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## Over surgery in breast cancer

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## ABSTRACT

Breast surgery remains the original and most effective ‘targeted’ therapy: excision of early cancer is curative and for more advanced disease surgery improves local disease control. However in well intentioned pursuit of cure and local disease control, some cancers are over-treated resulting in major physical and emotional morbidity.

Less breast surgery is safe, as evidenced by steady reductions in mortality and local recurrence; earlier diagnosis and widespread use of systemic therapies and radiotherapy have allowed more conservative surgery. As tumour biology dictates cancer outcomes not surgery extent, surgery can safely be ‘minimum required’ rather than ‘more is better’ with the focus on removal of disease rather than healthy tissue.

Surgeons can reduce the burden of surgery further but it is important that less surgery is not over-compensated by more radical or unnecessary systemic therapies and/or radiotherapy with their own toxicities and morbidity. We all need to be alert to the potential drivers of over treatment and over surgery such as failure to work within a multidisciplinary team, failure to design a multimodality treatment plan at diagnosis or overuse of novel assessment technologies of uncertain clinical utility. Pursuit of wide margins and the removal of the contra-lateral healthy breast for marginal risk-reduction gains are also to be discouraged as is routine local/regional surgery in stage 4 disease.

The surgeon has a pivotal role in minimizing breast surgery to what is required to achieve the best oncological, functional and aesthetic outcomes.

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## 1. Introduction

Breast cancer (BC) accounts for a quarter of female cancers [1] but as the result of better treatment fewer women in Europe are dying and in the UK just under 80% of women are alive a decade after diagnosis [2]: this is on a background of less (radical) surgery as surgeons embraced the multimodality approach to BC treatment and led multidisciplinary team (MDT) working. The primary goal of BC surgery is local disease control with the aim of achieving cure but other desirable outcomes include: better survival, reduction in risk of distant metastases and local recurrence, good cosmesis, relief of symptoms and crucially a return to a quality life as close as possible to that before diagnosis. With declining mortality and extended survival for advanced and metastatic cancers, limiting the impact of surgical morbidity is essential for high quality long-term

survivorship. Treatment morbidity is burdensome to the patient and escalates healthcare costs and for a disease that is reaching pandemic proportions this is neither desirable nor globally sustainable. In addition preservation of form (cosmesis) and function are increasingly important and should no longer be regarded as a necessary sacrifice.

As BC treatment becomes more individualised, not only tailored to the disease but also the patients age, natural life expectancy, preferences and values, we need to pay more attention to treatment ‘trade-off’ where the marginal gains (for a few) are outweighed by the harms (to the majority). For patients and surgeons the dilemma is deciding what percentage of absolute benefit is the morbidity of extensive surgery (un)acceptable. Unambiguous data on individual recurrence risk and treatment benefit is not yet available to guide the most appropriate use and extent of surgery, although improvements in predictive tumour genomic assays and targeted use of systemic therapies may hold the key longer term.

Localised low risk (Luminal A like) cancers probably require little more than targeted disease excision and for wide-spread

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disseminated disease surgery should be limited to managing symptomatic local disease. Where the primary role of surgery needs to be urgently and rapidly re-evaluated is for the higher risk (as determined by stage, biological tumour subtype and genomics) but early and potentially curable BC. For these cancers the multimodality treatment plan can function as a surgical tool, allowing surgeons to modulate the extent and requirement for surgery through the careful integration and sequencing of surgery with the other therapies. Fully exploiting the multimodality approach is crucial to limiting oversurgery in the breast and axilla. It is important however that the often visible harms of surgery are not simply swapped for another set of less immediately obvious treatment related morbidities such as radiation or anthracycline induced cardiac disease: less surgery must not mean more untargeted radiotherapy (RT) and/or systemic therapies, especially if chasing marginal or uncertain benefits. The association between the trend for less surgery but more extensive loco-regional RT with very modest improvements in outcomes [3] is not clear, particularly with the increasing use of systemic therapy [4] and is addressed elsewhere in this publication.

Patients must also understand and believe that less surgery is safe, but rational analysis of recurrence risks and treatment benefits and harms is challenging when overwhelmed by fear of recurrence and death. Fear of not doing enough now (anticipated regret) drives both the patient and surgeon towards more radical treatment/surgery [5,6]. For the surgeon fear that as a consequence of my (in) action, my patient may suffer the terrible consequences of uncontrolled local disease are powerful influencers towards 'just in case' radical surgery, but surgeons can alter practice safely when supported by MDT working and high quality, national and international guidelines. Surgeons can support patients in choosing optimal treatment by providing clear information about treatment gains and harms and giving time for discussion, emphasising that taking time to formulate the best integrated treatment plan is of more value than rushing into any treatment.

## 2. Reducing breast surgery for invasive cancer

### 2.1. Multidisciplinary working

Multidisciplinary team (MDT) working is essential to establish the ideal balance between treatment benefits and harms through amalgamating clinical experience and evidenced based knowledge into objective but individualised treatment recommendations at diagnosis. Although there is scant evidence that MDT working translates into measurable outcome benefits [7] as the relationship between tumour biology, disease heterogeneity and treatment options become more complex, formulating an early coherent treatment plan becomes ever more necessary, requiring input from radiologists, pathologists, surgeons, oncologists and nurse specialists. Good communication and close working between surgeons and the wider cancer team is ever more crucial to maximise the benefits that can be gained from adjusting the sequence of surgery with other therapies. Referring patients to the oncologists after primary surgery is not MDT working and may deny patients the benefits of primary systemic therapies (PST). This is illustrated by the fact that PST is underutilised: in 77,000 post-menopausal women being offered endocrine therapy in only 3% it was given as primary therapy (PET) [8] and of 95,000 women receiving chemotherapy in only 13% was it given as primary therapy (PCT) [9]. Working with the MDT at diagnosis may avoid oversurgery and is crucial to limit the totality of treatment burden regardless of modality.

### 2.2. Be aware of the potential for advancements in medical imaging to drive oversurgery [10]

As tempting as it is, do not look too hard for occult, early, low volume breast and axillary nodal disease. Modern technologies are effective and will always detect more occult loco-regional disease but up-staging risks driving more extensive surgery with little evidence it has or will further reduce mortality or loco-regional recurrences (LRR). Current mortality reductions and low LRR of 2–5% at 10 years [11] have been achieved using relatively 'low-tech' mammography and ultrasound to assess disease extent, reinforcing that residual low volume occult disease in the breast and axilla is treated by adjuvant therapies. Emerging technologies must be welcomed but require careful evaluation of clinical utility before being routinely employed.

Breast MRI should not be part of the standard diagnostic work-up. MRI detects additional low volume disease and alters surgical recommendations towards more radical surgery and MRI uncertainties may be one of the drivers for bilateral mastectomy (BMx) but MRI use has not shown a survival gain or reduction in LRR, even for invasive lobular cancer [12]. To avoid oversurgery, criteria for breast MRI need to be defined by each MDT with MRI mainly reserved to define the extent of the dominant disease and aid surgical planning for non-concordant clinical and standard imaging assessment.

In response to high re-excision rates after breast conservation surgery (BCS) a plethora of innovative intra-operative devices using different technologies [13] such as MRI, ultrasound, tissue impedance etc have been developed to assess tumour presence at the specimen resection edge and/or tumour cavity to then allow immediate re-excision. These new technologies are undoubtedly interesting but device utility is not yet established and the usual caveats regarding more comprehensive margin assessment driving removal of more tissue than is required and potentially reducing cosmetic outcomes with minimal oncological gains, apply.

### 2.3. Limit the need for mastectomy: aim for breast conservation where possible

Landmark level 1 trials with 20 year follow up have demonstrated that breast conservation surgery with whole breast radiotherapy (BCT) has equivalent oncological outcomes to mastectomy [14]. Systemic therapies have a powerful impact on local disease control and risk of LR is related to the inherent biological aggressiveness of the tumour as reflected in tumour subtype, not the extent of surgery [15]. Breast conservation (when compared with mastectomy) results in better patient satisfaction with lower psychological morbidity, less anxiety and depression and improved body image, sexuality, self-esteem [16]. Whilst respecting patients' values and treatment preferences, BCS should be the default recommendation where appropriate and the 2013 St Gallen conference found very few absolute contraindications to breast conservation other than failure to achieve clear margins [17].

In view of the above factors it is difficult to explain the large variations in mastectomy rates (and therefore BCT) across Europe: from 20% in France to 50% in the Netherlands for similar disease characteristics and stage [18]. In the 2013 UK NHS breast screening audit of 17000 invasive cancers, mastectomy for small tumours of <15 mm ranged from 2 to 21% [19]. Some variability is inevitable and will reflect patient preferences, breast size and limited access to radiotherapy (RT). Some variation will be less justifiable, for example: surgeon preferences (more must be better) [20], breast MDT's not considering/adopting/accepting oncoplastic surgery techniques for larger tumours and/or not utilising PST to downsize and facilitate conservation.

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