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● *Clinical Note*

ONE-LUNG FLOODING ENABLES ULTRASOUND-GUIDED TRANSTHORACIC NEEDLE BIOPSY OF PULMONARY NODULES WITH HIGH SENSITIVITY

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Abstract—Ultrasound-guided transthoracic needle biopsy (USgTTNB) can only be used for peripheral tumours that contact the pleura. Sonographic accessibility of the entire lung can be achieved using one-lung flooding. In this study, feasibility, sensitivity and complication rate of USgTTNB of lung nodules after one-lung flooding in an *ex vivo* and *in vivo* lung tumour model were assessed. USgTTNB was performed *ex vivo* after one-lung flooding in 10 resected human lung lobes containing carcinoma or metastasis. USgTTNB after one-lung flooding and simulation of a lung nodule was conducted *in vivo* in 5 animals. Transthoracic sonography and chest X-ray were obtained 30 min after reventilation. The lungs were examined macroscopically and histopathologically. The pathologic diagnosis was confirmed in 85.7% and 100% of tumours after first and second puncture attempts, respectively. The successful puncture rate *in vivo* was 90%. Neither pneumothorax nor bleeding was observed. One-lung flooding enables USgTTNB of lung nodules with a high sensitivity and minimal risk of complications in a pre-clinical model. (E-mail: Thomas.Lesser@srh.de)

Key Words: **One-lung flooding, Ultrasound, Transthoracic needle biopsy, Pulmonary nodules.**

INTRODUCTION

Since publication of the National Lung Screening Trial (NLST) results, lung cancer screening has gained considerable interest not only in the United States but also elsewhere in the world. Low-dose computed tomography (LD-CT) lung cancer screening leads to a high detection rate of pulmonary nodules. In the NLST, 51.8% of cancer patients with a positive LD-CT result had Stage IA tumours. However, 96.4% of positive screening results in the LD-CT group were false-positive results (National Lung Screening Trial Research Team 2011). Most small nodules are not malignant. The American College of Chest Physicians Guidelines for Diagnosis and Management of Lung Cancer recommend pathologic confirmation of pulmonary nodules, except when the clinical probability of malignancy is very low (<5%) or the clinical probability is low (<30%–40%) and the results of a functional imaging test are negative (Gould et al. 2013).

Current non-surgical biopsy methods, such as computed tomography (CT)-guided transthoracic needle biopsy (CTgTTNB) and transbronchial biopsy (TBB), have significant risks of complications and are frequently non-diagnostic. For nodules measuring up to 15 mm in diameter, a false-negative biopsy occurs in 10%–49% of CTgTTNB and 30%–70% of TTB (Fontaine-Delaruelle et al. 2015; Gould et al. 2013). Pneumothorax and haemorrhage are serious potential complications of CTgTTNB or TBB. Rzyman et al. (2013) reported that approximately 60% of patients with pulmonary nodules underwent surgery without earlier pathologic examination; 35% of these operations were unnecessary, as the lesions were benign. These findings emphasize the need for a safe, minimally invasive non-surgical biopsy method with sufficient sensitivity, accuracy and negative predictive value.

Traditional ultrasound-guided TTNB (USgTTNB) can only be used for peripheral tumours that contact the pleura. In ventilated lung, nodules localised to more central areas are not visible by ultrasound. Animal experiments have shown that sonographic accessibility of the entire lung can

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be achieved using one-lung flooding (OLF) (Lesser et al. 1998). OLF enables complete sonographic imaging of the whole lung, including parenchyma, vessels and bronchi, as well as lung tumours (Lesser et al. 2013). A good sonographic imaging of the lesion is indispensable for a successful biopsy. However, there are various aspects that influence the biopsy outcomes, such as lesion size, depth, localization, needle size, the approach path to the lesion, strategies for clear visualization of the needle. Although solid pancreatic masses were visible by ultrasound, percutaneous ultrasound-guided core needle biopsy resulted in a negative predictive value of 75% (Kahriman et al. 2016).

The objective of this study is to investigate the feasibility, sensitivity and safety of USgTTNB of pulmonary nodules, using OLF in pre-clinical *ex vivo* and *in vivo* lung tumour models.

MATERIALS AND METHODS

Ex vivo *examinations*

An *ex vivo* human lung model was used to obtain biopsy specimens of central pulmonary lung nodules. Lung lobes containing central tumours were obtained from 10 patients who underwent curative lobar resection. The experimental protocol was approved by a local institutional review board, and informed consent for the study was obtained from all patients. The lobes were flooded *ex vivo* with saline (Lesser et al. 2013). Biopsy was performed by placing the sonographic probe on the visceral pleura of the flooded lobe and inserting an automated cutting core biopsy needle (BARD MAX-CORE Disposable Core Biopsy Instrument, 14 gauge; BARD GmbH Karlsruhe, Germany) (Fig. 1). Each tumour was punctured up to three times. A sonographic hit was defined as the needle being visible within the nodule during B-mode imaging. A pathologic hit was defined as the needle biopsy results exhibiting the same histology as the final pathology results of the resected lobe. Of the 10 lung lobes (4 right lower lobe, 3 left upper lobe, 1 left lower lobe, 2 right upper lobe) examined, 5 contained non–small cell lung cancer (NSCLC; 2 adenocarcinoma, 2 neuroendocrine tumour, 1 squamous cell carcinoma) and 5 contained metastases (2 renal cell carcinoma, 1 colorectal cancer, 1 breast cancer, 1 lung carcinoma). The mean nodule diameter was 2.9 cm (1.8–4.5 cm) on CT examination.

In vivo *examinations*

In vivo experiments were performed using a large porcine model, with 5 female pigs ("Deutsches Landschwein," 30–34 kg) in the supine position. Permission for all animal experiments was granted by the Veterinary Department of the Thuringian State Authority for Food Protection and Fair Trading in compliance with the National Animal Protection Act.

After the animals were anaesthetized with propofol (10 mg kg^{-1} h^{-1}), sufentanil (0.02 µg kg^{-1} min^{-1}) and pancuronium bromide (2.5 µg kg^{-1} min^{-1}) a left-sided animal-specific Robertshaw double-lumen tube with an extra-long bronchial channel (39 Fr; special product by Mallinckrodt Medical, Dublin, Ireland) was inserted. The correct position of the tube was checked by fibre optic bronchoscopy (BF 3 C30; Olympus, Tokyo, Japan). Mechanical ventilation was performed with an intensive care unit respirator (Servo 900, Siemens AG, Munich, Germany) in volume-controlled mode (FiO_2 = 0.4; tidal volume = 10 mL kg^{-1} weight; respiratory rate adjusted to maintain an end-tidal CO_2 of 35–45 mm Hg; inspiratory:expiratory ratio = 1:1; positive end-expiratory pressure = 5 cm H_2O). After 30 min of double-lung ventilation with FiO_2 = 1.0, the right endobronchial channel was disconnected from the respirator. The infusion system was immediately connected to this channel, and the right lung was slowly filled

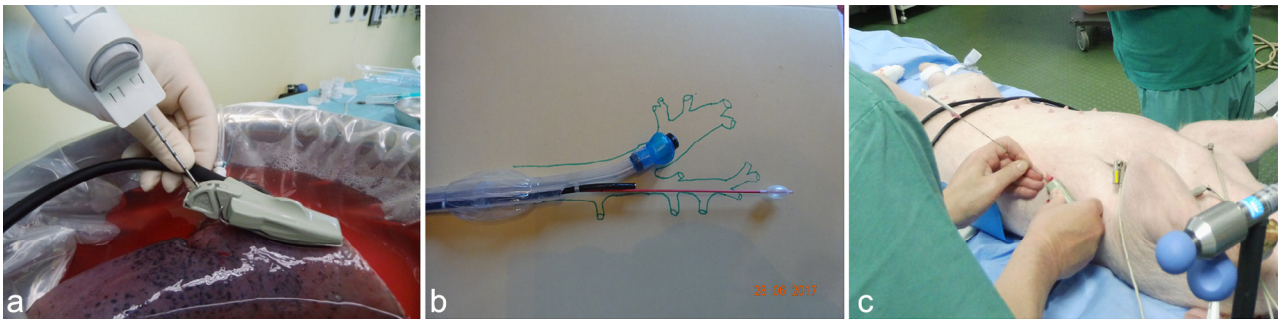

Fig. 1. Experimental setup. (a) Transpleural ultrasound-guided core needle biopsy (using a needle-guidance device) of a central localized lung malignancy after flooding of the resected human lobe *ex vivo*. (b) *In vivo* experimental setup of simulated lung lesion, showing transbronchial insertion of a Fogarty catheter in the flooded right lung *via* the right lumen of a double-lumen tube, using fibreoptic bronchoscopic control. The Fogarty balloon is filled with saline. (c) Ultrasound-guided transthoracic needle biopsy of a simulated lung lesion after one-lung flooding *in vivo*. A small-calibre core biopsy needle (18 gauge) was inserted by the "freehand" technique.