Radiomic Tools To Assess Early Response To Cancer Therapy

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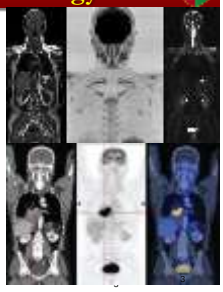
Disclosures

- None.

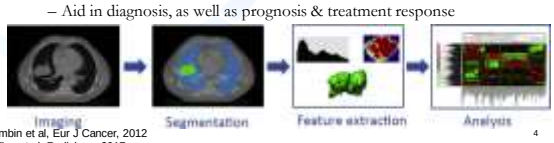
Role of Radiologic Imaging in Oncology

- 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



Lambin et al, Eur J Cancer, 2012
Gillies et al, Radiology, 2017

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Outline of this Talk

- Current status and recent developments in radiomics
  - Claimer: Not a comprehensive review (Lambin, Nat Rev Clin Oncol 2017)
  - Translational: how radiomic tools are applied to a clinical problem
  - 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

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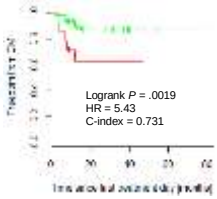
Radiomic Signature for Lung Cancer Prognosis

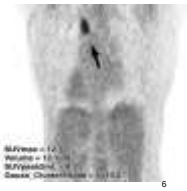
- Clinical problem: Unable to predict which patients will develop distant metastasis after SABR; this makes decision regarding adjuvant therapy uncertain.
- Image signature = 2.1 x SUV_{peak_2cc} + 3.6 x Gaussian_ClusterShade

Discovery Cohort (n=70)



Patient 1: Disease free 34 mo after SABR

Patient 2: distant metastasis 9 mo after SABR



Wu et al, *Radiology*, 2016

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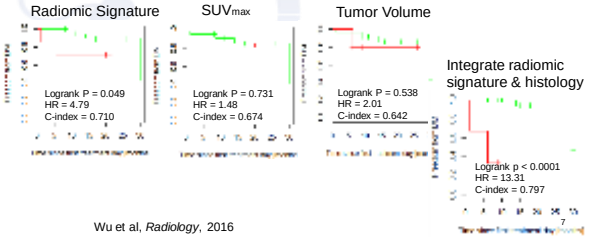
Independent Validation



Wu et al, *Radiology*, 2016

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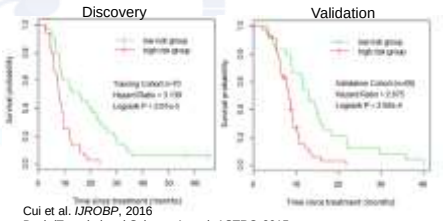
Prognostic Imaging Marker in Pancreatic Cancer

- 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

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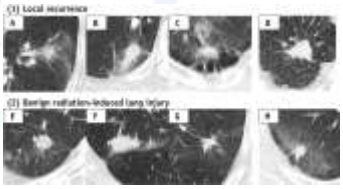
Gross Tumor Features To Detect Recurrence

- 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

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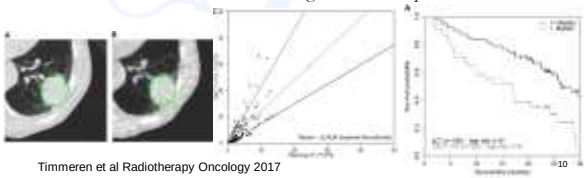
Gross Tumor Features To Evaluate Response

- 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?



Timmeren et al Radiotherapy Oncology 2017

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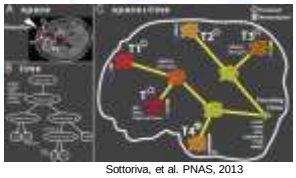
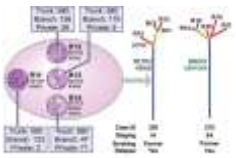
Beyond Gross Tumor: Multi-Region Analysis

- 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.

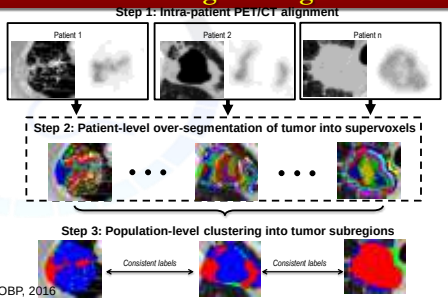


Sottoriva, et al. PNAS, 2013



Zhang et al: Science 2015

Intra-Tumor Partitioning of Lung Cancer



Wu et al. IJROBP, 2016

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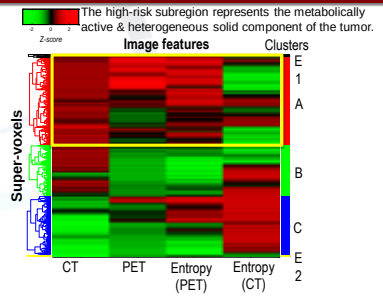
Unsupervised Clustering Revealed 3 Tumor Subregions



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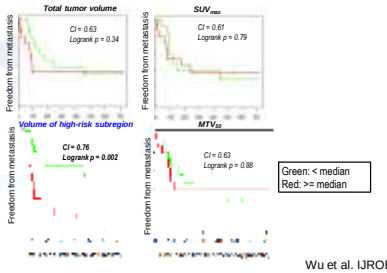
High-Risk Subvolume is Prognostic in Stage III NSCLC



Wu et al. IJROBP, 2016

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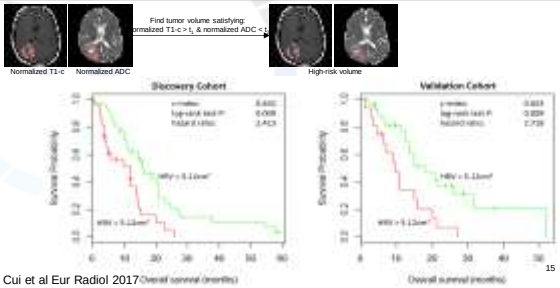
Imaging Reveals High-Risk Subregion in GBM



Cui et al Eur Radiol 2017

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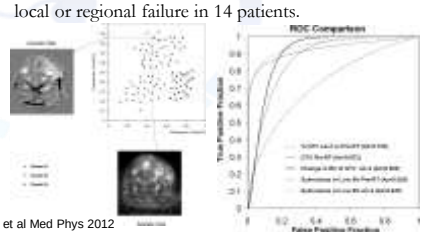
High-Risk Subvolume in HN Tumors

- 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

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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

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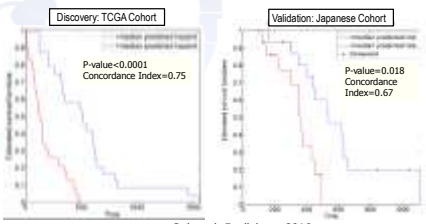
Prognostic Imaging Signature in GBM

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



Cui et al, *Radiology*, 2016

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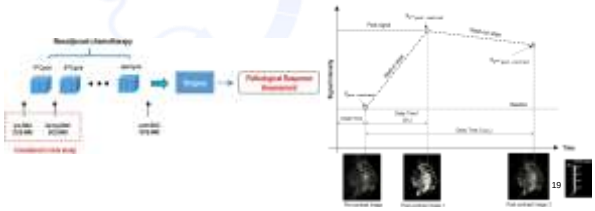
Early Response Prediction in Breast Cancer

- 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.



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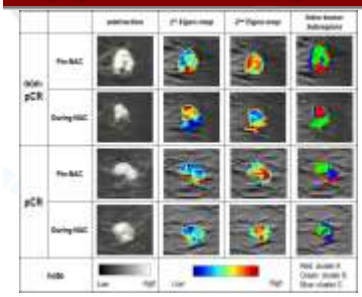
Imaging Predictors of Pathological Response



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

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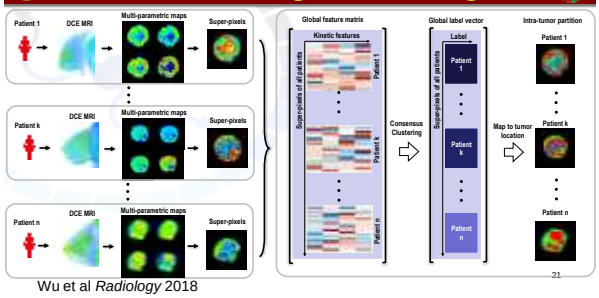
Spatial Interaction among Tumor Subregions



Wu et al *Radiology* 2018

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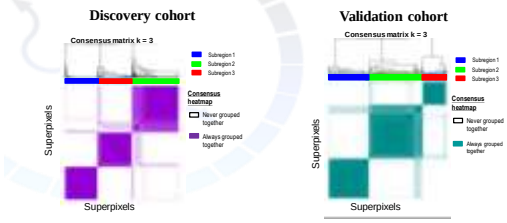
Breast Tumor Subregions



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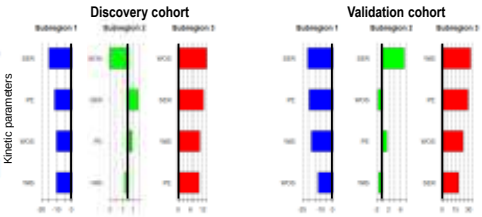
Imaging Characteristics of Tumor Subregions



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

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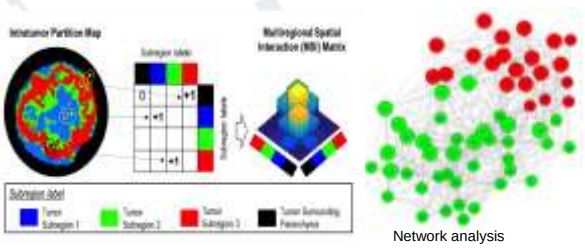
Spatial Interaction Index to Stratify Patients



Network analysis to stratify patients

Wu et al *Radiology* 2018

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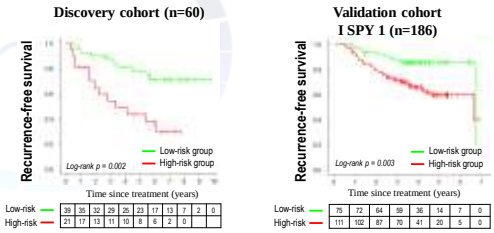
Prognostic Value of Image-Based Stratification



*Independent predictor of RFS adjusting for age, ER, PR, HER2, tumor volume. 25

Prognostic Value in Histopathological Subtypes

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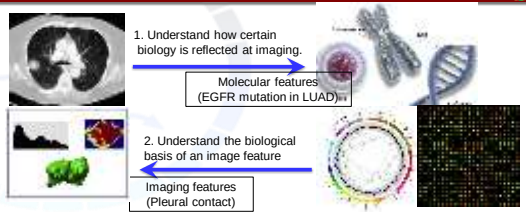
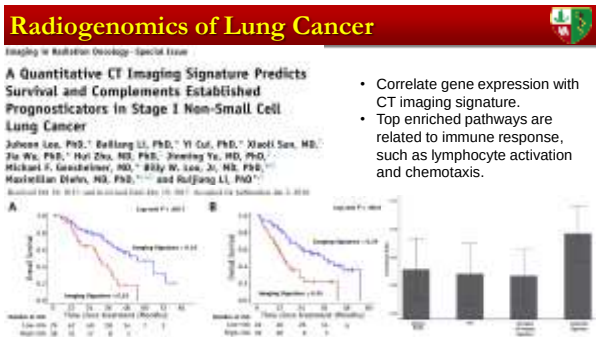
Wu et al *Radiology* 2018

Radiogenomics: Linking Imaging with Molecular Biology



Radiogenomics of Lung Cancer

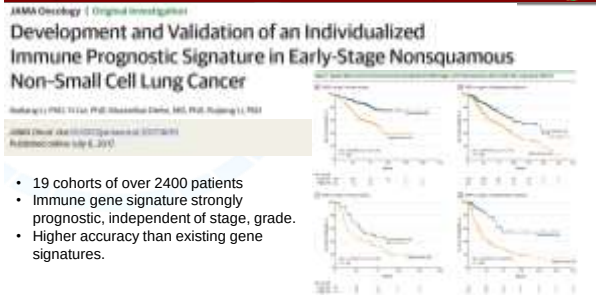

Imaging in Radiation Oncology–Special Issue

A Quantitative CT Imaging Signature Predicts Survival and Complements Established Prognosticators in Stage I Non-Small Cell Lung Cancer

Juhwan Lee, PhD,* Baiqiang Li, PhD,* Yi Cui, PhD,* Xiaoli Sun, MD,† Jie Wu, PhD,* Hui Zhu, MD, PhD,‡ Jinming Yu, MD, PhD,‡ Michael F. Gensheimer, MD,* Billy W. Loo, Jr, MD, PhD,§ Maximilian Diehn, MD, PhD,*,‖ and Ruijiang Li, PhD*,‖

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

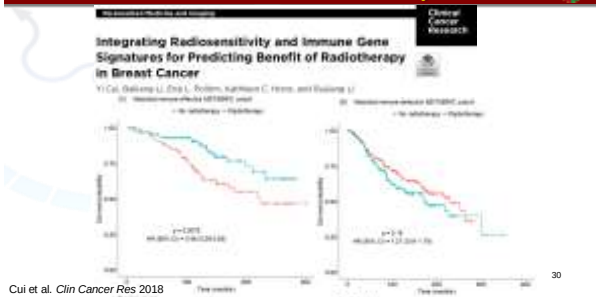
Prognostic Value of Tumor Immunity


JAMA Oncology | Original Investigation

Development and Validation of an Individualized Immune Prognostic Signature in Early-Stage Nonsquamous Non-Small Cell Lung Cancer

- 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


Clinical Cancer Research

Integrating Radiosensitivity and Immune Gene Signatures for Predicting Benefit of Radiotherapy in Breast Cancer

Cui et al. *Clin Cancer Res* 2018

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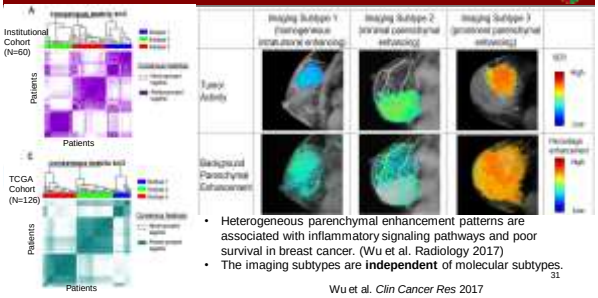
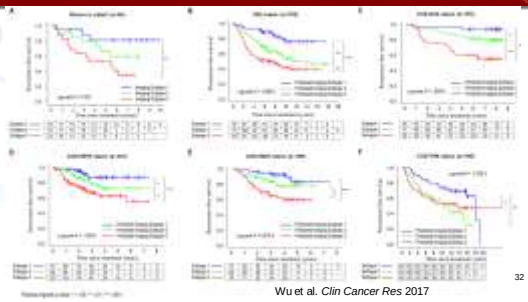
Breast Cancer Imaging Subtypes



- 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.

Wu et al. *Clin Cancer Res* 2017

Distinct Molecular Pathways and Prognoses



Wu et al. *Clin Cancer Res* 2017

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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Acknowledgment

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  - Kate Horst
  - Beth Beadle
  - Quynh Le

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