Radiomics / Radiogenomics

Elizabeth O’Flynn
Clinical Lecturer and Consultant Breast Radiologist
What is radiomics?

- Aims to capture imaging phenotypic differences automatically
- “radiomic signature” associated with underlying gene-expression patterns
- May provide more complex information on lesions that would be missed otherwise
ARTICLE
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Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

Hugo J.W.L. Aerts1,2,3,4,*, Emmanuel Rios Velazquez1,2,*, Ralph T.H. Leijenaar1, Chintan Parmar1,2, Patrick Grossmann2, Sara Carvalho1, Johan Bussink5, René Monshouwer5, Benjamin Haibe-Kains6, Derek Rietveld7, Frank Hoebers1, Michelle M. Rietbergen8, C. René Leemans8, Andre Dekker1, John Quackenbush4, Robert J. Gillies9 & Philippe Lambin1

Image credit: Aerts et al.
Nature Communications 5, Article number: 4006
Recent breast publications

Isabelle Trop, MD, MPH
Sophie M. Leflarue, MD
Julie Druval, MD
Lucia Lanvera, MD
Dau Tram-Thanh, MD
Manole Labbe, MD
Monia M. El Khoury, MD

Molecular Classification of Infiltrating Breast Cancer: Toward Personalized Therapy

Original Research
Breast Imaging

Radiogenomic Analysis of Breast Cancer: Luminal B Molecular Subtype Is Associated with Enhancement Dynamics at MR Imaging

Maciej A. Mazurowski, PhD, Jing Zhang, PhD, Lars J. Grimm, MD, MHS, Soro C. Yoon, MD, James I. Silber
From the Department of Radiology, Duke University Medical Center, 2301 Erwin Rd, Box 3808, Durham, NC 27710 (M.A.M., J.Z., L.J.G., S.C.Y.); and Department of Biomedical Engineering, Duke University, Pratt School of Engineering, Durham, NC (J.I.S.).

Identification of Intrinsic Imaging Phenotypes for Breast Cancer Tumors: Preliminary Associations with Gene Expression Profiles

Purpose:
To present a method for identifying intrinsic imaging phenotypes in breast cancer tumors and to investigate their association with prognostic gene expression profiles.

Materials and Methods:
The authors retrospectively analyzed dynamic contrast material-enhanced (DCE) magnetic resonance (MR) images of the breast in 25 women (mean age: 35 ± 11 years).

Computerized Image Analysis for Identifying Triple-Negative Breast Cancers and Differentiating Them from Other Molecular Subtypes of Breast Cancer on Dynamic Contrast-enhanced MR Images: A Feasibility Study

Purpose:
To determine the feasibility of using a computer-aided diagnosis (CAD) system to differentiate among triple-negative breast cancer, estrogen receptor (ER)-positive cancer, human epidermal growth factor receptor type 2 (HER2)-positive cancer, and benign breast causes on dynamic contrast material-enhanced (DCE) magnetic resonance (MR) images.

Materials and Methods:
This is a retrospective study of prospectively acquired breast MR imaging data collected from an institutional review board-approved HIPAA-compliant study between 2002 and 2005. Written informed consent was obtained from all patients. The authors collected DCE-MR images from...
Recent breast publications

Identification of Intrinsic Imaging Phenotypes for Breast Cancer Tumors: Preliminary Associations with Gene Expression Profiles

**Purpose:** To present a method for identifying intrinsic imaging phenotypes in breast cancer tumors and to investigate their association with prognostic gene expression profiles.

**Materials and Methods:** The authors retrospectively analyzed dynamic contrast material-enhanced (DCE) magnetic resonance (MR) images of the breast in 56 women (mean age, 55.6 years; age range, 33-72 years) with invasive ductal carcinoma of the breast.

Radiogenomic Analysis of Breast Cancer: Luminal B Molecular Subtype Is Associated with Enhancement Dynamics at MR Imaging

**Purpose:** To investigate associations between breast cancer molecular subtype and semiautomatically extracted magnetic resonance (MR) imaging features.

**Materials and Methods:** Imaging and genomic data from the Cancer Genome Atlas were used to identify associations between breast cancer molecular subtypes and imaging features.

Breast Cancer: Radiogenomic Biomarker Reveals Associations among Dynamic Contrast-enhanced MR Imaging, Long Noncoding RNA, and Metastasis

**Purpose:** To perform a radiogenomic analysis of women with breast cancer to study the multiscale relationships among quantitative computer vision–extracted dynamic contrast material-enhanced (DCE) magnetic resonance (MR) imaging phenotypes, early metastasis, and long noncoding RNA (lncRNA) expression determined by means of high-resolution next-generation RNA sequencing.

Computational Approach to Radiogenomics of Breast Cancer: Luminal A and Luminal B Molecular Subtypes Are Associated With Imaging Features on Routine Breast MRI Extracted Using Computer Vision Algorithms

**Purpose:** To identify associations between semiautomatically extracted MRI features and breast cancer molecular subtypes.

**Methods:** We analyzed routine clinical preoperative breast MRIs from 275 breast cancer patients at a single institution in this retrospective, Institutional Review Board–approved study. Six fellowship-trained breast radiologists reviewed the MRIs and annotated the cancers. Computer vision algorithms were then used to extract 56 imaging features from the cancers including morphologic, texture, and dynamic features. Surrogate markers (estrogen receptor [ER], progesterone receptor [PR], human epidermal growth factor receptor-2 [HER2]) were used to categorize tumors by molecular subtype: ER/PR+; HER2− (luminal A); ER/PR+; HER2+ (luminal B); ER/PR−; HER2+ (HER2); ER/PR+/HER2− (basal). A multivariate analysis was used to determine associations between the imaging features and molecular subtype.

**Results:** The imaging features were associated with both luminal A (P = 0.0027) and luminal B (P = 0.0063) molecular subtypes. No association was found for either HER2 (P = 0.2465) or basal (P = 0.1014) molecular subtype and the imaging features. A P-value of 0.0055 (0.0054) was considered significant.

**Conclusion:** Luminal A and luminal B molecular subtype breast cancer are associated with semiautomatically extracted features from routine contrast-enhanced breast MRI.
Websites

http://www.radiomics.org/

- www.oncoradiomics.com
- www.mastro.nl
- www.cerr.info
- www.moffitt.org
- www.cancerdata.org
- www.predictcancer.org
- www.quic-concept.eu
- www.pttheragnostic.com
Breast MRI Radiomics

Special types are homogeneous at the transcriptome level.

Weigert et al. J Pathol 2008
Molecular subtypes of breast cancer

<table>
<thead>
<tr>
<th>Molecular subtype</th>
<th>Biomarker profile</th>
<th>Prevalence</th>
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<tr>
<td>Luminal A</td>
<td>ER+ and/or PR+, HER2-, low Ki67&lt;14%</td>
<td>42-59%</td>
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<tr>
<td>Luminal B</td>
<td>ER+ and/or PR+ and HER2+, ER+ and/or PR+, HER2-, high Ki67&gt;14%</td>
<td>6-19%</td>
</tr>
<tr>
<td>Basal-like/ triple negative breast cancer (TNBC)</td>
<td>ER-, PR-, HER2-, cytokeratin 5/6+ and/or EGFR+</td>
<td>14-20%</td>
</tr>
<tr>
<td>HER2 +</td>
<td>ER-, PR-, HER2 +</td>
<td>7-12%</td>
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*ER = oestrogen receptor*  
*PR = progesterone receptor*  
*HER2 = human epidermal growth factor receptor 2*  
*EGFR = epidermal growth factor receptor*
## MRI assessing response through subtype

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Triple negative breast cancer

- High T2 centrally
- Enhancing rim
- Restricted diffusion rim

**Imaging Techniques**
- T2W MRI
- Early subtracted DCE-MRI
- DWI b=1150
- ADC map

*References*
Histology of triple negative breast cancer

Central necrosis

Smooth tumour edge

With kind permission of Dr Tan, Singapore General Hospital
Luminal breast cancer

- Intermediate signal mass
- Homogeneous spiculate enhancement
- Homogeneous restricted diffusion
- Low signal spiculated mass

T2W MRI  
Early subtracted DCE-MRI  
DWI b=800  
T1W MRI
Histology of luminal breast cancer

With kind permission of Professor Sarah Pinder
Functional MRI sequences

- Dynamic Contrast Enhanced MRI (DCE-MRI)
- Standard Measurements (RECIST)
- MR Spectroscopy
- Diffusion-Weighted Imaging (DWI)
- Intrinsic Susceptibility Weighted MRI (R2*)
**VASCULARITY**

- Dynamic Contrast Enhanced MRI (DCE-MRI)
  - Time signal intensity curves $K_{\text{trans}}, k_{\text{ep}}, v_e$

**CELLULARITY**

- Diffusion-Weighted Imaging (DWI)

**OXYGENATION**

- Intrinsic Susceptibility Weighted MRI ($R^2*$)

**METABOLISM**

- MR Spectroscopy
  - Choline peak at 3.2ppm

**MRI**

- Tumour Diameter
- Tumour Volume
- Standard Measurements (RECIST)

**Additional Text**

- Apparent Diffusion Coefficient (ADC)
- Choline peak at 3.2ppm
- $R^2* = 1/T^2*$
MRI Parameters

Standard Measurements (RECIST)

Tumour Diameter
Tumour Volume
MRI Parameters

VASCULARITY

**Semi-quantitative parameters:**
- Time-signal intensity curves
- Maximum signal intensity
- Absolute MRI signal intensity
- Relative MRI signal intensity
- Normalised MRI signal intensity
- Initial Area Under the Gadolinium Curve (IAUGC)
- Enhancement Fraction

**Pharmacokinetically modelled parameters:**
- $K_{\text{trans}}$
- $k_{\text{ep}}$
- $V_e$
- Textural analysis
MRI Parameters

**VASCULARITY**

*Dynamic Contrast Enhanced MRI (DCE-MRI)*

**Semi-quantitative parameters:**
- Time-signal intensity curves
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- Relative MRI signal intensity
- Normalised MRI signal intensity
- Initial Area Under the Gadolinium Curve (IAUGC)
- Enhancement Fraction

**Pharmacokinetically modelled parameters:**
- $K_{\text{trans}}$
- $k_e$
- $V_e$
- Textural analysis
Dynamic contrast enhanced (DCE)-MRI

- Gd-DTPA iv injection
- Blood plasma
- Extravascular extracellular space ($V_e$)
- Renal excretion
- Transfer constant ($K_{trans}$)
- Rate constant ($k_{ep}$)

Pharmacokinetic Modelling*

D.M. McDonald & P.L. Choyke
Imaging of angiogenesis: from microscope to clinic

*Tofts et al. JMRI 1999
Assessing response in breast cancer with dynamic contrast-enhanced magnetic resonance imaging: Are signal intensity–time curves adequate?

David K. Woolf · Anwar R. Padhani · N. Jane Taylor · Andrew Gogbashian · Sonia P. Li · Mark J. Beresford · Mei-Lin Ah-See · James Stirling · David J. Collins · Andreas Makris

Fig. 1 Classification scheme for SITCs adapted from: Daniel et al. Radiology; 1998; 209: 499–509 [22]

Table 1 Descriptions of signal intensity–time curve (SITC) shapes

<table>
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<th>SITC type</th>
<th>Description</th>
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<tr>
<td>1</td>
<td>No enhancement observed throughout without any upstroke</td>
</tr>
<tr>
<td>2</td>
<td>Slow rising curve for the entire observation period (&lt;70 % of total amplitude reached within 90 s)</td>
</tr>
<tr>
<td>3</td>
<td>Fast initial uptake (≥70 % of total amplitude reached within 90 s) followed up a continued rise of ≥10 % from the 90 s amplitude</td>
</tr>
<tr>
<td>4</td>
<td>Fast upstroke as in 3 followed by a plateau phase</td>
</tr>
<tr>
<td>5</td>
<td>Fast upstroke as in 3 followed by a decline in SI of ≥10 %</td>
</tr>
</tbody>
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MRI Parameters

**Cellularity**

Diffusion-Weighted Imaging (DWI)

**ADC** = Apparent Diffusion Coefficient
DWI and cellularity

Apparent Diffusion Coefficient map (ADC)

Histology of Grade 3 IDC

Mean ADC = 0.95 \times 10^{-3}\text{mm}^2/\text{s}
Diffusion Weighted Imaging (DWI)

\[ S = S_0 e^{-b \cdot ADC} \]

ADC = Apparent Diffusion Coefficient
DWI aiding tumour detection

DCE-MRI subtracted image

ADC map
\[ ADC = 0.79 \times 10^{-3} \text{mm}^2/\text{s} \]

• DWI can improve specificity up to 85%*

* Chen BMC Cancer 2010
Acknowledgements:

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Thank you for your attention