

Optimise not compromise: The importance of a multidisciplinary breast cancer patient pathway in the era of oncoplastic and reconstructive surgery

Madeleine C. Strach^{a,b,*}, Thiru Prasanna^{a,b}, Youlia M. Kirova^c, Severine Alran^d, Sandra O'Toole^{e,f,g}, Jane M. Beith^{a,b,f}, Philip Poortmans^c, Catriona M. McNeil^{a,b,f}, Susan Carroll^{b,f,h}

^a Department of Medical Oncology, Chris O'Brien Lifehouse, Camperdown, New South Wales, Australia

^b Royal Prince Alfred Hospital, Camperdown, New South Wales, Australia

^c Department of Radiation Oncology, Institut Curie, Paris, France

^d Department of Surgical Oncology, Groupe Hospitalier Paris St Joseph, France

^e Garvan Institute of Medical Research, Darlinghurst, New South Wales, Australia

^f Sydney Medical School, University of Sydney, New South Wales, Australia

^g Australian Clinical Labs, Bella Vista, New South Wales, Australia

^h Department of Radiation Oncology, Royal North Shore Hospital, St Leonards, New South Wales, Australia

ABSTRACT

Modern breast cancer care is a complex multidisciplinary undertaking in which the integrated function of multiple constituent parts is critical, and where changes to one therapeutic component may profoundly influence the delivery and outcomes of another. Oncoplastic and reconstructive breast surgery has evolved in the era of longer survival rates for women with breast cancer and aims to enhance oncological and cosmetic outcomes. However, concurrently there has been an expansion in the indications for post-mastectomy radiation therapy (Abdulkarim et al., 2011; Early Breast Cancer Trialists' Collaborative Group (EBCTCG), 2014; Poortmans et al., 2015; Wang et al., 2011), the recognition of several biologically distinct breast cancer subtypes (Perou et al., 2000; Sørlie et al., 2001, 2003; Cheang et al., 2008, 2009; Sotiriou et al., 2003; Millar et al., 2011; Blows et al., 2010; Schnitt, 2010; Haque et al., 2012; Dai et al., 2015) and the development of recommendations for prophylactic surgery for high-risk women, including BRCA-mutation carriers (James et al., 2006; Domchek et al., 2010). Primary systemic therapy is increasingly utilised yet has varying efficacy depending on tumour biology (Cortazar et al., 2014). In this paper we review the evidence which informs the multidisciplinary team opinion in the era of oncoplastic and reconstructive breast surgery. We aim to describe an optimal multidisciplinary approach which balances competing risks of multimodal therapies to optimise oncological and cosmetic outcomes.

1. Introduction

The term 'oncoplastic surgery' was first devised by Dr Werner Audretsch in the 1990s as an evolution from the pioneering breast conserving and reconstructive efforts of surgeons in the 1980s (Audretsch et al., 1993, 1998). It was originally described as a multidisciplinary approach to integrate chemotherapy and radiation planning with conservative breast surgery for locally advanced disease (Macmillan and McCulley, 2016). The term is now commonly used to describe breast surgery that prioritises both oncologic and cosmetic outcomes.

Oncoplastic and reconstructive breast surgery has arisen from the pursuit of optimal psychosocial adjustment and quality of life in women with curable breast cancer who mostly have long term survival (Pan et al., 2017). Postoperative breast asymmetry after breast conserving surgery (BCS) has been shown to correlate with poor psychosocial

functioning (Waljee et al., 2008) and oncoplastic breast surgery (OBS) attempts to overcome these deficits to improve patient satisfaction (Weber et al., 2017a). OBS is an amalgamation of oncologically focused surgery with reconstructive techniques and requires multidisciplinary planning from the outset to facilitate appropriate integration of adjunctive therapies.

OBS has evolved as a subspecialty over the last two decades with more than one thousand journal articles published since 1983 (Freitas-Junior et al., 2017). Most of these articles were written by plastic and breast surgeons, with minimal contribution of other oncological specialties such as medical or radiation oncologists despite these specialties being key contributors to the multidisciplinary management of breast cancer patients (Freitas-Junior et al., 2017). To date there has not been a published review comprehensively describing the multidisciplinary team's contribution to management plans in the era of OBS.

In recent years there has been an evolution in surgical techniques

* Corresponding author at: Chris O'Brien Lifehouse, 119-143 Missenden Rd, Camperdown NSW 2050, PO Box M33 Missenden Rd, NSW, 2050, Australia.
E-mail address: madeleine@strach.net (M.C. Strach).

with the development of OBS (Freitas-Junior et al., 2017; Clough et al., 2015). In 2011, a survey of 33 breast surgeons in France reported using OBS in 14% of patients receiving BCS (Clough et al., 2015) and a registry study of the period 2011–2012 revealed 25% of 1,798 women underwent OBS (Klit et al., 2017). Consequently, a number of countries are establishing oncoplastic breast surgical fellowships to formalise training in this rapidly expanding field (Yunaev and Hingston, 2013; Zucca Matthes et al., 2012; Maxwell et al., 2017). To complement the expansion of this field in the surgical sphere, this article will review the role of oncoplastic surgery in the management of localised breast cancer and the interplay between treatment pathways involving radiation and chemotherapy, along with pathologic, radiological, genetic and patient-focused considerations. We aim to elucidate a strategy of multidisciplinary integration of oncoplastic and reconstructive surgical methods helping to optimise outcomes for women with localised breast cancer without any compromise to their oncological care.

2. The multidisciplinary tumour board

Breast cancer multidisciplinary tumour board (MTB) meetings are standard and often even obligatory by national regulations in most institutions as they contribute to quality performance standards for health services (The Department of Health, 2018; Saini et al., 2012; Kesson et al., 2012). They involve a representation of a broad range of cancer specialists with significant experience and knowledge in the field of breast cancer to make recommendations regarding the optimal care for cancer patients (Cataliotti et al., 2007). Multiple authors discussing the role of OBS advocate for breast surgeons to discuss surgical plans pre- and postoperatively to facilitate planning of other therapies (Shah et al., 2018; Lebovic, 2010). The introduction of a dedicated oncoplastic MTB is being explored to assist clinician decision-making regarding optimal patient selection (Gammal El et al., 2017; Rusby et al., 2011). One group retrospectively reviewed surgical outcomes after introduction of an oncoplastic MTB, demonstrating an increased reconstruction rate (Gammal El et al., 2017). Therefore, we propose that each breast cancer specialist has an important contribution in the formulation of the comprehensive treatment plan for each individual patient and that the MTB is a suitable place to meet and discuss this.

3. Role of the breast surgeon

While the anatomical and technical decisions regarding surgery remain the realm of the surgeon, it is important that the proposed surgical technique is shared with the multidisciplinary team to ensure that all other treatment modalities are taken into account and not compromised by the surgical techniques utilised (Kümmel et al., 2014; Frasier et al., 2016; Rochlin et al., 2015; Cordeiro et al., 2014).

3.1. Oncoplastic breast surgery (OBS)

OBS has evolved from the need to reconcile optimal cosmetic outcomes without compromising the oncological aims (Benson and Down, 2017). Oncoplastic procedures are cosmetic and reconstructive

techniques developed by plastic surgeons which are utilised by breast surgeons in breast conserving surgery (Clough et al., 2010). The aim is to combine oncological surgery with techniques that aim to restore symmetry, preserve normal tissue, optimise cosmesis, and minimise postoperative complications while not exposing patients to the risk of local recurrence necessitating multiple further resections (Clough et al., 2010; van Paridon et al., 2017). Such strategies are increasingly utilised in the surgical management of breast cancer, with some commentators describing OBS as the “standard of care” (Macmillan and McCulley, 2016).

OBS encompasses multiple techniques to achieve volume displacement and replacement using autologous tissue or implants, however, there is no consensus as to which procedure is best suited for patients (Clough et al., 2010; van Paridon et al., 2017; Challoner et al., 2017; Clough et al., 2012). The decision to undertake OBS is based on certain assumptions as to the tumour stage and extent, risk factors of the tumour at the time of surgery, and the likely indications for cytotoxic chemotherapy and radiation therapy (RT). Where resection with clear margins can be predicted reliably in advance, the surgical approach should adhere to the oncological principle of clear margins integrated into the complete multidisciplinary treatment plan (O’Kelly Priddy et al., 2016; Singletary, 2002).

Van Paridon and colleagues retrospectively analysed the records of 42 women with 46 breast cancers to formulate a treatment algorithm of oncoplastic techniques based on diagnosis, tumour size, tumour location, and breast size and shape (van Paridon et al., 2017). In this cohort of women, 46% of whom had invasive ductal cancer, breast surgeons performed the resections and plastic surgeons the oncoplastic reconstructions. While this algorithm does not incorporate the multidisciplinary integration of other therapies such as chemotherapy or RT, it could form the basis for a broader algorithm incorporating the role of chemotherapy, RT and genetic risk factors.

Surgical techniques further refining the oncoplastic approach are being developed with the multidisciplinary pathway in mind, for example, Clough and colleagues sought to use evaluation of breast density to minimise complications of glandular necrosis which can delay postsurgical treatments (Clough et al., 2010). Detailed surgical guidelines exist in relation to the decision to undertake the various oncoplastic and reconstructive procedures and are beyond the scope of this review. The indications and contraindications for OBS are shown in Table 1 (Association of Breast Surgery at BASO et al., 2007; Nijenhuis and Rutgers, 2013; Agrawal, 2016a).

3.1.1. Oncological outcomes for OBS

Although several recent systematic reviews attest to the short-term safety of OBS, controversy persists as to the long-term oncological safety and cosmetic outcome (La Cruz De et al., 2016; Yiannakopoulou and Mathelin, 2016; Losken et al., 2014; Headon et al., 2016; Piper et al., 2016; Carter et al., 2016). Furthermore, breast cancer requires prompt initiation of adjuvant systemic cytotoxic and/or targeted therapy, for which delays related to wound healing, infection and multiple surgeries are best avoided (Fan et al., 2017).

Several controversies and criticisms of the OBS approach exist in the

Table 1

Indications and contraindications to oncoplastic techniques in breast conserving surgery (Association of Breast Surgery at BASO et al., 2007; Agrawal, 2016a,b).

Oncoplastic breast surgery	
Indications – where there is risk of significant deformity with adequate wide local excision	Contraindications
Resection of > 20% of breast volume	When clear margins cannot be assured without performing a mastectomy
Central, medial and lower quadrant resections	Patients with extensive and/or inflammatory T4 tumours
Axillary dissection via large lateral quadrant resection	Patients with multi-centric disease (becoming more and more contested)
Cosmetic considerations: macromastia, significant ptosis or breast asymmetry, patient desires smaller breasts	Patients with extensive malignant mammographic calcifications/ extensive DCIS
	Where radiation therapy cannot be given

context of breast conserving surgery and multidisciplinary adjunctive therapies. These include concern regarding sacrifice of resection margins, the pathological identification of positive resection margins after glandular mobilisation, accurate localisation of the tumour bed for postoperative RT, the upper size limit for safe breast conservation, sequencing of RT with two-stage breast reconstruction and (in)appropriate use of primary systemic chemotherapy (Mattingly et al., 2017).

Several recent and substantial meta-analyses evaluated the oncological outcomes of OBS. A meta-analysis of 8,659 patients (3,165 oncoplastic BCS vs 5,494 conventional BCS), showed superior margin control (12% vs 21% margin positivity), a lower local recurrence (LR) rate (4% vs 15%) and improved cosmetic outcome (90% vs 83% patient satisfaction) with an oncoplastic approach. However, the mean follow-up in the oncoplastic patient group was only 37 months, compared to 64 months in the conventional BCS group (Losken et al., 2014).

A systematic review of 6,011 patients undergoing OBS showed low rates of LR (3%) and distant relapse (DR) (9%) at a mean follow-up of 51 months, and a margin positivity rate of 10% (La Cruz De et al., 2016). Another systematic review of 2,830 patients undergoing OBS observed that most studies were of low quality, of small size and short follow-up (only 2 out of 40 studies had a median follow-up over 60 months) suggesting that the evidence around oncological outcomes of OBS is still limited (Yiannakopoulou and Mathelin, 2016).

Likewise, a systematic review of 1,324 oncoplastic reduction mammoplasty cases, with only 2 out of 17 studies having a median follow-up beyond 60 months, reported low LR and DR rates of 3%, with high levels of cosmetic satisfaction (Piper et al., 2016). Nevertheless, interpretation was hampered by a lack of consistency in selection and reporting of endpoints, the retrospective nature of the data and the limited number of patients per study.

A smaller single-institution study compared 454 OBS cases with 908 BCS cases, with a median follow-up of 7.2 years. With the exception of multifocality, which was more common in the oncoplastic group (26% vs 13%), all other clinicopathological features including use of adjuvant systemic therapies were well-balanced. All patients received postoperative RT. There was a non-significant increase in LR events with the oncoplastic approach (3.0% vs 1.8% at 5 years and 6.7% vs 4.2% at 10 years) and no difference in distant events or overall survival (OS) (De Lorenzi et al., 2016).

More recently Clough and colleagues published outcomes for 350 consecutive patients undergoing oncoplastic level 2 mammoplasties with prospective data collection between 2004 and 2016. Most patients had luminal A subtype and median follow up was 55 months with 12.5% overall margin positivity rate, 8.9% experiencing postoperative complications and 4.6% experiencing delay until postoperative treatment. Five-year incidence of locoregional recurrence (LRR) was 3.1% and of DR 12.4% (Clough et al., 2018). Although these rates are comparable to the literature regarding conventional BCS follow-up is short and lack of randomisation or a control arm are limitations to interpretation of this data.

Based on data that cavity shaving reduces margin positivity after partial mastectomy (Chagpar et al., 2015), Mukhtar and colleagues completed a retrospective cohort study of patients undergoing BCS for stage 1–3 invasive lobular cancer (ILC) between 1992 and 2017. They demonstrated that oncoplastic techniques and selective shave margins were associated with lower positive margin rates after adjustment for tumour size and multifocality (Mukhtar et al., 2018). This cohort demonstrated similar rates of margin positivity after initial surgery with margin positivity increasing with the complexity of oncoplastic techniques used. 27% of patients required a single re-excision and 1.8% two re-excisions.

Accepting the caveats surrounding these studies, the five-year LR rate of approximately 3% observed with OBS are comparable to those reported in the literature for both BCS and mastectomy, as conventional surgical approaches for primary breast cancer (Aalders et al., 2016a).

3.1.2. Patient reported outcomes for OBS

Mature data regarding patient-reported outcomes comparing OBS to conventional BCS are limited. In mostly single arm cohort studies, OBS generally results in good to high rates of patient satisfaction at short term follow-up. The largest data set is from a South African study where out of 251 patients who underwent therapeutic mammoplasty, 70% were happy with the cosmetic results, 24% were satisfied and 6% were dissatisfied (Grubnik et al., 2013). Furthermore, at one year post-operatively, a cohort of 353 women reported increased emotional health (Losken et al., 2017). A recent retrospective study from Iceland compared 85 patients who had OBS compared to 665 who had BCS. No significant difference in satisfaction rates for cosmetic outcome were seen (Palsdottir et al., 2018). Another small series assessing 71 patients who underwent OBS reported good or excellent cosmetic satisfaction scores in 90% of the 64 respondents (Crown et al., 2018). This is in contrast to data from a Dutch study where patients who had conventional BCS had higher scores for satisfactory cosmetic outcomes compared to OBS (Lansu et al., 2015). Despite the mostly positive patient-reported outcomes from these cohorts, there remains a lack of robust evidence. More evaluation of patient-reported outcomes and results of prospective trials such as the Dutch COSMAM [NTR5665] trial are eagerly awaited (Catsman et al., 2018).

3.1.3. OBS training

One of the important issues globally is the lack of formal training programmes and a common curriculum in breast oncoplastic surgery (Are et al., 2016). Training in this area is of utmost importance. In many countries breast surgical management has traditionally been by separate surgical subspecialties being on the one hand the general, gynaecological or breast surgeon with a focus on the removal of the cancer, and on the other hand the plastic and reconstructive surgeon with a focus on the maintenance of the cosmetic outcome. For a long time it was thought there to be an innate conflict between these approaches of eradication and preservation, a belief that even remained for a long time after the fall of the Halsted concept of sequential spreading of breast cancer (Benson and Down, 2017). The integration of both the oncological and the cosmetic approaches has the advantage that it ensures the integrity of breast surgery focusing on the oncological outcomes without compromising this for the purposes of the cosmetic outcome.

Standardised approaches to OBS training is required to ensure that the required competencies can be obtained by all oncoplastic breast surgeons. Further post-graduate educational courses are organised by professional societies, however, these are not always with an established credentialing or certification process in place (Chatterjee et al., 2018). A recent consensus for recommendations for standardisation of OBS was obtained from an international panel, which agreed that there is a need for prospective multicentre studies to standardise patient selection and define criteria to accredit training centres (Weber et al., 2017b).

In the early 2000s, the Royal College of Surgeons of England introduced an advanced breast surgery course and calls for a subspecialty training program in oncoplastic surgery were made (Association of Breast Surgery at BASO et al., 2007; Skillman and Humzah, 2003; Brown et al., 2004). As it is accepted that several surgical subspecialties, including general surgeons, plastic surgeons and gynaecological surgeons, can practice breast surgery (Cataliotti et al., 2007), standardising breast surgical training is complex and has struggled to gain a consensus globally (Urban et al., 2014). Most countries have introduced breast surgery and/or oncoplastic surgical fellowships (Brown et al., 2004; Khayat et al., 2017; Maxwell et al., 2017).

The British Association of Surgical Oncology (BASO) published a guide to good oncoplastic practice in 2007, which has become a reference to guide training competencies (Association of Breast Surgery at BASO et al. (2007)). ESSO, the European Society of Surgical Oncology,

initiated an “Advanced Course on Oncoplastic Breast Surgery” with a multidisciplinary faculty of specialists for a limited group of participants to optimise interactivity ([The European Society of Surgical Oncology, 2016](#)). It has only been recently that the American Society of Breast Surgeons Oncoplastic Surgery Committee was formed to recommend educational programs for its members ([Chatterjee et al., 2018](#)). A survey from this group showed the heterogeneity in oncoplastic surgical training with education obtained from courses, videos, teaming with a plastic surgeon, textbooks and via dedicated fellowships ([Chatterjee et al., 2018](#)). Countries outside of the UK and USA who have shown a keen and dedicated interest, yet with different models, in oncoplastic breast surgical training include France, Spain, Italy, Brazil, Portugal, Canada and Australia ([Yunaev and Hingston, 2013](#); [Maxwell et al., 2017](#)).

Oncoplastic surgical competencies have been classified based on tiers of complexity ([Association of Breast Surgery at BASO et al., 2007](#); [Urban et al., 2014](#)) that form the basis for training guidelines ([Lebovic, 2010](#)). Level I is the basic level of competence with no specific plastic surgical training required; level II requires competence in reduction mammoplasty techniques; level III requires attaining expander and implant techniques and finally level IV requires the ability to perform autologous flaps which requires advanced skills in plastic and reconstructive surgical techniques ([Association of Breast Surgery at BASO et al., 2007](#); [Urban et al., 2014](#)). Appropriate patient selection and mastering of these techniques at a standardised level is required to guarantee breast cancer patients optimal oncological and cosmetic outcomes ([Lebovic, 2010](#)).

3.1.4. Further developments in OBS

The literature describes attempts to apply oncoplastic techniques to BCS in settings when mastectomy traditionally is indicated. Silverstein and colleagues coined the concept of ‘extreme oncoplasty’ when evaluating outcomes for 66 patients who declined conventional mastectomy and after multidisciplinary discussion underwent breast conserving techniques for large multifocal and multicentric tumours larger than 5 cm followed by standard adjuvant RT and boost to the tumour bed ([Silverstein et al., 2015](#)). Despite only one patient experiencing LR this was over a short median follow-up of 24 months, and no pathological data were provided to provide risk stratification of this group, nor was information on systemic therapy provided. This raises an exploratory concept that requires further investigation and given the limited data for safety of oncological outcomes, this approach is not recommended. However, cases such as these clearly outline the important role of the multidisciplinary team in making appropriate treatment recommendations, especially in the less usual setting of patients declining standard oncological approaches.

3.2. Reconstruction after mastectomy

Mastectomy is required firstly, for breast cancers in women where BCS cannot achieve adequate oncological clearance, secondly, for women living in regions with limited access to radiotherapy, thirdly, for women who ask for a mastectomy and finally for prophylactic surgery for women with BRCA or cancer-predisposing genetic mutations ([Gu et al., 2018](#); [Meijers-Heijboer et al., 2001](#)). Increasingly, patients are considering breast reconstruction after mastectomy ([Jagsi et al., 2014](#)). However, the majority of patients (70–90%) having mastectomy will decide not to have a surgical breast reconstruction, for reasons relating to age, complications of unnecessary surgery, employment, and inadequate or unsatisfactory information provided by surgeons regarding reconstruction ([Héquet et al., 2013](#)). Autologous reconstruction utilises the patient’s own tissue to recreate the breast shape, while implant-based reconstruction uses a prosthetic implant. [Table 2](#) outlines the advantages and disadvantages of the respective procedures.

A vital missing component in most institutional reviews has been

patient-reported outcomes. The multi-institutional prospective study, Mastectomy Reconstruction Outcomes Consortium (MROC) involving 11 academic centres in North America aimed to address this issue through the collection of patient-reported outcome measure scores (PROMs). Of 1,632 women who were studied, 1,139 underwent implant reconstruction and 493 autologous reconstruction, 73% of women responded to a 1-year questionnaire. After covariate analysis autologous reconstruction was associated with significantly higher levels of breast satisfaction than implant reconstruction ([Pusic et al., 2017](#)).

The timing of reconstruction in the setting of breast cancer treatment is controversial and of ongoing debate. There has only been one randomised trial over 20 years ago assessing the effects of immediate compared to delayed reconstruction and the Cochrane review in 2011 pointed out this deficiency ([D’Souza et al., 2011](#)). Increasingly, breast reconstruction using temporary tissue expanders (TTE) is occurring at the time of oncological surgery with later change to permanent implants or autologous reconstruction. The use of implanted surgical devices needs careful scrutiny with some products officially withdrawn due to safety concerns ([Benson and Down, 2017](#)). Silicone-gel implants for cosmetic indications were banned temporarily 1992–2006 by the US Food and Drug administration ([Angell, 1996](#)) due to concerns regarding lack of proof for safety, not because they were proven to be dangerous. Only recently, epidemiological data have shown an association between breast implants and breast anaplastic large cell lymphoma ([de Jong et al., 2008](#); [de Boer et al., 2018](#)). Delayed autologous reconstruction has the advantage that it can be left until after completion of adjuvant chemotherapy and RT. Timing of reconstruction in relation to consideration of adjuvant RT is discussed in more detail in [Section 6.4](#).

3.3. Summary of impact of OBS and reconstructive breast surgery

While it is likely that the oncological outcomes from OBS and reconstructive surgery will not be inferior to conventional approaches, there are few large long-term follow-up studies with most reported series being of small to moderate size, or of relatively short follow-up duration. This latter point is important given the fact that many breast cancer relapses particularly luminal A subtypes occur after five years ([Saphner et al., 1996](#)) with a recent publication demonstrating the cumulative 13% risk of distance recurrence between years five to twenty ([Pan et al., 2017](#)).

Questions do remain as to the impact of breast reconstruction options on outcomes, especially where RT is a requirement for optimal oncological care. When post-mastectomy RT (PMRT) is anticipated, the evidence to date suggests no sequence, nor reconstructive choice is definitively superior to any other ([Nelson and Disa, 2017](#); [Panchal and Matros, 2017](#)). Furthermore, the impact on long-term quality of life is uncertain and cumulative treatment burden remains unquantified.

4. Role of the pathologist

It is critical that attention to pre-operative assessment of the histopathological phenotype of the tumour is undertaken. An example is the subtype of ILC with its diffuse growth pattern. This is a breast cancer subtype that has a higher prevalence of positive margins than other tumour subtypes ([Cheang et al., 2008, 2009](#); [Sotiriou et al., 2003](#)). Preoperative assessment with standard imaging is also less accurate ([Millar et al., 2011](#); [Blows et al., 2010](#); [Schnitt, 2010](#)).

Close dialogue with breast cancer pathologists can provide significant insights into potential tumour behaviour. For example, assessing the likelihood of response to primary systemic therapy (PST) allows the care team to reasonably predict the likelihood whether adjuvant chemotherapy and RT will be required, or the risk of margin positivity if OBS is planned. Standardisation of orientation of surgical specimens should be described to assist surgeons and pathologists better understand pathologic results including margin. While intra-

Table 2

Advantages and disadvantages of implant-based versus autologous reconstruction after total mastectomy (Association of Breast Surgery at BASO et al., 2007; Poppe and Agarwal, 2017; O'Halloran et al., 2018).

Reconstruction Technique	Advantages	Disadvantages
Implant-Based	<ol style="list-style-type: none"> 1. Reduced operating time and quicker return to normal activities (O'Halloran et al., 2018) 2. Excellent cosmesis when post-mastectomy RT is not required (Association of Breast Surgery at BASO et al., 2007) 3. Lack of donor site morbidity (O'Halloran et al., 2018) 	<ol style="list-style-type: none"> 1. Saline based tissue expanders require repeated inflations which can cause pain, be inconvenient and can cause breast asymmetry (O'Halloran et al., 2018) 2. 2-stage surgical procedure (O'Halloran et al., 2018) 3. Infective complications (Becker and Lind, 2013) 4. Red breast syndrome secondary to delayed type IV hypersensitivity (Wu et al., 2015) 5. Risk of capsular contraction (Headon et al., 2015; Stevens et al., 2013) 6. Implant associated anaplastic large cell lymphoma (Loch-Wilkinson et al., 2017) 7. Complications after adjuvant radiation: implant failure (El-Sabawi et al., 2015) capsular contracture and radiodermatitis (Nava et al., 2015) 8. Potential for complications to delay adjuvant therapies (Alderman et al., 2010; Jabo et al., 2018) 9. Need for adjuvant therapy may not be predicted up-front eg: postoperative RT if adverse histopathological features (Nijenhuis and Rutgers, 2013)
Autologous	<ol style="list-style-type: none"> 1. Longer time for decision-making if delayed approach used (O'Halloran et al., 2018) 2. When performed after adjuvant therapy is complete (PST and radiation therapy), avoids delay to adjuvant chemotherapy and RT (Association of Breast Surgery at BASO et al., 2007) 3. More natural breast shape (O'Halloran et al., 2018) 4. Higher patient satisfaction (Atisha et al., 2015) 5. More durable and consistent (Association of Breast Surgery at BASO et al., 2007) 6. Less likely to fail than implant after radiation (O'Halloran et al., 2018) 	<ol style="list-style-type: none"> 1. Surgery has high patient morbidity, longer operative time, hospital stay and recovery (O'Halloran et al., 2018; Platt et al., 2011) 2. Complications of tissue necrosis and loss at recipient site (O'Halloran et al., 2018) 3. Complications at donor site such as wound dehiscence and abdominal hernias (Kroll et al., 1995) 4. Requires replacement of a larger amount of skin (Association of Breast Surgery at BASO et al., 2007) 5. Flaps may be thin, scarred, contracted, irradiated or poorly positioned (Association of Breast Surgery at BASO et al., 2007) 6. Requires extra training and expertise (Nahabedian et al., 2002) 7. Unless a TTE is used at the time of initial oncological surgery, there may be a prolonged period without a breast mound (Association of Breast Surgery at BASO et al., 2007) 8. Increase in thrombotic events, flap complications for patients having microvascular reconstruction while on tamoxifen (Parikh et al., 2017)

operative frozen section of margins has been suggested as an approach to improve rates of complete excision in OBS, this is highly labour intensive and relatively insensitive (Schnitt and Morrow, 2012).

In formulating oncoplastic and reconstructive treatment plans it is also important to appreciate LRR rates in time and relation to molecular subtype and age. In an analysis of 2,233 patients treated with BCS in the pre-trastuzumab era (1998–2007), LRR rates at 8 years were 1.8%, 5.5%, 2.2%, 11.7% and 9.8% for luminal A, luminal B, luminal-human epidermal growth factor receptor 2 (HER2), HER2 and triple-negative breast cancer (TNBC) patients respectively (Braunstein et al., 2017). Luminal B (vs luminal A), HER2 and TNBC subtypes were independently associated with increased LR risk on multivariable analysis, as were age under 50 years and increasing nodal status (Braunstein et al., 2017). However, in the era of modern anti-neoplastic systemic therapy with taxane and trastuzumab use, the influence of tumour subtype on LRR is attenuated to some degree, particularly for HER2-positive and TNBC subtypes (Aalders et al., 2016a, b; Truong et al., 2014)

5. Role of the radiologist

Incorporation of imaging review in the multidisciplinary setting is important pre- and post-operatively as imaging may highlight multifocality and locoregional disease extent thus altering the surgical plan. OBS using volume-displacement techniques should be preceded by detailed imaging to assess disease extent, as tissue relocation may make subsequent margin identification and re-excision difficult. Placement of clips in the tumour bed helps to better identify margin resection and facilitate precise delivery of radiation to the tumour bed.

Use of magnetic resonance imaging (MRI) in addition to mammography and ultrasound may improve diagnostic sensitivity (Berg et al.,

2004) and assist in pre-operative planning for women with locally advanced breast cancer, those planning reconstructive surgery and those at risk of contralateral disease. However, it should be noted that routine use of pre-operative MRI has not resulted in improvements in LR rate, overall or cause-specific survival, suggesting that even with highly sensitive pre-operative imaging, it may be difficult to predict margin extent (Sung et al., 2014; Houssami et al., 2014; Gervais et al., 2017; Solin et al., 2008).

6. Role of the radiation oncologist

Adjuvant RT is an essential component of breast conserving therapy and has several indications in post-mastectomy settings where reconstruction may have occurred or is planned. Importantly, RT is not only a critical component in maximising local control, but also impacts distant disease control (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al., 2014; Headon et al., 2016; Shafiq et al., 2007). Recently the MROC published data on the impact of RT on complications and patient-reported outcomes after breast reconstruction, finding that RT significantly increased the odds of complications in implant compared to autologous reconstructions and that irradiated patients who received implant reconstruction had lower satisfaction at 2 years (Jagsi et al., 2018). Thus, patients need to understand the indications for RT, the possible benefits and toxicities of RT, including the potential implications for cosmesis, from the earliest part of the discussion of their oncological care plan. Reconstructive surgeries are safe procedures with no convincing evidence of compromise in relation to radiation efficacy, but the technical issues of radiation delivery, the timing of such procedures, and the reconstructive type are all critical, requiring a multidisciplinary approach at each institution and internal auditing of outcomes.

6.1. Radiation therapy and OBS

Whole breast irradiation (WBI) following BCS is well established with proven efficacy and safety compared to mastectomy (Fisher et al., 2002; Veronesi et al., 2002). A radiation boost to the tumour cavity site is well documented in the literature to improve outcomes with several randomised trials and incorporation into evidence-based guidelines. The 20 year outcomes of the EORTC 22881 where over 5300 women with stage I/II breast cancers resected with negative margins were randomised to a radiation boost of 16 Gy to the tumour cavity compared to no boost demonstrated reduced local recurrence (17% vs 12%) although with no breast cancer or overall survival advantage (Vrieling et al., 2017; Jones et al., 2009).

There are less data in the use of a boost to the tumour cavity site, in the setting of oncoplastic surgery, although it is reasonable to assume this benefit should be similar to that observed in conventional BCS (Boersma et al., 2012). Oncoplastic techniques may pose more challenges for the radiation oncologist. Due to significant parenchymal tissue rearrangement, the tissue surrounding the original tumour site is often dispersed and requires placement of several clips (Furet et al., 2014; Shah et al., 2018). Uncertainty regarding the position of the cavity site may result in larger boost volumes that worsen cosmesis (Immink et al., 2012). A retrospective review demonstrated that despite the displacement of breast tissue and surgical clips to breast quadrants outside of the original tumour location, most tumours recur in the original tumour quadrant (Eaton et al., 2014).

A recent systematic review of the use of boost RT (24 studies involving 1933 patients) in the setting of oncoplastic surgery found that the use or omission of a local boost dose and tumour bed marking was not reported in the majority of studies of OBS (Schaverien et al., 2013). One contemporary study from a group in the Netherlands reported their experience of 125 patients that included patient and physician reporting quality of life (QOL) data (Lansu et al., 2015). Those that had conventional surgery had a better QOL compared to those that had OBS. This negative result linked to oncoplastic surgery may be due to patient selection bias, over-enthusiastic devascularisation during surgery and/or to larger boost volumes. Larger numbers and longer follow-up are required to verify these findings.

Centres with a long history of the use of OBS suggest the optimal approach is for the intraoperative placement of at least four surgical clips to delineate the limits of the tumour bed to facilitate the delivery of a boost in those who have risk factors for LR (Vrieling et al., 2017; Furet et al., 2014; Kirova et al., 2008). Cooperative groups recognising these challenges have developed expert consensus guidelines such as those from the GEC-ESTRO group to aid in the planning process. Interdisciplinary dialogue and an understanding of techniques including clip placement are required between both groups in this setting.

Although the GEC-ESTRO group were unable to provide strong recommendations as to target definition and delineation in the setting of OBS, in selected cases of limited rotational flaps the clinical target volume (CTV) can be defined as the sum of the clipped area (CA) and the distance of 20 mm minus the smallest surgical free margin. The planning target volume (PTV) is defined at the CTV + 10 mm (Fig. 1) (Strnad et al., 2018). Novel tumour bed markers such as BioZorb® (Focal Therapeutics, Aliso Viejo, CA, USA) have been shown to reduce CTV and PTV, but not ipsilateral lung or heart irradiation (Ward et al., 2018; Wiens et al., 2018).

6.2. Intraoperative radiation therapy (IORT)

IORT has been proposed as a means of treating small (< 5 cm) tumour cavities prior to tissue rearrangement (Shah et al., 2018) although there is a lack of evidence for the safety of this approach in the context of OBS. IORT has been studied in the context of conventional BCS, showing a statistically equivalent, to slightly higher risk, of ipsilateral breast tumour recurrence compared with WBI. However this is still at

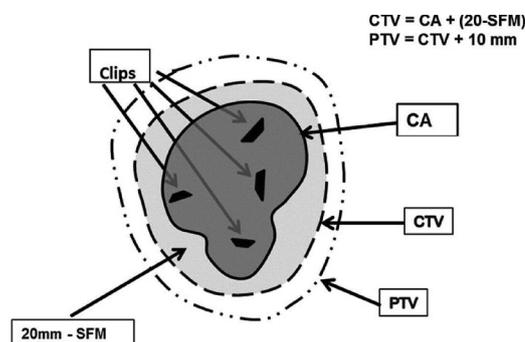


Fig. 1. Schedule of target definition following oncoplastic breast conservation surgery. [Reproduced with permission (Strnad et al., 2015)].

short term follow up (Vaidya et al., 2011; Fastner et al., 2013; Veronesi et al., 2013).

6.3. Neoadjuvant radiation therapy

With the increasing use of PST, there is growing interest in pre-operative RT (Tansley et al., 2013; Barrou et al., 2017; Lightowlers et al., 2017). This is particularly in the setting where women at presentation will require PST, mastectomy and radiation therapy, and also desire a one-stage reconstruction following completion of chemotherapy and RT. This pathway is attractive as it means adjuvant therapies are not delayed and also avoids expander complications and the traditional two-stage reconstruction pathway. European groups are discussing clinical trials and a British group has started a prospective study of this so-called “reverse-sequence” approach (Lightowlers et al., 2017). Promising single centre experiences have been published over the last decade suggesting equivalence in oncological outcome in chemotherapy responders and interest is growing (Tansley et al., 2013; Barrou et al., 2017; Zinzindohoué et al., 2016; Monrigal et al., 2011; Nestle-Krämling et al., 2016).

6.4. Post-mastectomy radiation therapy

Meta-analyses have reported a significant benefit from the use of PMRT in lowering LRR, distant metastasis and improving OS (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al., 2014; Headon et al., 2016). PMRT is widely accepted for those with more than four positive lymph nodes and is recommended for those with high-risk features including but not limited to T4 tumours, non-luminal T3 tumours, and involved resection margins. Updated guidelines further expand the indications for PMRT to include patients with one to three positive lymph nodes (National Comprehensive Cancer Network, 2018). Other aggressive biological features of the cancers are sometimes taken into consideration in decision-making such as presence of lymphovascular invasion, hormone receptor negativity and higher grade (Recht et al., 2017).

Breast reconstruction has been shown to result in favourable psychological and QOL outcomes (Heneghan et al., 2011), and as a consequence is offered early in contemporary breast surgical management. Adjuvant RT is an extra consideration for surgeons when recommending reconstruction type and timing, and adds to the complexity of discussion at the time of the patient's diagnosis (Nelson and Disa, 2017; Panchal and Matros, 2017). Patient decision tools are lacking, and most studies are single institutional.

Indications for PMRT have broadened over time (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al., 2014) and the decisions pertaining to the type and timing of reconstructive procedures in relation to radiation are not straightforward. Practices are evolving and preferences vary according to local institutional expertise. Reconstruction has higher rates of complications in the setting of PMRT irrespective of the timing of

radiation, or whether it is a TTE, direct-implant, or autologous reconstruction. In particular, implant based reconstructions are associated with a more than doubling in capsular contracture rate, failed reconstruction after RT (Cordeiro et al., 2014) and reduced QOL (Alborno et al., 2014). If a patient is not a candidate for an autologous reconstruction or prefers an immediate prosthesis-based reconstruction, generally placement of a TTE is performed with replacement by a permanent implant after PMRT (National Comprehensive Cancer Network, 2018). However, the optimal sequencing of RT particularly in the setting of implant-based reconstruction remains controversial.

The placement of TTEs prior to radiation (especially if bilateral) can create an anatomical barrier to chest wall tangents and nodal radiation (especially internal mammary nodes) when using commonly available three-dimensional (3D) conformal techniques (Motwani et al., 2006). The technical benefit of a TTE over an immediate implant is that it can be deflated prior to radiation to overcome these potential anatomical issues. Furthermore, the metallic ports in tissue expanders create a dose decrement on skin of 7% over 1.07cm in vivo on either side of the tangential beam using 3D treatment planning techniques (Gee et al., 2016). While this is unlikely to impact on local control, care should be taken in the radiation planning process especially for close or positive margins. Newer techniques of treatment delivery such as (volumetric) intensity-modulated radiation therapy including heliocoidal tomotherapy have moved into breast radiation planning and look promising in overcoming these deficiencies. However, they do come at a cost of low dose exposure to the lungs and contralateral breast with the potential of second cancer risk (Massabeau et al., 2012). Ongoing modelling of optimal radiation dose in the context of tissue expanders is being undertaken to improve dosing calculations (Yoon et al., 2018). Proton therapy might overcome this disadvantage, however, this is lacking clinical validation and is not readily accessible (Braunstein and Cahlon, 2018). The availability of these techniques is dependent on local technical expertise and resources, and hence the value in extrapolation of single institution reports is limited. The patient should be aware of all these variables prior to expander insertion, so as to make an informed decision.

The timing of autologous reconstructive surgery in the setting of PMRT is a subject of debate. Some surgeons avoid immediate reconstruction if PMRT is anticipated (Rogers and Allen, 2002; Spear et al., 2005) while others feel reconstruction with a well-vascularised tissue in the radiation field should not result in an adverse outcome (Crisera et al., 2011). Reports suggest increased rates of fat necrosis with RT, but patient satisfaction is good, and other complications are no greater (Rochlin et al., 2015). A delayed reconstruction, months to years after PMRT seems to be relatively safe with complication rates comparable to those who did not receive PMRT (Williams et al., 1995).

7. Role of the medical oncologist

7.1. Primary systemic treatment (PST)

Considerations for neoadjuvant chemotherapy or primary systemic treatment (PST) are important in the multidisciplinary pathway paradigm of breast cancer. Recent commentary suggests it be combined with oncoplastic surgery (Piper et al., 2015) and in this situation discussion at a MTB is paramount to optimise patient selection for this approach based on clinicopathological factors (Early Breast Cancer Trialists' and Collaborative Group (EBCTCG), 2018). The administration of cytotoxic chemotherapy prior to breast surgery compared to afterwards has been shown to result in similar long-term outcomes in progression-free survival and OS (Kümmel et al., 2014). Although a recent individual patient data meta-analysis concerning demonstrated an increased risk for local recurrence after BCS following neoadjuvant chemotherapy compared to with adjuvant chemotherapy (Symmans et al., 2017). The equivalence of pre- and post-surgery chemotherapy has been largely evaluated in aggregate studies and meta-analyses

where the nuances of breast cancer phenotype have not been addressed. This is of some concern when pathological complete response data from PST studies are considered. It is clear that while subtypes such as the TNBC group and HER2-positive/hormone receptor (HR)-negative group are extremely chemo-sensitive and may benefit from early introduction of systemic therapy, the luminal (HR-positive) groups are relatively chemo-insensitive (Cortazar et al., 2014). A single institutional study found that evaluating residual cancer burden (RCB) adds long-term prognostic data to pathological staging, and also demonstrated a higher proportion of extensive RCB (56%) in HR-positive/HER2-negative patients compared to in TNBC (23%) and HER2-positive (21%) patients (Symmans et al., 2017). Nevertheless, the PST approach has gained considerable traction because of the opportunity to assess chemo-sensitivity.

A more contentious benefit is improvement in breast conservation rate, especially when considered in the light of increased margin involvement post PST (Volders et al., 2016). Studies of post-PST resection specimens show the tumour response patterns range from concentric lesion shrinkage to fragmentation into a field of lesions (Tozaki et al., 2006). Thus, as the precise post-PST tumour extent is difficult to accurately assess pre-operatively, excision volumes are generally based on the pre-chemotherapy tumour size, nullifying the anticipated benefit in tumour downsizing. It should also be noted that the majority of data pertaining to the use of PST date from the pre-oncological era, and therefore the impact of PST on margin control in this setting is unknown. Given that oncoplastic tissue-displacement interventions make the management of positive margins difficult, this type of surgery requires careful multidisciplinary consideration in the post-PST setting.

7.2. Adjuvant chemotherapy

It has long been recognised that breast cancer is a systemic disease, and can become so at a small primary tumour size (Barinoff et al., 2013). Factors influencing propensity to microscopic metastatic spread include molecular phenotype and grade, which are intrinsically linked, and regional lymph node involvement (Kawano et al., 2013; Dawood et al., 2010). For aggressive chemo-sensitive cancers, such as the TNBC and HER2-positive subtypes, chemotherapy is likely to be required even in the setting of small, node negative disease (Tolaney et al., 2015; Blum et al., 2017). Furthermore, it is recognised that delays to chemotherapy initiation may influence long-term outcomes (Fan et al., 2017; Colleoni et al., 2000; Gagliato et al., 2014; Farolfi et al., 2015) with delays longer than 4 weeks considered suboptimal. It is in these patients where a PST approach may be especially advisable (Alexander et al., 2017).

While rates of complications and re-operation are expected to be higher with oncoplastic surgery than with BCS alone, available data do not necessarily support this (Losken et al., 2014). However, in the post mastectomy setting, immediate breast reconstructive procedures are associated with a higher complication rate. A large series from the MD Anderson Cancer Centre of over 10,000 breast surgical procedures noted that in the total mastectomy with immediate reconstruction group the infection rate was nearly double compared to the total mastectomy alone group (13% vs 8%) and there was a 17% implant complication rate (Carter et al., 2016). Thus, where adjuvant cytotoxic chemotherapy is anticipated for patients known to have operable TNBC and HER2-positive subtypes (for example if fertility preservation is required with its attendant delays to start chemotherapy) simpler surgery with a lower risk of infections or delayed wound healing may be preferable.

8. Genetic considerations

The identification of a mutation in a breast cancer susceptibility gene (such as BRCA1/2) may have profound implications for the type of breast surgery ultimately undertaken, and in some cases also leads to

consideration of risk-reducing oophorectomy (Ludwig et al., 2016). Women with the knowledge of their genetic predisposition before surgery may opt to undergo therapeutic mastectomy with or without contralateral prophylactic mastectomy, rather than BCS. Furthermore preventative surgery may be undertaken at a later stage when the urgency surrounding the management of the breast cancer presentation is less. Additionally, reconstructive techniques such as abdominoplasty may be avoided if future oophorectomy is considered. Thus, where a genetics review is flagged pre-operatively, it is judicious to undertake an approach that avoids unnecessary surgery and allows adequate time for measured counselling and multidisciplinary discussion (Association of Breast Surgery at BASO et al., 2007).

9. Patient perspective

OBS and reconstructive breast surgery provide additional approaches and techniques to the already complex schema of decision-making in early breast cancer. Ultimately, recommendations from multidisciplinary teams are discussed with patients to design individualised treatment plans. It is imperative that patients understand the limitations and benefits of oncoplastic approaches compared with conventional BCS. A recent survey of American oncoplastic surgeons demonstrated that only 51% discussed oncoplastic options suggesting that these options are either not offered due to skill and/or knowledge gaps, or that formal consent to oncoplastic procedures is lacking (Chatterjee et al., 2018).

There is significant interest in the literature regarding decision aids to assist patients making decisions regarding complex medical treatments (Stacey et al., 2011). A recently published systematic review evaluated the effectiveness of decision-making interventions regarding breast reconstruction (Paraskeva et al., 2018). Only two out of eight studies identified were of moderate or strong quality. The highest quality study evaluated a decision aid in an Australian context by qualitative methods and both patients and health practitioners found the intervention useful in decision-making (Sherman et al., 2017). Incorporation of OBS and reconstructive breast surgical approaches in decision-making interventions may help clarify treatment options to patients to optimise their oncological and cosmetic outcomes.

10. Current guidelines

Several recent excellent reviews from the literature are available to assist in the surgical decision-making surrounding oncoplastic and reconstructive breast surgery (Association of Breast Surgery at BASO et al., 2007; Agrawal, 2016b; Hamdi, 2013). However, the role of the non-surgical components of multidisciplinary cancer care is less frequently discussed in detail. In the setting of modern breast cancer multidisciplinary care the following are critical considerations:

- In appropriately selected patients OBS is safe without any significant compromise in oncological outcome with excellent cosmetic results and patient satisfaction.
- Radiation guidelines are based on traditional non-skin sparing mastectomies (Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al., 2014).
- The suitability for OBS should be assessed at a MTB with an oncoplastic-trained surgeon, medical oncologist, radiation oncologist, pathologist, genetics specialist and radiologist.
- In addition to patient factors and tumour biology, the likelihood of radiation and chemotherapy should be considered in surgical decision-making. Patients should be clearly educated and patient decision aids developed.
- PST should be considered in patients with highly chemo-sensitive tumours, although even this may not allow for significantly smaller resection volumes which should be identified prior to chemotherapy.

- Additional considerations should be given to the possibility of inherited mutations like BRCA and potential additional prophylactic surgeries if an inherited mutation is found.
- Close collaboration between radiologists, oncoplastic surgeons and pathologists is required so that margins, and multiple tissue specimens are understood and orientated.
- In the setting of OBS, the tumour cavity site must be marked with clips with interdisciplinary input, and radiation oncologists are encouraged to utilize published guidelines for delineation e.g. those published by GEC-ESTRO (Strnad et al., 2018), and to audit local results.
- The timing and sequencing of chemotherapy and RT are important and have implications for reconstructive complications, especially in the setting of implant-based reconstruction.
- Modern patient-centred breast cancer care involves close dialogue and collaboration between all disciplines involved in multidisciplinary care, paying attention to cosmetic outcomes while heeding the imperatives of optimal oncological care.

11. Conclusion

In the era of modern cancer care, treatment decisions should not be made in isolation. True multidisciplinary care requires upfront discussions between oncological and plastic surgeons, pathologists, imaging specialists, genetics specialists, radiation and medical oncologists. It is also critical that at a time of fear and uncertainty, patients are afforded adequate information as to the treatment options available to them to optimise both cancer and cosmetic outcomes without any compromise. Importantly, it should be recognised that for many evolving therapeutic interventions long-term outcome data remain limited in quality, quantity and consistency. While awaiting maturity of these data we recognise that clinical uncertainties and controversies remain. We are convinced that the integration of the OBS topic into the MTB can help to individualise and improve treatment plans for breast cancer patients including an optimisation of oncological and cosmetic outcomes. As the various components of breast cancer care evolve we suggest that each centre develops a system that allows them to monitor and evaluate outcomes as part of multidisciplinary care, integrating oncoplastic and reconstructive interventions into planned care pathways for the benefit of patients.

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Conflicts of interest

None

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