MRI Guided Adaptive Radiotherapy
Present and Future

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Disclosure

• Personal fees (speaking honorarium) from Viewray, Inc. outside this work
Outline

• Introduction to MRI guided radiotherapy (MRgRT)
• Rationale for adaptive radiotherapy
• Clinical workflow of MR guided adaptive radiotherapy
• Challenges in MR guided adaptive planning
• Future development
Advantages of MRI guided RT (MRgRT)

- Superior soft tissue contrast
- Functional and physiological imaging
- Real time dynamic imaging
- No radiation imaging dose

- Target/OAR delineation
- Treatment setup and verification
- Monitor treatment variations and response
- Motion management
Challenges for MRgRT

• MR safety

• Patient immobilization with MR coils

• Geometric distortion

• Lack of electron density info for dose calculation

• Magnetic field interference on dose distribution
<table>
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<tr>
<th>MRgRT system</th>
<th>Radiation</th>
<th>Magnet field</th>
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<tr>
<td></td>
<td>Configuration</td>
<td>Orientation</td>
</tr>
<tr>
<td>ViewRay MRIidian Cobalt</td>
<td>Cobalt-60 split</td>
<td>superconducting close bore</td>
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<tr>
<td>ViewRay MRIidian Linac</td>
<td>6 MV split</td>
<td>superconducting close bore</td>
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<tr>
<td>MagnetTx Aurora RT</td>
<td>6 MV superconducting rotating open bore</td>
<td>Parallel</td>
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<tr>
<td>Australian MRI-Linac</td>
<td>6 MV superconducting open bore</td>
<td>Parallel/Perpendicular</td>
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<tr>
<td>Elekta Unity</td>
<td>7 MV superconducting close bore</td>
<td>Perpendicular</td>
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Introduction to ViewRay MRIidian® system

RT components:

- **Cobalt system**: 3 cobalt heads, 500cGy/min, 3 independent MLC system (1cm leaf width, double focus, field size 27.3cm x 27.3cm)
- **MR-Linac**: 6MV Flattening Filter Free Linac, 600cGy/min, 0.4cm leaf width double focus double stack MLC

MRI components:

- Split superconductor MRI (0.345 T)
- 50cm FOV with 70cm bore size
- High resolution 3D MRI images in 17-172s
- Real time cine MRI image (4 frames/s for one sagittal plane)
• Adaptive radiation therapy (ART) is a close-loop process:
  • Systematic monitoring of treatment variations (e.g. IGRT)
  • Re-optimize the treatment plan to account for these variations
Intra-treatment variations

• Tumor anatomic changes
  - Regression/Progression (Systematic)
• Weight loss (Systematic)
• Positioning and posture
• Organ at risk
  - Morphological (volume, shape etc.) (Stochastic)
  - Position change in relative to target
• Respiratory motion
• Tumor and/or OAR biological changes (Systematic)

➢ Does the change lead to clinically unacceptable deviation of dose?
➢ How to account for it?
Online Adaptive Radiotherapy (On-ART)

- To account for stochastic changes of critical organs
- Potential advantages:
  - Dose escalation
  - Improve treatment tolerance
- Mandates on-board imaging guidance
- Heavily relies on image quality
- Efficient treatment planning tool is essential
Online MR guided adaptive treatment workflow

- Image
- Re-contour
- Predict dose
- Re-optimize
- Motion/Position verification
- QA
- Treat
Imaging and Contouring

• **MR imaging:**
  - TRUFI (true fast imaging with steady-state free precession) sequence
  - Abdomen: FOV 45x45x24cm, spatial resolution 0.15x0.3cm, acquisition time: 17s with breath hold
  - Pelvic: FOV 50x45x43cm, spatial resolution 0.15x0.15cm, acquisition time 172s with free breathing

• **Contouring**
  - **Deformable image registration** between daily MRI and the initial planning MRI
  - Initial planning contours deformed to the daily MRI
  - Reviewed and manually corrected by physician and physicist
Dose prediction and re-optimization

• Initial treatment planning is re-calculated to ascertain whether treatment plan is optimal for that day’s specific anatomy
  • Dosimetric metrics extracted automatically for evaluation
  • DVHs and dose distribution compared with the initial plan

• If adaptive planning deemed necessary:
  • Re-optimization using initial planning beam angles and optimization parameters
  • Optimization parameters can be adjusted if necessary
Plan Quality Assurance

- Online adaptive QA tools:
  - Secondary Monte Carlo dose calculation
    - DVHs, Dosimetric metric parameters
    - 3D Gamma analysis
  - Sanity check:
    - Structure volumes
    - Beam bixel-time
Motion management – Soft tissue based gating

Before coaching

With coaching

Gating based on breath hold
Early Clinical Data: Efficacy and Toxicity of MRgRT for Pancreas Cancer

Local Control

- MaxBED > 90
- MaxBED < 90

Overall Survival

- MaxBED > 90
- MaxBED < 90

Gr 3+ GI Toxicity

- MaxBED_{10>90} 0%
- MaxBED_{10<90} 15.8%
Challenges for online adaptive planning

- **Image quality:**
  - Tumor conspicuity and soft tissue contrast
  - Image artifacts (motion)

- **Plan quality:**
  - Contour quality
  - Electron density accuracy
  - Re-planning/optimization
  - Plan QA/QC

- **Other factors:**
  - Time and process management
  - Decision making
  - Staff coordination and training
Image quality

- Sub-optimal soft tissue contrast with TrueFISP sequence

- MRI is prone to motion artifacts due to volumetric acquisition with slow K space sampling
Accelerated 3D Balanced SSFP imaging

• Variable-density Poisson-Disk (VDPD) technique with 15x undersampling (12.5s)
Quality and Efficiency of Contouring

- Heavily relies on deformable image registration
- Usually requires labor-intensive manual correction
Automated contour segmentation

- Advanced auto-segmentation approaches:
  - Statistical shape model
  - Statistical appearance model
  - Machine learning based model
  - Biomechanical model
    - Rigidity of bones
    - Elasticity of organs
    - Boundary conditions between tissues

Time for adaptive re-contour

M=10 min

Sharp et al. Medical Physics, Vol. 41, No. 5, 2014

Biomechanics Of Bodies: bob-biomechanics.com
Re-planning/optimization

- With limited time, how to achieve the best possible plan dosimetry?
  - Quality of the initial plan is important
  - Improvement of optimization algorithm
  - Beam angle optimization
  - Knowledge based planning

Planning algorithms doesn’t know to avoid the kidney if minimal priority is not given – human judgement crucial
Process management and improvement

- Compressing many days of work in one setting with patient on table
- Median time of the adaptive process is about 24 minutes
- Room for improvement
  - Improve image acquisition speed and quality
  - Contouring accuracy and efficiency
  - Re-planning and QA efficiency
  - Staff training, coordination and communication

*Automation to maximize efficiency, quality and safety*

*Minimizing errors through application of risk analysis*
Functional imaging as biomarker

- Tumor exhibits complex and heterogeneous microenvironment
- Biological changes may occur before detectable morphological changes
- Functional MRI imaging as a biomarker to assess radiation treatment response:

<table>
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<tr>
<th>Biological Processes</th>
<th>Modalities</th>
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<td>Metabolism</td>
<td>1H -13C- MR Spectroscopic imaging (MRSI)</td>
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<tr>
<td>Hypoxia</td>
<td>Blood Oxygenation Level-Dependent (BOLD) MRI</td>
</tr>
<tr>
<td>Proliferation/Apoptosis</td>
<td>Diffusion Weighted MRI</td>
</tr>
<tr>
<td>Angiogenesis</td>
<td>Dynamic Contrast Enhanced (DEC) MRI</td>
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Diffusion weighted MRI (DWI)

• A technique to measure the movement of water molecules at cellular level through MR gradients

• Water perfusion and diffusion are influenced by tissue cellularity, tissue organization and extracellular space tortuosity and cell membrane function etc.

• Non-invasive and quantitative

• Dose not require any exogenous contrast agent

• Biomarker to assess treatment response

Sequence for DWI

- Standard diagnostic sequence: single-shot echo-planar-imaging (ssEPI)
  + Rapid acquisition
  + Less susceptible to ghosting
  - Low SNR
  - Low spatial resolution
  - Severe geometric distortion
Turbo spin echo (TSE) based DWI sequence

(a) DW-ssEPI, b=0  
(b) DP-TSE, b=0

Distortion (mm)

Distance to image center (mm)

Before Correction  
After correction

ADC Accuracy at Zero Degree

Concentration Level

ADC (10^-3 mm²/s)

DP-TSE

B value

Log(Signal)  
Log(Noise)

ADC Reproducibility

Level 1  
Level 2  
Level 3  
Level 4  
Level 5

GAO et al. Medical Physics, 44 (10), 2017
Longitudinal diffusion MRI for treatment response assessment: Preliminary experience using an MRI-guided tri-cobalt 60 radiotherapy system

Yingli Yang, Minsong Cao, Ke Sheng, Yu Gao, Allen Chen, Mitch Kamrave, Percy Lee, Nzhde Agazaryan, James Lamb, David Thomas, Daniel Low, and Peng Hu
Summary

• MRIgRT has tremendous potential in personalized precision-guided radiotherapy

• MRI-guided adaptive radiotherapy may become a new RT paradigm that allows us to offer high quality and personalized patient care

• Opportunities for improvement include high quality and fidelity imaging, better motion management and efficient adaptive workflow as well as biological and functional based adaption