

Incorporating Integrated Diagnostics into Precision Oncology

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Disclosures

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- External Advisory Board, CCC, Johns Hopkins
- International Advisory Board, Univ of Vienna
- Scientific Committee, DKFZ
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- Scientific Advisory Board, Euro-BioImaging, ERC

Exponential increase in Diagnostic test

Diagnostics - 2023



ILLUSTRATION BY DAVID PARKINS

Integrated Diagnostics - 2028



Requirements: big data, algorithmic decisions, and operational excellence

What is Integrated Diagnostics?

NO consensus on the definition or scope of ID

Different Perceptions - e.g.,

Integrating two or more diagnostic tests within the same specialty

Integrating two or more diagnostic tests from different specialties

Long-term goal – integrating all diagnostic domains of measurements!

Diagnostic Tests - all Domains of Measurement

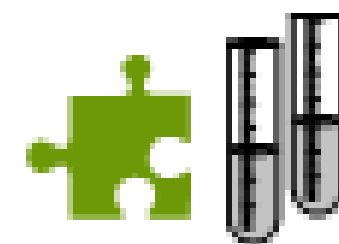
Nucleic Acids



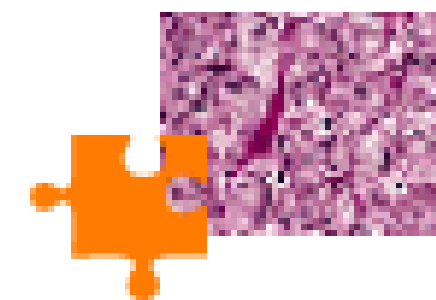
Proteins



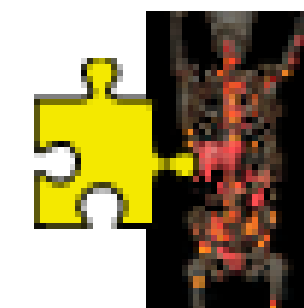
Laboratory Medicine



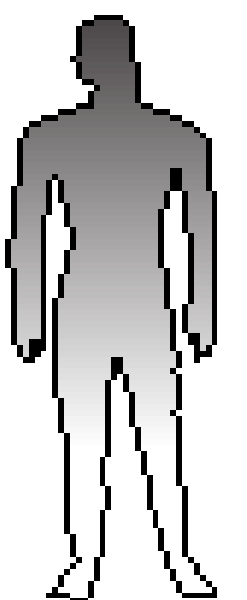
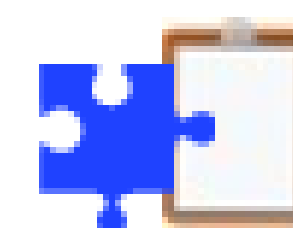
Pathology



Radiology

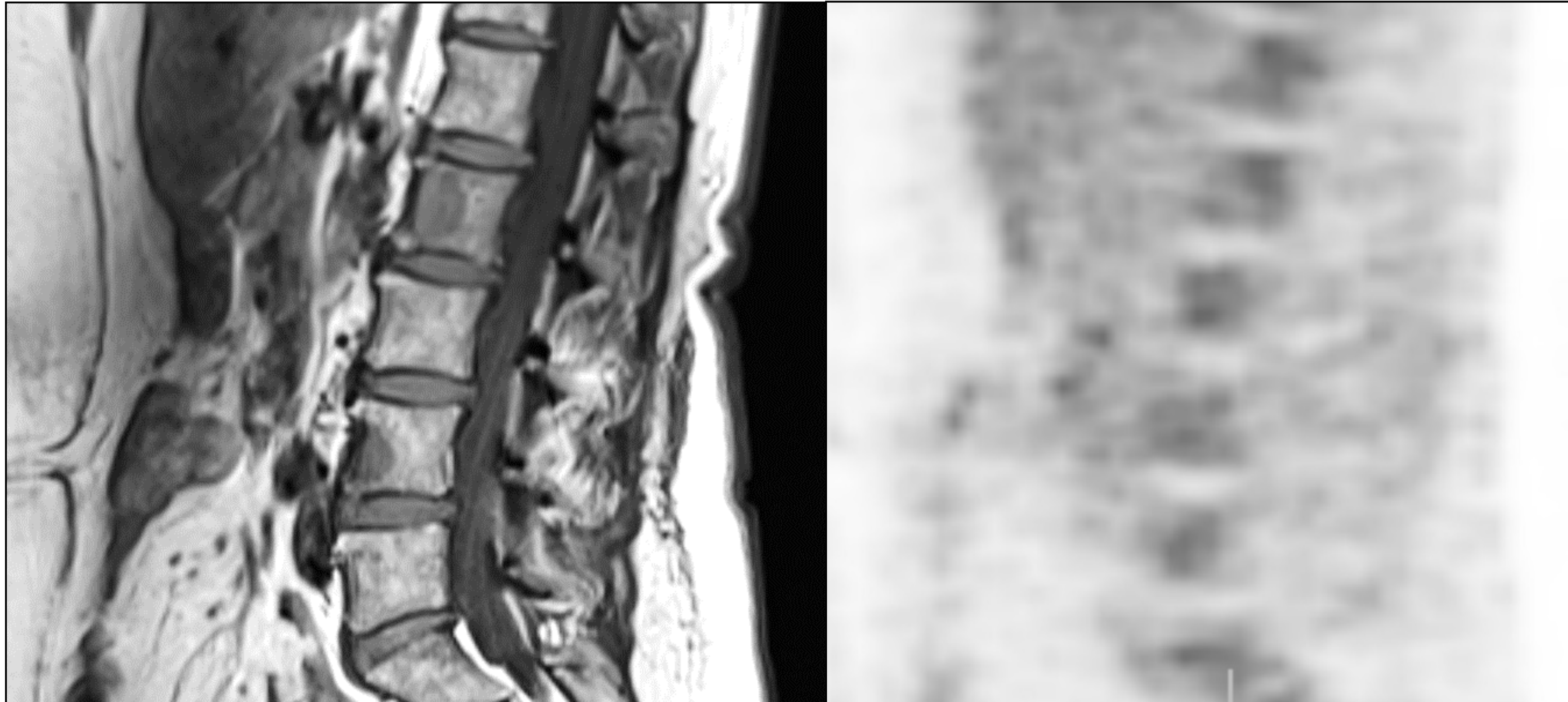


Clinical Data



Integrated Diagnostics - *MRI & ^{18}F FDG-PET*

Dx: Multiple Myeloma – R/o Bone metastasis



MRI

[18F]FDG-PET

[18F]FDG-PET is **negative** in 11% of multiple myeloma patients due to a lack of hexokinase-2 expression

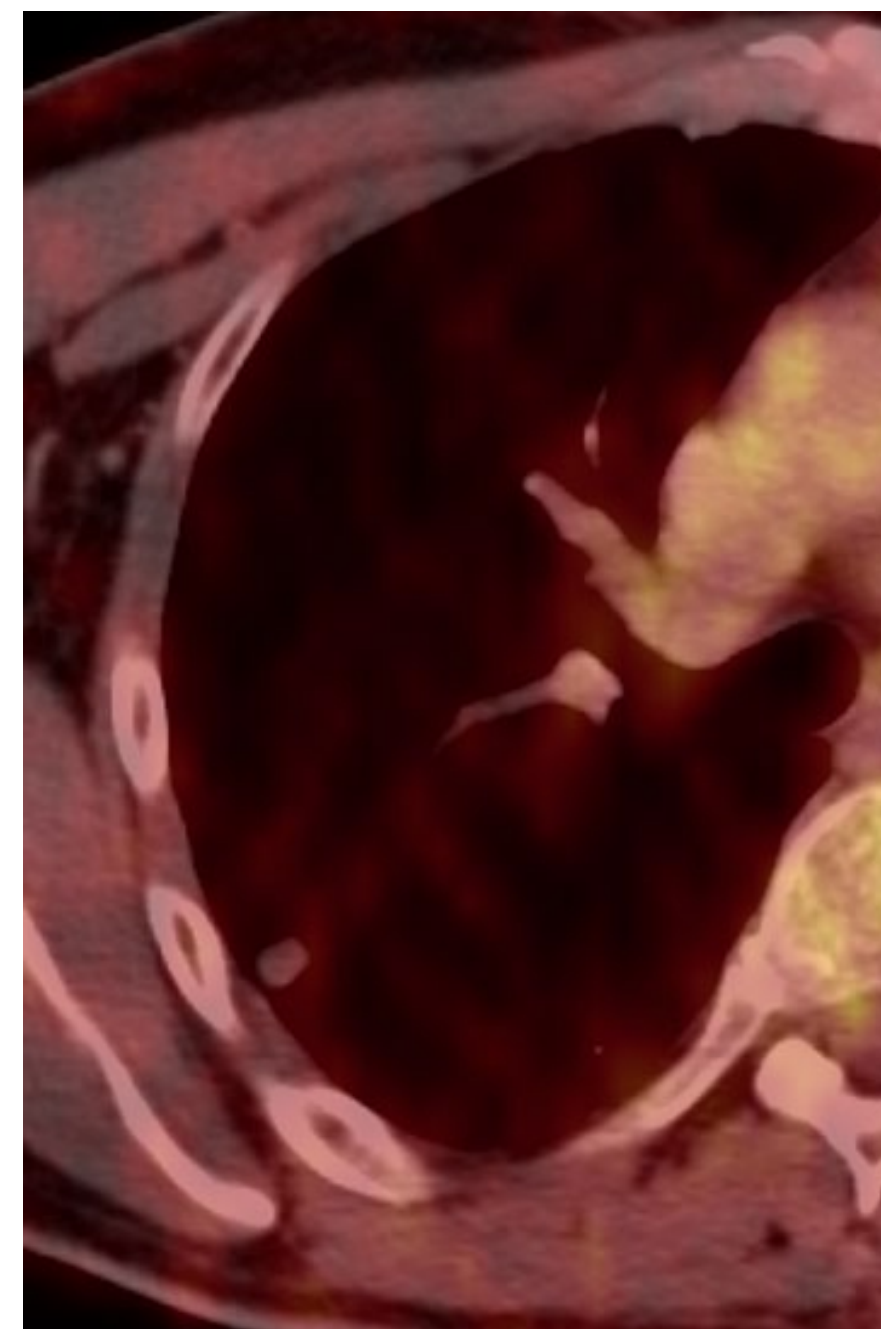
Rasche et al, Blood 2017

Integrated Diagnostics - *CT & ^{18}F FDG-PET*

63-year-old patient with cutaneous melanoma – lung lesion?



CT

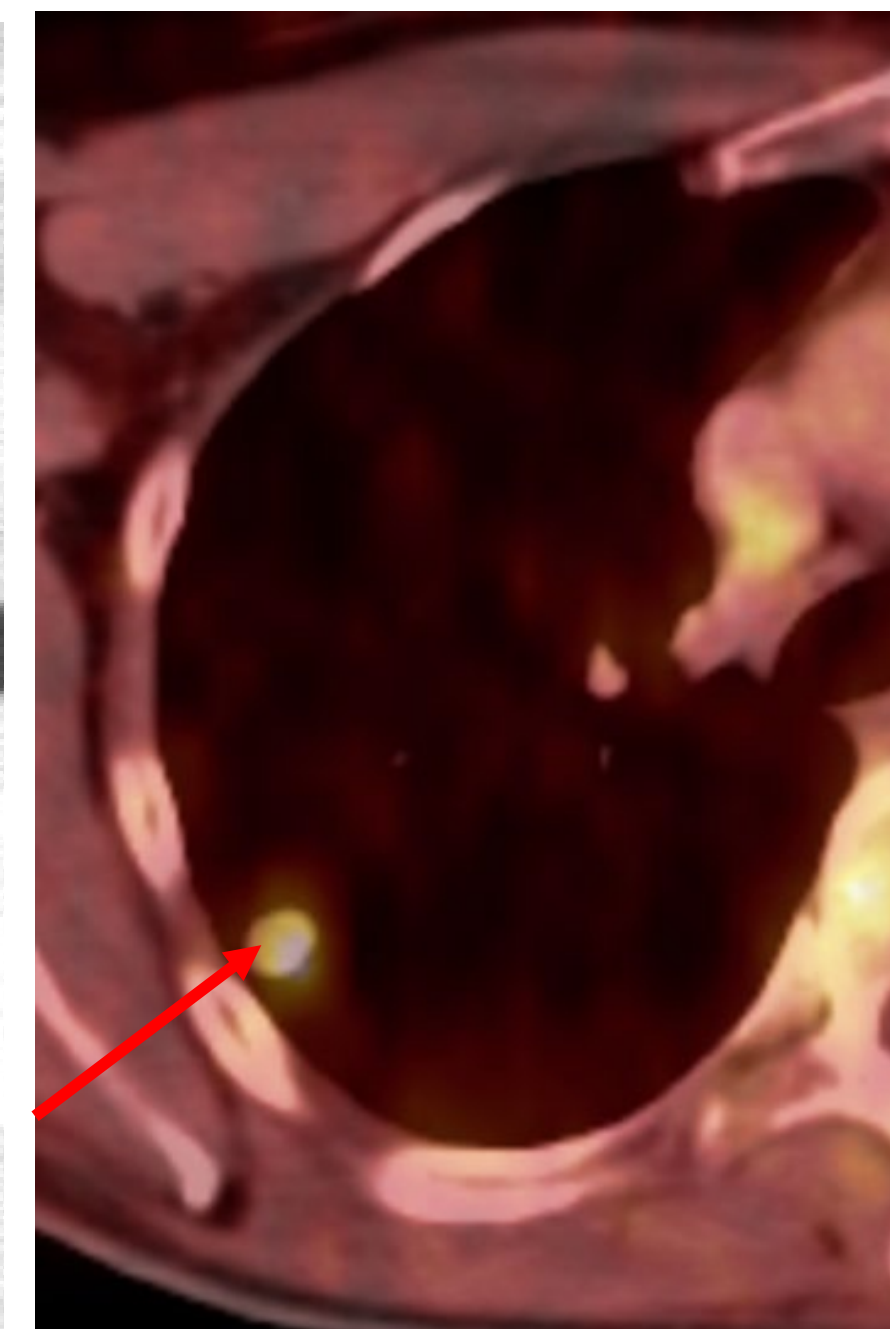


PET-CT

Initial Staging



CT

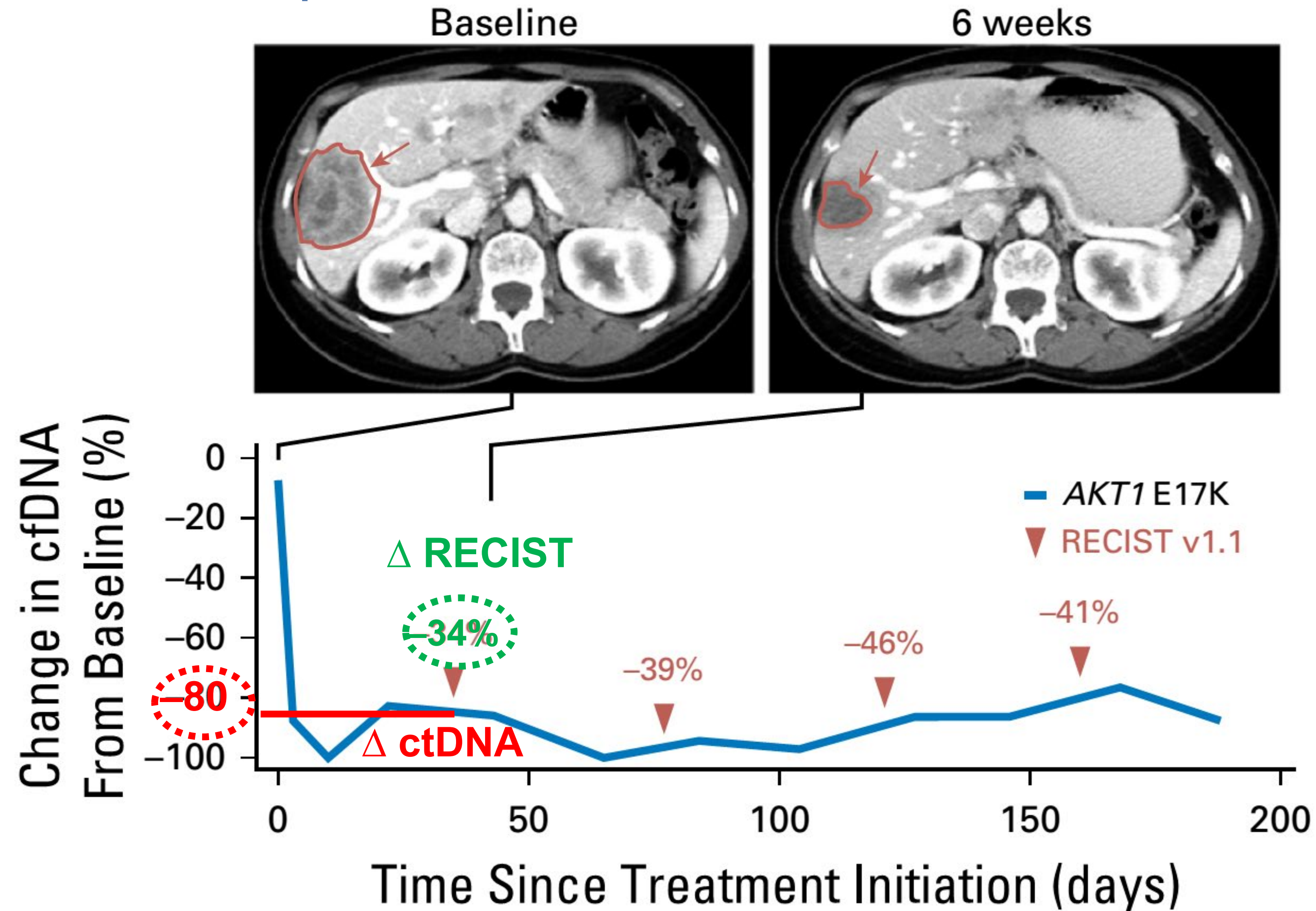


PET-CT

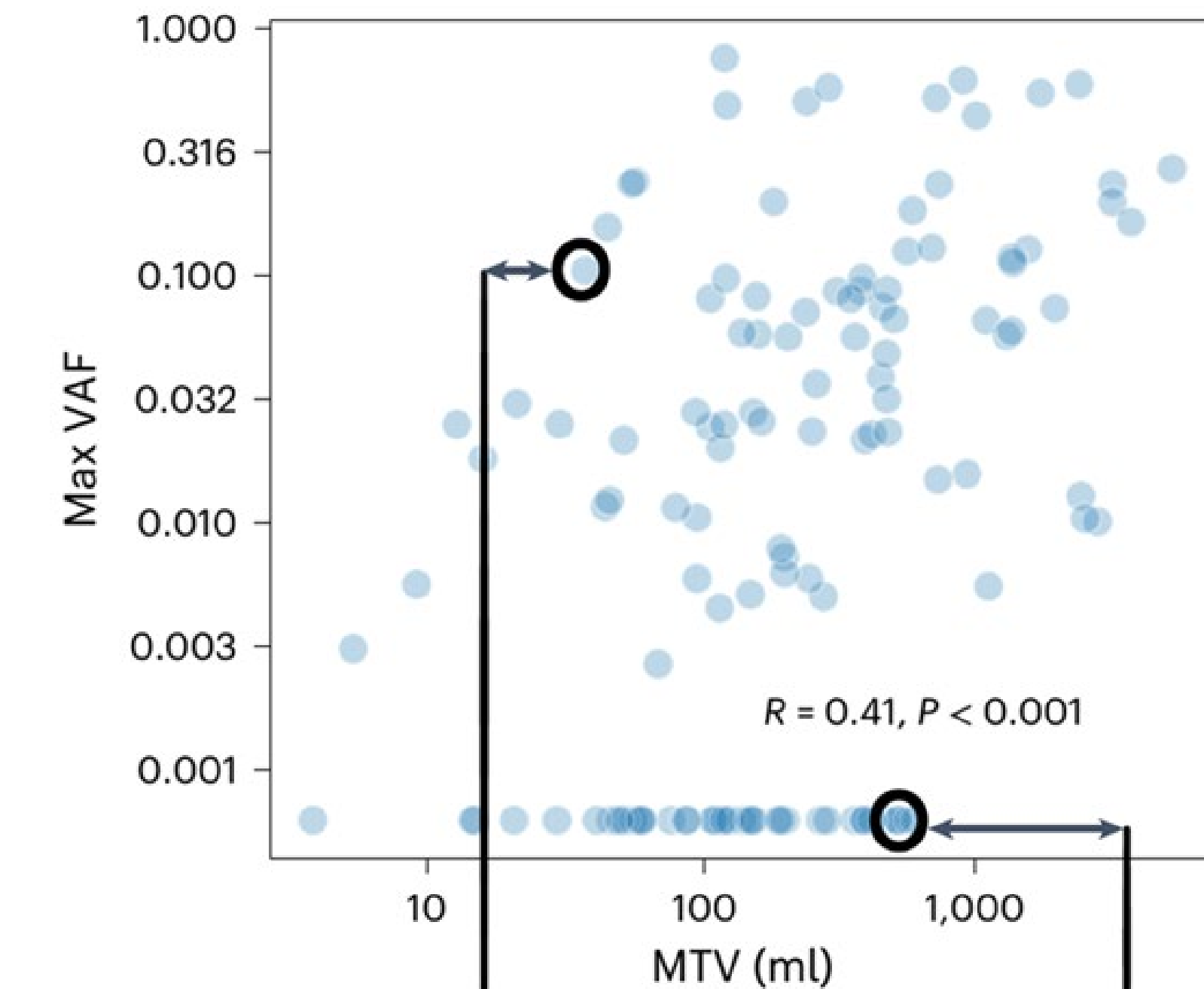
After 2 months

Integrated Diagnostics - *CT & ctDNA in Tumor Follow-up*

Pan-Akt inhibitor in multiple solid tumors



Integrated Diagnostics - MTV on PET/CT & ctDNA as Prognostic Biomarker



MSK-IMPACT

TP53 E339*
KRAS G12C
KEAP1 F211Y
STK11 D194Y

ctDx Lung

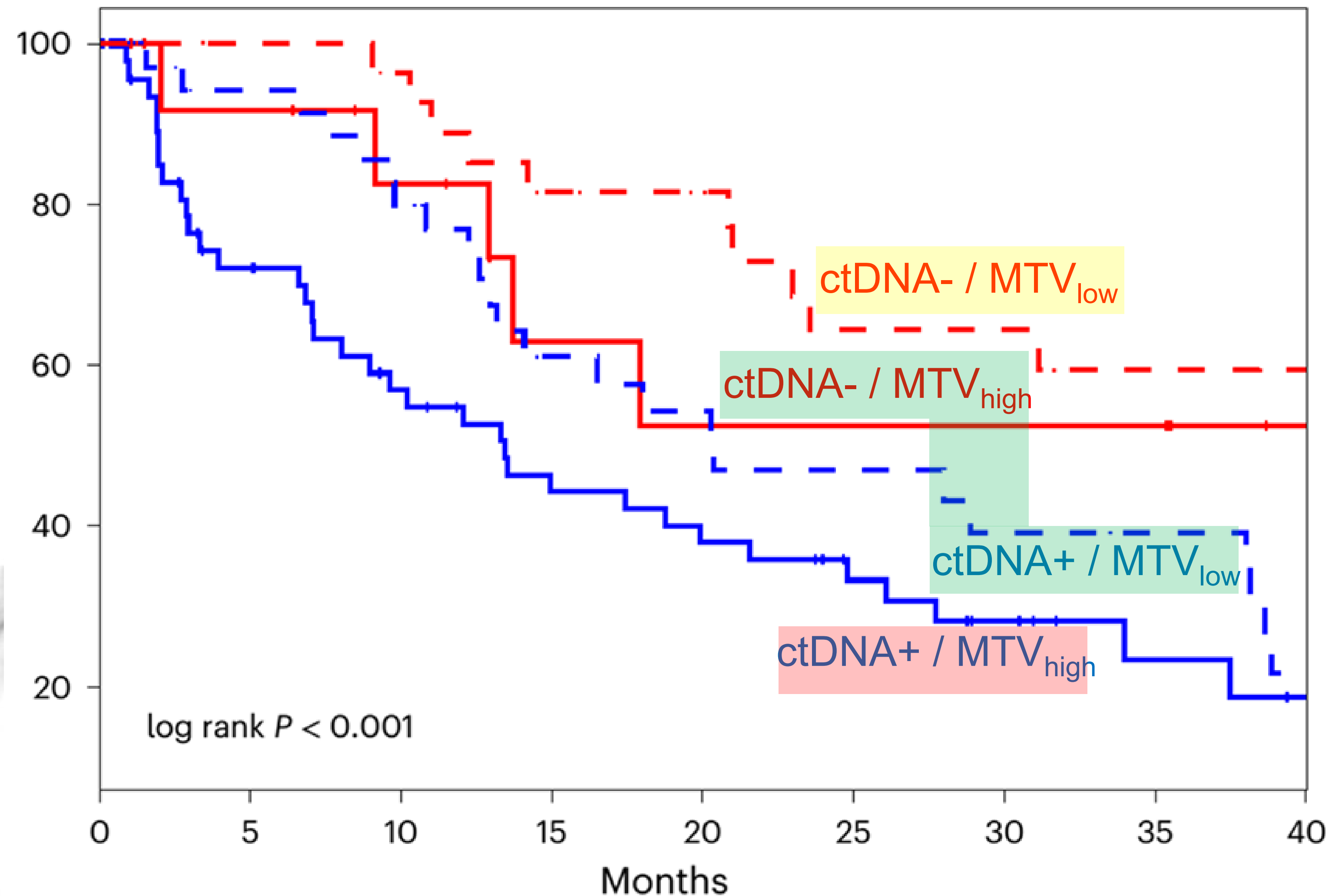
TP53 E339* 10.4%
KRAS G12C 9.7%

MSK-IMPACT

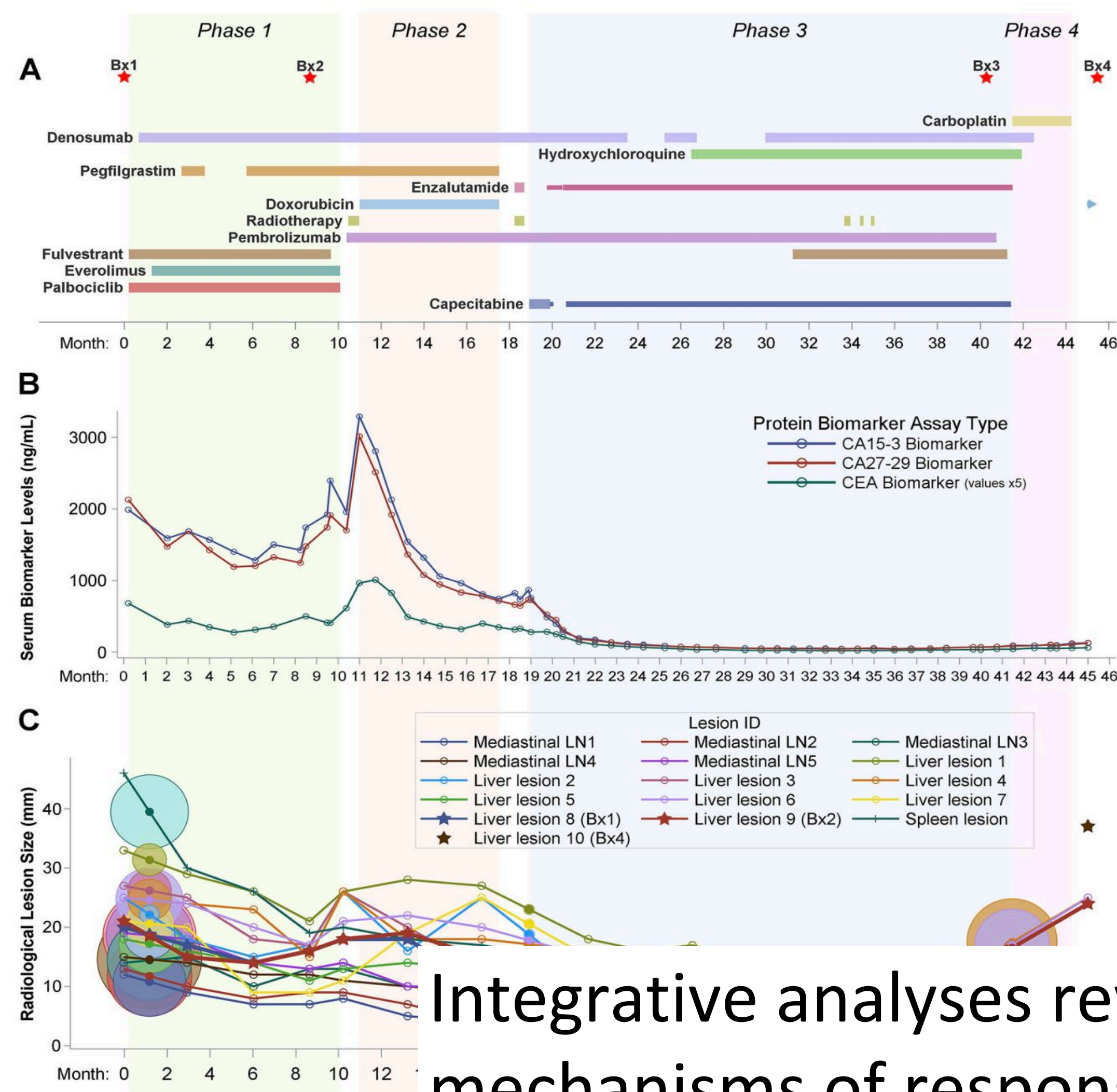
ROS1 rearrangement

ctDx Lung

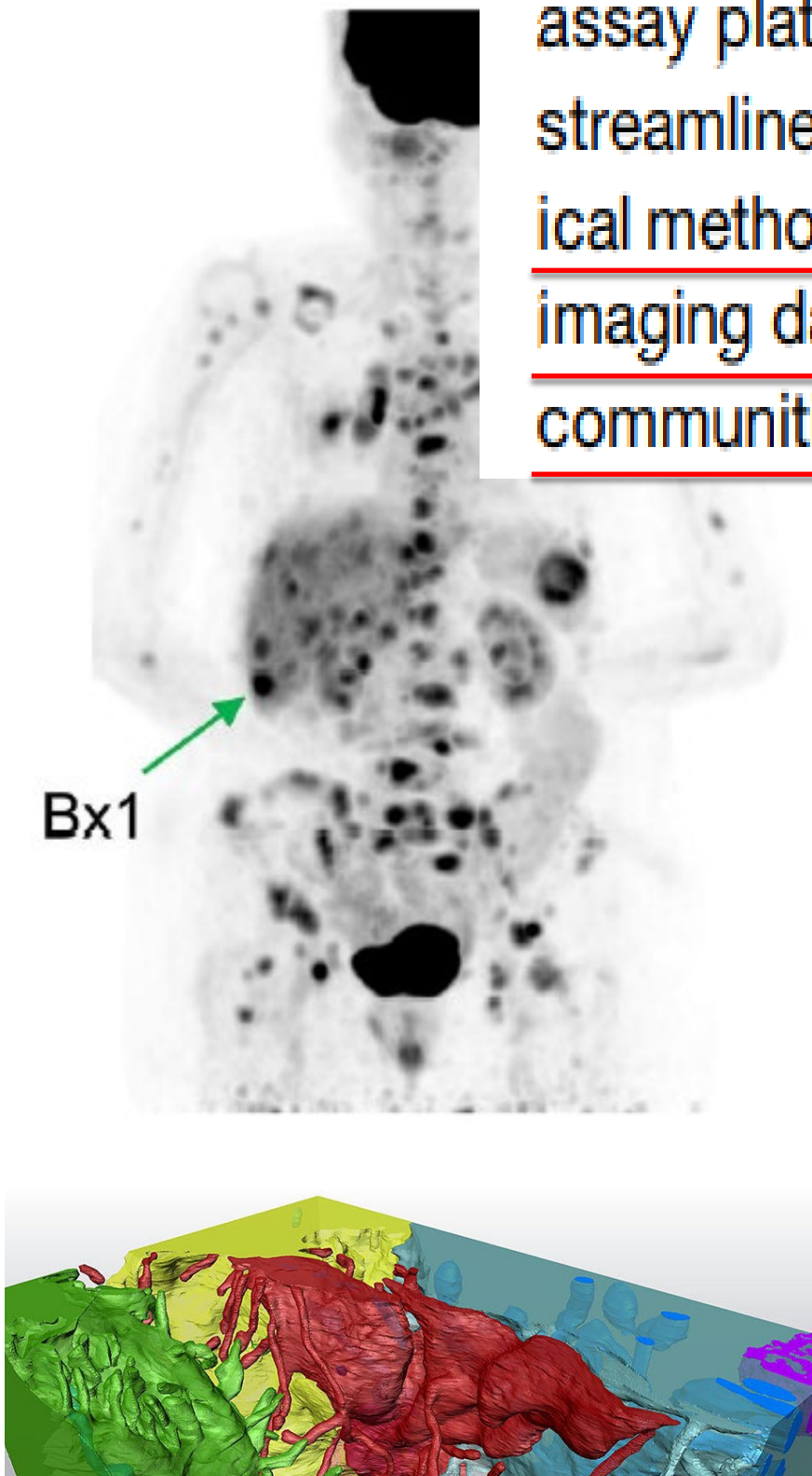
No alterations



Integrated Diagnostics – Multi-Platform Omics and Imaging



Several of our methods are too complex to be widely applied as currently implemented. However, when the utility of each assay platform is established, workflows can be simplified and streamlined. Our work shows that further development of analytical methods to integrate and interpret multi-platform omics and imaging datasets is clearly needed for the clinical and research communities. The OMS atlas can serve as a resource in that



JohnsonBE at al: An Omic and Multidimensional Spatial Atlas from Serial Biopsies of an Evolving Metastatic Breast Cancer; Cell Reproductive Med , 2022

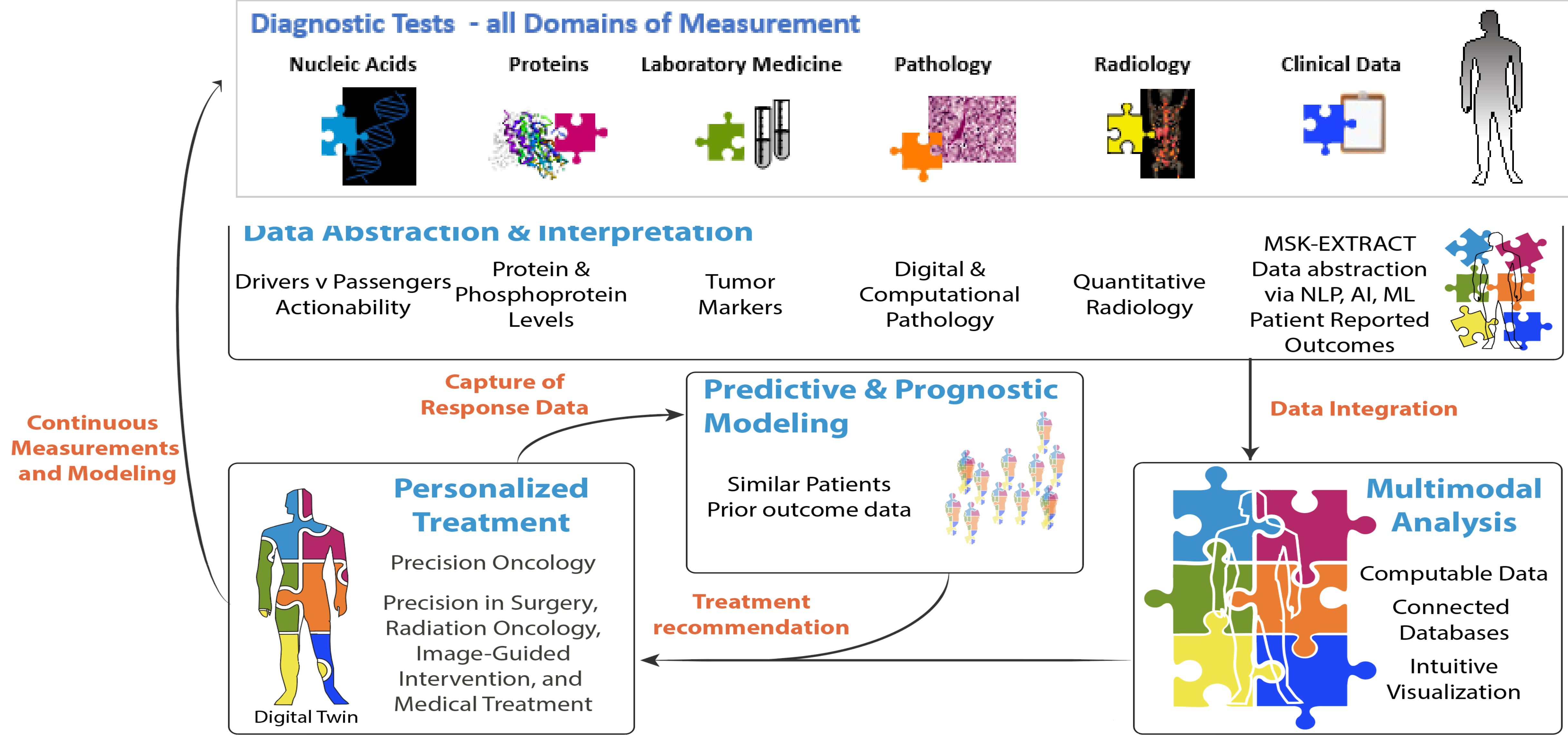
Integrative analyses reveal new potential mechanisms of response and resistance

Integrated Diagnostics – *Multifaced Opportunities*

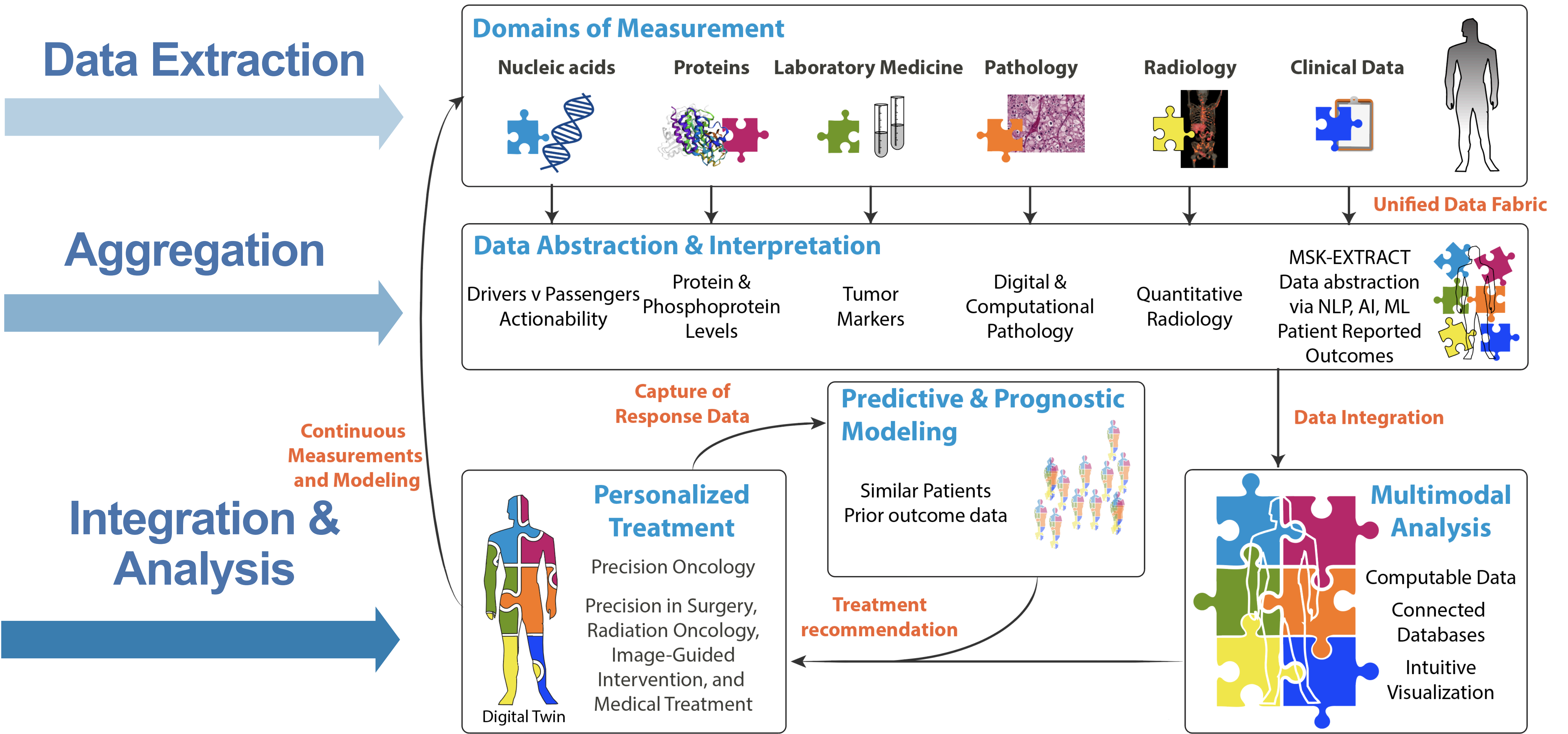
1. **Clinical:** “*AI-facilitated Tumor Boards*” - Multidisciplinary & Interdisciplinary workflow organized along disease-specific pathways
e.g., MSK pilot projects – (Neuroendocrine Tumors, Brain Tumors & Lymphoma)
2. **Research:** endless opportunities for new discoveries through annotated & curated large database
3. **Education**
4. **Patient access:** to data and shared decision making
5. **Health Equity:** Enabling personalized precision cancer care within the US and Globally

Towards Reducing Medical Errors & Improved Outcomes

Integrated Diagnostics – Ultimate Goal



Integrated Diagnostics – *Steps to take*



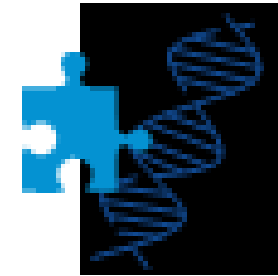
Integrated Diagnostics - *Challenges*

Data Extraction

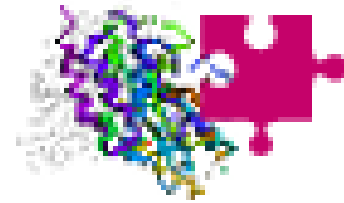


Diagnostic Tests - all Domains of Measurement

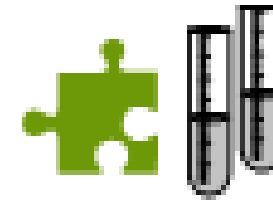
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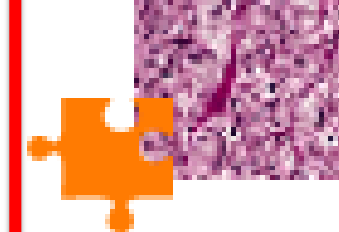
Proteins



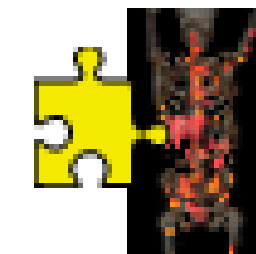
Laboratory Medicine



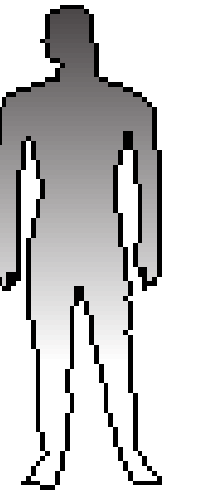
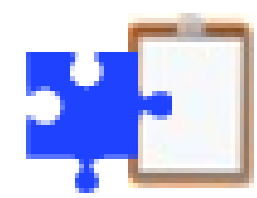
Pathology



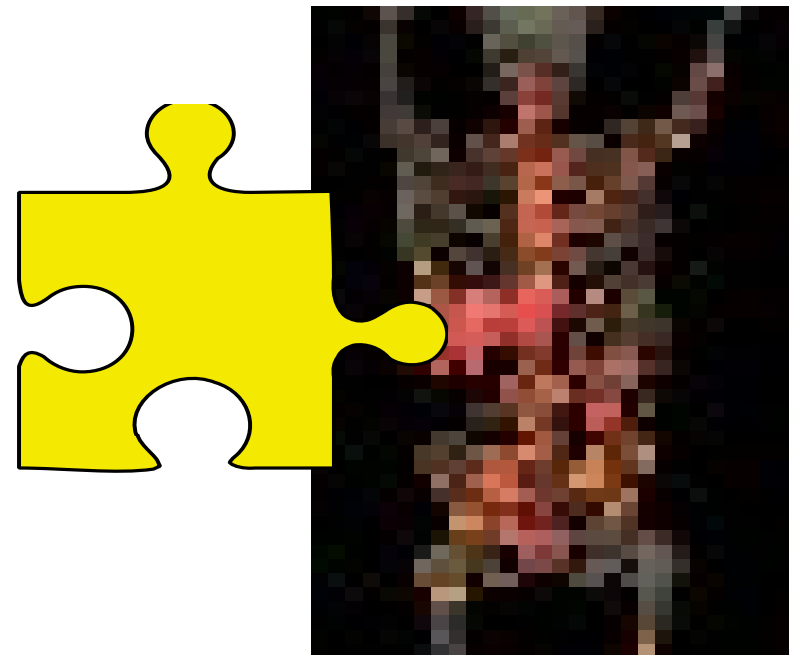
Radiology



Clinical Data



Radiology



- **Structured Reporting & Diagnostic Uncertainty**
- **AI for tumor segmentation, feature extraction & classification**
- **Automated Anatomic and Metabolic Total Tumor Burden Measurements**

Integrated Diagnostics – Challenges for Radiology

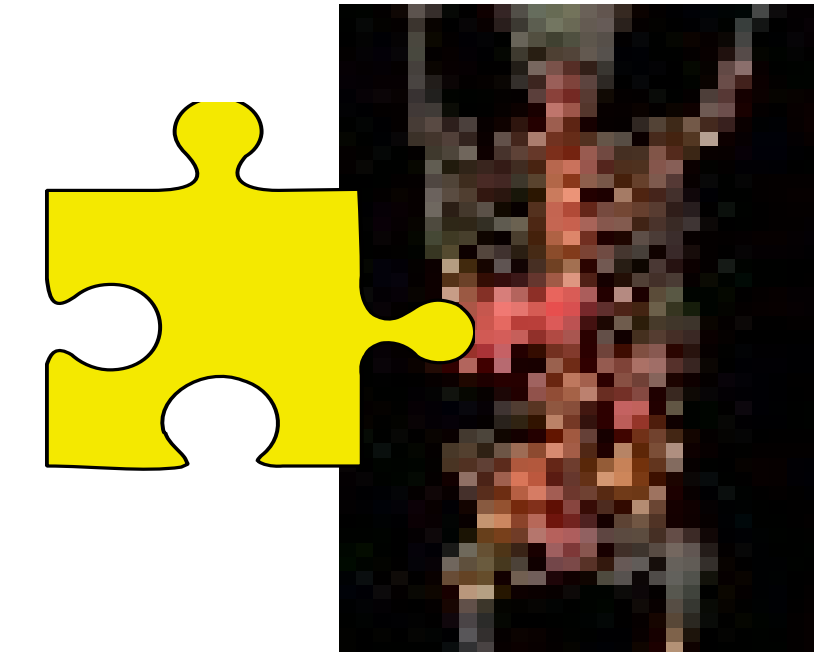
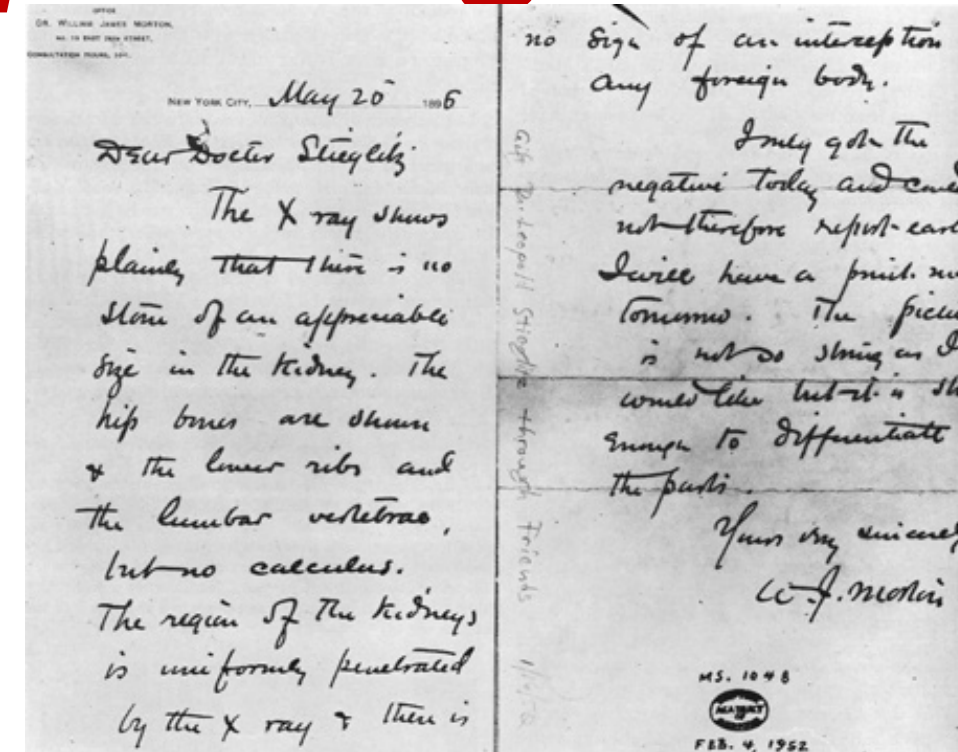
Structured & Synoptic Reporting

Radiology

Free text reporting:

Dear Dr Stieglitz: The X ray shows plainly that there is no stone of an appreciable size in the kidney. The hip bones are shown & the lower ribs and lumbar vertebrae, but no calculus. The region of the kidneys is uniformly penetrated by the X ray & there is no sign of an interception by any foreign body.

Dr William James Morton May 1896
Courtesy NY Academy of Medicine

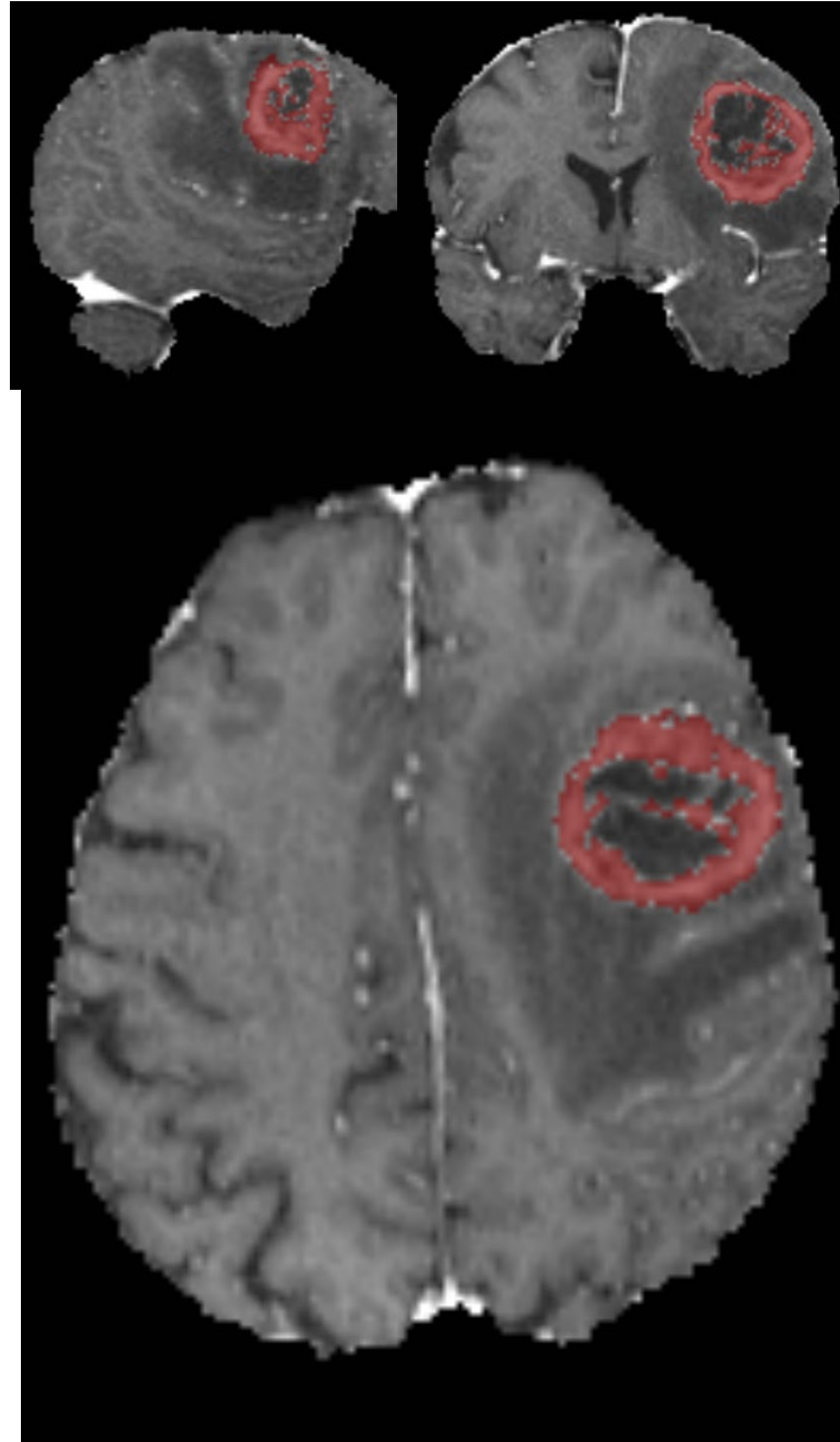
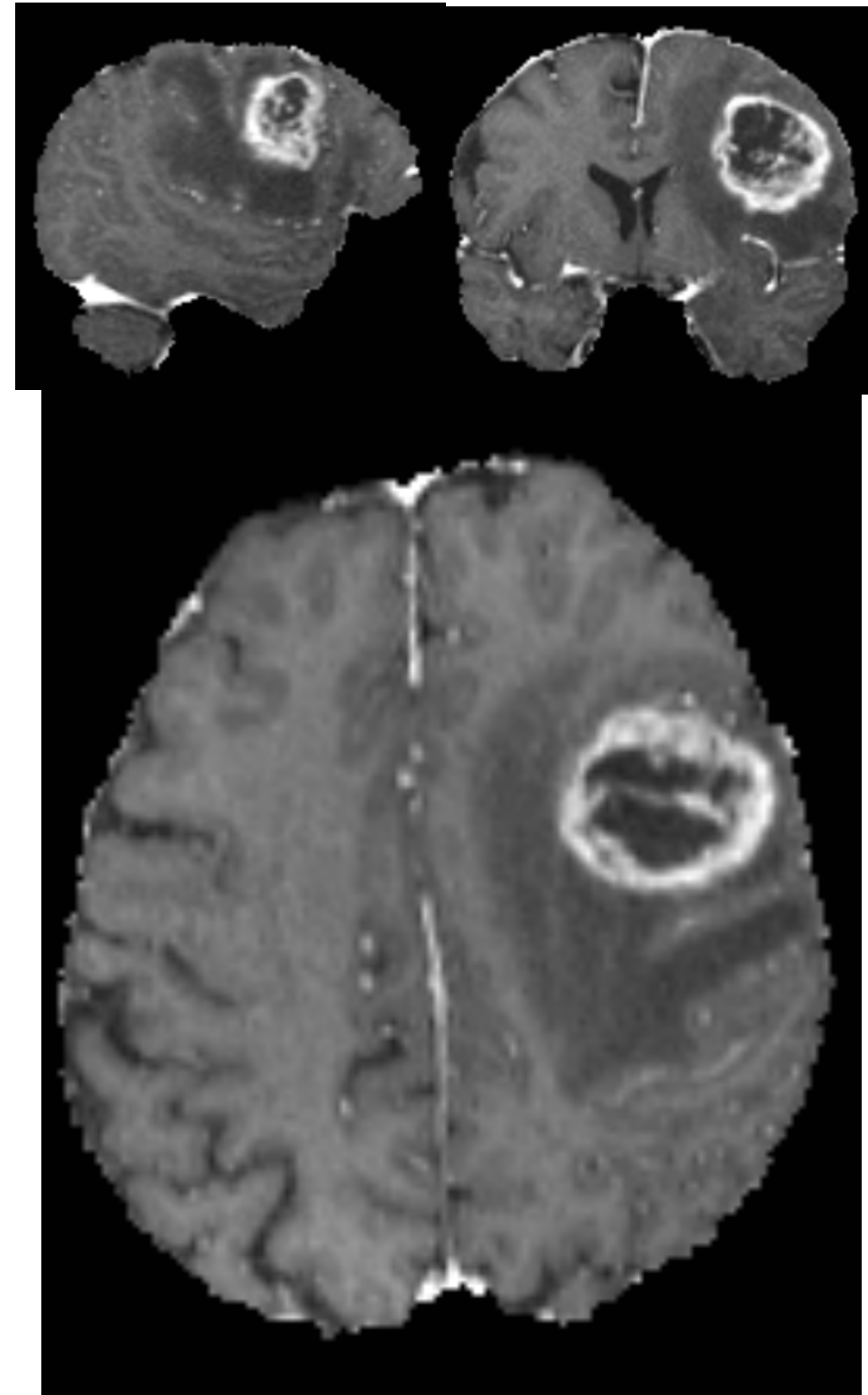


Addressing Diagnostic Uncertainty

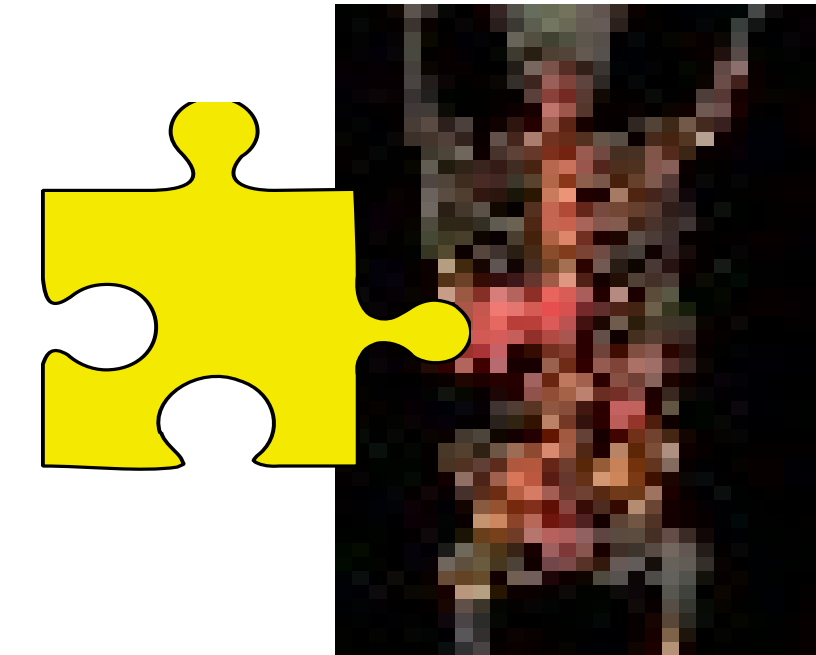
Consistent with	>90%
Suspicious for/Probable/Probably	~75%
Possible/Possibly	~50%
Less likely	~25%
Unlikely	<10%

Integrated Diagnostics – *Challenges for Radiology*

AI - Tumor Segmentation



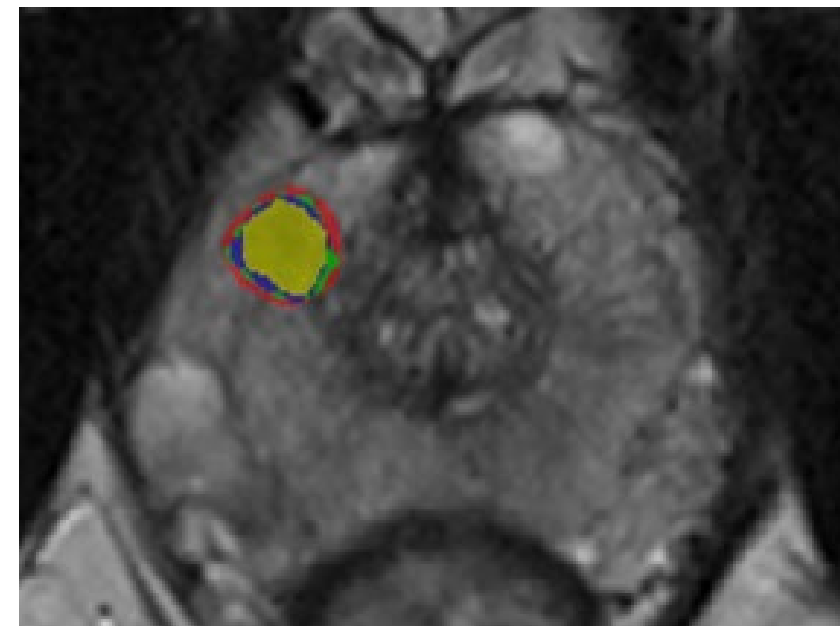
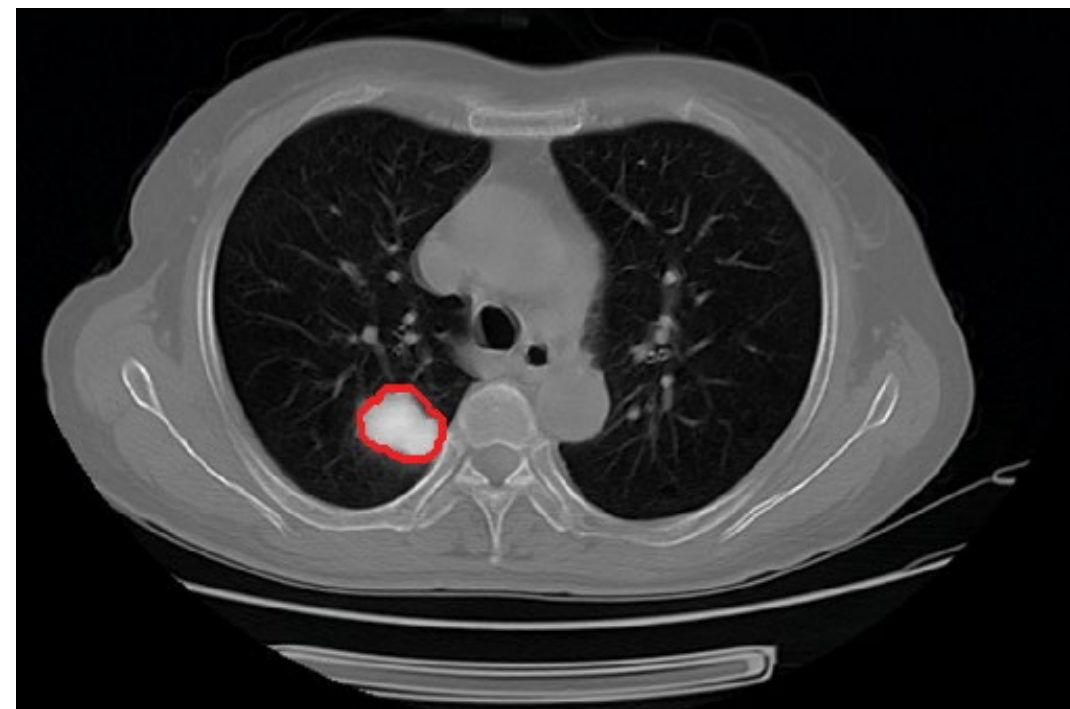
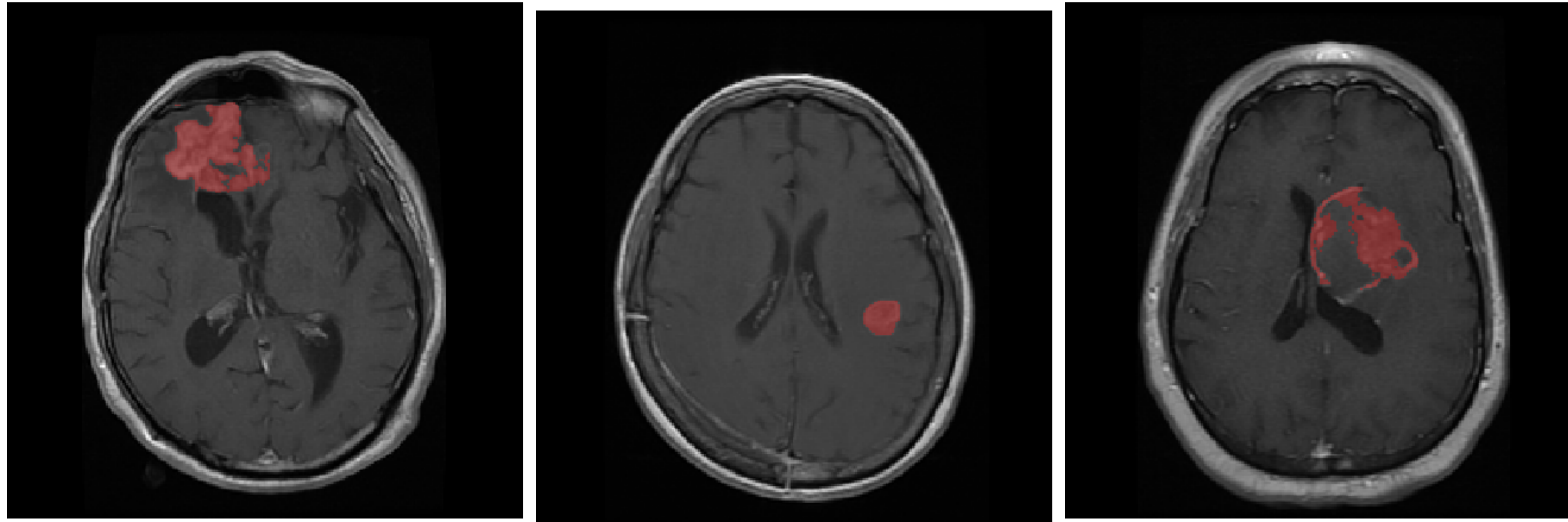
Radiology



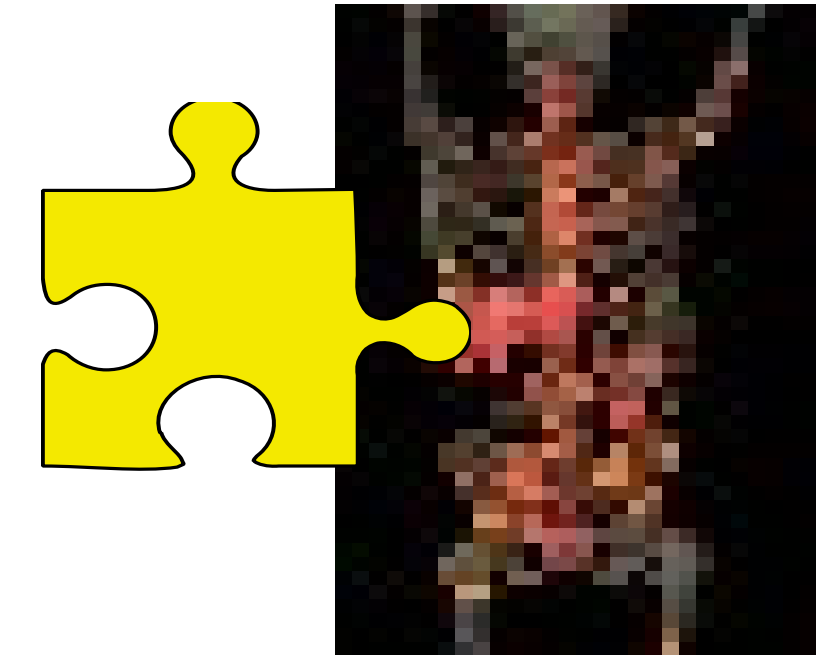
Manual tumor segmentation is a clinical and research bottleneck

Integrated Diagnostics – *Challenges for Radiology*

Tumor Segmentation



Radiology



Automated,
algorithmic
validated tumor
segmentation for
every site & every
modality!

Work in progress

Integrated Diagnostics – Challenges for both Radiology and Pathology

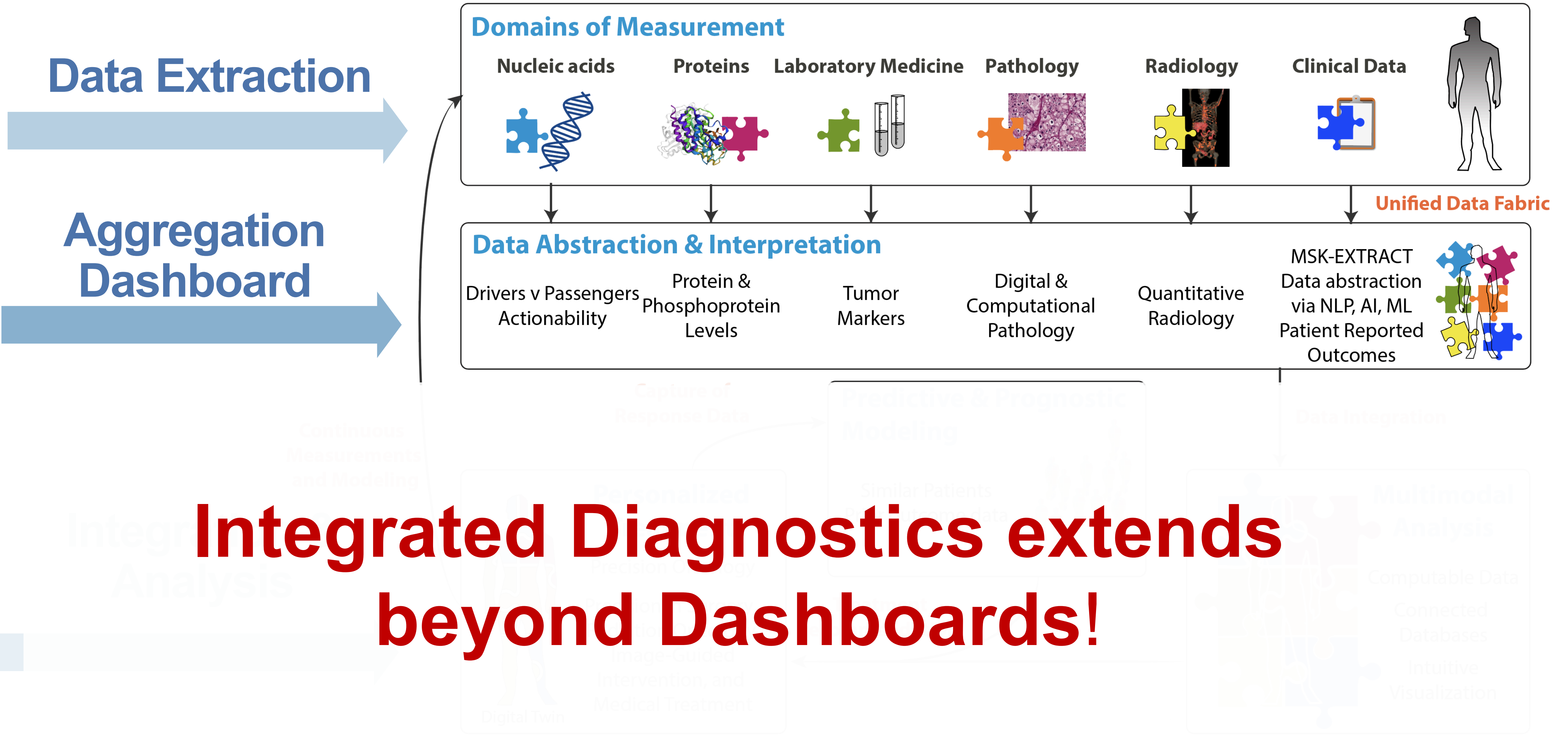
Data Governance/Culture!!!!

Data Sharing Requires Guardrails & Protections

- Prevent misuse and misinterpretation of data
- Protect interests of patients, faculty, MDT, departments and institutions
- Ensure proper recognition of contributions
- Mindful of both scientific and business interests of all parties

To correctly interpret results from patient-derived data, input from diagnostic and clinical experts is essential!

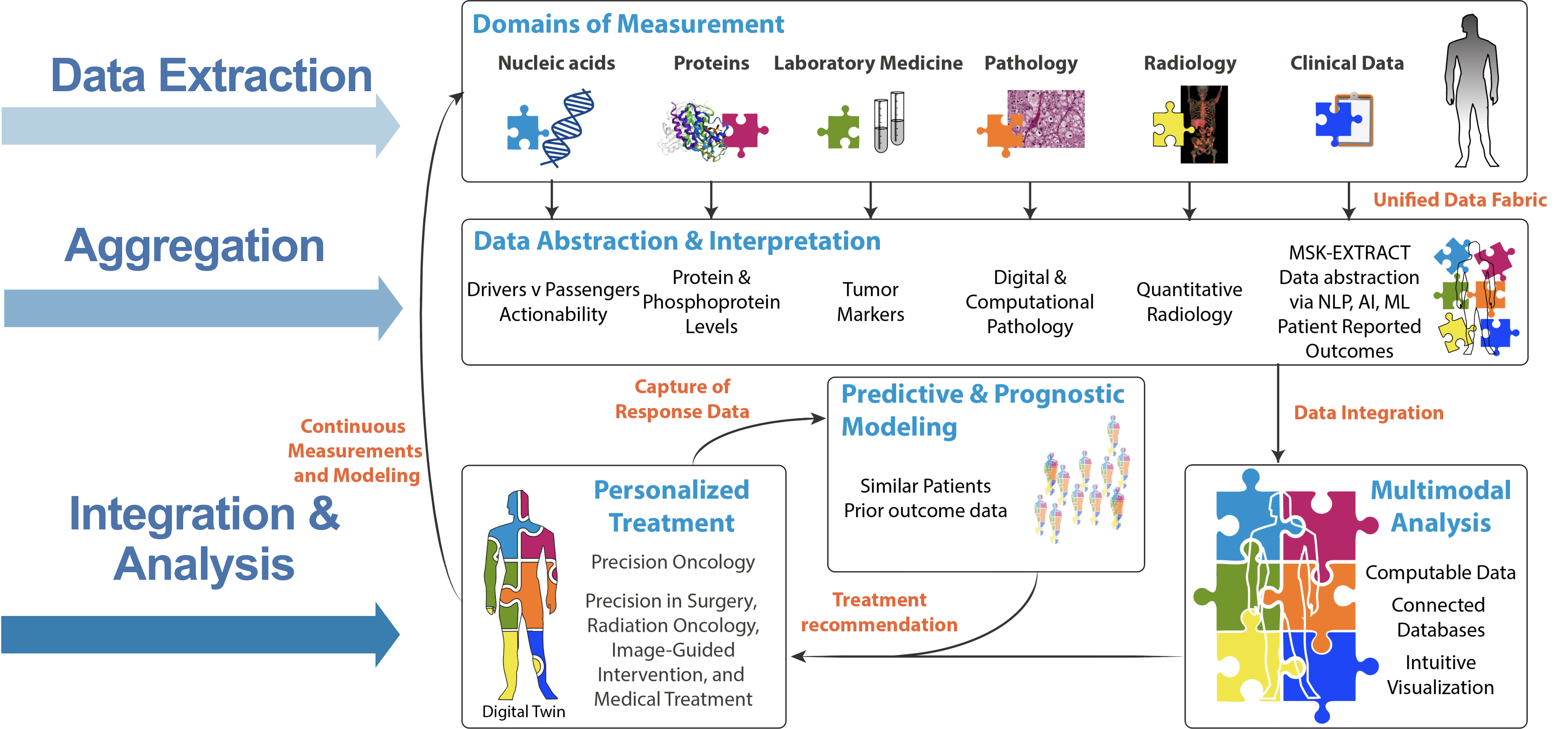
Integrated Diagnostics



“As much as new ideas are
fundamental to the advancement of
science, technologic innovations are
the engine of scientific progress”

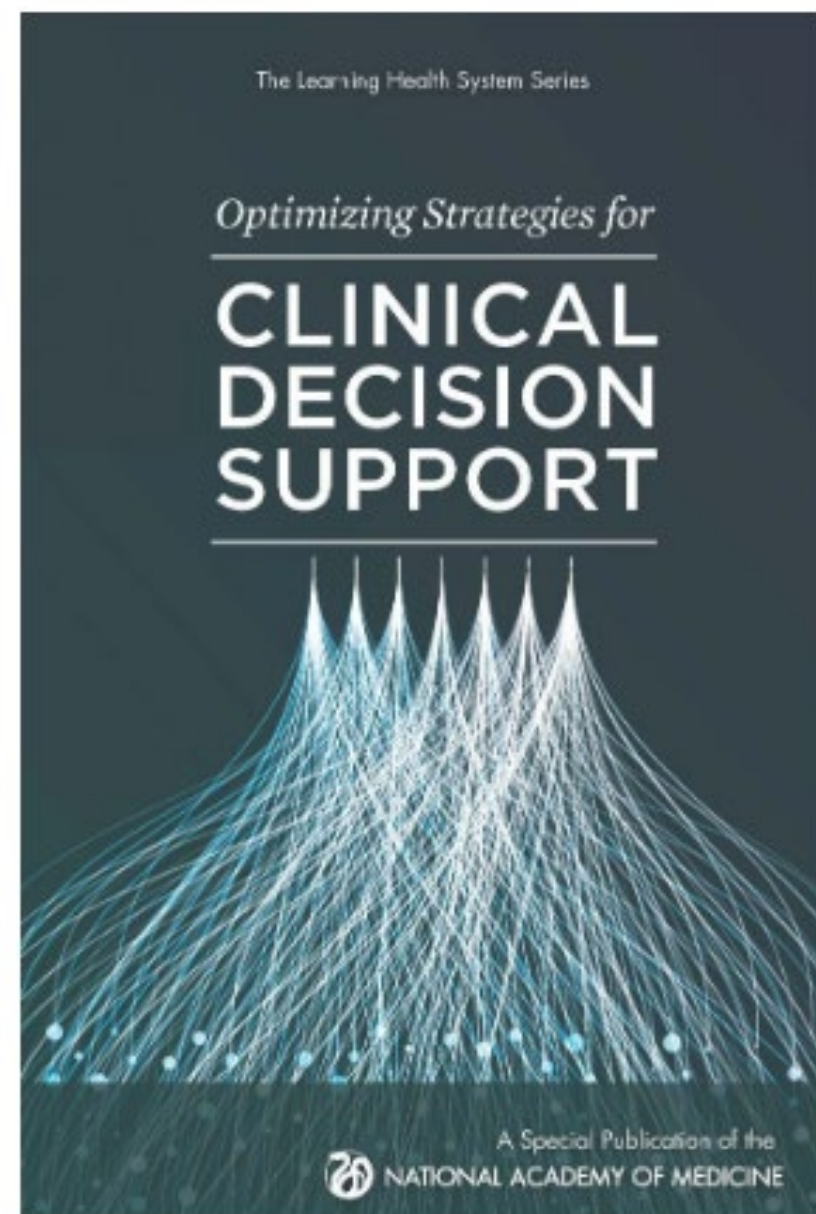
Shirley Tilghman
19th President, Princeton University

Integrated Diagnostics

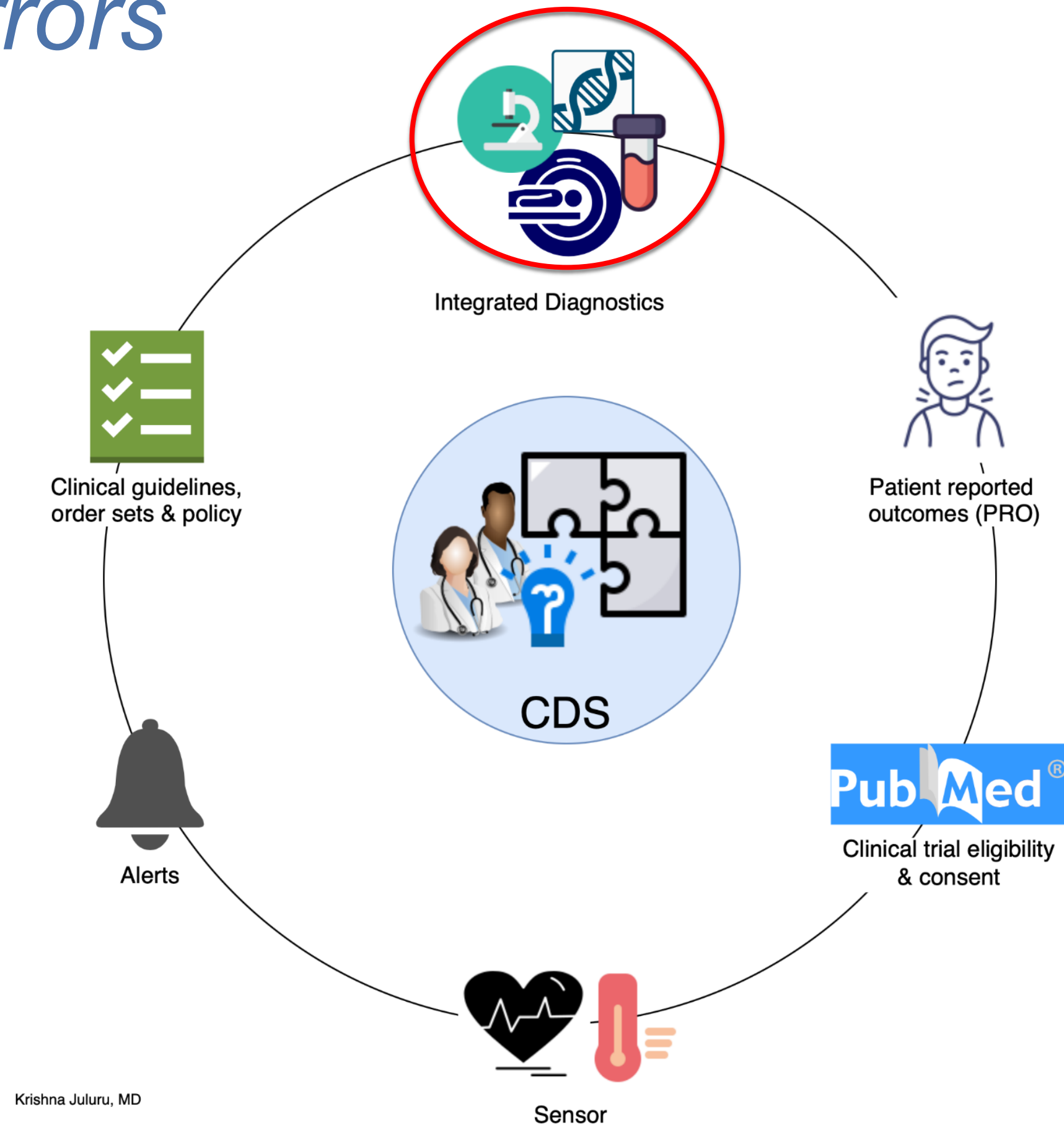


Clinical Decision Support & Integrated Diagnostics

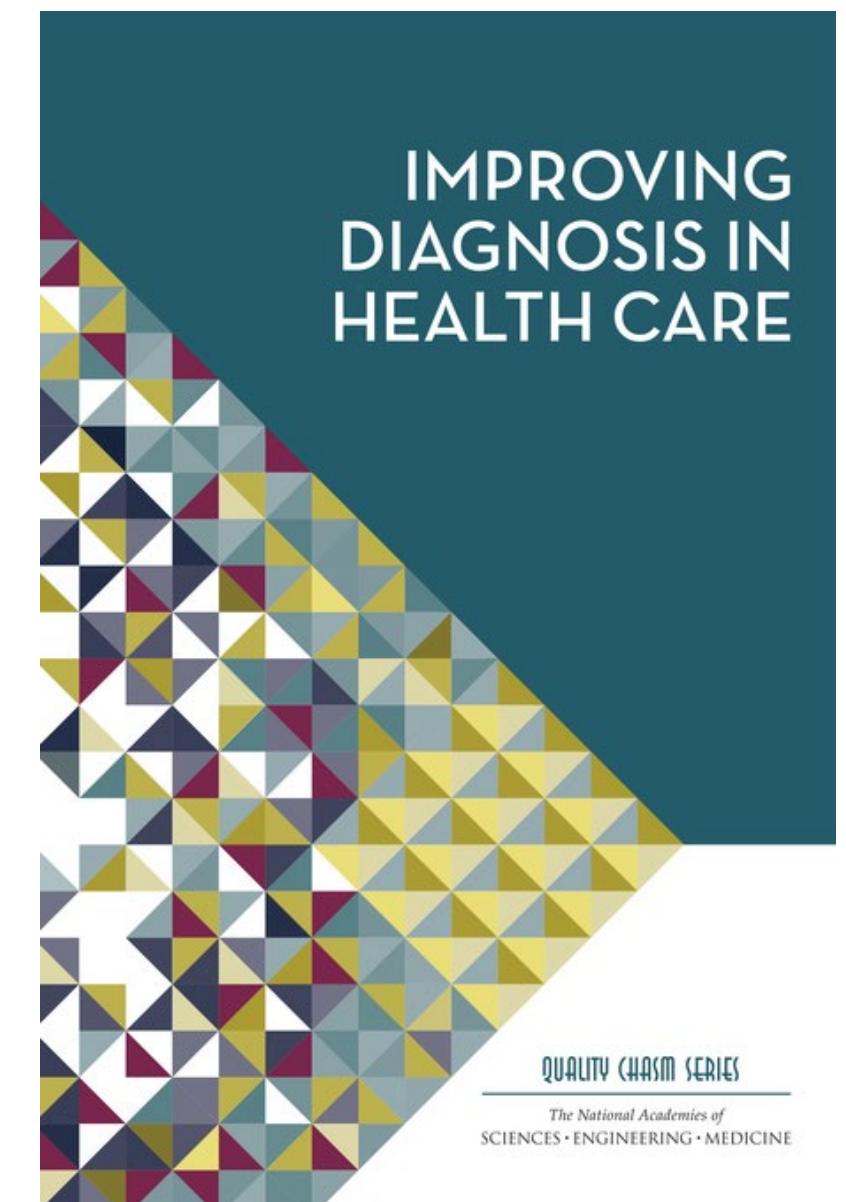
Reducing Medical Errors



2017



Krishna Juluru, MD



2015*

*“The definition of diagnostic error is *the failure to (a) establish an accurate and timely explanation of the patient's health problem(s) or (b) communicate that explanation to the patient.*”

Integrated Diagnostics – Myth or Reality?



Rene Magritte – “La Clairvoyance” (1936)

Vision, Courage, Agility, Collaboration & Perseverance

Thank You!!!