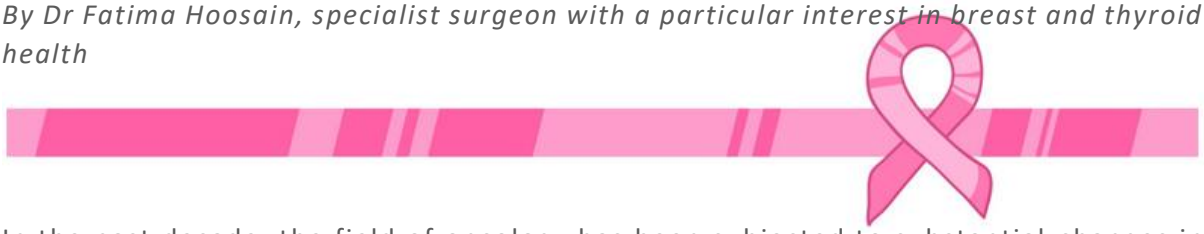
Using Genetic Testing to create custom breast cancer treatment plans

By Dr Fatima Hoosain, specialist surgeon with a particular interest in breast and thyroid health



In the past decade, the field of oncology has been subjected to substantial changes in the way patients with cancer are being treated. We have departed from a "one-size-fits-all" treatment approach and entered an era with increasing focus on precision medicine based on genomic variants[1].

In order to better understand cancer and to develop drugs to fight cancer, medical researchers have been studying genes and the changes in these genes for a very long time. The goal behind this research is to create therapies that disrupt various steps in cancer growth, but cause minimal damage to normal cells. These therapies are referred to as targeted drugs or targeted therapy. Researchers have noted that some types of cancers are frequently associated with specific genetic mutations. Not every cancer has a genetic source, but a significant percentage will. It is also noteworthy that cancers with these mutations usually have a more predictable response to certain drug treatments compared to cancers without these mutations[2].

Gene expression is the process where the body makes specific proteins from the information contained within genes. Different tissues express different sets of genes based on their function in the body. Within the cell, information from genes is used to make a template for building ribonucleic acid (RNA). This RNA is processed to create the protein that is required by the cell. In patients with breast cancer this is translated into multi-parameter gene expression tests[3].

Gene expression tests evaluate the RNA in a person's tissue sample to determine which genes are actively making proteins. These are tests that evaluate the products (RNA) of specific groups of genes in the malignant (cancerous) tissue from the breast in order to determine which genes are making proteins within the tumour. This information can then be used to predict the outcome by estimating the risk of recurrence of the cancer. It is also used to guide treatment[4].

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[1] E. R. Malone, M. Oliva, P. J. B. Sabatini, T. L. Stockley, and L. L. Siu, "Molecular profiling for precision cancer therapies," *Genome Med.*, vol. 12, no. 1, pp. 1–19, 2020.

[2] **https://labtestsonline.org/tests/genetic-tests-targeted-cancer-therapy**

[3] **https://labtestsonline.org/tests/breast-cancer-gene-expression-tests**

[4] **https://labtestsonline.org/tests/her2**

Each breast cancer has an individual set of genetic mutations that distinguishes it from the normal tissue. These mutations within the cancer cells and the related change to the expression of those genes regulate how rapidly the cancer grows. This also determines the likelihood of metastasis. It will determine whether or not its growth is supported by the hormones oestrogen and/or progesterone or whether it over-expresses certain proteins such as HER2. Ultimately, it influences how responsive the cancer will be to various treatment modalities.

Rather than evaluating a single gene, multiparameter gene expression tests analyse the RNA of multiple genes within a cancer at the same time. The result is a pattern of gene expression that is consolidated into a score and/or profile. This information is then used to help predict the likely behaviour of the cancer and its response to the available treatment options.

These tests are relatively new, but their use is increasing as they become more affordable and available. Their use is aimed ultimately, at developing a personalized approach to patient care and breast cancer therapy.

In Cape Town, a comprehensive breast centre has been using molecular genetic profiling and testing for more than 15 years and has documented the clinical progress of more than 300 patients, diagnosed with breast cancer, who had undergone molecular genetic profiling of their breast tumours.

The tumours were selected for molecular genetic profiling as part of the normal consultative process. The patients were older than 18 years with histopathological (microscopic examination of tissue in order to study the manifestations of disease) confirmation of an early breast cancer (the tumour was less than 5cm across and had spread to a maximum of 3 axillary lymph nodes). In these patients, it is often not clear whether they will benefit from the addition of chemotherapy after their surgical management. Oncologists are inclined to rather give chemotherapy than omit it, to avoid compromising patient outcome.

In these patients, chemotherapy was recommended if the molecular genetic profile indicated a high-risk of relapse; conversely, chemotherapy was not recommended if the molecular genetic profile indicated a low risk of relapse. Each patient was consulted by a team consisting of a surgical, medical and radiation oncologist. Once the decision on further treatment was taken, established protocols were followed.

These patients have been monitored and followed up, for over more than a decade, to determine whether the individual treatment plan based on the genetic markers in the tumour has resulted in a better outcome than standard treatment.

Out of more than 300 patients, half were low risk based on the outcome of the molecular genetic profiling; all have survived without relapse despite not having had chemotherapy. Conversely, out of the high-risk group, despite receiving chemotherapy, 3 patients have relapsed indicating that the risk assessment with molecular genetic profiling was accurate. The major outcome of the study, however, was that about more than half of the patients that ordinarily would have received chemotherapy, could

safely be spared chemotherapy with all its feared side effects without compromising the outcome. Also, a few patients which ordinarily would not have received chemotherapy were identified to have high risk tumours and received chemotherapy, a potentially life-saving addition to their treatment.

These outcomes are in accordance with experience in the best overseas cancer centres and confirm that molecular genetic testing can reduce the number of individuals who undergo chemotherapy and also save lives due to a more aggressive treatment regime being prescribed for individuals who at first diagnosis would be seen as low risk. It gives medical professionals a new level of information from which to determine prognosis and treatment options and ultimately, allows for a more individualised approach to cancer prognosis and treatment.

Apffelstaedt, Hoosain and Associates, a multi-disciplinary Breast, Thyroid and Parathyroid Health Centre in Cape Town, offers genetic counselling and testing for patients who have a family history of breast and ovarian cancers.

About the author

Dr Fatima Hoosain is a specialist surgeon who enjoys all aspects of General Surgery, with a particular interest in breast and thyroid health. This includes surgery for breast, thyroid and soft tissue tumours.

Dr Hoosain graduated with an MBChB from the University of Stellenbosch in 2009, subsequently specialised in General Surgery and qualified with an FCS (SA) and MMed (Surg) in 2019. She has been involved in the publication of several journal articles.

Dr Hoosain is also a member of the Breast Interest Group of South Africa (BIGOSA), the Association of Surgeons of South Africa (ASSA), the Surgical Research Society of South Africa (SRS) and the South African Colorectal Society.