High-Throughput Quantitative MRI Phenotyping of TCGA/TCIA Breast Cancers for Prognostic Prediction

Collaboration between The University of Chicago and the TCGA/TCIA Breast Phenotype Group

THE UNIVERSITY OF CHICAGO

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THE CANCER IMAGING ARCHIVE

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Purpose

We aim to demonstrate, using the TCGA/TCIA Breast image dataset, the performance of quantitative magnetic resonance imaging (MRI) analysis (i.e., MRI-based phenotyping) in characterizing the molecular subtypes of breast cancer. Understanding of the relationships between quantitative image analysis, molecular subtypes, and genomic data of breast cancer may ultimately improve prognostic assessment and contribute to more effective cancer treatment plans.

Quantitative Image Analysis and Image-based Phenotypes

Quantitative image analysis methods are being developed with the goal to serve as an aid in cancer diagnosis and patient management. In some instances – such as computer-aided detection in screening mammography – such methods have already become an integral part of today's clinical practice (1-2). Quantitative imaging aims to provide objective and effective tools for clinical decision making – serving as "measuring devices" rather than "imaging devices" (3). Quantitative image analyses address various biomedical questions using computer vision and artificial intelligence techniques. The role of quantitative medical image analysis in the detection and diagnosis of disease continues to increase, with methods being developed and evaluated for use in
- assessment of risk
- computer-aided detection (CADe)
- computer-aided diagnosis (CADx)
- assessment of prognosis
- assessment of response to therapy
- imaging genomics

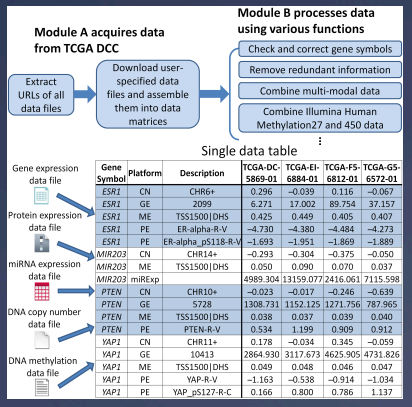
Computer Vision: Quantitatively extract lesion characteristics

Patient-specific: Image-based tumor signature for precision medicine

Population-based: Data-mining of computer-extracted features on large datasets for cancer discovery

TCGA/TCIA Dataset

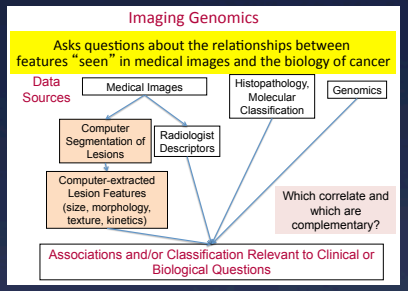
This study used the 98 breast cancer cases for which magnetic resonance images (MRIs) were available in The Cancer Imaging Archive (TCIA) and which corresponded to breast cancer cases available in the The Cancer Genome Atlas (TCGA). Clinical, genomics, epigenomics and proteomics data of these cancer cases were prepared using TCGA-Assembler (4), an open-source software freely available at *www.compgenome.org* for retrieving and processing TCGA Data.



Gene Symbol	Platform	Description	TCGA-DC-5869-01	TCGA-EI-6884-01	TCGA-F5-6812-01	TCGA-G5-6572-01
ESR1	CN	CHR6+	0.296	–0.039	0.116	–0.067
ESR1	GE	2099	6.271	17.002	89.754	37.157
ESR1	ME	TSS1500|DHS	0.425	0.449	0.405	0.407
ESR1	PE	ER-alpha-R-V	–4.730	–4.380	–4.484	–4.273
ESR1	PE	ER-alpha_pS118-R-V	–1.693	–1.951	–1.869	–1.889
MIR203	CN	CHR14+	–0.293	–0.304	–0.375	–0.050
MIR203	ME	TSS1500|DHS	0.050	0.090	0.070	0.037
MIR203	miRExp		4989.304	13159.077	2416.061	7115.598
PTEN	CN	CHR10+	–0.023	–0.017	–0.246	–0.639
PTEN	GE	5728	1308.731	1152.125	1271.756	787.965
PTEN	ME	TSS1500|DHS	0.038	0.037	0.039	0.040
PTEN	PE	PTEN-R-V	0.534	1.199	0.909	0.912
YAP1	CN	CHR11+	0.178	–0.034	0.345	–0.059
YAP1	GE	10413	2864.930	3117.673	4625.905	4731.826
YAP1	ME	TSS1500|DHS	0.049	0.048	0.046	0.047
YAP1	PE	YAP-R-V	–1.163	–0.538	–0.914	–1.034
YAP1	PE	YAP_pS127-R-C	0.166	0.800	0.786	1.137

Imaging Genomics

Imaging genomics involves the correlative investigation of image data, clinical data, histopathology data, and genomic data in order to understand the molecular biology behind the imaging characteristics of tumors and normal structures. [e.g., (7-13)]

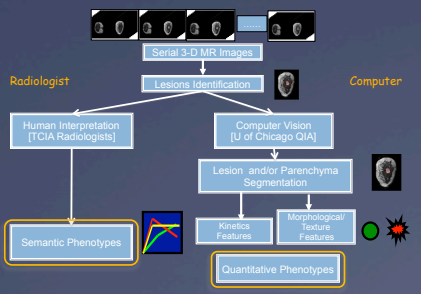


From medical images, either semantic descriptors, given subjectively by radiologists, or quantitative mathematical descriptors calculated using computer vision techniques, i.e., quantitative image-based phenotypes, can be used for input to data mining techniques and association analyses (2,5-12). By learning which phenotypes are correlated and which are complimentary to each other, investigators aim to merge the various multi-scale, multi-modality image-based phenotypes into advanced tumor signatures for predicting cancer risk and/or for patient management.

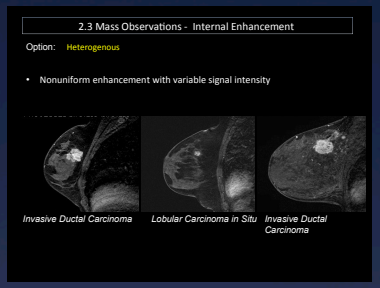
Computer output from quantitative image analysis is expected to aid in understanding disease by yielding methods of "high-throughput image-based phenotyping" (11,12), or "radiogenomics" (13). Thus, computer vision workstations need to effectively and efficiently analyze large populations in a user-friendly manner. The workstation below (demonstrated at RSNA 2010), automatically performs lesion segmentation, feature extraction (i.e., image-based phenotyping), and feature merging (i.e., classification) to yield image-based tumor signatures.

High-Throughput Diagnostic Phenotyping

Image Analysis Workflow

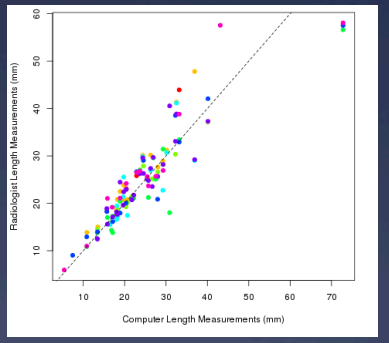


Radiologist Semantic Phenotypes



Above: Examples illustrating radiologist-extracted descriptors of internal enhancement.

Radiologist vs. Computer



Above: Size measurement visually determined by the radiologists and the size measurement automatically calculated by the computer workstation

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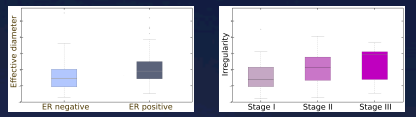
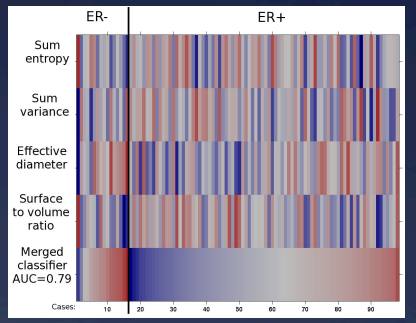
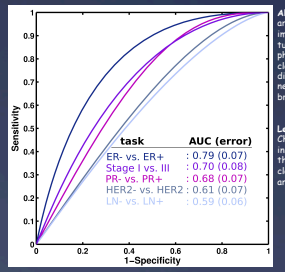
Image-based Quantitative Phenotypes



Above: Box plots of normalized image-based quantitative phenotypes for the 98 breast cancer cases stratified by ER status and pathological stage, respectively





Above: MRI-based phenotype array of computer-extracted image-based phenotypes and a tumor signature from phenotypes merged by a classifier in the task of distinguishing between ER-negative and ER -positive breast cancers

Left: Receiver Operating Characteristic (ROC) curves indicating the performance of the computer in several classification tasks. *AUC:* area under the curve.

Summary and Conclusion

Quantitative image analysis was performed on 98 de-identified MRI studies depicting biopsy-proven breast cancers from the NCI's multi-institutional The Cancer Imaging Archive (TCIA) and The Cancer Genome Atlas (TCGA) project. Computerized image-based phenotyping was completely automated apart from the indication of the lesion center and included: 1) 3D lesion segmentation, 2) feature extraction (i.e., extraction of image-based phenotypes) , 3) leave-one-case-out linear stepwise feature selection, and 4) leave-one-case-out cross-validation merging image-based phenotypes to form a prognostic predictive classifier. The performance of the classifier model for molecular subtyping was evaluated using ROC analysis with the area under the ROC curve (AUC) as the figure of merit.

The results from this study indicate that quantitative MRI analysis shows promise as a means for high-throughput image-based phenotyping in the discrimination of breast cancer subtypes. In the future, the merging of image-based phenotypes with genomic data may lead to improved prognostic predictors.