

Rotorua GP CME 2012

Genetics

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Breast Surgeon

Genes Known

- BRCA1 : breast, ovary :men prostate
- -BRCA2 : Breast Ovary Male breast ,prostate, pancreas
- Tp53b breast bone or soft tissue
Many other sites brain lung adrenal
- Mismatch repair genes

Genes



- Chromosome 17 BRCA1
- Chromosome 13 BRCA2
- Colorectal close on chr 17

Breast cancer & family history



-5-10% women with breast cancer

- Increased risk of breast/ovarian Ca
Breast Ca 60-80% lifetime risk

- Identify at risk, as screening altered
National Breast And Ovarian Cancer Centre
www.nbocc.org.au/

At or slightly above risk 95%



- No confirmed family hx
- One 1st degree relative >50yrs
- One 2nd degree relative any age
- Two 2nd degree rel same side > 50
- Two or one 2nd degree rel > 50yrs different sides

Treatment advise low risk



- Clarify risk
- Same as general population
- Most will NOT get breast cancer
- Risk increases with age
- Check factors you can change

Moderately increased risk <4%



- One 1st degree rel < 50yrs
- Two 1st degree rel same side
- Two 2nd degree rel same side but one under 50yrs
- 1 in 8 to 1 in 4 chance

Treatment advise moderate risk

- Most will NOT get cancer breast
- <50yrs 1st degree rel annual mammo if >40yrs
- Discuss tamoxifen
- Clinical trials
- Other risk factor
- (early babies breast feeding etc)

High risk family history



➤ 2 or more 1st/2nd degree relatives on the same side of the family <50 breast or ovarian

+ 1 or more high risk features:

<40 at diagnosis

bilateral breast cancer

Male breast cancer relative

breast and ovarian Ca in same pt

Ashkenazi Jewish ancestry

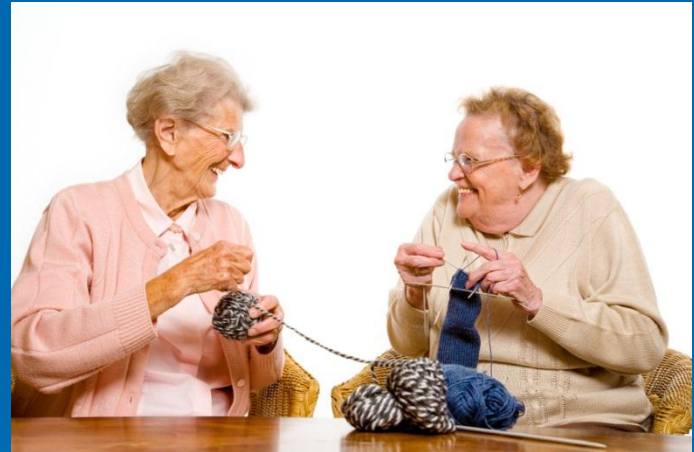
Treatment advise High Risk



- Referral to Family History Clinic or genetic counselling
- Discuss risk reduction surgery
- Discuss Tmx
- Trials
- Regular exam
- Mammography/ ultrasound/MRI
- Ovarian cancer risk

Risk Factors

- Increasing age
- Female gender
- Family History



Risk Factors



- INTRINSIC : endogenous hormones, familial genetic predisposition, benign breast lesions
- EXTRINSIC : exogenous hormones, geographic location, environmental exposure, diet

Breast Cancer : Facts



- Leading cause of death in women 30 to 50 yrs
- Leading cause of death from Cancer in non-Maori women
- Second after Lung Cancer in Maori women

Risk of developing Breast or Ovarian Cancer in next 10 years

Now aged	Breast	Ovarian
20	1 in 2500	1 in 3000
30	1 in 250	1 in 2000
40	1 in 70	1 in 900
50	1 in 40	1 in 450
60	1 in 30	1 in 300
70	1 in 30	1 in 200

Magnitude of Known Breast Cancer Risk Factors

Relative Risk < 2

- Early menarch
- Late menopause
- Nulliparity
- Age > 35 yr first birth
- HRT
- Obesity
- Alcohol use 1.4 times for each 24gm
- Prolif benign breast disease



Magnitude of Known Breast Cancer Risk Factors

Relative risk 2 to 4

- One 1st degree relative cancer breast
- Radiation exposure
- Prior ca breast
- Dense breast



Magnitude of Known Breast Cancer Risk Factors

Relative risk >4

- Two 1st degree relatives with cancer breast
- Gene Mutations
- LCIS
- DCIS

Atypical Hyperplasia

Risk Assessment Tools



- Gail Model
- Two breast biopsies prior to age 50yrs
- Any atypia ?
- At least one 1st degree rel
- First live birth age
- Age of menarche

Risk Assessment Tools



- Claus Model
- National Surgical Adjuvant Breast and Bowel Project (NSABP) to estimate a woman's risk of developing invasive breast cancer.
- BRACPRO
- Tyre-Cuzick

IMAGING HIGH RISK



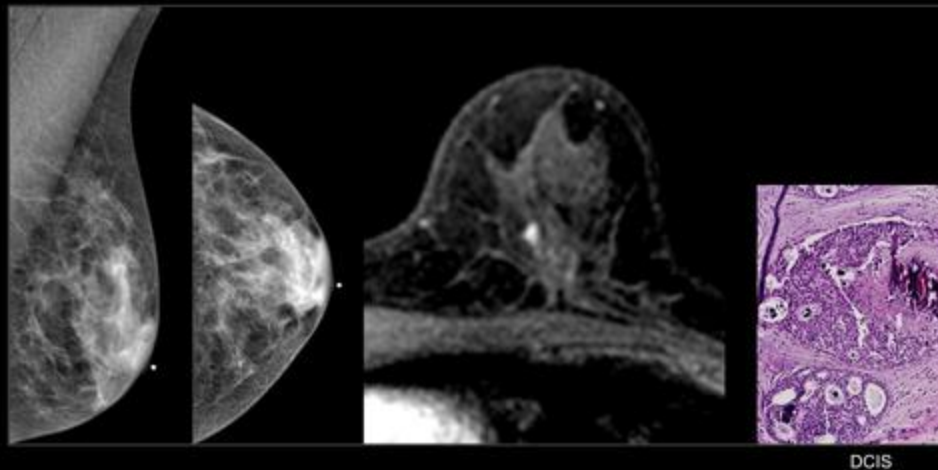
- Mammography 10 years prior to age of first relative 1 to 2 yrly
- MRI from age 30yrs annual
- Ultrasound for under 30 yrs

MRI Clinical Applications

- High Risk Screening
- Staging newly diagnosed breast cancer
- Positive axillary nodes ? Primary
- Close or positive margins post cancer excision
- Post Treatment evaluation
- Significant nipple discharge
- Monitoring Neoadjuvant Chemotherapy

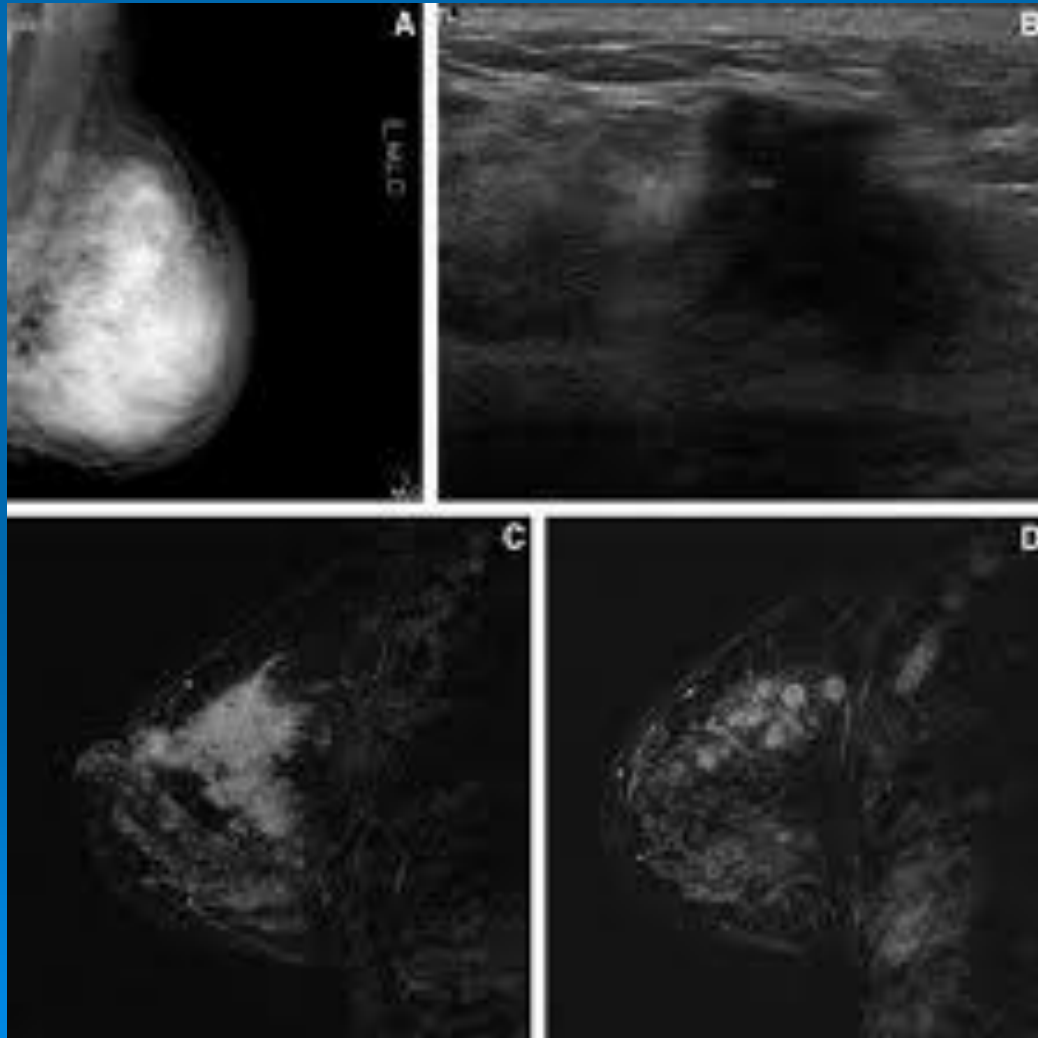
MRI

Breast MRI Screening



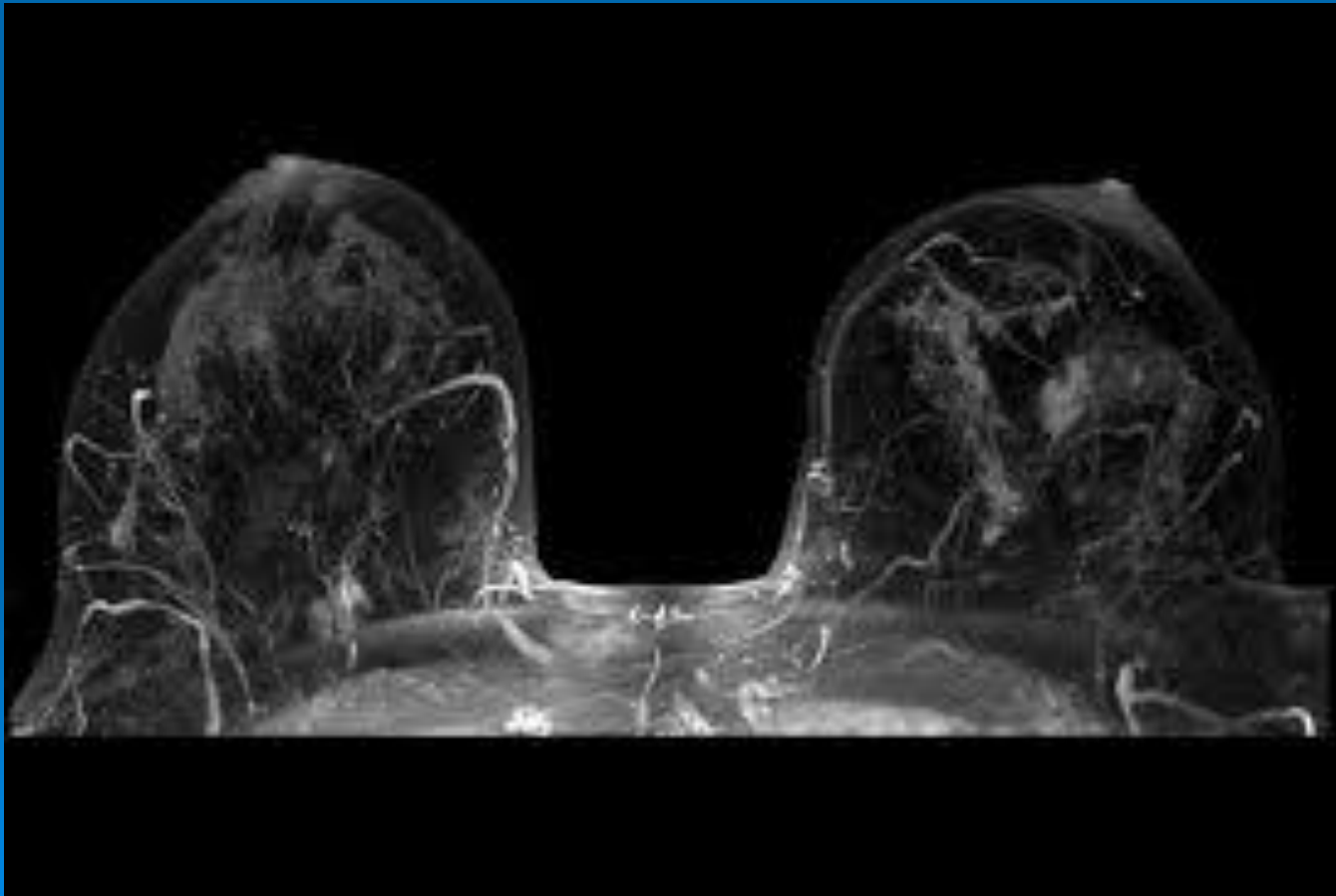
- A review of 10 studies using MR imaging as the screening method for high-risk women demonstrates a 3% prevalence for cancer detection at MRI for lesions occult at mammography.
- Sensitivity of 81% specificity combined with mammography of 92%.

MRI :Dense Breast clinical thickening



MRI

dense breasts ,young ,family history



Treatment High Risk

➤ Chemoprevention Tamoxifen

Aromatase Inhibitors

NSAPB 1 and 2

Side effects !



Treatment High Risk



Surgery

- Prophylactic mastectomy
Now nipple areolar sparing skin sparing
- Bilateral salpingo oophorectomy

Prophylactic Surgery



- BRCA1 or BRCA2
- Strong Family History
- Anxiety Overload
- Cancer Other Breast (Lobular)

Pre reduction strong family history



Previous reduction for Mastectomy



Post mastectomy implant alone



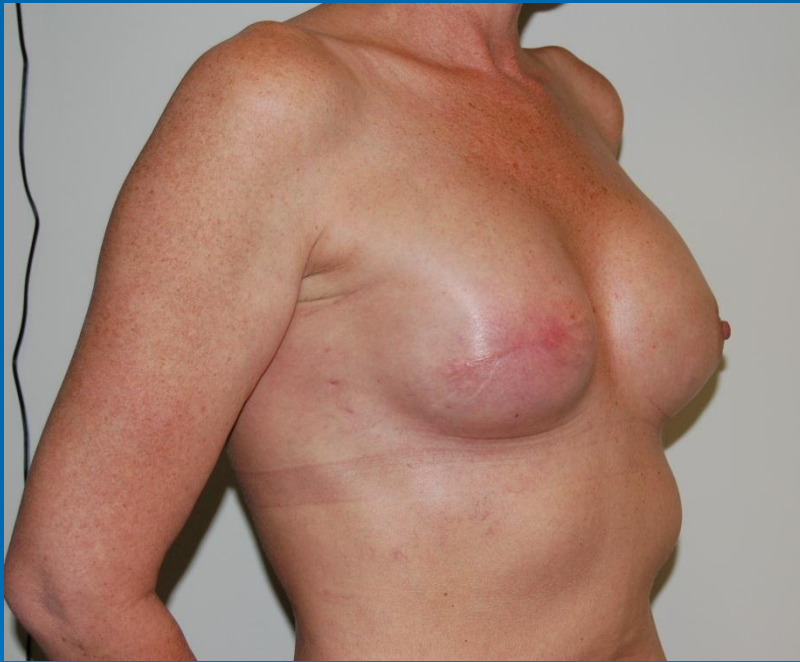
Prophylactic reconstruction



Prophylactic reconstruction



Post Implant Alloderm



Breast Cancer Tumour characteristics



Oncotype DX 21 gene signature

Mammaprint 70 gene signature

Stratify into low and high risk

Helps with treatment advise

10s to 1000s dollars

NEW tests



- UK ICH4
- Measures OR PR Her2 and Ki67
- Circulating tumour cells in the blood CTU
- Very early days

Current blood tests



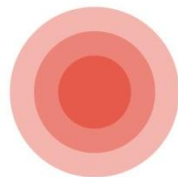
- Ca 15/3 Breast
- Ca/125 Ovarian
- CEA Colorectal Ovary
- PSA Prostate

DNA Oral testing



- Measures DNA from mucos
- Oral wash ONCOVUE
- Cheek swab
- Combine with lifestyle and risk factors
- May give an idea of risk in future

All aspects of breast care dealt with in a
caring and professional manner by our
multidisciplinary team.



BREAST
ASSOCIATES
for complete breast care



American Cancer Society Updated Guidelines

- MR screening is evidence-based and recommended for patients who meet 1 or more of these criteria:
 - *BRCA* mutation or *TPEN* of *TP53* gene
 - First-degree-relative *BRCA* carrier, but untested
 - 20%-25% or greater estimated lifetime risk by model
 - Radiation to chest between ages 10-30 yr; dose > 4 Gray (based on expert consensus)

MR screening beginning at age 30 as long as patient is in good health