

Localizing small lung lesions in video-assisted thoracoscopic surgery via radiofrequency identification marking

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Abstract

Background To facilitate accurate localization of small lung lesions in thoracoscopic surgery, we employed a micro-radiofrequency identification tag designed to be delivered through the 2-mm working channel of a flexible bronchoscope. This report presents the results of preclinical studies of our novel localizing technique in a canine model. **Methods** To evaluate functional placement, three types of tags [Group A, tag alone ($n = 18$); Group B, tag + resin anchor ($n = 15$); and Group C, tag + NiTi coil anchor ($n = 15$)] were bronchoscopically placed in subpleural areas and subsegmental bronchi via our new delivery device; tags were examined radiographically on days 0–7 and day 14. In addition, eight tags, which were placed at a

mean depth of 13.3 mm (range 9–15.7 mm) from visceral pleura in bronchi with a mean diameter of 1.46 mm (range 0.9–2.3 mm), were recovered by partial lung resection under video-assisted thoracoscopic surgery using a 13.56-MHz wand-shaped probe with a 30-mm communication range.

Results Peripheral airway placement: Group C had a significantly higher retention rate than the other two groups (retention rate at day 14: Group A, 11.1 %; Group B, 26.7 %; Group C, 100.0 %; $P < 0.0001$). Central airway placement: Overall retention rate was 73.3 % in Group C, and placement was possible in bronchi of up to 3.3 mm in diameter. Outcomes of partial resection: Tag recovery rate was 100 %, mean time required for tag detection was 10.8 s (range 8–15 s), and mean surgical margin from the delivered tag was 9.13 mm (range 6–13 mm).

Conclusion Radiofrequency identification marking enabled accurate localization with depth, which could ensure effective deep resection margins.

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Keywords Radiofrequency identification tag · Localization · Small lung lesion · Video-assisted thoracoscopic surgery · Wedge resection · Surgical navigation

According to the results of worldwide computed tomography (CT) screenings for lung cancer, the number of newly detected small cancers has been increasing in recent years [1–4]. Most of these small cancers are classified as early stage and can be curable when resected by minimally invasive video-assisted thoracoscopic surgery (VATS) with appropriate surgical margins [5]. However, as CT-detected lung lesions are small and faint, their localization is often challenging. Particularly in wedge resection, resection lines

with adequate surgical margins are not ensured, as there are no anatomical landmarks for orientation.

Some localization methods have been reported for preoperative marking to identify small lung lesions, but these methods have limitations in technical safety, ease, and positional accuracy [6]. To ensure the patient's preoperative safety, marking access is better performed via bronchoscopy-guided transairway access, as CT-guided transthoracic access can cause more severe complications, including fatal air embolism [7, 8]. The most accurate positional information can be obtained from the use of radiopaque material in combination with intraoperative fluoroscopy, ensuring a stable resection line with adequate surgical margins [9–13], even when the target lesion is deeply located from visceral pleura. Intraoperative fluoroscopic manipulation, however, requires additional assistants to use such a large apparatus and involves radiation exposure.

Hence, we have proposed a novel lung marking system using radiofrequency identification (RFID) technology to provide accurate positional information without the use of intraoperative fluoroscopy; the key advantages are a smaller-sized apparatus and the absence of radiation exposure. The feasibility and reliability of our RFID lung marking system were reported previously [14, 15]; however, three improvements had to be made before we could consider clinical application. The first was the maximum range of effective detection, which had been only 7 mm in our previous tags; a range of 30 mm, as achieved by our current tags, might be more appropriate for clinical application. Second, bronchoscopically delivered tags must be equipped with sufficient anchoring to maintain position in the bronchus despite pressure from coughing or sneezing. Finally, the long-term safety of tags in the lung must be clarified, as there may be potential harm caused by tags left behind in the remaining lung. The aim of the present study was to develop our RFID lung marking system for clinical application in localizing small lung lesions. The system is characterized by wireless surgical markers using RFID technology that can provide accurate location with depth.

Materials and methods

Radiofrequency identification lung marking system

The system consists of the following three components (Fig. 1): (1) RFID tags (13.56 MHz tag: $3.2 \times 1.6 \times 0.9$ mm; Murata Manufacturing, Kyoto, Japan); (2) tag delivery system through a bronchoscope with a 2-mm working channel (Asahi Intecc, Nagoya, Japan); (3) signal processing device with a wand-shaped probe (diameter, 10 mm; Welcat, Tokyo, Japan). The detailed algorithms used in the system and the proof of concept have been

reported previously [14, 15]. Briefly, RFID tags (passive transponders with no built-in battery) are activated by the electromagnetic field produced by a probe acting as both the power supply and receiver antenna. The activated tag returns the signal response at a fixed wavelength of 13.56 ± 0.423 MHz. The strength of the signal received by the probe is converted to five gradual changes in sound pitch by the signal processing unit, the pitch becoming higher as the probe approaches the tag. By improving our prototype system, the effective range was extended to 30 mm, with the highest pitch emitted within a 7-mm range in front of the probe tip.

Animal care

This study was performed in 14 canines (median weight 10.3 kg, range 8.6–11.8 kg) with the approval of the Committee for Animal Research of Kyoto University in Japan, which ensures the humane treatment of laboratory animals in compliance with the guidelines established by the Ministry of Education, Culture, Sports, Science and Technology of Japan. Animal studies were conducted between January 2015 and March 2016, and all dogs were euthanized after study completion. Before the bronchoscopic procedures, all dogs were sedated with intramuscular injection of 0.05 mg/kg atropine, 15 mg/kg ketamine hydrochloride, and 3 mg/kg xylazine hydrochloride. Local anesthesia of the upper respiratory tract was performed using 1 % lidocaine solution for bronchoscopic procedures. For surgical procedures, dogs were intubated with a Univent endotracheal tube with a bronchial blocker (Fuji Systems, Tokyo, Japan). Sevoflurane and intravenous injection of 0.1 mg/kg vecuronium bromide were used for maintenance of anesthesia under mechanical ventilation, and electrocardiographic and percutaneous oxygen saturation monitoring was conducted throughout the surgical procedures. Postoperatively, the muscle relaxation was fully reversed. Each dog was returned to its cage and cared for in the same way as prior to the operation.

Evaluation of functional placement

All intubated dogs were placed in the supine position on a fluoroscopy table (BRANSIST-Alexa F12; Shimadzu, Kyoto, Japan), followed by CT (Aquilion TSX-101A; Toshiba, Tokyo, Japan) measurement of bronchial diameters under breath-hold conditions (10 cm H₂O positive end-expiratory pressure). Three different types of tags were placed in the subpleural area and in the central airway of a subsegmental bronchus via a bronchoscope with a 2-mm working channel (BF240; Olympus, Tokyo, Japan): Group A (tag alone, $n = 18$), Group B (tag + resin anchor (width, 3 mm), $n = 15$), and Group C (tag + NiTi coil

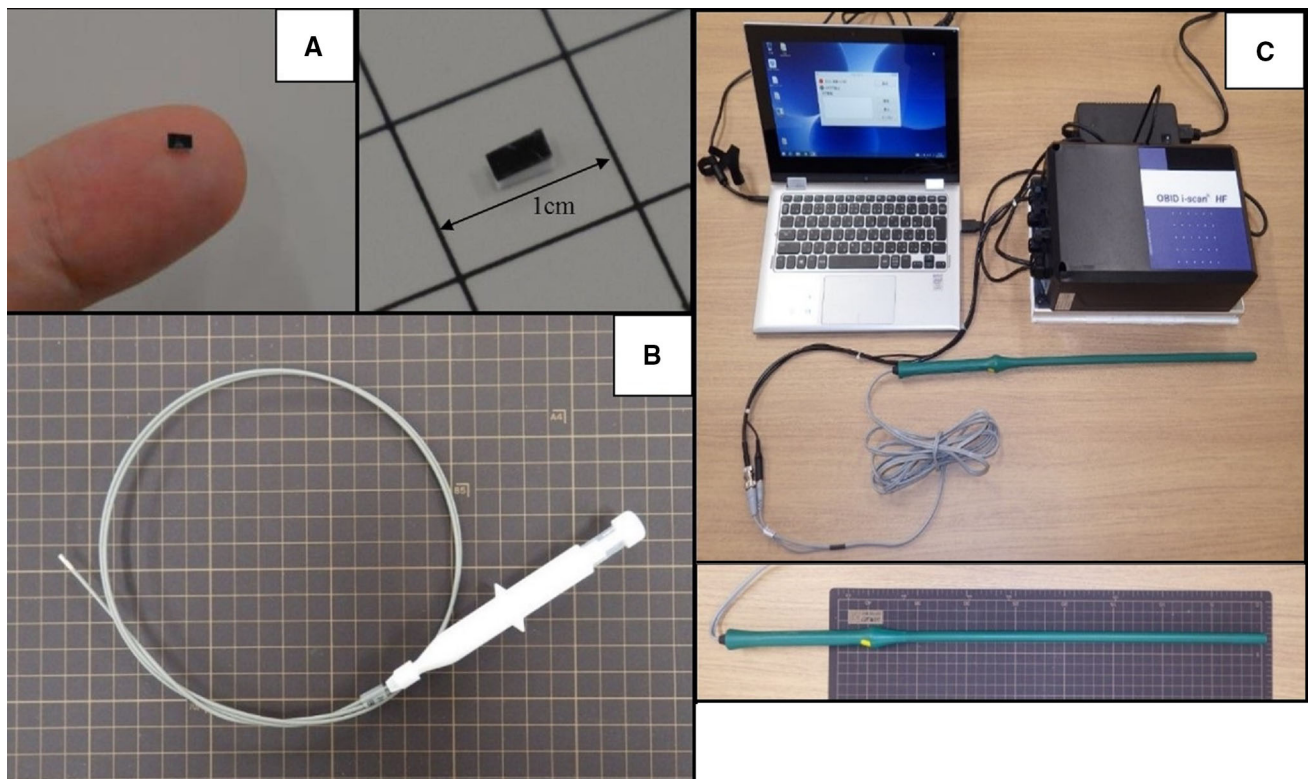


Fig. 1 Components for the radiofrequency identification (RFID) lung marking system, comprising a passive RFID tag (13.56 MHz; $3.2 \times 1.6 \times 0.9$ mm; **A**), a delivery device that can pass through a bronchoscope with a 2-mm working channel (**B**), and a detection

probe (diameter, 10 mm) with a signal processing device (**C**). The tip of the delivery device has a hanger with a maximum diameter of 1.88 mm, out of which the installed tag is released by a flexible pusher-wire

anchor (diameter, 5 mm), $n = 15$) (Fig. 2). Tags for all groups were implanted via a 2-mm working channel using our original delivery device (diameter, 1.88 mm) with a pushing wire, the tip of which had a hanger for the tag. The bronchi into which the tags were placed were blindly selected by a third party. Up to five tags were implanted per lung when the tip of the delivery device seemed to reach the subpleural area as indicated by fluoroscopic guidance and a feeling of airway resistance; great care was taken to avoid puncturing the visceral pleura. After bronchoscopic

delivery, we confirmed that all tags were placed in the terminal bronchi within 2 mm using CT performed under the same breath-hold conditions as used previously. The number of tags remaining at the implanted sites was examined via daily chest radiography from day 1 to 7 and then on day 14. The delivered tags were judged to be dislocated from the lung when chest radiography showed that the positional relationships of the tags had changed compared with previous examinations, or when the total number of tags had decreased. When tag dislocations were

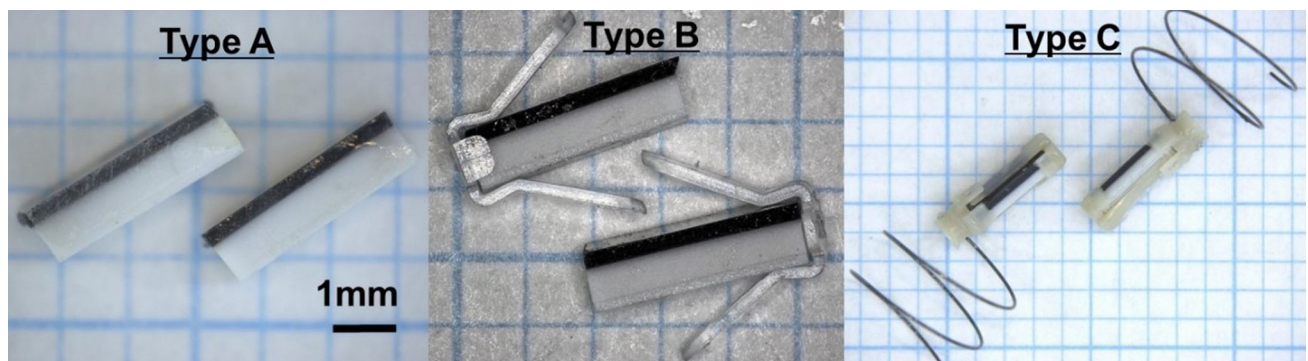


Fig. 2 Photographs showing the three types of tags: Type A: tag without any anchoring function, Type B: tag with resin anchor (width, 3 mm), and Type C: tag with NiTi coil (diameter, 5 mm; length, 4 mm)

confirmed, CT was performed to identify which tags had dislocated and whether the other remaining tags were fixed at the sites in which they were initially implanted.

Partial lung resection via video-assisted thoracoscopic surgery

To evaluate the accuracy of this RFID system (particularly regarding depth), tags were recovered by partial lung resection via VATS with a deep margin of 10 mm from the tag after evaluation of the previous fixation experiments. Initially, CT was used to select a target tag whose position was approximately in the outer third of a lung lobe [16]. General anesthesia was then induced, and the dog was placed in the lateral decubitus position with single-lung ventilation. After the administration of prophylactic intravenous ampicillin, the selected tags were excised under aseptic conditions through three ports with 10-mm incisions (one port for the endoscope and two for endoscopic forceps). Under thoracoscopic view, the lobe of interest was scanned with the locating probe from at least two different access ports to locate the tag. When the tag was located, ring-shaped forceps were introduced from the other port to grasp the target tag with lung tissue. The lung was resected with electrocautery, while the expected resection line was adjusted by scanning with the probe. After resection, the specimen was examined to ascertain the recovery of the implanted tag by confirming detection of the specimen outside the chest. Appropriate surgical margins were ensured by the directional probe with a distance resolution of 5 mm. Data were collected on tag implantation sites on CT, distance between the tag and the deep resection margin, time to scanning of the implanted tag (from beginning of scan to localization of tag position on hearing the highest pitch emitted from the system), and tag recovery rate.

Statistical analysis

For comparisons of tag retention rates, outcomes were measured with Kaplan–Meier models, and differences were analyzed using the log-rank test. JMP version 11.2.1 software (SAS Institute, Cary, NC) was used for statistical analysis.

Results

Evaluation of functional placement

Peripheral airway placement

Retention rates for the three groups are shown in Fig. 3. Chest CT performed immediately after the tag delivery

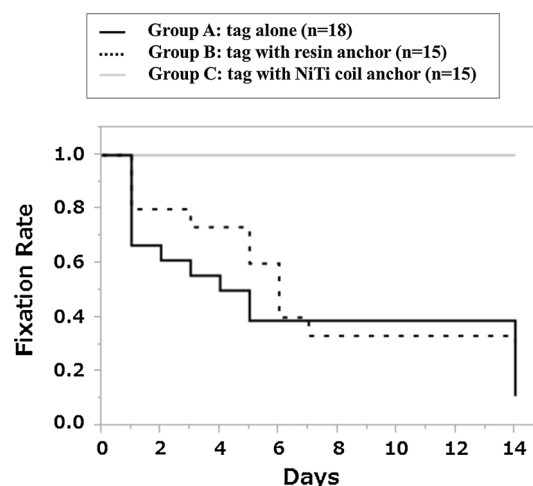


Fig. 3 Fixation rate in the peripheral airways among groups. Group A, tag alone ($n = 18$) is indicated by the *black line*; Group B, tag + resin anchor ($n = 15$) by the *black dotted line*; and Group C, tag + NiTi coil anchor ($n = 15$) by the *gray line*. Group C demonstrated significantly better functional placement than the other two groups (log-rank test, $P < 0.0001$)

revealed that the mean bronchial diameters in Groups A, B, and C were 1.02 mm (range 0.4–1.4 mm), 1.28 mm (range 0.6–1.9 mm), and 1.29 mm (range 0.6–1.9 mm), respectively; there were no significant differences in the size of the target airways among the groups.

Fixation rates on the first day after tag placement were 66.7 % (12 of 18 tags) in Group A, 80.0 % (12 of 15 tags) in Group B, and 100 % (15 of 15 tags) in Group C. Fixation rates on day 7 were 38.7 % (7 of 18 tags) in Group A, 33.3 % (5 of 15 tags) in Group B, and 100.0 % (15 of 15 tags) in Group C. On day 14, fixation rates were 11.1 % (2 of 18 tags) in Group A, 26.7 % (4 of 15 tags) in Group B, and 100.0 % (15 of 15 tags) in Group C. Although the fixation rate in Group B was higher than that in Group A until day 6, both groups had a similar rate after day 7, suggesting that the resin anchor was insufficient to maintain tag position. Group C demonstrated significantly better purposeful placement in comparison with the other two groups (log-rank test, $P < 0.0001$). The total fixation rate at day 28 was 100 % in Group C, indicating that the NiTi coil could provide sufficient anchoring function to maintain the position of delivered tags; hence, as central placement would be more difficult for maintenance of tag position because of larger bronchial diameters in the placement sites, the following central placement experiment was performed only with the tags employed in Group C.

Central airway placement

The relationship between bronchial diameter before implantation and the duration of tag retention at the

implanted site is illustrated in Fig. 4. Retention rates on days 7 and 14 were 80.0 % (12 of 15) and 73.3 % (11 of 15), respectively, and central placement indicated that bronchi of up to 3.3 mm in diameter were suitable for tag placement for at least 14 days.

Tags that dislocated from the implanted site were no longer visible in the chest on fluoroscopy, suggesting either complete expectoration or expectoration to the oral cavity and swallowing. Although swallowed tags were observed in some cases in the abdomen on fluoroscopy, they were excreted out of the body afterward. No dogs in which tags were implanted showed any complications such as persistent cough, radiographically apparent pneumonia, or atelectasis distal to the implantation site.

Outcome measures with video-assisted thoracoscopic surgery partial lung resection

Eight tags placed at a mean depth from the pleura of 13.3 mm (range 9–15.7 mm) and at a mean bronchial diameter of 1.46 mm (range 0.9–2.3 mm) were planned to be excised by partial lung resection via VATS. When the implanted tag was completely grasped and surrounded by the metallic ring grasper, the detecting function of the probe deteriorated owing to interference with magnetic flux generation; hence, a plastic ring grasper was applied instead. After application of the plastic ring grasper, the problems with detection were successfully resolved (Fig. 5). The mean time for tag detection was 10.8 s (range

8–15 s), mean distance between tag and deep resection margin was 9.13 mm (range 6–13 mm), and tag recovery rate was 100 % (Table 1).

Assessment of long-term safety at the tag implantation sites

A total of 15 implantation sites from Group C, located in five canines selected from some of the previous experiments, were observed by CT, bronchoscopy, and histological examination for up to 6 months in order to clarify the potential harm caused to the healthy lung when marking tags were left behind in the remaining lung. CT and bronchoscopy were performed every month. Three sites were pathologically examined 3 months after implantation, and another three sites were examined after 6 months.

CT showed that none of the five canines had apparent pneumonia or peripheral atelectasis from the tag implantation sites. Bronchoscopic examinations revealed that the NiTi coils had been gradually covered with slightly thickened mucosa, through which the shape of the NiTi wire could be observed. Six months after implantation, the tags were not embedded by granulomatous tissue and were relatively easily removed with bronchoscopic forceps. Microscopically, most of the tissue reaction was hyperplasia of the bronchial epithelium and mild granulomatous formation with no fibrous connective tissue; these findings were limited to areas where the NiTi coil contacted bronchial epithelium (Fig. 6).

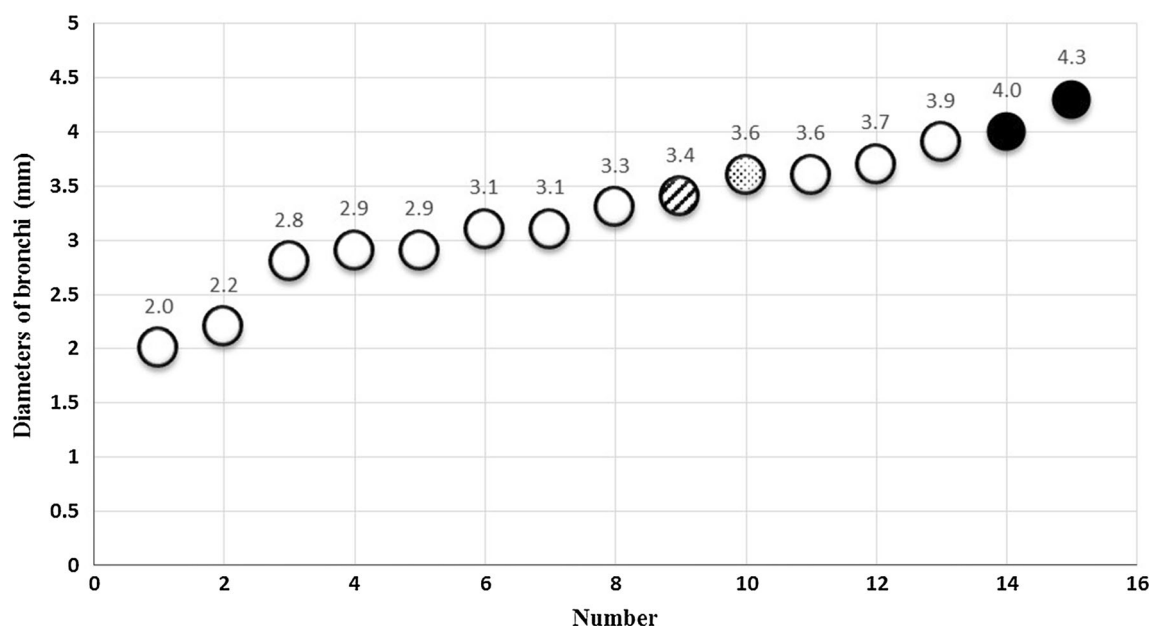


Fig. 4 Results of central implantation in Group C. This graph shows the relationship between the diameter of the selected bronchus and the fixation rate at the placed site ($n = 15$). The white circles indicate tags remaining at day 14. The two black circles (no. 14 and 15)

correspond to tags that dislocated 1 day after implantation. The dotted circle (no. 10) shows the tag lost at day 5, and the diagonally lined circle (no. 9) shows the tag lost at day 14

Fig. 5 Chest computed tomography demonstrates an implanted tag (indicated by the white arrow) at a depth of 13.3 mm in left S6 (A). Thoracoscopic view shows that the placed tag was elevated by a plastic grasper, and lung tissue was resected by electrocautery with accurate adjustment of the resection line by detecting tag position (B)

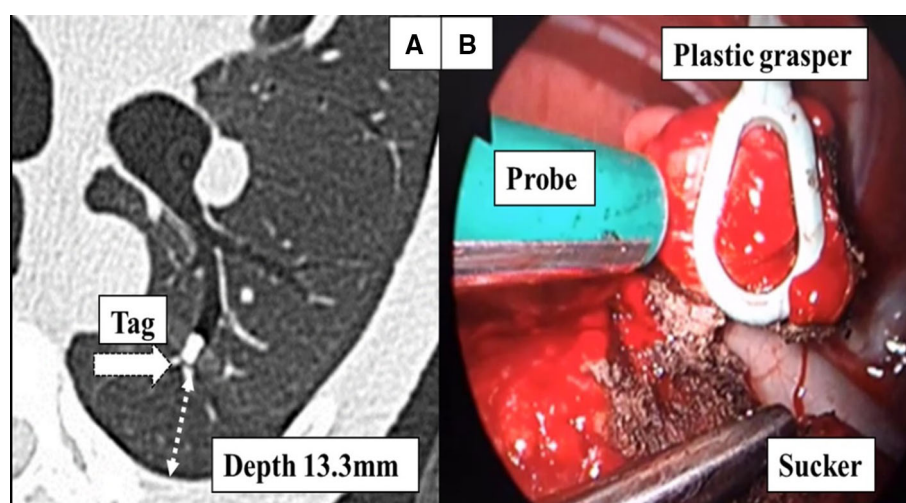


Table 1 Outcomes of video-assisted thoracoscopic surgery partial lung resection ($n = 8$)

	Mean	Range
Depth from visceral pleura (mm)	13.3	9.0–15.7
Bronchus diameter (mm)	1.46	0.9–2.3
Detection time (s)	10.8	8–15
Resection margin (mm)	9.13	6–13
Recovery rate	100 %	

Discussion

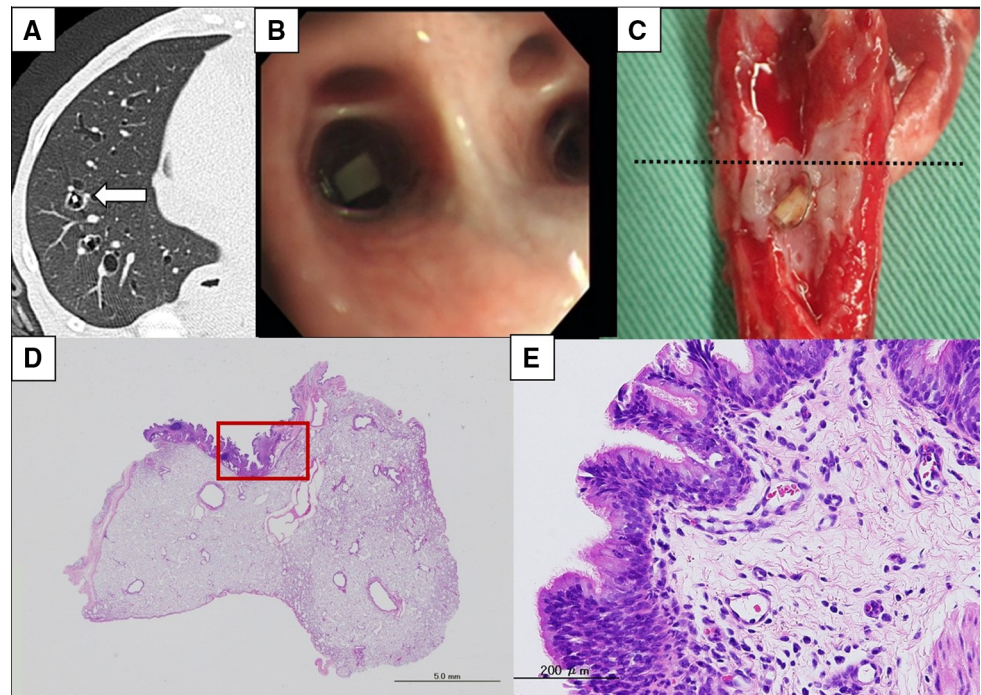
Lung cancer is the leading cause of cancer death. More than one-third of lung cancer patients die within 3 months of diagnosis; however, clinical outcomes are greatly improved when lung cancer is diagnosed at an early stage [17, 18]. In accordance with the clinical evidence from the National Lung Screening Trial, the first randomized controlled trial to investigate the efficacy of low-dose CT lung cancer screening in reducing lung cancer mortality [1], CT screening has become standard for lung cancer screening, which has resulted in an increase in the number of newly detected small lung cancers [2, 3]. Most of these cancers were detected at the early stage, when surgical resection can cure the disease.

According to the American Association for Thoracic Surgery guidelines for lung cancer screening, subcentimeter ground glass nodules showing sequential morphological changes suspicious for malignancy on follow-up CT should be surgically resected, as surgery is currently the most effective treatment for small lung lesions [19]. The American College of Chest Physicians recommends less invasive VATS wedge resection as a diagnostic approach for small peripheral lung lesions with a high clinical probability of malignancy [20]. As diagnostic yield for

subcentimeter nodules using non-surgical methods is unacceptably low [21, 22], VATS surgical biopsy is a last resort for the definitive diagnosis of small lung lesions. However, in subcentimeter ground glass nodules more than 5 mm deep to the visceral pleura, the probability of failure of localization is reportedly 63 % in thoracoscopic surgery [23], as such lesions are not easily identified by thoracoscopic view and are hardly palpable. Accurate localization of small lung lesions poses a significant challenge in VATS to ensure reliable resection for patients. Particularly in wedge resection for definitive diagnosis, surgeons currently have no reliable measure to secure stable deep resection margins, as the region lacks anatomical landmarks for orientation [24]. Therefore, the adequacy of the deep resection margin depends on the individual operator's skills.

Surgeons have overcome such difficulties by developing some preoperative marking techniques that facilitate the localization of small lesions while precluding unnecessary thoracotomy or lobectomy. However, there is currently no accepted standard method, as each of these marking methods has limitations. The ideal marking technique requires positional accuracy to locate the targets, technical ease, and low complication and failure rates, which depends on using material and access route to the target lesion in marking procedure. Conventionally used surgical markers include radiopaque metallic markers (hookwire and microcoils) and liquid markers (indigo carmine, indocyanine green, and lipiodol). When combined with intraoperative fluoroscopy, a radiopaque marker placed in the vicinity of the target can provide accurate positional information; however, this requires a large operation space and additional staff to use this apparatus and involves intraoperative radiation exposure. Pleural tattooing using liquid markers is also clinically accepted [25], but this method lacks positional accuracy (particularly with depth);

Fig. 6 Long-term effects on implanted tags. Tag implantation sites were followed for up to 6 months on computed tomography and by bronchoscopy. The *white arrow* in **A** indicates a tag implantation site. No pneumonia or peripheral atelectasis was observed (**A, B**). Coils were easily detached from the slightly thickened mucosa (**C**). The *black dotted line* in **C** indicates the cutting direction of the frozen section. Microscopically, the area that contacted the coil showed mild granulomatous formation and squamous metaplasia in respiratory epithelium (**D, E** H&E stain, $\times 1.25$ and $\times 10$ magnification, respectively)



the acquired information is limited to relative positional relationships between the target lesion and marked pleura. Moreover, pleural tattooing cannot be generally applied in anthracotic lung, as underlying lung conditions may make it difficult to identify the colored pleura [6]. Marking procedures are usually performed via CT-guided transthoracic access and bronchoscopic transairway access. CT-guided transthoracic access is available for lung lesions inaccessible by bronchial access, but is accompanied by higher complication rates of pneumothorax (8–50 %) due to puncture of visceral pleura; therefore, this access is contraindicated in emphysematous lung where additional drainage treatment may be required. CT-guided transthoracic access limits the number of marking procedures that can be conducted and also carries other risks including pulmonary hemorrhage (12–35 %) and potentially fatal air embolism (0.02 %) caused by perforation of the pulmonary vein [26, 27]. The ideal marking technique is a material that can be safely delivered bronchoscopically and accurately localized without use of intraoperative fluoroscopy.

To address these issues, we proposed our RFID marking system. Our marking system was characterized by wireless surgical markers that can be easily detected by a simple wand-shaped probe, with the key advantage of no radiation exposure [14, 15]. Moreover, the application of our new marker does not depend on the underlying severity of pulmonary emphysema or anthracosis. RFID technology has already been introduced into our daily lives and the healthcare industry, such as in patient identification and management of surgical instruments [28–30]. To date, this

technology has already received approval for implantation in humans by the US Food and Drug Administration, and one prospective clinical study has reported on wireless marking methods using 134.2 MHz RFID tags (Health Beacons, Seattle, WA) in the field of breast surgery [31]. Successful localization was reported in 20 consecutive cases with non-palpable breast lesions, using larger RFID tags (8 and 12 mm in length with an effective range of 6 cm) plus hookwire marking as a backup in case of tag migration [31]. They concluded that RFID technology could offer a feasible alternative to the hookwire marking conventionally used in the field of breast cancer.

In our previous report on tags without an anchoring function [14], implantation sites were limited to parenchyma near the visceral pleura because of the lack of fixation strength in lung parenchyma and the short communication range. For further clinical application, issues with tag fixation and extension of detection distance had to be overcome. A resin anchor was initially developed owing to potential interference with radio waves; however, the fixation rate was similar to that of tags without anchors. We then tested RFID tags with NiTi coils, which showed sufficient detection range and anchoring function in the canine lung. In the current study, we confirmed the accuracy of our marking system, assuming that the tags were implanted adjacent to small lung lesions. The enhanced marking system with the NiTi coil anchor can provide accurate positional information with depth in the marked organ by the wireless method, which could not be achieved using liquid markers that provide relative positional relationships

between a lesion and marked point. RFID tags placed adjacent to small lesions could have a higher yield for securing deep margins in non-anatomical wedge resection that lacks anatomical landmarks for orientation.

In order to take full advantage of our system, the surgical marker needs to be bronchoscopically delivered in the vicinity of small target lesions. This critical issue can be overcome using electromagnetic-navigated bronchoscopy (ENB) or a virtual bronchoscopic navigation system such as Synapse Vincent (Fuji Film Co., Ltd., Tokyo, Japan), or Lung Point (Broncus Medical, Inc., San Jose, USA). These bronchoscopic navigation systems have recently been used for image-guided bronchoscopy for biopsy of peripheral small lung nodules and for preoperative simulation or marking; these methods enabled successful navigation to the immediate vicinity of the lesion [32, 33]. ENB systems can monitor the distance to a target in real time, guiding the bronchoscope to reach an ideal site adjacent to targets unreachable by conventional bronchoscopy [22, 34, 35]. This ENB system navigates the bronchoscope to the exact locations of the target tumors, even if they are radiolucent, and could potentially be used for our RFID marking method in providing accurate tumor locations. Anayama et al. [36] proposed a new dying method for ENB-guided transbronchial injection using indocyanine green mixed with iopamidol, which was retained at depths of <12 mm in the deflated ex vivo porcine lung within 6 h after injection. An advantage of liquid marking is that the material is not permanently retained in the body; however, there is a time limitation, as the operation has to be conducted before the liquid diffuses into the pulmonary parenchyma.

Using microcoils, as was adopted in our anchoring shape, would enable more flexible schedules after marking procedures than using liquid markers and would also ensure adequate resection margins as they can be placed in the central airway. Toba et al. [37] reported a successful identification rate using fluoroscopy of 98.4 % (62 of 63 lesions) in 58 patients using 3-mm metallic coils at an average interval of 5.6 days after marking (range 0–30 days). One coil implanted in a bronchus of just 3 mm was unable to be identified owing to intraoperative migration resulting from manipulation of the lung [37]; this was addressed by subsequently applying a larger 6-mm coil. As dislocation of the implanted coil represents a major potential problem in surgery, unexpected dislocations have to be avoided by measuring the diameter of the target bronchus before the marking procedure. In the current study, our coil could be fixed in canine bronchi up to 3.3 mm in diameter for 14 days after marking, which is long enough for planning elective surgery, suggesting that our marking could be applicable to areas five or six generations beyond the main bronchus in humans [38]. To

minimize the potential risks of preoperative migration of our RFID marker, it may be reasonable to conduct the marking procedure in the operation room just before surgery.

As minimally invasive surgery in the field of endoscopic surgery has widely spread, the development of a surgical navigation system that can visualize the location of the target tumor and the surrounding anatomy is in great demand. In fact, technical advances have been made in the field of neurosurgery and orthopedic surgery wherein three-dimensional relationships of intraoperative anatomical structures are almost the same as the preoperative simulated images. However, in lung surgery, the development of such a surgical navigation system is lagging. This is mainly because the lung is greatly deformed by collapse to gain the workspace needed for endoscopic operation, and the intraoperative position of the target lesion may change markedly from its original preoperative CT position. Our proposed system can potentially realize surgical navigation in thoracoscopic settings; each tag bronchoscopically placed at the target anatomical position on preoperative CT has its own unique number and can be recognized individually by displaying the tag on three-dimensional lung imagery even after the lung is collapsed.

To apply our RFID marking system for clinical use, three concerns warrant consideration. The first is related to the fixation rate of our RFID markers. In our four-legged walking canine model where the bronchus divergence is horizontal to the ground, the bronchial diameters where markers were fixed within 14 days could be examined; however, the differences in the fixation rate between each lobe could not be evaluated. The fixation rate in the upper lobe may be lower than in the lower lobes in humans, as markers placed in the upper lobes would have to sustain their own weight against gravity. In the clinical cases where RFID markers will be placed in the subsegmental bronchus in the upper lobes, the period between the marking and the operation should probably be short in order to avoid preoperative migration.

The second study limitation is connected with the usability of our probe and delivery device. Usability of our system could not be sufficiently evaluated, as there are great differences between humans and canines in body size and bronchial structures. To consider clinical application, it must first be determined whether our RFID marker can be detected in human lungs as easily as in small canine lungs, and whether the delivery catheter can be directed in the vicinity of the target in all lobes of human lungs.

The third study limitation is associated with the safety of this system when a tag is left behind in the remaining lung. In the canine model, long-term implantation of up to 6 months did not harm healthy dogs; however, the sample size in this study was small. Inclusion of a greater number

of animals and observations with implantation sites for much longer than 6 months would increase the reliability of findings. As reliable data are not yet available, removal of migrated tags would be recommended in future clinical application owing to potential harmful effects associated with tag-triggered residual reactions in the lung.

Conclusion

Our RFID lung marking system provided accurate positional information with depth for localizing small lung lesions. Tags with NiTi anchors were effectively kept in position in the delivered bronchi and were recovered by VATS partial lung resection with adequate margins. These results suggest that our RFID marker is a promising pre-operative marking method for small lung lesions.

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Compliance with ethical standards

Disclosures We guarantee that all authors are aware of and agree to the contents of the paper and their being listed as an author on this paper. All authors have contributed significantly to the content of the article. All authors have read and approved the submission of the manuscript to *Surgical Endoscopy*. Subject to acceptance, authors will sign an exclusive license to publish. Drs. J. Zhang, Y. Muranishi, Y. Sakaguchi, T. Komatsu, F. Kojima, and T. Nakamura have no conflicts of interest or financial ties to disclose. Y. Yutaka, T. Sato, and H. Date have a financial relationship with Hoky Medical Co., Ltd., which developed the radiofrequency identification system used in this study. The results were collected and analyzed independent from any sponsor.

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