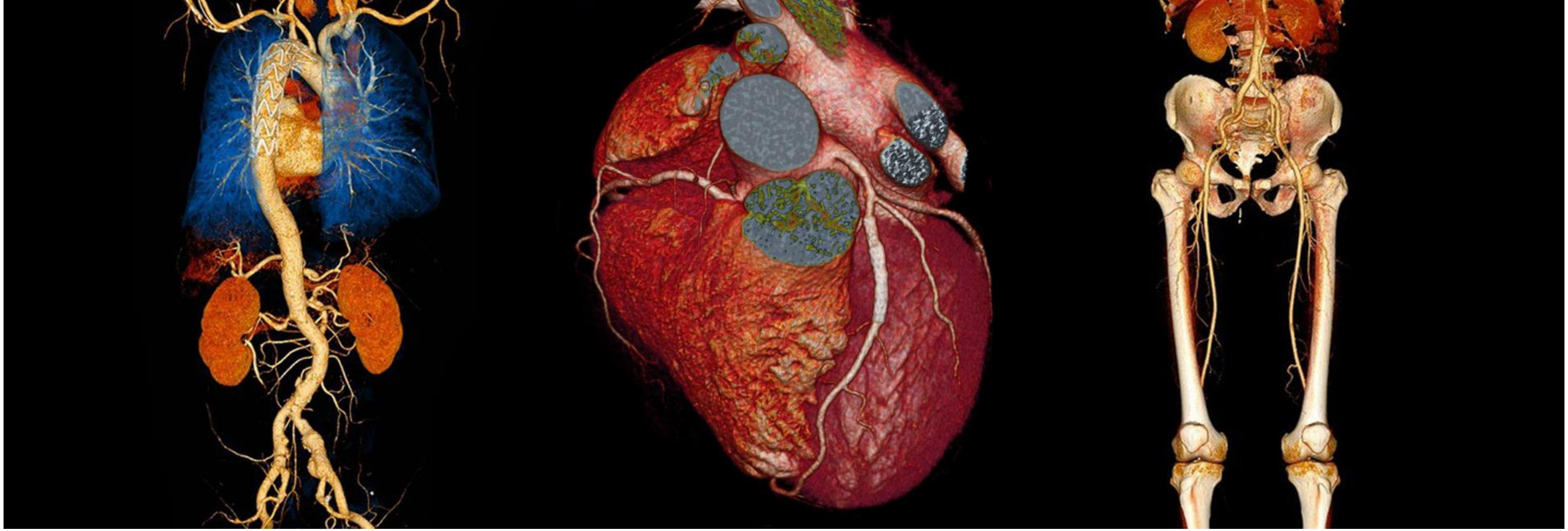

Visual Analytics in Bio-Medical Applications

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What is Visual Analytics (VA)?

- “Visual Analytics is the science of analytical reasoning supported by a highly interactive visual interface.” [Wong and Thomas 2004]

- “Visual Analytics combines automated analysis techniques with interactive visualisations for an effective understanding, reasoning and decision making on the basis of very large and complex datasets” [Keim 2010]

Visual Analytics Process

- First step: preprocess and transform data
  - Data cleaning, normalization, grouping, data fusion
- Automated methods

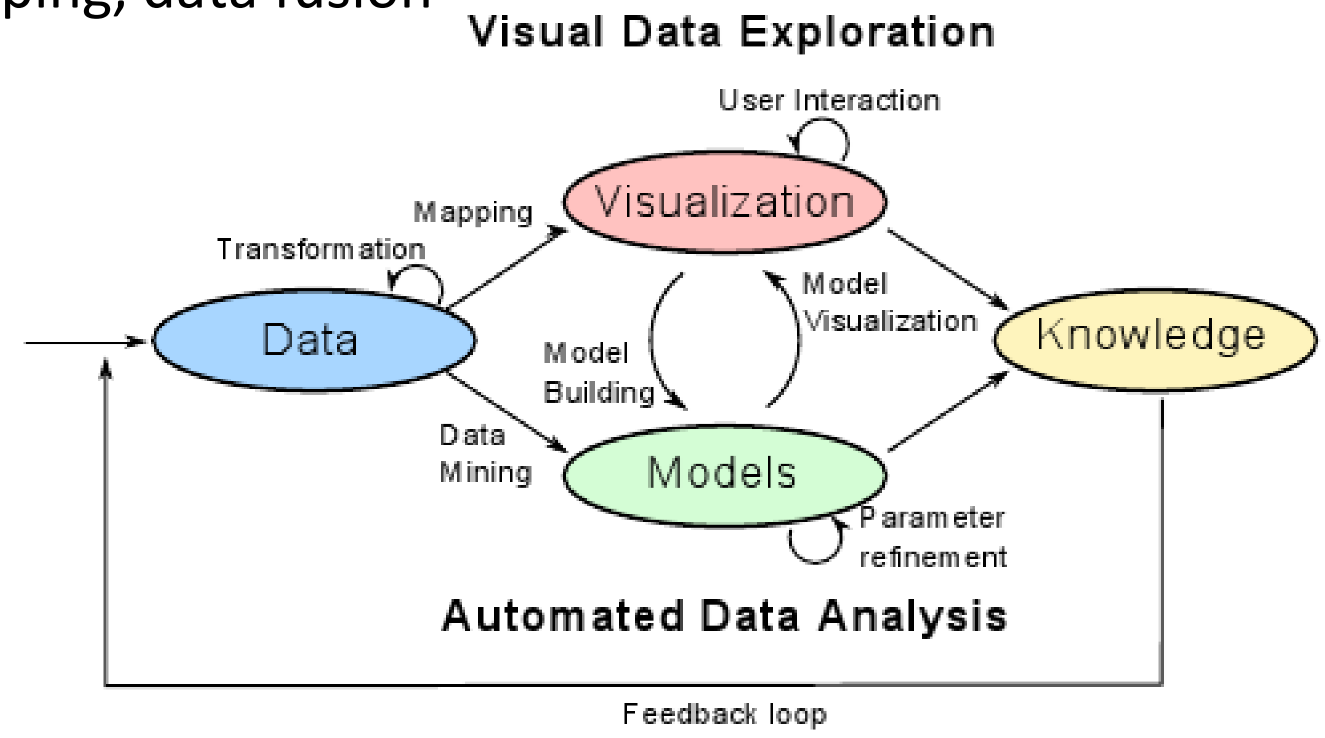
  + Scale well

  - Get stuck in local optima

  - Run in a black box fashion
- Visualization

  + Interactive data analysis

  - Scalability
- Visual Analytics integrates both
  - Tied together by the user
  - Alternating between visual and automatic methods



[Keim 2006]

Goals of Visual Analytics (VA)

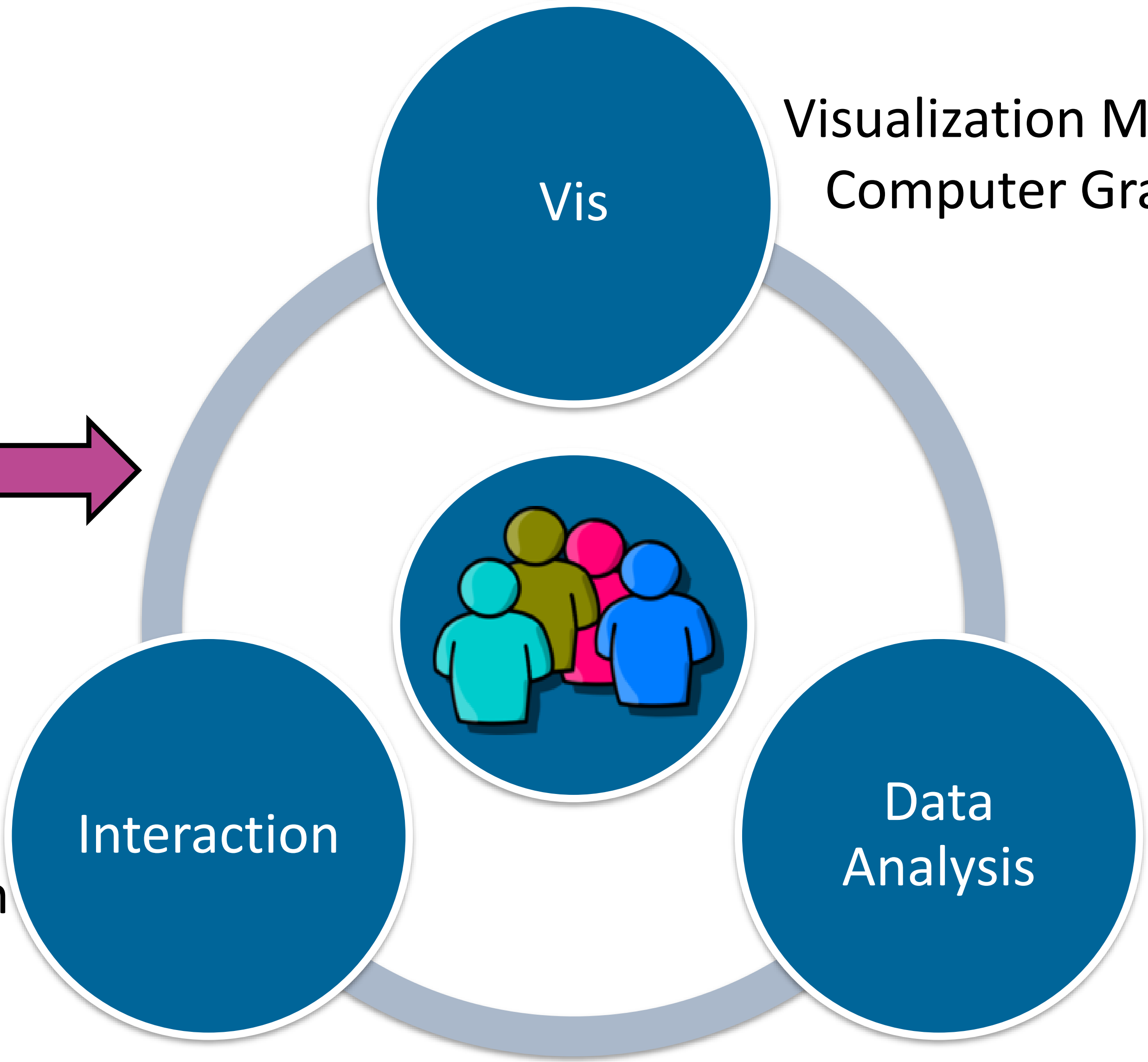
Creation of tools and techniques to enable users to:

- Synthesize information and derive insight from massive, dynamic, ambiguous, and often conflicting data
- Detect the expected and discover the unexpected
- Provide timely, defensible, and understandable assessments
- Communicate these assessment effectively for action

Visual Analytics

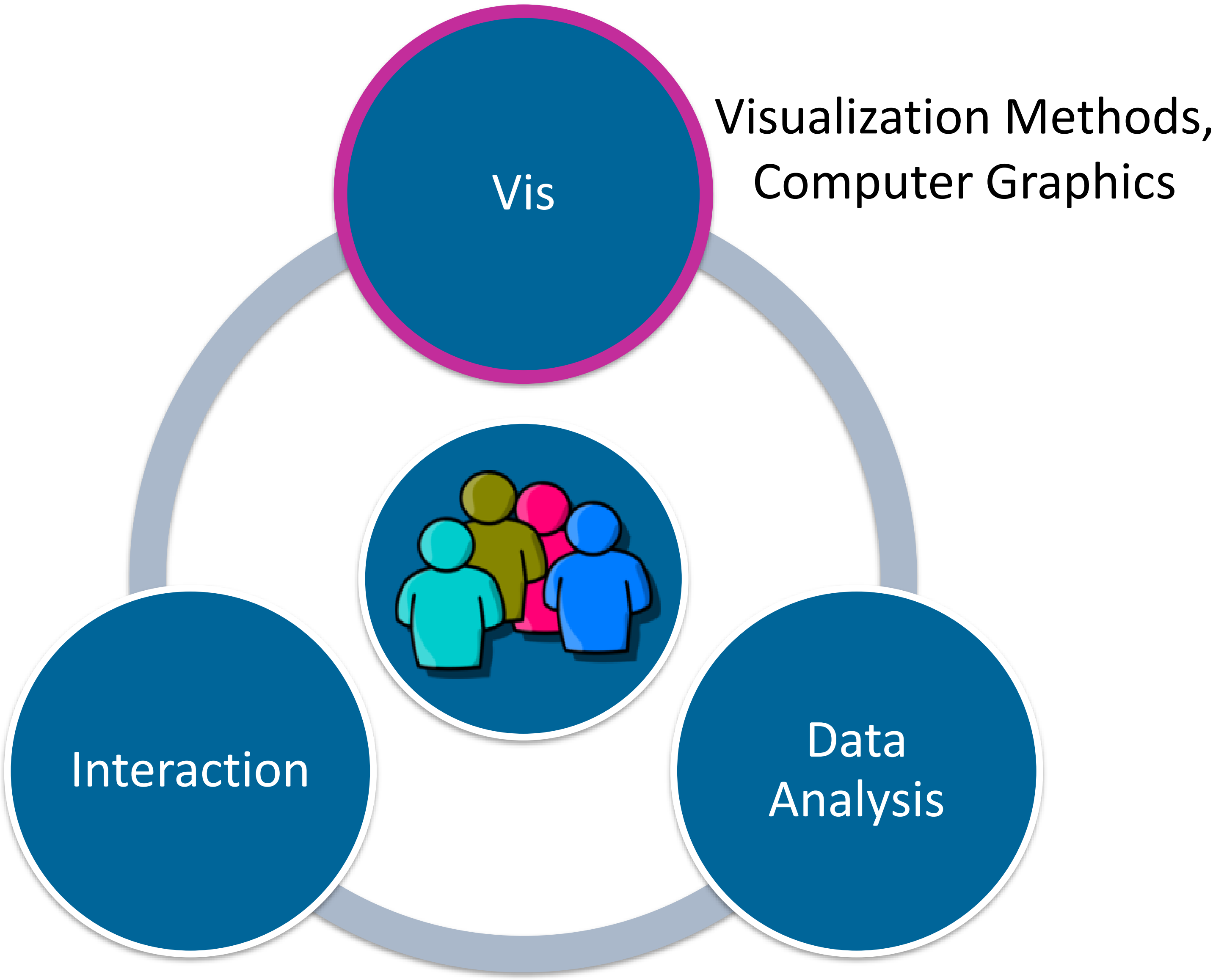
Visualization Methods,
Computer Graphics

Data Exploration
Knowledge Discovery
Hypothesis Confirmation
or Generation



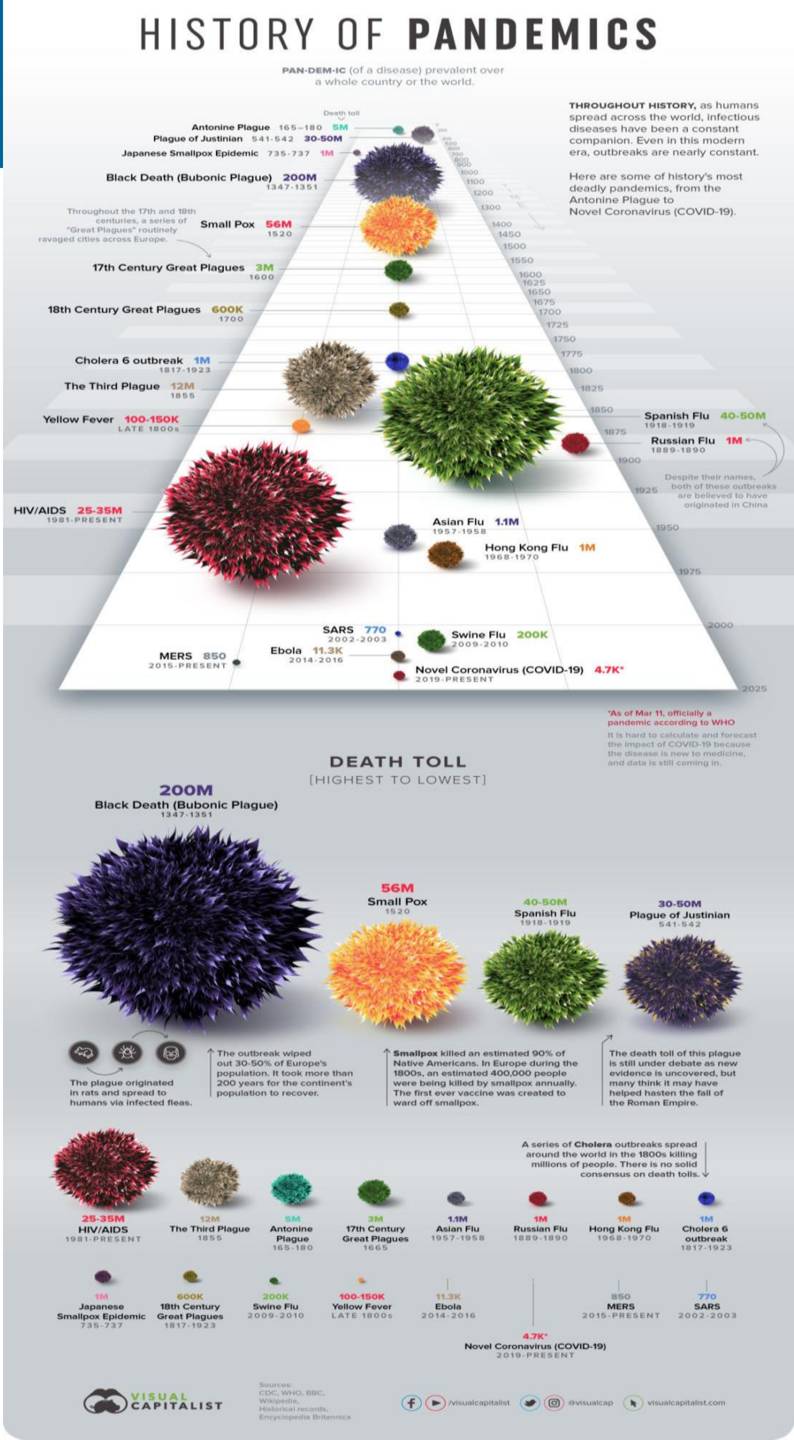
HC Interaction,
Cognition & Perception

Data Mining,
Machine Learning,
Statistics,…


Vis
Visualization Methods,
Computer Graphics
Interaction
Data
Analysis

Why Graphics?

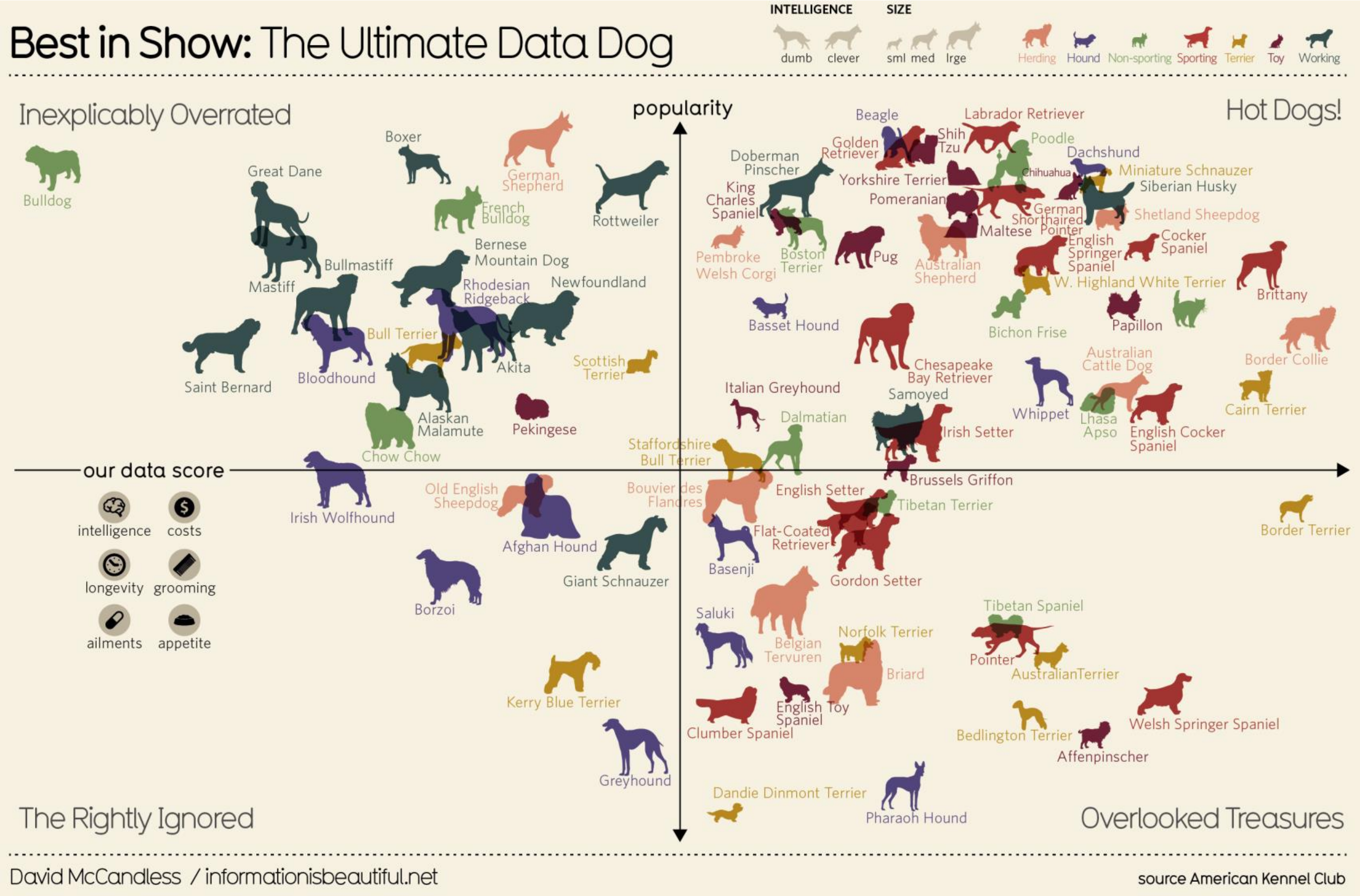
- Figures are richer; provide more information with less clutter and in less space.
- Figures provide the ‘Gestalt‘ effect: they give an overview; make structure more visible.
- Figures are more accessible, easier to understand, faster to grasp, more comprehensible, more memorable, more fun, and less formal.



Why Graphics?

"The art of making the unseen visible" [*Clifford Pickover*]

	A	C	E	AA	AB	AC
1	**Best in show?**	largest value				
2	we rated 87 dog breeds	smallest value				
3	**Sources - see bottom right**	**category**	**datadog score**	**ULTIMATE TOP DATA DOG MEGA RANKING - without kids**	**ULTIMATE TOP DATA DOG MEGA RANKING - with kids**	**ULTIMATE TOP DOG MEGA SCORE**
4	**Dog breed**	American Kennel Club group				intelligence + longevity + ailments + 50% (purchase price + food costs + grooming score). highest possible score: 4.5
5	Border Collie	herding	3.64	1	29	3.64
6	Border Terrier	terrier	3.61	2	1	3.61
7	Brittany	sporting	3.54	3	11	3.54
8	Cairn Terrier	terrier	3.53	4	2	3.53
9	Welsh Springer Spaniel	sporting	3.34	5	4	3.34
10	English Cocker Spaniel	sporting	3.33	6	5	3.33
11	Cocker Spaniel	sporting	3.3	7	6	3.30
12	Papillon	toy	3.26	8	22	3.26
13	Australian Cattle Dog	herding	3.25	9	52	3.25
14	Shetland Sheepdog	herding	3.22	11	8	3.22
15	Siberian Husky	working	3.22	10	3	3.22
16	Lhasa Apso	non-sporting	3.21	12	7	3.21
17	Affenpinscher	toy	3.2	13	26	3.20
18	Dachshund	hound	3.19	14	54	3.19
19	Miniature Schnauzer	terrier	3.19	14	27	3.19
20	Chihuahua	toy	3.15	16	55	3.15
21	Australian Terrier	terrier	3.11	17	30	3.11
22	Whippet	hound	3.11	17	30	3.11
23	English Springer Spaniel	sporting	3.09	19	9	3.09
24	West Highland White Terrier	terrier	3.08	20	10	3.08
25	Bedlington Terrier	terrier	3.07	21	35	3.07
26	Poodle	non-sporting	3.04	22	39	3.04
27	Bichon Frise	non-sporting	3.03	25	16	3.03
28	German Shorthaired Pointer	sporting	3.03	23	12	3.03
29	Pointer	sporting	3.03	24	13	3.03
30	Tibetan Spaniel	non-sporting	3.02	26	14	3.02
31	Labrador Retriever	sporting	2.97	27	15	2.97
32	Maltese	toy	2.93	29	65	2.93



Statistics vs. Visualization: Anscombe’s Quartet

Anscombe's quartet

I		II		III		IV	
x	y	x	y	x	y	x	y
10.0	8.04	10.0	9.14	10.0	7.46	8.0	6.58
8.0	6.95	8.0	8.14	8.0	6.77	8.0	5.76
13.0	7.58	13.0	8.74	13.0	12.74	8.0	7.71
9.0	8.81	9.0	8.77	9.0	7.11	8.0	8.84
11.0	8.33	11.0	9.26	11.0	7.81	8.0	8.47
14.0	9.96	14.0	8.10	14.0	8.84	8.0	7.04
6.0	7.24	6.0	6.13	6.0	6.08	8.0	5.25
4.0	4.26	4.0	3.10	4.0	5.39	19.0	12.50
12.0	10.84	12.0	9.13	12.0	8.15	8.0	5.56
7.0	4.82	7.0	7.26	7.0	6.42	8.0	7.91
5.0	5.68	5.0	4.74	5.0	5.73	8.0	6.89

Statistics vs. Visualization: Anscombe's Quartet

Statistics profile is the same for all!

Property	Value
Mean of x in each case	9 (exact)
Variance of x in each case	11 (exact)
Mean of y in each case	7.50 (to 2 decimal places)
Variance of y in each case	4.122 or 4.127 (to 3 decimal places)
Correlation between x and y in each case	0.816 (to 3 decimal places)
Linear regression line in each case	$y = 3.00 + 0.500x$ (to 2 and 3 decimal places, respectively)

Anscombe's Quartet

Four datasets that have identical simple statistical properties, yet appear very different when graphed.

Property	Value
Mean of x in each case	9 (exact)
Variance of x in each case	11 (exact)
Mean of y in each case	7.50 (to 2 decimal places)
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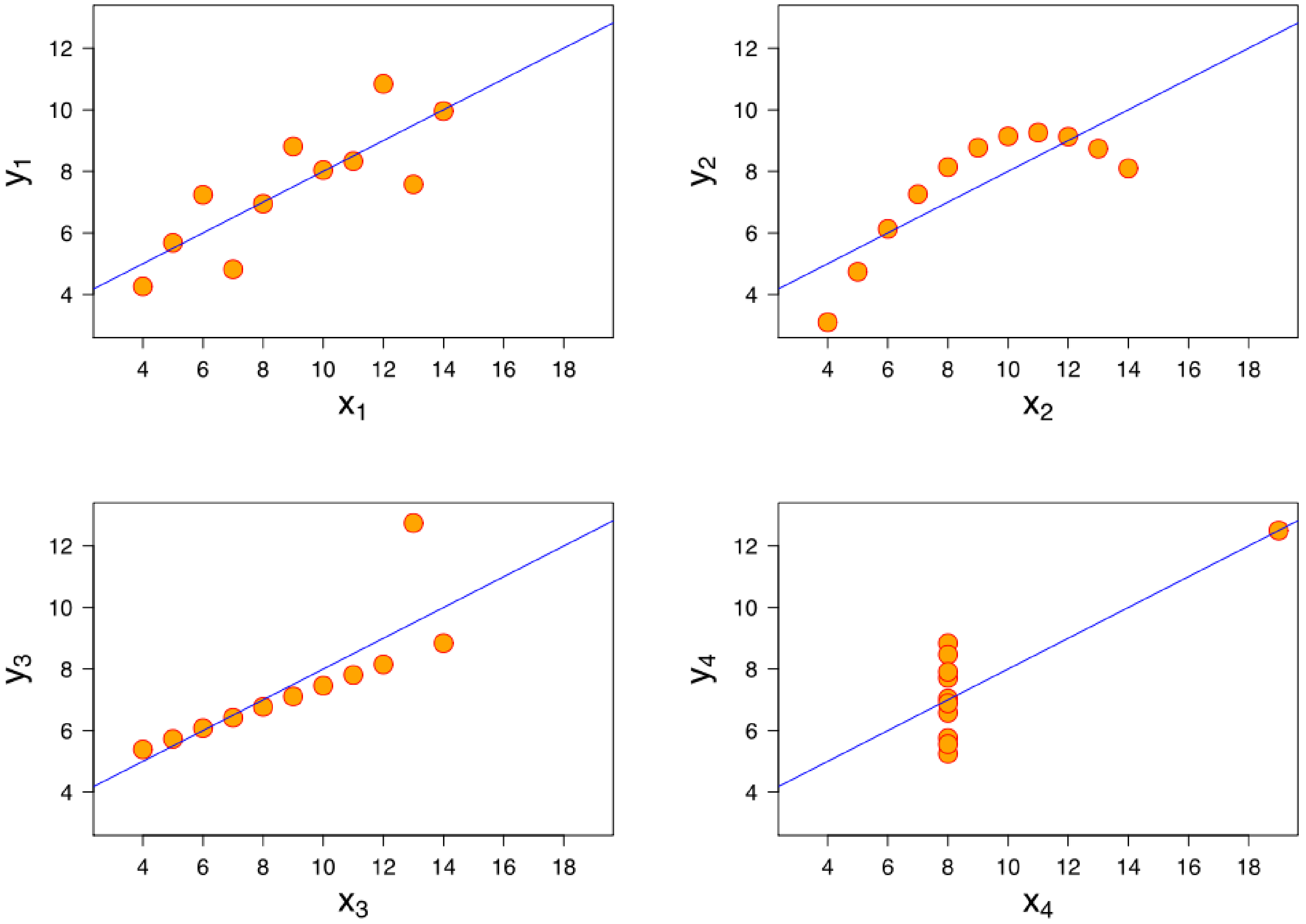
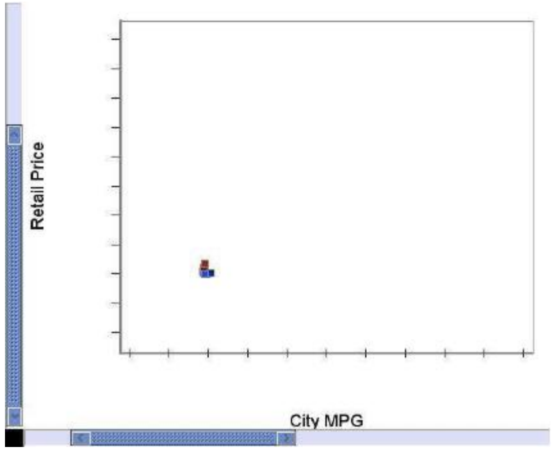


Wikimedia Commons

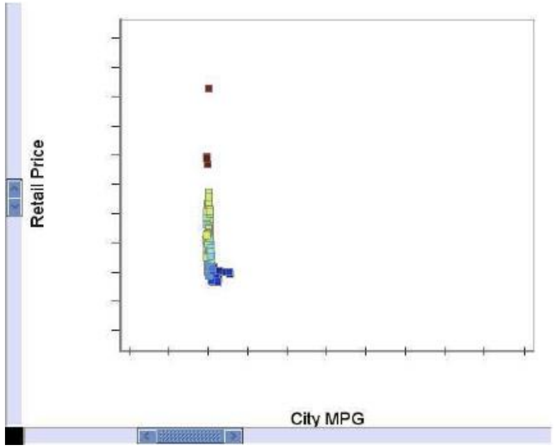
Visualization Can Be Biased

[Ward, Grinstein, Keim 2011]

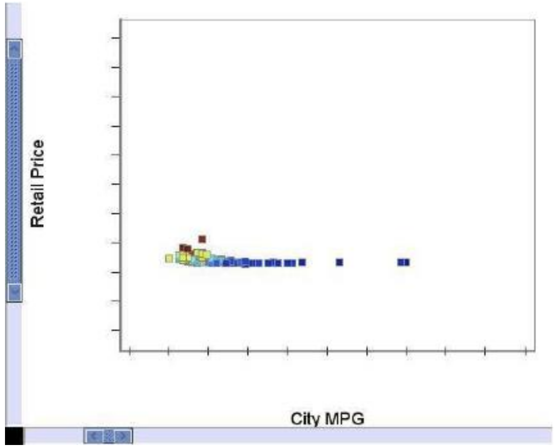
The same data plotted with different scales is perceived dramatically differently.



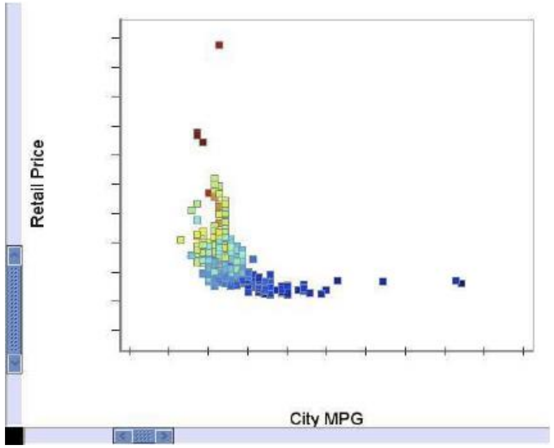
(a) Equally (uniformly) large scale in both *x* and *y*



(b) Large scale in *x*



(c) Large scale in *y*



(d) Scale determined by range of *x*- and *y*-values.

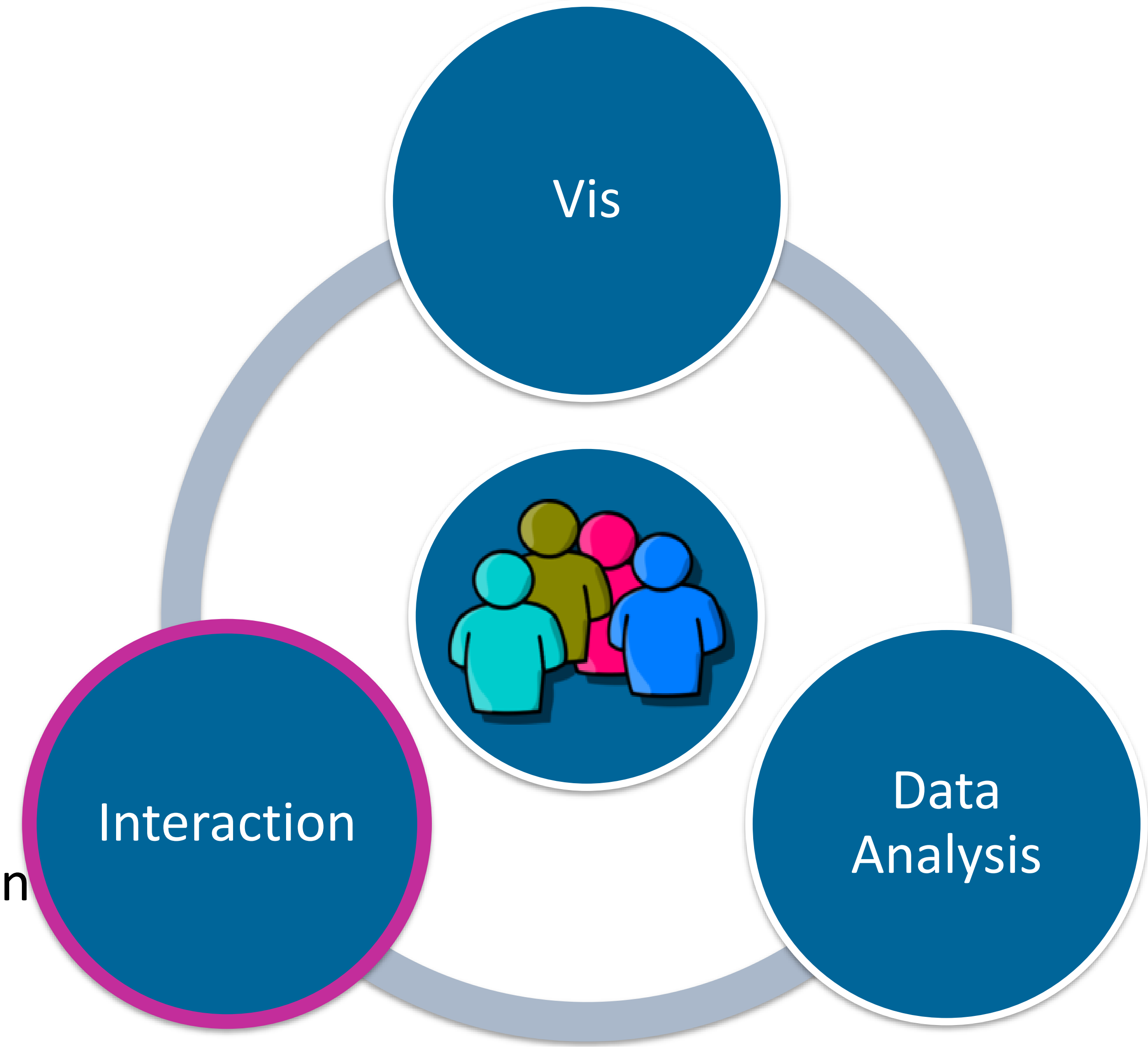
Mantras

Overview first, zoom/filter, details on demand

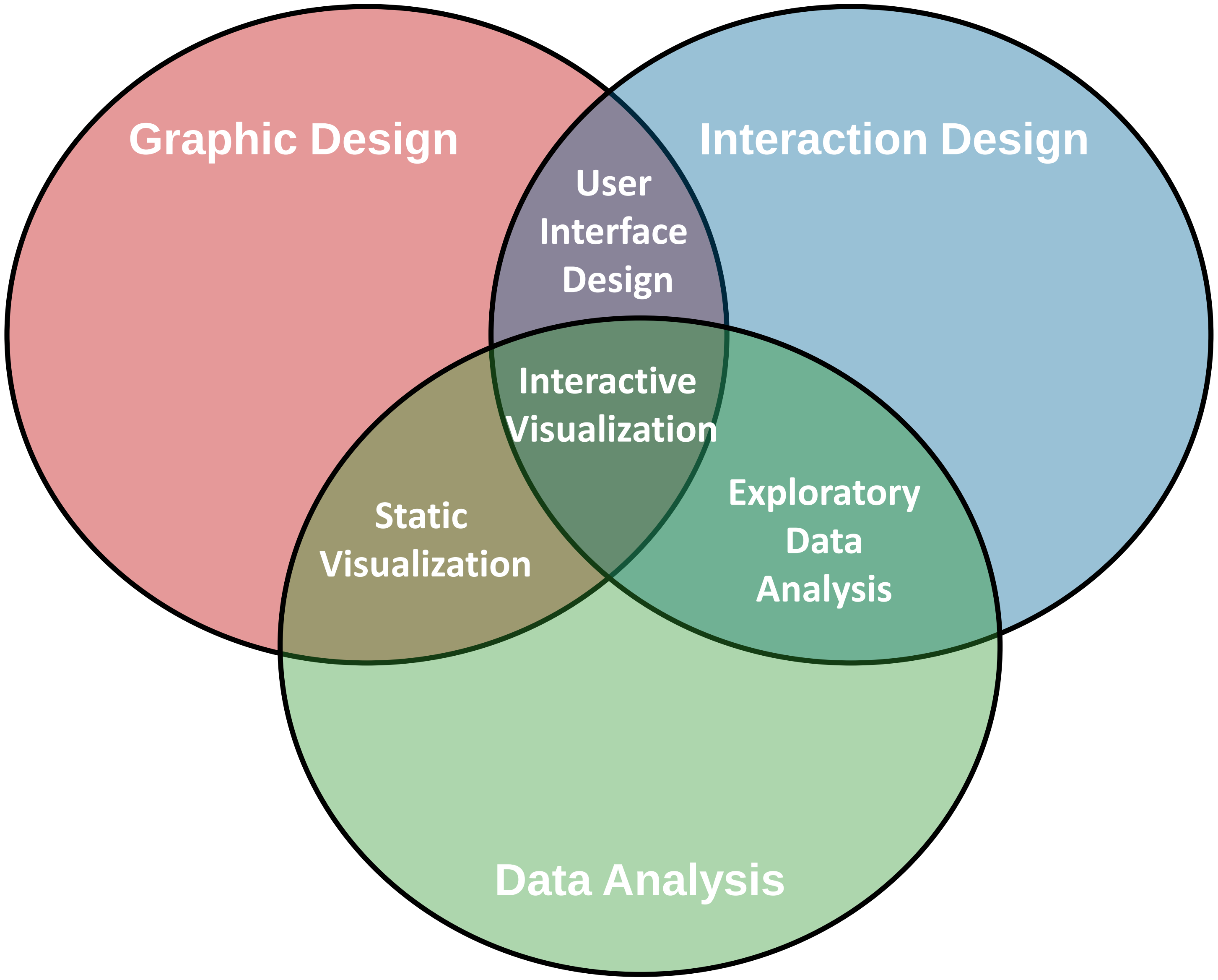
[Shneiderman, 1996]

Analyze first, show the important, zoom/filter, analyze further, details on demand [Keim, 2006]

HC Interaction,
Cognition & Perception

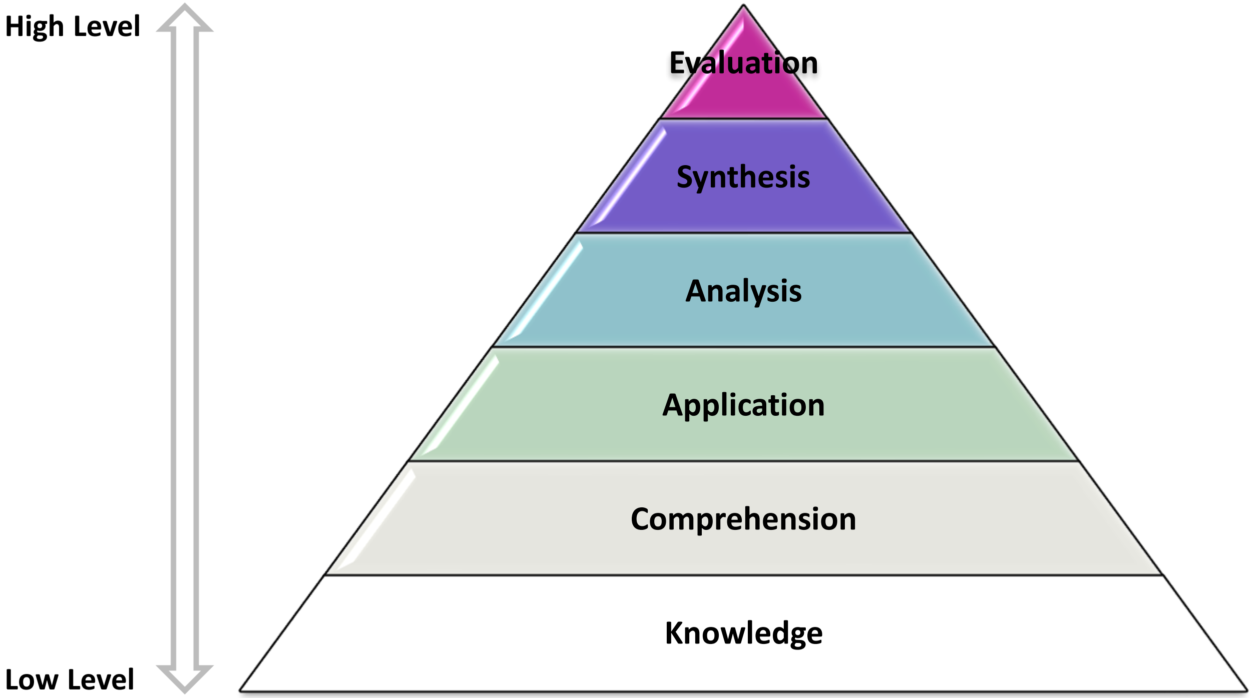


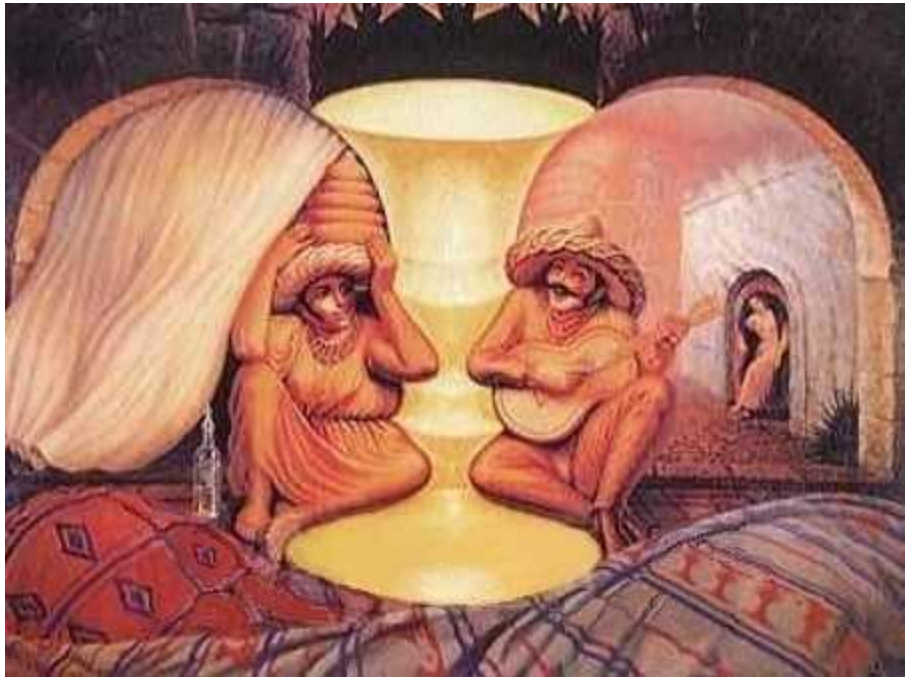
Interactive Visualization

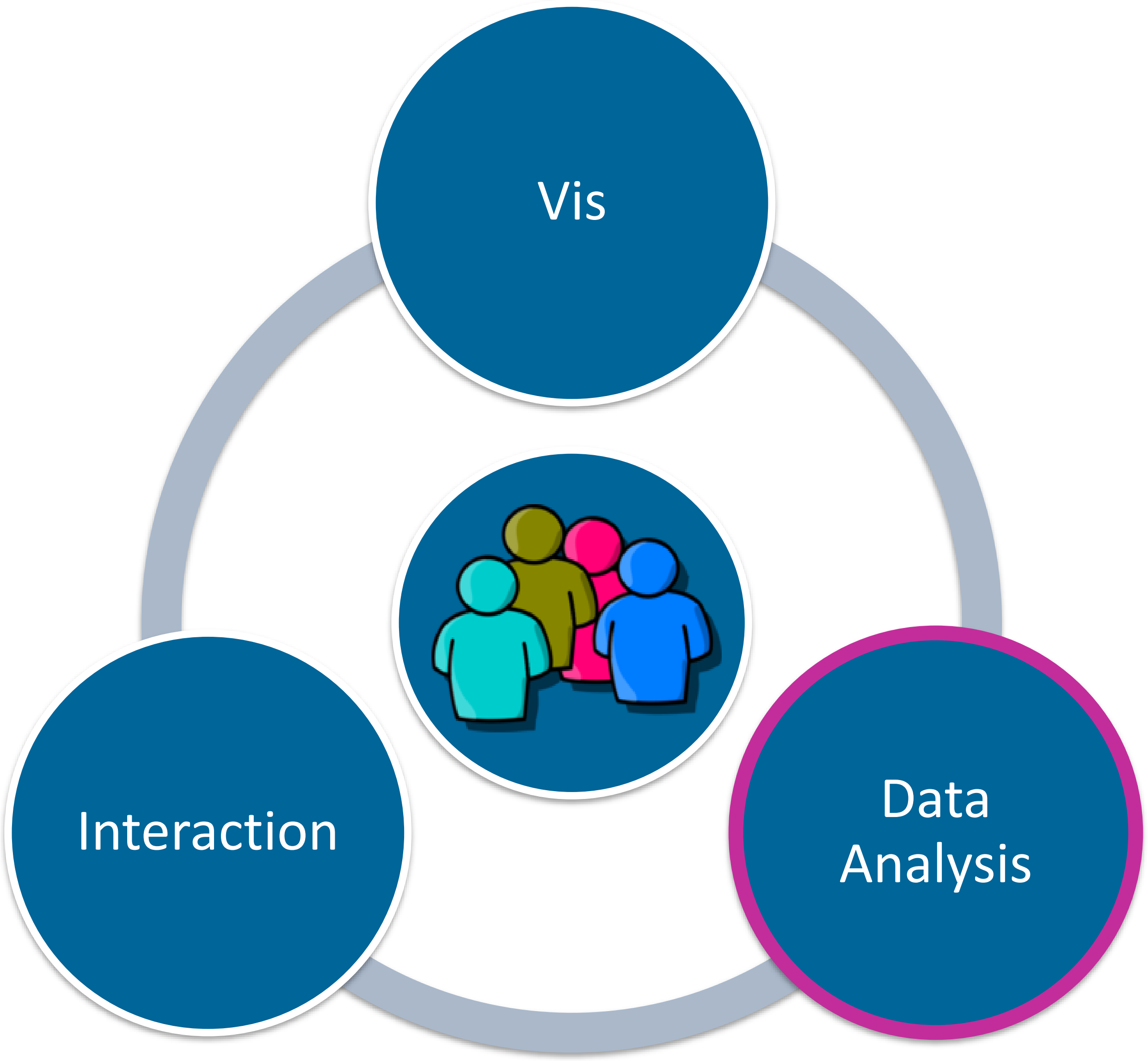


Cognition and Perception

- Cognition: the **mental processes** which assist us to remember, think, know, judge, solve problems, etc.
- Perception: the process by which we interpret the things around us **through sensory stimuli**.



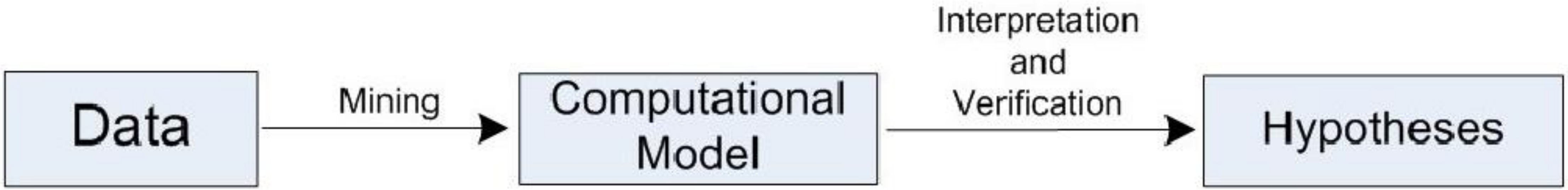




Data Mining,
Machine Learning,
Statistics,...

Data Mining Definition

Automatic algorithmic extraction of valuable information from raw data

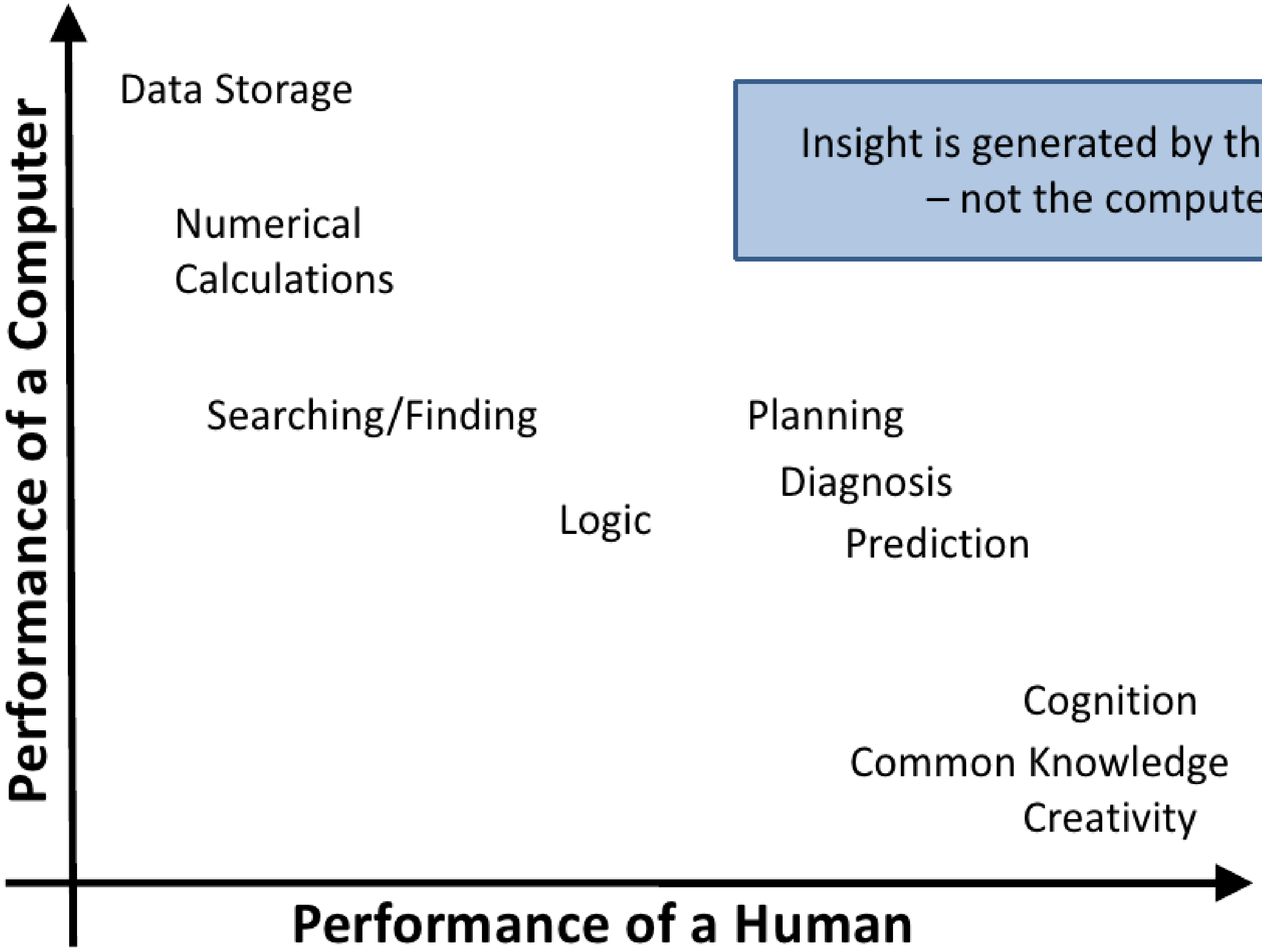


Descriptive vs. Predictive tasks

Knowledge Discovery and Data Mining (KDD)

- Semi or fully automated analysis of massive data sets
- Contributions are more about general methodologies
- Black-box methods in the hands of end users
  - Users need to understand the algorithms for using them
  - What attributes to use? What similarity measure? etc.
  - Often trial and error

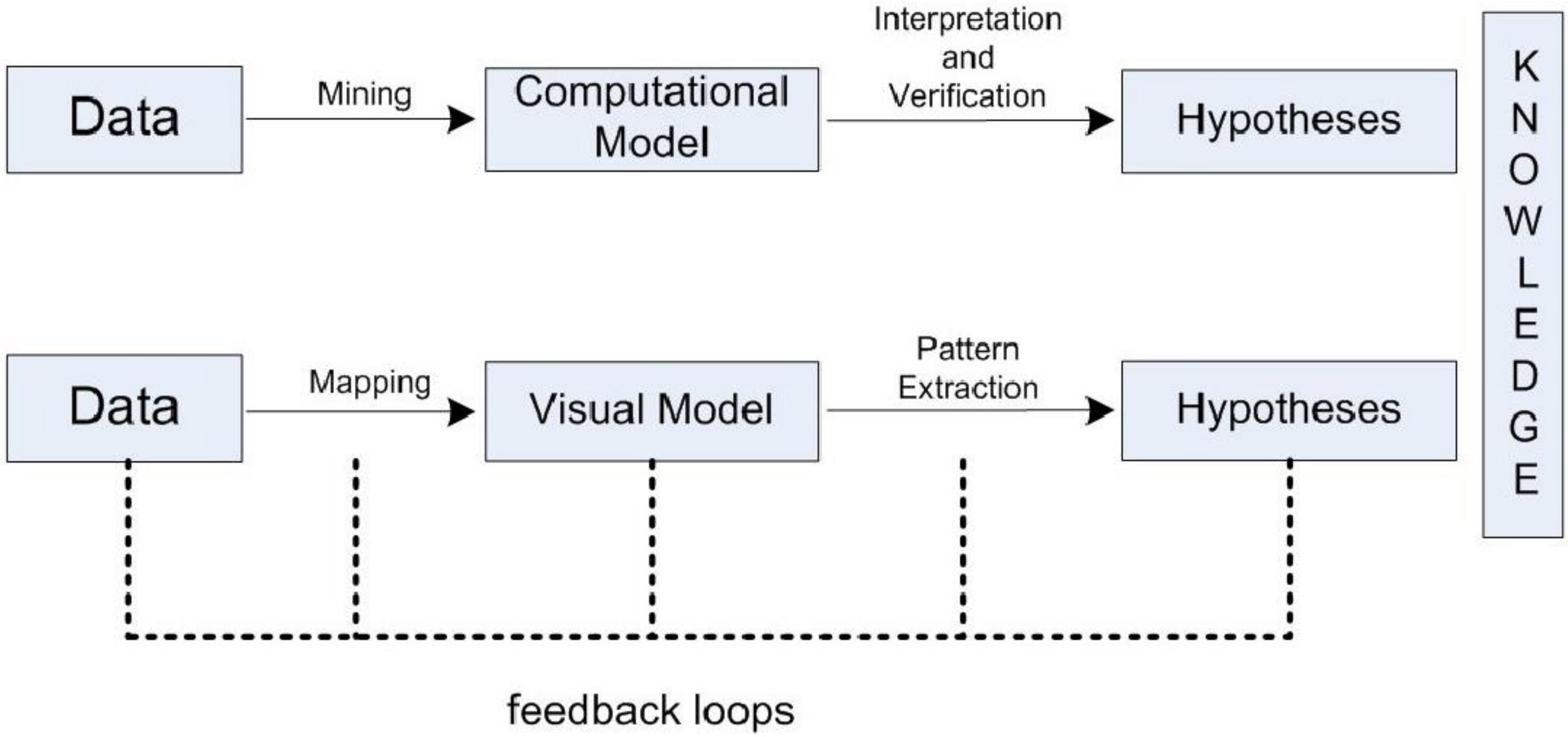
The Ability Matrix



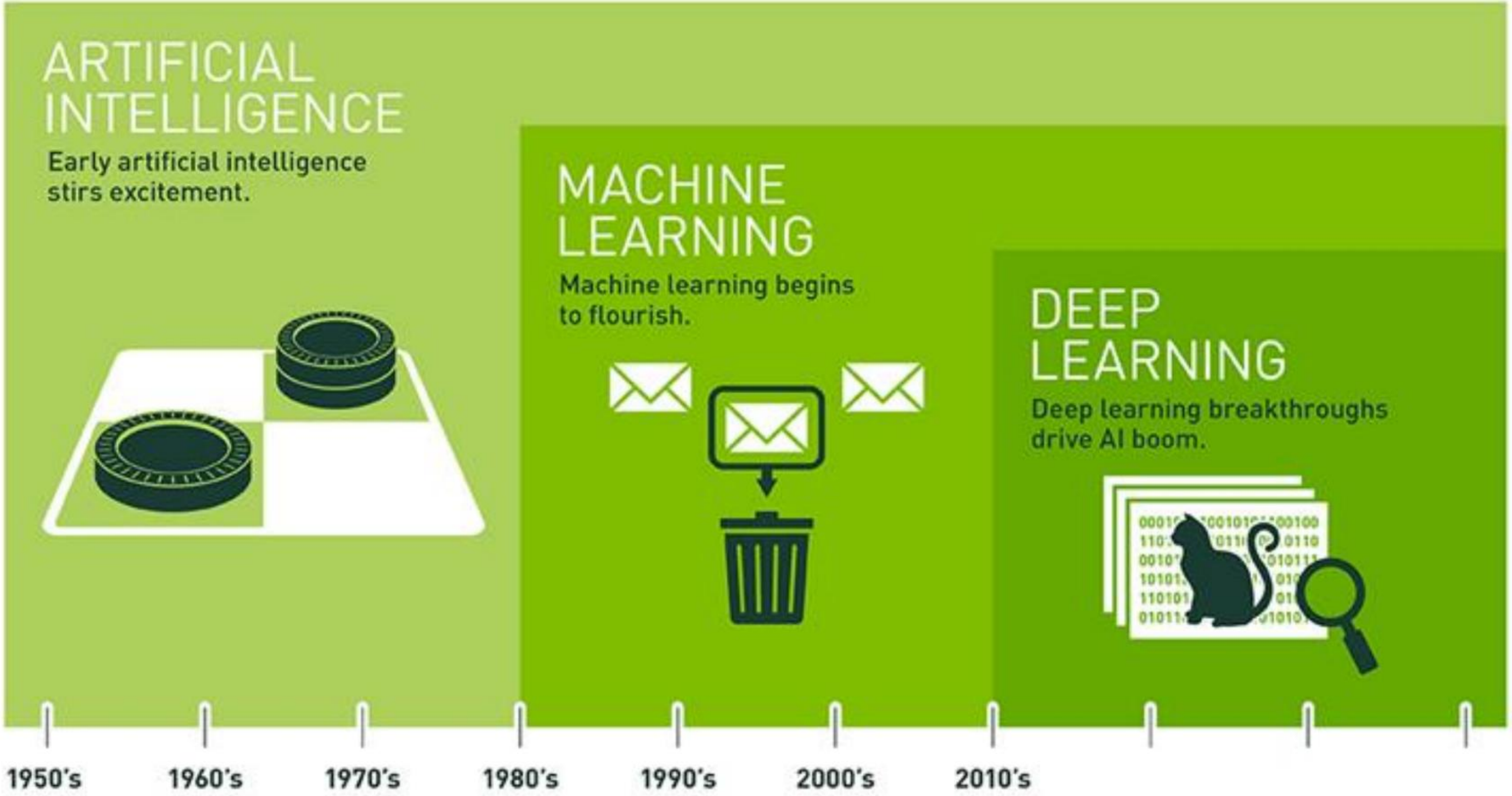
Insight is generated by the human – not the computer!

adapted from Daniel Keim, Uni. Konstanz

Traditional Data Mining vs. Visual Analysis Processes



Machine Learning

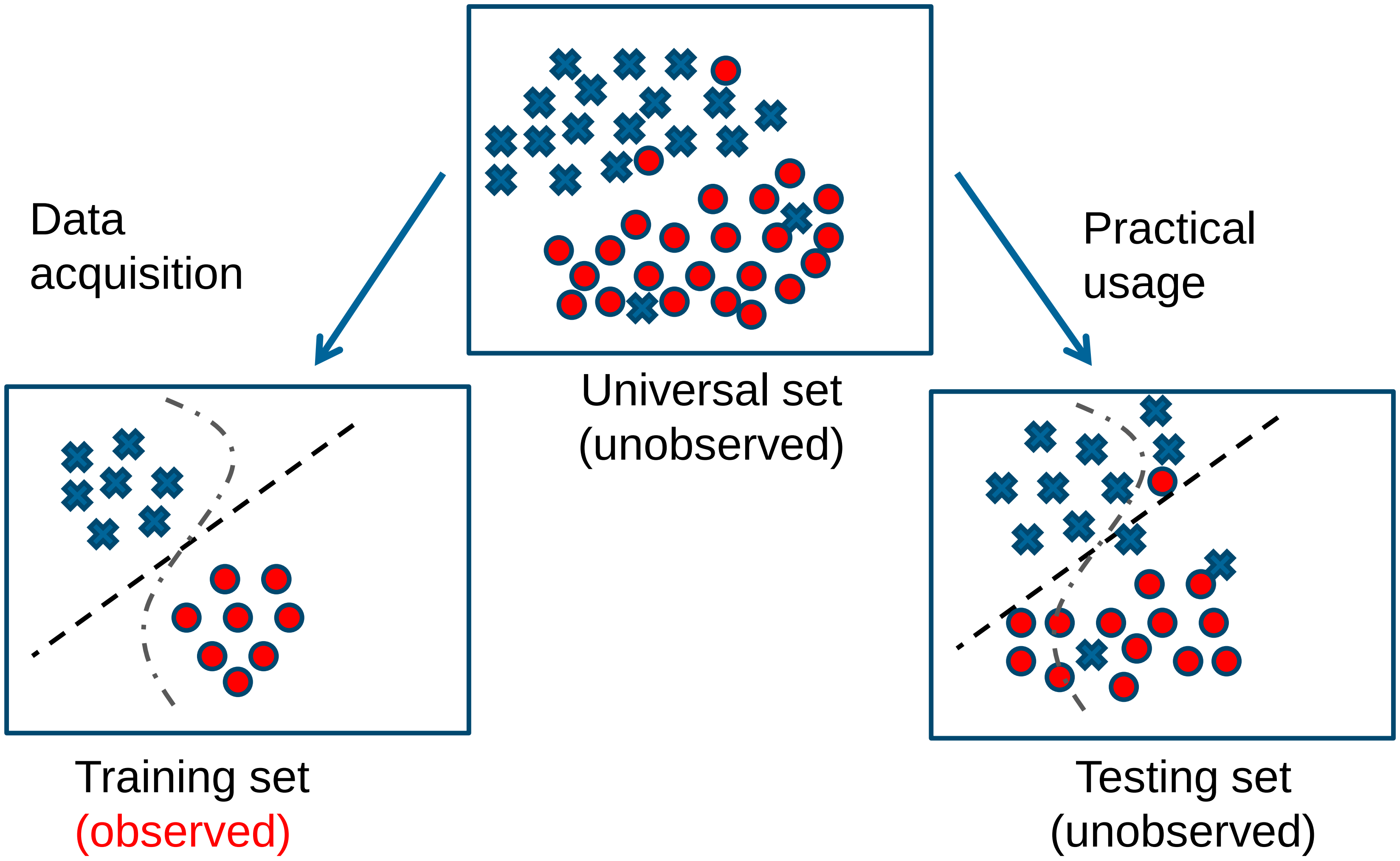


What is machine learning?

- A branch of artificial intelligence, concerned with the design and development of algorithms that allow computers to evolve behaviors based on empirical data.

- As intelligence requires knowledge, it is necessary for the computers to acquire knowledge.

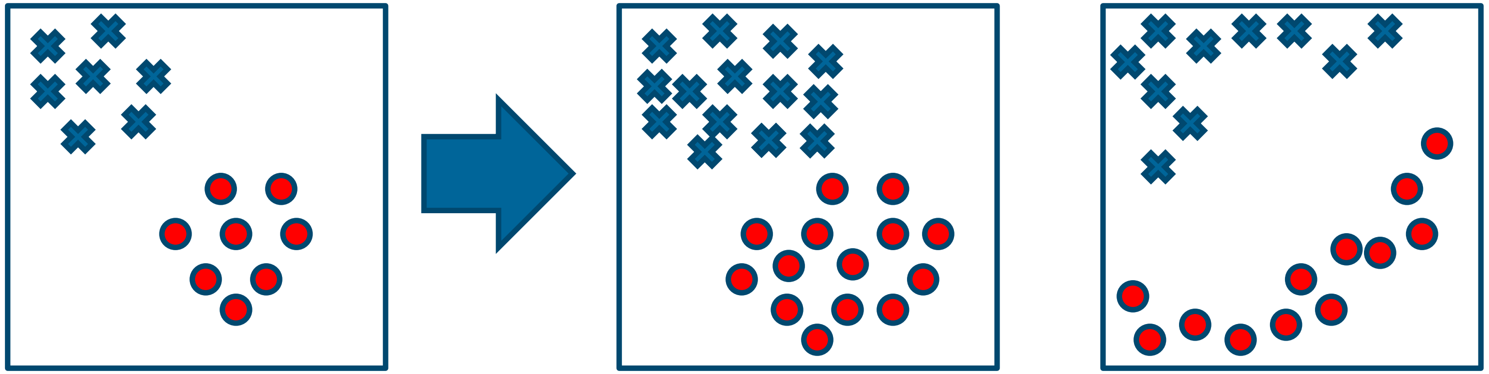
Training and testing



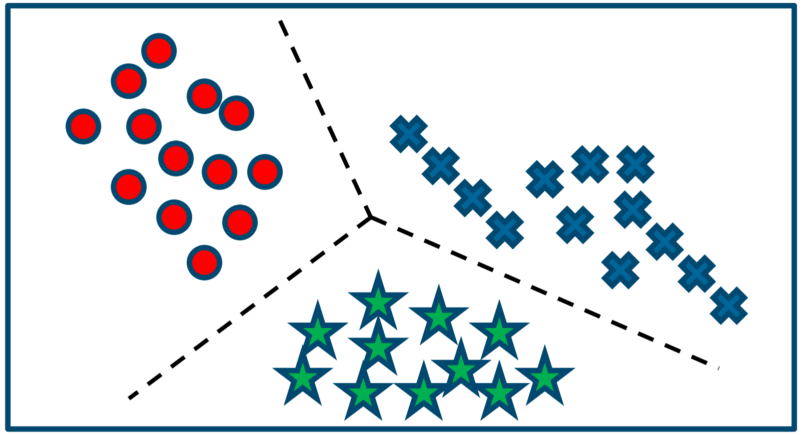
Training and testing

- Training is the process of making the system able to learn.

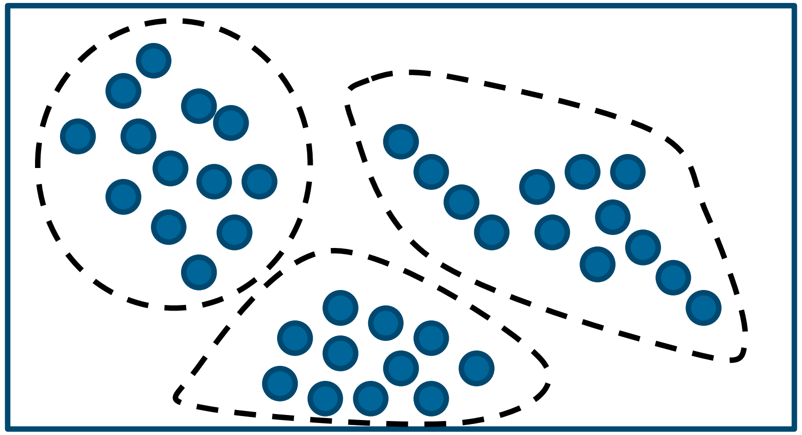
- No “free-lunch” rule:
  - Training set and testing set come from the same distribution
  - Need to make some assumptions or bias



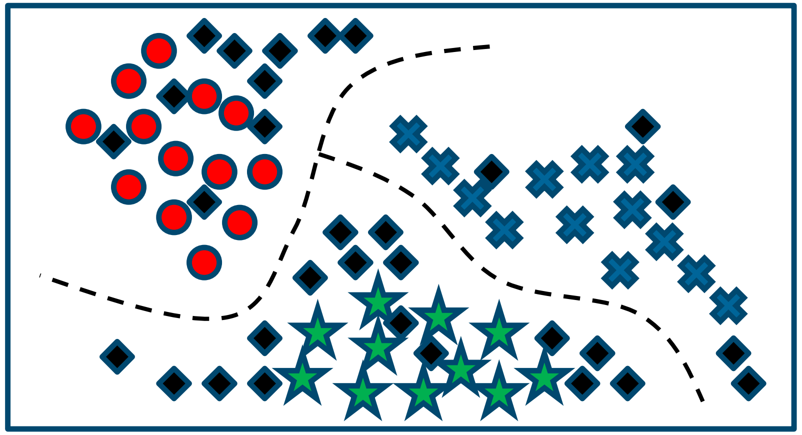
Algorithms



Supervised learning



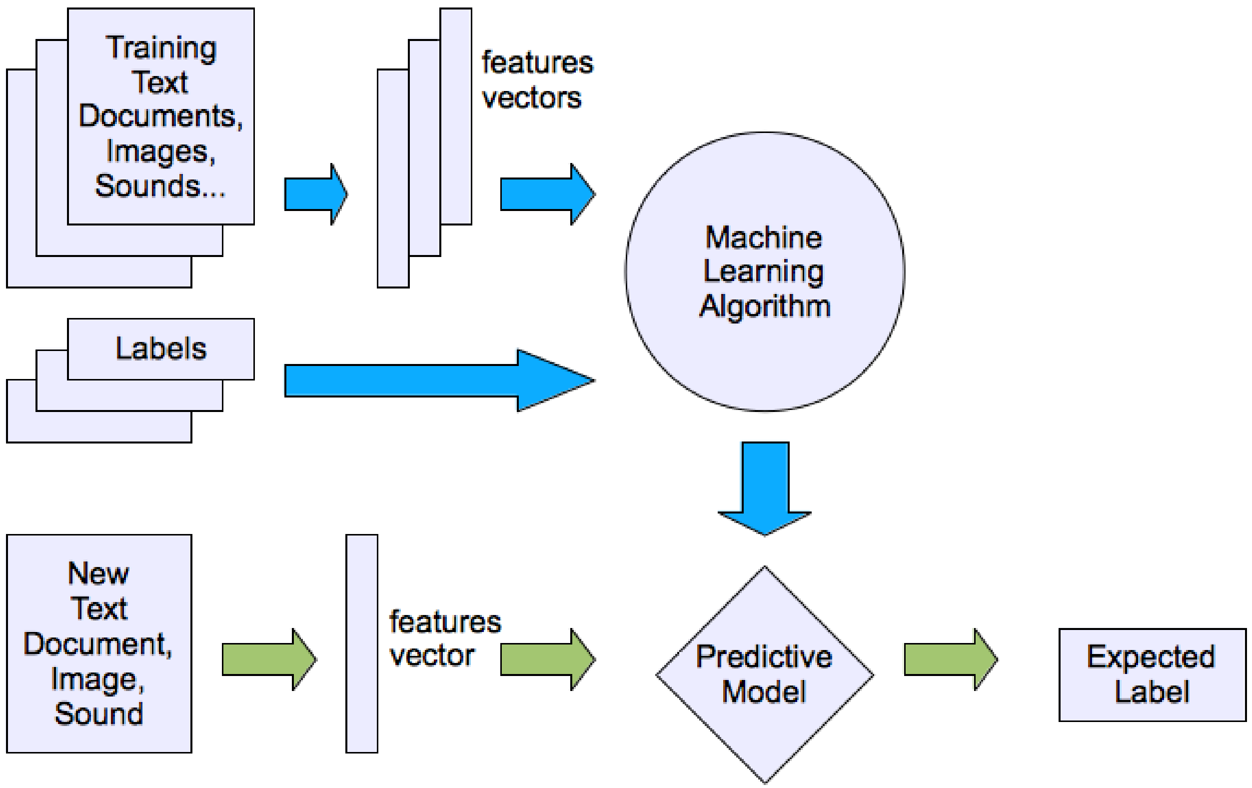
Unsupervised learning



Semi-supervised learning

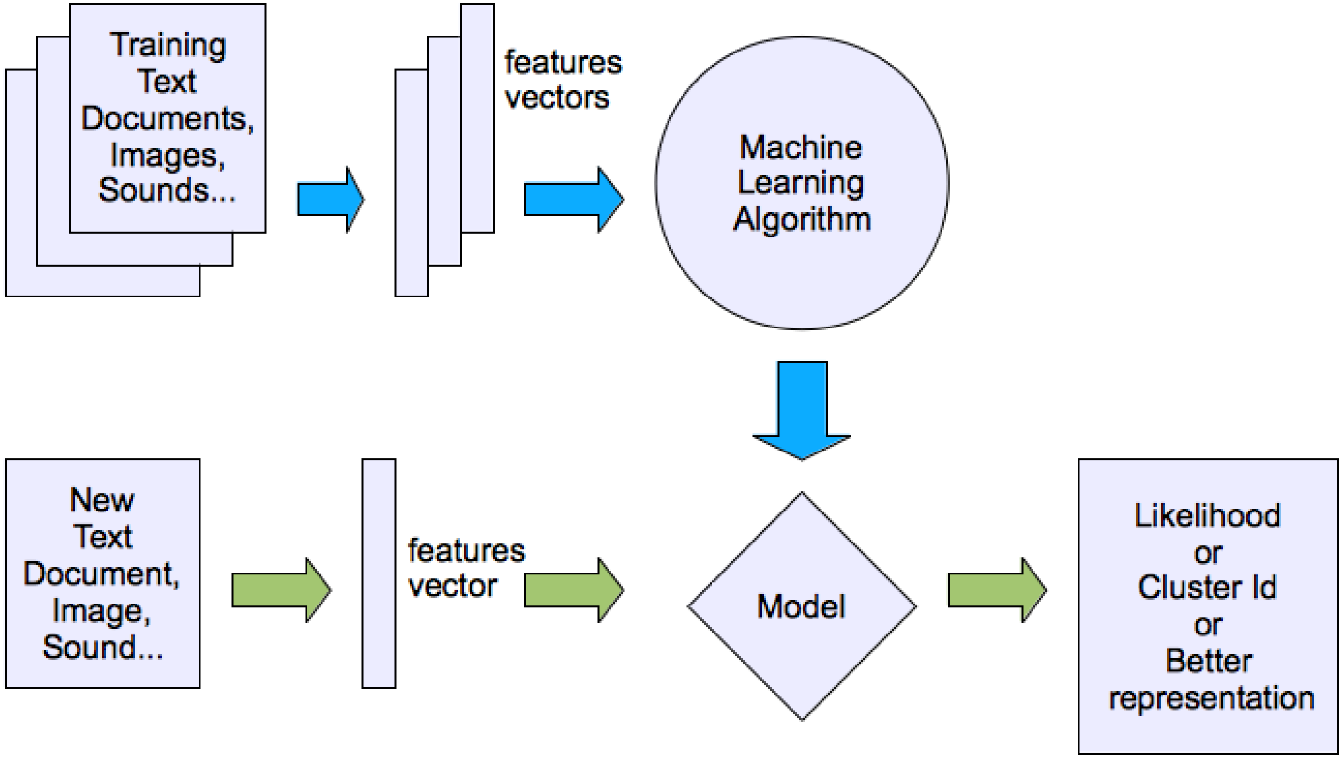
Machine learning structure

Supervised learning



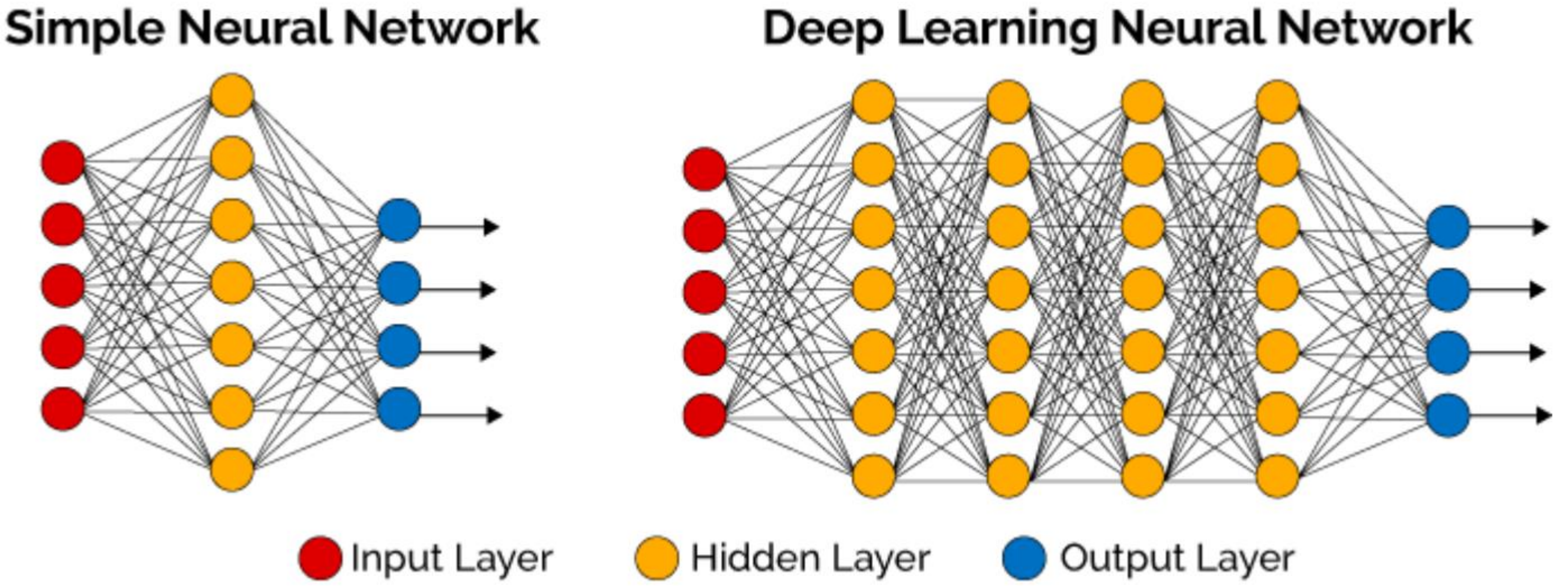
Machine learning structure

Unsupervised learning



Deep Learning

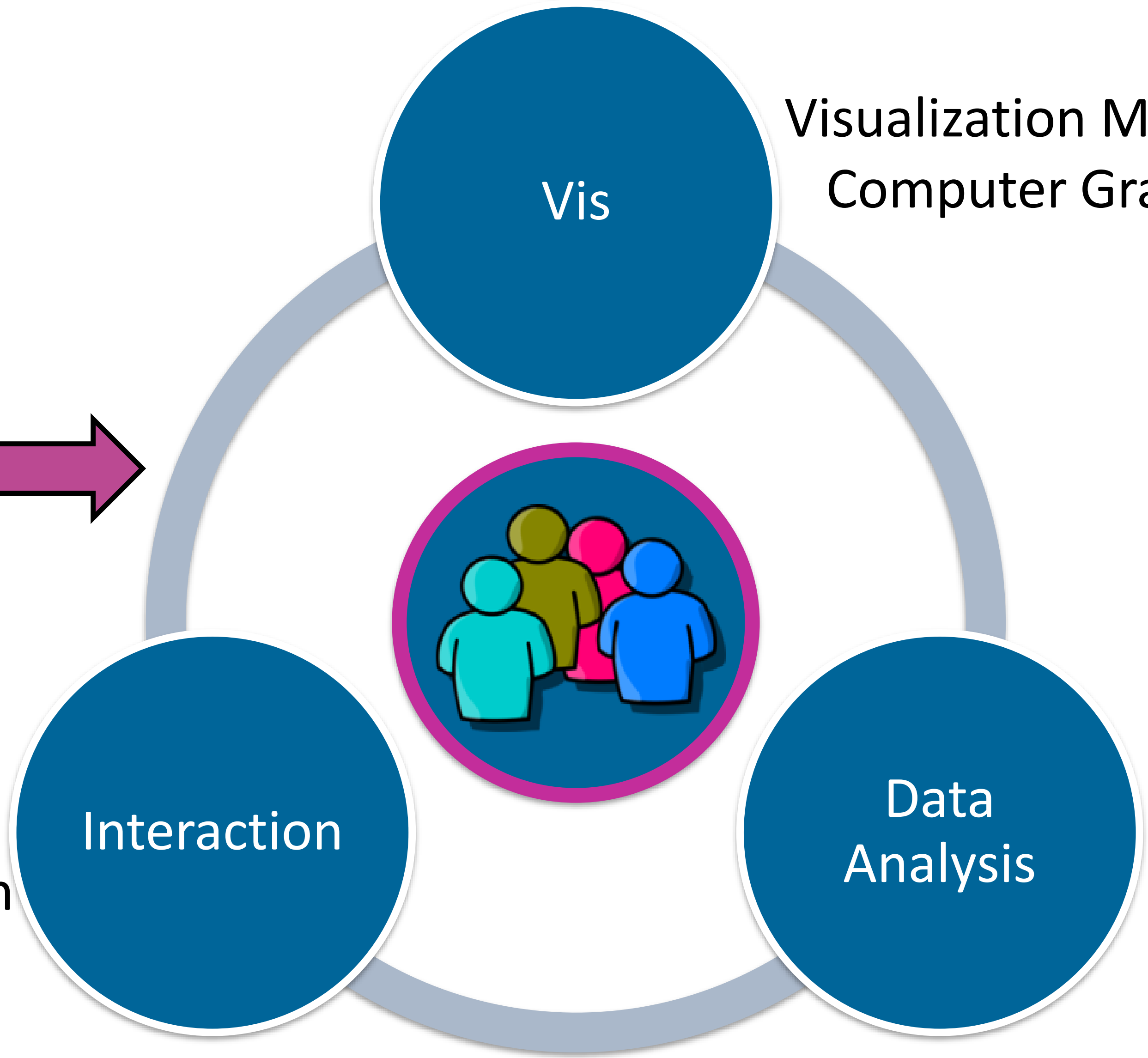
Construct layers of increasingly meaningful representations of the data



Visual Analytics

Visualization Methods,
Computer Graphics

Data Exploration
Knowledge Discovery
Hypothesis Confirmation
or Generation



HC Interaction,
Cognition & Perception

Data Mining,
Machine Learning,
Statistics,…

Challenges

- Data → Dealing with very large, diverse, variable quality datasets
- Users → Meeting the needs of the users
- Design → Assisting designers of visual analytic systems
- Technology → Providing the necessary infrastructure

Visual Analytics for :

1. … Tumor Tissue Characterization and Organ at Risk Segmentation → *Research and Treatment Planning in RT*

2. … Exploring Organ Variability for RT → *Research and Treatment Planning in RT*

Background: Prostate Cancer

WHO 2018

18.1 M Cancer Cases

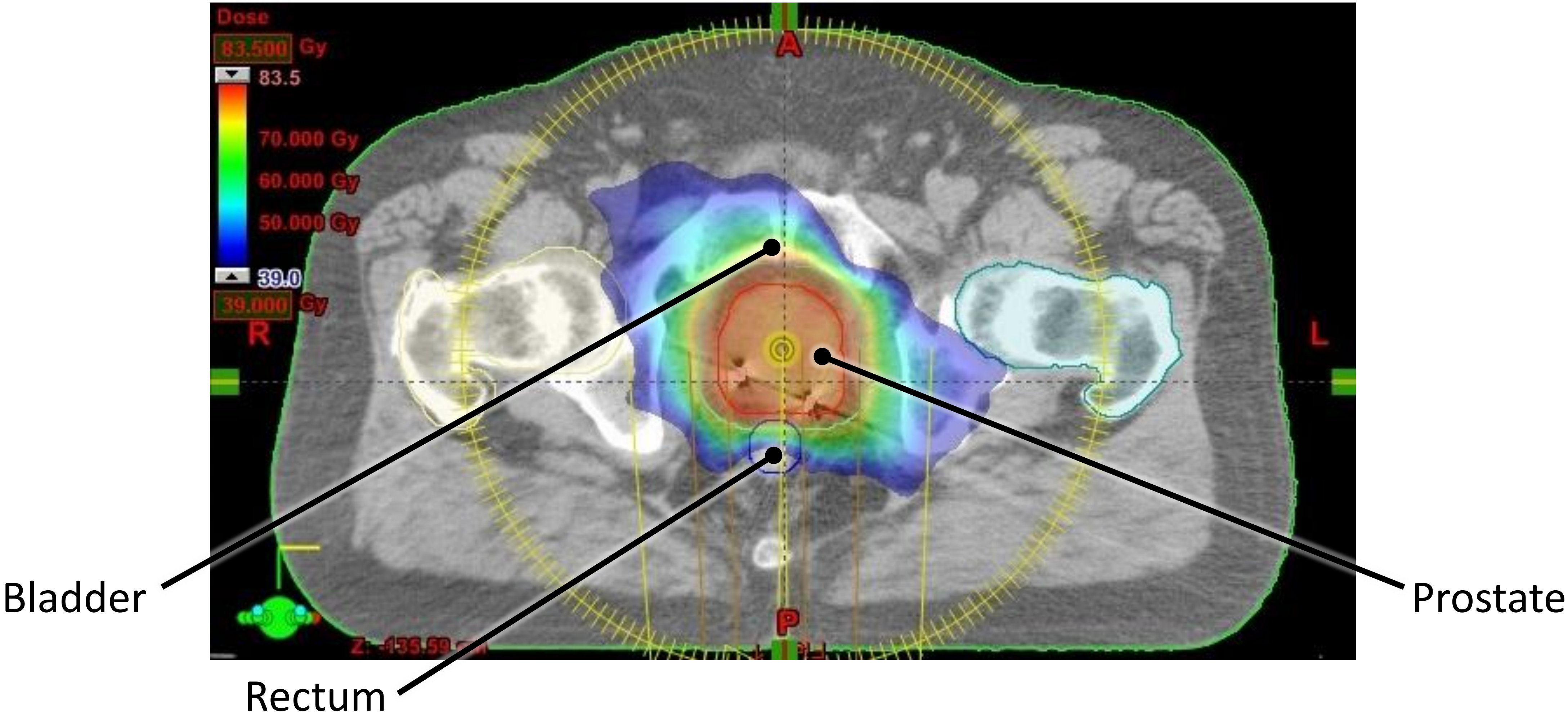
9.6 M Cancer Deaths

Prostate Cancer

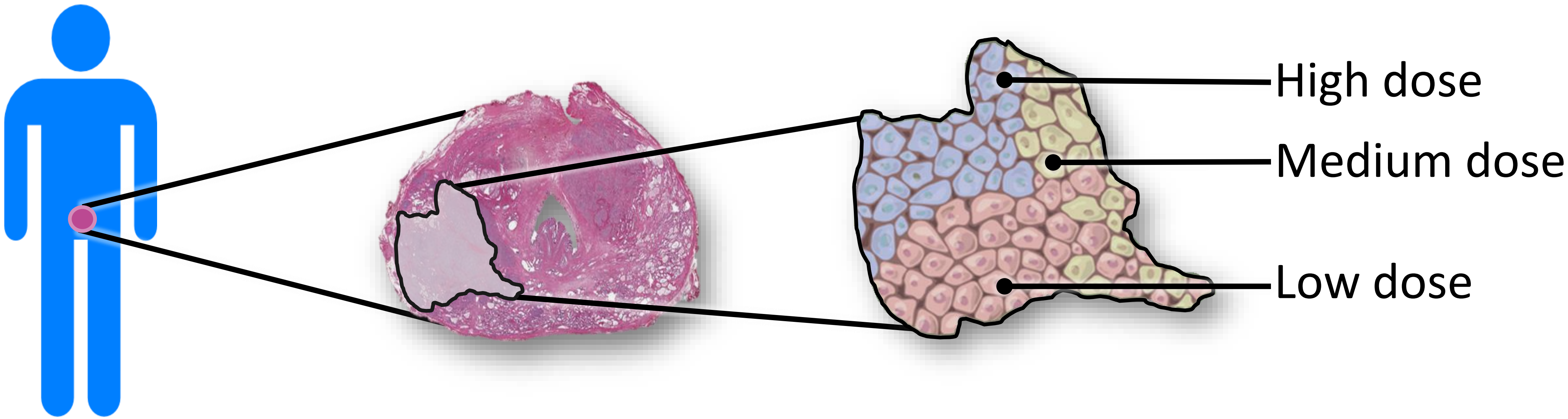
1 out of 6 men

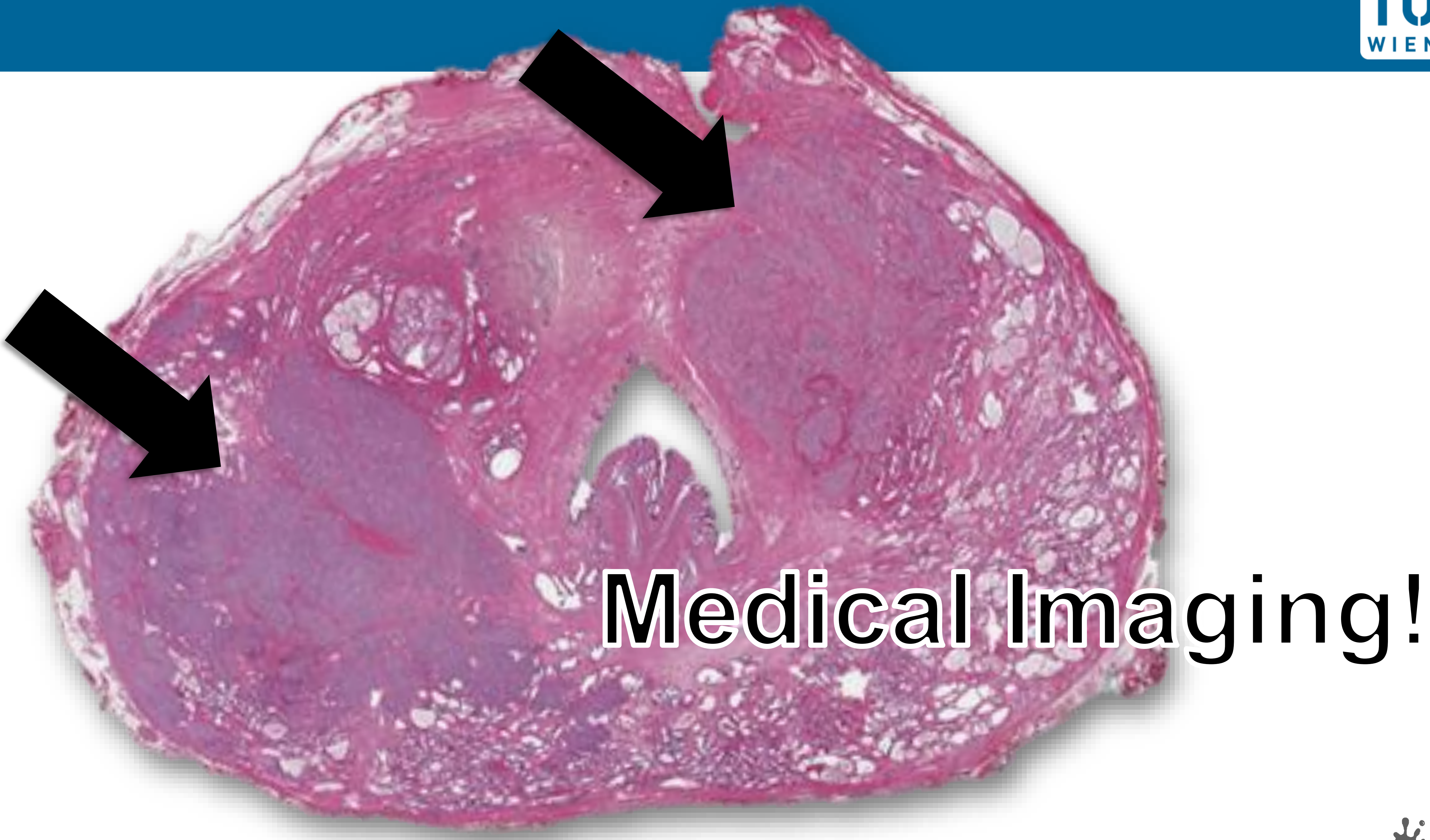
[WHO Report, 2018]

60% of patients receive radiotherapy treatment



Tailoring the Dose to Tumor Characteristics



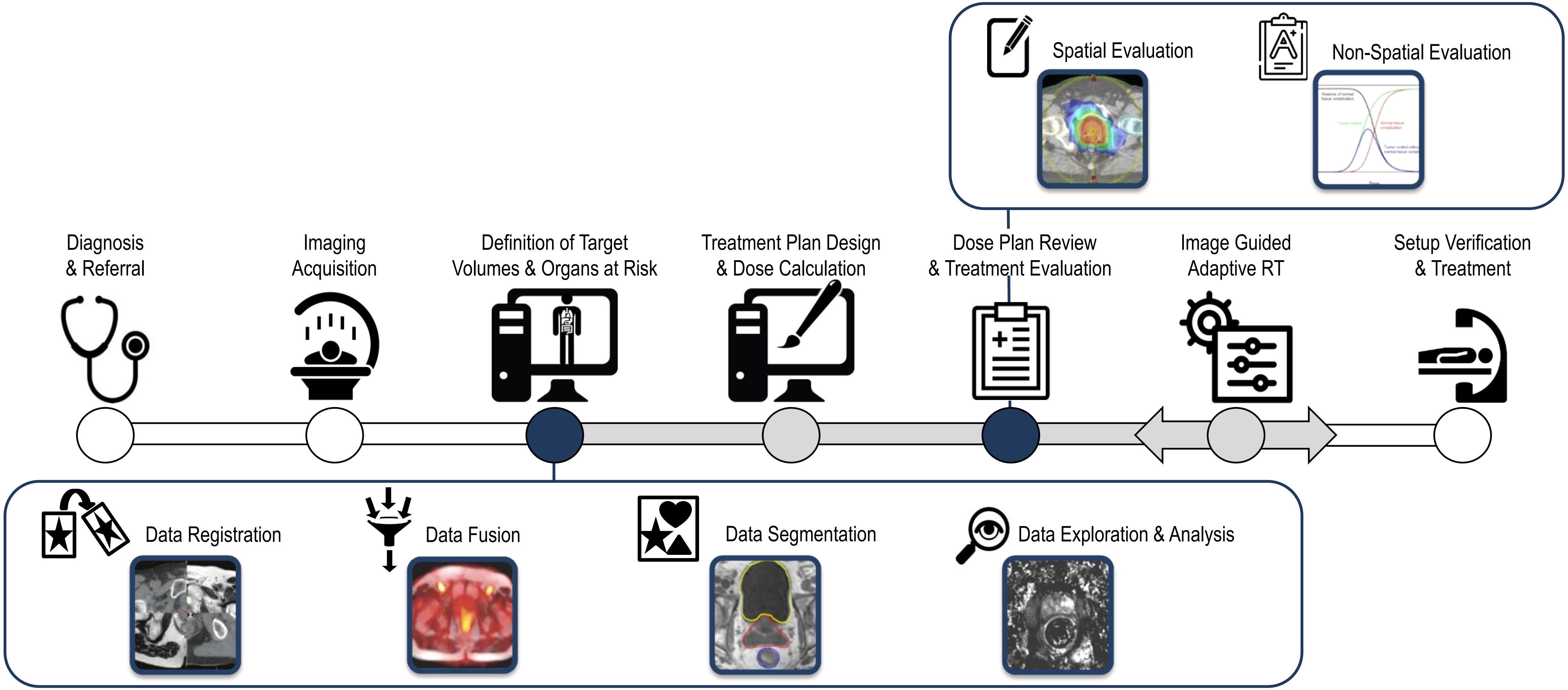

Medical Imaging!

RT Pipeline

[Schlachter, Raidou et al. 2019 STAR CGF]

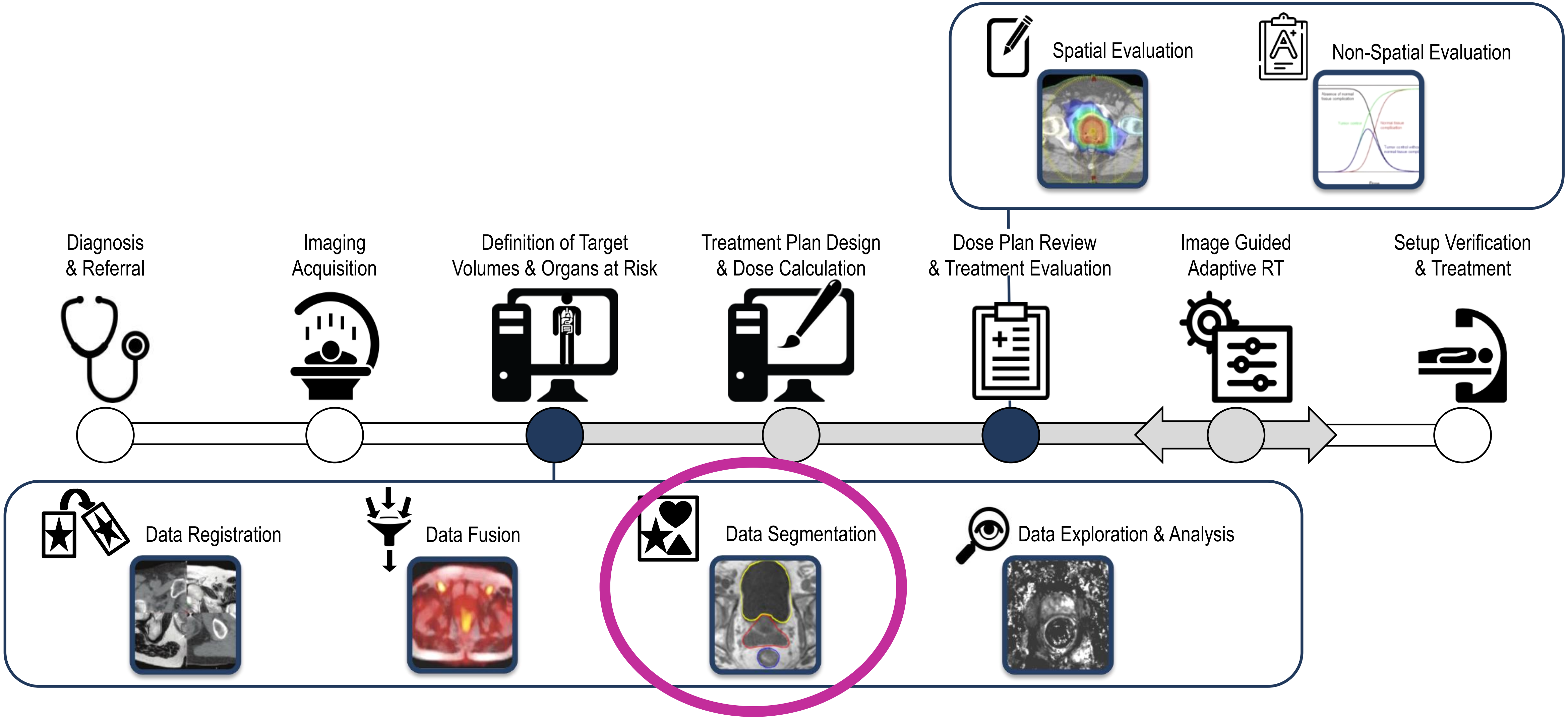
RT Pipeline

[Schlachter, Raidou et al. 2019 STAR CGF]



RT Pipeline

[Schlachter, Raidou et al. 2019 STAR CGF]



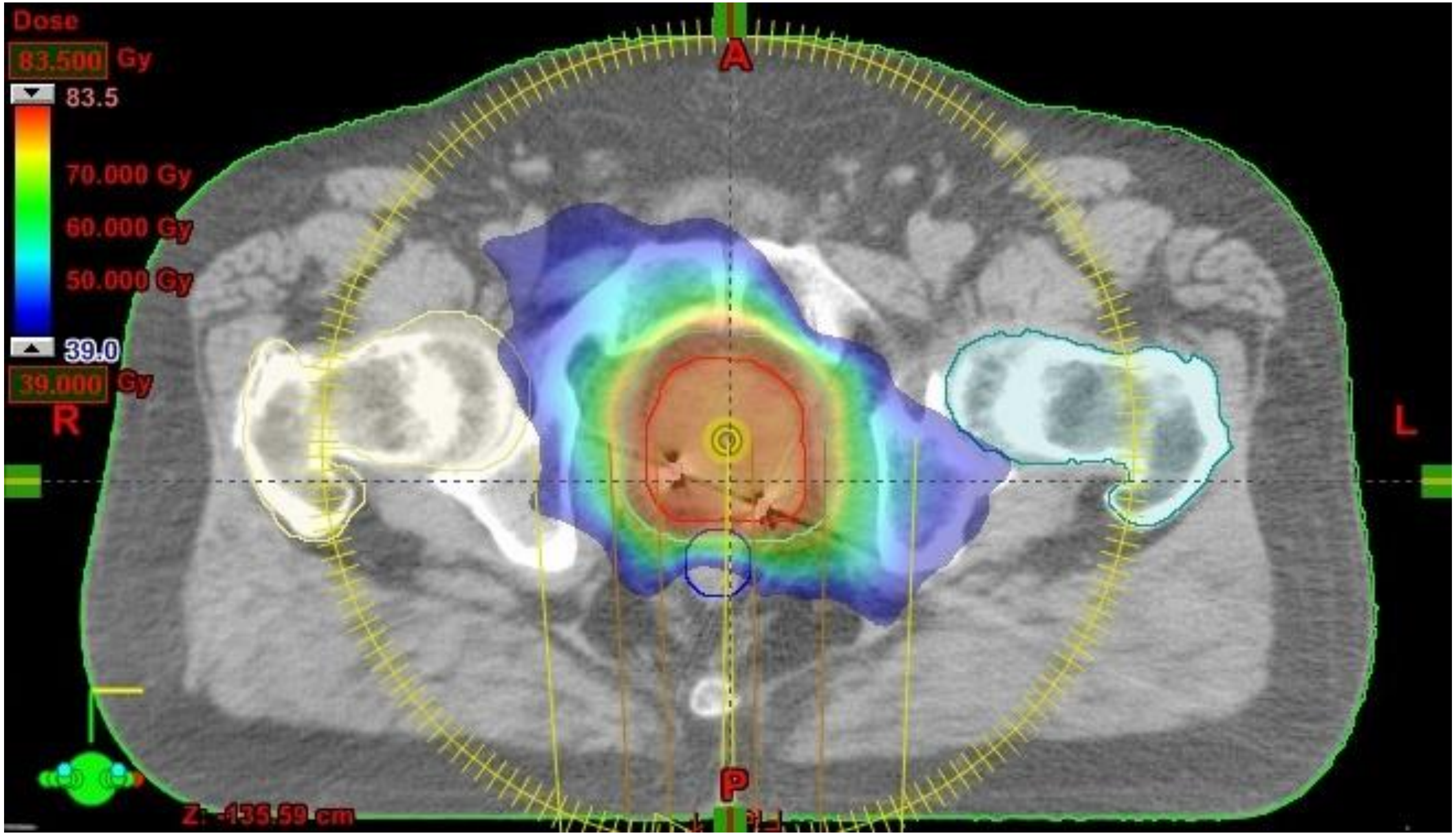
Visual Analytics Examples

Visual Analytics for :

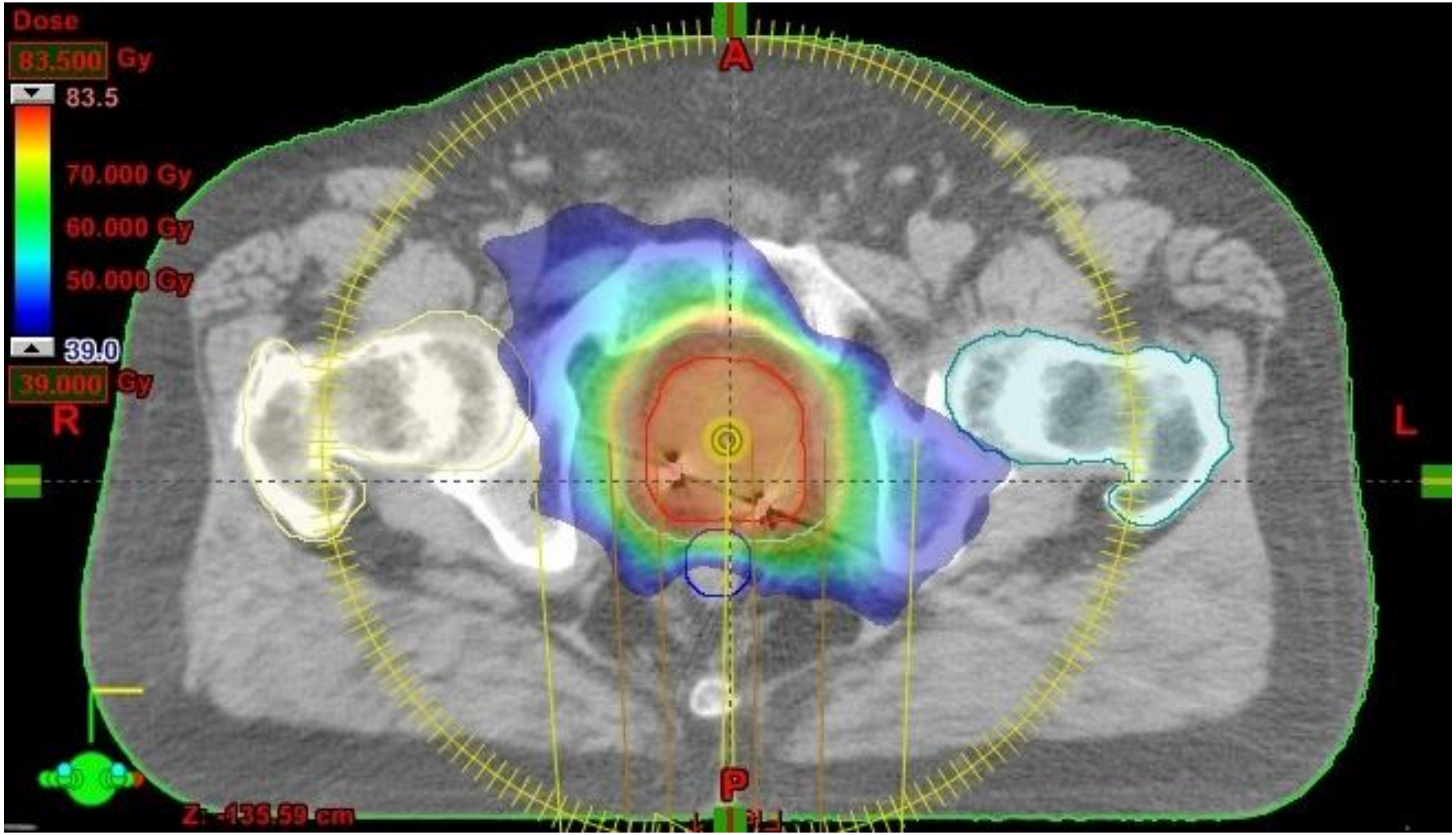
1. … Tumor Tissue Characterization

2. and Organ at Risk Segmentation

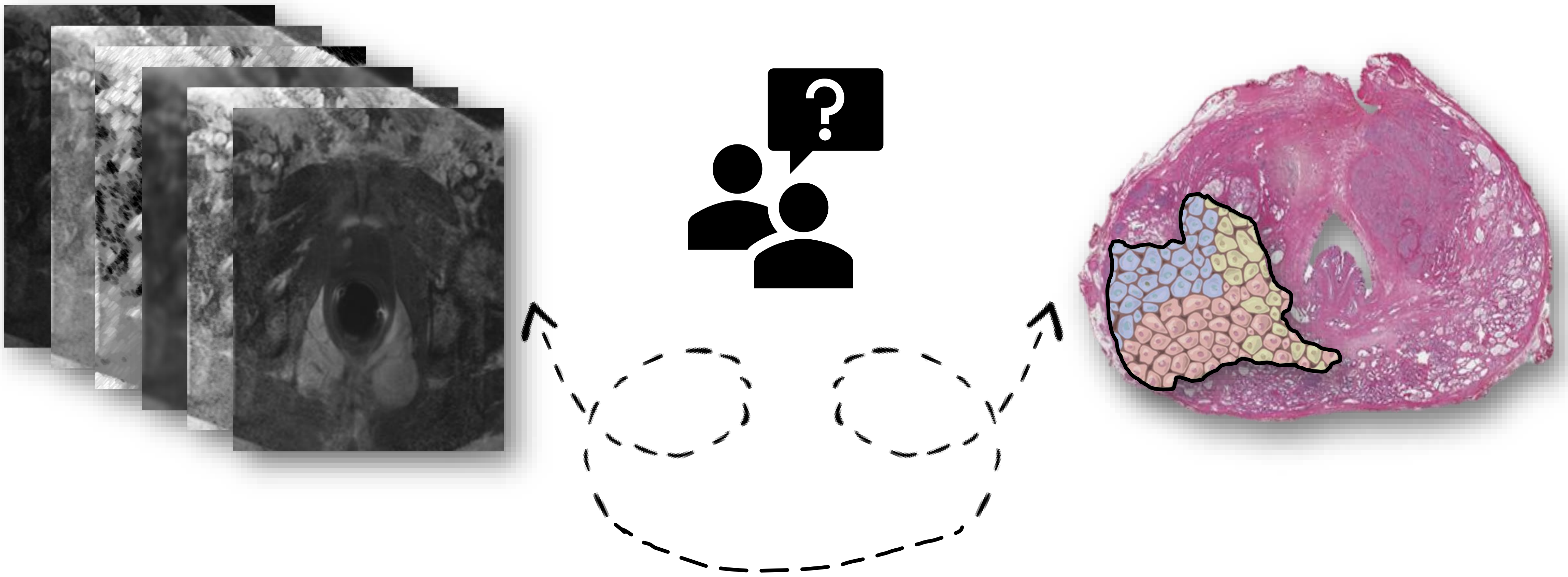
Tumors vs. Healthy Organs (at Risk)

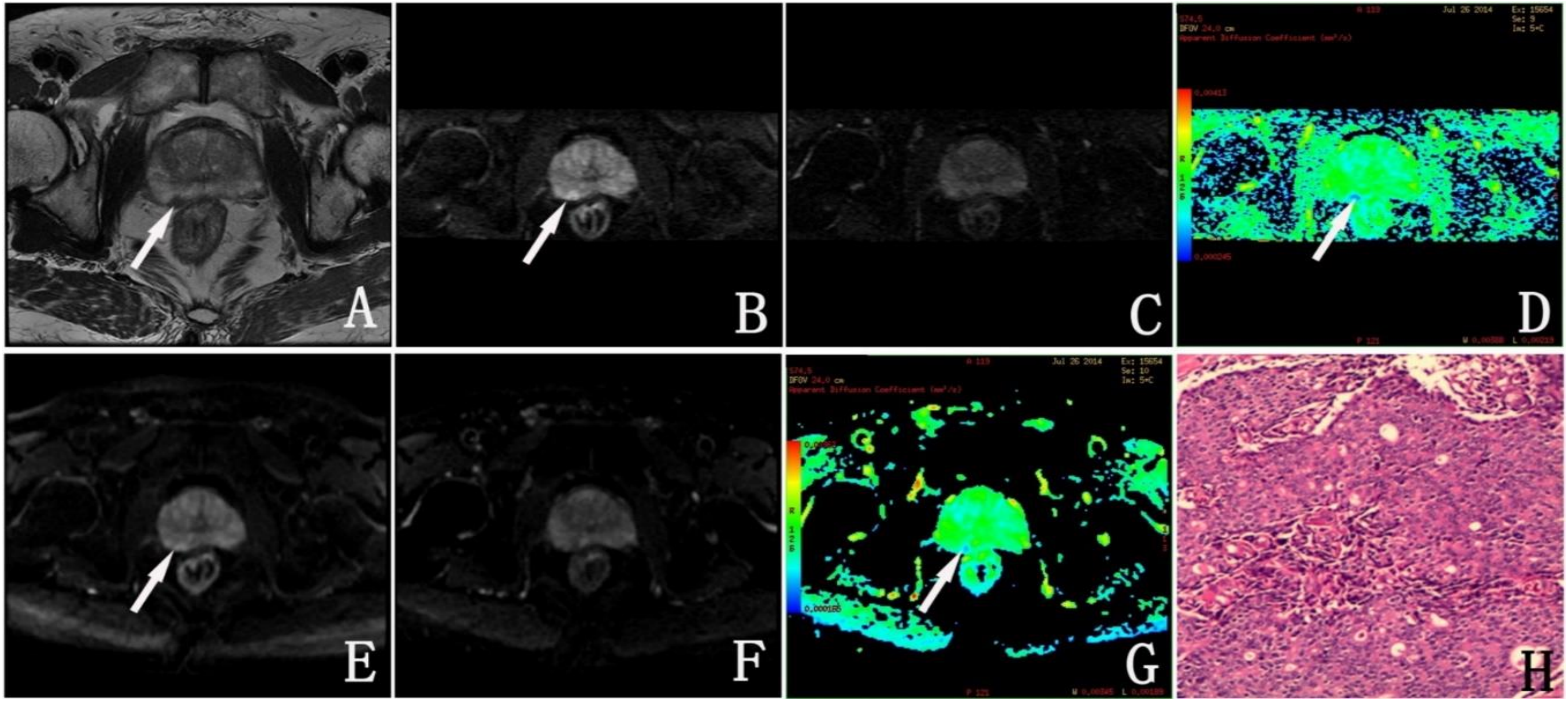


Tumors vs. Healthy Organs (at Risk)

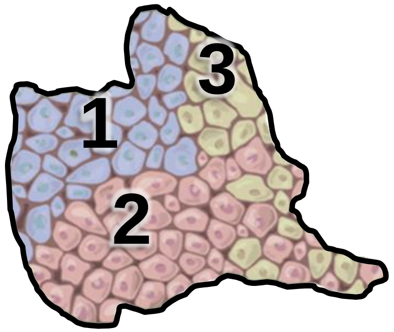


Exploration and analysis of intra-tumor tissue characteristics



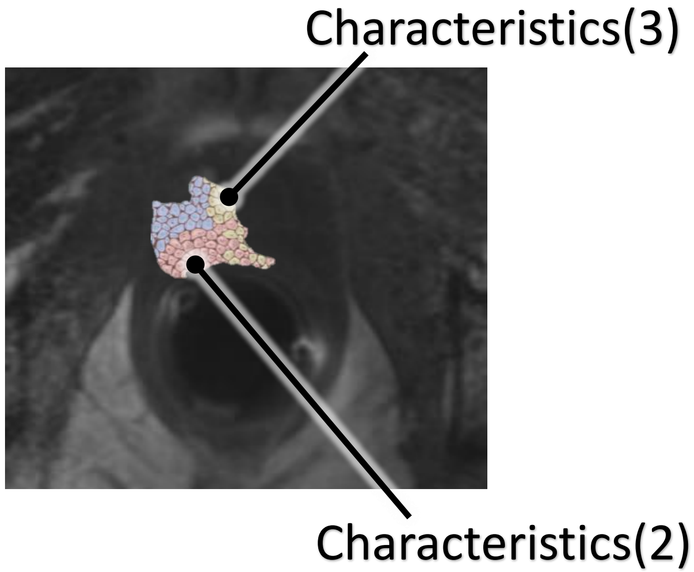


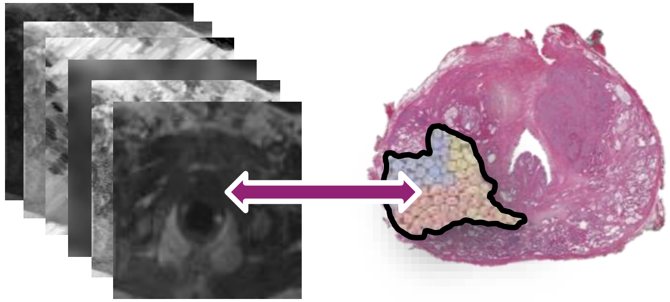
[Feng et al., ECR2015]



Identification and exploration of intra-tumor regions

Analysis and comparison of intra-tumor regions

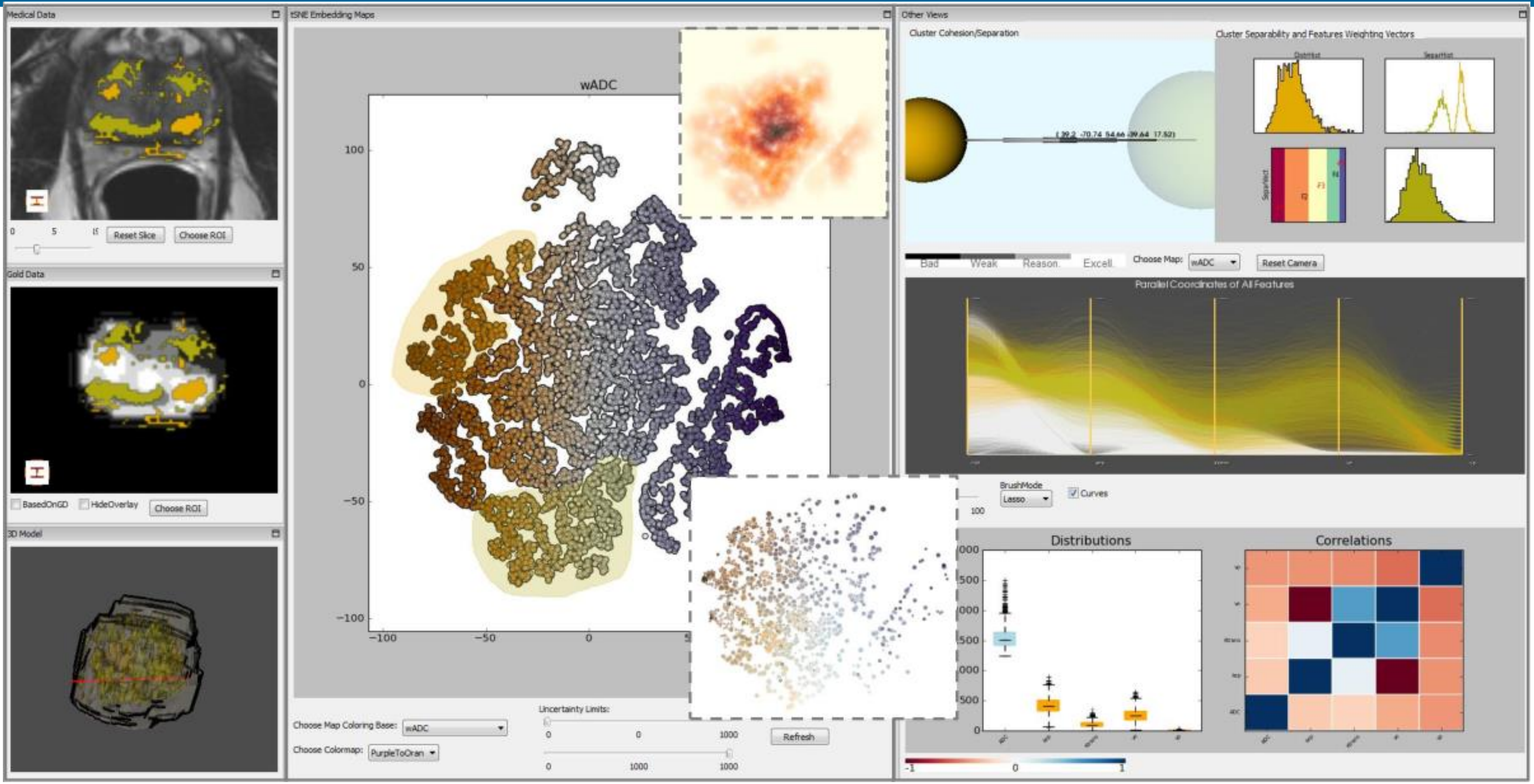




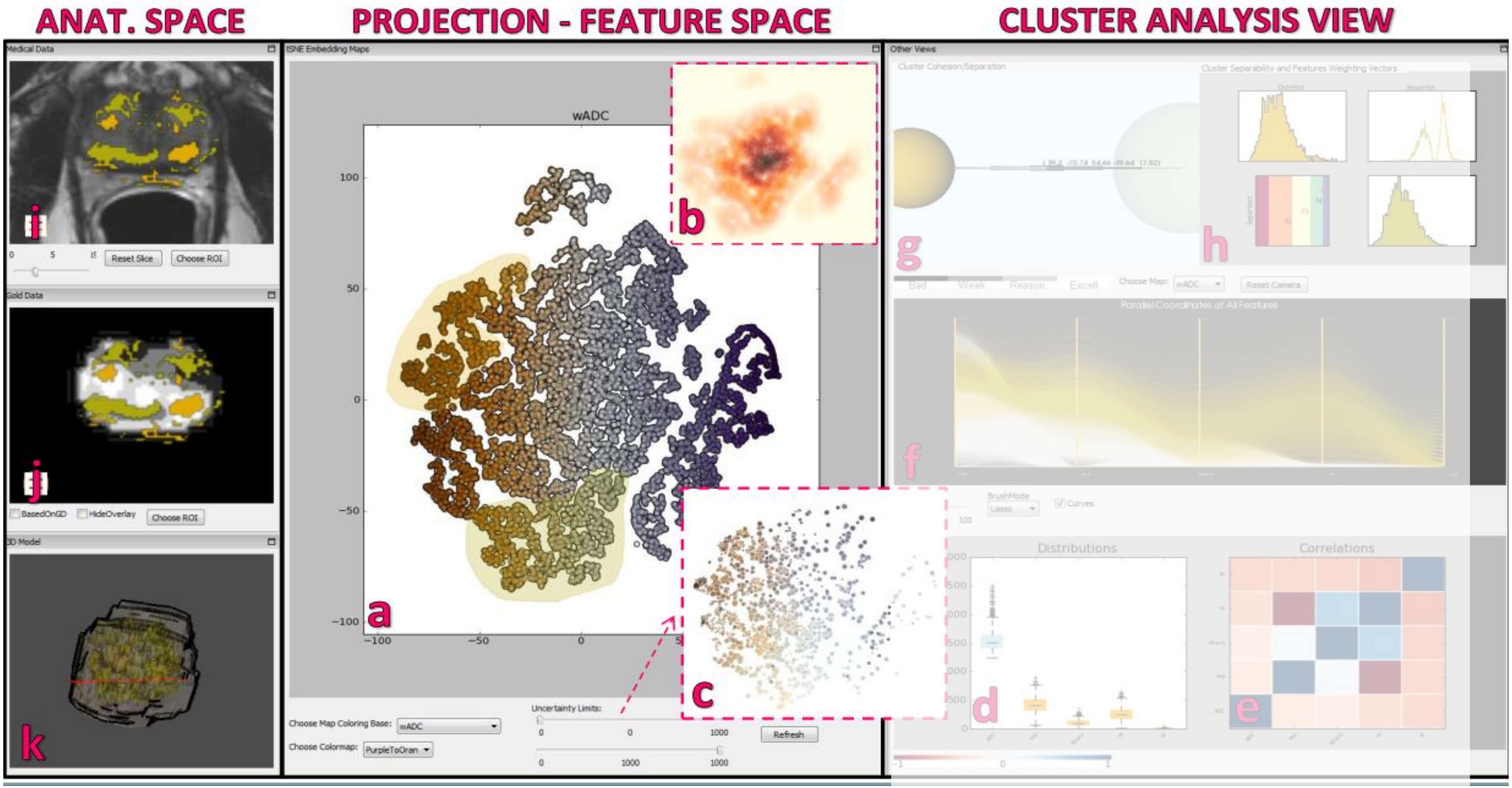
Association to other clinical reference data

Uncertainty impact on analysis

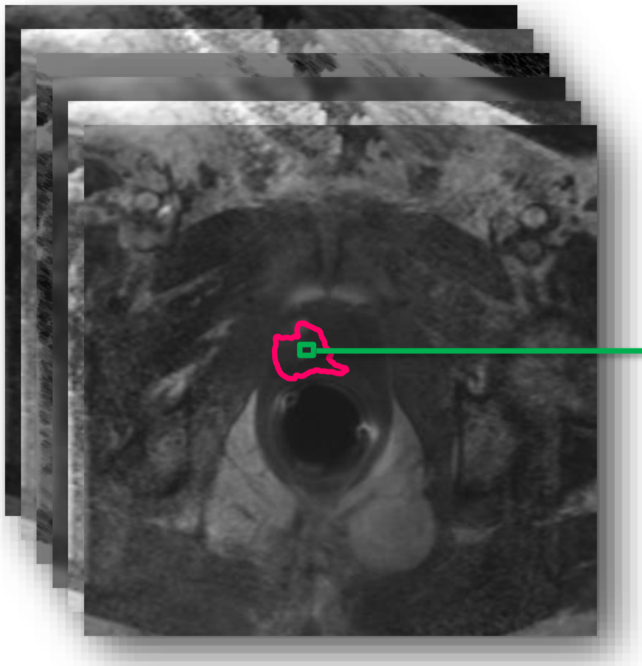
Visual Analytics Solution



1. Identification and Exploration of Intra-tumor Regions



1. Identification and Exploration of Intra-tumor Regions

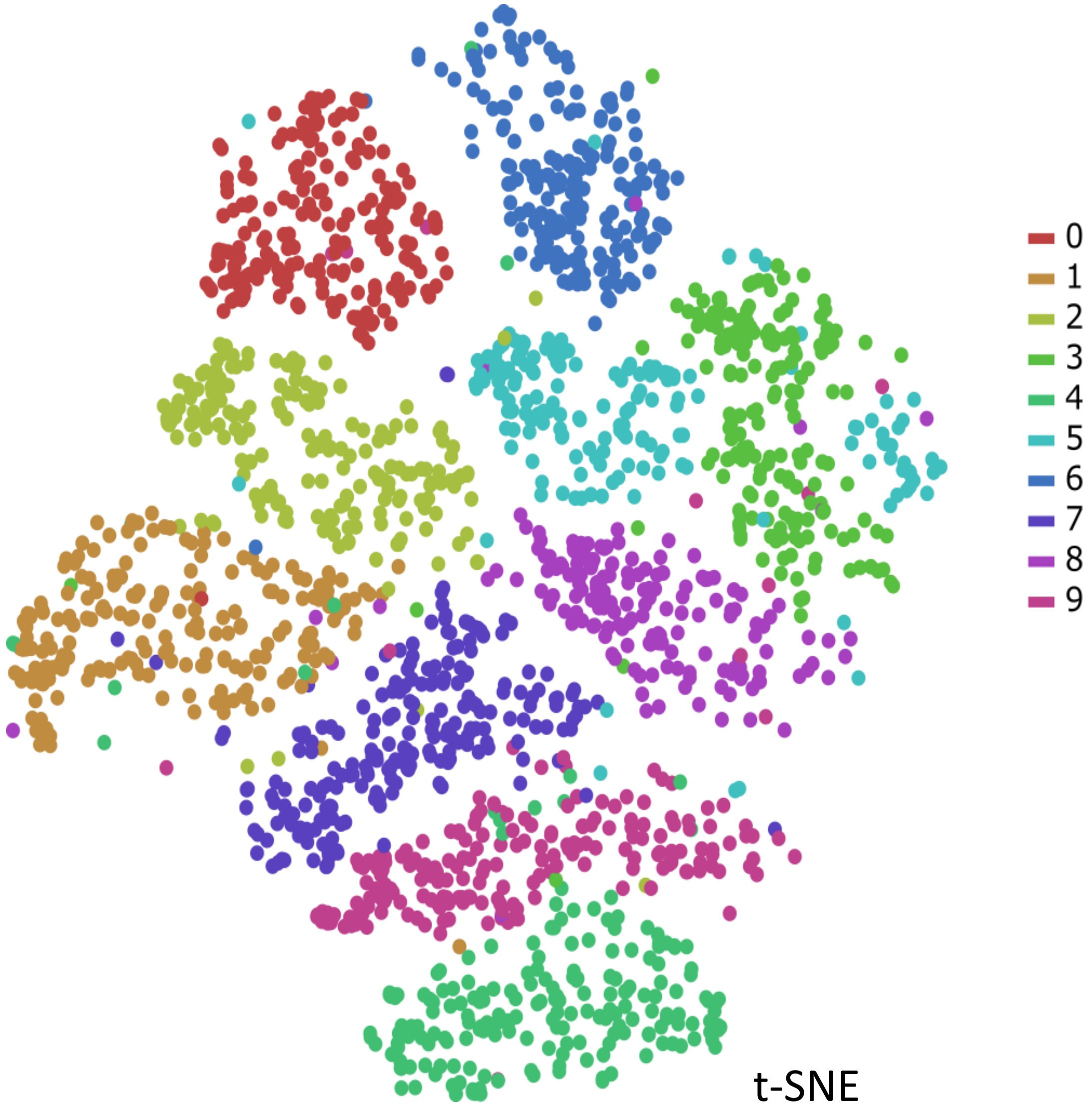


$$\boldsymbol{v} = \{\underbrace{ttc_1, ttc_2, \ldots, ttc_N}\}$$

Imaging-derived features per voxel

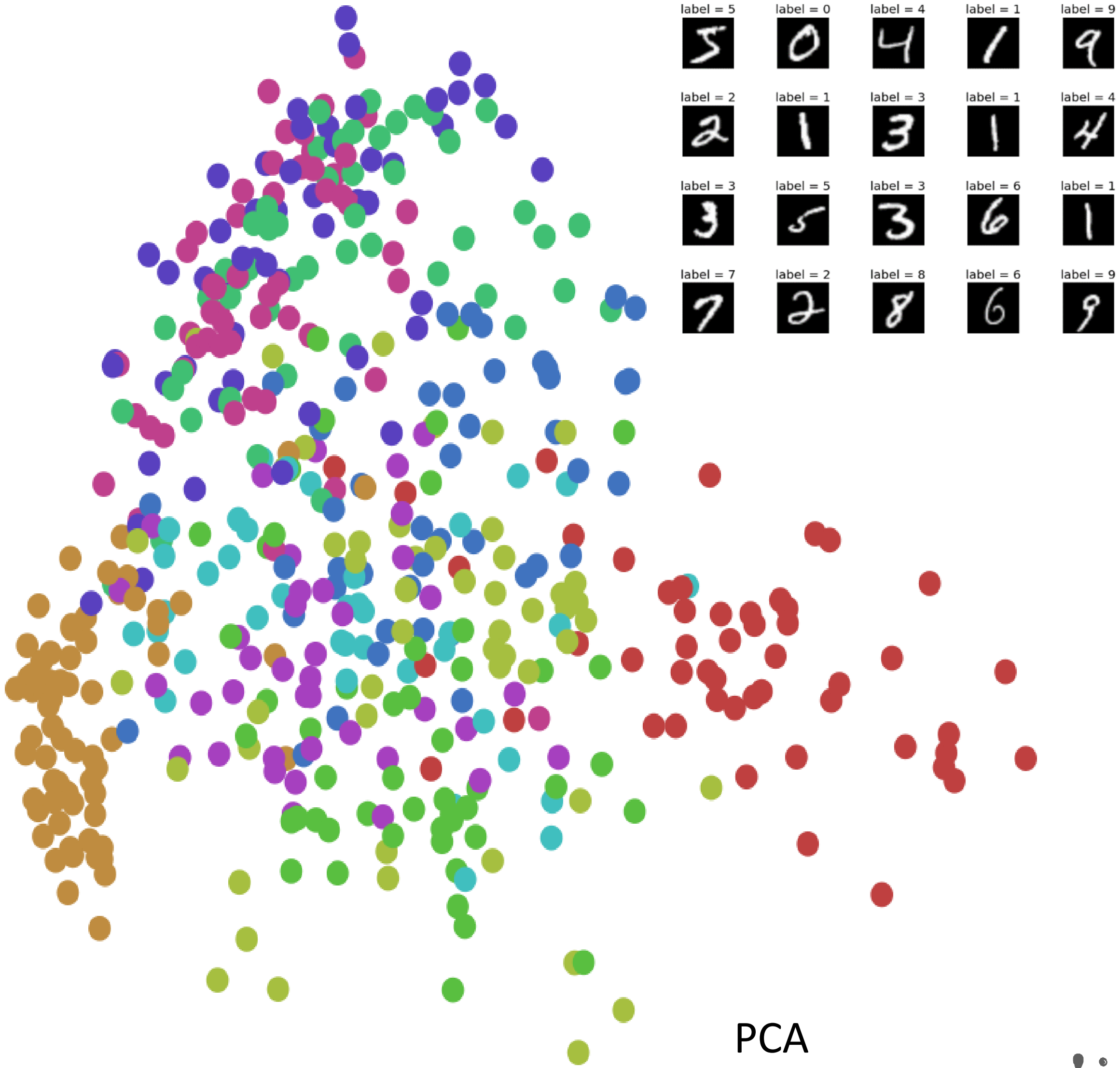
t-Distributed Stochastic Neighborhood Embedding (**tSNE**) - L. van der Maaten, 2008

PCA vs. t-SNE



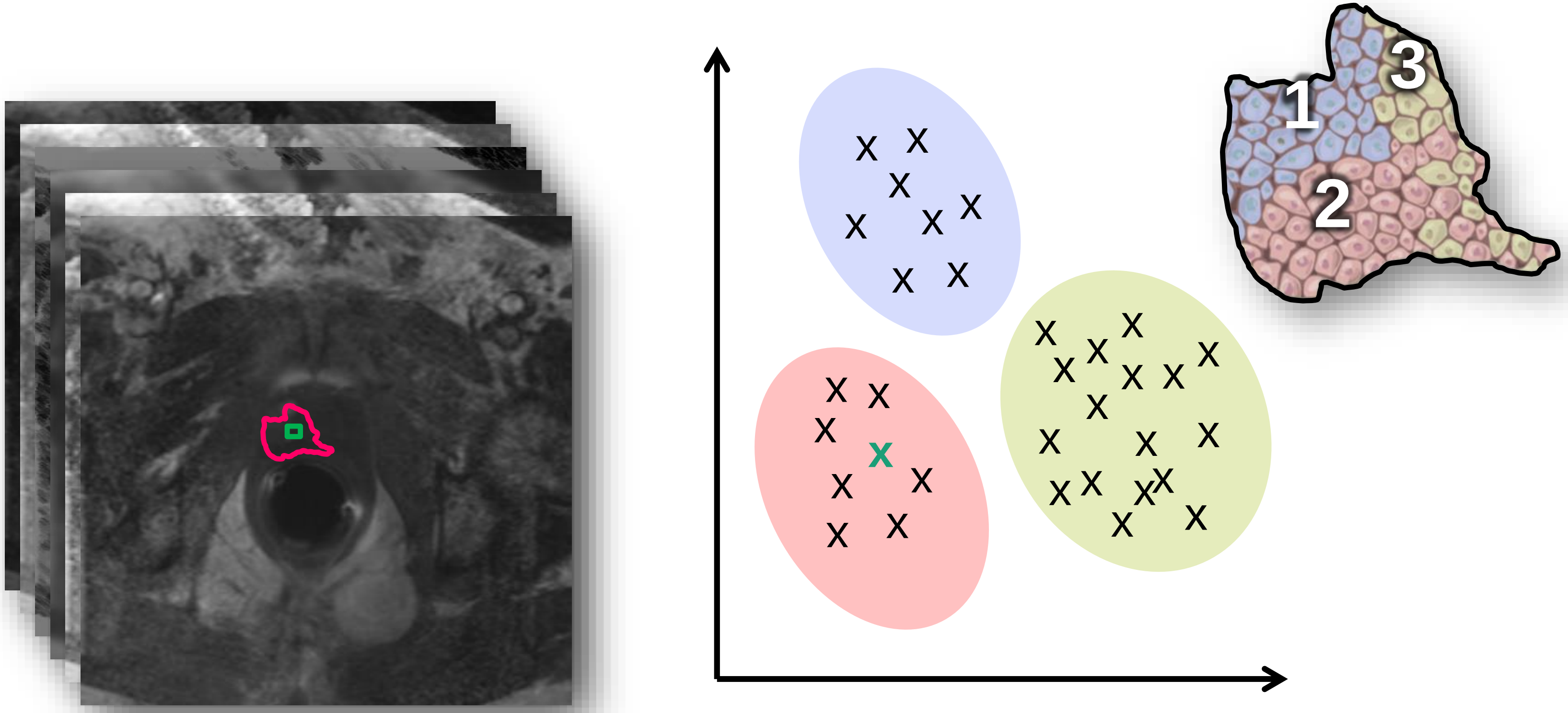
t-SNE

MNIST dataset example



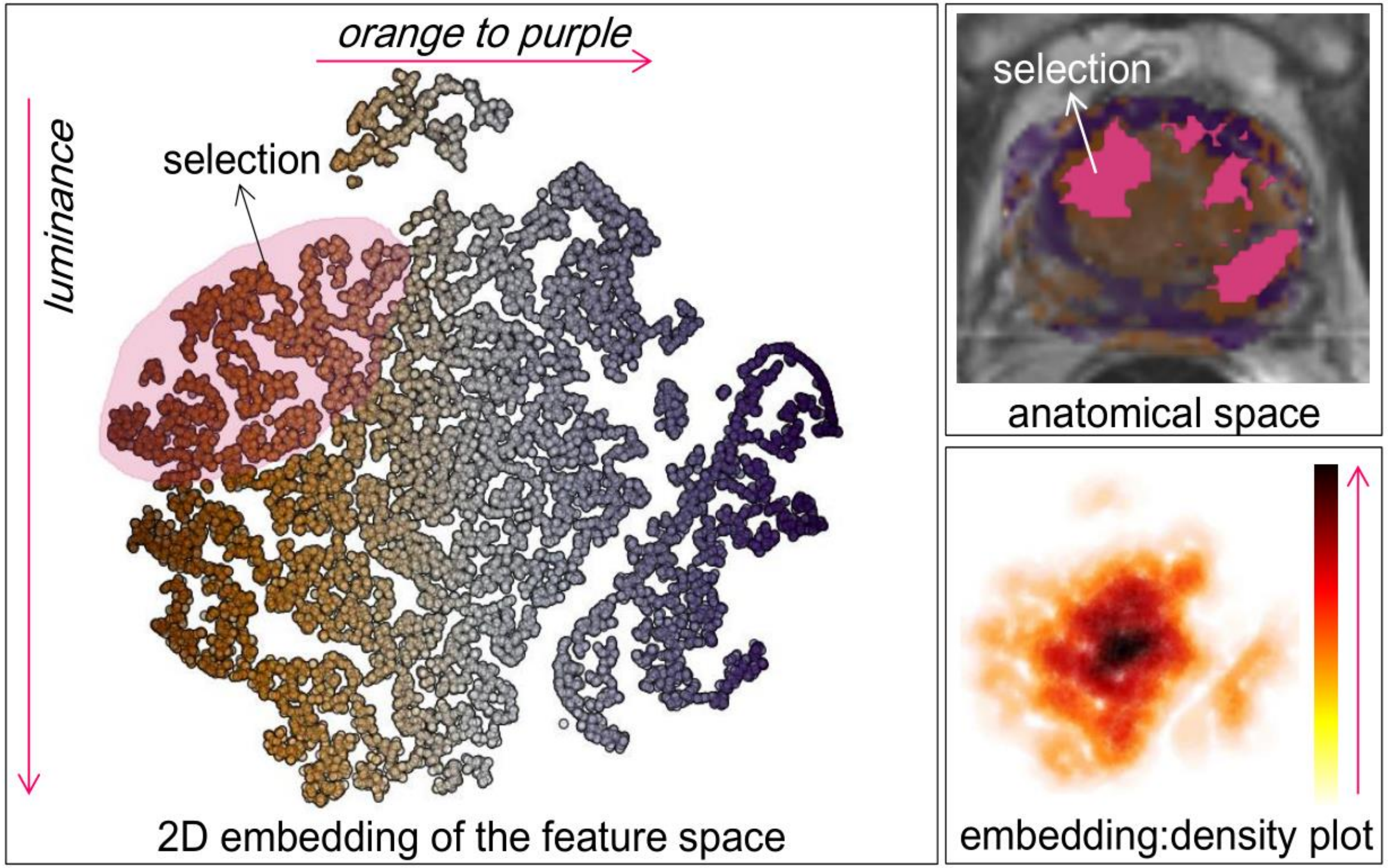
PCA

1. Identification and Exploration of Intra-tumor Regions

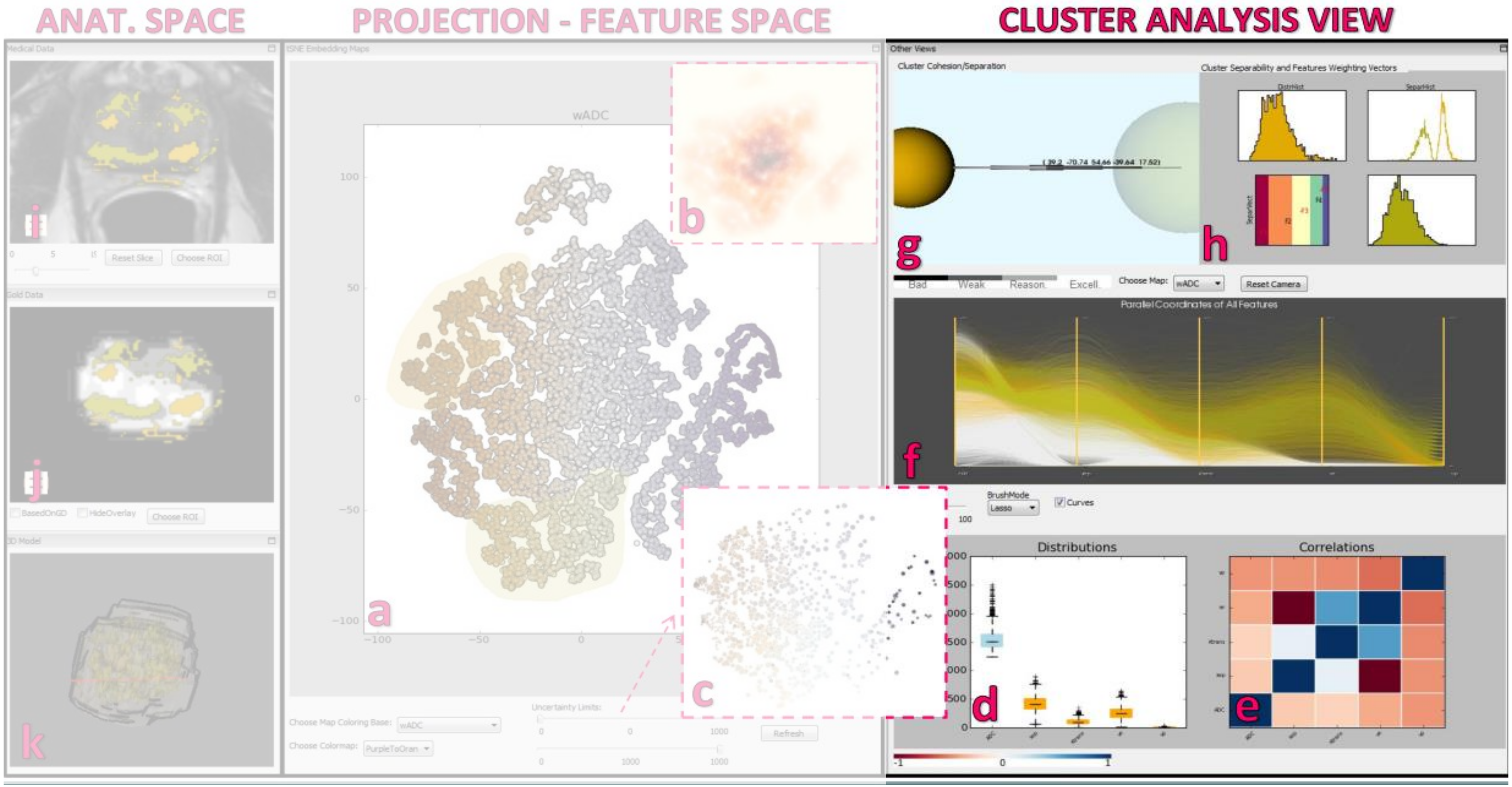


t-Distributed Stochastic Neighborhood Embedding (**tSNE**) - L. van der Maaten, 2008

1. Identification and Exploration of Intra-tumor Regions



2. Analysis and Comparison of Intra-tumor Regions



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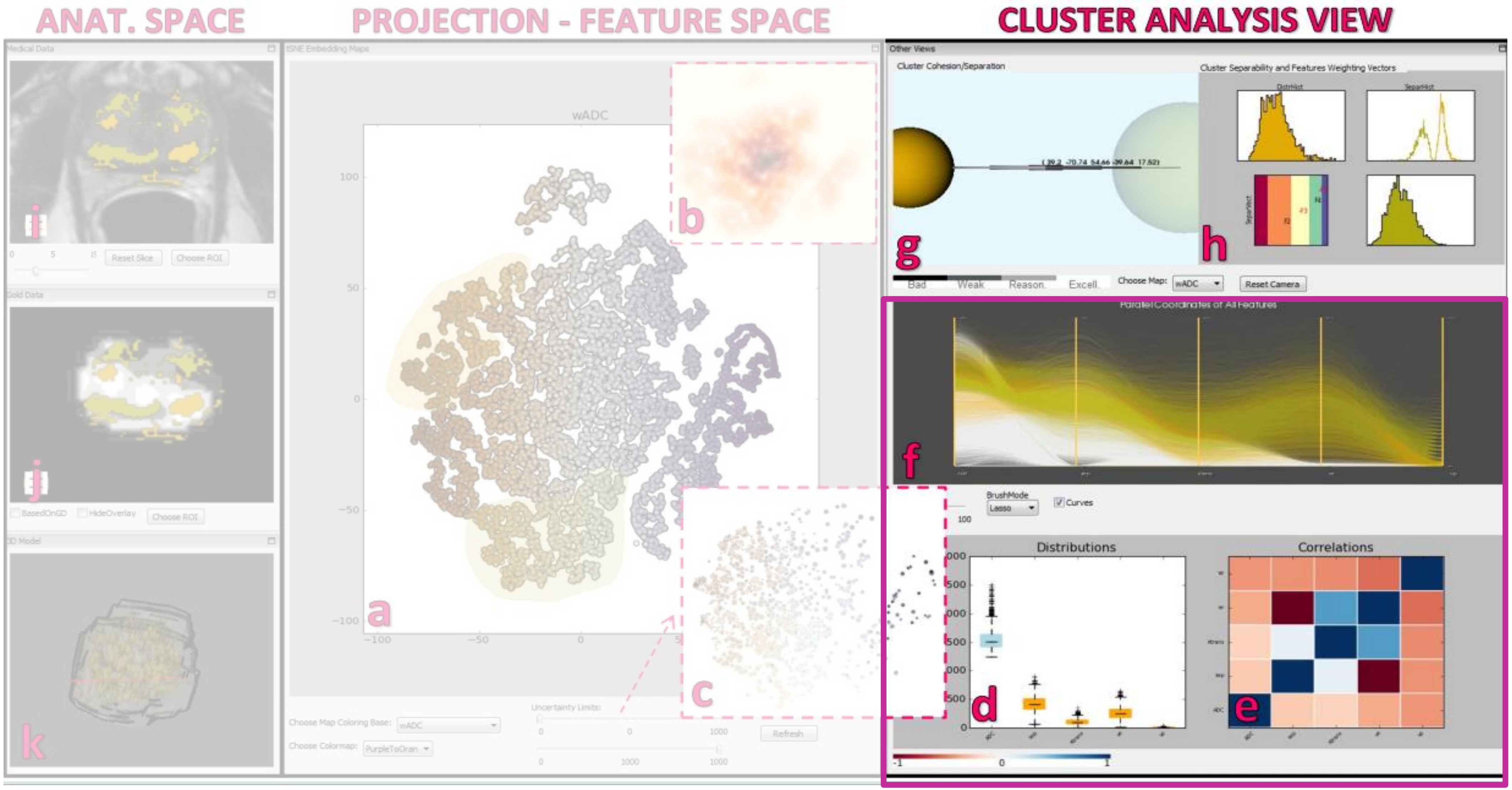

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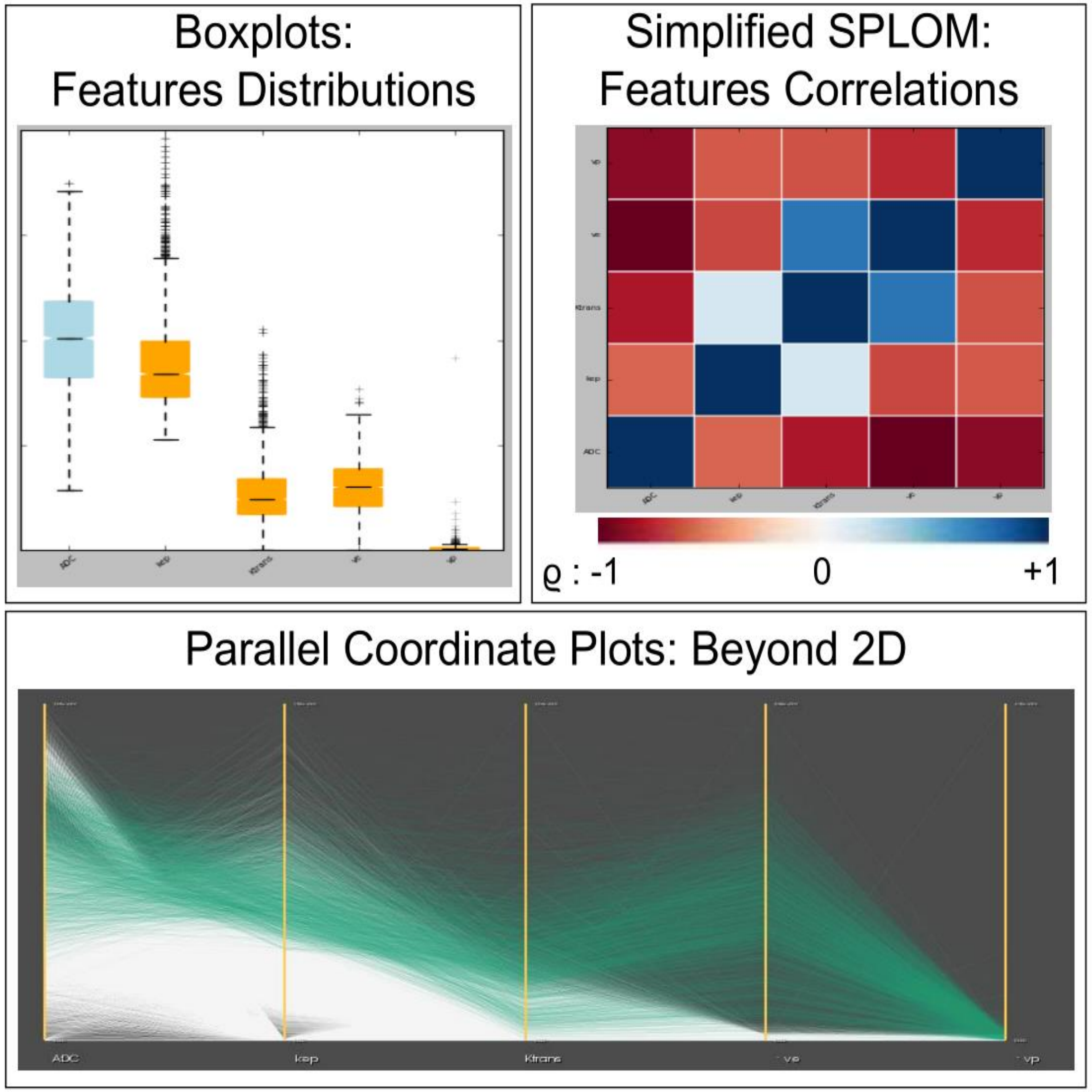

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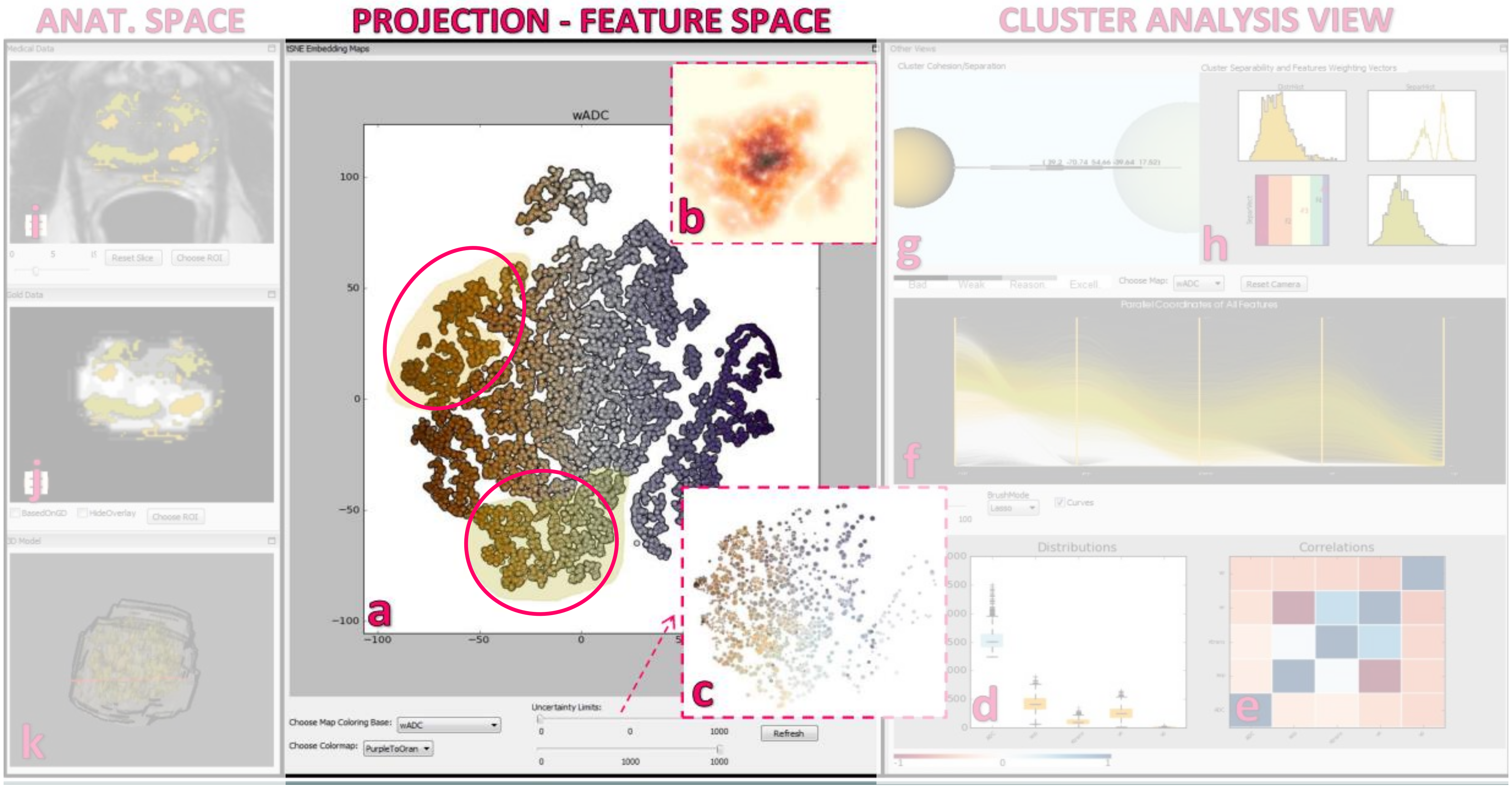

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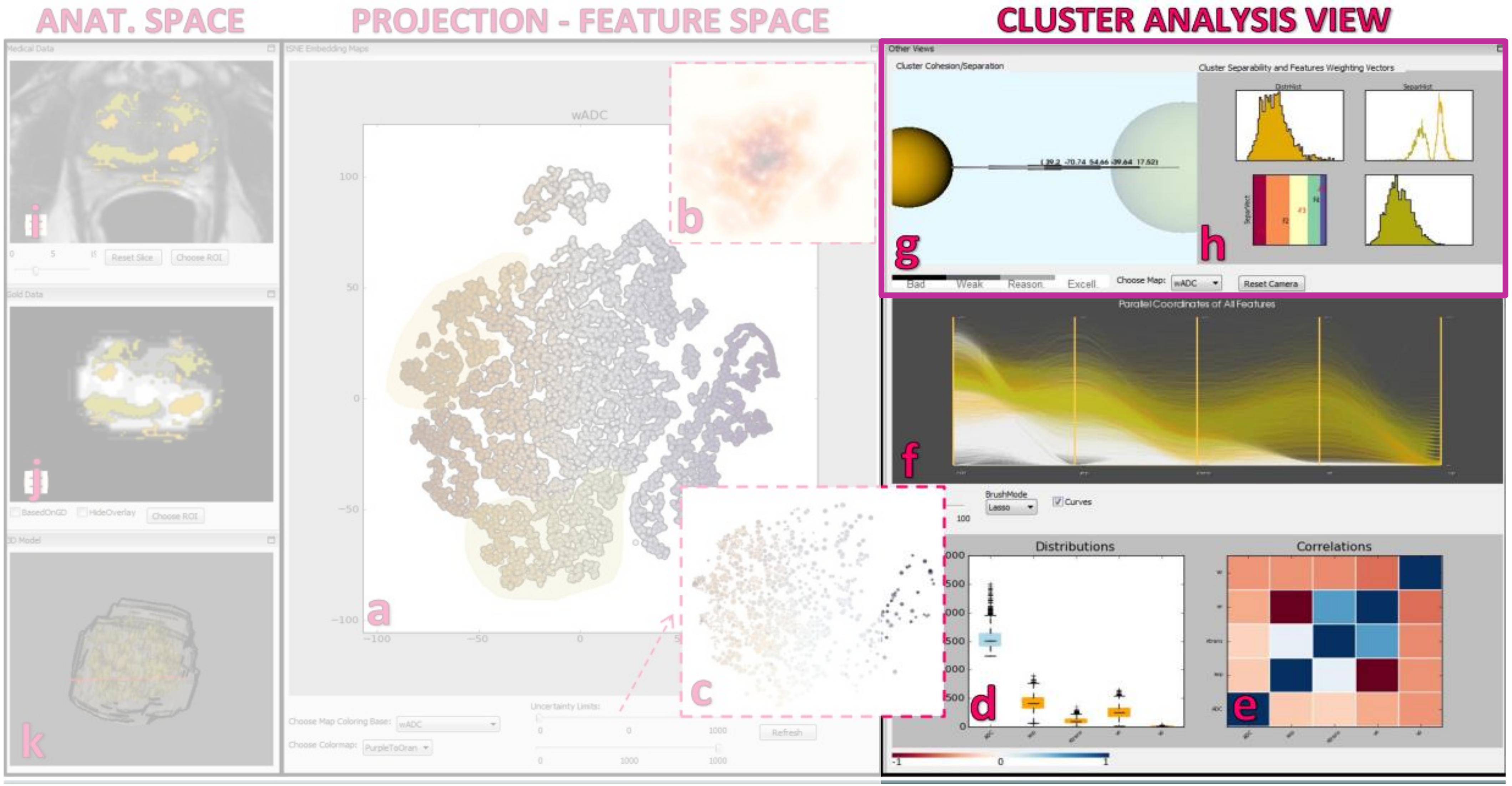
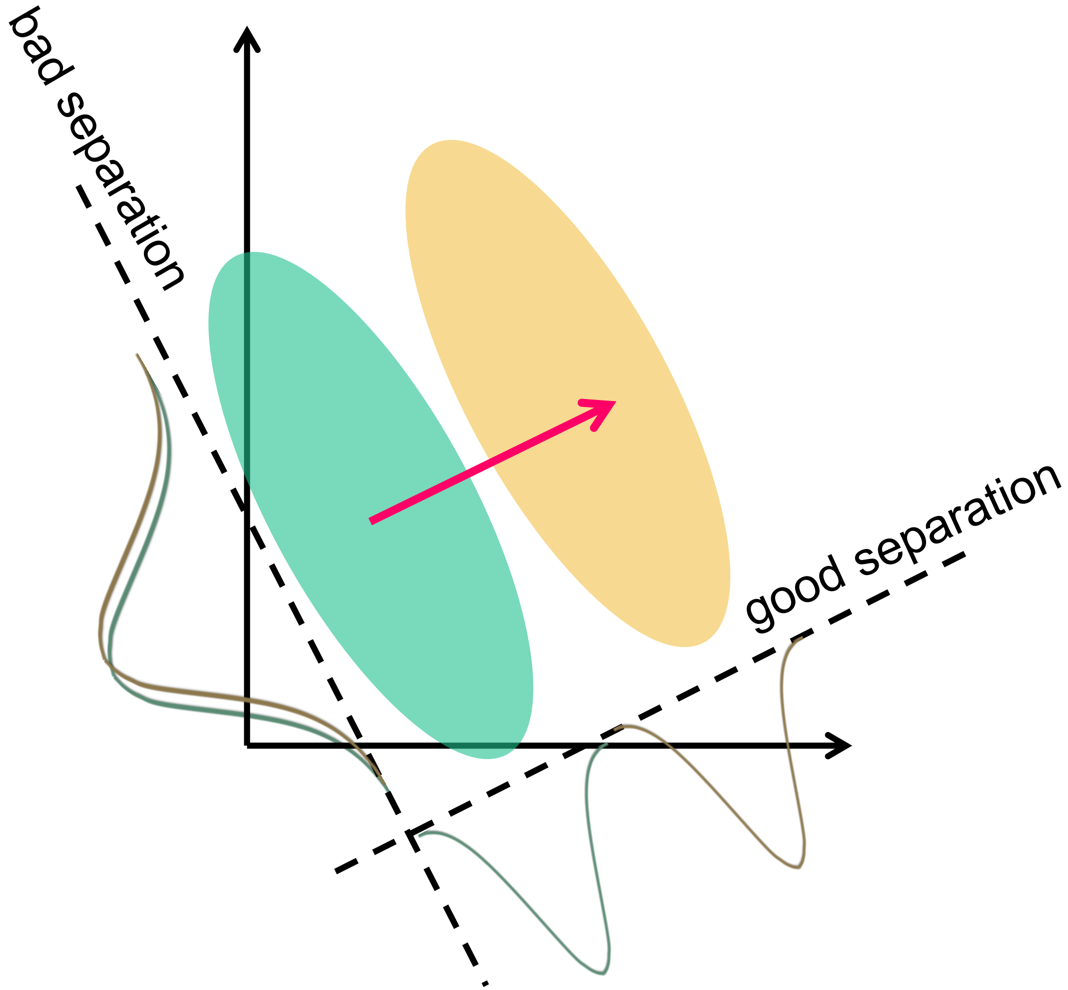
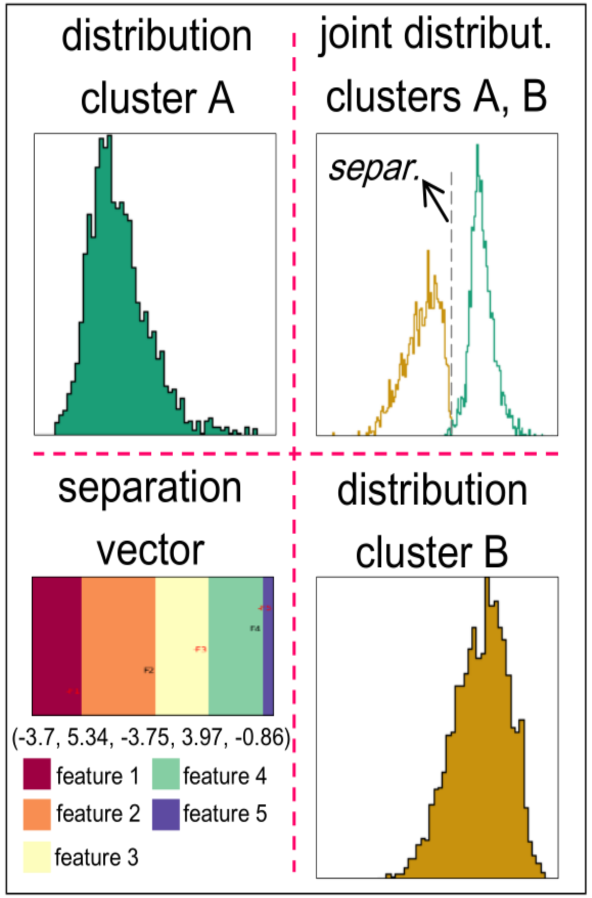
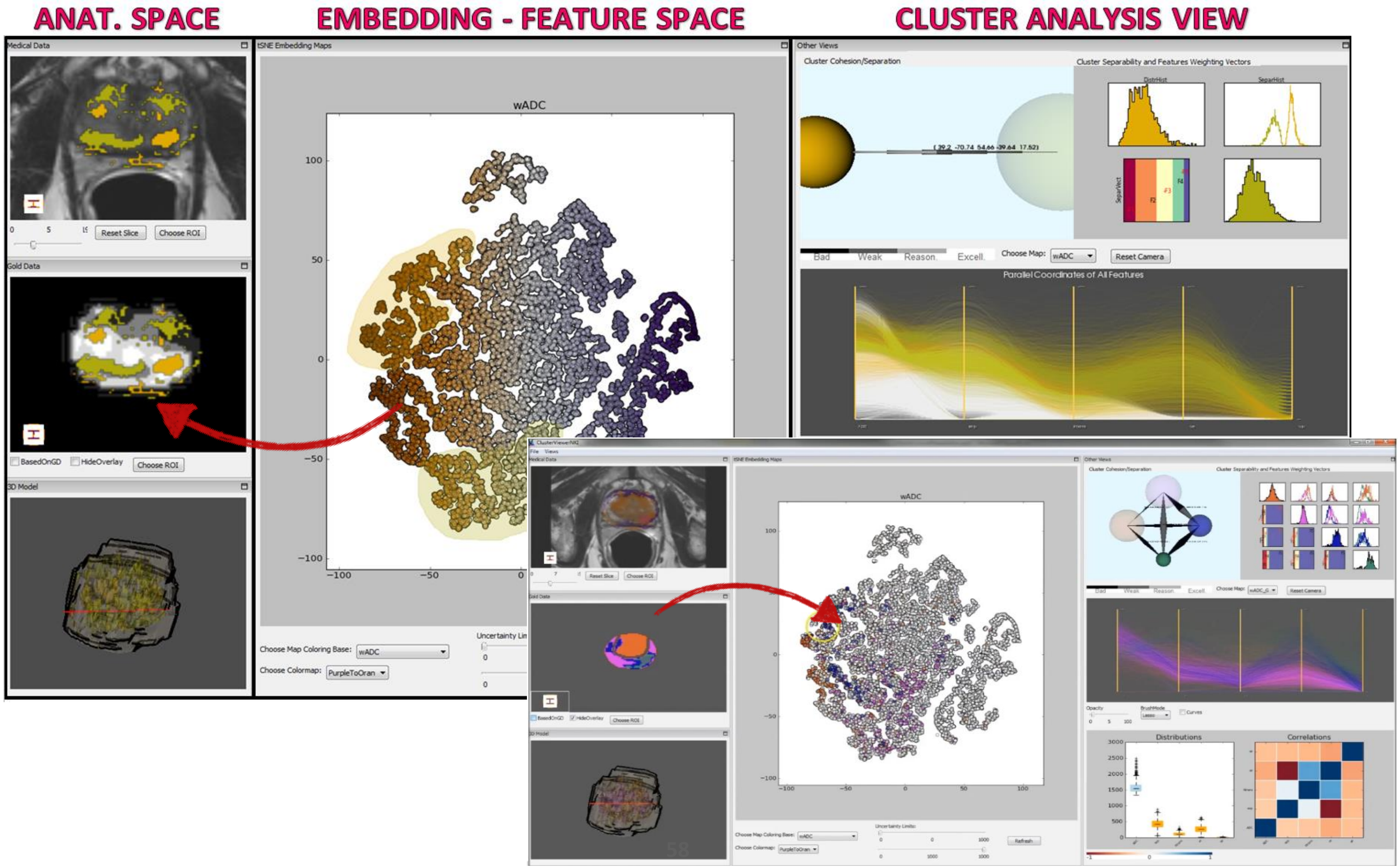


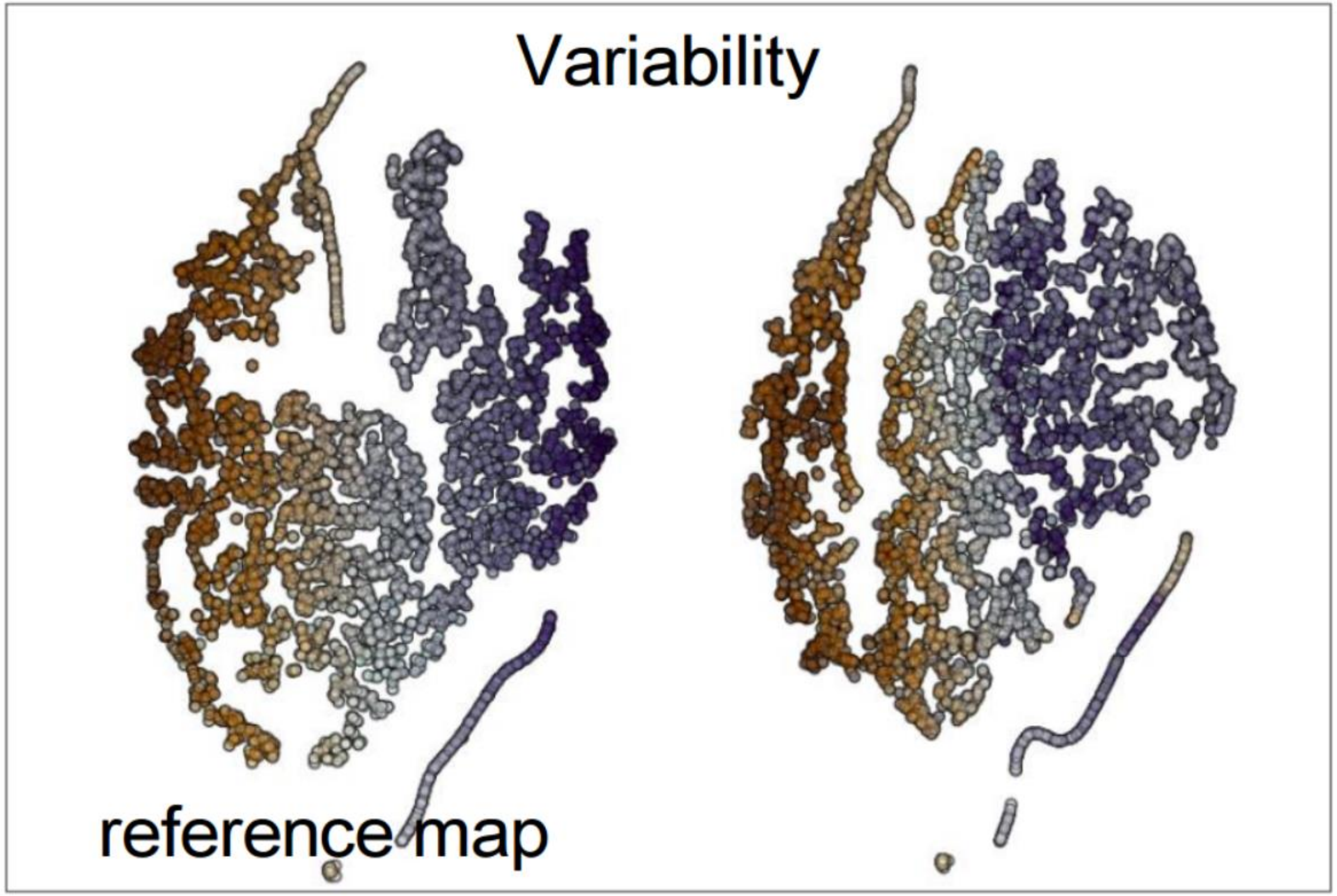

bad separation
good separation

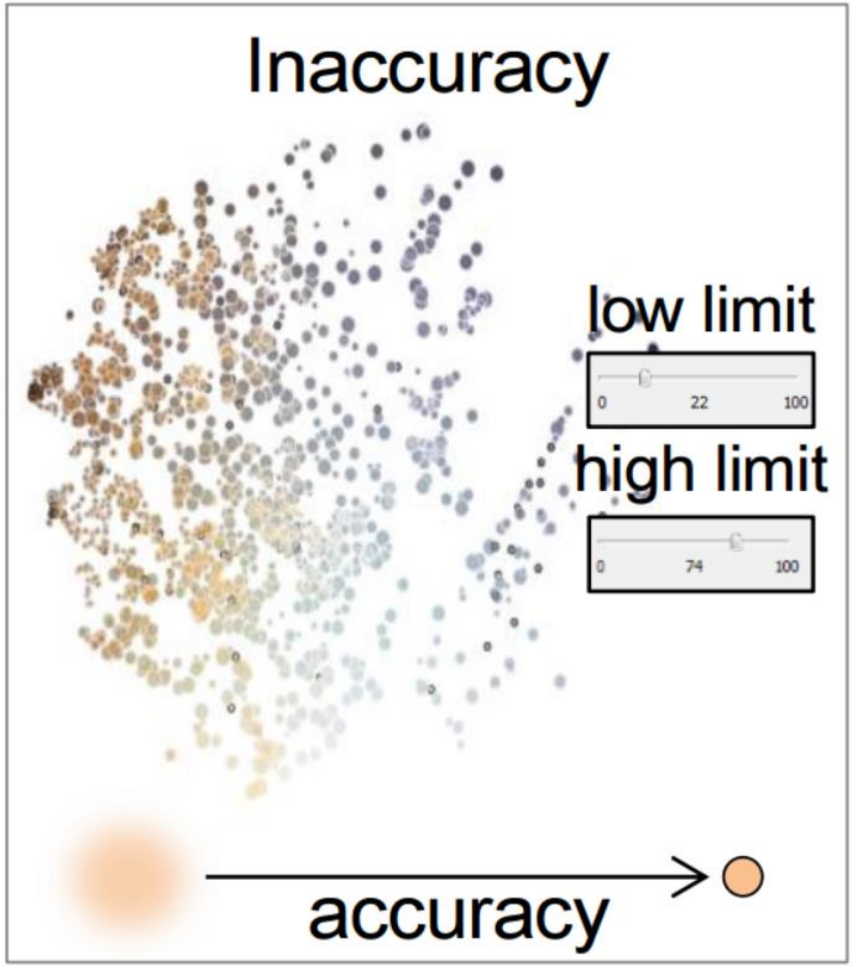

distribution
cluster A
joint distribut.
clusters A, B
separ.
separation
vector
distribution
cluster B
(-3.7, 5.34, -3.75, 3.97, -0.86)
feature 1
feature 2
feature 3
feature 4
feature 5

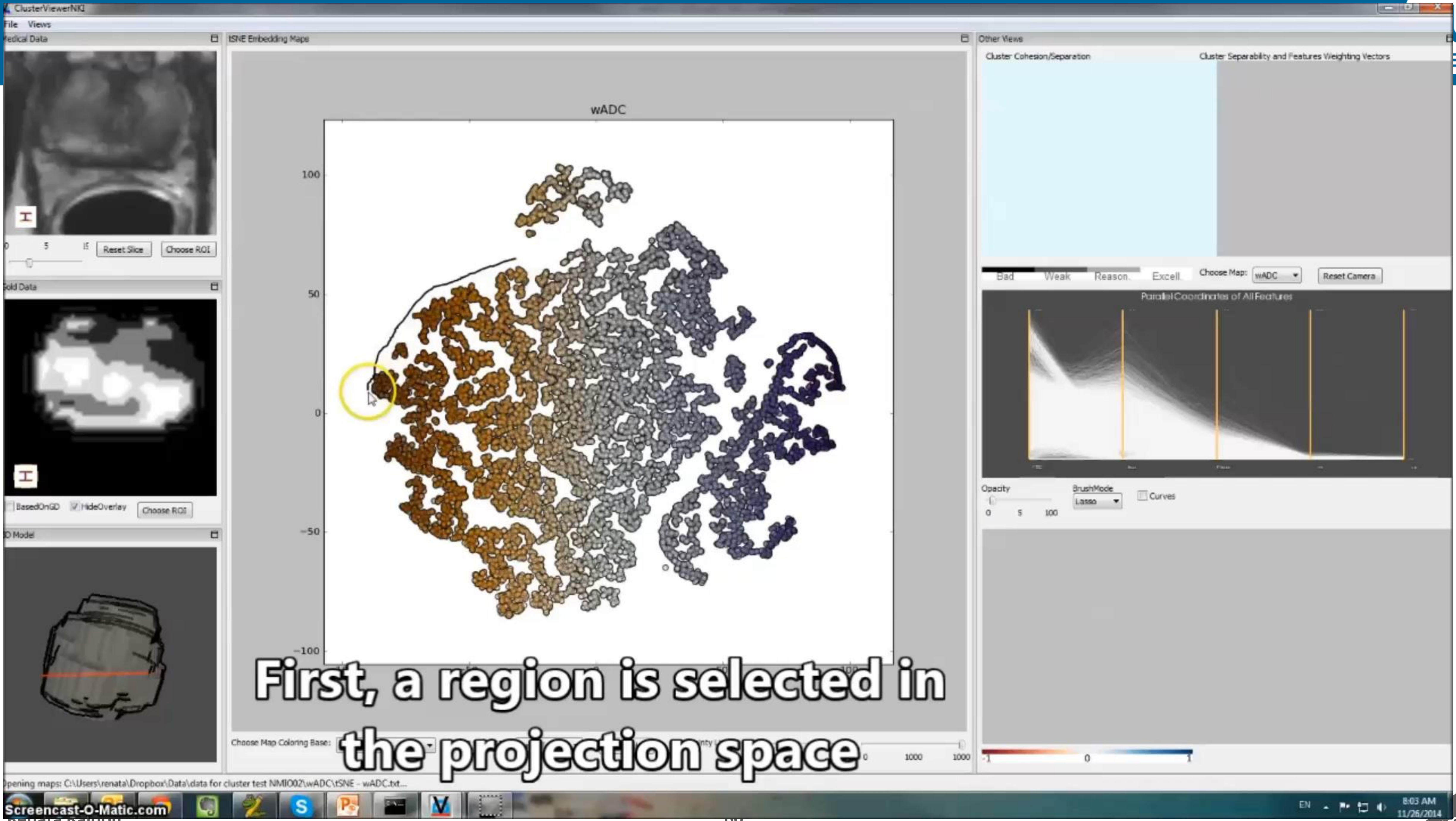
3. Association to clinical reference data

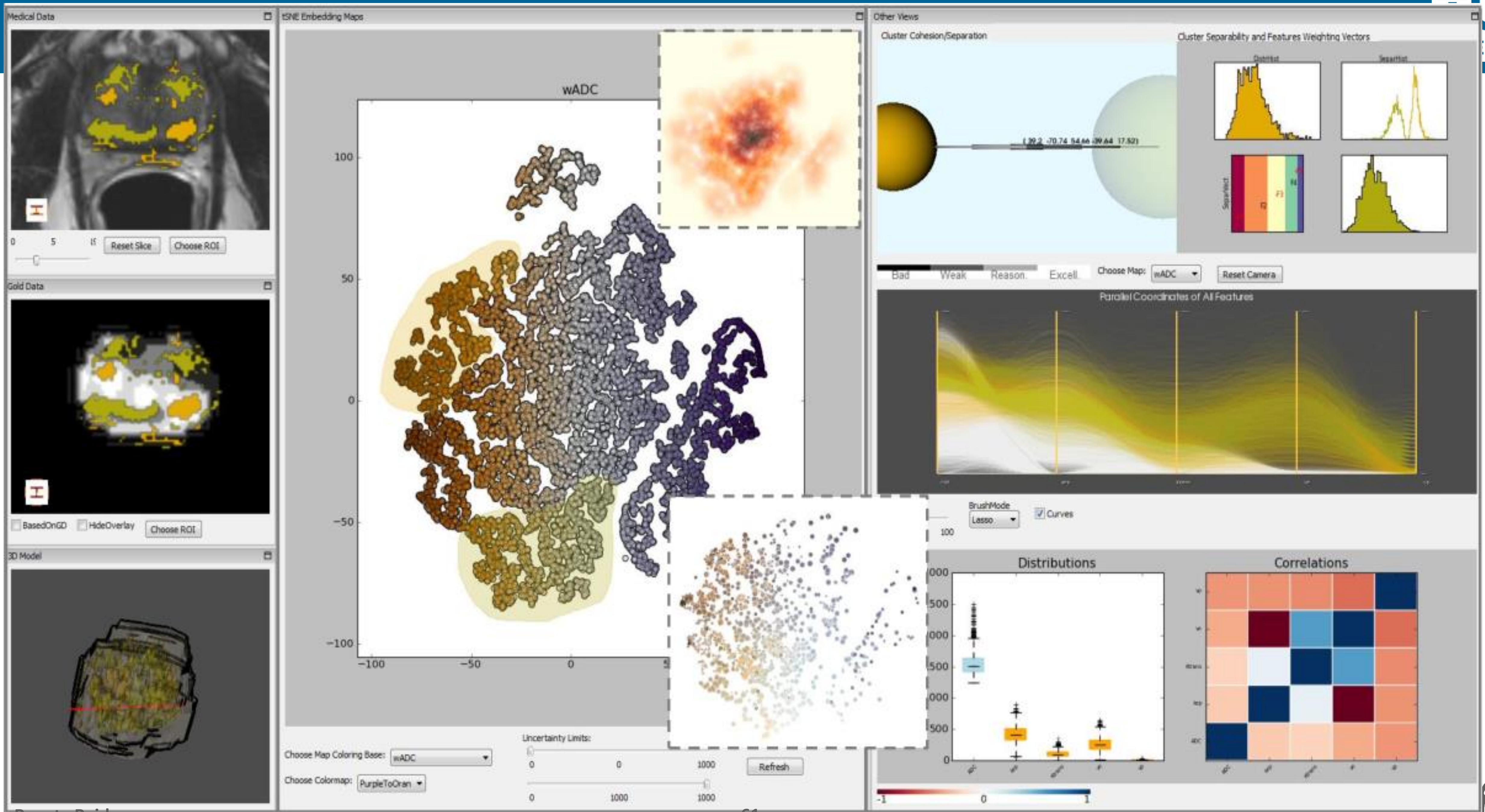


4. Effect of Variability/Inaccuracy






ClusterViewerNKI
File Views
tSNE Embedding Maps
Other Views
wADC
Cluster Cohesion/Separation
Cluster Separability and Features Weighting Vectors
Bad Weak Reason. Excell.
Choose Map: wADC
Reset Camera
Parallel Coordinates of All Features
Opacity
BrushMode Lasso
Curves
Reset Slice
Choose ROI
BasedOnGD
HideOverlay
Choose Map Coloring Base:
First, a region is selected in the projection space
Screencast-O-Matic.com


Medical Data
Reset Slice
Choose ROI
Gold Data
BasedOnGD
HideOverlay
Choose ROI
3D Model
tSNE Embedding Maps
wADC
Choose Map Coloring Base:
wADC
Choose Colormap:
PurpleToOran
Uncertainty Limits:
Refresh
Other Views
Cluster Cohesion/Separation
Cluster Separability and Features Weighting Vectors
Bad
Weak
Reason.
Excell.
Choose Map:
wADC
Reset Camera
Parallel Coordinates of All Features
BrushMode
Lasso
Curves
Distributions
Correlations

Applications

- Prostate Tumor Exploration
  - With Histopathological Data → Simple imaging features not enough for GS
  - With Risk Prediction Data → Current prediction models are sub-optimal

- Cervical Tumor Exploration
  - Validation of Different Models

- Lung Tumor Exploration
  - Evaluate the importance of multi-modal imaging in region detection

- Smart Feature Selection for Aiding the Design of Classifiers

Applications

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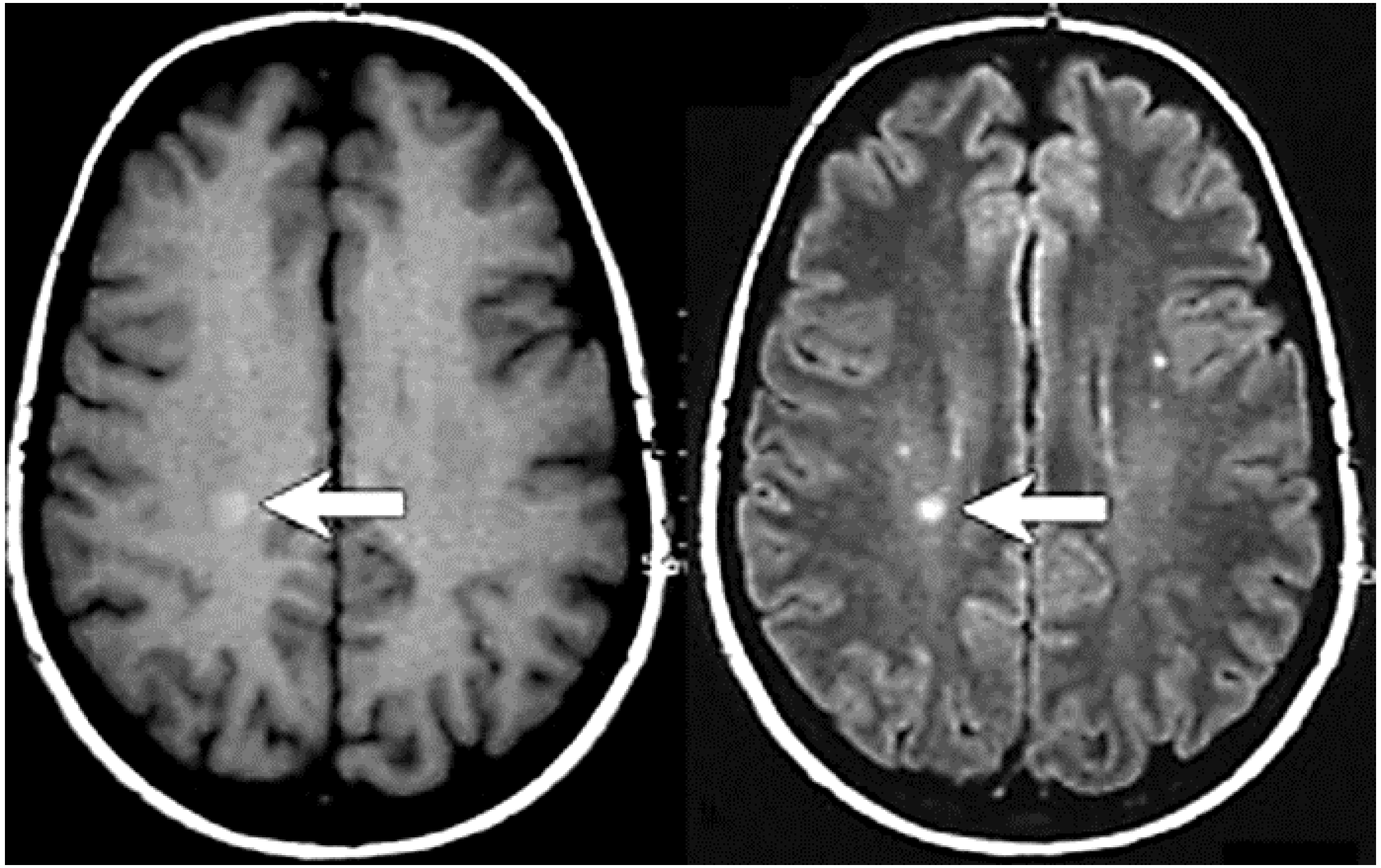
  - Evaluate the importance of multi-modal imaging in region detection

- **Smart Feature Selection for Aiding the Design of Classifiers**

White Matter Hyperintensities (WMH)



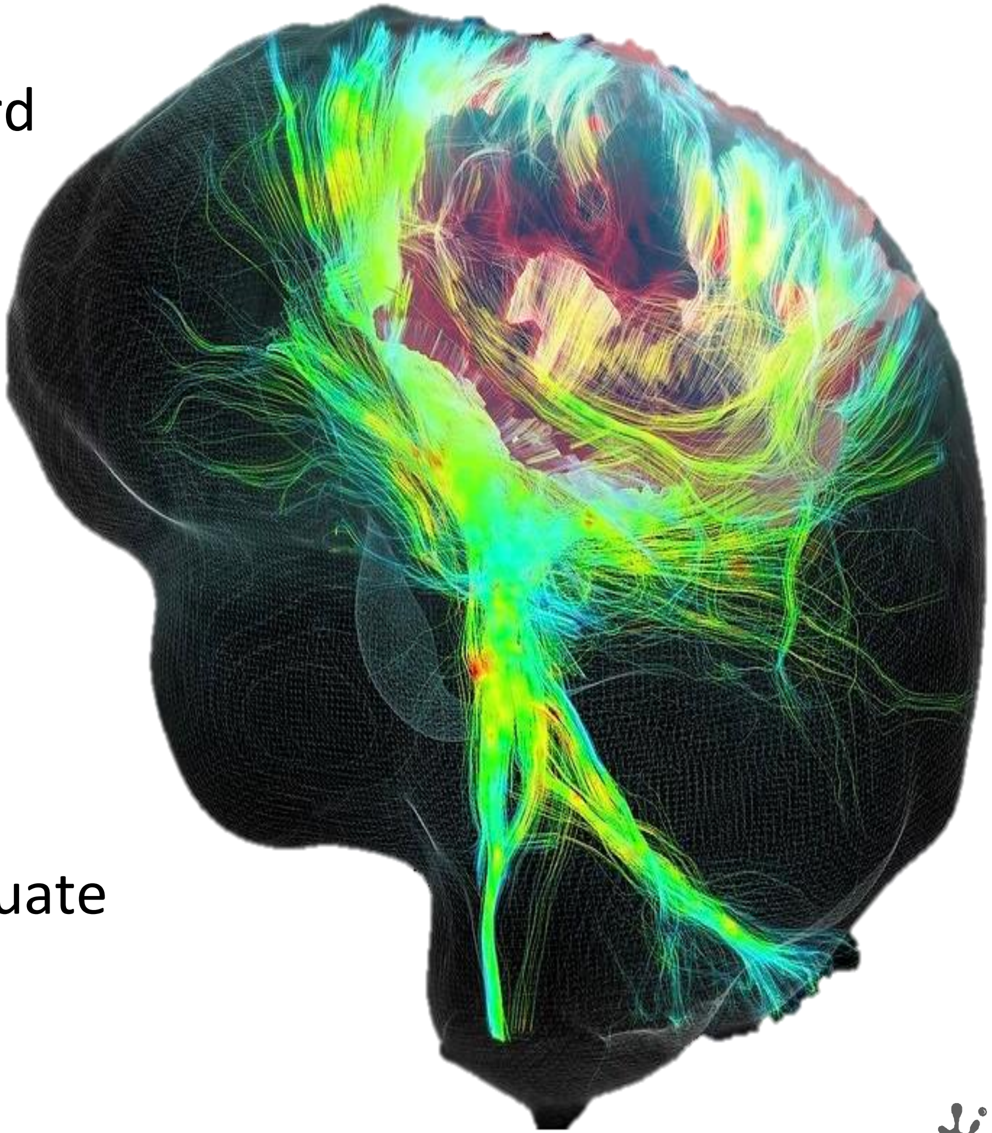
Segmentation for prognosis and disease monitoring

Motivation

- Conventionally: T1 and T2.
- Diffusion MRI can provide additional features [Maillard 2013, Kuijf 2014]. Which features of all?

- Careful selection of features is more important than chosen classification algorithm [Sweeney 2014].
- Currently, this is a black box!

- A new pipeline, to aid the design of WMH classifiers.
- It provides new insight into the entire classification procedure, especially, in the identification of an adequate feature list, and the analysis of the outcome.

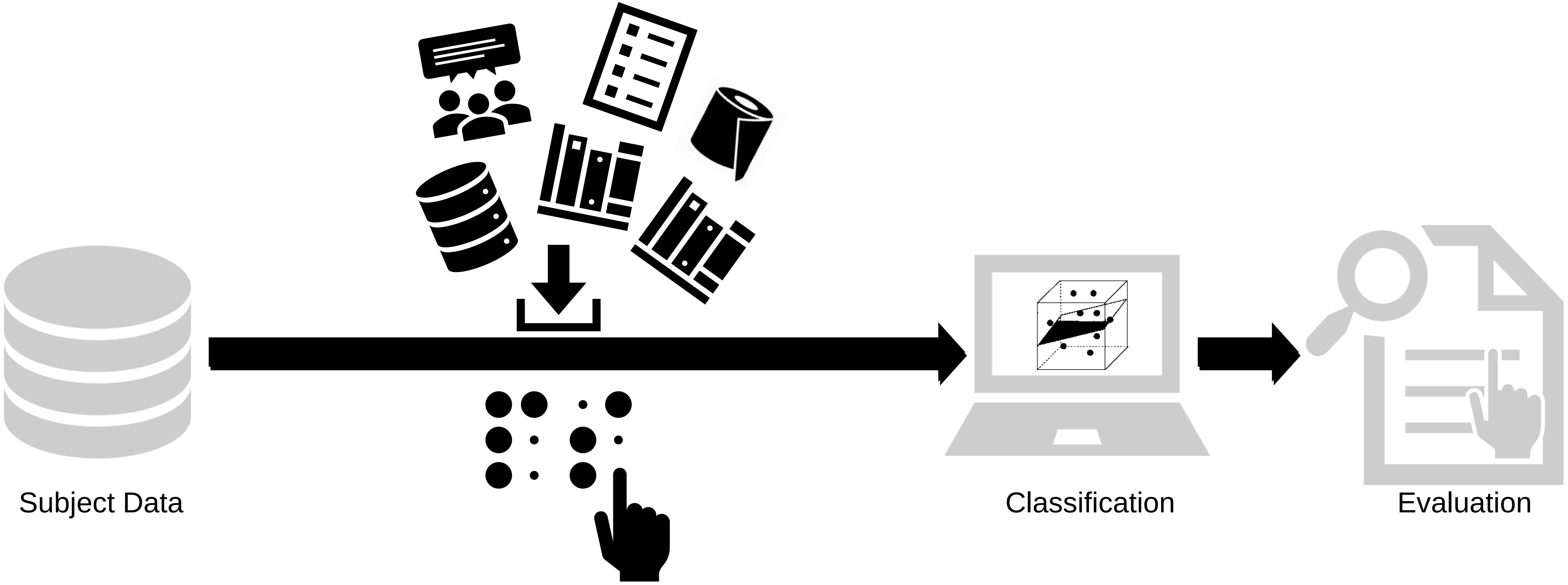


Materials

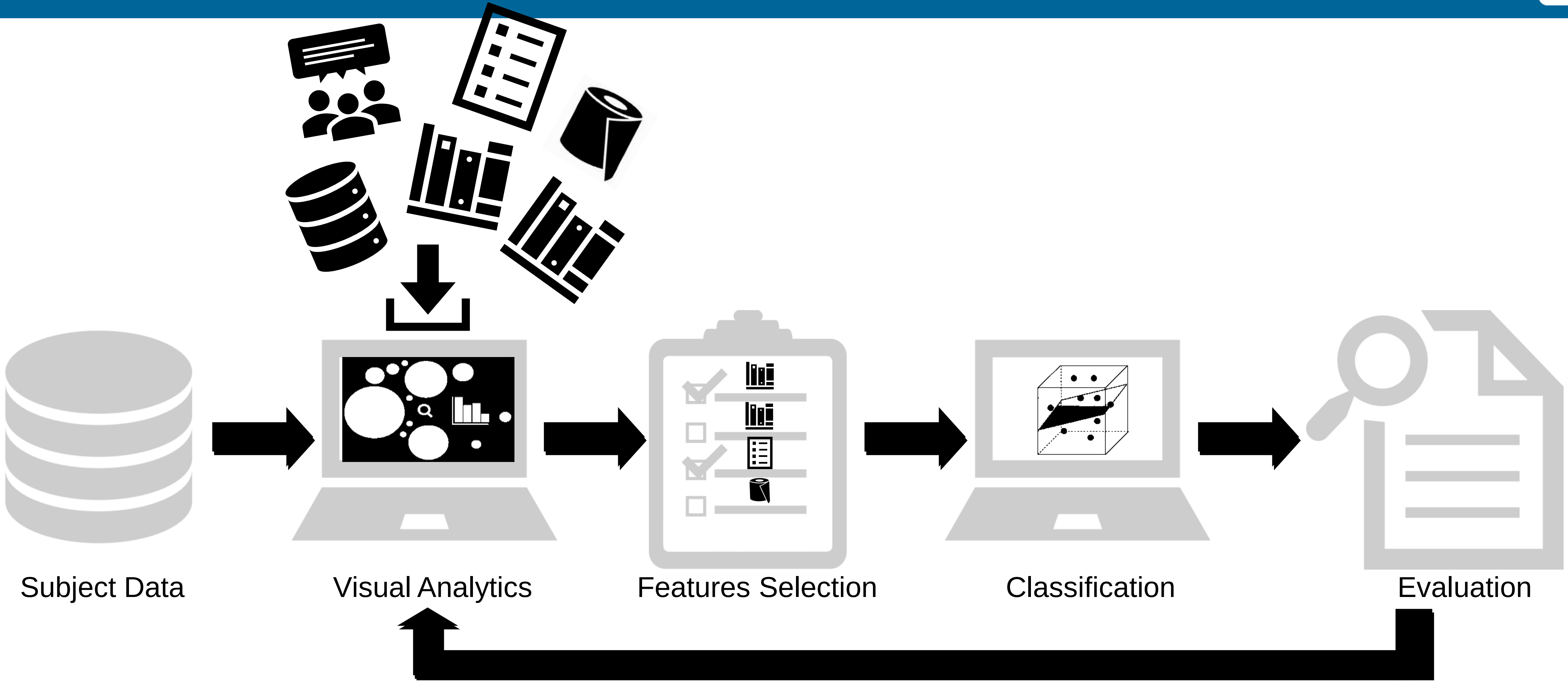
- 20 subjects of the MRBrainS13 challenge.
- Ground truth: manual delineations of WMH.

- 3T MR exam: T1-weighted, multi-slice FLAIR, multi-slice IR, single-shot EPI DTI sequence with 45 directions.
- Features: T1, FLAIR, IR, FA, MD, AD, RD, CL, CP, CS and the MNI152-normalized spatial coordinates [Kuijf 2014].

Current Method

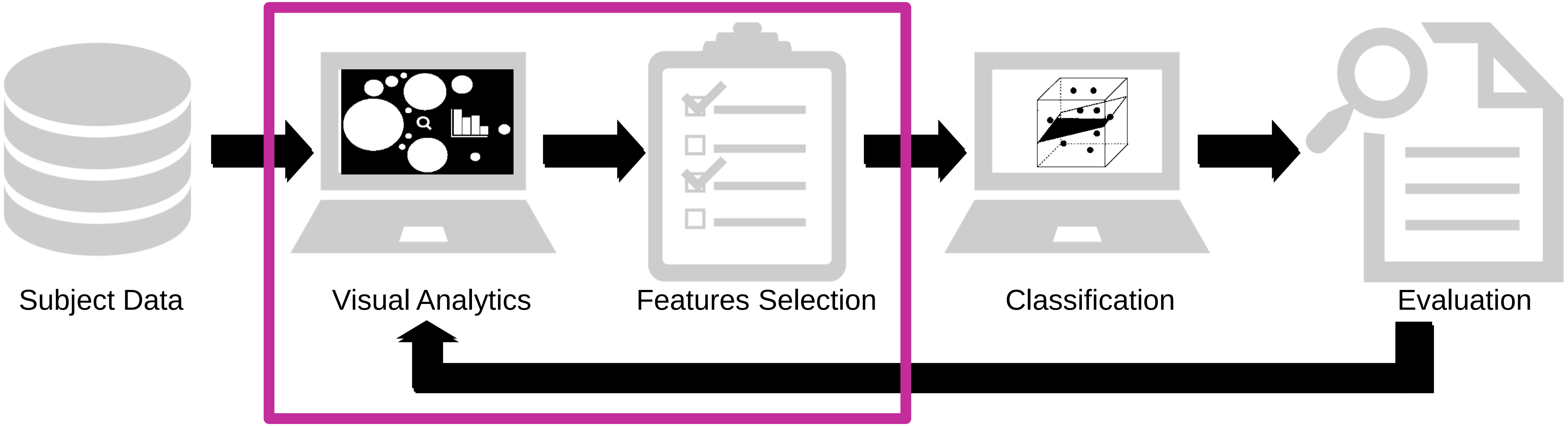


Our Method

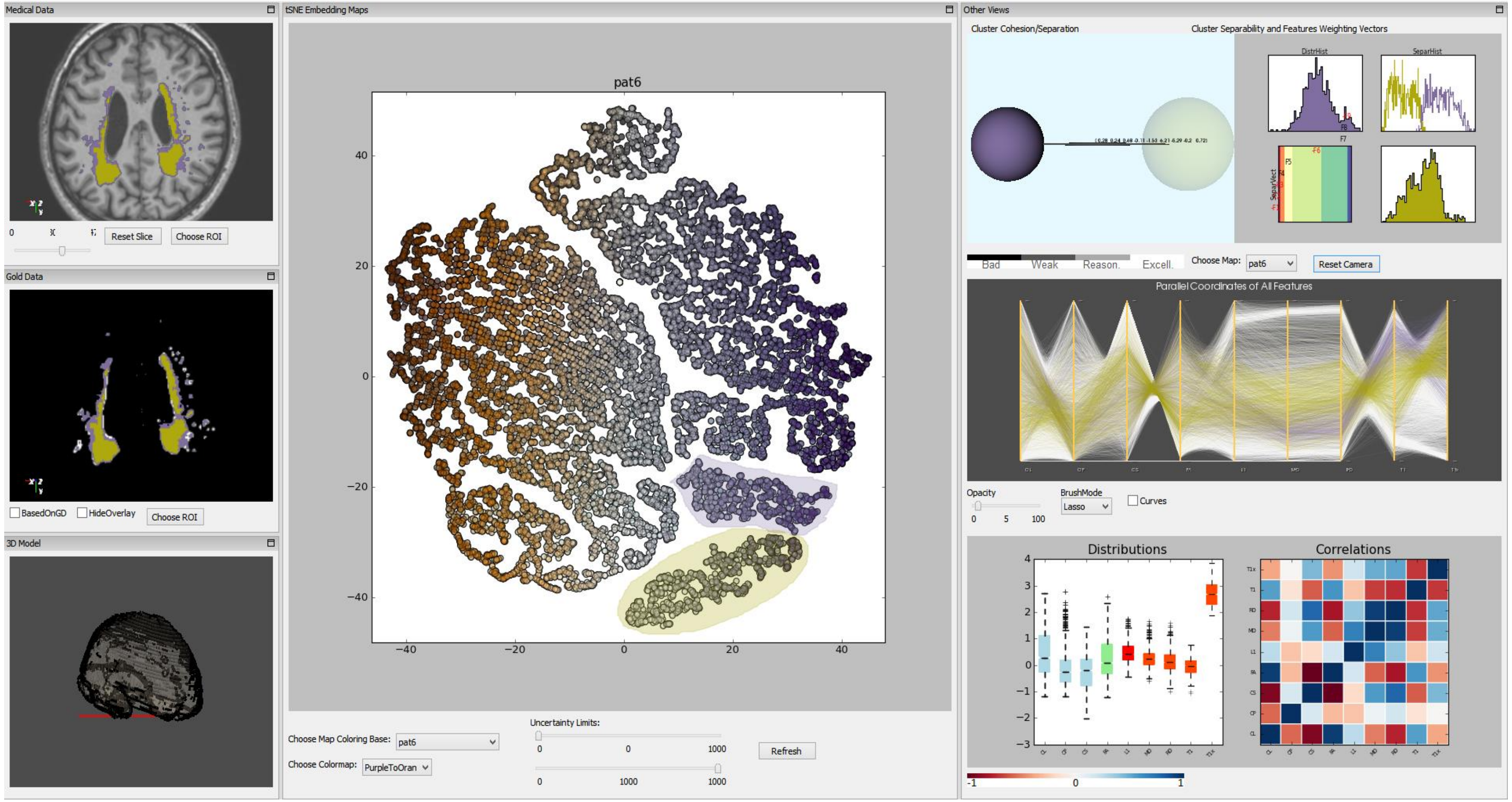


Subject Data
Visual Analytics
Features Selection
Classification
Evaluation

Step-by-step Approach and Results

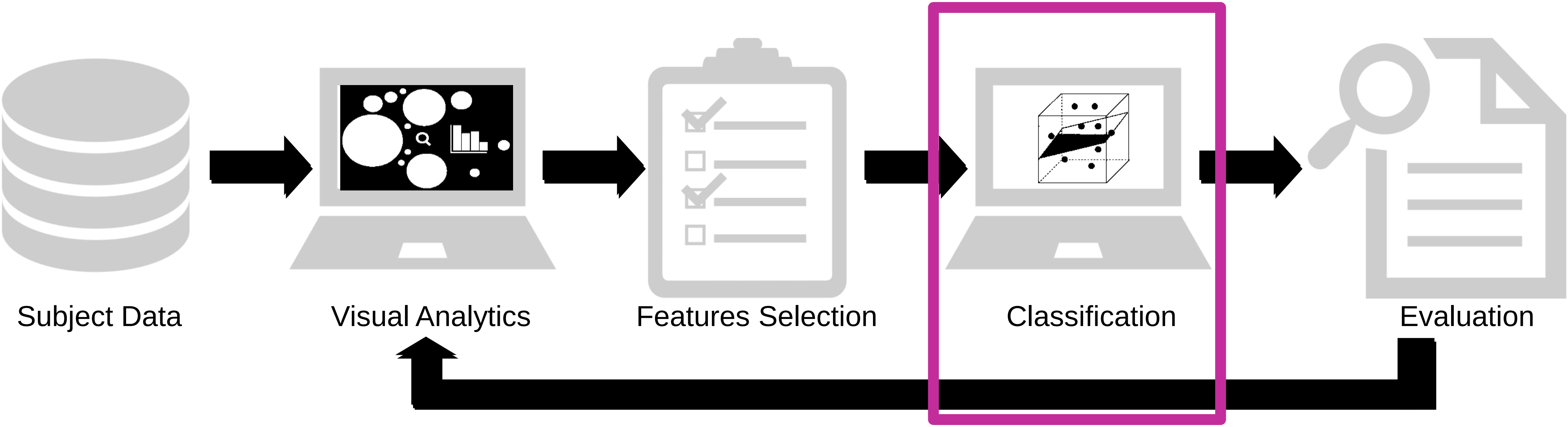


- Interactive exploration of the WMH structures and their intrinsic imaging-derived characteristics.
- Optimal set of features for the classifier is the combination of (T2-FLAIR, MD, RD, FA, Cs) + T1 & MNI152-normalized spatial coordinates → IR, AD, CL, CP out!



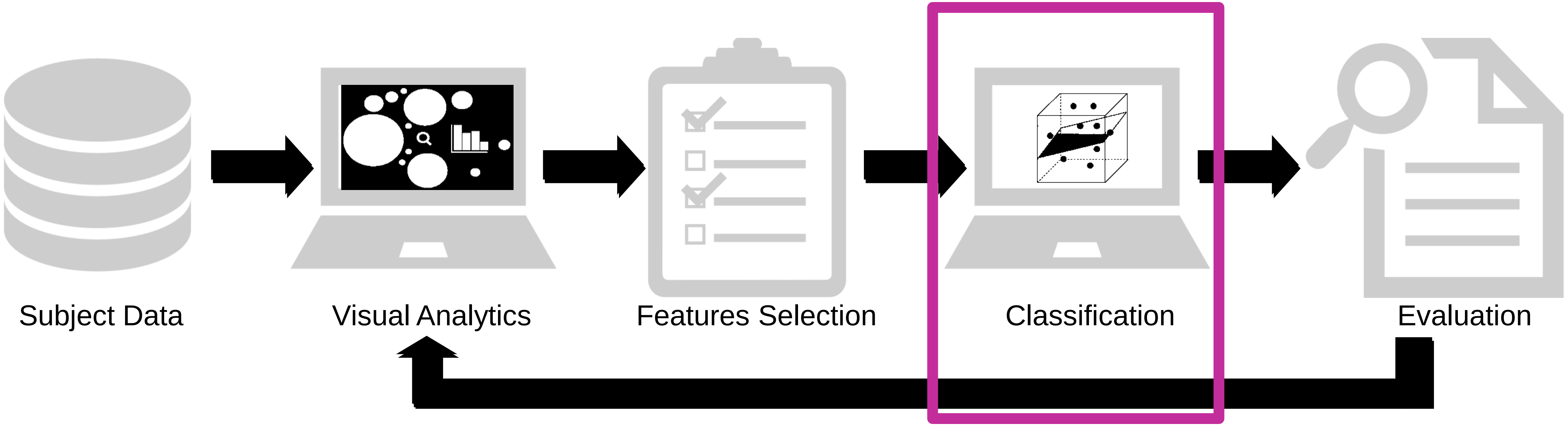
Step-by-step Approach and Results

As proof-of-concept and for comparison to previous work:
k-nearest-neighbor classifiers [Kuijf, 2014]
(k = 50, 75, or 100, uniform or distance-based)



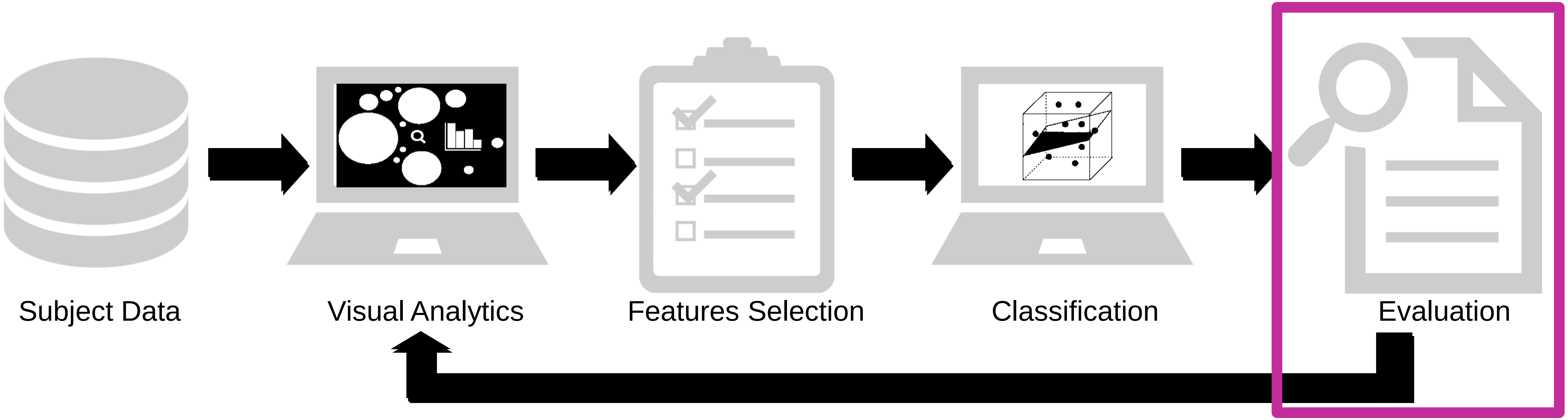
Step-by-step Approach and Results

Comparable results with previous automated approaches
Less features than in previous work
(saving scanning and computational time)
Smarter selection of features, not brute-force



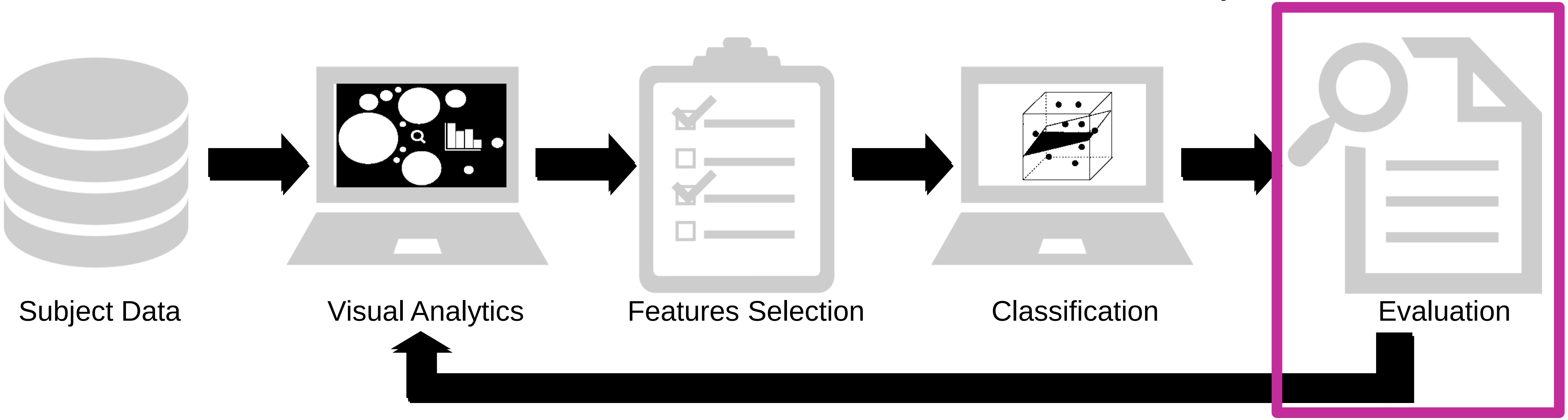
Step-by-step Approach and Results

Again with the VA tool
- What was missed?
- How the classifier works?
- How can the classifier be improved?



Step-by-step Approach and Results

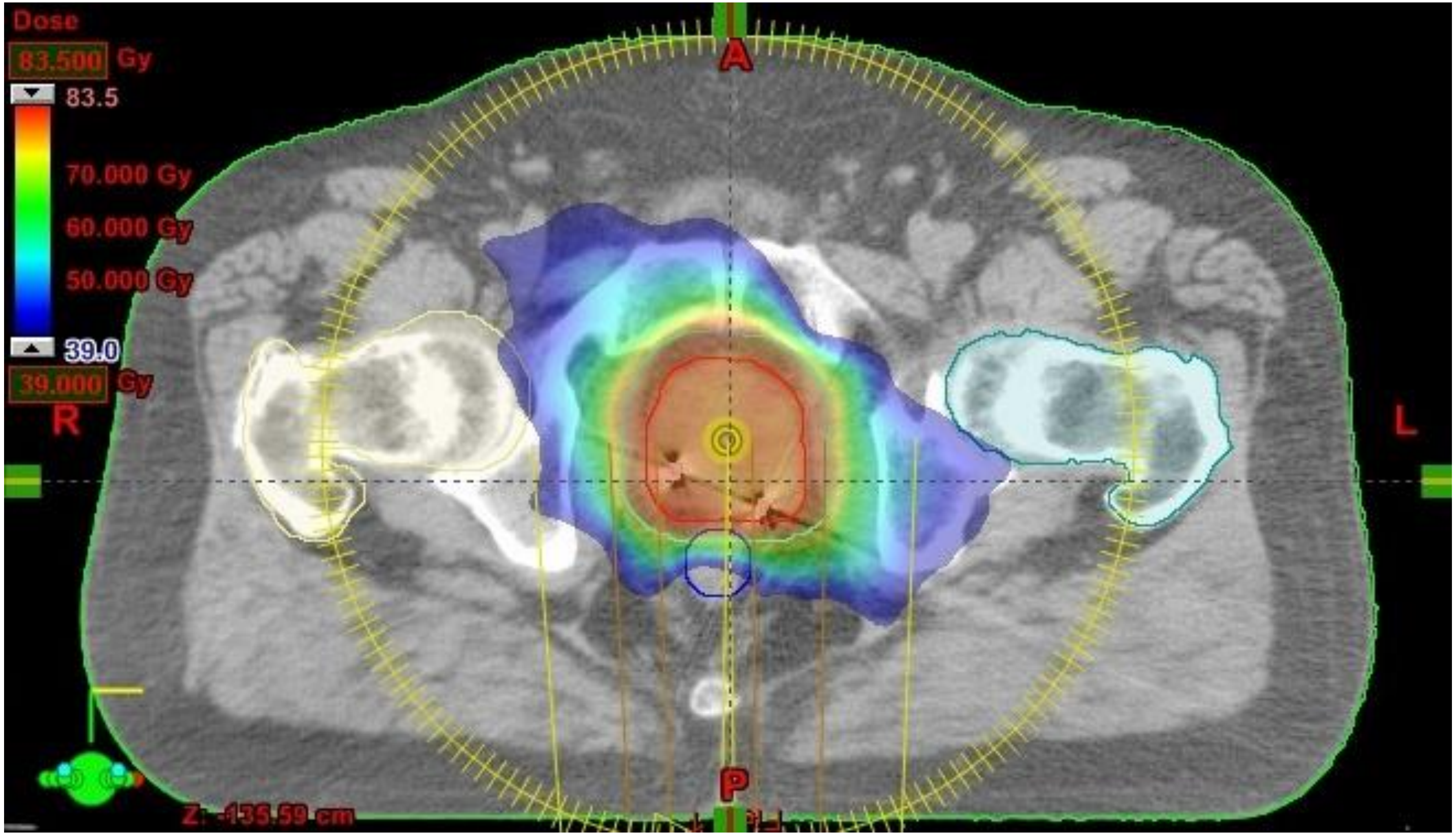
- Core is always detected, periphery is missed – different TCs?
- Posterior WMHs more often missed.
- For different sized WMHs different features more important.

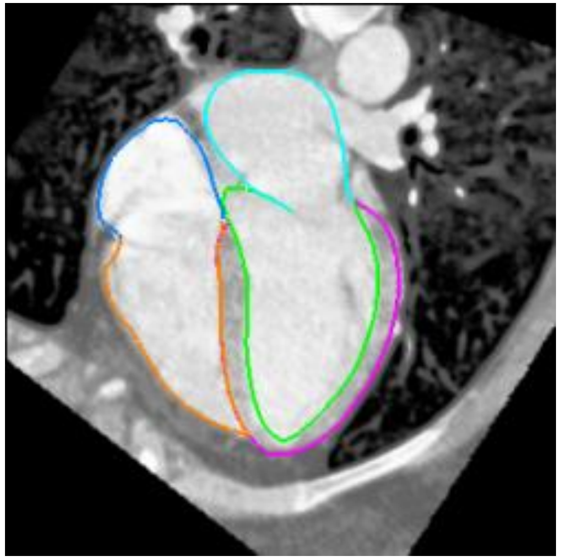


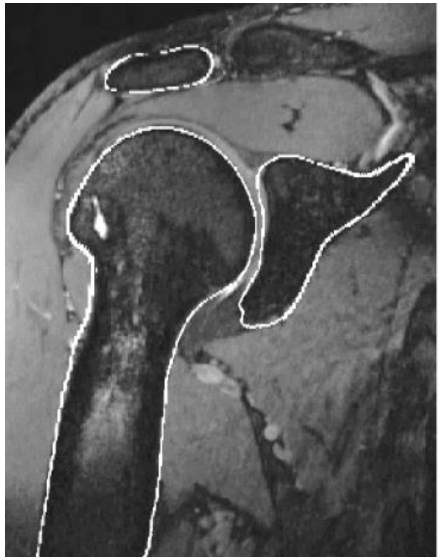
Conclusions

- Aiding the design of tissue classifiers in a “smart” way
- Understanding how features affect the result of the classifications
- Different parts of WMHs potentially require different features
- Better understanding of a complex problem

Tumors vs. Healthy Organs (at Risk)







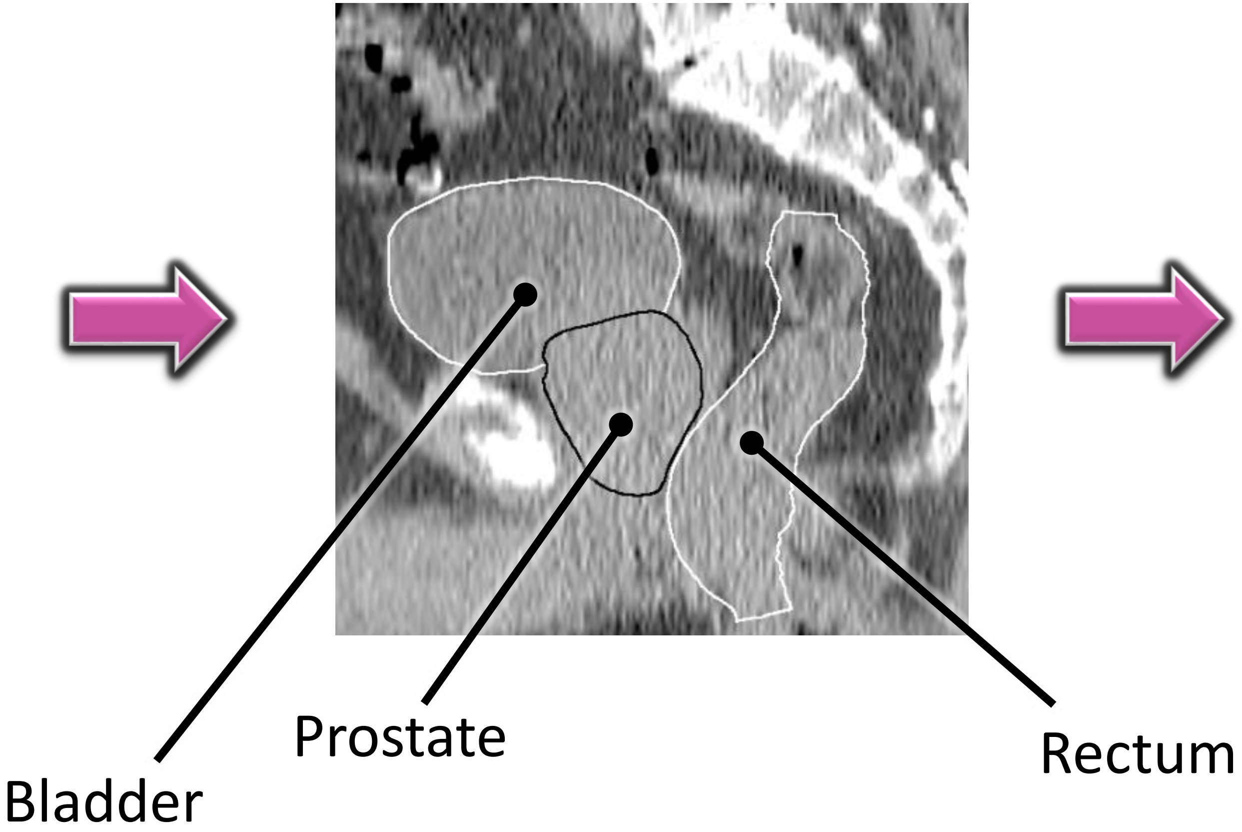
Manually

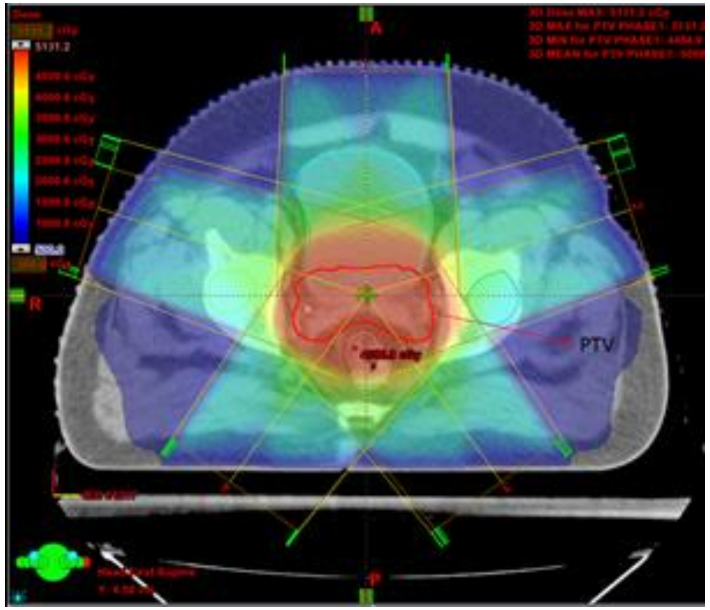
Semi-automatically

$\boxed{\text{Automatically}}$

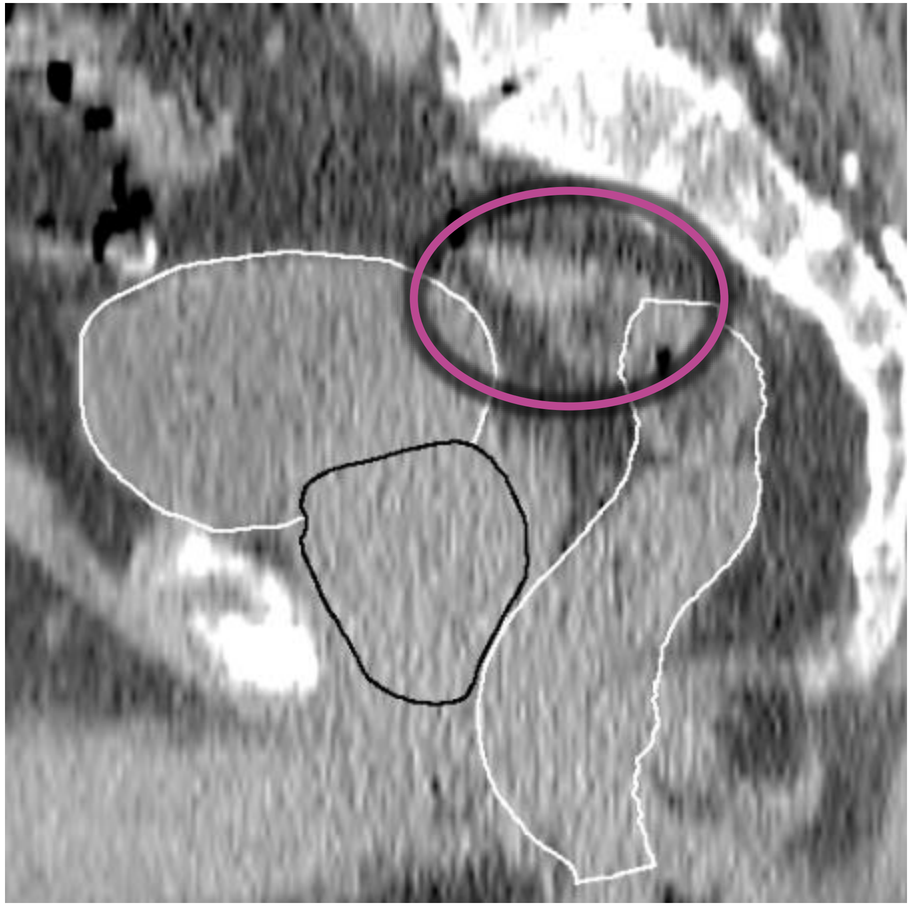
Active Shape Modeling

Initial | After 5 it.s | 10 it.s | Converged (18 it.s)


Bladder
Prostate
Rectum


PTV

[Schadewaldt et al., 2013]

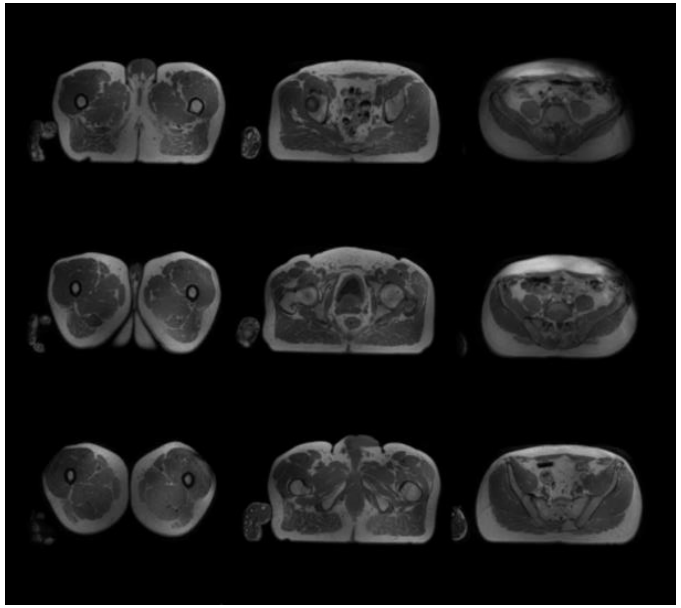


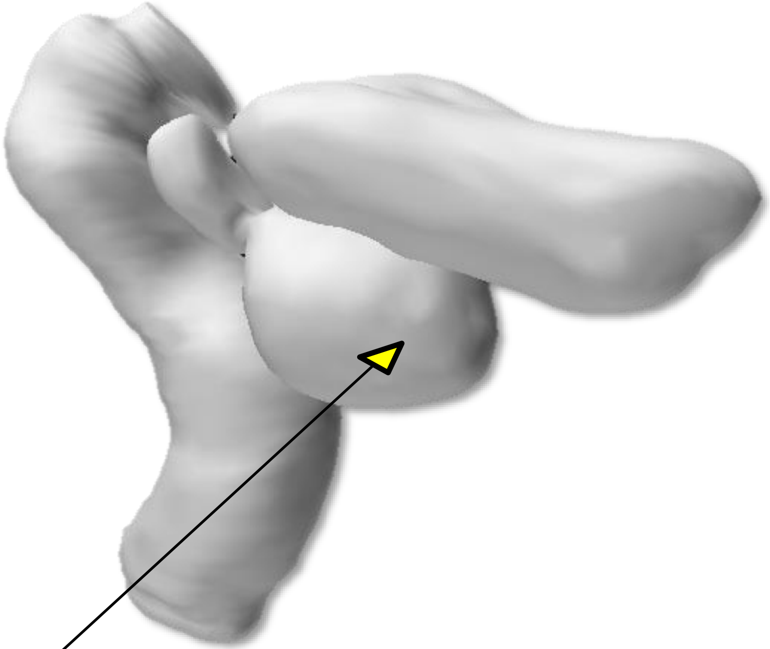
Why was it missed?

How can it be improved?

Awareness/prediction of inaccuracies?

Data

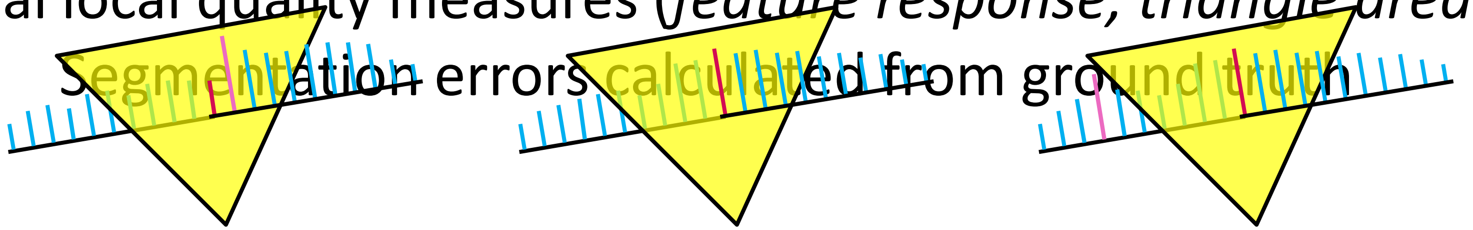


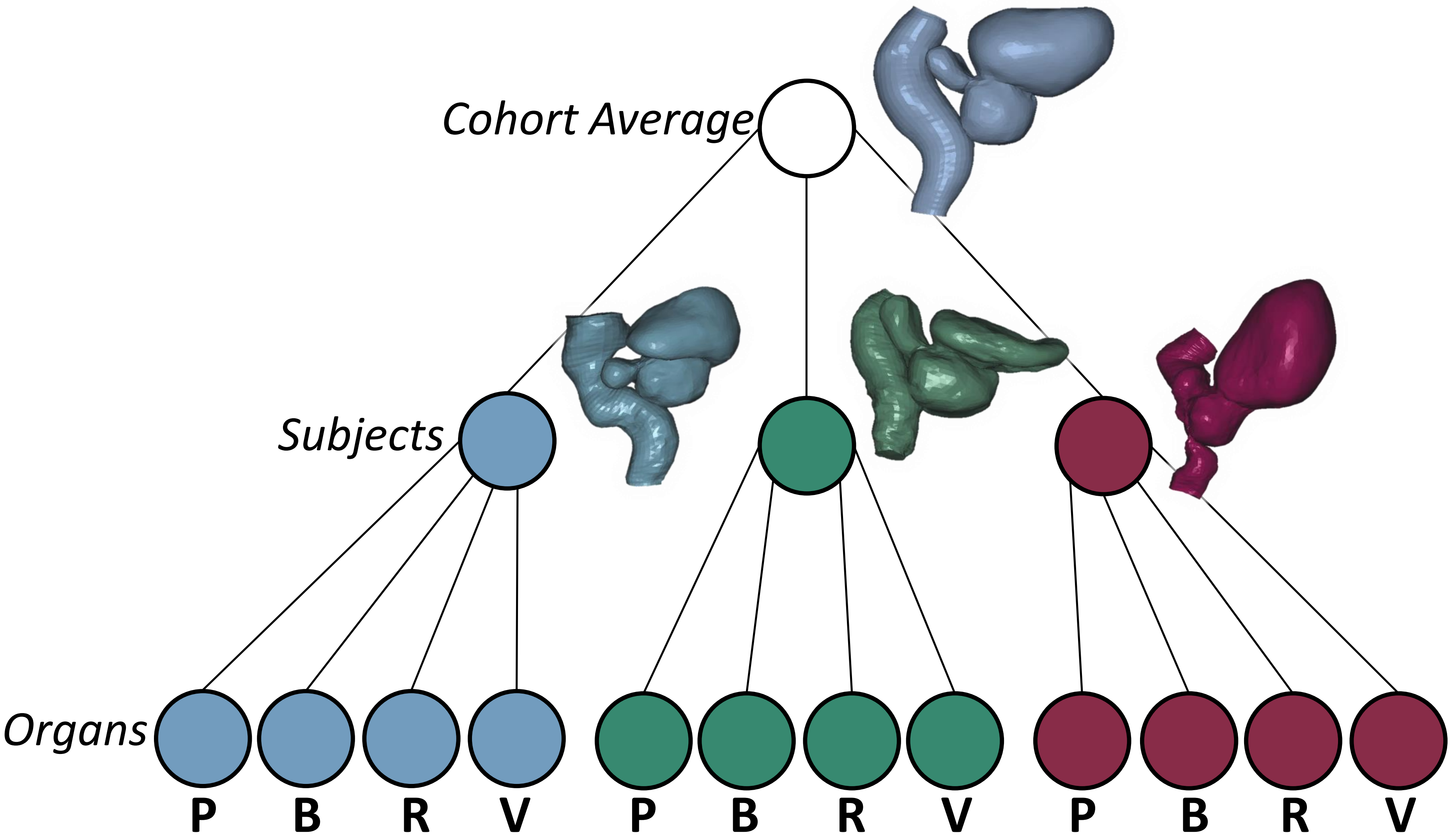


Feature Response Profile

Several local quality measures (*feature response, triangle area*,…)

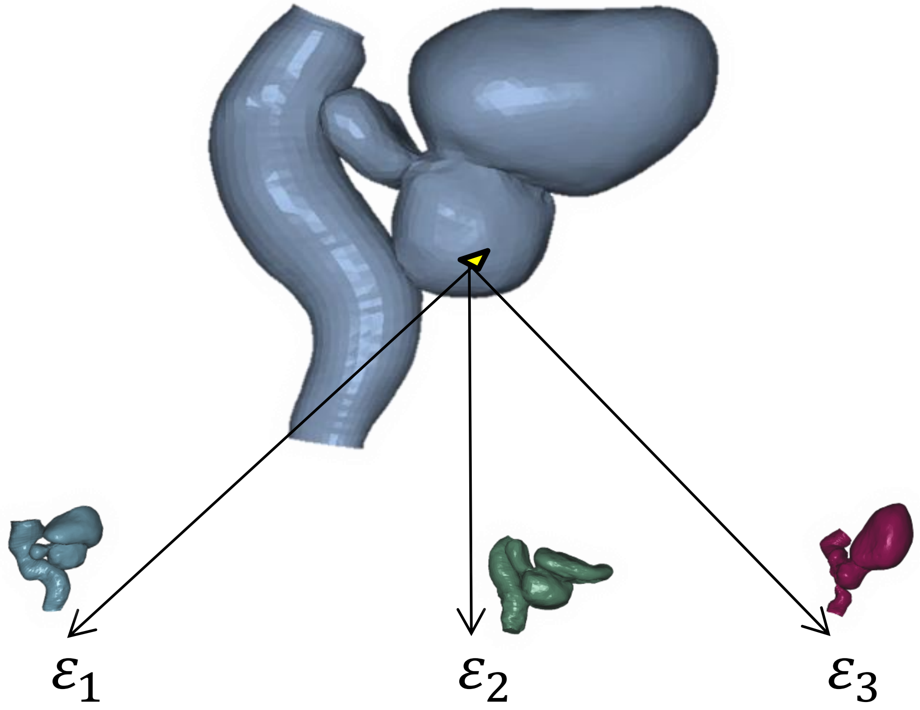
Segmentation errors calculated from ground truth



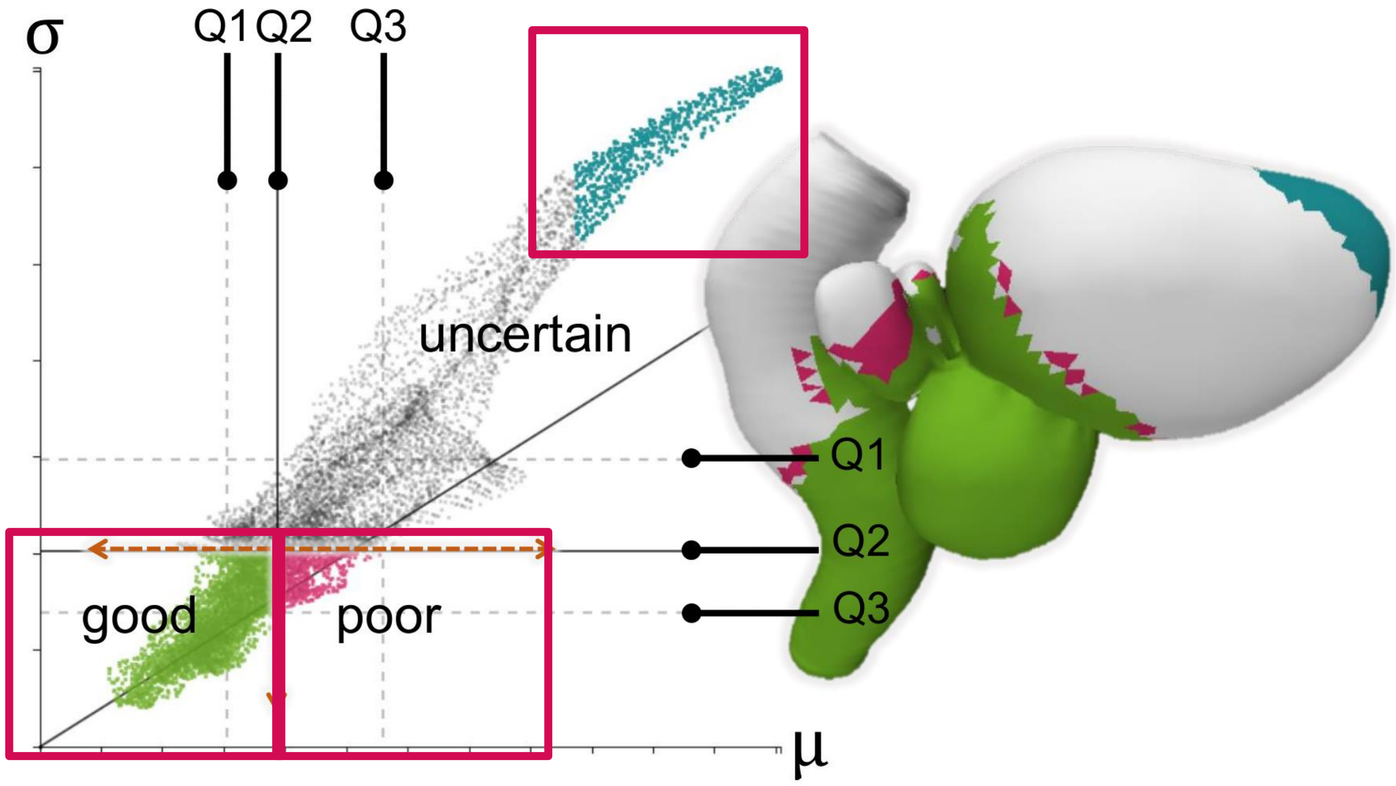

Cohort Average
Subjects
Organs
P
B
R
V
P
B
R
V
P
B
R
V

Full Cohort Exploration and Analysis

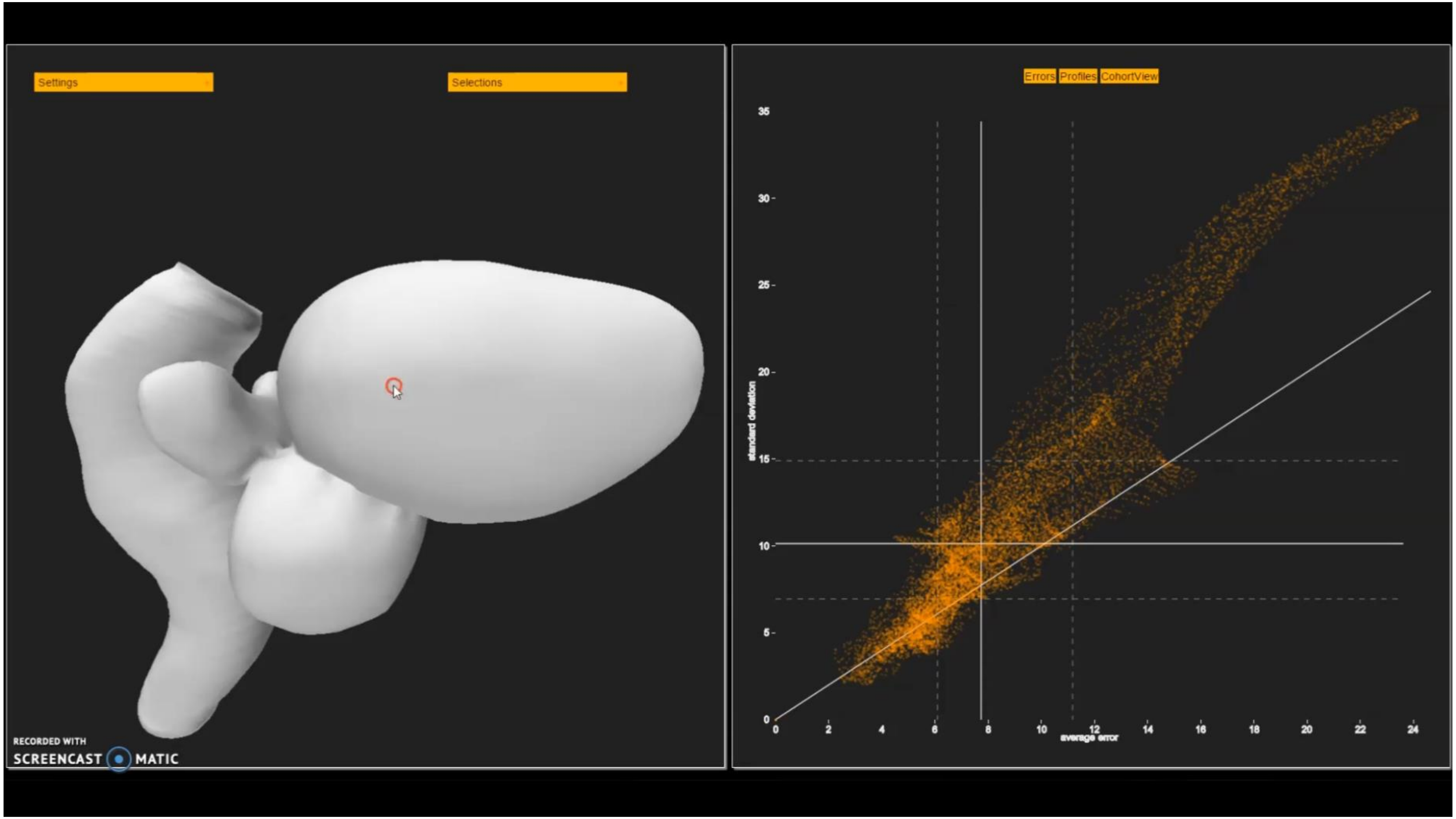
Cohort Average Mesh



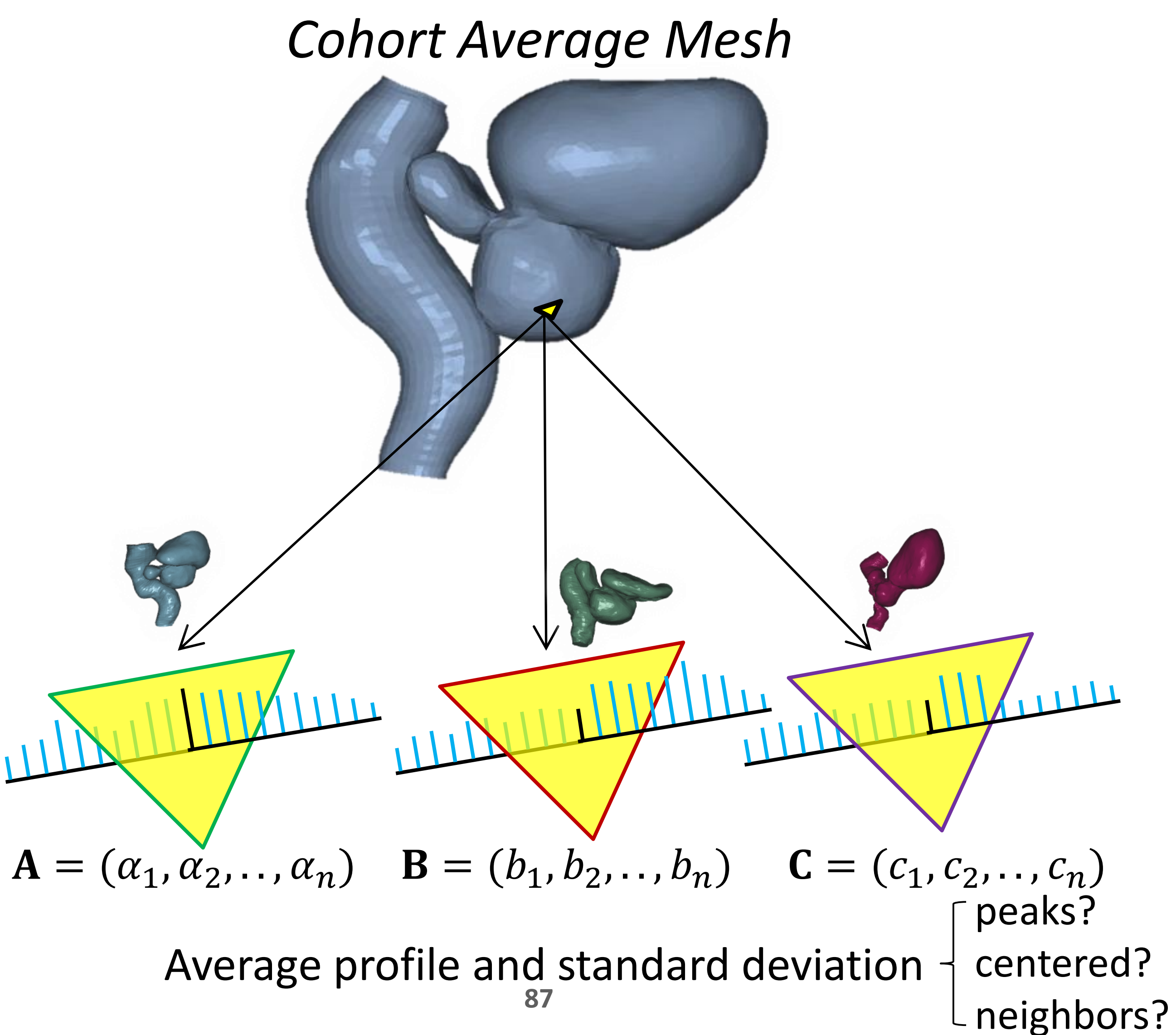
Triangle–to–triangle correspondence between subjects $\rightarrow (\mu, \sigma)$


σ
Q1
Q2
Q3
uncertain
good
poor
Q1
Q2
Q3
μ

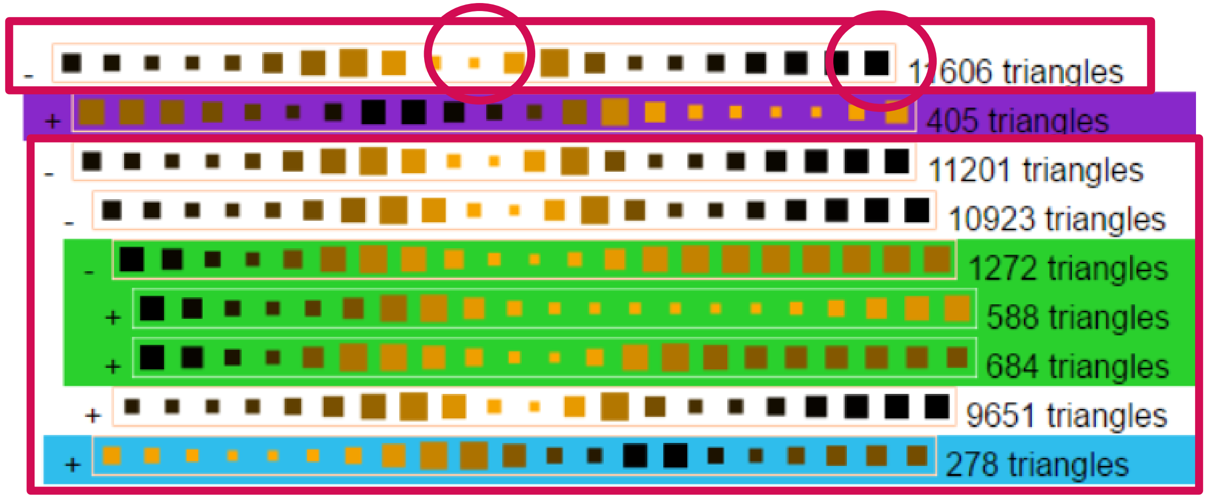
Full Cohort Exploration and Analysis

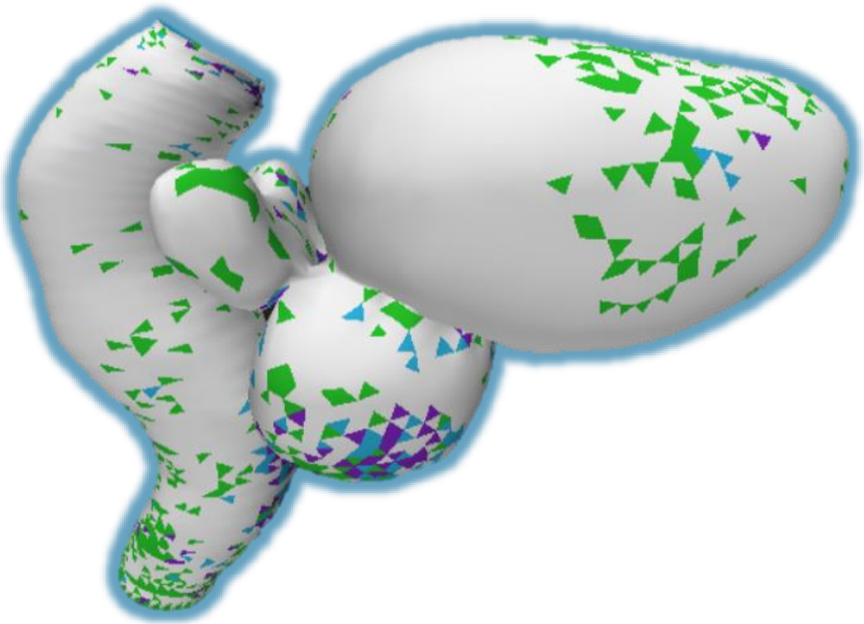


Full Cohort Exploration and Analysis

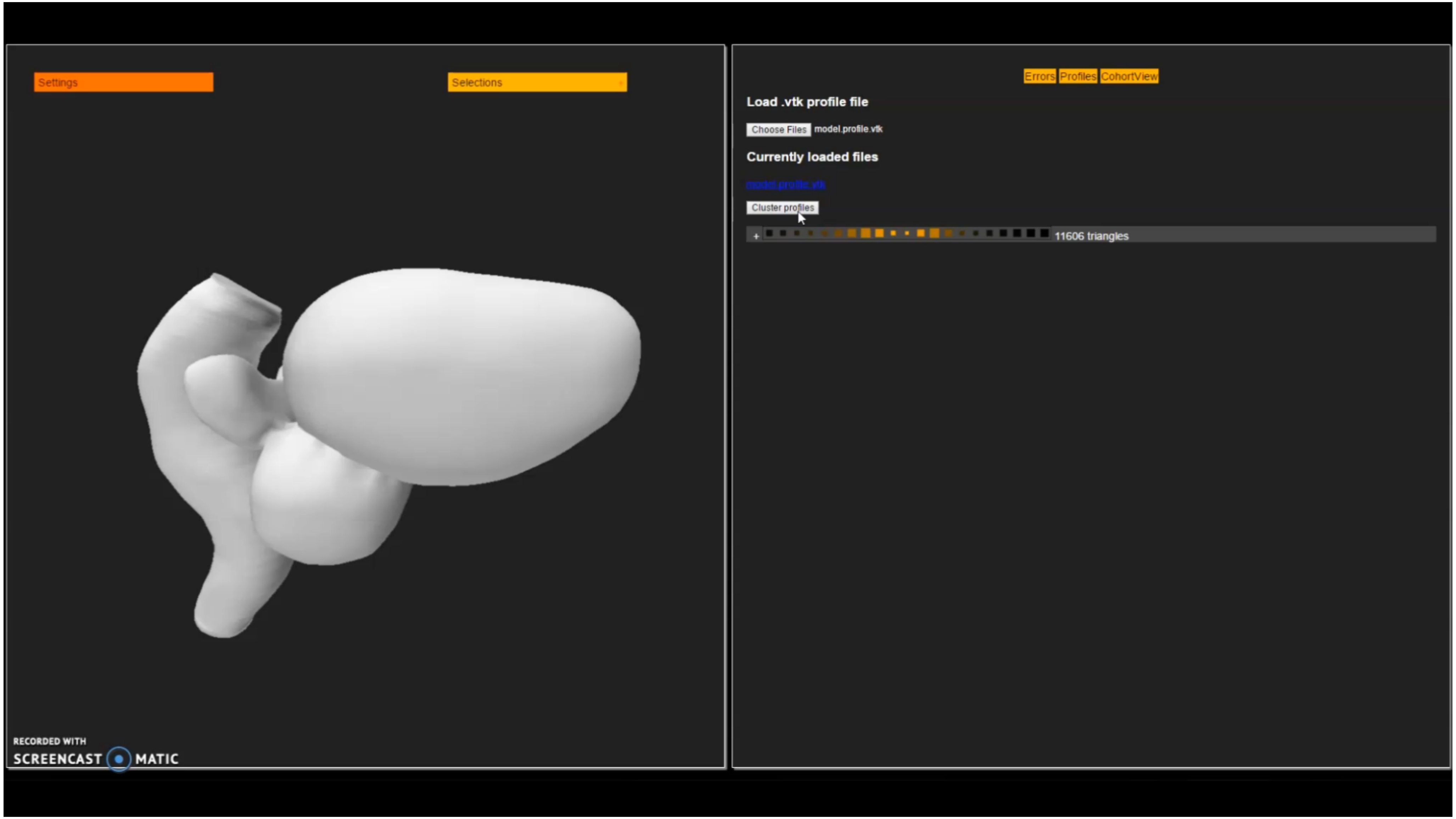


Full Cohort Exploration and Analysis

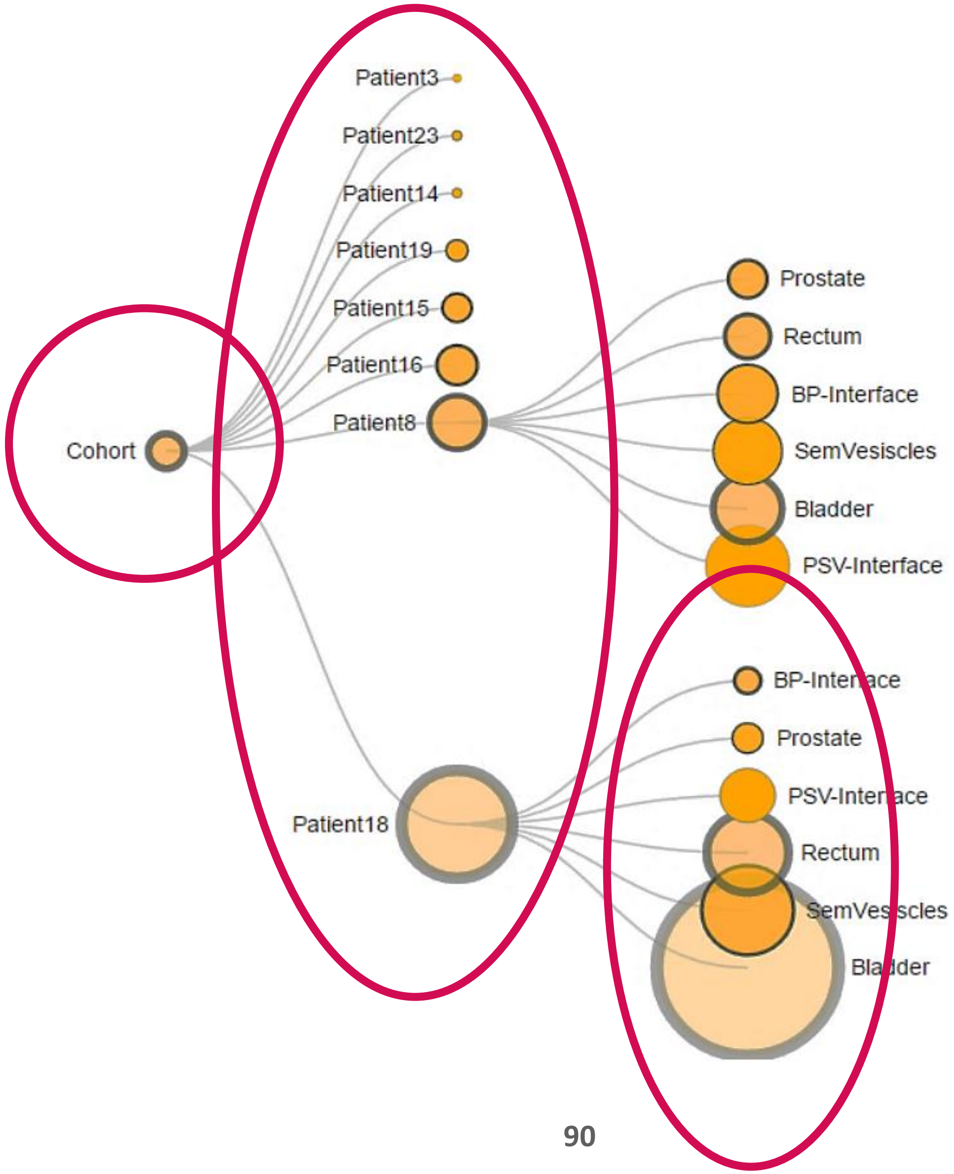




Full Cohort Exploration and Analysis

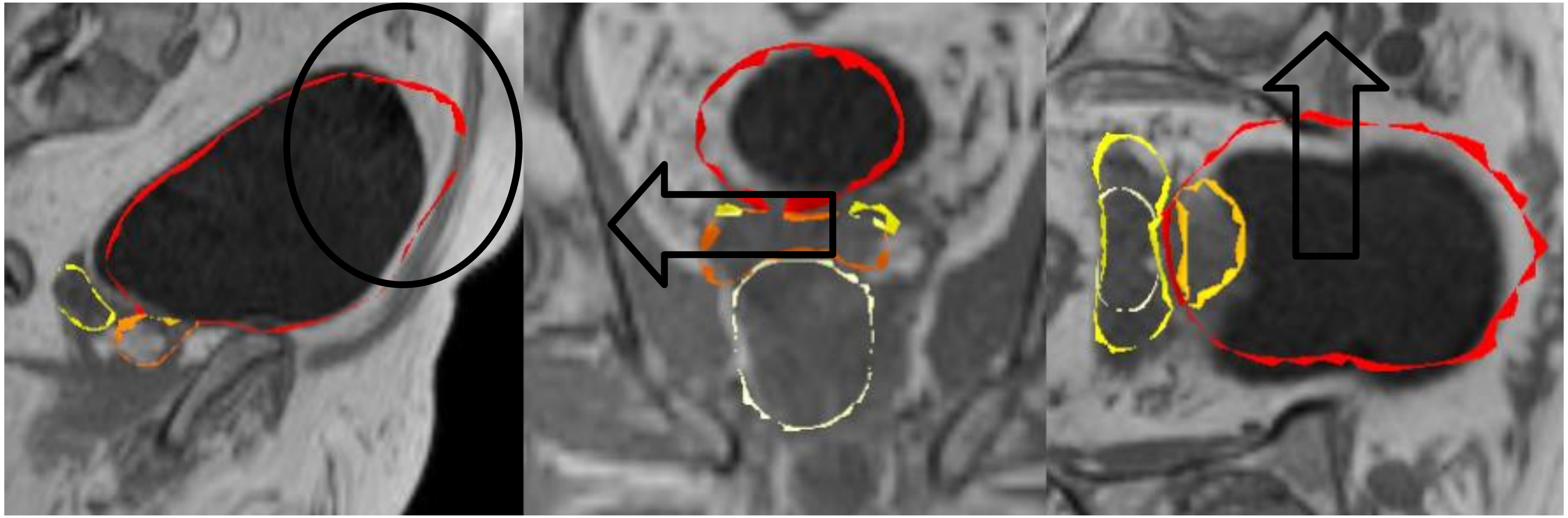


Cohort Error Hierarchy Exploration

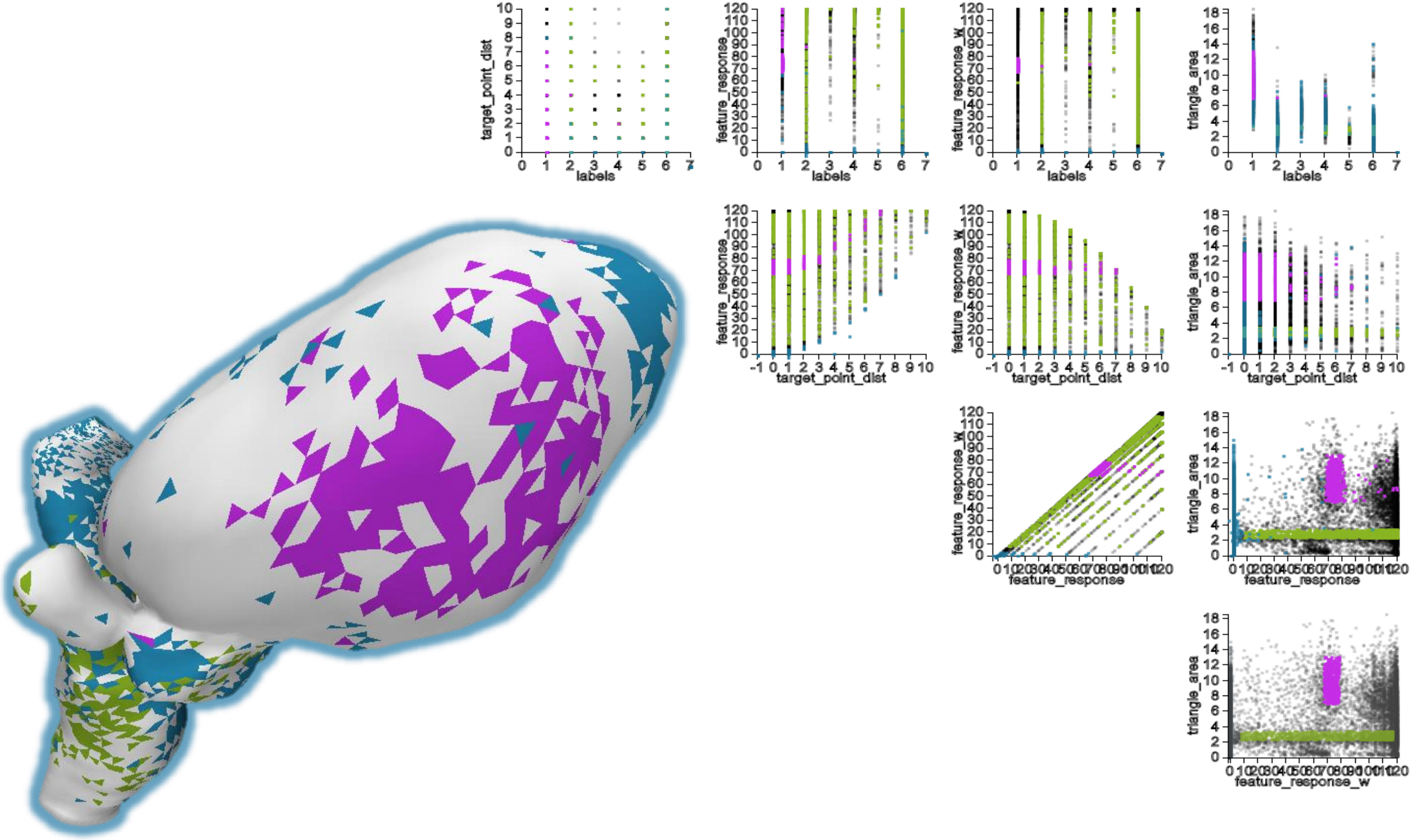


Individual Subject Exploration and Analysis

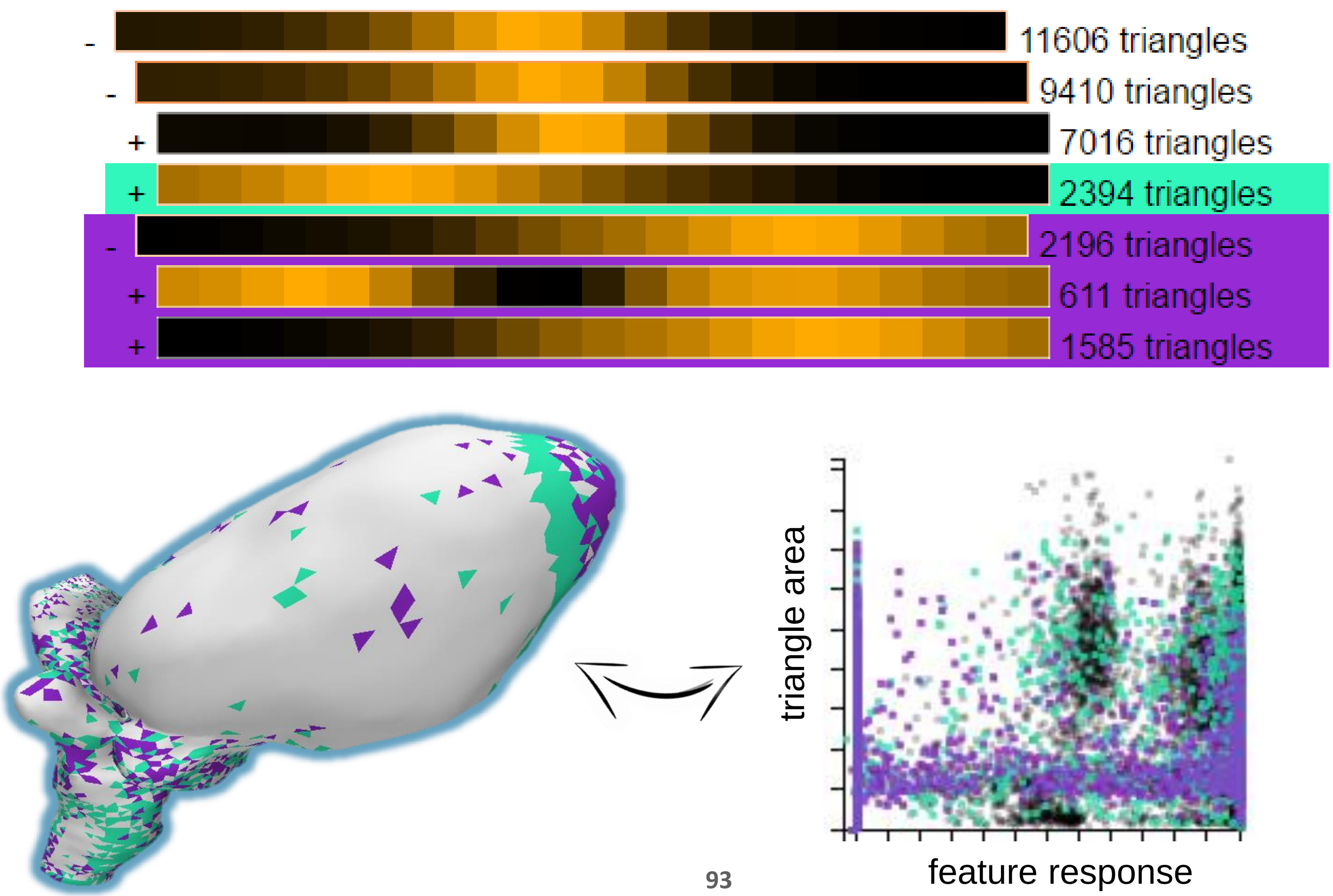
- Initial qualitative inspection w.r.t. imaging data



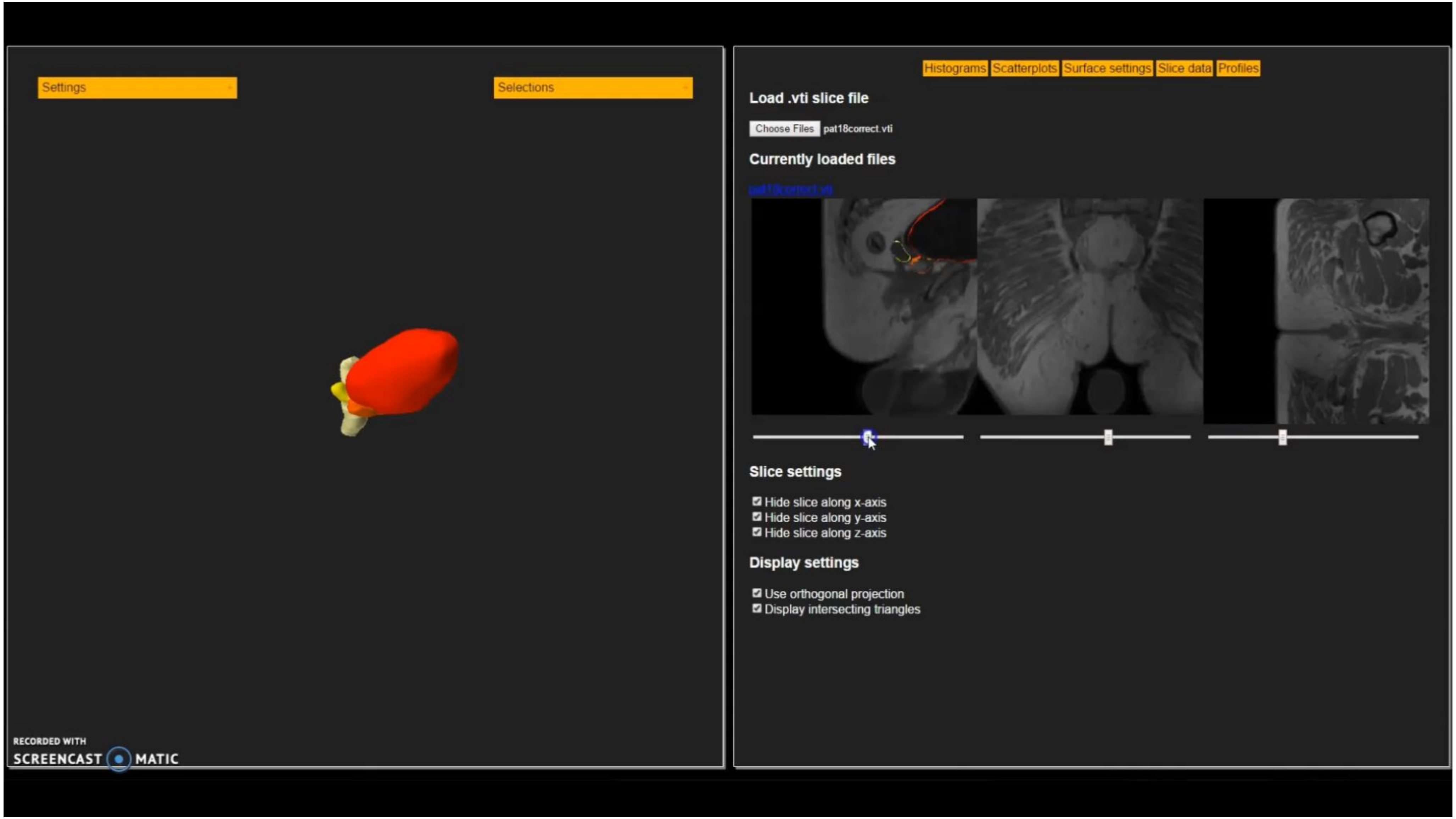
Individual Subject Exploration and Analysis



Individual Subject Exploration and Analysis



Individual Subject Exploration and Analysis



Conclusions

- Visual tool for the exploration and assessment of the results and errors of automated segmentation processes.
- Better understanding of how the employed algorithm works.
- Going from an entire cohort to single cases.

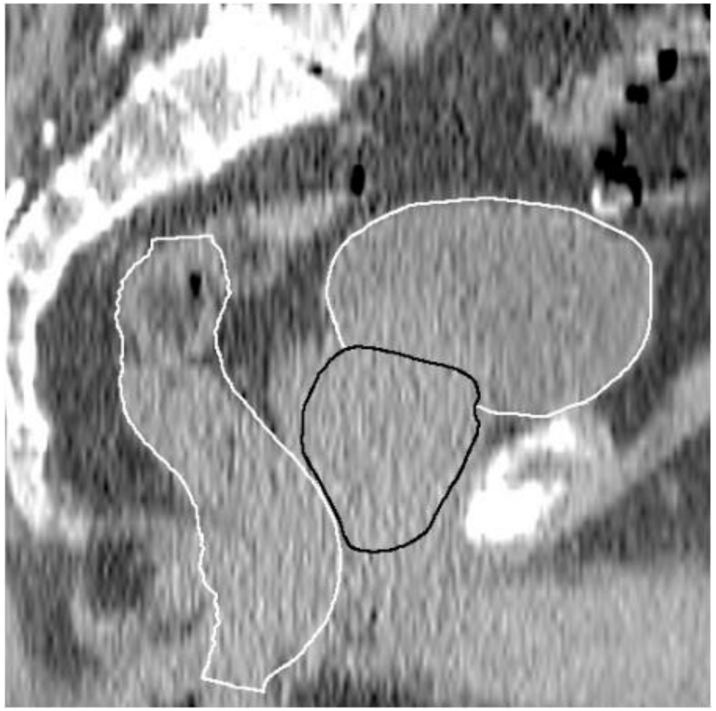
Comparative Visual Analysis of Pelvic Organ Segmentations

Oliver Reiter[1], Marcel Breeuwer[2;3], M. Eduard Gröller[1;4], Renata G. Raidou[1]

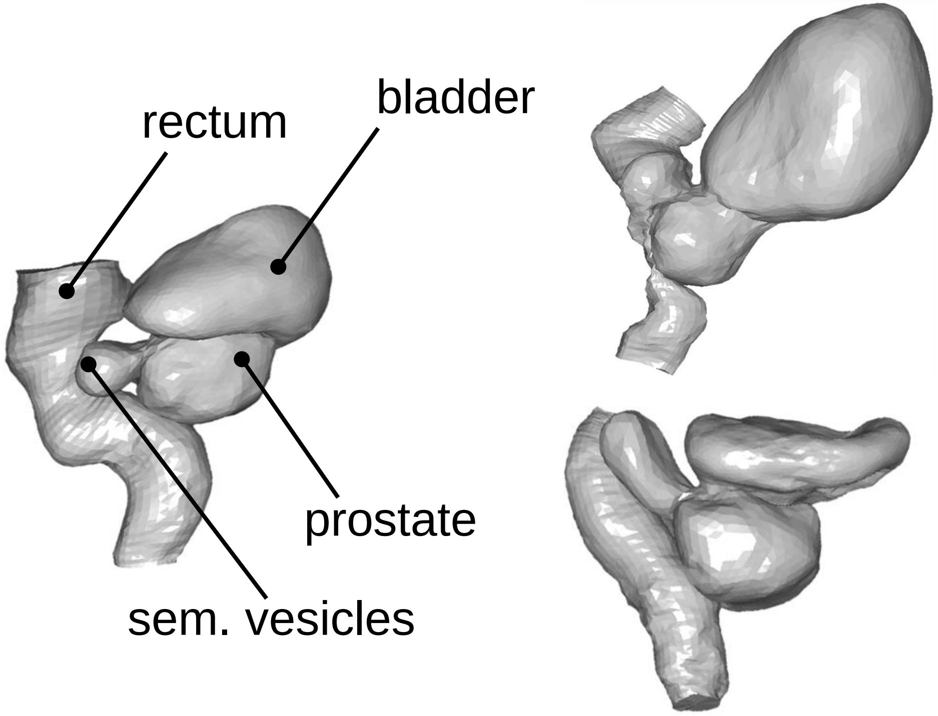
[1]Institute of Visual Computing & Human-Centered Technology, TU Wien, Austria
[2]Eindhoven University of Technology, the Netherlands
[3]Philips Healthcare Best, the Netherlands
[4]VRVis Research Center, Austria

Motivation

<u>Hypothesis</u>: inaccuracy related to high variability of organs



Schadewaldt et al., 2013



Anatomical Variability Across Patients

Contribution

A **web-based** framework for:

1. easy exploration and detailed analysis of pelvic organ **shape variability**

2. hypothesis generation w.r.t. the impact of shape variability on the **performance of segmentation** algorithms

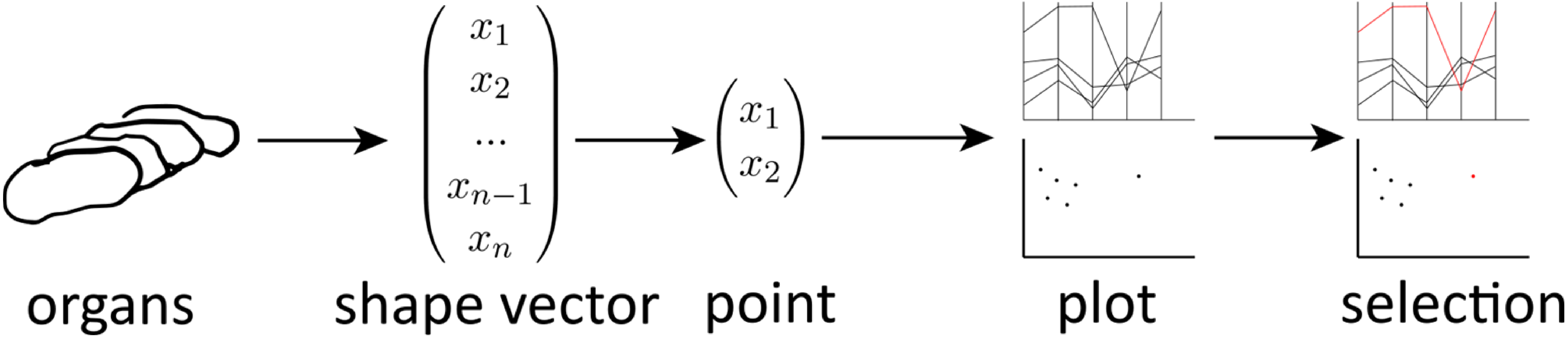
for each **individual** organ and for **all** organs at the same time.

Tasks and Challenges

1. Quantification and Visualization of Organ Shape Variability
   - Per individual organ
   - Across all pelvic organs
   - Quantification requires adequate metrics

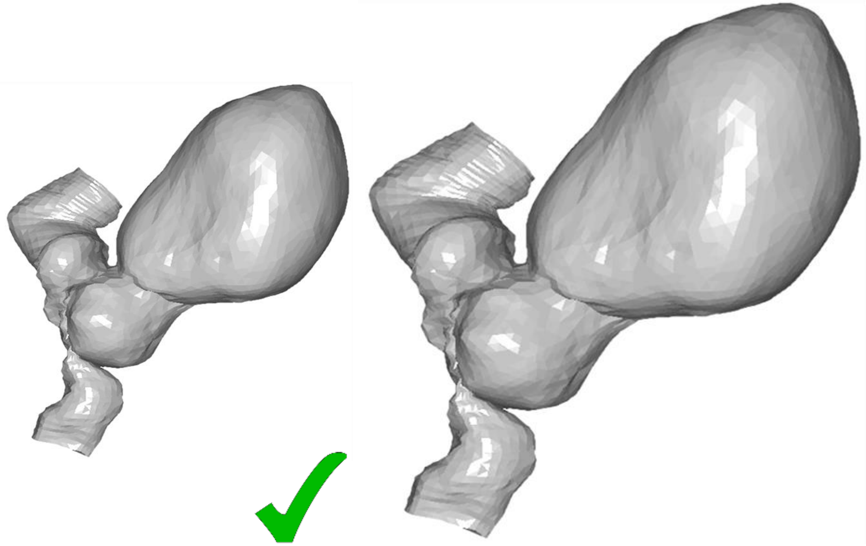
2. Comparative Visualization of Pelvic Organs
   - Across multiple patients
   - Multiple pelvic organs per patient
   - Organ interfaces

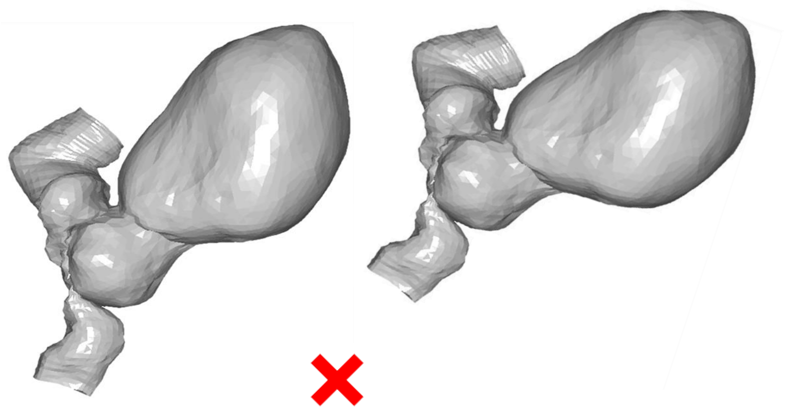
Task 1: Quantification and Visualization of Shape Variability



- Shape descriptors
  - Represent shapes as vectors
  - Translation/rotation/scale invariance

- In this work: no scale invariance, but translation/rotation





Shape Descriptors

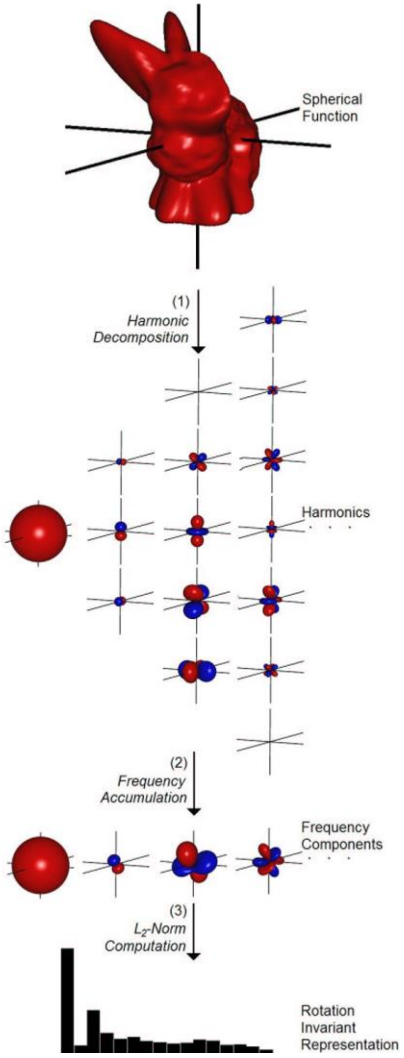
- Global feature based
- Graph based
- Zernike moments

[Zhang et al. **Survey of 3D Shape Descriptors**, 2004]

Spherical Harmonics-based Descriptors

- Decompose spherical function into its harmonics
- Accumulate based on the frequency
- Compute L2 Norm
- Rotation invariant for each frequency component

- Result: Shape vector of frequencies



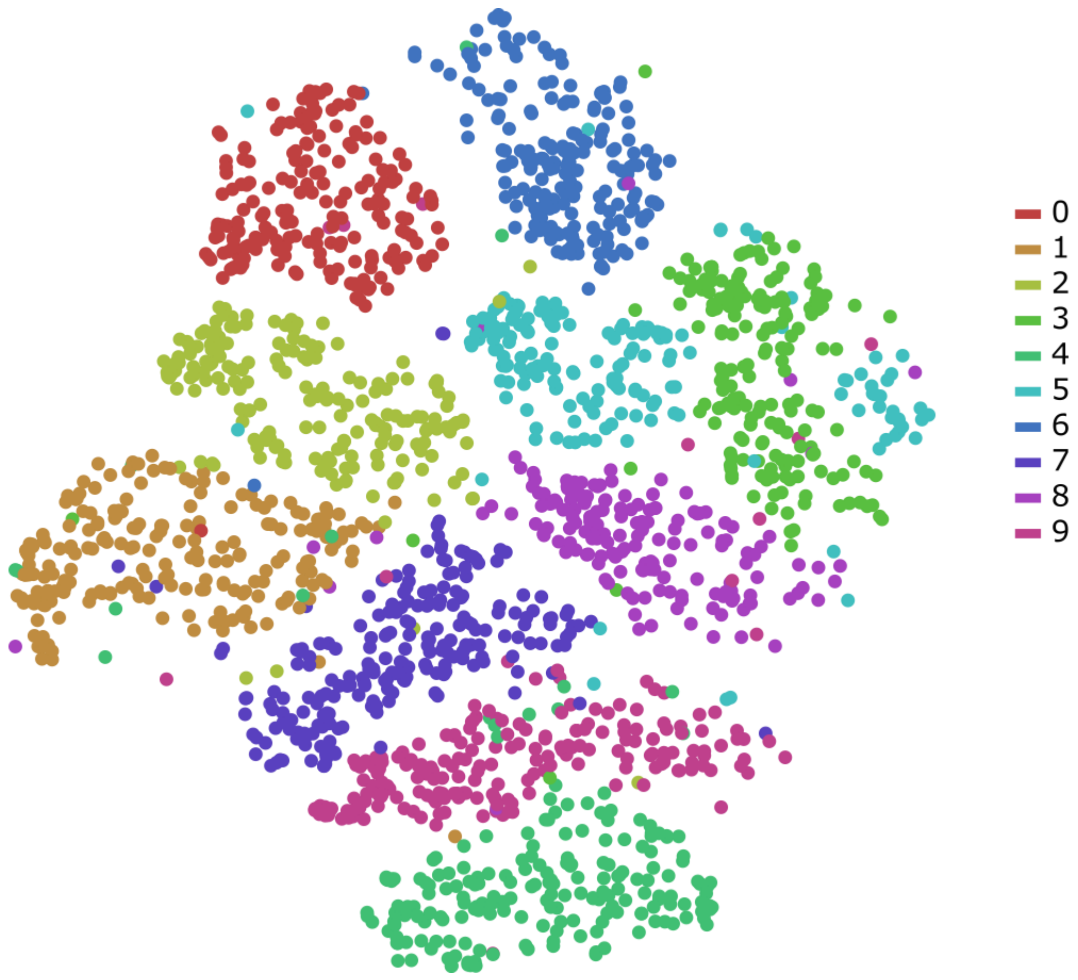
Kazhdan, Funkhouser and Rusinkiewicz, 2003

Dimensionality Reduction

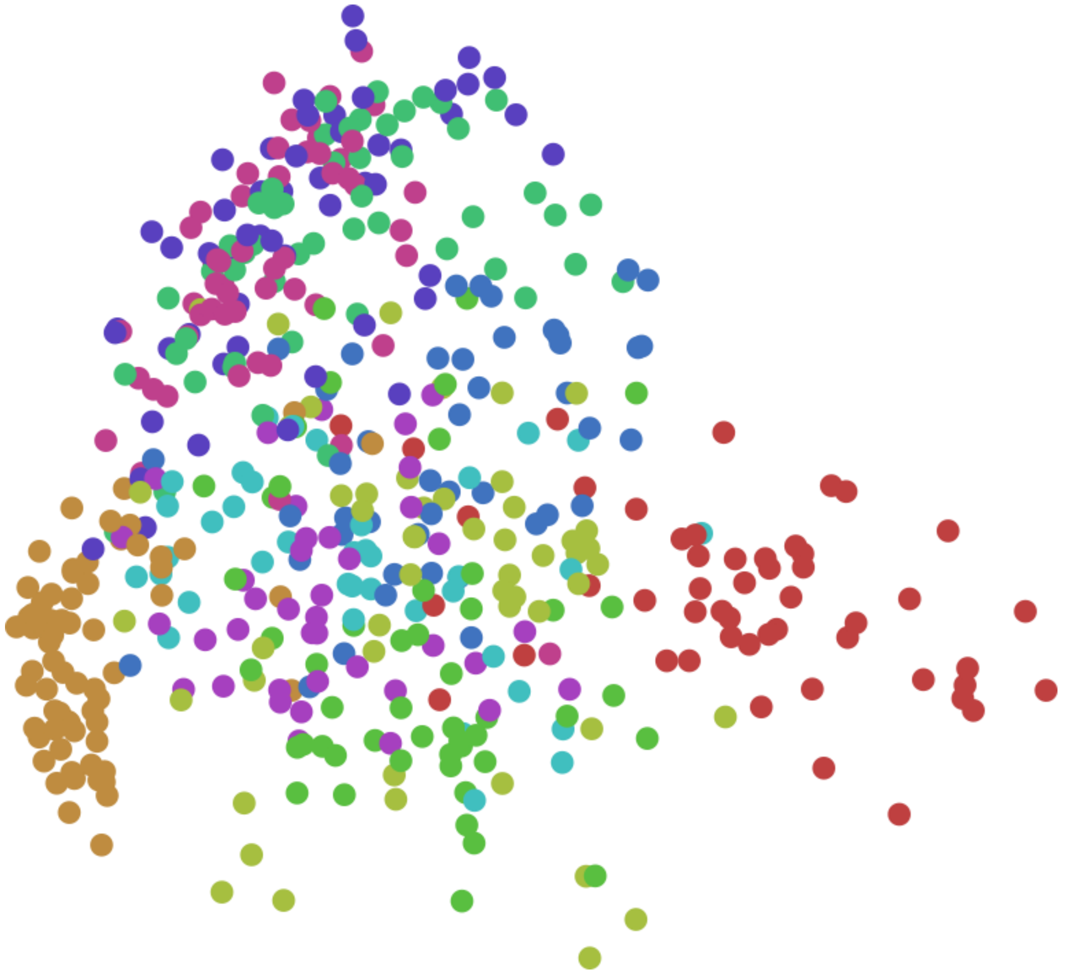
- Eight-dimensional shape description vector for each organ

- Dimensionality reduction necessary in order to visualize:
  - PCA for individual organ (within class visualization)
  - t-SNE for multiple organs (between class visualization)

Dimensionality Reduction - MNIST Dataset

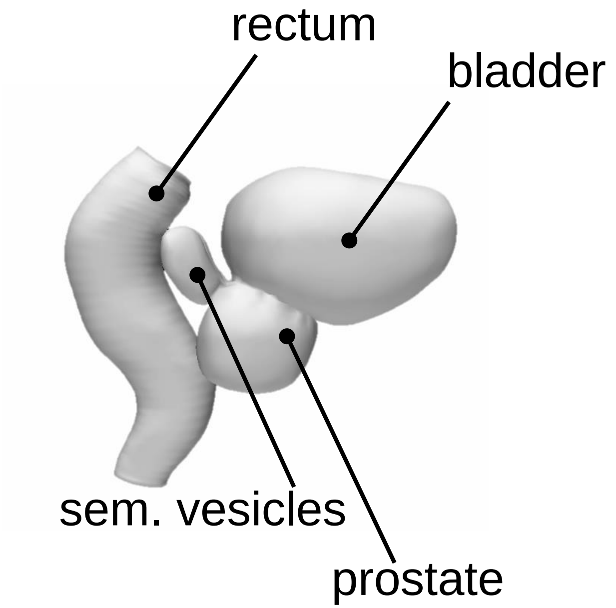


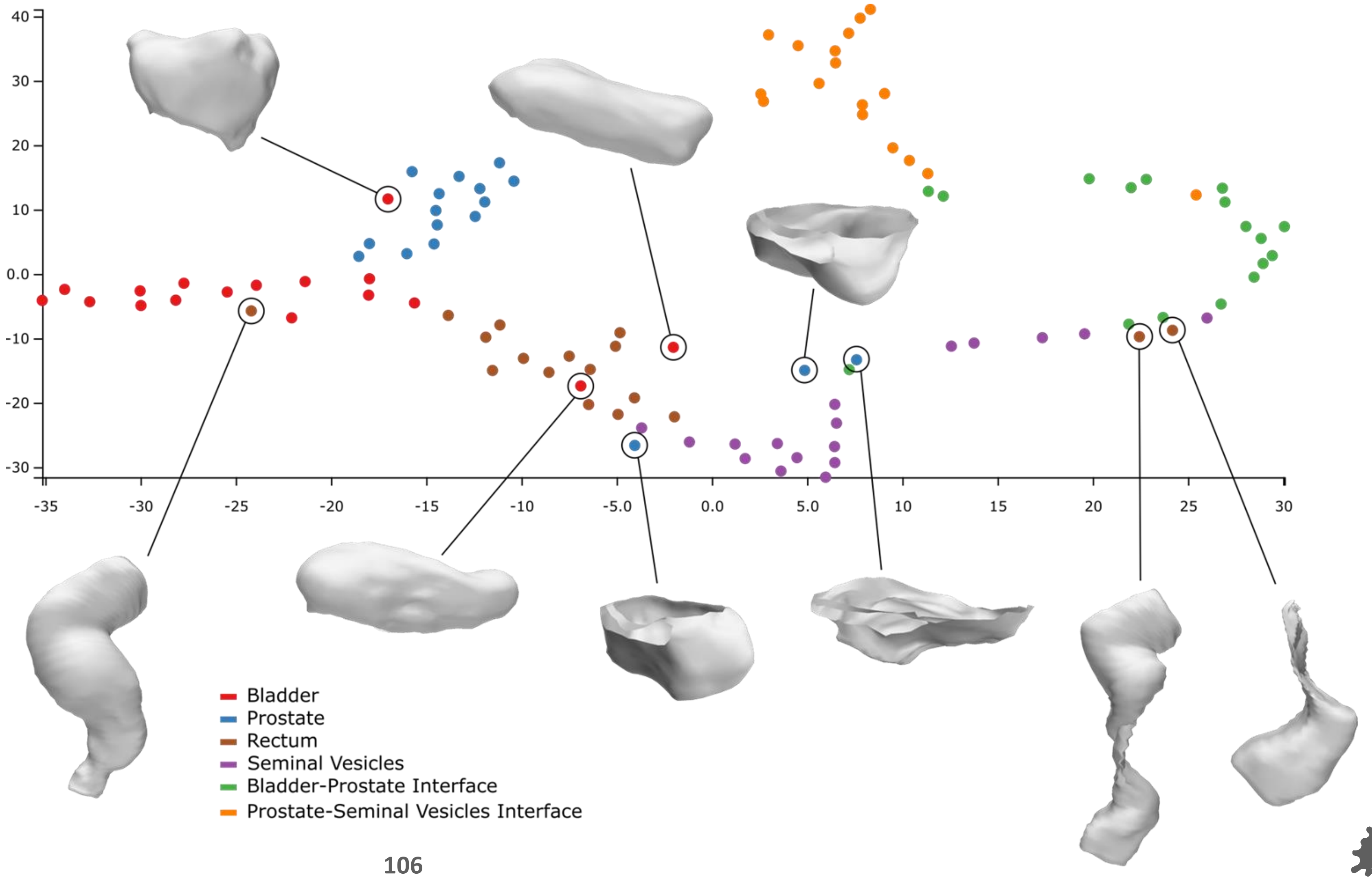
t-SNE



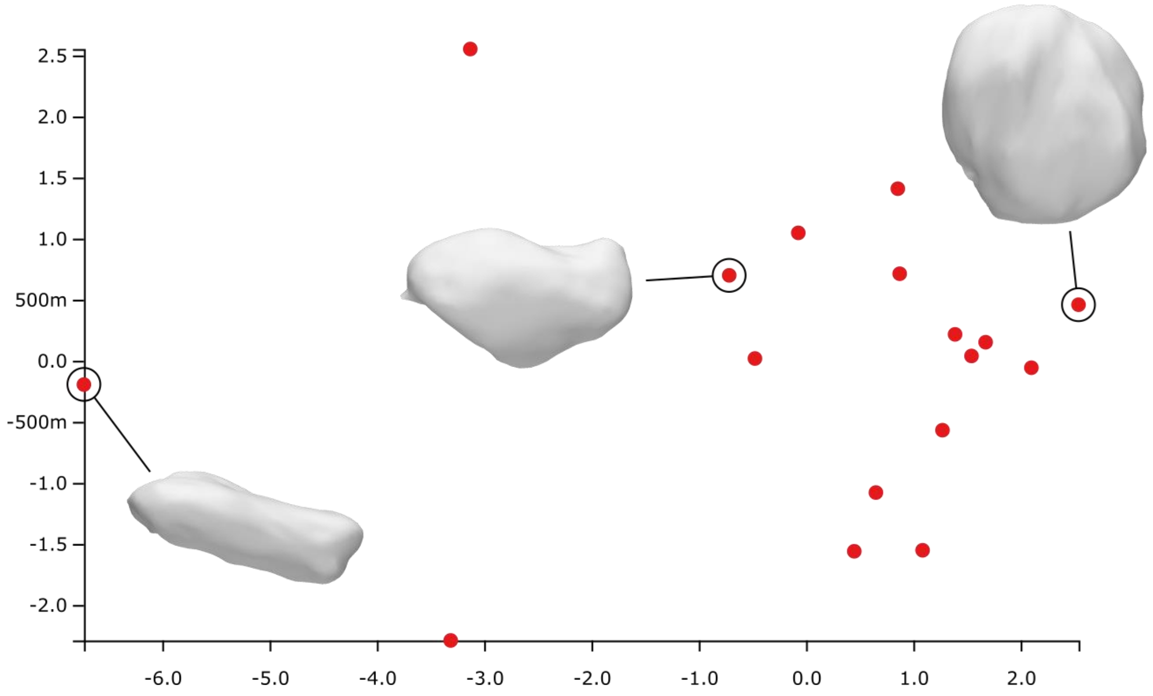
PCA

2D Visualization of Multiple Organs (t-SNE)

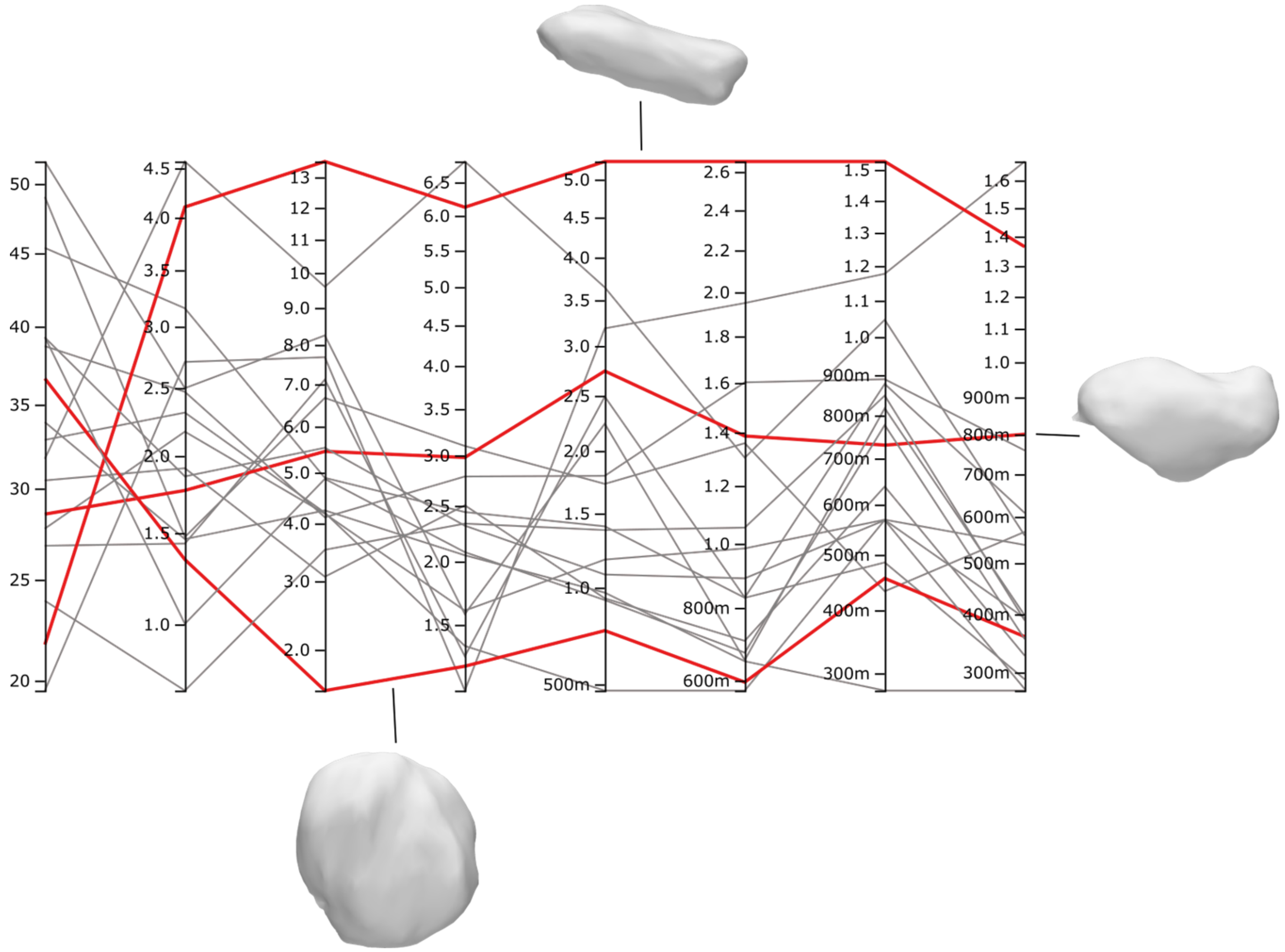




2D Visualization of an Individual Organ (PCA) (Bladder)



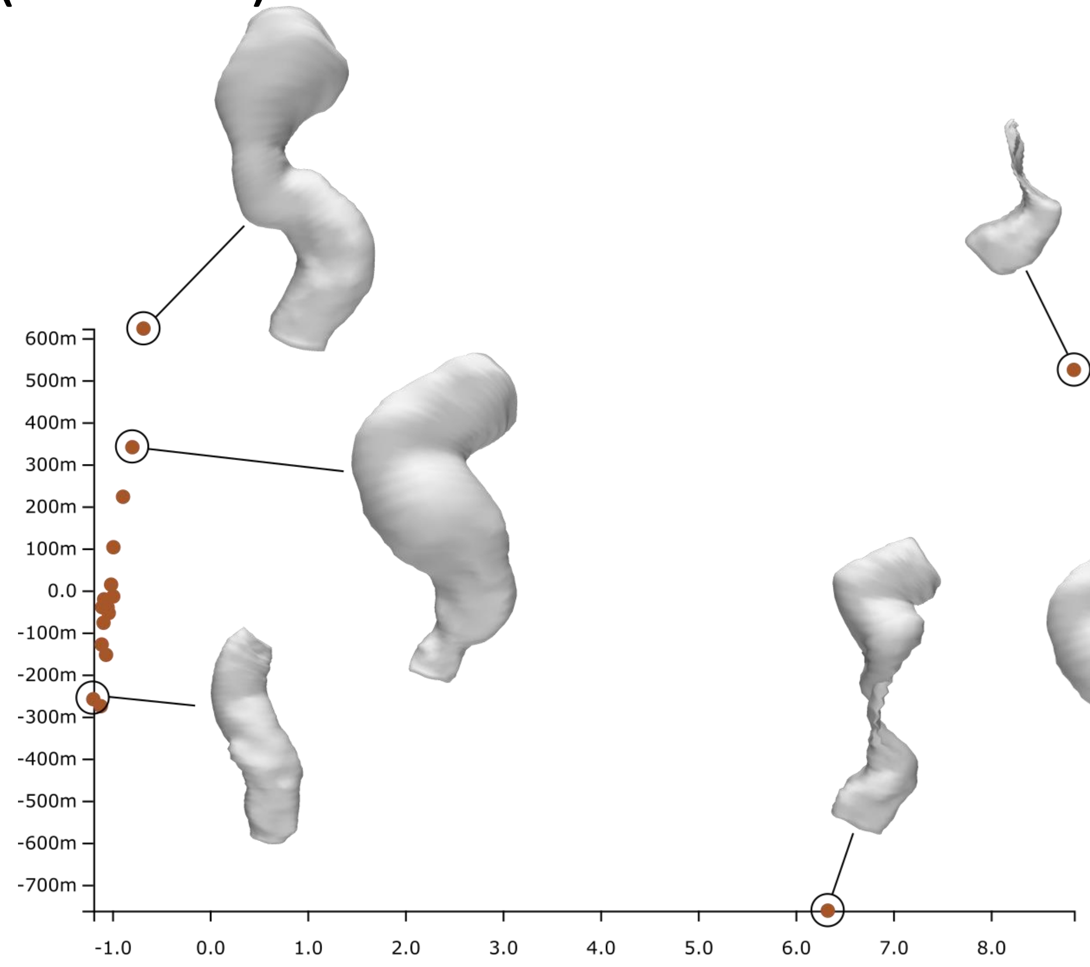
PCA plot



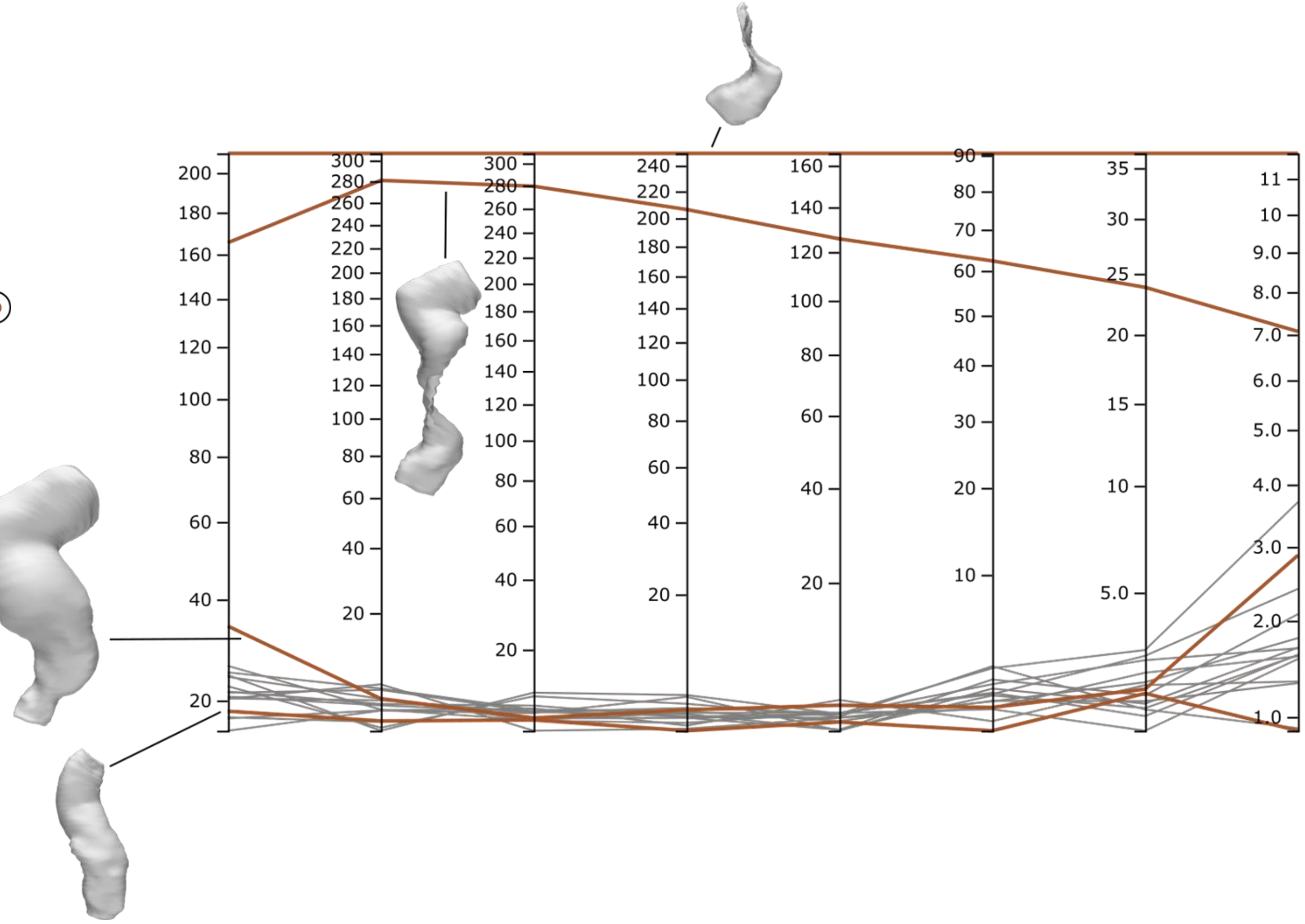
Parallel Coordinates Plot

2D Visualization of an Individual Organ (PCA)

(Rectum)

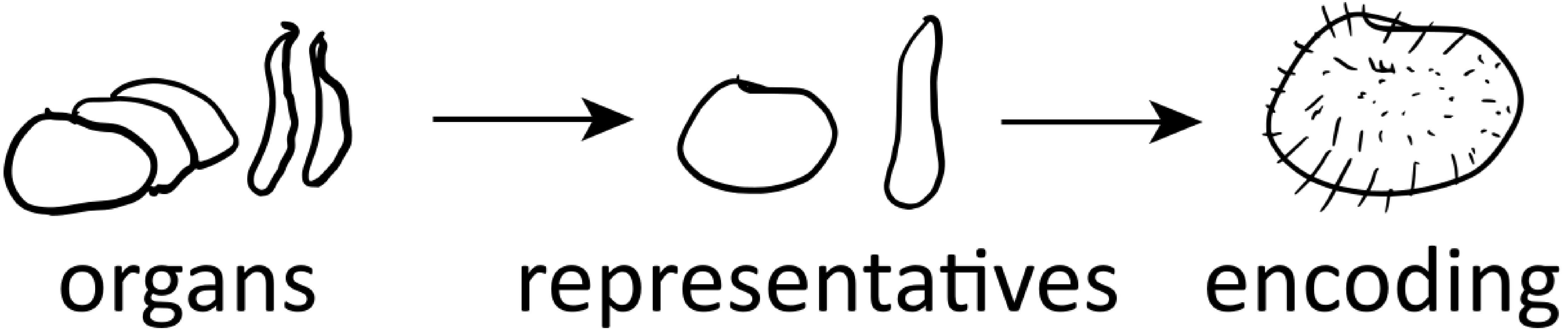


PCA plot



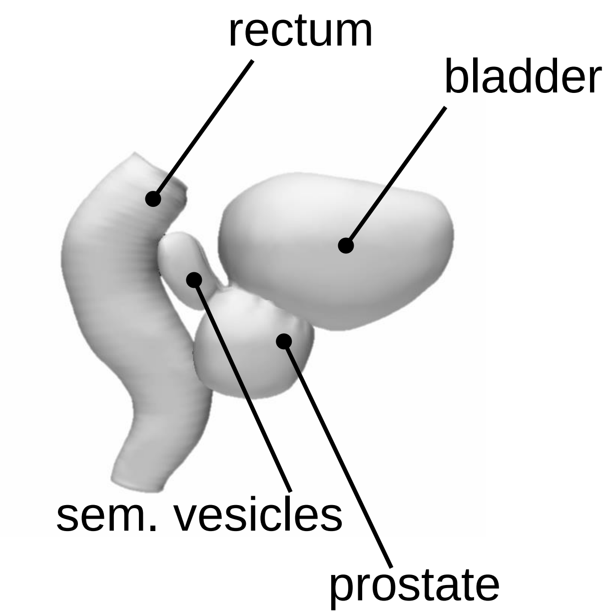
Parallel Coordinates Plot

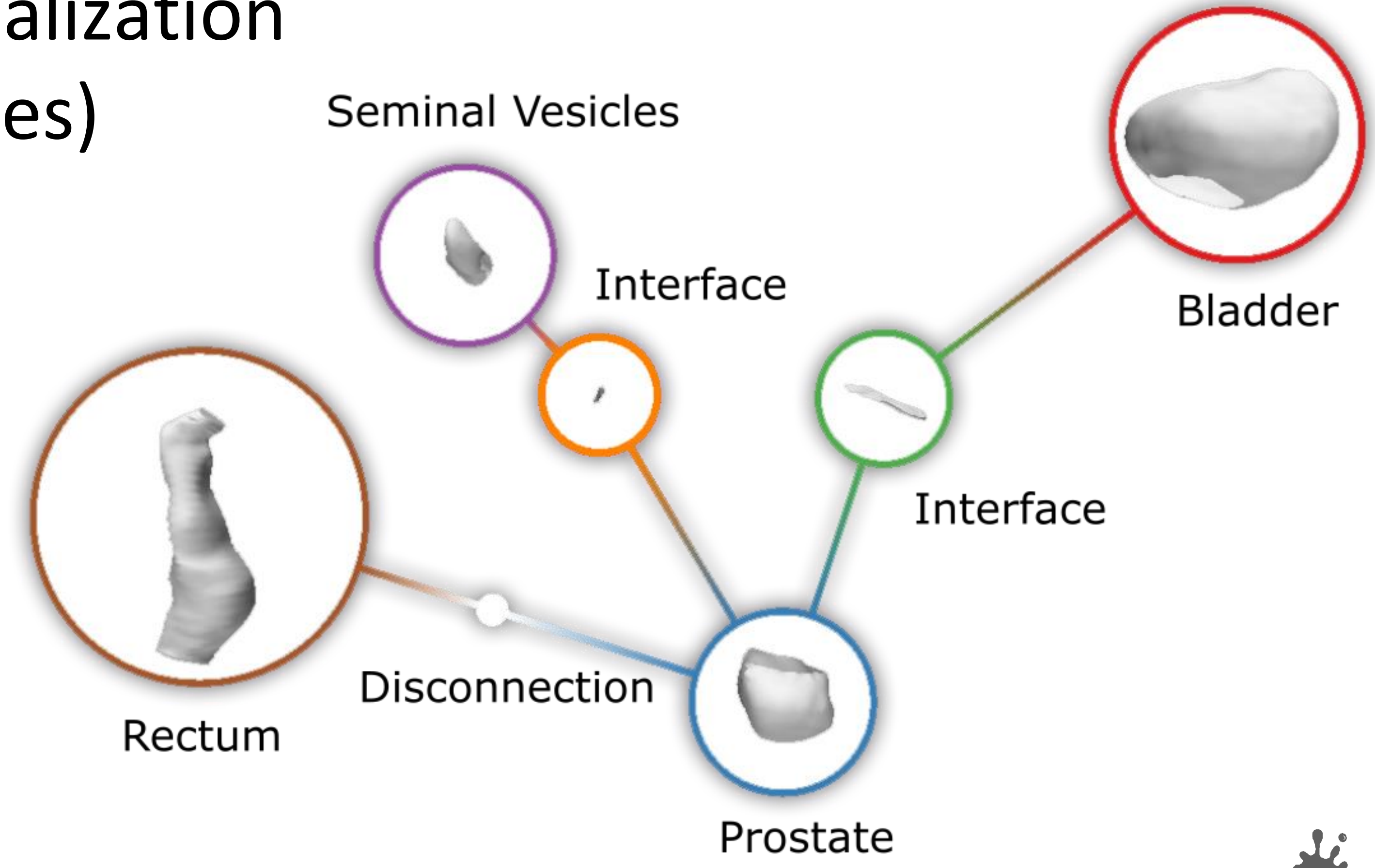
Task 2: Comparative Visualization of Multiple Organs



Dealing with Multiple Organs

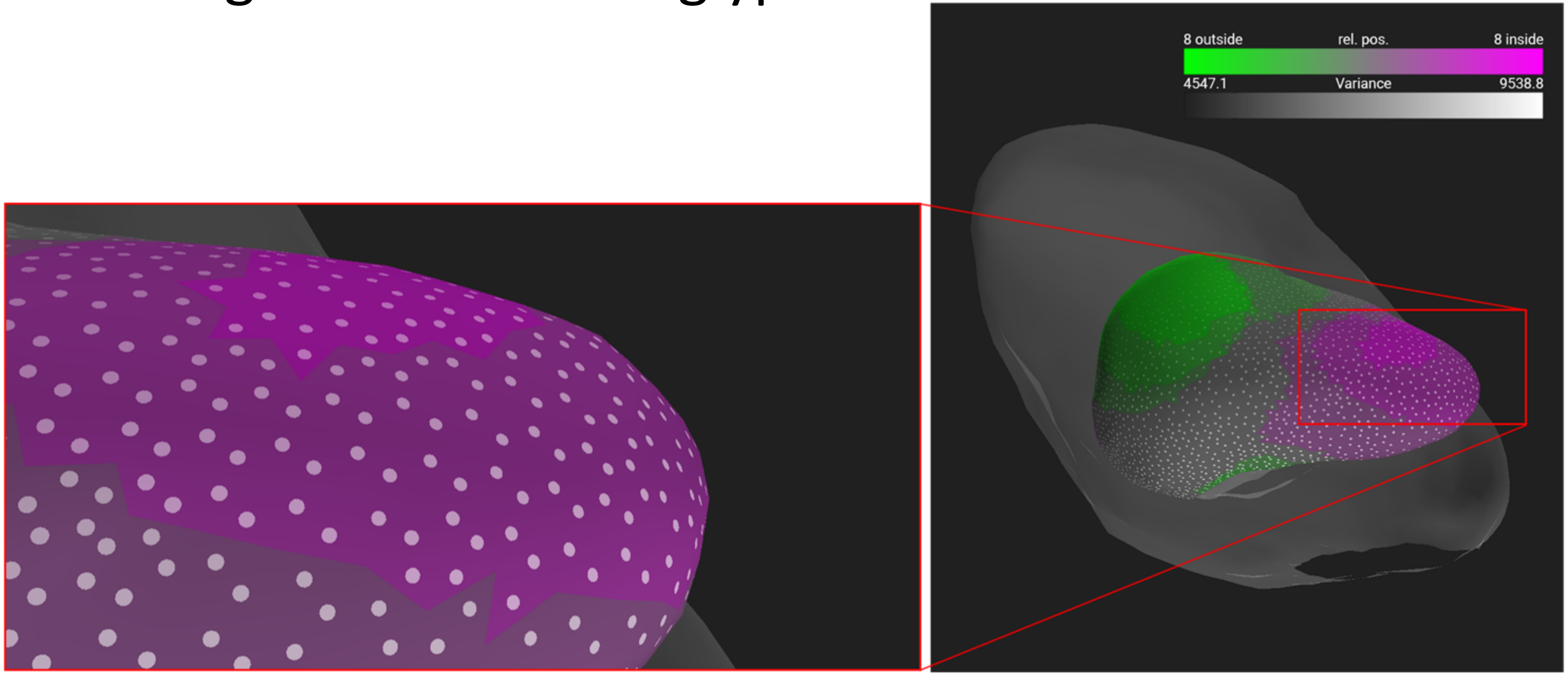
- Show median shape per organ
- Display relative position
- Preserve context of 2D visualization
- Show connections (interfaces)



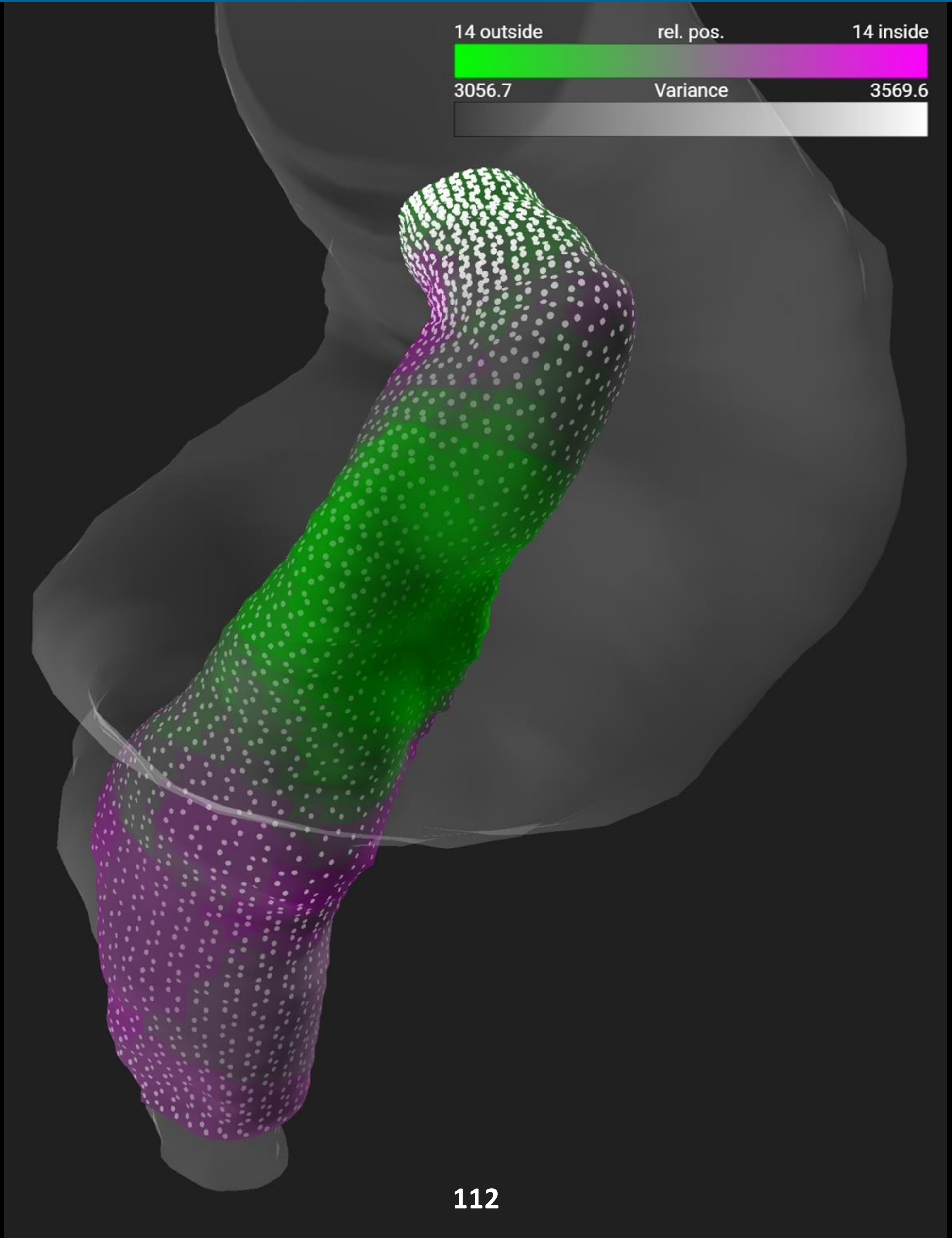


Detail-on-Demand View

- Relative extent of median shape compared to all others: color
- Per-triangle variance: dot glyps



Detail-on-Demand View of Rectum Cohort



Evaluation

- Informal evaluation with an experienced segmentation expert
- “Easy to learn and easy to understand”
- Positively judged as an interesting basis for future work

- Original image data not accessible
- No scale to see the actual size

Limitations

- Shape descriptor not suitable for organ interfaces
- t-SNE requires experience to find good parameters
- Little interaction possibilities in the exploded view

Conclusions

- Compare segmentations of multiple organs across multiple patients
  - Measure and visualize shape variability
  - Comparative visualization of pelvic organs
- Quickly identify mis-segmented shapes
- Provides quick and easy insight into shape variability
- Hypothesis generation for segmentation algorithms performance

Summary

- "Visual Analytics combines automated analysis techniques with interactive visualisations for an effective understanding, reasoning and decision making on the basis of very large and complex datasets" [Keim 2010]

- Few examples applied on the domain of RT treatment planning

- The purpose of computing is insight, not numbers [Hamming, 1962]

- The purpose of visualization is insight, not pictures [Shneiderman, 2005]