The iBiopsy plateform –

imaging phenomics and the limits of genomics

Hubert Beaumont, PhD

Lead Scientist

Meet Ups – March 30, 2017

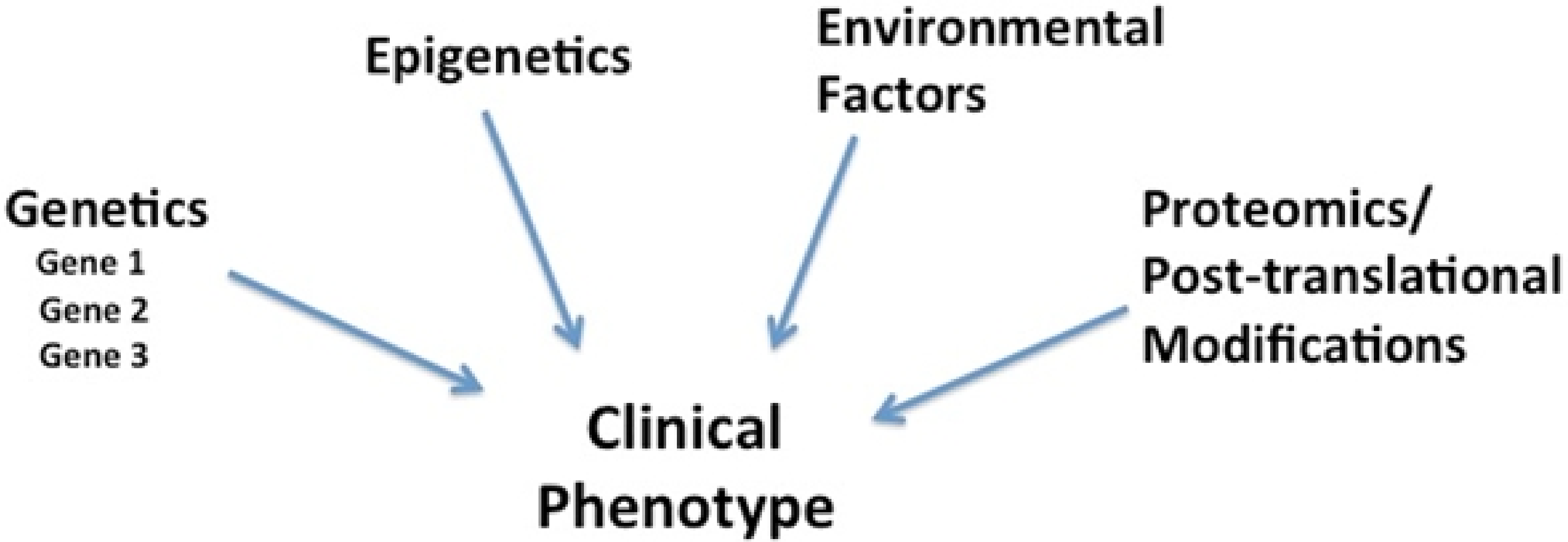
Precision Medicine

Problem Statement

- **There is a need to identify which patients are likely to derive the most benefit from targeted therapies**
- **Biomarkers—especially predictive biomarkers—are crucial tools** in the field of personalized medicine and health economics, in particular, as they enable definition of the populations of patients who are most likely to benefit from targeted therapies.
- **Some groups report that current pharmacogenetic approaches are suboptimal**. More-effective patient selection and treatment assessment is mandatory to improve the success rate of new therapies.
- **Multiplex phenotype**: Complex contribution of numerous genes, the epigenome and environmental factors.

The Genotype-Phenotype Relationship

Genotype is not the only contributor to Phenotype



Genetics
Gene 1
Gene 2
Gene 3

Epigenetics

Environmental Factors

Proteomics/
Post-translational
Modifications

Clinical Phenotype

Limitations of Genomics to Precision Medicine

Not the single Risk Predictor

- **Most clinical traits are polygenic**. Height is affected by more than 180 genes.
- **The genome only contributes a fraction of the expressed trait**. For height it less than 10%.
- **Downstream modifying factors, the epigenome, the environment, have a significant contributing influence**.

Although partial risk prediction will be feasible and medically useful in some cases, there are likely to be fundamental limits on precise prediction due to the complex architecture of common traits, including common variants of tiny effect, rare variants that cannot be fully enumerated and complex epistatic interactions, as well as many non-genetic factors.

Dr. Eric Lander : "Initial impact of the sequencing of the human genome", Nature, 2011

New Paradigm Needed

From Genome to Phenome

- Whole genome sequencing approaches can be suboptimal at assessing risk for most common diseases. **Most disease risk factors are not purely genetic.**
- Paradigm shift away from a **genocentric to a phenocentric** view, is what is really needed to improve our understanding of complex diseases and deliver targeted therapies.

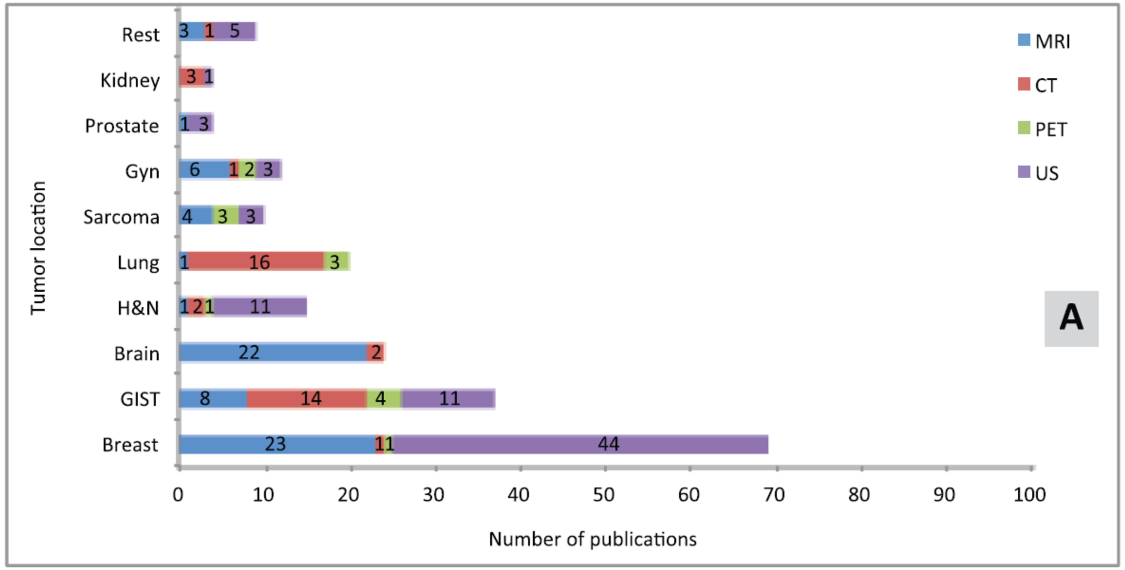
Focus may be on Phenotype not Genotype

The phenotype is the expressed trait that physicians look for

Radiomics/Phenomics: State of the art

A very active area

- **Reproducibility generally not addressed**



Features		N	%
Imaging method	MRI	75	36%
	CT	40	19%
	PET	14	7%
	US	81	39%
Study goal	Diagnosis/staging/outcome pred.	182	56%
	Response	63	30%

L. Alic et Al. "Quantification of Heterogeneity as a Biomarker in Tumor Imaging: A Systematic Review," PLoS One, vol. 9, no. 10, p. e110300, 2014

Radiomics/Phenomics: A new start

A reference study

nature
COMMUNICATIONS

ARTICLE

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

DOI: 10.1038/ncomms5006

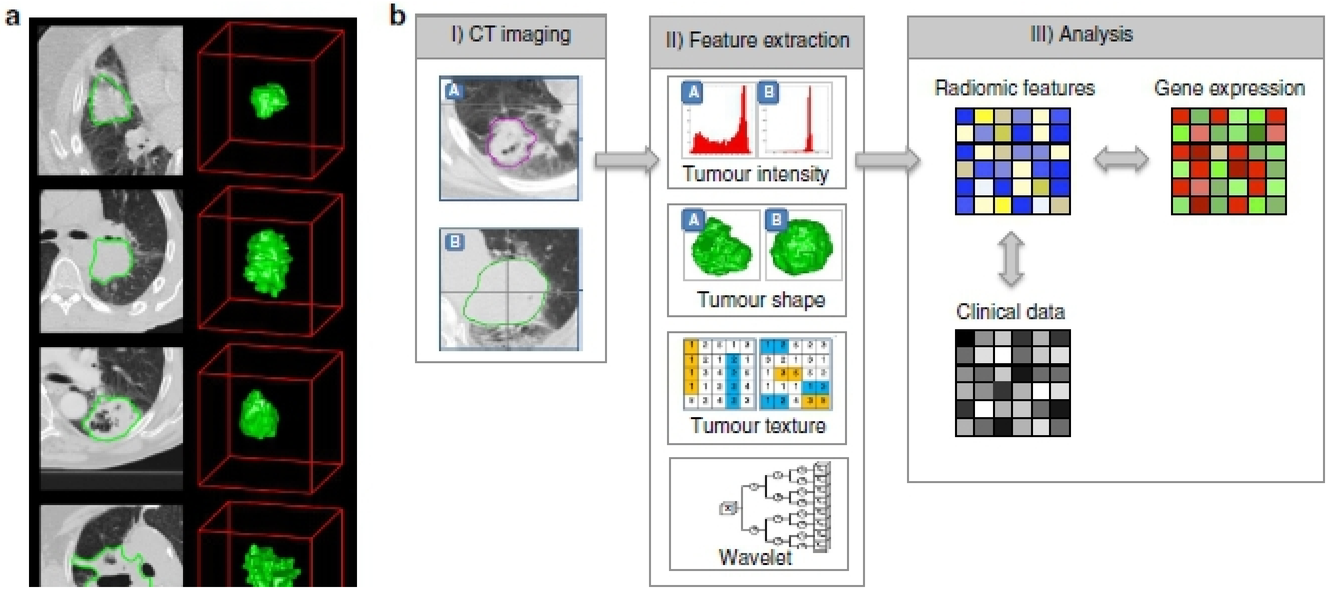
OPEN

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]

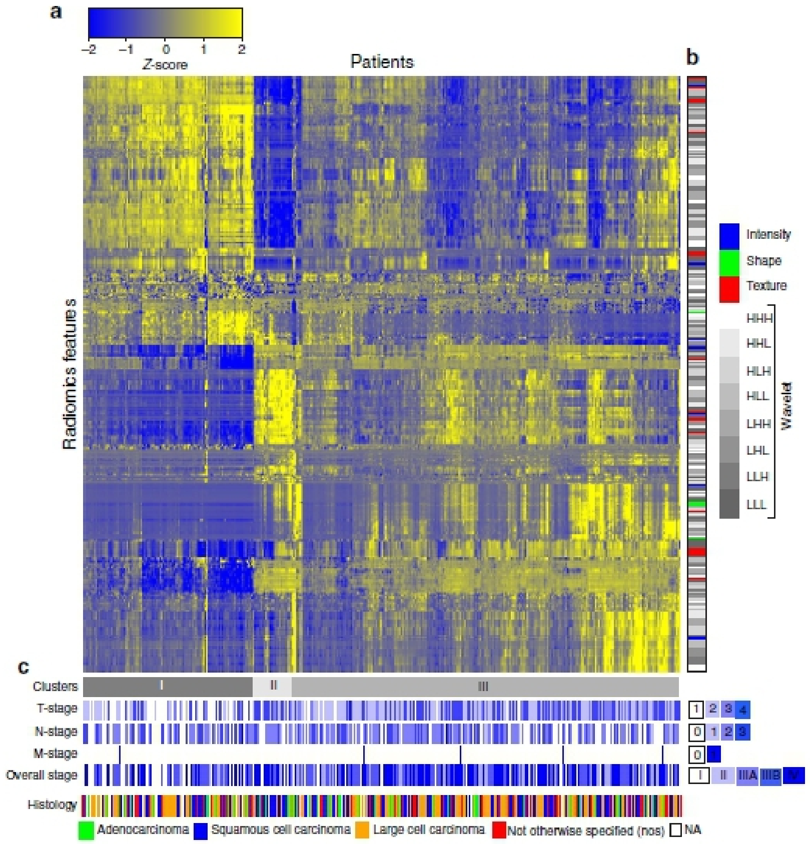
Radiomics/Phenomics: A new start

Material & Methods



Radiomics/Phenomics: A new start

Results



Radiomics/Phenomics: A new start

Conclusions

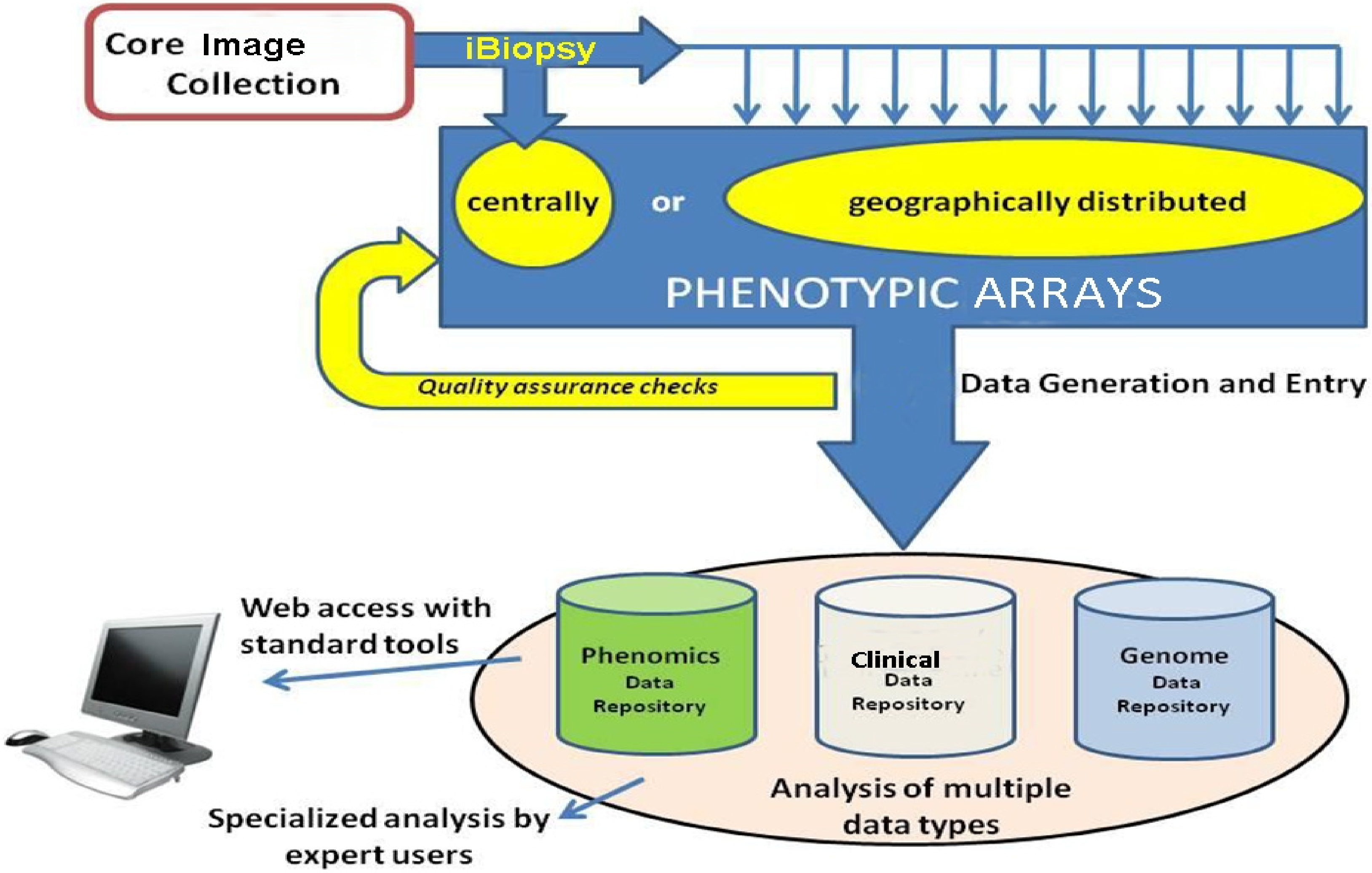
- “ Prognostic validation of radiomic signature ”
- “ Combining the radiomic signature with TNM staging showed a significant improvement ”
- “ We did not find a significant association between radiomic signature prediction and Human Papilloma Virus status. However, we found that the signature preserved its prognostic performance in the HPV negative group ”
- “ We found significant associations between the signature features and gene-expression patterns ”

Phenomics

The Science of Biomarkers

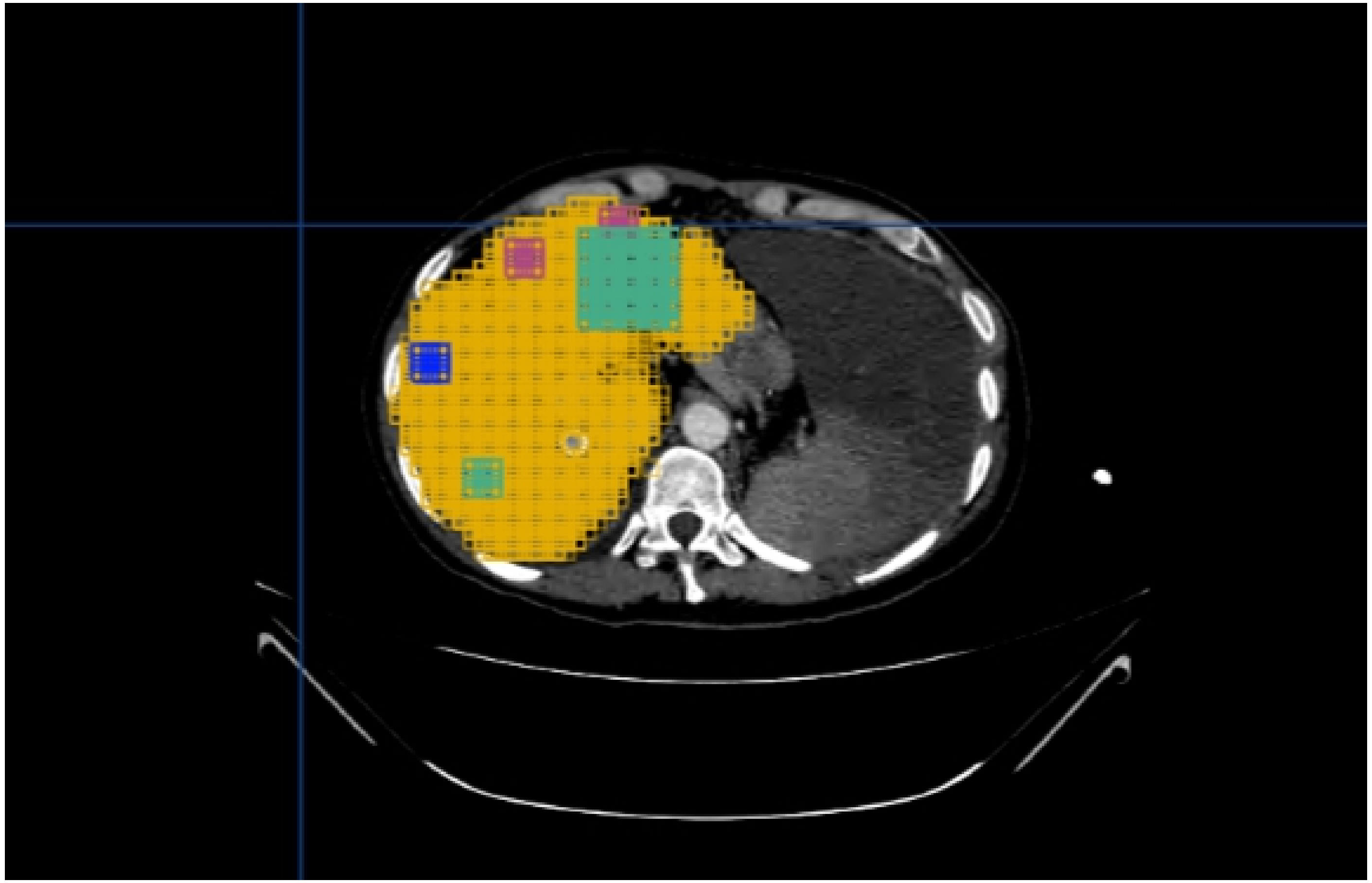
- Phenomics is the large-scale collection and analysis of phenotypic data or biomarkers
- The phenotype is the expressed clinical trait
- The phenome is the catalog of phenotypic biomarkers
- Starting point should be the study of phenotypic variability
- Phenomics captures genomic, epigenetic, metabolic and environmental associations
- Phenotype may be more predictive than genotype
- Phenomics requires a **big data**, **high throughput analytics** approach

iBiopsy: from Imaging to Phenomics



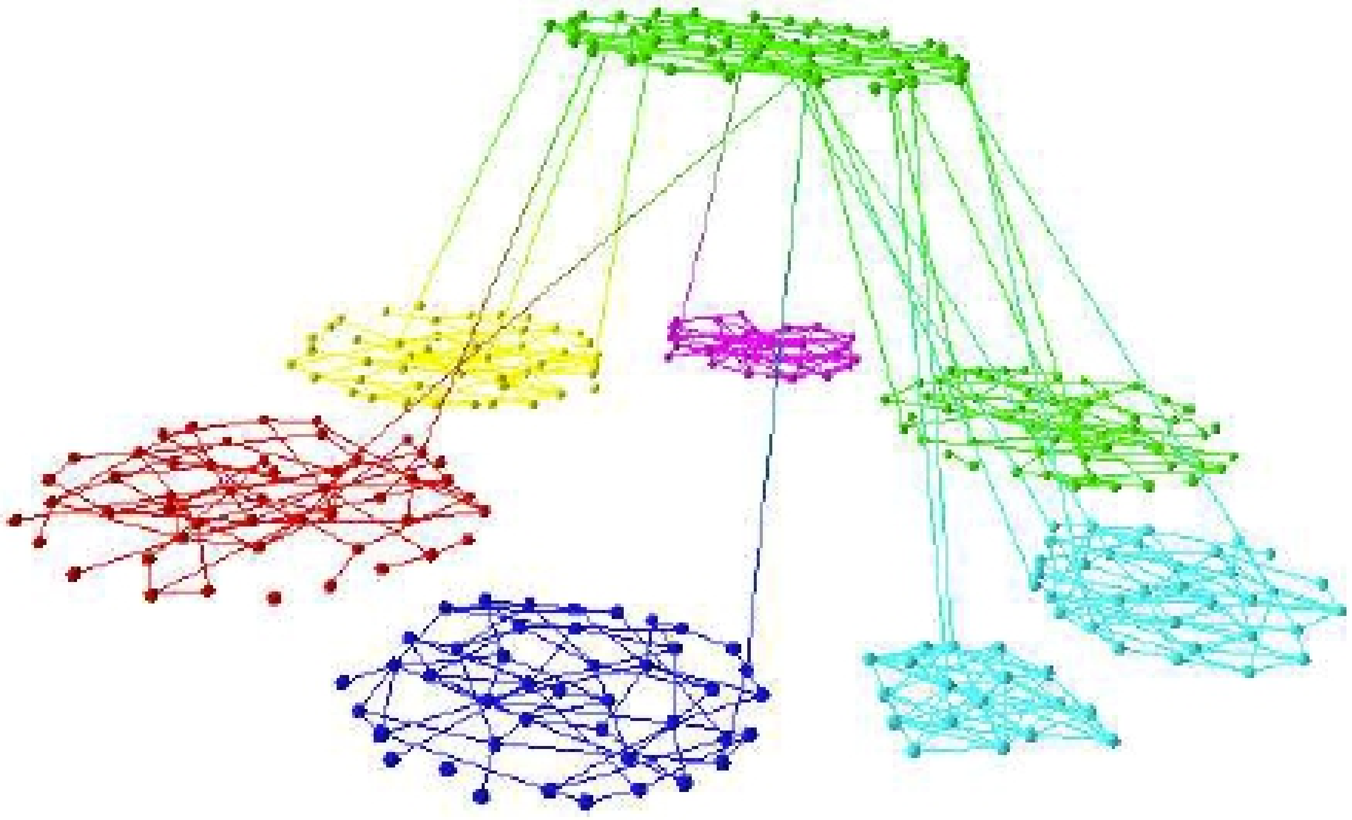
Decoding the Image

Step 1: Automated organ segmentation, ROI identification and multi-resolution tiling



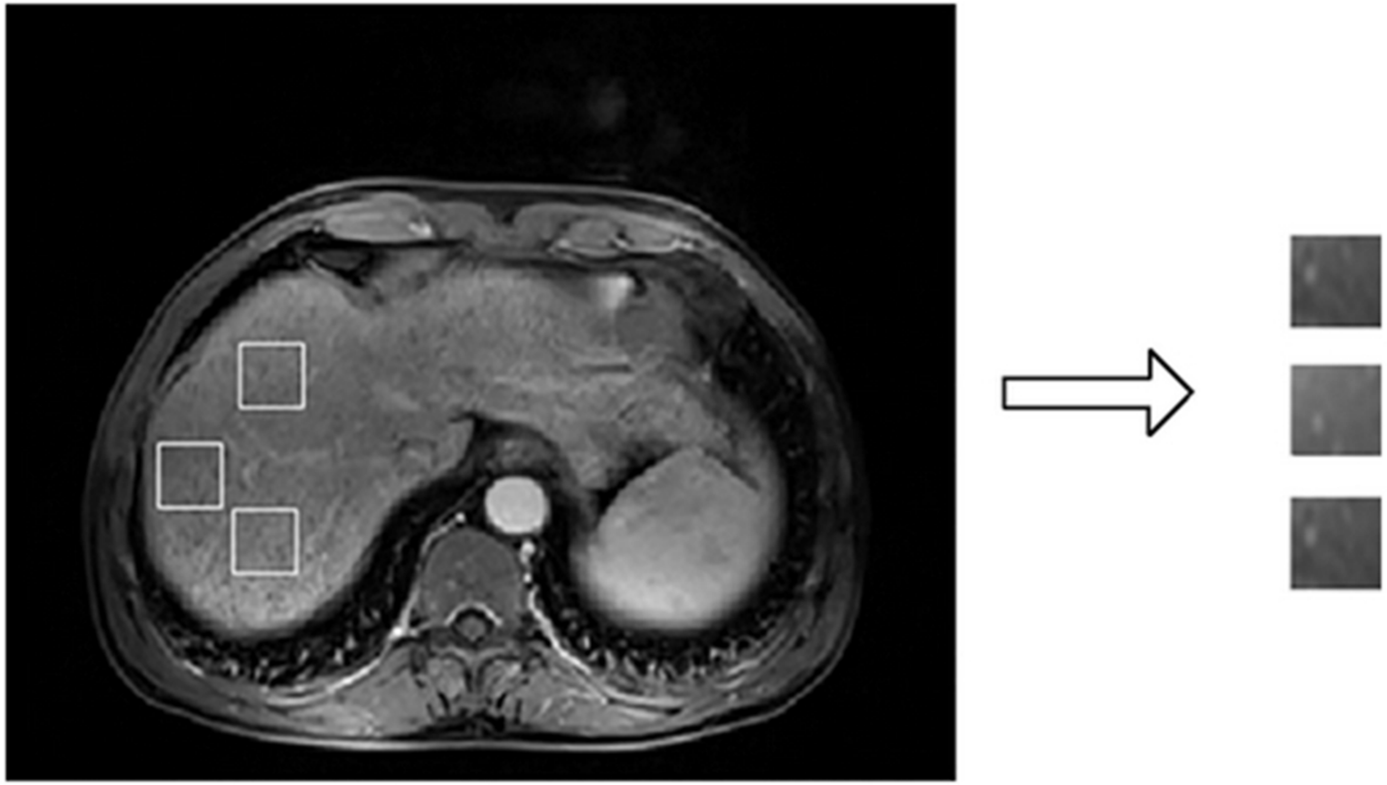
Indexing the Phenotypes

Step 2: Organizing individual phenotypes in clusters by



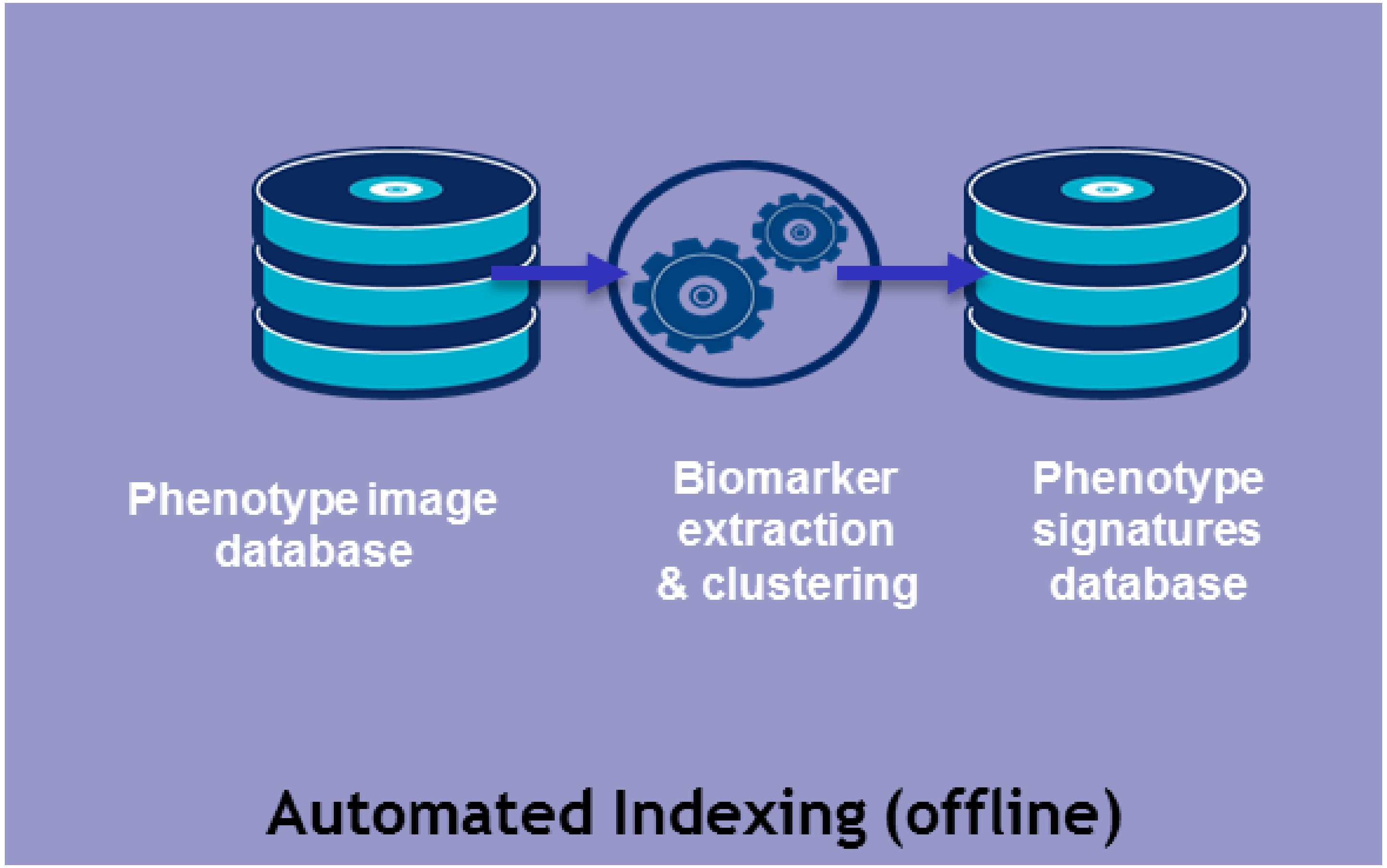
Automated Biomarker Extraction

Thousands of Biomarkers Extracted per Phenotype



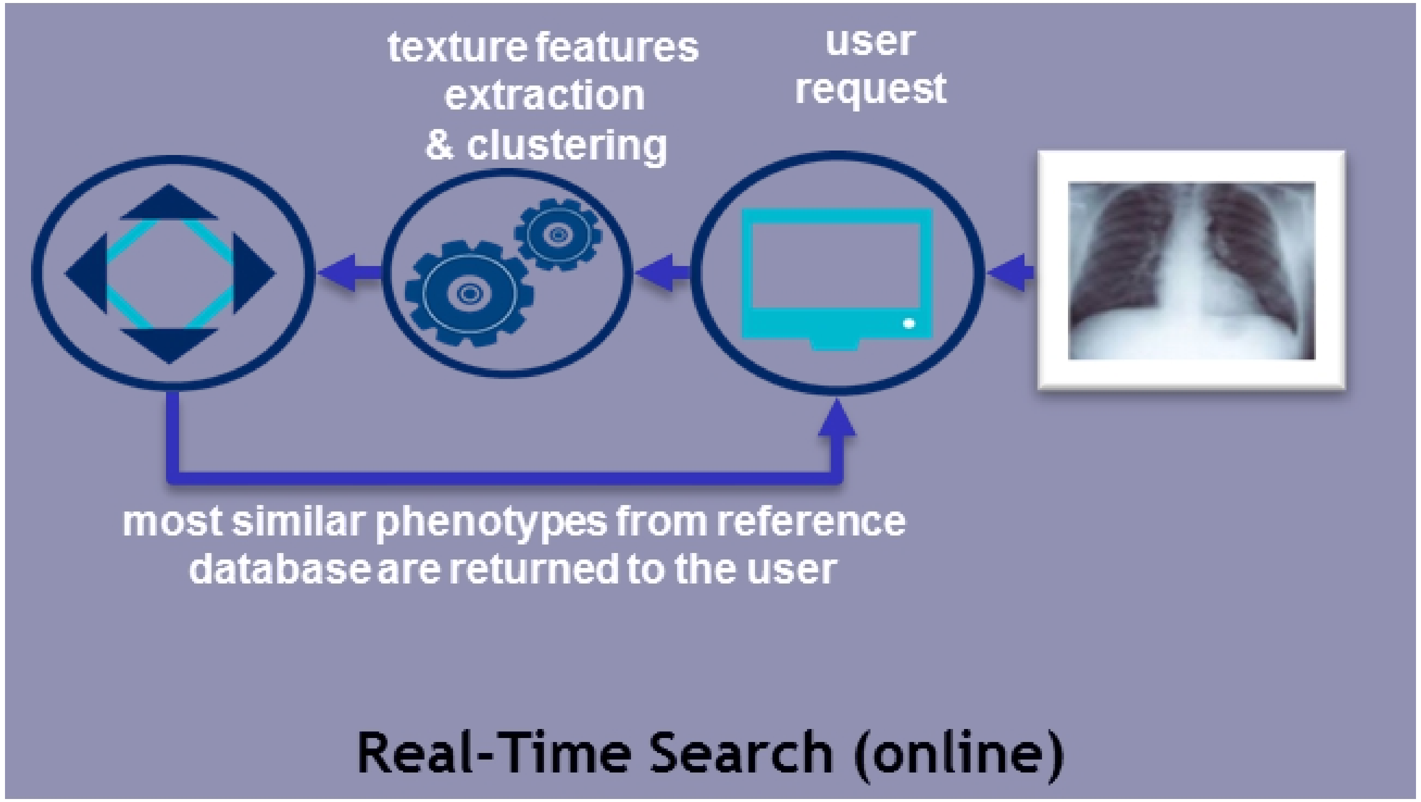
Creation Of Phenotype Reference Database

High Throughput Data Extraction & Indexing



Phenotype Search Engine

Content-based phenotype retrieval in real-time from Cloud



texture features extraction & clustering

user request

most similar phenotypes from reference database are returned to the user

Real-Time Search (online)

Imaging Phenomics

The New Paradigm

BIG DATA ANALYTICS

End to end imaging platform for:

- Large scale data acquisition
- Massively parallel feature extraction
- Biomarker computation
- Predictive Analytics

IMAGING

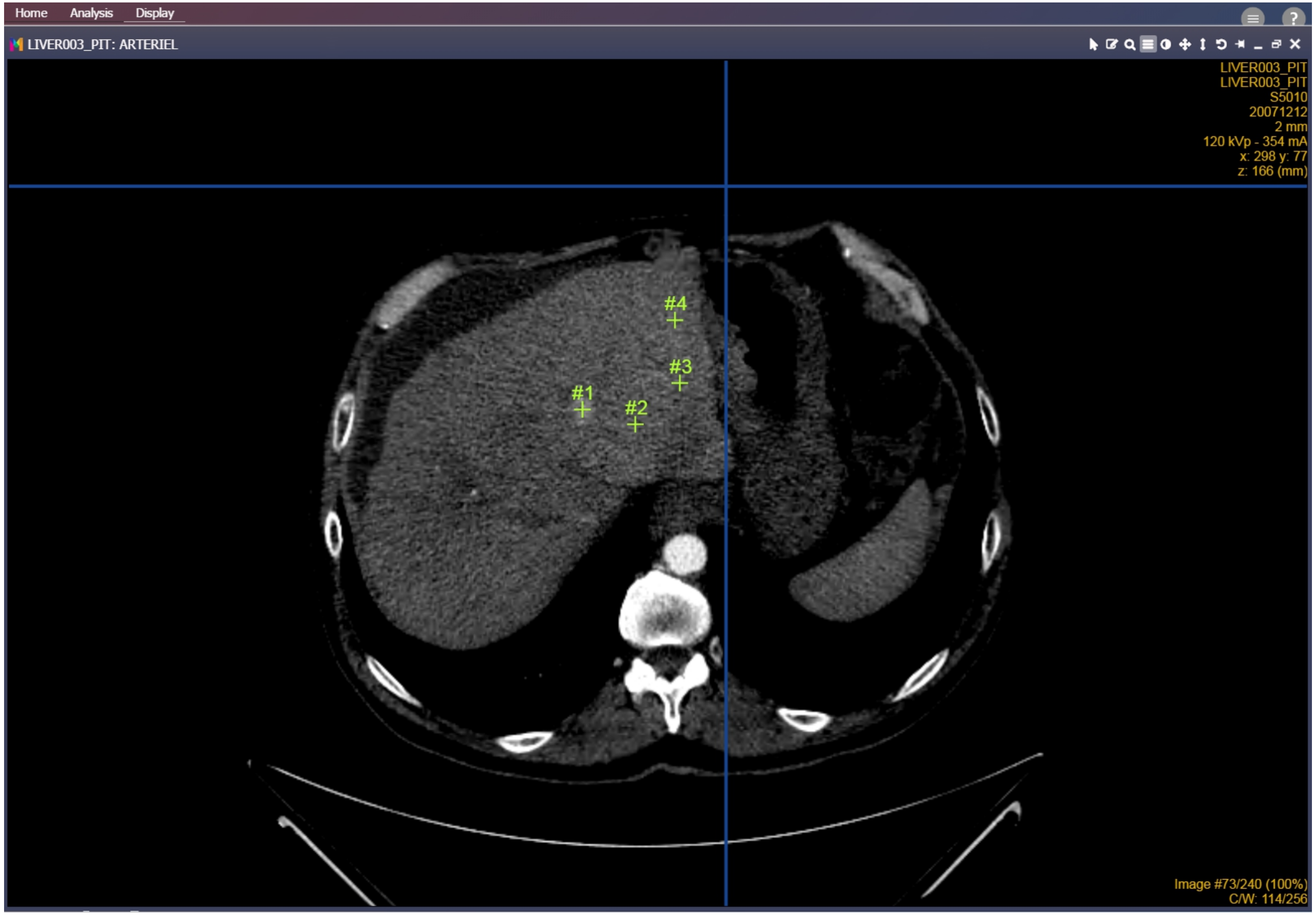
Imaging Biomarkers correlate to:

- Gene-expression
- Disease biology
- Patient status (TNM)
- Treatment outcome
- Personalized medicine

Advantages of Imaging Biomarkers

- Non invasive methods
- Suited for heterogeneous tissues
- Analyzes the entire tumor at once
- Biomarkers can be quantified
- Imaging acquisition methods are standardized
- Available for routine clinical use
- Biomarker extraction can be automated
- Big data makes the analysis of millions of phenotypes feasible

The User Interface

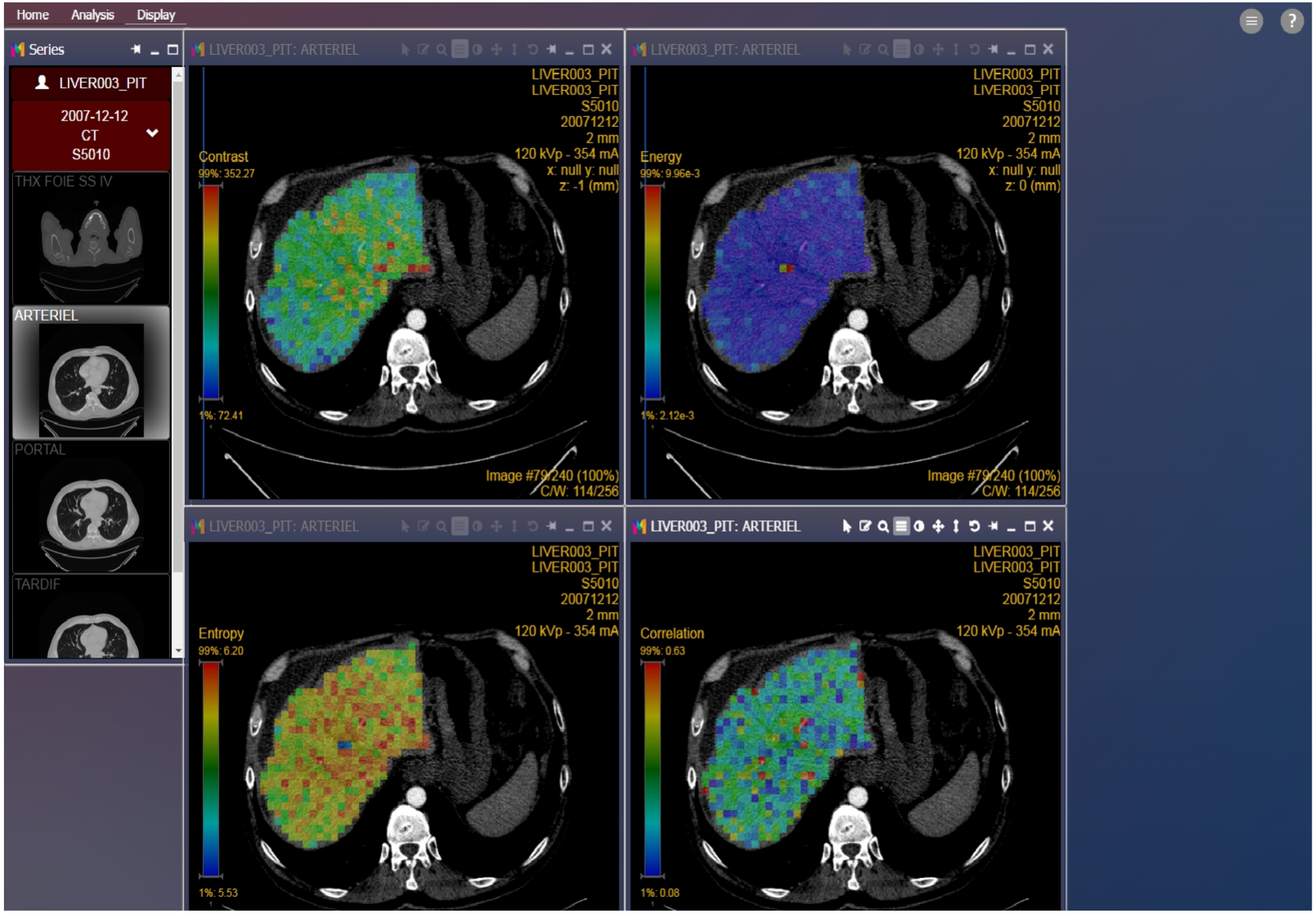


LIVER003_PIT: ARTERIEL

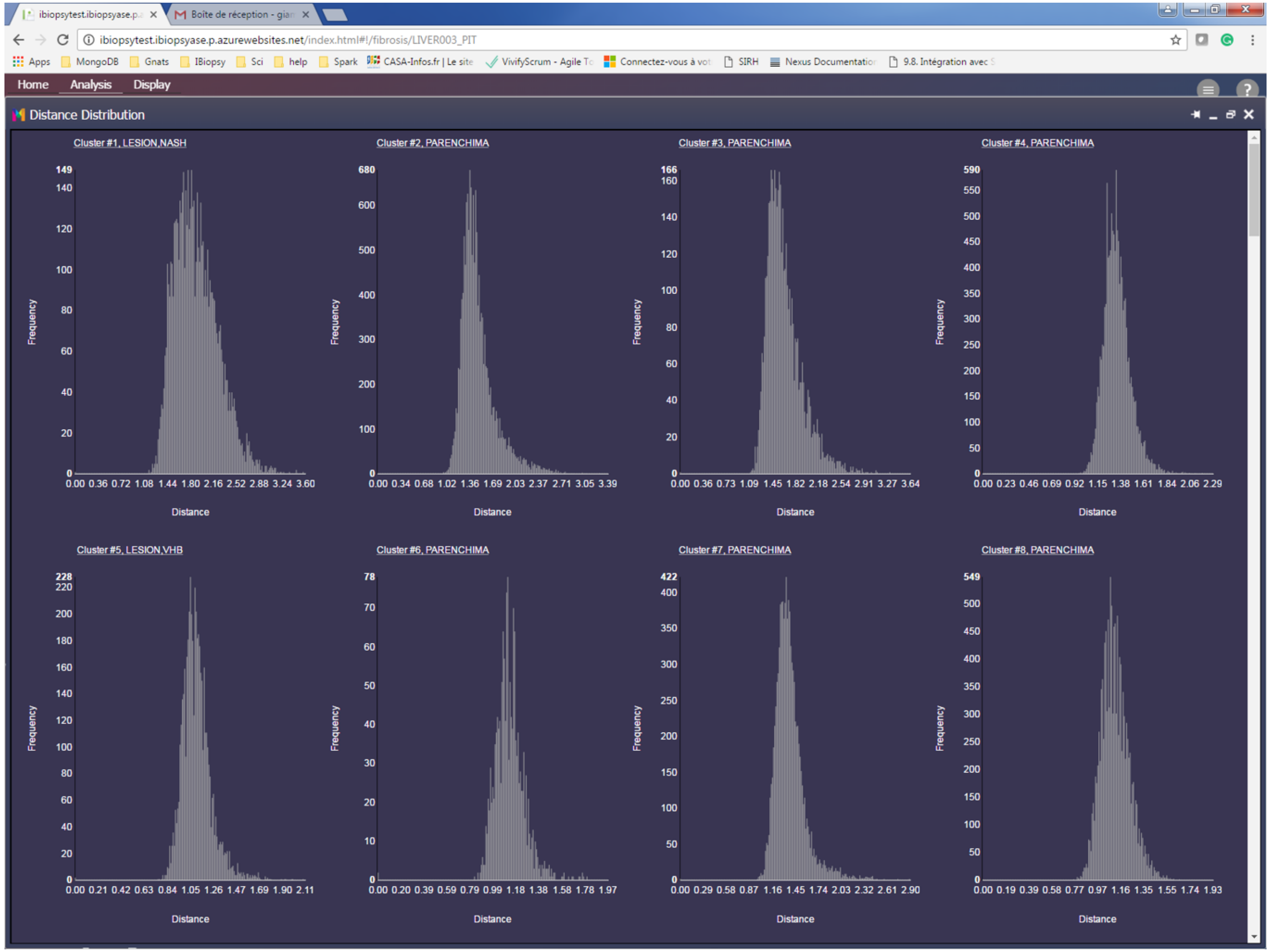
LIVER003_PIT
LIVER003_PIT
S5010
20071212
2 mm
120 kVp - 354 mA
x: 298 y: 77
z: 166 (mm)

Image #73/240 (100%)
C/W: 114/256

The User Interface



Analytics


ibiopsytest.ibiopsyase.p
Boite de réception - gian
ibiopsytest.ibiopsyase.p.azurewebsites.net/index.html#!/fibrosis/LIVER003_PIT
Apps
MongoDB
Gnats
IBiopsy
Sci
help
Spark
CASA-Infos.fr | Le site
VivifyScrum - Agile T
Connectez-vous à vot
SIRH
Nexus Documentatio
9.8. Intégration avec
Home
Analysis
Display
Distance Distribution
Cluster #1, LESION.NASH
Cluster #2, PARENCHIMA
Cluster #3, PARENCHIMA
Cluster #4, PARENCHIMA
Cluster #5, LESION.VHB
Cluster #6, PARENCHIMA
Cluster #7, PARENCHIMA
Cluster #8, PARENCHIMA
Frequency
Distance
149
680
166
590
228
78
422
549
0.00 0.36 0.72 1.08 1.44 1.80 2.16 2.52 2.88 3.24 3.60
0.00 0.34 0.68 1.02 1.36 1.69 2.03 2.37 2.71 3.05 3.39
0.00 0.36 0.73 1.09 1.45 1.82 2.18 2.54 2.91 3.27 3.64
0.00 0.23 0.46 0.69 0.92 1.15 1.38 1.61 1.84 2.06 2.29
0.00 0.21 0.42 0.63 0.84 1.05 1.26 1.47 1.69 1.90 2.11
0.00 0.20 0.39 0.59 0.79 0.99 1.18 1.38 1.58 1.78 1.97
0.00 0.29 0.58 0.87 1.16 1.45 1.74 2.03 2.32 2.61 2.90
0.00 0.19 0.39 0.58 0.77 0.97 1.16 1.35 1.55 1.74 1.93

Used technologies

mongoDB

Spark

Microsoft
Azure

Value Proposition

Target Applications

- Early detection of cancers and other chronic diseases (NASH)
- Predicting treatment response
- Predicting patient prognosis or outcome
- Selecting patients for clinical trials
- Identifying biological processes at individual level
- High throughput screening for development of targeted compounds

Requirements for Phenomics

Phenomics requires a Big Data Computing Platform for large scale phenotypic data collection and analysis.

- High-dimensional imaging biomarker discovery and validation
- Tens of thousands of variables and feature combinations
- Millions of computations per image require high throughput architectures
- Supervised and unsupervised analysis using Big Data Analytics Tools

High quality, fully indexed databases of phenotypic traits images and biomarkers.

Median iBiopsy Platform

Highly differentiated based on proprietary technology & processes

MEDIAN is uniquely positioned to offer a high-throughput, comprehensive, accurate, end-to-end **image mapping and analysis platform** for large scale extraction of imaging biomarkers and phenotypic signatures.

iBiopsy is based on state-of-the-art “big-data” architecture highly optimized for automated phenotype indexing and analysis.

Cloud Computing Platform in collaboration with Microsoft.