Radiomics Certificate, AAPM 2018

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- Laurence Court, University of Texas MD Anderson Cancer Center

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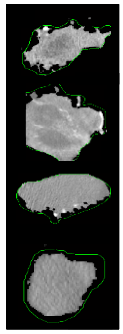
- Jeff Layton, NVIDIA
- Mark Hill, NVIDIA
- Chintan Parmar, Dana-Farber Cancer Institute
- Roman Zeleznik, Dana-Farber Cancer Institute



Radiomics Certificate, AAPM 2018

1. Introduction to radiomics – including radiomics features and statistics
2. Machine learning for radiomics – intro to machine learning, deep learning
3. Convolution neural nets – including radiomics case studies
4. Deep learning lab (NVIDIA) – hands-on experience
5. Radiomics proffered abstracts – 12 radiomics papers
6. Deep learning with medical images – including 1-hour hands-on lab

REMINDER: Lab sessions are for Radiomics course registrants – Bring your laptop (fully charged!!)

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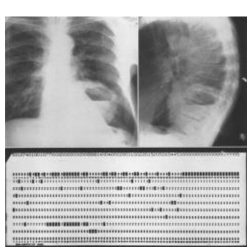
Introduction to Radiomics

- Introduction to radiomics – Laurence Court, University of Texas MD Anderson Cancer Center
- Radiomics features – Xenia Fave, University of California San Diego
- Statistics for radiomics - Shouhao Zhou, University of Texas MD Anderson Cancer Center

University of Chicago 1994 Prototype System for Computer-Aided Detection

Photograph (1994) courtesy of Maryellen Giger



LODWICK, G. S., et al 1963. The coding of Rontgen images for computer analysis as applied to lung cancer, Radiology 81(2), 185-200

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Learning Objectives

1. To introduce the goals and objectives of radiomics research
2. To describe where radiomics research is today
3. To understand the workflow when using quantitative image features for radiomics research
4. To understand the key statistical techniques used in radiomics

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LETTERS

nature biotechnology

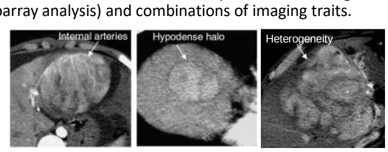
Decoding global gene expression programs in liver cancer by noninvasive imaging

Eran Segal[1], Claude B Sirlin[2], Clara Ooi[4], Adam S Adler[3], Jeremy Gollub[6], Xin Chen[8], Bryan K Chan[2], George R Matcuk[7], Christopher T Barry[3], Howard Y Chang[3] & Michael D Kuo[2]

NATURE BIOTECHNOLOGY VOLUME 25 NUMBER 6 JUNE 2007

Imaging features and radiomics

- Radiologists identified 138 different imaging traits on contrast-CT scans of hepatocellular carcinomas (n=28)
- Filtered traits based on reproducibility and independence (->32)
- Searched for associations between expression of 6,732 genes (clustered) (microarray analysis) and combinations of imaging traits.



Examples from: E. Segal *et al.* Decoding global gene expression programs in liver cancer by noninvasive imaging (2007)

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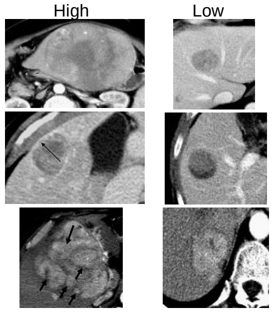
High Low

- Cross-sectional area
- Liver capsule abutment
- Number of regions of necrosis



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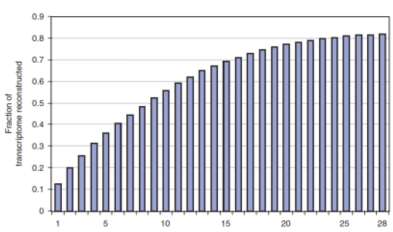
28 imaging traits could reconstruct 78% of gene expression profile (116 modules)



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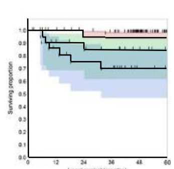
Imaging for precision medicine



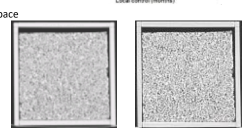
Elhawani et al, Sci. Rep. 8, 1524, 2018

Advantages of imaging for precision medicine

- Appearance is somehow related to tumor phenotype – and related outcomes
- Performed non-invasively
- Provides a 3D picture of the entire cancer
- Already performed in clinical practice
- Multiple times during treatment for diagnosis, staging, radiation oncology planning, response assessment
- Captures the cancers appearance over time (delta radiomics) and space

Disadvantages/challenges of imaging for precision medicine

- Proves the cancer at the macroscopic level
- Can be qualitative not quantitative
- Patient heterogeneity – means we need lots of data
- Heterogeneous acquisition protocols
  - Comparisons between patients difficult
  - Comparisons between same patient in time difficult



Siemens B30f Siemens B70f

Data from Dennis Mackin, 2018

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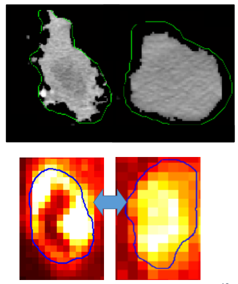
So, what is radiomics?



Hypothesis: Quantitative image features are related to underlying gene expression and phenotype

Goals:
- To provide a comprehensive quantification of the phenotype of the tumor
- To provide patient-specific predictions of their "outcome" given a specific treatment

The outcome could be genetic expression, treatment response (pathology), overall survival, freedom from metastases, ……..

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General Radiomics Hypothesis: Quantitative image features are related to underlying gene expression and phenotype

Classifying Tumors
- Benign v. Malignant, Wang 2010
- SCC v. ACC, Basu 2011

Links to Genomics
- K-ras mutant, Weiss 2014
- MAPK pathway, Miles 2016

Predicting Outcomes
- Aerts 2014
- Fried 2015

Monitoring Response
- Fave 2017

•Patient stratification in order to decide on alternative treatments	Predict
•Analysis of heterogeneity within and across lesions *(can assess varying pharmacokinetics, receptor status, proliferative/apoptotic rates, …)*	Virtual Biopsy
•Early prediction of treatment response •Basis for modifying therapy	During Tx
•Monitoring for Treatment Efficacy	After Tx
•Longitudinal monitoring and evaluation *(can be done before then after treatment, substituting for longitudinal tissue biopsy)*	Follow-up

Buckler, *et al.*, A Collaborative Enterprise for Multi-Stakeholder Participation in the Advancement of Quantitative Imaging, *Radiology* 258:906-914, 2011

Based slides from Xenia Fave and Ed Jackson

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Radiomics workflow

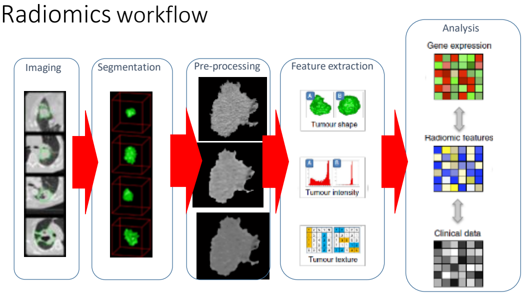
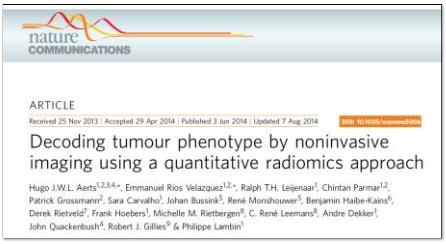


Figure adapted from Aerts et al, Nature Communications 2015


nature COMMUNICATIONS

ARTICLE

Received 25 Nov 2013 | Accepted 29 Apr 2014 | Published 3 Jun 2014 | Updated 7 Aug 2014

DOI: 10.1038/ncomms5006

Decoding tumour phenotype by noninvasive imaging using a quantitative radiomics approach

Hugo J.W.L. Aerts[1,2,3,4,*], Emmanuel Rios Velazquez[1,2,*], Ralph T.H. Leijenaar[1], Chintan Parmar[1,2], Patrick Grossmann[2], Sara Carvalho[1], Johan Bussink[5], René Monshouwer[5], Benjamin Haibe-Kains[6], Derek Rietveld[7], Frank Hoebers[1], Michelle M. Rietbergen[8], C. René Leemans[8], Andre Dekker[1], John Quackenbush[4], Robert J. Gillies[9] & Philippe Lambin[1]

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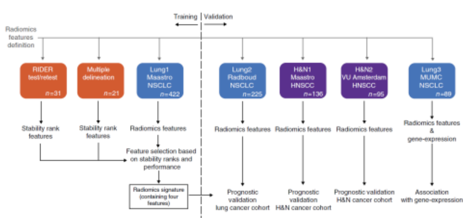
Decoding the tumor phenotype



Multivariate Cox proportional hazards regression model for prediction of survival

Aerts et al

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Methodology

- Identify stable features
- Select most stable feature from each feature category
- Multivariate Cox proportional hazards regression model for prediction of survival
- Four final features:
  - Statistics energy – overall tumor density (intensity histogram)
  - Shape compactness – compactness of the tumor (shape)
  - Grey level nonuniformity – intratumor heterogeneity (texture)
  - Wavelet grey level nonuniformity HLH – heterogeneity after decomposing the image in mid-frequencies (wavelet)

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Prognostic performance

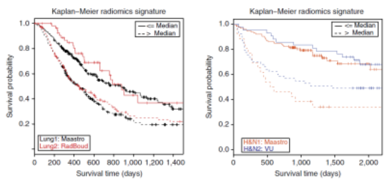

Figure 4 | Prognostic performance and gene-expression association of the radiomics signature. (**a**) Radiomic signature performance. Kaplan–Meier curves demonstrating performance of the radiomic signature on the lung cancer data sets (left) and the head-and-neck cancer data sets (right). The signature was built on the Lung1 data ($n = 422$). The signature had a good performance in the Lung2 (CI = 0.65, $P = 2.91 \times 10^{-09}$, Wilcoxon test, $n = 225$), and a high performance in H&N1 (CI = 0.69, $P = 7.99 \times 10^{-07}$, Wilcoxon test, $n = 136$) and H&N2 (CI = 0.69, $P = 3.53 \times 10^{-06}$, Wilcoxon test, $n = 95$) validation data sets. (**b**) Association of radiomic signature features and gene expression using gene-set enrichment analysis (GSEA) in the Lung3

Aerts et al

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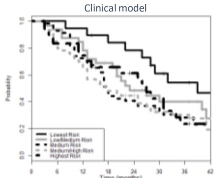
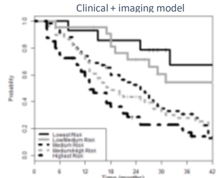
Can we do this with PET images?

- 195 Patients, stage III NSCLC w/ definitive XRT
- 11 conventional prognostic factors
- MIM PETedge: Semi-automated delineation
- 47 Quantitative Image Features (QIFs) [IBEX]
- Clustering to try to identify multiple risk groups

Clinical model



Clinical + imaging model



Fried et al., Radiology 278, 2016

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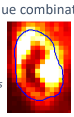
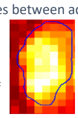
Important features: PET

- COM Energy: Measure of primary tumor SUV uniformity
  - Sum(Probability of unique combinations of SUV values between adjacent pixels)

Low Energy
Volume = 165 cc
DWD @ 5 months

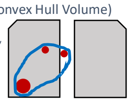


High Energy
Volume = 163 cc
NED @ 24 months

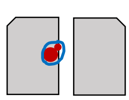


- Solidity: Measure of local-regional disease dispersion
  - (Disease Volume/Convex Hull Volume)

Low solidity
(RLL
Hilar Node
Subcarinal)



High solidity
(RML
Paratracheal
Node)



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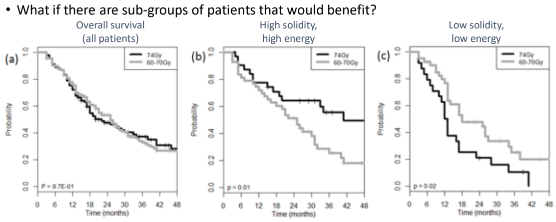
Radiomics to determine appropriate treatments

- RTOG 0617 showed no benefit (possible harm) in dose escalation for stage III NSCLC patients
- What if there are sub-groups of patients that would benefit?



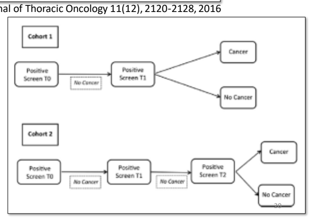
Fried et al. IJROBP 94, 368-376, 2016

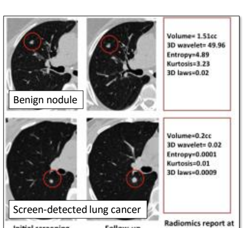
Predicting Malignant Nodules from Screening CT Scans

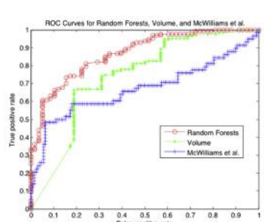
Samuel Hawkins, MS,[a] Hua Wang, PhD,[b,c] Ying Liu, MD,[b,c] Alberto Garcia, AA,[c]
Olya Stringfield, PhD,[c] Henry Krewer, BS,[a] Qian Li, MD,[b,c] Dmitry Cherezov, MS,[a]
Robert A. Gatenby, MD,[d] Yoganand Balagurunathan, PhD,[c] Dmitry Goldgof, PhD,[a]
Matthew B. Schabath, PhD,[e] Lawrence Hall, PhD,[a] Robert J. Gillies, PhD[c,d,*]

Journal of Thoracic Oncology 11(12), 2120-2128, 2016

- Particular challenge of CT screening for lung cancer is the high detection of 4-12mm pulmonary nodules – only 3.6% of which are actually cancers
- Used features that are stable, prognostic and predictive
- Used several machine learning algorithms for classification including:
  - Support vector machines (SVMs), random forest







Journal of Thoracic Oncology 11(12), 2120-2128, 2016

- Hawkins et al achieved accuracies > 90% for some patient groups (low and high risk extreme phenotypes, around 55% of patients)

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Radiomics workflow

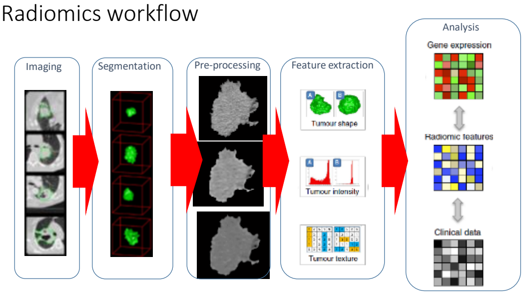
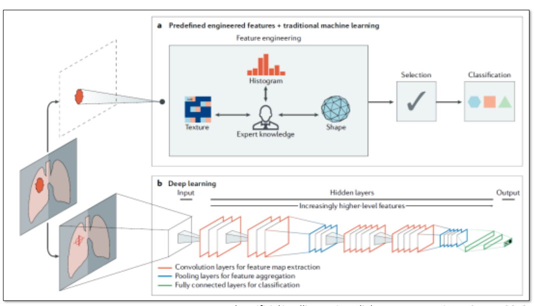


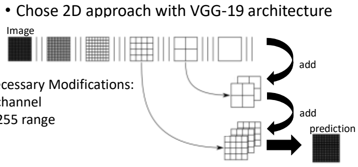
Figure adapted from Aerts et al, Nature Communications 2015



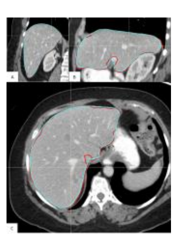
Hosny et al, Artificial intelligence in radiology, Nature Reviews: Cancer, 2018

Deep learning for autocontouring

- Chose 2D approach with VGG-19 architecture



Necessary Modifications:
3 channel
0-255 range

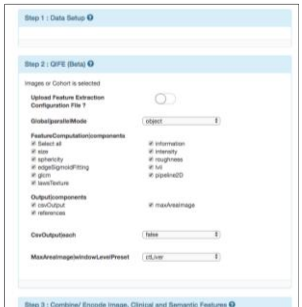


Long, Shelhamer, Darrel Fully Convolutional Networks for Semantic Segmentation IEEE CVPR 2015

Slide from Brian Anderson, MD Anderson

Resources

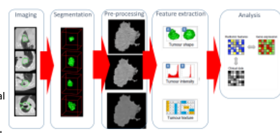
- Many different tools for feature calculation, statistics, machine learning etc.
  - Court et al, Computational resources for radiomics, Translational Cancer Research 5(4), 340-348, 2016
  - Larue et al, Quantitative radiomics studies for tissue characterization: A review of technology and methodological procedures, Brit. J. Radiol. 90, 20160665, 2017
- 3D slicer/Pyradiomics – Aerts group's python library and pipeline
- www.Radiomics.world – Radiomics Quality Score (Lambin group)

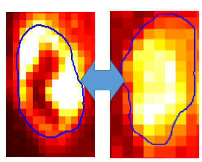


Stanford radiomics pipeline, courtesy of Sandy Napel

Summary

- Radiomics image features have potential for:
  - Improving risk stratification compared with conventional prognostic factors
  - Understanding genetic expression
  - Predicting patient-specific response to treatment (e.g. dose escalation)
- The use of these features is:
  - Non-invasive
  - Routinely obtained images
- Our understanding is still basic:
  - Why do specific image features work? – what are we actually detecting?
  - How can we optimize the features? – filtering, reproducibility
  - What about multimodality approaches? CT/PET/MRI
- We can expect results to improve as we improve our control of the various noise sources
- Also, new modeling/image handling techniques will improve models (especially deep learning)





Research group and collaborators

Our group (past and present)
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- Luke Hunter
- David Fried
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- Joe Chang
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- Susan Tucker
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