

# Utility of intraparenchymal blood patch testing following CT-guided lung biopsy

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Lung cancer remains the leading cause of cancer-related deaths among men and women in the United States (1,2), with lung nodule prevalence ranging from 14–36% (3). With improved access to computed tomography (CT) scanners and the implementation of low-dose CT lung cancer screening in the United States and Europe, lung nodule detection rates will likely increase. Despite technological advances and the development of surveillance guidelines, confidence in our imaging technology's discriminatory capability to differentiate intermediate-risk lesions is still lacking (3,4). As advances in oncological treatments continue to evolve and therapies become increasingly tailored to specific mutations, tissue biopsies will likely continue to play a significant role in allowing precision treatments to be designed in the future (5).

Multiple options exist to obtain tissue for histological and molecular analysis. These include image-guided transthoracic biopsies, bronchoscopy-guided biopsies, and surgical biopsies. The chosen method depends on multiple factors, including location, lesion size, available expertise, and underlying comorbid conditions (6). A United States-based proprietary claims database review reveals that most patients undergo CT-guided needle biopsy (CTNB) for peripheral pulmonary nodules (7-9). CTNB has excellent

specificity and accuracy, with literature reporting pooled diagnostic accuracy of 92.1% (9,567/10,383), a sensitivity of 92.1% (7,343/7,975), and a specificity close to 100% for the diagnosis of malignancy (7,10). However, despite the excellent accuracy of CTNB, risks exist, including, most commonly, pneumothorax. Multiple studies put the incidence of pneumothorax at 15–62% (4,6,7,10,11). In this issue of *Precision Cancer Medicine*, Dr. Jain and colleagues explore an intervention to mitigate the incidence risk of pneumothorax (12).

The authors performed a retrospective analysis of all CTNB lung nodule biopsies carried out at two hospitals between January 2013 and January 2020. Of the 848 biopsies performed, 536 met the inclusion criteria. Cases were excluded if a chest tube was already in place, an alternative sealant material was used, or the guiding needle did not traverse the lung parenchyma to reach the sampled lesion. The control group consisted of 227 patients who underwent CTNB between 2013–2015. A total of 309 patients who had a CTNB from 2016 onwards received an intraparenchymal blood patch (IPB), which utilizes 10–15 mL of the patient's blood obtained while securing intravenous access. The blood was then instilled into the biopsy tract as the introducer needle was removed.

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The primary endpoints examined were post-biopsy pneumothorax, the need for chest tube placement, and the requirement of hospital admission. Thirty-seven percent of patients (84/227) who did not receive IPB developed a pneumothorax post-biopsy, while only 14.6% (45/309) of patients who received an IPB developed a pneumothorax. The difference was statistically significant ( $P < 0.0001$ ), with an absolute risk reduction of 22.4% and a number needed to treat (NNT) of 4.4. In addition, there was a significant decrease in the incidence of chest tube placement from 17.2% (39/227) in the control group to 3.9% (12/309) ( $P < 0.0001$ ) among patients who received IPB, with an absolute risk reduction of 13.3%. Similarly, there was a significant decrease in hospital admissions from 16.3% (37/227) to 2.9% (9/309) in patients who received an IPB ( $P < 0.0001$ ).

Caveats exist when interpreting the results of this study. First, there was a statistical difference between the prevalence of patients with underlying chronic obstructive pulmonary disease (COPD) in the two groups (46.7% in the control arm *vs.* 35.4% in the treatment arm,  $P = 0.008$ ). Previous studies have shown COPD to be a risk factor for developing pneumothorax post-biopsy (7,13). Second, the two groups differed in home oxygen usage (7.1% in the control arm *vs.* 1.9% in the treatment arm,  $P = 0.003$ ). Although this finding may reflect the difference between the prevalence of COPD in the two groups, it may also indicate a difference in COPD severity between the groups. Third, one physician performed all the biopsies with IPB, while multiple physicians may have performed the earlier biopsies. Thus, the difference in pneumothorax rate may reflect differences in expertise and technique. Finally, as this study was a retrospective analysis, readers should be cognizant of biases associated with retrospective analyses, namely selection bias and confounding bias. Multivariate analysis could have mitigated potentially confounding bias by controlling for underlying pulmonary disease, severity, and the operator's expertise level. Without that further analysis, however, the observed effect may be due to other variables, such as technique, patient rollover, needle removal during expiration, patient factors, or keeping the biopsied lung dependent (14). Unfortunately, these variables were also not uniform across all cases, and further details are unavailable.

Jain *et al.*'s (12) findings highlight the need for updated guidelines governing CTNB. Image-guided percutaneous lung biopsies have been performed since 1960 (13). Pneumothorax and bleeding were the most frequent complications initially. In 1974, McCartney *et al.*

described their experience of 25 cases where autologous blood patching or gel foam was used to seal the needle track, preventing pneumothoraces (15). Two subsequent studies, however, failed to show any statistical difference in pneumothorax rate with IPB (16,17). The quest to decrease the incidence of post-biopsy pneumothorax continued. After lab models reaffirmed the utility of blood patching (18), Lang *et al.* revisited IBP with a multicenter randomized control trial (RCT), reaffirming its benefits (19). Despite encouraging results, the only formal guideline dedicated to CTNB did not endorse IBP and questioned its utility (20).

Over the years, many other materials have been trialed to help seal the needle track, including normal saline, compressed collagen foam plugs, fibrin glue, and absorbable hemostat gelatin powder (21-24). In addition, many maneuvers, such as rapid rollover (puncture site down) and breath-hold after expiration during needle extraction, have been developed and trialed to decrease the incidence of pneumothorax, chest tube insertion, and hospital admission (14,20). Even without formal endorsement from any specialty society, many physicians have been using IBP and other maneuvers to help decrease pneumothorax rates following CTNB (21,25). Huo *et al.* systematically reviewed post-biopsy maneuvers from 21 articles, totaling more than 7,000 patients (21). The maneuvers included IBP, needle tract plugs, changes in patient position, and needle extraction during exhalation. The pooled odds in six studies that evaluated IBP (including four RCTs) reduced the risk of pneumothorax by half and chest tube insertion by three-fold, indicating that efforts to reduce the incidence of complications appear effective.

Multiple studies have examined the economic burden associated with diagnostic testing of lung nodules and the substantial cost incurred after complications, which can be as much as four times the cost of the actual procedure (8-9,11). For example, Huo *et al.* revealed that the additional cost of minor to intermediate complications, such as pneumothorax without or with a chest tube, ranges from \$5,881 to \$20,457 (9). Thus, efforts to decrease the risk of complications are certainly needed.

As the era of precision medicine continues to evolve, the biopsy of pulmonary nodules will continue to play an integral role in establishing a diagnosis and developing a treatment plan. CTNB will remain a mainstay of lung nodule evaluation for the foreseeable future. Unfortunately, pneumothorax will also likely remain the most common complication of this procedure. IPB appears to be a safe procedure when performed after CTNB to seal the needle

tract and decrease the incidence of pneumothorax. The reproducible decrease in pneumothorax rate with IPB seen in numerous trials lends support for its routine use following the withdrawal of the introducer needle after CTNB. Incorporating IPB into future guidelines for the performance of CTNB should be considered.

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