# Breast Cancer Awareness Month

by Dr. Nimallen Naicker

Breast cancer is the second most common cancer in the world and the most common cancer in women.

The latest cancer registry data shows that, in South Africa, breast cancer is the single most common cancer, accounting for over 23% of cancer diagnoses. In 2019, there were 10172 cases of breast cancer, far above second place, which was cervical cancer at 6945.

Diagnosis and treatment of breast cancer has advanced over the years and there are many new modalities to detect and treat this pervasive entity.

The diagnostic journey starts in the clinical arena, with physical examination and radiological tools including mammogram and ultrasound. The diagnosis is confirmed on histology specimens, which is usually a core needle biopsy done by the surgeon or radiologist. Apart from the elementary diagnosis made on standard H & E stains, the histopathologist will undertake numerous ancillary tests in order to fully classify the tumour so that the patient can receive the correct treatment and have a good understanding of the prognosis.
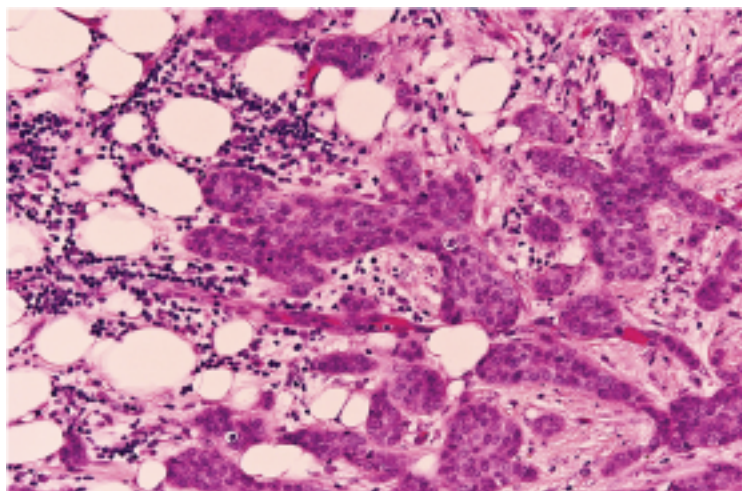
Invasive breast carcinoma of no special type (previously called invasive ductal carcinoma). *Hematoxylin and eosin-stained section.*

The aetiology of breast cancer is multifactorial and includes genetic predisposition, age, window of oestrogen exposure, gender, family history and exogenous hormone use. Invasive breast carcinomas are categorized by histologic features and molecular features.

Because molecular tests are expensive and not readily available, immunohistochemistry is used as a surrogate to extrapolate the molecular subtypes.

Although this is not perfect, it is still a relatively accurate measure of the underlying genetic alterations.

As such, these tumours can be classified as depicted in the following tables:

Table 1. Modified Bloom-Richardson Score (histologic grade)

Feature	Qualifiers	Score
Tubal Formation	> 75%	1
	25 - 75%	2
	< 25%	3
Nuclear Pleomorphism	Small, regular uniform cells	1
	Moderate increase in size & variability	2
	Marked variation	3
Mitotic Count	0 - 8	1
	9 - 17	2
	≥ 18	3

Score of 3 - 5 = well-differentiated (Grade 1).
Score of 6 - 7 = moderately differentiated (Grade 2).
Score of 8 - 9 = poorly differentiated (Grade 3).

Further molecular studies have elucidated other molecular subtypes, which currently don't have acceptable immunohistochemical surrogates. These include claudin-low and molecular apocrine.

Table 2. Allred score for oestrogen and progesterone
receptor

Positive cells %	Proportion score	Intensity	Intensity score
0	0	None	0
< 1	1	Weak	1
1 - 10	3	Intermediate	2
11 - 33	3	Strong	3
34 - 66	4		
≥ 67	5		

The Allred score combines the percentage of positive cells and the intensity of the reaction in most of the carcinoma. The 2 scores are added together for a final score with 8 possible values. Scores of 0 and 2 are considered negative. Scores of 3 - 8 are considered positive.

In addition to the above, other prognostic tests have been developed to guide treatment, particularly when guiding the inclusion of chemotherapy. The most widely used of these assays are Oncotype Dx and Mammaprint. These tools help the oncologist to decide whether a patient will require adjuvant chemotherapy or if they can be spared the side effects of these drugs.

The importance of classifying breast cancer is in the prognostic and treatment benefits of the systems used to segregate the different types. Depending on the molecular alterations, there are numerous targeted therapies that can be used to treat patients.
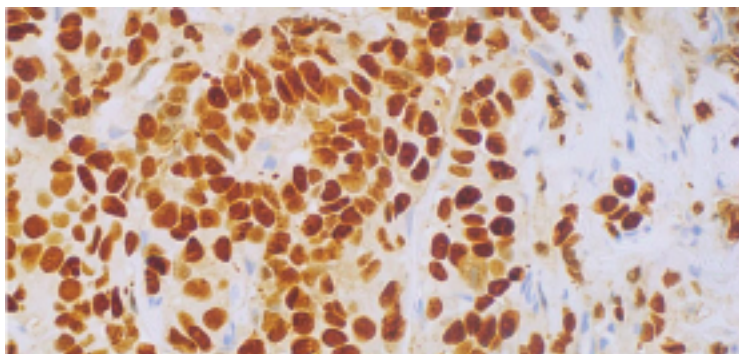
Strong oestrogen receptor nuclear positivity (400x magnification)

Herceptin (trastuzumab) is a tried and tested targeted treatment for patients with HER2 positive breast cancer.

Newer medications such as PI3K inhibitors and CDK4/6 inhibitors have also been introduced and can be used depending on the particular subtype of breast cancer.

CDK4/6 inhibitors are used for patients with hormone positive (ER/PR), HER2 negative breast carcinomas. If the patient has a mutation in the PI3K pathway (PIK3CA), then these drugs can also be utilized for management.

Surgery is also a mainstay for most stages of breast cancer and other adjuvant treatments such as chemo-therapy and radiotherapy are also core modalities. Early diagnosis and treatment are key in the management of breast cancer. Patient education is pivotal in decreasing morbidity and mortality of the disease. Patients should be aware of their family history and must be educated in conducting self-breast examinations.

The future of breast cancer diagnosis and treatment resides in more advanced molecular testing including genomics and development of sophisticated targeted therapies in addition to new surgical techniques.

Table 3. Molecular Subtypes
(Immunohistochemical surrogates)

Molecular Subtype	Oestrogen receptor	Progesterone receptor	HER2	Ki67
Luminal A	+	+	-	Low
Luminal B	+	+	-	High
HER2-amplified	-	-	+	Usually high
Triple negative	-	-	-	Usually high

References

1. Singh E. National Cancer Registry: Cancer in South Africa. 2017 ed. South Africa: National Institute for Communicable Diseases; 2019.
2. Dabbs DJ. Breast pathology. Elsevier Health Sciences; 2016 Nov 4.