



Will the ultra-low-dose intraoperative X-ray imager change thoracoscopic surgery?

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Lung cancer is the most frequent cancer worldwide and is the leading cause of cancer-related death (1). Most lung cancers are already in an advanced stage at the time of their diagnosis and are difficult to treat even with the administration of recent molecular-targeted chemotherapy and immune checkpoint inhibitors. In contrast, early-stage lung cancer, such as stage IA, can be treated with a very high 5-year survival rate (2). The introduction of lung cancer screening using low-dose computed tomography (CT) is expected to increase the early detection of lung cancer, as randomized trials have found that mass CT screening of high-risk groups is beneficial (3-5). The increased detection rate of early-stage lung cancer has led to an increase in the popularity of minimally invasive techniques such as video-assisted and robot-assisted thoracoscopic surgery. In comparison with traditional open thoracotomy, these minimally invasive techniques allow the removal of early lung cancer lesions with decreased postoperative pain, air leak duration, length of hospital stay, and overall complication rates, with equivalent oncologic results (6-8).

One of the clinical challenges in minimally invasive techniques is the intraoperative localization of small tumors. The skin incision for video-assisted thoracoscopic surgery is usually too small to enable the detection of tumors via tactile sensation. Furthermore, sublobar resection is considered less reproducible because the surgical margins in sublobar resection are unclear, more subjective, and less reproducible compared with lobectomy, which is anatomically well-defined. Therefore, there is a need for techniques to not only identify lesions intraoperatively, but

also to perform sublobar resection while ensuring that the margins are appropriate.

Many marking techniques have already been proposed, such as percutaneous CT-guided hook-wire placement (9,10), microcoil placement (11), or CT-guided lipiodol marking (12,13), virtual-assisted lung mapping (14), and a radiofrequency identification marking system (15). However, these techniques require preoperative invasive preparations that carry risks of pneumothorax, intrapulmonary hemorrhage, or air embolism. The marker may also migrate to another position between preoperative placement and surgery, potentially causing the surgeon to resect the incorrect part of the lung. Moreover, the use of fluoroscopy exposes both patients and staff to intraoperative radiation in the catheterization laboratory or the operating theater.

Park *et al.* described the use of an ultra-low-dose X-ray imager to identify lung nodules intraoperatively (16). This device is a hand-held, clamp-shaped endoscopic instrument that employs a carbon nanotube, which allows a compact design. The authors assembled this device from small components and demonstrated its feasibility by applying it to an animal model in which a simulated tumor was created in swine lungs. Furthermore, the authors confirmed that the device could identify lesions in surgically resected human lung specimens, suggesting the usefulness of the device.

The ultra-low-dose X-ray imager may have several positive aspects. (I) The lesion can be identified in real time during surgery, enabling sublobar resection to be performed with adequate margins. (II) There is no risk of a marker being intraoperatively dislodged or lost. (III)

The radiation dose is only 0.1 $\mu\text{Sv/h}$, which is extremely small compared with conventional C-arm fluoroscopy and virtually eliminates the need to worry about radiation exposure of patients and medical staff. (IV) If the tumor can be detected without contrast agents there is no need for extra preoperative procedures. This avoids complications associated with percutaneous puncture (e.g., pneumothorax, intrapulmonary hemorrhage, air embolization), which are a concern with other methods.

Based on our experience, I believe that the ultra-low-dose X-ray imager has another advantage. We conducted a clinical study in which we used a very small intrathoracic ultrasound probe to intraoperatively identify lung tumors (17), similarly to the purpose of the ultra-low-dose X-ray imager. This ultrasound probe was equally satisfactory regarding the abovementioned four advantages of the ultra-low-dose X-ray imager. However, it was impossible to identify the lesion via ultrasonography when the lung was insufflated. Therefore, when using ultrasonography intraoperatively, it is important to know how to achieve a totally collapsed lung. In clinical practice, we intraoperatively use cone-beam CT in the hybrid operating room to roughly locate the lesion in an insufflated lung, and then use ultrasonography to accurately identify the location of the lesion in a collapsed lung and perform sublobar resection. I believe that the ultra-low-dose X-ray imager could have a great advantage in that it is expected to allow the procedure to proceed without the need for pulmonary collapse.

I believe that the proposed ultra-low-dose X-ray imager also has the following issues. One issue is the large size of the device. The authors report that it is 46 mm in the “with shields” condition. A 20-mm skin incision must be made to prepare the port, as in many cases it is necessary to remove the lung through the port hole. Thus, assuming that the device is inserted through that port, it would need to be reduced to about 15 mm in diameter. The size of the ultrasonography probe used in the aforementioned report (17) is less than 10 mm in size. A reduction in the size of the ultra-low-dose X-ray imager is essential for clinical application.

It has been reported that surgeons who are highly skilled in thoracoscopic surgery can palpate any tumor during thoracoscopic maneuvers (18). In our clinical experience, solid lesions are often palpable. In contrast, the lesions that require imaging assistance are often pure ground-glass opacity nodules or partially solid ground-glass opacity nodules with a small solid part. In such cases, it is presumed that lesion identification will be difficult unless the lungs are still somewhat insufflated. Therefore, it is expected that

the ultra-low-dose X-ray imager will be used in the limited space of the chest cavity, necessitating a reduction in the size of the device.

The second issue with the ultra-low-dose X-ray imager is that Park *et al.* identified lesions containing contrast media (16). In clinical practice, the insertion of a contrast agent into a lesion involves an extra procedure, which involves additional radiation exposure and procedural risks. Ideally, lesions should be identifiable in the absence of contrast. Improvements in image resolution are necessary to achieve such a result.

Aside from these issues, I believe that the ultra-low-dose X-ray imager is very promising. The authors have used this device as a prototype, and further improvements are expected in the future. If the size and resolution can be improved, this device has the potential to change minimally invasive thoracic surgery, and I hope that further progress will be made in the development of this device.

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