: 35.0 ppb, $P = 0.028$) using PEAK.

This study further evaluated the concentration distribution of 87 VOCs using conventional electrosurgical knives under different electrocautery power conditions (Table 2). The analytical results show that the median level of 87 VOCs from skin tissues using an electrocautery power of ≥ 27.5 watts (2905.8 ppb) was significantly higher than that using an electrocautery power of < 27.5 watts (381.7 ppb). However, no difference was found in the median level of 87 VOCs from adipose tissues and mammary glands under different electrocautery power conditions.

4. Discussion

To the best of our knowledge, this study first attempted to analyze the VOC profile of surgical smoke samples from breast surgeries. The predominant component of air samples collected from the skin disinfection procedure was methanol. The source of methanol in the air samples warrants further evaluation. Moreover, the level of methanol in the surgical smoke samples from different tissues of breast surgeries using conventional electrosurgical knives and PEAK was 29.6-to-172.7-fold higher than that in surgical smoke samples during skin disinfection. Thus, the level of methanol exposure among surgeons and other medical care personnel in ORs should be evaluated. An *in vitro* experiment from NIOSH showed that the surgical smoke samples from five fibroadipose tissues from breast reduction surgeries and one below knee amputation surgery was mainly composed of ethanol (average value: 1200 μg/m^3; 37,158 ppb) and isopropanol (average value: 600 μg/m^3; 18,579 ppb) (Lee et al., 2018). In this study, ethanol and isopropanol were not included in the standard quantitative analysis of 87 VOCs. However, the semiquantitative analysis showed that the surgical smoke from breast surgery had ethanol (484–917,000 ppb) and isopropanol (11.5–62.6 ppb), which is similar to results of the NIOSH study with high percentages of ethanol (83–90%) and isopropanol (80–86%) (Lee et al., 2018). The above difference in the concentration of two VOCs might be related to the different tissues, air sampling, and electrocautery power conditions.

Methanol can be absorbed through skin contact and inhalation. Exposure to excessive amounts of methanol vapor can suppress the central nervous system and cause optic nerve injury, such as eye irritation, headache, fatigue, and drowsiness. Exposure to 50,000 ppm of methanol causes death within 1–2 h (U.S. Coast Guard, 1999). The US OSHA recommended that the permissible exposure limits - short-term exposure limit and ceiling for methanol should not exceed 250 ppm and 1000 ppm, respectively, to avoid the risk of developing intolerable irritation and chronic or irreversible tissue lesions, prevent accidents, or avoid the reduction in work efficiency (Occupational Safety and Health Administration OSHA, 2020). In this study, the methanol concentration in surgical smoke samples from breast surgeries in the ORs did not exceed the recommended level set by the US OSHA (Occupational Safety and Health Administration OSHA, 2020); the potential toxicity of

Table 2
Concentrations of 87 VOCs in surgical smoke from breast surgeries using electrosurgical knives under different electrocautery power conditions.

ppb	Skin tissues		P	Adipose tissues		P	Mammary glands		P
	≥27.5 W (n = 5)	<27.5 W (n = 5)		≥35 W (n = 7)	<35 W (n = 5)		≥35 W (n = 5)	<35 W (n = 5)	
Mean	3758.8	980.4	0.047	3189.8	1729.3	0.462	12,275.9	9529.6	0.602
SD	2332.2	1542.5		3875.6	2185.1		6120.9	1965.8	
Median	2905.8	381.7		1865.9	1080.0		13,809.3	9552.8	
25 percentiles	2724.0	129.6		758.0	111.7		6439.1	8604.1	
75 percentiles	4387.5	606.5		2701.1	2697.4		15,132.2	10,354.2	

Skin tissues included breast and abdominal subcutaneous tissues; Adipose tissues came from breast and abdomen.

methanol for humans, such as headache and vision impairment, should be investigated. The removal of surgical smoke in the operation area using a smoke evacuation system to reduce the exposure risk of medical care personnel is recommended.

A previous study showed that the concentration of 18 VOCs in surgical smoke samples from 20 surgical patients who underwent laparoscopic nephrectomy was 3759–7531 μg/m^3 (977.3–1958.1 ppb) (Choi et al., 2014). Our study indicated the concentration of 87 VOCs in surgical smoke during breast surgeries seemed to be higher than above study. The possible reasons for the concentration difference between studies might be related to the type of surgery, electrocautery power, electrocautery time, sampling period, and the number of VOCs analyzed. In this study, the substances of IARC group 1 detected in the surgical smoke samples from skin tissue, adipose tissue, mammary gland, and tumor in breast surgeries included benzene (26.35–222.65 ppb), 1, 3-butadiene (15.55–856.2 ppb), and vinyl chloride (0.55–3.11 ppb). The levels of benzene and 1,3-butadiene in the surgical smoke samples from breast surgeries were higher than those from an *in vitro* study of pig liver tissues (benzene: 6.21 ppb, 1,3-butadiene: 2.45 ppb) and pork tissues (benzene: 19.06 ppb, 1,3-butadiene: 15.4 ppb) in Switzerland (Kocher et al., 2019). Additionally, 1,2-dichloropropane and trichloroethylene were not detected in the surgical smoke samples from breast surgeries in our study. Previous studies have found that exposure to 10 ppm of benzene for 30 years was associated with death from leukemia (Austin et al., 1998). The incidence of lung cancer was also related to the monthly cumulative exposure to benzene and working years (Wong, 1987). Moreover, long-term exposure (6 h/d, 5 d/week, 104 weeks) to 1,3-butadiene was associated with lung tumor growth in female mice (Melnick et al., 1990). Exposure to vinyl chloride (600 ppm, 4 h/d, 5 d/week, 12 months) resulted in liver tumors in male rats (Radike et al., 1981). Therefore, the health risk of exposure to relatively low concentrations of surgical smoke in health care personnel in the ORs during breast surgery warrants further investigation.

With regard to the type of electrosurgical unit, a US study found that the mean level of benzene in surgical smoke samples from laparoscopic surgery using electrosurgical knives (85 ppb) was significantly higher than that using ultrasonic scalpels (1 ppb) (Fitzgerald et al., 2012). Results of our study indicate that the median levels of benzene, styrene, and toluene in the surgical smoke samples from mammary glands using electrosurgical knives were significantly higher than those using PEAK, which might be due to the operation conditions and the materials of electrosurgical units. The surface temperature of PEAK (40–170 °C) was lower than that of a conventional electrosurgical knife (200–350 °C) (Spektor et al., 2016), possibly resulting in lower VOC production from PEAK. Additionally, this study found that the changes in the concentrations of 87 VOCs in the surgical smoke samples from skin tissues in breast surgeries using conventional electrosurgical knives were associated with the electrocautery power setting. Our results differed from those reported in the Switzerland study (Kocher et al., 2019), which indicated that electrocautery power was not associated with the concentrations of VOCs, including 1,3-butadiene, benzene, and furfural. The relationship between electrocautery power and the composition of VOCs in surgical smoke samples should also be evaluated further.

To avoid personal exposure to surgical smoke, effective methods should be adopted, such as using an efficient local smoke evacuation system, increasing the ventilation rate in ORs, and wearing a fit personal protective mask. Controlling the pollution source is the best way to reduce the VOCs exposure in health care personnel. An efficient local smoke evacuation system can be direct to remove the VOCs in surgical smokes during operations. The suction efficiency of a local smoke evacuation system deserves further concerns. According to ASHRAE/ASHE 170 standard and Facility Guidelines Institute (FGI) standard, the minimum suggested OR ventilation rate were 20 ACH and 15 ACH, respectively (American Society of Heating Refrigerating and Air-Conditioning Engineers, 2017; Facility Guidelines Institute (FGI), 2018). Until recently, no standard or guideline was established for exposure of OR health care personnel to VOCs. Additionally, surgical masks have a limited ability to remove the VOCs in surgical smokes. The use of powered air purifying respirators (PAPR) might be alternative personal protective equipment for health care personnel in ORs. Thus, this study recommends that health care settings should regularly monitor the air quality of ORs and maintain the ventilation systems to ensure the health and safety of health care personnel in the ORs.

This study had several limitations. First, the study evaluated the exposure to VOCs using area sampling, not personal sampling, because it was impossible to perform the personal sampling during operations. Second, the operation time of breast surgery ranged from 39 to 807 min in the study, however, the actual cauterization time in patients was not measured. A grab sampling was adopted using an evacuated canister for only 30 s during cauterization period, so that the VOCs exposure of OR health care personnel may be underestimated. Thus, the time of exposure to surgical smoke warrants further evaluation. Third, the surgical smoke samples were collected near the surgical site to avoid interfering with the operations. The analytical results might not directly reflect the actual exposure of VOCs in OR health care personnel in the study.

5. Conclusions

The median level of 87 VOCs in the surgical smoke samples from mammary glands using conventional electrosurgical knives was the highest. High levels of methanol and IARC group 1 compounds, including benzene, 1,3-butadiene, and vinyl chloride were found in breast surgeries using conventional electrosurgical knives. The concentration of 87 VOCs was affected by the electrocautery power used in cutting the subcutaneous tissues.

CRediT authorship contribution statement

Ming-Huei Cheng: Conceptualization, Investigation, Writing - review & editing. **Chun-Hui Chiu:** Methodology, Formal analysis, Writing - original draft. **Chi-Tsung Chen:** Investigation, Formal analysis, Writing - original draft. **Hsu-Huan Chou:** Investigation. **Li-Heng Pao:** Project administration, Funding acquisition. **Gwo-Hwa Wan:** Conceptualization, Methodology, Investigation, Writing - original draft, Writing - review & editing, Project administration, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank the Ministry of Science and Technology (107–2314-B-182–054), Chang Gung University of Science and Technology (ZRRPF3H0081), and Chang Gung Medical Foundation (BMRP441), Taiwan, for financially supporting this research. Also, the authors thank Mrs. Chi Wang for her assistance on administration affairs of the operating rooms in this study.

References

Al Sahaf, O.S., Vega-Carrascal, I., Cunningham, F.O., McGrath, J.P., Bloomfield, F.J., 2007. Chemical composition of smoke produced by high-frequency electrosurgery. Ir. J. Med. Sci. 176, 229–232.

American Society of Heating Refrigerating and Air-Conditioning Engineers, 2017. ANSI/ASHRAE/ASHE Standard 170-2017: ASHRAE/ASHE Standard Ventilation of Health Care Facilities.

Austin, H., Delzell, E., Cole, P., 1998. Benzene and leukemia. A review of the literature and a risk assessment. Am. J. Epidemiol. 127, 419–439.

Choi, S.H., Kwon, T.G., Chung, S.K., Kim, T.H., 2014. Surgical smoke may be a biohazard to surgeons performing laparoscopic surgery. Surg. Endosc. 28, 2374–2380.

Environmental Analytical Laboratory (EAL), 2014. Environmental Protection Administration, Taiwan. Analytical method for determining volatile organic compound in air - stainless steel canister / gas chromatography-mass spectrometry (NIEA A715.15B). https://www.epa.gov.tw/DisplayFile.aspx?FileID=18E7C2F1DB13EBCB. (Accessed 20 August 2020). [In Chinese].
Facility Guidelines Institute (FGI), 2018. Status update, edition of the Guidelines for Design and Construction of Health Care Facilities, FGI - Facilities Guidelines Institute. http://www.fgiguidelines.org. (Accessed 10 November 2020).
Fitzgerald, J.E., Malik, M., Ahmed, I., 2012. A single-blind controlled study of electrocautery and ultrasonic scalpel smoke plumes in laparoscopic surgery. Surg. Endosc. 26, 337–342.
Gates, M.A., Feskanich, D., Speizer, F.E., Hankinson, S.E., 2007. Operating room nursing and lung cancer risk in a cohort of female registered nurses. Scand. J. Work Environ. Health 33, 140–147.
Hill, D.S., O'Neill, J.K., Powell, R.J., Oliver, D.W., 2012. Surgical smoke - a health hazard in the operating theatre: a study to quantify exposure and a survey of the use of smoke extractor systems in UK plastic surgery units. J. Plast. Reconstr. Aesthet. Surg. 65, 911–916.
ISO (International Organization for Standardization), 2015. Cleanrooms and Associated Controlled Environments. Part 1: Classification of Air Cleanliness by Particle Concentration; ISO standard 14644–1:1999. International Organization for Standardization: Geneva, Switzerland.
Kalil, J., Pessine, F.B., Fidelis, C.H., Menezes, F.H., Palma, P.C., 2016. Analysis of electrocautery generated smoke by chromatographic-mass spectrometry. Rev. Col. Bras. Cir. 43, 124–128.
Kocher, G.J., Sesia, S.B., Lopez-Hilfiker, F., Schmid, R.A., 2019. Surgical smoke: still an underestimated health hazard in the operating theatre. Eur. J. Cardiothorac. Surg. 55, 626–631.
Le Moual, N., Varraso, R., Zock, J.P., Henneberger, P., Speizer, F.E., Kauffmann, F., Camargo, C.A., 2013. Are operating room nurses at higher risk of severe persistent asthma? The Nurses' Health Study. J. Occup. Environ. Med. 55, 973–977.
LeBouf, R.F., Stefaniak, A.B., Virji, M.A., 2012. Validation of evacuated canisters for sampling volatile organic compounds in healthcare settings. J. Environ. Monit. 14, 977–983.
Lee, T., Soo, J.C., LeBouf, R.F., Burns, D., Schwegler-Berry, D., Kashon, M., Bowers, J., Harper, M., 2018. Surgical smoke control with local exhaust ventilation: experimental study. J. Occup. Environ. Hyg. 15, 341–350.
Liang, C.C., Wu, F.J., Chien, T.Y., Lee, S.T., Chen, C.T., Wang, C., Wan, G.H., 2020. Effect of ventilation rate on the optimal air quality of trauma and colorectal operating rooms. Build. Environ. 169, 106548.
Massarweh, N.N., Cosgriff, N., Slakey, D.P., 2006. Electrosurgery: history, principles, and current and future uses. J. Am. Coll. Surg. 202, 520–530.
Melnick, R.L., Huff, J., Chou, B.J., Miller, R.A., 1990. Carcinogenicity of 1,3-butadiene in C57BL/6 x C3H F1 mice at low exposure concentrations. Cancer Res 50, 6592–6599.
Occupational Safety and Health Administration (OSHA), 2008. Laser/Electrosurgery Plume. https://www.osha.gov/SLTC/laserelectrosurgeryplume/index.html. (Accessed February 22, 2019).
Occupational Safety and Health Administration (OSHA), 2020. METHYL ALCOHOL (METHANOL). http://www.osha.gov/chemicaldata/chemResult.html?RecNo=474. (Accessed 20 August 2020).
Radike, M.J., Stemmer, K.L., Bingham, E., 1981. Effect of ethanol on vinyl chloride carcinogenesis. Environ. Health Perspect. 41, 59–62.
Sisler, J.D., Shaffer, J., Soo, J.C., LeBouf, R.F., Harper, M., Qian, Y., Lee, T., 2018. In vitro toxicological evaluation of surgical smoke from human tissue. J. Occup. Med. Toxicol. 13, 12.
Spektor, Z., Kay, D.J., Mandell, D.L., 2016. Prospective comparative study of pulsed-electron avalanche knife (PEAK) and bipolar radiofrequency ablation (coblation) pediatric tonsillectomy and adenoidectomy. Am. J. Otolaryngol. 37, 528–533.
U.S. Coast Guard, 1999. Chemical Hazard Response Information System (CHRIS)-Hazardous Chemical Data. Commandant Instruction 16465.12C. U.S. Government Printing Office, Washington, D.C.
Ulmer, B.C., 2008. The hazards of surgical smoke. AORN J. 87, 721–734.
Wong, O., 1987. An industry wide mortality study of chemical workers occupationally exposed to benzene. II. Dose response analyses. Br. J. Ind. Med. 44, 382–395.