Introduction

In recent years, due to the widespread diffusion of imaging techniques, the detection of peripheral pulmonary nodules/masses (PPN/M) has become even more frequent. A prompt diagnosis of lung cancer represents a crucial point to substantially improve the 5-year survival-rate, as, despite new perspectives in the therapeutic landscape, it remains the leading cause of cancer death worldwide (1). Therefore, the goal is to quickly identify malignant nodules in order to allow a curative surgical resection, while avoiding unnecessary invasive interventions in case of benign lesions.

Transbronchial needle aspirations vs. percutaneous needle aspirations

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Abstract: Over the last decade, the increasing diffusion of innovative and more powerful imaging guided techniques has further broadened the bronchoscopist’s horizons in the diagnostic work-up of peripheral pulmonary nodules/masses (PPN/M). However, in most of institutions worldwide, due to the lack of resources and specific skills, the routinely diagnostic approach to PPN/M is still represented by imaging-guided transbronchial needle aspirations (TBNA) and percutaneous needle aspirations (PCNA). So far, no randomized clinical trials directly comparing the accuracy of the two procedures are available, and a standardized strategy that defines the proper role of each technique has yet to be established. In fact, the choice between these procedures is mostly influenced by “environmental” factors, such as operator’s experience and local resources, rather than by an established algorithm, based on selected clinical scenarios. Data from literature indirectly suggest a higher sensitivity of PCNA compared to transbronchial approach, especially when lesions are peripheral and less than 2 cm. On the other hand, the transbronchial approach has been shown to have a better safety profile. Moreover, it offers the advantages to provide, during a single examination, a pathological diagnosis of nodules, information on mediastinal staging and airways involvement, and to identify potential synchronous lesions. In this context, it would be reasonable to firstly perform flexible bronchoscopy with TBNA, and, in case of inconclusive results, PCNA. In conclusions, both the techniques have been shown to be useful in the diagnostic pre-operative work-up of PPN/M. In order to optimize the diagnostic yield and to minimize the risk of patients they should not to be considered as two alternative options, but, rather, as two complementary techniques integrated in a standardized algorithm.

Keywords: Transbronchial needle aspirations (TBNA); percutaneous needle aspirations (PCNA); peripheral nodules/masses; accuracy; safety

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In fact, up to 60% of removed nodules are not malignant, underlying the importance of a diagnostic approach that better enables lung preservation. Mini-invasive diagnostic options in this context include imaging-guided transthoracic (or percutaneous) and transbronchial approach.

The transthoracic approach to PPN/M was first described by Tsuboi in 1967, employing a curette introduced through a catheter (Metras). The advent of the bronchofiberscope and the subsequent development of new tools of sampling, such as flexible transbronchial needles, have largely improved the yield of the technique, generally performed under fluoroscopic guidance.

The percutaneous approach to PPN/M became widely used after the introduction of the fine-needle technique by Nordenström in 1965 (2). Several large studies have subsequently confirmed the accuracy of this method, independently of the imaging guidance employed either fluoroscopy or computed tomography (CT).

No randomized clinical trials directly comparing the accuracy of the two procedures are available, and, to date, a standardized strategy that defines the proper role of each technique in the diagnostic work-up of PPN/M has yet to be established. In fact, the choice between these procedures is mostly influenced by “environmental” factors, such as operator’s experience and local resources, rather than by an established algorithm, based on selected clinical scenarios.

Transthoracic/percutaneous needle aspiration (TTNA/PCNA)

Transthoracic needle aspiration (TTNA), also named percutaneous needle aspiration (PCNA) allows both cytological and histological samples of pulmonary lesions, and it could be performed under biplane fluoroscopy or, more frequently, under CT-guidance. Ultrasound can be also used when the lesion is adjacent to the thoracic wall.

Overall, the sensitivity of PCNA ranges from 70% to 97%, since it depends on several clinical and procedure-related factors. A peripheral location of nodules has been widely recognized as a predictor of a successful aspirate, while data on lesion size documented an excellent accuracy even for nodules smaller than 1 cm (3). The interinstitutional variability in the technical performance, such as operator skills, number of needle passes, and the presence of onsite cytological examination, is also likely to highly influence the results. With reference to guidance system, although there are no randomized trials definitely showing the superiority of CT compared to biplane fluoroscopy, the first one has become the most widely employed imaging guide, as it allows to determine the safest needle trajectory, to approach small lesions not visible on fluoroscopy, and to avoid radiation exposure to the operators. Again, data on the proper choice of needle size are still controversial, but, overall, the core needle biopsy is recommended especially when either a benign lesion or a malignancy other than lung cancer is suspected.

Although the diagnostic yield seems to be outstandingly satisfying, especially in suspected lung cancer patients, it is important to underline that a not diagnostic or negative result does not rule out the possibility of malignancy. On the other hand, the specificity is excellent, as the false positives are nearly anecdotal (3).

However, concerns have risen about the safety profile of PCNA. The most frequent complications include pneumothorax and hemorrhage. Among studies, pneumothorax rate varied hugely, ranging approximately from 10% to 50% and requiring tube placement in less than 10% of cases. Several risk factors for pneumothorax onset have been suggested: older age, deeper and smaller lesions, location proximal to lung fissures, a long needle path length, repeated punctures, lateral patient position, and the presence of emphysema (3-5).

Hemoptysis occurs up to 5-10% of cases and is usually mild and self-limiting. Other adverse events have been rarely described and include air embolism (<1%), haemothorax, empyema, tumor diffusion along the needle tract and haemoparicardioum (3,6).

Overall, absolute contraindications of PCNA are contralateral pneumonectomy, bleeding disorders, an uncontrollable cough, suspected arteriovenous malformation or hydatid cyst; relative contraindications include respiratory failure, severe chronic obstructive pulmonary disease, pulmonary hypertension and unstable ischemic heart disease.

Transbronchial approach

Peripheral pulmonary lesions might also be approached by standard flexible bronchoscopy with different sampling instruments (forceps biopsy, flexible needles, brushing) that can be inserted through the working channel of the flexible bronchoscope and pushed into the peripheral airways to obtain cyto-hystological specimens from lesions located outside the visible range of the bronchoscope (2). In case of localized pulmonary nodules/masses, the use of guidance systems is required, as it allows more accurate visualization and sampling. The traditional guidance system in this context is fluoroscopy. The only prospective randomized
trial comparing CT fluoroscopy versus standard fluoroscopy for the diagnosis of peripheral lung lesions and mediastinal lymph nodes failed to show any significant difference between the guidance systems in terms of accuracy (7).

The third edition of the American College of chest Physician (ACCP) evidence-based clinical practice guidelines reported a transbronchial approach sensitivity for PPN/M ranging from 5% to 76%, mostly derived from retrospective studies (3). More recently, two large studies have prospectively assessed the role of flexible bronchoscopy in the pre-operative work-up of peripheral pulmonary nodules (8,9). Schwarz et al. reported an unexpected malignant involvement of the central airways in 5% of cases, and anatomic variants of bronchial tree in 7%, sometimes useful for the surgeon to know exactly the lesion location (8). In the study by Trisolini et al., the sensitivity of transbronchial needle aspirations (TBNA) for peripheral lesions was 65% (95% CI: 57.7-71.5), and the ROC curve analysis showed that it was the single bronchoscopic procedure with the best performance characteristics, if compared to transbronchial lung biopsy and bronchial brushing, confirming data from previous large investigations (2,9). This might be due to the ability of the needle to penetrate the lesion, even if it does not infiltrate the bronchial wall.

Overall, a number of features have been identified as strong predictors of a higher TBNA accuracy, and these include an underlying malignant disease, a lesion size >2 cm, the presence of the bronchus sign, and location in the middle lobe (3,9).

About the safety profile, major adverse events, including pneumothorax and bleeding, occurred in less than 5% of cases.

**Transbronchial needle aspirations (TBNA) vs. percutaneous needle aspiration (PCNA)**

Over the last decade, the increasing diffusion of innovative and more powerful imaging guided techniques, such as endobronchial ultrasound (EBUS) and electromagnetic navigation, has further broadened the bronchoscopist’s horizons in the management of peripheral pulmonary nodules. However, in most of institutions worldwide, due to the lack of resources and specific skills, the routinely diagnostic approach to PPN/M is still represented by bronchoscopic approach with fluoroscopic guidance and PCNA.

The lack of studies directly comparing such two procedures does not yet allow to definitely provide evidence based recommendation on the best choice between them. Data from literature strongly suggest a higher sensitivity of PCNA compared to transbronchial approach, especially when lesions are peripheral and less than 2 cm. On the other hand, as the success of a diagnostic test should result from a proper balance between accuracy and procedure-related complications, transbronchial approach has been shown to have a better safety profile. Moreover, it offers the advantages to provide, during a single examination, a pathological diagnosis of nodules, information on mediastinal staging and airways involvement, and to identify potential synchronous lesions.

In this context, it is reasonable to propose a sequential diagnostic algorithm, as previously suggested (2), in which flexible bronchoscopy with TBNA should be performed first, due to the safer profile and the possibility to obtain a simultaneous mediastinal staging, and PCNA after, in case of inconclusive results.

In conclusions, both the techniques have been shown to be useful in the diagnostic pre-operative work-up of PPN/M. In order to optimize the diagnostic yield and to minimize the risk of patients they should not to be considered as two alternative options, but, rather, as two complementary techniques integrated in a standardized algorithm.

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**Footnote**

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

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