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AAPM 2019: AI for predicting response session

Radiomics and Machine Learning in Predicting Response from Medical Imaging

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University of Chicago

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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

Biomedical Question	Computer-extracted Image-based Biomarker (Radiomics/ML)
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?	CADe = 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 Giger AAPM 2019

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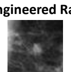
Machine Learning in Breast Cancer Diagnosis and Management

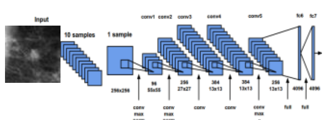
Human-Engineered Radiomics



Computerized Tumor Segmentation

Computer-Extracted Tumor Features

Deep Learning Radiomics
Convolutional Neural Networks (CNN)



CNN Schematic

Classification on clinical question

Huynh B, Li H, Giger ML: Digital mammographic tumor classification using transfer learning from deep convolutional neural networks. J Medical Imaging 3(3), 034501 (2016).

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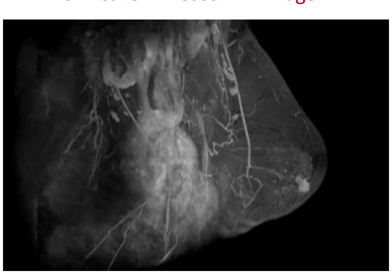
Clinical 3D Breast MRI image



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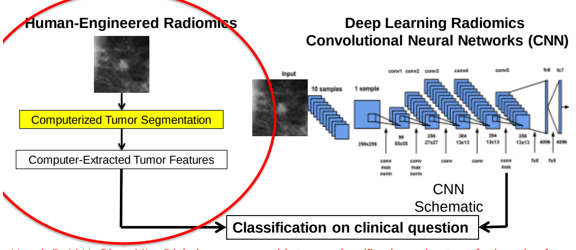
Machine Learning in Breast Cancer Diagnosis and Management



Huynh B, Li H, Giger ML: Digital mammographic tumor classification using transfer learning from deep convolutional neural networks. J Medical Imaging 3(3), 034501 (2016).

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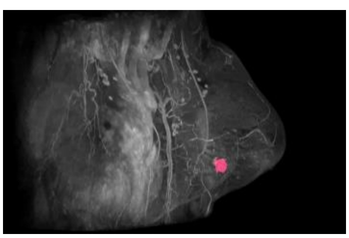
Computer-extracted Breast Cancer on MRI
(can analyze as a "virtual" digital biopsy of the tumor)



- non-invasive
- covers complete tumor
- repeatable

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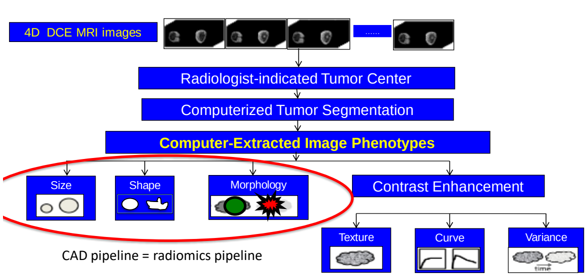
Quantitative Radiomics and Deep Learning in Breast Cancer Diagnosis



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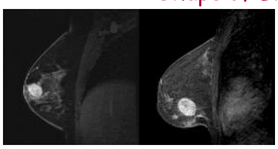
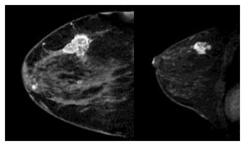
Example of quantitative radiomic features

Computer-extracted objective phenotypes from breast MRIs

Shape of Breast Tumors





Sphericity: 0.80; 0.85 Irregularity: 0.65; 0.78

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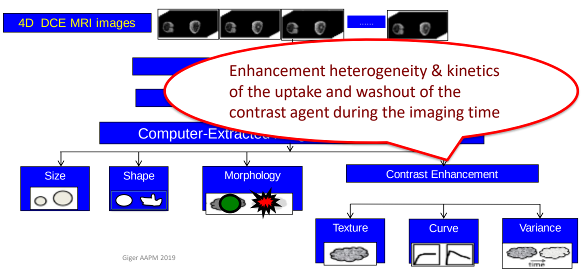
Quantitative Radiomics and Deep Learning in Breast Cancer Diagnosis



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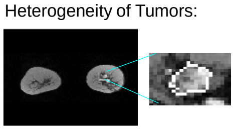
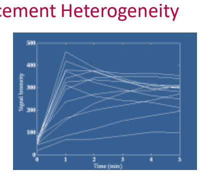
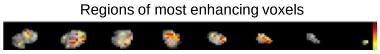
Tumors are Heterogeneous:
e.g., Contrast Enhancement Heterogeneity

Heterogeneity of Tumors:





Regions of most enhancing voxels



Radiomics of texture giving a measure of the heterogeneity of contrast uptake; also called "habitat" image analysis.

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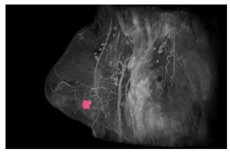
Conventional Mathematically-Engineered Radiomics CADx

- Center of the lesion is indicated
- Followed by automatic lesion segmentation
- After the lesion is segmented, image features (i.e., mathematical descriptors) areextracted from the lesion:
  - Lesion size
  - Lesion shape
  - Intensity features (e.g., average gray 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)



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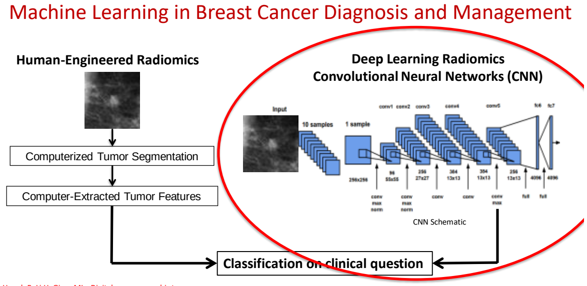
Machine Learning in Breast Cancer Diagnosis and Management



Huynh B, Li H, Giger ML: Digital mammographic tumor classification using transfer learning from deep convolutional neural networks. J Medical Imaging 3(3), 034501 (2016).

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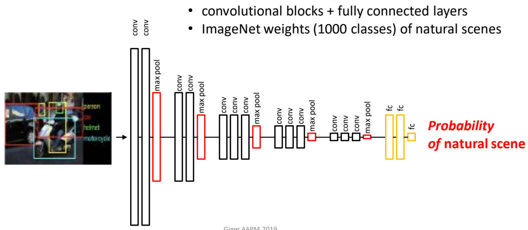
CNN structure – Transfer Learning

- Use: trained Alexnet or VGG19
- convolutional blocks + fully connected layers
- ImageNet weights (1000 classes) of natural scenes



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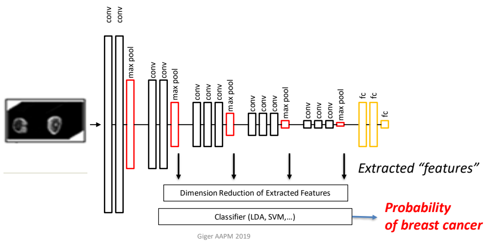
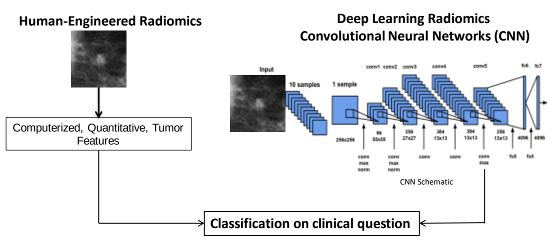
Transfer Learning: **Feature Extractor**



Machine Learning in Breast Cancer Diagnosis and Management

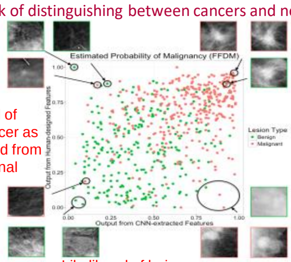


Antropova N, Huynh BQ, Giger ML: A deep fusion methodology for breast cancer diagnosis demonstrated on three imaging modality datasets. Medical Physics online doi.org/10.1002/mp.12453, 2017. Giger AAPM 2019

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

RED = CANCER

GREEN = Non-CANCER

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Human-Engineered CADx & Deep Learning CADx
(**diagnostic** task of distinguishing between cancers and non cancers across breast imaging modalities; ROC analysis)

Breast Imaging Modality	Number of Cases	Conventional CADx (AUC)	Deep Learning CNN (AUC)	Combination Conventional CADx & CNN (AUC)
Digital Mammography	245	0.79	0.81	0.86
Ultrasound	1125	0.84	0.87	0.90
DCE-MRI	690	0.86	0.87	0.89

Antropova N, Huynh BQ, Giger ML: A deep fusion methodology for breast cancer diagnosis demonstrated on three imaging modality datasets. Medical Physics online doi.org/10.1002/mp.12453, 2017.

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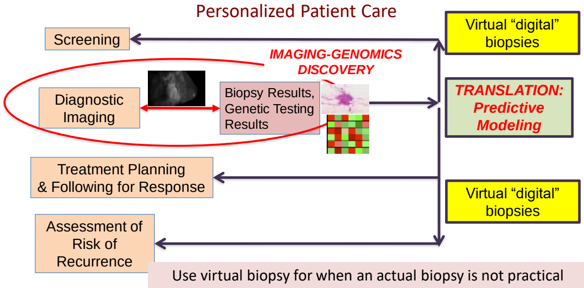
Two Stage Process: Discovery and Predictive Modeling for Personalized Patient Care



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

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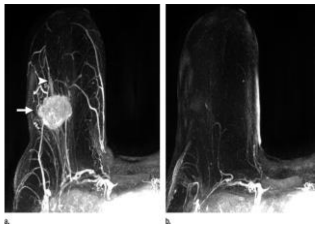
Imaging Neoadjuvant Therapy Response in Breast Cancer
(Fowler AM, Mankoff DA, Joe BN, Radiology 2017)

Images of a newly diagnosed clinical stage IIA 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 shows resolution of the abnormal enhancement. Final pathologic findings after breast-conserving surgery showed complete pathologic response.



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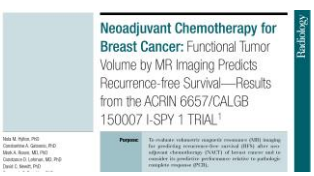

Neoadjuvant Chemotherapy for Breast Cancer: Functional Tumor Volume by MR Imaging Predicts Recurrence-free Survival—Results from the ACRIN 6657/CALGB 150007 I-SPY 1 TRIAL[1]

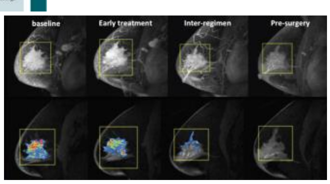
Radiology

Functional Tumor Volume Predicts Recurrence-free Survival

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

Hylton NM, et al. Radiology 2012



Drukker *et al. Cancer Imaging* (2018) 18:12
https://doi.org/10.1186/s40644-018-0145-9

Cancer Imaging

RESEARCH ARTICLE Open Access

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

Karen Drukker*, Hui Li, Natalia Antropova, Alexandra Edwards, John Papaioannou and Maryellen L. Giger

Applied automatic calculation of quantitative radiomics to cases from the I-SPY 1 (ACRIN 6657) study of dynamic contrast-enhanced MR images.

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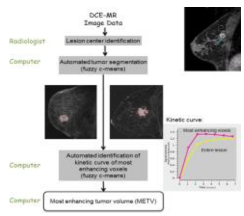
Most-Enhancing Tumor Volume by MRI radiomics **predicts recurrence-free survival "early on"** in neoadjuvant treatment of breast cancer

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 (143 women: 37 with a recurrence vs. 105 without).



Drukker K, Li H, Antropova N, Edwards A, Papaioannou J, Giger ML: Most-enhancing tumor volume by MRI radiomics predicts recurrence-free survival "early on" in neoadjuvant treatment of breast cancer. Cancer Imaging 18:12, 2018

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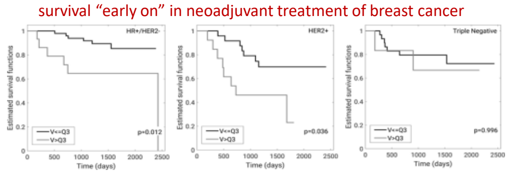

Kaplan-Meier recurrence-free survival estimates for METV at the early treatment time point using the highest quartile cut-point (Q3) with corresponding p-values by hormone-receptor status subgroup: hormone-receptor positive and HER2 negative (N=66, left), HER2 positive (N=38, middle), and triple negative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

Drukker K, Li H, Antropova N, Edwards A, Papaioannou J, Giger ML: Most-enhancing tumor volume by MRI radiomics predicts recurrence-free survival "early on" in neoadjuvant treatment of breast cancer. Cancer Imaging 18:12, 2018

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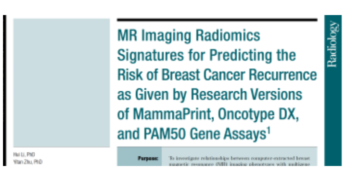

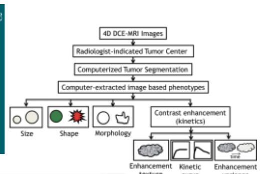

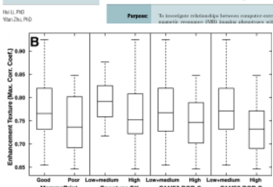

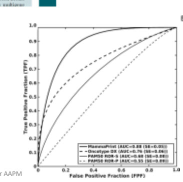

Li H, Zhu Y, Burnside ES, ... Perou CM, Ji Y*, Giger ML*: MRI radiomics signatures for predicting the risk of breast cancer recurrence as given by research versions of gene assays of MammaPrint, Oncotype DX, and PAM50. Radiology DOI: http://dx.doi.org/10.1148/radiol.2016152110, 2016.

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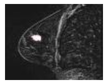
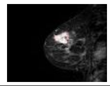
Predicting Risk of Recurrence





Multi-gene assays of risk of recurrence

Radiomics for "virtual" biopsy

	Good Prognosis Case (left)	Poor Prognosis Case (right)
Cancer Subtype	Luminal A	Basal-like
OncotypeDX Range [0, 100]	14.4 (low risk of breast cancer recurrence)	100 (high risk of breast cancer recurrence)
MammaPrint Range [0.848, -0.748]	0.67 (good prognosis)	-0.54 (poor prognosis)
PAM50 ROR-S (Subtype) Range [-7.42, 71.76]	-2.2 (low risk of breast cancer recurrence)	56.3 (high risk of breast cancer recurrence)
PAM50 ROR-P (Subtype+Proliferation) Range [-13.21, 72.38]	0.96 (low risk of breast cancer recurrence)	53.2 (high risk of breast cancer recurrence)
MRI Tumor Size (Effective Diameter) Range [7.8 54.0]	16.8 mm	21.7 mm
MRI Tumor Irregularity Range [0.40 0.84]	0.438	0.592
MRI Tumor Heterogeneity (Entropy) Range [6.00 6.59]	6.27	6.51

Li H, Zhu Y, Burnside ES, …. Perou CM, Ji Y*, Giger ML*: MRI radiomics signatures for predicting the risk of breast cancer recurrence as given by research versions of gene assays of MammaPrint, Oncotype DX, and PAM50. Radiology DOI: http://dx.doi.org/10.1148/radiol.2016152110, 2016.

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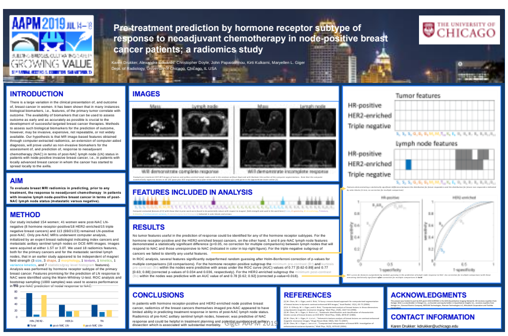

Use of Deep Learning to Assess Response

PROCEEDINGS OF SPIE

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

Benjamin Q. Huynh, Natasha Antropova, Maryellen L. Giger

Journal of Digital Imaging

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

Richard Ha[1] · Christine Chin[2] · Jenika Karcich[1] · Michael Z. Liu[3] · Peter Chang[4] · Simukayi Mutasa[1] · Eduardo Pascual Van Sant[1] · Ralph T. Wynn[1] · Eileen Connolly[2] · Sachin Jambawalikar[3]

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Abstract
We hypothesize that convolutional neural networks (CNN) can be used to predict neoadjuvant chemotherapy (NAC) response using a breast MRI tumor dataset prior to initiation of chemotherapy. An institutional review board-approved retrospective review of our

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AI for predicting response session

Learning Objectives:

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  - Monitoring the therapy
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- Assessing risk of recurrence
  - Recurrence-free survival

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

Recent & Current Graduate Students
Joel Wilkie, PhD
Martin King, PhD
Nick Gruszauskas, PhD
Yading Yuan, PhD
Robert Tomek, MS
Neha Bhooshan, PhD
Andrew Jamieson, PhD
Hsien-Chi Kuo, PhD
Martin Andrews, PhD
William Weiss, PhD
Chris Haddad, PhD
Natasha Antropova, PhD
Kayla Mendel Robinson, PhD
Adam Sibley
Jennie Crosby
Isabelle (Qiyuan) Hu
Jordan Fuhrman
Lindsay Douglas

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Heather Whitney, PhD
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John Lee, PhD
Li Lan, MS
John Papaioannou, MS
Sasha Edwards, MA
Chun Wai Chan, MS
Thomas Rhines
Summer medical students, undergraduates, and high school students

Collaborators
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Suzanne Conzen, MD
Marcus Clark, MD
Yuan Ji, PhD
Greg Karczmar, PhD
Milica Medved, PhD
Yulei Jiang, PhD
Hiro Abe, MD
Deepa Shah, MD

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