Article Commentary

Synchronized Tissue Acquisition Techniques for Novel Biomarker Discovery: Are You Ready to Waltz?

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Revolutionary progress in biomarker-driven treatment has enhanced survival and preserved quality of life for patients and has become a standard of care in cancer management today.[1] Over the last 2 decades, global efforts have been made toward improving the quality of tumor tissue retrieved for histopathologic and genomic analysis and biomarker discovery. The US Precision Medicine Initiative[2] was one such step forward and underscored the need for accurate representative tissue acquisition, emphasizing the need for new age biospecimen collection. The role for primary biopsy specimens has already been established to better understand tumor evolution and heterogeneity, and now, longitudinal biopsy specimens are being advocated in clinical practice and clinical trials.[3] However, nearly one-third of core biopsy specimens are unable to yield the appropriate tissue quality for histopathologic testing, next-generation sequencing (NGS), and novel biomarker discovery, especially immune biomarkers. Observations from the MERIT and the BATTLE lung trials underline these challenges and NCI-MATCH, TAPUR, and M-PACT, a few of the most ambitious precision trials with a biomarker backbone, have also identified tissue acquisition as a barrier to an ideal conduct of the precision methods for investigation.[4–6]

Image-guided biopsy procedures yield higher quality tissue samples for analysis and have become a standard of care in the field of oncology.[7] Computed tomography or ultrasound-guided biopsy procedures are most commonly performed. To enhance tissue capture, more recently, newer radiologic tests, such as magnetic resonance imaging or positron-emission tomography/computed tomography–guided biopsy procedures, are being investigated and practiced at some centers.[7] In the current times when clinical practices and research strategies are based on longitudinal efforts at biomarker discovery, it becomes imperative to ensure adequate representative tissue collection that would yield material for routine tests as well as novel attempts at biomarker discovery.[8–10] Many such initiatives require a higher level of coordination between and within multidisciplinary teams, including medical oncology, surgical oncology, radiation oncology, interventional radiology, histopathology, molecular biology, and sometimes even anesthesiology. Such coordinated efforts could be challenging and make longitudinal efforts difficult and fraught with errors.

The need for "next-generation biospecimens" brings to the fore the necessity for designing well-synchronized, coordinated efforts that would improve the quality and the reliability of biospecimen acquired, enhance feasibility, and reduce the scope for errors in these challenging situations.[8] The minimum representative tumor required for NGS to be performed is different for DNA and RNA extraction and requires different levels of understanding and coordination. Immune biomarkers and tumor microenvironment analysis are new age biomarkers being studied extensively over the last decade, and quality and integrity of tissue requirement for these are different from the routine.[10] Management of lung cancer has revolutionized and transformed the approach to advanced disease. Initial and longitudinal biopsy specimens are imperative and central to the management of lung cancer. Barriers to acquiring the right tissue and risks associated with tissue retrieval in lung cancer are widely described and nearly 30% samples are known to not meet quality standards.[11] Each new lung biopsy specimen could cost nearly $US10,000 to 14,000 and any complication could raise this cost to nearly US$35,000 to 40,000, underscoring the need to reduce errors and reduce the need for repeat biopsy procedures.[12]

The original research article by Xu et al,[13] recently published in the *Journal of Immunotherapy and Precision Oncology*, presents results from implementation of a novel web-based lesion selection tool (LST) to improve

acquisition of tumor biopsy specimens. Debut of the so-called *Naing tool* is an example of a coordinated effort to enhance the reliability and integrity of the tissue acquired for testing. In this analysis, they included a total of 145 patients; the LST was used in 88 patients and 57 patients served as controls. The authors studied the consistency of lesions biopsied in longitudinal samples, total number of cores obtained, and adequacy of tumor cellularity for NGS testing from those specimens. The investigators reported 100% consistency in the lesions biopsied with the LST group versus 75% in the control group. The chances of yielding the representative tissue specimen increased when at least five cores were collected per biopsy procedure.

In summary, this analysis demonstrates that the novel LST platform was able to identify the representative tumor specimen more accurately in longitudinal sample collection, especially when at least five cores were collected per biopsy.[13] The enhanced accuracy reduces the need and risk of repeat biopsy procedures, enhances appropriate resource utilization, and improves patient care. In addition, radiotherapy can alter the tissue architecture and impair immune monitoring strategies. Using the Naing tool to predesignate different lesions for radiotherapy and for longitudinal sampling is a remarkable strategy that will likely pay rich dividends. Identifying lesions to follow consistently is invaluable for evaluating response to treatment in RECIST (response evaluation criteria in solid tumors) and immune-related RECIST (irRECIST) criteria. The Naing tool does just that and prevents inadvertent sampling of lesions followed for response.

The most striking point about the research of Xu et al[13] is that one can biopsy the same site consistently at baseline, on treatment, and after treatment with longitudinal sampling. This will provide valuable information on dynamic changes in the tumor microenvironment. The Naing tool will facilitate more accurate serial monitoring of biomarkers for response or resistance, rendering this an invaluable tool in this era of NGS and biomarker development.

However, the study was limited by a small sample size and further testing is required in a larger population to become a standard of care. Funding for the effort of involved staff for synchronized tissue acquisition techniques should be considered. In addition, because the LST method is novel, the feasibility and adaptability into the implementation of this method is still unknown and needs further validation. The lack of integration to the current existing electronic medical record system poses an additional limitation to adaptability for a novel technique like LST.

Despite all the challenges seen with the implementation of a novel technique, it does stand clear that the LST method could be a value addition to the diagnostic methods and procurement of representative patient tissue for genomically driven cancer care. A well-synchronized method, like LST, with strategic integration is the need of the hour to elevate the level of tissue retrieval for the next generation of biospecimen procurement and novel biomarker discovery.

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