Thoracoscopic ultrasonography for localization of subcentimetre lung nodules

Hironobu Wadaa,b, Takashi Anayamaa, Kentaro Hirohashia, Takahiro Nakajimaab, Tatsuya Katoa, Thomas K. Waddella, Shaf Keshavjeea, Ichiro Yoshinoa and Kazuhiro Yasufukua,*

a Division of Thoracic Surgery, Toronto General Hospital, University Health Network, Toronto, Canada
b Department of General Thoracic Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

* Corresponding author. Division of Thoracic Surgery, University of Toronto, Toronto General Hospital, University Health Network, 200 Elizabeth St, 9N-957, Toronto, ON, Canada M5G2C4. Tel: +1-416-3404290; fax: +1-416-3403660; e-mail: kazuhiro.yasufuku@uhn.ca (K. Yasufuku).

Received 23 October 2014; received in revised form 10 February 2015; accepted 4 March 2015

Abstract

OBJECTIVES: Localization of small, non-visible and non-palpable subcentimetre nodules can be challenging during video-assisted thoracoscopic surgery (VATS). Intraoperative ultrasonography is an option for localization of such lesions, yet this technology has not been fully adapted to thoracic surgery. The objective of this study was to assess a newly developed thoracoscopic ultrasound for localization and biopsy of subcentimetre pulmonary nodules in animal models.

METHODS: A prototype convex probe ultrasound thoracoscope (XLTF-UC180, Olympus Medical Systems Corp.) was used in this study. Multiple 5% agar pseudo-tumours were created in porcine lungs (n = 10) and assessed for localization with different frequencies (5.0–12.0 MHz) in deflated lungs. The evaluated pseudo-tumours were divided into two groups based on the distinctness of the tumour margin on the ultrasound images and compared in terms of the size and depth of the tumours. The visualization of real tumours and the biopsy capability were assessed using rabbit VX2 lung tumour models (n = 7).

RESULTS: The thoracoscopic ultrasound clearly visualized normal lung structures within a 1.5-cm depth including small vessels and bronchioles less than 5 mm in diameter in the completely deflated lung. Twenty-eight of 30 agar pseudo-tumours (93.3%) were successfully detected in deflated lungs (average size: 8.5 ± 2.1 mm; average depth: 7.4 ± 7.5 mm and depth range: 0–24.8 mm). Two tumours were not detected due to residual air surrounding the tumour. Higher frequency (12 MHz) tended to show more distinct margins of the targets. Indistinct tumours were located significantly deeper in the lung than the distinct tumours (14.11 vs 2.42 mm), regardless of them being in a similar size range. VX2 tumours were identified as heterogeneous isoechoic lesions and adequate tissue sampling for diagnosis was achieved using a dedicated needle.

CONCLUSIONS: The newly developed convex probe ultrasound thoracoscope was capable of localizing subcentimetre nodules in the porcine deflated lung as well as of obtaining sufficient sampling from lung tumours in the rabbit model, which may enable single-port VATS lung nodule biopsy in a human clinical setting. However, the depth of the tumours significantly influenced the quality of ultrasound images. Complete collapse of the lung and use of high frequency may facilitate achieving distinct visualization of the targets.

Keywords: Thoracoscopy/VATS • Imaging • Lung wedge resection • Surgical equipment • Ultrasound

INTRODUCTION

The results of the National Lung Screening Trial showing reduced lung cancer mortality with low-dose CT screening have led to the adoption of lung cancer screening in centres around the world [1]. Due to this, thoracic surgeons will be faced with small pulmonary nodules requiring surgical resection. Video-assisted thoracoscopic surgery (VATS) wedge resection has been widely applied to patients with small peripheral pulmonary nodules, including metastatic tumours and indeterminate lesions. One of the clinical challenges during VATS wedge resection is real-time precise localization of the tumour, in particular for small, non-visible and non-palpable lesions. Failure of localization may result in larger resections or conversion to thoracotomy. Preoperative CT-guided metal tag placement (such as a microcoil or a hook wire) has been prevalently performed to localize small pulmonary lesions with intraoperative fluoroscopic assistance, and has shown excellent results with more than 97% localizability [2, 3]. However, these techniques require a preoperative invasive procedure, which can cause patient discomfort, dislodgement...
of the tag and complications such as pneumothorax and haemoptysis. Furthermore, intraoperative radiation exposure is also inevitable to patients as well as operating staff. Alternatively, thorascopic ultrasonography is an option as it is a real-time, convenient and less invasive technique not requiring any preoperative additional procedure for localization of small lung lesions during VATS. Previous small-scale, single-centre studies have demonstrated the feasibility of intraoperative thorascopic ultrasound for localization of small lung nodules [4–12] and even for ground-glass opacities (GGOs) [5]. This technology also facilitates wedge resection of the lung in children [6, 13]. However, there is limited use of thorascoscopic ultrasound in thoracic surgery likely due to the current available probes which were originally made for abdominal surgery and not for thoracic surgery. Therefore, we have been developing a thorascoscopic ultrasound system that enables precise visualization and real-time biopsy of small lung nodules during VATS. The aim of this study was to assess the prototype thorascoscopic ultrasound in animal models in preparation of translation to clinical use, and explore optimal ultrasound settings for intraoperative lung nodule localization.

MATERIALS AND METHODS

Convex probe thorascoscopic ultrasound

All experiments and data analysis were performed at University Health Network (UHN). A newly developed prototype thorascoscopic ultrasound (XLTF-UC180, Olympus Medical Systems Corp., Tokyo, Japan) was used for this study (Fig. 1). This is a semi-rigid thorascoscope with a 1-direction flexible tip (up and down). It has a convex ultrasound probe on its tip similar to that used in the endobronchial ultrasound scope. The device operates at the frequencies of 5, 7.5, 10 and 12 MHz. The scanning direction of the probe is parallel to the insertion direction. The scanning range is 60°. A dedicated 22-G needle can be used to obtain tissue samples. The obtained echo images can be recorded in an ultrasound scanner (EU-Y0005, Olympus Medical Systems Corp.) and used for the analysis described later.

Animal models and thorascoscopic ultrasound evaluation

This study was approved by the Animal Care Committees at UHN. All animals were provided humane care in accordance with the policies formulated by the UHN Animal Care Committee, the Animal for Research Act of the Province of Ontario and the Canadian Council on Animal Care.

Porcine pseudo-tumour models (n = 10, average body weight: 35.3 ± 4.5 kg) and rabbit VX2 lung tumour models (n = 7) were used for the evaluation of the new device. In the porcine pseudo-tumour models (Yorkshire pigs purchased from Caughell Farms, Fingal, Canada), tracheotomy was performed and an endobronchial tube or an endotracheal tube with an intrabronchial blocker was placed to apply appropriate one-lung ventilation under general anaesthesia. After left thoracotomy, pseudo-tumours were created by transpleural injection of 5% agar mixed with Iohexol (Omnipaque®, GE Healthcare, Mississauga, Canada) into inflated porcine lungs at different depths from the lung surface. For collapsing the lung, the probe of the thorascoscopic ultrasound was placed on the lung surface through the thoracotomy window, and the porcine normal lung structures and small agar pseudo-tumours were evaluated. All evaluation was performed at a frequency of 12 MHz except for the first case which was evaluated with 10 MHz. The lungs were deflated as much as possible since air remaining in the lung causes the scattering of the ultrasound, leading to low-quality ultrasound imaging. No acoustic coupling agent, such as ultrasound gel, was used for visualizing the structure. The Doppler mode was used

Figure 1: (A) Tip of the prototype thorascoscopic ultrasound (XLTF-UC180) with a dedicated 22-G needle. (B) The outer diameter is 10 mm for the use of minimally invasive surgery. A CCD camera and two light sources are on the tip of the thorascoscope. The accessory channel diameter is 2.2 mm. (C) The convex probe placed on the porcine lung surface to localize pseudo-tumours.
in distinguishing vessels from other structures. Different frequencies (5, 7.5, 10 and 12 MHz) were tested to compare each ultrasound image in 3 of 10 pigs. Of 10 porcine models, two ex vivo lungs were used for creation and evaluation of pseudo-tumours in the aforementioned manner. After the evaluation, the entire lungs with the trachea were removed and a tracheal tube was inserted into the trachea to create an ex vivo inflated state. The left lung was examined by micro-CT to determine the depth of the pseudo-tumours from the lung surface in the inflated state. The cross-section of the pseudo-tumours was recorded and their sizes were measured by Image J, which was then compared with the sizes in the obtained ultrasound images. We also evaluated the feasibility of carbon dioxide (CO2) insufflation into the thoracic cavity maintaining an intrathoracic pressure of 8 mmHg with intratracheal suction to obtain complete deflation of the lung. A thoracic port was placed and a thoracoscope was used to visualize the process of deflation. The completely deflated lung was defined as a dark red-coloured lung, whereas the inflated lung exhibited a pinkish tone due to air in the lung. Three of 10 pigs were used for the evaluation.

We also used a rabbit VX2 lung tumour model developed in our laboratory [14] to explore the feasibility of visualization of and biopsy capability with regard to a real lung tumor. Seven New Zealand white rabbits (Charles River, St Constant, Canada) were used in this study. The VX2 tumour-bearing rabbit underwent right thoracotomy under appropriate general anaesthesia and the probe of the thoracosopic ultrasound was placed on the tumour in the deflated lung without an acoustic coupling agent. Visualization of tumours was evaluated and subsequently fine-needle aspiration biopsies were performed using the dedicated 22-G needle in 3 of 7 cases. The aspirates in the needle were air-blown onto a glass slide and smeared for cytological evaluation using Diff-Quick staining.

**Ultrasound image evaluation**

The large tumour axis in the ultrasound images was compared with the actual size calculated by Image J to determine the correlation between those sizes. Digital images of all the pseudo-tumours obtained by the thorascoscopic ultrasound were reviewed by three different individuals (Hironobu Wada, Kentaro Hirohashi and Tatsuya Kato) blinded to the exact location of the tumours. The tumours were divided into two groups based on the margin of the tumour (distinct or indistinct). A distinct tumour was defined as the tumour visualized with more than half of the margin being clear. When the margin was unclear (less than half of the margin being distinct), we determined them to be indistinct. The depth, actual size and echoic size of the tumour were compared between the two groups.

**Statistical analysis**

The Mann–Whitney U-test was used to compare continuous variables such as the tumour size and the depth from the lung surface in the two groups. A two-by-two contingency table was created for Fisher’s exact test to compare the distinctness of tumour border between in vivo and ex vivo states. The square of the Pearson correlation coefficient ($R^2$) was computed between the actual and ultrasound diameter of the pseudo-tumours. All data analysis was conducted with the GraphPad Prism software (version 5.01, La Jolla, CA, USA). All P-values were based on a two-sided hypothesis, and a P-value of <0.05 was considered to have statistical significance.

**RESULTS**

In the porcine lung, both normal structures and agar pseudo-tumours were assessed by XLTFF–UC180 after deflation of the lung. The device clearly visualized pulmonary vessels in the peripheral lung at 12 MHz even though the vessel was 2 mm in diameter at 15 mm depth when the lung was completely deflated (Fig. 2). The pulmonary arterioles and venules showed a homogeneous hypoechoic area, and bronchioles exhibited a hyperechoic area adjacent to pulmonary arterioles. Thirty pseudo-tumours (the averaged actual size: 8.5 ± 2.1 mm) were created; this includes 21 in porcine lungs in vivo, and 9 in ex vivo lungs, both at a depth of 7.4 ± 5.7 mm (0–24.8 mm) from the inflated lung surface. Twenty-eight of 30 pseudo-tumours (93.3%) were successfully detected in the deflated lungs (Fig. 3A and B). All detectable pseudo-tumours were visualized within a 14-mm depth from the probe surface on ultrasound images. The deep edge of the pseudo-tumours was exhibited at a depth of 8.5 mm on average (5–14 mm). Two undetectable tumours were surrounded by the lung parenchyma with massive amount of residual air. The average size and depth of those two non-detectable pseudo-tumours were 8.5 and 6.7 mm, respectively. The ultrasound images of incompletely deflated lung showed a harsh heterogeneous hyperechoic area that made it difficult to identify either normal structures or pseudo-tumours (Fig. 3C). The pseudo-tumours were visualized as a homogeneous hypoechogenic area distinguished from pulmonary vessels by the Doppler mode. They sometimes contained white dots inside the tumour images due to the mixed air in the tumour. Nineteen of 28 identified pseudo-tumours showed a partially or entirely hyperechoic border that contributed to the successful localization of the tumour.

Different frequencies (5, 7.5, 10 and 12 MHz) were tested for visualization of normal structures and pseudo-tumours to determine the optimal setting for localization of the lung tumour. Seven pseudo-tumours and two normal structures were selected in 3 of 10 pigs examined. Each of them was evaluated at different frequencies and compared. Based on intraoperative subjective judgements of surgeons (Hironobu Wada and Takashi Anayama) and retrospective review of ultrasound images, a higher frequency tended to show distinct margins of the tumours and normal lung structures, and the ultrasound at 12 MHz reached a 15-mm depth in the deflated lung (Fig. 4). The frequency of 12 MHz appeared to be the best among the frequencies for visualization of the targets that aided surgeons to localize the tumour.

Of the 28 identified pseudo-tumours, the long axis of actual size and ultrasound measurement showed statistically significant and moderate correlation ($R^2 = 0.46$, $P < 0.001$, $Y = 0.81X + 1.73$). Of those, 16 pseudo-tumours were categorized in the distinct margin group, and the remaining 12 pseudo-tumours were categorized in the indistinct margin group. The indistinct pseudo-tumours were located in a significantly deeper part of the lung when compared with the distinct pseudo-tumours (14.11 mm for indistinct tumours and 2.42 mm for distinct tumours, $P < 0.001$), though there was no significant difference in actual size ($P = 0.63$) and ultrasound measurement ($P = 0.44$) of the pseudo-tumours (Fig. 5A). The ex vivo lung condition attributed to an indistinct tumour border in contrast to the in vivo lung condition ($P = 0.017$), likely due to the difficulty in achieving a completely deflated lung state ex vivo. Therefore, further analysis using in vivo data alone was
Conducted and demonstrated similar results, showing a significant difference in depth ($P = 0.004$), and no difference in sizes ($P = 0.96$ in actual size, $P = 0.75$ on ultrasound measurement; Fig. 5B).

The efficacy of CO$_2$ insufflation for achieving complete lung deflation was evaluated in three pigs. CO$_2$ insufflation maintaining an intrathoracic pressure of 8 mmHg was applied combined with intratracheal suction. This intervention achieved complete lung deflation within 180 s with satisfactory reproducibility. No complications were observed in any of the pigs during the procedure.

Real tumour visualization and biopsy capability of the thoracoscopic ultrasound were evaluated in rabbit VX2 lung tumour models. The average actual tumour size was 11.3 mm by 9.4 mm. The VX2 tumour in the rabbit lung exhibited a heterogeneous iso-echoic area that had similar ultrasound characteristics to deflated normal lung parenchyma. In 6 of 7 cases, distinct hyperechoic margins facilitated distinguishing the tumour from the lung parenchyma. The other case failed to visualize the tumour due to a thin tumour wall with a large cavity containing air. After visualization
of the tumour, the dedicated 22-G needle was inserted into the
tumour in 3 cases. We were able to successfully aspirate tumour
cells using the dedicated needle. The dedicated needle was clearly
visualized in the tumour during the aspiration. Diff-Quick staining
demonstrated adequate sampling for diagnosis of the tumour
(Fig. 6).

**DISCUSSION**

A thoracoscopic ultrasound is one of the feasible modalities for
localization of small lung tumours during VATS. Previous articles in-
dicate several advantages of thoracoscopic ultrasonography over
other modalities: it is real-time, convenient and less invasive, and

---

**Figure 4:** Comparison of both normal structures (top) and a pseudo-tumour (bottom) among the different frequencies. The frequency of 12 MHz showed a clear margin of the target, especially at the deep edge of the pseudo-tumour. Arrows show small vessels in the deflated lung. Scale bar: 5 mm. Left to right: 5, 7.5, 10 and 12 MHz.

**Figure 5:** (A) The pseudo-tumours with a distinct border were located significantly closer to the lung surface than those with an indistinct border ($P > 0.001$), even though the size of the tumours showed no difference. The largest depth in each group was 13.3 and 24.8 mm, respectively. White circles show the ex vivo evaluation. (B) In vivo tumours alone showed similar results ($P = 0.004$ in the depth comparison).
can potentially be done at a low cost since additional preoperative procedure is not necessary. Ultrasound technology provides accessibility to most of the pleural surface during VATS, including the surface of complete fissures, which may be a challenge for finger palpation as well as preoperative CT-guided metal tag placement [15]. It is also a safe technique without complications [7], such as pneumothorax and haemoptysis, since preoperative procedures are not required. On the other hand, several drawbacks of thoracoscopic ultrasonography have been reported. First, the thoracoscopic ultrasound requires complete deflation of the lung because residual air in the lung causes inferior ultrasound images [5, 6, 9, 11, 12]. Second, it requires experience in ultrasound interpretation [7, 15]. Careful port placement is also needed for successful localization of small lung nodules using thoracoscopic ultrasound, especially in paediatrics with a small chest cavity [6]. This study was conducted to validate thoracoscopic ultrasound technology for localization of small lung

**Figure 6:** Real-time thoracoscopic ultrasound-guided fine-needle aspiration biopsy of lung tumours in a rabbit model. (A) Endoscopic view of a VX2 tumour in the right lower lobe. (B) Cross-section of the tumour. The large arrow head shows the pulmonary artery adjacent to the tumour. (C and D) Echo images of a VX2 tumour with (D) and without (C) a needle. Scale bar: 5 mm. Arrows delineate the tumour. Large and small arrow heads show the corresponding pulmonary artery and the needle, respectively. (E) Adequate sampling was achieved for the diagnosis. Scale bar: 100 µm.
nODULES USING A NEW PROTOTYPE THORACOSCOPIC ULTRASOUND DEVICE IN MULTIPLE ANIMAL MODELS. FURTHERMORE, LITERATURE RELATED TO ULTRASONOGRAPHY FOR LUNG SURGERY FROM THE LAST DECADE WAS REVIEWED.

The success rate of the new device for localization of small lung nodules was 93.3%, which is similar to that of the previous reports (72.3%–100%; Table 1). The deepest detectable nodule was located at a depth of 24.8 mm from the inflated lung surface. However, there was a wide variability of quality in ultrasound images of pseudo-tumours despite the fact that similar structures were evaluated. The distance from the lung surface significantly influenced the quality of the pseudo-tumours. Some pseudo-tumours located deep in the lung were clearly visualized by the thoracoscopic ultrasound; however, many pseudo-tumours located more than 10 mm in depth showed indistinct margins. This is likely due to a small amount of residual air surrounding the target in the lungs. The probe had to be firmly pressed against the lung surface to localize the pseudo-tumours that were in the deep areas of the lung, so that the residual air was pushed away and the probe was close to the target. In our study, all detectable pseudo-tumours were visualized within 14 mm from the probe surface on ultrasound images. Sortini et al. [7] have insisted that the presence of a small amount of air in the pulmonary parenchyma is useful for localization of the tumour that has a hypoechoic ultrasound pattern because an incompletely deflated lung showed a hyperechoic pattern. However, we contend that a completely deflated lung without residual air is needed to obtain high-quality ultrasound images, even though localization is possible in the incompletely deflated lung with a small amount of air.

To improve the detectability of the targets, several devices have been combined with thoracoscopic ultrasonography. Some surgeons introduce saline into the thoracic cavity and submerge the lung in the saline as an acoustic coupling for the ultrasound probe [6, 9, 10, 12]. CO₂ insufflation into the thoracic cavity has been used to expedite collapse of the lung for visualization of intrathoracic structures. Ohtsuka et al. [16] have demonstrated that low-flow CO₂ insufflation with an intra-pleural pressure of 8–10 mmHg does not cause harmful haemodynamic effects during the thoracoscopic harvest of the internal mammary artery. Gow et al. [6] used 5 mmHg CO₂ insufflation to minimize intraparenchymal air during VATS in children. Our study has shown that CO₂ insufflation achieves complete lung collapse within 180 s in healthy porcine models, which is feasible during VATS and we believe this may be helpful for the success of thoracoscopic ultrasonography.

The added value of the current thoracoscopic ultrasound system is the capability of real-time fine-needle aspiration using a dedicated needle. This function enables surgeons to take a biopsy from lung nodules through a single port. In some instances, this may allow surgeons to avoid diagnostic wedge resections and to proceed with an anatomical resection of the lung.

Table 1 presents the overview of the literature on thoracoscopic ultrasound. The linear-type probe without optics has mainly been used for localization during VATS. Owing to the structure of the existing linear probes made for the use in the abdomen, some parts of the lung such as the posterior segment and lesions close to the spine may be difficult to access [4]. In addition, the linear-type probe is suitable for visualization of the flat part of deflated lung, but may be unsuitable for parts of the lung with a curve. The convex probe has the advantage of being able to visualize the targets over a wider range. The available frequencies of the current ultrasound devices mainly range from 4 to 10 MHz. Some of the works in the literature have described the use of higher frequencies. Kondo et al. [5] have demonstrated that GGO lesions can be detected by thoracoscopic ultrasonography at 7.5 or 18 MHz. Pseudo-tumours made of 200 µl of ultrasound gel were successfully visualized by a 15-MHz ultrasound in a rabbit lung [17]. In our experience, higher frequency appeared to be better for obtaining high-quality ultrasound images of the targets in the deflated lung. According to the indications of VTAS wedge resection, target tumours generally are located on the outer one-third (approximately at a depth of 30 mm) of the inflated lung. Furthermore, the CT evaluation in this study showed that the tumour depth from the lung surface in the deflated lung was less than half of that in the inflated lung (data not shown). Therefore, the thoracoscopic ultrasound will be useful if it can detect a target within a 15-mm depth in a completely deflated lung. In theory, high frequency is better to clearly visualize such targets in shallow parts (within 15 mm from the lung surface) with a high resolution. In

### Table 1: The thoracoscopic ultrasound probe and its localization capability

<table>
<thead>
<tr>
<th>Author and study</th>
<th>Transducer type</th>
<th>Frequency (MHz)</th>
<th>Contact area (mm)</th>
<th>Sensitivity (%) (detected/evaluated)</th>
<th>Average size (range) (mm)</th>
<th>Average depth (range) (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Khereba et al. [4]</td>
<td>Linear</td>
<td>5–10</td>
<td>NS</td>
<td>93.5 (43/46)</td>
<td>13.8 (2–62)</td>
<td>8.57 (1–24.1)</td>
</tr>
<tr>
<td>Kondo et al. [5]</td>
<td>Linear</td>
<td>7.5 or 18</td>
<td>38 × 10</td>
<td>100 (53/53)</td>
<td>9.9 ± 3.5, 12.1 ± 3.8</td>
<td>NS</td>
</tr>
<tr>
<td>Gow et al. [6]</td>
<td>NS</td>
<td>4–10</td>
<td>10</td>
<td>87.5 (7/8)</td>
<td>10.9, 9.7</td>
<td>NS</td>
</tr>
<tr>
<td>Sortini et al. [7]</td>
<td>Linear</td>
<td>5–8</td>
<td>NS</td>
<td>96 (24/25)</td>
<td>12.6 ± 2.2</td>
<td>26 ± 5</td>
</tr>
<tr>
<td>Mattioli et al. [8]</td>
<td>Linear</td>
<td>7.5–10</td>
<td>10</td>
<td>93.3 (42/45)</td>
<td>15 (3–30)</td>
<td>NS</td>
</tr>
<tr>
<td>Ambrogi et al. [9]</td>
<td>Linear</td>
<td>5–10</td>
<td>NS</td>
<td>72.3 (34/47)</td>
<td>17 (4–30)</td>
<td>15 (0–30)</td>
</tr>
<tr>
<td>Matsumoto et al. [10]</td>
<td>Linear</td>
<td>7.5</td>
<td>NS</td>
<td>100 (25/25)</td>
<td>&lt;30</td>
<td>&lt;14^d</td>
</tr>
<tr>
<td>Yamamoto et al. [11]</td>
<td>NS</td>
<td>7.5</td>
<td>NS</td>
<td>80.8 (21/26)</td>
<td>19.5 ± 8.5 (8–40)</td>
<td>NS</td>
</tr>
<tr>
<td>Piolanti et al. [12]</td>
<td>NS</td>
<td>5–7.5</td>
<td>NS</td>
<td>92.9 (39/42)</td>
<td>13.2 ± 5.9 (3–22)</td>
<td>16.1 ± 14.7 (0–54)</td>
</tr>
</tbody>
</table>

Inclusion criteria: English language, peer-reviewed articles and studies reporting sensitivity of localization of the lung nodules (more than 5 cases) using a thoracoscopic ultrasound from 2000 to 2013. The data are expressed as the average value ± the standard deviation.

NS: not stated.

^aBased on pathological measurement.

^bBased on preoperative CT measurement.

^cMedian.

^dWithin one-third from the lung surface.
reality, the high frequency of 12 MHz successfully visualized targets at a 15-mm depth. An even higher frequency may facilitate the distinct visualization of targets in this range.

The major limitation of this study was the tumour model used for the evaluation. Agar pseudo-tumours show hypoechoic lesions with sharp contrasting borders, which may have been an advantage for ultrasound localization/visualization of the nodule. Even though VX2 lung tumours were also evaluated in this study, we do not have data on the use of this device in patients. Secondly, GGOs were not assessed in this study, which frequently are the targets requiring preoperative marking. Since there are no pseudo-tumour models mimicking a GGO, we are currently planning a trial to test the same device in resected ex vivo lung cancers/GGO specimens.

In conclusion, the prototype convex probe thoracoscopic ultrasound was capable of localizing subcentimetre nodules in the porcine deflated lung as deep as 24 mm from the inflated lung surface. Moreover, this device enabled intraoperative real-time needle biopsy with adequate sampling for diagnosis from lung tumours in the rabbit model. However, the depth of the pseudo-tumours significantly influenced the quality of the ultrasound images, even though the targets were successfully localized. The completeness of the collapse of the lung was one of the factors that affected the visualization of small nodules. Complete lung deflation, use of a high frequency and targeting nodules within 15 mm from the probe surface may be the key factors to successful thoracoscopic ultrasound localization of small lung nodules.

ACKNOWLEDGEMENT

The authors acknowledge Sandra Lafrance, Deborah Scollard and Lisa Di Diodato for technical assistance in the animal imaging studies.

Funding

This work was supported by Olympus Medical Systems Corp. to Kazuhiro Yasufuku who provided the prototype thoracoscopic ultrasound (XLT-UC180). Hironobu Wada received a research scholarship from the Honjo International Scholarship Foundation.

Conflict of interest: Kazuhiro Yasufuku received research support from Olympus Medical Systems Corp. for conducting the current study. None of the others declared any conflict of interest.

REFERENCES