Radiomic Tools To Assess Early Response To Cancer Therapy

Ruijiang Li, PhD
Assistant Professor of Radiation Oncology
Bio-X & Stanford Cancer Institute
Stanford Biomedical Informatics Graduate Program
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Disclosures

• None.

Role of Radiologic Imaging in Oncology

• Diagnosis, staging, response evaluation
• Routinely used, noninvasive, repeatable
• Image entire tumor & surrounding tissue
• Current radiology interpretation is limited.
  – Subjective: inter/intra-observer variations
  – Diagnostic: few semantic features (typically <10)
  – Response criteria: tumor size, SUVpeak
• We need to do better.
  – Quantitative
  – Comprehensive
Radiomics: the Rationale and Process

- Imaging phenotypes are driven by underlying pathophysiology
  - FDG-PET SUV and metabolism.
- Tumor segmentation, high-throughput feature extraction
  - Convert radiologic image to quantitative ‘omic’ data
- Correlate with clinical outcomes: putative imaging markers
  - Aid in diagnosis, as well as prognosis & treatment response

Outline of this Talk

- Current status and recent developments in radiomics
  - Claimer: Not a comprehensive review (Lambin, Nat Rev Clin Oncol 2017)
  - Theme: better characterize intra-tumor heterogeneity
- Conventional radiomics: Gross tumor
  - Histogram, morphology, texture
- Emerging paradigms: Tumor subregions/habitats
  - Volume; Texture
  - Spatial interaction
- Radiogenomics
- Challenge, outlook

Radiomic Signature for Lung Cancer Prognosis

- Clinical problem: Unable to predict which patients will develop distant metastasis after SABR; this makes decision regarding adjuvant therapy uncertain.
- Image signature = 2.1 x SUVpeak_2cc + 3.6 x Gaussian_ClusterShade
Independent Validation

Wu et al, Radiology, 2016

Prognostic Imaging Marker in Pancreatic Cancer

- An FDG-PET radiomic signature improved survival prediction.
- C-index: 0.67 for radiomics vs 0.56-0.58 for SUV and tumor volume

Cui et al. IJROBP, 2016
Basic/Translational Science Award, ASTRO 2015

Gross Tumor Features To Detect Recurrence

- A radiomic signature measured at post-treatment CT detected local recurrence after SABR for lung cancer, with an error rate of 24% in 45 patients, compared with physicians (average 35%).

Mattonen et al IJROB 2016
Gross Tumor Features To Evaluate Response

- 13.3% (149 out of 1119) of the radiomic features showed an $R^2$ above 0.85 between planning CT and CBCT.
- CBCT preserved prognostic value: CI=0.66 (0.69 for CT).
- Potential of CBCT for monitoring radiation response?

![Image](image1.png)

Timmen et al Radiotherapy Oncology 2017

Beyond Gross Tumor: Multi-Region Analysis

- Current radiomics approach
  - Aggregate features from the bulk tumor
  - Assuming tumor is well mixed. Not spatially explicit.
- Branched evolution causes regional differences within a tumor.

![Image](image2.png)

Setton et al. PNAS, 2015

Zhang et al. Science 2015

Intra-Tumor Partitioning of Lung Cancer

![Image](image3.png)

Wu et al. IJROBP, 2016
Unsupervised Clustering Revealed 3 Tumor Subregions

The high-risk subregion represents the metabolically active & heterogeneous solid component of the tumor.

High-Risk Subvolume is Prognostic in Stage III NSCLC

Imaging Reveals High-Risk Subregion in GBM
High-Risk Subvolume in HN Tumors

- Large poorly perfused subvolumes of HNC at DCE MRI persisting during the early course of chemo-RT associated with local or regional failure in 14 patients.

Wang et al Med Phys 2012

Combine Radiomics with Multi-Region Analysis

- Intra-tumor partitioning using multi-parametric MRI of GBM
- Extract radiomic features for each subregion and gross tumor.

T1w T2w FLAIR Tumor Subregions

Cui et al. Radiology, 2016

Prognostic Imaging Signature in GBM

- A radiomic signature of 5 features predicted overall survival, independent of age, gender, extent of resection.

Cui et al. Radiology, 2016
Early Response Prediction in Breast Cancer

- Neoadjuvant chemotherapy is used to shrink tumor for breast-conserving surgery.
- 30% of patients have poor response, and yet suffer from the toxicity.
- Early response prediction would enable the use of alternative therapies.

Imaging Predictors of Pathological Response

The change in texture of tumor subregion associated with rapid wash-out pattern on DCE-MRI predicted pathological complete response.

- ΔTumor Volume: AUC=0.53
- ΔTumor Texture: AUC=0.65
- ΔSubregion Volume: AUC=0.57
- ΔSubregion Texture: AUC=0.79

Wu et al. JMRI 2016

Spatial Interaction among Tumor Subregions

Wu et al. Radiology 2018
Breast Tumor Subregions

Subregions correspond to the highly, moderately, poorly perfused portion of the tumor.

Imaging Characteristics of Tumor Subregions

Subregions correspond to the highly, moderately, poorly perfused portion of the tumor.

Spatial Interaction Index to Stratify Patients

Network analysis to stratify patients.
Prognostic Value of Image-Based Stratification

Discovery cohort (n=60)

Validation cohort 1SPY 1 (n=186)

Low-risk group

High-risk group

Log-rank p = 0.002

Time since treatment (years)

Low-risk

High-risk

*Independent predictor of RFS adjusting for age, ER, PR, HER2, tumor volume.

Prognostic Value in Histopathological Subtypes

ER+ (n=103)

HER2+ (n=56)

Wu et al. Radiology 2018

Radiogenomics: Linking Imaging with Molecular Biology

1. Understand how certain biology is reflected at imaging.

2. Understand the biological basis of an image feature

Molecular features:
- EGFR mutation in LUAD

Imaging features:
- Pleural contact

*Independent predictor of RFS adjusting for age, ER, PR, HER2, tumor volume.*
Radiogenomics of Lung Cancer

- Correlate gene expression with CT imaging signature.
- Top enriched pathways are related to immune response, such as lymphocyte activation and chemotaxis.

Prognostic Value of Tumor Immunity

- 19 cohorts of over 2400 patients
- Immune gene signature strongly prognostic, independent of stage, grade.
- Higher accuracy than existing gene signatures.

Predictive Value of Tumor Immunity

Cui et al. Clin Cancer Res 2018
• Heterogeneous parenchymal enhancement patterns are associated with inflammatory signaling pathways and poor survival in breast cancer. (Wu et al. Radiology 2017)

• The imaging subtypes are independent of molecular subtypes.

**Breast Cancer Imaging Subtypes**

**Distinct Molecular Pathways and Prognoses**

**Challenges & Potential Solutions**

• Standardization – NIH QIN, RSNA QIBA
  – Technical: Image acquisition: scanner, protocol, techniques
  – Analytical: Image reconstruction, feature definition, calculation

• Small sample size may lead to spurious findings
  – Collaboration & data sharing – TCIA; both imaging & clinical information

• Reproducibility
  – Need rigorous, truly independent validation.

• Biological interpretation
  – Correlating imaging with genomics may help – beware of caveat
Conclusion & Outlook

- Radiomics is a useful tool to discover new imaging markers.
  - Beyond gross tumor: intratumoral subregions/habitats
  - Mostly for initial characterization; less for response
  - Delta radiomics may not be optimal/sensitive to evaluate response
  - Need better tools specific for detecting changes at serial imaging
- Prospective validation in RCT is required to establish clinical utility.

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