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Measurement of ventilation- and perfusion-mediated cooling during laser ablation in ex vivo human lung tumors

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ABSTRACT

Purpose: Perfusion-mediated tissue cooling has often been described in the literature for thermal ablation therapies of liver tumors. The objective of this study was to investigate the cooling effects of both perfusion and ventilation during laser ablation of lung malignancies.
Materials and methods: An ex vivo lung model was used to maintain near physiological conditions for the specimens. Fourteen human lung lobes containing only primary lung tumors (non-small cell lung cancer) were used. Laser ablation was carried out using a Nd:YAG laser with a wavelength of 1064 nm and laser fibers with 30 mm diffusing tips. Continuous invasive temperature measurement in 10 mm distance from the laser fiber was performed. Laser power was increased at 2 W increments starting at 10 W up to a maximum power of 12–20 W until a temperature plateau around 60 °C was reached at one sensor. Ventilation and perfusion were discontinued for 6 min each to assess their effects on temperature development.
Results: The experiments lead to 25 usable temperature profiles. A significant temperature increase was observed for both discontinued ventilation and perfusion. In 6 min without perfusion, the temperature rose about 5.5 °C (mean value, $P < 0.05$); without ventilation it increased about 7.0 °C (mean value, $P < 0.05$).
Conclusion: Ventilation- and perfusion-mediated tissue cooling are significant influencing factors on temperature development during thermal ablation. They should be taken into account during the planning and preparation of minimally invasive lung tumor treatment in order to achieve complete ablation.

1. Introduction

Thermal ablation techniques (e.g. techniques using laser, radiofrequency or microwave) are established methods for treating focal malignant lesions in various organs, such as the liver, kidneys and lung. A decrease in temperature caused by perfusion, known as perfusion-mediated cooling, has often been investigated in the liver [1–5]. The use of radiofrequency and laser ablation in the lung also becomes more frequent and several studies on this topic have been published during the last years [6–9].

When these ablation procedures are applied to tumors in different organs, there are special characteristics that have to be taken into account. For example in the lung, it is possible that there is both perfusion- and ventilation-mediated cooling during ablation, which can have negative effects on the therapy, such as smaller areas of coagulation necrosis, as Anai et al. demonstrated in a porcine model using normal lung tissue [10]. However, obtaining large lesions is especially important since the ablation volume should be at least four times larger than the tumor to warrant complete ablation results without any viable cells left behind, as De Baère et al. observed [9].

Linder et al. developed a physiologically accurate ex vivo model which uses resected human lung tissue containing focal tumors. The tumor-bearing lung tissue gives us the opportunity to demonstrate ventilation-mediated cooling in a clinically relevant way and to obtain realistic temperature measurement in focal laser ablation since energy may propagate differently in solid and air-filled tissue [11].

The objective of our study was to investigate the influence of ventilation and perfusion on temperature development during laser ablation of focal lung tumors.

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2. Materials and methods

2.1. Experimental overview

The experiments were performed in the Department of Thoracic Surgery of a Center for Lung Disease (Lungenklinik Hemer, Germany, 1300 lung resections annually). Resected tumor-bearing lung lobes (only non-small cell lung cancer) were used for the study. The regional ethics committee had approved the study protocol including the use of resected human lung specimens in the ex vivo isolated, perfused, and ventilated human lung model [12]. Patients had given written informed consent to this procedure. The type of resection and treatment of the resected specimens were dictated only by medical necessity in each case.

The experiments were carried out with 14 lobes and temperatures were measured on two sides of the laser fiber, i.e. 28 temperature profiles were recorded. Three profiles had to be excluded because they were not logged correctly for technical reasons, resulting in 25 temperature profiles in 10 mm distance available for analysis.

The two authors who performed the experiments were trained and supervised in the use of the lung model by its developer. They carried out about 25 training procedures before this study was started.

Tumor-bearing lobes, bilobes or whole lungs were used. Each specimen contained one tumor; both centrally and peripherally located tumors were included in the study. Decaying tumors with cavitation seen on preoperative CT were excluded. Since the tumors in the used specimens were large, there were no major airways or vessels near the laser fiber and temperature sensors. Technical feasibility of the connection to the isolated human lung perfusion model was a prerequisite.

2.2. Ex vivo model

The resected lung specimens were prepared for the experiments immediately after surgery. Veins and arteries were opened to allow evacuation of blood. In the artery stumps plastic cannulae were inserted and fixed. Bronchi were connected end-to-end to a bronchial tube by sutures. Veins remained open (Fig. 1). The lobes were connected to the roller pumps of a heart-lung machine and perfused with a solution of Dulbecco's phosphate-buffered saline (Sigma–Aldrich Chemie, Steinheim, Germany), glucose (0.99 g/l) and calcium chloride (2.5 mM). $NaHCO_3$ was added to adjust pH to 7.4. The perfusate mixed with residual blood in the specimens to oxygenate tumor tissue via hemoglobin in the blood and circulated at a temperature of 37 °C.

The bronchial tube was connected to a respirator (Dräger UV1, Dräger Werke AG, Luebeck, Germany). The preparations were ventilated with room air to which O_2 or CO_2 was added as necessary. Respiratory rate was 10–16 min^{-1}. The tidal volume was manually adjusted between 100 ml (single lobe) and 500 ml (whole lung). O_2 partial pressure was kept between 80 and 120 mmHg and CO_2 partial pressure between 35 and 45 mmHg by changing the O_2 and CO_2 fractions or the ratio of inspiration to expiration time. Regular blood gas analysis including glucose and lactate values served to monitor and adjust several parameters of the perfusate.

2.3. Laser ablation and temperature measurement

Laser ablation has been described elsewhere [13,14]. It was performed using a Nd:YAG laser (Medilas fibertom 5100, Dornier MedTech, Germering, Germany) with a wavelength of 1064 nm. The laser was combined with a miniaturized, open applicator (Monocath®, Trumpf, Umkirch, Germany) and a Teflon tube with a y-shaped entrance for the laser fiber and infusion line. Cooling was provided by a flow of 80 ml/h saline solution (0.9% at room temperature) inside and out of the tube containing the laser fiber. This was necessary to prevent carbonization around the fiber during ablation which would have negative effects on the energy deposition in the tissue. The laser fiber had a core diameter of 400 μm and a diffuser length of 30 mm, where the laser light was emitted (Microflexx 30, KLS Martin, Umkirch, Germany). The 5.5-F Teflon catheter was placed in the tumor with the help of a mandrin. After the removal of the mandrin, the cooled laser fiber was inserted into the catheter. Temperature probes (NiCr–Ni, −50 °C to +260 °C, B+B Thermotechnik, Donaueschingen, Germany) were manually positioned within the tumor parallel to the laser applicator on two opposing sides at a distance of 10 mm under palpation guidance by passing them through a plastic barrow with parallel holes (Fig. 2), i.e. two temperature profiles were recorded in each experiment. Temperatures were continuously logged using an 8-channel USB data logger (RedLab TC, software: Tracer Daq, Meilhaus Electronic, Puchheim, Germany).

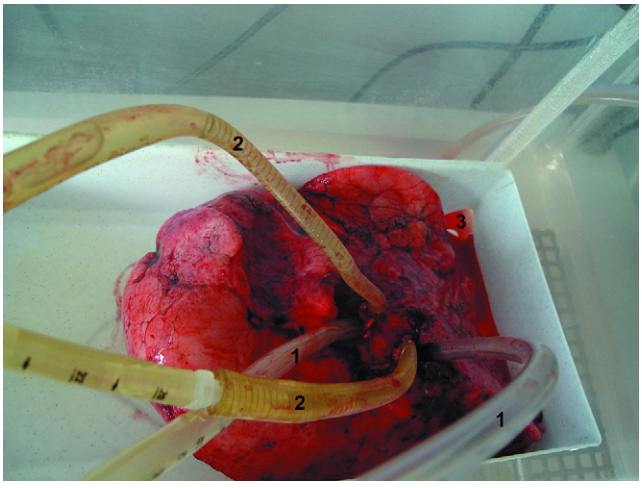

Fig. 1. Left upper lobe connected to the IHLP. (1) Bronchial tubes connected to the respirator, (2) perfusion cannulae and (3) run-off for recirculation of the perfusate.

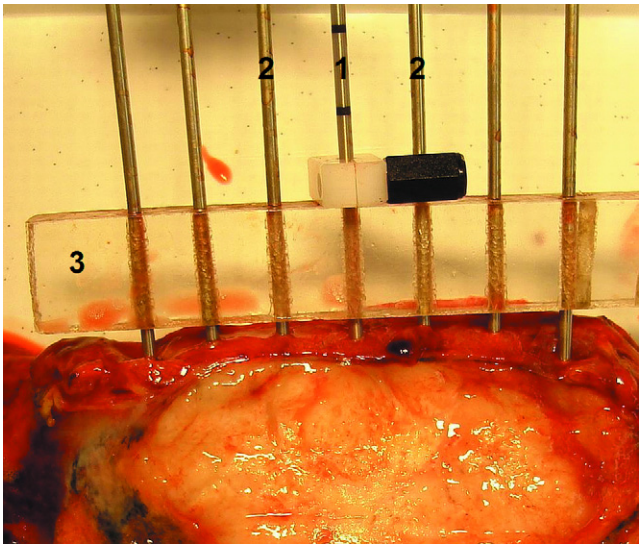

Fig. 2. Specimen cut along the laser fiber and temperature probes to verify their correct position after the experiment. (1) Applicator containing the laser fiber, (2) temperature probes on both sides of the laser fiber in 10, 20 and 30 mm distance and (3) plastic barrow used as spacer.