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# The Role of Next Generation Sequencing in the Breast Cancer Prognosis

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## Introduction

In the last two decades, Sanger sequencing has dominated genomics research and made significant advances, such as the sequencing of the entire human genome, which allowed for the discovery of single gene disorders and the detection of capable of attacking genetic abnormalities for clinical molecular diagnosis [1, 2]. There has been a dramatic increase in the sense and richness of genetic alterations in cancer, such as point mutations, small insertions or deletions, copy number changes, and structural variations, as a result of the application of next generation sequencing (NGS), particularly through whole genome (WGS) and whole excavation technology (WES). A comprehensive transcriptome technique (RNA-Seq) may identify fusion transcripts, alternative splicing, and RNA editing in addition to measuring gene expression levels. The NGS, also known as massively parallel sequencing (MPS), is frequently performed on breast cancer patients to find specific alterations in the illness after it has spread or progressed. We now understand much more about breast variety and heterogeneity thanks to advances in cDNA genotyping profiling of gene expression, gene expression-based prediction biomarkers, targeted Sequence analysis, WGS, and NGS [3]. Breast cancer treatment plans are influenced by the disease's biomolecular features, histological subtypes, and clinical and pathological stages. Breast cancer can be diagnosed and classified into biomolecular subgroups, such as luminal A, luminal B, human epidermal growth factor receptor 2 (HER2) luminal B, HER2-enriched, or basal-like subtypes, using analysis of eosin and hematoxylin (HandE)-stained tissue sections and immunohistochemistry (IHC). The most frequent type of cancer among women is breast cancer. Discovery of "curable" drug target for diagnostic screening of individuals having lateral lymph node metastases from carcinoma of unknown origin with early, advanced, and metastatic breast cancer. Link between original breast cancer and relapse in breast cancer.

## Methods and Treatment

The volume of data is greatly increased by the parallel processing sequencing of millions of DNA molecules made feasible by NGS technology. Sequencing of previously broken-up, ligated-together, and amplified DNA fragments, often known as "short reads", is the foundation of second-generation techniques, which are currently most frequently utilized in standard diagnostic labs. Short-read sequencing, which enables the sequencing of gene panels, WES, and WGS, all of which give useful information in cancer, is particularly ideal for DNA taken from partly digested formalin-fixed paraffin-embedded (FFPE) tissues. Point mutations, minor base additions, deletions, copy number alterations, and structural rearrangements can all be found using NGS. In order to analyses genes of interest, modern sequencing technologies can sequence up to a billion or more of reads per specimen, providing a wide coverage area equal to the amount of reads at a particular region. For the identification of sub-clonal cancer mutations or alterations in specimens with poor tumors cellularity, the great depth is very important. The same sequencing technologies may be used to study RNA by reverse transcribed (RT) RNA particles into cDNA molecules. The most significant recognized and targetable oncogenes may be quickly and affordably analyzed using a modest screen of a few dozen genes. Based on recently discovered molecular changes, tumors DNA analysis may be retrieved from FFPE, 6 frozen tissues, or fluids like blood, and a wider panel of numerous genes can be utilized to find novel treatment targets and new indicators for cancer monitoring and testing. This method may soon prove to be an efficient and affordable tool to pinpoint patients who might profit from poly-ADP-ribose polymerase inhibitor therapy (PARPi). Also, this technique is appropriate for FFPE samples and only generates a minimal quantity of recordable data. According to how beneficial they are to patients' genomic changes are categorized as target for precision cancer therapy.

The changes that have grade I proof are the ones that have been linked to better results in clinical studies. When feasible under safe and appropriate circumstances, those who have recently been diagnosed with recurrent or metastatic breast cancer are encouraged to get a biopsy of the

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metastatic disease to assess the metastatic disease phenotype (ER, PR, and HER2). Because the Olympia trial findings revealed an increase in 3-year invasion illness survival (3yIDFS) from 77.1% to 85.9% when BRCA1-BRCA2 mutations are addressed with adjuvant treatment, this is additionally done in early-stage breast cancer (triple-negative or luminal). NGS has also made it possible to analyze therapy-resistant breast cancer, which has been shown to have 40 recurring alterations. Pi3Kca or AKT mutations causing treatment resistance have been found by genetic profiling of HR cancers [4, 5]. It is possible to extract tumors DNA for analysis from FFPE, 6 frozen body parts or liquids, such as blood. Then, a larger array of several hundred genes may be used to identify new disease indicators, discover novel therapy targets, and verify testing. Based on recently found molecular alterations, of a clinical study. This method may soon prove to be an efficient and affordable tool to pinpoint patients who might profit from PARPi therapy. Since the administration of messenger RNA-dependent rapamycin (mTOR) and PI3K inhibitors in animals was authorized for use in this situation together with hormone treatment, it changed the standard of care [6].

Another useful tool for the treatment of breast cancer patients is the use of circulating tumour DNA (ctDNA) to track the disease's development. With aromatase inhibitor therapy, oestrogen receptor 1 gene (ESR1) alterations are acquired and are sub clonal in malignancies. Modern polymerase chain reaction can quickly identify them in ctDNA, making it more accurate (PCR) [7]. When reproduced in the initial trial, the PADA-1 investigation examined the existence of ESR1 mutations in baseline ctDNA. Palbociclib and aromatase inhibitors were used in conjunction to treat metastatic ER HER2 breast cancer [8]. Upon early discovery of an ESR1 mutation, patients who were randomly shifted from aromatase inhibitors to fulvestrant saw a twofold increase in median PFS. Two additional molecular alterations, neurotrophic receptor tyrosine kinase (NTRK) fusion detection for larotrectinib or entrectinib, both tyrosine kinase (TRK) inhibitors, and microsatellite instability (MSI) for immune checkpoint inhibitors, have been identified as predictive markers for ESCAT level of evidence IC in breast cancer. IHC is a potent technique that can enable case selection for molecular testing to establish mismatch repair (MMR) status or NTRK fusions, even if the ideal testing approach is still up for dispute. The term "carcinoma of unknown primary" (CUP) refers to occult metastatic cancer. 2 - 3% of newly diagnosed cases of metastatic cancer are caused by it [9]. Just 15% of them have axillary lymph nodes in a particular place, and more than half of them have disseminated illness. An essential step in figuring out the cancer's potential origin and the best course of action is the biopsy of the metastases. To pinpoint the source of metastatic malignancies, Institute Curie has developed RNA sequencing with a deep learning classifier. By contrasting it with the recurring profile, NGS enables the identification of the genetic profile of initial breast cancer. While reflecting at most some of the molecular abnormalities of the primary breast cancer, metastases can have a substantially diverse genomic profile, especially in luminal A and late metastases [10]. Dominant driver mutations that were previously present in the initial tumors are also acquired by metastatic illnesses under increased treatment strain, including modifications to the ERS1 and MAPK (mitogen-activated protein kinase) pathways. using olaparib as an adjuvant [11]. NGS has also made it possible to analyze therapy-resistant breast cancer, which has been shown to have 40 recurring alterations. Pi3Kca or AKT mutations causing treatment resistance have been found by genomic profiling of HR cancers [12, 13].

## Conclusion

These tests are mostly utilized to look for therapeutic indicators more than ten years after the launch of NGS. Just two mutations, germline BRCA1 and BRCA2 variations, are now recognized as evidence-based IA treatment markers for breast cancer patients internationally for the indication of PARP inhibitors in patient populations with triple-negative or luminal breast cancer, and PIK3CA mutations, given that PI3K inhibitors are not permitted in many but not all countries [14]. With the clinical studies use of antibody-drug conjugates, a key advancement in the treatment of breast cancer, his technique appears to have become even more crucial. With the current usage of antibody-drug-antibody-drug in clinical practice, the immunotherapy antagonist partnering testing is programmed death mediator 1 (PD-L1) status assessed by IHC in the metastatic scenario, which looks to become increasingly crucial. a major breakthrough in breast cancer treatment. PD-L1 status is now assessed by IHC in a metastatic situation by immune checkpoint inhibitor test.

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