APPLICATIONS AND CHALLENGES USING RADIOMICS FOR RADIATION THERAPY TREATMENT ASSESSMENT

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RADIOMICS: DEFINITION AND MOTIVATION

- 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


RADIOMICS APPROACHES AND MACHINE LEARNING

- Four major steps for radiomics applications:
  - Step 1: To acquire quality medical image
  - Step 2: To define volumes for feature analysis
  - Step 3: To represent quantitative information
  - Step 4: 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


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

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- Duke Kunshan University: professor
**RADIOMICS APPROACH 3: FEATURE EXTRACTION**

- 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 grey level co-occurrence matrix (GLCM) and grey-level run length matrix (GLRLM), etc., arranging over all thirteen directions (9x3).
  - **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 cofif wavelet transformation.


**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 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.
CLASSIFICATION OF NSCLC HISTOLOGY FROM RADIOMICS

Example for feature classification – supervised training

- 43 radiomics features
- Logistic Regression Modeling w/ LASSO Regularization
- 31 Patient Cohort
- 50 Bootstrapped Models of 10 fold CV each
- ROC Curve / AUC


FEATURE CLASSIFICATION: QUANTUM LANGEVIN CLUSTERING

An example of unsupervised training for feature classification:

- Map radiomics feature vectors, $\mathbf{x}_i$, to a function space, $\mathcal{H}(\mathbf{x})$
- Inversely search for corresponding Potential Function, $V(\mathbf{x})$, as “clustered wells”
  - Satisfies the Schrödinger Equation with solution for $\psi(\mathbf{x})$
- Propagate feature vectors through $V(\mathbf{x})$ via Langevin dynamics

Step I

$\mathbf{x} = \psi(\mathbf{x}_i) \Rightarrow \psi = \mathcal{H}(\mathbf{x}_i)$

Step II

$\mathbf{c} = \mathcal{F}(\mathbf{x}_i)$

Step III

$\gamma = \mathcal{G}(\mathbf{x}_i)$

Lafata et al - Quarterly of Applied Mathematics 2018

CORRELATION BETWEEN RADIOMICS DATA AND FEV1

A significant correlation was found between radiomics data and lung function (FEV1)

Feature Space:

- 65 patients
- 39 features from segmented lung volume

Lafata et al Scientific Reports 2019

PREDICTING TREATMENT OUTCOME BY PRE-TREATMENT CT

Image acquisition → Image segmentation → GTV

Post-SBRT Cancer Recurrence

Feature analysis → Image feature extraction

Association of pre-treatment radiomic features with lung cancer recurrence following SBRT

Lafata et al 2019 PMB

OUTCOME PREDICTION USING DELTA-RADIOMIC FEATURES

Investigate machine learning methods in delta-radiomic feature analysis for patients with recurrent malignant gliomas using concurrent SRS and bevacizumab treatment,

- Effectiveness for predicting overall survival (OS)
- Effectiveness for feature selection and building classification models

Wang et al JRSRBT 2018

Chang et al PLOS One 2019

AUC data indicated:

- Delta data performed better than single time point data
- Delta after 1 week performed better than data after two months
- Combinations of (RF-selector/KSVM-classifier) and (RF-selector/NN-classifier) showed the highest AUCs

Chang et al PLOS One 2019
**RADIOGENOMICS: HYBRID BIOMARKERS FOR PREDICTING LUNG CANCER PATIENT SURVIVAL**

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

**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

**CHARACTERIZING INCONSISTENCIES AMONG RADIOMICS EXTRACTION TOOLBOXES USING DIGITAL PHANTOMS**

- Three toolboxes:
  - CERR (Computational Environment for Radiological Research)
  - IBEX (imaging biomarker explorer)
  - In-house radiomics platform
- Workflow for evaluating consistencies

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61 features typically extracted from three radiomics toolboxes


Features with Pearson correlation lower than 0.95

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

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