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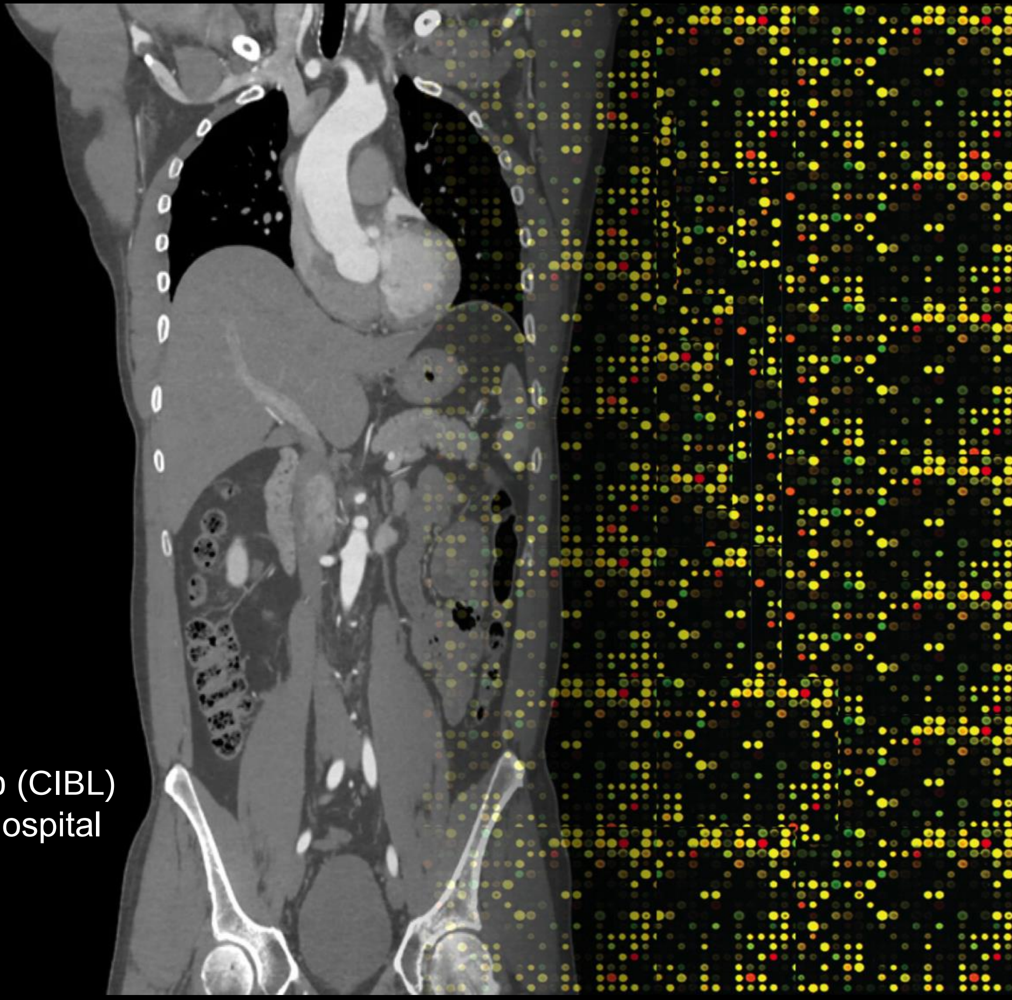
Quantitative Radiomics System: Decoding the Tumor Phenotype



Hugo Aerts

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Dana-Farber Cancer Institute, Brigham and Women’s Hospital
Harvard Medical School

Objectives

- Describe the motivation and methodology underlying quantitative radiomic analysis
- Describe biomarker quantification studies in Radiomics and Imaging-Genomics (Radiogenomics)
- Describe radiomic informatics platform (U24 ITCR)

Imaging for precision medicine

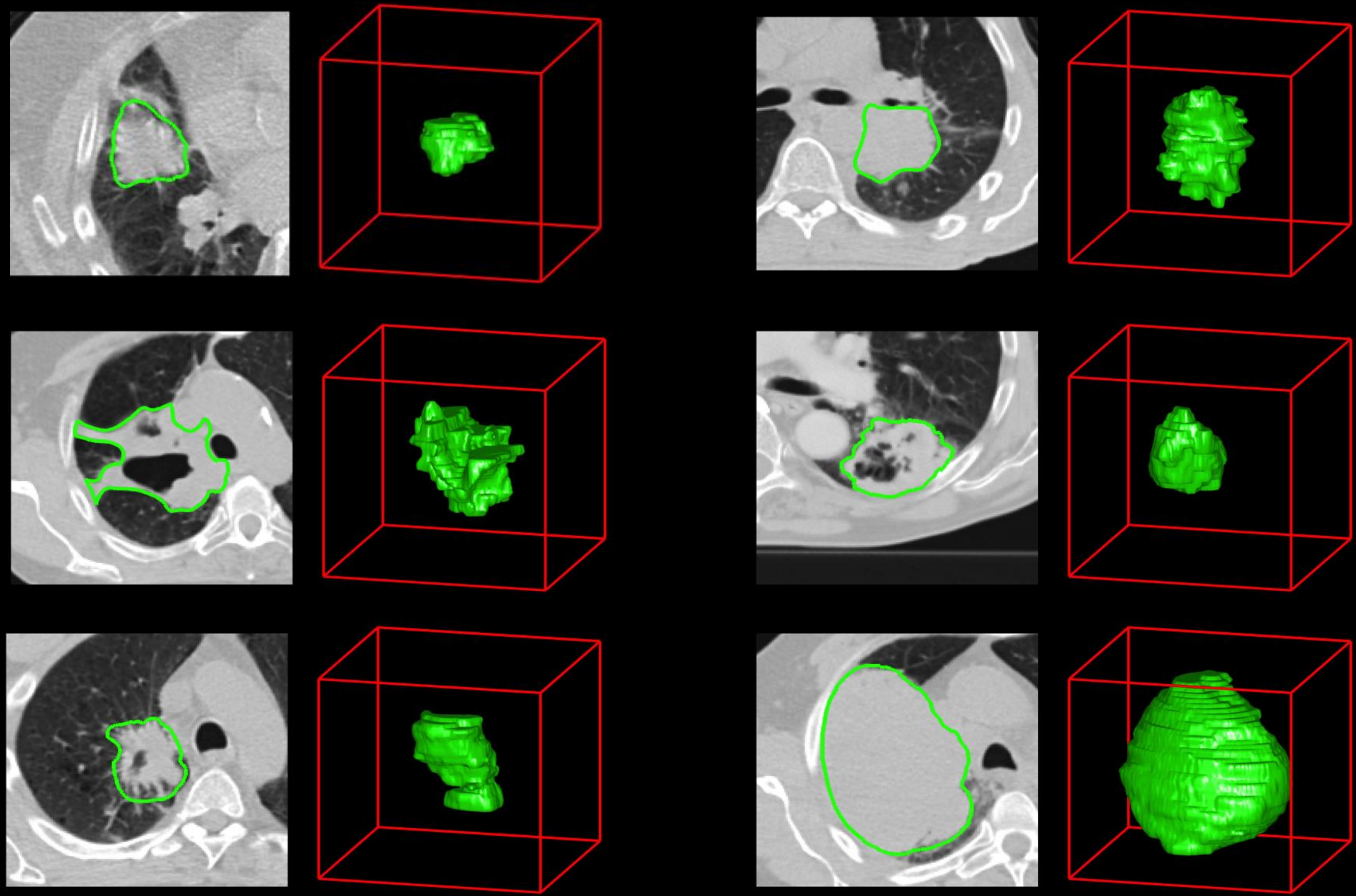
Advantages of Imaging:

- Performed non-invasively
- Provides 3D picture of the entire phenotype
- Already performed in clinical practice
- Multiple times before, during and after treatment
- Captures a disease’s appearance over time and space

Disadvantages of Imaging:

- Probes the disease at the macroscopic level
- Often qualitative not quantitative
- Very heterogeneous acquisition protocols:
  - comparisons between patients difficult
  - comparisons same patient in time difficult
- Storage of only reconstructed images (not the raw data)

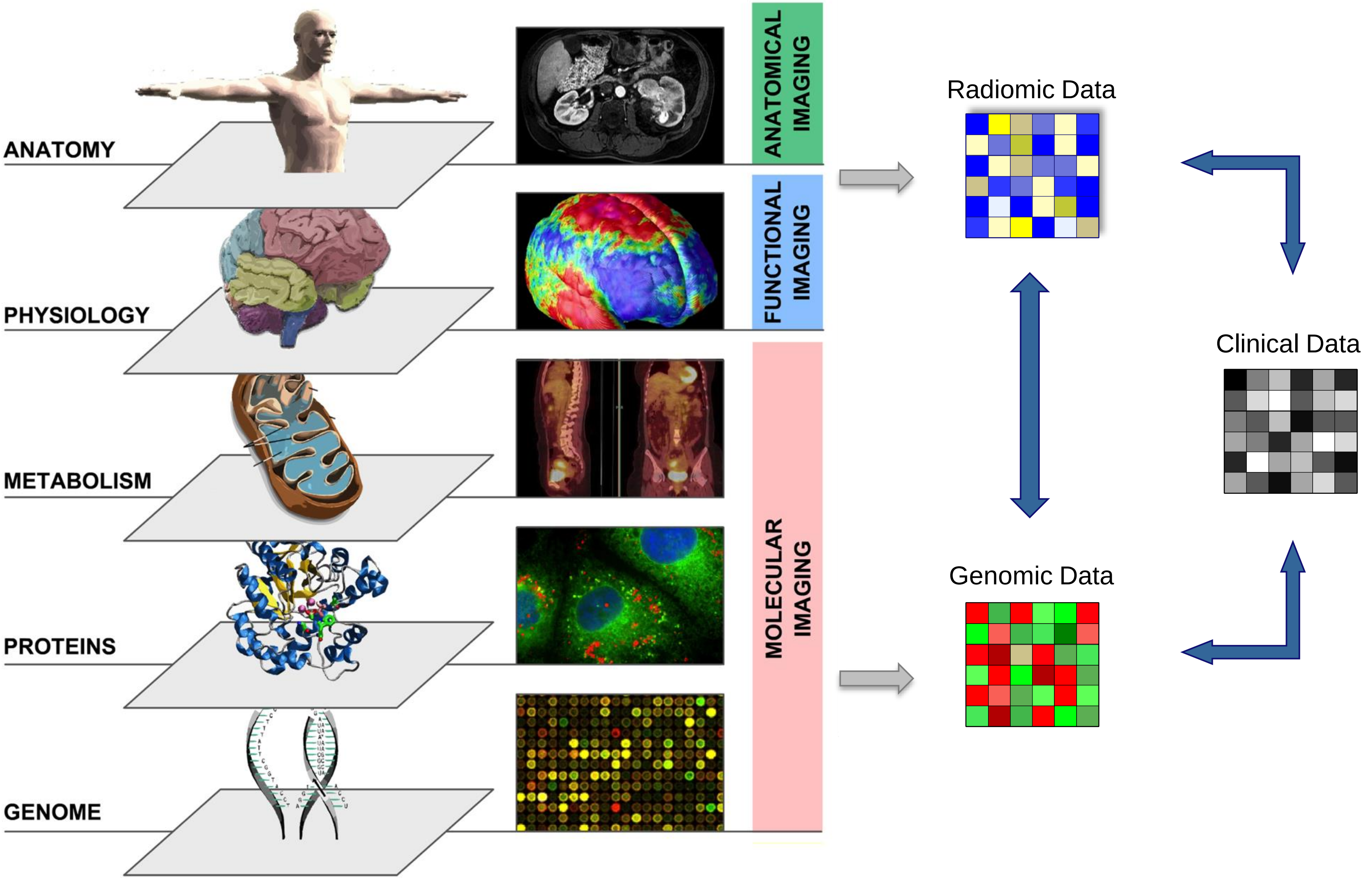
Representative CT images of lung cancer



Tumors are different

Medical imaging can capture these phenotypic differences

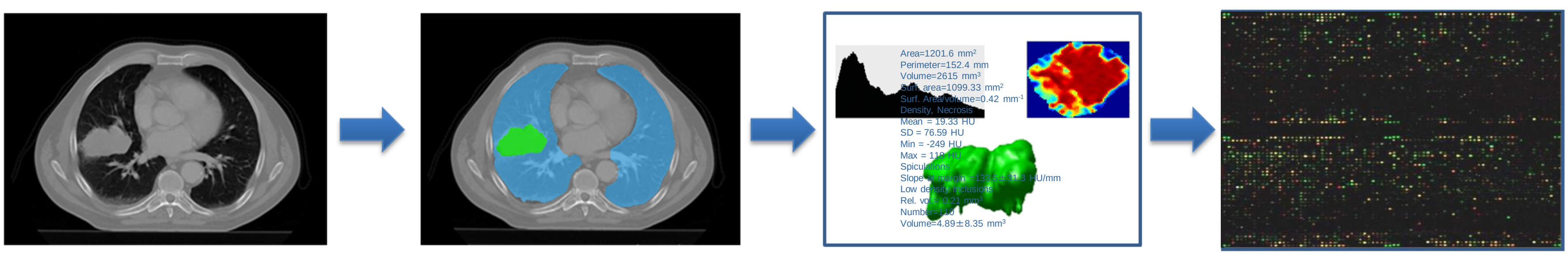
Integrating Imaging and Genomic Data



Radiomics (rā'dē-ō'mĭks) n.

Radiomics involves extracting quantitative & automated features from images and producing data elements

Radiomic data aims to provide a comprehensive quantification of the imaging phenotype

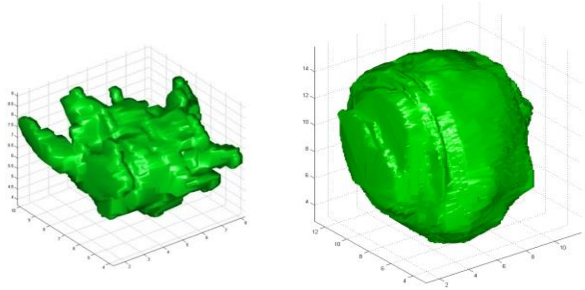


Imaging | Segmentation | Feature extraction | Analysis

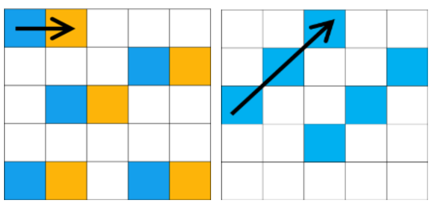
*Lambin *et al.* Eur J Cancer 2012
*Aerts *et al*, Nature Comm 2014

Radiomic Feature Set (current release ~1600 features)

Shape

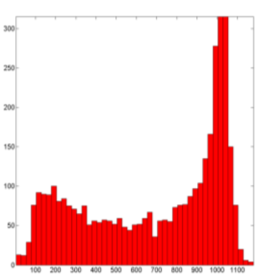


Texture



GLCM GLRL

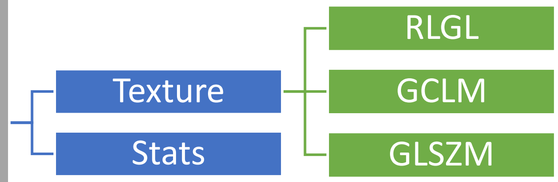
Stats



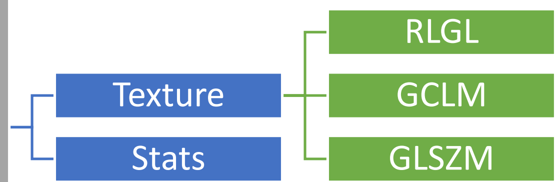
Kurtosis: $Kur = \frac{1}{XY}\sum_{x=1}^{X}\sum_{y=1}^{Y}\left\{\left[\frac{I(x,y)-\mu}{\sigma}\right]^4\right\} - 3$

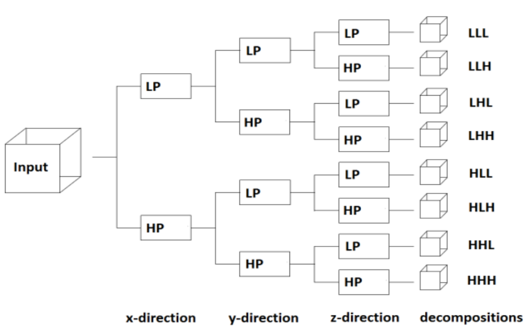
Entropy: $H = -\sum_{i=1}^{XY} P(i)\cdot \log_2 P(i)$

LoG



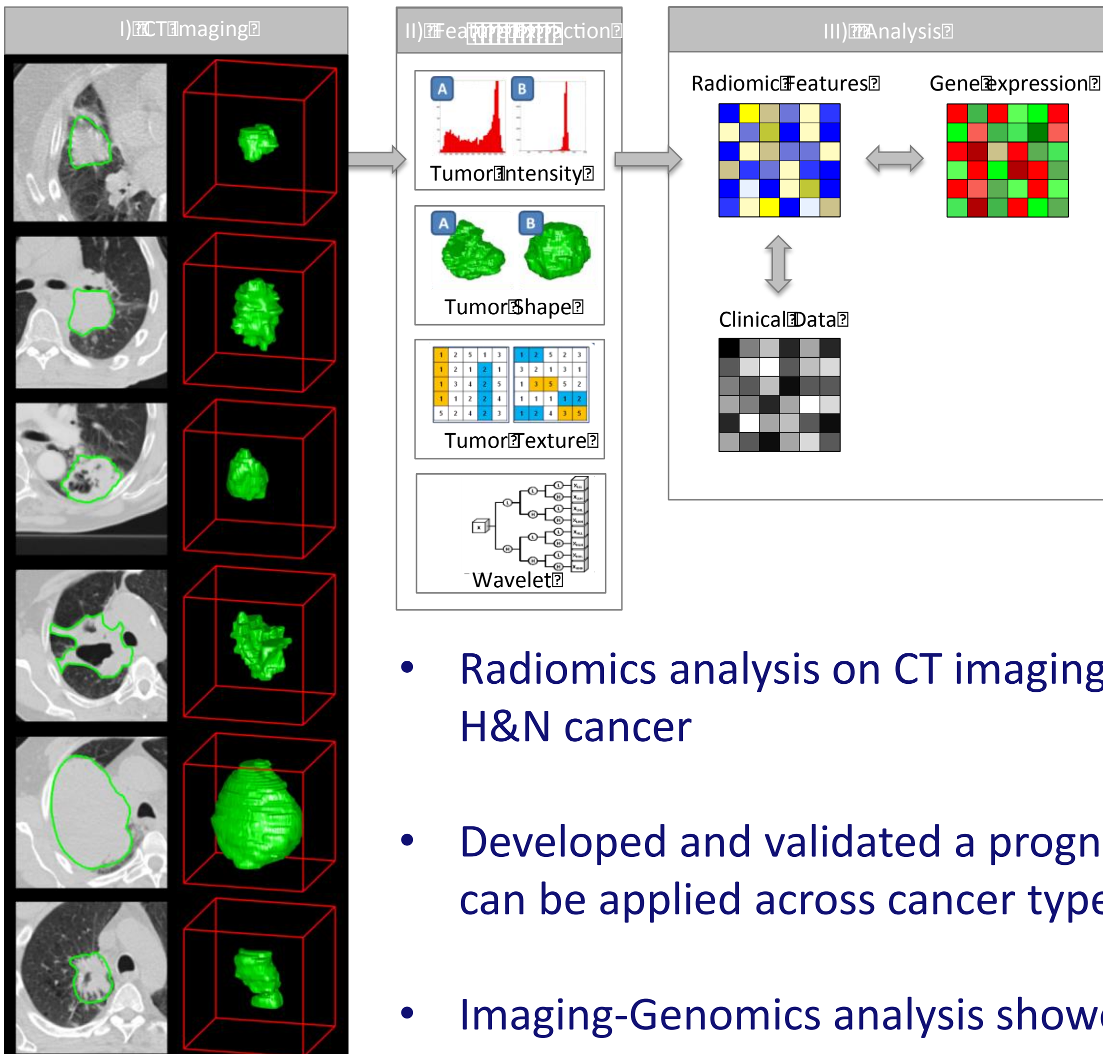
Wavelet





Radiomic features can capture phenotypic details

Imaging-Genomics across cancer types

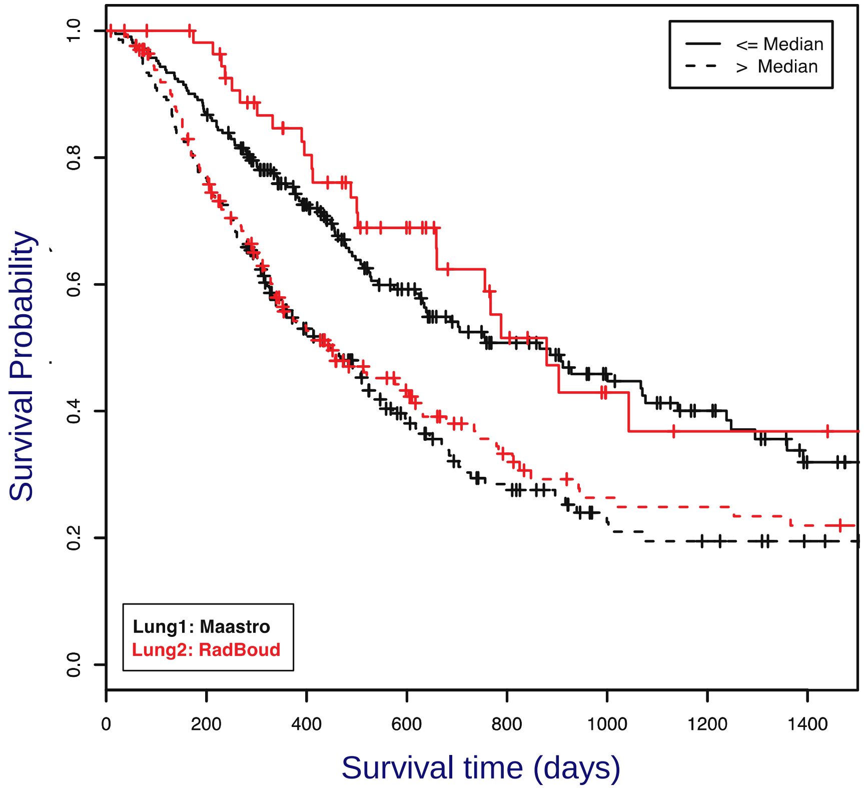


*Aerts *et al.* Nature Comm. 2014

- Radiomics analysis on CT imaging of >1000 patients with Lung or H&N cancer
- Developed and validated a prognostic radiomics signature that can be applied across cancer types
- Imaging-Genomics analysis showed strong correlations between radiomics and genomics data

Radiomics CT Signature Performance

Lung cancer cohorts



Performance Model:

- CI = 0.65 on the Lung2 Validation Dataset (n=225)

*Aerts *et al.* Nature Comm. 2014

Radiomics CT Signature Performance

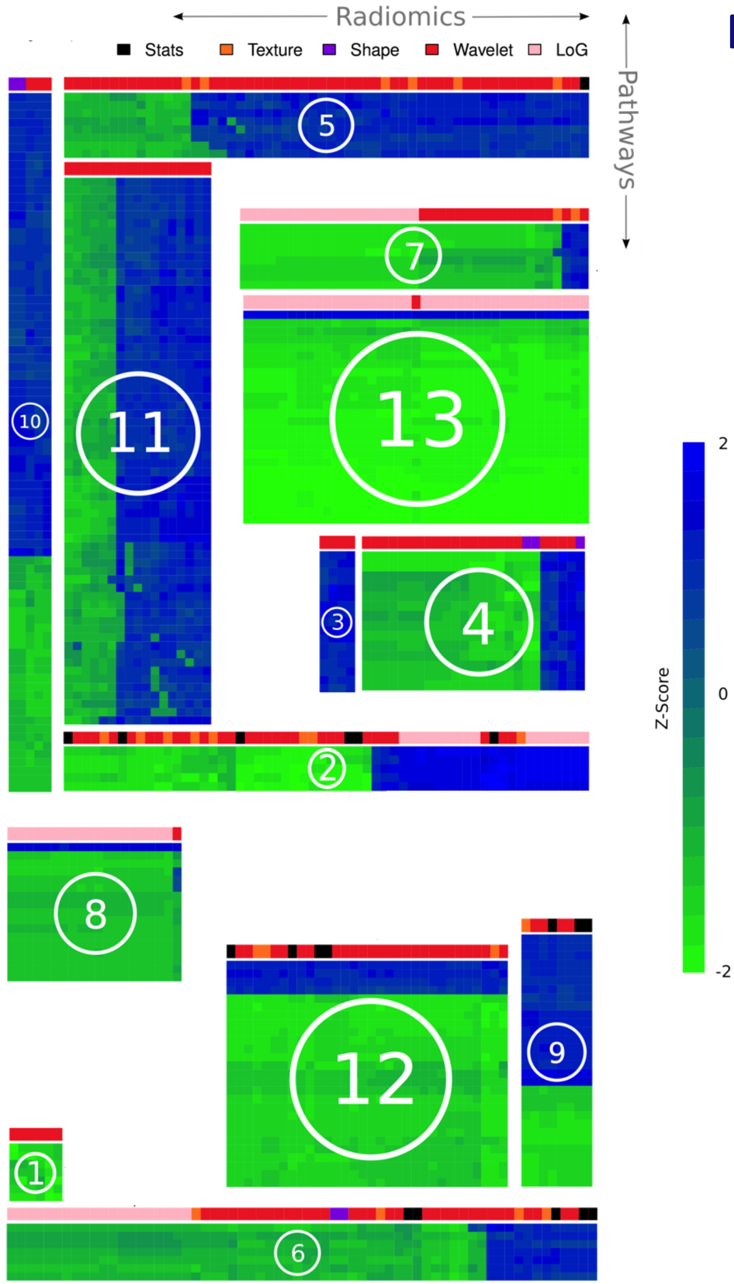
Extended Data Table 1 | Prognostic performance in validation datasets (Concordance Index CI)

Dataset	TNM	Volume	Radiomics	TNM-Radiomics	Volume-Radiomics	TNM vs. Radiomics	Volume vs. Radiomics	TNM vs. TNM-Radiomics	Volume vs. Volume-Radiomics
Lung2	0.60	0.63	0.65	0.64	0.65	**1.42×10^{-04}**	**6.29×10^{-07}**	**1.40×10^{-05}**	**7.52×10^{-08}**
H&N1	0.69	0.68	0.69	0.70	0.69	0.12	**1.70×10^{-02}**	**3.79×10^{-04}**	**8.55×10^{-03}**
H&N2	0.66	0.65	0.69	0.69	0.68	**6.48×10^{-08}**	**3.72×10^{-18}**	**3.06×10^{-10}**	**2.52×10^{-18}**

Prognostic performance in validation datasets (Concordance Index CI)

- Signature performed significantly better compared to volume in all datasets.
- Signature performance was better than TNM staging in Lung2 and H&N2, and comparable in the H&N1 dataset.
- Combining the signature with TNM showed significant improvement in all datasets.

Radiomics-Genomics association modules



13 association modules were identified and independently validated

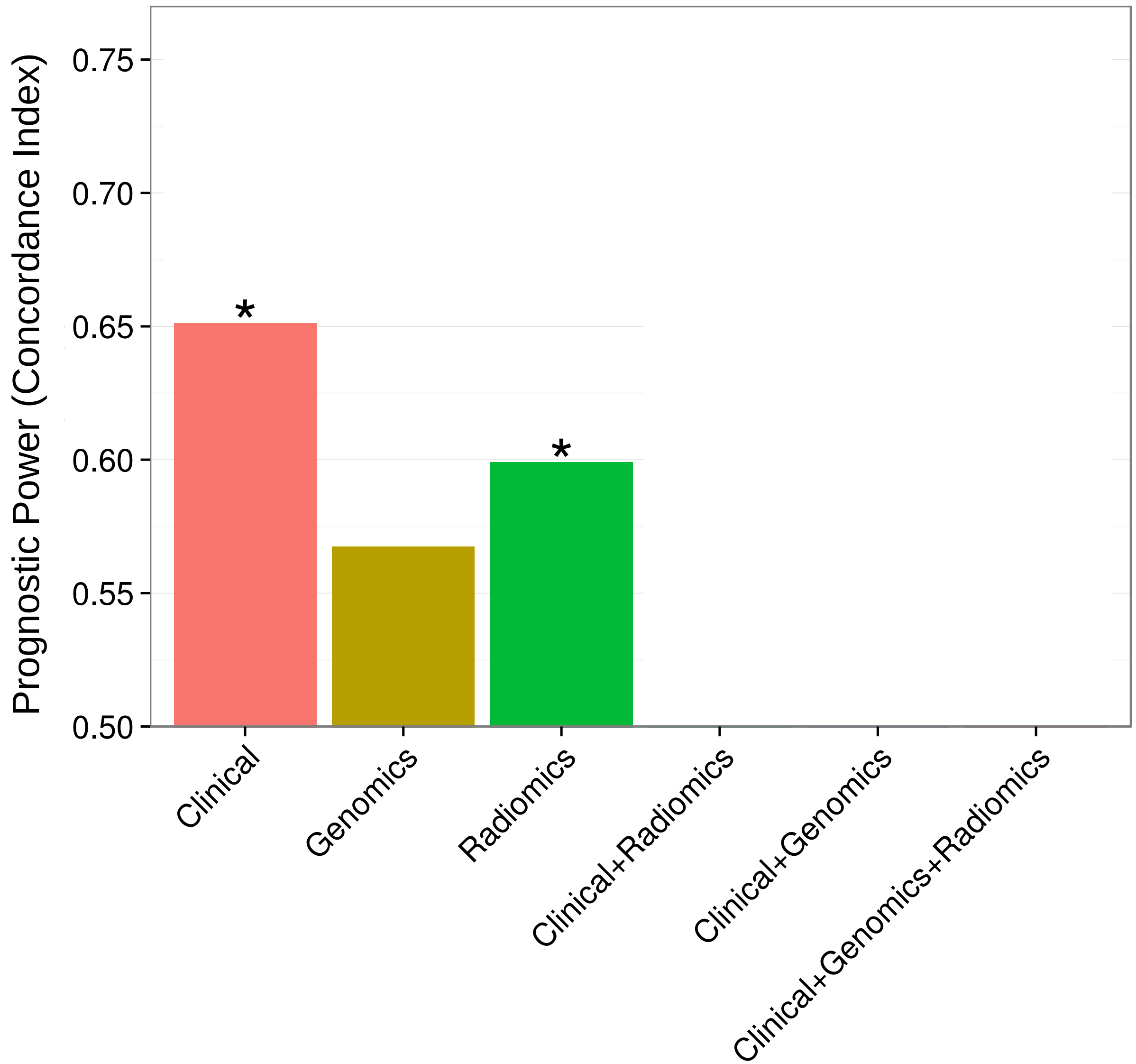
Radiomics Modules associate with distinct biological processes

Modules are significantly associated with clinical parameters:
survival (3), histology (5), stage (10)

Clinical-Radiomics-Genomics Prognostic Signatures

Genomic Signature:
Hou et al., 2010
17 genes for
Post-treatment survival

Radiomics Signature:
Aerts et al., 2014
(I) Statistics Energy
(II) Shape Compactness
(III) Grey Level Nonuniformity
(IV) Wavelet Grey Level
Nonuniformity HLH



Radiomics significantly adds to prognostic gene-signatures

Radiomics: Current Status

- Imaging moves towards a computational data science (bioinformatics)
- Due to advances in imaging, quantitative imaging is currently possible
- Large retrospective and prospective potential

- Large number of imaging features defined & successfully implemented
- Feature extraction pipeline implemented in 3D-Slicer (Python / Matlab)

- Radiomics signatures are prognostic across cancer types
- Radiomics are strongly connected with genomic patterns
- Integration of multiple datasets to improve performance

Radiomics: Challenges

Clinical/Radiology challenges:

- Image quality has to be optimized (QIN).
- Segmentations have to be accurate and robust (QIN).
- Feature algorithms must have high performance and stability (QIN).
- Exact role in personalized medicine has to be defined: how to improve diagnostic, prognostic and predictive power (QIN)

Informatics Challenges:

- Technical platforms have to be generalized (ITCR).
- Radiomics feature definitions have to be generalized (ITCR).
- Generalize across disease site and imaging modality (ITCR).
- Complex nature of imaging data has made it difficult for experts in genomics and bioinformatics to directly apply their methods to radiomics data (ITCR).

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ITCR radiomics informatics platform

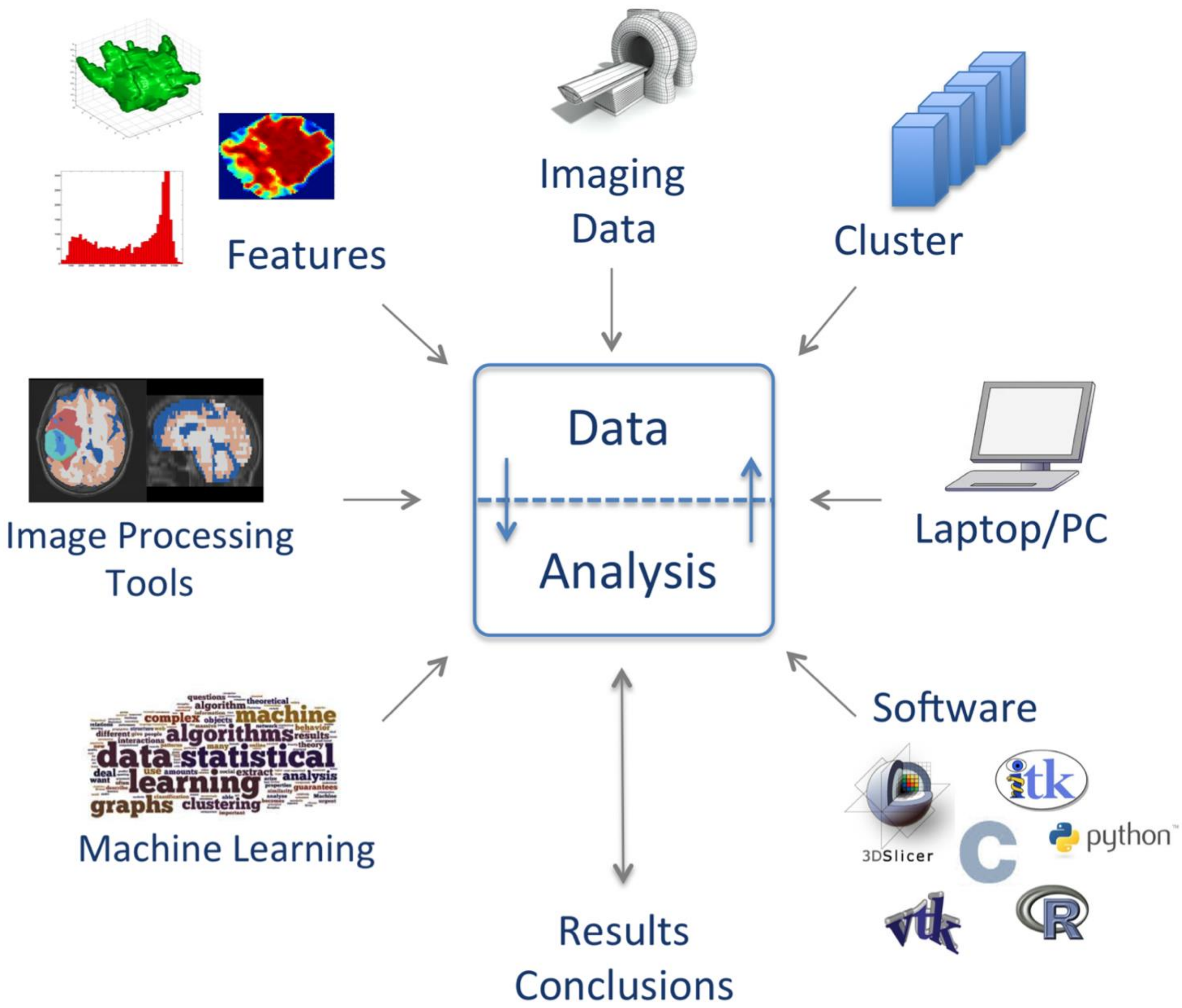
Radiomics Informatics Platform

Advanced Radiomics System implemented in 3D-Slicer (ITCR-U24)

PIs: Hugo Aerts, John Quackenbush (start April 2015)

- Publically available radiomics platform for automated extraction of imaging features (biomarkers)
- Platform designed to be open, generalized, portable, and widely applicable across image modality and cancer type.
- Flexible platform for experts and non-experts (bioinformatics/physicians)
- Validate developments by integrating radiomics, genomics, and clinical data -> prognostic performance and examine associations

Radiomics Informatics Platform



DANA-FARBER CANCER INSTITUTE

BWH BRIGHAM AND WOMEN'S HOSPITAL
A Teaching Affiliate of Harvard Medical School

Kitware

Isomics

PyRadiomics

- Radiomics package integrated within python
  (runs stand-alone and inside of Slicer)

- Large number of Radiomics feature algorithms are implemented.

- Image processing modules are based on ITK/VTK

- Stability tests at several partner sites are currently ongoing

- Public Release is expected fall 2016:
  radiomics.github.io

Horizon

- Open-source sever based system for medical image processing.
- Advanced DICOM image viewing and editing capabilities.
- Based on several open source packages: for example Cornerstone (OHIF), GIRDER (Kitware)
- Image-handling and processing tools will be included (including radiomic feature extraction)

- Developments ongoing:

https://github.com/crad

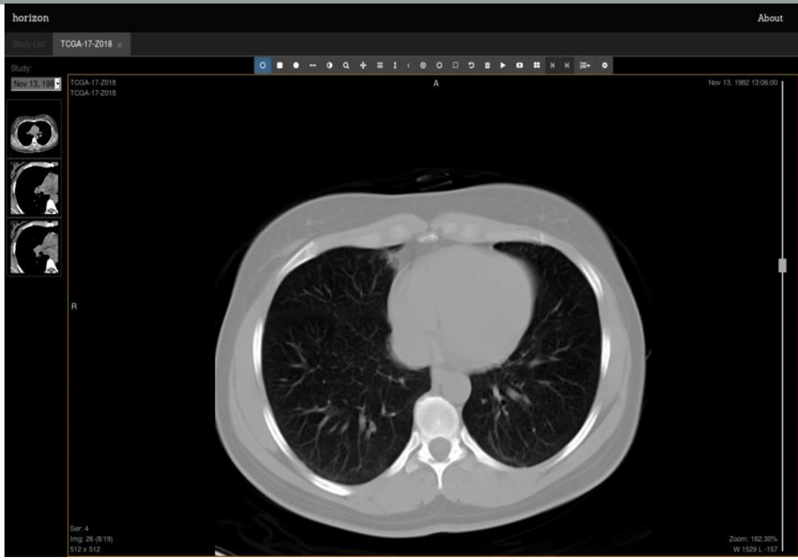
https://github.com/HorizonPlatform

Horizon

Partners:

- Dana-Farber Cancer Institute
- Brigham and Women's Hospital
- Harvard Medical School
- Kitware
- Isomics
- Open Health Imaging Foundation (OHIF)
- Intel (Comprehensive Cancer Cloud)

Horizon Infrastructure



Client Side – Viewer

- Open Source
- Based on OHIF Viewer / Cornerstone
- Segmentation viewer & editor
  - Paint brushes
  - Adaptive brushes
  - Cutting tools

Server Side – User Management

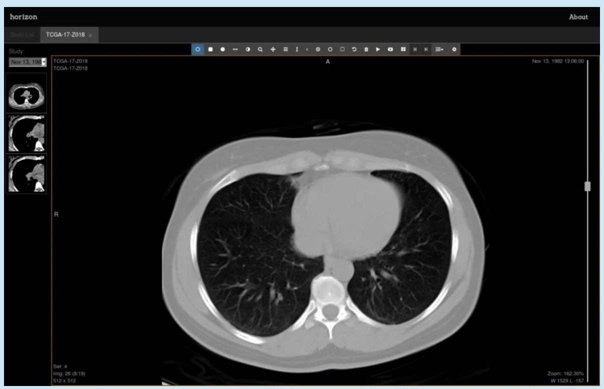
- Access control
- Data conversion
- Data storage

Server Side – Data Management

- Girder data management platform
- Open source
- Running on Partners Server / Amazon AWS / Intel Cluster /

Horizon Infrastructure

Client



Open Health
Imaging Foundation

Server

Client APIs

Backend APIs

Kitware
Girder

DEMO

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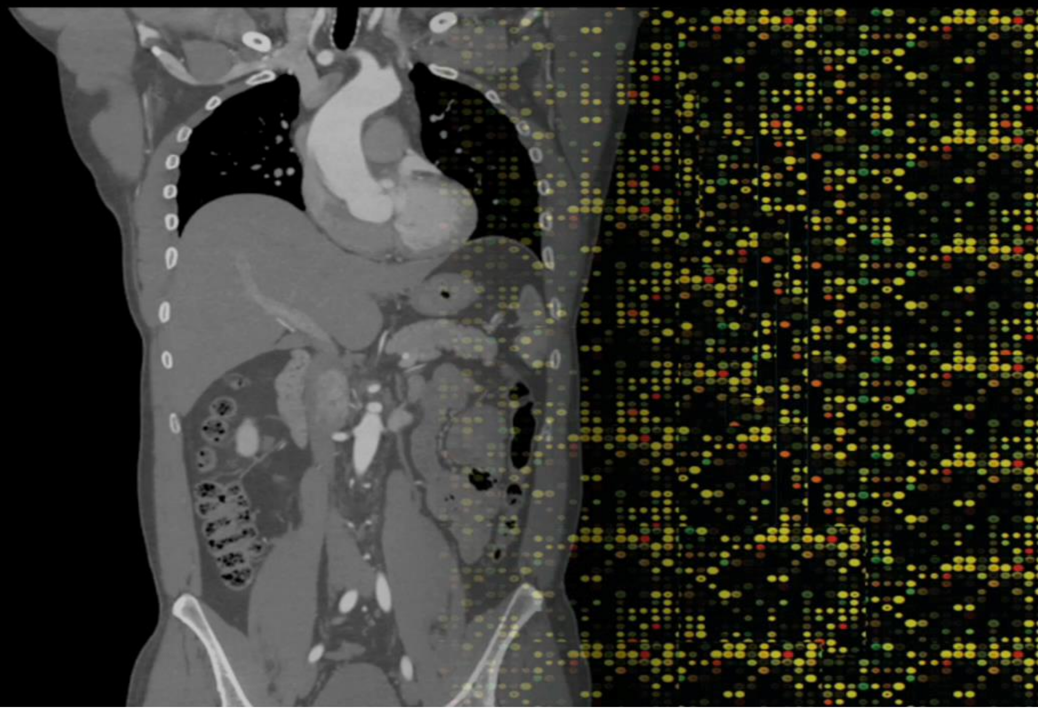
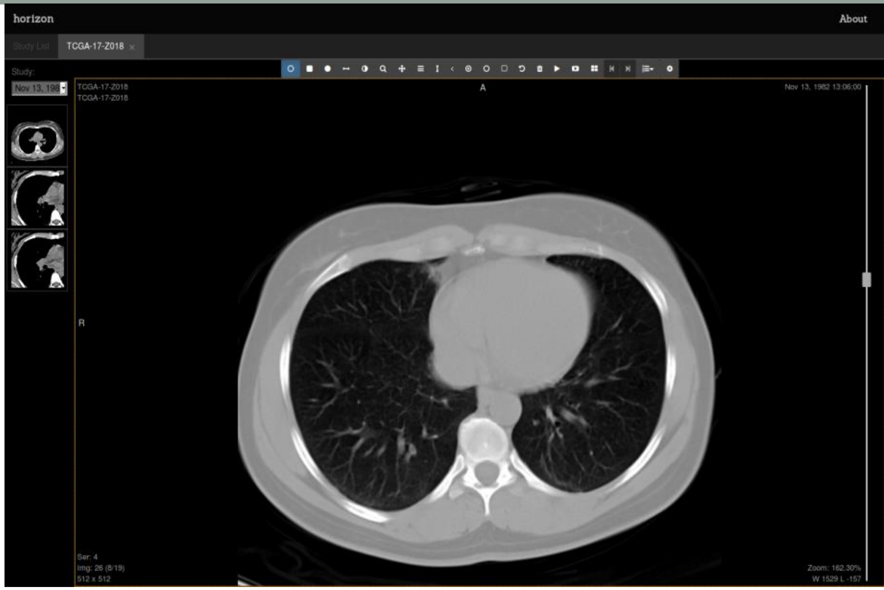


Want to know more?



Contact us:

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- Ron Kikinis (Harvard-BWH)
- Roman Zeleznik (Harvard-DFCI)
- Jean-Christophe Fillion-Robin (Kitware)
- Nicole Aucoin (Harvard-BWH)

https://github.com/crad

https://github.com/HorizonPlatform

https://radiomics.github.io