Newly Diagnosed Breast Cancer: Preoperative Imaging and Localization

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no disclosures

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Preoperative Imaging

- stage disease index breast
- contralateral assessment
- axillary lymph node evaluation
- chemotherapy response
- localization for excision
Cancer Staging: Index Breast

- **diagnosis:** mammo/US (conventional)

- **extent of disease evaluation:**
  - ipsilateral tumor size and extent
  - surrounding structures
Cancer Staging: Index Breast

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MRI
MR-only additional disease

**additional lesions:** 16-20%

**additional malignancy:** 11-14%

MR biopsy capability lacking in many of these studies

20% from 50 studies, N=10,811 (Plana 2012 Eur Radiol)
16% from 19 studies, N=2610 (Houssami 2008 J Clin Oncol)
MR-only additional disease

- **2015 U.S** - 2021 CA patients, 2001-2011
  - 14% additional malignancy with MR

- **2015 Germany** - 1102 consecutive CA pts
  - 23% additional malignancy with MR

- **2015 Canada** - 2309 MR / 582 new CA pts
  - 34% additional malignancy with MR
MR-only additional disease

incidence of additional CA\(^\uparrow\) over time

additional lesions up to 45%

additional cancer up to 34%
Are additional lesions important? (beyond Mammo/US)

“NO – no MRI, don’t look for it”:

1. unlikely to affect prognosis (stage)
2. doesn’t help with surgical management
   - taken care of with radiation and chemo
Are additional lesions important? for prognosis (staging)

- not by the TNM system

- Tumor: sized only by the largest lesion
TNM Staging

• started in 1959

• absence of:
  – screening mammography
  – effective chemo
  – knowledge of tumor biology
Current TNM Staging fails to account for:

- tumor grade
- receptor status
- multifocal/multicentric disease

role in prognostication should be updated
Are additional lesions important?

- evaluation period 1963-2007
- 2 groups, 288 each
  - unifocal disease
  - multifocal/multicentric (mf/mc)
- matched for size of largest tumor
  as well as grade and hormone receptor status

Weissenbacher et al. BrCaResTreat 2010
Are additional lesions important?

<table>
<thead>
<tr>
<th></th>
<th>unifocal</th>
<th>mf / mc</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>local recurrence</td>
<td>7.3%</td>
<td>17.4%</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>distant mets</td>
<td>13%</td>
<td>21%</td>
<td>.004</td>
</tr>
<tr>
<td>relapse-free surv months</td>
<td>206</td>
<td>170</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>survival</td>
<td>222</td>
<td>203</td>
<td>&lt;.0001</td>
</tr>
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Weissenbacher et al. BrCaResTreat 2010
Are additional lesions important?

“NO – don’t look for it”:

1. unlikely to affect prognosis (stage)
## MR: Surgical Impact

2009-2012 meta-analysis
9 studies, N=3112

<table>
<thead>
<tr>
<th></th>
<th>MR</th>
<th>noMR</th>
<th>p</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>re-excision after BCS</td>
<td>11.6</td>
<td>11.4</td>
<td>-</td>
<td>0.95</td>
</tr>
<tr>
<td>overall mastectomy</td>
<td>25.5</td>
<td>18.2</td>
<td>&lt;0.001</td>
<td>1.5</td>
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</tbody>
</table>

# MR: Surgical Impact

## Newer Data 2013-2015

**PreOP MR in 123pts**

<table>
<thead>
<tr>
<th></th>
<th>MR</th>
<th>no MR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive margins</td>
<td>15.8%</td>
<td>29.3%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>re-operation rate</td>
<td>18.9%</td>
<td>37.4%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**PreOP MR in 348 pts***

<table>
<thead>
<tr>
<th></th>
<th>MR</th>
<th>no MR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>re-excision rate</td>
<td>29%</td>
<td>45%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

*controlled for surgeon

Sung et al. AJR 2014   Obdeijn et al. AJR 2013
MR: Surgical Impact

Newer Data 2013-2015

- new RCT 2014, Sweden
  - young women (<56 yo)
  - N=440 (220 each group)
  - lacking MR biopsy
MR: Surgical Impact

- new RCT 2014, Sweden

<table>
<thead>
<tr>
<th></th>
<th>MR group</th>
<th>NoMR group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>reoperation rate overall</td>
<td>5%</td>
<td>15%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>planned BCT reoperation</td>
<td>5%</td>
<td>22%</td>
<td>&lt;.0001</td>
</tr>
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</table>
Are additional lesions important?

“NO – don’t look for it”:

1. unlikely to affect prognosis (stage)

2. doesn’t help with surgical management
Are additional lesions important?

“NO – don’t look for it”:

1. unlikely to affect prognosis (stage)

2. doesn’t help with surgical management

evidence of re-operation with MRI
MR: Impact

- an asset in the newly diagnosed CA pt
- doesn’t help everyone
- benefits higher in some populations
MR: Impact

Invasive Lobular Histology

2014 population (SEER) based / ILC = 1928

MR = 40% reduction in re-operation rate for ILC

MR = without increasing mastectomy for ILC

Fortune-Greeley et al. 2014 Br Cancer Res Treat

MR: Impact

• benefits higher in some populations
  – invasive lobular carcinoma
  – other biology based?
  – other factors?
Who benefits most?

- Netherlands 2014
- N=685; all had MRI (2000-2008)
- most likely to have additional disease at MR vs conventional imaging?

Pengel et al. 2014 EurJRad
Who benefits most?

Significantly associated with add’l disease at MR:

• age
• preOp lym node positive
• Her2 positive
• tumor size discrepancy mammo v US
• presence of ILC

Pengel et al. 2014 EurJRad
Who benefits most?

Significantly more tumor discrepancy:

- younger patients

- heterogeneous or dense breasts

P<0.001 for both

Pengel et al. 2014 EurJRad
Who benefits most?

Any of these, do MRI:

- age under 60
- heterogeneously or extremely dense
- preOp lymph node positive
- mammo vs ultrasound discrepancy
- lobular histology

Pengel et al. 2014 EurJRad
Who benefits most?

• Netherlands 2014
• most likely to have additional disease?

- <60
- dense
- +ax ln
- mam≠US
- ILC

• Applied retrospectively: ↓20% in MRIs

7% of add’l CA would be undetected

Pengel et al. 2014 EurJRad
Who benefits most?

- Germany 2015
- N= 1102; all had mammo, US, MRI
- MRI only add’l cancers 23%
- most likely to have additional disease?

Debald et al. 2015 BrCaResTreat
Who benefits most?

- Germany 2015

Significantly associated with add’l ds at MR:

- Premenopausal
- ILC
- Heterogeneously or extremely dense

Debald et al. 2015 BrCaResTreat
Who benefits most?

- Germany 2015
- most likely to have additional disease?
  - premenopausal
  - dense
  - ILC
- Applied retrospectively: ↓ 32% in MR

Debald et al. 2015 BrCaResTreat
Who benefits most?

- U.S. 2014
- N=441

- Her2+ (ER PR +/-, Her2+)
  - more multifocal/centric
  - more lymph node mets

Grimm et al. 2015 Radiology
Who benefits most?

- Korea 2016
- Triple negative breast cancer (TNBC)
- N=398 with stage I or II

Independently associated with recurrence:

- absence of MR (HR 2.66)
- dense tissue (HR 2.77)

Bae et al. 2016 Radiology
Who benefits most?

- Canada 2015
- N=582; evaluated tissue density and MR

Additional disease at MR:

- extremely dense 5X more likely than fatty
- h/e dense 2X more likely than fatty/sfg

Occult disease in 33% of fatty breasts

Seely et al. 2015 Eur Radiol
Preoperative MR imaging

subsets of patients who will be most likely to have additional disease

- ILC
- age < 60
- dense breasts
- mammo/US discrepancy
- Her2+
- TNBC
- axillary node+
Cancer Staging: Index Breast

disease occult to conventional imaging is important

ignoring it is not a viable option
Summary:

PreOP Eval New Breast Cancer

Staging the Index breast

- finding more disease, must manage it
- important for treatment, likely prognosis
- MR directed at those who benefit most
Preoperative Imaging

- stage disease index breast
- contralateral assessment
- axillary lymph node evaluation
- chemotherapy response
- localization for excision
Lesion Localization

Wire localization

– portion external to patient
– wire can move / be dislodged
– must operate same day
– can limit surgical approach
– if cut, need to fish it out
Lesion Localization

- Radioactive Seed (RSL)
- E-magnetic reflector / IR detection
- Magnetic lesion localization
Seed Localization

- radioactive seed: I-125
- half life: 59 days
- beta emitter, external dose very low
Seed Localization

Advantages

• nothing left exterior to patient
• seed migration is minimal to none
• specimen volumes are less
Seed Localization
Advantages

• surgeon can optimize incision site
• probe is same one used for SLN
• loc and surgery no longer linked
Seed Localization
Disadvantages

- highly regulated
  - need a plan for every step
  - start-up can be onerous

- need multidepartment cooperation
  - follow seed everywhere it goes

- seed has to come out surgically
RSL Challenges

• positive axillary node retrieval after NAC
  – in Europe – seed placed prior to NAC
  – in U.S. – target the clip

  can be difficult after chemo response
RSL Challenges

• positive axillary node retrieval after NAC
  – removal beneficial to treatment plan
  – seeds allow removal where wire would not
  – care in placement in NAC response
RSL Challenges

- placement of seed in fatty tissue
  - not an issue in vivo
  - problem if surgeon cuts close
RSL

• easier than wires

• more regulatory hurdles

• some special situations not seen with wire
Lesion Localization

- Radioactive Seed (RSL)
- E-magnetic reflector / IR detection
- Magnetic lesion localization
Reflector Localization

- E-magnetic reflector / IR detection
  - reflector inserted up to 7 days prior
  - non-radioactive
  - handpiece emits IR / e-magnetic waves
    activates transistor on reflector
Reflector Localization

- Pilot study 2016 / 50 patients
  - insertion: long16g / hard for mammo
    1 of 2 sites did only with US
  - tissue depth an issue
    3cm in study; maybe 4.5cm lesion depth possible
  - radiologists liked less than wires
    1 of 2 sites did only under anesthesia in OR

Reflector Localization

- E-magnetic reflector / IR detection
  - no regulatory hurdles
  - reflector larger than seed / more cumbersome
  - more expensive
Lesion Localization

- Radioactive Seed (RSL)
- E-magnetic reflector / IR detection
- Magnetic lesion localization
Magnetic Lesion Localization

- injection of superparamagnetic iron oxide
- detection with magnetometer
- no regulatory hurdles / no Nucs
- used successfully for SLNB
- localize tumor + SNLB with one injection

SentiMag Trials UK and Central Europe

Douek et al. 2014 AnnSurgOncol
Magnetic Lesion Localization

- first dual use pilot 2015
- 33 cancers in 32 patients

- injection day prior to surgery
- all breast tumors localized successfully
- SLNB needed addition of dye

Ahmed et al. BJS 2015
Summary:

PreOP Eval New Breast Cancer

Lesion Localization

- wires being replaced by other devices
- seed localization: many advantages
- other viable options being developed
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THANK YOU

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