

APPENDICES





GLOSSARY

Adjuvant chemotherapy

A postoperative treatment for eradicating residual microscopic cancer cells that could lead to recurrence when these are not yet detectable clinically.

Axillary dissection

A surgical procedure to remove the lymph nodes in the armpit (axillary nodes) hidden under the pectoral major and minor muscles. It is normally performed when there is evidence of cancerous cells in lymph nodes by palpation or imaging, or upon sentinel lymph node biopsy.

Bilateral breast cancer

Cancer occurring in both breasts at the same time or within six months of each other (synchronous), or at different times at least six months apart (metachronous).

Biological subtype

Breast cancer is well known to be a heterogeneous disease and can be further classified into several biological subtypes by immunohistochemical staining of several biological markers [estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and Ki-67 index]. By assessing these biological markers in the primary tumour together rather than separately, further prognostic and predictive information can be obtained. The biological subtypes of breast cancer include luminal A (ER+ and/or PR+, HER2-, and low Ki-67 index), luminal B (HER2 negative) (ER+ and/or PR+, HER2-, and high Ki-67 index), luminal B (HER2 positive) (ER+ and/or PR+, HER2+, and any Ki-67 index), HER2 positive (ER-, PR-, HER2+, and any Ki-67 index) and triple negative (ER-, PR-, HER2-, and any Ki-67 index).⁴⁸

Breast-conserving surgery

The surgical removal of a cancerous breast lump with a rim of non-cancerous tissue around the lump, without removing the entire breast. The surgery can be lumpectomy, wide local excision, partial mastectomy or segmentectomy.

Breast reconstruction surgery

A surgical treatment that rebuilds the breast contour after mastectomy. A breast implant of the woman's own tissue provides the contour. If desired, the nipple and areola may also be preserved or recreated. Reconstruction is usually done at the time of mastectomy, but it can be done any time later.

Breast surgery

A local operation to remove the breast tumour.

Cancer staging

Appendix II refers.

Cancer specific death

A death with the underlying cause indicated as cancer. Cancer patients who die of other causes are not counted.

Chemotherapy

A treatment that uses one or more cytotoxic drugs to destroy cancer cells. Chemotherapy is often used in addition to surgery or radiotherapy to treat cancer when metastasis (spread) is proven or suspected, when the cancer has come back (recurred), or when there is a strong likelihood that the cancer could recur.

Distant recurrence

Cancer that reoccurs in organs or tissues distant from the original site or regional lymph nodes, such as lungs, liver, bone marrow, or brain.

Endocrine therapy

A treatment with hormonal drugs that interfere with hormone production or hormone action, or surgical removal of hormone-producing glands, to slow or stop the growth of cancer.

Estrogen receptor positive

It is one of the breast cancer biological characteristics. The status of cancer cells with receptor that binds with estrogen. Cancer cells that are estrogen receptor positive need estrogen to grow, and may stop growing when treated with substances that block their binding with estrogen.

Human epidermal growth factor receptor 2 (HER2) positive

It is one of the breast cancer biological characteristics. In HER2 positive breast cancer, the cancer cells have an abnormally large copy number of HER2 genes per cell. When this happens, excessive HER2 protein appears on the surface of these cancer cells. This is called HER2 protein over-expression. When excessive HER2 receptor-ligand binding complex existed, it would cause cancer cells to grow and divide more quickly. This is why HER2 positive breast cancer is considered aggressive.

In situ breast cancer

This term refers to early stage breast cancer, when it is confined to the layer of cells where it began. In breast cancer, in situ means that the cancer cells remain confined to ducts (ductal carcinoma in situ). They have not grown into deeper tissues in the breast or spread to other organs in the body, and are sometimes referred to as pre-invasive breast cancer.

Invasive breast cancer

Cancer that has already grown beyond the outer lining of myoepithelial cells or basement membrane where it started, for example breast ducts or lobules. Most breast cancer cases are invasive carcinoma.

Ki-67 index

Ki-67 protein is a biological marker for cell proliferation. It presents at low levels in quiescent cells but increases in proliferating cells. Ki-67 index refers to the percentage of tumour cells staining positive as measured by immunohistochemical (IHC) staining. High level of Ki-67 indicates an aggressive tumour. At present, an index of 14% or above is regarded as high Ki-67 index.

Latissimus dorsi flap (LD flap)

A method of breast reconstruction that rotates the fan-shaped flat muscle of the back to the chest area.

Locoregional recurrence

Locoregional recurrence occurs when cancer returns after treatment, and occurs at the same site as the original cancer or in the lymph nodes near the site of origin.

Mastectomy

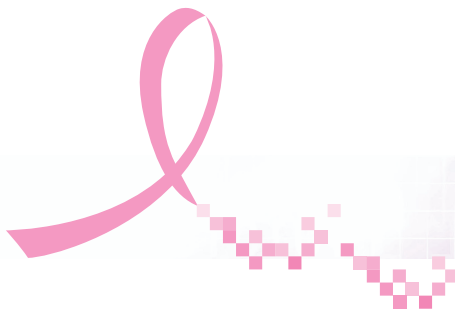
The surgical removal of the entire breast. It is usually used for treating serious breast disease, such as breast cancer.

Metastasis

The spread of cancer cells from the place where they first formed to another part of the body.

Mortality

The incidence of death in a population.



Multicentricity

A breast is divided into four quadrants. Breast cancer occurring in multiple quadrants of a breast is considered as multicentric.

Multifocality

Multifocality in breast cancer is defined as the presence of two or more tumour foci (five mm or more apart) within a single quadrant of the breast.

Necrosis

A term used for describing the death of cellular tissue. Necrosis within a cancerous tumour may indicate that the tumour is growing rapidly that blood vessels are not able to multiply fast enough to nourish some of the cancer cells. Necrosis usually indicates that the tumour is very aggressive and can spread quickly.

Neoadjuvant chemotherapy

Neoadjuvant chemotherapy (preoperative treatment) is administered to shrink the primary tumour, thereby rendering local therapy (surgery or radiotherapy) less destructive or more effective.

Progesterone receptor positive

It is one of the breast cancer biological characteristics. The hormone progesterone will bind to receptor on the cell surface. Cancer cells that are progesterone receptor positive need progesterone to grow and will usually inhibit growing when endocrine therapy drugs block progesterone from binding.

Proliferative diseases with atypia

A type of benign breast disease in which there is an overgrowth of cells in the ducts or lobules of the breast tissue, with some of the cells no longer appearing normal. Proliferative disease with atypia include atypical ductal hyperplasia and lobular neoplasia [e.g. atypical lobular hyperplasia and lobular carcinoma in situ (LCIS)], which are linked to variably increased risk of breast cancer.

Radiotherapy

The use of radiation to destroy cancer cells. This type of treatment may be used to reduce the size of tumour before surgery, or to destroy any remaining cancer cells after surgery.

Risk factors

Risk factors are associated with an increased probability of a specified outcome, for example, the occurrence of breast cancer. Risk factors are not necessarily the cause.

Sentinel node biopsy

A surgical procedure to remove the first few lymph nodes to which cancer cells are likely to spread from the breast tumour, more commonly in clinically node-negative cancer. This is to determine if breast cancer has spread to the armpit (axillary) lymph node basin.

Survival time

The duration of time from initial diagnosis until death.

Targeted therapy

A type of medication that inhibits the growth of cancer cells by interfering with specific targeted molecules needed for carcinogenesis and tumour growth.

Time to recurrence

The duration of time from initial diagnosis until the occurrence of recurrence.

Transverse rectus abdominus muscle flap (TRAM flap)

A method of breast reconstruction in which tissues from the lower abdominal wall receiving its blood supply from the rectus abdominus muscle are used. The tissues from this area are moved up to the chest to create a breast mound and an implant is usually not required. Moving muscles and tissues from the lower abdomen to the chest results in flattening of the lower abdomen.

Triple negative breast cancer

It is one of the breast cancer biological subtypes. It describes breast cancer (usually invasive ductal carcinoma) in which the cells lack estrogen receptors and progesterone receptors, and do not have an excess of HER2 protein on their surfaces.

AJCC CANCER STAGING SYSTEM (8TH EDITION)

The American Joint Committee on Cancer (AJCC) Breast Cancer Staging System (8th edition)⁴⁶ is used for determining cancer staging in the patient cohort. There are two stage groups according to this system: anatomic and prognostic stage groups. The anatomic stage group assigns a cancer stage based on the anatomic information on the tumour (T), regional nodes (N), and distant metastases (M) categories. The prognostic stage group, in conjunction with the aforementioned anatomic information (i.e. TNM categories), also takes into account other factors, including the tumour grade, biomarkers [human epidermal growth factor receptor 2 (HER2), estrogen receptor (ER), progesterone receptor (PR)] expression and genomic assays, in assigning a stage.

Although prognostic stage group was recommended for patient care and was used for reporting of all cancer patients in the United States starting from 2018, it was not used in this report. The reason for this was that patients in the cohort were mostly diagnosed in 2006 to 2017 and the treatment offered to patients in the cohort was based on the prevailing anatomic stage group. It is noted that there is only minimal difference in the TNM anatomic staging between the 7th and 8th edition.

Anatomic stage groups

Stage	Tumour	Node	Metastasis
0	Tis	N0	M0
IA	T1*	N0	M0
IB	T0	N1mi	M0
	T1*	N1mi	M0
IIA	T0	N1**	M0
	T1*	N1**	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1*	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

T0: no tumour; Tis: carcinoma in situ; T1: tumour size ≤ 20 mm;

T2: 20 mm < tumour size ≤ 50 mm; T3: tumour size > 50 mm;

T4: any size with direct extension to the chest wall and/or to the skin (ulceration or skin nodules)

N0: no positive nodes;

N1mi: 0.2 mm < metastasis size ≤ 2.0 mm or a cluster of more than 200 tumour cells;

N1: 1-3 positive axillary nodes;

N2: 4-9 positive axillary nodes or positive internal mammary nodes;

N3: ≥ 10 positive axillary nodes, or positive axillary and internal mammary nodes, or positive supraclavicular or infraclavicular nodes

M0: no metastasis; M1: evidence of metastasis

* T1 includes T1mi.

** T0 and T1 tumour with nodal micrometastases only are excluded from stage IIA and are classified as stage IB.

Clinical prognostic stage groups

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Clinical Prognostic Stage Group is		
Tis N0 M0	Any	Any	Any	Any	0		
T1*N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA		
				Negative	IA		
				Negative	IA		
			Negative	Positive	IA		
				Negative	IA		
				Negative	IB		
		G2	Positive	Positive	Positive	IA	
					Negative	IA	
					Negative	IA	
				Negative	Positive	IA	
					Negative	IA	
					Negative	IB	
	G3		Positive	Positive	Positive	IA	
					Negative	IA	
					Negative	IA	
				Negative	Positive	IA	
					Negative	IB	
					Negative	IB	
		T0 N1** M0 T1* N1** M0 T2 N0 M0	G1	Positive	Positive	Positive	IB
						Negative	IIA
						Negative	IIA
					Negative	Positive	IB
						Negative	IIA
						Negative	IIA
G2	Positive			Positive	IB		
				Negative	IIA		
				Negative	IIA		
	Negative			Positive	IB		
				Negative	IIA		
				Negative	IIB		

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Clinical Prognostic Stage Group is		
T0 N1** M0 T1* N1** M0 T2 N0 M0	G3	Positive	Positive	Positive	IB		
				Negative	IIA		
				Negative	IIA		
			Negative	Positive	IIA		
				Negative	IIB		
				Negative	IIB		
		T2 N1*** M0 T3 N0 M0	G1	Positive	Positive	Positive	IB
						Negative	IIA
						Negative	IIB
					Negative	Positive	IIA
						Negative	IIB
						Negative	IIB
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G2			Positive	Positive	Positive	IB
						Negative	IIA
						Negative	IIB
					Negative	Positive	IIA
						Negative	IIB
						Negative	IIIB
		G3	Positive	Positive	IB		
				Negative	IIB		
				Negative	IIB		
			Negative	Positive	IIB		
				Negative	IIIA		
				Negative	IIIB		



Clinical prognostic stage groups

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Clinical Prognostic Stage Group is	
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G2	Positive	Positive	Positive	IIA	
				Negative	IIIA	
			Negative	Positive	IIA	
				Negative	IIIB	
		G3	Positive	Positive	Positive	IIB
					Negative	IIIA
	Negative			Positive	IIIA	
			Negative	IIIB		
			Negative	IIIC		
	T4 N0 M0 T4 N1*** M0 T4 N2 M0 Any T N3 M0		G1	Positive	Positive	Positive
		Negative				IIIB
		Negative			Positive	IIIB
Negative				IIIB		
Negative				IIIC		
G2		Positive		Positive	Positive	IIIA
			Negative		IIIB	
			Negative	Positive	IIIB	
		Negative		IIIB		
		Negative		IIIC		

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Clinical Prognostic Stage Group is
T4 N0 M0 T4 N1*** M0 T4 N2 M0 Any T N3 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
		Negative		IIIC	
		Negative		IIIC	
		Any T Any N M1	Any	Any	Any

- * T1 includes T1mi.
- ** N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.
- *** N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1 and T4 N1, respectively.

Pathological prognostic stage groups

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Pathological Prognostic Stage Group is	
Tis N0 M0	Any	Any	Any	Any	0	
T1*N0 M0 T0 N1mi M0 T1* N1mi M0	G1	Positive	Positive	Positive	IA	
				Negative	IA	
				Negative	IA	
			Negative	Positive	IA	
				Negative	IA	
				Negative	IA	
		G2	Positive	Positive	Positive	IA
					Negative	IA
					Negative	IA
				Negative	Positive	IA
					Negative	IA
					Negative	IB
	G3		Positive	Positive	IA	
				Negative	IA	
				Negative	IA	
			Negative	Positive	IA	
				Negative	IA	
				Negative	IB	
	T0 N1** M0 T1* N1** M0 T2 N0 M0	G1	Positive	Positive	Positive	IA
					Negative	IB
					Negative	IB
				Negative	Positive	IA
					Negative	IB
					Negative	IB
G2			Positive	Positive	IA	
				Negative	IB	
				Negative	IIA	
			Negative	Positive	IA	
				Negative	IIA	
				Negative	IIA	

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Pathological Prognostic Stage Group is		
T0 N1** M0 T1* N1** M0 T2 N0 M0	G3	Positive	Positive	Positive	IA		
				Negative	IIA		
				Negative	IIA		
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
		G1		Positive	Positive	Positive	IA
						Negative	IIA
						Negative	IIA
			Negative	Positive	Positive	IIA	
					Negative	IIA	
					Negative	IIA	
T2 N1*** M0 T3 N0 M0	G1	Positive	Positive	Positive	IA		
				Negative	IIA		
				Negative	IIA		
			Negative	Positive	Positive	IA	
					Negative	IIA	
					Negative	IIA	
		G2	Positive	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
T0 N1** M0 T1* N1** M0 T2 N0 M0	G2	Positive	Positive	Positive	IB		
				Negative	IIA		
				Negative	IIA		
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
		G3	Positive	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G1	Positive	Positive	Positive	IB		
				Negative	IIA		
				Negative	IIA		
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
		G2	Positive	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	
			Negative	Positive	Positive	IB	
					Negative	IIA	
					Negative	IIA	



Pathological prognostic stage groups

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Pathological Prognostic Stage Group is	
T0 N2 M0 T1* N2 M0 T2 N2 M0 T3 N1*** M0 T3 N2 M0	G2	Positive	Positive	Positive	IB	
				Negative	IIIA	
			Negative	Positive	IIIA	
		Positive		IIIA		
		Negative		IIIB		
		G3	Positive	Positive	Positive	IIA
	Negative				IIIA	
	Negative			Positive	IIIB	
			Positive	IIIA		
			Negative	IIIC		
	T4 N0 M0 T4 N1*** M0 T4 N2 M0 Any T N3 M0		G1	Positive	Positive	Positive
		Negative				IIIB
Negative		Positive			IIIA	
		Positive		IIIB		
		Negative		IIIB		
G2		Positive		Positive	Positive	IIIA
			Negative		IIIB	
			Negative	Positive	IIIA	
		Positive		IIIB		
		Negative		IIIC		

When TNM is	And Grade is	And HER2 Status is	And ER Status is	And PR Status is	Then the Pathological Prognostic Stage Group is
T4 N0 M0 T4 N1*** M0 T4 N2 M0 Any T N3 M0	G3	Positive	Positive	Positive	IIIB
				Negative	IIIB
			Negative	Positive	IIIB
		Positive		IIIC	
		Negative		IIIC	
		Any T Any N M1	Any	Any	Any

* T1 includes T1mi.

** N1 does not include N1mi. T1 N1mi M0 and T0 N1mi M0 cancers are included for prognostic staging with T1 N0 M0 cancers of the same prognostic factor status.

*** N1 includes N1mi. T2, T3, and T4 cancers and N1mi are included for prognostic staging with T2 N1, T3 N1 and T4 N1, respectively.