APPLICATIONS AND CHALLENGES USING RADIOMICS FOR RADIATION THERAPY TREATMENT ASSESSMENT

FANG-FANG YIN, DUKE UNIVERSITY

AAPM 2020 VIRTUAL ANNUAL MEETING 07-15-2020

DISCLOSURES

- NIH: served as PI or co-PI for the following grants
  R21CA218940, R01CA184173, R21CA195317, R01EB028324
- Varian Medical Systems: research grants
- Duke Kunshan University: professor

RADIOMICS: DEFINITION AND MOTIVATION

Radiomics:

- Converts medical images into high-dimensional quantitative features
- Analyzes combined features with other patient data to provide clinical decision support. It has been investigated for
  - Evaluating tumor prognostic or predictive abilities
  - Stratification of tumor histology or stages
  - Describing the relationship between images and clinical outcomes
  - Association with underlying gene expression patterns

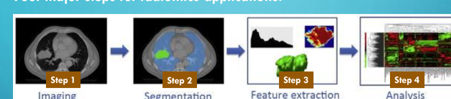
Advantages:

- Noninvasive
- Individualized
- Low cost
- Potentially routine procedure

Lambin et al Eur J Cancer (2012)
Parmar et al. Sci. Rep. 5, 13087 (2015)

RADIOMICS APPROACHES AND MACHINE LEARNING

- Four major steps for radiomics applications:



To acquire quality medical image | To define volumes for feature analysis | To represent quantitative information | To build radiomics model for decision

- Machine-learning drives the success of radiomic applications through feature selection and classification to achieve high accuracy, reliability, efficiency and to reduce overfitting of models

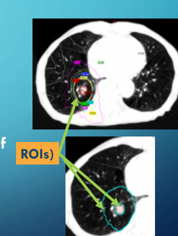
Lambin et al Eur J Cancer (2012)
Parmar et al. Sci. Rep. 5, 13087 (2015)

RADIOMICS APPROACH 1: IMAGE ACQUISITION

- Potential variations in imaging for radiomics feature calculation:
  - Different imaging modalities (such as MRI, CT, PET, etc.)
  - Different imaging units (different CTs used in a hospital, etc.)
  - Different imaging parameters and dates used in the same imaging modality
  - Different reconstruction methods/parameters (i.e., CT/CBCT, MRI)
  - Different calculated datasets from 4D CT dataset (MIP, inhale, AveIP …)
  - ……
- These variations affect calculated feature values
- Data harmonization minimizes variations between image data sets and should be done before any application

RADIOMICS APPROACH 2: IMAGE SEGMENTATION

- Features can be calculated from
  - Whole image
  - Region-of-interest (ROI):
    tumor, lung, a specific structure/organ, or a volume inside lung as shown in figures
- Feature values could be very different if using different ROIs
- Accurate image segmentation is very critical: manual, automatic, and semi-automatic segmentation

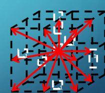


RADIOMICS APPROACH 3: FEATURE EXTRACTION

Software packages used for feature calculation should be validated!

Typical four feature groups:

- **Intensity:** estimate the first order statistics of the intensity histogram
- **Shape:** describe the 3D geometric properties of the tumor (or ROIs)
- **Textural features:** quantify the intra-tumor heterogeneity. They can be derived from the gray level co-occurrence matrix (GLCM) and gray-level run length matrix (GLRLM), etc., averaging over all thirteen directions (fig)



- **Wavelet features:** transform domain representations of the intensity and textural features - They can be computed on different wavelet decompositions of the original image using a coiflet wavelet transformation

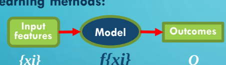
Parmar et al. Sci. Rep. 5, 13087 (2015)

RADIOMICS APPROACH 4: FEATURE ANALYSES

- The issues related to the extracted features
  - Number of features: in the order of 10th, 100th, and 1000th.
  - Nature of features: Similar or correlated
  - Small data set compared to feature number: over fit to models
- Feature selection
  - To minimize the number of features for decision models
    – use machine-learning (or deep-learning) algorithms
- Feature classification
  - To build a model which classifies input features into corresponding output endpoint(s)
    – use machine-learning (or deep learning) algorithms

RADIOMICS APPROACH 4: FEATURE ANALYSES

- Build a decision model using machine learning methods:



{xi} f{xi} O

(Training using training/validation data)

O = f{xi}

(Testing using test data to evaluate the trained model)

- **Evaluation method:**
  Area under ROC curve (AUC)

Parmar, C. et al. Sci. Rep. 5, 13087 (2015)

Classification method acronym	Classification method name	Feature Selection method acronym	Feature selection method name
Nnet	Neural network	RELF	Relief
DT	Decision Tree	FSCR	Fisher score
BST	Boosting	GINI	Gini index
BY	Bayesian	CHSQ	Chi-square score
BAG	Bagging	JMI	Joint mutual information
RF	Random Forset	CIFE	Conditional infomax feature extraction
MARS	Multi adaptive regression splines	DISR	Double input symmetric relevance
SVM	Support vector machines	MIM	Mutual information maximization
DA	Discriminant analysis	CMIM	Conditional mutual information maximization
NN	Neirest neighbour	ICAP	Interaction capping
GLM	Generalized linear models	TSCR	T-test score
PLSR	Partial least squares and prinicipal componenet regression	MRMR	Minimum redundancy maximum relevance
—	—	MIFS	Mutual information feature selection
—	—	WLCX	Wilcoxon

12 machine-learning selectors/classifiers

RADIOMICS APPLICATIONS IN RADIATION THERAPY

Processes in RT

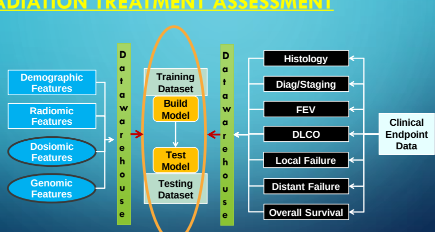
- Diagnosis
- Simulation
- Planning
- Localization
- Treatment
- Assessment
- Quality assurance

AI/Radiomics applications

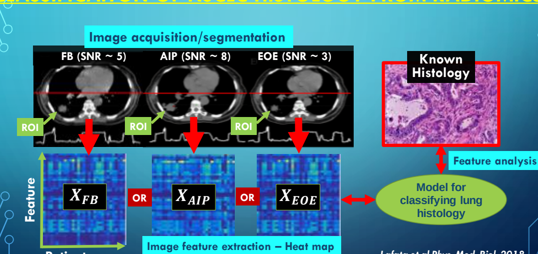
- Computer-aided diagnosis, etc.
- Low-dose imaging/Prediction
- Auto- segmentation/planning
- Imaging/analysis
- Optimization/tracking
- Outcome modeling and prediction
- Automation

To address the most complex challenges across every RT function and process, we need to combine radiomics/AI technology and human clinical expertise

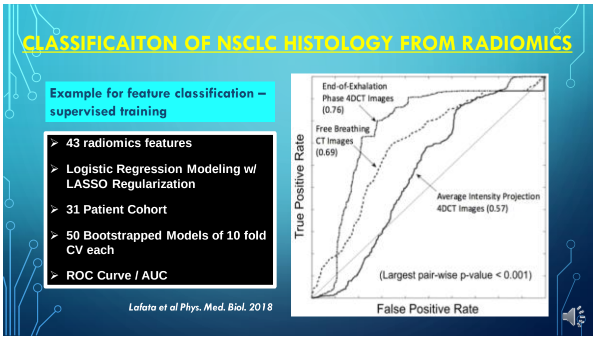
SAMPLE PLATFORM USING ~OMICS FOR LUNG RADIATION TREATMENT ASSESSMENT

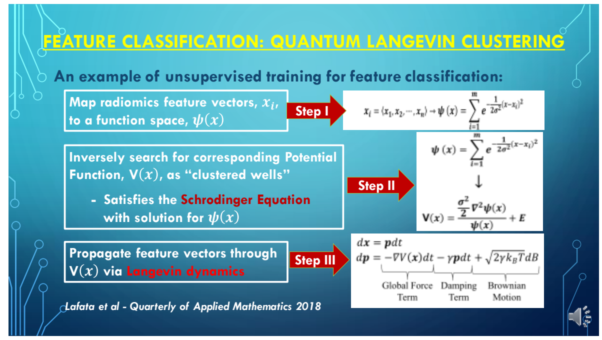


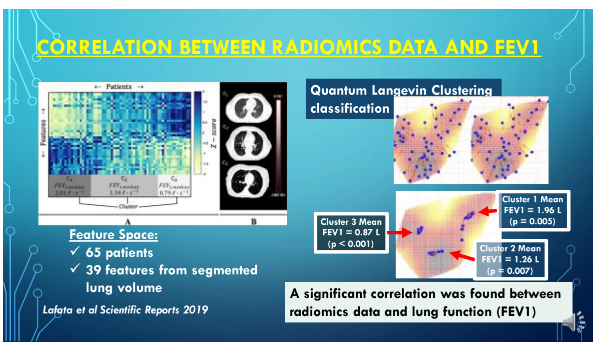
CLASSIFICAITON OF NSCLC HISTOLOGY FROM RADIOMICS

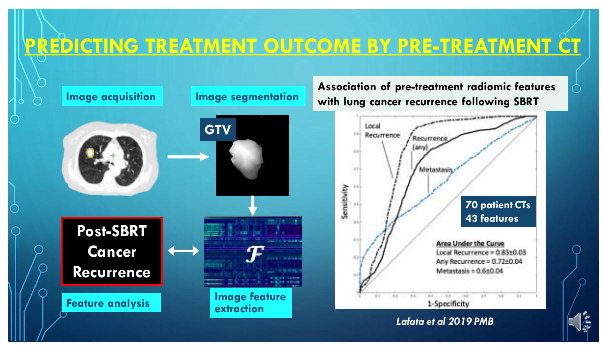


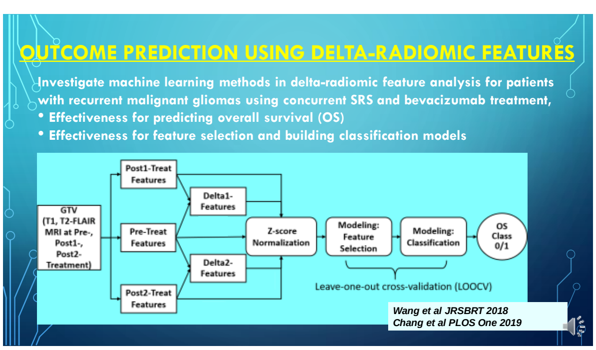
Lafata et al Phys. Med. Biol. 2018

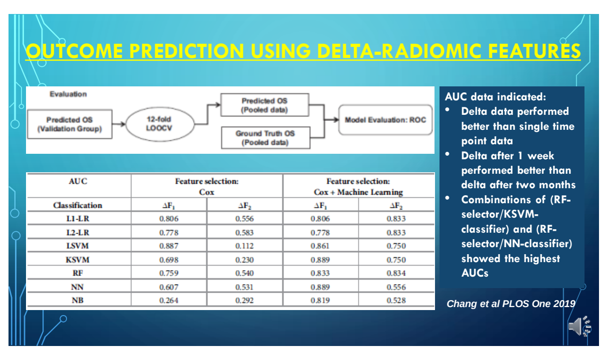






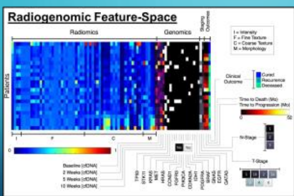


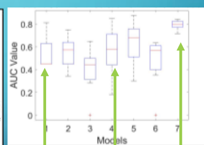




AUC	Feature selection: Cox		Feature selection: Cox + Machine Learning	
Classification	ΔF_1	ΔF_2	ΔF_1	ΔF_2
L1-LR	0.806	0.556	0.806	0.833
L2-LR	0.778	0.583	0.778	0.833
LSVM	0.887	0.112	0.861	0.750
KSVM	0.698	0.230	0.889	0.750
RF	0.759	0.540	0.833	0.834
NN	0.607	0.531	0.889	0.556
NB	0.264	0.292	0.819	0.528

RADIOGENOMICS: HYBRID BIOMARKERS FOR PREDICTING LUNG CANCER PATIENT SURVIVAL





p53 mutation

Delta radiogenomics

Post-Tx delta radiomics

Radiogenomic data detailing the information collected from 24 cases as part of treatment response assessment

Weng et al MS thesis 2018

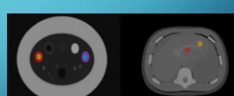
FEATURE EXTRACTION: REPRODUCIBILITY/CONSISTENCY

- Issues
  - Different modalities and different parameters are used for imaging and reconstruction
  - Different software packages are available for feature extraction with the same names but different calculation methods, etc.
- Solutions
  - Reproducibility check for imaging systems: a phantom is scanned by different units and features are calculated using the same software package
  - Consistency check for different software packages: digital phantoms are used for feature calculation using different software packages

PHANTOMS FOR RADIOMICS REPRODUCIBILITY

Testing for reproducibility radiomics features – as the fundamental requirement for generalizability of radiomics-based clinical prediction models

- Three phantoms: 1) Catphan 700, 2) COPD Gene Phantom II, 3) Triple modality 3D Abdominal Phantom
- Three Dutch medical centers
- Three CT scanners: two from Siemens one from Philips
- CT scanner details and image acquisition parameters for baseline scans were tabulated
- Data are publically available



COPD Gene Phantom II

Triple modality 3D Abdominal Phantoms

Kalendralis et al.: CT phantoms public dataset for radiomics Med Phys 2019

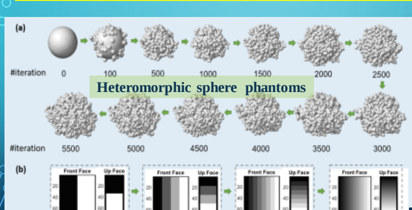
PHANTOMS FOR RADIOMICS REPRODUCIBILITY

Sample CT scanner details and image acquisition parameters for baseline scans

Parameters	DICOM tags	*MAASTRO Clinic (MAAS)*	Radboud University Medical Center (RADB)	University Medical Center Groningen (UMCG)
Catphan 700/COPDGene Phantom II baseline scan parameters				
Manufacturer	(0008, 0070)	Siemens	Phillips	Siemens
Model	(0008, 1090)	Biograph 40	Brilliance Big Bore	Biograph 64
Software Version	(0018, 1020)	syngo CT 2006A	3.6.6	VG60A
Slice thickness (mm)	(0018, 0050)	3	3	3
TUBE VOLTAGE (KV)	(0018, 0060)	120	120	80
Reconstruction diameter (mm)	(0018, 1100)	500	255	239
Tube current (mA)	(0018, 1151)	39	134	149
EXPOSURE (mAs)	(0018, 1152)	24	124	53
Convolution kernel	(0018, 1210)	B31f	B	I30f
Rows	(0028, 0010)	512	1024	512
Columns	(0028, 0011)	512	1024	512
Pixel spacing	(0028, 0030)	0.98	0.25	0.46
Bits stored	(0028, 0101)	12	12	12
High bit	(0028, 0102)	11	11	11
Rescale offset	(0028, 1052)	−1024	−1024	−1024
Rescale slope	(0028, 1053)	1	1	1

Kalendralis et al.: CT phantoms public dataset for radiomics Med Phys 2019

CHARACTERIZING INCONSISTENCIES AMONG RADIOMICS EXTRACTION TOOLBOXES USING DIGITAL PHANTOMS



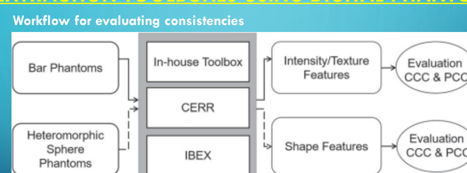
Three toolboxes:

- CERR (Computational Environment for Radiological Research)
- IBEX (imaging biomarker explorer)
- An in-house radiomics platform

Chang et al Biomed. Phys. Eng. Express 6 (2020)

CHARACTERIZING INCONSISTENCIES AMONG RADIOMICS EXTRACTION TOOLBOXES USING DIGITAL PHANTOMS

Workflow for evaluating consistencies



CCC: concordance correlation coefficient

PCC: Pearson correlation coefficient

Chang et al Biomed. Phys. Eng. Express 6 (2020)

CHARACTERIZING INCONSISTENCIES AMONG RADIOMICS EXTRACTION TOOLBOXES USING DIGITAL PHANTOMS

	Number of Features	Perfect Agreement (CCC = 1)	Strong Agreement (CCC > =0.8)	Moderate Agreement (0.5 < CCC < 0.8)	Weak Agreement (CCC < 0.5)
CCC(IH/CERR)	55	52.7%	70.9%	3.6%	25.5%
CCC(IH /IBEX)	31	45.2%	61.3%	0%	38.7%
CCC(CERR/IBEX)	31	54.8%	61.3%	0%	38.7%

Percentage of score categories in CCC pair-comparison.

61 features typically extracted from three radiomics toolboxes

Toolboxes	Feature Name	PCC
IH versus CERR	Variation Of Intensity	−0.735
IH versus IBEX	Differential Entropy	−0.387
	Info Measure Correlation1	0.452
	Variation Of Intensity	−0.735
	Coarseness	−0.381
	Complexity	−0.114
CERR versus IBEX	Differential Entropy	−0.386
	Info Measure Correlation1	0.479
	Busyness	−0.387
	Coarseness	−0.382
	Complexity	−0.113
	Contrast	−0.386

Features with Pearson correlation lower than 0.95

3 key sources of discrepancy:
1. Mathematical definitions
2. Pre-processing steps inherent to toolboxes
3. Differences in calculation methods

Chang et al Biomed. Phys. Eng. Express 6 (2020)

AI/RADIOMICS TECHNOLOGIES FOR CLINICAL TRIALS

Guidelines for the Use of Radiomics in NRG Clinical Trials Involving Brain Tumors

I. Introduction

Radiomics is an emerging science of mining medical imaging data sets for new information in non-traditional ways that can be used for clinical decision making. Radiomics features are extracted from medical images and then are typically modeled using some machine learning techniques to draw clinical decisions. The applications of radiomics in the treatment of brain

NRG medical physics Sub-Committee formed a workgroup to develop guidelines for the use of radiomics in NRG clinical trials involving brain tumors to ensure the quality of the trial.

SUMMARY

- Radiomics is an emerging and rapidly developing field, which uses extracted radiographic features as biomarkers for disease diagnosis, prediction and treatment assessment
- Applications of radiomics in radiation oncology have demonstrated some encouraging results for treatment prediction and assessment
- Quality assurance for applying radiomics and/or radiogenomics to evaluate clinical outcomes is essential

ACKNOWLEDGEMENTS

Duke Faculty:
Kyle Lafata, PhD
Zheng Chang, PhD
Chunhao Wang, PhD
Chris Kelsey, MD
John Kirkpatrick, MD, PhD
Yunfeng Cui, PhD
Jackie Wu, PhD
Lei Ren, PhD
Jordan Torok, MD
Chris Willett, MD
David Brizel, MD
Yvonne Mowery, MD, PhD

Students:
Yushi Chang, MS
Xiaoyu Duan, MS
Ruiqi Geng, MS
Zhenyu Yang, MS
Yin Gao, MS
Xinru Chen, MS
Nathan Shaffer, BS
Wenzheng Sun, PhD

Other collaborators:
Jian-guo Liu, PhD
Zhennan Zhou, PhD
Jing Cai, PhD
Julian Hong, MD, MS
Bradley G Ackerson, MD
Betty Tong, MD
Michael Corradetti, MD, PhD
Ying Xiao, PhD
Duke Woo Center
Duke Kunshan University

And others whose names may not be listed

THANK YOU FOR YOUR ATTENTION