

Surgery after Neo adjuvant
chemotherapy:
New Rules for large
cancers

Dr C Benn



Background

- The importance of systemic nature of breast cancer was recognized as early as Hypocrates (400 BC),
- In the 1940's Haagenson and Stout described criteria for operability and recognized that cancers with certain features could not be cured by even the most radical surgery.
- Preoperative, neo adjuvant or primary systematic therapy (PST) refers to the administration of chemotherapy before loco regional treatment with surgery and/or radiation

Facts

- Primary chemotherapy is the gold standard for locally advanced breast cancer,
- Now being used for operable stage 3 and stage 2 breast cancers that desire breast conserving surgery. .
- In South Africa 60% of tumours are classified as locally advanced. The use of breast conserving surgery in this group needs to be addressed.
- The vast majority of our patients should be receiving primary chemotherapy.

NSABP B-18 trial

- Preoperative chemotherapy is a reasonable alternative for patients with operable breast cancer who wish to have less-extensive surgery.
- The rate of successful breast-conserving surgery correlates with clinical response of the primary tumor (patients who experience a complete clinical response have a 90% chance of successful breast-conserving surgery.)
- Patients who were under 50 years of age show a greater survival benefit from preoperative rather than postoperative chemotherapy.
- NSABP B-18 study also has a marginally significant increase in local recurrence in patients who were converted from proposed mastectomy to lumpectomy after preoperative chemotherapy, (at 9 years, it was 15.9% compared with 9.9% in preoperative patients)

Assessing response to chemotherapy

- Clinical
- ~~Radiology~~
- Pathologically

Rule 1

- The initial assessment of the breast radiologically is pivotal to determining use of breast conservation



The role of surgery

- The role of surgery after neo adjuvant chemotherapy in patients with LABC is to ensure local control.
- Radiation therapy (RT) alone, especially in cases of complete clinical response cannot control residual microscopic disease, (most studies report a much higher rate of local recurrence (30%) with RT only).
- Postoperative complications are not increased with the use of preoperative chemotherapy.



Rule 2

- Successful use of the incorporation of primary chemotherapy requires a coordinated multidisciplinary approach

Rule 3

- Types of surgical procedures that need to be discussed after primary chemotherapy are the use and indications for mastectomies, breast conservation surgery, and reconstruction (immediate and delayed)
- This discussion starts prior to chemotherapy

What do you know

- The standard surgical therapeutic option for patients for patients with stage 1 and 2 breast cancer in the 21-century is breast conservation with radiation therapy.
- The change is well supported by level 1 and 2 research data and is not just the thrust of women empowerment groups and patient promotion.
- Central to the acceptance of breast conservation is the prerequisite understanding that there is preservation of a normal appearing breast. Breast conserving surgery should therefore be considered both an oncological as well as cosmetic

Mastectomy

- persistent skin oedema,
- extensive inflammatory lymphatic invasion
- lobular carcinoma.
- inflammatory breast cancer,
- extensive microcalcifications throughout the breast,
- multifocal disease in separate quadrants of the breast;
- In our unit subset analysis reveals patients with DCIS surrounding the tumour are more likely to have loco-regional recurrence



Breast conserving surgery

Tumour Size

- several publications support that local resection should be practiced irrespective of the size of the tumour (the critical issue is not the size of the tumour but the relationship to the size of the breast).
- The EORTC 10801 with 5569 patients with stage 1 or 2 breast cancer showed no impact on survival when practicing local excision on tumours more than 5 cm.
- In terms of local recurrence, it has been well shown that boosting of the tumour bed during radiation therapy **decreases the chance of local recurrence irrespective of the size of the tumour.**
- It should be noted that breast conservation surgery on large tumours usually requires some form of onco reconstruction to maintain a good aesthetic result

Margins

- The question as to what the required margin should be macroscopically and microscopically does not have consensus..
- intra-operative pathology can aid the surgeon

Rule 4

In our unit a minimum margin of 10mm is excepted in women over 35 and 20mm in women under 35

The average margin is 15mm

??????

- The unanswered question as to what the resection volume in patients undergoing breast conserving therapy post primary adjuvant therapy will be addressed by watching the recurrence rate in these patients.
- A suggestion of wide local excision with good documentation in trials of both macroscopic and microscopic margins will aid the setting of guidelines. So this answer remains elusive as we wait for long-term follow-up on these patients.
- However analysis of the data to date shows no increase in loco-regional recurrence.

Local Recurrence

- The main determinants of local recurrence in breast conserving surgery are the following;
- residual tumour, positive margins(R1 and R2),
- residual malignant micro-calcifications on mammogram ,
- extensive intraduct component with positive margins,
- lymphatic vessel invasion, vascular invasion ,
- high proliferative rate
- young age less than 35 year

- Studies evaluating local recurrence after neo adjuvant therapy and BCT have shown conflicting results.
- Three large, randomised, prospective trials comparing preoperative or postoperative chemotherapy did not demonstrate a difference in local recurrence
- except in those patients with positive margins, young age and significant residual disease

In our unit

- breast conserving surgery post primary chemotherapy is reserved for a select group of patients who have a good clinical and radiological response to chemotherapy.
- Its use is increased by 5 -27% when primary chemotherapy is used.
- Pre-treatment placements of clips and coils improves subsequent localisation particularly if a significant response occurs,
- Adequate localization of the tumour for BCT would have not been possible in > 30% of cases without the preoperative placement of a tissue clip.

In our unit

- At the time of definitive segmental mastectomy (wide local), the tissue resected must include all residual palpable and radiographic abnormalities.
- Not all of the initial tumour volume needs to be excised but all residual radiological and palpable disease should be excised,
- Meticulous assessment of margins is imperative
- Pathologically negative margins remain essential, just as in patients who have not had preoperative chemotherapy.
- Again in our unit a minimum margin clearance of 10 mm at time of intra-operative pathological assessment is the rule

Axilla

- The axilla is down staged in 25% of the cases that have primary chemotherapy and optimal staging and treatment of the axilla is undergoing re-evaluation
- The use of sentinel lymph node biopsies (SLNB) is controversial
- Theoretically fibrosis in lymphatic channels and chemotherapy changes in the SLN may result in difficulty identifying the SLN and higher false negatives.
- Identification rate in the studies demonstrated range from 84% to 98% with a accuracies of 77% to 100% and false negatives of 0% to 33%..

In our unit

- ultrasound assessment and guided core biopsies .The ultrasound sensitivity with a good operator is above 97%. (number of nodes are counted)
- In the ultrasound node negative axilla SLNB prior to chemotherapy with a 4 lymph node sampling

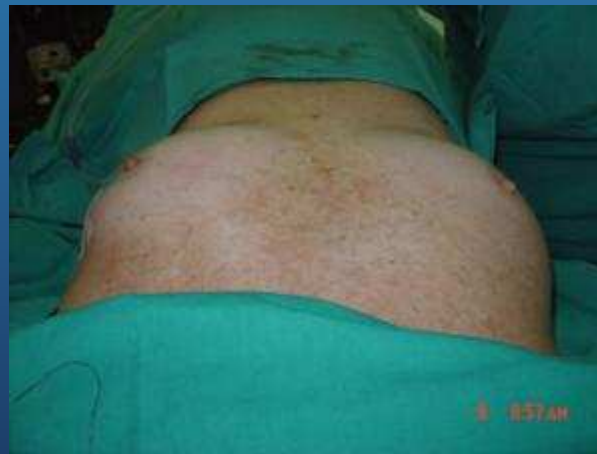
Why

The level of radiation and need should be determined prior to starting chemotherapy

Reconstructive surgery

- Breast reconstruction after mastectomy or breast conservation for breast cancer is now a standard option offered to women.
- Many studies have demonstrated the oncological safety of immediate breast reconstruction with no increase in local recurrence or difficulty in detecting recurrence.
- In patients requiring radiation no prosthetic material, or TRAM flap reconstructions are done
- (It is not because you can't ...ensure the lowest complication rate)





the use of stringent guidelines is strictly adhered to.

- Pre-operative tumour size (clinically, radiologically)
- Nodal assessment is carefully determined prior to any treatment as this influences the level of radiation and type of reconstruction offered to the patient
- All patients requiring radiation therapy as per international guidelines i.e. all locally advanced breast cancers prior to chemo; more than 3 nodes positive do not get prosthetic reconstruction
- intra-operative margin assessment
- Onco reconstructive procedures for all patients receiving breast conservation (either volume replacement or volume displacement)

Unit Data

- In our unit of 8000 active patients, and 2200 cancer patients, (180 patients underwent primary chemotherapy) the data of patients undergoing breast conserving surgery is recorded and local recurrence rates are similar in those having surgery post primary chemotherapy to those patients having breast conserving surgery and adjuvant treatment



Conclusions

- The use of primary chemotherapy both as a gold standard for locally advanced breast cancers and for select patients with pre-operative large tumour to breast ratios and radiologically extensive nodal disease is an important therapeutic addition to the specialist management of breast cancer.
- Close multidisciplinary communication and team assessment is imperative in these patients.
- **Surgical therapy is an essential component for treatment and breast conservation, with reconstructive procedures can be offered to these patients safely.**