ADVANCES IN IMAGE-GUIDED RADIATION ONCOLOGY: CHANGING THE WAY WE TREAT CANCER

Jared R. Robbins MD
Assistant Professor
Department of Radiation Oncology
Medical College of Wisconsin

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DISCLOSURES

- Elekta-travel support
- The Medical College of Wisconsin is part of the Elekta MR-Consortium
OBJECTIVES

- Review the various modalities for image-guided radiation therapy and how they have evolved over time
- Review how the various information obtained through image-guidance and how it can be used to guide treatment and predict response or toxicity
- Discuss the emergence of MR-Guided radiation therapy and the potential treatment planning implications

IMPORTANT DEVELOPMENTS FOR MODERN EBRT

1895
William Roentgen discovers X-rays

1896
Emil Grubbe treats first cancer patient with X-rays

1898
Marie Curie discovers radium

1900
Type of IGRT

1950
Surface/ skin markings

1970
portals x-rays

1980
1980’s Multi-leaf collimator developed

1982
1972 first CT scans

1984
1980 MRIs clinically available

1988
1988 IMRT

1990’s
Computer based 3D planning

1995
Dynamic MLC

2000’s
SBRT

2006
Dose escalation

2010’s
hypofrac

2014
First MRgRT patient treated

Need for precision image guidance
**COMPARING 2D/3D TO IMRT**

- Increasing conformality, dose escalation, and OAR protection requires improved IGRT imaging

![CT slices](image)

*Fig. 1 Axial planning CT slice showing typical dose-wash of (a) conventional radiotherapy (2D-RT), (b) 3D-CRT, and (c) IMRT plan for head-neck cancer. Note the progressive high-dose conformation to the target volume and sparing of surrounding normal structures.*

Tejpal IJSO 2010

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**USE OF ADDITIONAL IMAGING FOR TARGET DELINEATION IN RADIATION PLANNING**

![Graph](image)

<table>
<thead>
<tr>
<th>Disease Site</th>
<th>Number of Users (% of All Users)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>286 (79.0)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>289 (79.8)</td>
</tr>
<tr>
<td>Breast</td>
<td>72 (19.9)</td>
</tr>
<tr>
<td>Lung</td>
<td>302 (83.4)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>193 (53.3)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>159 (43.9)</td>
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<tr>
<td>Gynecologic</td>
<td>166 (45.9)</td>
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<tr>
<td>Pediatrics</td>
<td>52 (14.4)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>203 (56.1)</td>
</tr>
<tr>
<td>Palliative</td>
<td>94 (26.0)</td>
</tr>
</tbody>
</table>

*Simpson et al. 2009 J Am Coll Radiol*
IMAGE-GUIDED RT

- With improved imaging capabilities, image-guidance technology was integrated into radiation oncology equipment to ensure what was seen on the outside reflected actual tumor position
  - Allows for greater assurance of tumor control
  - Decreased margins
  - Less normal tissue being irradiated
  - Requires volumetric 3D information to accurately assess setup and target location
  - Quality assurance that the planned treatment is delivered correctly

IGRT INCREASES EFFICACY AND DECREASES SIDE EFFECTS

- Retrospective study evaluating benefits of IGRT in prostate cancer patients (n=376) treated IMRT radiation (86.4 Gy) with or without IGRT (daily fiducial tracking with kV imaging) comparison of toxicity and efficacy

Zelefsky et al. 2012 IJROBP
SOURCES OF UNCERTAINTY AND VARIABILITY

- **Setup Errors:**
  - Incorrect positioning/rotation
  - Weight loss
  - Contour deformation
  - Skin mark shifts
  - Involuntary motion
  - Tensing of muscles

- **Motion and Deformation of Organs:**
  - Volume changes
  - Bladder and/or Rectal filling
  - Intra-abdominal pressure
  - Bowel gas
  - Respiration
  - Peristalsis
  - Cardiac motion

- Classified into two subcategories:
  - **Intrafraction Variability:**
    - Uncertainty occurs within a treatment fraction
    - Mainly due to organ motion (e.g., respiration, peristalsis, involuntary motion, etc)
  - **Interfraction Variability:**
    - Uncertainty occurs from fraction to fraction
    - Mainly due to irreproducibility of setup (e.g., anatomy changes, positioning errors, etc)

Corrected by pre-treatment IGRT
Corrected by real-time IGRT and daily adaption

Organs and tumors move between... and during daily treatments!
**IGRT Modalities**

- **Pre-Treatment IGRT:**
  - CTOR
  - kV CBCT
  - Tomo MVCT
  - IBL
  - MVCBCT

- **Real-time IGRT:**
  - kV Fluoroscopy
  - Ultrasound
  - RF transponders
  - MRI

<table>
<thead>
<tr>
<th>Energy</th>
<th>Fan Beam</th>
<th>Cone Beam</th>
</tr>
</thead>
<tbody>
<tr>
<td>kV</td>
<td>CTOR</td>
<td>kV CBCT</td>
</tr>
<tr>
<td>MV</td>
<td>Tomo</td>
<td>MV CBCT</td>
</tr>
</tbody>
</table>

- MV CBCT: Low Quality
- Ultrasound: Low Quality
- Tomo CBCT: Low Quality
- kV Fluoro: Low Quality
- CTOR: Medium Quality
- MRI: High Quality
**Quality of Image Guidance**

- **Low Quality**
  - MV CBCT
  - TOMO CT
  - kV CBCT
  - CTOR
  - MRI

- **High Quality**
  - MV CBCT
  - Ultrasound
  - Tomo CBCT
  - kV Fluoro
  - CTOR
  - MRI

**Improvements in Imaging and Technology**

- The ability to use 3D volumetric information in creating radiation plans has led to the development of better radiation treatments.
- As conformality increases, so does need for precise imaging.

**Intent**

- 2-D
- 4-field box
- CRT
- 3D-CRT
- CTg-IMRT
- MRg-IMRT
**CONE BEAM CT (CBCT)**

- 2D diverging x-ray source and flat panel detector mounted to linac gantry
- As gantry rotates around patient, planar projection images are acquired
- Reconstructs into a true 3D volumetric CT image set:
  - Conventional CT is multi-slice 2D
- Permits imaging and treatment to be performed in identical patient position

**MV CONE BEAM CT (MV CBCT)**

- Conventional CBCT imaging approach
- Uses combination of MV x-ray beam and EPID
- Advantages:
  - No additional hardware required
  - Less susceptible to artifacts from metallic objects compared to kV CBCT (due to Compton effect)
  - Calculation of imaging dose possible
- Disadvantages:
  - Poor image contrast and quality
  - Higher imaging RT dose vs kV
Kv Cone Beam CT (Kv CBCT)

- Conventional kv x-ray tube mounted on a retractable arm fixed to gantry
- Additional flat panel mounted on retractable arm opposite kv x-ray source on gantry
- Advantages:
  - Better soft tissue contrast at much lower imaging doses than MVCT
  - High compatibility with planning CT
  - Permits acquisition of 3D CBCT, 4D CBCT, 2D radiography, and 2D kv fluoroscopy with same source and detector
- Disadvantages:
  - Requires additional hardware
  - Difficult to match kv and MV isocenters

Tomotherapy

- Combines linac and helical CT scanner for IMRT (and static) delivery
- MV fan-beam
- Arc-shaped detector array consisting of 738 Xenon ion chambers
CT-ON-RAILS (CTOR)

- kV fan-beam CT with gantry on sliders
- Couch isocentrically rotated to CT scanner axis after patient is setup; rotated back for treatment

Advantages:
- Diagnostic quality CT images

Disadvantages:
- Time between imaging and treatment
- Cost of separate CT scanner
- Patient must be rotated after imaging

MR-GUIDED RT

ViewRay MRIdian Linac

Elekta Atlantic

ViewRay MRIdian Cobalt
The value of MR-guidance

- MRI based image guided RT will allow for superior tumor and organ at risk delineation, superior motion management, and greater avoidance of adjacent organs/tissues resulting in:
  - similar tumor control with decrease toxicity versus standard treatment = **fewer side effects**
  - more accurate targeting and OAR avoidance in turn enabling safe dose escalation = **improved local tumor control**
  - possibility of novel biologic targets/biomarkers
  - No additional radiation exposure for IGRT
**THE USE OF IGRT MODALITIES**

Nabavizadeh et al. IJROBP 2016

**THE FREQUENCY OF IGRT USE**

Nabavizadeh et al. IJROBP 2016

Fig. 2. Physician-reported image guided radiation therapy frequency (black) and on-line image verification frequency (gray) for standard fractionation treatments, by disease site. Abbreviations: 3D-CRT = 3-dimensional conformal radiation therapy; fx = fractions; IMRT = intensity modulated RT.
HOW IS HIGH QUALITY IGRT CHANGING THE WAY WE TREAT CANCER?

- Improved assurance of target and OAR location/delineation prior to treatment
- Gives insight into anatomic and tumor changes during treatment to allow for precise adaptive therapy
- Provide potential functional or biological information about the tumor (radiomics) that could help predict outcome or toxicity
- Allows deviation from standard fraction sizes (hypofractionation)

VERIFYING TUMOR/OAR POSITION

- Motion management
  - Assessment of tumor and OAR
  - Static (4D CBCT)
  - Real time (fiducial or transmitter tracking vs MRI)
  - Gating based on tumor position vs respiratory cycle
- Delineation of tumor from critical structure
  - Must be able to distinguish tumor from OAR
- Allow for dose escalation and margin reduction
4D-CT vs 4D-MRI

Figure 3. Real-time tumor tracking using the tri²¹⁳C system.
Successive snapshots of a liver lesion as visualized using the real-time cine-MRI functionality of the tri²¹³C system. The thick crimson outline indicates the “envelope” within which the radiation treatment will be delivered, while the softer crimson outline indicates the location of the tumor as it moves in real-time. The lesion is outside the “envelope” in the top row (radiation beam is off), and moves into the “envelope” in the bottom row (radiation beam is on).

Henke et al. Radiotherapy and Oncology 2018

Courtesy of Dr. Eric Paulsen
Effect of image quality: Variation in identifying prostate

Manual registration by 20 users

Image contrast is an important issue for tumor delineation and mid-treatment adaption

Li, MCW unpublished

Fig. 1. GTV for oropharyngeal cancer delineated on T2-w MR image. Each color depicts a different observer.

- There is great variability in the delineation of oropharyngeal tumors on MRI even among International H&N specialists.
- Guidelines for MRI-directed tumor delineation is needed

Blinde ASTRO 2017
ADAPTIVE RADIATION THERAPY

• A state-of-the-art approach that uses a feedback process to account for patient-specific anatomic and/or biological changes during the treatment, thus, delivering highly individualized radiation therapy for cancer patients.

ADAPTIVE RADIATION THERAPY

• Precision medicine
• Off-line vs on-line
• Reactionary vs planned
  • Daily vs weekly vs “as needed”
• Reasons for adaption
  • Anatomic change
    • Weight loss/gain
    • Change in tumor or OAR spatial relationship to each other
    • Changes in size or position OAR from the treatment plan
  • Tumor change
    • Response to treatment
    • Progression or more extensive disease
Tumor Response for squamous cell carcinoma of the left tonsil as observed over time on daily “diagnostic-quality in-room CT” scan taken for image-guided radiation therapy

### ADAPTIVE RE-PLANNING

- First prospective trial using offline ART for oropharyngeal tumors
- 24 patients, one or two mid-treatment re-plans
- 31 month median follow-up
- 100% local and 95% regional control at 2 years with low acute toxicity
Dose is 69.96 Gy in 33 fractions with RT given once daily, 5 days a week, over 6 weeks and 3 days.

The RT plan will be adapted to target the tumor volume on MRI obtained biweekly during treatment.

Treatment volume will shrink during treatment to potentially reduce dose to OARs and minimize late effects.

**CLINICAL MR-LINAC PROTOCOL**

**MR-LINAC CONSORTIUM – OROPHARYNX-TSG**

- Eligibility:
  1) T1-2N0-2M0, unchallenged squamous cell carcinoma
  2) Age 18-56
  3) ECOG ≤ 2
  4) Lifetime nonsmoker

- **Stage 1**: Enroll 10 patients to experimental arm (MRgRT)

- **Stage 2A**: Enroll 30 patients

- **Stage 2B**: Enroll 30 patients
**CAN IGRT IMAGES REVEAL A NEED FOR DAILY ADAPTIVE RT FOR ABDOMINAL TUMORS?**

- Abdominal organs move with respiration, distention, and peristalsis
- Retrospective study of 30 liver SBRT patients evaluating the interfraction dose differences to the OARS using daily IGRT (CTOR) images
- Two phases
  - Phase 1 (10 patients)
    - 7 organs contoured for all
  - Phase 2 (20 additional)
    - Only contoured organs in close proximity to target (5 cm)

Schmidt R and Robbins JR (ASTRO 2017)

Schmidt R and Robbins JR (RSNA 2016)
Variations in interfractional max dose to OARs during liver SBRT

Schmidt R and Robbins JR (ASTRO 2017)

While some violation of daily constraints were due to changes in the OAR shape or position, the majority were due to variation in position between the GTV and the OARs.

These constraint violations would likely have been prevented with daily adaptive RT

Schmidt R and Robbins JR (ASTRO 2017)
MRI-GUIDED ADAPTIVE TREATMENT OF OLIGOMETASTATIC DISEASE IN ABDOMEN

Phase I trial

Phase I trial of stereotactic MR-guided online adaptive radiation therapy (SMART) for the treatment of oligometastatic or unresectable primary malignancies of the abdomen

Lauren Henke 1, Rojano Kashani 2, Clifford Robinson 3, Austen Curcuru 4, Todd DeWees 4, Jeffrey Bradley 4, Olga Green 5, Jeff Michalski 5, Sasa Mutic 5, Parag Parikh 6, 7, Jeffrey Olsen 7

1 Department of Radiation Oncology, Washington University School of Medicine, St. Louis, and 2 Department of Radiation Oncology, University of Colorado School of Medicine, Aurora, United States
Adapted Fractions

- In the 20 patients, 81/97 fractions (84%) adaptive plans were generated
  - 61/81 (75%) due to OAR constraint violation
  - 20/81 (25%) opportunity for PTV dose escalations
- After adaption no constraints were violated
- No ≥ grade 3 toxicity observed

**Time cost for on-line adaptive therapy**

<table>
<thead>
<tr>
<th>Time Cost Metric</th>
<th>Median (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median on-table time in min (range)</td>
<td>79 (36–160)</td>
</tr>
<tr>
<td>Median re-contour time in min (range)</td>
<td>9 (2–24)</td>
</tr>
<tr>
<td>Median re-plan time in min (range)</td>
<td>10 (1–19)</td>
</tr>
<tr>
<td>Median QA time in min (range)</td>
<td>4 (1–14)</td>
</tr>
</tbody>
</table>

Henke *et al.* Radiotherapy and Oncology 2018
Para-aortic node  
Liver metastasis 
Pancreatic metastasis  
Dose escalated liver metastasis

Henke et al. Radiotherapy and Oncology 2018
ABDOMINAL OLIGOMETASTASIS

SBRT to painful abdominal metastasis (surrounded by small bowel)
- PTV prescribed 21 Gy in 3 fractions of 7 Gy/fraction at 95% IDL

Courtesy of Dr. Salim Siddiqui at Henry Ford Hospital

3 months later

ABDOMINAL OLIGOMETASTASIS

0

3 months later
~3 months later

Courtesy of Dr. Salim Siddiqui at Henry Ford Hospital
First clinical outcome data supporting MR guided and adaptive RT paradigm

- 4 institutional retrospective review of 42 patients with unresectable pancreatic cancer
- Treated with various fractionation schemes
- Some patients treated with on-table adaptive treatment
- Patients compared by dose maxBED$_{10} \geq$90 Gy vs <90 Gy
- Median follow-up of survivors was 21 months

<table>
<thead>
<tr>
<th>Radiation Factors</th>
<th>maxBED$_{10}$ $\geq$ 90 Gy</th>
<th>maxBED$_{10}$ &lt; 90 Gy</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BED$_{10}$ of Rx (Gy)</td>
<td>72.0</td>
<td>59.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>maxBED$_{10}$</td>
<td>101.1</td>
<td>66.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median Fractions Adapted per patient</td>
<td>5</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GTV (cc)</td>
<td>38</td>
<td>36</td>
<td>0.714</td>
</tr>
</tbody>
</table>

Rudra et al. ASTRO 2017

**Radiation Fractionation Scheme**

<table>
<thead>
<tr>
<th>RT Technique</th>
<th>Dose and Fractionation</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional</td>
<td>50.4 Gy in 28 Fractions</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>40 - 55 Gy in 25 Fractions</td>
<td>7</td>
</tr>
<tr>
<td>Hypofractionated</td>
<td>50 - 67.5 Gy in 10-15 Fractions</td>
<td>8</td>
</tr>
<tr>
<td>SBRT (maxBED$_{10}$ &lt; 90)</td>
<td>30 – 40 Gy in 5 Fractions</td>
<td>6</td>
</tr>
<tr>
<td>SBRT (maxBED$_{10}$ &gt; 90)</td>
<td>40 – 52 Gy in 5 Fractions</td>
<td>15</td>
</tr>
</tbody>
</table>

Rudra et al ASTRO 2017
Lee et al AMAC 2018

**MR-gRT WORKFLOW EVOLUTION**

- What is anatomy and motion of the day?
- Truth-in-delivery: How much dose did target and OARs actually receive?

**Gr 3+ GI Toxicity**

<table>
<thead>
<tr>
<th>maxBED_{\text{cl}} &gt; 90</th>
<th>0%</th>
</tr>
</thead>
<tbody>
<tr>
<td>maxBED_{\text{cl}} &lt; 90</td>
<td>15.8%</td>
</tr>
</tbody>
</table>

Courtesy of Dr. Christopher Schultz
GLEANING INFORMATION FROM IGRT

- Vast quantity of data is collected with IGRT
  - Some keys to better understanding outcome and toxicity could be extracted from these images
- Treatment response
  - Can early treatment response be a predictor of long-term outcomes?
  - Can early response act as a biomarker for dose personalization?
  - Can changes in normal organs during treatment predict for toxicity?
- Radiomics
  - How do the basic characteristics of the tissue change with dose?
- Radiogenomics
  - Are there correlation between the tumor genetics and the imaging characteristic changes?

EARLY RESPONSE PREDICTS OUTCOME

- Retrospective study of 96 patients using CT taken on 15th fraction
  - Median tumor reduction was 18.7%.
  - Total tumor reduction and primary tumor reduction were significant predictors of local failure.

Kabarritti (Wisconsin) IJROBP (2018 in press)
TREATMENT RESPONSE BY MRI

- Patient imaged every two weeks starting first week of RT
  - Patient with T2N2b squamous cell carcinoma of the left oropharynx, p16+, receiving treatment with concurrent cisplatin

Diffusion Weighted MRI images taken: A. Week 1 B. Week 3 C. Week 5 D. Week 7

MCW Solid Tumor Imaging MR-Linac (STIM) Study

- IRB approved study for all solid tumors
- Patient volunteers will receive 1.5 T MRIs in the treatment position at various time points during their treatment
- MRIs can be acquired at any treatment related appointment up to 6 months after RT

- Objectives
  - Improve variables related to MR image quality (e.g., signal-to-noise ratio, image contrast, acquisition time, etc.)
  - Determine the feasibility of the MR guided adaptive workflow for MR-linac radiation therapy. This will include improvement in variables related to simulated (i.e., not given to the patient) MRI radiation treatment delivery (e.g., contours, auto segmentation software, organ deformation and volume change, etc.) to determine the feasibility of intra- and interfraction adaptive radiation therapy.
  - Obtain imaging data and clinical data from participants, for additional research focused on MRI use for Radiation Therapy
**Radiomics**

- Extracting quantitative features from images to create “mineable” data elements.
- These elements may give insight into treatment outcome or normal tissue response.
- Can require lots of data, computational power, and clinical outcomes to establish correlations.

![Radiomics Workflow](image)

**Example of Radiomic Features**

<table>
<thead>
<tr>
<th>Energy</th>
<th>Contrast</th>
<th>Dissimilarity</th>
<th>Homogeneity</th>
<th>Maximum Probability</th>
<th>Sum Average</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Energy Image" /></td>
<td><img src="image" alt="Contrast Image" /></td>
<td><img src="image" alt="Dissimilarity Image" /></td>
<td><img src="image" alt="Homogeneity Image" /></td>
<td><img src="image" alt="Maximum Probability Image" /></td>
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</table>

<table>
<thead>
<tr>
<th>Entropy</th>
<th>Sum Entropy</th>
<th>Difference Entropy</th>
<th>Variance</th>
<th>Sum Variance</th>
<th>Inverse Variance</th>
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<tbody>
<tr>
<td><img src="image" alt="Entropy Image" /></td>
<td><img src="image" alt="Sum Entropy Image" /></td>
<td><img src="image" alt="Difference Entropy Image" /></td>
<td><img src="image" alt="Variance Image" /></td>
<td><img src="image" alt="Sum Variance Image" /></td>
<td><img src="image" alt="Inverse Variance Image" /></td>
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</table>

<table>
<thead>
<tr>
<th>Cluster Shade</th>
<th>Cluster Prominence</th>
<th>Cluster Tendency</th>
<th>Correlation</th>
<th>Auto Correlation</th>
<th>Information Measure of Correlation (1)</th>
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<tbody>
<tr>
<td><img src="image" alt="Cluster Shade Image" /></td>
<td><img src="image" alt="Cluster Prominence Image" /></td>
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<td><img src="image" alt="Information Measure Image" /></td>
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</tbody>
</table>

Courtesy of Dr. Christopher Schultz
Early Assessment of Treatment Responses During Radiation Therapy for Lung Cancer Using Quantitative Analysis of Daily Computed Tomography

PMID: 28543105

Other Radiomics features

Lung cancer Hounsfield Unit response during RT

Paul 2017 IJROBP
Xerostomia Project-Radiomics

- Can CT radiomic features of the parotid glands during radiotherapy (RT) predict severity of xerostomia?
- Daily diagnostic-quality CT-on-rails imaging were analyzed for 23 patients with HNSCC.
- Contours of parotid glands were generated on each selected daily CT.

Wu IJROBP (2018 in press)
XEROSTOMIA PROJECT-RADIOIMICS (CONT)

- Six histogram-based radiomic metrics including the mean CT number (MCTN), measured by Hounsfield unit (HU), volume, standard deviation (STD), skewness, kurtosis, and entropy for parotid glands were calculated for each fraction.
- Correlations between these metrics, radiation dose to bilateral parotid glands, and the observed grade and severity of xerostomia were analyzed.
- A CT-Based Xerostomia Score (CTXS) was developed and evaluated.

Wu ASTRO 2017, (manuscript in preparation)
The CTXS showed a significant strong correlation to the observed xerostomia grades ($\rho=0.757$, $P=0.000029$)

The xerostomia grade observed at the end of treatment can be predicted based on the CTXS determined at the 5th week during the treatment.

The precision of the prediction is 80% with a sensitivity of 100%.

CT radiomic data may be a helpful tool in predicting treatment related toxicity.

Wu 2018 IJROBP (in press)

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**MRI-BASED BIOMARKERS FOR DETECTING ACUTE RT-INJURY**

- Review of 32 patients who received EBRT for HNSCC who received pre, mid, and post-RT DCE-MRI scans
- MRIs were co-registered to dosimetric maps from EBRT to correlate changes in the mandibular vascularity as measured by $K_{\text{trans}}$ and $V_e$
- DCE-MRI detected dose-dependent changes in bone vascularity at the end of treatment
- First to demonstrate with DCE-MRI RT-related dose changes in bone perfusion.
- Imaging biomarkers like $K_{\text{trans}}$ and $V_e$ can identify subclinical radiation induced damage

MDACC 2016 Sci Rep
Figure 2. DCE-MRI Detects Focal Vascularity Changes During EBRT. Evaluation of DCE-MRI acquired $K_{trans}$ across the entire mandibular volume allows for identification of geographically distinct perturbations which can then be correlated to the dosimetric map for each individual patient. (A) Arrows in top and bottom rows identify the area of altered $K_{trans}$. Middle row demonstrates no appreciable change in $K_{trans}$ across the entire mandibular volume regardless of administered EBRT dose. (B) Arrows in top and bottom rows identify the area of altered $V_e$. Middle row demonstrates no appreciable change in $V_e$ across the entire mandibular volume regardless of administered EBRT dose. Panels A and B represent distinct patients.
**RADIO-GENOMICS**

- The intersection of imaging-based molecular phenotyping and genetic assays derived from biopsy
- Used in radiation oncology to reference the linkage between genotype and the radio-sensitivity of tissue or organs

PERSONALIZED RADIATION DOSING

- Genomic-Adjusted Radiation Dose (GARD)
  - Based on gene-expression-based radiosensitivity index and the linear quadratic model
  - Potential to adjust RT dose to match individual tumor's radiosensitivity

Scott, Lancet 2016

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Figure 3: GARD and distant-metastasis-free survival in the Ercanmus Breast Cancer Cohort
(A) GARD values for each individual patient are presented ranked from the highest to lowest value; each line represents an individual patient and colour relates to radiotherapy dose received. The number of patients in each group and the GARD ranges are online (appendix p. 4). (B) Kaplan-Meier plot for distant-metastasis-free survival comparing patients with high GARD (>38; the 75th percentile) with patients with low GARD (<38). HR is from univariable analysis. If no event occurred, then cases were censored at 5 years. GARD=genomic-adjusted radiation dose. HR=hazard ratio.
Pancreatic MRI and CT radiomic metrics correlate with pathologic molecular markers

<table>
<thead>
<tr>
<th>Radiometric Metric</th>
<th>Molecular Profile Correlation</th>
<th>Statistical Rs, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of T1 enhancement</td>
<td>% TOP1</td>
<td>Rs = 0.399, p = 0.29</td>
</tr>
<tr>
<td>Peak height</td>
<td>% ERCC1</td>
<td>Rs = 0.441, p = 0.04</td>
</tr>
<tr>
<td>Time to peak contrast enhancement</td>
<td>% FYM5</td>
<td>Rs = -0.431, p = 0.04</td>
</tr>
<tr>
<td>Uptake rate</td>
<td>% ENT1</td>
<td>Rs = -0.369, p = 0.045</td>
</tr>
<tr>
<td>ADC Value</td>
<td>% RRM1</td>
<td>Rs = 0.440, p = 0.036</td>
</tr>
</tbody>
</table>

Hall et al. ASTRO 2017
CONCLUSIONS

- IGRT has improved how we treat cancer and improved outcomes
- There are various options for IGRT and the modality should reflect the clinical scenario
- Advance IGRT techniques will continue improve the way we treat cancer
- There are many opportunities to use the information gleaned from IGRT to adapt and personalize radiation treatments
THANKS YOU

Medical College of Wisconsin
- Radiation Oncologist
- Dosimetrists
- Physicists
- Treatment and support staff

Contributors
- Dr. Christopher Schultz
- Dr. William H. Hall
- Dr. Eric Paulsen
- Dr. Salim Siddiqui