PET/CT Radiomics for Tumor Response Evaluation

August 1, 2016
Wei Lu, PhD
Department of Medical Physics
www.MSKCC.org
Department of Radiation Oncology
www.umaryland.edu

Anatomic Tumor Response Assessment in CT or MRI

- Imaging as surrogate for
  - Survival, response, time to tumor progression
- RECIST criteria based on longest diameter
  - Complete response (CR): disappear
  - Partial response (PR): ≥ 50% decrease
  - Stable disease (SD): others
  - Progressive disease (PD): ≥ 25% increase or new tumor

Metabolic Tumor Response Assessment in FDG-PET

- Strong correlation between FDG uptake and cancer cell number
- Metabolic (functional) change may occur earlier and more markedly than tumor size (anatomic) change

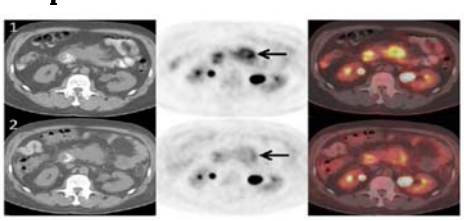
Qualitative (Visual) PET Response Evaluation

- Distribution and intensity of FDG uptake in tumor are visually compared with uptake in normal tissues
- Requires clinical experience, knowledge of disease patterns

Semi-Quantitative PET Response Assessment

- Clinic: SUVmax
- PERCIST criteria (SULpeak hottest tumor)
  - CMR: normalize to background level
  - PMR: ≥ 30% decrease and ≥ 0.8 unit in SUL
  - SMR: others
  - PMD: ≥ 30% increase and ≥ 0.8 unit in SUL or visible increase in extent of uptake, or new FDG-avid lesion

PET/CT for Tumor Response: An Example in Pancreatic Tumor



Large decline in SUL (-41%) despite stable pancreatic mass anatomically (arrows) → Partial metabolic response.

Wahl, J Nucl Med. 50(Suppl 1): 122S–150S.

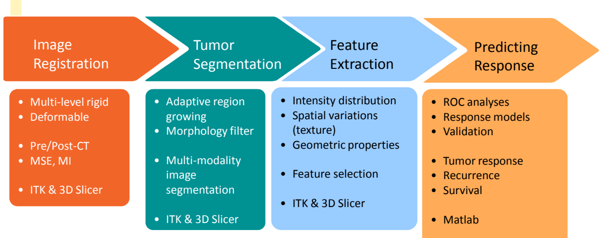
Rationales for PET/CT Radiomics?

- In population-based cancer therapy, large differences in tumor response among patients
- To make a personalized clinic decision, ≥ 90% response assessment accuracy is needed
- Solid tumors have high spatial and temporal heterogeneity at different levels
- PET/CT Radiomics quantify comprehensive tumor properties in a non-invasive way

What are Radiomics?

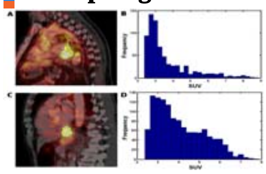
- Lambin, *et al.* 2012. *Eur J Cancer* ***48: 441-6.***
- The automatic extraction of a large number of image features from medical images
- Hypothesis: these image features could capture additional information not currently used that has prognostic value

A Framework of PET/CT Radiomics for Tumor Response Evaluation



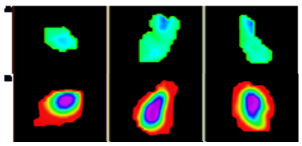
Lu, et al. 2015. Br J Radiol: 20140625.

Esophageal Cancer



SUV skewness pre-CRT
- Top: responder, more skewed (fewer higher SUVs)
- Bottom: non-responder, less skewed (more higher SUVs)

Three texture features post-CRT – Inertia, Correlation, and Cluster Prominence
- Top: responder, homogeneous FDG uptake post-CRT
- Bottom: non-responder, heterogeneous FDG uptake post-CRT

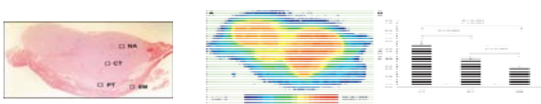


University of Maryland School of Medicine

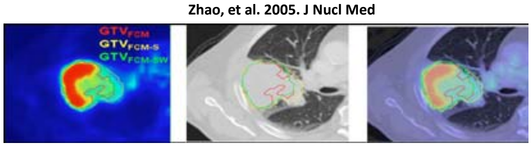
Tan, Lu et al. 2013. Int J Radiat Oncol Biol Phys 85: 1375-82.

Memorial Sloan Kettering Cancer Center

Texture: Spatial Variation in FDG Uptake is Important Prognostic Factor



Zhao, et al. 2005. J Nucl Med



Belhassen and Zaidi 2010. Med Phys

Memorial Sloan Kettering Cancer Center

Accuracy of Individual FDG-PET Features

Table 3 AUC and *P* values of the most accurate SUV features for the prediction of pathologic response to neoadjuvant chemoradiation therapy in patients with esophageal cancer

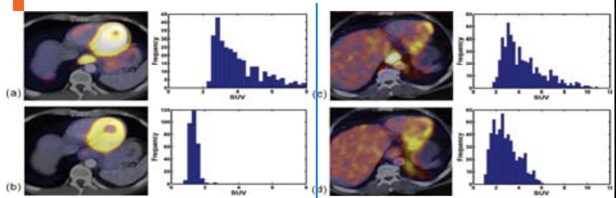
Feature	VOI	Image	AUC	*P* value
Traditional SUV intensity features				
SUV_{max} decline*	SUV_{max} point	Pre, Post	0.76	.05
SUV_{max} ratio†	SUV_{max} point	Pre, Post	0.76	.05
SUV_{max} Pre	SUV_{max} point	Pre	0.70	.14
SUV_{max} Post	SUV_{max} point	Post	0.61	.47
Intensity features				
SUV_{mean} decline*	VOI_$SUV_{2.5}$	Diff	0.79	.03
Skewness	VOI_$SUV_{2.5}$	Pre	0.76	.05
Texture features				
Inertia	VOI_$SUV_{2.5}$	Post	0.85	.01
Correlation	VOI_$SUV_{2.5}$	Post	0.80	.03
Cluster prominence	VOI_$SUV_{2.5}$	Post	0.78	.04
Geometry features				
Roundness	VOI_$SUV_{2.5}$	Pre	0.71	.12
Volume change*	VOI_$SUV_{2.5}$	Pre, Post	0.71	.12
Diameter change*	VOI_$SUV_{2.5}$	Pre, Post	0.64	.30
Geometry-intensity feature				
TGV change*	VOI_$SUV_{2.5}$	Diff	0.74	.06

Abbreviations: Diff = Pre−Post; Post = Post-CRT SUV; Pre = Pre-CRT SUV; TGV = total glycolytic volume; VOI = volumes of interest.
* Decline or change = Pre−Post.
† Ratio = Post:Pre.

Tan, Lu et al. 2013. Int J Radiat Oncol Biol Phys 85: 1375-82.

Memorial Sloan Kettering Cancer Center

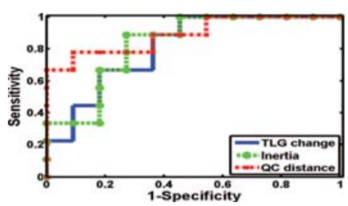
FDG-PET Histogram Distances



- A responder shows larger histogram distance (1.71)
- A non-responder shows smaller histogram distance (1.37)

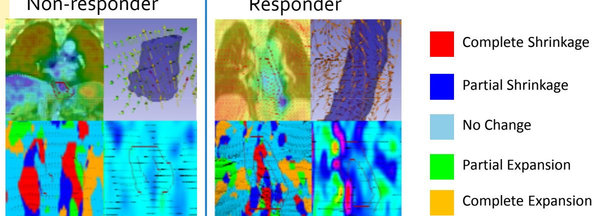
Accuracy of Histogram Distances

- More complete description of changes at all SUV levels
- Bin-to-bin or cross-bin
- 14 histogram distances have higher AUCs than conventional PET/CT response measures



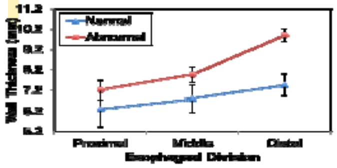
Structural Evolution Maps Computed from Deformation Vector Field (Riyahi SU-F-R-19)

Non-responder Responder

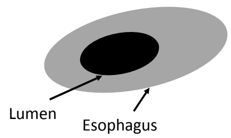


- Contraction map - localized tumor shrinking/growth
- Hessian map – magnitude/direction of displacement change

Disease Specific Features: Esophageal Wall Thickness and Asymmetry



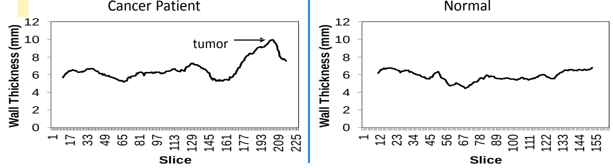
- Cancer patients: mean 8.4 (±1.2) mm
- Normal: 6.9 (± 0.7) mm, $p < 0.05$



- Tumor growth results in asymmetry in wall thickness

Wang, Lu et al. 2015. Proc. SPIE 941708.

Variation in Wall Thickness along the Esophagus

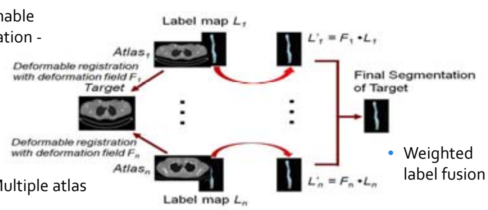


Standard Deviation: $p = 0.02$
Flatness: $p = 0.04$

Wang, Lu et al. 2015. Proc. SPIE 941708.

Extracting Esophageal Wall using Atlas-based Segmentation in CT

- Deformable registration - ANTs

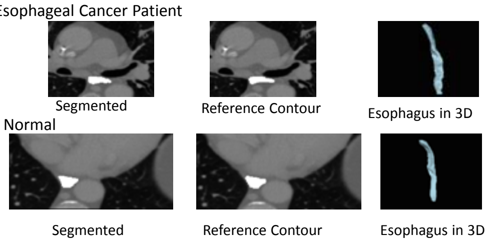


- Weighted label fusion
- Multiple atlas

Wang, Lu et al. 2015. Proc. SPIE 941708.

Segmentation Results

Esophageal Cancer Patient



- Segmentation accuracy: Dice = 0.69, need improvements

Wang, Lu et al. 2015. Proc. SPIE 941708.

University of Maryland School of Medicine — Memorial Sloan Kettering Cancer Center

Predictive Model

- Conventional criteria using cutoff values of a single measure (30% of SUL) have limitations
  - A single measure, either anatomic or metabolic
  - The optimal cutoff values depend on disease, timing after treatment, treatment, and its goal

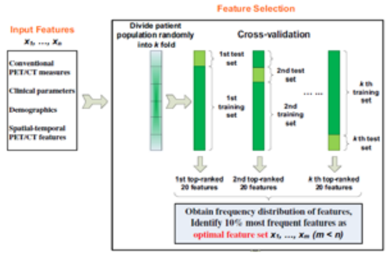
University of Maryland School of Medicine — Memorial Sloan Kettering Cancer Center

Predictive Model

- More than 100 image features, plus clinical parameters and demographics
- Feature selection
- Constructing predictive model using machine learning techniques

University of Maryland School of Medicine — Memorial Sloan Kettering Cancer Center

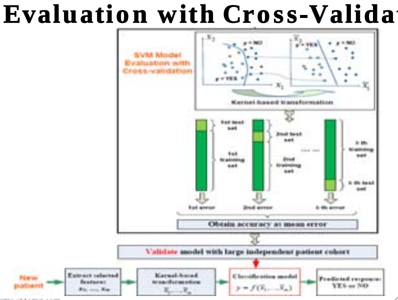
Feature Selection with Cross-Validation



Zhang, Lu et al. 2014. Int J Radiat Oncol Biol Phys 88: 195-203

University of Maryland School of Medicine — Memorial Sloan Kettering Cancer Center

Response Model Construction and Evaluation with Cross-Validation

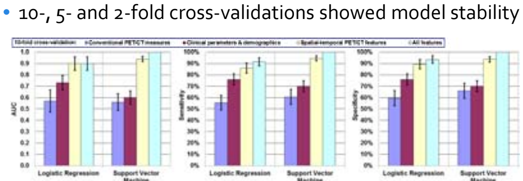


Zhang, Lu et al. 2014. Int J Radiat Oncol Biol Phys 88: 195-203

University of Maryland School of Medicine — Memorial Sloan Kettering Cancer Center

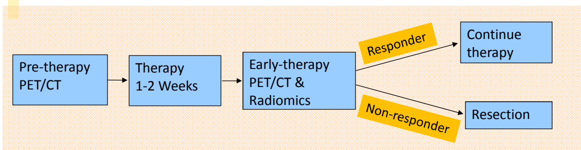
Results: Predicting Pathologic Response to Chemoradiotherapy

- SVM model with 17 selected features: AUC = 1.0
- Models with conventional response measures AUCs < 0.75
- 10-, 5- and 2-fold cross-validations showed model stability



University of Maryland School of Medicine — Zhang, Lu et al. 2014. Int J Radiat Oncol Biol Phys 88: 195-203 — Memorial Sloan Kettering Cancer Center

A Design of a Prospective Trial



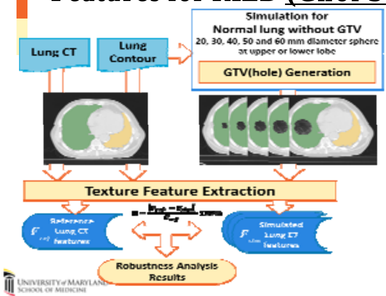
Feature Discovery vs. Candidate Feature Approach

- Feature discovery
  - A large number of features are extracted
  - Features are selected that are independent, robust, and prominent on the data
  - Usefulness of a feature is not known *a priori*
- Candidate feature approach
  - Candidates are selected based on prior knowledge
- Both require validation

Robustness of Radiomics Features

- CT features, Hunter, et al. 2013. Med Phys 40: 121916.
  - Test-retest reproducibility
  - Inter-scanner stability
  - About 40% of all features were stable
- PET features, Leijenaar, et al. 2013. Acta Oncol 52: 1391-7.
  - 71 % test-retest reproducibility
  - 91% inter-observer (tumor delineation) stability

Identify Robust Normal Lung CT Texture Features for RILD (Choi SU-F-R-31)

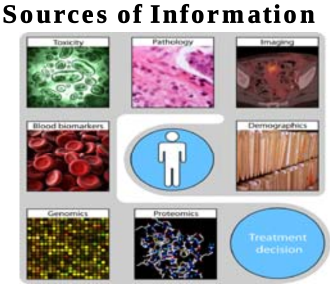


- Invariant (robust) to tumor size
- NOT correlated with lung volume
- Simulate tumors in healthy lung
- 11 of 27 features were robust

Challenges

- Validation of Radiomics features and response models on high-quality data sets
- Clinic or biological interpretation of Radiomics features
- Data sharing & standards Gillies, et al. 2016. Radiology 278: 563-77.
- Implementation and clinical acceptance

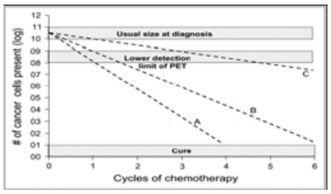
Other Sources of Information



Lambin et al. Eur J of Cancer (2012) 48, 441– 446

Limitation of Metabolic Tumor Response Assessment in PET

- Poor resolution: smallest tumors PET can detect: 4-10 mm diameter, 10^8 cells
- Depends on time to normalization (positive to negative) of the PET scan
- Hard to differentiate inflammatory tissue uptake from viable residual tumor uptake



Wahl, J Nucl Med. 50(Suppl 1): 122S–150S.

Summary

- PET/CT Radiomics revealed new, promising, prognostic information in esophageal cancer
- Combining with other sources of information to make personalized clinical decision

Acknowledgements

- Radiation Oncology, UMM
  - Shan Tan, Howard Zhang, Jiahui Wang, Steven Feigenberg, Mohan Suntha, Warren D. D'Souza
- Radiation Oncology, UMM & Medical Physics, MSKCC
  - Sadegh Riyahi, Wookjin Choi
- Diagnostic Radiology and Nuclear Medicine, UMM
  - Wengen Chen, Seth Kligerman
- NIH: R01 CA172638