Chapter 4
Breast Cancer

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Introduction

Breast cancer is the most common cancer among Canadian women with the exception of non-melanoma skin cancer. An estimated 24,400 new cases occurred in Canada in 2014. Breast cancer is responsible for 26 % of all cancers in females and 14 % of all cancer-related deaths in females. 1 in every 9 women is expected to develop breast cancer during her lifetime and 1 in 30 women will die of breast cancer [1].

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Presentation	Prognosis 5-Year overall survival (OS)
• Early breast cancer[a] (75–80 %)	90–100 %
• Locally advanced breast cancer[a] (10–20 %)	36–67 %
• Distant metastasis (5 %)	26 %

[a]See definitions in the chapter

The recommended staging system is the 7th edition of American Joint Committee on Cancer (AJCC) [2].

The surgical management of breast cancer requires an understanding of the complete spectrum of breast pathology, both malignant and premalignant. As a result, an overview of this continuum is presented: from high-risk pathologies, through pre-invasive disease, to invasive disease and the management of some of its various subtypes.

Benign, but Worrisome

Within the pathological examination of breast tissue, there exist spectrums of conditions, which often bridge the divide between benign and malignant. They can present difficulty to the clinician, in terms of their appropriate management and—like many aspects of breast treatment—they are under constant review. Below we have summarised several of the more commonly encountered entities:

Entity	Definition and diagnosis	Treatment	Comments
Atypical ductal hyperplasia (ADH)	• A proliferation of uniform epithelial cells with monomorphic round nuclei filling part, but not all the involved duct • Diagnosis: no symptoms, incidental, often calcifications	• If found on CNB, the area should be removed to ensure that no adjacent carcinoma is present • If found at the margins of an excised lesion, re-excision is not generally considered necessary	• Atypical hyperplasia confers a substantial increase in the risk of subsequent breast cancer (RR 3.7–5.3) [3]
Atypical lobular hyperplasia (ALH)	• Monomorphic, evenly spaced, dyshesive cells filling part, but not all, of the involved lobule. ALH can also involve ducts • Diagnosis: no symptoms, incidental	• If found on CNB, the area should be removed to ensure that no adjacent carcinoma is present • If found at the margins of an excised lesion, re-excision is not generally considered necessary	• ALH is associated with an increased risk of both ipsilateral and contralateral breast cancer, with the Nurses' Health Study demonstrating that only 56 % of cancers developing in women with ALH occurred in the ipsilateral breast. The cumulative incidence of breast cancer over 30 years in patients with ALH approached 35 % [4]
Lobular carcinoma in situ (LCIS)	• Abnormal cell growth in the lobules of the breast that represents an increased risk of cancer rather than being a premalignant condition per se • Distinguish between classic (cLCIS) and pleomorphic (pLCIS) to plan treatment • Diagnosis: no symptoms, incidental	• If found on CNB, the area should be removed to ensure no adjacent carcinoma is present • If found at the margins of an excised lesion, re-excision is not generally considered necessary	• In a NSABP study of 180 women with LCIS, 5 % developed an ipsilateral invasive carcinoma after 12 years of follow-up, while a similar fraction (5.6 %) developed a contralateral invasive tumour [5] • Pleomorphic LCIS is an aggressive variant of LCIS, which is a newly categorised entity, often treated as DCIS sharing pathologic features with DCIS, and is often treated with excision to clear margins, similar to DCIS [6]
Intraductal papilloma	• Intraluminal epithelial fronds that can exhibit a variety of alterations from hyperplasia to carcinoma • Diagnosis: breast lump, nipple discharge (often bloody), or nodule on ultrasound or by ductoscopy	• Generally, the advice is for excision given the risk of malignancy. If the absence of atypia can be proven, however, there might be a role for observation	• Without atypia, the chance of malignancy is very small (<3 %), but with atypia, some authors have reported the associated rate of coexistent cancer to be as high as 67 % [7] – One of the largest multicentre series (n=238), reported an upgrade rate of 14.4 %, with only 3.7 % upgraded to invasive. Older age and presence of atypia on core biopsy were associated with risk of malignancy [8]
Sclerosing adenosis	• A benign condition, which involves the development of excessive tissue in the breast lobules • Diagnosis: occasional lump/nodules or pain, and occasional microcalcifications. Perform CNB	• After CNB, excision is only recommended in the following situations: – Limited sampling – Presence of atypia – Radiological discordance	• The risk of malignancy from sclerosing adenosis is linked to its potential to become ADH, ALH, LCIS, or DCIS, which has made some authors quote an increased risk of 1.5 times, above baseline risks of 1.5 times the normal risk [9]

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Entity	Definition and diagnosis	Treatment	Comments
Microglandular adenosis	• A rare type of adenosis, resembling tubular carcinoma, where irregular clusters of small tubules are present in adipose or fibrous tissues • Diagnosis: may present as mass • Perform CNB	– Given risk of carcinoma, perform excision	– Microglandular adenosis is poorly studied, but is associated with a carcinoma rate of approximately 23 % [9, 10]
Radial scars and complex sclerosing lesions	• Benign, spiculated masses, characterised by a sclerotic-appearing (scar like) centre with peripheral entrapped normal breast ducts and lobules • Diagnosis: no symptoms. Perform imaging and CNB	• The standard management is to excise if detected as a mammographic lesion • However, if the diagnosis is made incidentally on a CNB and atypia is not identified, there may be a role for observation	• A large study looked at about 157 non-palpable lesions across 11 institutions. With atypia, the rate of cancer was 28 % but with no atypia, it was 4 % • Carcinoma was missed in 9 % of spring-loaded biopsy devices and in 0 % of vacuum-assisted biopsy devices. Carcinoma was also missed in 8 % of lesions sampled with less fewer than 12 specimens or more specimens [11]
Pseudoangiomatous stromal hyperplasia (PASH)	• Benign, stromal proliferation • More common in pre-menopausal women, possible hormonal etiology • Diagnosis: single, well-circumscribed, palpable mass	• If diagnosed conclusively on CNB, PASH can be managed expectantly • Excise if discordance with imaging or increase in size of lesion	• Although PASH is benign, recurrence after excision is reported in 15–22 % of cases
Flat epithelial atypia (FEA)	• A morphologically diverse group consisting of atypia within columnar cell change and hyperplasia • Diagnosis: no symptoms. Perform imaging and CNB	• The current standard of care is to excise lesions where FEA has been diagnosed on CNB • The current standard of care is surgical excision; however there is controversy regarding the management of pure FEA on CNB	• Retrospective data shows upgrade to DCIS or IDC in 9.5 % of pure FEA [12]. The data here is very poor, with a handful of retrospective studies • The largest prospective studies show an upgrade to carcinoma on surgical excision in 3.2 %–4.2 % in pure FEA [13, 14]. The upgrade rate increased to 18.6 % when ADH was present with FEA on original CNB [13] • Original small studies questioned the need to excise FEA following core biopsy [15]. The largest, albeit still quite small ($n=95$ pure FEA) [14] series, however, demonstrated a 9.5 % rate of finding of either invasive carcinoma (4.2 %) or DCIS (5.3 %) [11]

NSABP national surgical adjuvant breast and bowel project, *DCIS* ductal carcinoma in situ, *RR* relative risk, *FEA* flat epithelial atypia, *CNB* core needle biopsy

Ductal Carcinoma In Situ

Ductal carcinoma in situ (DCIS) is a pre-invasive breast cancer that does not penetrate the basement membrane. The incidence of DCIS markedly increased from 5.8 per 100,000 women in the 1970s to 32.5 per 100,000 women in 2004 and then reached a plateau [16]. Approximately 90 % are asymptomatic and not palpable, with the remainder presenting as a lump, discharge, or Paget's disease of the nipple.

Although evidence suggests that a significant amount of DCIS does not progress to invasive cancer, our inability to distinguish which will progress and which will not has led to an aggressive approach to all DCIS [17, 18].

The indications for lumpectomy vs. mastectomy are similar in DCIS as with invasive disease, with mastectomy indicated where:

1. Area of DCIS is large, relative to breast size.
2. Disease is multicentric.
3. Radiotherapy is contraindicated.
4. Clear margins cannot be obtained with breast conservation.

The lack of true randomised data regarding breast conservative surgery (BCS) and mastectomy for DCIS should be noted. The first indication that BCS—in conjunction with adjuvant radiotherapy—was acceptable treatment for DCIS came from a subset analysis of 78 patients in the NSABP B-06 [19]. Originally enrolled because of presumed invasive breast cancer, these women were downgraded to DCIS on pathologic reanalysis. The local recurrence rate was 9 % in those that underwent radiotherapy vs. 43 % in those that did not. Retrospective studies have since confirmed that BCS provides survival rates similar to mastectomy; however local recurrence is higher, even with radiotherapy [20].

As mentioned, similar to invasive disease, there is good evidence for radiotherapy following a breast-conserving approach:

Study	Methods	Results
NSABP-B17 Fisher et al. [21]	• *N* = 818 • RCT • Patients assigned to lumpectomy alone vs. lumpectomy and RT	• At 7.5 years, RT reduced the incidence of ipsilateral invasive disease (13.4 % to 3.9 %) as well as ipsilateral DCIS (13.4 % to 8.2 %) • A subset analysis from this study also demonstrated that comedo necrosis was a risk factor for recurrence
EORTC 10853 Julien et al. [22]	• *N* = 1010 • RCT • Patients with DCIS and BCS randomised to receive no further treatment or RT	• RT reduced overall non-invasive recurrence at 10.5 years by 48 % and invasive recurrence by 42 %
UK/ANZ DCIS Cuzick et al. [23]	• *N* = 1701 • RCT • Patients with excised DCIS randomised to receive RT, tamoxifen, both or none	• RT reduced ipsilateral invasive recurrence at 12.7 years by 68 % and DCIS by 62 %, but with no effect on contralateral breast cancer

RCT randomised controlled trial, *HR* hazard ratio, *RT* radiotherapy

It is worth noting that both NSABP B-17 [21] and EORTC 10853 [22] came under some criticism for not providing mammographic correlation with the specimen or pre-operative evaluation and in NSABP B-17 [21] sampling of the surgical specimen was unable to exclude invasive disease or involved margins. This questioned the completeness of excision in both studies. As a result, many believe that this strengthens the argument for complete surgical resection rather than an approach that relies on radiotherapy as a means of dealing with residual disease.

There is some evidence, however, that radiotherapy may be safely omitted in some cases of DCIS:

1. Tumour less than 1.5 cm
2. Margins greater than 10 mm
3. Non-high grade, without necrosis (nuclear grade 1 or 2)
4. Patient age over 60 [24]

The EORTC 10853 [22] study demonstrated a recurrence rate of less than 4 % at 5 years of low-grade DCIS, making an argument for the omission of radiotherapy in this circumstance. More recently, a prospective study of 670 patients [25] demonstrated a 5-year recurrence of 15 % for high-grade DCIS, but only 6 % for low- or intermediate-grade DCIS, when excised with a minimum of 3 mm margins. However, the authors note an increase in recurrences beyond 5 years for all grades of DCIS and urge caution in applying these results to clinical practice. Another prospective trial of wide excision alone for low-to-intermediate-grade DCIS found an unacceptably high local recurrence rate of 12 % at 5 years and 15.6 % at 10 years [26].

Given the difficulty in determining which patients DCIS may be safely treated with wide excision alone, it remains the standard of practice at the University of Toronto to offer radiation to all patients having undergone breast-conserving surgery (BCS) for DCIS.

DCIS Recurrence

Approximately 25–50 % of recurrences are invasive disease. Factors involved in recurrence include:

1. Margin status
2. High-grade/comedo necrosis
3. Histological type and architecture
4. Age at diagnosis

Margin status has three times the power of tumour grade at predicting local recurrence [20]. The NSABP-B17 [21], NSABP-B24 [27] and EORTC clinical trials [22] have all revealed that clear margins significantly decrease recurrence.

No trials, however, have rigorously examined the optimum excision width. An analysis of pooled data from both randomised and non-randomised studies in 2009 concluded that a margin of 2 mm when excising DCIS was as safe as a larger margin when followed by radiotherapy [28]. Contributing to the debate is another meta-analysis, published in 2012, which showed a statistically significant decrease in recurrence for 10 mm margins compared to 2 mm margins (OR = 0.46; 95 % CI = 0.29–0.69) [29].

Although a high-grade lesion was originally thought to be a risk factor for recurrence, a 2006 review of the EORTC data [22] with a 10-year follow-up suggested that this may not be the case. It has, however, confirmed that comedo necrosis is an independent risk factor for recurrence, with 3 of 10 patients recurring by 10 years [22].

Age is also a significant factor in DCIS recurrence. The EORTC trial [22] demonstrated a higher recurrence rate in young women under 40, quoting a hazard ratio (HR) of 2.54 [22]. Similarly, the NSABP B-24 [27] trial found that the rate of ipsilateral cancer in women under 49 was 33/1000 women years as opposed to 13/1000 for those over 49 [30].

The management of recurrence is largely dependent on whether radiotherapy has been administered. If not, then a local resection may be possible; otherwise a mastectomy should be offered. There has been some suggestion that repeat resection and irradiation may be safe in the setting of recurrence. The data, however, is limited by short follow-up and is largely confined to the setting of invasive disease rather than DCIS [31] and this approach is, therefore, not universally accepted.

DCIS and the Axilla

The incidence of axillary metastases in DCIS is <1 % and these are likely to represent missed invasive disease, rather than true DCIS metastases. It should be borne in mind that the majority of reported sentinel lymph node (SLN) involvement in DCIS is revealed by immunohistochemical (IHC) techniques as isolated tumour cells or micrometastases, and the clinical significance of these is uncertain even in true invasive disease [32].

A joint committee of the American College of Surgeons, American College of Radiology and the College of American Pathologist recommended that axillary staging in patients with DCIS treated by BCS be reserved for those with invasive disease. For those undergoing mastectomy for DCIS, sentinel lymph node biopsy (SLNB) was recommended. This recommendation is made with a view to avoid axillary lymph dissection in the event of an upgrade from DCIS to invasive carcinoma on final pathology of the mastectomy specimen, as SLNB is not possible after mastectomy.

Invasive Breast Cancer

In this section, the management of invasive breast cancer is discussed, focusing on tumours less than 5 cm with no evidence of matted or fixed axillary lymph nodes, corresponding to T0, T1, T2 and N0, N1 (stages 0, I, IIA and IIB).

Work-up	Surgical management	Follow-up (F/U)
• History and physical exam • Imaging: – Review bilateral mammogram and ultrasound (assess for multifocal/multicentric disease, as well as contralateral disease) – Axillary US – Breast MRI if indicated (see below) • Core needle biopsy to confirm the diagnosis • Apply clip if neoadjuvant therapy is considered • CCO staging recommendations [33]: – Routine bone scanning, liver ultrasonography and chest radiography are not indicated before surgery • Post-operatively: – In women with stage I tumours, routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging – In women who have pathological stage II tumours, a postoperative bone scan is recommended as part of baseline staging – In women who have pathological stage III tumours, bone scan, chest radiography and liver ultrasound are recommended post-operatively	• Breast (local): – Breast-conservative surgery plus breast irradiation or mastectomy +/− post-mastectomy radiation therapy [34] • Axilla (regional): – Sentinel lymph node biopsy for clinical N0 patients – Axillary lymph node dissection for clinical N1 • Consider and discuss neoadjuvant chemotherapy in the following cases: – Triple-negative – Young patients (<40) – Her2/neu + – Reducing the size of tumour to facilitate BCS – Node-positive patients	• Regular clinical breast exam • Mammogram every 12 months

BCS breast-conserving surgery, *MRI* magnetic resonance imaging, *CCO* Cancer Care Ontario

Special Notes

- It is standard of care to obtain the diagnosis of invasive breast cancer with core needle biopsy. While the primary use of core needle biopsy is to establish a diagnosis, it is also useful in providing receptor status if neoadjuvant chemotherapy is considered. Furthermore, positive margin rates and the need for reoperation are reduced in women who have been assessed with core needle biopsy preoperatively [35].
- In breast cancer of a more advanced stage, Cancer Care Ontario has recommended that in women with pathological stage III tumours, bone scanning, liver ultraso-

nography or CT abdomen and chest radiography are recommended post-operatively as part of baseline staging. However, in women for whom treatment options are restricted to tamoxifen or hormone therapy, or for whom no further treatment is indicated because of age or other factors, routine bone scanning, liver ultrasonography and chest radiography are not indicated as part of baseline staging [33].

- Mammography remains the mainstay of breast imaging. MRI of the breast is considered an adjunct to mammography. Pre-operative diagnostic MRI detects additional ipsilateral lesions in up to 32 % of patients and contralateral lesions in 7 % of patients. Sensitivity ranges from 75 to 100 % and specificity from 80 to 100 % [35]. However, several studies have failed to show a decreased rate of positive margins in BCS for patients undergoing MRI [37, 38] while also showing an increased likelihood of mastectomy in such patients [38].
- According to the American College of Radiology, current indications for diagnostic MRI are:
  - Axillary adenocarcinoma with unknown primary
  - Evaluation of response to neoadjuvant chemotherapy
  - Assessment of extent of DCIS and IDC
  - Assessment of invasion of deep fascia
  - Evaluation of possible recurrence
- Diagnostic MRI can also be considered in patients with invasive lobular carcinoma, as there is some evidence that MRI reduces the need for re-excision surgery in this subset of patients, but at the cost of an increased likelihood of upfront mastectomy [38].

Breast-Conserving Surgery

The aim of breast conservation is to achieve a balance between complete resection of the tumour with negative margins and preservation of as much normal breast tissue as possible. Volume loss is the major determinant of cosmesis after BCS. A good cosmetic outcome maximises the psychosocial benefits of breast preservation [39].

In patients with no contraindication to BCS, there are several points to be discussed with the patient	BCS includes the lumpectomy to a negative margin, margin revision being necessary in about 20 % of cases If the margin is positive after appropriate attempts at therapeutic breast-conserving surgery, the patient should be considered for mastectomy
	BCS for DCIS and IDC includes administration of radiotherapy
	When compared with mastectomy, BCS may have a slightly higher risk of local recurrence. Both approaches, however, have equivalent survival outcomes

Absolute Contraindications to BCS

1. Early pregnancy, if radiation deemed necessary to be performed during pregnancy.
2. Multicentric IDC—diffuse-appearing suspicious 19 % microcalcifications or inability to resect the evident disease with acceptable cosmetic results.
3. Any contraindication to radiation therapy (e.g. active collagen vascular disease with severe vasculitis, ataxia telangiectasia).

Relative Contraindications to BCS

1. A history of collagen vascular disease, in remission.
2. Large tumour size in relation to the breast size.
3. A history of prior therapeutic irradiation to the breast region.

For invasive cancer, another consideration in the choice of surgical treatment of the primary tumour is the management of the axilla after positive SLNB. The ACOSOG Z0011 trial—detailed in section IV of this chapter—supports omission of axillary lymph node dissection (ALND) after positive SLNB in many patients treated with BCS. However, patients treated with mastectomy were excluded and the current standard remains completion of ALND in those cases. This may factor into the decision-making process for the patient and surgeon.

Trials for BCS vs. Mastectomy

Study	Methods	Results
NSABP-B06 Fisher et al. [31]	• *N* = 1851 • RCT • Patients in stages I and II were assigned total mastectomy/ALND, lumpectomy/ALND alone or lumpectomy/ALND + breast irradiation • Margins—no cancer cell at the surgical margin	• Follow-up—20 years • No significant differences in disease-free survival and overall survival • Recurrence rate in the ipsilateral breast was 14.3 % in the lumpectomy/ALND plus breast irradiation group and 39.2 % in the lumpectomy/ALND-alone group
Milan Group Veronesi et al. [32]	• *N* = 701 • RCT • Patients with tumour <2 cm were assigned radical mastectomy vs. quadrantectomy/ALND + radiotherapy • Margins—1.5–2.0 cm, with the overlying skin and deep fascia	• Follow-up—20 years • No statistical difference in overall survival • Recurrence rate higher in the BCS group (8.8 % vs. 2.3 %)

RCT randomised controlled trial

Meta-Analysis to Assess Surgical Margins in BCS for Early Breast Cancer

Study	Methods	Results
Houssami et al. [39]	• 33 studies • *N* = 28,162 patients (1506 with LR) • Impact of surgical margins on LR • Model 1—effect of margin status in relation to LR • Model 2—effect of margin distance to LR (1 mm vs. 2 mm vs. 5 mm)	• Higher probability of LR associated with positive/close margins vs. negative margins (OR 1.97) • No difference in LR with 1 mm vs. 2 mm vs. 5 mm margin distance • Wider margins unlikely to increase long-term local control

LR local recurrence, *OR* odds ratio

This work by Houssami et al. formed the basis of the Society of Surgical Oncology-American Society for Radiation Oncology (SSO-ASTRO) consensus guidelines for breast-conserving surgery for early-stage breast cancer. Using this data, a multidisciplinary panel concluded that "no ink on tumour" should be adopted as the standard for an adequate margin for invasive breast cancer [39]; this guideline has since been endorsed by the American Society of Clinical Oncology (ASCO) and the American Society of Breast Surgeons (ASBS) [41].

The Axilla

Management of the axilla is arguably the most controversial aspect of the breast cancer treatment paradigm. From considering axillary lymph node dissection (ALND) as the standard of care for all breast cancer patients, to now omitting patients with proven axillary metastases from further surgery, it is a complex facet of the management of invasive breast cancer.

Authors such as Steele et al. [42] in the 1980s challenged the belief that all breast cancer patients should have an ALND. They endorsed a system of axillary node sampling, whereby four nodes were "cherry picked" from level one of the axilla, and if negative for disease, no further surgery was performed. This limited axillary node sampling may be seen as the grandfather of SLNB, a technique which has supplanted ALND as the standard of care in staging the clinically negative axilla.

Several key trials have demonstrated the efficacy of SLNB

Study	Methods	Results
Multicenter Validation Study Krag et al. [43]	• $N=443$ • All patients underwent both SLNB and then ALND	• It demonstrated that this technique could be used by surgeons • At least 1 SLN was identified in 98 % of cases and the predictive value of a negative SLN was 96 %, with a false-negative rate of 11 %
ASCO Review Lyman et al. [44]	• $N=8059$ • Systematic review of 69 SLNB trials	• SLN identification was successful in 95 % of patients • The false-negative rate was 7.3 % (range 0–29 %). Using both radiocolloid and blue dye was more successful than blue dye alone
ALMANAC Mansel et al. [45]	• $N=1031$ • RCT • Patients randomly assigned to ALND vs. SLNB with delayed ALND if SLN positive	• SLNB group had less arm morbidity • SLNB group had better quality of life and arm functioning scores

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Study	Methods	Results
NSABP B-32 Krag et al. [46]	• $N=5611$ • RCT • Comparing SLNB, followed by ALND vs. SLNB, followed by ALND for positive SLN	• Lymphatic mapping was successful in 97 %, and the false-negative rate was 9.8 % • No significant differences were observed in regional control or survival between the groups at follow-up of 8 years

ASCO American Society of Clinical Oncology, *SLN* sentinel lymph node, *SLNB* sentinel lymph node biopsy, *RCT* randomised controlled trial, *ALND* axillary lymph node dissection

Sentinel Lymph Node Biopsy and Axillary Dissection

The contribution of ALND to survival in women with breast cancer has been questioned since the publication of the NSABP B-04 [47] trial. It has often been the basis of argument against mandatory ALND. In this study, clinically node-negative patients were randomised to radical mastectomy (RM), total mastectomy (TM) plus axillary irradiation or TM alone. Forty percent of the RM group had lymph node involvement. However, axillary recurrence, as a first failure, was only in the TM-alone group. Moreover, the three groups had a similar overall survival [49]. In the era of SLNB, the contribution of axillary dissection to survival was revisited in the ACOSOG Z0011 trial [50]. In this prospective randomised non-inferiority trial, breast cancer patients receiving breast-conserving therapy with only one or two positive SLNs and with no gross extracapsular extension were randomised to SNLB-alone vs. ALND groups. The main criticism of this study is that it is underpowered, with a relatively short follow-up (median: 6.3 years) period. The overall survival and the disease-free survival of the SLNB-alone group appeared to be non-inferior to the ALND group.

The conclusions of the Z0011 trial are supported by another randomised non-inferiority trial (IBCSG 23-01). Patients with tumour size less than 5 cm and one or more micrometastatic sentinel lymph node were randomised to completion axillary dissection ($n=465$) or no further axillary surgery ($n=469$). In both groups, 9 % of patients received mastectomy for the primary tumour, unlike the Z011 trial. In those randomised to completion axillary dissection, there was a significantly higher rate of sensory neuropathy, motor neuropathy and lymphedema; 13 % had at least one additional lymph node involved. There was no significant difference in 5-year disease-free survival (84.4 % in the group with axillary dissection vs. 87.8 % in the group without) or cumulative incidence of breast cancer events (10.6 % in the group with axillary dissection vs. 10.8 % in the group without).

Studies in support of ALND *after positive SLNB*

Study	Methods	Results
Meta-Analysis Orr, 1999 [51]	• 6 RTCs • *N* = 3000 • Patients assigned to ALND or no ALND	• Limited by very few T1a tumours, no women over 70 years, no adjuvant treatment and a timeline of 1951–1987 • Demonstrated an improvement in absolute survival with ALND (range 4–16 %) using Bayesian statistics
SEER Database Analysis Joslyn, 2002 [52]	• Retrospective review • *N* = 257,157 • Women diagnosed with breast cancer in the SEER database between 1988 and 2000	• Women undergoing ALND had an increased survival • Also, with an increasing ratio of positive nodes to total number removed, there was a consistent trend towards reduced survival
Truong et al. [53]	• Retrospective population-based cohort • *N* = 8038 • Patients treated for T1–2 breast cancer in British Columbia between 1989 and 1998	• Overall and cancer-specific 5-year survival rates were significantly worse in those who had not undergone ALND (68 % vs. 85 % and 86 % vs. 91 %, respectively). Note that the much larger difference in overall survival suggests large heterogeneity between groups
Early Breast Cancer Trialists' Collaborative Group Analysis Clarke et al. [52]	• 78 RCTs • *N* = 42,000 • Comparing the effect of different types of local treatment on recurrence and survival	• While not directly examining ALND, the study showed that local control affects overall survival, a fact which is often used in support of ALND • Local recurrence positively impacted on the 15-year survival

RCT randomised controlled trials, *ALND* axillary lymph node dissection, *SEER* surveillance epidemiology and end results (US National Cancer Institute)

Studies in support of ALND omission *after positive SLNB*

Study	Methods	Results
NSABP B-04 Fisher et al. [55]	• *N* = 1843 • RCT • Women were assigned to radical mastectomy vs. simple mastectomy plus local nodal irradiation, or simple mastectomy with ALND delayed if needed	• This study is criticised for being underpowered and also for including many women with simple mastectomy who had some nodes removed with the breast specimen • There was no effect on survival of prophylactic ALND vs. nodal radiotherapy vs. no initial axillary treatment

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Study	Methods	Results
The Breast Carcinoma Collaborative Group of the Institut Curie Cabanes et al. [56]	• *N* = 658 • RCT • Patients assigned to lumpectomy alone or lumpectomy plus ALND • All received RT, and women with positive LNs received chemotherapy	• Initially, ALND was associated with significantly better 5-year survival (97 % vs. 93 %) • However, after the data was reviewed with longer follow-up of 10–15 years, survival rates were similar (approximately 75 %) • The instance of regional recurrence was lower in women who had ALND. The results however were skewed, as the only women to receive chemotherapy were in the ALND group
Systematic Review and Meta-Analysis Sanghani et al. [57]	• 3 RCTs • Comparing ALND vs. no ALND (2000 and 2007) and a 4th trial comparing axillary radiotherapy vs. no axillary therapy	• No difference in overall survival or recurrence with axillary treatment • It is felt that the widespread use of adjuvant radiotherapy and chemotherapy contributed to these results
Z0011 Guiliano et al. [50]	• *N* = 891 • RCT • ALND vs. no ALND for women with positive SLNB	• At median follow-up of 6.3 years, the 5-year overall survival was 91.8 % in ALND and 92.5 % in those with SLNB. Importantly, disease-free survival was also similar with 82.2 % in ALND and 83.9 % with SLNB • It is criticised for its low numbers and an approximately 20 % lost to follow-up rate (unlike NSABP-B32 <1 %) • Powered for 1900 patients but closed earlier due to lower than expected mortality rate

RCT randomised controlled trials, *ALND* axillary lymph node dissection, *LN* lymph node, *SLNB* sentinel lymph node biopsy, *RT* radiotherapy

Special Notes

- Although by no means an exhaustive examination of the literature, the above studies do help demonstrate the controversy surrounding ALND. It should be always remembered that with the rapid changes in adjuvant therapy for breast cancer, one must examine the older literature with a certain degree of care. Certainly, it seems that the benefit of extensive axillary surgery is questionable in this era of effective adjuvant therapy. Given the limitations of the Z0011 study, however, it is difficult at the present time to completely advocate a definitive move away from the procedure.

- At the University of Toronto, we forego axillary dissection in patients meeting the Z011 inclusion criteria.

Management of Macrometastatic Axillary Disease

The Z0011 study results were practice changing and incorporated quickly into management guidelines (i.e. national comprehensive cancer network). Two recent studies, AMAROS and MA20, have contributed to the discussion regarding the axillary management of pathologically macrometastatic positive SLNs. These two trials are summarised below:

Study	Methods	Results
AMAROS Donker et al. [58]	• $N=4806 \rightarrow 1425$ (29.7 %) found to have +ve SLNB • RCT, non-inferiority trial • From 2001 to 2010, patients with cT1–2N0 invasive breast cancer were enrolled in the EORTC phase III non-inferiority AMAROS trial. Patients with previous neoadjuvant systemic treatment were excluded from the study • Patients were randomised to ALND or ART prior to SLNB and breast-conserving surgery or mastectomy. Patients with positive SLNs were then included in analysis. ART included radiation to level I, II, III and supraclavicular lymph nodes • Primary endpoint was 5-year axillary recurrence rate	• 5-year axillary recurrence was 0.43 % after axillary lymph node dissection and 1.19 % after axillary radiotherapy. Due to the unexpectedly low number of events, the non-inferiority test was underpowered and did not meet non-inferiority criteria. The axillary recurrence rate for patients with a negative sentinel node biopsy was 0.72 % (25 out of 3131 patients) during the entire follow-up period (median 6.1 year) • Clinical signs of lymphedema were noted more often following ALND than ART, 23 % versus 11 % at 5 years ($p<0.0001$). Rates of subjectively measured lymphedema were not different between groups. Range of motion and quality of life measurements were not significantly different between the two groups

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Study	Methods	Results
MA 20 Whelan et al. (abstract) [59]	• $N=1832$ • RCT • Women with high-risk node-negative or node-positive breast cancer treated with BCS and adjuvant chemotherapy and/or endocrine therapy were randomised to WBI (50 Gy in 25 fractions +/– boost irradiation) or WBI plus RNI (45 Gy in 25 fractions) to the internal mammary, supraclavicular and high axillary lymph nodes. The primary outcome was OS	• Overall 5-year survival: 90.7 % (WBI) vs. 92.3 % (RNI) non-significant difference, trend only, $p=0.07$ • Locoregional recurrence: 94.%% (WBI) vs. 96.8 % (RNI), $p=0.02$ • 5-year DFS: 84 % (WBI) vs. 89.7 % (RNI), $p=0.003$ • Toxicities: Pneumonitis 0.2 % (WBI) vs. 1.3 % (RNI) and lymphedema 4.1 % (WBI) vs. 7.3 % (RNI)

EORTC European Organisation for Research and Treatment of Cancer, *AMAROS* the after-mapping of the axilla: radiotherapy or surgery?, *ART* axillary radiation therapy, *RCT* randomised control trial, *BCS* breast-conserving surgery, *WBI* whole-breast irradiation, *RNI* regional nodal irradiation, *OS* overall survival

Isolated Tumour Cells and Micrometastases

Isolated tumour cells (ITCs)	Micrometastases
• Defined by the 7th edition of AJCC as "small clusters of cells not greater than 0.2 mm, or nonconfluent or nearly confluent clusters of cells not exceeding 200 cells in a single histologic lymph node cross section are classified as isolated tumour cells" [2] (pN0(i+)) • No further surgery, radiotherapy or chemotherapy is indicated by their presence	• Defined by a separate designation of pN1mi (>0.2 mm and no greater than 2.0 mm) to indicate micrometastases alone [2] • Although larger than ITCs, their clinical significance is also questionable: NSABP B-32 showed a 1.2 % lower 5-year survival in patients with micrometastases, compared to those that were pathologically node negative [46]

Special Notes

- The literature is populated by much discussion regarding the significance of isolated tumour cells (ITCs) and micrometastases. This debate has been largely superseded by the publication of Z0011 and its findings relating to the significance of macrometastases [50], along with Weaver et al. who demonstrated statistical, but no clinical significance to their presence [32].

Summary: Management of the Clinically Node-Negative Axilla

- SLNs are pathologically negative or contain only ITCs:
  - SLNB is the standard for staging and axillary surgery [60].

- SLNs contain micrometastatic disease on pathologic examination:
  - SLNB alone can safely manage burden of disease. However case should be discussed at Multidisciplinary Cancer Conference (MCC) to determine if identification of macrometastases will alter adjuvant therapy recommendations. If so, completion ALND may be considered [60].
- SLNs contain macrometastatic disease on pathologic examination:
  - If meets all inclusion criteria for Z0011 (T1 or T2 tumour, 1 or 2 positive SLNs, no gross extranodal extension, breast-conserving therapy, whole-breast radiotherapy planned, no neoadjuvant chemotherapy), no further ALND is required [60].

    If three or more positive SLNs and/or gross extranodal disease, consider completion ALND [60].
  - If patient has undergone mastectomy, consider completion ALND [60]. However, may discuss at MCC to review benefits/risks of completion ALND vs. axillary radiotherapy.

Locally Advanced Breast Cancer

Locally advanced breast cancer (LABC) is a heterogeneous entity. The term includes T3: tumours greater than 5 cm in maximum diameter, T4: tumours that directly invade skin or chest wall, as well as inflammatory breast cancer, and tumours that have extensive regional lymph node involvement (matted ipsilateral lymph nodes N2–N3) without evidence of distant metastatic disease at initial presentation. These tumours fall into the category of stage IIB and III disease as per AJCC 7th edition staging. It is clinically useful to separate LABC into operable and inoperable, or situations in which upfront surgery is of questionable overall benefit. Approximately 25–30 % of LABC are inoperable on presentation. Up to 20 % of patients with clinically LABC are metastatic after staging [61]. Signs of questionable operable benefit or inoperability include [62]:

1. Extensive skin edema
2. Satellite nodule in the skin
3. Inflammatory breast cancer
4. Involvement of supraclavicular or internal mammary lymph nodes
5. Pre-operative upper limb edema
6. Skin ulceration
7. Fixation to the chest wall
8. Fixed, matted ALN

Optimal management of LABC requires multimodality treatment. The usual order of treatment varies according to the patient and the tumour clinical stage and characteristics:

Work-up	Inoperable LABC	Operable LABC	Follow-up (F/U)
• Obtain the ER, PR and HER2/neu status • Imaging: – Breast MRI – CT scan chest, abdomen and pelvis – Bone scan • Apply a radiologic marker pre-initiation of chemotherapy • Precise tumour measurement and documentation of skin changes. • Record tumour site with transparent film or skin tattoo. • Consider discussion in MCC	• Neoadjuvant chemotherapy and reassess response after each cycle • If response—continue until completion of planned treatment or maximal response—then surgical management • If no response—discuss again in MCC. Options: – Alternate systemic therapy regimen – If operable: Surgical management – If non-operable: radiotherapy +/− planned surgical treatment	• Consider neoadjuvant chemotherapy in: – Any patient who will need adjuvant chemotherapy [63] and in whom surgical pathology information is not required to determine regimen – High-grade tumours [64] – HER2+ [64] – Triple negative (ER/PR/HER2$^-$) [65] – Young patients <35 years [66] – Patient has large tumour and seeks breast conservation – Patients with node-positive disease • Surgical management of the breast (usually mastectomy unless downstaging) and axilla (see below: SLNB vs. axillary dissection)	• Regular clinical breast exam • Mammogram every 12 months

ER estrogen receptor, *PR* progesterone receptor, *HER2* human epidermal growth factor receptor 2, *MCC* Multidisciplinary Cancer Conferences, *SLNB* sentinel lymph node biopsy

Special Notes

- Radiation therapy will be recommended post-mastectomy or post-BCS to patients with LABC
- Advantages of neoadjuvant chemotherapy:
  - Evaluation of in vivo response to chemotherapy
  - Downstaging to facilitate breast conservation

    Conversion from mastectomy to BCT occurs in approximately 23 % of patients [65]

    Local recurrence rates in this conversion group are slightly higher than in the mastectomy group (10.7 % vs. 7.6 %) [68]
  - Early introduction of chemotherapy to treat occult potential systemic metastases

- Potential candidates for BCT after neoadjuvant chemotherapy:
  - Unifocal disease
  - No inflammatory skin involvement
  - Radiographic abnormalities resectable with lumpectomy
  - No contraindication to adjuvant radiotherapy
  - Willing to accept slightly higher risk of local recurrence in conversion from mastectomy to BCT
- SLNB has been investigated both before and after the completion of neoadjuvant chemotherapy [69]. When performed before neoadjuvant chemotherapy, it is both accurate (identification rate between 93 and 100 %) and safe, with a low rate of regional recurrence reported. However, it potentially delays the initiation of chemotherapy in an era where lymph node status does not influence the choice of chemotherapy. Conversely, SLN biopsy after neoadjuvant chemotherapy has the advantage of reducing the number of operative procedures needed, as well as being both accurate and safe [69]. A 2011 meta-analysis examining the accuracy rate of SLNB after neoadjuvant chemotherapy reported that the detection rate was 82 to 100 %, with a false-negative rate of 0 to 20 % [70]. However, the data with regard to the axillary recurrence in this setting are limited [69]. Furthermore, the ACOSG Z01071 (Alliance) Trial demonstrated a false-negative rate of greater than 10 % in women with cN1 breast cancer and 2 or more sentinel lymph nodes examined following neoadjuvant chemotherapy [71]. The Canadian SN FNAC study showed a suboptimal identification rate of SLN after chemotherapy, but has shown an acceptable false-negative rate of 8.4 % when immunohistochemistry (IHC) is used and sentinel node metastases of any size are considered positive. After neoadjuvant therapy, accuracy is further increased by the use of both blue dye and radiolabelled tracer, as well as by harvesting more than one sentinel node if possible [72]. The clinical relevance of residual nodal disease in the axilla following neoadjuvant treatment remains undetermined. As a result, in patients who are node positive on presentation, axillary lymph node dissection is the standard of care following neoadjuvant chemotherapy, although there is a role for tailoring this to our individual patients with input from an MCC [69, 70].

Neoadjuvant chemotherapy studies

Study	Methods	Results
NSAPB B18 Wolmark et al. [68]	• *N* = 1493 • RCT • Operable T1–3 N0–1 M0 patients assigned to pre-operative chemo (4 cycles of AC) vs. post-operative chemo (4 cycles of AC)	• Follow-up—9 years • No differences in OS (70 % and 69 %) or DFS (53 % and 55 %) • Marginally statistically significant treatment by age interactions appears to be emerging for survival and DFS, suggesting that younger patients may benefit from preoperative therapy, whereas the reverse may be true for older patients

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Study	Methods	Results
EORTC Trial 10902 van der Hage et al. [67]	• *N* = 698 • RCT • Patients with T1c, T2, T3, T4b, N0 to 1 and M0 breast cancer were assigned to pre-operative vs. post-operative chemotherapy (4 cycles—FEC)	• Median follow-up—56 months • No differences in terms of PFS, OS and LRR • Pre-operative chemotherapy enabled more patients to be treated with breast-conserving surgery (rate of downstaging was 23 %)
Fisher et al. 2011 [73]	• *N* = 385 • Retrospective chart review • Patients stage I, II or III and triple-negative treated with neoadjuvant or adjuvant chemotherapy	• There is a trend towards survival benefit in patients with pCR following neoadjuvant chemotherapy • However, patients undergoing neoadjuvant chemotherapy with residual disease had significantly worse survival compared to patients receiving adjuvant therapy, with a trend towards worse survival compared to patients receiving neoadjuvant chemotherapy with pCR

AC doxorubicin/adriamycin + cyclophosphomide, *RCT* randomised controlled trial, *DFS* disease-free survival, *FEC* fluorouracil, epirubicin and cyclophosphamide, *OS* overall survival, *PFS* progression-free survival, *LRR* locoregional recurrence, *pCR* complete pathologic response

Inflammatory Breast Cancer

Inflammatory breast cancer (IBC) is a rare clinicopathological entity characterised by rapid progression and aggressive behaviour which, as originally described, presents with erythema and edema with exaggerated hair-follicle pits, causing a peau d'orange appearance of the skin [75]. The rapid progression, along with diffuse erythema of more than one-third of the skin overlying the breast, distinguishes IBC from neglected LABC with skin involvement [75].

After ruling out metastasis, patients are usually treated with pre-operative chemotherapy followed by surgery and radiation [75, 76]. The combined approach improves the outcome of those patients with IBC. In a recent study, Li et al. reported a 5-year survival rate of 35–40 % [75].

Pregnancy and Breast Cancer

Pregnancy-associated breast cancer (PABC) is defined as breast cancer diagnosed during pregnancy, within 1 year of delivery, or while lactating [77]. It is considered one of the most common cancers diagnosed during pregnancy, with an incidence of 1 in 3000 pregnancies [78] and is usually of high grade. The management of PABC requires a multimodality approach and thorough discussion with the patient. Treatment depends on the stage of the cancer and the gestational age of the pregnancy.

Work-up	Before week 20	After week 20
• Mammogram (with fetal protection) • Breast ultrasound • Discuss at MCC	• Breast surgery is safe throughout the pregnancy: – Mastectomy and SLNB/axillary dissection – BCT: not common – Radiation can be delayed until after delivery. A typical patient undergoing BCT will have a lumpectomy performed followed by chemotherapy (see below) and RT after delivery – SLNB with technetium and excluding blue dye • Chemotherapy can be administered after the first trimester: – If the patient is planned for neoadjuvant chemotherapy, then breast conservation is possible	• If there is no contraindication to BCT, it can be preformed, with plans for post-partum radiation • SLNB with radiolabelled sulfur colloid and excluding blue dye

BCT breast-conserving therapy, *SLNB* sentinel lymph node biopsy, *RT* radiotherapy

Special Notes

- Fluorouracil, doxorubicin and cyclophosphamide can be used during the second and third trimesters of pregnancy; no complications were observed for the foetus or infant [79].
- NCCN guidelines suggest that insufficient evidence exists regarding the general use of taxanes in any trimester; however, the use of weekly paclitaxel after the first trimester may be acceptable if clinically indicated [80].
- The use of trastuzumab is contraindicated in all trimesters [80].
- Data would suggest that SLNB is safe in the pregnant population using Tc-99 m for lymphoscintigraphy [81, 80] but avoiding blue dye [83].
- MRI cannot be performed due to inability to administer gadolinium.

Metastatic Breast Cancer

Approximately 4.1 % of newly diagnosed breast cancer patients will have metastases at presentation. Improved systemic therapy has seen an increase in the 5-year survival of such patients in the past 5 years [84].

Until recently, surgery had a limited role in the management of patients with metastasis [85, 86]. However, there is an emerging body of evidence to support the concept that removing the primary may provide a survival advantage for such patients [84–86]. A retrospective review of 16,023 patients from the national cancer data base examined this issue. Overall survival was improved in women who underwent surgical resection, with 3-year survival rates of 17 % for the no-surgery group, 28 % for the partial mastectomy group and 32 % for the mastectomy group [85]. Several other retrospective studies showed survival benefits for surgery [87–95].

However, Cady et al. [96] challenged this view through a case-matched retrospective analysis of 808 patients with metastatic breast cancer. They found that case matching either diminishes or eliminates the survival advantage obtained with surgery. More recently, Badwe et al. demonstrated that locoregional treatment of the primary tumour and axillary nodes has no impact on overall survival in patients with metastatic disease at presentation who have responded to frontline chemotherapy [97]. Soran et al. drew a similar conclusion with respect to local therapy in metastatic disease, regardless of response to systemic treatment [98]. Additional trials are ongoing and should help to further clarify the issue [99, 100]. We believe that these cases constitute special situations that need a multidisciplinary approach. Each decision needs to be tailored according to patients' symptoms (pain, bleeding, non-healing wound), comorbidities and life expectancy. There are other ongoing phase III trials examining the value of early local therapy for the intact primary tumour in patients with metastatic breast cancer.

Locoregional Recurrence of Breast Cancer

Breast cancer recurrence can be divided into breast recurrence after breast-conserving therapy, recurrence after mastectomy and axillary recurrences [99].

Breast recurrence after BCT	Recurrence after mastectomy	Axillary recurrence
• Rate of LR after BCT—0.5–1 % per year [102] • Risk factors: – Age <45 years – High grade – Extensive DCIS – Node positive – HER2/neu overexpression – Positive margins • Most recurrences occur in the same quadrant as the primary tumour • Usually detected by physical examination and/or mammography • Metastatic work-up is required to rule out systemic disease • Due to previous radiotherapy, mastectomy is the standard of care, although data is beginning to emerge examining possible repeat excision and radiotherapy [31]	• Rate of chest wall recurrence: 5–7 % • The main predicting factor of chest wall recurrence is the stage of the initial tumour • Usually the recurrence after mastectomy carries a worse outcome than that after BCT • Metastatic work-up is indicated • If systemic disease is ruled out, the local treatment involves wide local excision with or without radiotherapy	• Rule out distant metastases and then patients treated with surgical excision of gross disease have better regional control than those treated by radiation therapy [103] • Isolated axillary recurrence has a 5-year survival of 50 % [104] • There is limited data on repeat irradiation of an already irradiated axilla and it should be discussed in the setting of a multidisciplinary meeting

BCT breast-conserving therapy, *LR* local recurrence

Referral to Medical Oncology

1. All invasive breast cancers need to be evaluated by medical oncology or discussed in MCC for consideration of systemic therapy.

Referral to Radiation Oncology

1. In situ or invasive carcinoma treated with breast-conserving therapy.
2. Positive or very close margins after mastectomy.
3. Any tumour more than 5 cm irrespective of the surgical treatment offered.
4. Locally advanced and inflammatory breast cancer.
5. Node-positive breast cancer.

Referring to Multidisciplinary Cancer Conference

Ideally all patients where time allows; however the following should be discussed:

1. Any case in which a deviation from the standard of care is considered.
2. Axillary lymph node metastases.
3. To review imaging and assess the extent of the disease for the purpose of planning surgical therapy.
4. Disease progression on neoadjuvant chemotherapy with borderline operability.
5. Patient with metastasis to contralateral axilla.
6. Patient with axillary metastasis and unknown primary cancer.
7. Chest wall recurrence after breast reconstruction.
8. Metastatic breast cancer in which surgery is being considered.

Breast Reconstruction

Over the last decade, there has been an increase in post-mastectomy breast reconstruction rates [105]. Research has shown that immediate and delayed breast reconstruction following mastectomy can improve patients' quality of life [104, 105] and is both technically and oncologically successful in the appropriate patients [108, 109]. Due to these advantages, we discuss and offer breast reconstruction as part of our initial management consultation. If a patient expresses interest in this option, a referral to plastic surgery is made.

Important considerations for reconstruction can be divided into pre-op, intra-op and post-operative concerns.

Pre-operative Considerations

Post-mastectomy reconstruction can be divided into implant-based and autologous methods. Implant-based reconstruction includes both direct to implant and tissue expander to implant procedures. Autologous methods include deep inferior epigastric perforator (DIEP) flaps, free and pedicled transverse rectus abdominis myocutaneous (TRAM) flaps, latissimus dorsi flaps and less commonly superficial inferior epigastric artery flaps (SIEA).

Post-mastectomy reconstruction can be done immediately (i.e. at the time of mastectomy) or in a delayed fashion. Delayed reconstruction is typically done at least 6 months following completion of any adjuvant treatment, but can technically be performed at any interval if the patient remains healthy and a good reconstruction candidate.

Mastectomy in the setting of immediate reconstruction can be done with a skin- or nipple-sparing technique. There are important oncologic factors to consider in such cases:

- A meta-analysis of >3700 patients demonstrated that skin-sparing mastectomy (SSM) with immediate reconstruction is equivalent to conventional mastectomy without reconstruction with respect to local and distant recurrence [110].
- Nipple-sparing mastectomy (NSM) can achieve good cosmetic results without an increased risk of recurrence in patients with disease >2 cm from the nipple [111]; however there are currently no randomised control trials on the oncologic safety of NSM vs. SSM. Similarly, there is minimal data on the oncologic safety of NSM in BRCA mutation carriers [112]. Overall, NSM should be carefully considered on a case-by-case basis in a multidisciplinary setting.

There are many clinical factors to consider when deciding on timing and type of reconstruction [113]. Immediate reconstruction is generally not recommended in:

- T3–T4 tumours
- Inflammatory breast cancer
- Axillary nodal metastases
- Before adjuvant radiotherapy
- When waiting for immediate reconstruction will considerably delay therapeutic surgery

Delayed breast reconstruction is acceptable in most circumstances.

Important patient factors that may adversely affect reconstruction outcomes include:

- Obesity
- Diabetes
- Smoking
- Older age

Intra-operative Considerations

Technically, SSM and NSM are more challenging than conventional mastectomy.

- Pectoralis coverage of the expander or implant is important. Therefore, when dissecting the breast and pectoralis fascia off the chest wall, it is imperative to avoid damaging the pectoralis major and compromising the muscle.
- Serratus fascia is used to form the inferior portion of the pocket for the expander or implant. This fascia must be kept intact. Occasionally this is augmented with an acellular dermal matrix.
- Excessive trauma to the mastectomy flaps must be avoided. Flaps must be thin enough to remove all breast tissue and constitute a sound oncologic procedure without compromising their viability.
- SLN biopsy at the time of SSM may be done through a separate incision in the conventional location, or via the SSM incision if nodes are easily accessible. Consider the need for excessive traction on the skin flap when making this decision. NSM requires a separate incision for SLN access as the NSM incision is often in the inframammary fold.
- ALND requires a separate incision in both SSM and NSM.

Post-operative Considerations

Complications [111]:

Autologous reconstruction	Implant-based reconstruction
Flap necrosis	Flap necrosis
Infection	Infection
Seroma	Seroma
Hematoma	Hematoma
Chronic back pain	Chronic breast pain
Abdominal weakness, bugle or hernia	Implant malposition
	Capsular contracture
TRAM flaps have a higher rate of donor site morbidity than DIEP flaps; conversely, DIEP flaps have a higher risk of necrosis [114–116]	Implant rupture

Surveillance [113, 117].

Surveillance is completed clinically. There is no evidence to support radiographic screening of the reconstructed breast unless the patient has palpable findings suggestive of recurrence. Suspicious masses or symptoms should be imaged and completely worked up. Fat necrosis is relatively common and benign following breast reconstruction.

Toronto Pearls

- When localising a lesion for breast conservation, some radiologists will mark the site of the lesion on the skin, but this is not always true. It is helpful to remember that the point of entry and the nipple are the only fixed points. The cranial-caudal (CC) view of a pre-operative mammogram defines medial vs. lateral and lesion along the nipples line will be either 12 or 6 o'clock. The medial-lateral (ML) view defines upper vs. lower half and lesions located at the nipple line will be located at either 3 or 9 o'clock.
- Z0011 results are integrated into our surgical practice: patients who have undergone lumpectomy and SLNB with positive nodes and who meet Z0011 criteria are not routinely offered completion axillary dissection.
- In cases of locally advanced breast cancer, we perform the SLNB after the neoadjuvant chemotherapy if nodes were clinically and radiologically negative prior to treatment. FNA of any suspicious axillary nodes is attempted pre-treatment. If nodes were positive, we recommend axillary lymph node dissection.
- Oncoplastic procedures in breast conservation are considered in conjunction with plastic surgery on a case-by-case basis, as are contralateral balancing procedures such as reduction mammoplasty.
- Contralateral prophylactic mastectomy (CPM) is not routinely recommended in the absence of a genetic mutation resulting in increased lifetime risk of developing a new breast cancer. In discussing CPM for patients without a gene mutation, the following must be considered: CPM does not offer an overall survival benefit in comparison to clinical and radiographic surveillance. It does decrease the risk of developing a contralateral breast cancer. CPM has no effect on local recurrence of the ipsilateral cancer. CPM may be considered in non-gene mutation carriers who are unable/unwilling to undergo continued surveillance and in those who wish to have immediate autologous flap-based reconstruction for optimal symmetry.

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