Radiomics and Machine Learning in Predicting Response from Medical Imaging

Maryellen L. Giger, PhD
University of Chicago

MLG is a cofounder and shareholder in Quantitative Insights (now Qlarity Imaging), a stockholder in R2 technology/InSight and Qview Medical, receives royalties from InSight, GE Medical Systems, MEDIAN Technologies, Riverain Medical, Mitsubishi and Toshiba.

AI for predicting response session

Learning Objectives:
1. Describe the use of artificial intelligence to predict treatment outcomes
2. Illustrate examples of predicting response in liver, breast, lung, and head and neck cancer treatment
3. Explain how imaging characteristics can be quantified for characterization of treatment response

Radiomics and Machine Learning in Predicting Response

- Radiomics and machine learning in imaging for precision medicine involves research in discovery, predictive modeling, and robust clinical translation.
- Quantitative radiomic analyses, an extension of computer-aided diagnosis (CAD) methods, are yielding novel image-based tumor characteristics, i.e., signatures that may ultimately contribute to the design of patient-specific breast cancer diagnostics and treatments.
- These “virtual biopsies” have a role in predicting response prior to or during the early stages of cancer treatment.
### Quantitative Radiomics and Machine Learning in Breast Cancer Image Analysis

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<th>Biomedical Question</th>
<th>Computer-extracted Image-based Biomarker (Radiomics/ML)</th>
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| What is a person’s risk of future breast cancer? | Computerized assessment of risk  
- Image-based cancer risk biomarkers |
| Screening - Is there a potential cancer in an asymptomatic person? | CADx = computer-aided detection  
- Localization detection task  
- Second reader IN SCREENING |
| What is the likelihood that the suspect lesion is cancer? | CADx = computer-aided diagnosis  
- Characterization/classification task  
- Diagnostic image-based biomarker |
| How aggressive is the cancer? | Computerized assessment of prognosis  
- Image-based prognostic marker |
| Is the cancer responding to treatment? | Computerized assessment of response to therapy |

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**Machine Learning in Breast Cancer Diagnosis and Management**

- **Human-Engineered Radiomics**
  - Computerized Tumor Segmentation
  - Computer-Extracted Tumor Features
  - Classification on clinical question

- **Deep Learning Radiomics**
  - Convolutional Neural Networks (CNN)

Clinical 3D Breast MRI image
Machine Learning in Breast Cancer Diagnosis and Management

Human-Engineered Radiomics

Deep Learning Radiomics
Convolutional Neural Networks (CNN)

Classification on clinical question


Computer-extracted Breast Cancer on MRI
(can analyze as a “virtual” digital biopsy of the tumor)

- non-invasive
- covers complete tumor
- repeatable

Quantitative Radiomics and Deep Learning in Breast Cancer Diagnosis

CAD pipeline = radiomics pipeline

Schematic
Example of quantitative radiomic features

Computer-extracted **objective** phenotypes from breast MRIs

**Shape of Breast Tumors**

- **Sphericity:** 0.80; 0.85
- **Irregularity:** 0.65; 0.78

Quantitative Radiomics and Deep Learning in Breast Cancer Diagnosis

- **4D DCE MRI images**
- **Enhancement heterogeneity & kinetics**
  - of the uptake and washout of the contrast agent during the imaging time

Tumors are Heterogeneous:
- e.g., **Contrast Enhancement Heterogeneity**

Heterogeneity of Tumors:

- **Regions of most enhancing voxels**
Conventional Mathematically-Engineered Radiomics CADx

- Center of the lesion is indicated
- Followed by automatic lesion segmentation
- After the lesion is segmented, image features (i.e., mathematical descriptors) are extracted from the lesion:
  - Lesion size
  - Lesion shape
  - Intensity features (e.g., average grey level, contrast)
  - Texture within the lesion
  - Margin morphology (e.g., spiculation and sharpness) of the mass
  - Kinetic enhancement features
- Features then merged by a classifier (e.g., LDA, SVM) to yield a signature indicating an estimate of the likelihood of malignancy (or some other clinical state)

Machine Learning in Breast Cancer Diagnosis and Management

Human-Engineered Radiomics

Deep Learning Radiomics

Convolutional Neural Networks (CNN)

CNN structure – Transfer Learning

- Use: trained Alexnet or VGG19
- Convolutional blocks + fully connected layers
- ImageNet weights (1000 classes) of natural scenes
Transfer Learning: **Feature Extractor**

Machine Learning in Breast Cancer Diagnosis and Management

- **Human-Engineered Radiomics**
  - Computerized, Quantitative, Tumor Features
  - Classification on clinical question

- **Deep Learning Radiomics**
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Human-Engineered CAD/Radiomics & Deep Learning CAD/Radiomics (task of distinguishing between cancers and non-cancers)

- Likelihood of being cancer as determined from conventional CADx
- Likelihood of being cancer as determined from deep learning

Likelihood of being cancer as determined from deep learning

RED = CANCER
GREEN = Non-CANCER

References:
Human-Engineered CADx & Deep Learning CADx

(diagnostic task of distinguishing between cancers and non cancers across breast imaging modalities; ROC analysis)

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<tr>
<th>Breast Imaging Modality</th>
<th>Number of Cases</th>
<th>Conventional CADx (AUC)</th>
<th>Deep Learning CNN (AUC)</th>
<th>Combination Conventional CADx &amp; CNN (AUC)</th>
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<td>Digital Mammmography</td>
<td>245</td>
<td>0.79</td>
<td>0.81</td>
<td>0.86</td>
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<tr>
<td>Ultrasound</td>
<td>1125</td>
<td>0.84</td>
<td>0.87</td>
<td>0.90</td>
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<tr>
<td>DCE-MRI</td>
<td>690</td>
<td>0.86</td>
<td>0.87</td>
<td>0.89</td>
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Two Stage Process: Discovery and Predictive Modeling for Personalized Patient Care

Screening

Diagnostic Imaging

Biopsy Results, Genetic Testing Results

MAGNO-GENOMICS DISCOVERY

Virtual "digital" biopsies

TRANSLATION: Predictive Modeling

Treatment Planning & Following for Response

Assessment of Risk of Recurrence

Virtual "digital" biopsies

Use virtual biopsy for when an actual biopsy is not practical

AI for predicting response

- Predicting response to treatment
  - Assessing extent of cancer within the breast
  - Assessing response as complete response, partial response, no response, or progression
  - Assessing lymph node involvement
  - Choosing the appropriate therapy
- Predicting response during treatment
  - Monitoring the therapy
  - Assessing need to change therapy
- Assessing risk of recurrence
  - Recurrence-free survival
Imaging Neoadjuvant Therapy Response in Breast Cancer
(Fowler AM, Mankoff DA, Joe BN, Radiology 2017)

Images of a newly diagnosed clinical stage II A right breast cancer.

Left: Maximum intensity projection from contrast material-enhanced breast MR imaging performed prior to neoadjuvant chemotherapy.

Right: Breast MR images after neoadjuvant chemotherapy show resolution of the abnormal enhancement. Final pathologic findings after breast-conserving surgery showed complete pathologic response.

Functional Tumor Volume Predicts Recurrence-free Survival

Giger AAPM 2019

Top row: Maximum intensity projection images

Bottom row: Corresponding FTV maps for a patient with an excellent clinical response and disseminated residual disease.

Semi-manual delineation of FTV

Hytonen NM, et al. Radiology 2012

Most-enhancing tumor volume by MRI radiomics predicts recurrence-free survival "early on" in neoadjuvant treatment of breast cancer

Karm (Khelifa) N, Li N, Natra Antropova, Alexandra Edwards, John Papacostas, and Marellen J, Giger

Applied automatic calculation of quantitative radiomics to cases from the i-SPY 1 (ACRIN 6657) study of dynamic contrast-enhanced MR images.
Most-Enhancing Tumor Volume by MRI radiomics predicts recurrence-free survival “early on” in neoadjuvant treatment of breast cancer

A subset, based on availability, of the ACRIN 6657 dynamic contrast-enhanced MR images was used in which we analyzed images of all women imaged at

- pre-treatment baseline (141 women: 40 with a recurrence, 101 without) and
- all those imaged after completion of the first cycle of chemotherapy, i.e., at early treatment (141 women: 37 with a recurrence vs. 105 without).

Kaplan-Meier recurrence-free survival estimates for METV at the early treatment time point using the highest quartile cut-point (Q3) with corresponding p-values by hormone-receptor status subgroup: hormone-receptor positive and HER2 negative (N=66, left), HER2 positive (N=38, middle), and triple negative (N=36, right) with corresponding p-values (for 2 cases the hormone receptor status was unknown).

MRI Imaging Radiomics
Signatures for Predicting the Risk of Breast Cancer Recurrence as Given by Research Versions of MammaPrint, Oncotype DX, and PAM50 Gene Assays

Use of Deep Learning to Assess Response

Comparison of breast DCE-MRI contrast time points for predicting response to neoadjuvant chemotherapy using deep convolutional neural network features with transfer learning


Prior to Initiation of Chemotherapy, Can We Predict Breast Tumor Response? Deep Learning Convolutional Neural Networks Approach Using a Breast MRI Tumor Dataset

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Discussion & Summary

- Radiomics from computer-aided diagnosis (CAD) can be applied to the task of evaluating tumors for therapy assessment
  - Human-engineered radiomics
  - Deep learning
- Collecting and curating datasets for training and testing
  - Accurate truth labels of cancers undergoing therapy
  - Correct database distributions
  - Correct separation of cases in training OR testing
  - Appropriate statistical evaluations
Thank you

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