

Experimental study of the potential hazards of surgical smoke from powered instruments

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Background: Many surgical instruments have been replaced with powered devices in open gastrointestinal and laparoscopic surgery. The production of smoke as a result of vaporization of surgical tissue is inevitable, and exposure to surgical smoke is a long-standing concern. These vapours are potentially hazardous to patients and surgical teams. The present research was designed to compare various surgical devices to determine whether viable cells exist in their surgical smoke.

Methods: The search for viable cells in surgical smoke was conducted using both *in vitro* and *in vivo* experiments. Various cancers were cauterized with electrocautery, radiofrequency ablation and ultrasonic scalpels, and the resulting surgical smoke was aspirated with Transwell[®] membrane; viable cells were sought in the surgical smoke. In an *in vivo* experiment, samples of SCC7 were cauterized with an ultrasonic scalpel and the sediment from the rinsed Transwell[®] membrane liquid after centrifugation was injected subcutaneously into the lower back of mice.

Results: Viable cells were found only in the smoke from ultrasonic scalpels (in all 25 samples taken 5 cm from the cautery; 2 of 25 samples at 10 cm). Viable cells in the surgical smoke from ultrasonic scalpels implanted in mice grew in 16 of 40 injection sites. Histological and biochemical analyses revealed that these cancer cells were identical to the cancer cells cauterized by the ultrasonic scalpel.

Conclusion: Viable tumour cells are produced in the surgical smoke from tumour dissection by ultrasonic scalpel.

Surgical relevance

Surgical smoke is a byproduct of dissection using a number of powered devices. Hazards to operating room personnel and patients are unclear.

This study has shown that use of an ultrasonic dissection device can produce smoke that contains viable tumour cells.

Although the model is somewhat artificial, a theoretical risk exists, and measures to evacuate surgical smoke efficiently are important.

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Introduction

Electrocautery (also known as electrosurgery), laser, radiofrequency ablation and ultrasonic scalpels are used for cutting, dissecting and coagulating during surgery. Both patients and operating room staff are exposed to surgical smoke generated by these devices. Surgical smoke is composed of the gaseous byproduct of vaporized tissue. It consists of 95 per cent water vapour and 5 per cent combustion byproducts (particulate matter). The

latter is composed of chemicals, blood and tissue particles, viruses and bacteria¹. Surgical smoke varies greatly in its nature depending on the energy device that creates it. Other factors that can affect the amount and content of smoke include the type of procedure, the surgeon's technique, the pathology of the target tissue, the power level used, and the amount of cutting, coagulation or ablation.

Surgical smoke produces an unpleasant odour and releases potentially harmful substances (various chemicals,

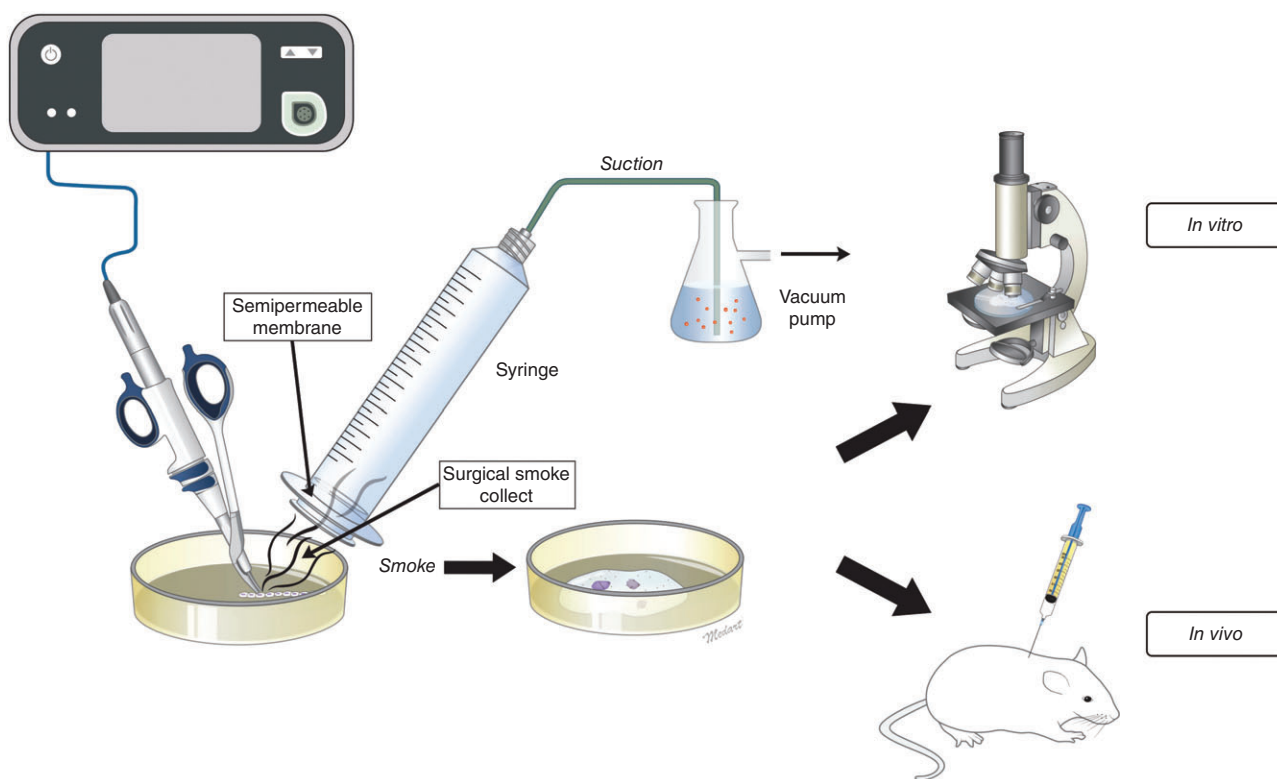


Fig. 1 Experimental settings for *in vitro* and *in vivo* experiments

particles, virulent viruses and bacteria) into the surrounding area. Concerns have been raised regarding the infection risk, mutagenesis and spread of malignant cells. Exposure to surgical smoke is associated with adverse effects on the cardiovascular and respiratory system as well as with increased mortality². Surgical smoke has been demonstrated to have cytotoxic, genotoxic and mutagenic effects^{3–5}. It is also a potential biohazard, containing carcinogens^{6,7}. Despite this, smoke evacuators are not employed routinely in conjunction with intraoperative energized dissection.

Experimental studies have shown that various surgical devices produce different particle sizes^{8–11} and thermal damage to tissue^{12–14}. The aim of the present study was to compare the contents of the smoke from various surgical devices and to see whether viable tumour cells could be found. The secondary aim was to determine whether any malignant cells found in surgical smoke had the potential to grow in other animals.

Methods

This study was conducted in two parts (*in vitro* and *in vivo* experiments). The *in vitro* experiment aimed to determine whether viable cells were present in surgical smoke. If

viable tumour cells were found, the *in vivo* study was to evaluate their carcinogenicity. Both experiments were performed in an operating theatre.

In vitro experiment

Various tumour cell lines (NCI-H292, FaDu, KB, AGS, ARO), obtained from the American Type Culture Collection (Rockville, Maryland, USA) were used. The FaDu and KB cells were grown *in vitro* in minimal essential medium supplemented with 10 per cent fetal bovine serum (FBS), 20 mmol/l HEPES, 50 units/ml penicillin and 50 µl/ml streptomycin. The other cells (NCI-H292, AGS, ARO) were grown in Rosewell Park Memorial Institute (RPMI) 1640 medium supplemented with 10 per cent FBS as well as 1 per cent penicillin and streptomycin. These cells were maintained at 37°C in a 5 per cent carbon dioxide incubator and passaged every 3 days. For injection, the cancer cell monolayers were disaggregated with 0.25 per cent trypsin–EDTA for 3 min at 37°C and adjusted to 2×10^6 cells/ml in RPMI. The following powered devices were tested: bipolar electrocautery (Valleylab™, Force FX™-8C; Covidien, Dublin, Ireland), radiofrequency ablation (Coblator II™ surgery

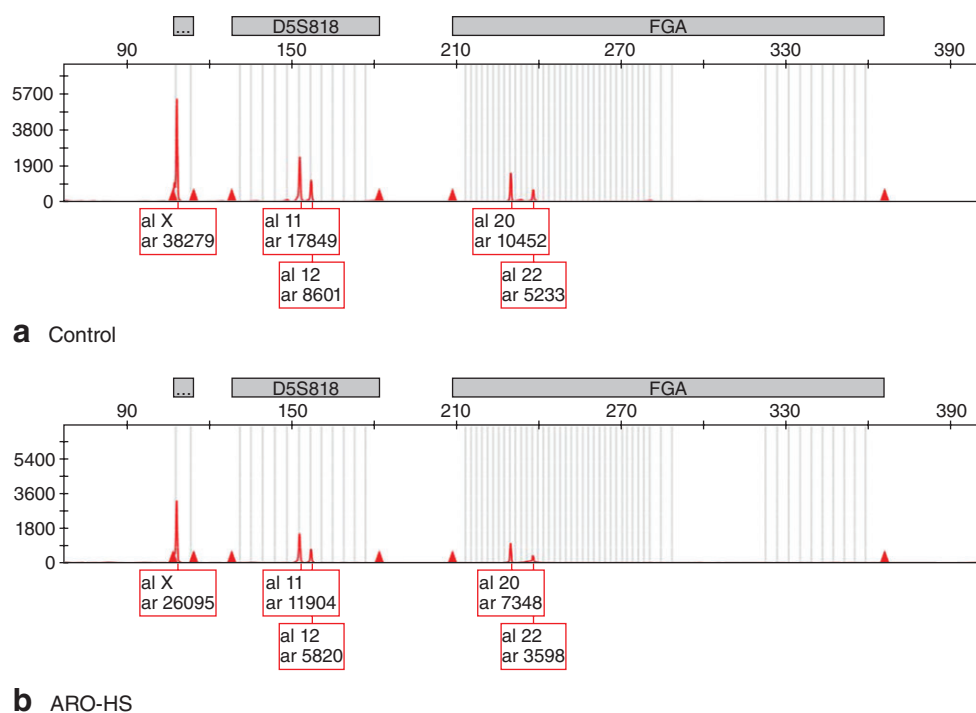


Fig. 2 Example of DNA analysis. All alleles for 16 markers are identical between the cell lines used in the vaporization experiment (**a** control) and cultured cells collected from the smoke (**b** ARO-HS), indicating that the two cell groups are genetically the same

system, ReFlex Ultra[®] 45 Plasma wand[™]; Arthrocare, Austin, Texas, USA) and ultrasonic scalpel (Ultracision Harmonic[®] scalpel generator 300; Ethicon Endo-Surgery, Cincinnati, Ohio, USA). The settings used were those usually employed during surgery. Costar[®] Transwell[®] Clear inserts (0.4 µm pore size, diameter 24 mm, semipermeable polyester membrane; Corning, New York, USA) were used to collect cells from the surgical smoke. These inserts were fixed tightly to the tip of a 50-ml syringe so that there was no space between them. The surgical smoke was aspirated by vacuum pump (15 cmHg) using the syringe with fitted Transwell[®] membrane, which was positioned at 5 and 10 cm from the target cell line (Fig. 1). The particles trapped in the Transwell[®] membrane were diluted with 3 ml medium. The diluted medium with surgical smoke was cultured at 37°C in a 5 per cent carbon dioxide incubator to see whether any cells remained viable. DNA genotyping analysis was used where cellular proliferation was observed to determine whether cells in the surgical smoke were consistent with the original tumour cells.

***In vivo* experiment**

SCC7 mouse cancer cells were grown in RPMI 1640 medium supplemented with 10 per cent FBS as well as 1

per cent penicillin and streptomycin, maintained at 37°C in a 5 per cent carbon dioxide incubator and adjusted to 5×10^5 cells/ml. The surgical smoke was collected as in the *in vitro* experiment. The rinsed Transwell[®] membrane liquid with RPMI 1640 medium was collected without a cell culture process. The rinsed Transwell[®] membrane liquid was isolated by centrifugation (5 min at 550g) and washed three times in RPMI 1640.

Table 1 Proportion of experiments with viable cells in surgical smoke produced by various surgical devices

Cell line	Proportion with viable cells					
	Radiofrequency ablation		Electrosurgery		Harmonic [®] scalpel	
	5 cm	10 cm	5 cm	10 cm	5 cm	10 cm
KB	0 of 5	0 of 5	0 of 5	0 of 5	5 of 5	1 of 5
FaDu	0 of 5	0 of 5	0 of 5	0 of 5	5 of 5	0 of 5
NCI-H292	0 of 5	0 of 5	0 of 5	0 of 5	5 of 5	1 of 5
AGS	0 of 5	0 of 5	0 of 5	0 of 5	5 of 5	0 of 5
ARO	0 of 5	0 of 5	0 of 5	0 of 5	5 of 5	0 of 5
Total	0 of 25	0 of 25	0 of 25	0 of 25	25 of 25	2 of 25

Results are shown for distances of 5 and 10 cm between the target cell line and Transwell[®] membrane.

Forty 5-week-old male C3H mice (Orient Bio, Seoul, Korea) were prepared. The sediment of rinsed Transwell® membrane liquid was injected subcutaneously into either side of the lower back of 20 C3H mice. The other 20 C3H mice, used as the control group, were injected on either side of the lower back with phosphate-buffered saline. The mice were observed for growth of cancer cells. After 14 days, the animals were anaesthetized with 3 per cent halothane by mask and killed by intracardiac injection of pentobarbital. The injection site was shaved and cleaned with alcohol, and any subcutaneous nodules were exposed using an aseptic technique. The nodules were bisected for microscopic examination. Haematoxylin and eosin-stained sections were examined at 400× magnification using an inverted microscope. All animal studies received prior institutional review board approval (IACUC 2014–0003).

Results

In vitro experiment

Viable cells were identified in smoke retrieved from a distance of 5 cm, but only from the Harmonic® scalpel (25 of 25 experiments); at 10 cm distance the rate was much lower (2 of 25) (Table 1). There were no viable cells in surgical smoke from the electrosurgical unit or radiofrequency ablation device.

Microscopic analysis of cultures from the cellular debris in surgical smoke was undertaken. Where cellular proliferation was observed, viable cells were seen on the first day and vigorous cellular proliferation was observed within 3 weeks of incubation. Culture of smoke from electrosurgery or radiofrequency ablation did not reveal any growth over 4 weeks. DNA genotyping analysis, used where cellular proliferation was seen, showed that all alleles were identical between cell lines used in the vaporization experiment and cultured cells collected from the smoke (Fig. 2).

In vivo experiments

As the *in vitro* experiment demonstrated viable cells only after Harmonic® scalpel use, the *in vivo* study was conducted with this device. Sediment collected from smoke of the SCC7 mouse cancer cell line treated with an ultrasonic scalpel was injected on both sides of the lower back of 20 mice. Two weeks after injection, tumour growth was seen on one side in eight of 20 animals that received an injection of smoke particles, and on both sides in four of 20; in total 16 of 40 injection sites (Table 2, Fig. 3). The animals were killed at 21 days, and any palpable mass was biopsied for morphological assessment. All tumours were located in

Table 2 Results of injection of surgical smoke from SCC7 cauterization in *in vivo* study

	PBS injection (n = 20)	SCC7 smoke injection (n = 20)
Tumour growth on one side	0 of 20	8 of 20
Tumour growth on both sides	0 of 20	4 of 20
Total animals with tumour growth	0 of 20	12 of 20
Total injection sites with tumour growth	0 of 40	16 of 40

PBS, phosphate-buffered saline.

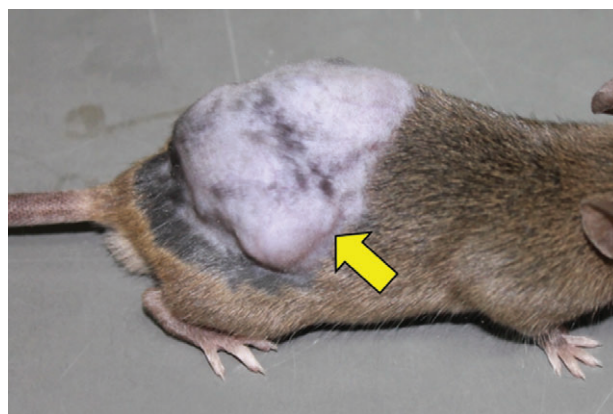


Fig. 3 Palpable mass found at injection site 14 days after injection of sediment

the subcutaneous layer. All contained highly mitotic cells including irregularly shaped nuclei, consistent with malignant tumours.

Discussion

This study demonstrated viable malignant cells only in surgical smoke from an ultrasonic scalpel. Their presence was dependent on the distance between the collecting membrane and the tip of the device generating the surgical smoke. Cells were always found at 5 cm distance between the Transwell® membrane and the tip of the device, but this reduced to 8 per cent (2 of 25) at 10 cm. This suggests that malignant cells may be aerosolized by the application of an ultrasonic scalpel to tumour-bearing tissue, and may account for the phenomenon of tumour recurrence in a port site remote from where a tumour was extracted after laparoscopic resection^{15–17}.

In contrast to surgery with an ultrasonic scalpel, radiofrequency ablation did not yield viable cells in the surgical smoke. Radiofrequency ablation and ultrasonic scalpels have a similar mechanism of action, and are operated at a

similar temperature of 50–100°C. They do not use a burning process like electrocautery or laser. During a burning process, target cells are heated to boiling point, causing the membrane to rupture and disperse fine particles into the surrounding area. The application of an electric current in the radiofrequency ablation range (450–500 kHz) results in ion movement and generation of heat due to friction (electrically resistive heating), and subsequent tissue death owing to protein coagulation¹⁸. Ultrasonic scalpels use ultrasonic energy to disrupt tissue by cavitation and produce a dense cloud of cellular debris that may contain viable cells. The heat generated by ultrasonic scalpels is a result of internal tissue friction caused by the high-frequency vibrations (about 55 000 per s)¹⁹. Cooler aerosols have a greater chance of carrying infectious and viable materials than the higher-temperature aerosols. Low-temperature vaporization by ultrasonic scalpels causes less thermal damage to tissue^{12–14}.

There is evidence showing the presence of viable bacteria and viruses in surgical smoke. Capizzi and colleagues²⁰ showed that, of 13 bacterial cultures, five resulted in growth of coagulase-negative *Staphylococcus* in laser resurfacing plume. Garden and co-workers²¹ demonstrated intact viral DNA in the smoke collected during carbon dioxide laser therapy of papillomavirus-infected verrucas. The same authors²² subsequently confirmed the infectivity of the particles by inoculation into the skin of calves. It has been reported that a surgeon contracted laryngeal papillomatosis after treating anogenital condyloma with a surgical laser²³.

The presence of viable cells in surgical smoke remains controversial. Although some studies failed to identify aerosolized cells in the peritoneal cavity during laparoscopic surgery²⁴, others have demonstrated the presence of cell-sized fragments, morphologically intact but non-viable cells¹⁹ and viable cells^{14,25,26} in surgical smoke. One study²⁷ noted that very few morphologically intact, but no viable cells were found in the surgical smoke of ultrasonic scalpels. In another study²⁸, viable melanoma cells were demonstrated in smoke generated by electrocautery of mouse melanoma cells. However, proliferation of these viable cells was not successful. It can be concluded that viable cells (including malignant cells) may survive in surgical smoke.

Previous experiments used surgical smoke directly aspirated through a long tube. In the present study, a Transwell[®] membrane with pores smaller than the cells was used to increase cell collection. When surgical smoke passed through the membrane, gaseous components were collected through a vacuum pump, whereas cells larger than the pore were filtered out and collected. The cell collection in this experiment may have

been more accurate than in previous studies as a result of this.

Even with the use of a smoke evacuator, operating theatre personnel can usually detect the smell of burnt tissue when energized dissection is used. This means that surgical smoke is inadequately removed for staff and patients. It is seldom the case that a tumour mass is cut directly because a safe resection margin is usually dissected. However, a tumour mass could be dissected directly because of a distorted surgical field, extensive malignancy or surgical error. Therefore, surgical smoke must be contained and a smoke evacuation system employed to protect surgical team members and patients.

A number of previous studies have demonstrated large quantities of cellular debris in the surgical smoke from various instruments; however, viable tumour cells have rarely been isolated. The present study suggests that the surgical smoke from ultrasonic scalpels may contain viable tumour cells, and that there is a theoretical risk of transfer to anyone close to the surgical procedure.

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