

# Rethinking the strategy for improving the diagnostic yield of bronchoscopic fine needle aspiration biopsies

## Abstract

To be useful in rendering a definitive histological and molecular diagnosis, bronchoscopic and similar Fine Needle Aspiration biopsies need to be processed in a manner that enhances yield and minimizes tissue (cell) waste. Field data and author's own observations suggest that improved imaging technology and the availability of liquid fixative-based concentration techniques in cytopathology processing make it possible to achieve such a goal. It is proposed that both, definitive diagnosis with adequate residual material for molecular and special studies, as well as increased patient comfort with reduced demand on operators' and pathologists' time can be achieved by simply procuring the FNA material and placing it in liquid fixative to be concentrated by the cytology lab and used to prepare representative (filter-based) smears and cell blocks instead of the conventional approach of waiting for on-site assessment by the pathologist on conventionally prepared and quick-stained smears.

**Keywords:** lung, fine needle aspiration, bronchoscopy, ultrasound, thinprep, smear, cell block

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**Abbreviations:** EBUS, endobronchial ultrasound; FNA, fine needle aspiration; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase

## Introduction

For many years, bronchoscopic ultrasound-guided fine needle aspiration biopsies have been utilized as a relatively safe and simple tool for sampling deep-seated lung or hilar mass lesions with the goal of securing a pathological diagnosis.<sup>1</sup> Towards that goal, it has been considered essential that adequacy of the aspirated material be assessed on the spot by a pathologist or trained cytotechnologist.<sup>2,3</sup> However, this paradigm is now being questioned or re-addressed thanks to recent developments in the fields of imaging and diagnostic Cytopathology.<sup>4-7</sup> Bronchoscopic Imaging technology, such as EBUS and the so-called "Electromagnetic Navigational Bronchoscopy" has become much more reliable and accurate in identifying lesions and thus accurately sampling those lesions while the increased demand for molecular-augmented tissue diagnosis hastened the need for either procuring larger FNA samples or minimizing cellular waste of the usual size FNAs. Until recently, in most venues, FNA's sample adequacy assessment has been considered a standard of care. In this process, a significant portion of the aspirated material or all of it is used to prepare smears that are used by the pathologist to render adequacy assessment and cytopathological diagnosis.

The pathologist or cytotechnologist attending the procedure may have to "stick around" for up to an hour or more at times until the bronchoscopic operator eventually succeeds in obtaining diagnostic material or gives up on that goal (unable to do so after several

passes). In most such scenarios, there is usually little material left to perform additional pathology work up such as histochemical or immunohistochemical stains or molecular (genetic) studies.<sup>8</sup> The latter is rapidly becoming equally important to making the primary pathology diagnosis itself especially in advanced non-small cell carcinoma of the lung, whereby a molecular profile of the tumor (mutations in several genes like EGFR, ALK and others) is critical to designing a "personalized" chemotherapeutic regimen.<sup>9,10</sup> In such cases, usually, additional material is still needed for molecular studies, hence the patient may have to submit to a much more invasive, core needle or open incisional, biopsy. Therefore, it is imperative that we rethink the way in which FNA's material is being utilized so as to maximize its diagnostic utility. Towards that goal, many pathologists, including this author, have begun questioning the need for wasting time and material on the classic process of preparing quick smears and examining them in the bronchoscopy suite.

The bronchoscopist's need to know that the needle is actually sampling the intended lesion should be less of an issue nowadays, considering the substantially improved imaging accuracy of the modern imaging devices. If we accept this premise, it follows that on-site examination by the pathologist or cytotechnologist is no longer consistent with procedure efficiency or substantially needed and thus instead of wasting material on "smears", the entire FNA yield can be placed in liquid fixative (such as that used in the ThinPrep concentration technique; Hologic, Inc, Marlborough, MA, USA) and submitted to the cytology lab to be concentrated and used to prepare one or more representative (filter-based) smears (Thinpreps) while the remaining concentrate is processed to make a paraffin-embedded cell block. Cell block sections can then be used to make routine (H&E-

stained) slides as well as slides that can be used for histochemical or immunohistochemical stains and molecular studies.<sup>11</sup> This is a win-win strategy that accomplishes a better diagnostic yield with less time invested by all involved: the pathologist, who doesn't need to attend the procedure; the bronchoscopy team, who don't need to wait for pathologist's on-site assessment and the patient, who doesn't have to endure a longer than necessary procedure.

The author examined the utility of this paradigm by assessing the outcomes of bronchoscopic FNAs in a hospital setting, whereby the pathologist had a working arrangement with the pulmonary bronchoscopy team, under which on-site adequacy assessment by a pathologist (the conventional way) would only be offered during certain hours of the day, only if a pathologist were available and only up to 3 FNA passes from a single site. In all such cases, any material left after "smearing" would be placed in liquid fixative and submitted to the lab for processing into concentrated smears and cell blocks. In cases outside these limits, the bronchoscopy team was advised to proceed with their planned procedure but to place the entire yield (as much as they can procure) in liquid fixative and submit it to the laboratory. The author compared the diagnostic yield (ability to make a definitive diagnosis, confirmed by additional histology or clinical correlation, on aspirated material and ability to obtain adequate material for special studies afterward) of FNA's processed the conventional way (with on-site preparation of smears and pathologist's on-site assessment) with FNA's processed using liquid fixatives without on-site pathologist's participation. Of the last 100 cases of each processing approach that were handled by the group up to the end of 2015, conventional processing yielded a definitive diagnosis on-site in 43% of the cases and in 78% of the cases after augmentation by processing residual material (unused to prepare on-site smears) in liquid fixative and preparing cell block when possible; however, adequate material for molecular studies was left only in about 60% of the diagnostic cases. In contrast, liquid fixative processing without on-site smear preparation or pathologist assessment yielded a slightly better rate of definitive diagnosis at 80% but provided adequate material for molecular studies in about 80% of the diagnostic cases.

## Conclusion

Logic, improved imaging and liquid fixative technologies, and available data from actual studies indicate that the diagnostic yield of FNAs of mass lesions from the lung and other deep sites can be improved or at least maintained at current rates but much lower cost and patient discomfort if those procedures are performed by skilled bronchoscopists who procure as much as they can with a minimally invasive needle and submit the entire material in liquid fixative to the cytology lab without the need for the added cost in wasted professional time and supplies associated with on-site adequacy assessment by a pathologist or cytotechnologist. Furthermore, in the age of molecular diagnostics, this paradigm shift can more reliably secure additional material for molecular (tumor genetic) studies that are now an integral part of cancer diagnosis and treatment.

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## Conflict of interest

The author declares no conflict of interest.

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