Seize the Opportunity With Small Tissue Samples: The Tailor Teaches!

To the Editor:

We read with great interest the study by Diep et al.,[1] which compared complication rates and success for molecular profiling through next-generation sequencing (NGS) of different biopsy methods and needle sizes in NSCLC. The Authors conclude that, among the needle-based techniques, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) yields more DNA and causes less complications than computed tomography-guided biopsy.

Nevertheless, what strikes the most of this study is, in our opinion, the low success rate of NGS for both EBUS-TBNA (58.1%) and computed tomography-guided biopsy (53.2%). Besides the externalization of the analytical component,[2] several factors may explain this result, and at least two of them are worth commenting. First, the molecular profiling was performed through either a 592-gene panel or whole exome sequencing, regardless of the amount of nucleic acids extracted from the samples. These panels, that are well beyond what is needed in clinical practice, require a large amount of DNA and RNA, which may be difficult to retrieve with the small-bore needles currently available for EBUS-TBNA. As a consequence, a more flexible strategy encompassing the use of a smaller NGS panel in cases with suboptimal quantity of nucleic acids would have most likely allowed a higher proportion of patients to have the genetic information essential for a correct treatment planning.[3] Second, the genomic profiling was carried out exclusively on formalin-fixed, paraffin-embedded (FFPE) material, a decision that may have significantly contributed to increase the failure rate of EBUS-derived samples. Comparative studies have clearly revealed that the smears prepared from EBUS-TBNA specimens contain a significantly higher amount of DNA and have a significantly lower failure rate for NGS testing as compared with the FFPE cell blocks.[4] This is true even when large gene panels are tested. Stoy et al.[5] reported a 91% success rate of a 1213-NGS gene panel by using cytologic samples obtained with EBUS-TBNA; interestingly, in 84.4% of the cases, the smears were used, whereas in the remaining 15.6%, the FFPE cell blocks were chosen for the genomic profiling.

In conclusion, it is key that the stakeholders involved in the tissue sampling and the molecular profiling processes coordinate to implement a strategy that allows to successfully test as many patients with advanced lung cancer as possible regardless of the biopsy method and the needle size. For this to be possible, a clear knowledge of the strength and limitations of the biopsy methods and a flexible use of different NGS panels on the basis of the characteristics of the sample are essential. Diep et al.[1] clearly reveal that with the "rigid" use of a single large gene panel, nearly 55% of the patients with NSCLC will have an extensive molecular profiling with a large amount of data not yet useful for clinical practice, whereas more than 45% of patients will not have any molecular profile, with serious clinical and ethical implications.

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