# Chemical composition of surgical smoke produced during Loop electrosurgical excision procedure treating cervical intraepithelial neoplasia

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# Abstract

Background

As LEEP (Loop electrosurgical excision procedure) is being increasingly used for diagnosis and treatment of uterine cervical intraepithelial neoplasia, the surgical smoke during LEEP becomes an inevitable health issue.Therefore in this study, the exposure to chemical substances of surgical smoke produced during LEEP was assessed.

Methods

Smoke samples from patients with high-grade cervical intraepithelial neoplasia undergoing LEEP were collected by smoke absorbing devices situated 1 meter away the operating table and near the nose of operator during LEEP, respectively. Each plume sample was collected after 5 patients proceeding LEEP and each patient take 5 min for smoke collection. The expected chemicals of exposure to surgical smoke includedbenzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, hendecane, acetone, acrylonitrile, 1,2-dichloroethane, phenol, chlorine, cyanide and hydrogen cyanide. Additionally,hazards classes of these chemical components were observed in International Agency for Research on Cancer.

Results

Qualitative analysis of the smoke produced during LEEP revealed the varieties of potentially toxic chemicals were under the standard detection, such as benzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, acrylonitrile, 1,2-dichloroethane, phenol, chlorine, cyanide and hydrogen cyanide. Additionally, the average concentrations of carbon dioxide were 0.098±0.015 during the surgery and higher than before the surgery (0.072±0.007), $P < 0.001$, and formaldehyde was significantly higher during the surgery (0.023±0.009) than before it (0.012±0.001), $P < 0.05$.

Conclusions

The most of detected chemicals in smoke generated during LEEP were under the exposure limits when local exhaust ventilation procedures were efficiently used. However, concentrations of carbon dioxide and formaldehyde found in the smoke were significantly higher after the surgery. To use evacuation devices routinely and consistently when performing LEEP was recommended to protect the perioperative personnel.

# Introduction

Surgical smoke is the gaseous byproduct rising from tissue being dissected, excised and coagulated by heat generating devices such as laser and electrocautery[1]. During these procedures, the target cells are heated to the point that they start boiling and cell membranes are ruptured, and subsequently ultrafine particles are dispersed into the operating theater[2]. There are mounting disadvantages of surgical smoke, such as obscuring the operating field, producing an unpleasant odor, releasing hazardous chemicals including mutagens and carcinogens, harboring contagious, viable malignant cells, and even to contain live bacteria and viruses[3, 4].Each year, a total of approximately 500,000 personnel in America such as surgeons, nurses, anesthesiologists, and technicians are exposed to surgical smoke in the operating rooms[5].

Surgical smoke is composed of 95 percent water vapor and 5 percent particulate matter[6]. The latter consists of dead and living cellular material, lung-damaging particulates, blood fragments, bacteria, viruses and toxic chemicals[6]. The chemical constituents and amount of noxious smoke varies widely, depending on type of surgery, type of energy and period of surgery time[7]. So far, in vitro experiments have identified more than 80 chemical compounds in the surgical smoke[8]. Emerging evidence illustrates that exposure to these chemicals may result in harmful effects to surgeons, such as headaches, watery eyes, coughs, burning throats, nausea, bad odors absorbed in the hair, drowsiness, dizziness, sneezing and rhinitis[9].

Cervical cancer is becoming one of the leading causes of cancer-related death in women. An estimated 13,240 patients will be diagnosed and about 4,170 cases will die because of this deadly disease in the United States in 2018[10].Therefore, to obtain the better treatment outcomes, loop electrosurgical excisional procedure (LEEP) have been considered as accurate techniques in cervical cancer prevention for excision of high-grade cervical intraepithelial neoplasia (CINII and CINIII)[11–13]. However,LEEP uses low-voltage, high-frequency alternating current of electricity through a thin wire loop to complete surgery, resulting in the generation of a smoke plume[14]. Unfortunately, the operating room personnel expose to the toxic chemicals from the beginning to the end of the procedure, which is regarded to be an occupational hazard to the staff in the operating theater. To date, there was no study focusing on the potential dangers associated with the exposure to the smoke generated during LEEP. Therefore, in this study, smoke samples from patients with high-grade cervical intraepithelial neoplasia undergoing LEEP were collected and the expected chemicals of exposure to surgical smoke were detected, in order to explore the chemical component and its potential hazards of surgical smoke produced during LEEP.

# Material And Methods

Smoke samples were collected from patients who harbored high-grade cervical intraepithelial neoplasia and underwent LEEP at the outpatient departments of the second affiliated hospital of Wenzhou medical university, China from May 2016 to Dec 2017. The operating rooms were equipped with local exhaust ventilation procedures, which were connected with the vaginal speculum through a tube. In addition, a vacuum suction device was also used in the operating room. The entire dissection and coagulation during LEEP was carried out using monopolar electrocautery. And the energy mode was set at 50W for cutting and 30W for coagulation. Ethical approval was obtained from the Ethical Committee of the Second Affiliated Hospital of Wenzhou Medical University. All subjects agreed and provided written informed consent before starting the study.

# Gas sampling

The surgical smoke was collected and detected according to Chinese indoor air quality standard (GB/T 18883 – 2002)[15],Chinese national standard (GB/T 160.68–2004,GB/T 160.29–2004, GB/T 18204.2–2014, GB/T 160.51–2007)[16]. Air samples of circumstance before and during the LEEP from the same operating room were also collected to minimize the background contamination (Fig. 1). Each plume sample was collected after 5 patients proceeding LEEP. Nine plume samples collected to analyze expected volatile organic chemical such as benzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, hendecane, acetone, acrylonitrile, 1,2-dichloroethane, phenol, chlorine, cyanide, hydrogen, carbon monoxide, carbon dioxide andformaldehyde.

# Collection of gas

Gas sampling was performed by activated charcoal tube, absorption liquid, silica gel and microporous filter adsorption. And these apparatuses were situated in the 1 meter away the operating table and within the breathing zone of medical operator (20 cm from diathermy tip, near the nose of operator), respectively (Fig. 1). Smoke samples were only collected immediately when the electrocautery was activated with a vacuum suction device. And the total time of collecting different chemical component was 5 min for every patient. The flow rates used to collect different chemical components varied from 0.1 to 1.0 L/min according to the Chinese national standard. It was set by sampling pumps named GilAir Plus.

# Analysis of gas

Analysis was carried out at Wenzhou Center for Disease Control and Prevention, China. Chlorine, cyanide and hydrogen cyanide in the collected smoke were determined by barbital sodium based spectrophotometric method[17].Chlorine, cyanide and hydrogen cyanide could react with chloramine to form cyanogen chloride in circumstance of a weakly acidic solution, and then react with isonicotinic acid sodium to produce Glutaconaldehyde acid which could react with barbituric acid and produce purple compounds. Added 1 drop of phenolphthalein solution to standard cyanide solution, neutralize with acetic acid solution. Then added 1.5 ml buffer and 0.2 ml chloramine T solution covered for 5 min, subsequently 2.5 ml color solution, placed in a water bath at 25 °C – 40 °C for 40 min. Then wavelength absorbance was determined at 600 nm, reflecting the concentration of Chlorine, cyanide and hydrogen cyanide.

Automated Thermal Desorber-Gas Chromatography was used to detect benzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, hendecane, acetone, acrylonitrile, 1,2-dichloroethane, phenol. The Gas Chromatography analysis was performed by using an Agilent 789013 gas chromatograph system coupled with a Flame ionization detector. HP-Innowax column (30 m × 0.32 mm × 0.5 μm) was used for chromatographic separations. Thermal desorption was required for samplegetting into the gas chromatography system for the separation step. Thermal desorption of the compounds concentrated was carried out at 250 °C for 5 min,during which time the eluted volatile organic compounds were transferred to the cold trap maintained at 10 °C. Then the cold trap was rapidly heated from 10 °C to 250 °C and maintained at this temperature for 3 min. During this time, volatile organic compounds were injected onto the HP-Innowax column. The thermal desorption system transfer line temperature was

150 °C. The Gas Chromatography conditions were set as following. The initial temperature was held at 45°C for 1 min, which was then increased to 85°C at a rate of 8°C/min, and then maintained at 85°C for 3 min. Finally the temperature was increased to 200°C at a rate of 20°C/min. The flame ionization detector temperature was set at 300°C. The retention time of the known components in the standard sample was used to identify the compositions in tested samples. If retention time of the sample was same as the retention time of the standard gas under the same gas chromatographic conditions, the composition in the sample was same as that in the standard. And the peak area was used to quantify the concentration of the compounds in samples. The ratio of the tested sample peak area to the standard sample peak area was equal to the ratio of the sample concentration to that of the standard gas under the same gas chromatographic analysis conditions.

In addition, carbon monoxide, carbon dioxide andformaldehyde levels were analyzed using portableTesto 435 multi-function meter JL-5-145 and Formaldehyde tester XP-308B.

# Gas hazards

Hazards classes of chemical components were observed in International Agency for Research on Cancer (IARC)[18]. Carcinogenic risks to human was evaluated by IARC and classified as 5 groups. Group 1 was carcinogenic to humans, and this category was used in case of sufficient evidence of carcinogenicity in humans. Group 2A was probably carcinogenic to humans,when there was limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. Group 2B was possibly carcinogenic to humans, as compared to Group 2A, Group 2B has less than sufficient evidence of carcinogenicity in experimental animals. Group 3 was not classifiable as to its carcinogenicity to humans, which was used when the evidence of carcinogenicity was inadequate in humans and inadequate or limited in experimental animals. Group 4 was probably not carcinogenic to humans, lacking evidence of carcinogenicity in humans and in experimental animals.

# Methods of statistical analysis

All analyses were performed using SPSS 17.0 software. The Student t test was performed to compare the differences of volatile chemical compounds before and during procedures. The level of significance used for statistical tests was P value $< 0.05$.

## Results

Among the LEEP smoke samples, volatile organic chemicals containing benzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, hendecane, acetone, acrylonitrile, 1,2-dichloroethane, phenol, chlorine, cyanide, hydrogen cyanide were found to be under the lowest mass of detection (LMD) both in the gas from circumstance and produced during LEEP and vaporization (Table 1). No significant differences were found between the concentrations of these chemicals determined pre- and postoperatively. Interestingly, the level of carbon monoxide was 0 $mg/m^3$.

Table 1

The hazards class and concentration of each common chemical in surgical smoke during LEEP

| Chemicals | Hazards class (IARC) | LMD ($mg/m^3$) | Air sample before LEEP ($mg/m^3$) | Smoke sample during LEEP ($mg/m^3$) |
|---|---|---|---|---|
| Benzene | 1 | 0.01 | < 0.01 | < 0.01 |
| Toluene | 3 | 0.01 | < 0.01 | < 0.01 |
| Xylene | 3 | 0.01 | < 0.01 | < 0.01 |
| Ethylbenzene | 2B | 0.01 | < 0.01 | < 0.01 |
| Styrene | 2A | 0.01 | < 0.01 | < 0.01 |
| butyl acetate | 3 | 0.02 | < 0.02 | < 0.02 |
| Hendecane | NA | 0.01 | < 0.01 | < 0.01 |
| Acetone | NA | 0.02 | < 0.02 | < 0.02 |
| Acrylonitrile | 2B | 0.02 | < 0.02 | < 0.02 |
| 1,2-dichloroethane | 2B | 0.02 | < 0.02 | < 0.02 |
| Phenol | 3 | 0.5 | < 0.5 | < 0.5 |
| chlorine | 3 | 0.2 | < 0.2 | < 0.2 |
| cyanide | 1 | 0.02 | < 0.02 | < 0.02 |
| hydrogen cyanide | 1 | 0.1 | < 0.1 | < 0.1 |
| Carbon monoxide | NA | 0.1 | 0 | 0 |

LEEP: loop electrosurgical excisional procedure; LMD: lowest mass of detection; IARC: International Agency for Research on Cancer, 1: carcinogenic to humans; 2A: probably carcinogenic to humans; 2B: possibly carcinogenic to humans, less than sufficient evidence; 3: not classifiable as to its carcinogenicity to humans; NA: not available in IARC.

As shown in Table 2, concentration of carbon dioxide in the surgical smoke during LEEP was on average $0.098 \pm 0.015$ and it was higher than before the surgery ($0.072 \pm 0.007$), $P < 0.001$. In the case of formaldehyde, the average concentrations of the compound in the plume during the LEEP were also significantly higher than before it, $0.012 \pm 0.001$ (before the surgery) compared to $0.023 \pm 0.009$ (during the surgery), $P < 0.05$.

Table 2
The hazards class and concentration of carbon dioxide, formaldehyde, and carbon monoxide in surgical smoke before and during LEEP

| Chemicals | Hazards class (IARC) | LMD | Before LEEP | During LEEP | P value |
|---|---|---|---|---|---|
| carbon dioxide | NA | 0.01 | 0.072 ± 0.007% | 0.098 ± 0.015% | < 0.001 |
| formaldehyde | 1 | 0.01 | 0.012 ± 0.001 $mg/m^3$ | 0.023 ± 0.009 $mg/m^3$ | < 0.05 |

LEEP: loop electrosurgical excisional procedure; IARC: International Agency for Research on Cancer, 1: carcinogenic to humans; 2A: probably carcinogenic to humans; 2B: possibly carcinogenic to humans, less than sufficient evidence; 3: not classifiable as to its carcinogenicity to humans; NA: not available in IARC; LMD: lowest mass of detection.

Chemicals among the smoke samples were further analyzed in the IARC to illustrate its potential hazards. Notably, benzene, cyanide, hydrogen cyanide and formaldehyde were classified as Group 1, which was carcinogenic to humans. Styrene was recognized as Group 2A, which was probably carcinogenic to humans and ethylbenzene, acrylonitrile, as well as 1,2-dichloroethane were recognized as Group 2B, which was possibly carcinogenic to humans. Furthermore, toluene, xylene, butyl acetate, phenol, chlorine were recognized as Group 3, not classifiable as to its carcinogenicity to humans. Additionally, hendecane, acetone, carbon monoxide and carbon dioxide were not available in IARC(Table 1 and Table 2).

# Discussion

As electrocautery devices being increasingly used in the modern surgery worldwide, the surgical smoke becomes an inevitable health issue. The potential hazards of surgical smoke give rise to serious concern. To date, emerging study describes the chemical constituents of diathermy plume produced during various surgeries on live humans.Sagar et al. [19] detected low levels of benzene, styrene, ethyl benzene, carbon disulphide and methyl benzene in the plume generated during colorectal surgery.Hollmann and his colleagues [20] identified 11 different gases in surgical smoke collected at 2 cm from the tip of the unipolar electrocautery device during reduction mammaplasty. Among these chemical components, the concentration of 2-furancarboxaldehyde was measured 12 times outstandingly higher than the occupational exposure limit. Another group collected plumes as close as possible(< 2 cm) to the point of electrocautery pencil during laparotomy for abdominal surgery and demonstrated hydrogen cyanide (3–51 parts per million (ppm)), acetylene (2–8 ppm), and 1,3-butadiene (0.15–0.69 ppm) were existed in the plume[21]. In addition, emerging evidence identified the chemical components during transurethral resection of prostates (TURP). One group detected sixteen chemical constituents in the gaseous plume collected from 15 cm above the end of the resectoscope, in whichcarbon monoxide has been found to be significantly high level, causing detrimental side effects to the medical operators such as headache, fatigue, and nausea[22]. In line with previous study, another group also collected 12 smoke samples from

TURP and vaporization and identified 16 main chemical constituents in surgical smoke including allene, propylene, isobutylene, 1,3-butadiene, vinyl acetylene, ethyl acetylene, mecaptomethane, diacetylene, 1-pentene, ethyl alcohol, piperylene, 1,4-pentadiene, propenylacetylene, acrylonitrile, cyclopentadiene, and butyrolactone[4].Later, Lin et al. [23] quantified five volatile organic compounds (toluene, styrene, xylene, phenol and furfural) in the smoke collected from the tip ofmonopolar electrocautery using in mammoplasty. Specially, higher concentrations of toluene were detected in patients undergoing modified radical mastectomy and in patients with high body mass index, as well as in longer duration of electrocautery as compared to partial mastectomy, low body mass index and shorter duration on electrocautery[23].Remarkably, a recent study collected 36 surgical smoke samples using an electrocautery surgical device in humanbreast reduction surgeries. They detected 17 different volatile organic compounds, among which acetaldehyde, ethanol and isopropyl alcohol were detected to be highly concentrated in every sample predominantly[24].Similarly,Sigrist et al. [25] identified carbon monoxide, hydrogen fluoride, sevoflurane, methane, ethane, ethylene during minimal-invasice surgery. Notably, twenty renal cell carcinoma patients undergoing transperitoneal laparoscopic radical nephrectomy was performed in Choi's experiment. As a result of this research, five carcinogenic volatile organic compounds (ethanol, 1,2-dichloroethane, benzene, ethylbenzene, and styrene) and 13 noncarcinogenic chemical compounds were identified, suggesting that more attention should be paid to the long-term adverse effects associated with exposure to surgical smoke[5]. All these experiments revealed theabundant chemicals in electrocautery smoke. However, most of these volatile organic compounds have been classified as carcinogens such as acrolein, acetaldehyde, acrylonitrile, benzene, cyclohexanone, furfural, formaldehyde, polyaromatic hydrocarbons, styrene, toluene and xylene[26].

Interestingly, harmless concentrations of chemical components were also detected in some articles. Gianella et al. [27] quantitatively evaluated the levels of chemicals in plume from a vessel-sealing device during laparoscopic surgery and indicated that the concentrations of methane, ethane, and ethylene in smoke were below the recommended exposure limit. In another study, sample collecting during laparoscopic cholecystectomy was performed within the breathing zone of medical staffs located near the operating table. Aldehydes, benzene, toluene, ethylbenzene, xylene, ozone, dioxins and furans were indentified. But all of them were lower than the hygienic standards allowed by the European Union Maximum Acceptable Concentration[28].

This is the first time to evaluate chemical composition of smoke produced during LEEP. Higher concentrations of formaldehyde and carbon dioxide were identified during LEEP as compared to before LEEP in this study. And other toxic compounds (benzene, toluene, xylene, ethylbenzene, styrene, butyl acetate, hendecane, acetone, acrylonitrile, 1,2-dichloroethane, phenol, chlorine, cyanide, hydrogen cyanide, and carbon monoxide) detected in the present study has been observed under the LMD.

It is well acknowledged that high concentration of carbon dioxide has been documented direct health effects on humans in previous research[29]. A maximum acceptable indoor carbon dioxide concentration was 800 ppm (a 0.08% concentration) [30]. When the concentration was higher than 20,000 ppm (a 2% concentration), carbon dioxide could cause deepened breathing. When higher than 40,000 ppm (a 4%

concentration), could increase respiration markedly. When higher than 100,000 ppm (a 10% concentration), could cause visual disturbances and tremors and loss of consciousness. And 250,000 ppm (a 25% concentration) can cause death[29]. However, carbon dioxide in the surgical smoke during LEEP was detected to be on average 0.098 ± 0.015%, beyond the maximum acceptable indoor carbon dioxide (0.08%), which was significantly higher than before the LEEP, suggesting that surgeons in this circumstance should take some useful methods to minimize carbon dioxide.

Formaldehyde was classified as a known human carcinogen. The threshold value for indoor formaldehyde concentration was 0.1 mg/m$^3$[31].Short-term exposure may result in eye irritation, nausea, vomiting, headache, weakness, edema, dizziness, fatigue, and chest tightness[32]. Long-term exposure may link to higher incidences of cancer in humans such as leukemia[33], even result in pregnant women fetal malformations[32]. Our result has detected the average concentrations of formaldehyde in the surgical plume during LEEP were significantly higher than before surgery. Even if the concentration of formaldehyde was under the exposure limit (0.1 mg/m$^3$), attention should be paid and preventive measures should be carried for gynecologists and other operating room staff members in order to minimize contact with formaldehyde and prevent excessive exposure. Moreover, the majority of the previous studies concerning the composition of surgical smoke collected the smoke sample near the tip of the diathermy pencil[20, 23]. While in our study, the gas concentration was measured directly at the height of the nose of gynecologists, which was diluted by the air. However, the gas concentration measured within the breathing zone exactly reflected the exposure of chemicals absorbed by operators in the operating room.

Besides, emerging evidence has declared that the suction devices were often ignored by operators. For example, a web-based survey examined current surgical smoke practices of local exhaust ventilators. The researchers found that only 14% of total 4533 respondents reported that local exhaust ventilators were always used during the procedures of electrosurgery[34]. It is indispensable that the suction devices were used in the hospital and executed their protective function. Suction clearance of the diathermy plume with smoke extraction systems resulted in a significant reduction in the amount of smoke in thyroid surgery[35].With the use of wall suction, Wang et al. [36] found that fine particle inhalation significantly decreased 48% in superficial surgeries, 52% in abdominal surgeries and 65% in pelvic surgeries. In our experiment, suction devices were effectively used in the operating room, which resulted in the negative consequence.Therefore, we recommended practitioners to use suction system routinely and consistently when performing LEEP.

In addition, Zhao et al. [37]identified 39 types of gases generated during transurethral resection of the malignant bladder tumor tissues, while only 16 types of gases during transurethral resection of benign hypertrophic prostate. The differences in the types of gases between benign hypertrophic prostate and malignant bladder tumor tissues indicated that electrosurgery of malignant tissue was probably more hazardous. LEEP is usually used to treat cervical high-grade CIN, which is potentially premalignant[38]. Thus, we suspected that the chemical composition of smoke produced during LEEP may be less than the level of cervical cancer. And the potential hazard of gases during the surgery of cervical cancer needs to be further investigated.

In summary, the present investigation shows the relatively low levels of the most common chemical compounds in the smoke from LEEP, in contrast to these determined compounds, the average concentrations of carbon dioxide and formaldehyde in the plume were significantly higher during LEEP than before it. Although exposure of the patient in operating room to emerging chemical compounds is usually a one-time and short-term incident,awareness should be strengthened and preventive measures should be carried for surgeons having operations frequently in the operating room to protect themselves from long-term exposure. We recommend practitioners to use evacuation devices routinely and consistently when performing LEEP. However, there are few studies that detect the long-term effects of surgical smoke. Further research is required to investigate potential long-term effects on theatre staff performing LEEP.

# Abbreviations

CIN: cervical intraepithelial neoplasia

IARC: International Agency for Research on Cancer

LEEP: Loop electrosurgical excision procedure

LMD: lowest mass of detection

TURP: transurethral resection of prostates

# Declarations

***Authors' contributions***: Xueqiong Zhu was involved in the conception and design of the study.Yi Liu and Menghuang Zhao analyzed and interpreted the data and wrote the manuscript. Yongqiang Shao and Linzhi Yan assisted in analyzing and interpreting data. Yi Liu and Xueqiong Zhu were involved in the conception and design of the study and critically reviewed the manuscript. All authors read and approved the final manuscript.

***Ethics approval and consent to participate***

Not applicable.

***Consent for publication***

Not applicable.

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### *Availability of data and materials*

All data generated or analysed during this study are included in this published article

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### *Competing Interests*

The authors have declared that no competing interest exists.

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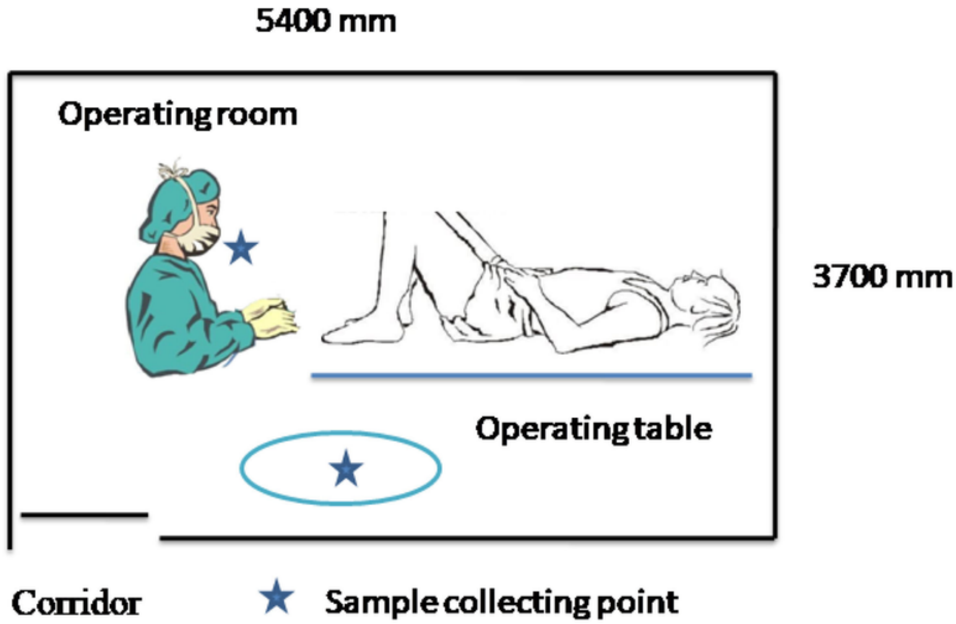
# Figures




## Figure 2

Operating room of LEEP and collection of smoke samples