Research infrastructures and medical image analysis

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HES-SO

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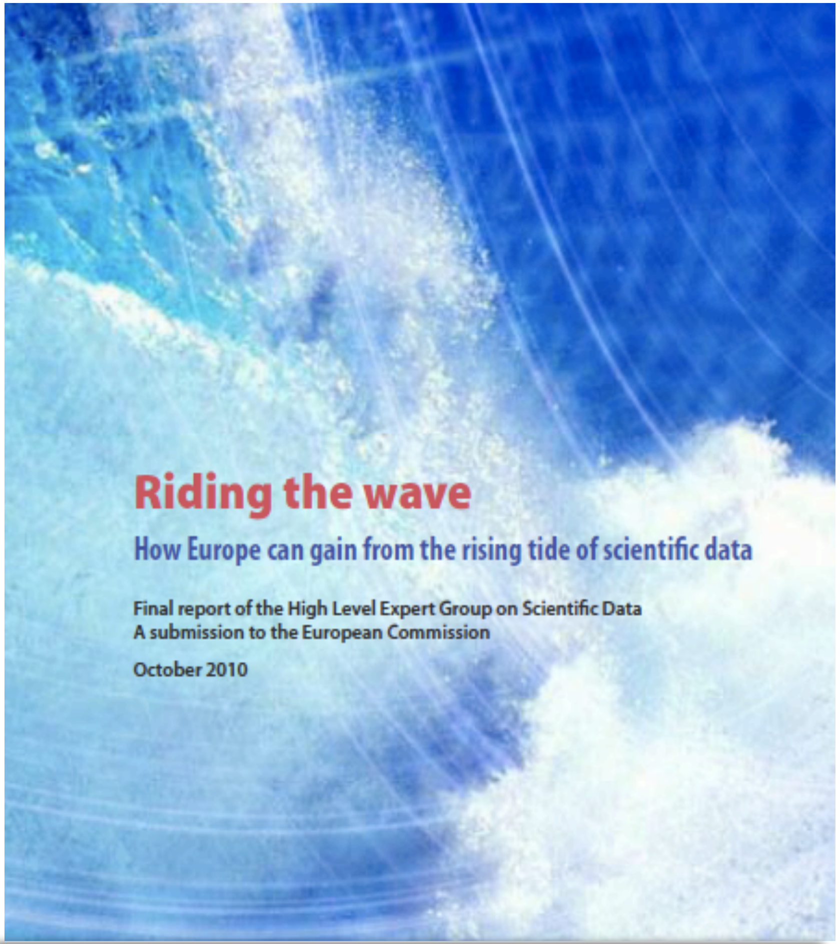
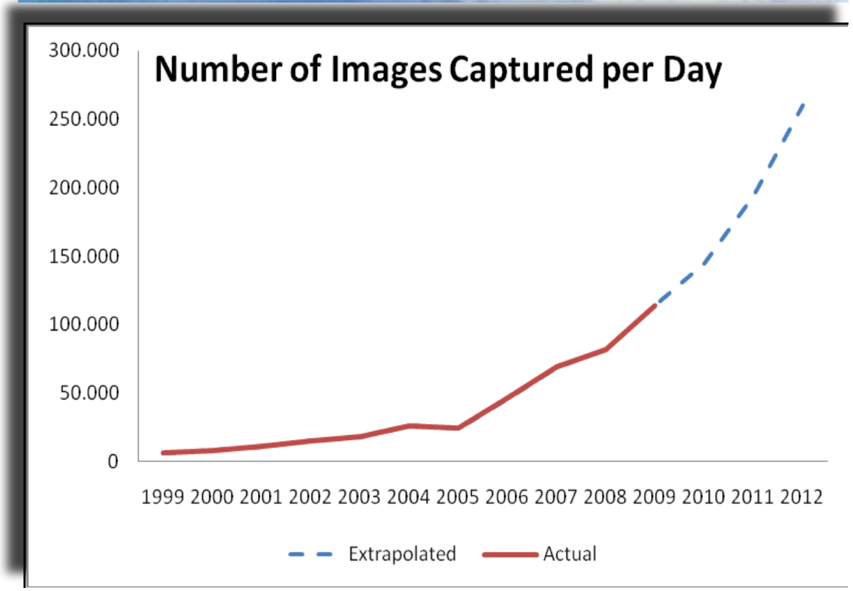
Who I am

- Medical informatics studies in Heidelberg, Germany (1992-1997)
  - Exchange with Daimler Benz research,
- PhD in image processing, image retrieval, Geneva, Switzerland (1998-2002)
  - Exchange with Monash University, Melbourne, AUS
- Professor in radiology and medical informatics at the University of Geneva (2014-)
- Professor in Computer Science at the HES-SO, Sierre, Switzerland (2007-)
  - Visiting faculty at Martinos Center (2015-2016)

Motivation

- Digital medicine and artificial intelligence are starting to change clinical practice
  - Strongly data driven
    - Almost unlimited amounts could possibly be used
- Massive amounts of data are being produced
  - Exponentially growing
  - Imaging, genetics, …
  - Also public data with TCIA TCGA, NLST, ...





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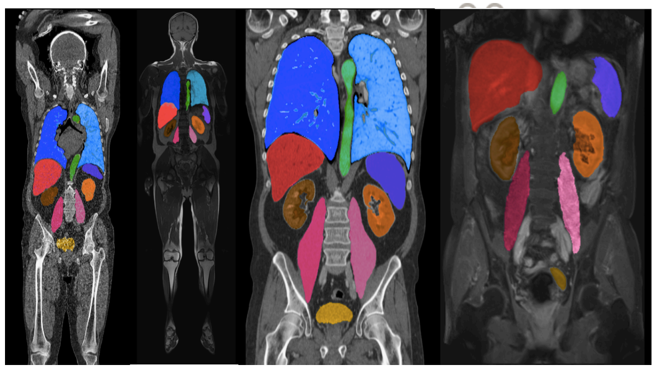
A medical environment



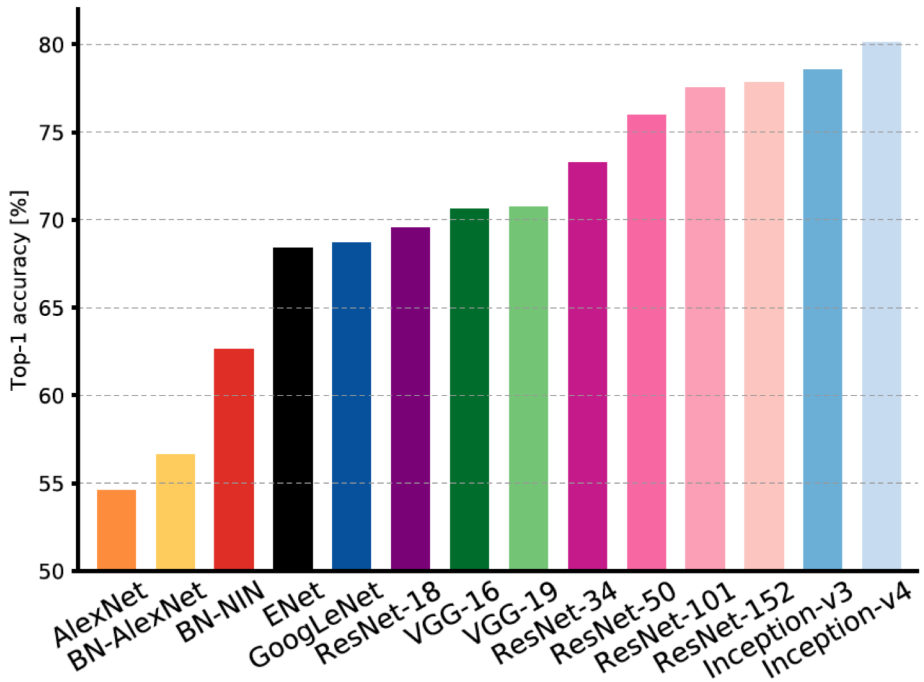
- Access to medical data is not easy
  - There are ethical and privacy constraints
    - Medical data are personal, sensitive
  - Annotations by experts are very expensive
  - Central storage is often not considered!
    - Usually hospitals do not give away data
      - Also for legal reasons
    - Requires to bring the algorithms to the data
- The risk is not sharing one data set itself but mixing several data sets
  - Risk of revealing the identity, backups, …

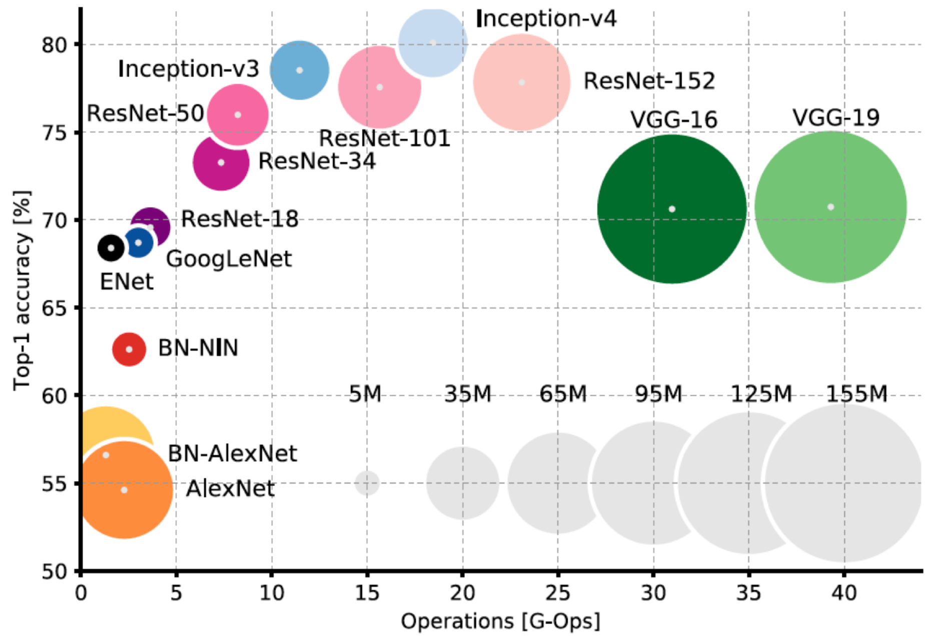
Success factors of artificial intelligence (deep learning)

- Large data sets can be stored and sometimes be made available (web, such as ImageNet)
- Labels and annotations can be obtained with limited costs for non-medical data
  - Allows to build more complex models
- Computing resources have increased, particularly GPUs had an influence on DL
- Open source frameworks have been shared and build upon (Caffe, Tensorflow, libsvm)
  - This should not be underestimated!
    - Things do not need to be built from scratch
    - Creates an extreme dynamic

Machine learning complexity

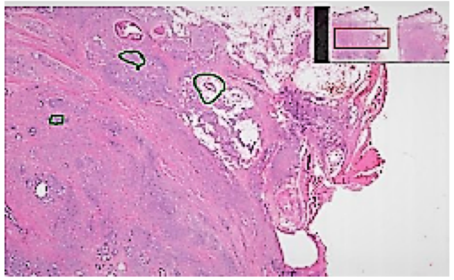
- Most often the big models win
  - More complex models can be built if data are available





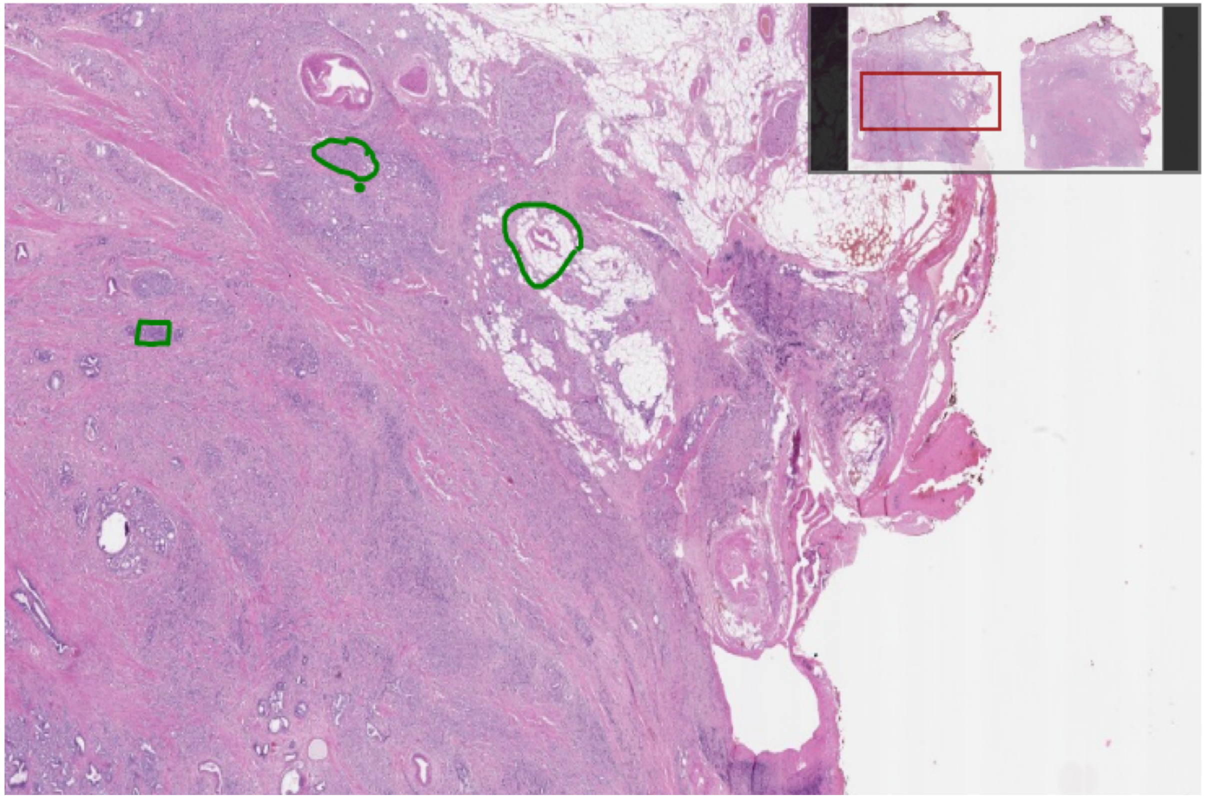
Canziani et al., 2017

- Towards exascale computing
- 3 computing centers (Leibnitz, Cyfronet, Amsterdam)
- 5 use cases
  - Science
  - Industry
  - Several domains
    - Medicine
    - Airlines
    - Agriculture
    - Astronomy



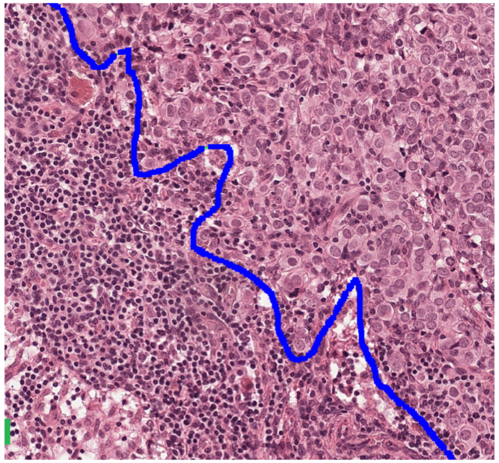
Histopathology imaging

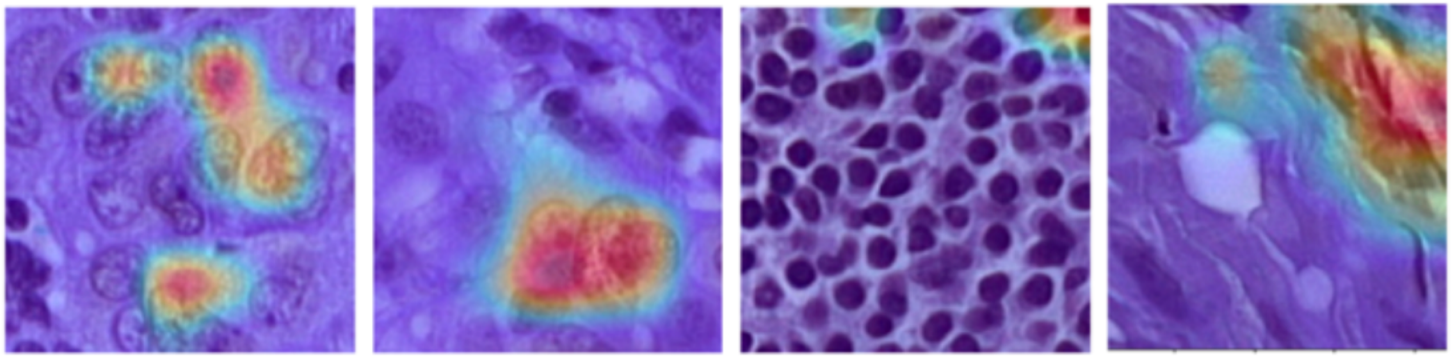
- Very large images (100,000x100,000 pixels, 30 GB)
  - Structures are visible at different scales
- Several images per patient and tumor (12 for needle biopsies for example)
  - Hundreds of patients a day
- Classification on a pixel scale
  - Currently on a patch-scale
- Mostly not digital



Tasks on histopathology images

- Grading and staging (i.e. prostate cancer)
  – Determines the treatment decisions
- Finding metastases
  – Needle in the haystack
- Interactive tools that highlight regions to inspect (harmonize interpretation)
- Allow interpretability of the results

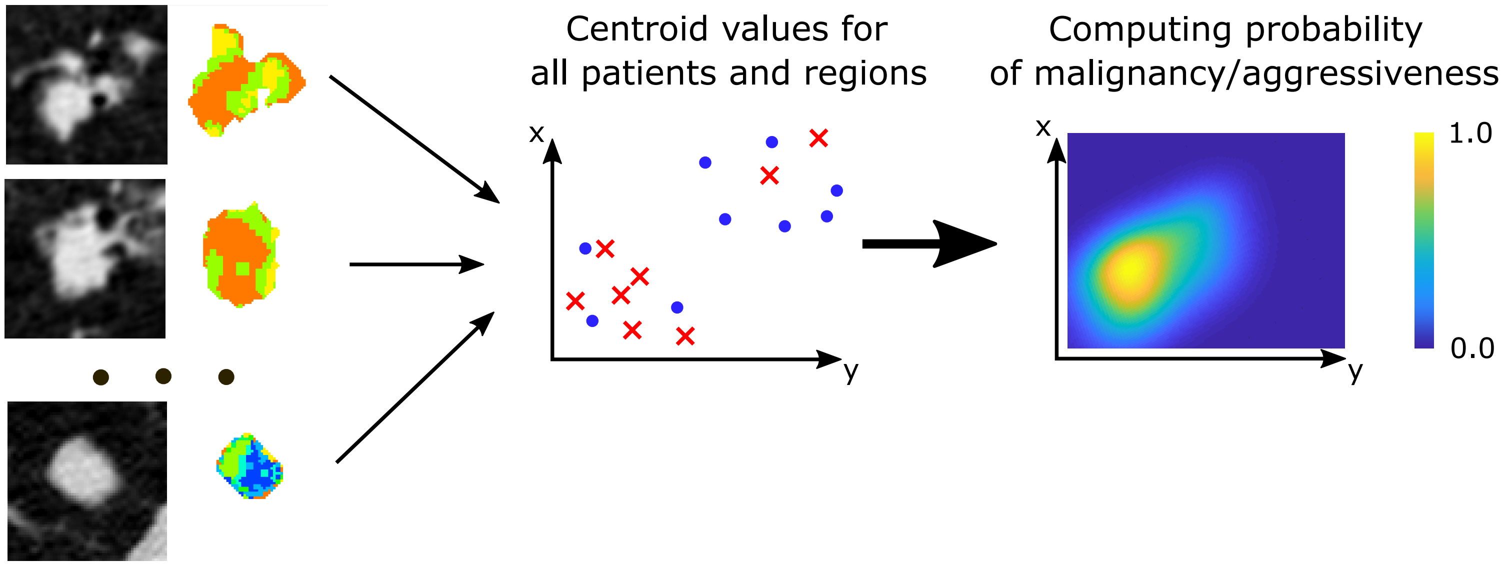




(a) tumor, $p = 0.994$ (b) tumor, $p = 0.999$ (c) non-tumor, $p = 4.7e-4$ (d) non-tumor, $p = 0.841$

Radiomics & tumor heterogeneity

- Using NLST lung screening data set & Moffitt data
  - Publicly available



- For larger tumors the results are very good and complementary to radiomics features
  - For small tumors only a small increase

Texture analysis (2D->3D->4D)

- Describe various tissue types
  - Brain, lung, …
  - Concentration on 3D and 4D data
  - Mainly texture descriptors
- Extract visual features/signatures
  - Learned, so relation to deep learning

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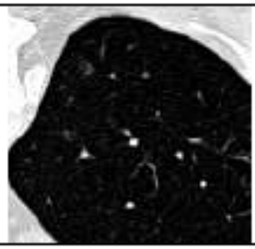
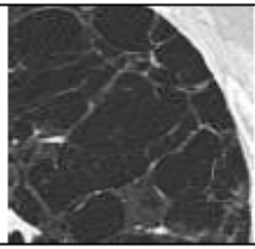
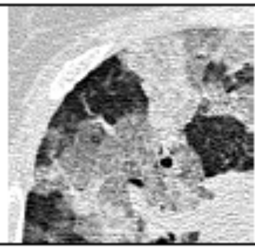
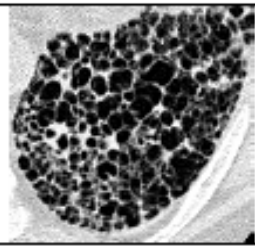
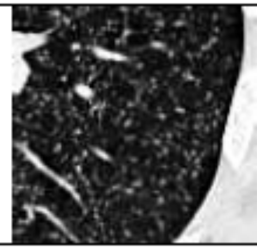
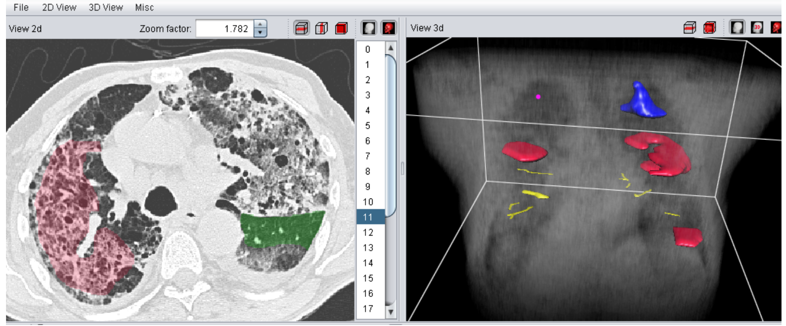
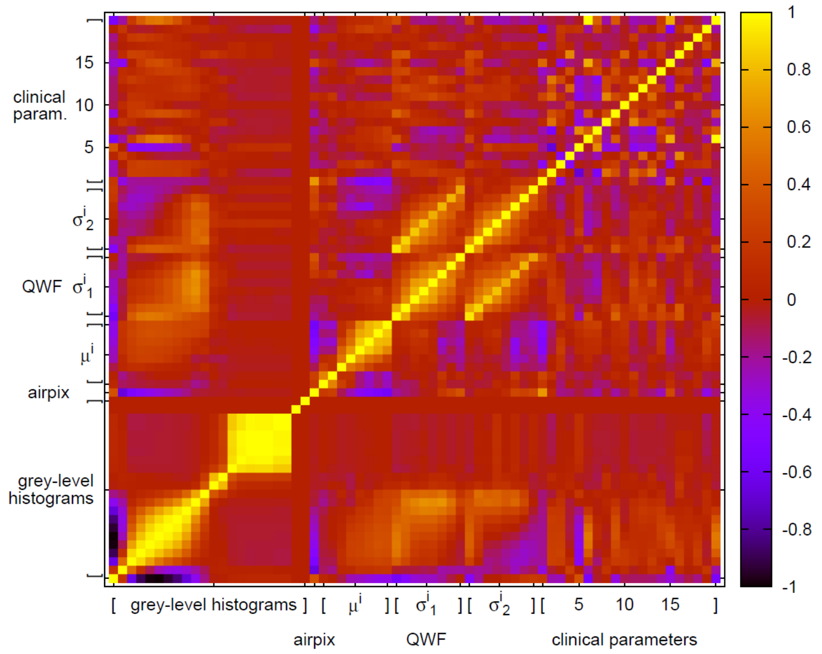
visual aspect					
class	healthy	emphysema	ground glass	fibrosis	micronodules

Adrien Depeursinge, Antonio Foncubierta–Rodriguez, Dimitri Van de Ville, and Henning Müller, Three–dimensional solid texture analysis and retrieval: review and opportunities, Medical Image Analysis, volume 18, number 1, pages 176-196, 2014.

Database with CT image of interstitial lung diseases



- 128 cases with CT image series and biopsy confirmed diagnosis
- Manually annotated regions for tissue classes (1946)
  - 6 tissue types of 13 with a larger number of examples
- 159 clinical parameters extracted (sparse)
  - Smoking history, age, gender hematocrit, …
- Available after signing a license agreement



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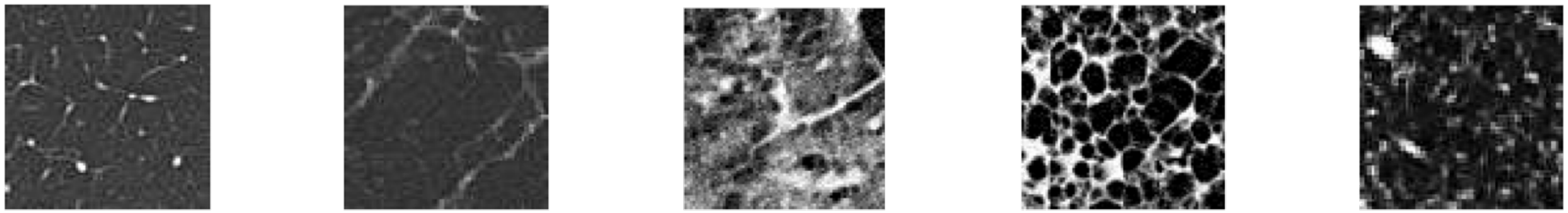
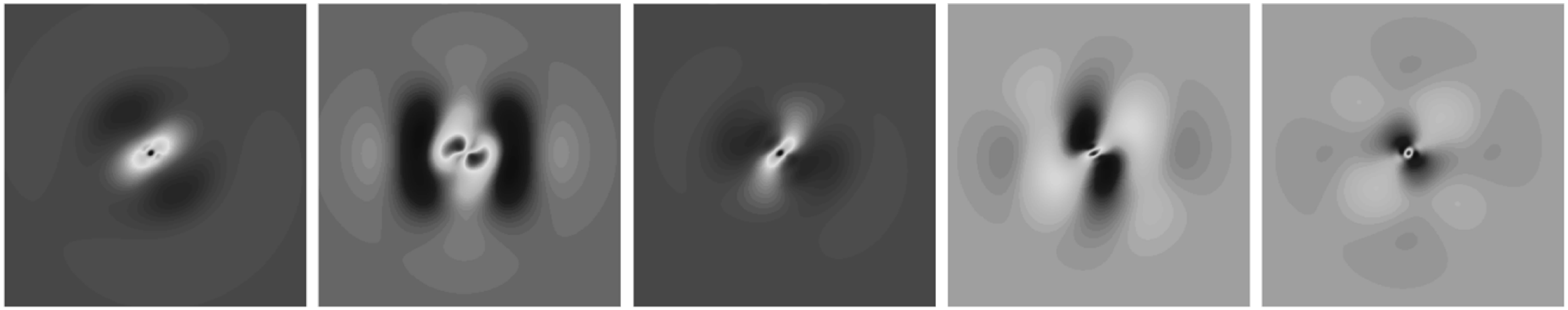
Learned texture signatures

- Learn combinations of Riesz wavelets as digital signatures using SVMs (steerable filters)
  - Create signatures to detect small local lesions and visualize them

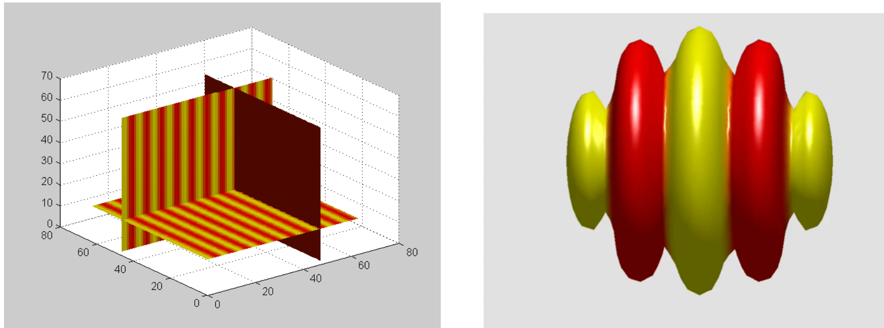




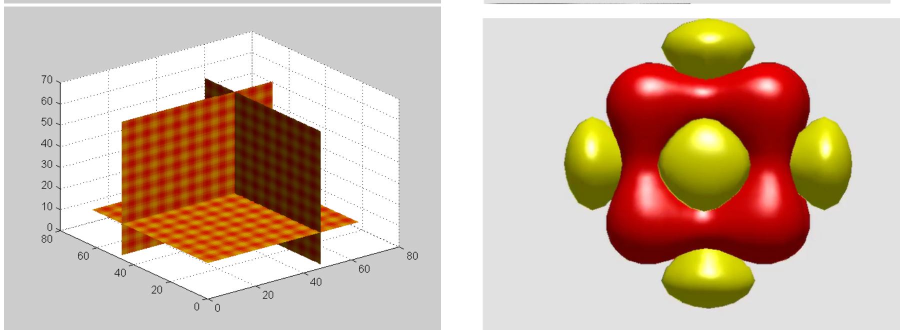
Adrien Depeursinge, Antonio Foncubierta–Rodriguez, Dimitri Van de Ville, and Henning Müller, Rotation–covariant feature learning using steerable Riesz wavelets, IEEE Transactions on Image Processing, volume 23, number 2, page 898-908, 2014.

Learning Riesz in 3D

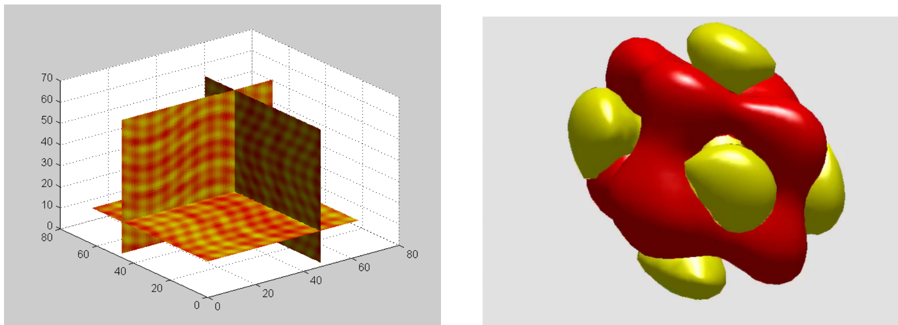
- Most medical tissues are naturally 3D
- But modeling gets much more complex
  - Vertical planes



  - 3-D checkerboard



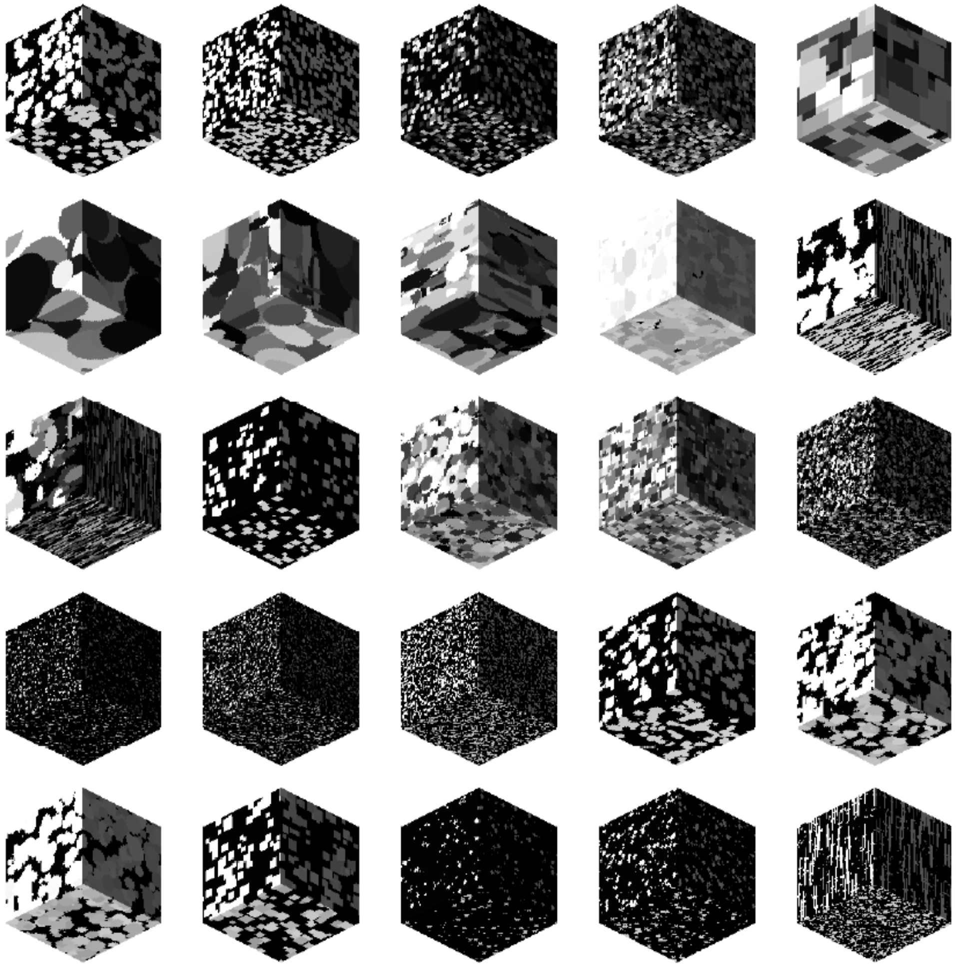
  - 3-D wiggled checkerboard

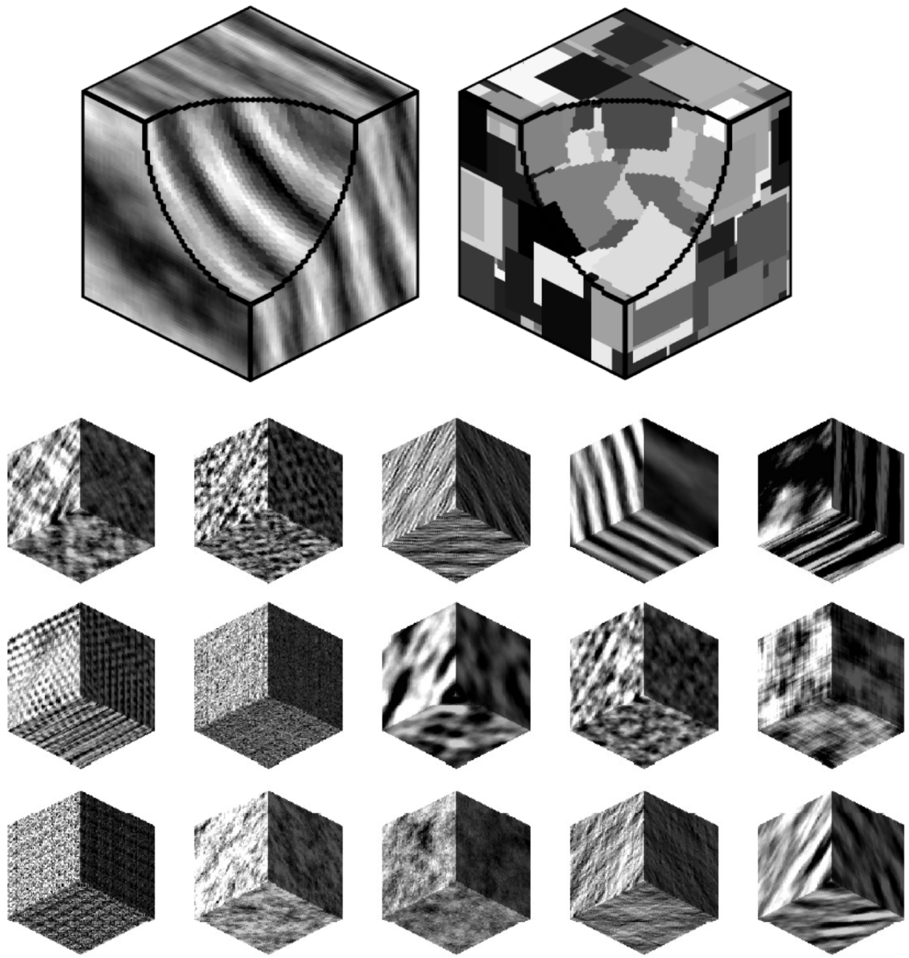


Solid 3D texture

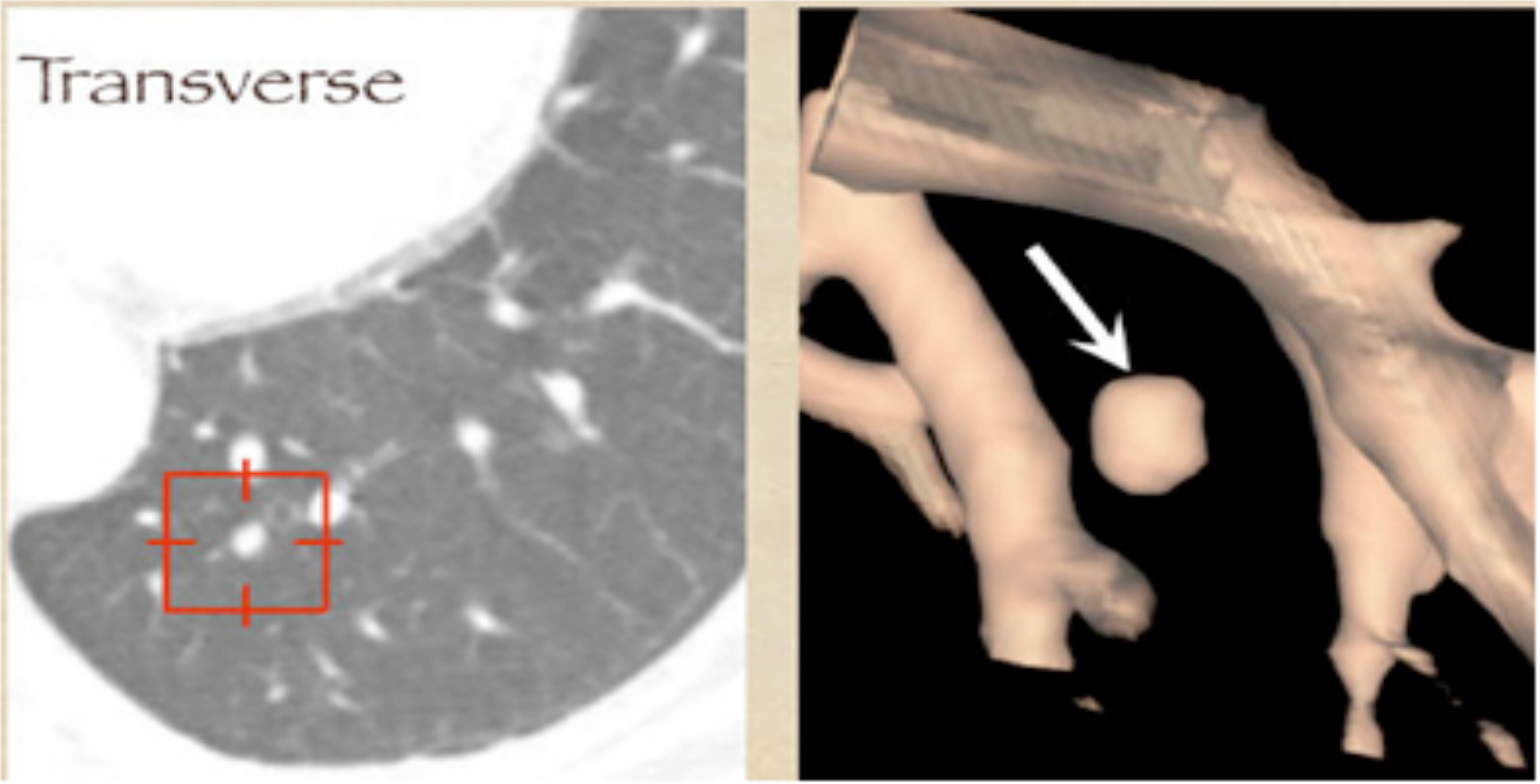
- Hard to visualize
- Most texture measures are translated to 3D

Y. Dicente Cid, H. Müller, A. Platon, PA Poletti, A. Depeursinge, Locall Oriented Wavelet Transforms for 3–D Solid Texture Classification, *IEEE Transactions on Image Processing*, 2017.





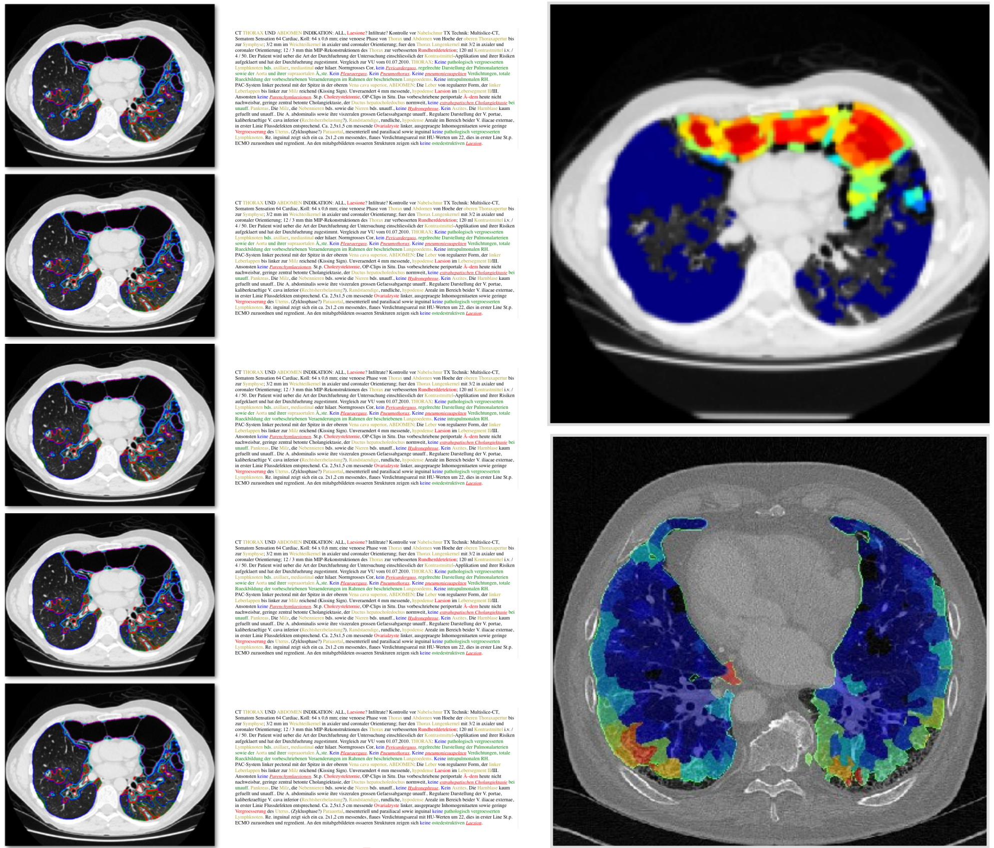
3D can be really important



CT finding (left) has the appearance of an adjacent vessel in transverse-section reconstruction and was not called by any of the four LIDC readers. After viewing transverse, coronal, sagittal, and volume-rendered reconstructions (right), all four university readers called the finding a lung nodule.

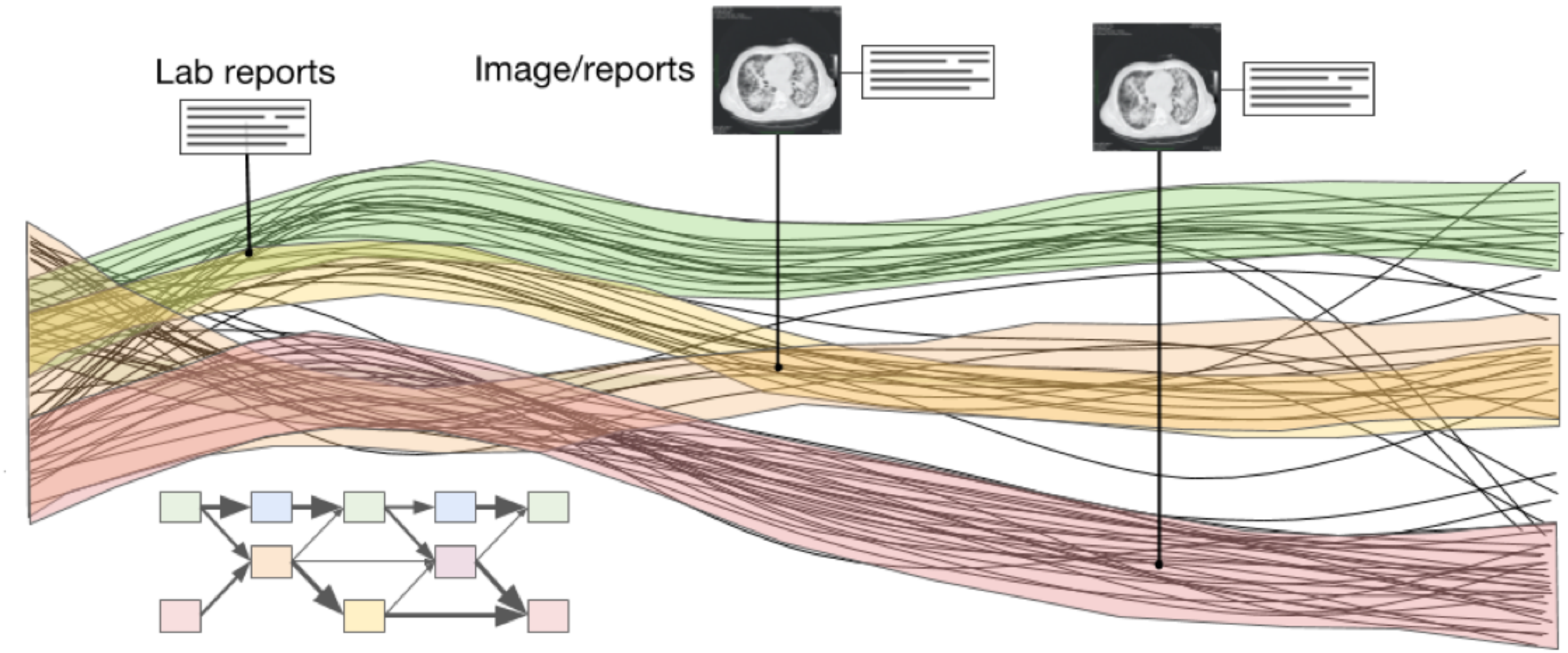
Semi-supervised learning

- Thousand of CT volumes with reports
  - Detect concepts
  - Find negations
- Analyze texture
  - Link with positive and negative concepts
- Localize difference maps without requiring manual region labeling
  - Manual interventions are expensive
- Work of the Medical University of Vienna



Trajectories of patients

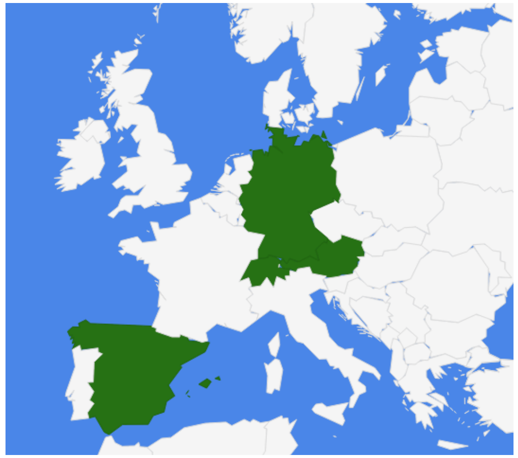
- Changes often matter more than absolute values
  – Which direction is a patient coming from
  – Longitudinal data are needed but hard to obtain
- Makes computation even more complex …
  – Much possible noise in the data



Research infrastructures

The VISCERAL project

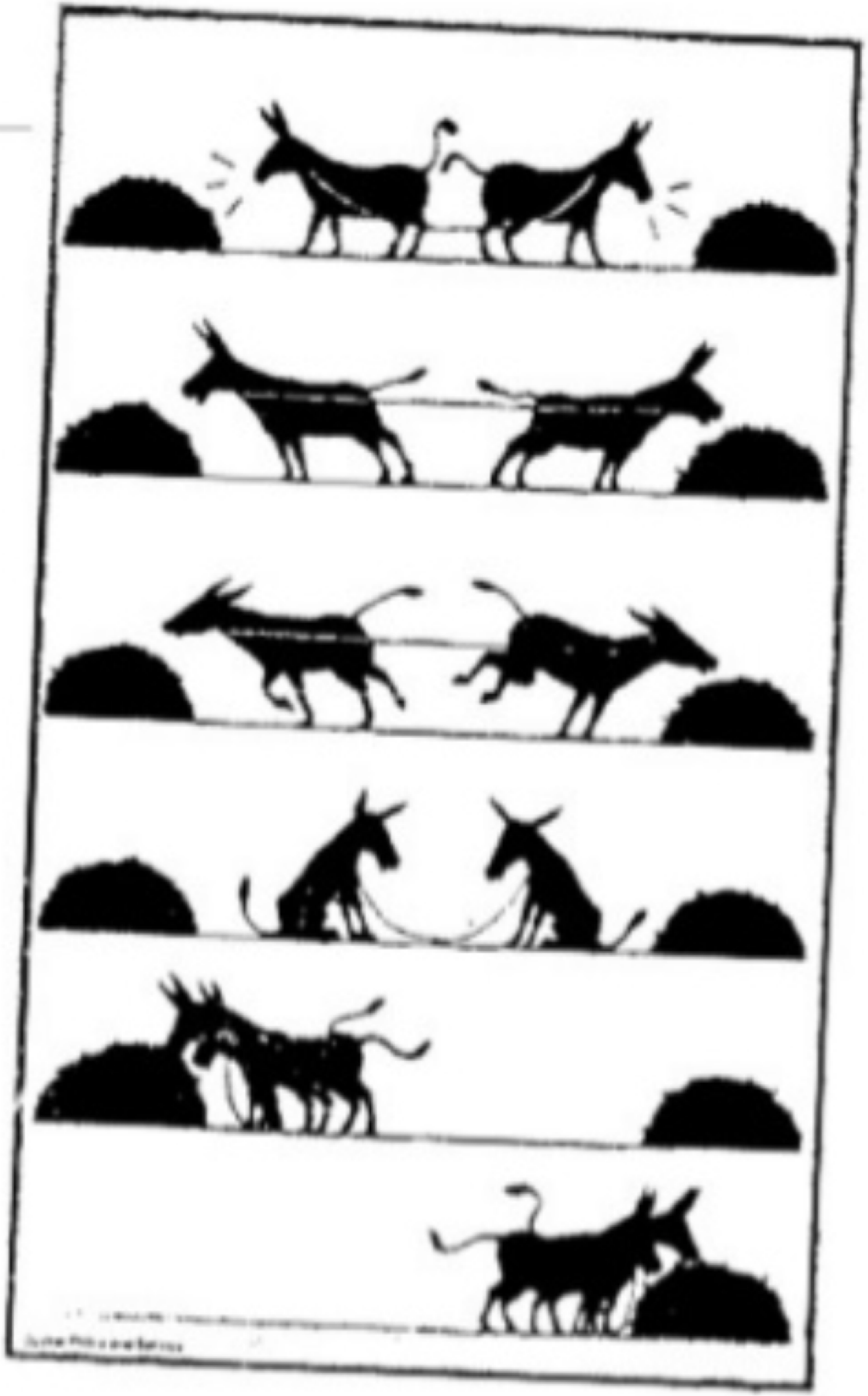
- Visual Concept Extraction challenge in Radiology
- Partners:
  - Technical University of Vienna, Austria
  - Medical University of Vienna, Austria
  - HES-SO, Sierre, Switzerland
  - ETHZ, Zürich, Switzerland
  - University of Heidelberg, Germany
  - Catalonia Health Authority, Barcelona, Spain



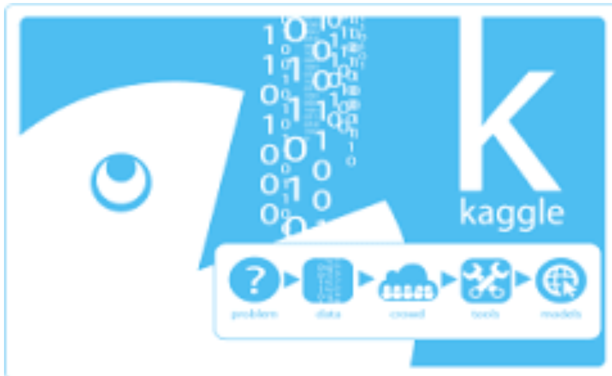
- 1.11.2012-30.4.2015 (30 months)
- Run challenges on medical organ segmentation, similar case retrieval and lesion detection

Scientific environment

- Competition
- Coopetition
- Cooperation



- Data science challenge on multimodal image retrieval
  - Run since 2003, medical task since 2004
  - Part of the Cross Language Evaluation Forum (CLEF)
- Many tasks related to medical image retrieval
  - Image classification
  - Image-based retrieval
  - Case-based retrieval
  - Compound figure separation
  - Caption prediction
  - …

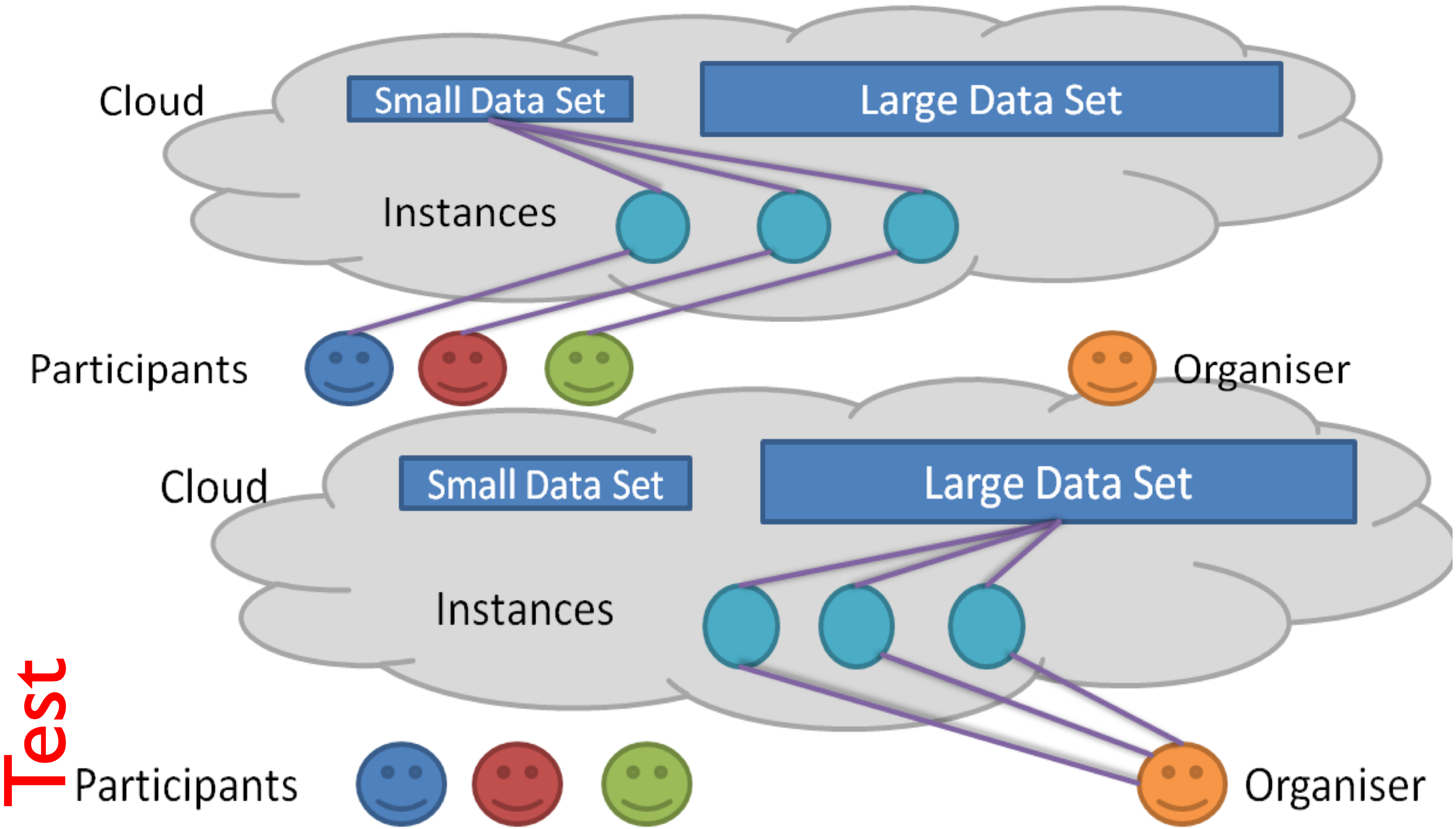


- Many old databases remain available, imageclef.org

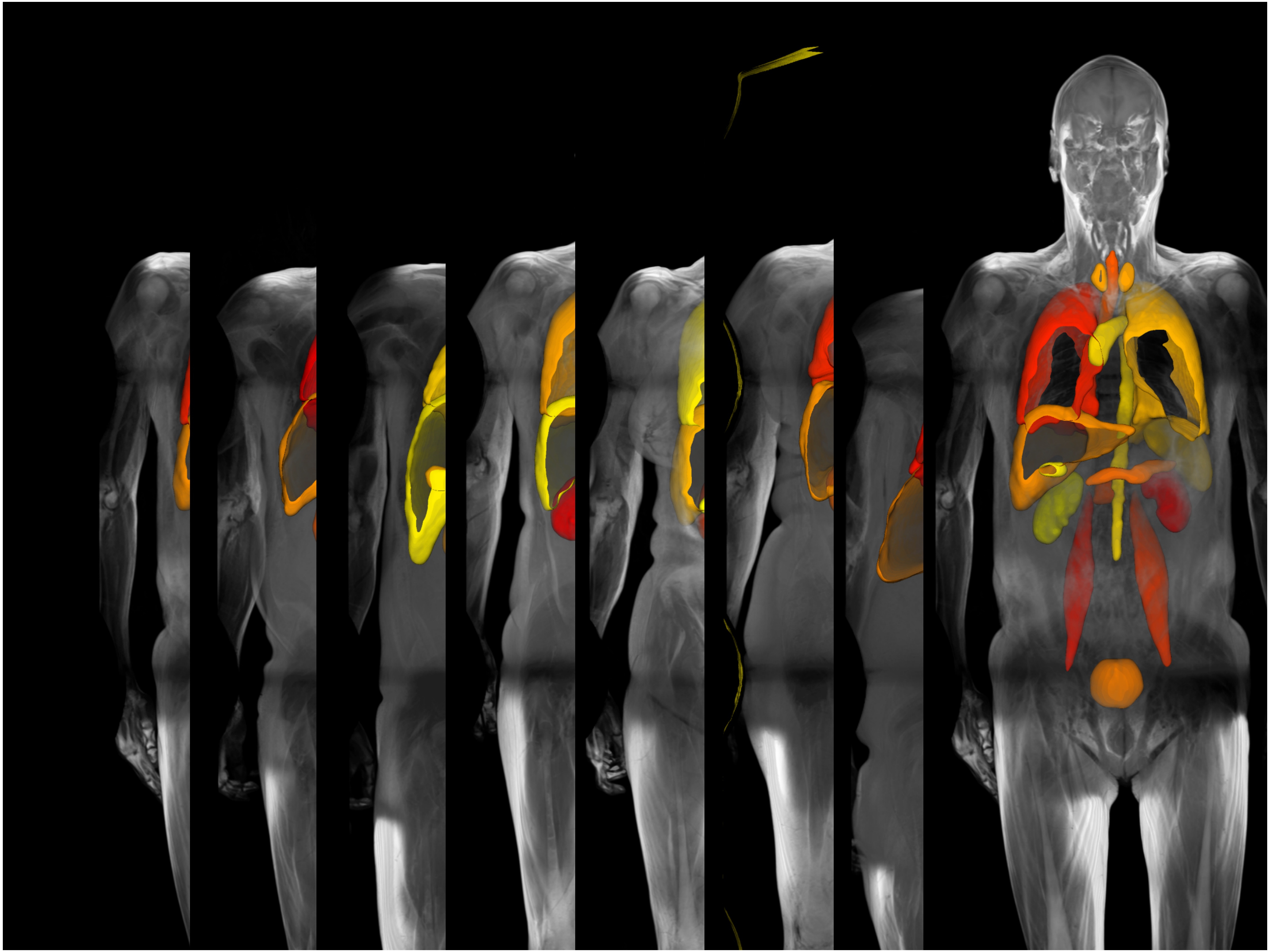
Challenges with challenges

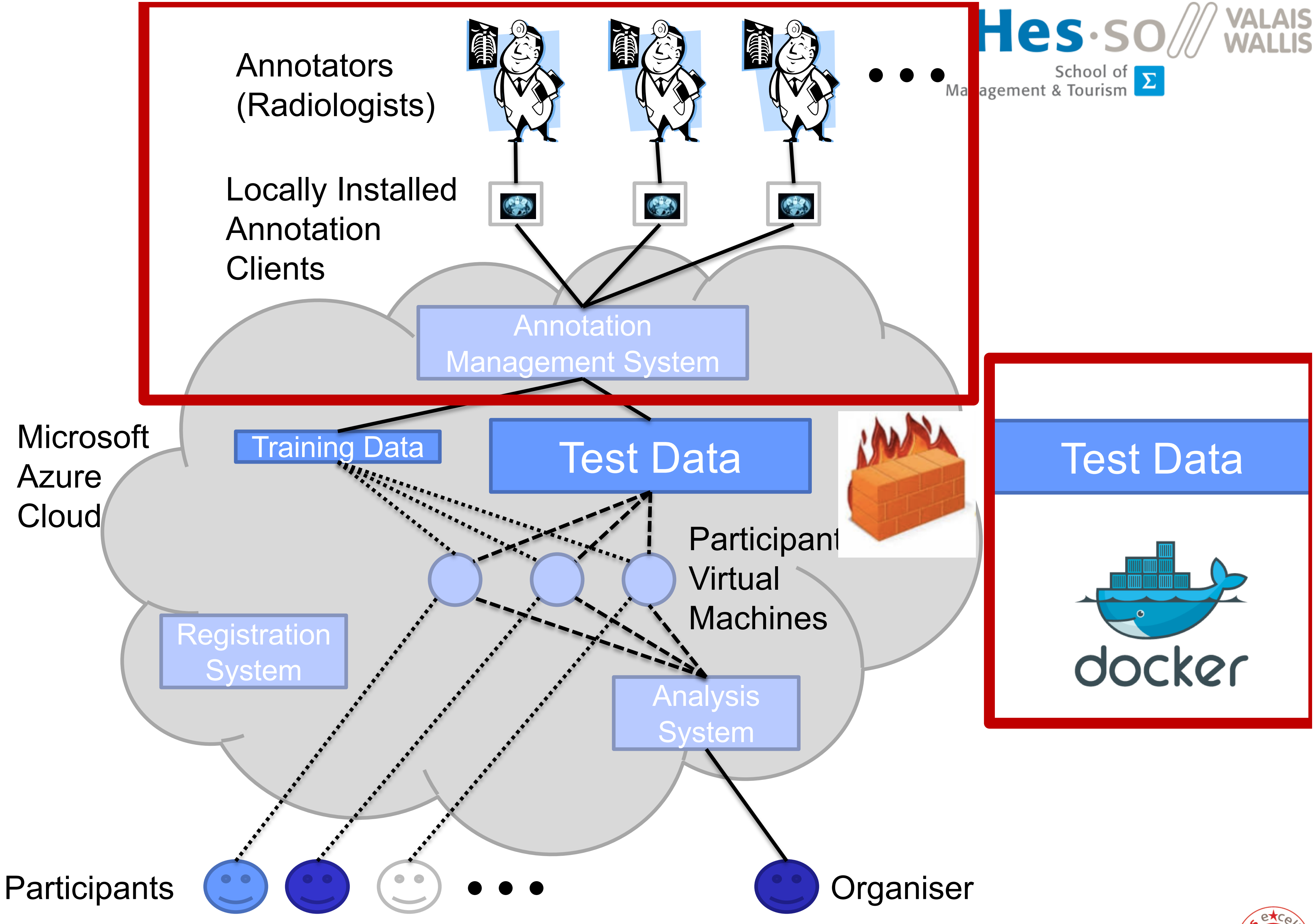
- Difficult to distribute very big datasets
  - Sending around hard disks? risky, expensive
- Sharing confidential data
  - Big data are impossible to anonymize automatically
- Quickly changing data sets
  - Outdated when a test collection is being created

- Optimizations on the test data are possible
  - Manual adaptations, etc.
  - Often hard to fully reproduce results
- Groups without large computing infrastructures are disadvantaged



A. Hanbury, H. Müller, G. Langs, M. A. Weber, B. H. Menze, T. Salas Fernandez, Bringing the algorithms to the data: cloud–based benchmarking for medical image analysis, CLEF conference, Springer Lecture Notes in Computer Science, 2012.



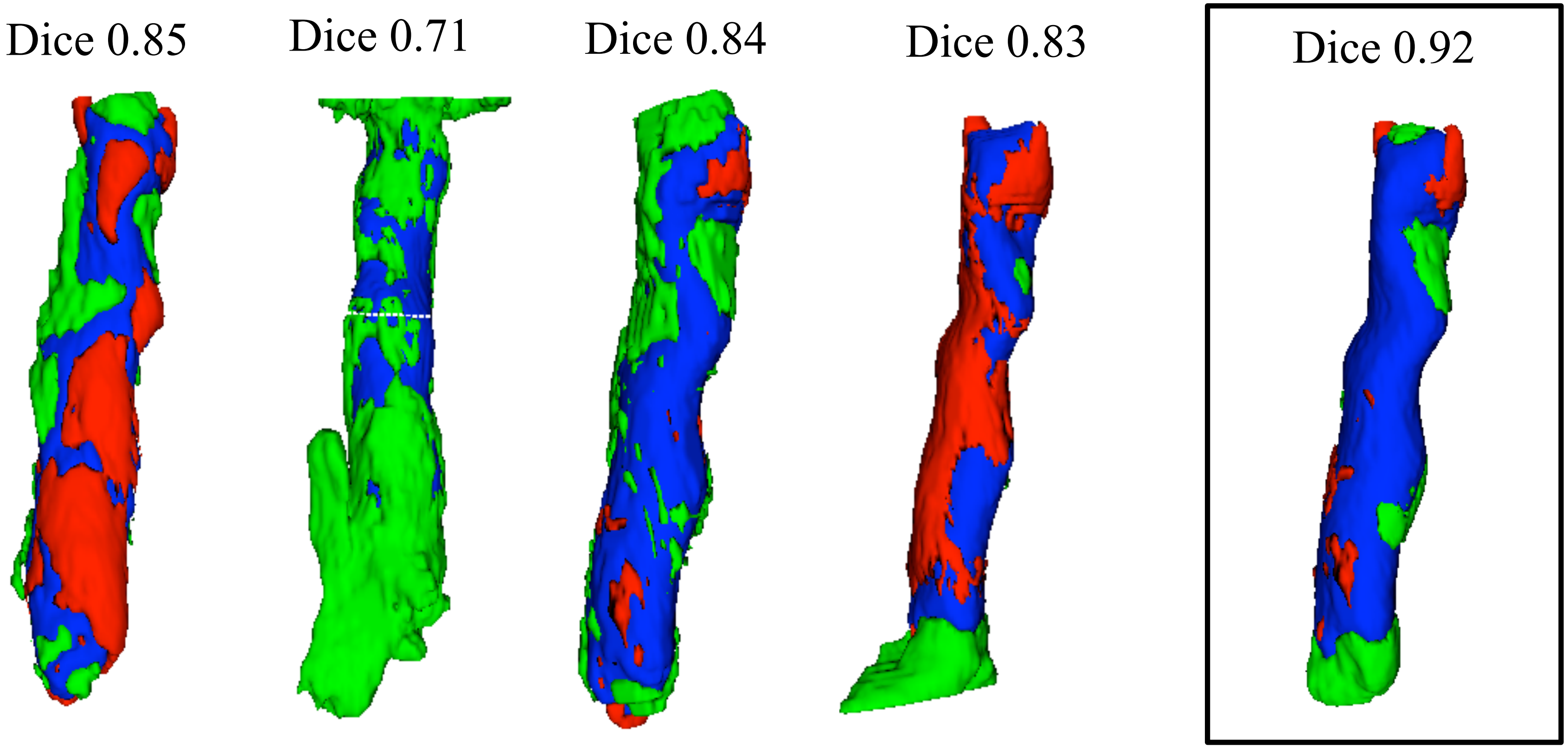

Annotators
(Radiologists)
Locally Installed
Annotation
Clients
Annotation
Management System
Microsoft
Azure
Cloud
Training Data
Test Data
Participant
Virtual
Machines
Registration
System
Analysis
System
Test Data
docker
Participants
Organiser

Silver corpus (example trachea)

- Executable code of all participants
  - Run it on new data, do label fusion

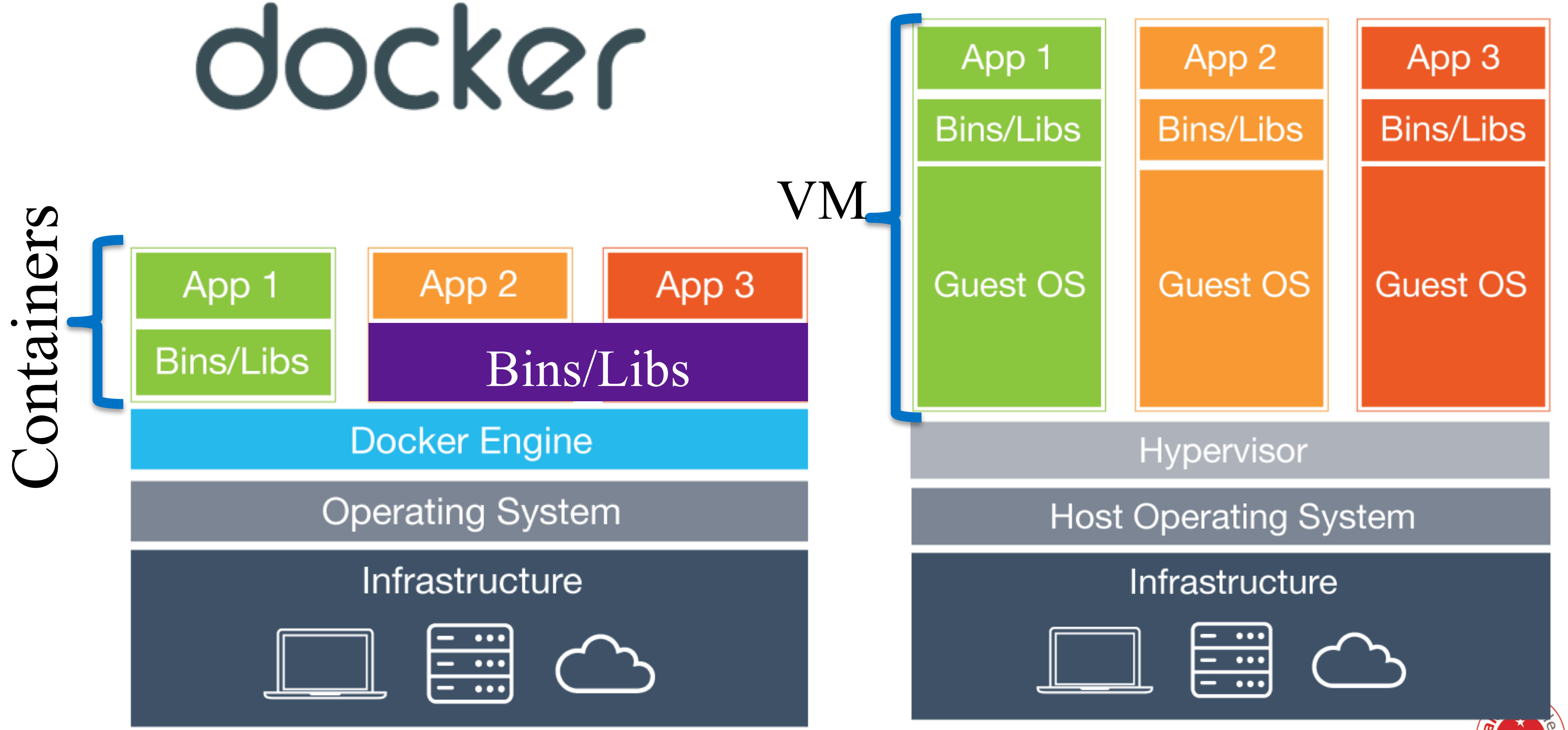
Participant segmentations

Silver Corpus



Docker vs. Virtual Machines

VS.



Evaluation-as-a-Service (EaaS)

- Moving the algorithms to the data, not vice versa
  - Required when data are: very large, changing quickly, confidential (medical, commercial, …)
- Different approaches
  - Source code submission, APIs, VMs local or in the cloud, Docker containers, specific frameworks
- Allows for continuous evaluation, component-based evaluation, total reproducibility, updates, …
  - Workshop March 2015 in Sierre on EaaS
  - Workshop November 2015 in Boston on cloud-based evaluation (http://www.martinos.org/cloudWorkshop/)

Allan Hanbury, Henning Müller, Krisztian Balog, Torben Brodt, Gordon V. Cormack, Ivan Eggel, Tim Gollub, Frank Hopfgartner, Jayashree Kalpathy-Cramer, Noriko Kando, Anastasia Krithara, Jimmy Lin, Simon Mercer, Martin Potthast, Evaluation-as-a-Service: Overview and Outlook, ArXiv, 2015.

EaaS aspects

Sharing images, research data

- Very important aspect of research is to have solid methods, data, large if possible
  - If data not available, results can not be reproduced
  - If data are small, results may be meaningless
- Many multi-center projects spend most money on data acquisition, often delayed no time for analysis
  - IRB takes long, sometimes restrictions are strange
- NIH is great to push data availability
  - But data can be made available in an unusable way

Why Most Published Research Findings Are False

John P. A. Ioannidis

Summary

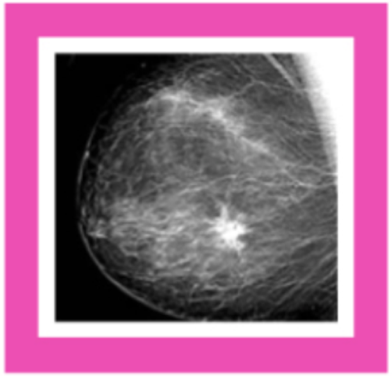
There is increasing concern that most

factors that influence this problem and some corollaries thereof.

Modeling the Framework for False

is characteristic of the field and can vary a lot depending on whether the field targets highly likely relationships

Hes·so // VALAIS WALLIS
School of Management & Tourism



The Digital Mammography DREAM Challenge

Build a model to help reduce the recall rate for breast cancer screening

Learn more & register to participate here: www.synapse.org/Digital_Mammography_DREAM_Challenge

Funded by ljaf

Enabled by DREAM Challenges · Sage · Coding4Cancer · GroupHealth · IBM · BCSC · amazon web services · Icahn School of Medicine at Mount Sinai · Seattle Cancer Care Alliance · RADISH

The Digital Mammography DREAM Challenge

Out of every 1000 women screened, only 5 will have breast cancer. But 100 will be recalled for further testing.

We can do better.

Build a model to help reduce the recall rate for breast cancer screening.

Calling all coders to join the Challenge.

Up to a **$1,000,000** in cash prizes for winning models.

May the best model win.

Future of medical research

- Much more centered around data!!
  - *Nature Scientific Data* underlines the importance!
- Data need to be available and in a meaningful way
  - Infrastructure needs to be available and ways to evaluate on the data with specific, precise tasks
    - Work on data preparation in line with IRB
  - Analysis inside medical institutions (MGH started)
- Code is becoming increasingly portable
  - Docker helps enormously and develops quickly
- Total reproducibility, long term, sharing tools
    - Much higher efficiency in research
- Adapt HPC to common frameworks (open source)

Conclusions

- Medical data science requires new infrastructures
  - Use routine data, not only manually curated data, work on large scale, accommodate for errors
    - Active learning and interactive data curation
  - Use large data sets from data warehouses
  - Keep data where they are produced
    - More “local” computation, so where data are
  - Sharing infrastructures, data and more
    - **Make code and data available! Impact!**
- Image-based decision support relies on data
  - With outcomes, including clinical data, longitudinal
  - Create personalized patient trajectories

Contact

- More information can be found at
  - http://visceral.eu/
  - http://medgift.hevs.ch/
  - http://publications.hevs.ch/
- Contact:
  - Henning.mueller@hevs.ch