Research in MRI-guided breast radiotherapy at UMC Utrecht

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Overview

• MRI Linac at UMC Utrecht
• Skin dose effects in breast RT in a magnetic field
• MRI of individual LNs for regional RT
• Intra-fraction motion of breast (tumours)
• Conclusions
**Why MRI?**

**MRI:** superior soft-tissue contrast, high resolution, geometric accuracy

Lumen

**Three rectal wall layers:**

- Mucosal layer
- Submucosal Layer
- Muscle layer

Mesorectal fat

Mesorectal fascie

Rectum

T2 weighted imaging

Breast

Courtesy of Martijn Intven
MRI Linac

Elekta accelerator

Philips Achieva 1.5 T MRI
MRI Linac combines 1.5 T MRI scanner with 8 MV photon linear accelerator
MRI-guided radiotherapy at UMC Utrecht

**1.5 T MRI scanner with 8 MV photon linear accelerator**

- Clinical model of MRI Linac being constructed
- Allows motion tracking, real-time position verification and on-line adaptive (re)planning
- Research line in MR-guided RT at UMC Utrecht
  - *bone metastasis, pancreas, rectum, etc.*
- Towards GTV boosting, stereotaxy
- My PhD: MRI-guided RT of the breast (physics) - MRI Linac
Skin dose effects: treatment planning study

- Electron Return Effect (ERE): Lorentz force acts perpendicularly on moving electrons

*Whole-breast irradiation and the ERE*

![Diagram showing electron return effect at 0 T and 1.5 T fields.](image-url)
Skin dose effects: treatment planning study

- Electron Return Effect (ERE): Lorentz force acts perpendicularly on moving electrons
- Result: higher skin dose!
- Expected in whole-breast irradiation (WBI)
  - *Large targets, large areas of skin involved*
- Also dependent on inclination of fields with the tissue
Skin dose effects: treatment planning study

- Electron Return Effect (ERE): Lorentz force acts perpendicularly on moving electrons
- Result: higher skin dose!
- Expected in whole-breast irradiation (WBI)
  Large targets, large areas of skin involved
- Also dependent on inclination of fields with the tissue
- What about accelerated partial-breast RT (APBI) with several fields?

**Purpose**: investigate magnetic-field effects on skin dose

Van Heijst et al. 2013 PMB
Skin dose effects: treatment planning study

Methods and materials

- CT scans from 12 BCT patients in supine RT position
- Three RT techniques

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose Calculation</th>
<th>Equivalent Dose</th>
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<tr>
<td>WBI by 2 fields</td>
<td>$16 \times 2.66 \text{ Gy} = 42.56 \text{ Gy}$</td>
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*APBI: focus on tumour bed (with margin)*

Van Heijst et al. 2013 PMB
Skin dose effects: treatment planning study

Methods and materials

- CT scans from 12 BCT patients in supine RT position
- Three RT techniques
- Specially developed treatment-planning software
- Calculations at 0 T, 0.35 T and 1.5 T
- Delineations by radiation oncologist
- Organs-at-risk, including skin (first 5 mm)

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Van Heijst et al. 2013 PMB
Skin dose effects: treatment planning study

Results

• Typical dose volume histograms
• Dose differences at 0.35 T and 1.5 T are evident in WBI

Van Heijst et al. 2013 PMB
Skin dose effects: treatment planning study

Results

• Typical dose volume histograms
• Dose differences at 0.35 T and 1.5 T are evident in WBI
• Clinically significant: 35 Gy and higher
• No significant effects in APBI

Van Heijst et al. 2013 PMB
Skin dose effects: treatment planning study

Conclusion

• Skin dose higher at 1.5 T in WBI, not in APBI
  - Conventional WBI for MRL: potential problem
  - APBI in MRI Linac: no toxicity hazards expected ( > 35 Gy )
  - Smaller targets, less superficial: no disadvantages

MRI Linac:

Focus on RT of the tumour (bed) instead of whole breast
MRI of individual LNs for regional RT planning

- Regional RT preferred over axillary LN dissection (ALND) based on AMAROS/Z0011 trials

2010 Leonor Garcia del Valle

MRI of individual LNs for regional RT planning

- Regional RT preferred over axillary LN dissection (ALND) based on AMAROS/Z0011 trials
- ALND associated with high toxicity (up to 60%)

2010 Leonor Garcia del Valle

MRI of individual LNs for regional RT planning

- Standard delineations performed on CT
- Delineation guidelines\(^4\) based on anatomical boundaries
- RT-induced toxicity\(^5,6\) up to 14%

MRI of individual LNs for regional RT planning

- Standard delineations performed on CT
- Delineation guidelines\(^4\) based on anatomical boundaries
- RT-induced toxicity\(^5,6\) up to 14%

- Target definition more accurate: lower toxicity?
- MRI enables direct visualization of LNs
- Diagnostic MRI not optimized for this

**Purpose:**
Develop and optimize MRI for LN imaging in RT planning!

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MRI of individual LNs for regional RT planning

Methods and materials

• 1.5 T wide-bore MRI scanner (Ingenia, Philips)
• Healthy female volunteers ($n = 12 + 4$)
• Supine RT position, wedge board
• Anterior coil on perspex stand

• Five MRI sequences optimized
  – 1x T1w, 3x T2w, 1x DWI

• Evaluation qualitatively and quantitatively for RT planning suitability
MRI of individual LNs for regional RT planning

Results

• Qualitatively: scans complementary
  
  – Contrast of LNs, anatomical information, blood suppression, fat suppression, sensitivity to motion artefacts, geometric accuracy
MRI of individual LNs for regional RT planning

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MRI of individual LNs for regional RT planning

Conclusions

• Achieved direct, individual LN imaging with MRI, in RT position
• Facilitates more accurate target definition/delineation
• Possibilities for MR-guided RT of the regional LNs

Van Heijst et al.
Discussion

- Near future: feasibility study in patients
  - Reproducibility of MRI, set-up
  - Do we see all LNs?
  - Effects of surgery
  - Added value of CT-based delineations

MRI of individual LNs for regional RT planning
Discussion

• Near future: feasibility study in patients
  • Reproducibility of MRI, set-up
  • Do we see all LNs?
  • Effects of surgery
  • Added value of CT-based delineations

• Targets based on individual LNs may be significantly smaller!
  • More distant future: staging with MRI

MRI of individual LNs for regional RT planning
Discussion

- Near future: feasibility study in patients
  - Reproducibility of MRI, set-up
  - Do we see all LNs?
  - Effects of surgery
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- Targets based on individual LNs may be significantly smaller!
  - More distant future: staging with MRI
  - Develop MR-guided RT of individual LNs
  - Stereotactic single high-dose, SIB, ...?

MRI of individual LNs for regional RT planning
Intra-fraction motion

- Increasingly important
  - targets smaller
  - fewer fractions
  - towards stereotactic (ablative) RT

- Previous studies
  - Projections (EPID);
  - Geometric information of breast (tumour) motion lost
Intra-fraction motion

• Increasingly important
  – *targets smaller*
  – *hypofractionation*
  – *towards stereotactic (ablative) RT*

• Previous studies
  – *Projections (EPID)*;
  – *Geometric information of breast (tumour) motion lost*

• MRI
  – *Superior soft-tissue contrast*
  – *Geometrical accuracy*
  – *MRI Linac*

*Purpose:* quantification of intra-fraction motion using MRI

Douglas et al. IJRBO 1996
Intra-fraction motion

Methods and materials

• 20 patients in RT position @ 1.5 T
  – Preoperatively and postoperatively

• 2D cine-MRI sequences
  – Oriented through the tumour
  – Sagittal, and transverse, acquired alternately
  – Every 0.3 s during 2 min

• 3D MRI
  – Radiation oncologist delineated breast (+tumour, cavity)
  – Transferred to reference frame on 2D cine-MRI

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Intra-fraction motion

- Reference frame registered rigidly to each scan

Reference scan ($t = t_0$)

Rigid registration

$t = t_1$
Intra-fraction motion

- Reference frame registered rigidly to each scan
Intra-fraction motion

- Reference frame registered rigidly to each scan
- Delineations transformed accordingly
- Deformation vector field to determine displacements

Reference scan ($t = t_0$)

Rigid registration

$t = t_1$

$t = t_2$

$t = t_3$
Time-series acquired in the transverse (left) and sagittal (right) plane; in-plane resolution: 1x1 mm²
Intra-fraction motion

• Motion can be observed

Respiratory motion
Motion amplitude limited
Similar motion observed in most patients
  - Breast and tumour (bed)
  - All in-plane directions (AP, LR, CC)
  - Preoperatively and postoperatively
Intra-fraction motion

- Motion amplitude limited
- Similar motion observed in most patients
  - *Breast and tumour (bed)*
  - *All in-plane directions (AP, LR, CC)*
  - *Preoperatively and postoperatively*
- Rarely observed: irregular motion (up to 14 mm!)
Conclusions

- Intra-fraction motion of breast (tumors) can be observed and quantified using cine-MRI
- Motion amplitudes in supine RT position are limited
- Motion tracking not necessary?
  - *Exception gating on the MRI Linac*
CONCLUSIONS

MRI-guided RT for breast-cancer patients

• Effects of magnetic field detrimental for WBI, not for smaller targets (tumour bed)

• Regional LNs can be individually imaged using new MRI: potential for new RT techniques
  • Near future: patient feasibility study

• Motion amplitudes in supine RT position are limited

• MRI Linac: Information can be used to develop new RT techniques
  • small targets and hypofractionation
  • single high-dose levels: GTV boosting and stereotactic approach
Clinical studies

- High correlation between microscopic tumor size and preoperative (diagnostic) MRI
  *Schmitz 2010 Radiother Oncol*

- High interobserver variability in postoperative (CT, and CT+MRI) delineations
  *Den Hartogh 2014, Radiat Oncol*

Next step: at UMC Utrecht, feasibility study (ABLATIVE) will start soon:

- *Elderly, low-risk breast-cancer patients*
- *Preop. single-dose: 20 Gy on GTV, 15 on CTV, using VMAT*
- *On supine CT and MRI*
Acknowledgements

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- Alexander Raaijmakers
- Martijn Intven
- Gijsbert Bol

Thank you for your attention!
1. Skin dose: treatment planning study

Results

- Dose difference maps per voxel
- Dose differences at 0.35 T and 1.5 T are evident in WBI
- Not in APBI!
2. MRI of individual LNs for regional RT planning

- Diagnostic MRI not optimized for regional RT planning
  - *Not in RT position (supine, arms in abduction)*
  - *Contrast (T1w) possibly insufficient*
  - *Breast coil not suitable*

- Purpose: develop MRI for imaging of LNs

- MRI developed and optimized in healthy volunteers
Intra-fraction motion

Preoperative \( (n = 18) \)

Postoperative \( (n = 19) \)

Breast

Tumour

Tumour bed
Intra-fraction motion

- Intra-fraction motion quantification
  - \( P95\%: \text{distance that includes 95\% of surface voxels} \)

- Anterior-posterior (AP), left-right (LR), and caudal-cranial (CC)

- Preoperative and postoperative analysis