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Ujjwal Karki
Beaumont Health Resident

Bipin Ghimire
Beaumont Health Resident

Emma Herrman
Beaumont Health Resident

Siddhartha Yadav

Mohammad Muhsin Chisti
Beaumont Health

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Detection of progression or regression of breast cancer by circulating tumor DNA (ctDNA)

Presenting Author(s) and Co-Author(s):

Ujjwal Karki, MBBS, *Resident Physician - Internal Medicine, Beaumont Hospital, Royal Oak, Michigan*
Country: United States

Bipin Ghimire, MBBS, *Resident Physician - Internal Medicine, Beaumont Hospital, Royal Oak, Michigan*
Country: United States

Emma Herrman, MD, *Resident Physician - Internal Medicine, Beaumont Hospital, Royal Oak, Michigan*
Country: United States

Siddhartha Yadav, MD, *Assistant Professor of Medicine and Oncology - Mayo Clinic*
Country: United States

Mohammad Muhsin Chisti, MD, *Associate Professor of Hematology and Medical Oncology - Oakland University William Beaumont School of Medicine*
Country: United States

Background:
Circulating tumor DNA (ctDNA) are short DNA sequences shed by tumor cells into the systemic circulation. Studies have shown potential utility of the test to predict relapse or recurrence following treatment in solid tumors, but sensitivity and specificity have varied widely, ranging from 19-100% and 80-100% respectively, in breast cancer specifically. Moreover, literature describing the utility of monitoring dynamic changes in ctDNA trends is limited. We aim to evaluate the correlation between ctDNA test, both single test as well as dynamic trends in value over time, with imaging findings.

Methods:
We retrospectively analyzed the medical records of all adult patients diagnosed with breast cancer who underwent ctDNA testing at the hematology-oncology clinic at William Beaumont - Royal Oak and Troy Hospitals, Michigan, from August 2017 to June 2022. Patients who had ctDNA testing done but did not have imaging to correlate it with were excluded from the study. We calculated the sensitivity and specificity of a single positive ctDNA test to detect disease progression or residual disease on imaging. In patients with multiple ctDNA tests, we calculated the sensitivity and specificity of dynamic trends in ctDNA values to detect progression, regression, or absence of disease on imaging. Moreover, we calculated the lead time for positive ctDNA results to detect disease progression compared to imaging.

Results:
Nineteen patients were included in the study, with 34 total ctDNA test results, each utilized as a separate data point to compare with corresponding imaging findings (Table 1). Ten out of the 19 patients had multiple(>=2) ctDNA test results reported, with a total of 15 pairs of ctDNA values and each pair was analyzed separately as up trending (N=7), down trending (N=4), or persistent negative (N=4) to compare with a corresponding pair of imaging findings (Table 2). The median age at diagnosis was 55 years, and 94.7% were female. At diagnosis, majority of

patients (68.4%) had either stage III or IV disease. Our primary endpoint, the correlation of single positive ctDNA result with imaging showing either progression or residual disease, showed a sensitivity and specificity of 100% and 93.3%, respectively. Secondarily, serial ctDNA trend analysis in ten patients revealed both sensitivity and specificity of 100% for up-trending ctDNA values to detect progression, down-trending to detect regression, and persistent negative results to detect absence of disease on imaging, respectively. The positive ctDNA results detected disease progression with a median lead time of 44.5 days compared to imaging.

Conclusion:
Given the high sensitivity and specificity to detect disease progression and regression in breast cancer patients by single ctDNA results and dynamic ctDNA trends in our study, we conclude that this may be a valid way to reliably monitor for changes in disease status before they become evident in imaging studies. Further clinical studies are required to prove the utility of ctDNA to detect changes in disease status and to guide therapeutic interventions in breast cancer.

Correlation of single ctDNA result with imaging findings

Table 1: Correlation of single ctDNA result with imaging finding

CtDNA result	Imaging finding		
	Progression/residual disease	No progression/residual disease	Total
Positive	19	1	20
Negative	0	14	14
Total	19	15	34

Correlation of dynamic trends in ctDNA values with imaging findings

Table 2: Correlation of dynamic trends of serial ctDNA values with imaging finding

CtDNA values	Imaging/biopsy finding			
	Progression	Regression	Absence of disease	Total
Up-trending	7	0	0	7
Down-trending	0	4	0	4
Persistent negative	0	0	4	4
Total	7	4	4	15

Disclosure(s):
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