Advanced Application of MRI: Towards Quantitative Analysis & Biological Insights of Disease

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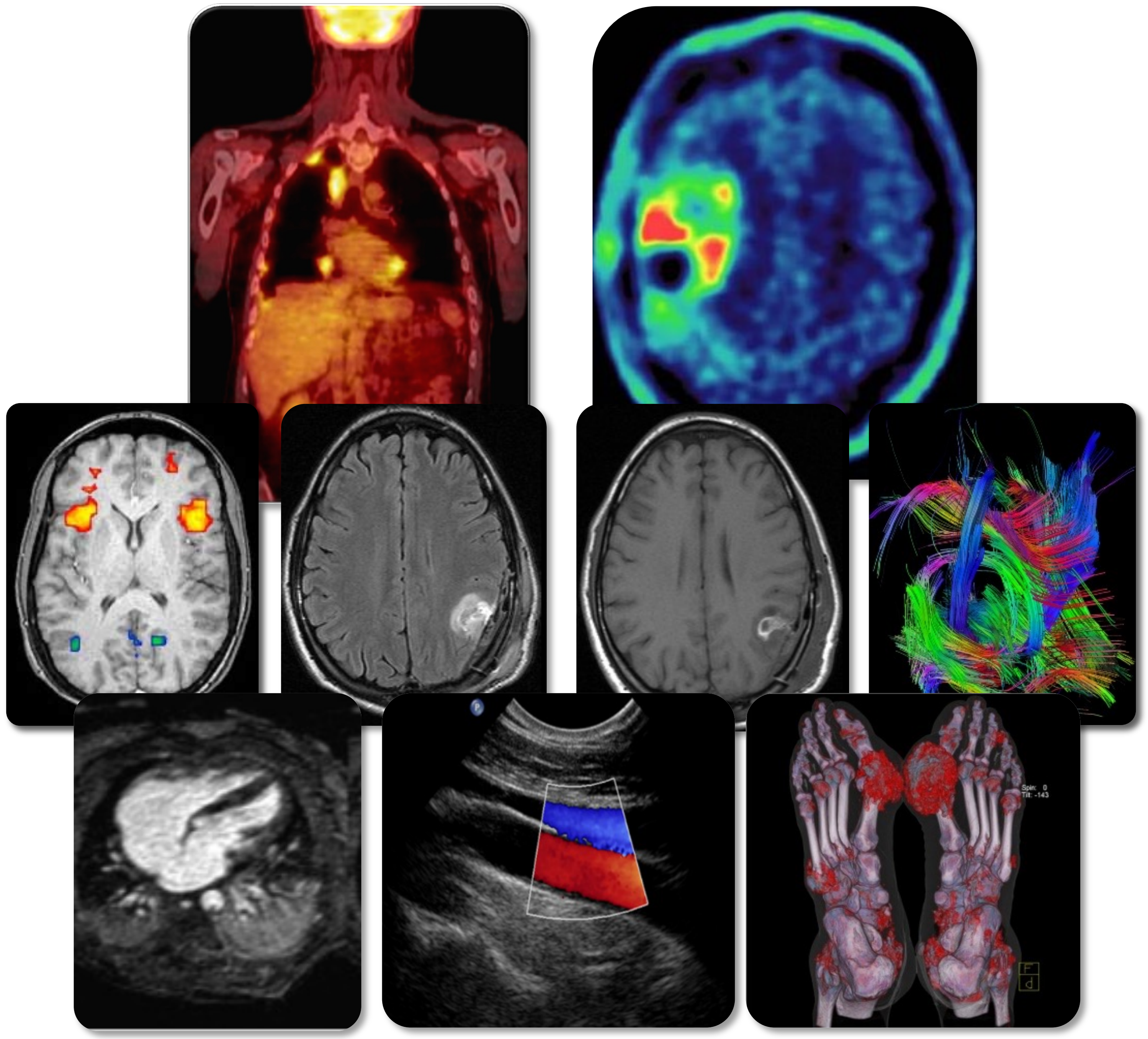
Medical & Imaging Informatics

The role of multimodal imaging

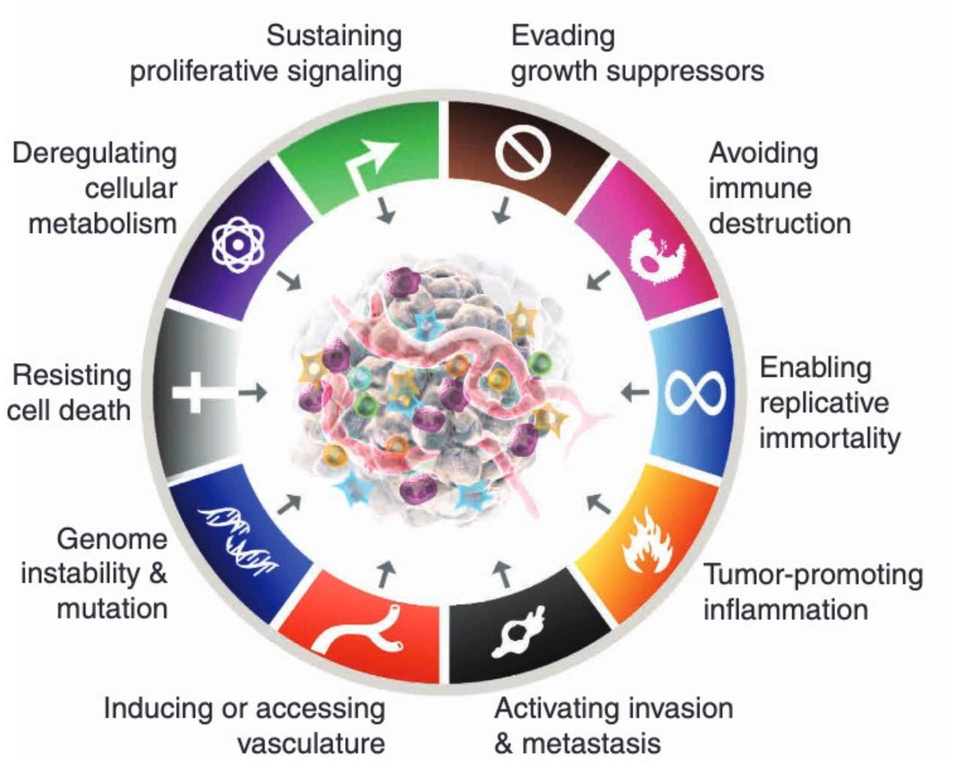
- Unique, in vivo, multi-scale view of anatomic and physiologic processes
- Utilized in the diagnosis, characterization, and clinical management of many diseases
- Biomarker of survival or treatment response
- A bridge between clinically observable level and lower biological scales

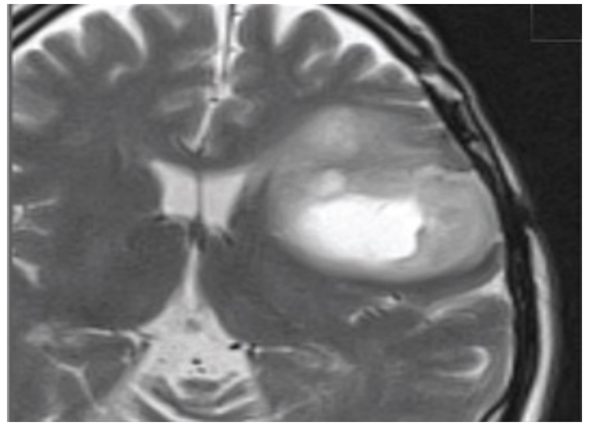


Hsu, W. et al. (2013). Biomedical imaging informatics in the era of precision medicine: progress, challenges, and opportunities. Journal of the American Medical Informatics Association : JAMIA, 20(6), 1010–3.

Imaging the "Hallmarks of Cancer"

NORMAL





Altered Metabolism & Hypoxia

^{18}FDG-PET
^{1}H and ^{13}C MRS
BOLD-MRI

Metastasis

DW-MRI
CT
^{18}FDG-PET

Angiogenesis

DCE-CT/MRI/US

Proliferation

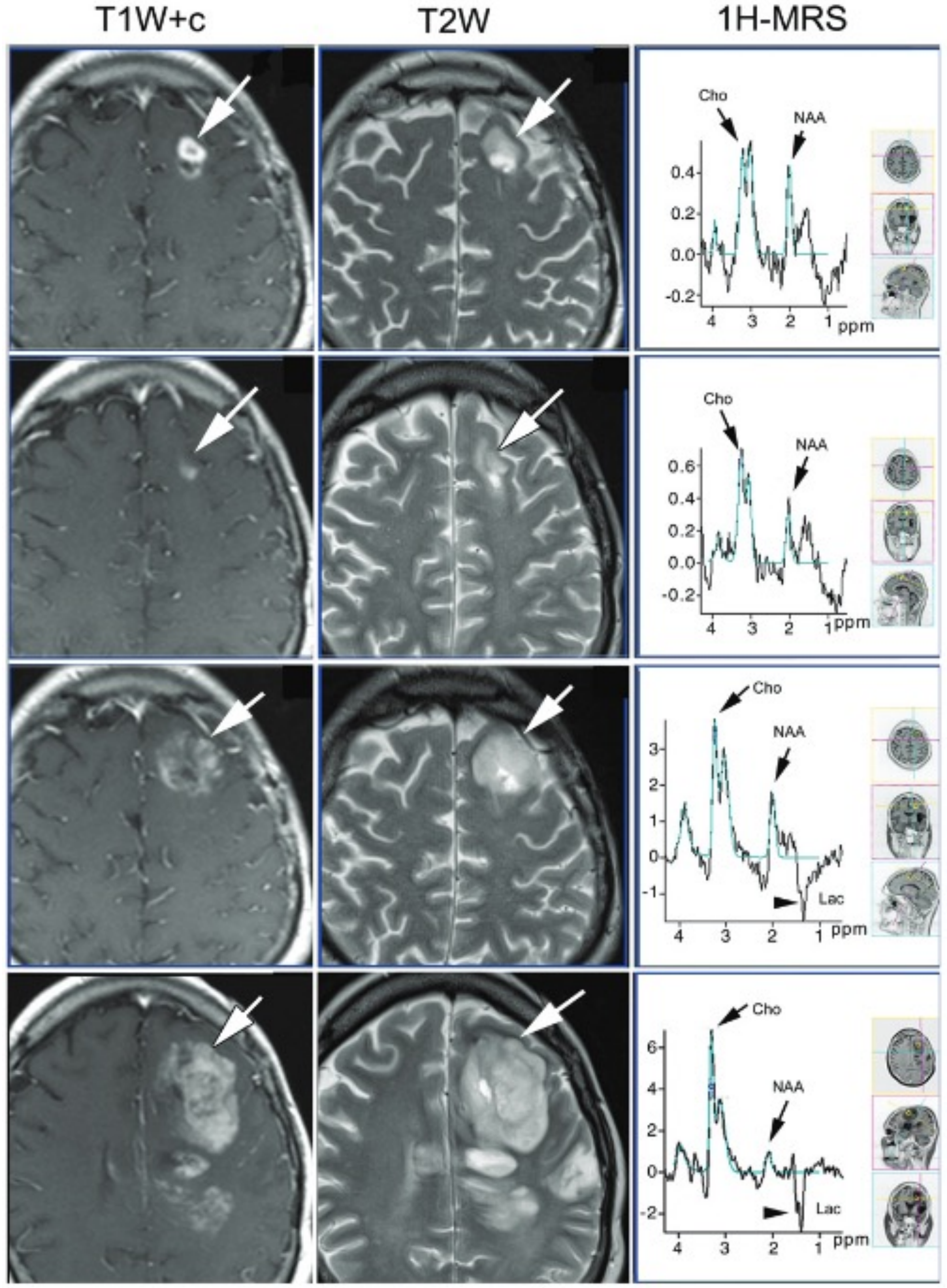
^{18}FLT-PET
^{1}H MRS
DW-MRI

Apoptosis

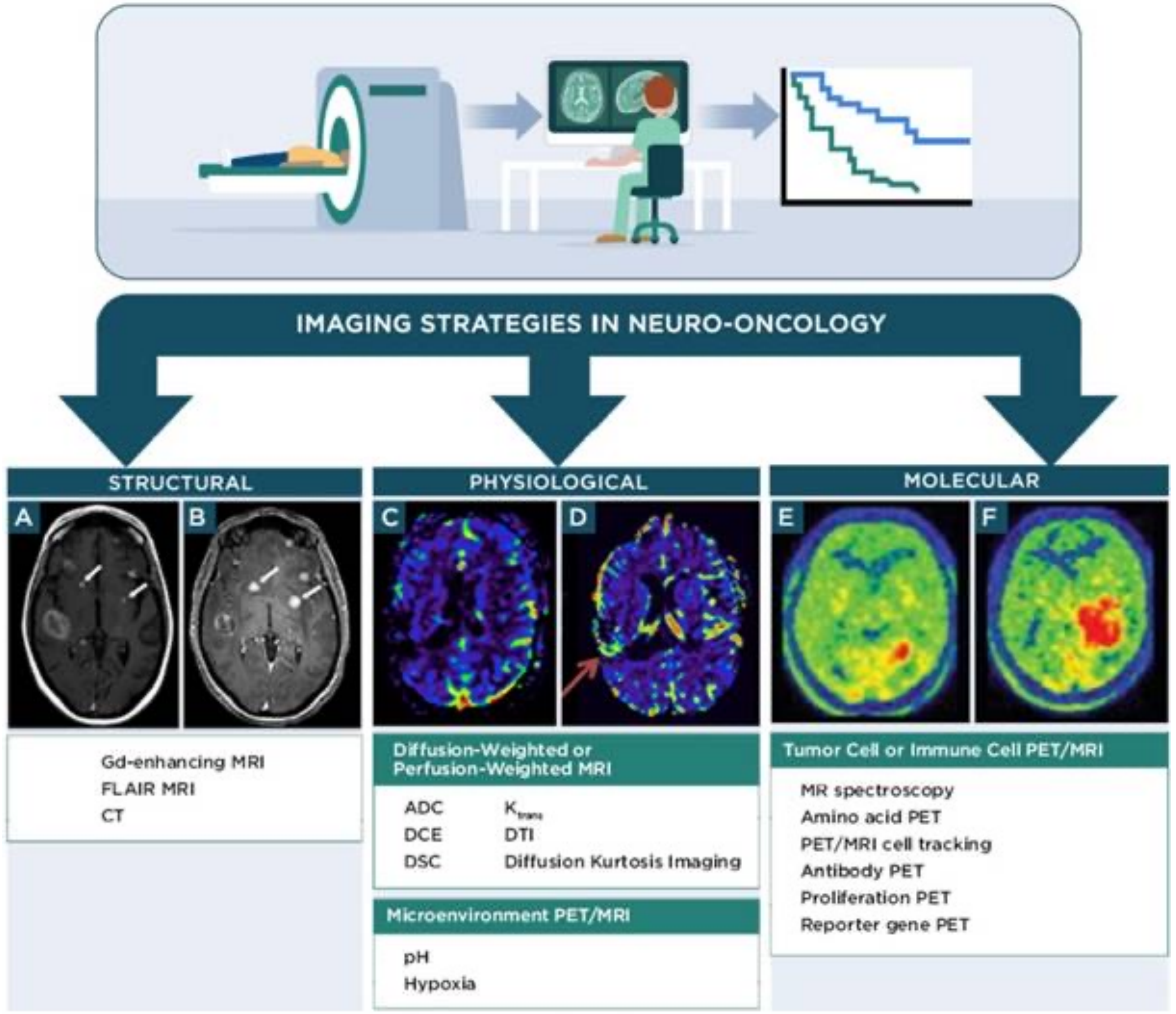
DW-MRI

Hanahan, D. Hallmarks of Cancer: New Dimensions. *Cancer Discov* **12**, 31–46 (2022).
Padhani, A. R. & Miles, K. A. Multiparametric Imaging of Tumor Response to Therapy. *Radiology* **256**, 348–364 (2010).

Imaging treatment response

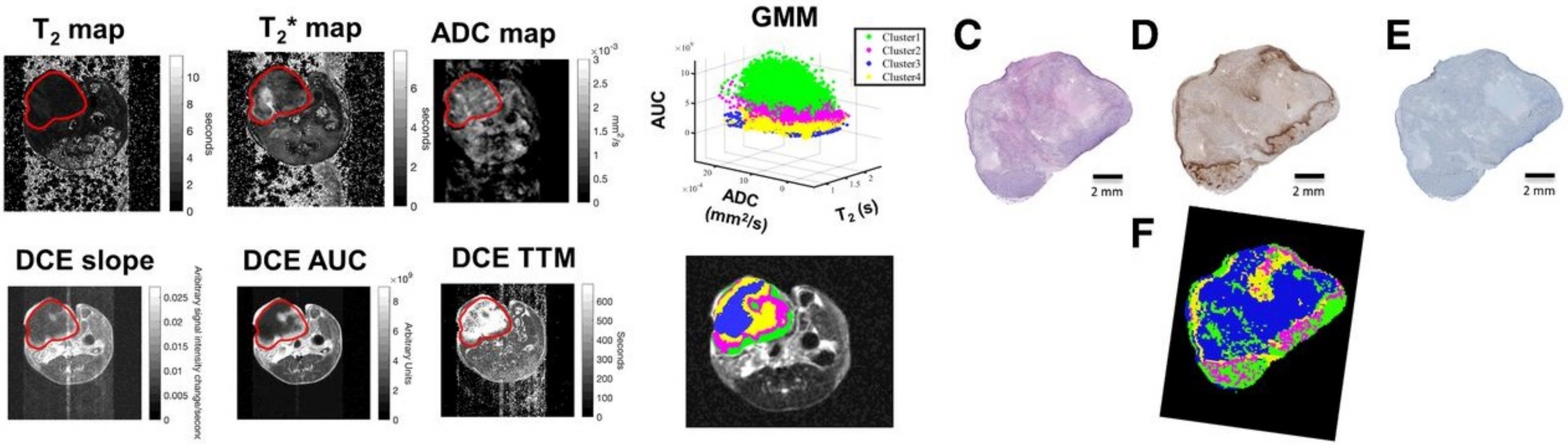


Padhani, A. R. & Miles, K. A. *Radiology* **256**, 348–364 (2010).



Kasten, B. B. *et al.* *Theranostics* **9**, 5085–5104 (2019).

Habitat maps combining MRI and histopathology



Jardim-Perassi, B. V. *et al.* Multiparametric MRI and Coregistered Histology Identify Tumor Habitats in Breast Cancer Mouse Models. *Cancer Res* **79**, 3952–3964 (2019).

Driving questions

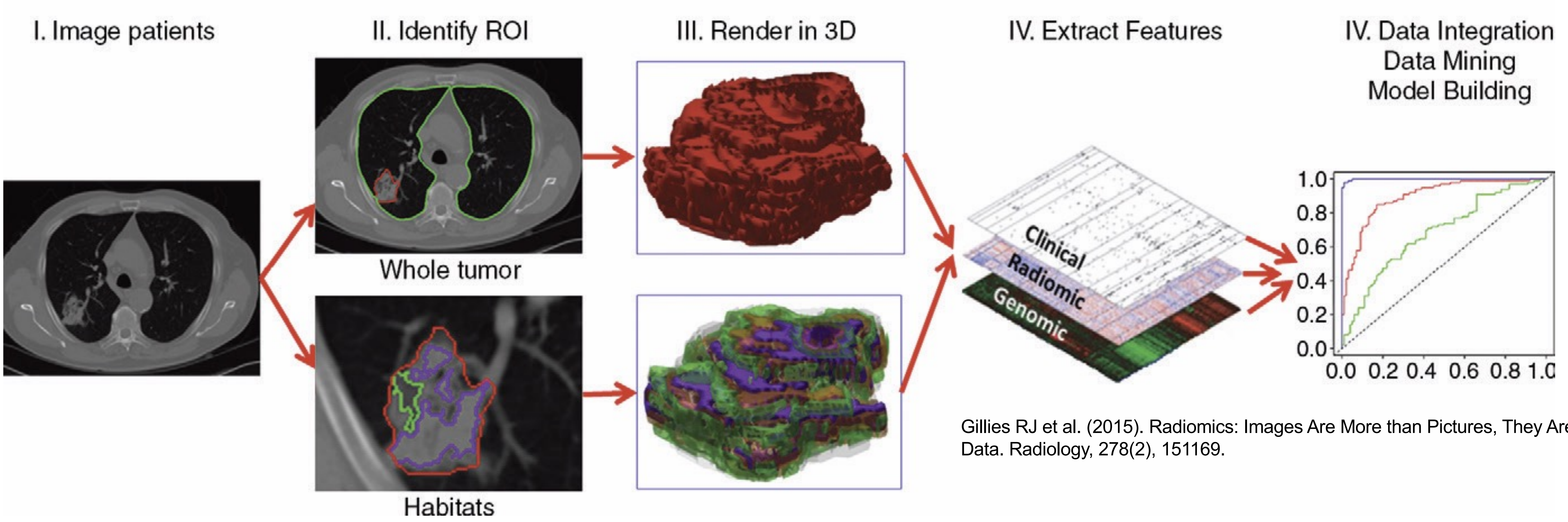
- What techniques exist for extracting biological knowledge using quantitative analysis of (MR) images?
- What barriers need to be addressed before biological insights can be reliably obtained?
- What role does imaging informatics play in the integration and analysis of biological information?

Outline

- Radiomics
- Mitigating variability due to image acquisition
- Spatially registering multimodal images
- Multimodal data fusion
- Ongoing efforts and concluding thoughts

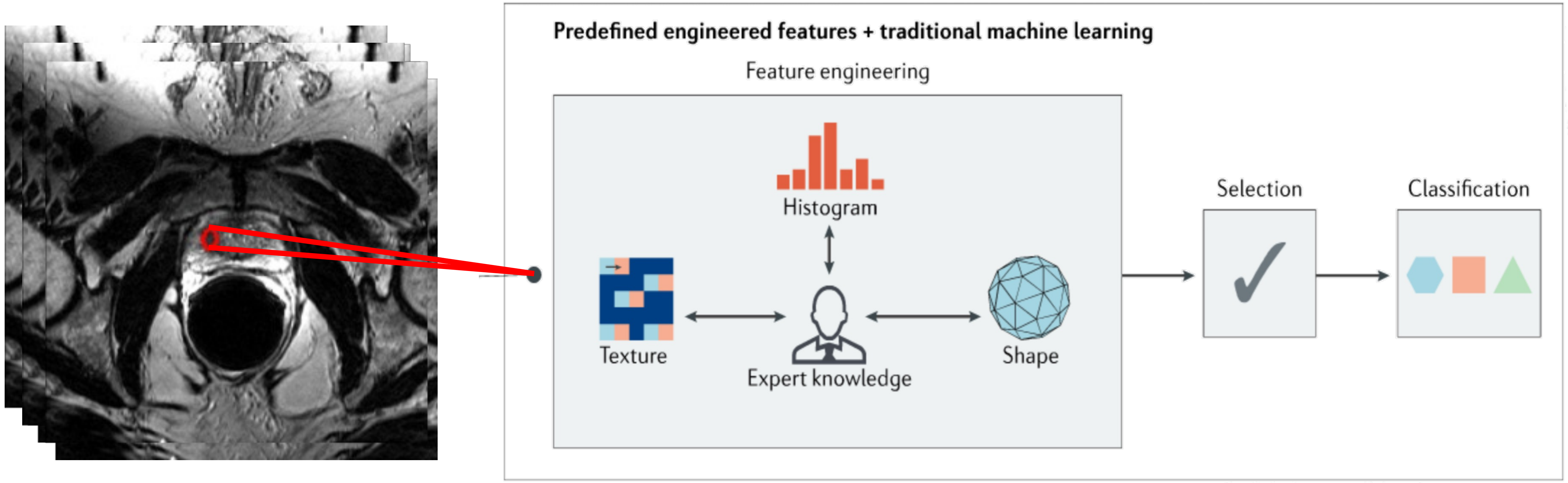
Radiomics

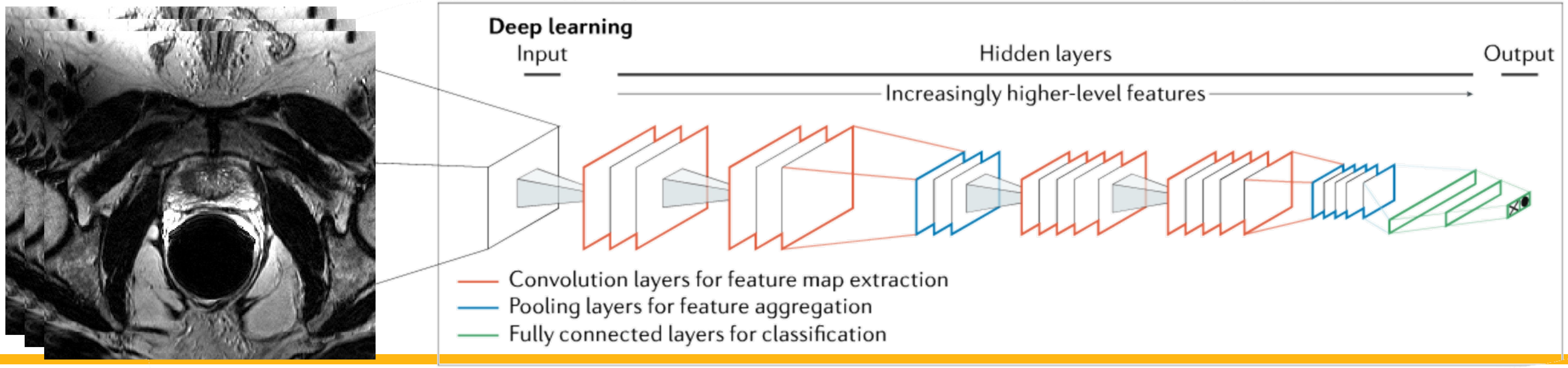
What is radiomics



Gillies RJ et al. (2015). Radiomics: Images Are More than Pictures, They Are Data. Radiology, 278(2), 151169.

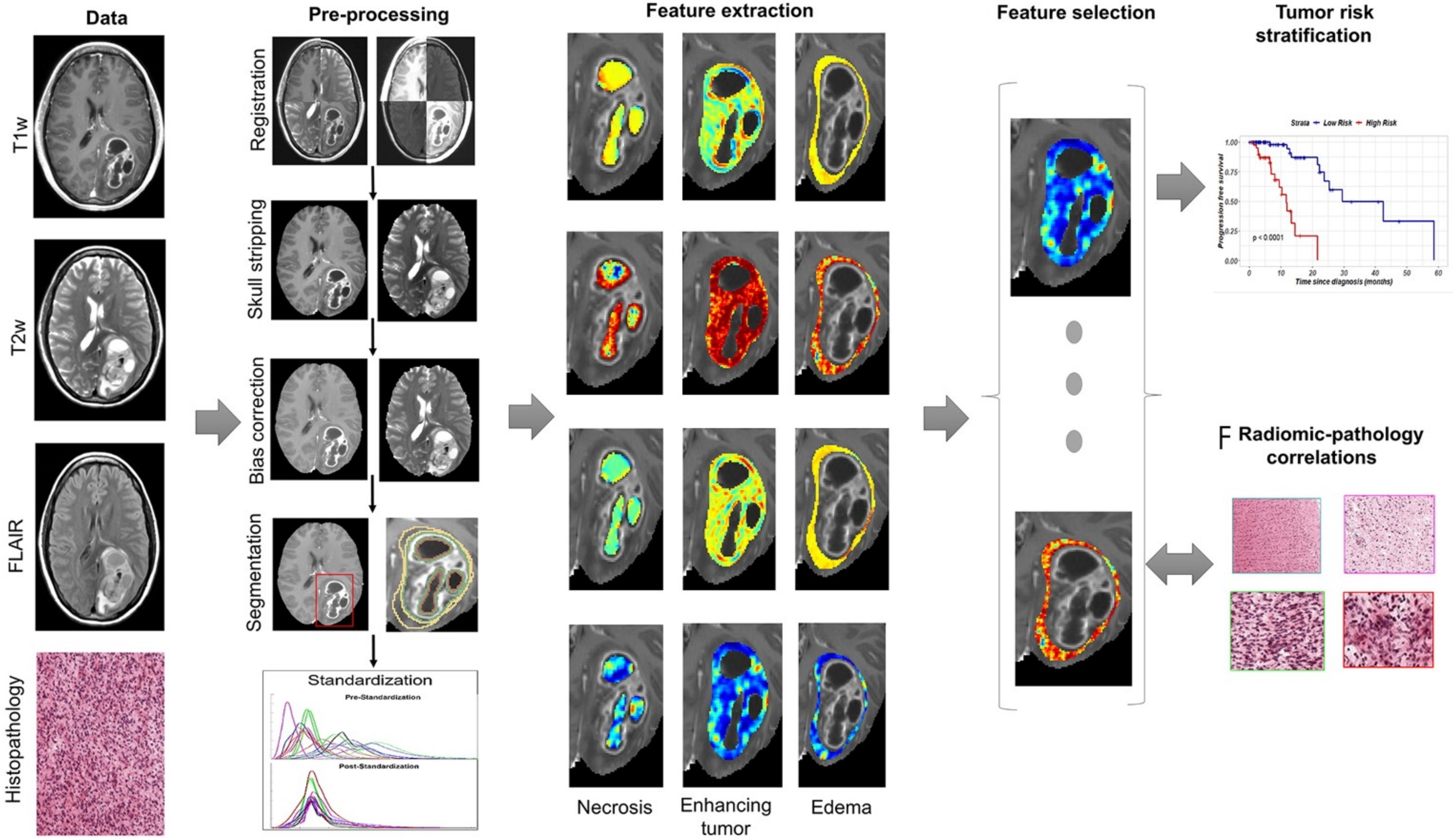
Radiomic vs deep features





Adapted from Hosny A, et al. Nature Reviews Cancer 2018: 18:500-51

Typical radiomic analysis pipeline



Verma et al (2020) https://pubs.rsna.org/doi/full/10.1148/ryai.2020190168

Families of radiomic features

		ROI mask		
Feature family	**count**	**morph.**	**int.**	**discr.**
morphology	29	✔	✔	×
local intensity	2	×	✔ [a]	×
intensity-based statistics	18	×	✔	×
intensity histogram	23	×	✔	✔
intensity-volume histogram	5	×	✔	✔ [b]
grey level co-occurrence matrix	25	×	✔	✔
grey level run length matrix	16	×	✔	✔
grey level size zone matrix	16	×	✔	✔
grey level distance zone matrix	16	✔	✔	✔
neighbourhood grey tone difference matrix	5	×	✔	✔
neighbouring grey level dependence matrix	17	×	✔	✔

- Number of features in the document
- The required input of a morphological (morph.) and/or intensity (int.) ROI mask
- Requirement of image discretization (discr.)

[a] *The entire image volume should be available when computing local intensity features*

[b] *Image discretization for the intensity-volume histogram is performed with finer discretization than required for e.g. textural features*

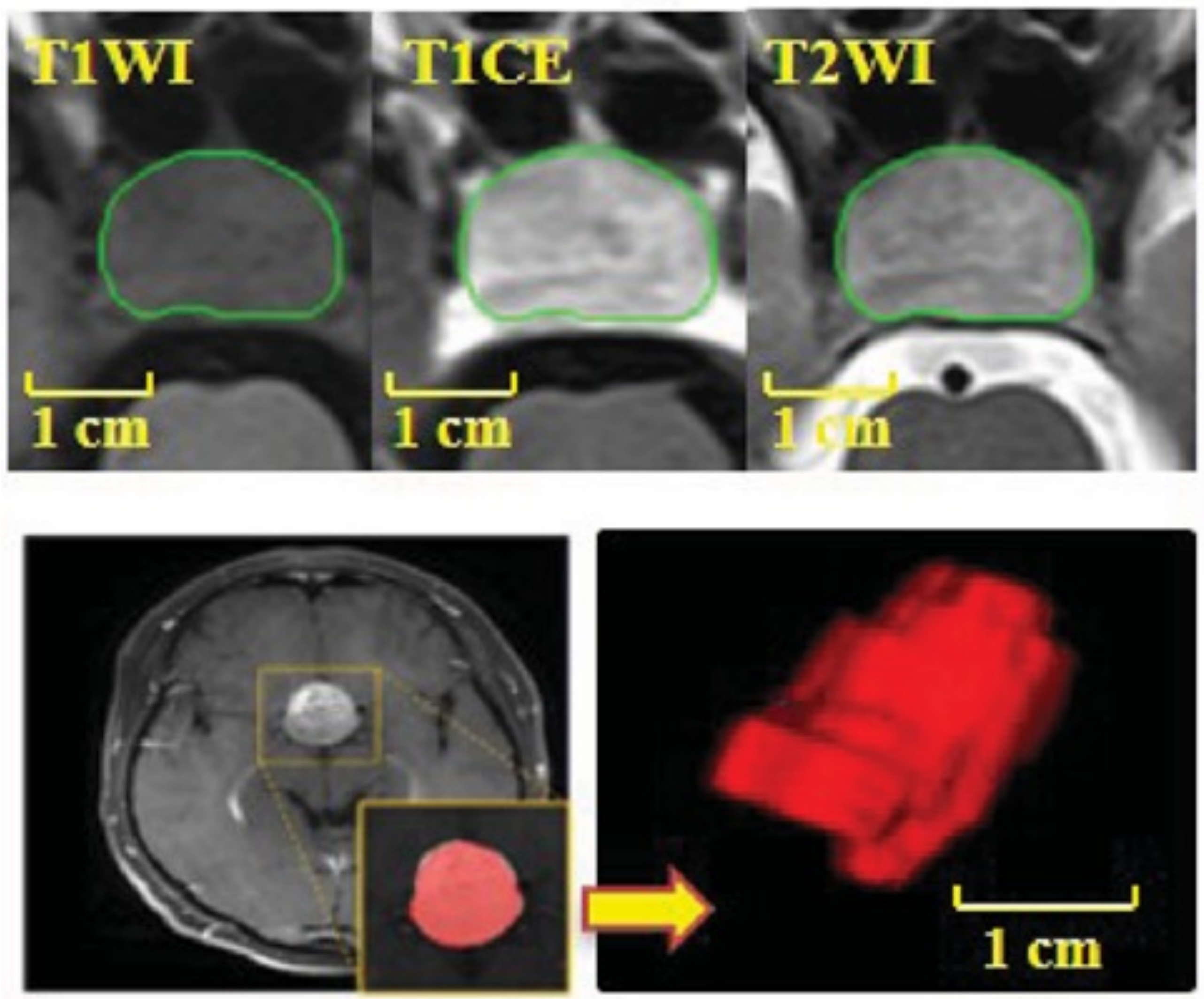
Discretization

- Intensity-resampling step applied to the image before computing features (used widely in intensity and texture features)
  - Matrix dimensions are determined by the number of intensity values obtained after this resampling
  - One approach: assign intensity value to bin based on:

$$I_B = B \times \frac{I - I_{min}}{I_{max} - I_{min}}$$

B = number of bins (8, 16, 32, 64…)
I_{min}, I_{max} = min/max intensity values in image

Morphology



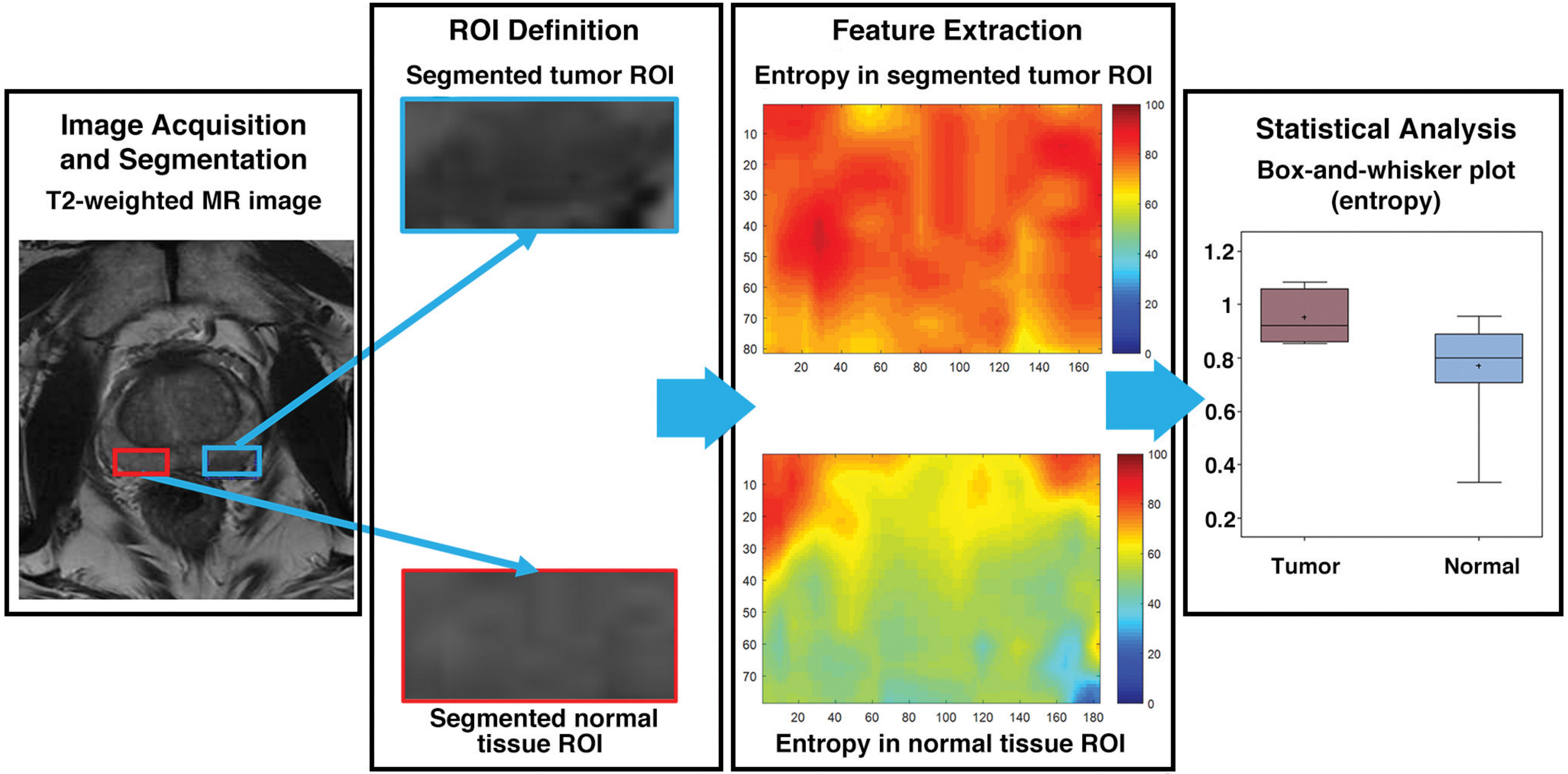
Source: https://onlinelibrary.wiley.com/doi/10.1002/jmri.27930

- Volume
- Surface area
- Sphericity
- …

Intensity

- **Local intensity features**: computed from voxel intensities within a defined neighborhood around a center voxel
- **Intensity-based statistical features**: description of how intensities within an ROI are distributed
- **Intensity histogram features**: characterization of the histogram profile after discretizing the original intensity distribution into bins
- **Intensity-volume histogram features**: description of the relationship between a defined discretized intensity bin and the fraction of the ROI that have voxel intensities within this bin

Texture



Source: https://www.ajronline.org/doi/pdf/10.2214/AJR.18.20624

Co-Occurrence Matrix

- **Co-occurrence matrix** is defined over an image to be the distribution of co-occurring values at a given offset
  - How combinations of (discretized) grey levels of neighboring pixels or voxels in a 3D volume are distributed along one of the image directions
- **Grey Level Co-occurrence Matrix** (GLCM aka Harlick features) calculates how often a pixel with grey-level value i occurs either horizontally, vertically, or diagonally to adjacent pixels with the value j
  - Relationship between the reference and neighboring pixel (e.g., second order feature)

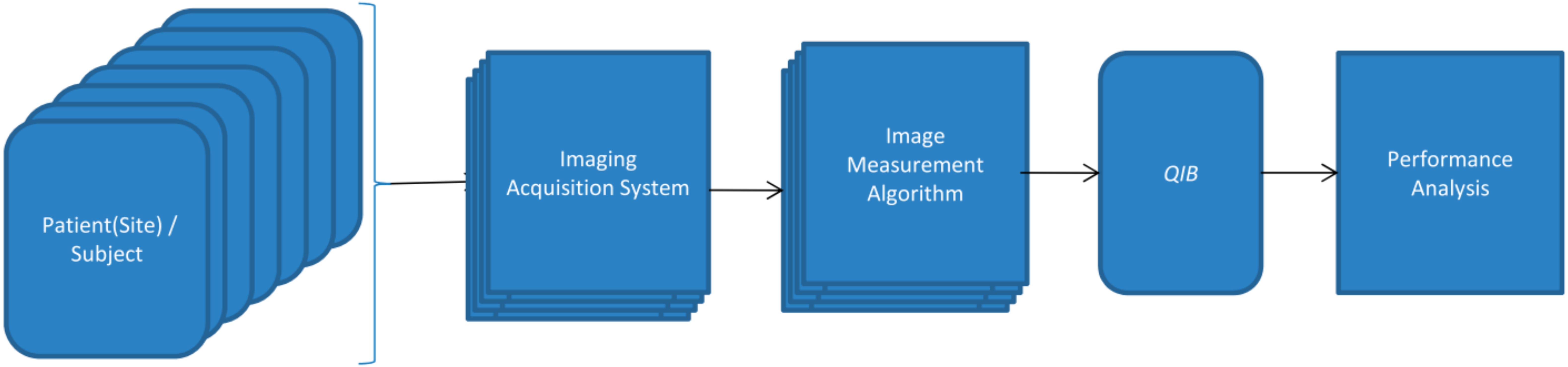
Calculating GLCM

0	0	1	1
0	0	1	1
0	2	2	2
2	2	3	3

1. Discretize the image
2. Create a framework matrix
3. Decide on the spatial relation between the reference and neighbor
4. Count the occurrences and complete the framework matrix
5. Add the matrix to its transpose to make it symmetrical
6. Normalize the matrix

Mitigating variability due to image acquisition

Sources of variability



Patient Variability

Instrument / Acquisition Variability

Algorithm / Measurement Variability

Repeatability vs reproducibility

- **Repeatability** refers to "variability of the quantitative image biomarker when repeated measurements are acquired on the same experimental unit under identical or nearly identical conditions" to determine the measurement error

- **Reproducibility** refers to "variability in the quantitative image biomarker measurements associated with using the imaging instrument in real-world clinical settings"

Raunig, D. L. *et al.* Quantitative imaging biomarkers: A review of statistical methods for technical performance assessment. *Stat Methods Med Res* **24**, 27–67 (2015).

Factors that influence radiomics stability

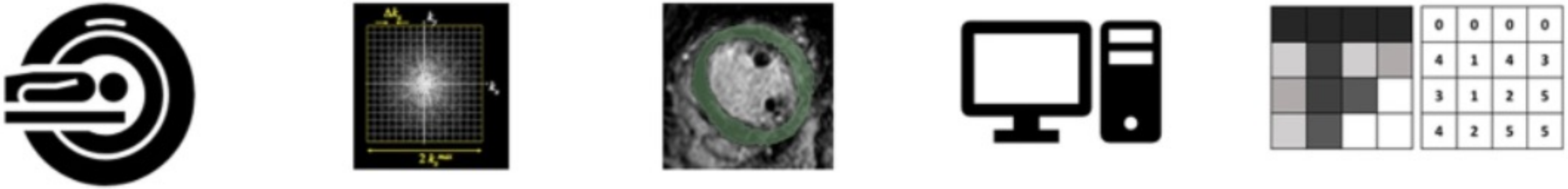


	Image acquisition	Reconstruction	Segmentation	Post-processing	Feature extraction

MRI	• Field strength
	• Sequence design
	• Matrix size (acquired)
	• Field of view
	• Slice thickness
	• Acceleration techniques
	• Vendor
	• Contrast timing
	• Movement
		• Matrix size (reconstructed)
		• Reconstruction technique
			• Manual 2D
			• Manual 3D
			• Semi-automated 2D
			• Semi-automated 3D
			• Automated 2D
			• Automated 3D
			• Size of the ROI
				• Image interpolation ('resampling' / 'rescaling')
				  • Grid alignment
				  • Pixel sizing
				• Intensity discretisation ('rebinning')
				• Normalisation
					• Mathematical formula
					• Post-processing platform

Timmeren, J. E. van, Cester, D., Tanadini-Lang, S., Alkadhi, H. & Baessler, B. Radiomics in medical imaging—"how-to" guide and critical reflection. *Insights Imaging* **11**, 91 (2020).

Measuring agreement

- Intraclass correlation (ICC)

$$Y_{ij} = \mu + \alpha_j + \varepsilon_{ij},$$

$$\frac{\sigma_\alpha^2}{\sigma_\alpha^2 + \sigma_\varepsilon^2}.$$

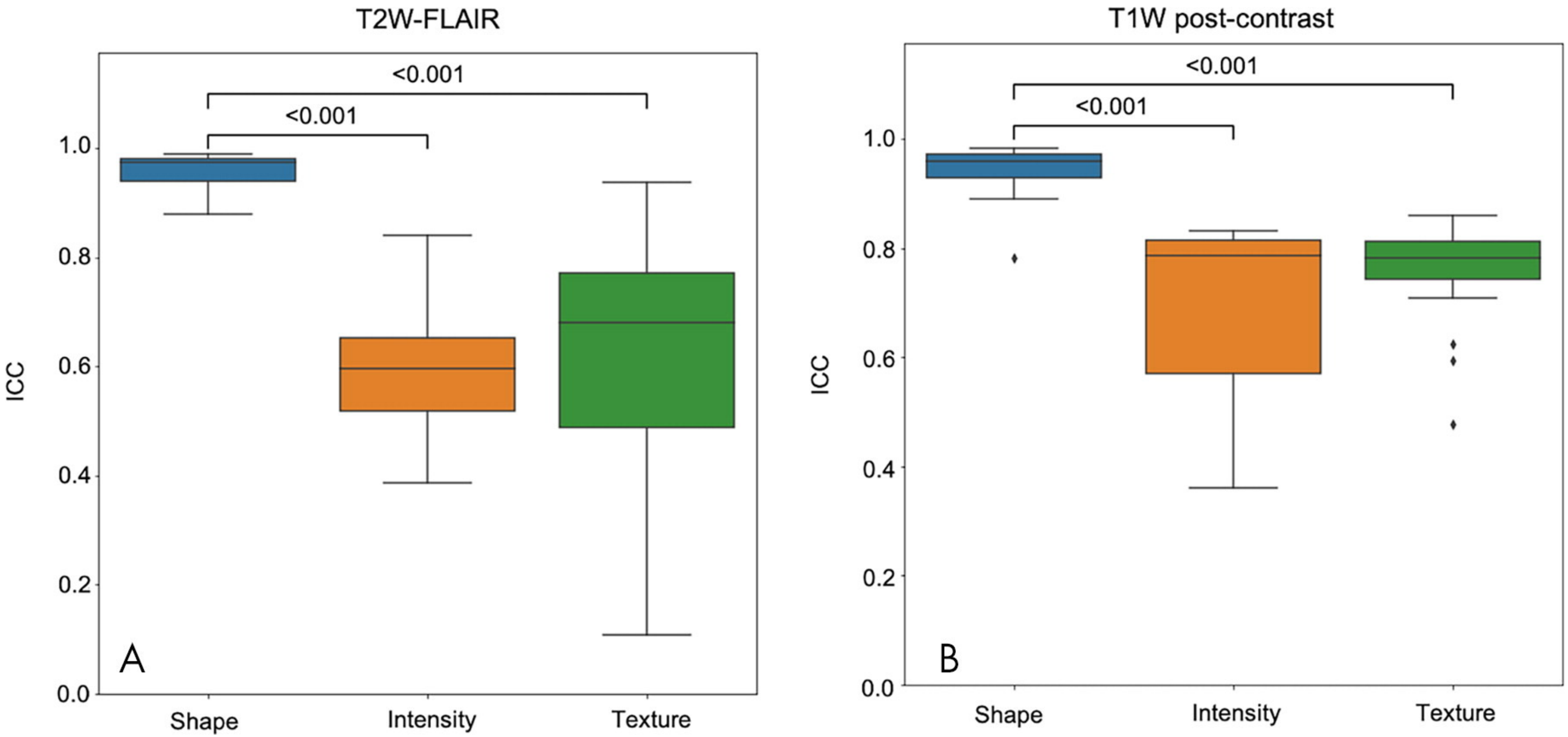
- Assumes linear relationship between variables
- Takes into account differences in the means of the measures being considered
- Can be generalized to multiple readers

- Concordance correlation (CCC)

$$P_{CCC} = \frac{2\sigma_{12}}{\sigma_\beta^2 + \sigma_\beta^2 + (\mu_1 - \mu_2)^2}.$$

- No statistical model is assumed in the definition
- Does not assume a common mean for judges' ratings
- Applies to only two judges at a time

ICC values from scan/rescan of same patient



UCLA Health | David Geffen School of Medicine

Hoebel, K. V. *et al.* Radiomics Repeatability Pitfalls in a Scan-Rescan MRI Study of Glioblastoma. *Radiology Artif Intell* **3**, e190199 (2020).

THE HSU LAB UCLA MII MEDICAL & IMAGING INFORMATICS

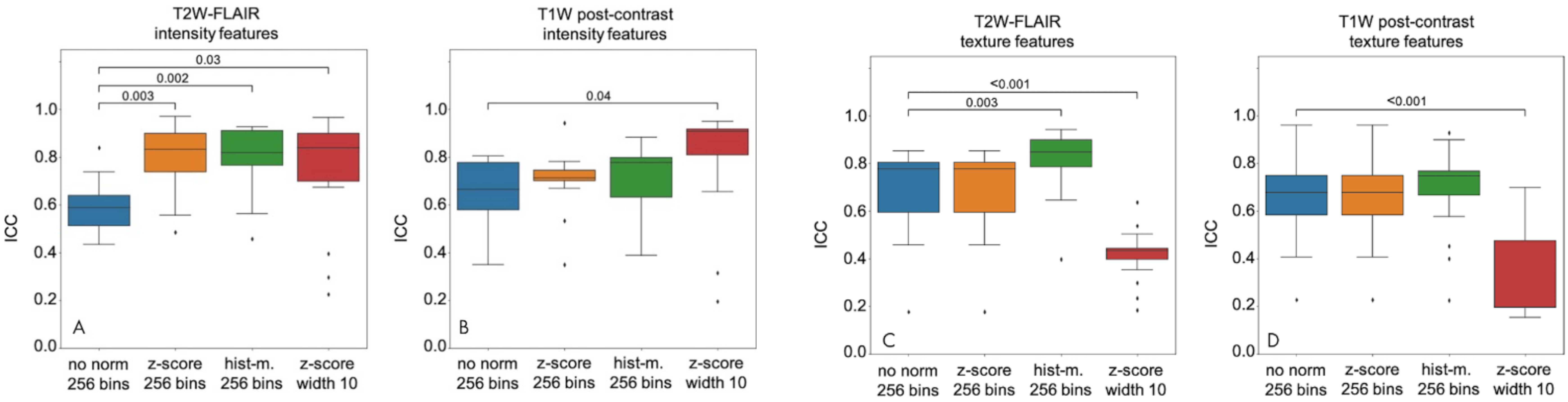
Normalization techniques

- Z score normalization
  - Subtract the mean intensity of the entire image or a region of interest from each voxel value and dividing it by the corresponding standard deviation
  - Mean of the voxel intensity distribution is centered at zero with unit variance

- Histogram matching
  - Modify the contrast level of one scan according to another
  - Piecewise linear transformation is applied such that the histogram of a source image is matched to that of a chosen reference image

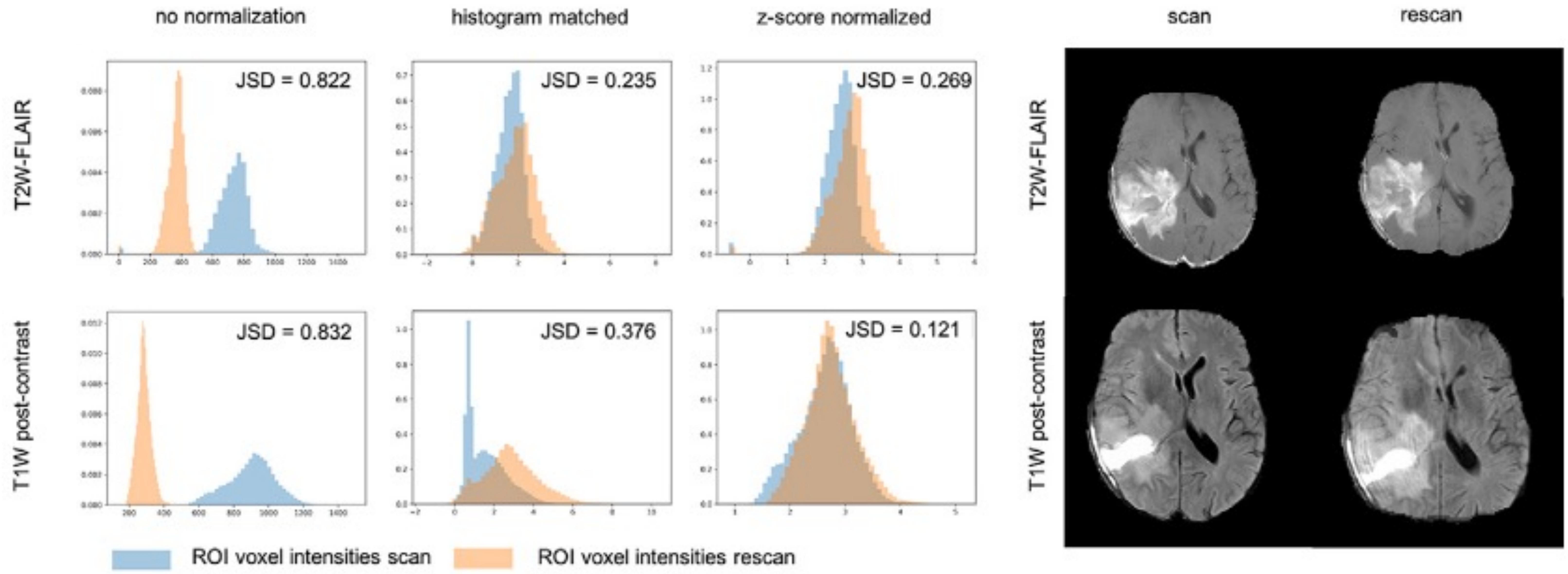
Nyúl LG, Udupa JK. On standardizing the MR image intensity scale. Magn Reson Med 1999;42(6):1072–1081.

Effect of normalization



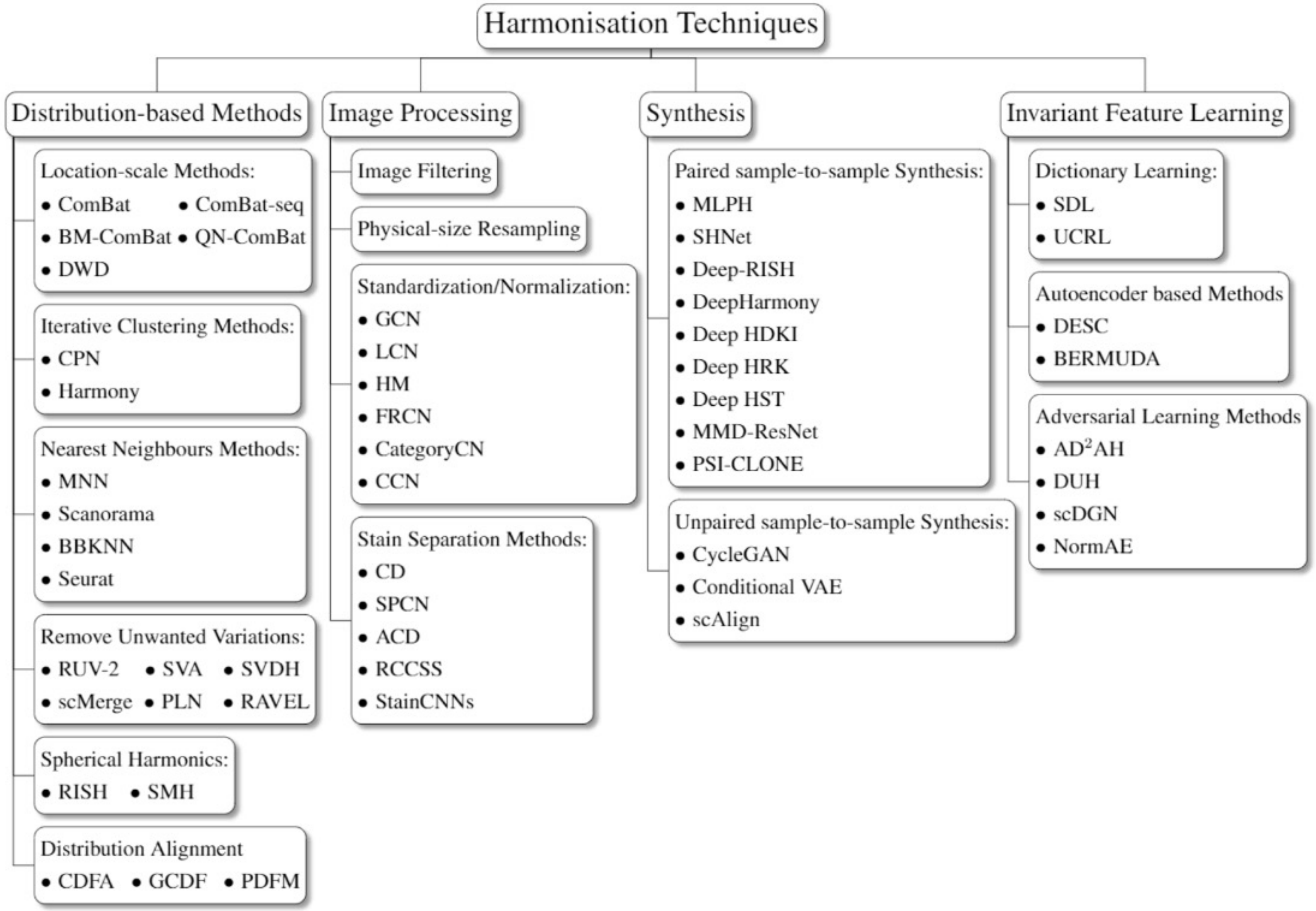
Hoebel, K. V. *et al.* Radiomics Repeatability Pitfalls in a Scan-Rescan MRI Study of Glioblastoma. *Radiology Artif Intell* **3**, e190199 (2020).

Effect of normalization



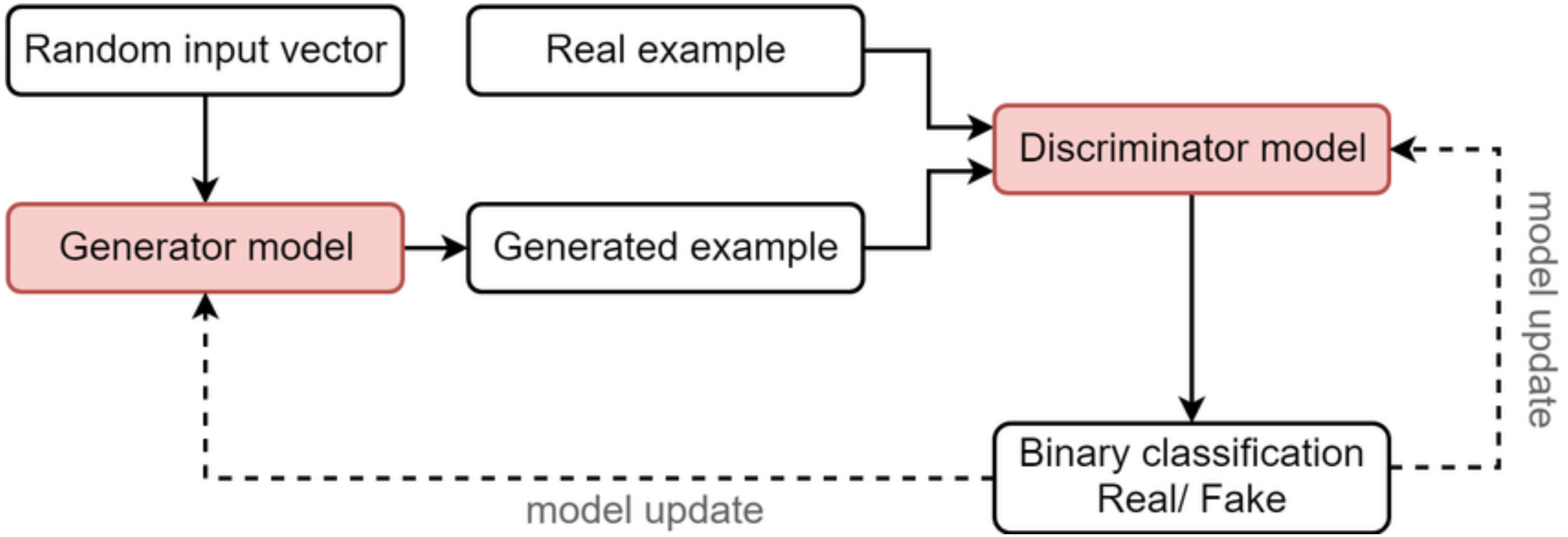
Hoebel, K. V. *et al.* Radiomics Repeatability Pitfalls in a Scan-Rescan MRI Study of Glioblastoma. *Radiology Artif Intell* **3**, e190199 (2020).

Methods for normalization

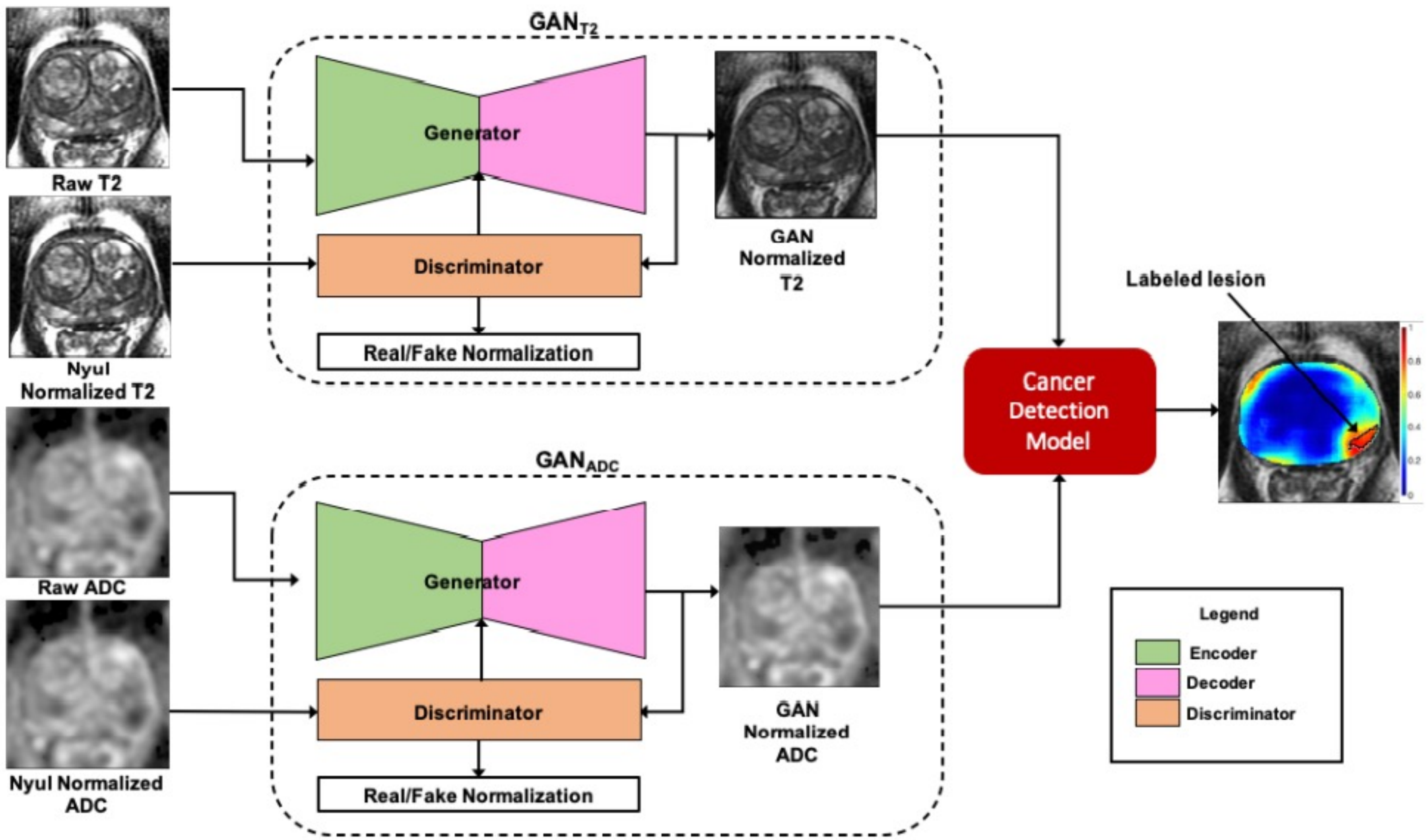


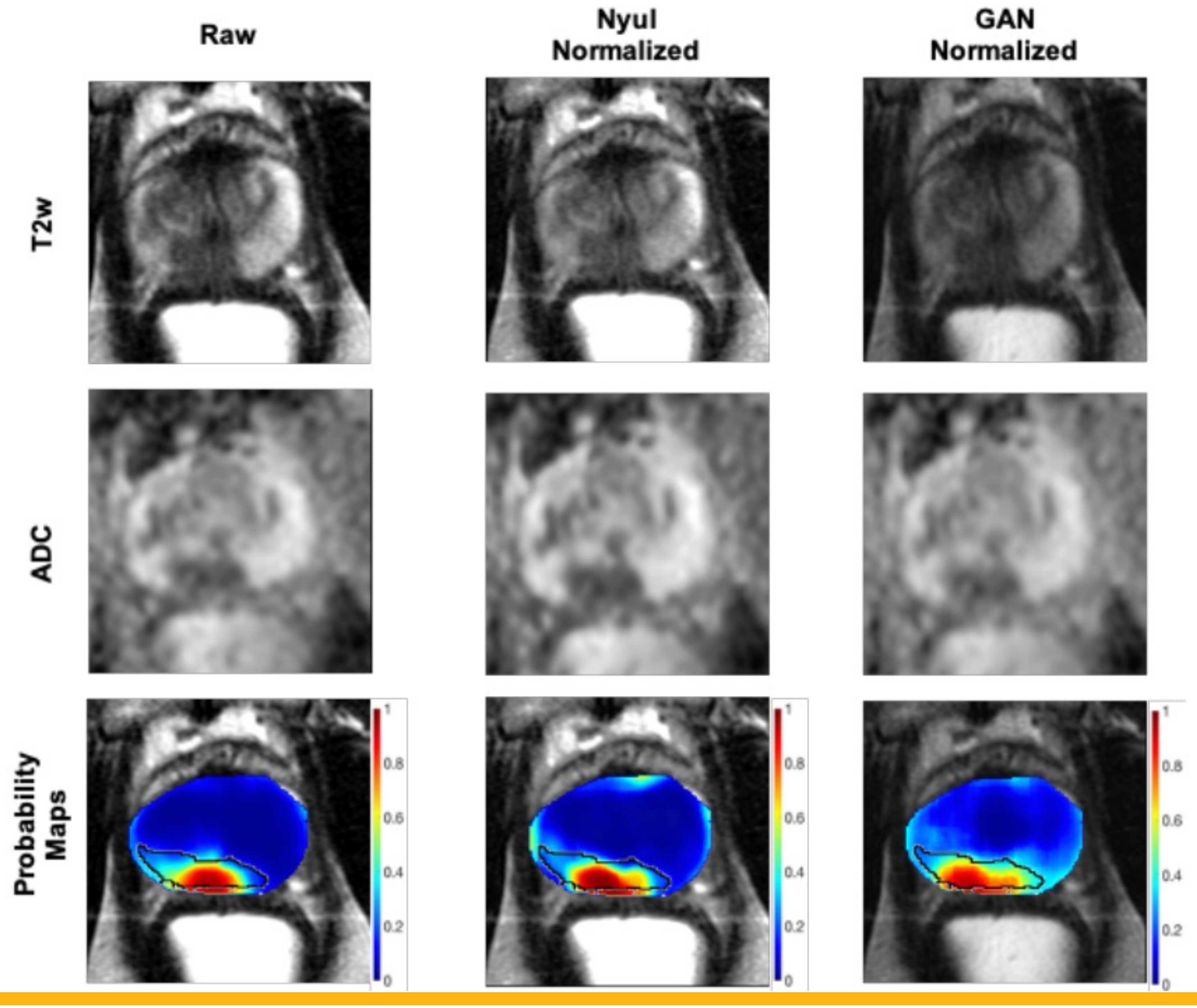
Nan, Y. *et al.* Data harmonisation for information fusion in digital healthcare: A state-of-the-art systematic review, meta-analysis and future research directions. *Inform Fusion* **82**, 99–122 (2022).

Normalization via synthesis



GAN-based normalization example



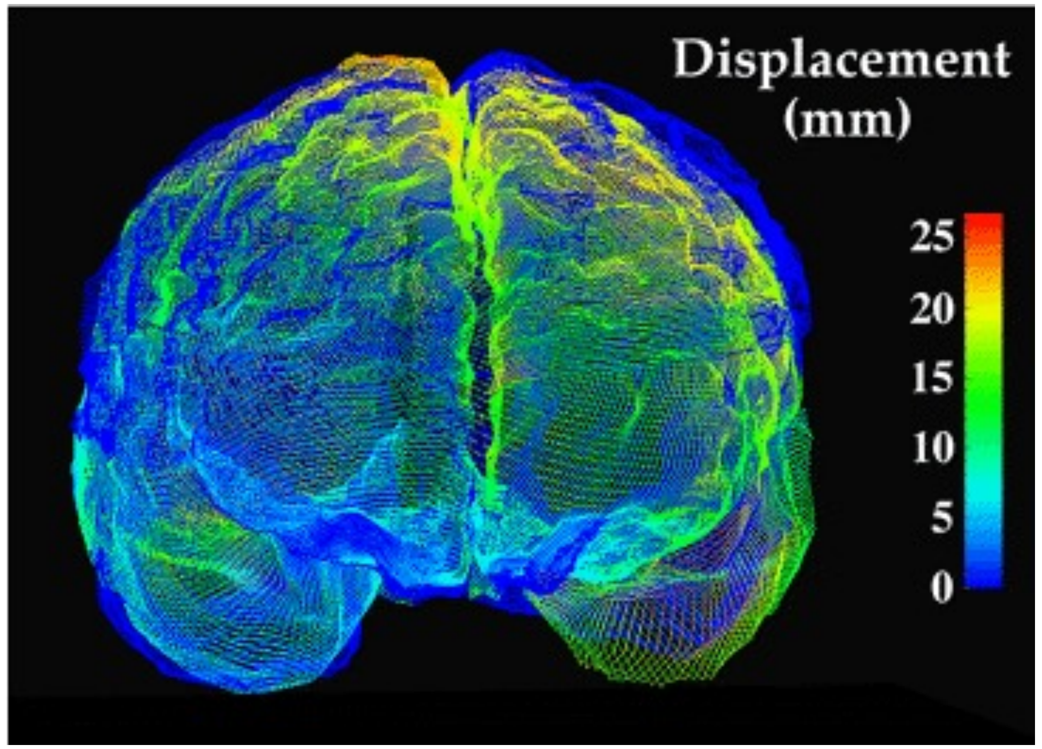


Spatially registering multimodal images

Some slides were adapted from David S. Paik (Stanford University)

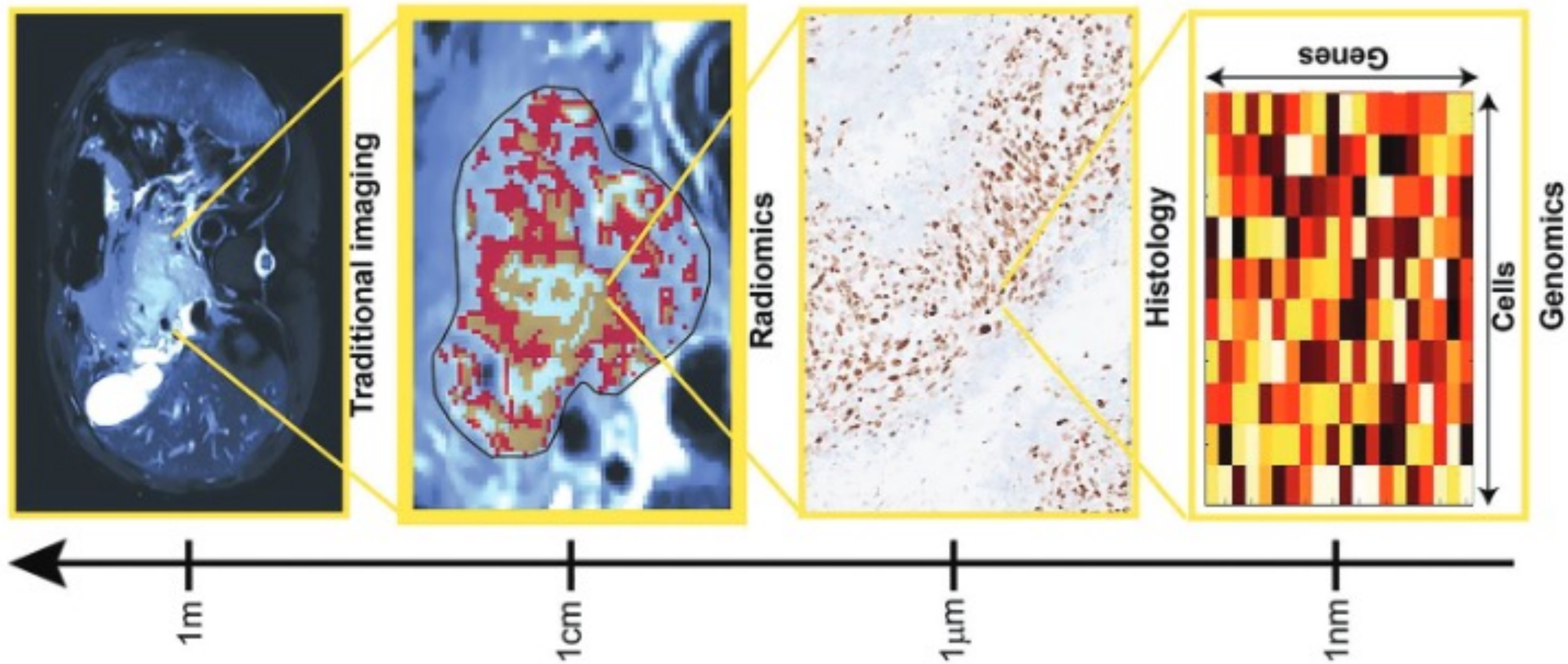
The need for spatial registration

- Two or more images of the same or different patients that you wish to spatially align with each other
  - << Multiparametric images of the same patient
  - Imaging studies from a cohort of patients from which you wish to build an atlas >>



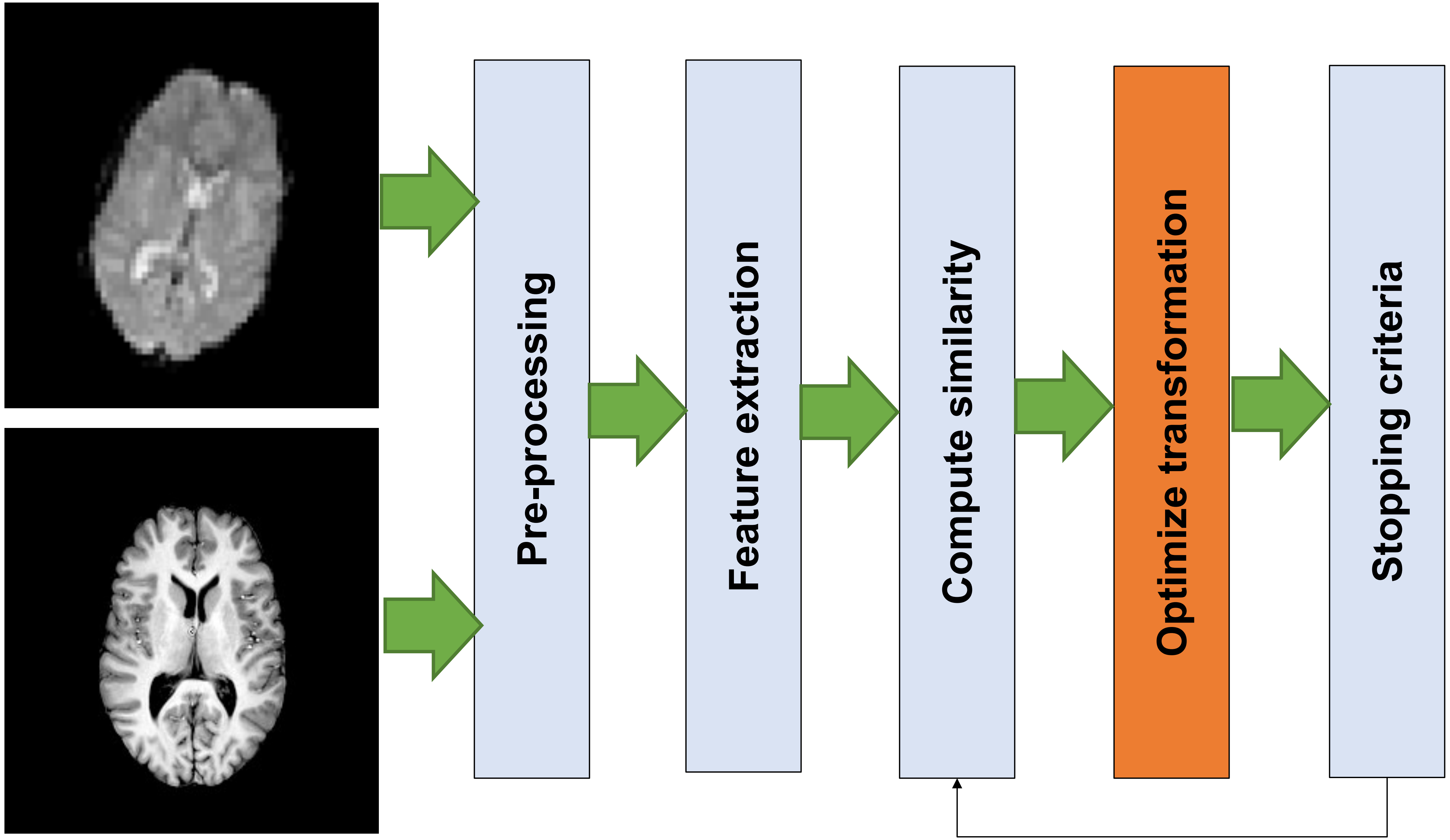
Source: http://users.loni.usc.edu/~thompson/hbm97abs.html

Aligning modalities

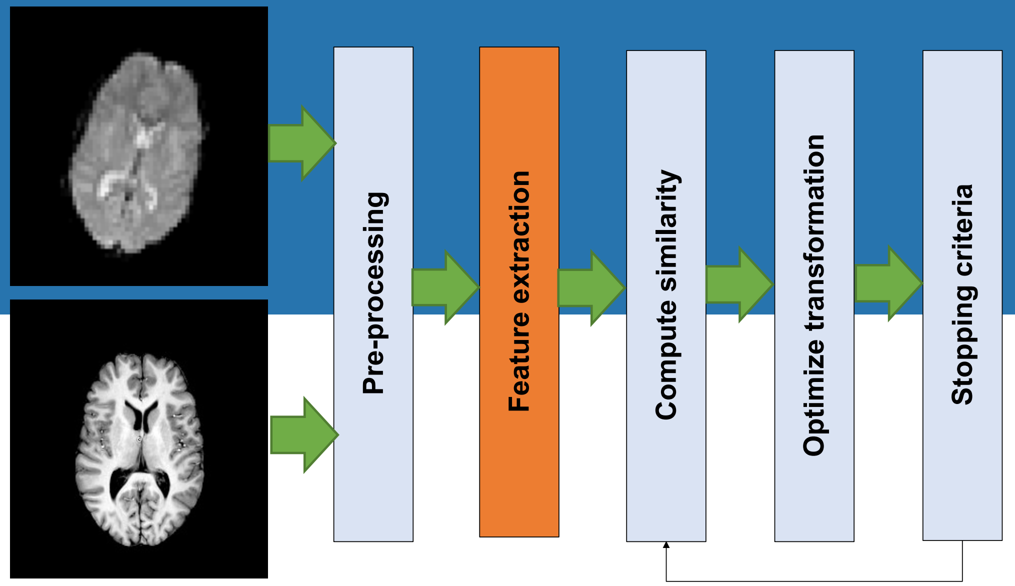


Tomaszewski, M. R. & Gillies, R. J. The Biological Meaning of Radiomic Features. *Radiology* 202553 (2021) doi:10.1148/radiol.2021202553.

Registration framework

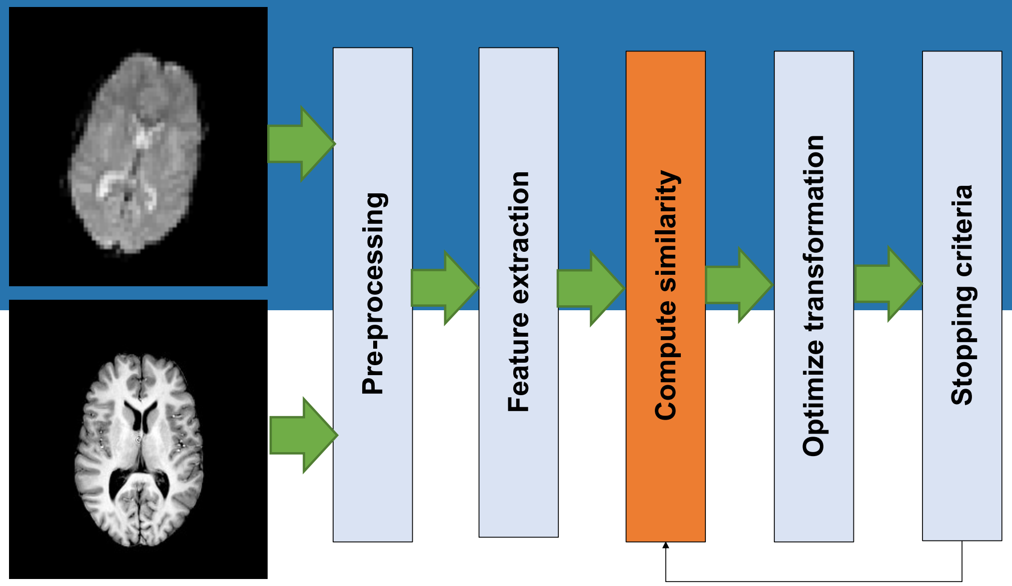


Feature extraction

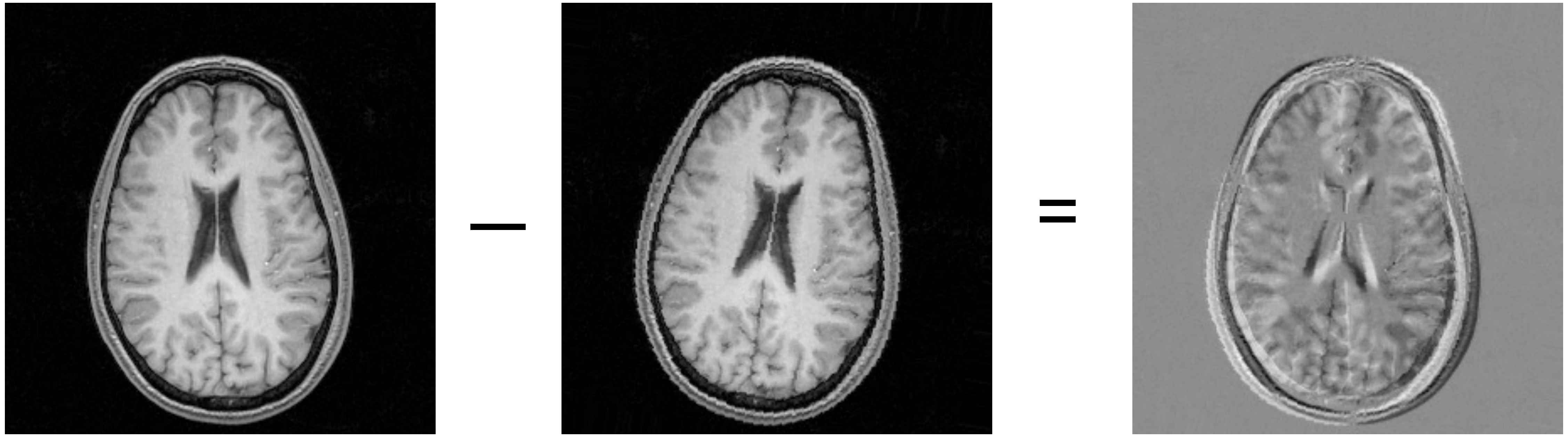


- Raw intensity values
- Edges
- Salient features
  - Points of locally maximum curvature on contour line
  - Centers of windows having locally maximum variance
  - Line intersections
- Statistical features
  - Moment invariants
  - Centroid/principal axes
- Higher level features
- Matching against models
  - Anatomic atlas

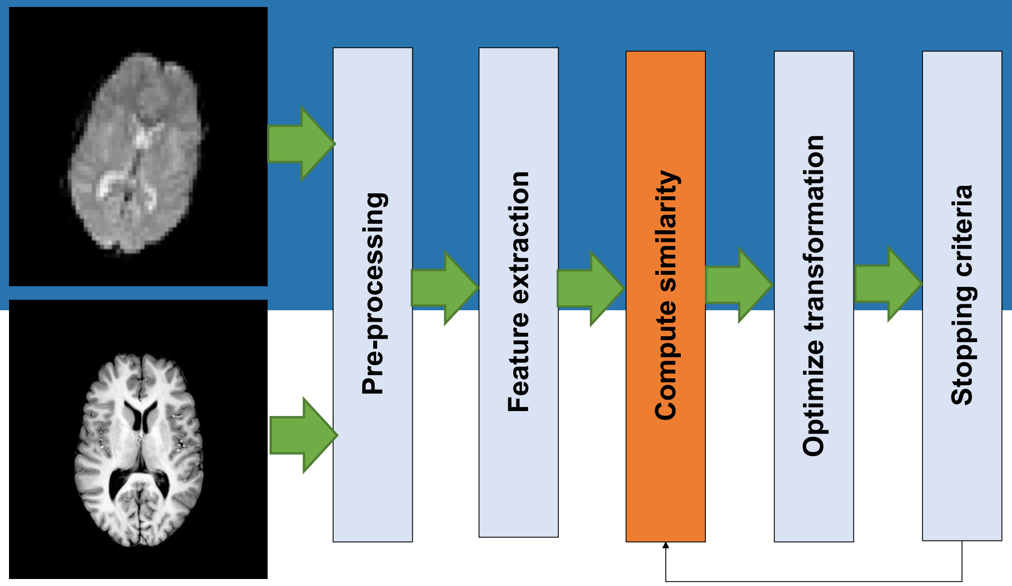
Compute similarity



- Similarity measure: maximum when images are perfectly aligned
  - Mutual information
  - Gradient correlation
  - Correlation coefficient
- Distance measure: minimum when images are perfectly aligned
  - Sum of squared differences
  - Sum of absolute differences

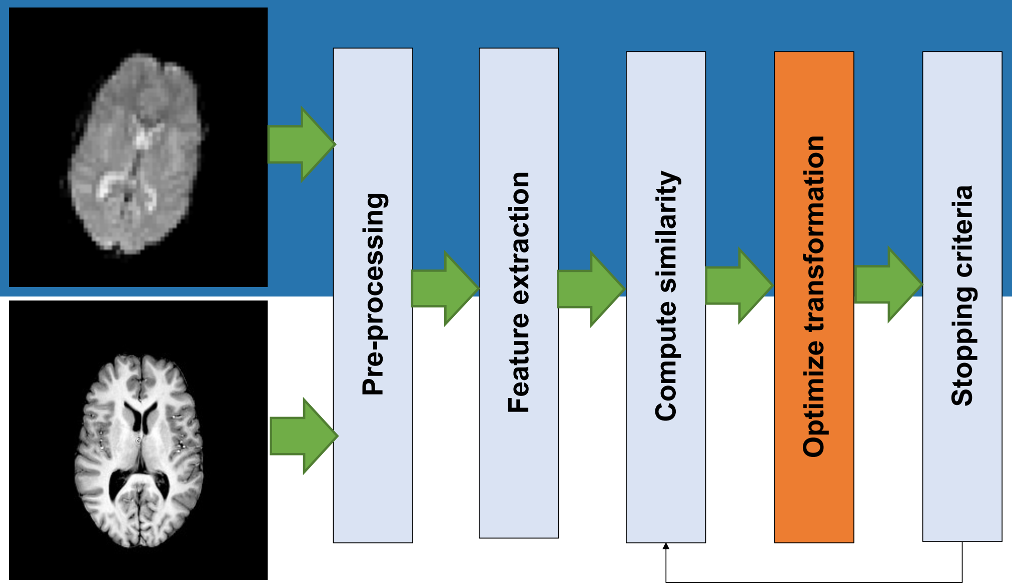


Compute similarity

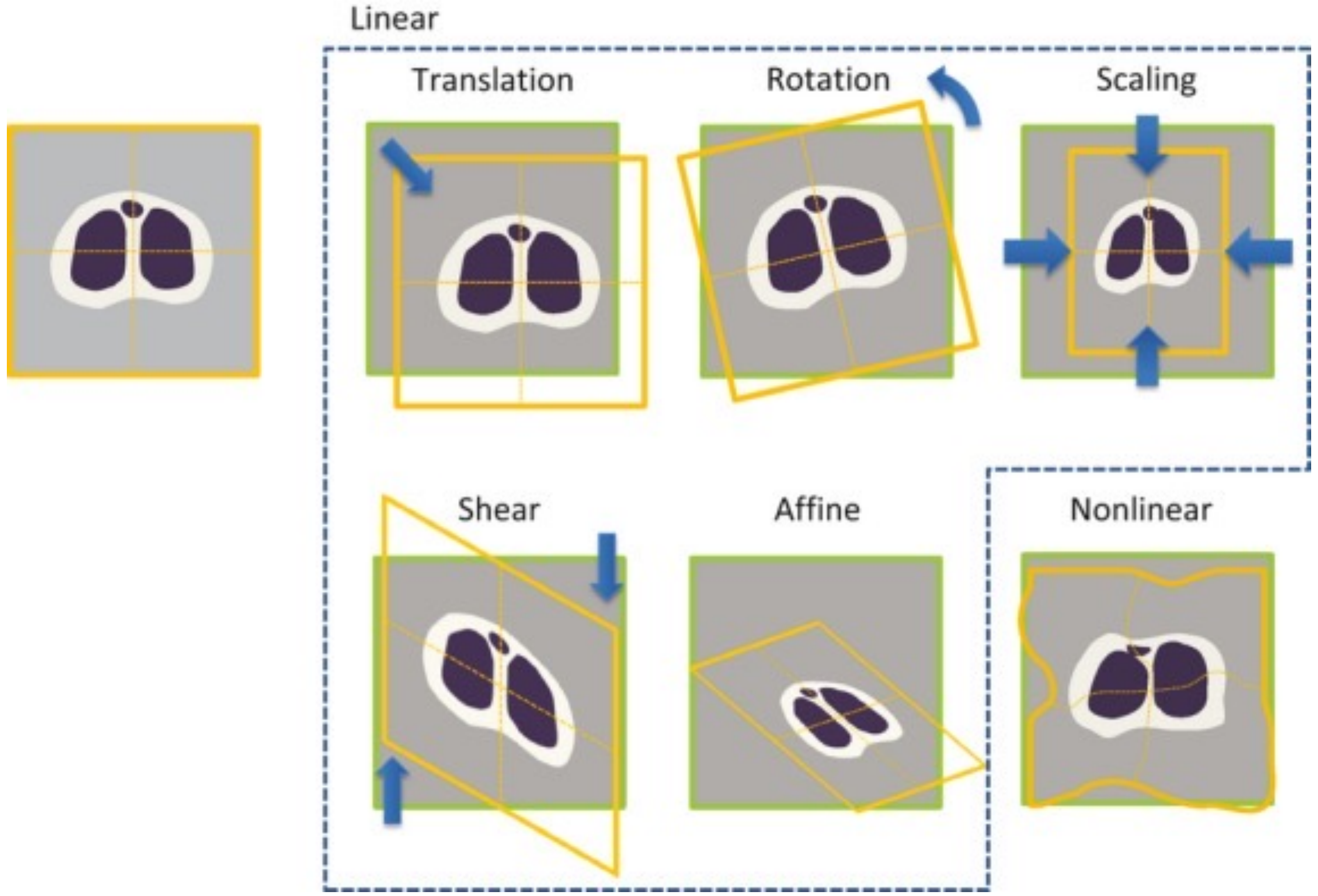


- Feature Similarity
  - Point to point distances $$D = \sum_i \sum_j \left\| x_i - y_j \right\|^2$$
- Image Similarity
  - Cross Correlation (Matched Filter, Template Matching) $$CC = \sum_i \sum_j I_1(i,j) I_2(i-u, j-v)$$
  - Sum of squared differences $$SSD = \sum_i \sum_j \left(I_1(i,j) - I_2(i-u, j-v) \right)^2$$
  - Ratio image uniformity $$RIU = \frac{\sigma_R}{\mu_R} \quad where\ R(i,j) = \frac{I_1(i,j)}{I_2(i,j)}$$
  - Mutual Information $$MI = -\sum_{g_1} \sum_{g_2} p(g_1, g_2) \log \left\{ \frac{p(g_1, g_2)}{p(g_1) p(g_2)} \right\}$$

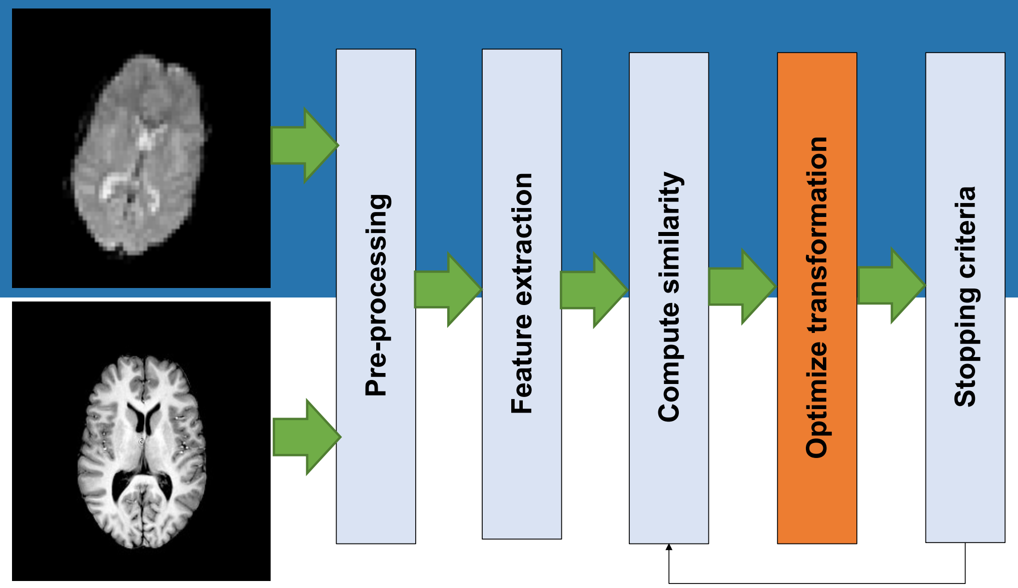
Transformations



- For images to become aligned, they must be transformed
- Maps points in the "moving" image to new locations on the "transformed" image
- **Degrees of freedom (DOF)**
  - Rigid body (6 DOF)
  - Affine (12 DOF)
  - Non-linear/deformable (>12 DOF)



Optimize transformation

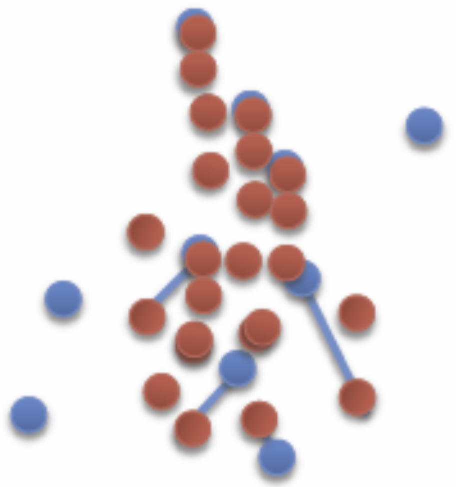


- Iterative Closest Point (ICP) Algorithm
  - Initial transformation is identity matrix
  - Repeat
    - For each point in A, find closest point in B
    - Estimate the combination of rotation and translation that will best align each source point to its match
    - Compute mean squared error

$$MSE = \frac{1}{N}\sum_{i=1}^{N}\left\| p_{A,i} - R(p_{B,i}) - T \right\|^2$$

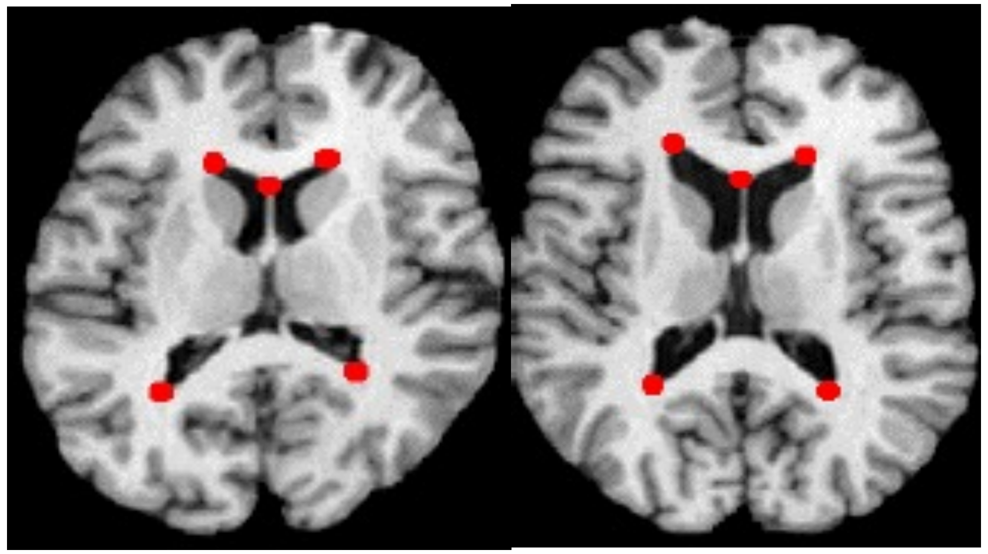
A and B are unstructured point clouds with unknown correspondence of points

A is the smaller set



Landmark based

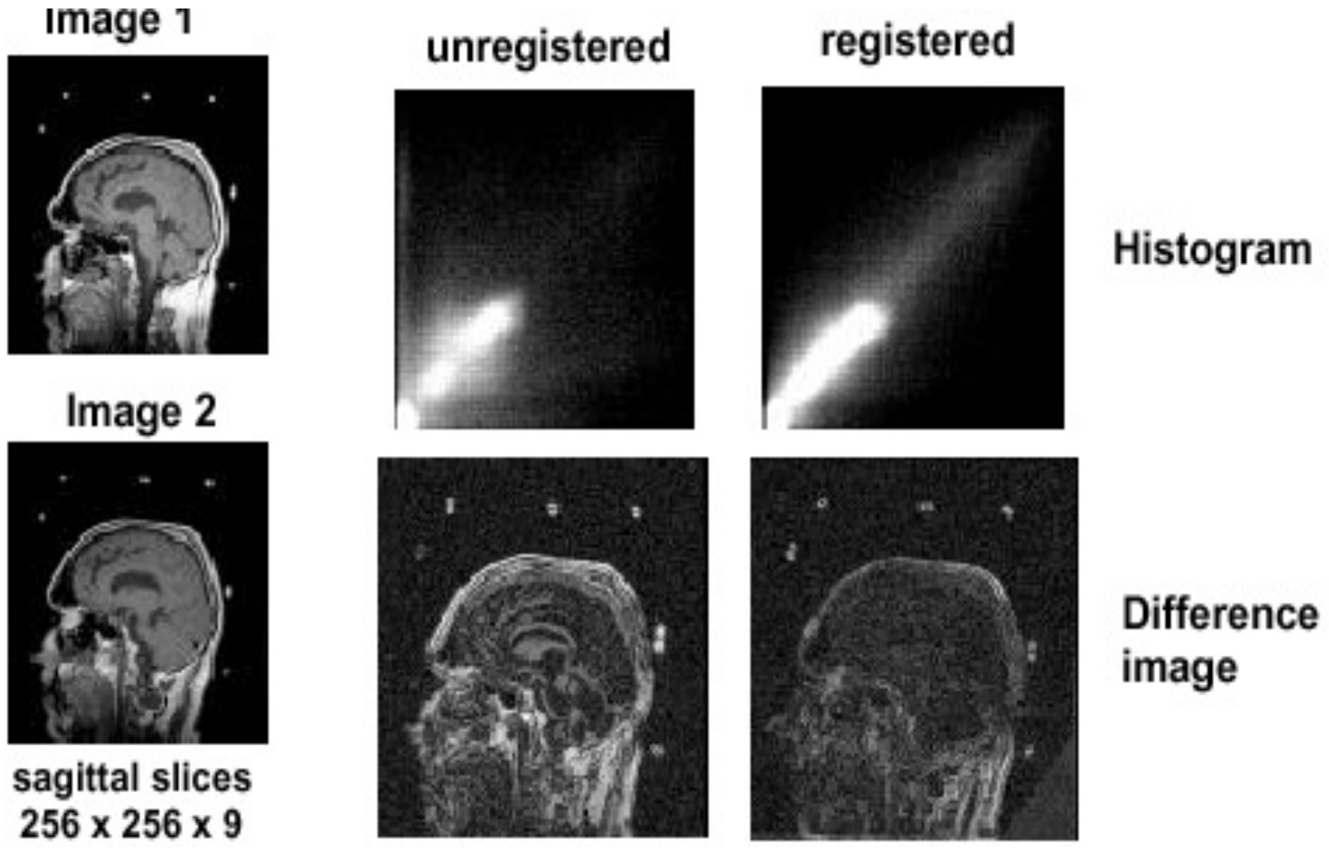
- Identifying corresponding points in the images and inferring the image transformation
- Types of landmarks (fiducial marker)
  - Extrinsic
    - artificial objects attached to the patient
  - Intrinsic
    - internal anatomical structures



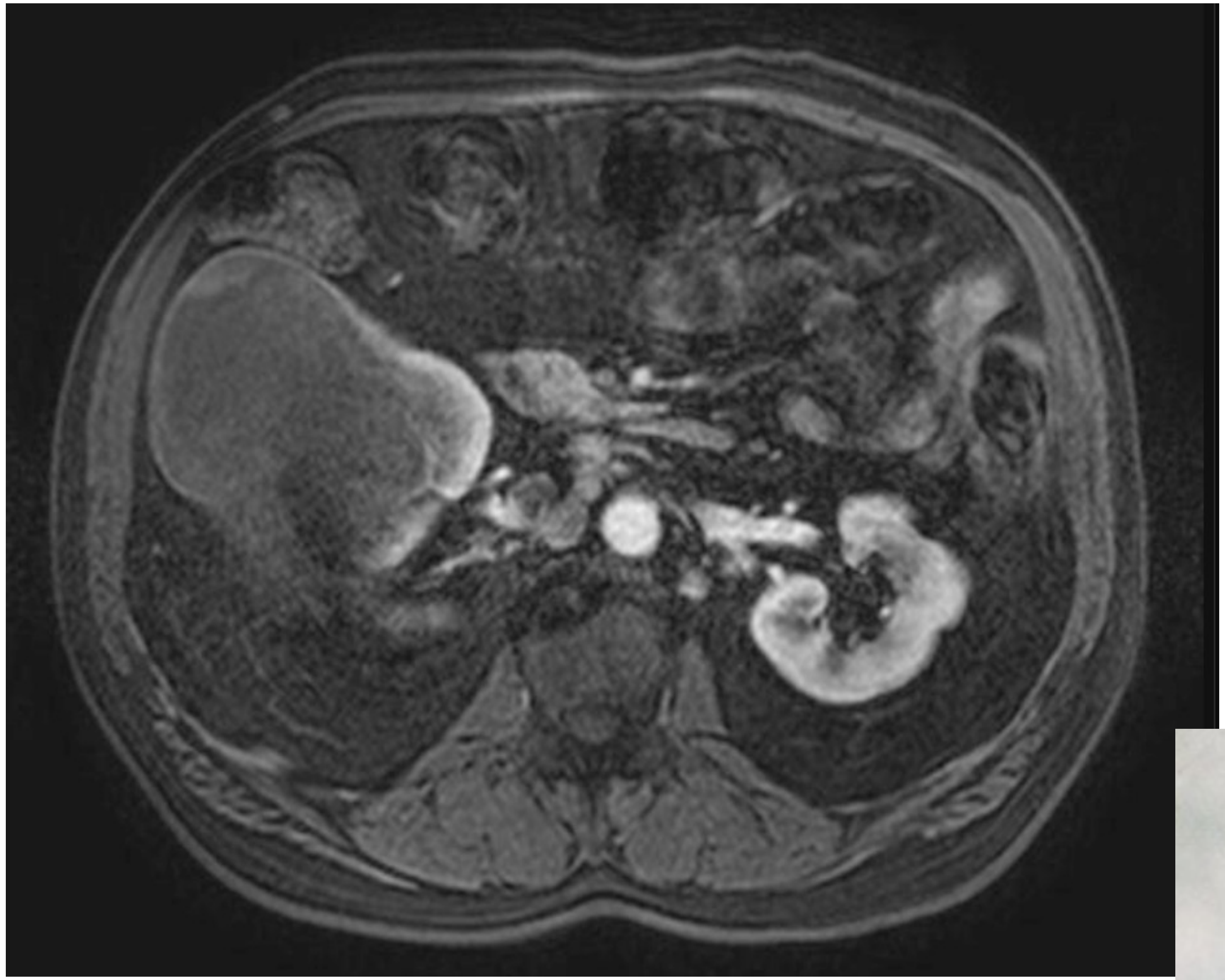
- Compute the average or “centroid” of each set of points → translation
- Rotate this point set about the new centroid difference between images is minimized

Voxel intensity based

- Method
  - Calculate the registration transformation by optimizing some measure derived from the voxel values in the image
- Algorithms used
  - Registration by minimizing intensity difference
  - Correlation techniques
  - Ratio image uniformity
  - Partitioned Intensity Uniformity

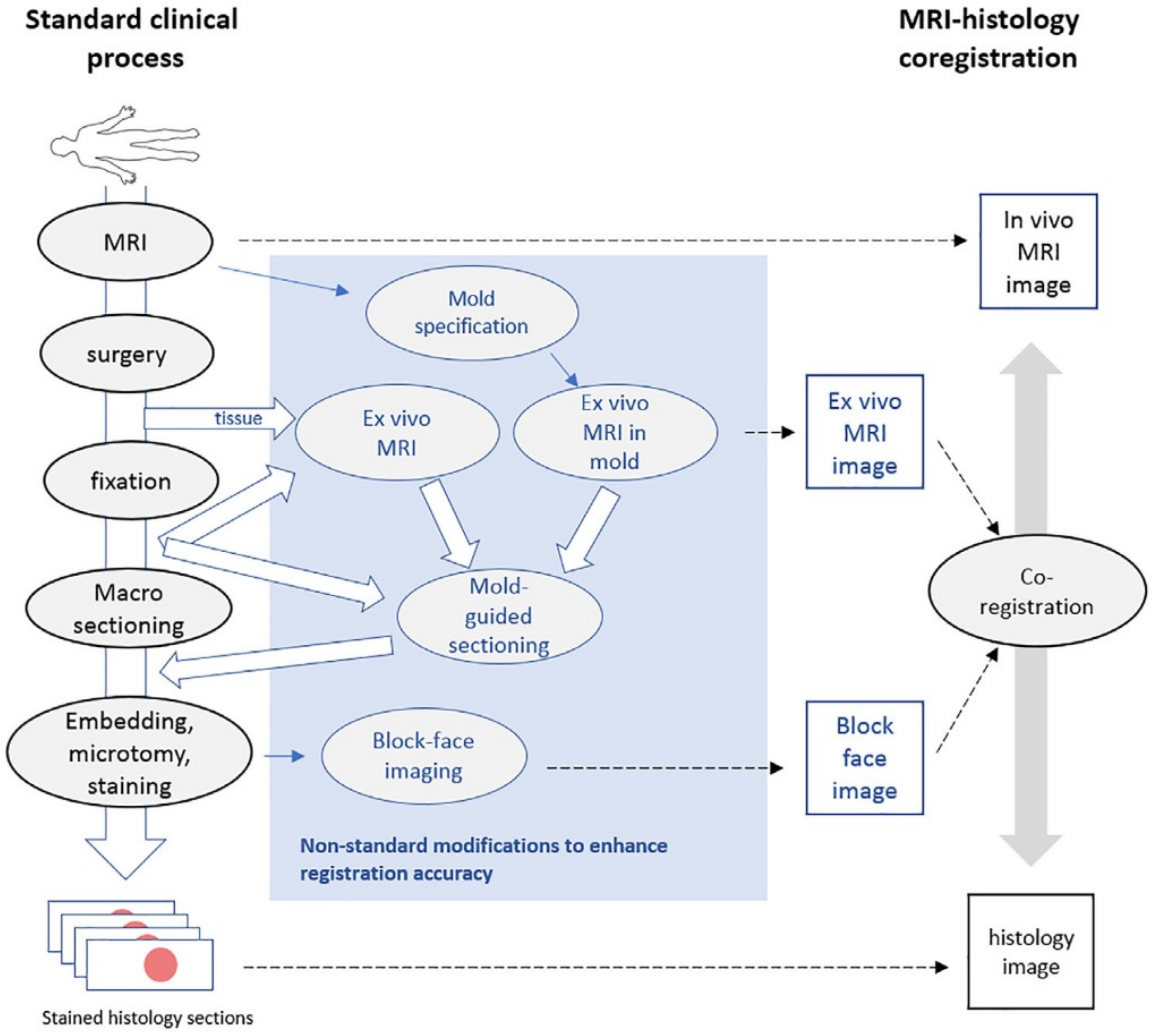


Radiology to pathology matching



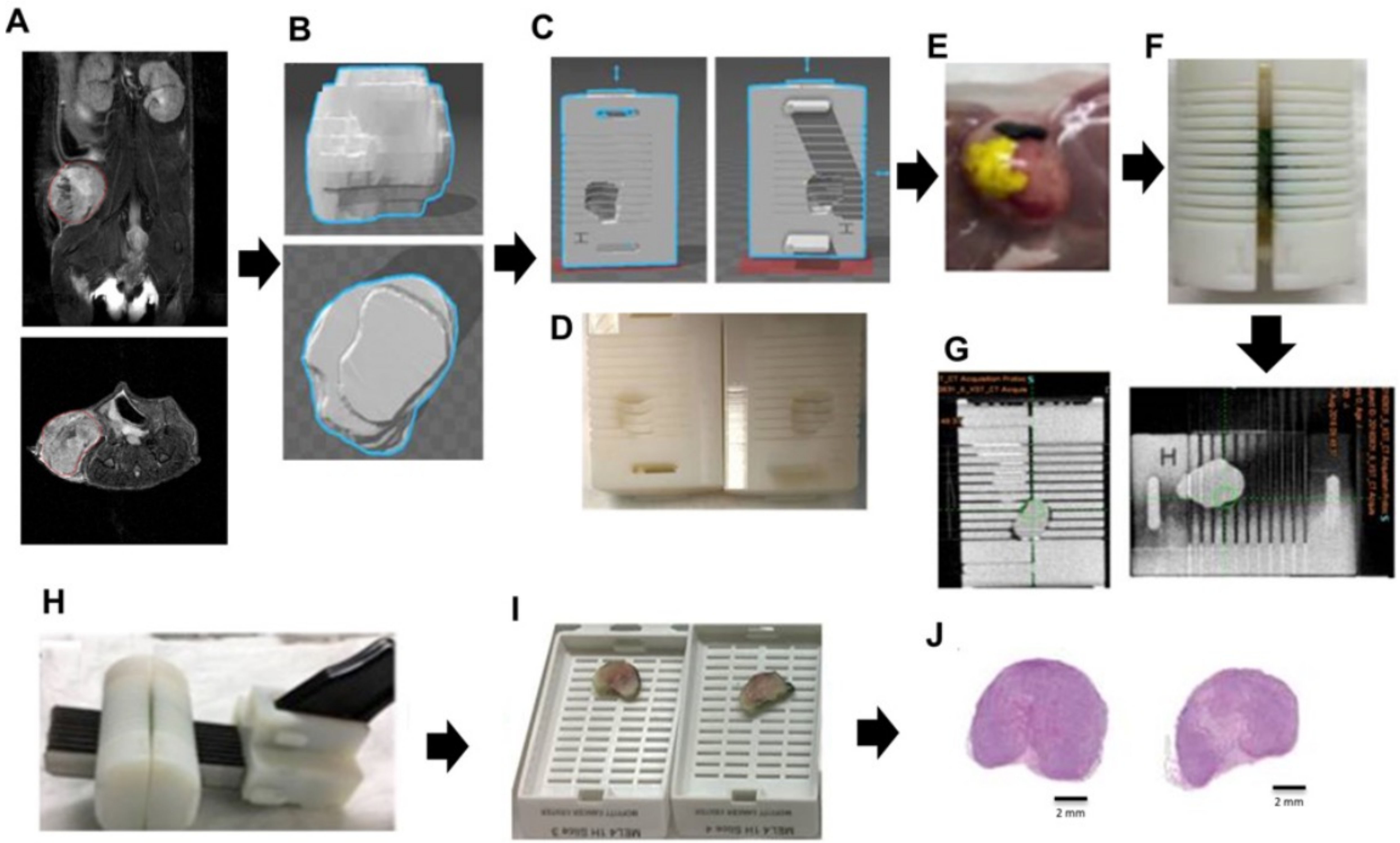
Matching MRI to pathology: Challenges

- Deformation of resected tissue
- Devascularization
- Difficulty orientating amorphous specimens
- Tissue shrinkage
- Thin-sectioning compression,
- Misalignment of macroscopic tissue sections
- Subdivision of macro tissue sections
- Slice thickness mismatch between sections prepared forlight microscopy



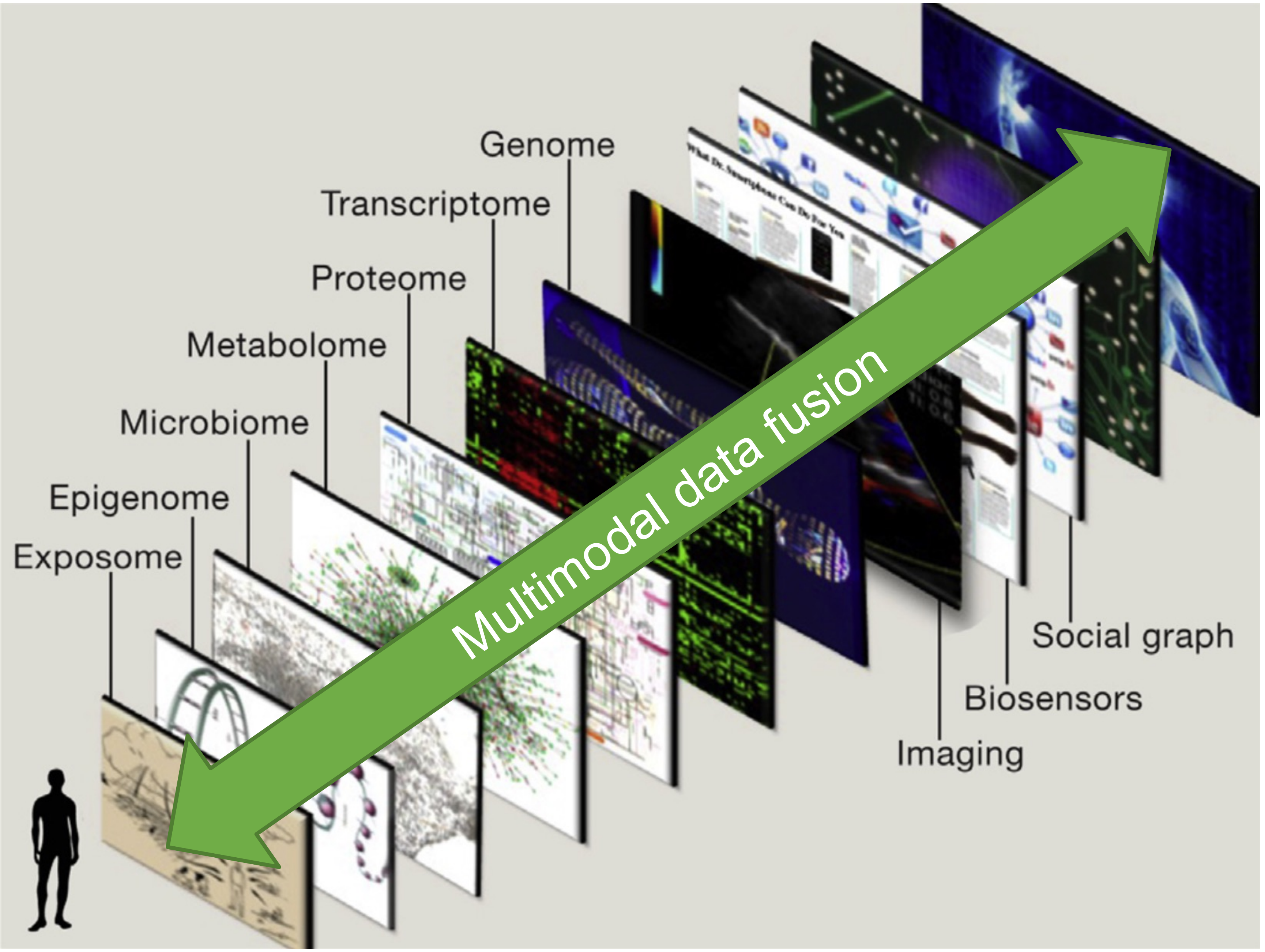
Alyami, W., Kyme, A. & Bourne, R. Histological Validation of MRI: A Review of Challenges in Registration of Imaging and Whole-Mount Histopathology. *J Magn Reson Imaging* **55**, 11–22 (2022).

Registering in vivo and histopathology images



Multimodal data fusion

Motivation

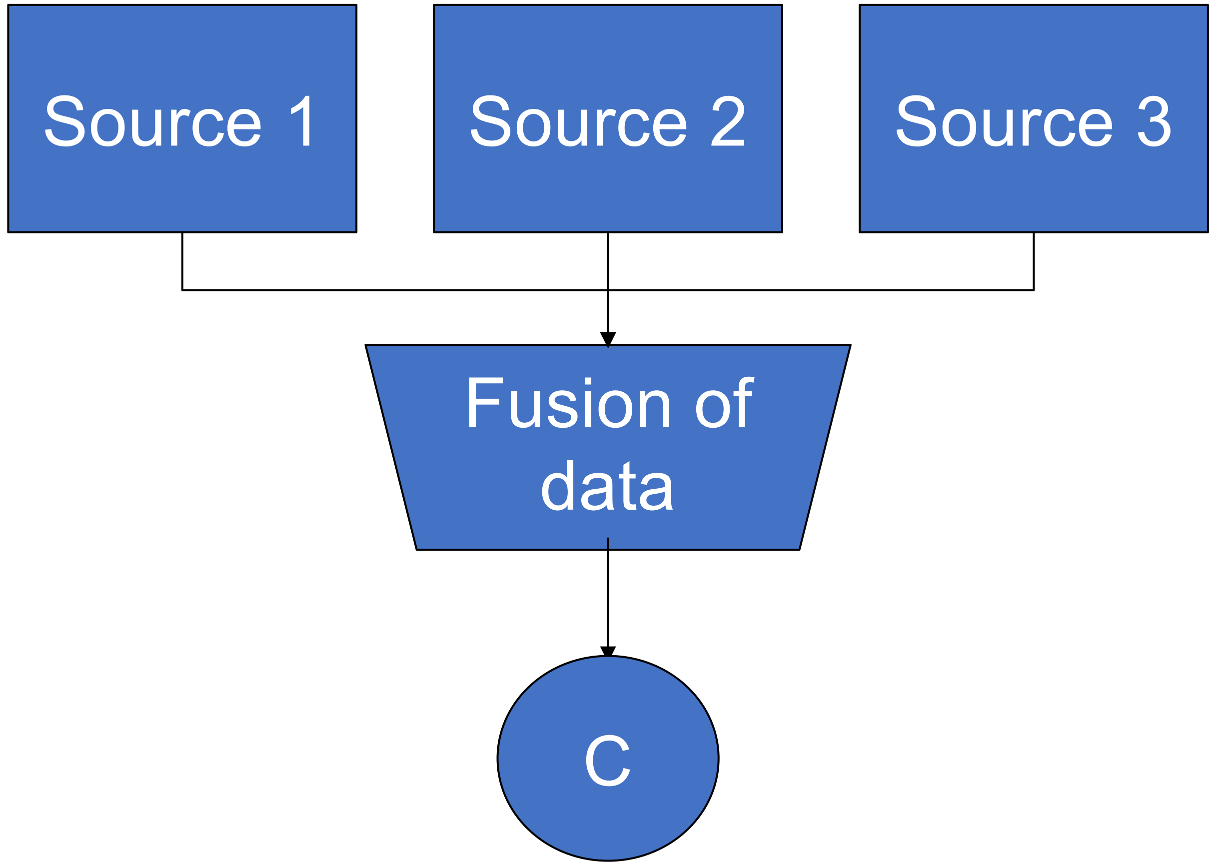


Topol EJ. **Individualized medicine from prewomb to tomb**. Cell. 2014 Mar 27;157(1):241-53.

Basic types of multimodal fusion

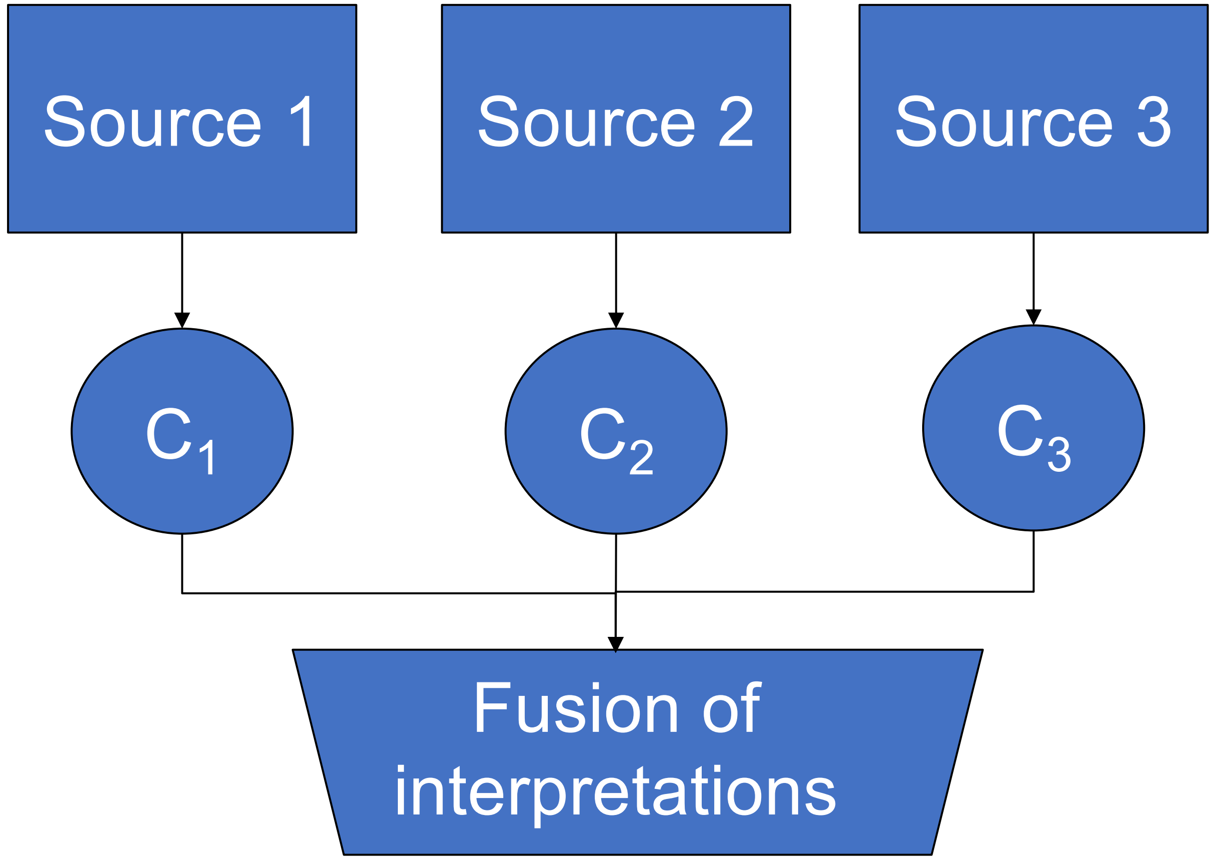
Combination of data (CoD):

Combine features across sources to generate a single feature vector for classification



Combination of interpretations (CoI):

Classify data from each source independently then aggregate the results



Lee G et al. **A knowledge representation framework for integration, classification of multi-scale imaging and non-imaging data: Preliminary results in predicting prostate cancer recurrence by fusing mass spectrometry and histology**. ISBI 2009 (pp. 77-80).

General approach

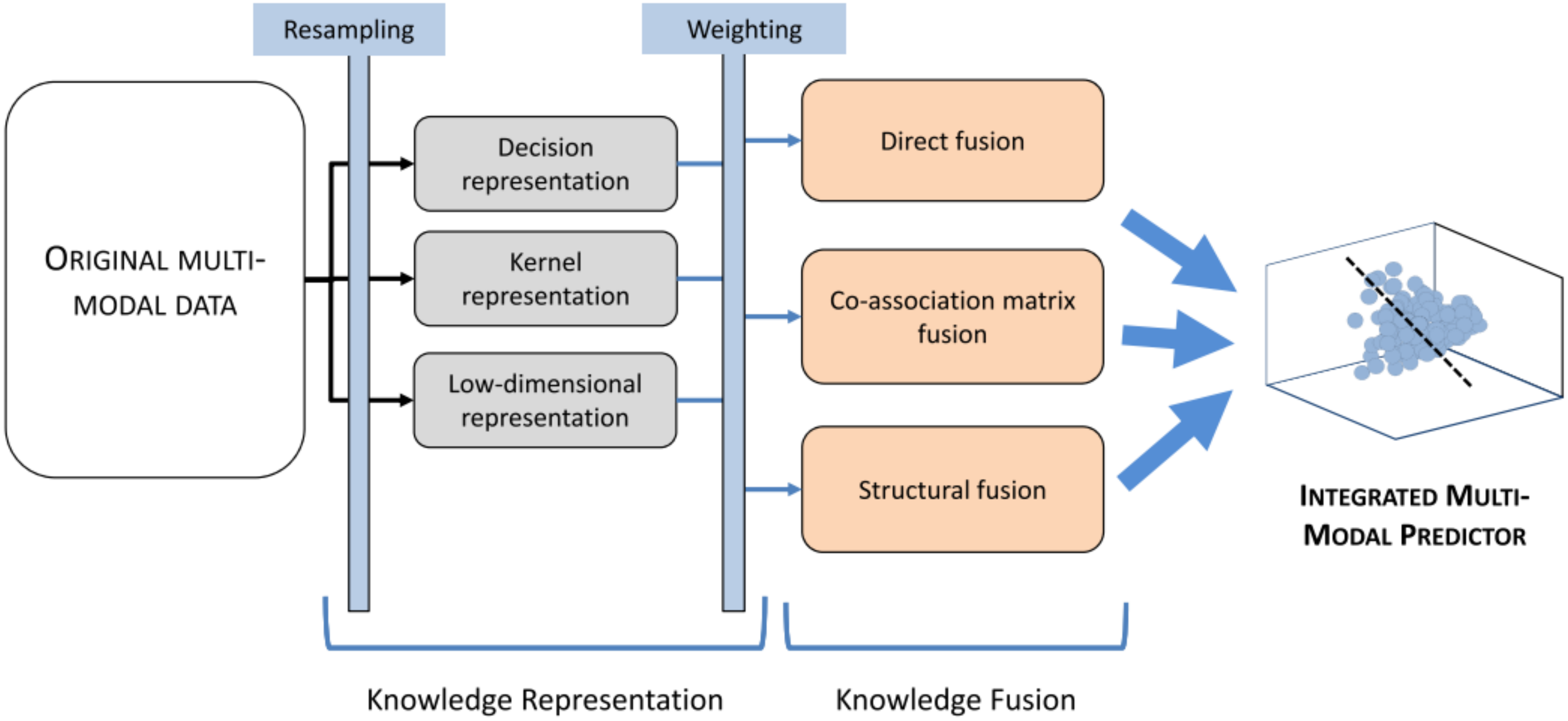
Data pre-processing
- Extract features from different data sources

Feature representation
- Transform features into a **common** representation

Feature fusion
- Combine features into a **single** representation

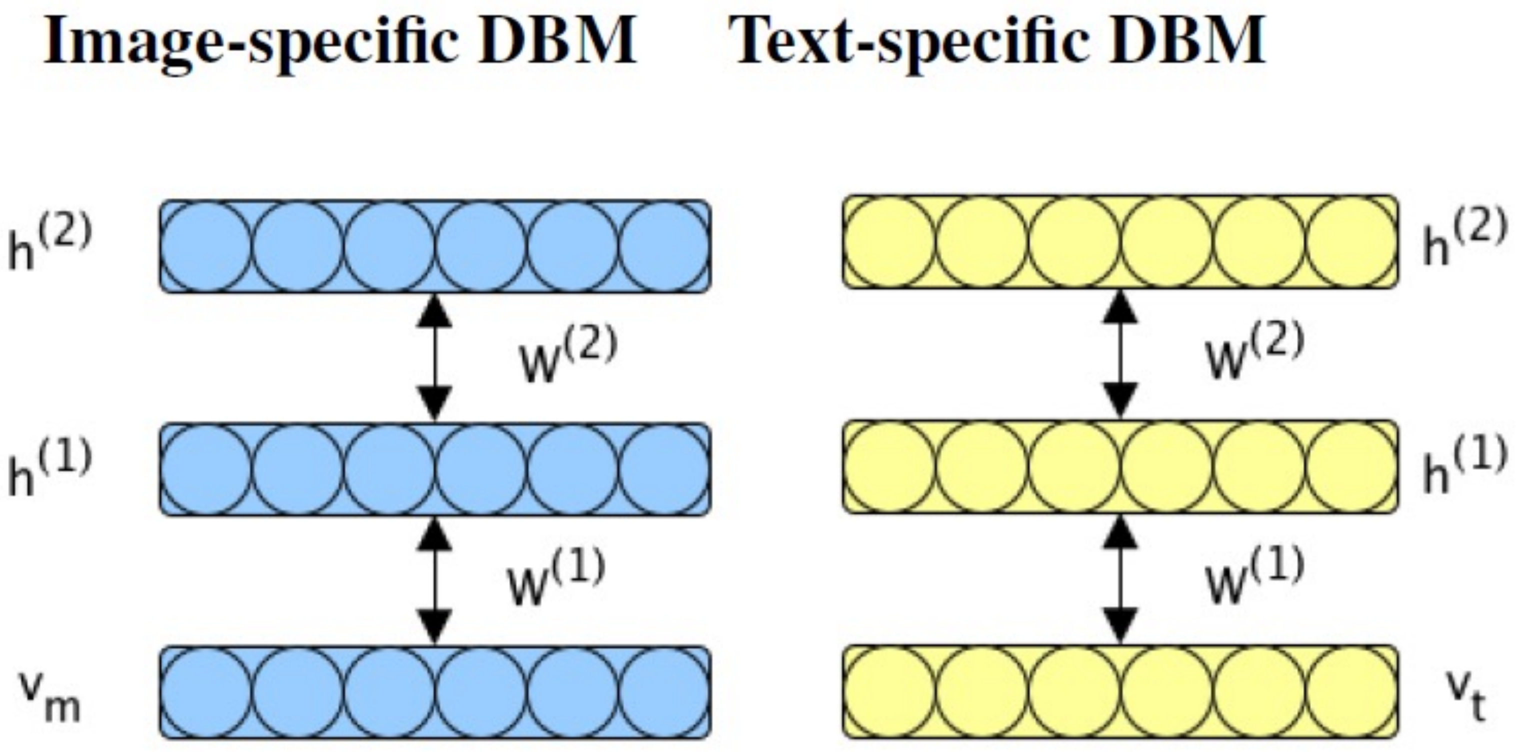
Classification
- Feed combined feature set into classifier

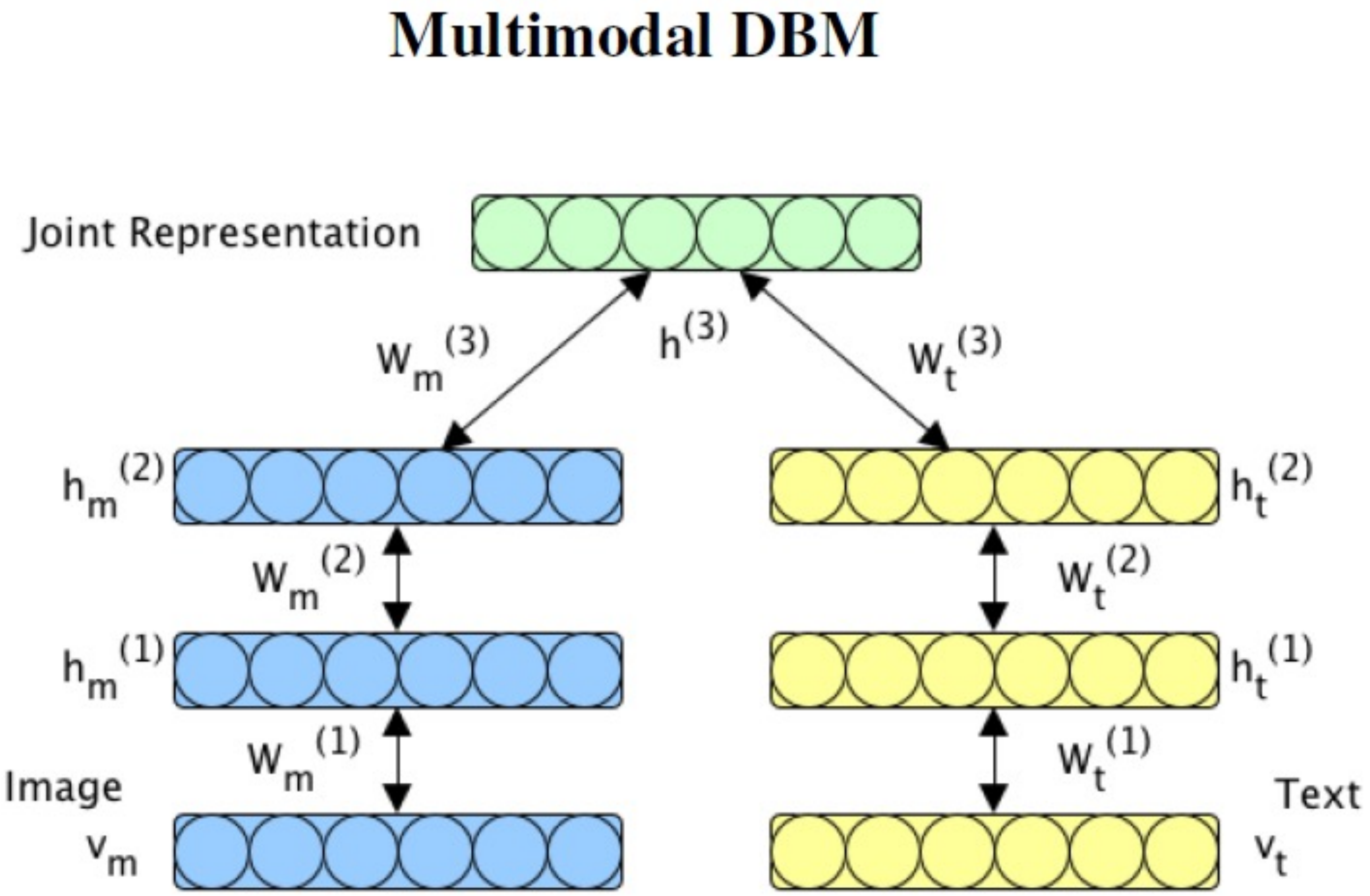
Examples of approaches



Viswanath SE, et al, **Dimensionality reduction-based fusion approaches for imaging and non-imaging biomedical data: concepts, workflow, and use-cases**. BMC medical imaging. 2017 Dec 1;17(1):2.

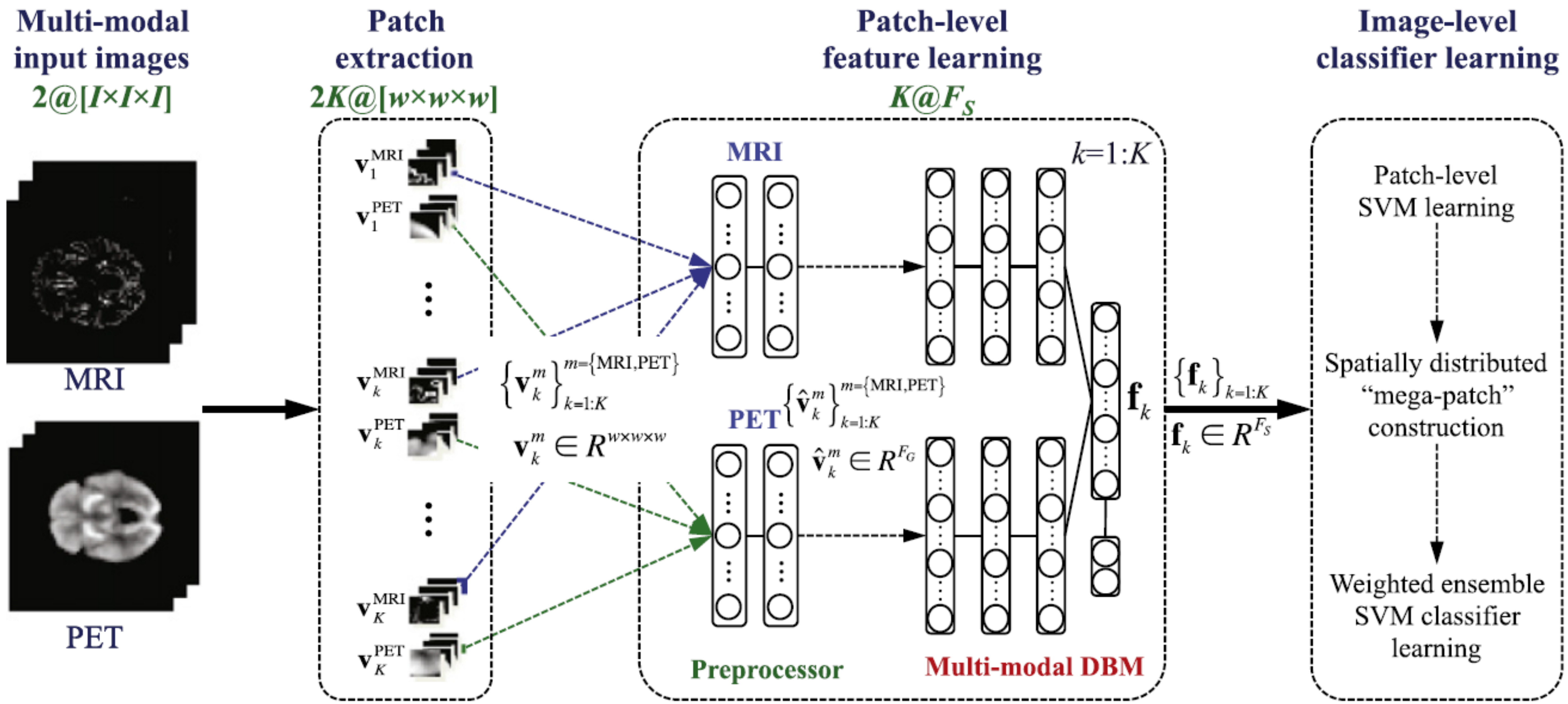
Examples of approaches





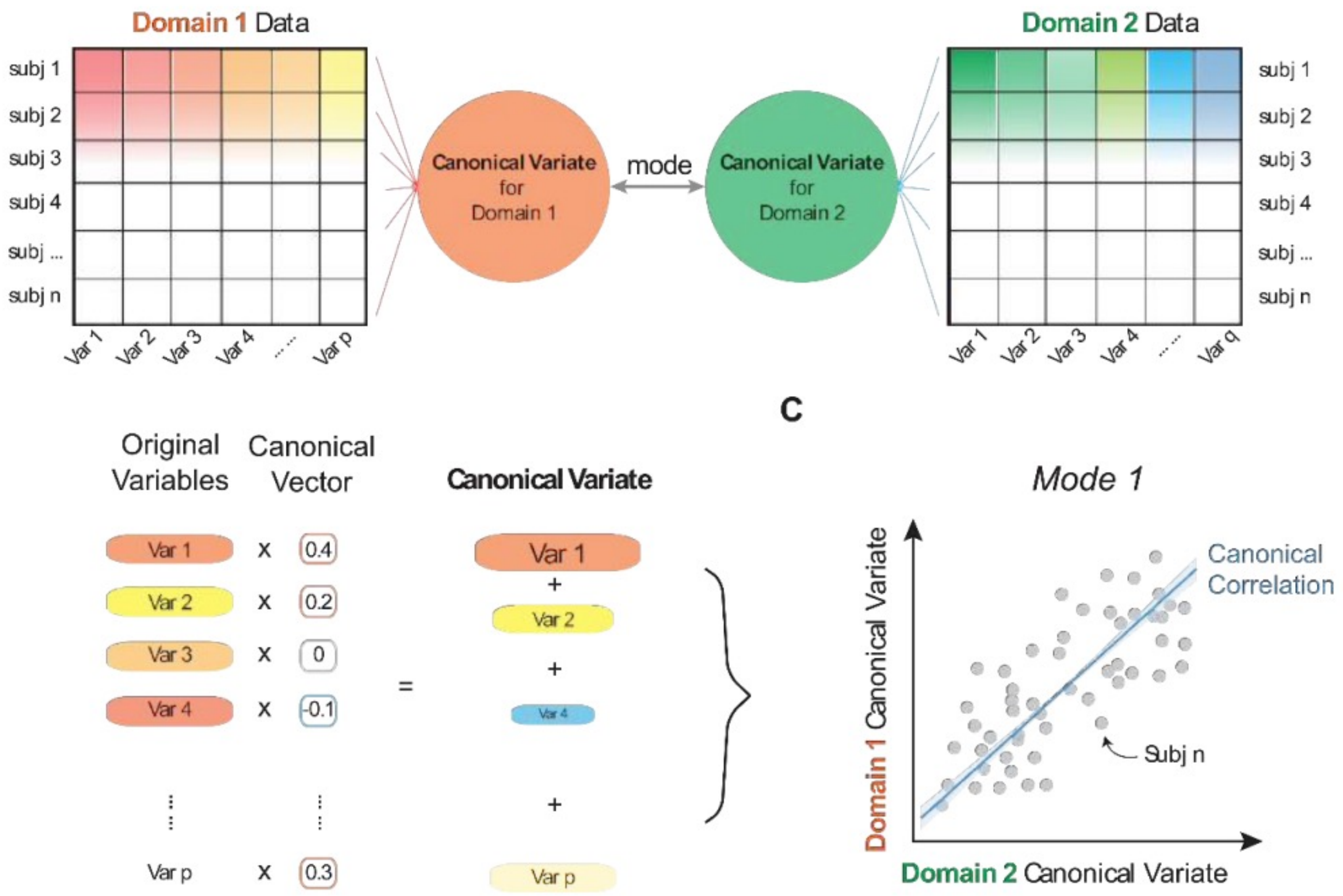
Srivastava N, Salakhutdinov RR. Multimodal learning with deep boltzmann machines. NeurIPS 2012 (pp. 2222-2230).

Examples of approaches



Suk HI et al. **Hierarchical feature representation and multimodal fusion with deep learning for AD/MCI diagnosis.** NeuroImage. 2014 Nov 1;101:569-82.

Examples of approaches



https://arxiv.org/ftp/arxiv/papers/1812/1812.02598.pdf

Ongoing efforts & concluding thoughts

Integrated Diagnostics Shared Resource

Mission: Catalyze innovative research and tool development through data integration and curation to improve early detection, diagnosis and treatment of cancer

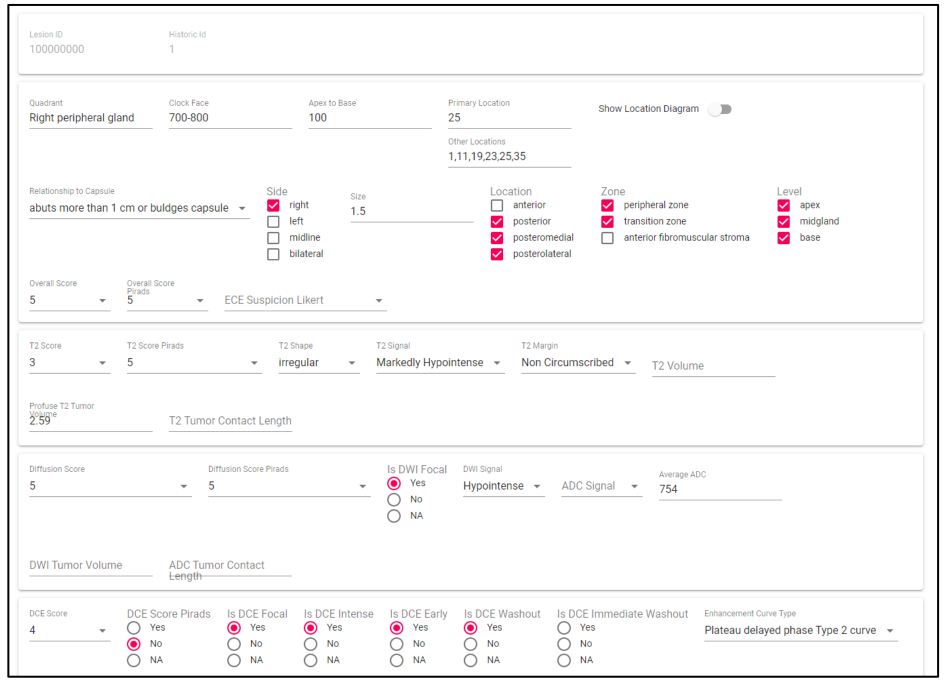
By systematically collecting

- **Clinical and Outcomes Data**
- **Imaging Data**
- **Pathology Data**
- **Prospective biospecimens**
- **Multi-omics Data**

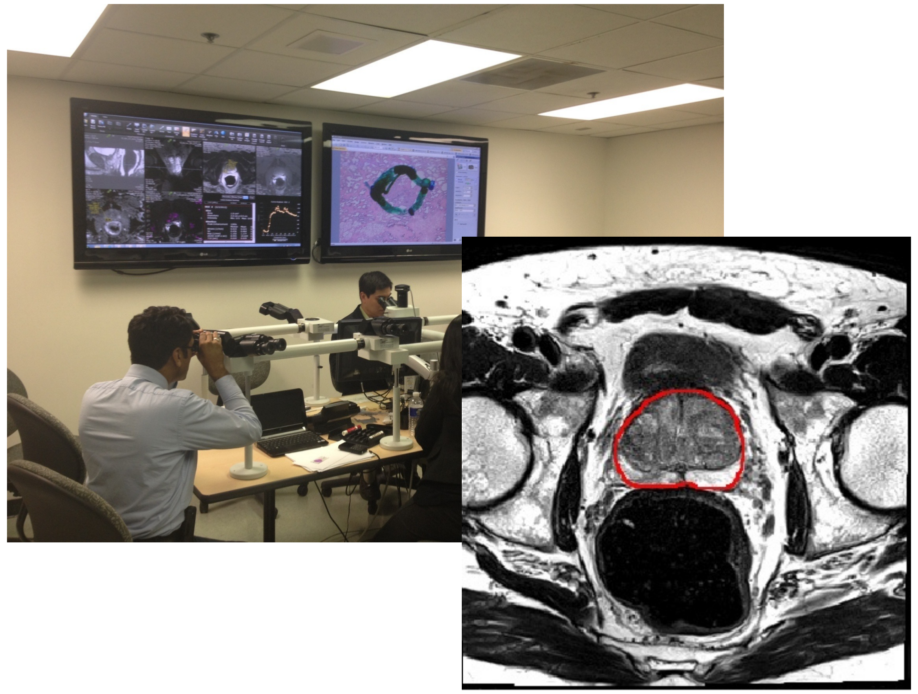
With the goal of

1. Developing and validating of novel AI/ML algorithms and imaging biomarkers to assist clinicians with cancer diagnosis and treatment
2. Generating new biological knowledge through the lens of imaging
3. Discovering actionable information that can inform clinical management of patients

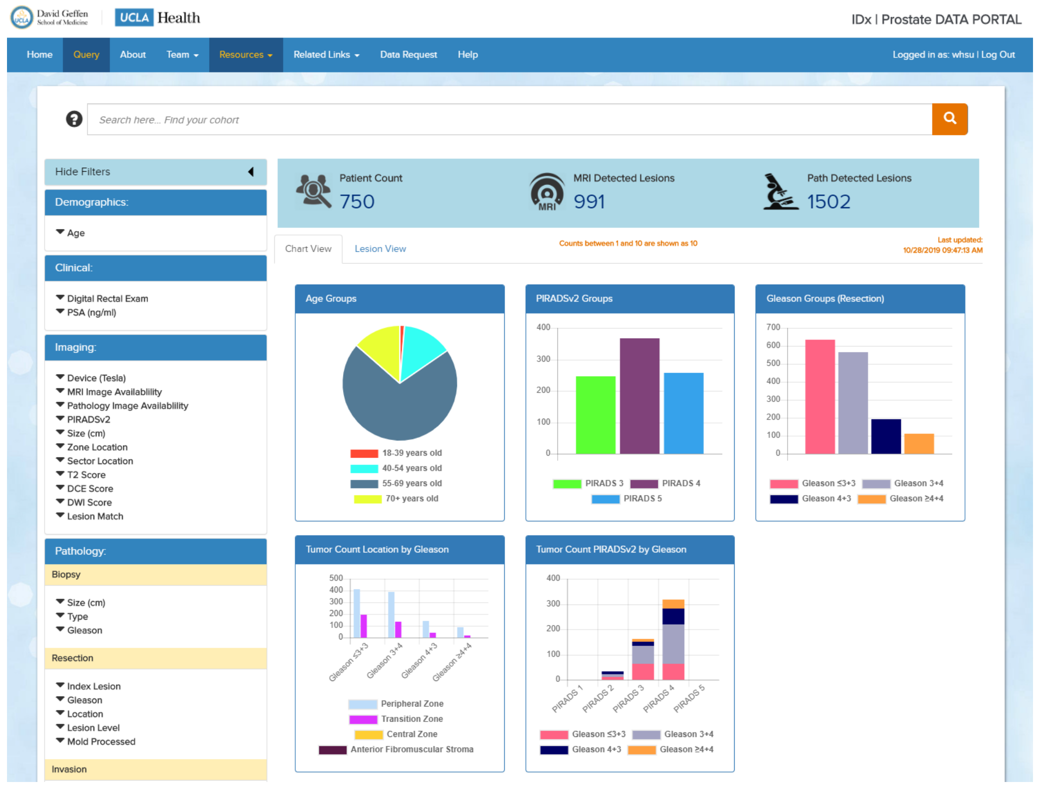
Functions of the shared resource



Data and specimen collection

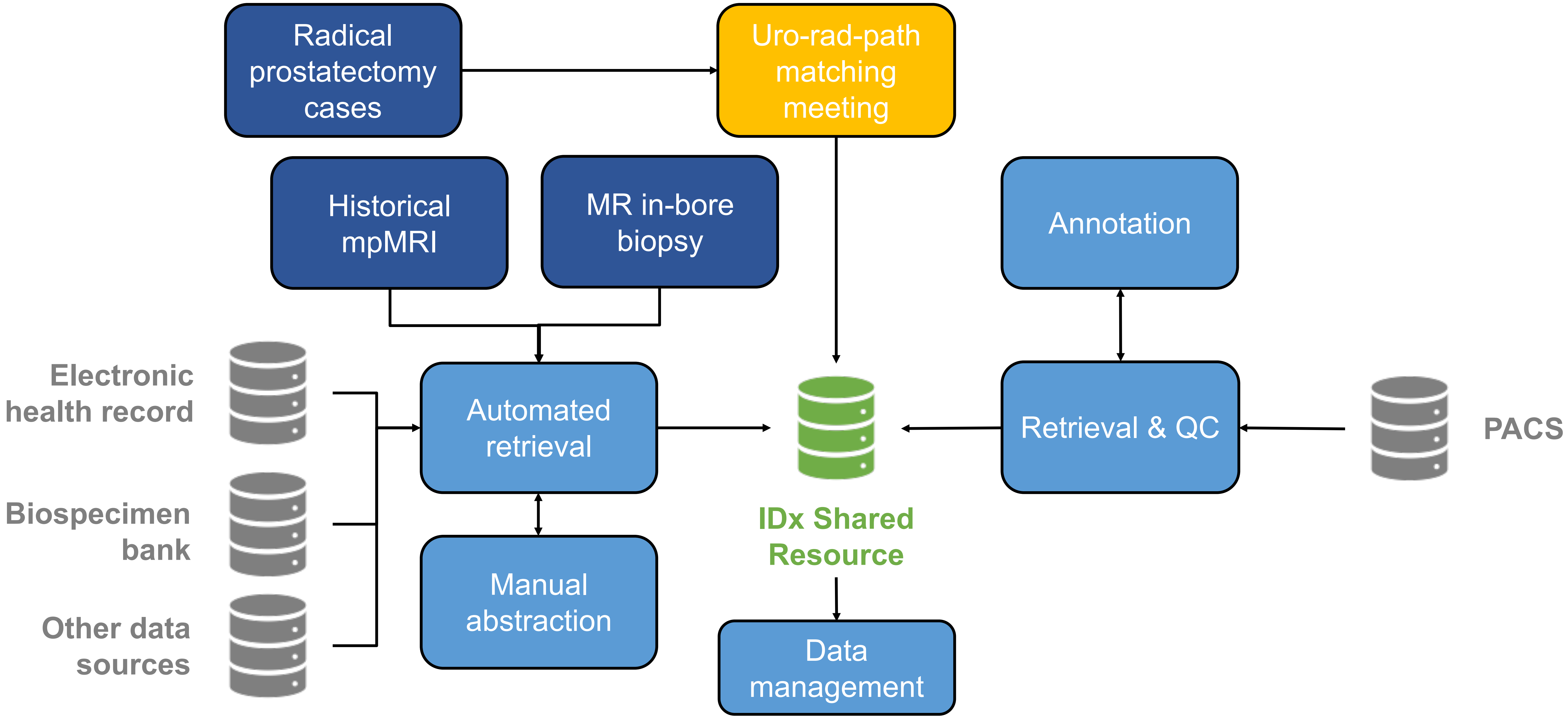


Annotation and data curation



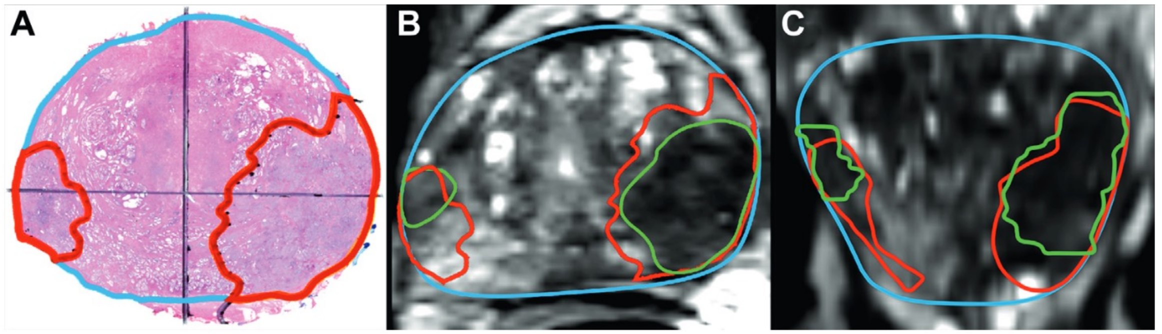
Data delivery and knowledge discovery

Database architecture

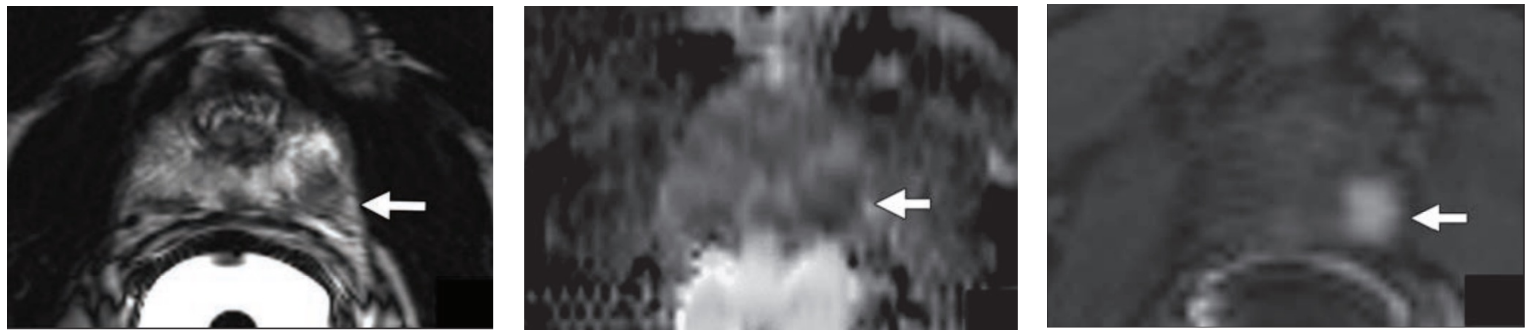


Example: IDx Prostate

(Priester A, J Urology, 2017)

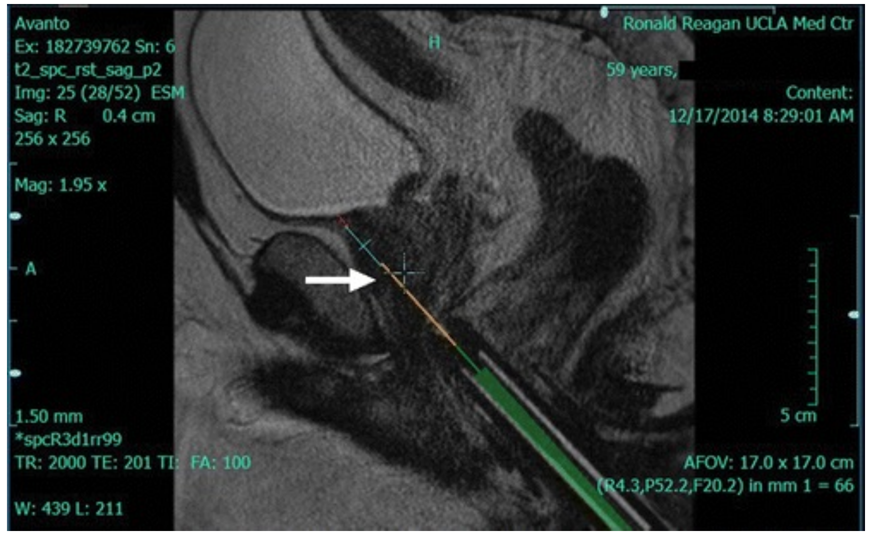


Resection cases N = 750
Archived images N = 741
Annotations N = 491



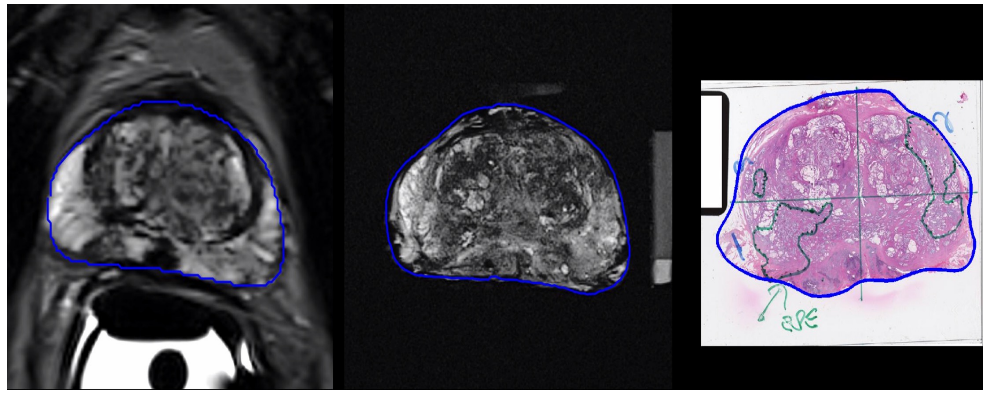
Historical mpMRI cases N = 4,071

(Tan N, Radiology, 2016)



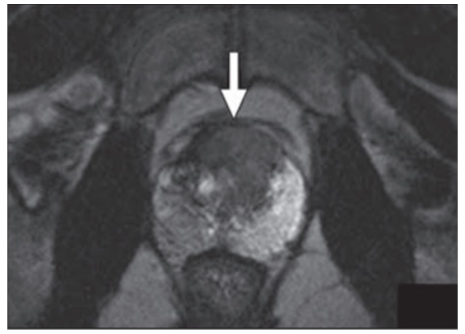
MR-guided Targeted Biopsy N = 254
Archived Images (biopsy + pre) N = 219
Annotations (pre) N = 150
Banked specimens N = 219

(Wu HH, JMRI, 2019)

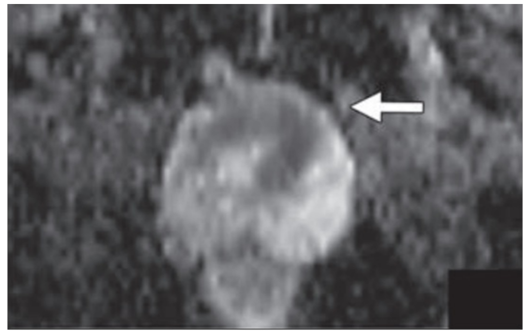


Ex vivo cases N=60+

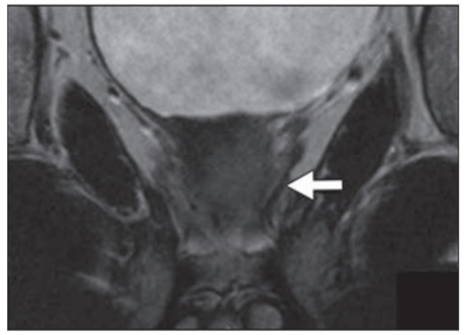
Precise MRI to whole mount correlation



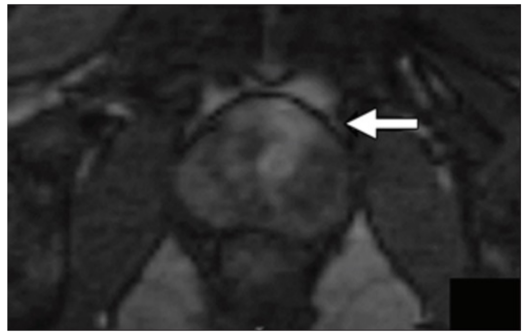
Axial (T2W)



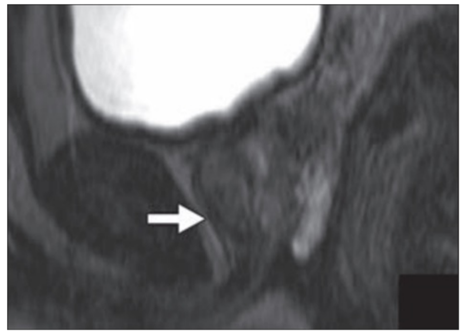
ADC Map (DWI)



Coronal (T2W)

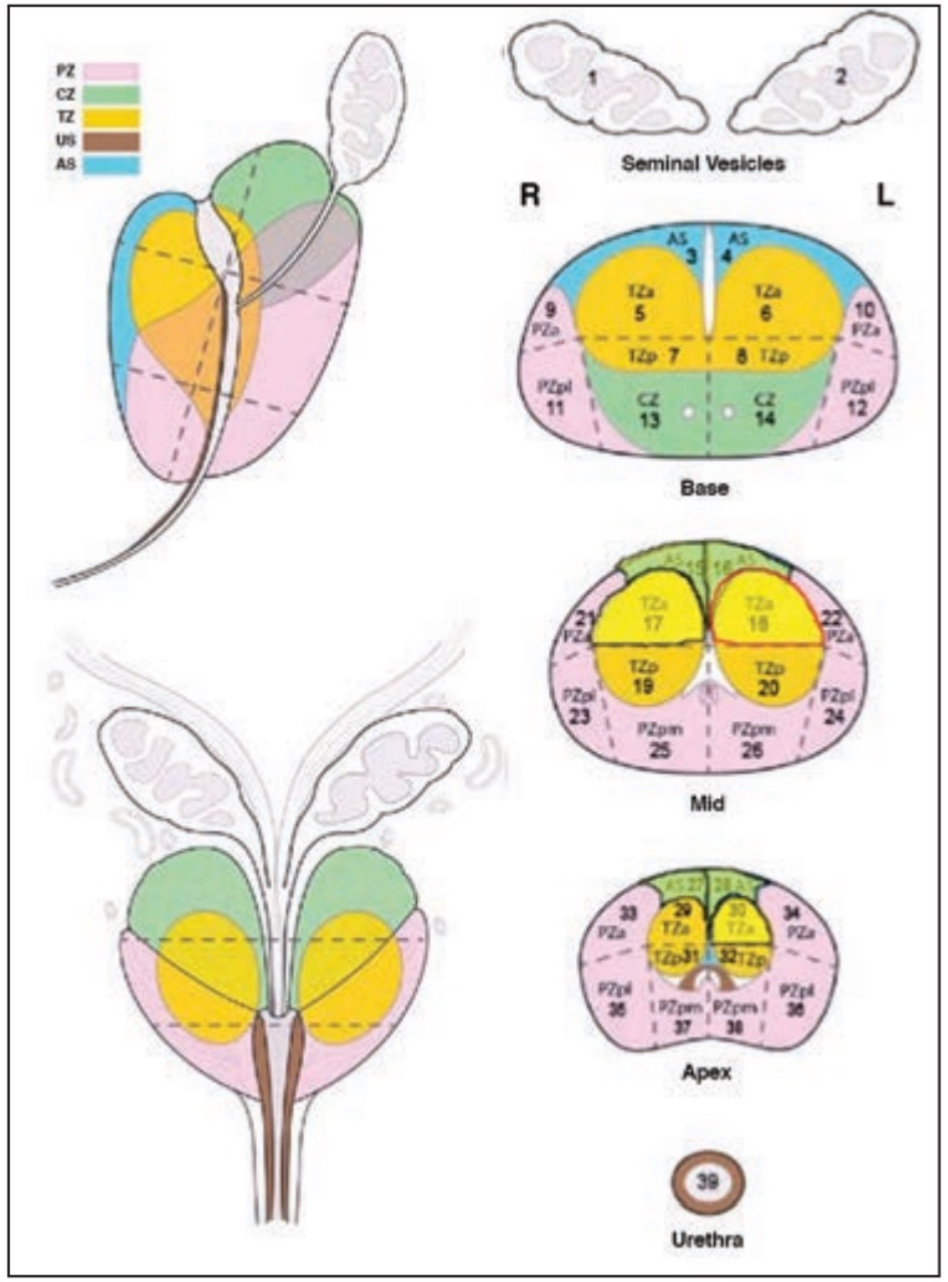


DCE MRI

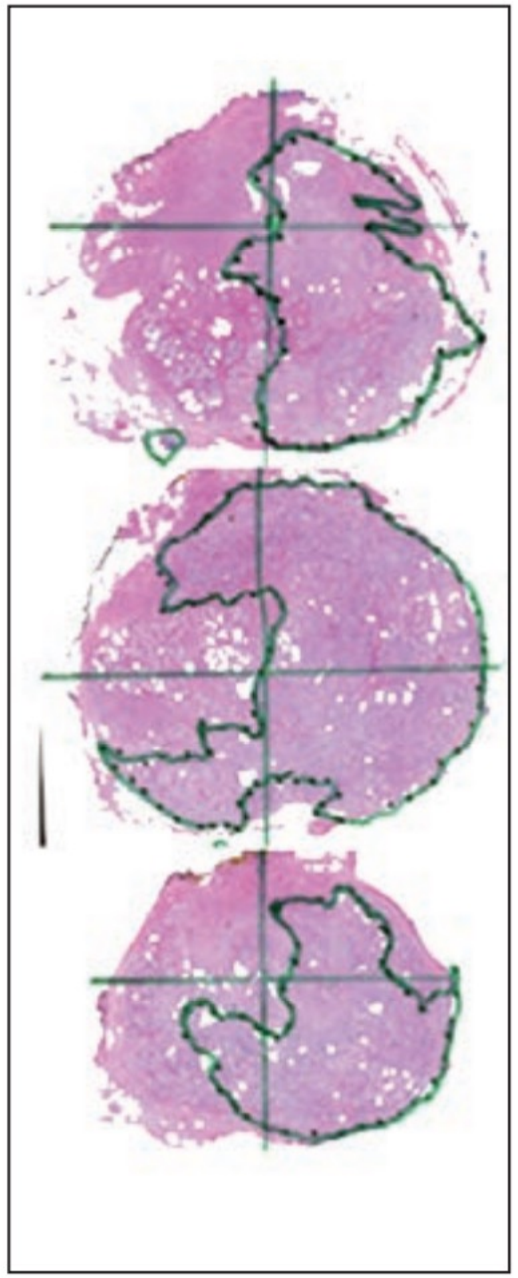


Sagittal (T2W)

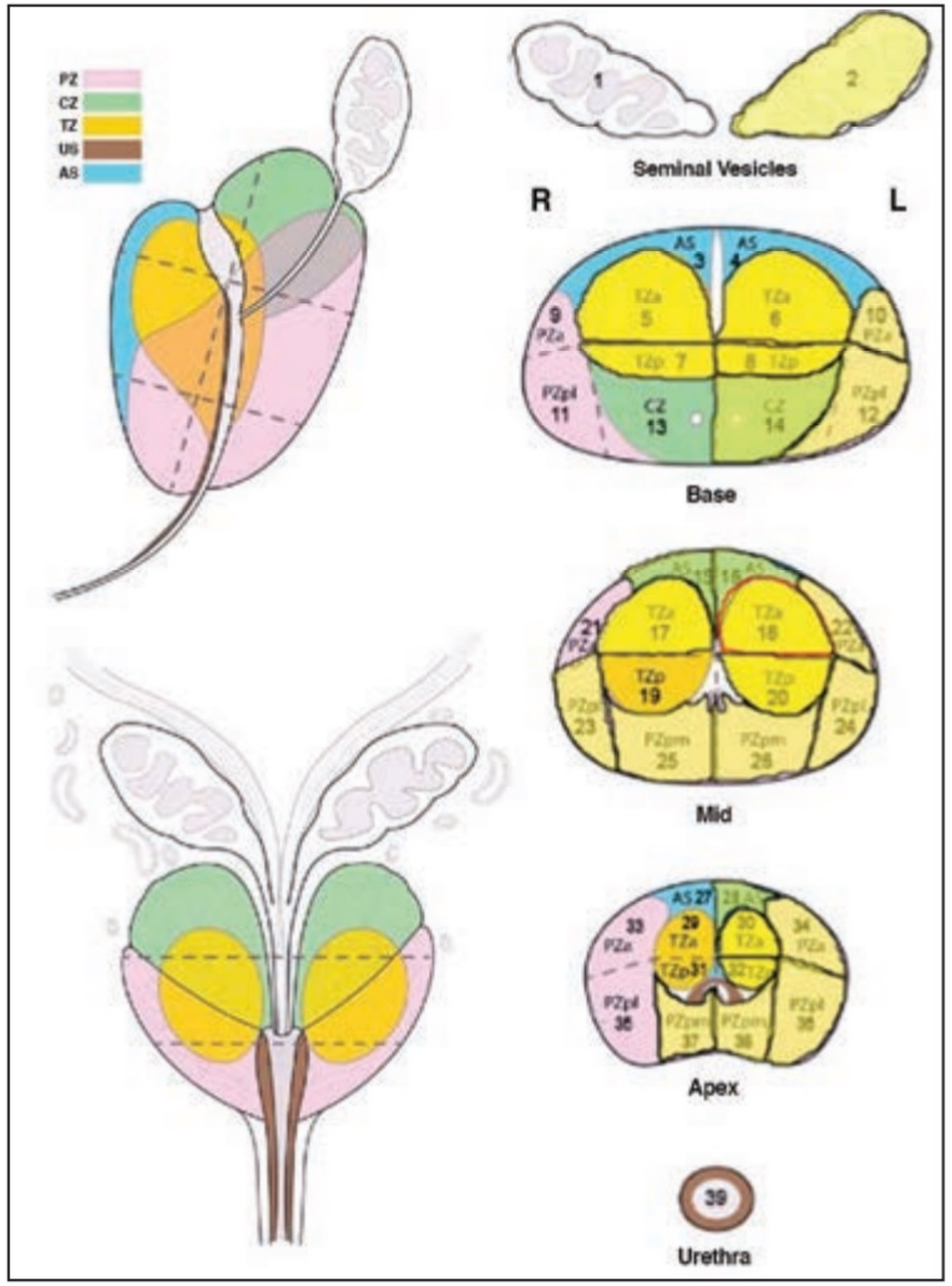
mpMRI images



Radiology Sector Map

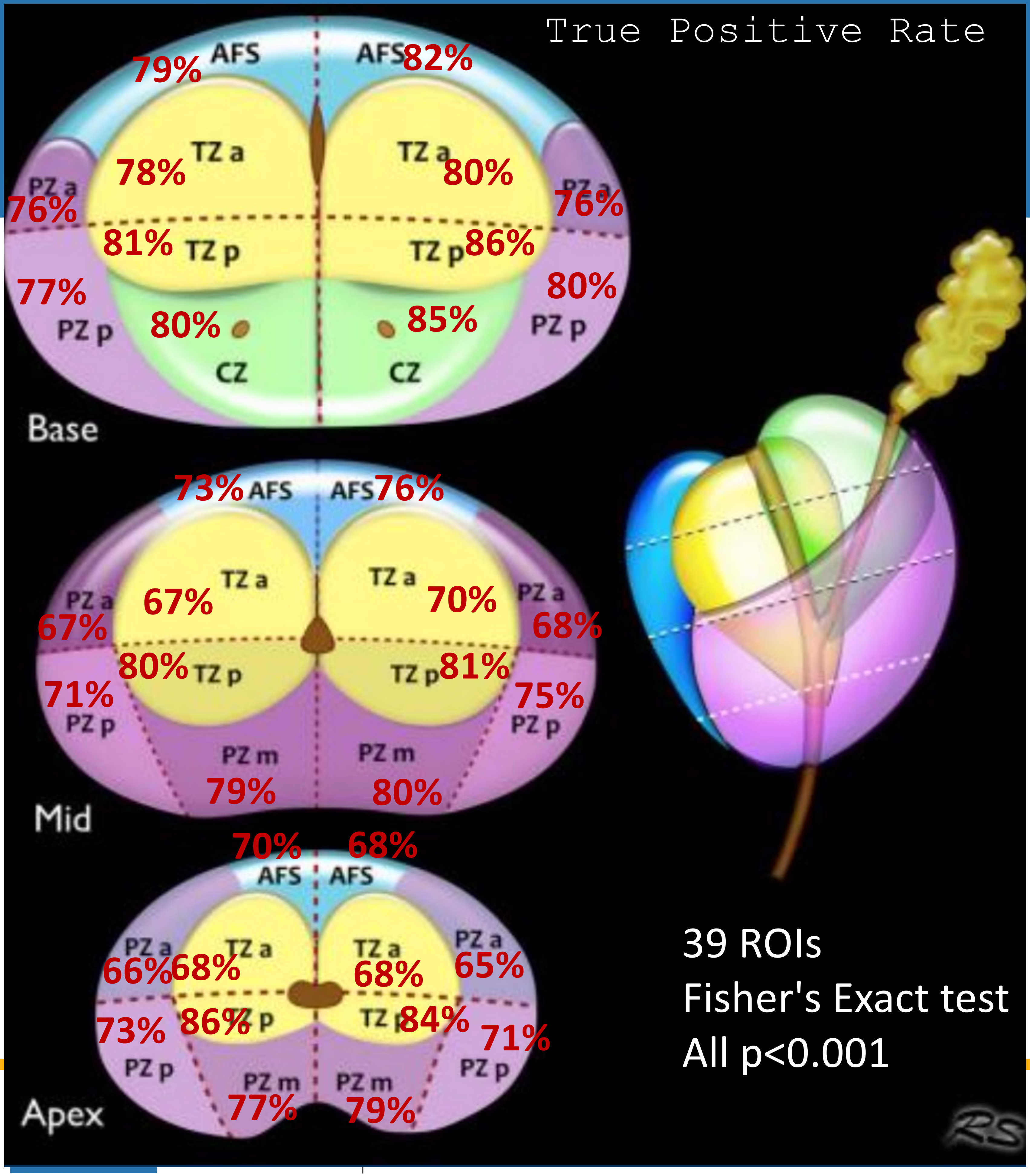


WM images



Pathology Sector Map

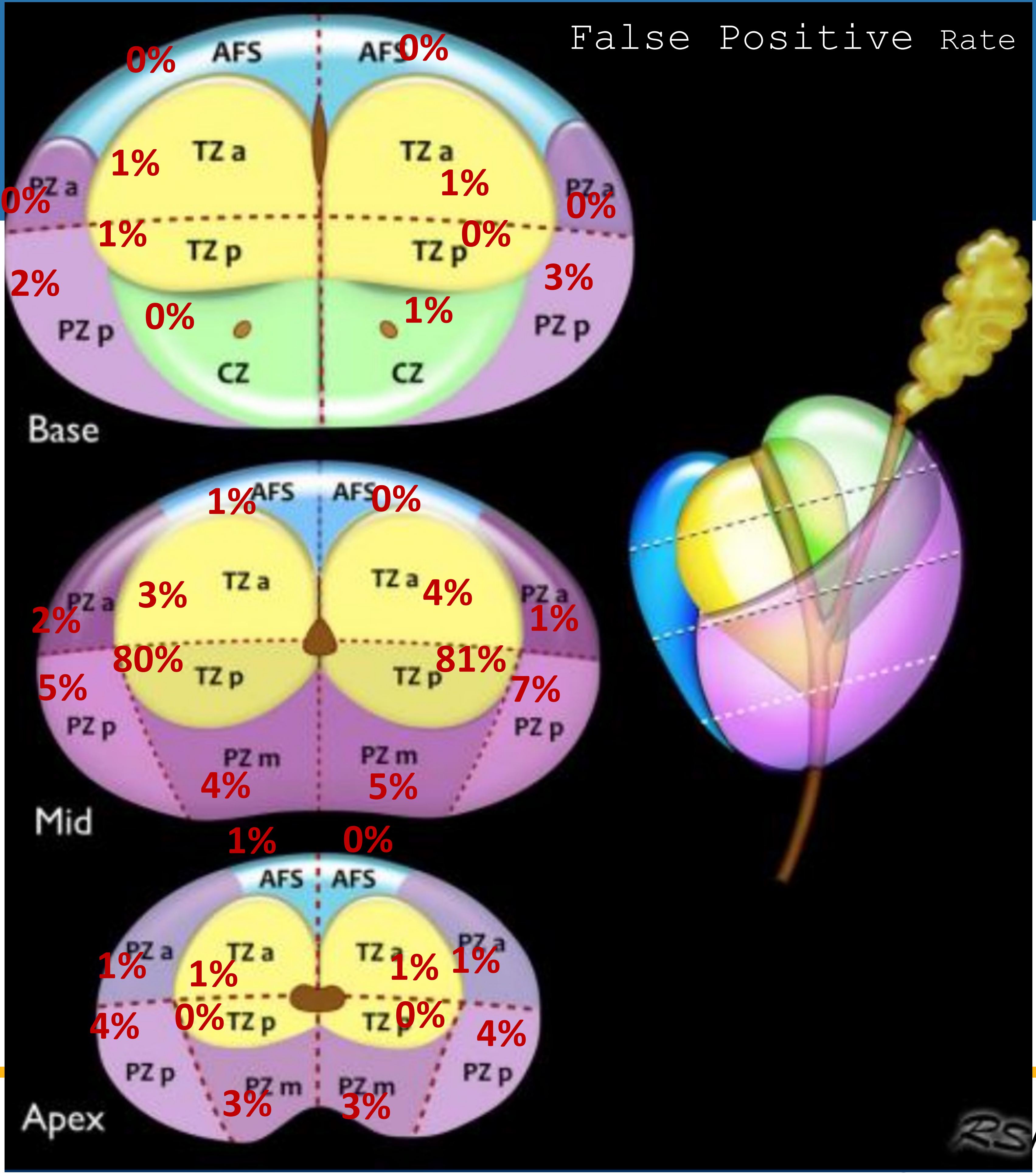
Wibulpolprasert P et al, AJR, 2019



39 ROIs

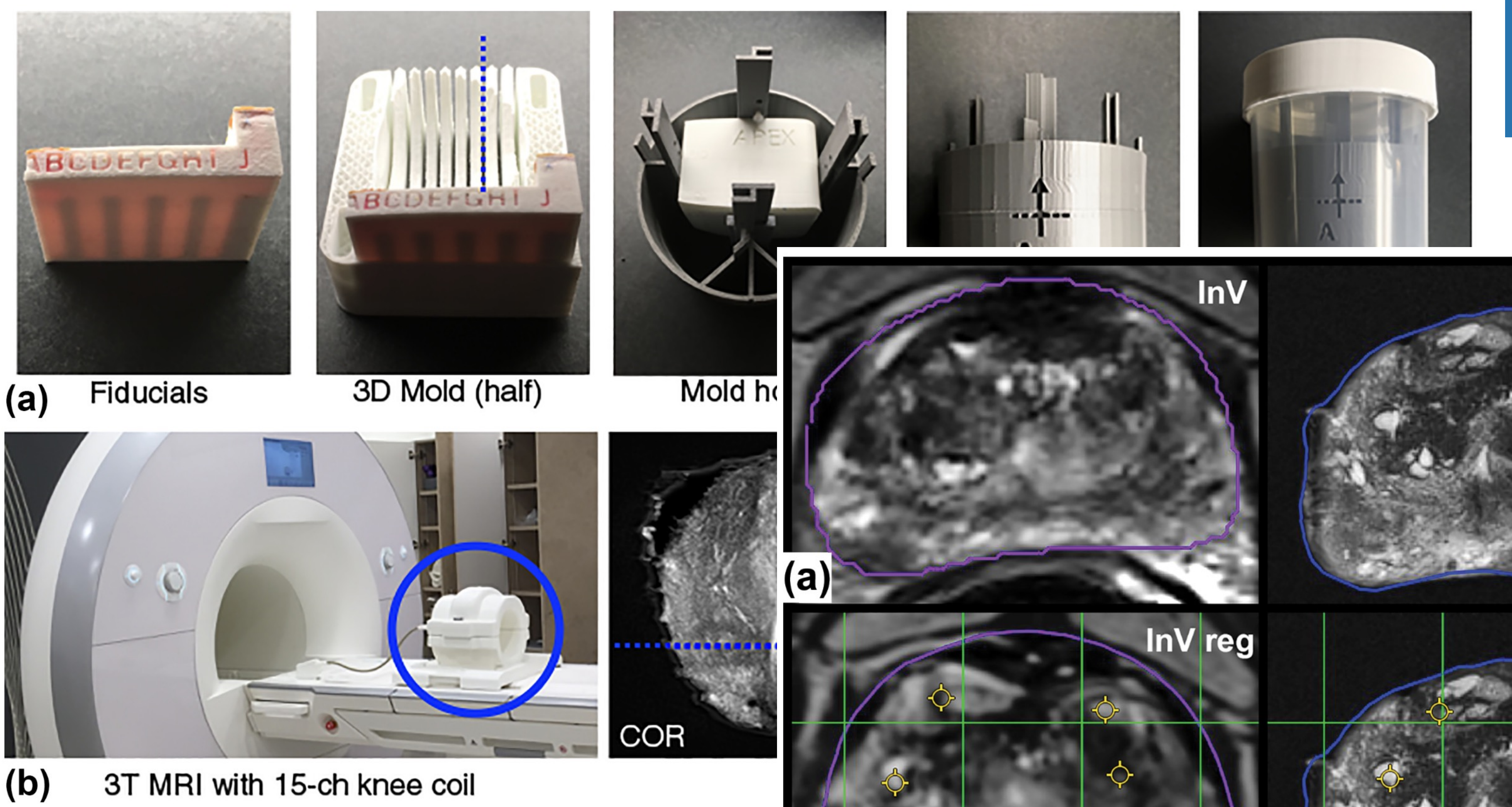
Fisher's Exact test

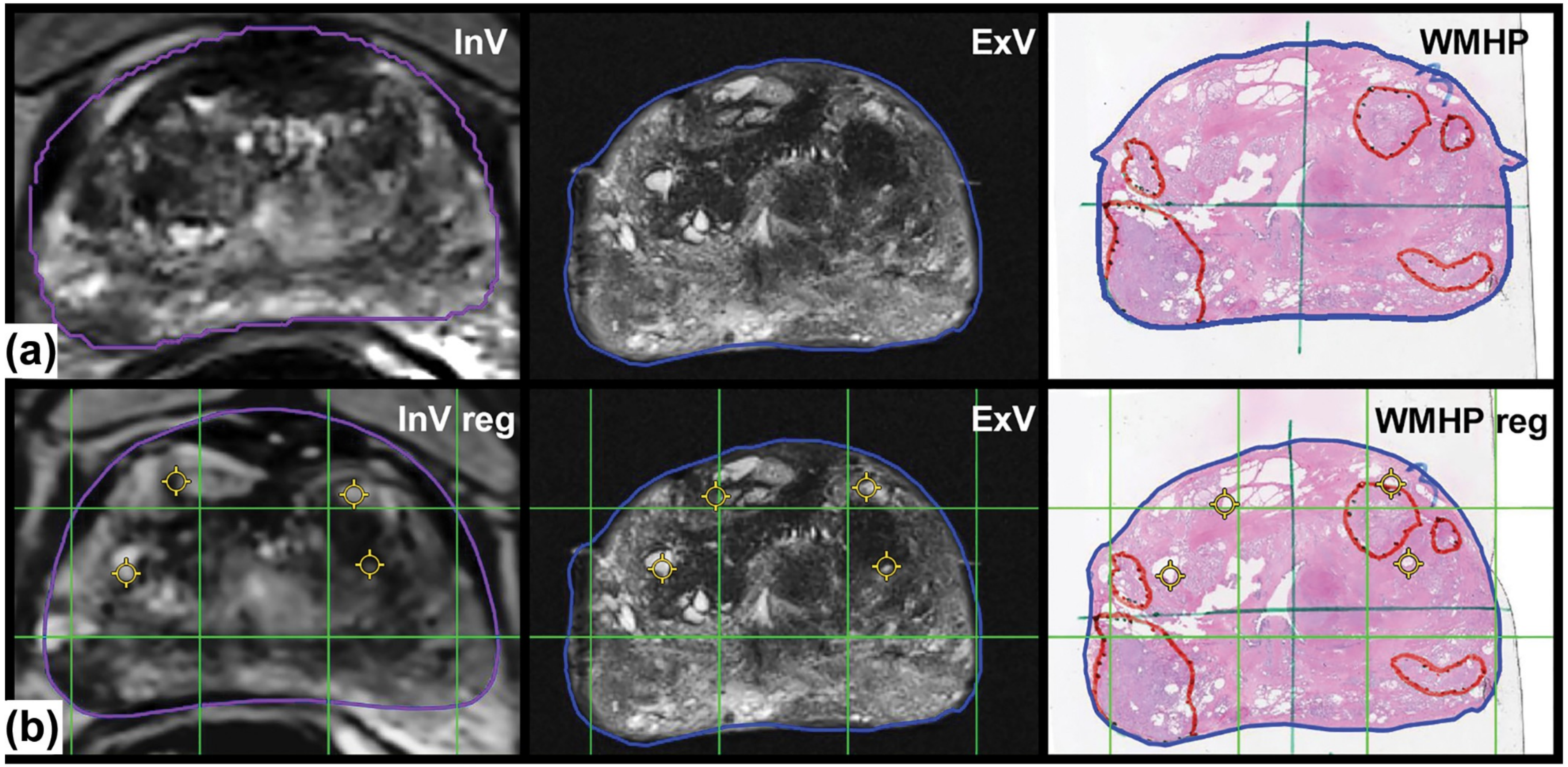
All p<0.001



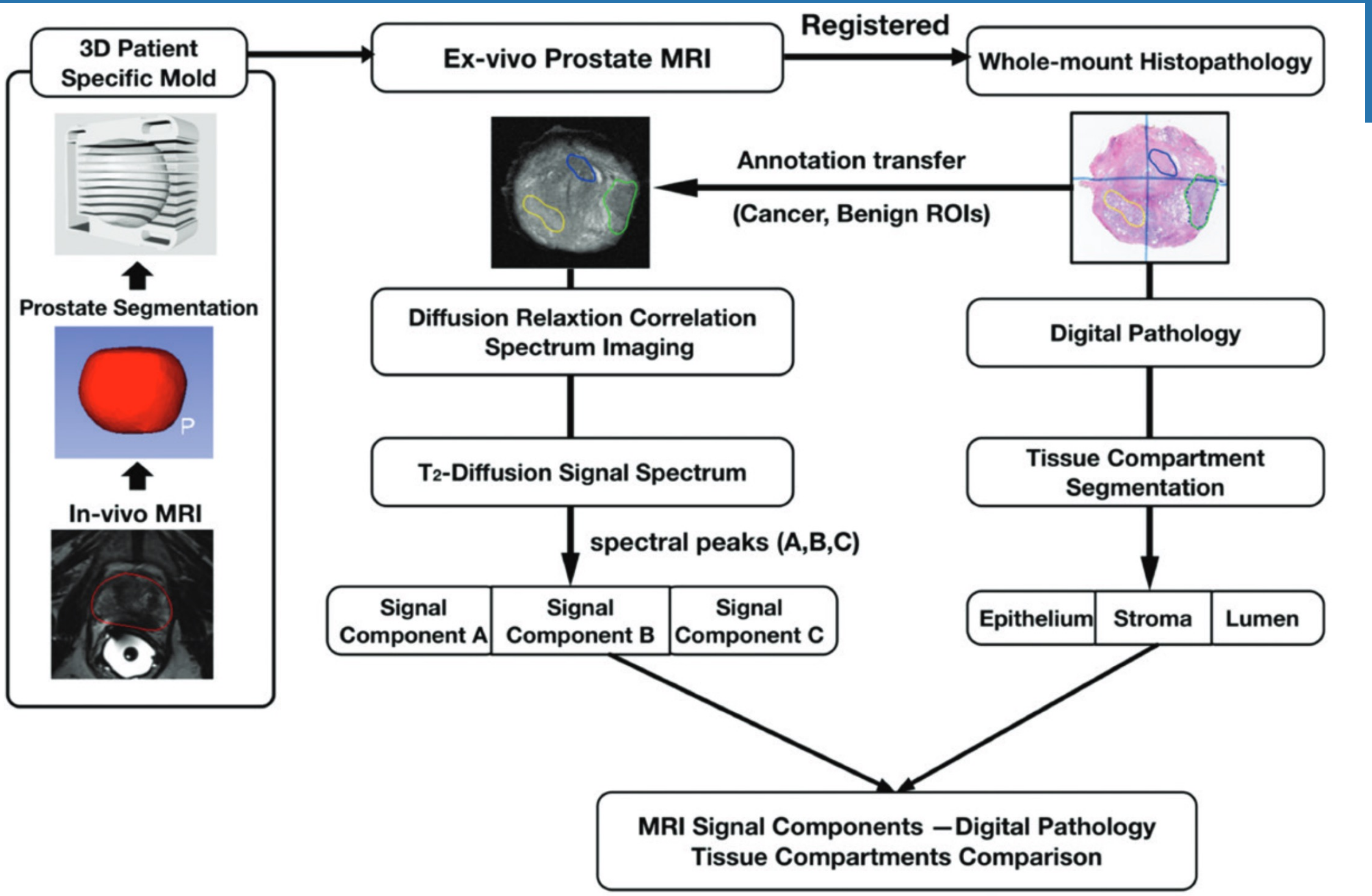
MEDICAL & IMAGING INFORMATICS

Slide courtesy of Grace Kim, PhD (UCLA)





Zhang, Z., Wu H.H., ... Enzmann, D. (2020). **Prostate Microstructure in Prostate Cancer Using 3-T MRI with Diffusion-Relaxation Correlation Spectrum Imaging: Validation with Whole-Mount Digital Histopathology** Radiology
https://dx.doi.org/10.1148/radiol.2020192330



Zhang, Z., Wu H.H., ... Enzmann, D. (2020). **Prostate Microstructure in Prostate Cancer Using 3-T MRI with Diffusion-Relaxation Correlation Spectrum Imaging: Validation with Whole-Mount Digital Histopathology** Radiology
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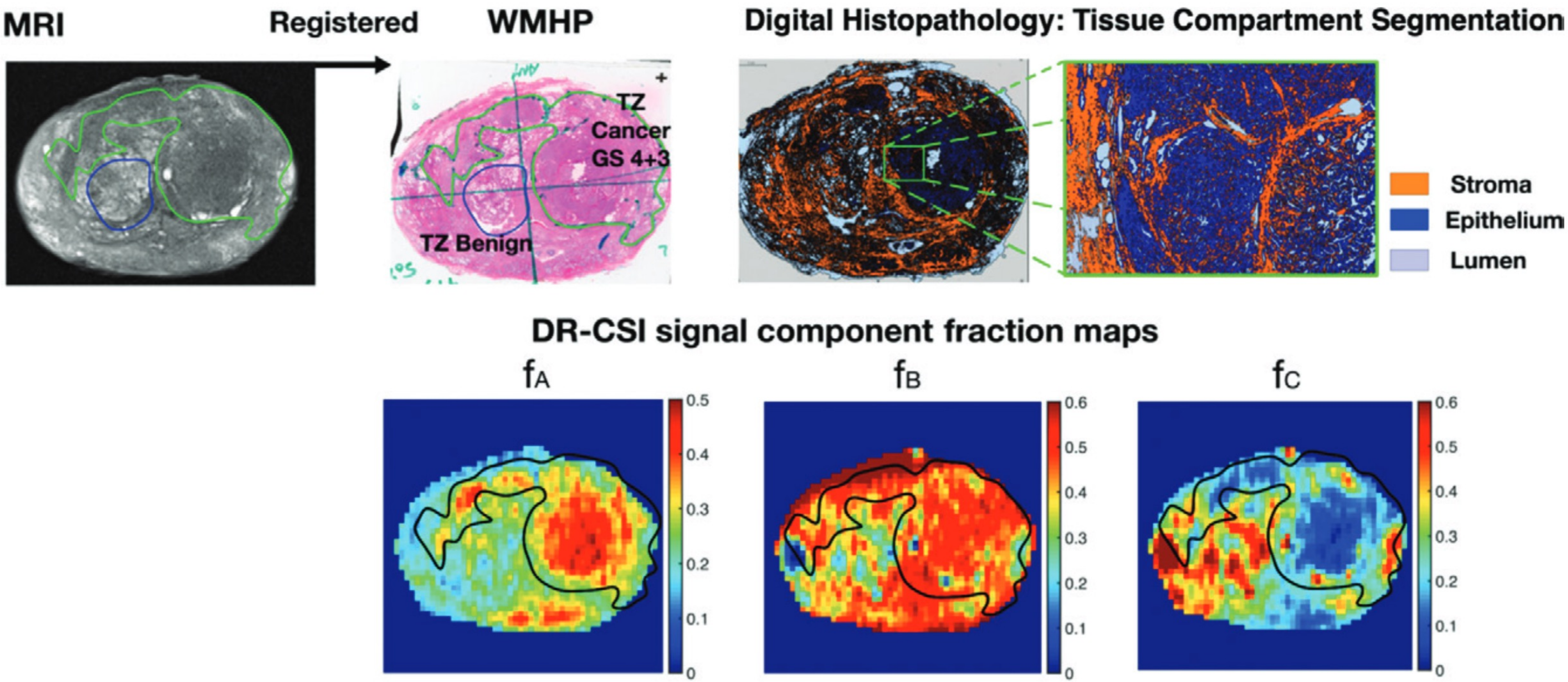
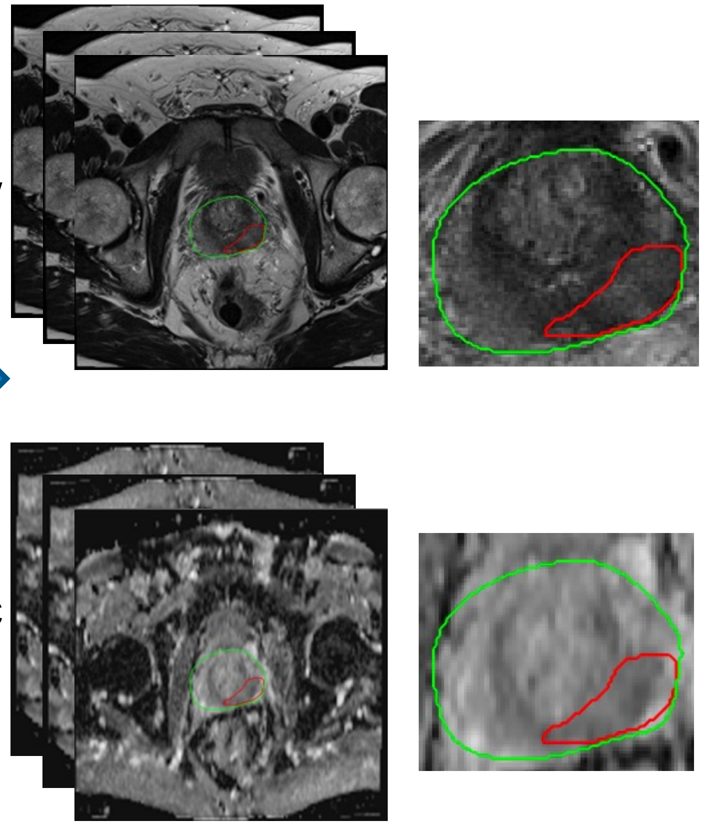


Zhang, Z., Wu H.H., ... Enzmann, D. (2020). **Prostate Microstructure in Prostate Cancer Using 3-T MRI with Diffusion-Relaxation Correlation Spectrum Imaging: Validation with Whole-Mount Digital Histopathology** Radiology
https://dx.doi.org/10.1148/radiol.2020192330

Radiomic analysis to predict outcomes

Normalization and intensity artifacts correction

MRI slices with annotations (red: tumor; green: prostate)

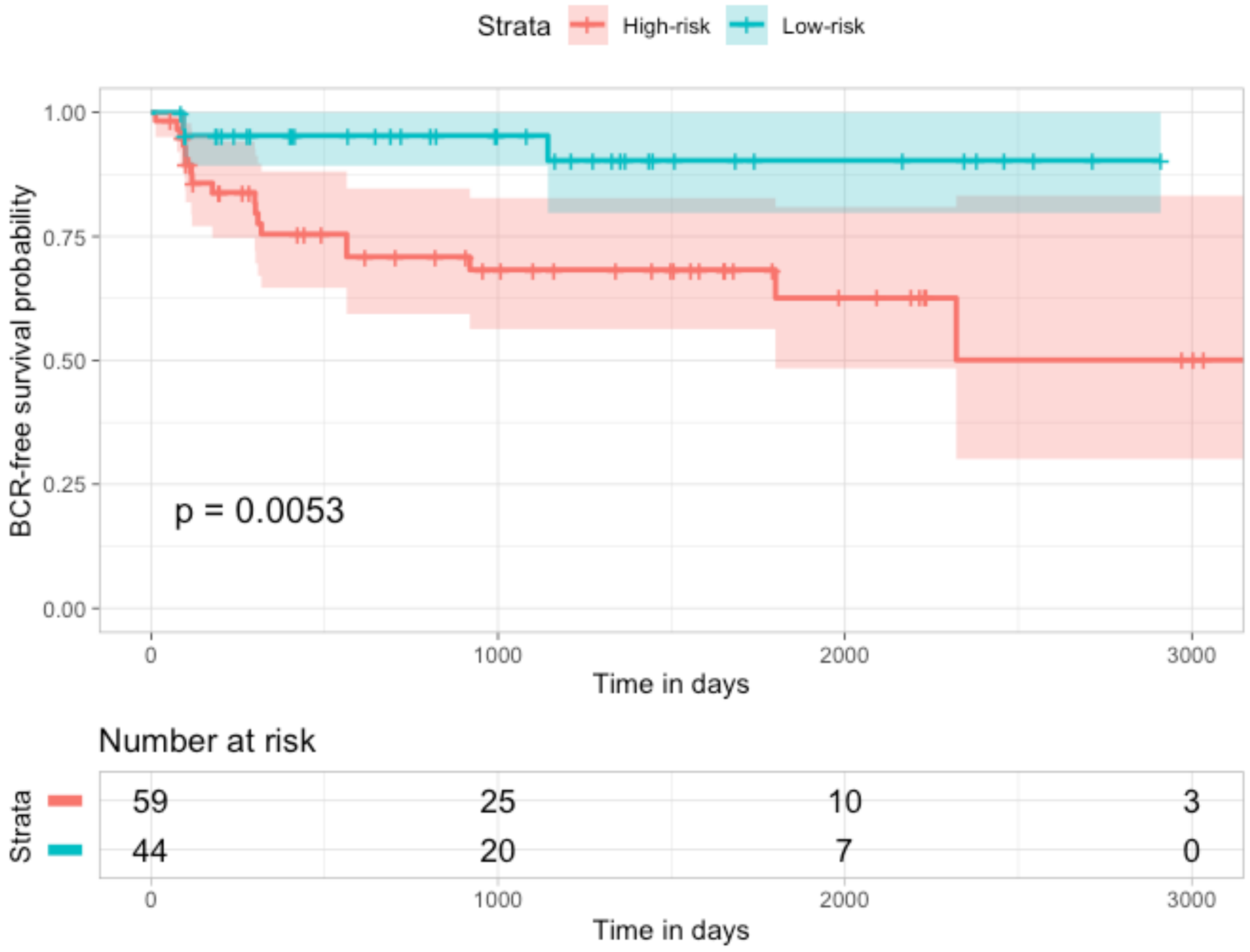


Combine slices to extract features from 3D

Shape features
- Major axis length
- Maximum 3D Diameter
- Surface volume ratio
- …

Intensity distribution features
- Mean
- 10 percentile
- Range
- …

Texture features
- Gray level co-occurrence matrix
- Gray level run length matrix
- Gray level size zone matrix
- …



Current domains

Prostate

- 960+ resection cases
- 64 ex vivo cases
- 5,000+ mpMRI cases
- 310+ MR-guided biopsies

Kidney

- 1,020+ retrospective RCC cases
- 80+ CT/US-guided biopsies

Liver

- 1,700+ ablation cases
- 110+ CT/US-guided biopsies

Lung

- 3,500+ screening cases
- 990+ CT-guided biopsies

Breast

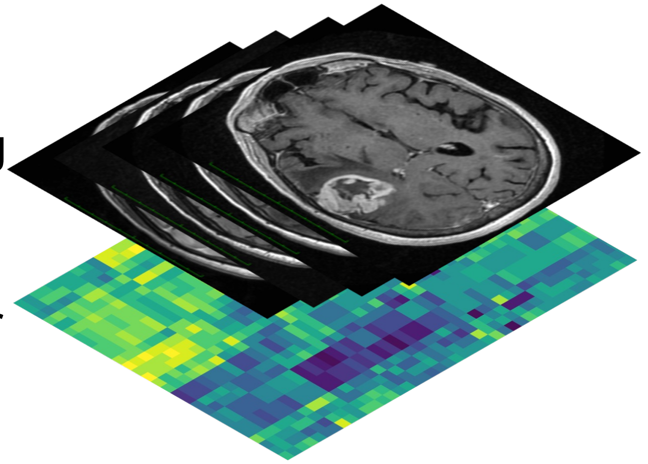
- 240+ US-guided biopsies

Patient data → Data integration → Disease trajectory

inputs

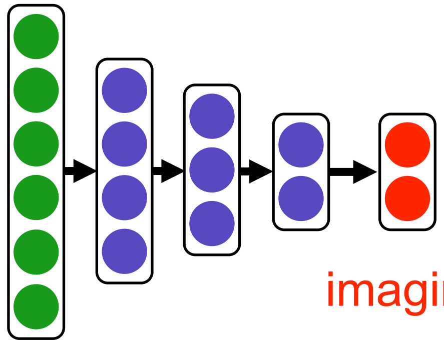
imaging

molecular



modeling

radiogenomic mapping

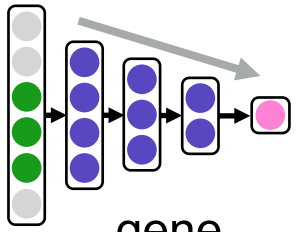


imaging

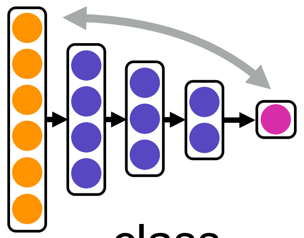
molecular

interpretation

interpretability methods



gene masking

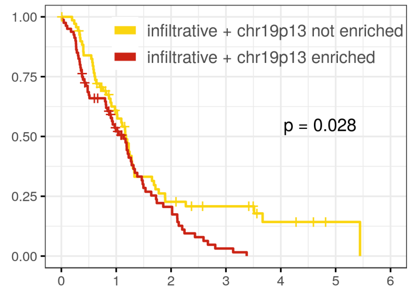


class saliency

outcomes

- progression-free survival
- overall survival

probability of survival

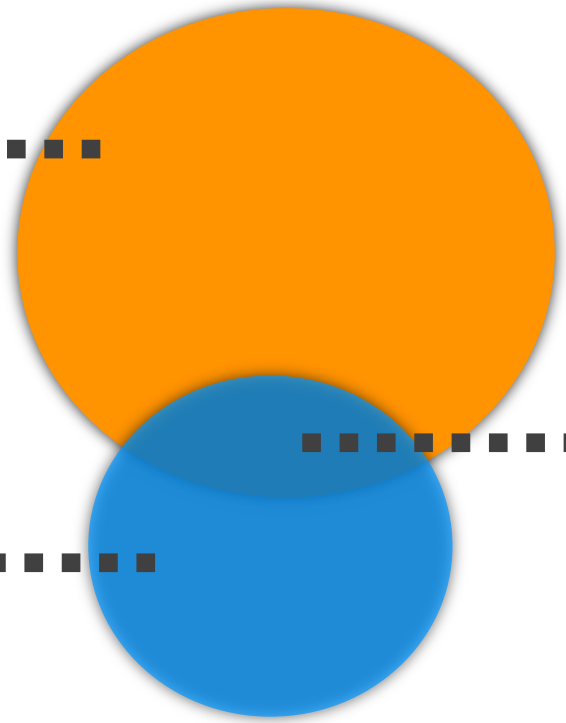


years

Data

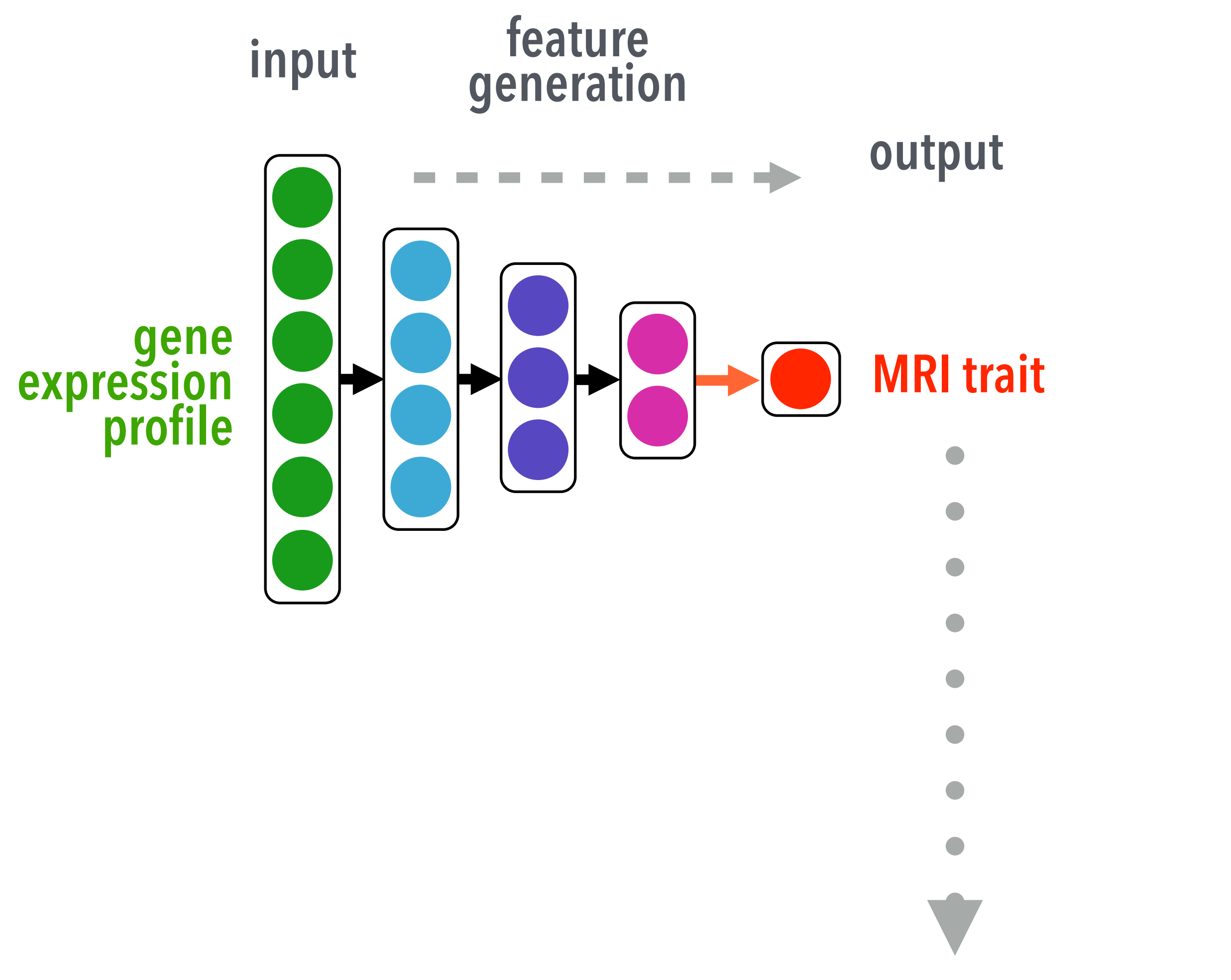
The Cancer Genome Atlas (TCGA)
n = 528 GBM patients
microarray
untreated, primary tumors

The Cancer Imaging Archive (TCIA)
n = 262 GBM patients
multiple image modalities



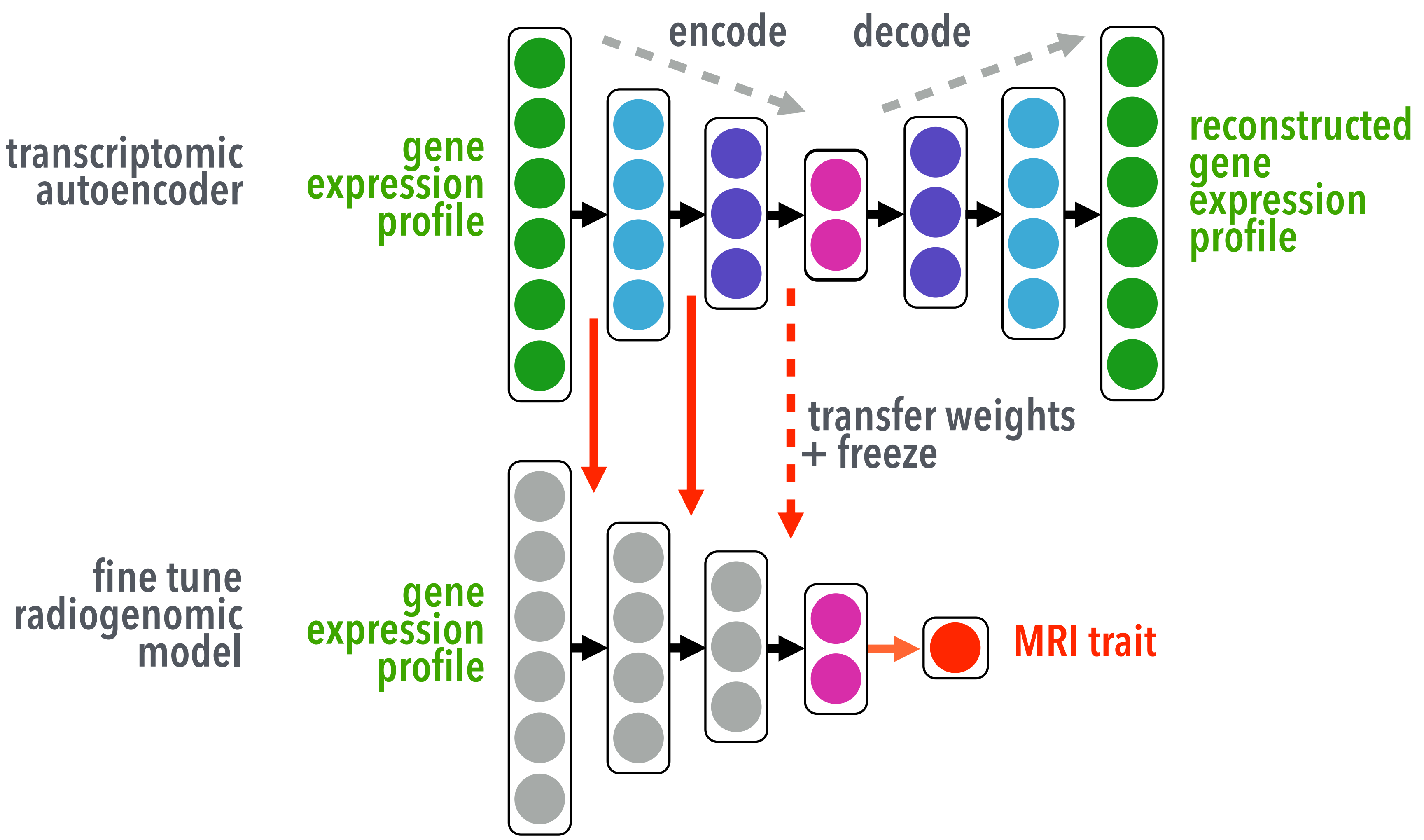
- n = 109 paired, radiogenomic samples
- gene expression profile *and* pre-operative MR imaging

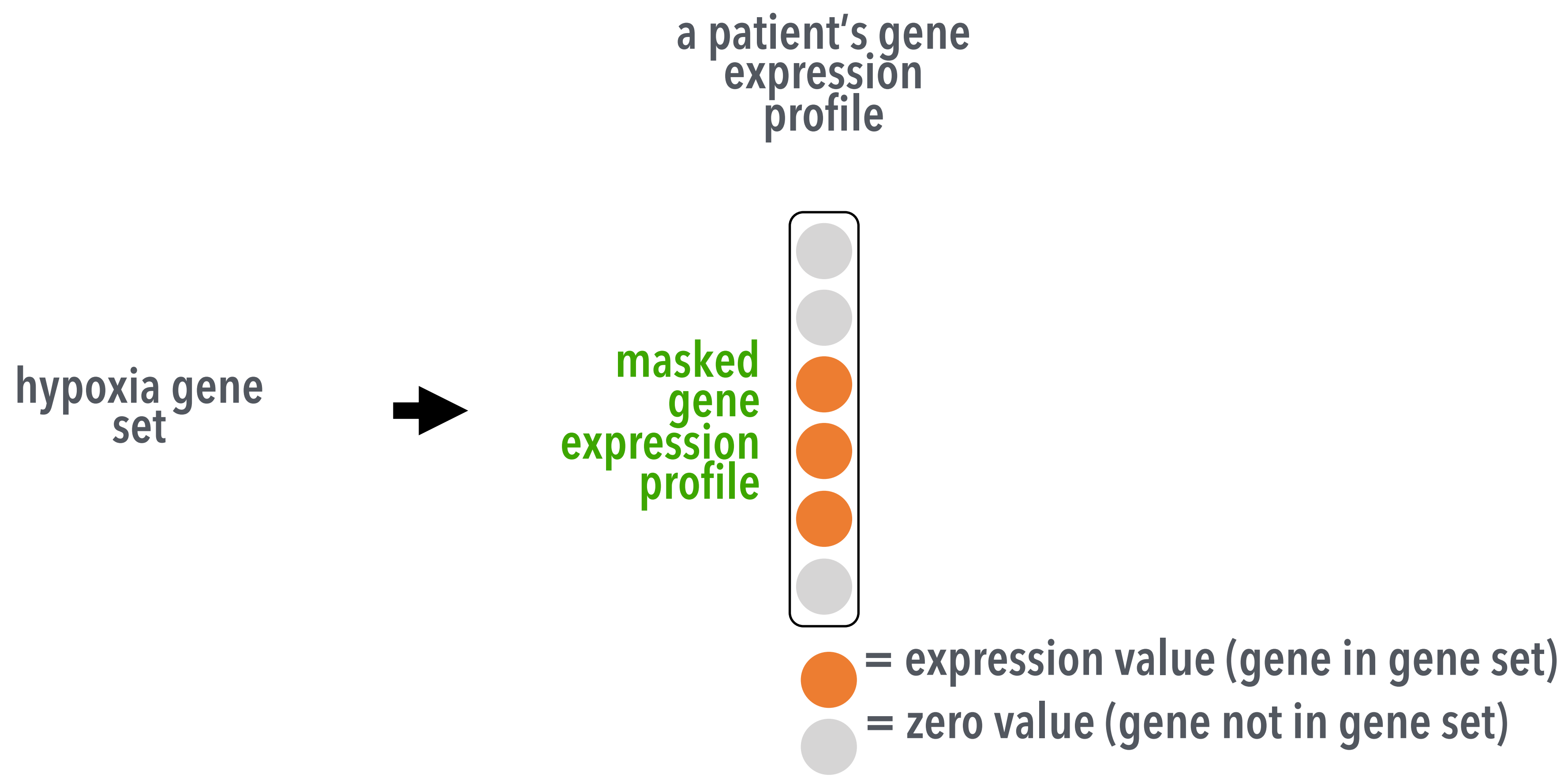
Radiogenomic neural network



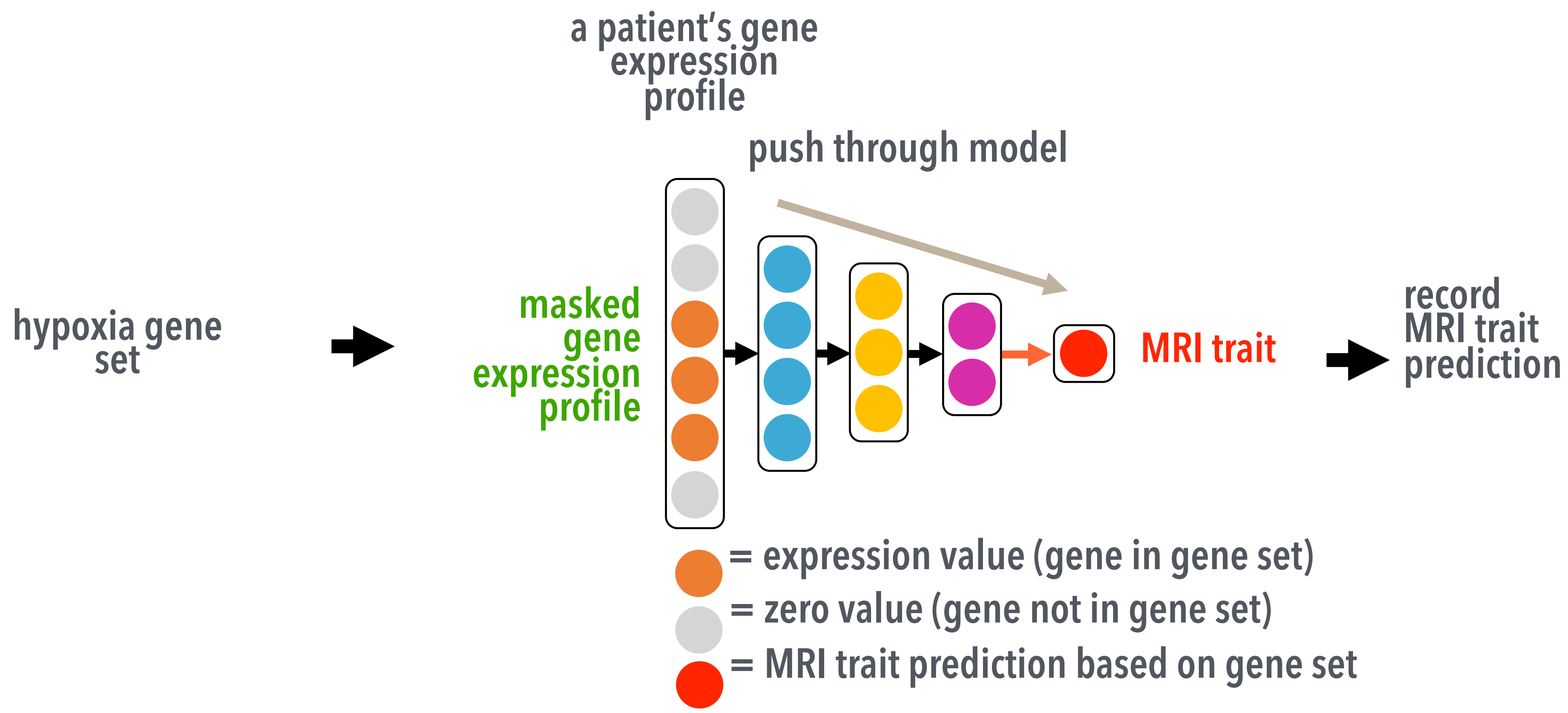
prediction of one or more imaging traits

Training:

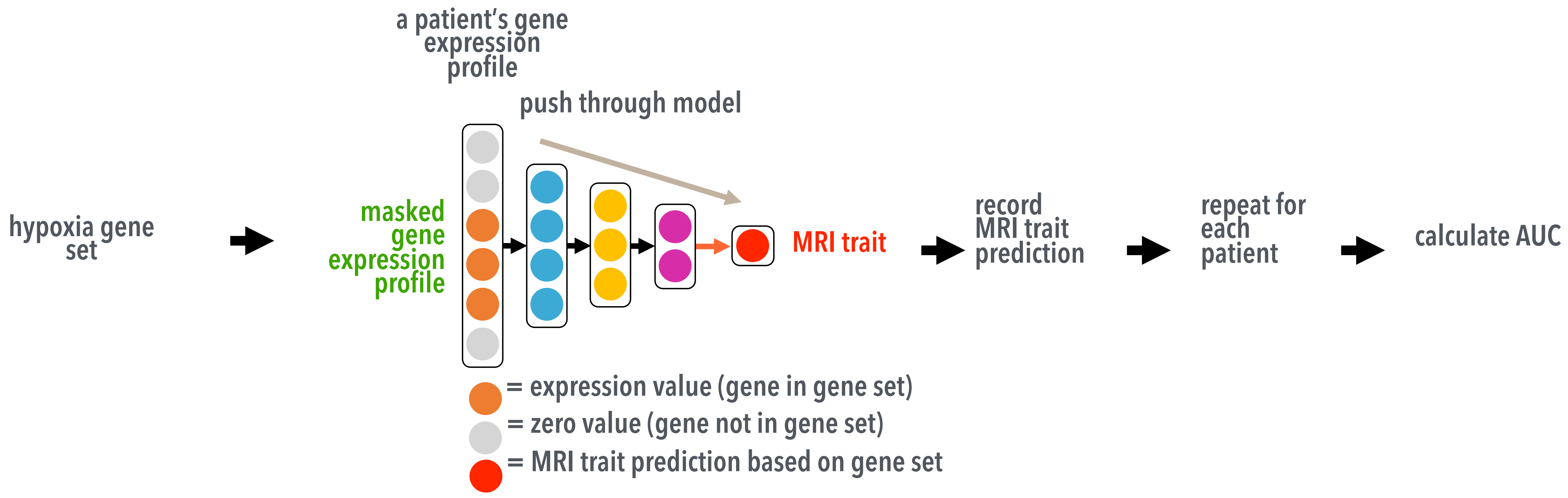




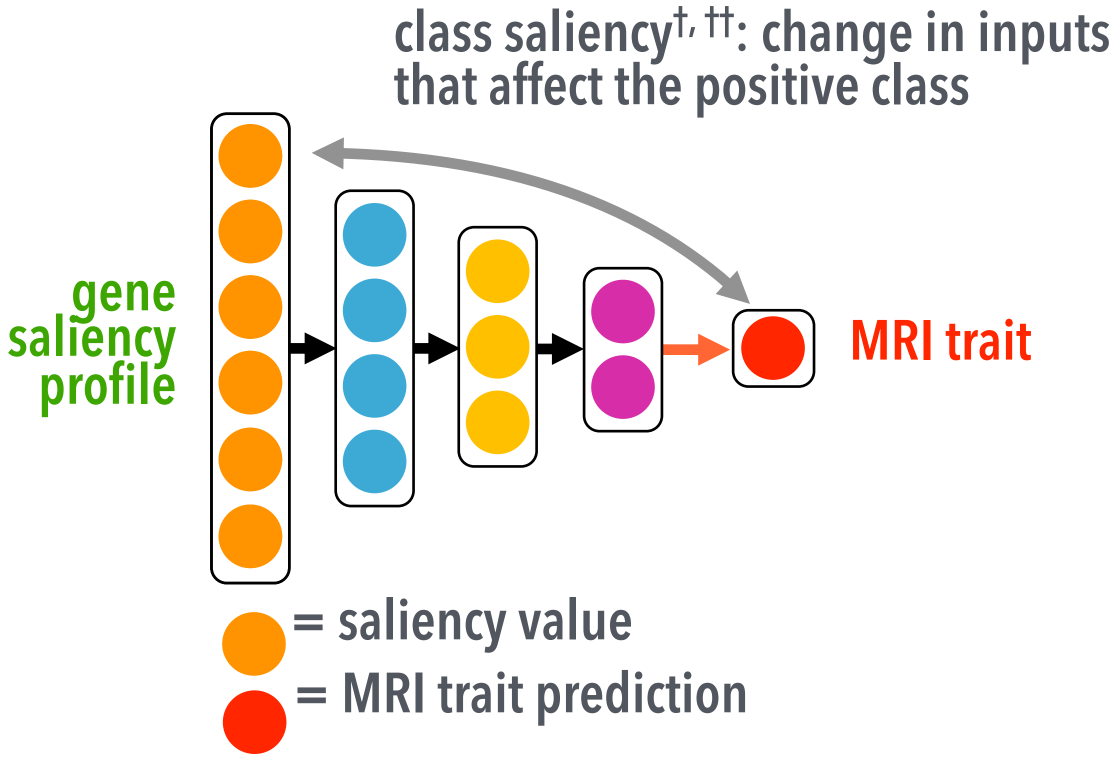
- mask the input



- mask the input
- measure the output

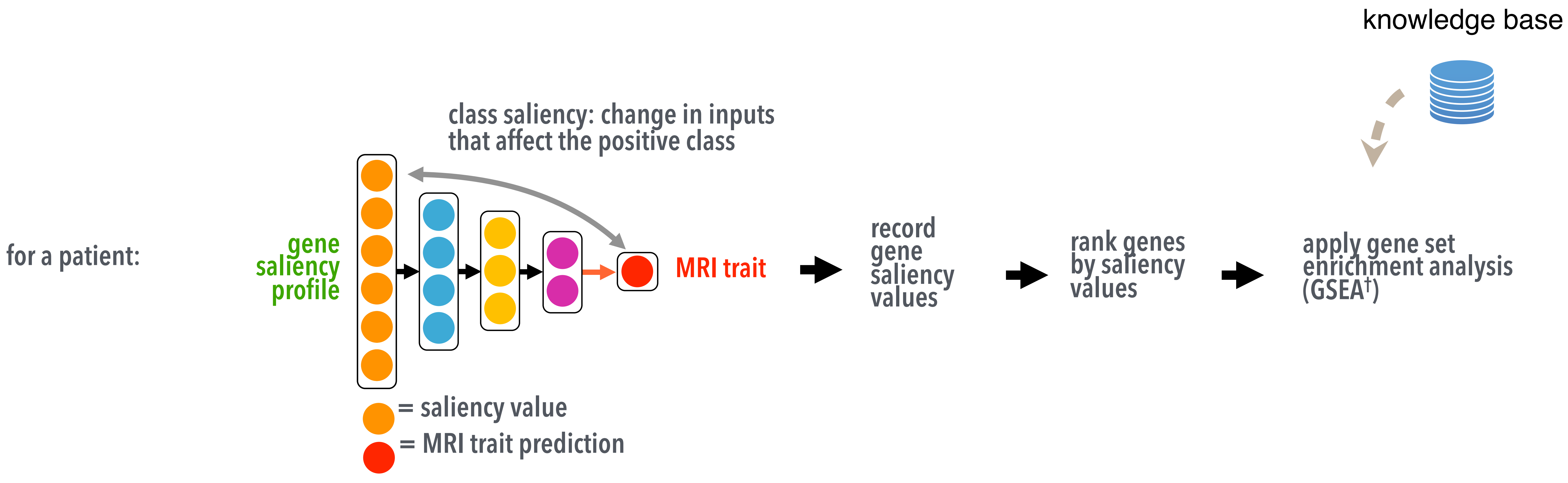


- measures performance of model when only using genes from a gene set
- use AUC as strength of association



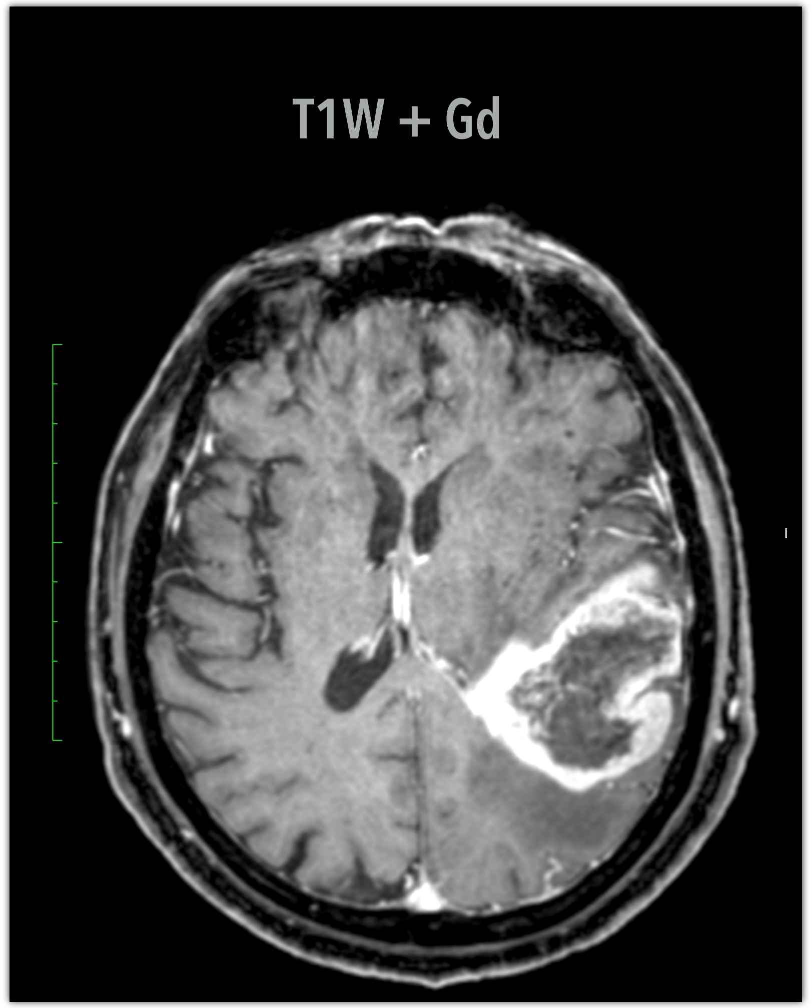
- attach weights to genes based on their importance in predicting a class label

† Simonyan, Karen, Andrea Vedaldi, and Andrew Zisserman. "Deep inside convolutional networks: Visualising image classification models and saliency maps." *arXiv preprint* (2013)
† † Kotikalapudi, Raghavendra, et al.“keras-vis.” (2017)



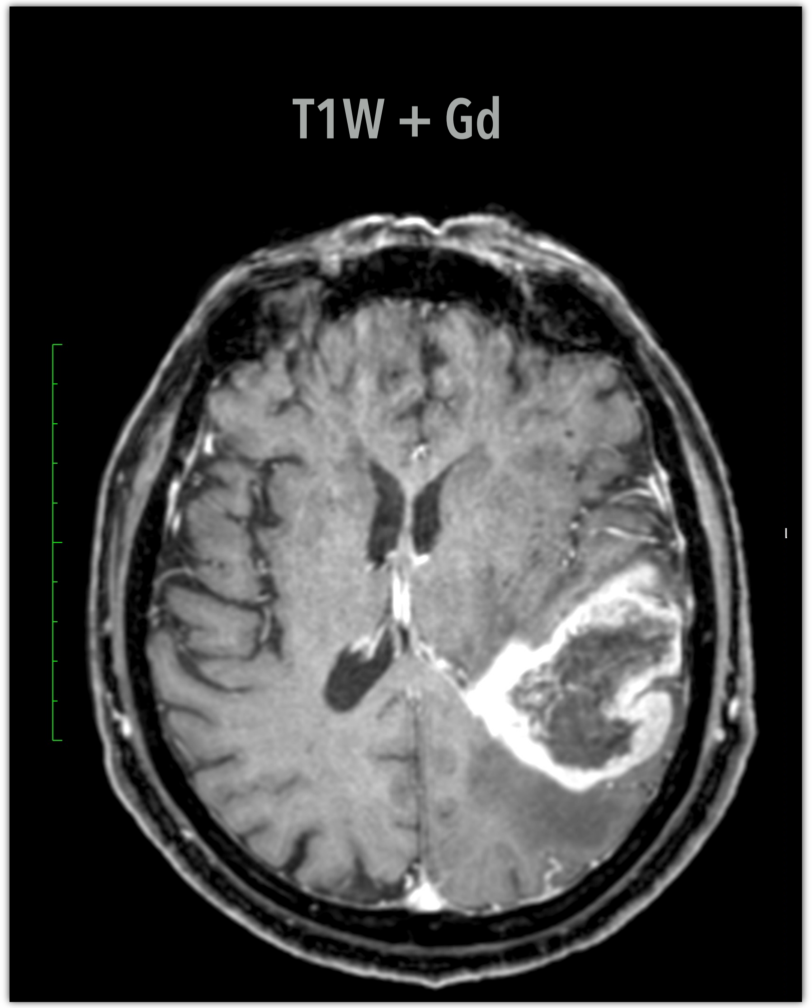
- attach weights to genes based on their importance in predicting a class label
- use of GSEA to determine what gene sets (pathways, biological processes etc.) were at the top of ranked genes

Model interpretation using gene masking



- high grade, aggressive tumor
- abnormal, leaky blood vessels
- disrupted blood-brain barrier

Model interpretation using gene masking



	transcriptomic drivers				
MRI trait	theme	gene set (collection*, query†)	**AUC**	**AP**	**see also**
enhancing	growth/death	growth (GO, *PTEN*)	0.86	0.84	
		sensory organ development (GO, *EGFR, KCNK3*)	0.85	0.84	[JDB14, GCH13]
	immune system	IL2/STAT5 signaling (H)	0.77	0.76	
		complement system (H)	0.79	0.75	
		activation of immune response (GO, *PTEN*)	0.90	0.89	
		leukocyte & lymphocyte activation (GO, *PIK3R1*)	0.86, 0.85	0.85, 0.83	
		immune effector process (GO, *PIK3CA*)	0.87	0.84	
	hormones	early & late responses to estrogen (H)	0.79, 0.78	0.73, 0.73	
		response to steroid hormone (GO, *RBI*)	0.88	0.88	
		regulation of hormone levels (GO, *PARK2*)	0.87	0.84	
	ECM	related to ECM proteins (C, ECM)	0.77–0.84	0.73–0.76	[DNW08]
		apical junction (H)	0.80	0.75	
	vasculature	heme metabolism (H)	0.77	0.65	
		vasculature & heart development (GO, *LTBP1*)	0.81, 0.78	0.80, 0.77	[JDB14]
	kinases activity	multiple (GO, *EGFR, LTBP1, KCNK3*)	all 0.87	all 0.85	[JDB14, GCH13]

- high grade, aggressive tumor
- abnormal, leaky blood vessels
- disrupted blood-brain barrier

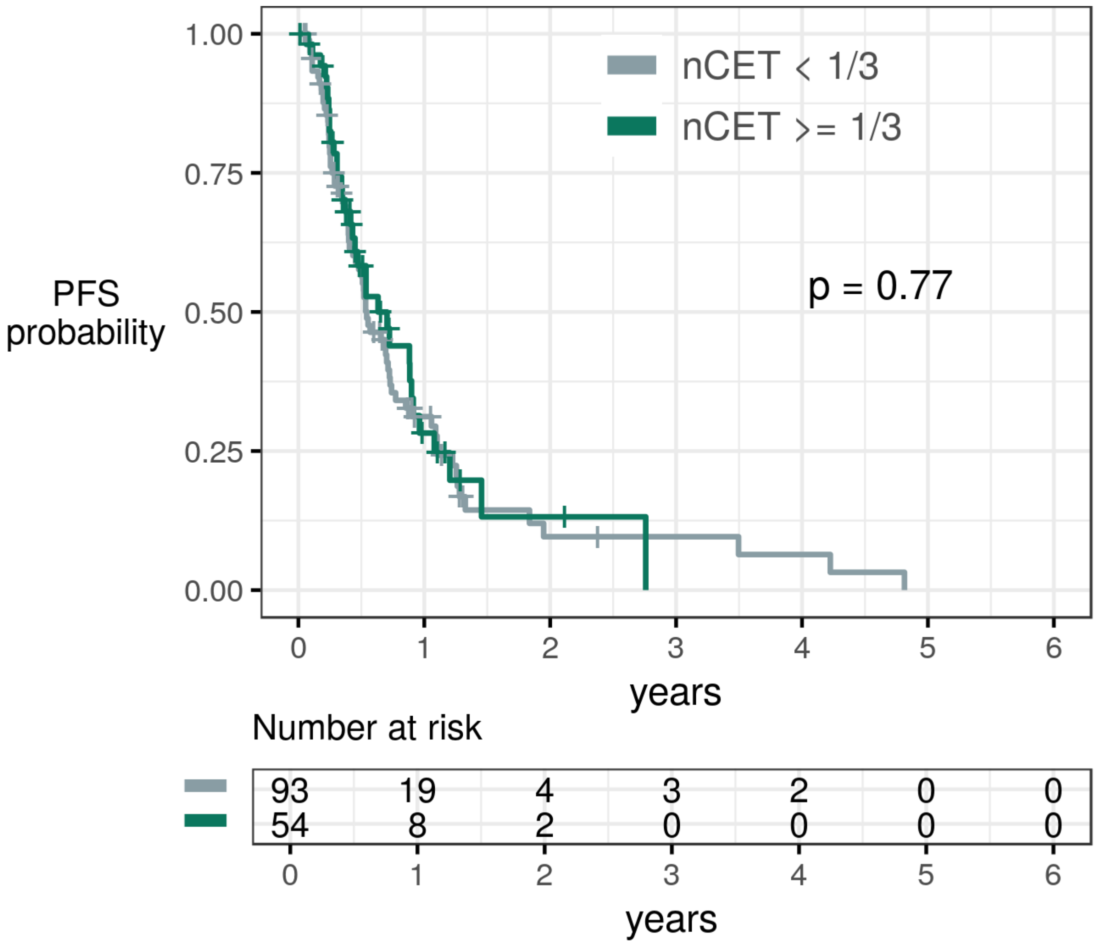
- identified the most predictive gene sets
- gene sets are related to growth, vasculature, immune system processes, and involved *EGFR*
- gene sets associated with prior radiogenomic work
- repeated analysis for all VASARI traits

Using class saliency to predict progression

- identify radiogenomic traits using class saliency
- Kaplan Meier survival curves
- **radiogenomic traits were able to differentiate progression free survival better than imaging traits alone**

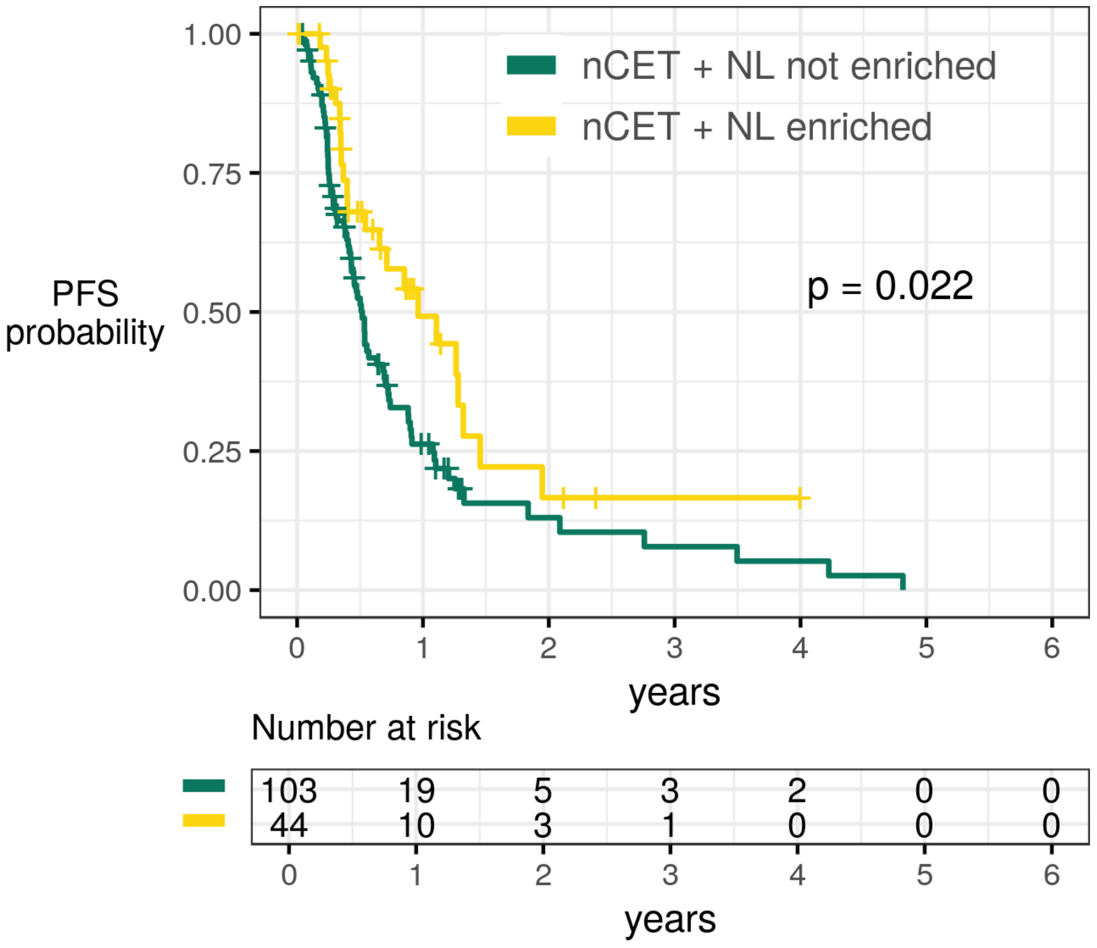
imaging trait

proportion of non-contrast enhancing tumor (nCET)



radiogenomic trait

prediction of nCET involved neural (NL) subtype genes



Concluding thoughts (1/2)

- A lot of biological information can be extracted from MRI
  - Incorporating information across biological scales and modalities can lead to improved predictions of prognosis and treatment response
- Different modalities carry different kinds of information
- Optimal techniques for normalization, registration, and fusion are open challenges
  - Driven by the increasing availability of multimodal datasets
  - Need high quality annotations and data collection workflows
- Need better model validation tools
  - Further investigation into how multi-modal features relate, model interpretability

Concluding thoughts (2/2)

- Desiderata of a good multimodal learning model (Srivastava and Salakhutdinov)
  - Similarity in the representation space implies similarity of the corresponding concepts
  - Robust to missing information / fill-in missing modalities given observed ones
- Need better model validation tools
  - Further investigation into how multi-modal features relate, model interpretability
- Additional resources
  - Survey and taxonomy of multimodal learning (Baltrusaitis et al, https://doi.org/10.1109/TPAMI.2018.2798607)
  - Recent special issue on multimodal data fusion in IEEE Journal of Biomedical and Health Informatics https://ieeexplore.ieee.org/xpl/tocresult.jsp?isnumber=8949677

Thank you

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  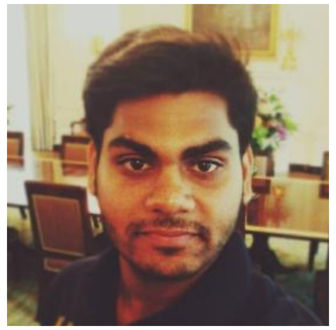 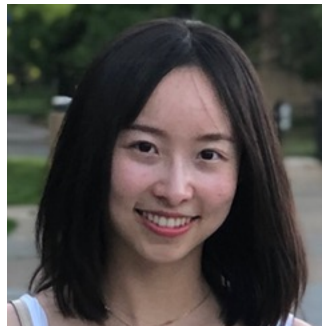
  

   
 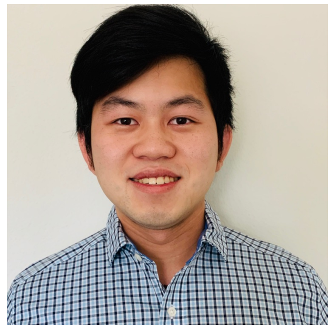  

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