Virtual Biopsy: Shift from microscope to imaging console

The term "biopsy" was coined into medical arena in 1879 by Ernest Besnier and the first diagnostic biopsy was performed by M. M. Rudnev in 1875 in Russia.[1] Biopsy is the sentinel component of diagnostic paradigm in all clinical specialties as it provides information about the biological existence and behavior of tissue being examined. It is a Greek word comprised of *Bios* for life and *Opsis* for sight.

In current practice biopsy or ***Tissue Biopsy*** refers to a medical procedure that involves taking a sample of tissue through either a needle or surgically like incisional or excisional depending upon bulk of tissue removed to examine under a microscope. Use of various staining techniques like immunohistochemistry, it has become a robust gold standard diagnostic modality.

The other type of biopsy is ***Liquid Biopsy*** which involves to looking blood for circulating tumor cells (CTCs). Thomas Ashworth in 1869 first observed CTCs in a cancer patient s blood and suggested that these tumor cells were thrown into the bloodstream leading to metastasis.[2] It was 1948 when researchers first detected and quantified Cell-free Deoxyribose Nucleic Acid (cfDNA) in both healthy and diseased patients. In 1966, researchers discovered high levels of cfDNA in lupus patients, and in the 1980s, cfDNA was first discovered in oncology patients.[2] Continuous and robust work, in 1994 researchers were able to detect specific mutations in cfDNA and in 2000, Veridex introduced the first commercially available liquid biopsy assay, the CELLSEARCHfi CTC test.[3] Journey goes on and in 2016, the Food and Drug Administration (FDA) approved the first liquid biopsy test, the cobasfi EGFR Mutation Test (detects cfDNA for the EGFR gene mutation in lung cancer patients).[4]

Since current era is dominated by humongous development in medical imaging and artificial intelligence (AI), a new modality ***Virtual Biopsy*** has been introduced. Virtual biopsy is a non-invasive technique to characterize tissue appreciable in imaging studies. Since 2015 when it was introduced, number of publications on PubMed has doubled in 2021.[5] The virtual biopsy could be used with tissue biopsy to guide doctors about tissue nature and behavior. This would minimize the likelihood of false negative results in cancer diagnosis and would also minimize number of samples taken from the patient. For optimists, virtual biopsy along with artificial intelligence (AI) would open the doors for less invasive and highly personalized arena of decision making. For skeptics, virtual biopsy would be a hollow vesicle and credibility of its results without seeing the tissue will be a major factor for its acceptability by patients, medical community, regulators and insurance companies. Currently virtual biopsies are being explored within realm of research and many vistas of oncological applications are being emerged. Regarding the axillary nodal status in breast cancer, researchers have compared imaging modalities like 18-FDG PET/MRI and ultrasound with histopathology as a reference standard.[6] They concluded that if both 18F-FDG PET/MRI and sonography are positive for axillary nodes, one might consider dispensing with axillary histopathologic sampling.

So, currently virtual biopsy is in front row of a flourishing and robust growing research effort. Despite its challenges like acceptability by medical fraternity, regulatory and reimbursement people, it is a potential logical next step in patient care.

Conflict of Interest: None

REFERENCE:

1. D DZerbino. Biopsy: its history, current and future outlook. LikSprava1994; **3-4:** 1-9.

2. Zhang H, Lin X, Huang Y, Wang M, Cen C, Tang S, Dique MR, et al. Detection Methods and Clinical Applications of Circulating Tumor Cells in Breast Cancer. Front Oncol. 2021 Jun 2; **11:** 652253.

3. Wang L, Balasubramanian P, Chen AP, Kummar S, Evrard YA, Kinders RJ. Promise and limits of the Cell Search platform for evaluating pharmacodynamics in circulating tumor cells. SeminOncol. 2016; **43(4):** 464-75.

4. Torres S, GonzÆlez `, Cunquero Tomas AJ, Calabuig Fariæas S, Ferrero M, Mirda D, et al. A profile on cobasfi EGFR Mutation Test v2 as companion diagnostic for first-line treatment of patients with non-small cell lung cancer. Expert Rev MolDiagn. 2020; **20(6):** 575-82.

5. Murray JM, Wiegand B, Hadaschik B, Herrmann K, Kleesiek J. Virtual Biopsy: Just an AI Software or a Medical Procedure? JNM 2022; **63(4):** 511-13.

6. Morawitz J, Bruckmann N-M, Dietzel F. Determining the axillary nodal statuswith 4 current imaging modalities, including 18F-FDG PET/MRI, in newly diagnosedbreast cancer: acomparative study using histopathology as the reference standard. J Nucl Med. 2021; **62:** 1677-83.

Maseeh uz Zaman,[1] **Nosheen Fatima,**[1] **Areeba Zaman,**[2] **Sidra Zaman,**[3] **Unaiza Zaman**[4]

[1] *Section of PET/CT and NM Imaging, Department of Radiology, Aga Khan University Hospital (AKUH), Karachi, Pakistan*

[2] *Department of Medicine, Sunny Downstate Hospital NY, USA.*

[3] *Dr. Ruth K. M. Pfau, Civil Hospital (DUHS), Karachi, Pakistan.*

[4] *Department of Haem-Oncology, Oklahoma University, Oklahoma, USA.*