Editorial

Need for preoperative marking of pulmonary nodules and a more useful technique

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Lung cancer is a malignancy with a high incidence and high mortality rates worldwide. An estimated 2.2 million new cases were diagnosed in 2020, accounting for 11.4% of all cancers, and ranking second only to breast cancer worldwide. In terms of mortality, approximately 1.8 million people died of lung cancer in 2020, accounting for 18% of all cancer deaths and ranking first worldwide (1). Early detection and treatment are therefore critically important to improve patient prognosis.

Lung cancer screening can be facilitated using low-dose helical computed tomography (CT) (2) as well as artificial intelligence, and computer-aided diagnosis. These techniques are expected to increase the detection of lung nodule shadows.

Furthermore, approximately 700,000 chest and/or abdominal CTs scans are performed annually in the United Kingdom, and the number of examinations is increasing each year, resulting in the incidental detection of lung nodules (3). The prevalence of lung nodules has been reported to be 13% in a population not screened for lung cancer and 33% in a population screened for lung cancer. The prevalence of lung cancer among incidentally detected lung nodules is approximately 1.5% (4). Increased nodule detection in the lung field is therefore expected to uncover more early stage lung cancers.

Transbronchial biopsy (TBB) and CT-guided transthoracic needle biopsy (CT-TNB) are generally recommended as non-surgical diagnostic modalities for peripheral lung lesions (5). A systematic review and meta-analysis that evaluated the effectiveness of CT-TNB *vs.* transbronchial lung biopsy with radial endobronchial ultrasound (TBLB-rEBUS) and virtual bronchoscopic navigation (VBN) for the diagnosis of small pulmonary lesions reported that the diagnostic rates of CT-TNB were 93% and 75% for TBLB-rEBUS and VBN (6). However, although CT-TNB has a high diagnostic rate, it is also associated with a high risk of complications including hemorrhage and pneumothorax. In contrast, TBB is associated with fewer complications; however, raising diagnostic yields may prove challenging. Various methods have recently been investigated to improve diagnostic yields, including the use of ultrathin bronchoscopes (7).

Small lung nodules are more likely to be early stage lung cancers. Treatment opinions vary among the guidelines, with some recommending surgical resection without preoperative pathology when the clinical probability of early stage lung cancer is high (4,5,8). However, 12.7% of cases in which surgical resection was performed without preoperative pathology had benign tumors (9), and 18/76 (20%) cases in the present study were reported to be benign, indicating that surgery was not necessary in these cases.

In addition, the current standard treatment for lung cancer is generally based on disease-associated variants/mutations and programmed death-ligand 1 (PD-L1) expression. These tests require more tissue volume, which

may necessitate surgical resection. Surgical resection is likely to be increasingly required for diagnosis and treatment decisions, but it is important to reduce the patient burden as much as possible in all cases, including benign cases, elderly patients, and those with poor respiratory function.

Identification of the nodule sites and resection locations are the main problems associated with the surgical resection of small nodules. Depending on the location of the nodule, the nodule site may be identified and judged by actual touch, but lesions that are distant from the pleura, or less than 1 cm in size, or of ground glass opacity are difficult to palpate. Therefore, preoperative marking may be used to facilitate identification of the nodule site.

Recently, Vollmer *et al.* (10) compared the efficacy and safety of radiotracer injection [radioguided occult lesion localization (ROLL)] to those of hookwire localization for the preoperative localization of lung nodules. The factors that determine the performance of ROLL compared to hookwire and how they affect resected lung volume have not yet been examined. To date, various methods of preoperative marking have been proposed, including methylene blue, lipiodol, coils, hookwires, and ROLL. In a meta-analysis comparing the hookwire, microcoil, and lipiodol methods, Park *et al.* reported successful localization rates of 94% for hookwire and 97% for microcoil, *vs.* 99% for lipiodol. In terms of complications, they reported the highest rates of pneumothorax and hemorrhage, 35% and 16% for hookwire and 31% and 12% for lipiodol, respectively, compared with 16% and 6% for microcoils (11). Hookwires and microcoils are the most commonly used methods, selected for convenience. A comparison of the two methods using propensity score matching by Yang *et al.* reported a 94.4% success rate for hookwires and a 97.2% success rate for microcoils, with no significant differences between the two methods. However, the complication rates were 31% and 15.5%, respectively, indicating that complications were significantly higher for hookwires (12). In contrast, ROLL is a method of marking pulmonary nodules proposed in 2000 (13) and can be used in the resection of other diseases, such as breast nodules. ROLL allows for the intraoperative evaluation of lesion resection margins using a gamma detector probe, leading to a reduction in resection volumes. A report by Galetta *et al.* examining ROLL in patients with pulmonary nodules smaller than 1 cm and/or deeper below the visceral pleura found that all patients underwent successful resection, but pneumothorax and bleeding occurred in 13.4% and 13.7% of cases, respectively (14). Ricciardi *et al.* also reported a success rate of 98% and pneumothorax in 3.3% of cases, indicating a high success rate and an acceptable complication rate (15).

In the study by Vollmer *et al.* (10), both the hookwire and ROLL were able to identify nodules in all cases, with resection success rates of 100%. The success rate of ROLL was almost the same as that of previous reports, and the success rate of the hookwire was better than that of previous reports; no significant difference was found. However, despite migration of the hookwire in of 3/52 (5.8%) cases, resection success was attributed to bleeding in the puncture pathway. The nodule distance was predominantly longer in ROLL than in hookwire cases, and is also considered to be more versatile in nodules that are distant and deeper from the surface. This report also indicated that ROLL tended to reduce the resection volume compared with hookwire, although the difference was not statistically significant. This is because the hookwire method requires resection of the entire intrapulmonary track of the marker, leading to an increase in resection volume, whereas ROLL allows resection confirmation with a gamma detector probe, which limits the resection area. This is in line with the previously reported results of resection in other diseases. The ability to reduce lung resection volumes can lighten the physical burden on patients and reduce the burden on the respiratory function. Furthermore, in terms of complications, although there were no significant differences in bleeding between ROLL (44.4%) and hookwire (48.1%) cases, however, there was a significant difference in the occurrence of pneumothorax between ROLL (24.2%) and hookwire (69.2%) cases, indicating that ROLL is superior in terms of safety.

The usefulness of ROLL is high; however, its disadvantage is that it requires a gamma detector probe, a nuclear medicine specialist to guide the surgeon during resection, and scintigraphy after tracer injection, which limits the number of facilities where the procedure can be performed. The success rate and safety of this technique are similar to those of other methods reported in the past, and it also reduces the patient burden.

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