



## **1. Screening, Diagnosis and Surgical Management of Breast Cancer**

*Dr Melanie Walker, MBBS, FRACS (Breast Surgeon)*

### **Oncoplastic Breast Surgery**

- Combination of optimal cancer surgery with plastic surgical techniques to achieve the best oncological and aesthetic outcome after breast surgery
- The aim: to improve women's long term quality of life and body image after breast cancer treatment
- Involves a range of simple through to complex rearrangements of breast volume (volume displacement)
  - Includes therapeutic mammoplasty
- Or breast volume replacement, where adjacent or remote tissues are used for various types of flap reconstructions to maintain breast shape

### **Types of Mastectomy**

- Radical
- Simple
- Skin sparing
- Nipple sparing (total skin sparing)
  - Prophylactic/risk reducing surgery
  - Therapeutic
  - Local recurrence after therapeutic NSM <5%
  - <1% cancer in retained nipple after risk reducing NSM
  - Partial necrosis up to 16%
  - Full necrosis up to 8%

### **Breast Imaging**

- Women with breast symptoms should be referred for diagnostic imaging assessment, **not** to a breast screening service

### **Screening Mammography**

- Patient should be asymptomatic
- Generally, the radiologist does not see films until the patient has left the radiology department

### **Diagnostic Mammography**

- Patients with breast signs or symptoms (palpable lump, pain, nipple discharge)
- Patients with abnormality detected on screening mammogram
- Performed under the supervision of a radiologist
- Additional specialized mammographic views +/- US



## **Breast Density**

- Cannot be predicted based on physical exam
  - Unrelated to breast size or consistency
- More common in younger women during breast feeding, women using hormone replacement therapy
- 60% of women under 50, 40% of women in their 50s and 25% of women in their 60s have radiographically dense breasts
- Sensitivity and specificity reduced
  - Sensitivity 33-81%
  - False positives increased
- Breast density is a significant independent risk factor for breast cancer
  - 4-5x relative risk

## **Breast MRI**

- Very high sensitivity for the detection of breast cancer (>90%)
- Vast majority of malignant lesions enhance
- High NPV
- Lower specificity
  - ~30-60% PPV
- Some benign lesions enhance
- Normal breast parenchyma may enhance
- Low PPV
- 6 prospective non-randomized trials in high risk women (20-80% lifetime risk)
- Sensitivity 71-100%
  - vs. 16-40% with mammo or US
- Specificity lower than mammo in all trials
  - Call back 8-17%
  - Biopsies 3-15%
- No mortality/survival data
- No RCTs

## **Limitations and Problems**

- Contra indications-METAL
- Patient claustrophobia/noisy/obesity/prone position
- Pregnancy – gadolinium contrast contra indicated
- Breast feeding – cease for 24 hours
- IV line
- Time consuming – 25 minutes
- Scheduling difficulties (day 6-16 menstrual cycle)
- Expensive
- Limited equipment



- Limited trained technologists
- Need expert, experienced interpretation
- MR guided biopsy time consuming

### Indications for Breast MRI

- Screening for breast cancer in young high risk women
- Assessment for women with a new breast cancer diagnosis for:
  - Assessment of extent of disease (local staging) in women with a recent breast cancer diagnosis
  - The role of MRI in this situation is controversial:
    - It can estimate tumour size and diagnose unsuspected multifocality/multicentricity with a high sensitivity
    - May lead to more extensive surgery without definite evidence of benefit
  - Screening the contralateral breast for cancer in women with a recent (ipsilateral) breast cancer diagnosis (the role of MRI in this situation is also uncertain)

### Other Uses of Breast MRI

- Assessing the integrity of breast prosthesis
- Assessment of the breast in occult primary breast cancer
- Monitoring response to neo-adjuvant chemotherapy in women with breast cancer
- Problem solving: e.g. scar vs. recurrence in treated breast, lesion characterization (multiple or indeterminate on US/mammo)

### **Digital vs. Film Mammography**

- Both use x-rays

#### Film

- Image captured on film

#### Digital

- Image captured electronically and stored digitally
- Viewed directly on a computer, radiologist can alter contrast/brightness/magnify without additional x-rays
- Digital more expensive
- More accurate than film in those:
  - <50 years of age
  - Perimenopausal or premenopausal
  - Dense breast tissue



### *Studies*

- 4 major prospective studies comparing clinical results of digital vs. film-screen in breast cancer detection
- No study has shown statistically significant difference in breast cancer detection
- No study has evaluated the effect of digital mammography on breast cancer mortality

### *Potential Advantages*

- Greater contrast resolution
- Storage issues
- Post-processing image enhancement
  - Alter contrast
  - Alter brightness
  - Magnify
- Reduced recall rate
- Slightly lower average dose
- More speed of image acquisition, display, retrieval
- Added applications: PACS, teleradiology, CAD

### **Tomosynthesis**

- Uses modified digital mammography unit to create 3D images
- 3D principle of operation
  - X-ray tube moves in an arc across the breast
  - A series of low dose images are acquired from different angles
  - Total dose approx. the same as one 2D mammogram
  - Projection images are reconstructed into 1mm slices
- Prelim studies suggest tomo has the potential to decrease the no. of recalls & possible to improve cancer detection rates (improve sensitivity)
- Increased reading time
- Potential to reduce compression force
- May improve cancer detection by mammography by enabling readers to detect lesions which are very difficult or impossible to visualize on conventional imaging due to overlying glandular tissue
  - Major factor contributing to the limited performance of mammography: tissue superimposition that is created by the overlap of normal breast structures in a two-dimensional mammographic projection
  - These overlapping structures can obscure a lesion making it more difficult to perceive or rendering it completely mammographically occult



## **2. Recent Developments in Radiation in Management of Breast Cancer**

*Dr David Blakey MBBS, FRANZCR (Radiation Oncologist)*

### **Altered Fractionation**

#### Hypofractionated RT

- Started as an empirical practice in government-run health care systems of UK and Canada
- Initially, a purely logistical exercise to reduce treatment duration & create machine space
- Recently, 2 large trials, START-A and START-B, have validated that clinically as well, hypofractionated RT is safe and effective
- In fact, even while delivering a lower BED, the hypofractionated regimens have shown a survival advantage over conventional fractionation

#### ASTRO 2008 Plenary

- Canadian trial 1993-1996
- N= 1234 women
- 42.5Gy in 16# vs 50Gy in 25#
- Median follow up – 12 years
- Local recurrence at 10 years – 6%
- Excellent cosmesis at 10 yrs – 70%
- No difference between 16 and 25 fractions

#### START-A (1998-2002)

- 1998-2002
- N=2236
- EBC (pT1-T3a, pN0-N1, M0)
- BCS=1900 (85%) & MRM = 336 (15%)
- Locoregional relapse rates were 3.6%, 3.5% and 5.2%, respectively
- Late effects, based on photographs and patient assessments, were significantly lower with 39Gy as compared to 50Gy
- 3 Arms:
  - 50Gy/25#/5 weeks
  - 41.6Gy/13#/5 weeks
  - 39Gy/13#/5 weeks
  - Median FU = 5.1 years

#### START-B (1992-2001)

- N=2215
- EBC (pT1-T3a, pN0-N1, M0)
- BCS=2038 (92%) & MRM = 177 (8%)



- Locoregional relapse rates were 3.3% and 2.2%, respectively
- Absolute differences in locoregional relapse was =0.7% (95%CI-1.7% to 0.9%), meaning that with 40Gy the relapse rate would be at most 1% worse and at best 1.7% better

### **Partial Breast Irradiation**

- Conform RT to uniformly cover lumpectomy cavity plus 1-2cm margin
- Minimal RT to normal uninvolved breast
- Provide comparable tumouricidal RT dose as conventional whole breast irradiation
- Deliver homogenous dose:
  - Optimize cosmetic result
  - Avoid fibrosis and fat necrosis

### Rationale

- Approximately 90% of tumour recurrence is local in the vicinity of lumpectomy cavity
- Concentrates radiation on the most likely area for tumour recurrence
- Recurrences away from tumour bed (elsewhere failures) appear unaffected by whole breast radiation therapy

### Benefits

- Accelerated radiation therapy decreasing treatment time from 6 weeks to 4-5 days
- Consistent and reproducible dose distribution and delivery
- Eliminates cardiac/pulmonary dose
- Reduced skin reaction in large breasted patients

### Advantages of Breast Brachytherapy vs. External Beam RT

#### *Breast Brachytherapy*

- 5 days (10 fractions)
- Dose is higher to tissue at greatest risk for sub-clinical malignant cells
- Reduction in skin, cardiac and lung dose
- Ideal for patients who live far from RT centre
- Convenient
- May increase number of women treated with BCT

#### *External Beam RT*

- 6 weeks (30 fractions)
- Homogeneous dose
- Logistical problem for patients



- Difficult for frail, elderly, or chronically ill patients
- Interferes with schedule of working women
- Some BCT candidates will opt for mastectomy

### Disadvantages of PBI vs. EBRT

#### *PBI*

- Invasive
- Not useful for treatment of nodal basins
- May miss tumour foci in other quadrants
- Low, but definite risk of infection and/or fat necrosis
- Requires special skills for performing; in placing catheters and dosimetry

#### *EBRT*

- Non-invasive
- Can cover nodal regions
- Treats multi-centric carcinoma
- Low complication rate
- Linear accelerators widely available
- Most radiation oncologists experienced

### **Respiratory Gating**

- Trilogy includes the RPM Gating System
  - Infrared camera
  - External marker block
  - Gating workstation
- Process
  - Place block on patient's abdomen
  - Camera monitors block motion
  - Respiratory waveform shows how the block moves
  - User sets upper and lower thresholds; the beam is on
  - Whenever the block moves outside the thresholds; the beam is off
  - Free-breathing and breath hold protocols are supported, as are gating at inhalation or exhalation or at any other point in the respiratory cycle



### **3. Systemic Therapy of Breast Cancer, Including Recent Developments**

*Dr Min Ne Wu MBBS, FRACP (Medical Oncologist)*

- Population risk for breast cancer for Australian women: 12%
- New diagnosis of breast cancer (2015): ~16000 cases
- Breast cancer accounts for 12% of all cancer diagnosis in Australia each year
- Breast cancer specific mortality (2015): ~3000 deaths

#### **Systemic Therapy**

##### Primary prevention

###### *Tamoxifen*

- When taken preventively daily for 5 years, reduces risk of developing breast cancer in Australian women, who are at increased risk of breast cancer, by more than 30% over 20-year period
- PBS listed for this indication recently

##### Neo-adjuvant therapy

##### Adjuvant therapy (secondary prevention)

###### *Endocrine therapy*

- Pre-menopausal women with hormone receptor positive, HER 2 negative breast cancer
- Exemestane plus ovarian function suppression vs. Tamoxifen alone
  - 10-15% improvement in 5 year breast cancer free interval in high recurrence risk group
  - At least 5% improvement in intermediate risk group
  - Minimal improvement for low risk group

###### *Extended endocrine therapy*

- After 5 years of Tamoxifen, additional 5 years of Tamoxifen or Aromatase Inhibitors (AI)
  - Reduces distant recurrence, new primary breast cancer
  - Improves disease free and overall survival
  - Benefit particularly after year 10
- After 5 years of AI, additional 5 years of AI
  - Reduces the risk of recurrence and new contralateral breast cancer
  - Improves disease free survival
  - No difference in overall survival
- No direct comparison using AI vs. Tamoxifen as extended endocrine therapy after 5 years of Tamoxifen





- Toxicities:
  - Extended Tamoxifen vs. Placebo
    - Increased incidence of endometrial cancer and pulmonary embolus
    - Reduced rate of ischaemic heart disease
  - Extended AI vs. Placebo
    - Increases risk of bone-related toxicity

*Targeted therapy (Anti-HER 2 therapy)*

*Chemotherapy*

Metastatic breast cancer

*Endocrine therapy*

*Targeted therapy (Anti-HER 2 therapy)*

- Trastuzumab (Herceptin) - Monoclonal ab
- Pertuzumab (Perjeta) – monoclonal ab
- Lapatinib (Tykerb) – tyrosine kinase inhibitor

*Chemotherapy*

Immunotherapy

- In clinical trial