



# Percutaneous transthoracic needle biopsy of the lung in the era of precision medicine

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Lung biopsy is a reliable procedure performed to inform treatment strategy for patients with abnormal findings of the lung. Cytology of biopsy specimens has long been a major diagnostic modality for initial evaluation of patients with lung cancer. Recent insight into the molecular basis of lung cancer, however, has led to changes in the diagnosis and treatment of this disease. The identification of driver genetic alterations, such as those affecting the epidermal growth factor receptor (*EGFR*), *ALK*, and *ROS1* genes, in lung cancer has already been successfully translated into clinical practice with the development of drugs targeted to the corresponding mutant proteins. Selective investigational new drugs are also under clinical evaluation for the treatment of lung cancer patients with other oncogenic drivers such as *HER2* mutations, *MET* exon-14 skipping mutations, as well as *NTRK* and *RET* fusions. Given that the clinical implementation of genomic profiling for non-small cell lung cancer (NSCLC) with high-throughput and multiplex genotyping tests is under way to allow prioritization of appropriate therapies for individual patients, the availability of sufficient tumor tissue as a source of DNA for these tests is increasingly important (1). Furthermore, a second biopsy for assessment of genetic changes during targeted therapy, such as the emergence of the T790M mutation of *EGFR* that is responsible for the development of resistance to tyrosine kinase inhibitors in patients with NSCLC positive for activating mutations of *EGFR*, is also now commonly performed (2).

Methods for lung biopsy other than general thoracotomy or thoracoscopic biopsy under general anesthesia include bronchoscopic lung biopsy and percutaneous transthoracic

needle biopsy (PTNB) with guidance by computed tomography (CT) (3). PTNB is performed to collect small pieces of lung tissue for the diagnosis of lung abnormalities. Zhou *et al.* have recently summarized the indications for and methods of PTNB as performed for the diagnosis of lung cancer (4). In general, bronchoscopy is the procedure of first choice for lung biopsy, with PTNB being selected for patients who are not able to tolerate bronchoscopy, in cases when a pathological diagnosis cannot be made even after bronchoscopy, and for new or enlarging abnormal lesions detected on a chest radiograph or CT scan that are unlikely to be accessible by bronchoscopy (3). PTNB is more accurate for peripheral pulmonary nodules or lesions, which are difficult to diagnose with the use of a bronchoscope (5). Guidelines for radiologically guided lung biopsy previously published by the British Thoracic Society mention relative contraindications for percutaneous transthoracic lung biopsy (PTLB, another name for PTNB) and state that the balance of benefit against risk for the procedure should be assessed at a multidisciplinary meeting (3). Zhou *et al.* now describe the contraindications for PTNB in detail (4). Previous pneumonectomy and other instances of a single lung, suspected hydatid cyst, and vascular malformation are absolute contraindications for PTNB (6). On the other hand, uncooperative patients, a high risk of bleeding, positive pressure ventilation, severe respiratory compromise, pulmonary artery hypertension, and severe interstitial lung disease are relative contraindications for the procedure. Patients who use anticoagulants or antiplatelet agents and who need to undergo an interventional pulmonary procedure are often encountered (7). A prospective cohort

study of 604 patients who underwent transbronchial lung biopsy found that the bleeding rate was higher in patients treated with clopidogrel (89%) than in a control group (3.4%) (8). On the other hand, a retrospective review of 63 patients with recent clopidogrel use who underwent image-guided percutaneous biopsy included 12 patients who underwent lung biopsy, and only one of these latter individuals experienced clinically significant bleeding (9). Whether the taking of anticoagulants or antiplatelet agents should be considered a contraindication for PTNB thus remains unsettled. The importance of obtaining tissue for the diagnosis and management of lung cancer (10) should not be underestimated, however, and the balance between the benefits and risks of the biopsy procedure should be carefully evaluated.

“Isolated pulmonary lesions that are highly suspected to be malignant and are potentially surgically resectable” are included as a contraindication for PTNB by Zhou *et al.* (4) “in order to minimize potential risks of PTNB-related cancer seeding and dissemination.” They also mentioned that “needle-tract seeding of tumor cells is a relatively common complication of percutaneous lung puncture biopsy,” citing three studies (11-13). Komiya *et al.* (11) reported only one instance of seeding of cancer cells along the needle tract out of a total of 420 PTNB procedures performed in 408 patients. Požek *et al.* (12) described the case of a 71-year-old patient with lung cancer whose cancer cells were implanted in the fine-needle aspiration biopsy track. Yan *et al.* (13) did not describe the complication of needle-tract seeding of tumor cells in their systematic review. Given that the frequency of tumor seeding varies among reports, it may be an overstatement to say that tumor seeding is relatively common during PTNB. A study of 9,783 biopsies collected from 124 centers in Japan found that needle-tract seeding occurred in only 6 (0.061%) cases (14). Pleural recurrence was found to be more common when CT-guided PTNB was performed for subpleural lesions (15). We agree that the incidence of tumor seeding may be underestimated because it is a late complication, but we do not believe that it should be a determining factor as to whether CT-guided biopsy is performed or not.

In order to avoid unnecessary invasive surgery for a patient, it is in principle necessary to obtain a tissue diagnosis beforehand. However, given the risk of complications including pneumothorax and bleeding and the time required for the procedure (16), PTNB is usually not performed for isolated pulmonary lesions that are highly suspected to be malignant and are potentially surgically

resectable, even if a pathological diagnosis cannot be made by bronchoscopy.

In summary, the demand for biopsied tissue is increasing for molecular and genomic profiling of NSCLC. To meet this demand, we need to understand the indications and contraindications for PTNB so that the procedure can be performed safely. In their consensus report, Zhou *et al.* describe the types of needles, guiding devices, and techniques of PTNB in detail (4), providing a useful overview of the procedure.

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### Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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