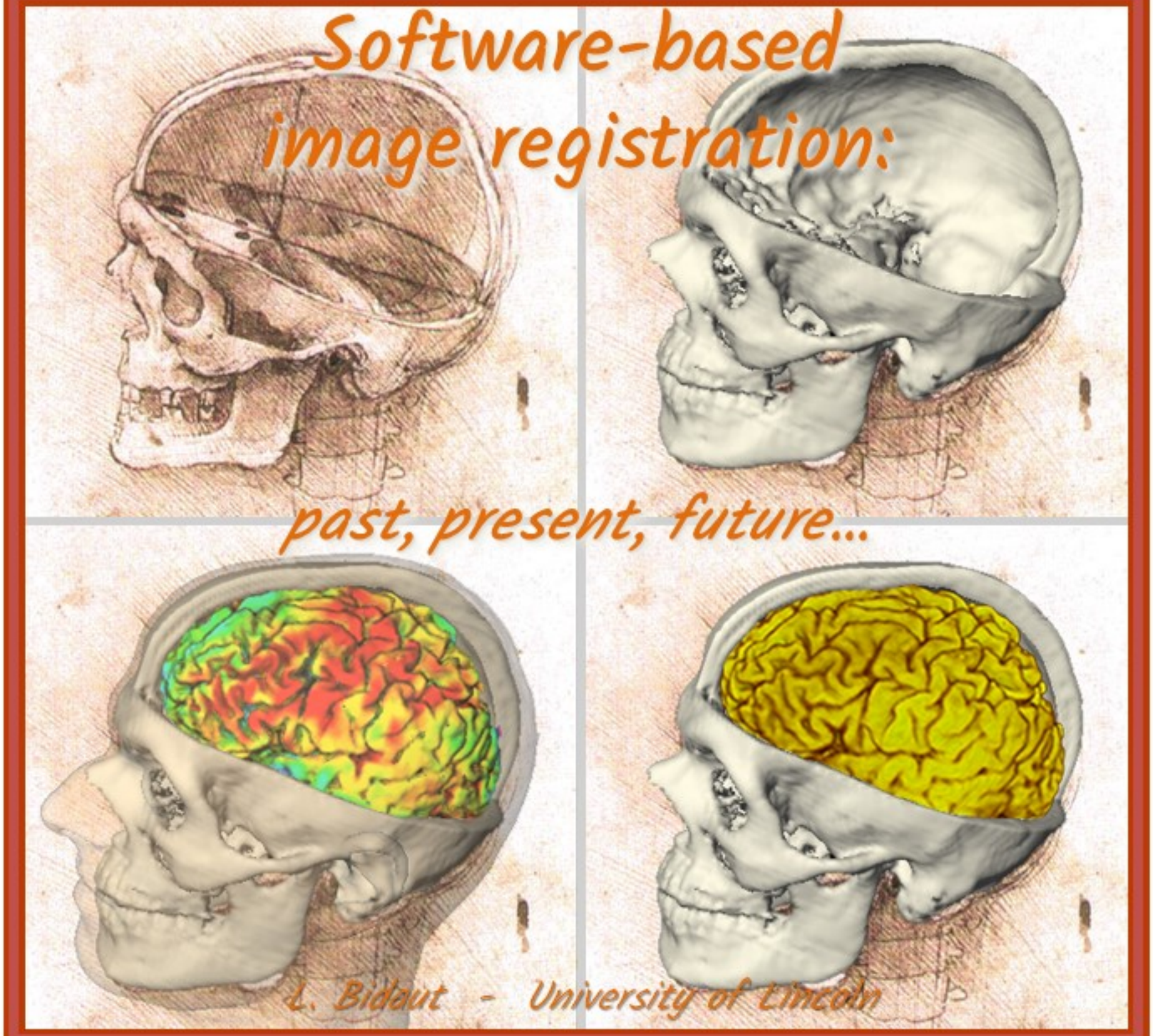
Software-based image registration:

past, present, future...



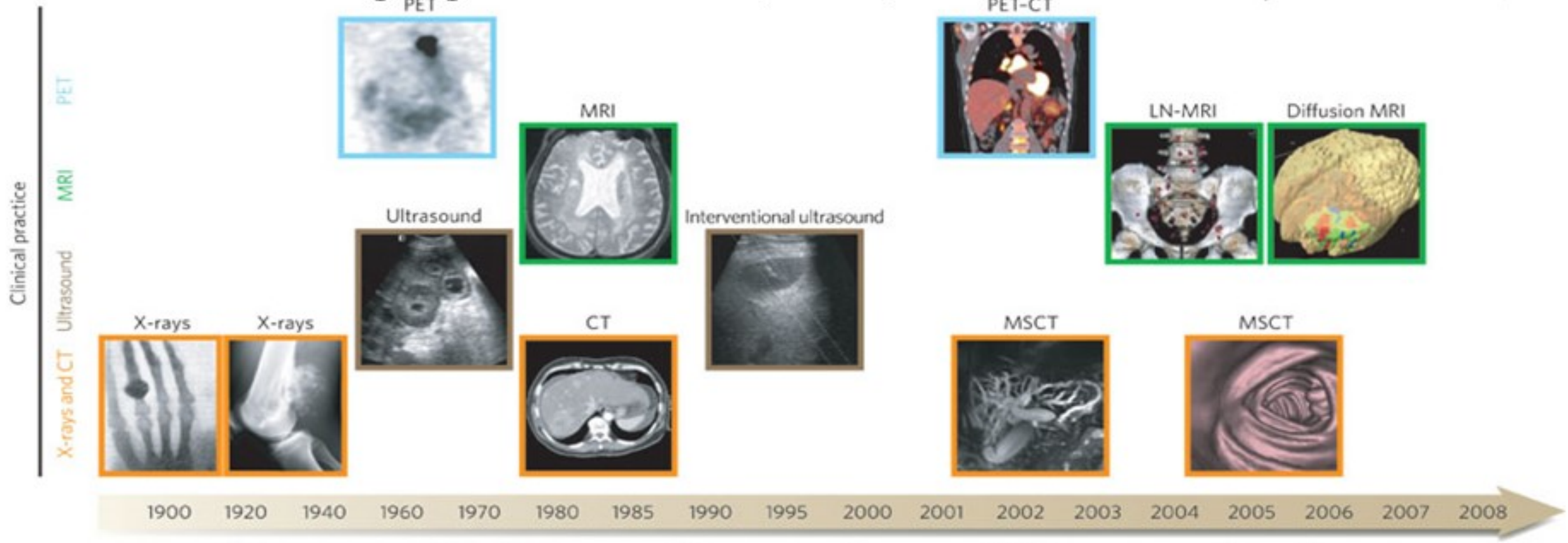
L. Bidaut - University of Lincoln

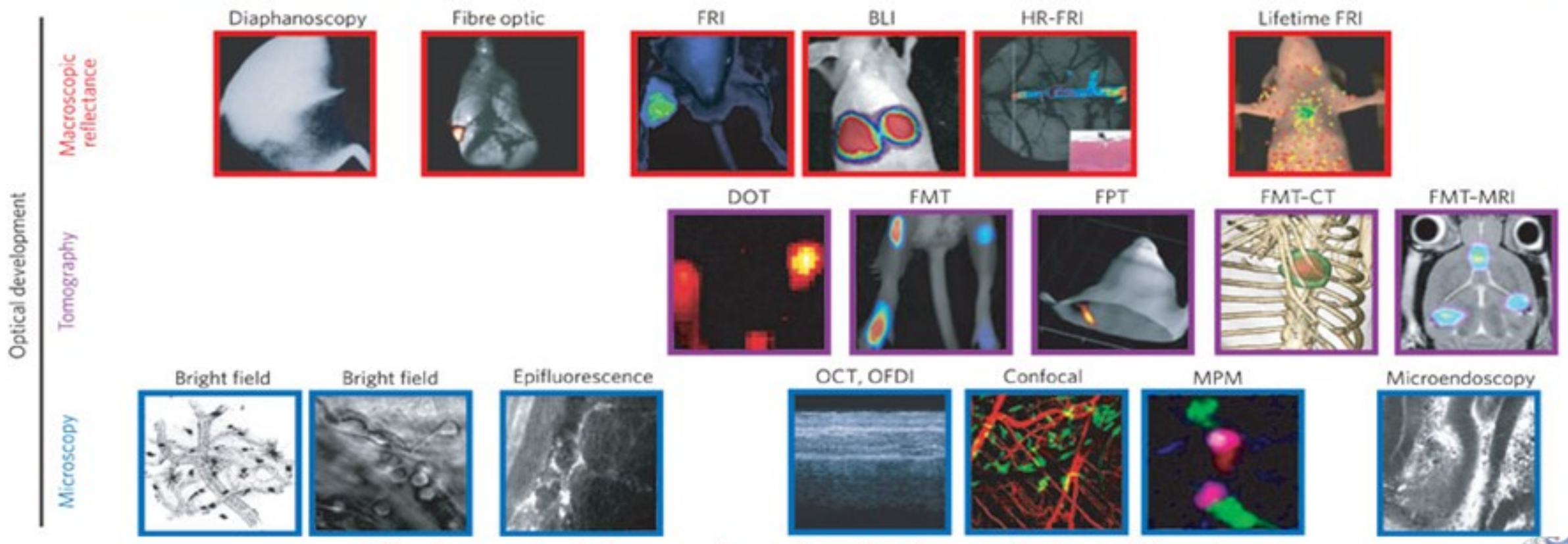
Once upon a time: Wilhelm Roentgen discovers X-rays in 1895 while experimenting on his wife Anna-Berthe …

and the rest is History…

Biomedical imaging: it isn't so simple anymore...

(from Nature 452, 2008)



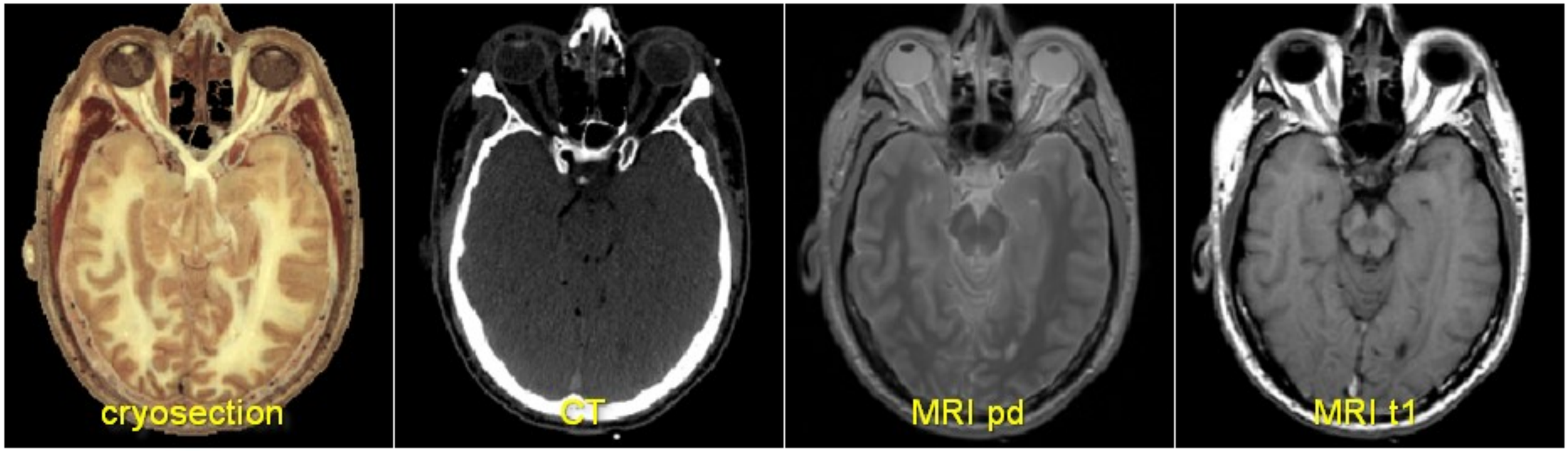


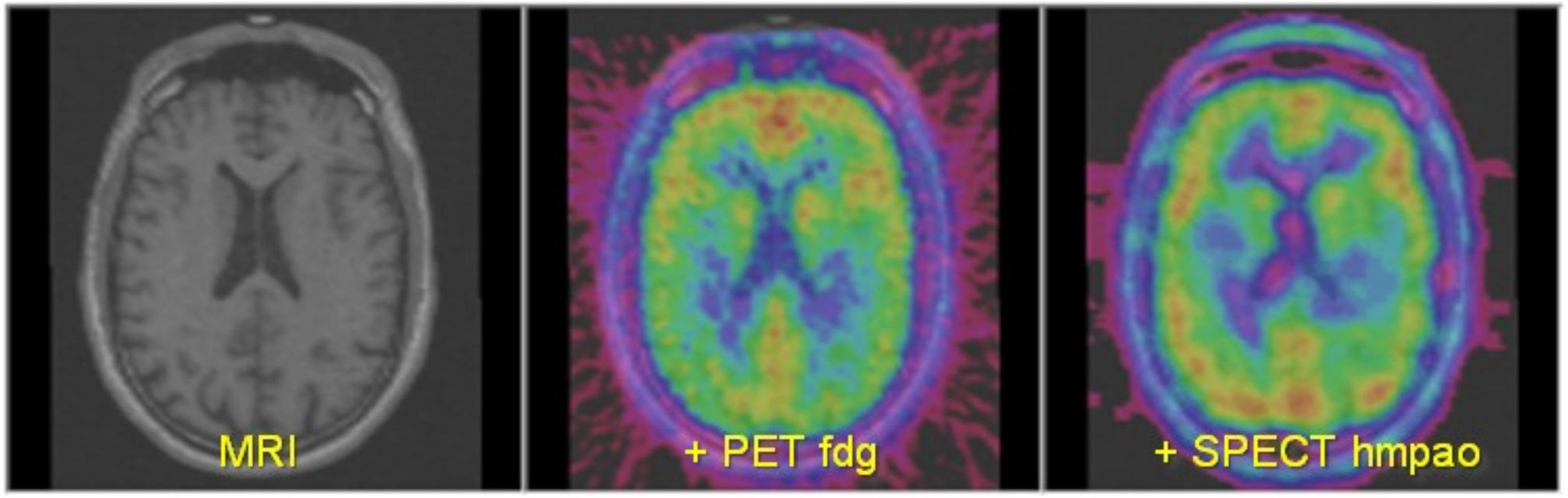
... differing principles and scales (both spatial and time)

=> show different things...

Multimodality/-sensor <= modalities

(collab. VH - NLM, HUG)



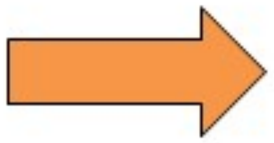


… differing principles and scales (both spatial and time)
=> show different things…

assumption: "the sum is greater than the parts"

Multi-modality imaging

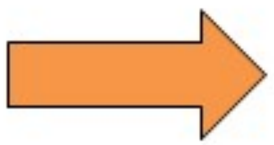
- Many different types of images
- They have different properties, such as resolution, contrast, property being imaged such as anatomy vs. physiology
- Combining such information can provide additional information (e.g., sum greater than the parts)



need for **fusion**

Various clinical imaging data sets

- Each modality (data set) has its own spatial reference system and, to make things slightly worse,
  time and physiology also matter...



need for **registration**

Multimodality Imaging: 2 complementary concepts

- **Registration**

<=> establishes the spatial relationship between two (or more) data sets

- **Fusion**

<=> combines data from different sources, times, procedures for extracting and exploiting complementary information

Registration/Fusion contexts:

- Intra-patient: same patient
- Inter-patient: different patients
- Intra-modality: same modality (e.g., protocol)
- Inter-modality: different modalities (or protocol)

=>> research or clinical registration can be
of interest for any combination(s) of the above

Registration techniques

Goal:

find the optimal geometric transformation so that
a location (point, pixel, voxel) in one data set
can be linked in a unique and reversible manner
to the corresponding one in the other data set

Means:

images
points, landmarks, features (surfaces, etc.)
contents

Multimodality registration:

chain of process; most relevant items between parentheses

acquisition, transfer -> reference data set and source one

conversion (e.g., Dicom to other)

segmentation (various techniques; manual to semi-auto.)

estimate/initialize current geometric transformation (# of DOF: e.g., rigid vs non-rigid)

transform source and compare to ref. (geometric transformation: DOFs, interpolation, etc.)

compare source and ref. (cost definition, e.g., analog to a distance)

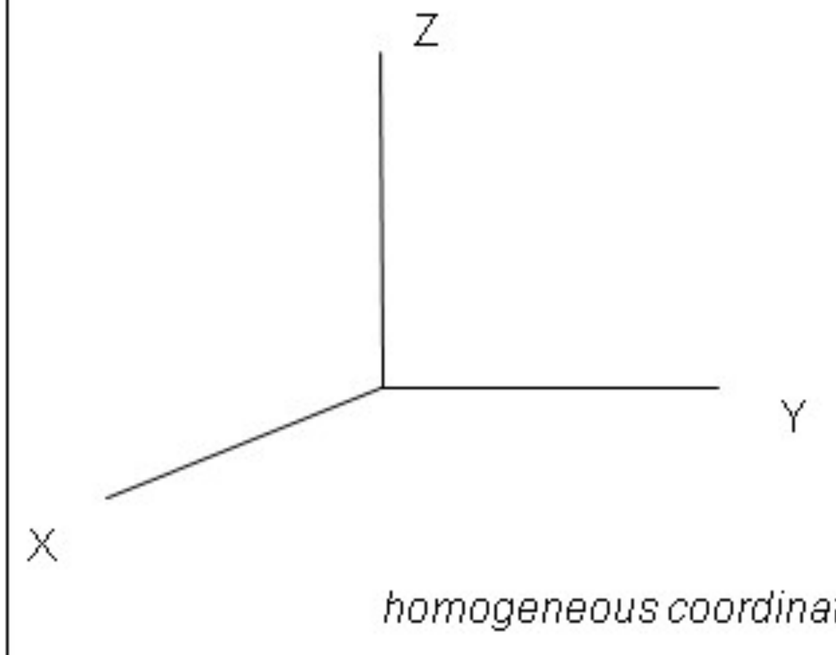
optimization (iterative techniques; multiscale, constraints, multicost, etc.
to avoid local extremas)

assess results (visual, stats, etc.)

visualize (various paradigms)

exploit …

Registration techniques: 3D transformation:



homogeneous coordinates

$$P_{tr}[Xtr,Ytr,Ztr] = [Sc][Ro][Tr]\ P_{ini}[X,Y,Z]$$

Rigid

TrX TrY TrZ

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ TrX & TrY & TrZ & 1 \end{bmatrix}$$

RoZ

$$\begin{bmatrix} cosZ & sinZ & 0 & 0 \\ -sinZ & cosZ & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

RoY

$$\begin{bmatrix} cosY & 0 & -sinY & 0 \\ 0 & 1 & 0 & 0 \\ sinY & 0 & cosY & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

RoX

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & cosX & sinX & 0 \\ 0 & -sinX & cosX & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

Affine

ScX ScY ScZ

$$\begin{bmatrix} ScX & 0 & 0 & 0 \\ 0 & ScY & 0 & 0 \\ 0 & 0 & ScZ & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

polynomial, etc. functions

Warps

warps are dangerous!

Registration techniques: costs based on:

- images: interactive techniques

  => minimize visual differences between paired images

- points, landmarks, features (lines, planes, surfaces): direct or iterative techniques

  => minimize distance analog between paired features

- contents: iterative techniques

  values: differences, ratios

  => minimize sum or variance of squared ds. or rs.

probability distribution: statistics

entropy: measure of randomness

$H(X) = -Ex[\log(Px)] = -sum[Px \log(Px)]$

joint entropy: measure of Y's randomness given X => minimize JE

$H(X,Y) = -Ex[Ey[\log(P(X,Y))]] = H(X)+H(Y)$ if X and Y are independent

mutual information: measure of the reduction of Hy given X => maximize MI

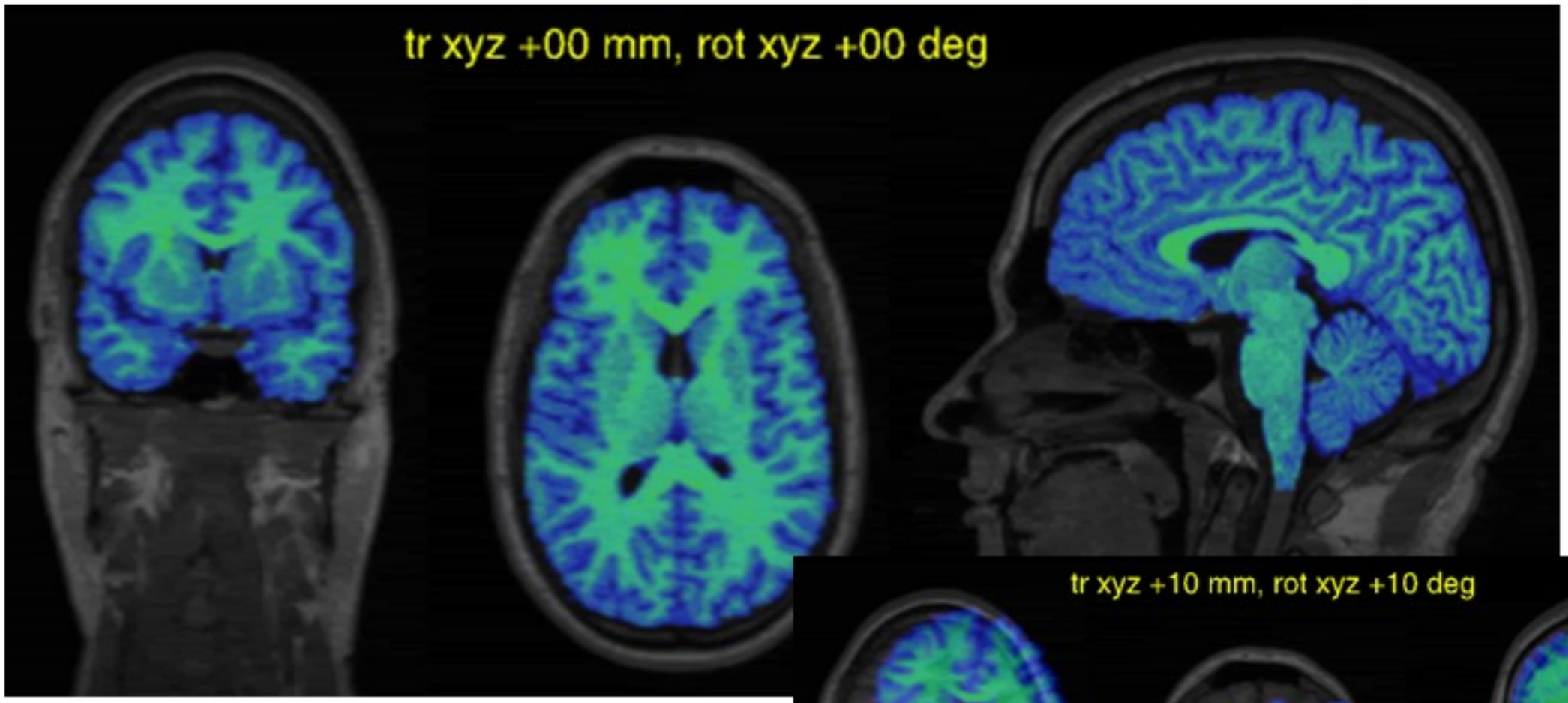
$MI(X,Y) = H(X) + H(Y) - H(X,Y)$ $NMI:(X,Y) = H(X)H(Y)/H(X,Y)$

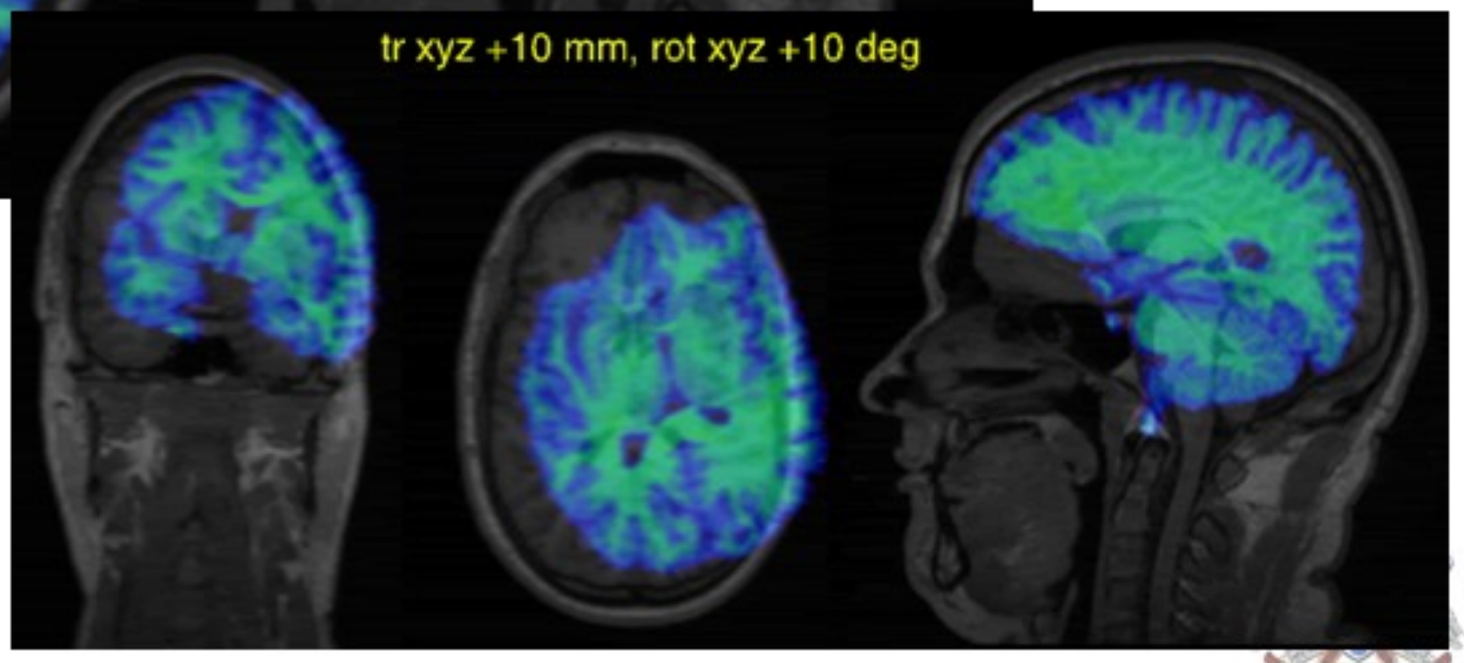
Registration techniques: cost based on:

- images: interactive techniques

  => minimize visual differences between paired images

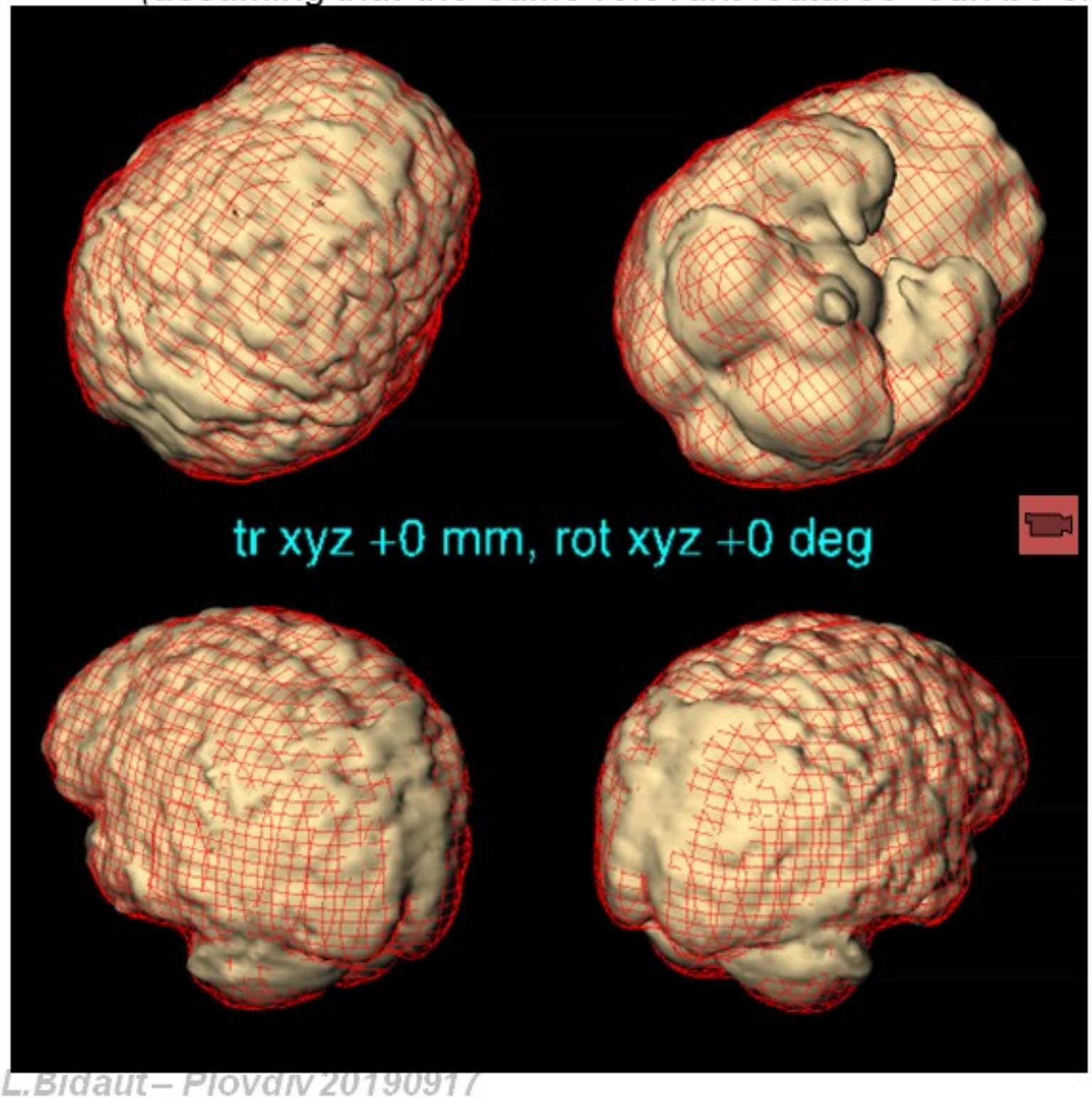
  (assuming that similar visual clues are visible on both IMref and IMali)



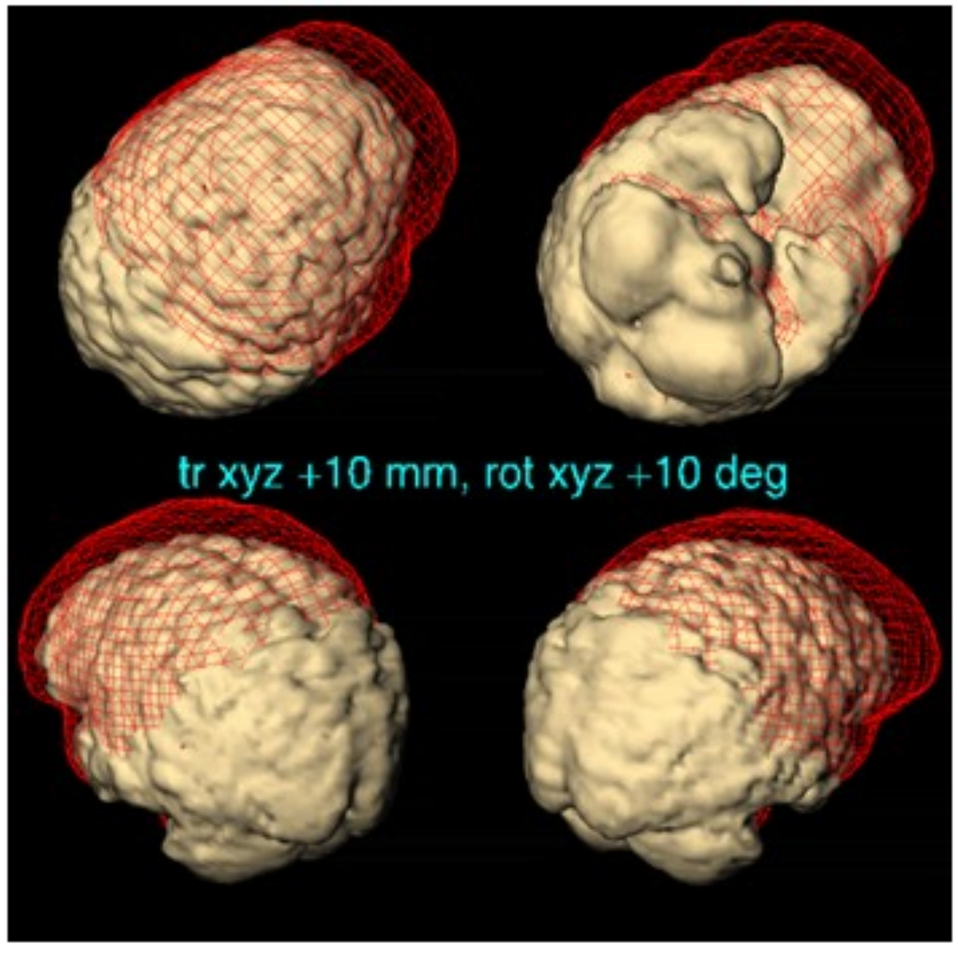


Registration techniques: cost based on:

- points, landmarks, features (lines, planes, surfaces): direct or iterative techniques
  => minimize distance (euclidean, chamfer, etc.) analog between paired features
  (assuming that the same relevant features can be extracted in both IMref and IMali)*



*intrinsic: belong to the data set
extrinsic: e.g., artificial markers, apparatus (stereotaxy,...), etc.



Registration techniques: cost based on:

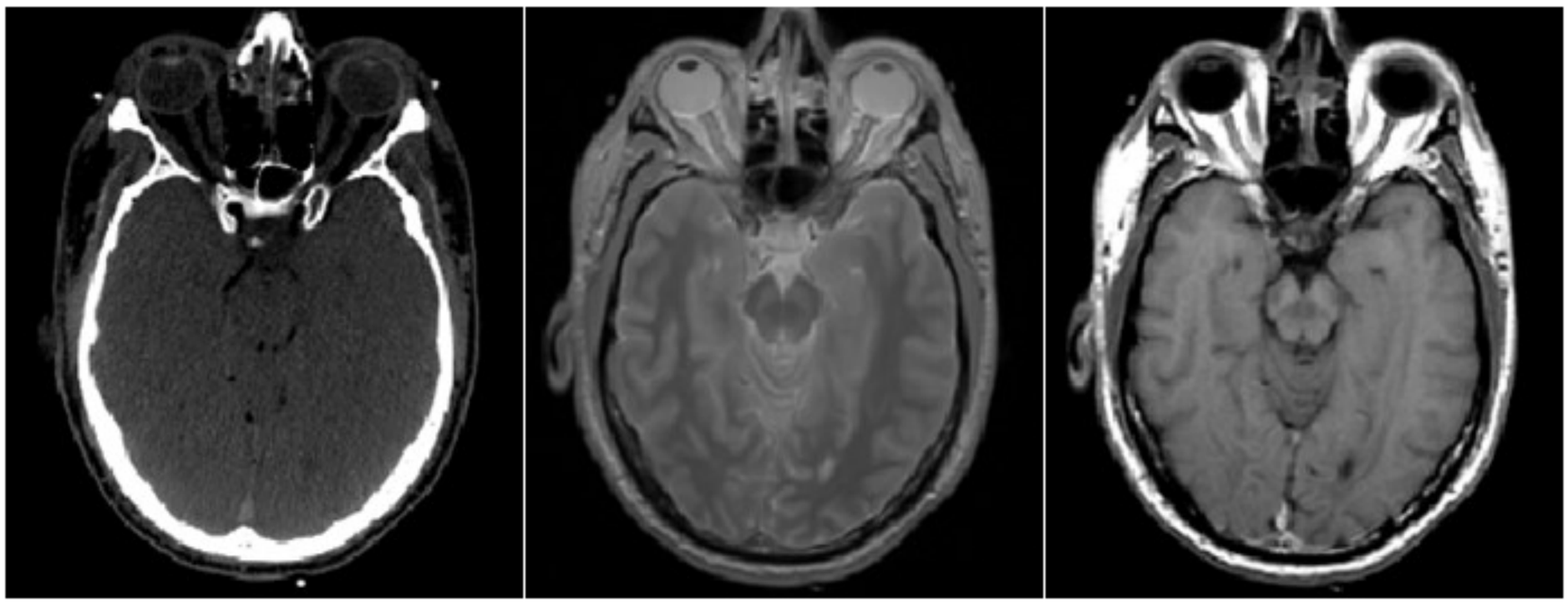
- contents: iterative techniques  *MR/CT iter*   *MR/PT iter*

  <u>direct values' comparison:</u> differences *(assuming that IMali ≈ IMref)*

  or ratios *(assuming that IMali ≈ a IMref + b)*

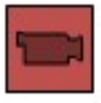
  in relevant tissue classes/structures

  => minimize sum or variance of squared ds. or rs.



CT MRI pd MRI t1

Registration techniques: cost based on:

- contents: iterative techniques  *MR/CT iter*   *MR/PT iter*

probability distribution: statistics *(assuming that IMali <≈> IMref)*

entropy: measure of randomness

$H(X) = -Ex[\log(Px)] = -sum[Px \log(Px)]$

joint entropy: measure of Y's randomness given X => minimize JE

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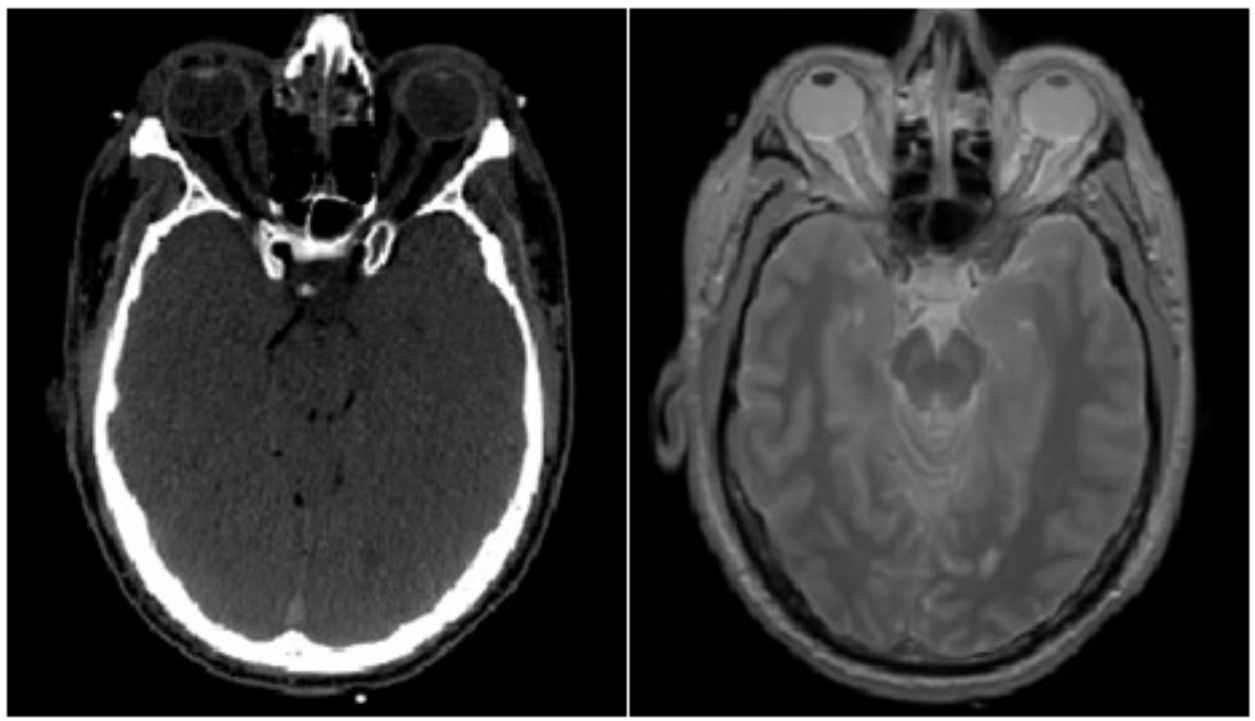
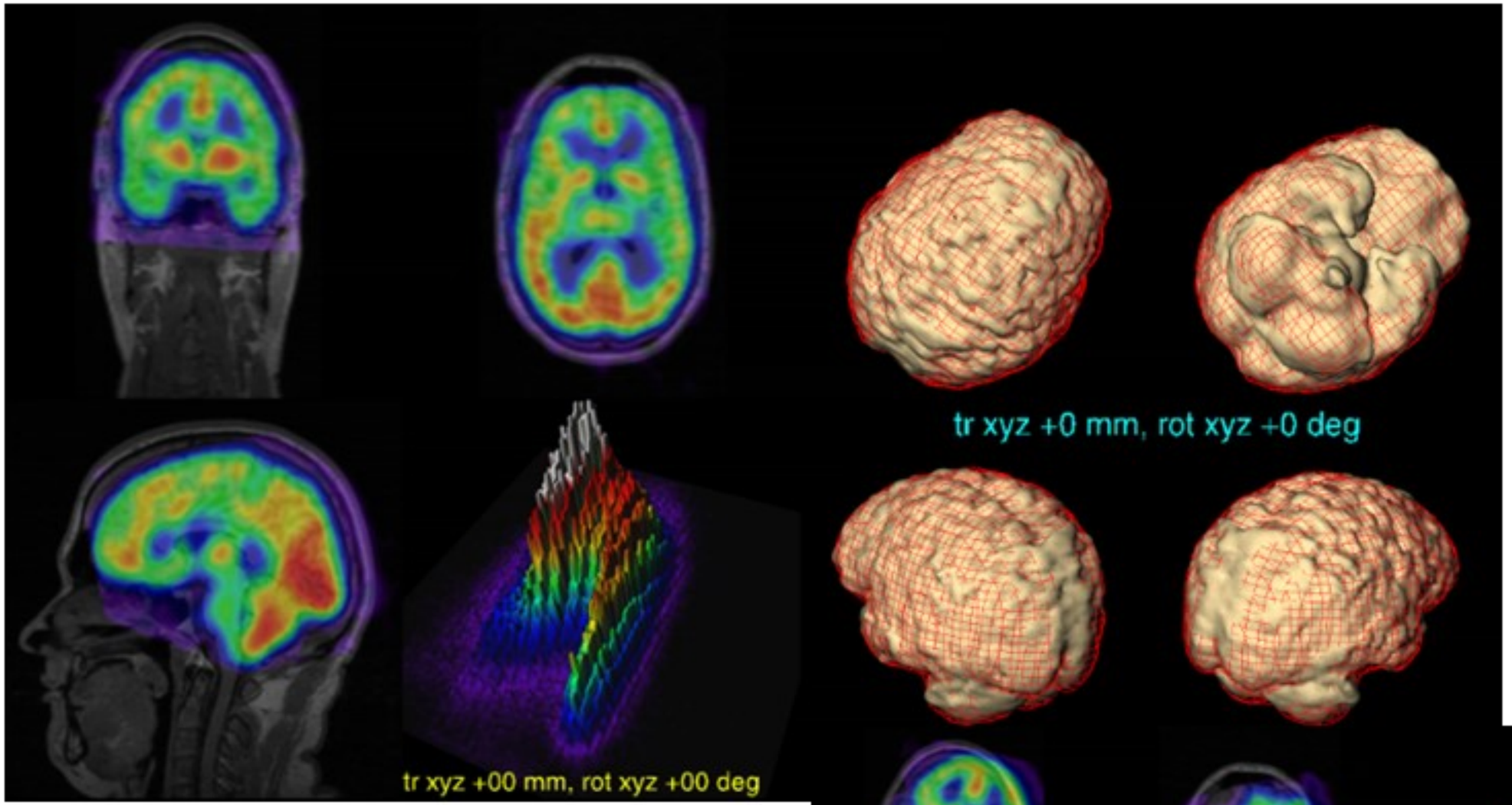
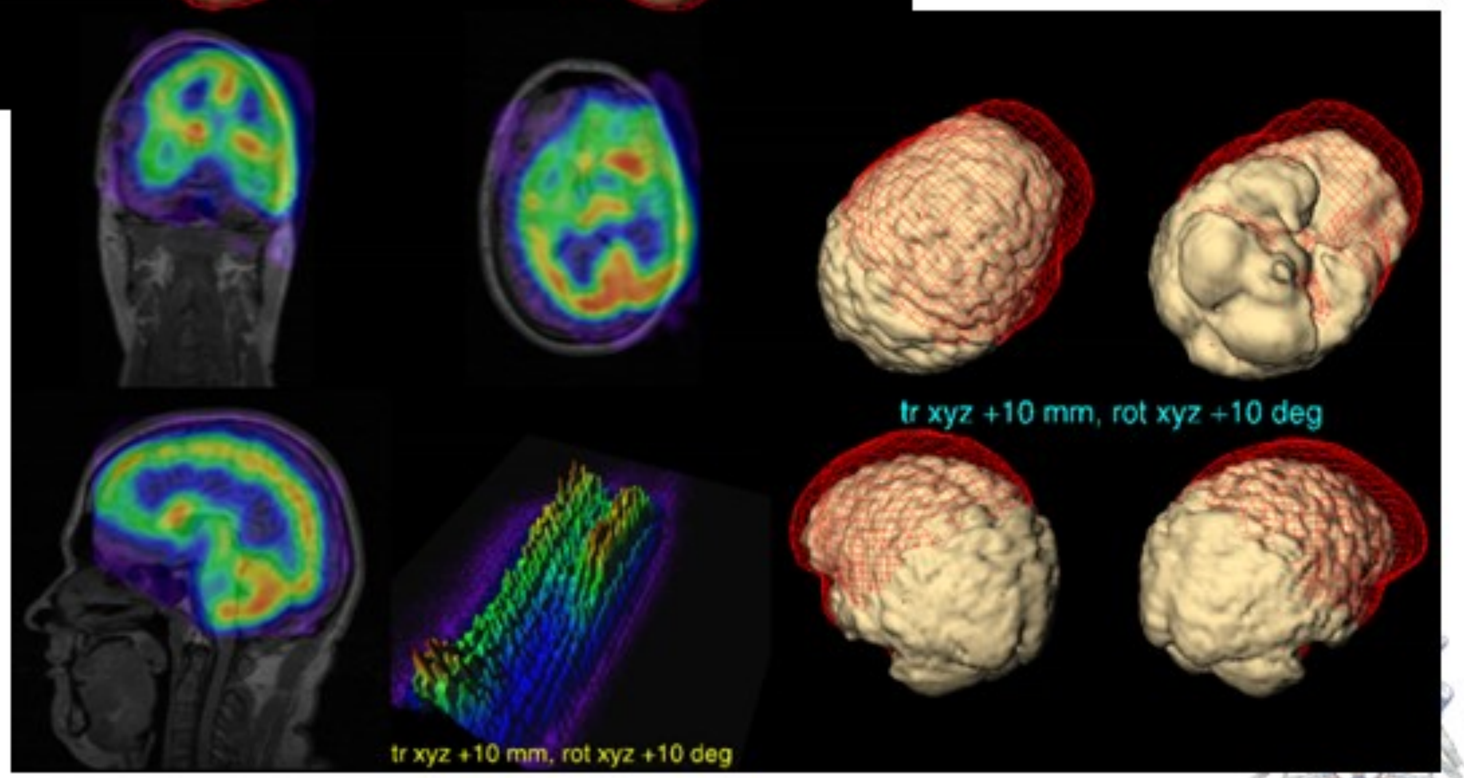


CT MRI pd

Registration techniques: summary





MR/CT iter *MR/PT iter*

Iterative techniques

To optimize the search for the optimal geometric registration transformation and ensure its convergence, e.g. through:

- multiresolution/multiscale approaches

- additional (adaptative) constraints to restrict the search (parameter) space

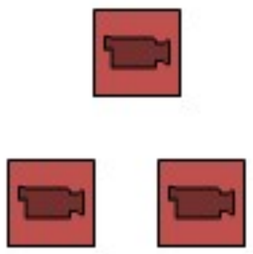
- "intelligent" use of various optimization strategies and/or cost functions

- initialization close enough to the likely solution, e.g. via controlled positioning and/or processing/registration sequence

- etc.

Iterative registration (CT to MR):

MR/CT iter



MR/PT iter

Non-rigid registration:

Two distinct approaches:

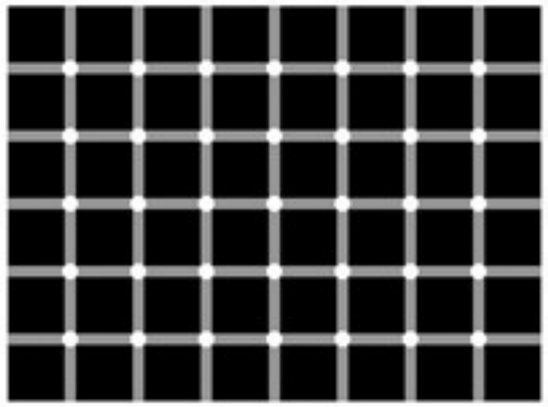
- linear combination of basis functions:
  polynomials,
  B-Splines,
  Thin Plate Splines (TPS),
  Radial Basis Functions (RBF)

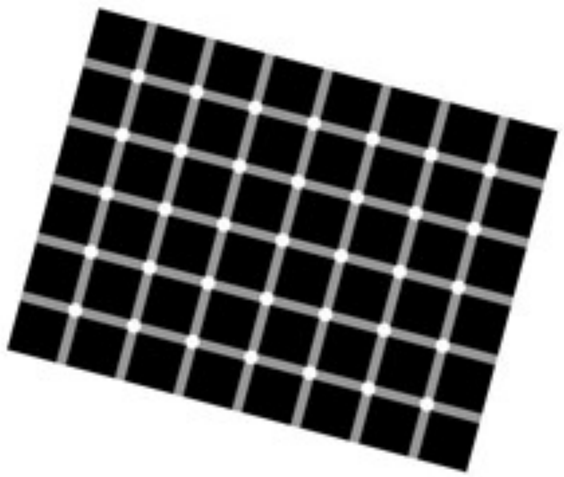
- modelling deformations as a physical process:
  e.g., viscous fluids (or other models) that deform images under the influence of external forces

=>> estimates a 3D vector field describing the displacement or deformation at each voxel in the image

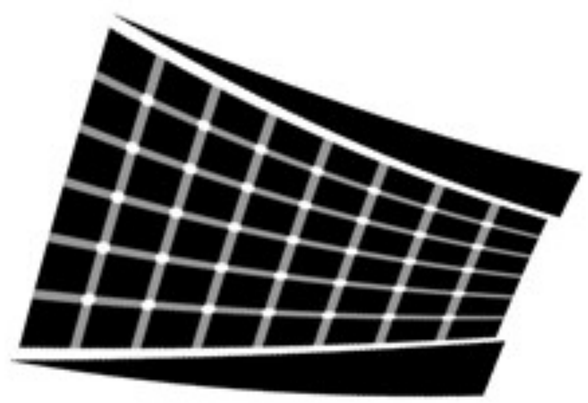
Non-rigid registration

Original





Rotate and Shift
Rigid

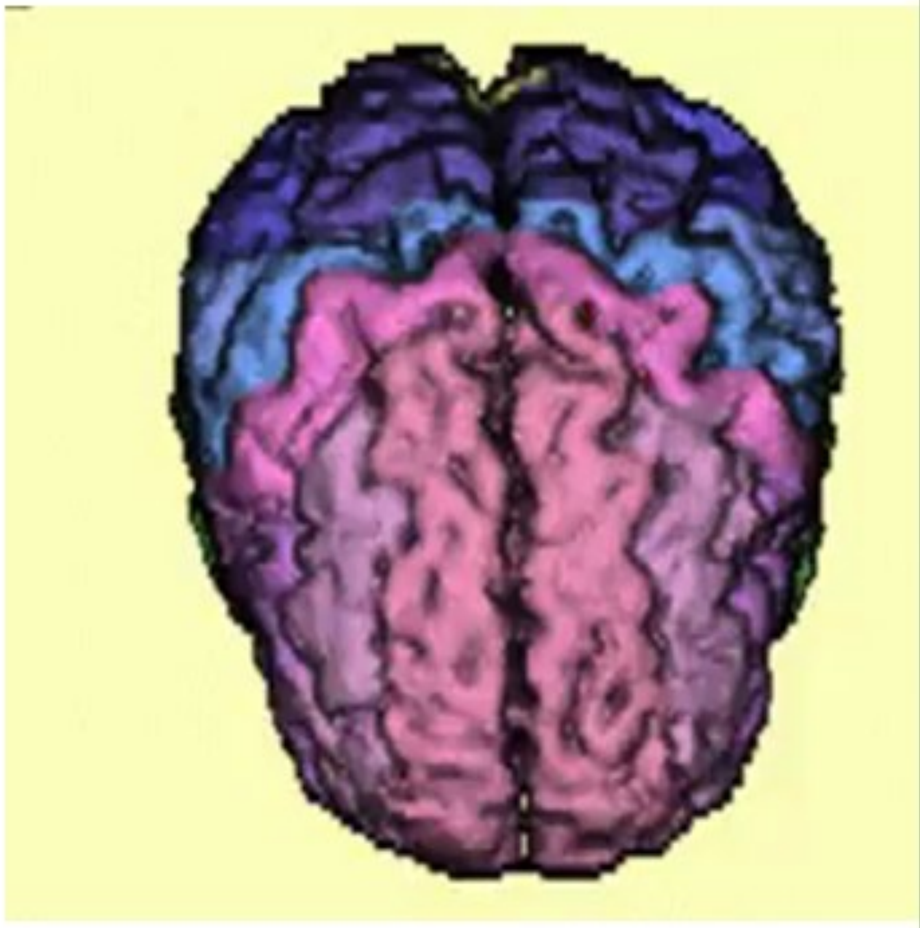


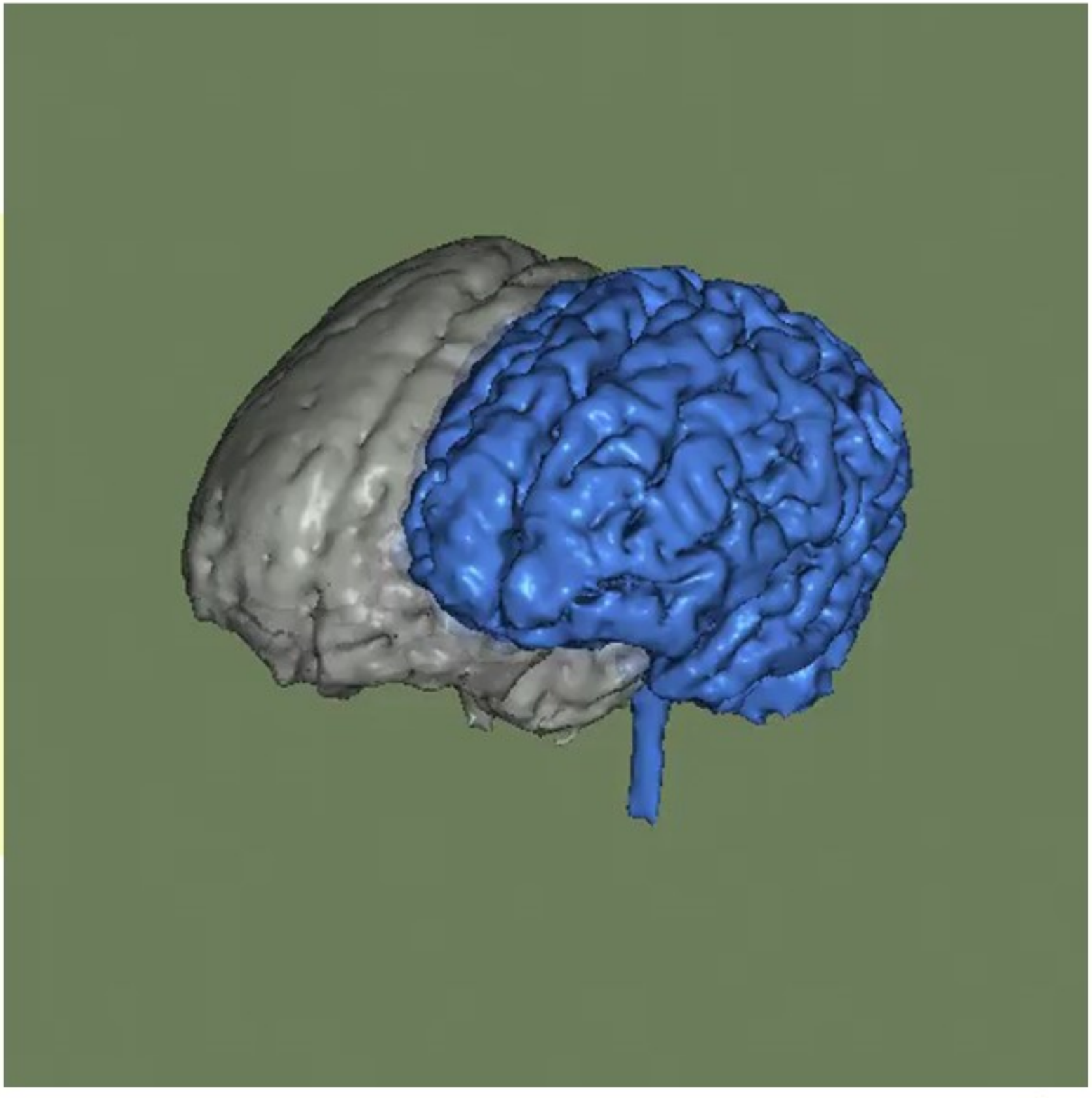
Affine

Warp
Non Rigid

Non-rigid iterative registration: brain(s)

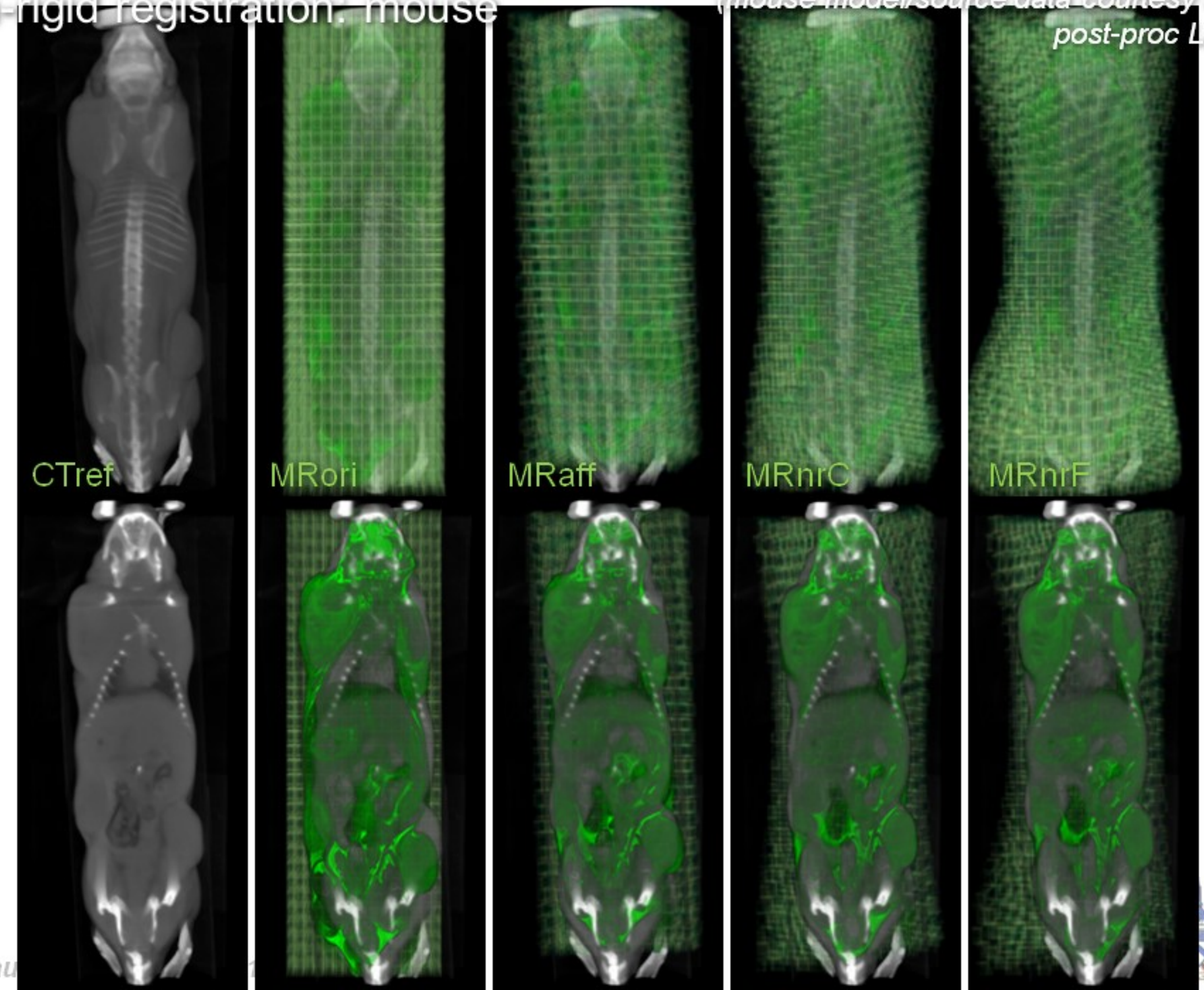
(courtesy SPL)





Non-rigid registration: mouse

(mouse model/source data courtesy SKI; post-proc LMB)



sli

3D

Non-rigid registration

Need for:

- an interpolation/deformation model
  - Optic flow
  - Thin plate spline, etc.
- spatial constraints
- an optimization technique

=>> Much more computer intensive than rigid registration

+ validation?

Registration validation: rationale <=> how-to

To provide a measure of likely error for a given case:

- landmarks: Root Mean Square error (≈distance)
- content: Least Square difference, correlation ratio

To provide an estimation of maximum/typical error for perfect and degraded cases:

- simulations:
  - numerical (total control),
  - realistic (closer to real life)
- phantoms, cadavers
- reference clinical data sets
- actual clinical data sets

BUT think of the various/individual components within the global registration system!!!

Multimodality registration:

chain of process; most relevant items between parentheses

acquisition, transfer -> reference data set and source one

conversion (e.g., Dicom to other)

segmentation (various techniques; manual to semi-auto.)

estimate/initialize current geometric transformation (# of DOF: e.g., rigid vs non-rigid)

transform source and compare to ref. (geometric transformation: DOFs, interpolation, etc.)

compare source and ref. (cost definition, e.g., analog to a distance)

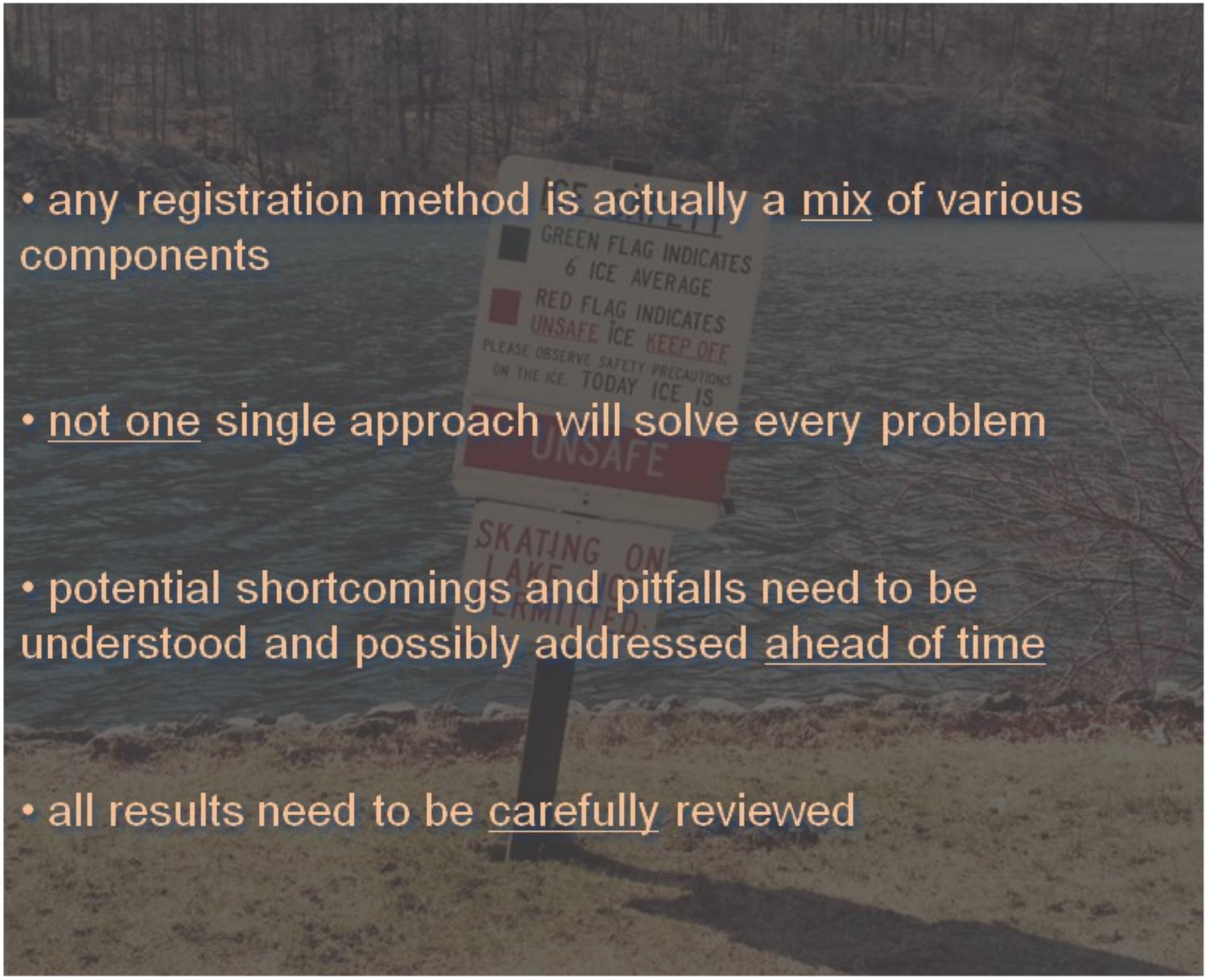
optimization (iterative techniques; multiscale, constraints, multicost, etc.
to avoid local extremas)

assess results (visual, stats, etc.)

visualize (various paradigms)

exploit ...

Multimodality alignment: you can never be too careful (or warned)



Multimodality Imaging: 2 complementary concepts

- Registration

<=> establishes the spatial relationship between two (or more) data sets

- **Fusion**

<=> combines data from different sources, times, procedures for extracting and exploiting complementary information

Visualization techniques:

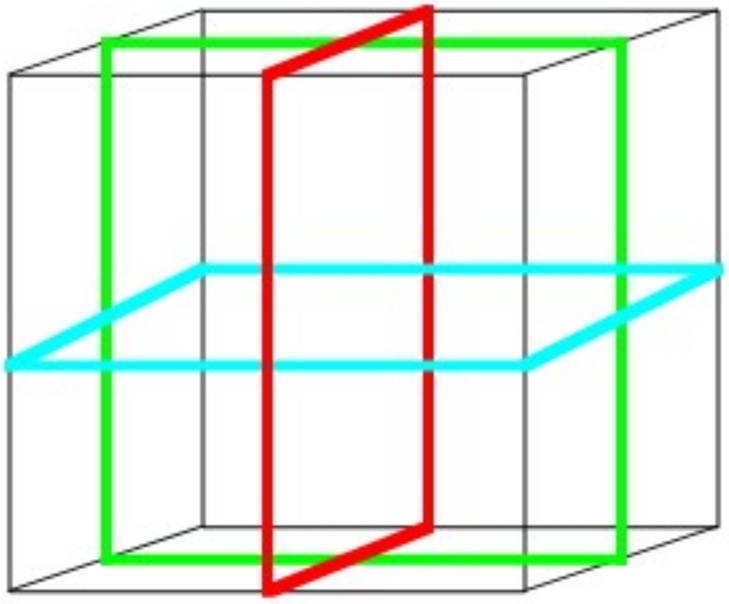
slices: Multi-Planar Reconstruction (MPR)
side by side images with coupled cursors
colorwash/fusion

3D surfaces:
segmented structures
textured by another modality
or other (parametric) data

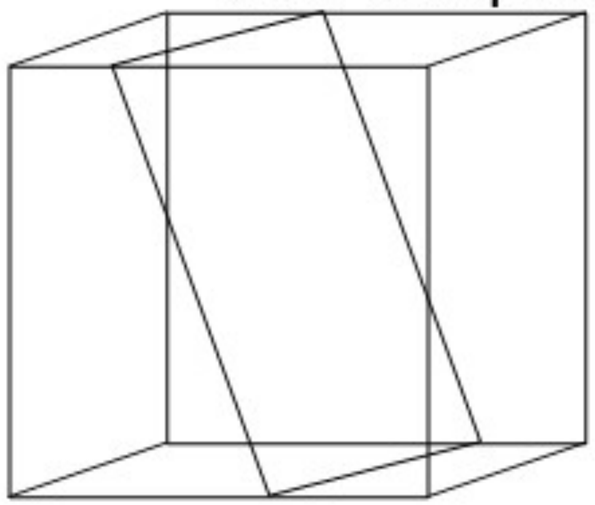
Volume Rendering:
Maximum Intensity Projection
ray-tracing/casting

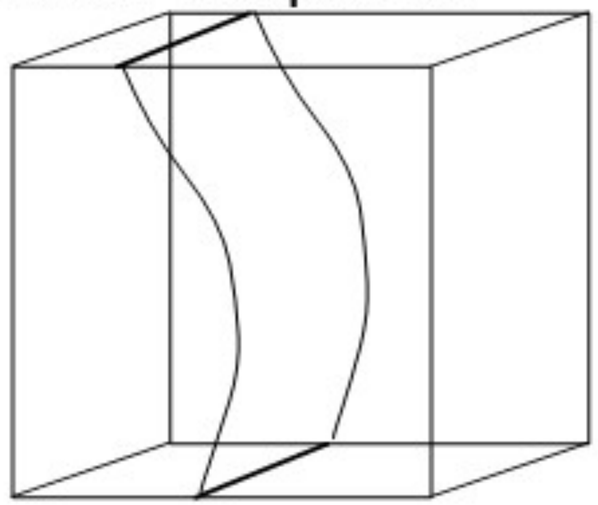
Multidimensional visualization techniques: slices and MPR

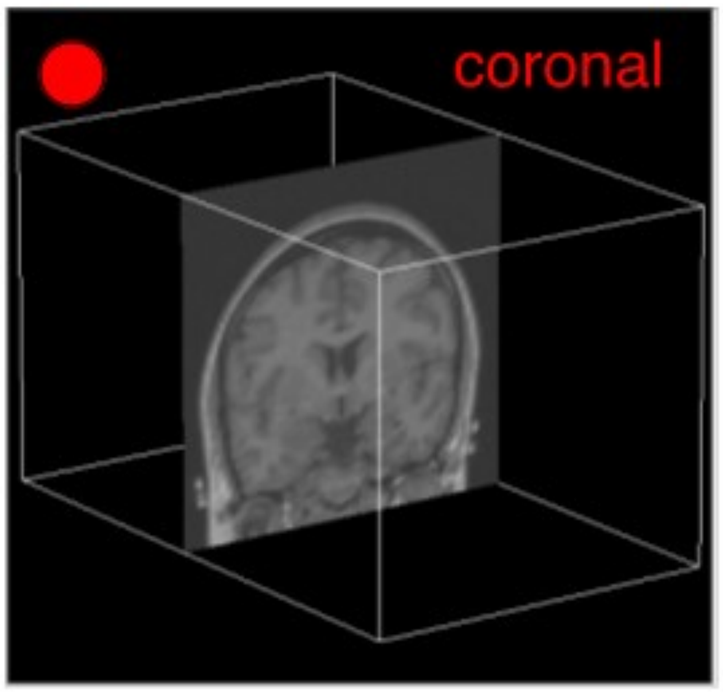
Multi-Planar Reconstruction (MPR)

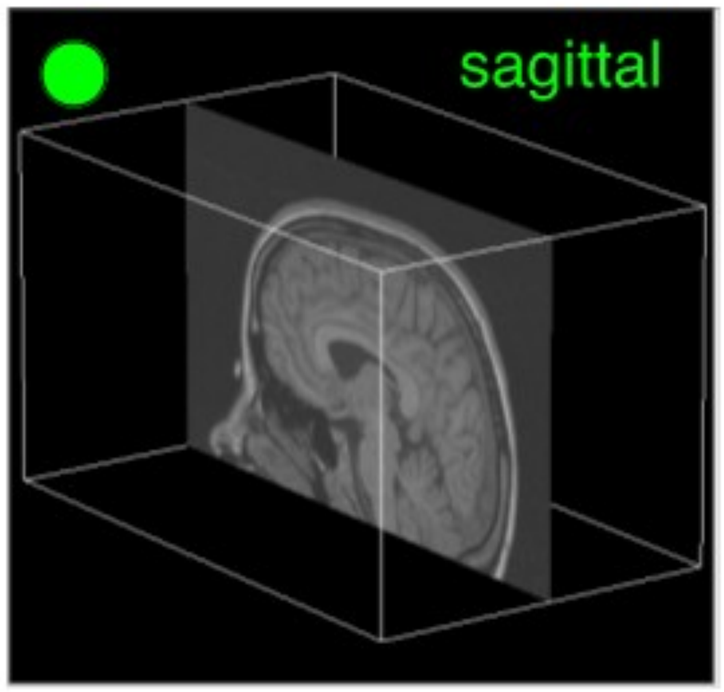


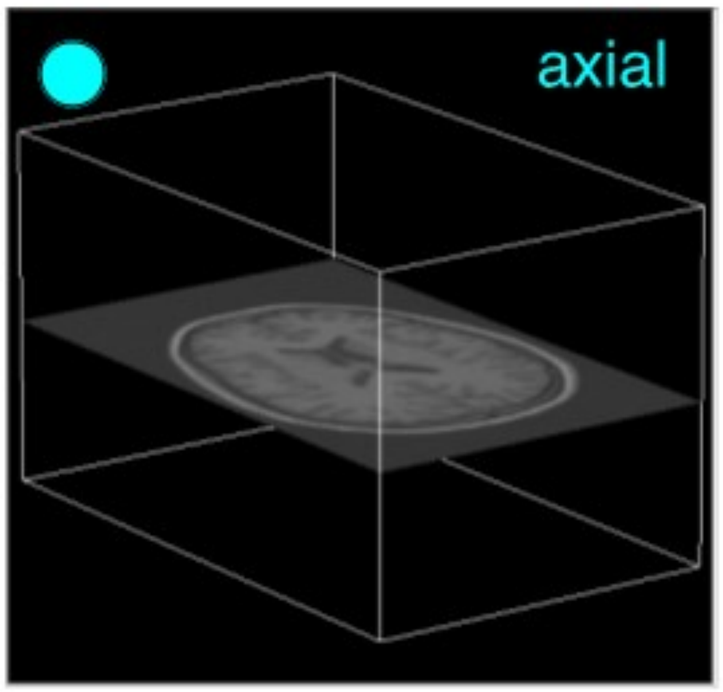
also oblique and curved planes



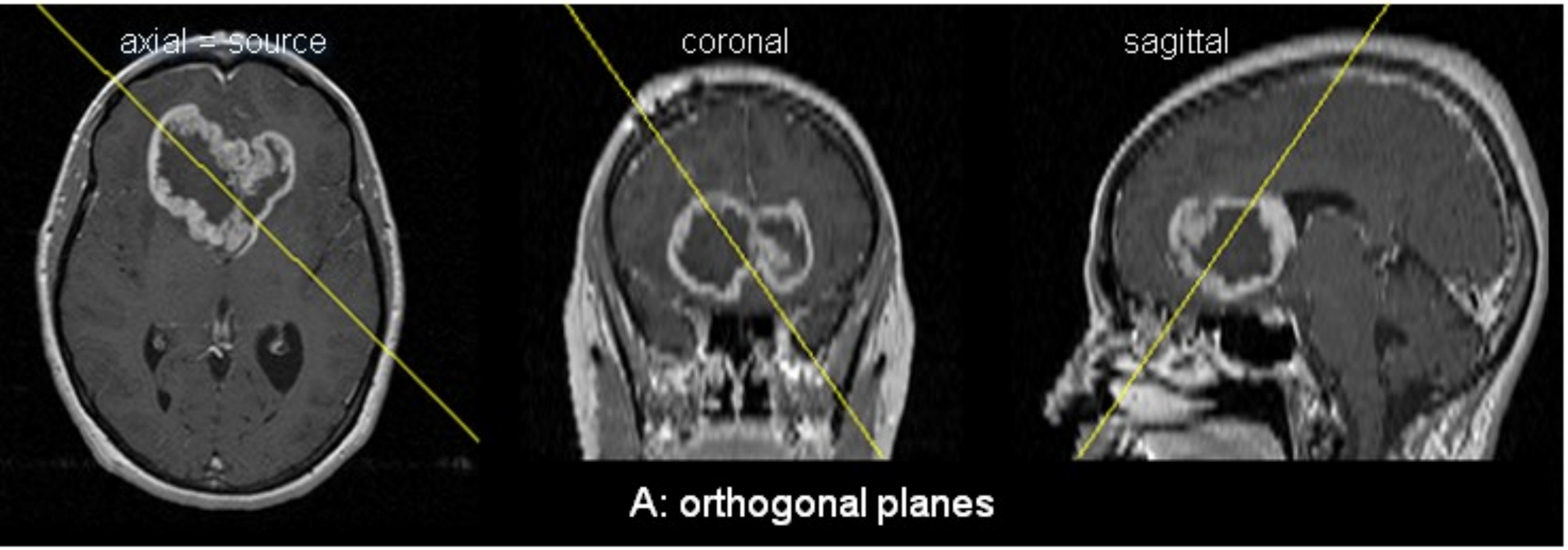


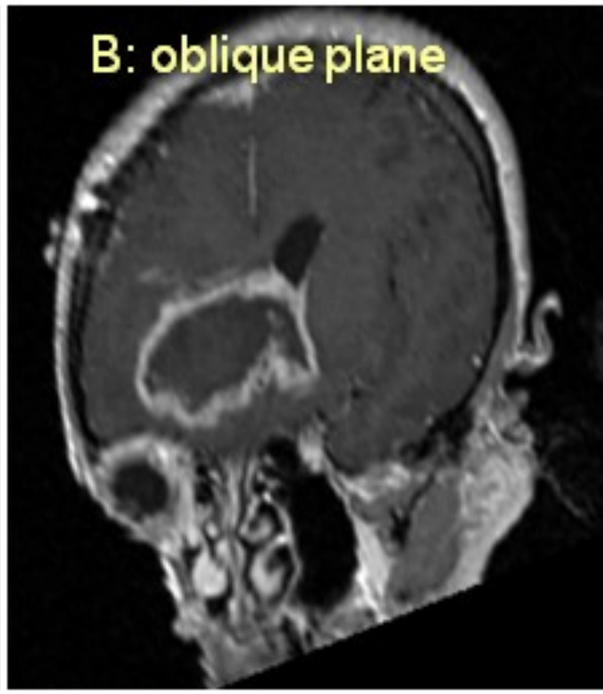


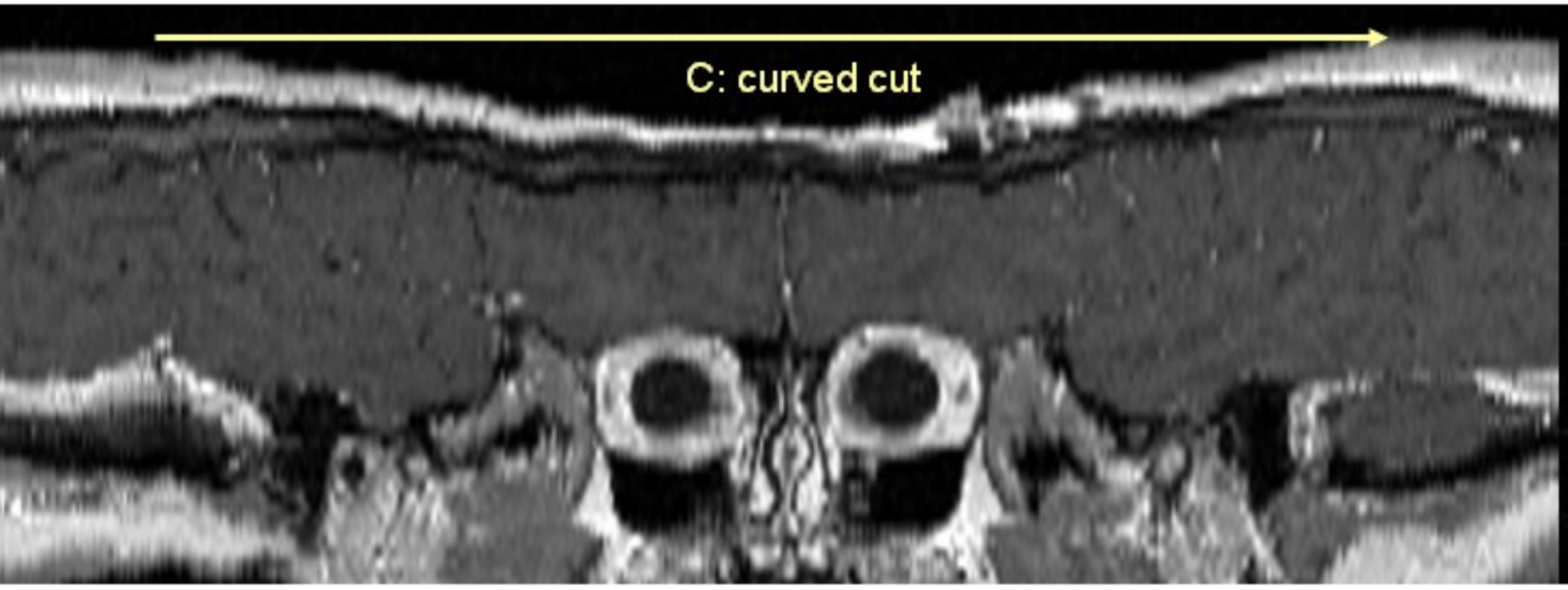


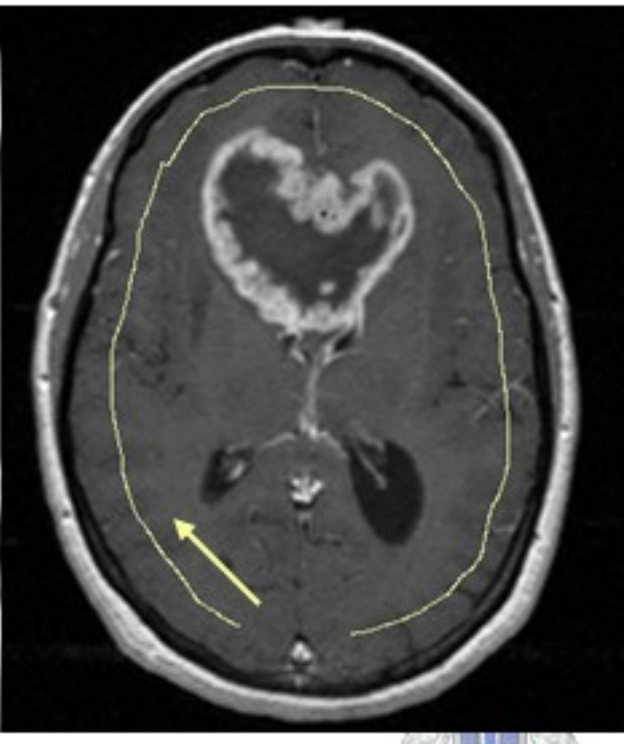


Multidimensional visualization techniques: slices and MPR

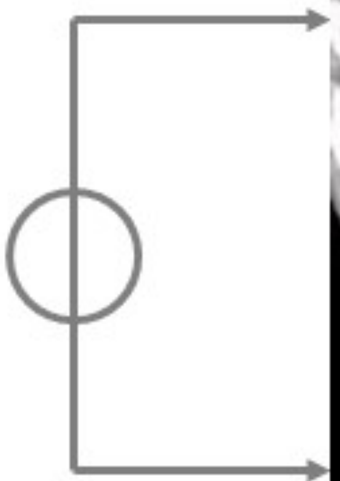


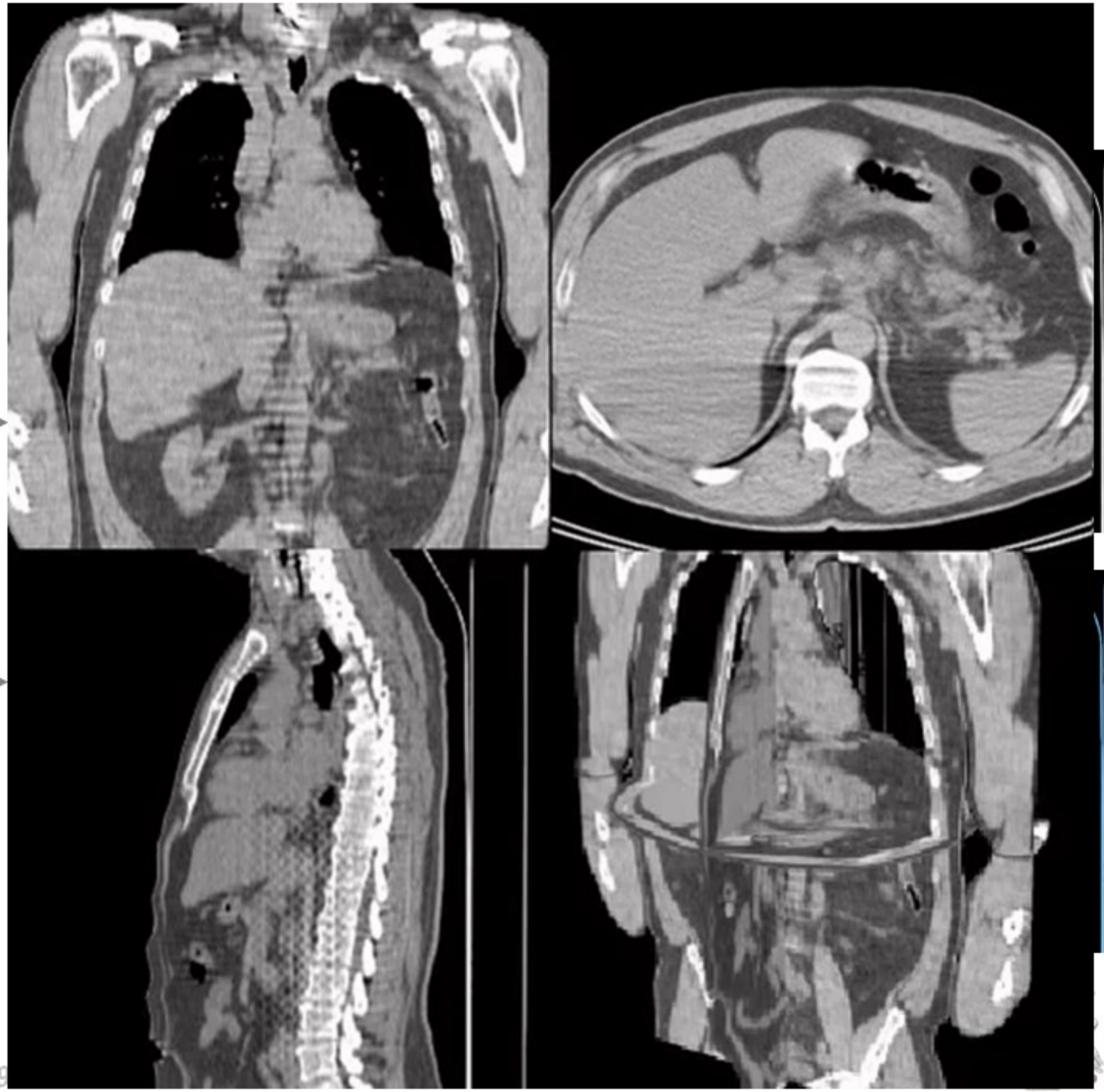






Multimodality MPR: colorwash





rot

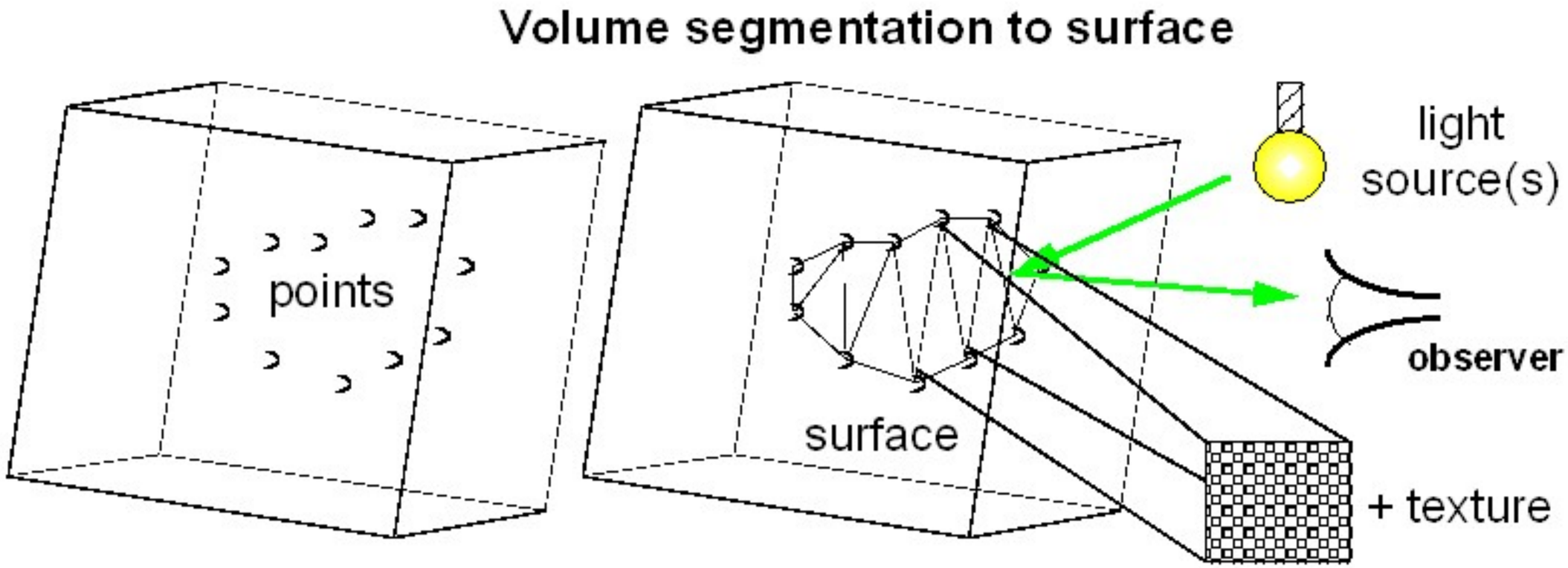
Visualization techniques:

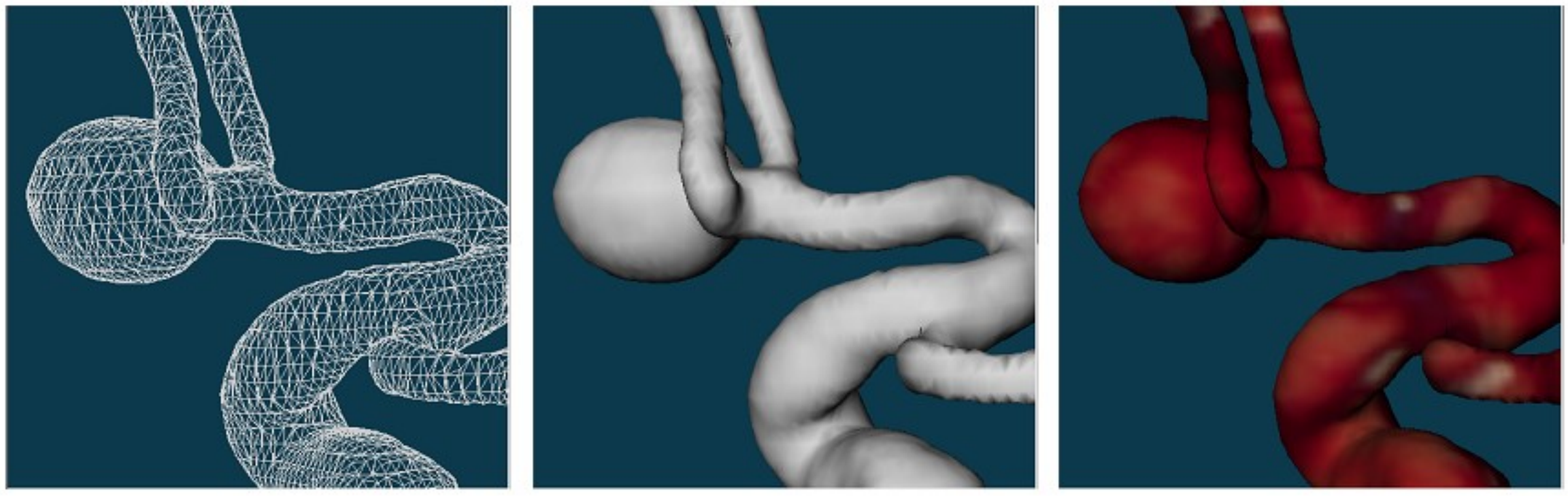
slices: Multi-Planar Reconstruction (MPR)
side by side images with coupled cursors
colorwash/fusion

3D surfaces:
segmented structures
textured by another modality
or other (parametric) data

Volume Rendering:
Maximum Intensity Projection
ray-tracing/casting

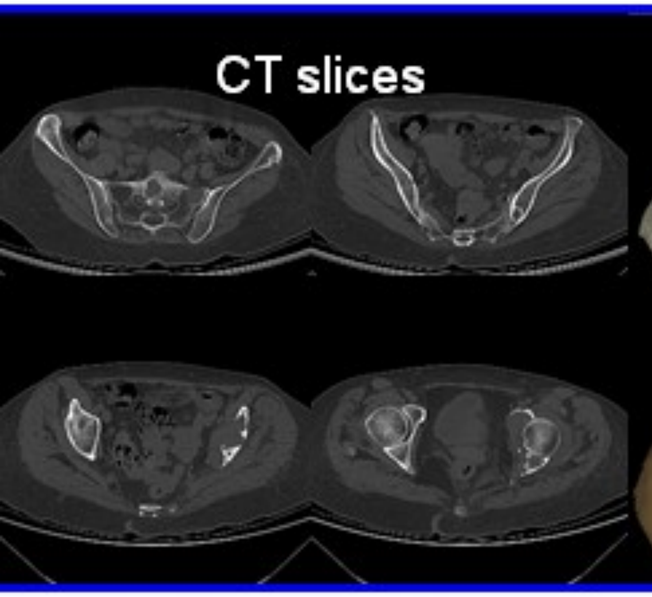
Multidimensional visualization techniques: surface rendering

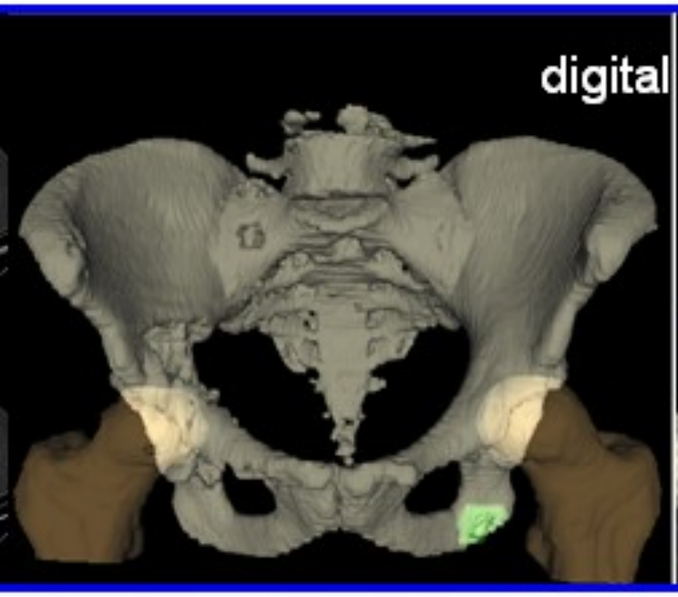


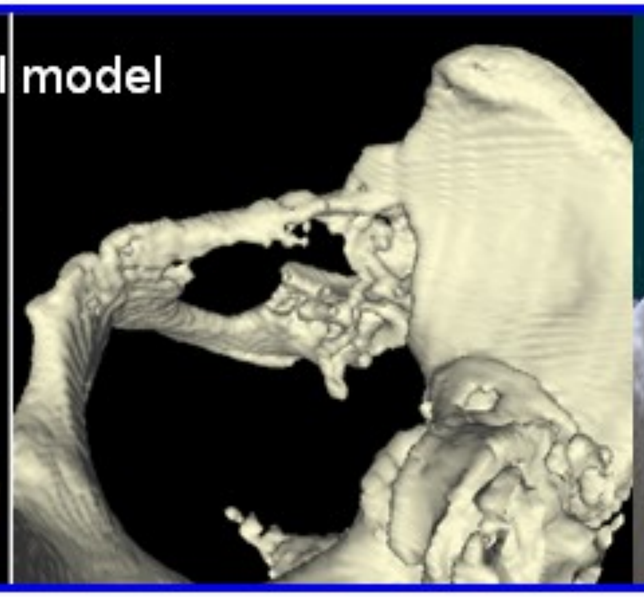


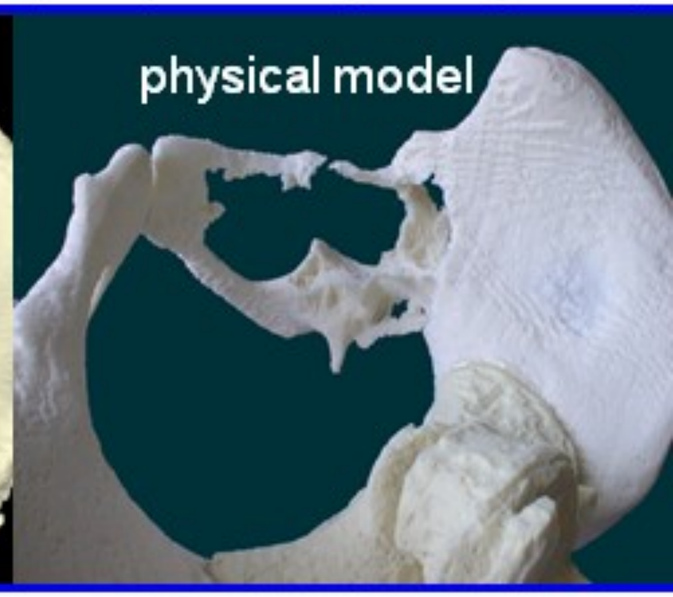
Rapid prototyping

(source CT's courtesy HUG; post-proc./3D printing LMB)

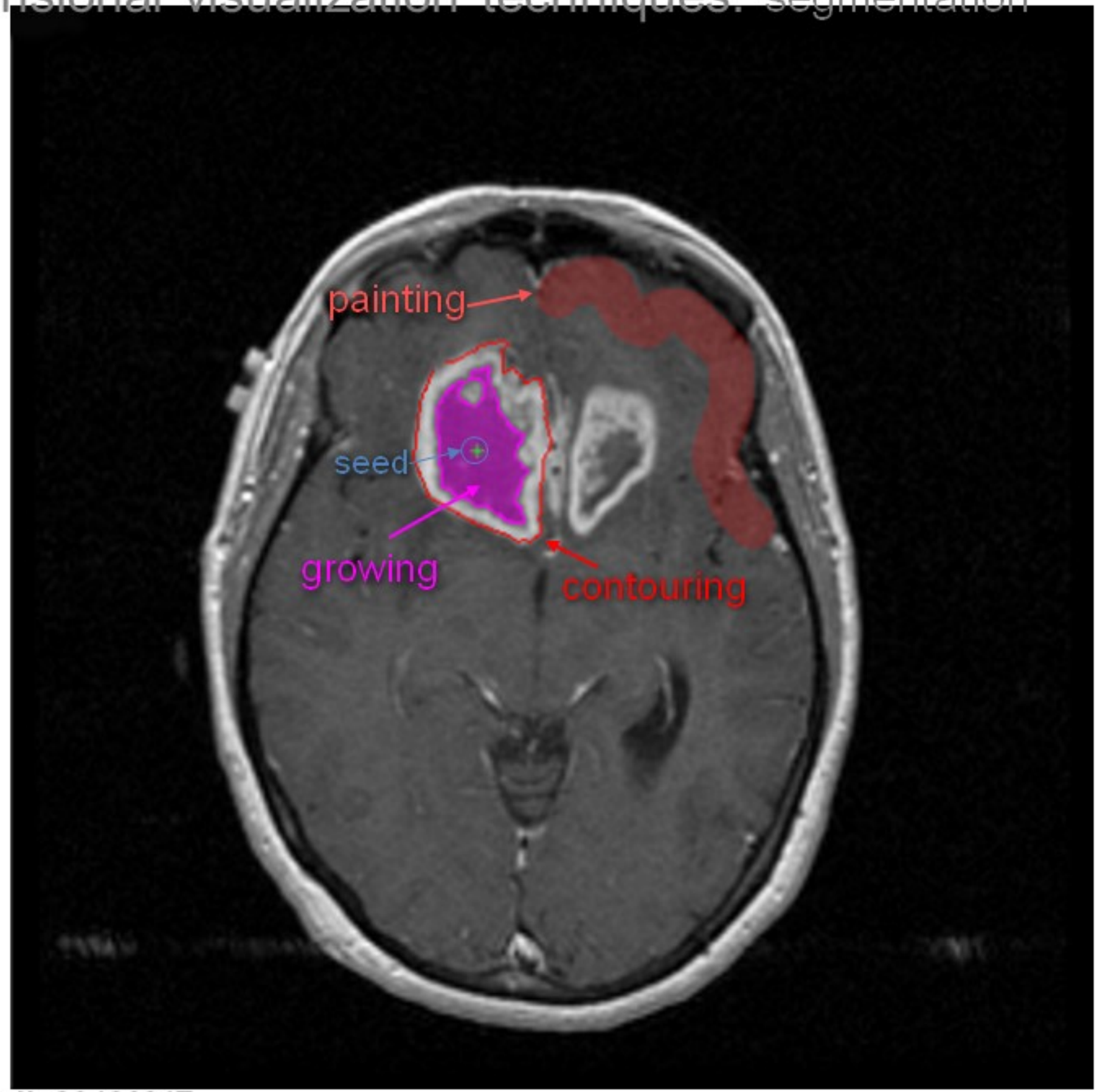




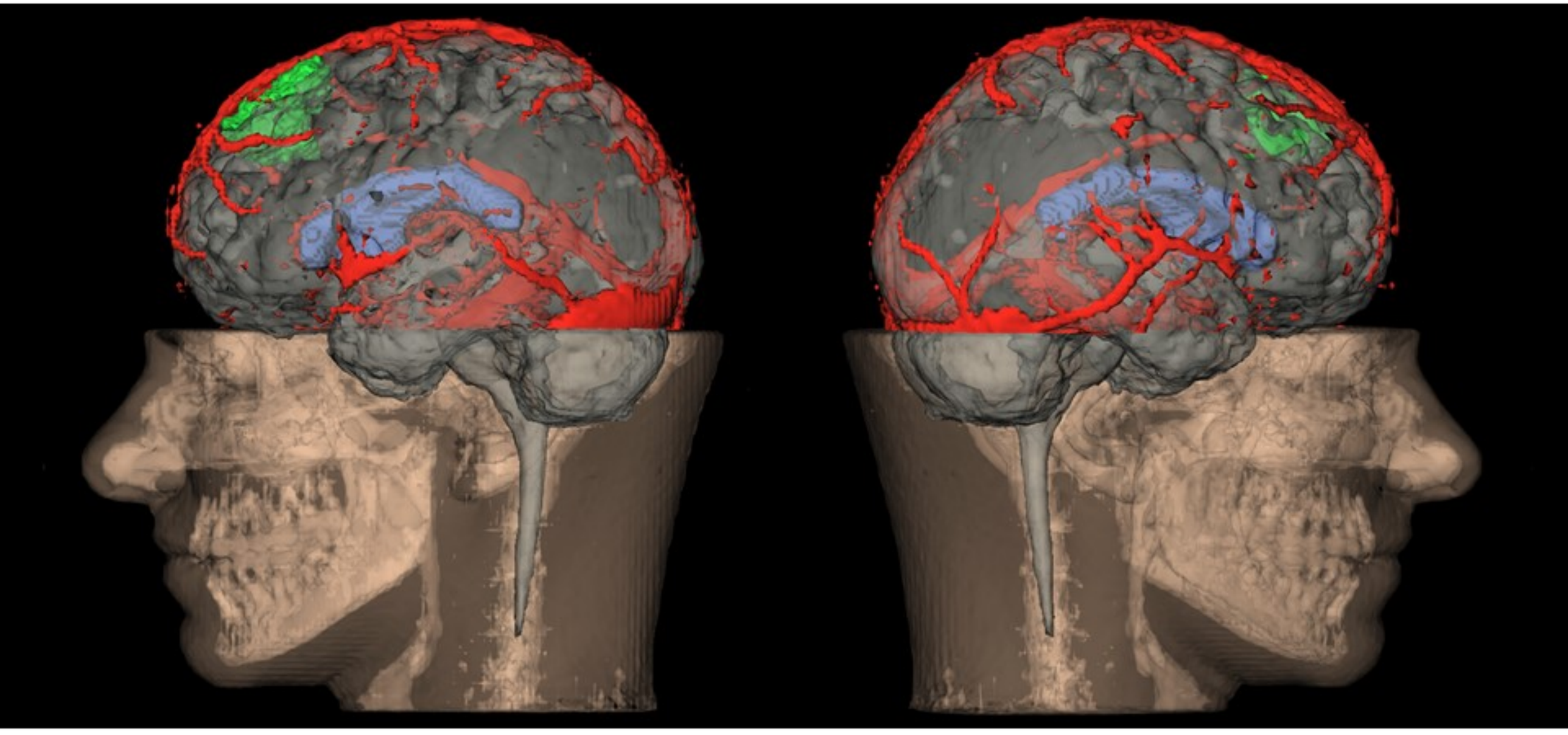




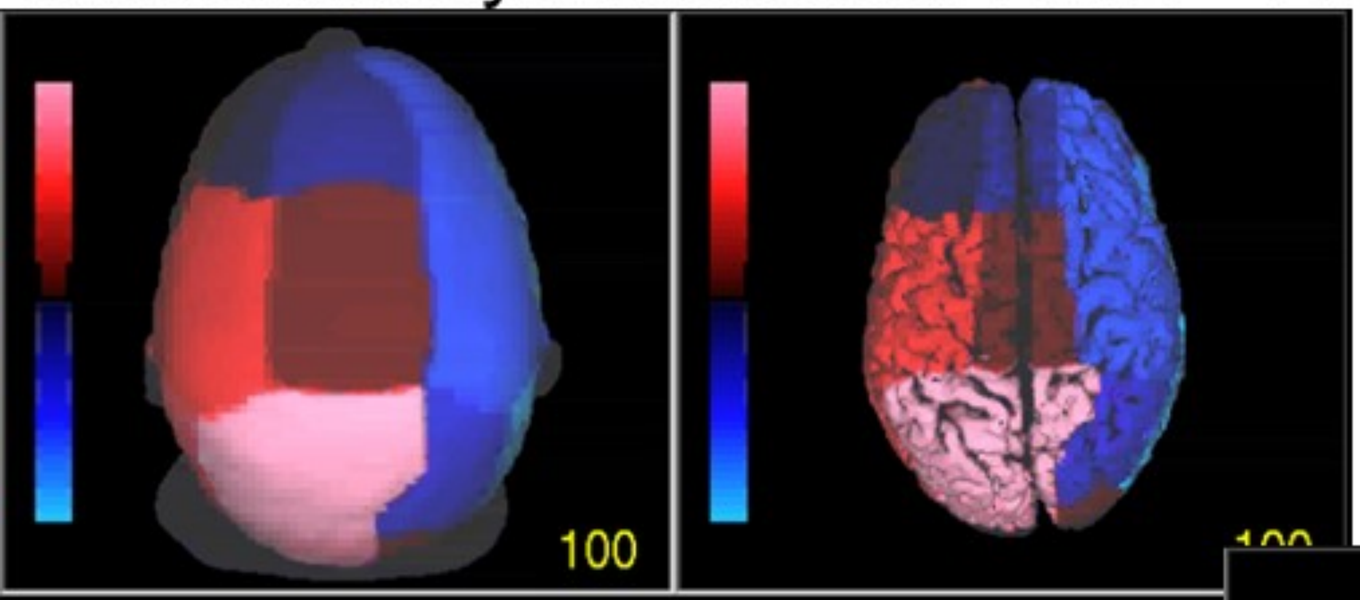
Multidimensional visualization techniques: segmentation

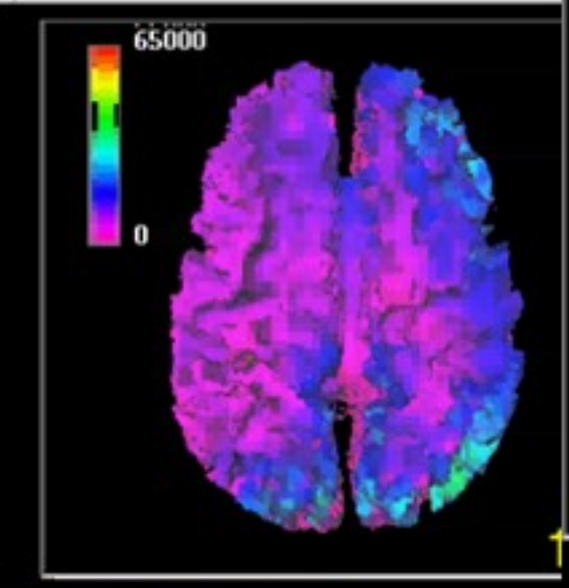


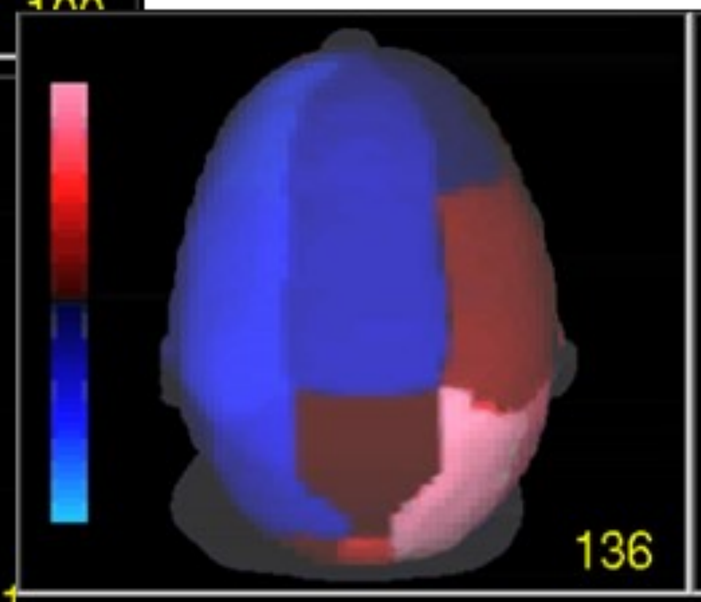
Brain tumor: *(source MR courtesy HUG; post-proc./visu. LMB)*

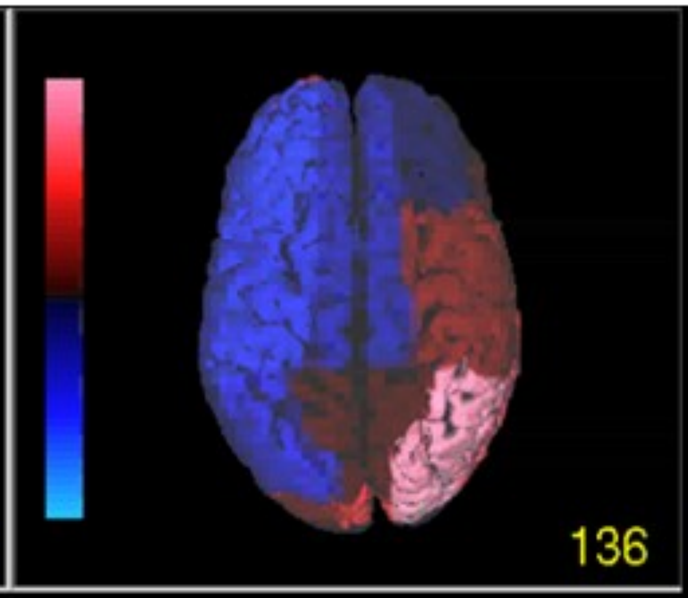


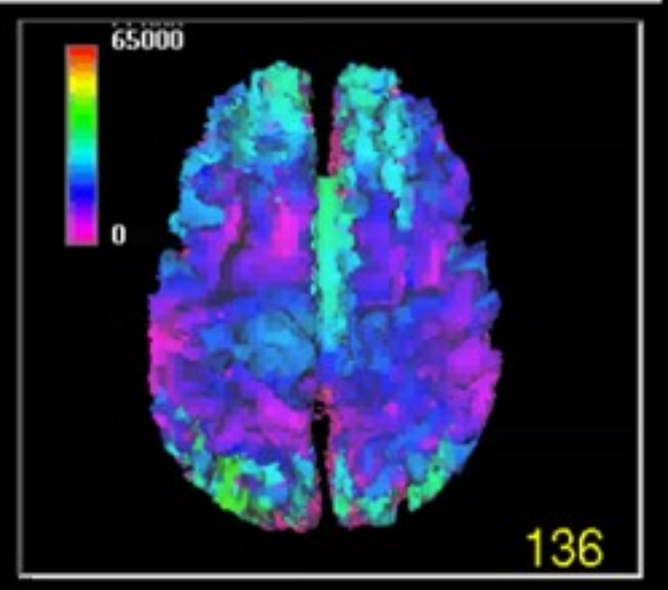
Multimodality/Multisensor: MR + ERP (EEG+EMT) *(source MR/EMT courtesy HUG; post-proc./visu. LMB)*











Visualization techniques:

slices: Multi-Planar Reconstruction (MPR)
side by side images with coupled cursors
colorwash/fusion

3D surfaces:
segmented structures
textured by another modality
or other (parametric) data

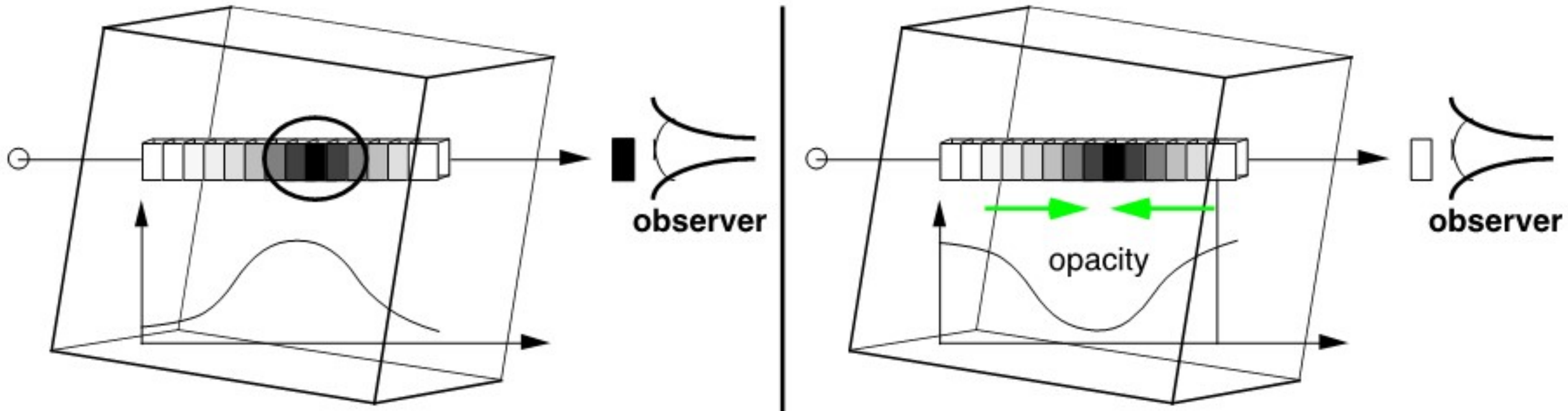
Volume Rendering:
Maximum Intensity Projection
ray-tracing/casting

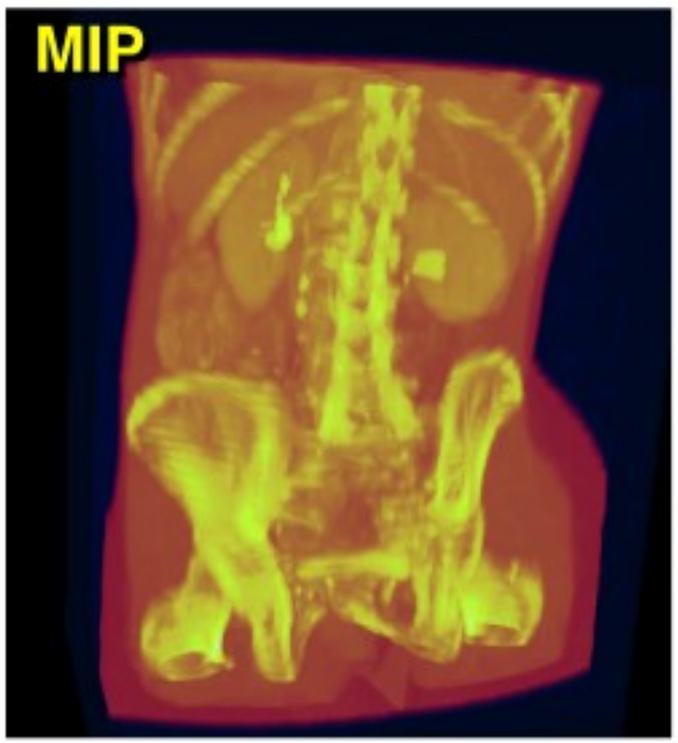
Multidimensional visualization techniques: volume rendering

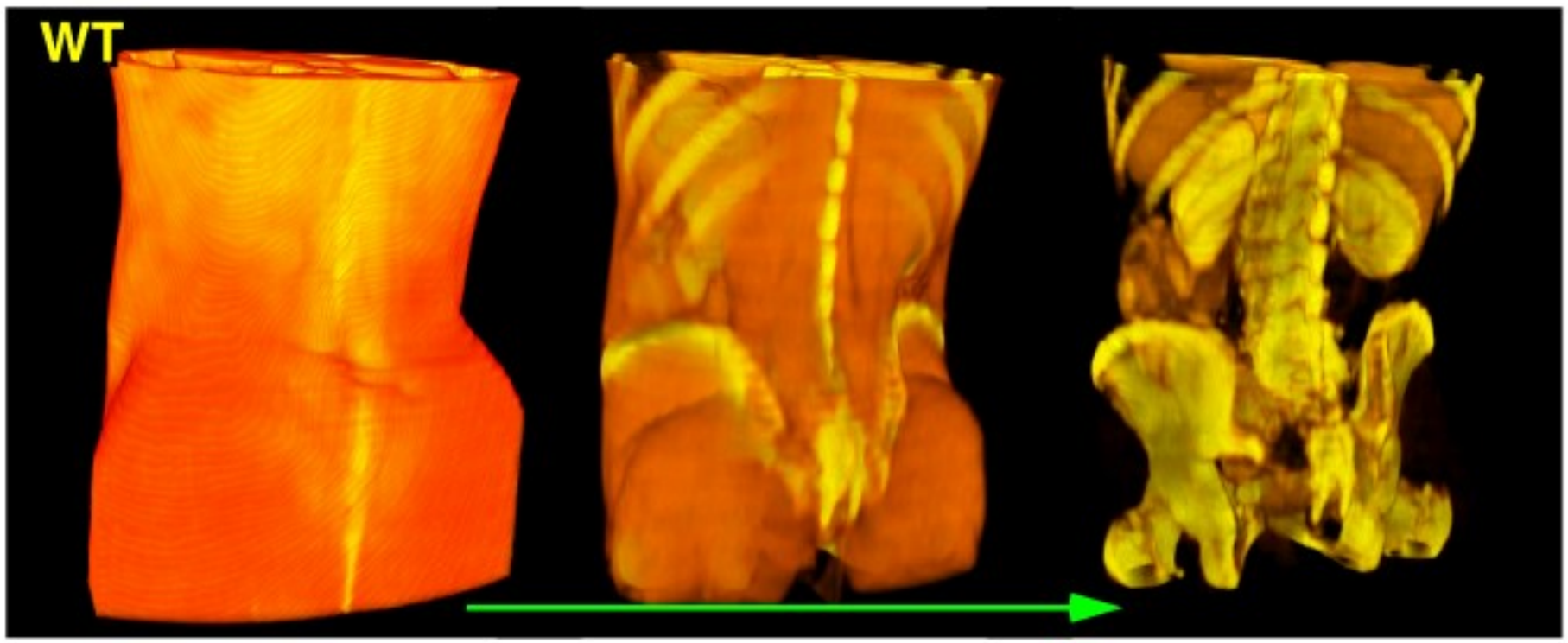
Maximum Intensity Projection
maximum value <-> projection

Volume Rendering

Weighted Transparency
value <-> opacity



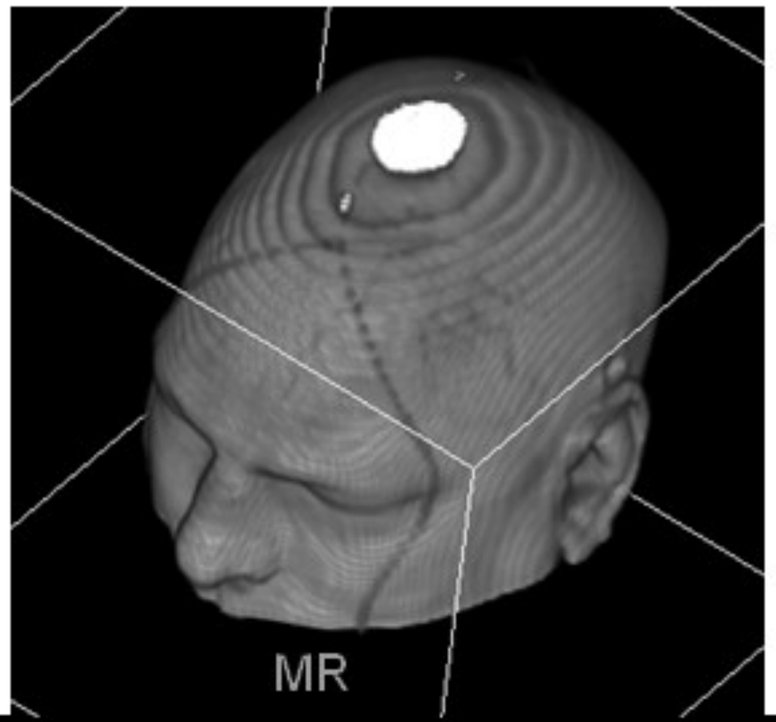


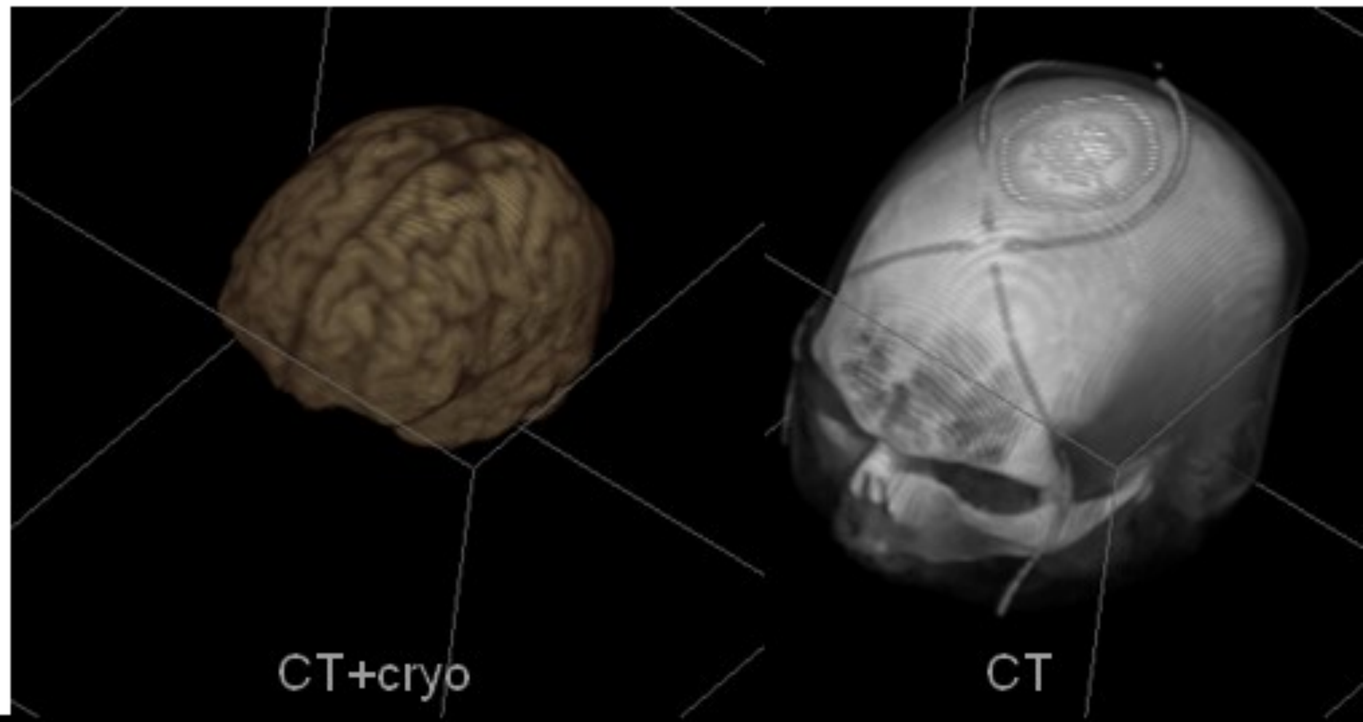


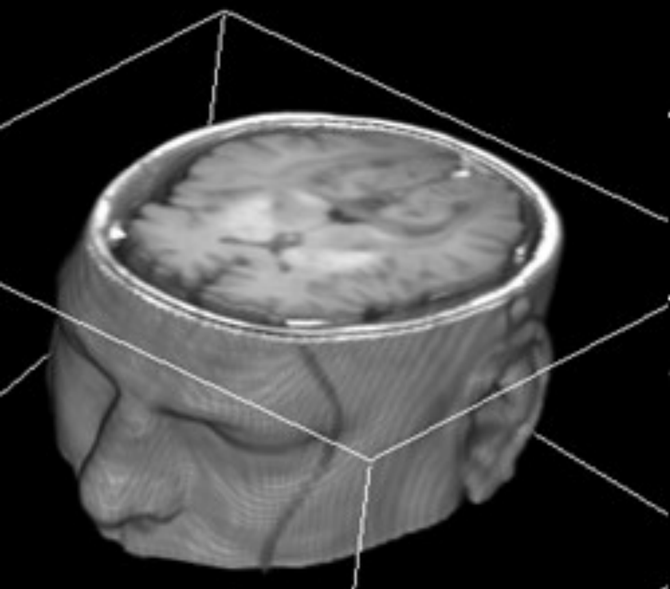
(CT courtesy HUG)

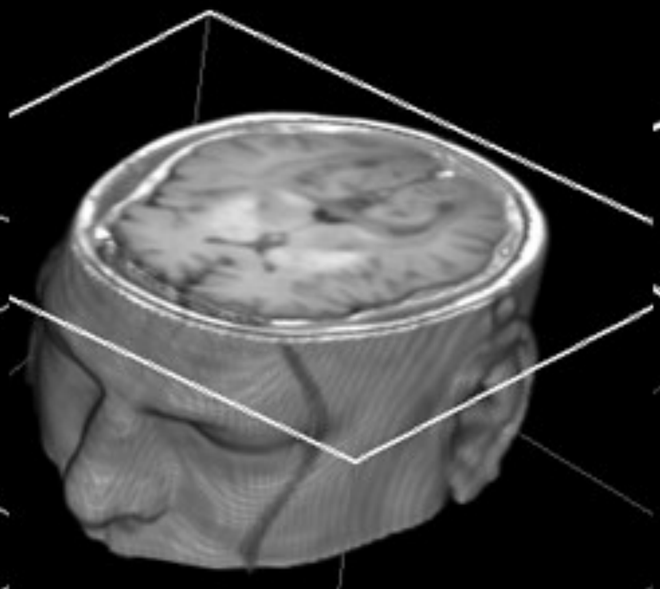
Multimodality visualization techniques: volume rendering (VH)

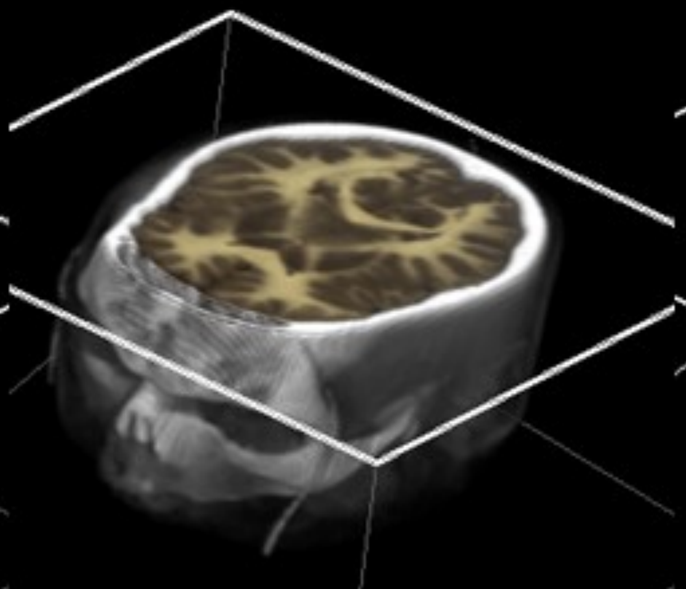
(source VH datasets courtesy NLM; post-proc./visu. LMB)

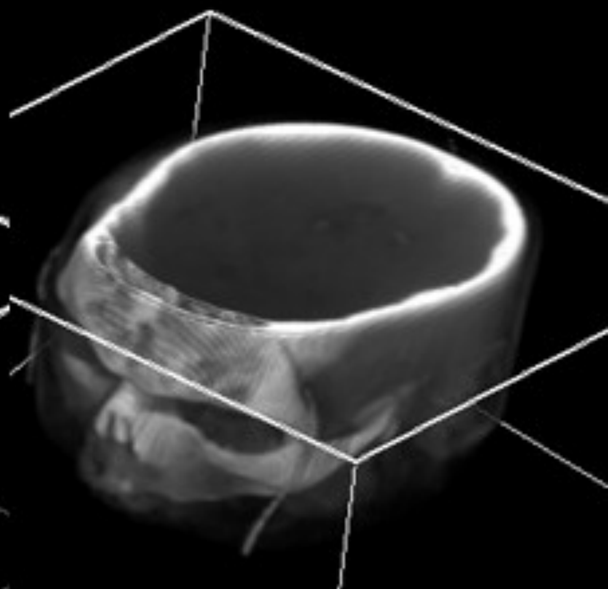


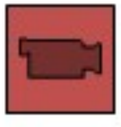


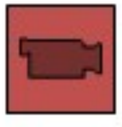






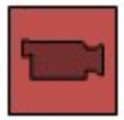






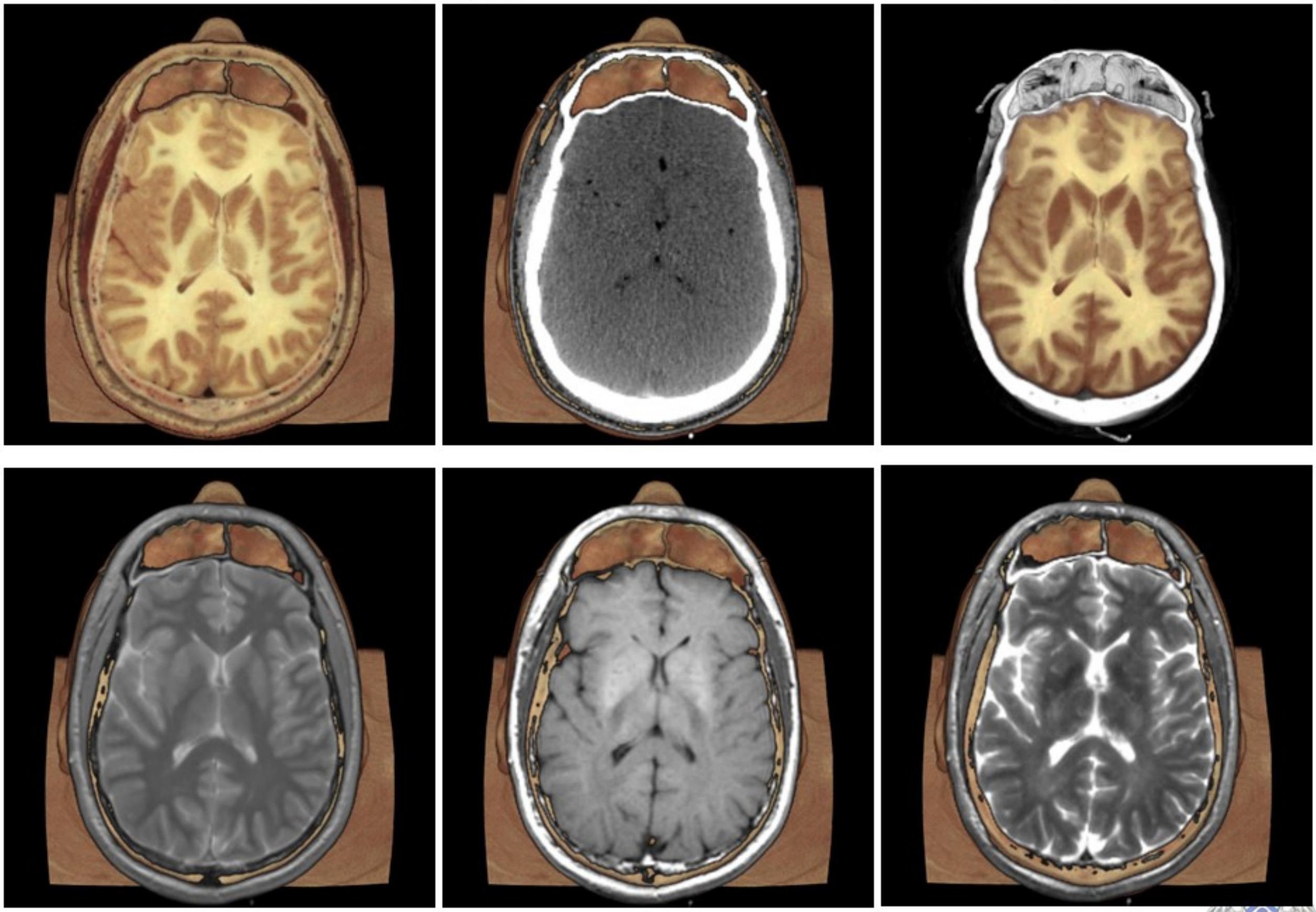
ali.slices

VH multimodality



rot

(source VH datasets courtesy NLM; post-proc./visu. LMB)



Imaging uses:

- diagnosis/staging
- treatment selection

<- planning/targeting

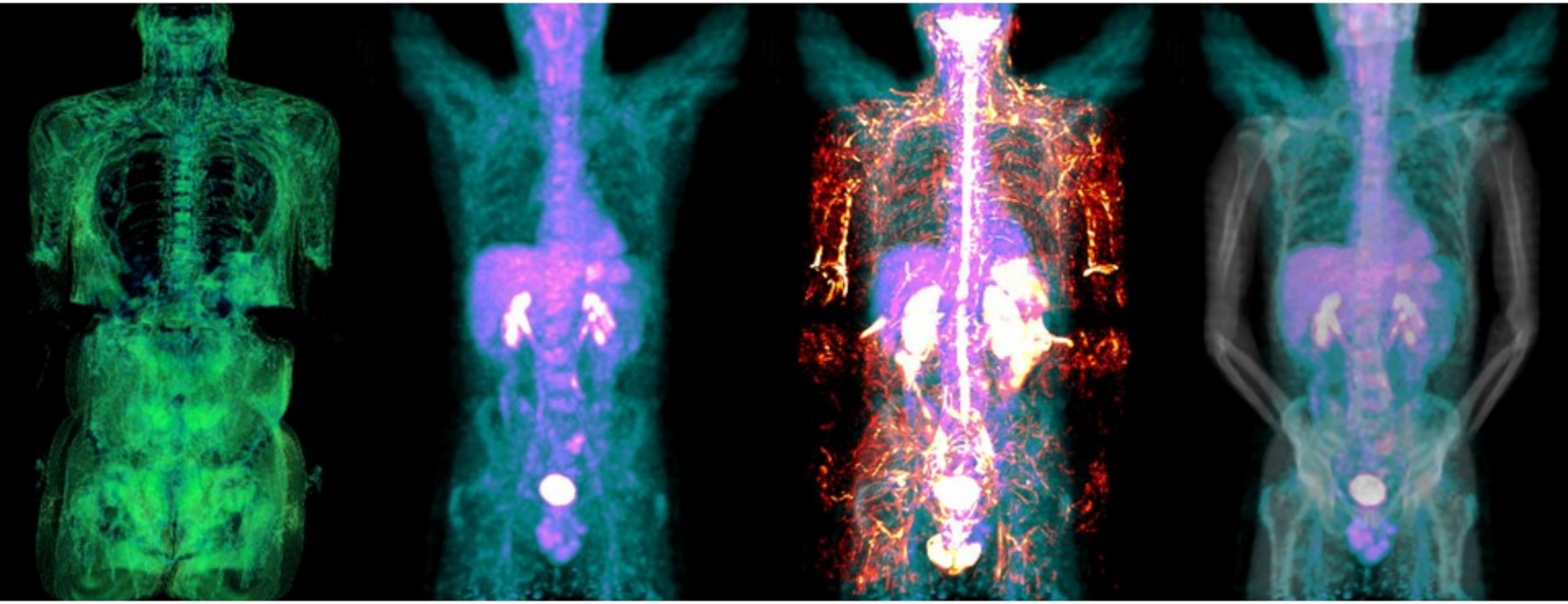
<- guidance

- response monitoring
- follow-up and restaging

Image-Guided Therapy…

Whole body MultiModality imaging

(source MR,PT(CT) courtesy MSKCC; post-proc./visu. LMB)

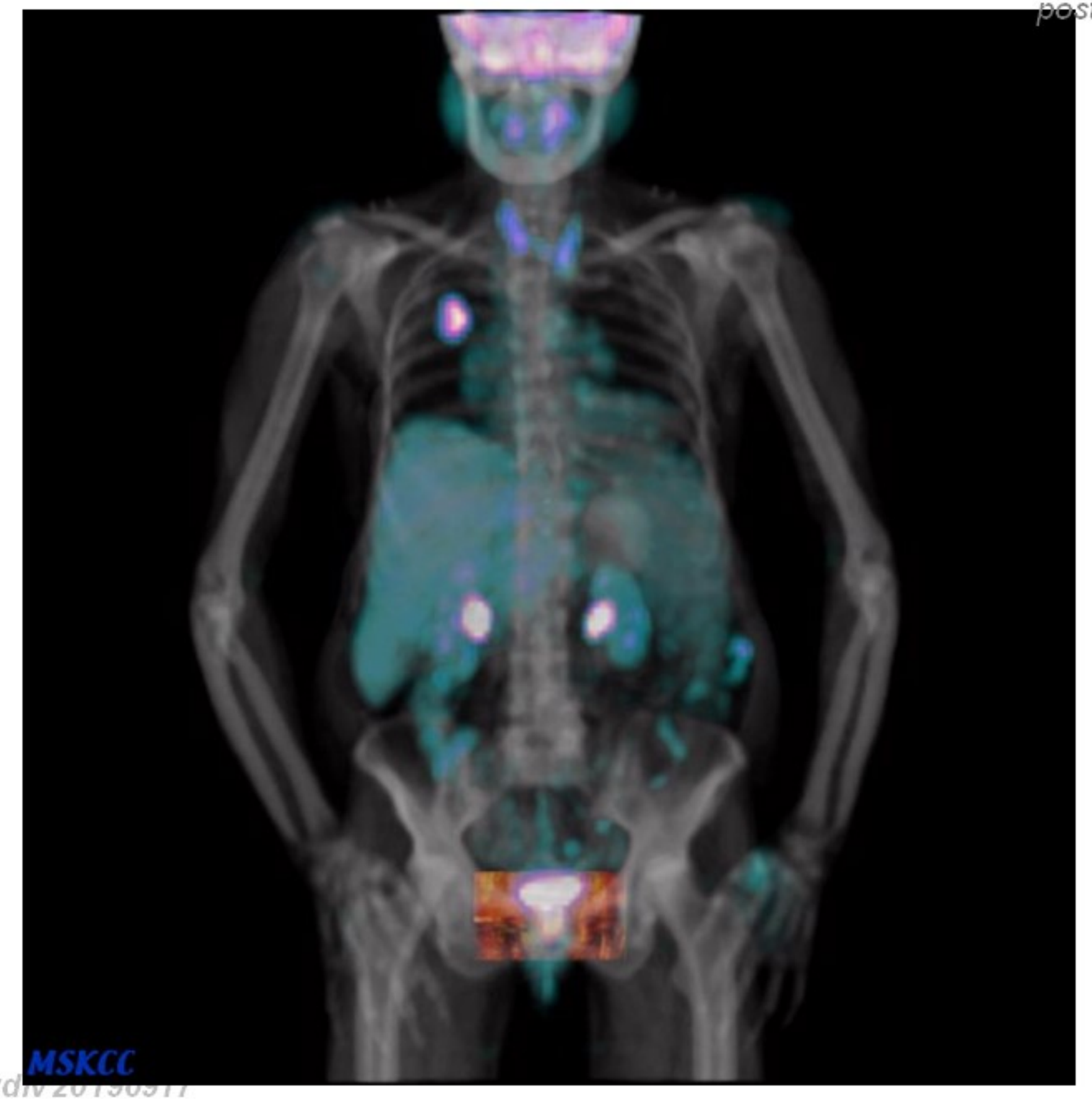


MRt1 PET PET+MRir PET+CT

vr

Whole body MultiModality imaging

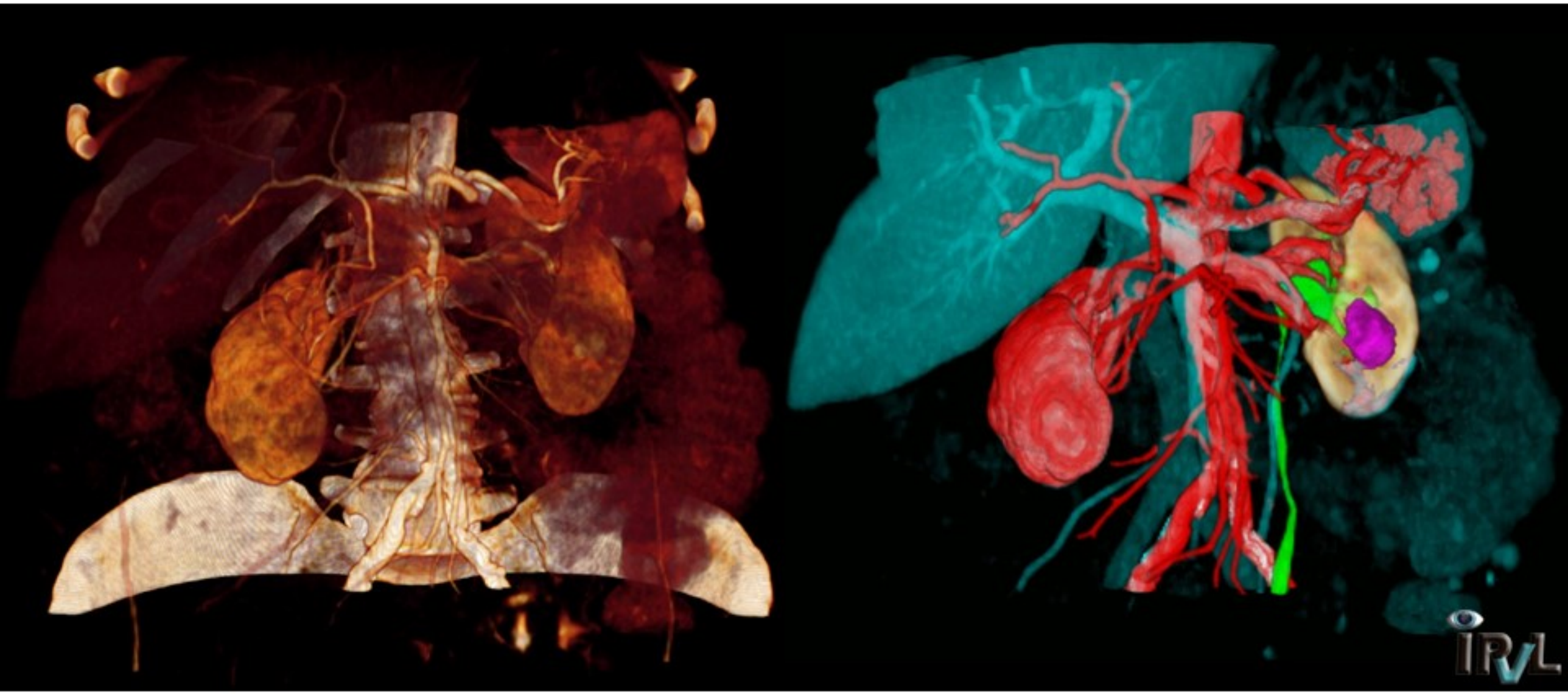
(source 3Dus,PT/CT courtesy MSKCC; post-proc./visu. LMB)



mov

Pre-op AI: multiphase CT (kidney)

(source CTs courtesy MDACC; post-proc./visu. LMB)



Pre-op AI: multiphase CT (liver)

(collab. MeVis)

tumor

HA+PV+BD

PV

PV segm.

PV territories

Risk PV
0,2,5,10mm

Risk territories
0,2,5,10mm

Left hemihepatectomy
HA+PV+BD

Left hemihepatectomy
HV segm.

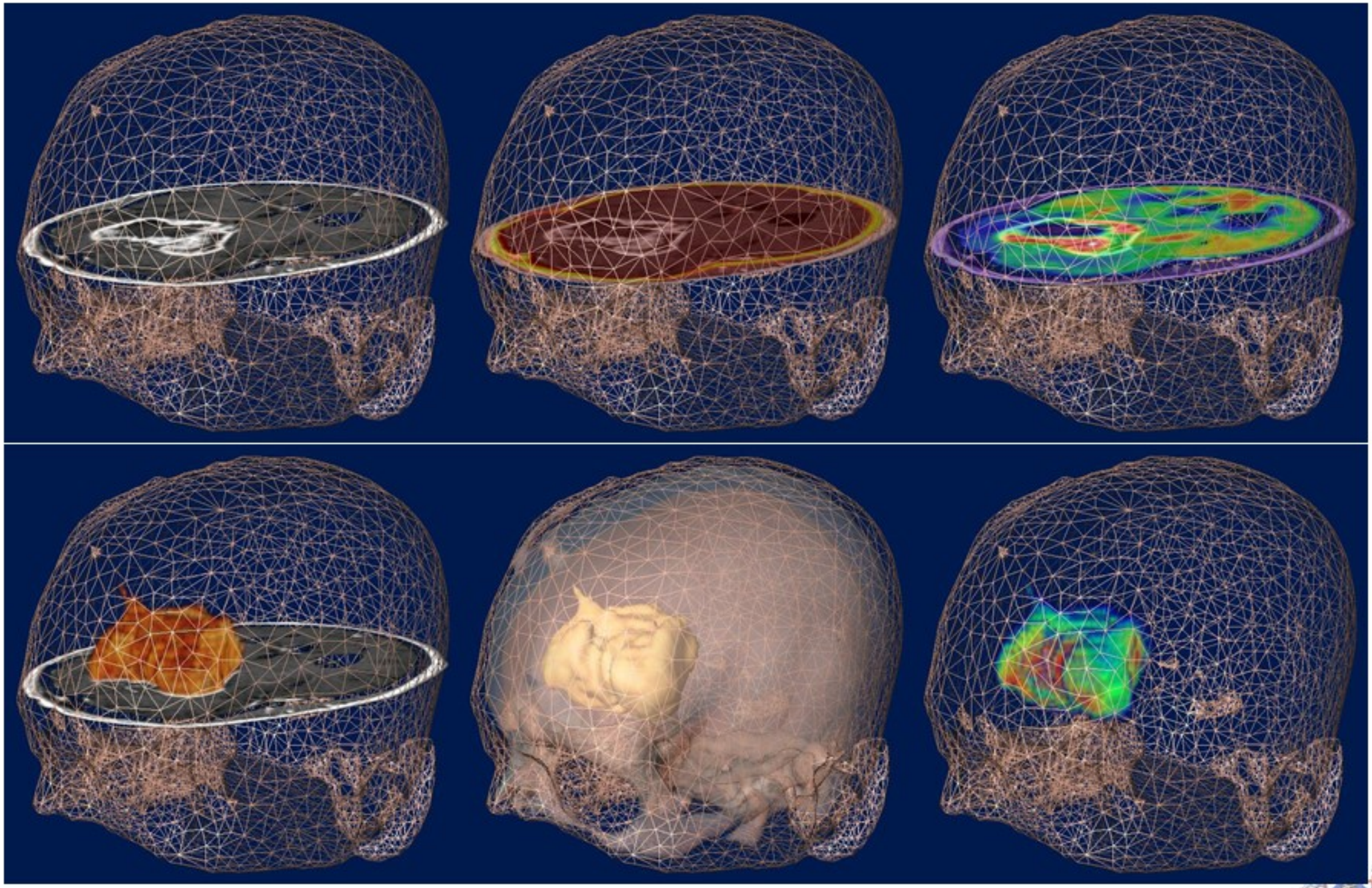
mos

vr

rep

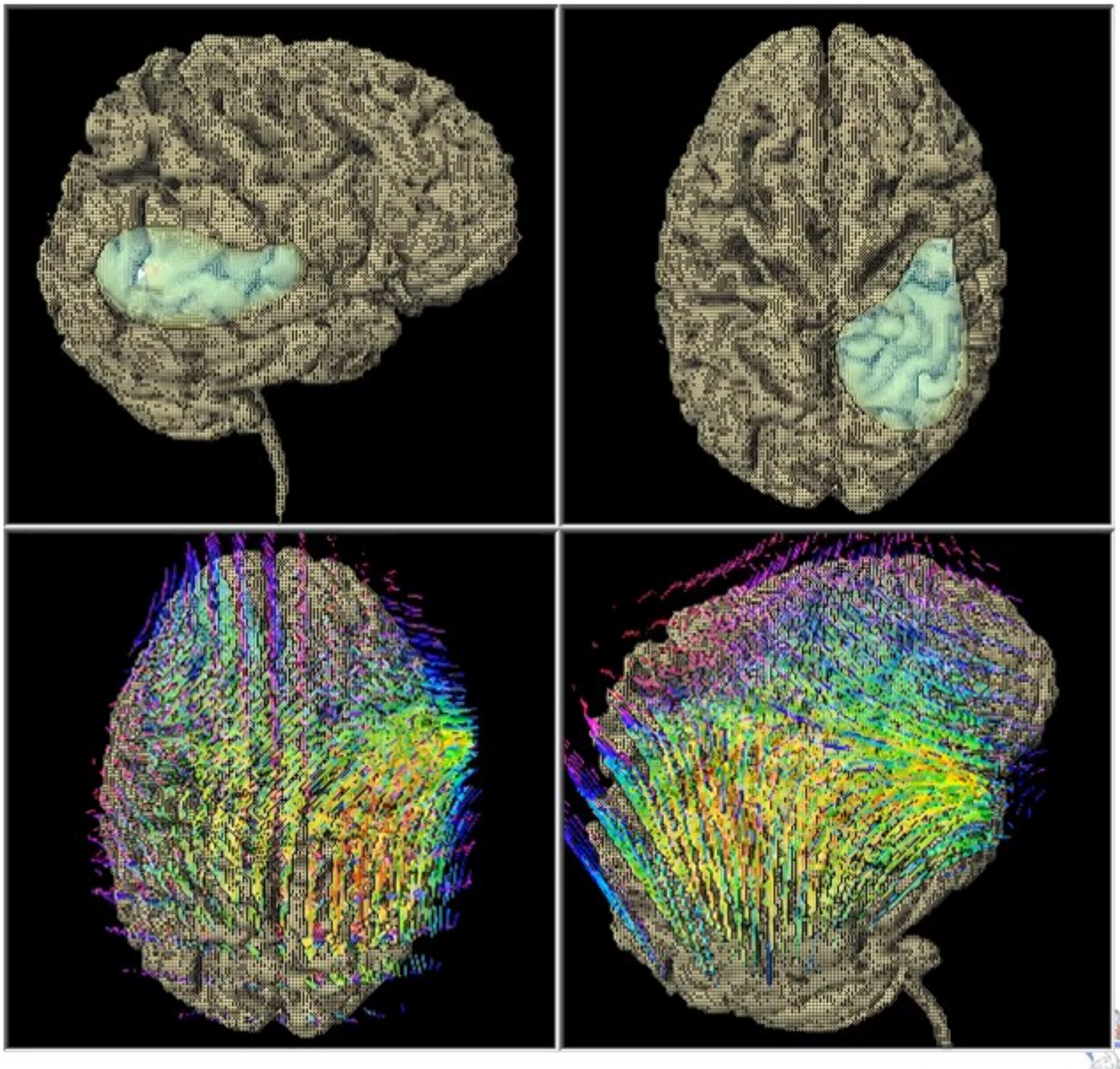
Brain tumor: MR + FDG-PET

(source data + collab. P. Gutin et al., MSKCC; post-proc./visu. LMB)



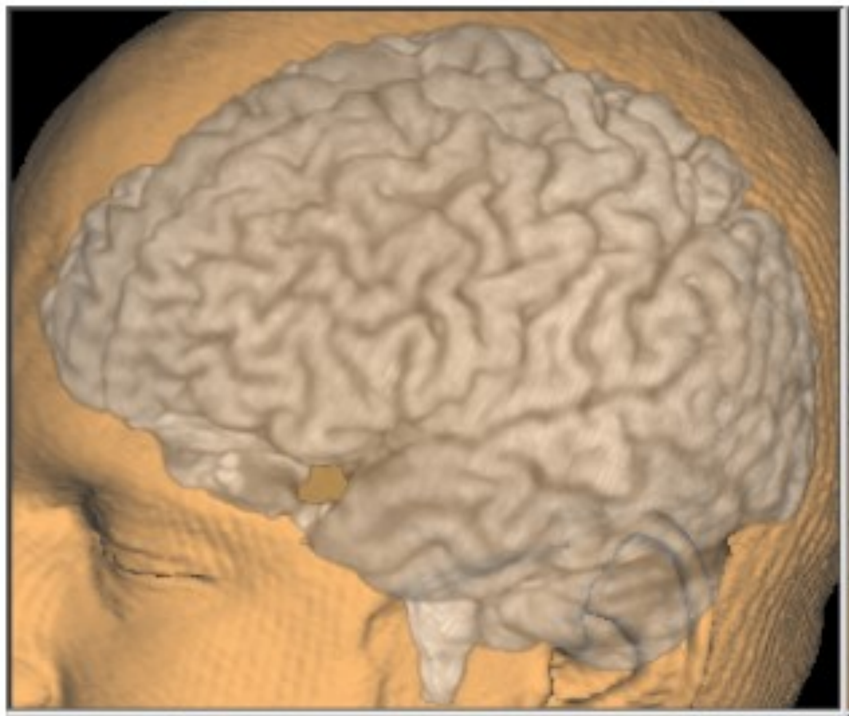
Brain function: EMT in epilepsy (from 1kHz EEG)

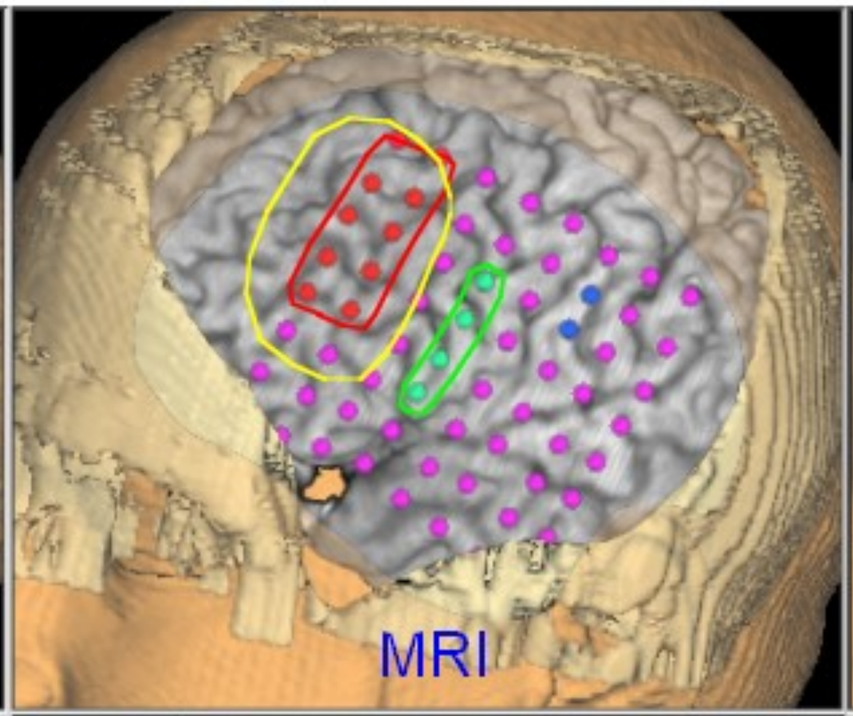
(source data + collabs. HUG & CHUV; post-proc./visu. LMB)

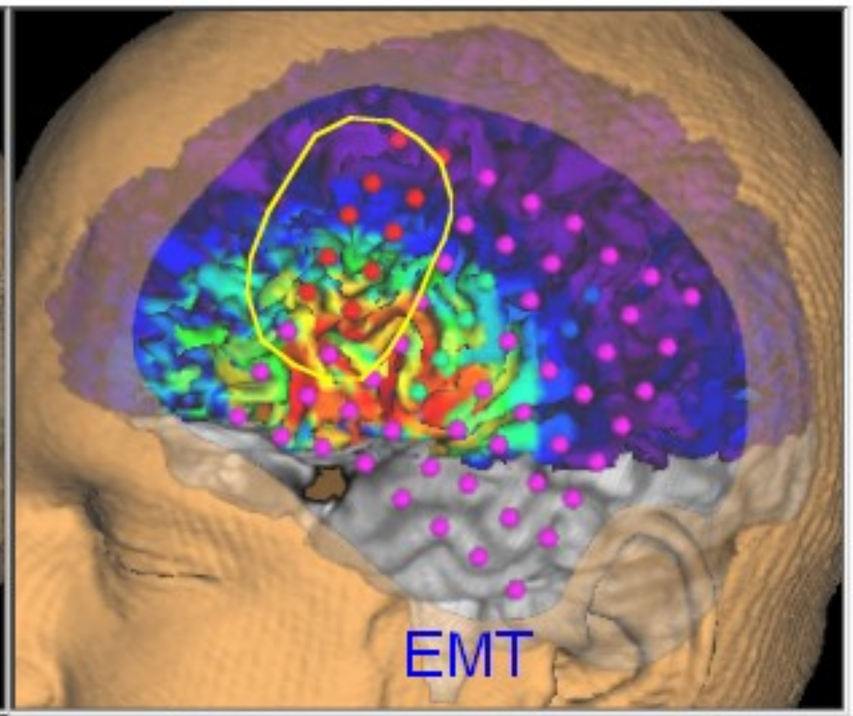


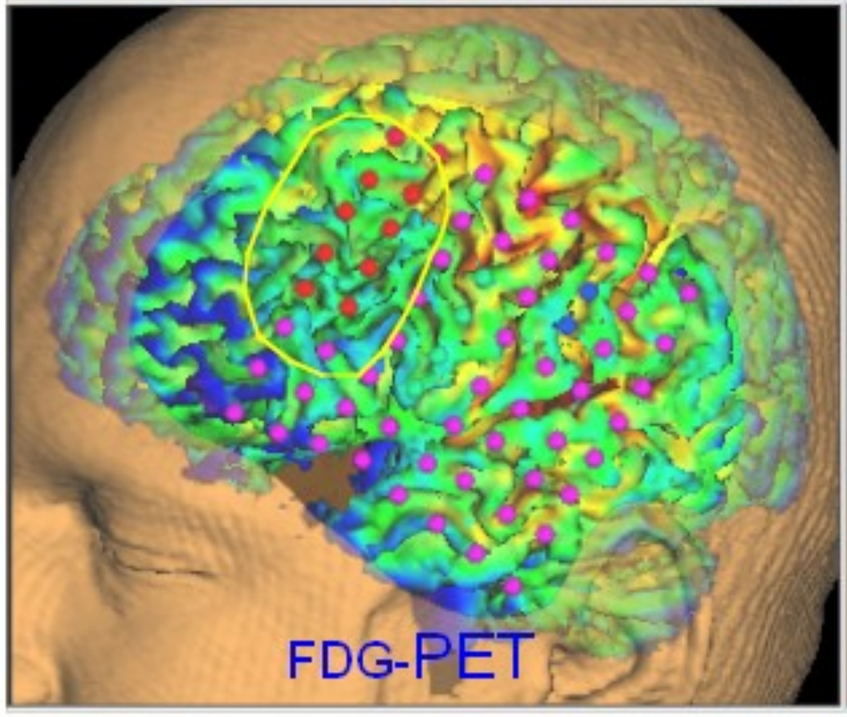
Pre/Post-op AI: neuro-epilepsy (MR + PET + SPECT + EMT + grid)

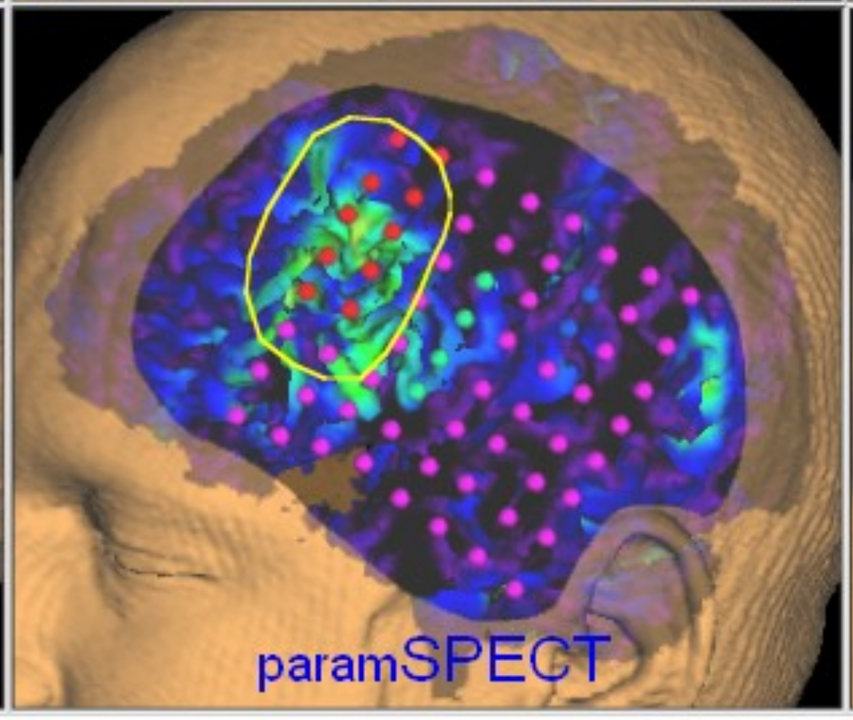
(source data + collabs. HUG & CHUV; post-proc./visu. LMB)

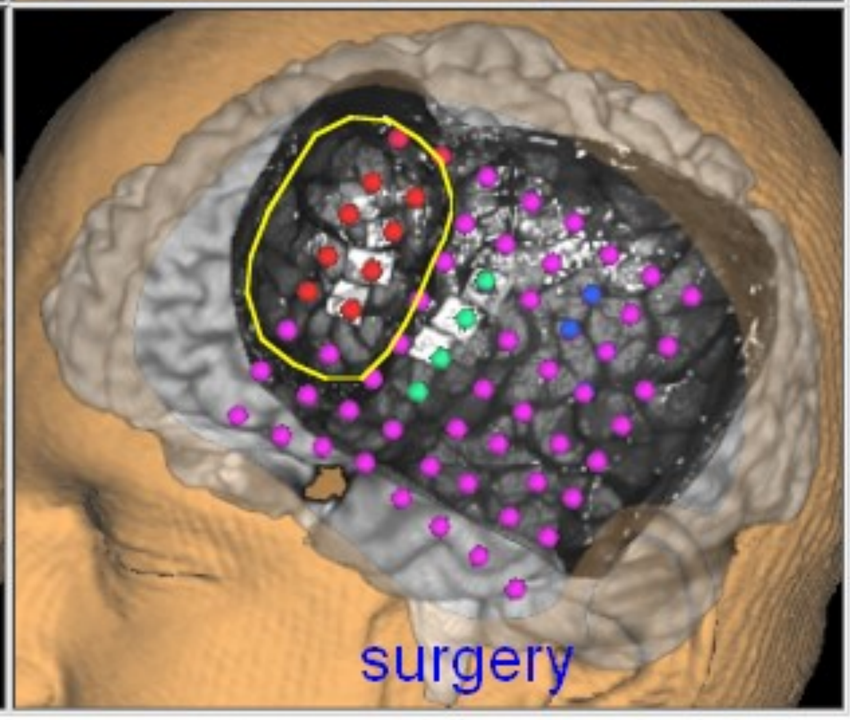






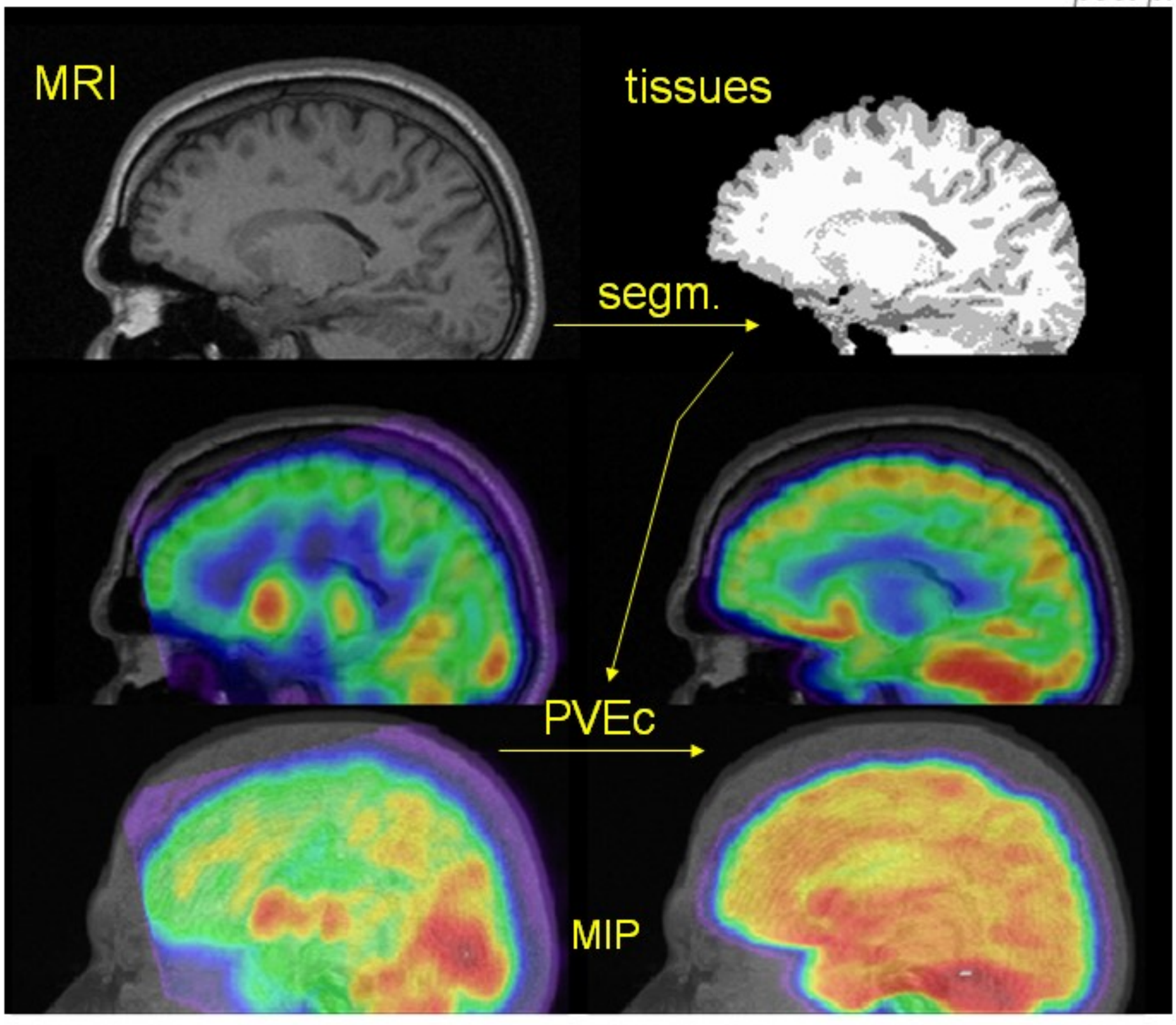






Refined 3D segmentation: Partial Volume Effect correction

(source MR/SPECT/PET courtesy HUG; post-proc./visu. LMB)



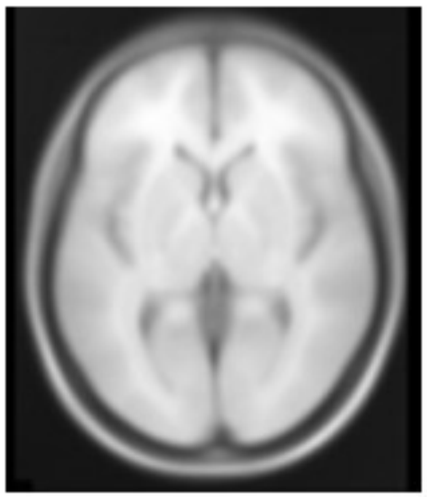
Inter subject registration:

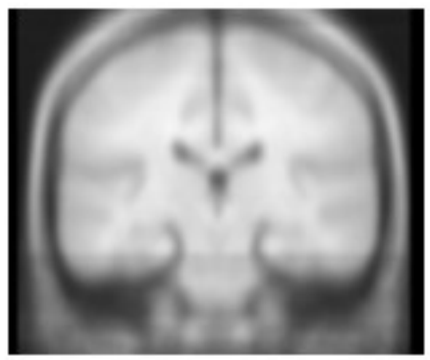
Registering:

acquisition

registration
rigid
affine

averaging → *average MR brain*

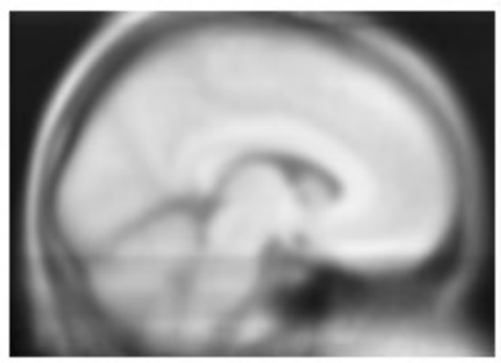




Exploitation ('à la' SPM):

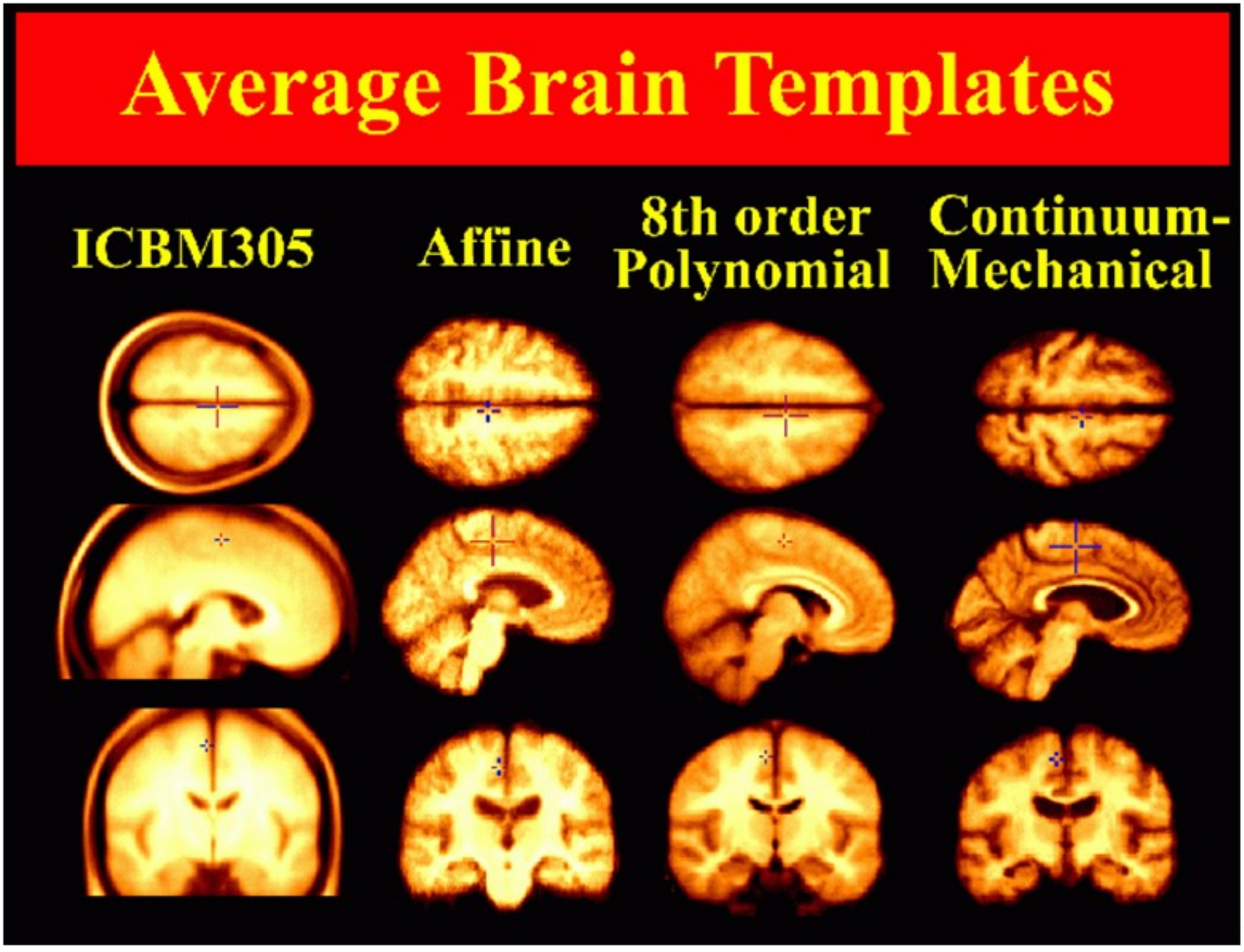
high (spatial) frequency smoothing

statistical analysis



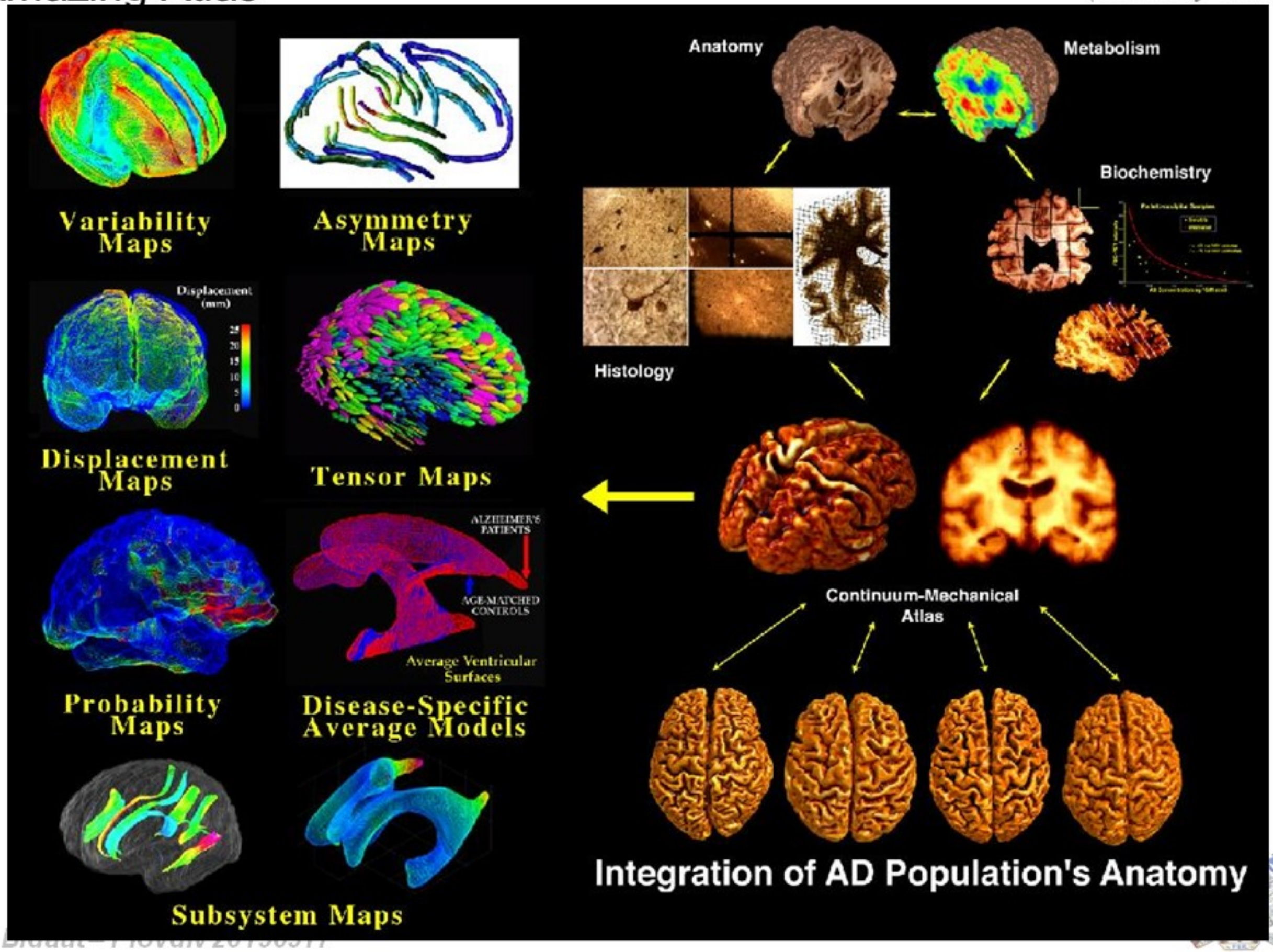
Creating a better average atlas

(courtesy LONI)

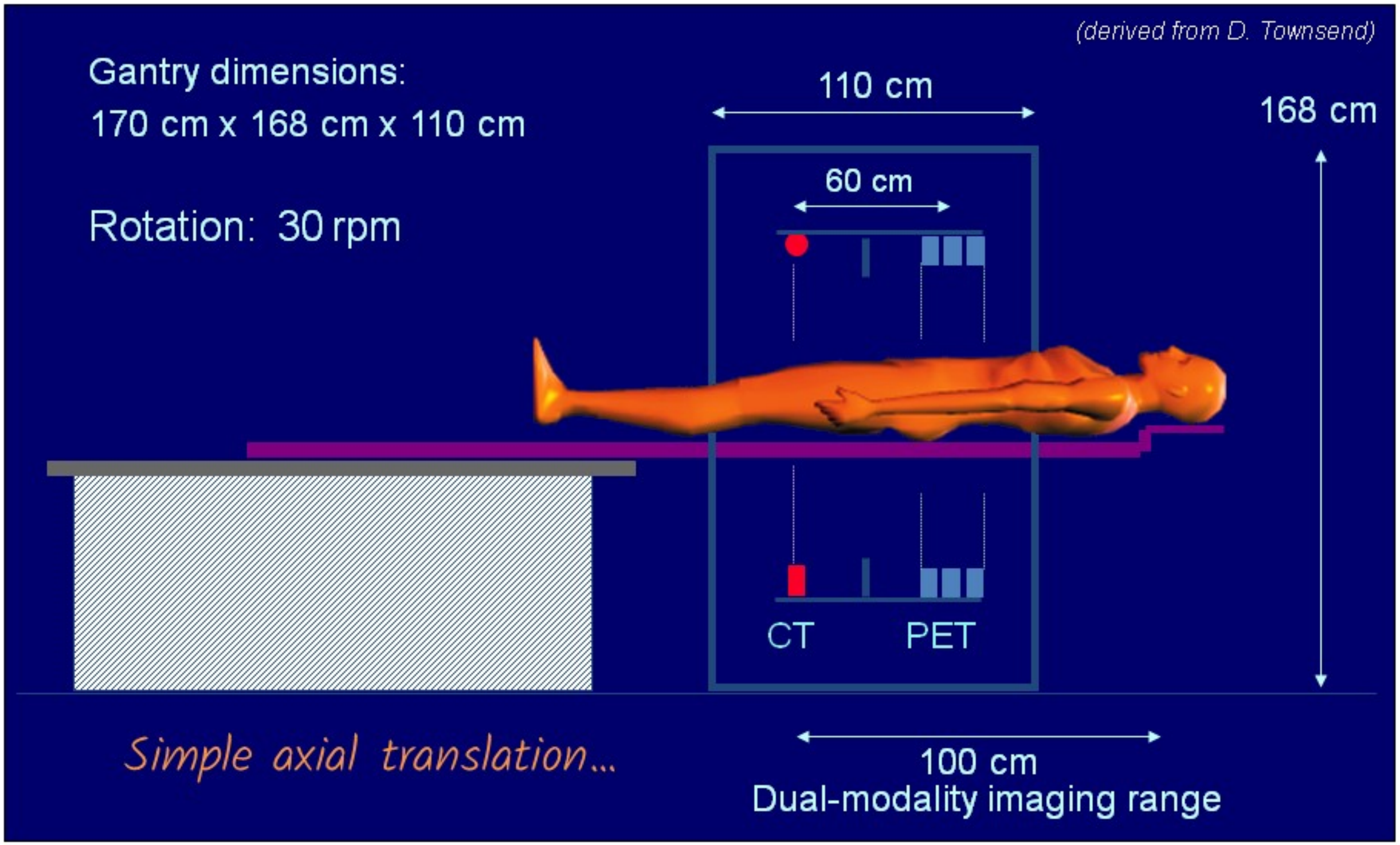


Amazing Atlas

(courtesy LONI)



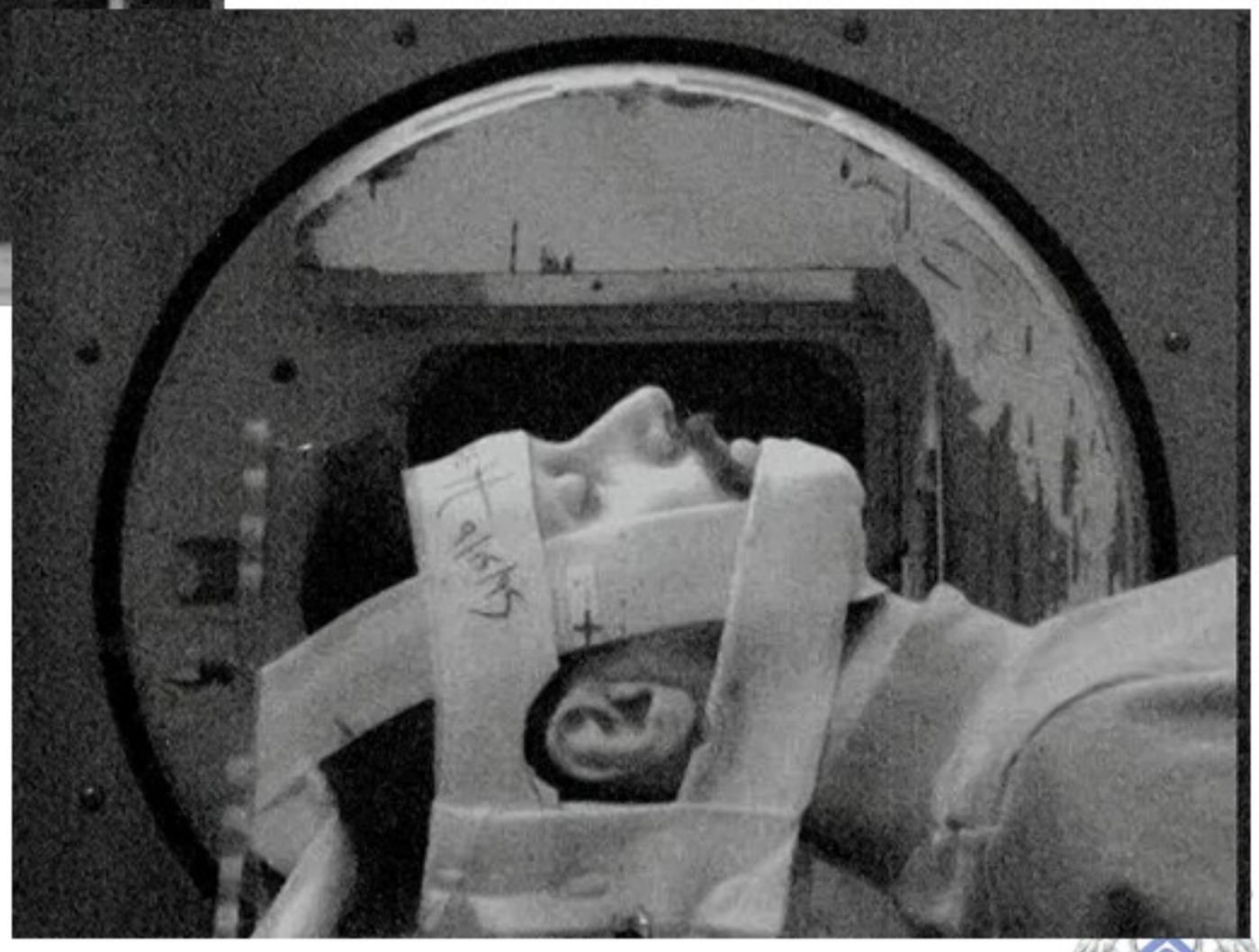
Multimodality/sensor: hybrid machines: PET/CTs, etc… mark II design



- non simultaneous
- different time scale (CT: few secs.; PT: several mins.)

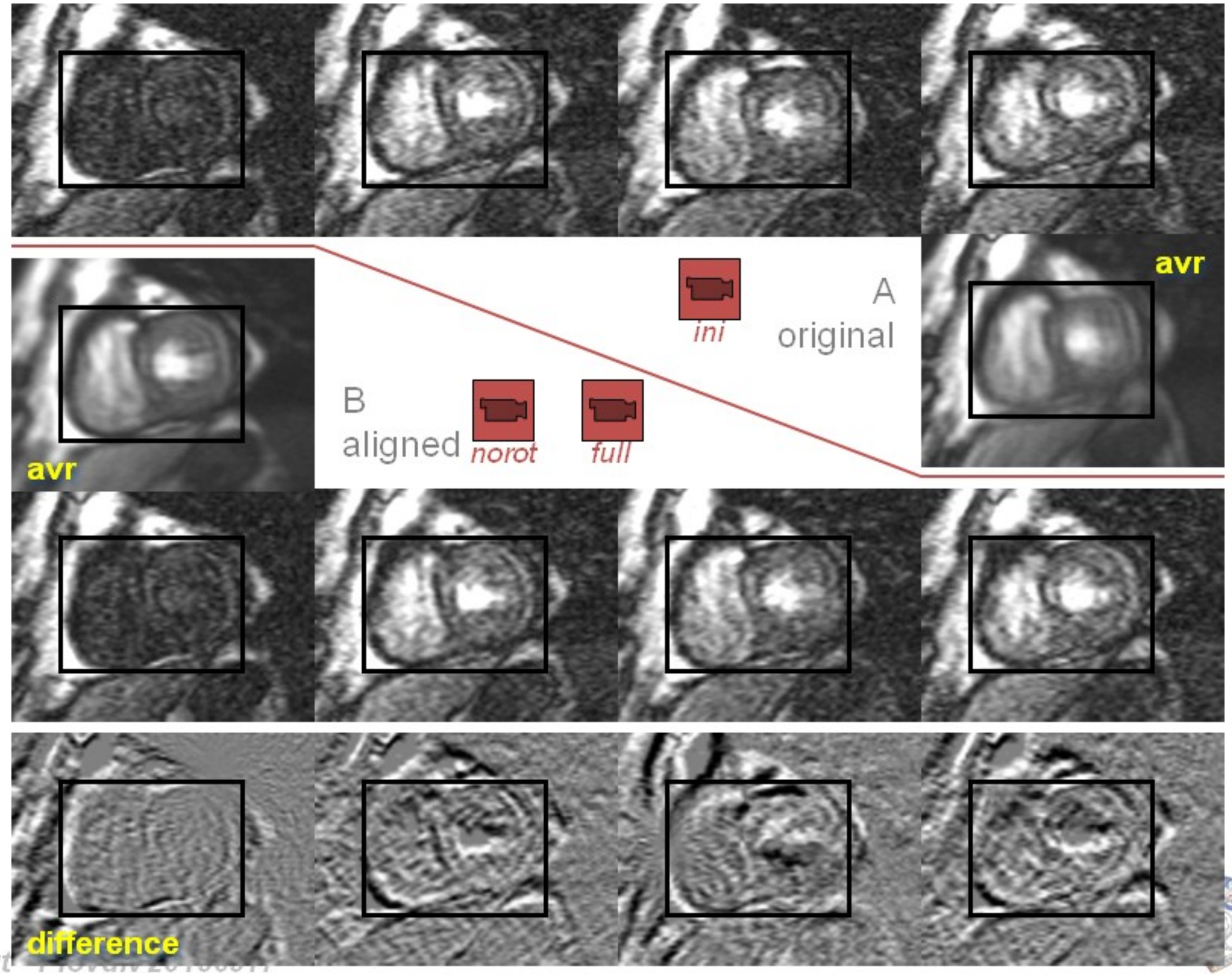
and motions…

Real need for registration? (motion…)



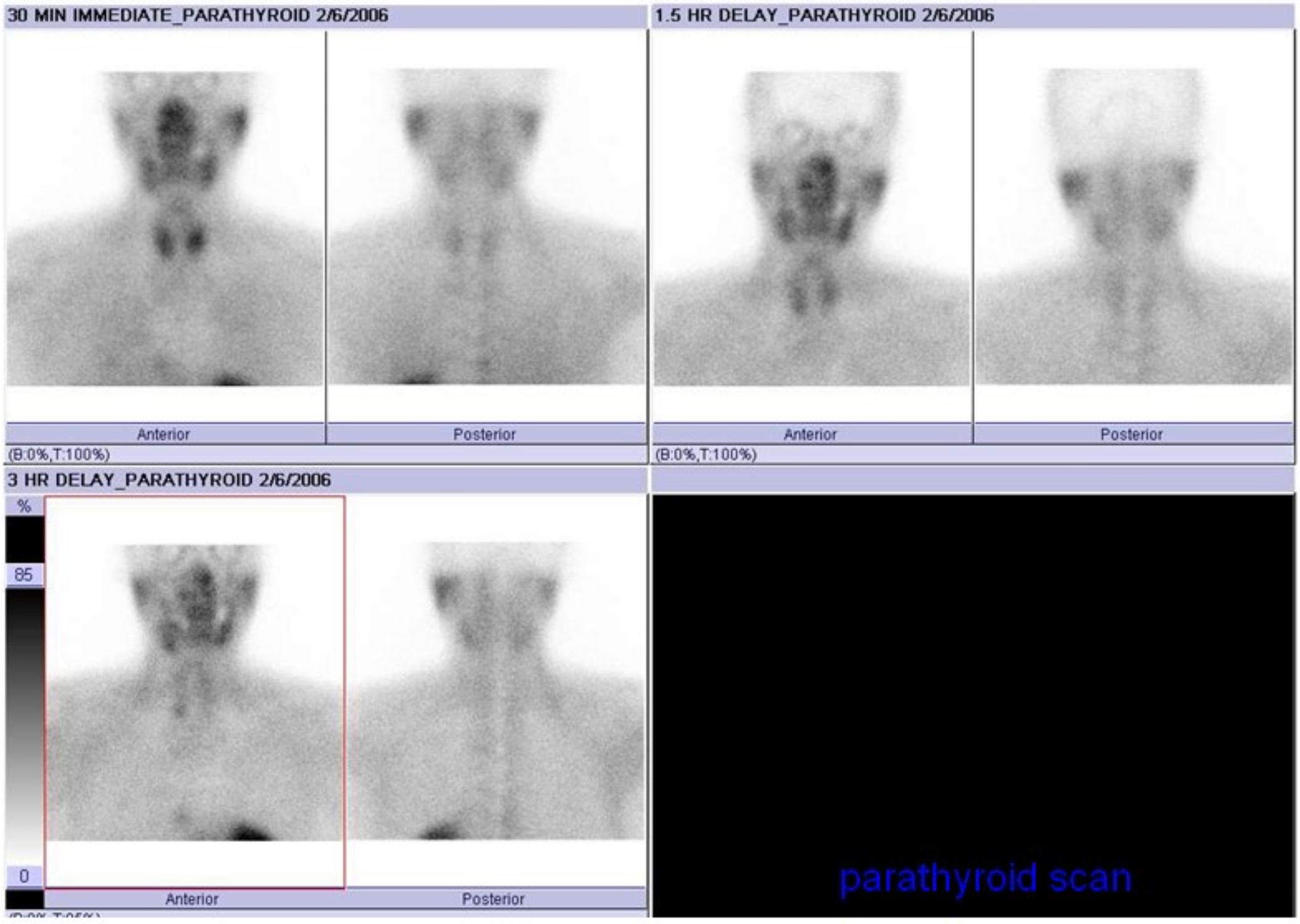
(courtesy University of Chicago)

Time based registration: breathing correction for cardiac MR *(MR courtesy HUG)*



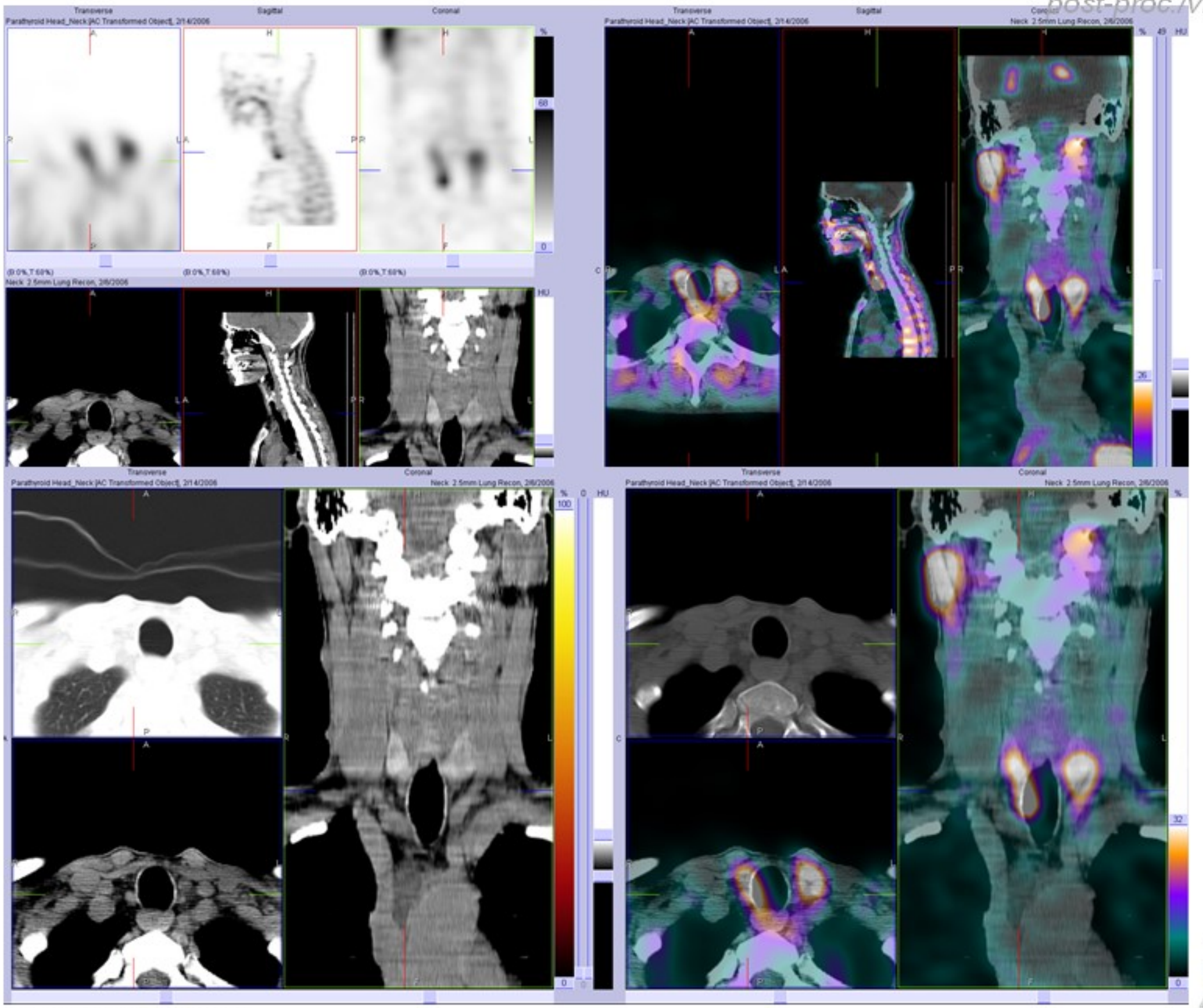
Parathyroid adenoma (KK)

(source data MDACC; post-proc./visu. LMB)



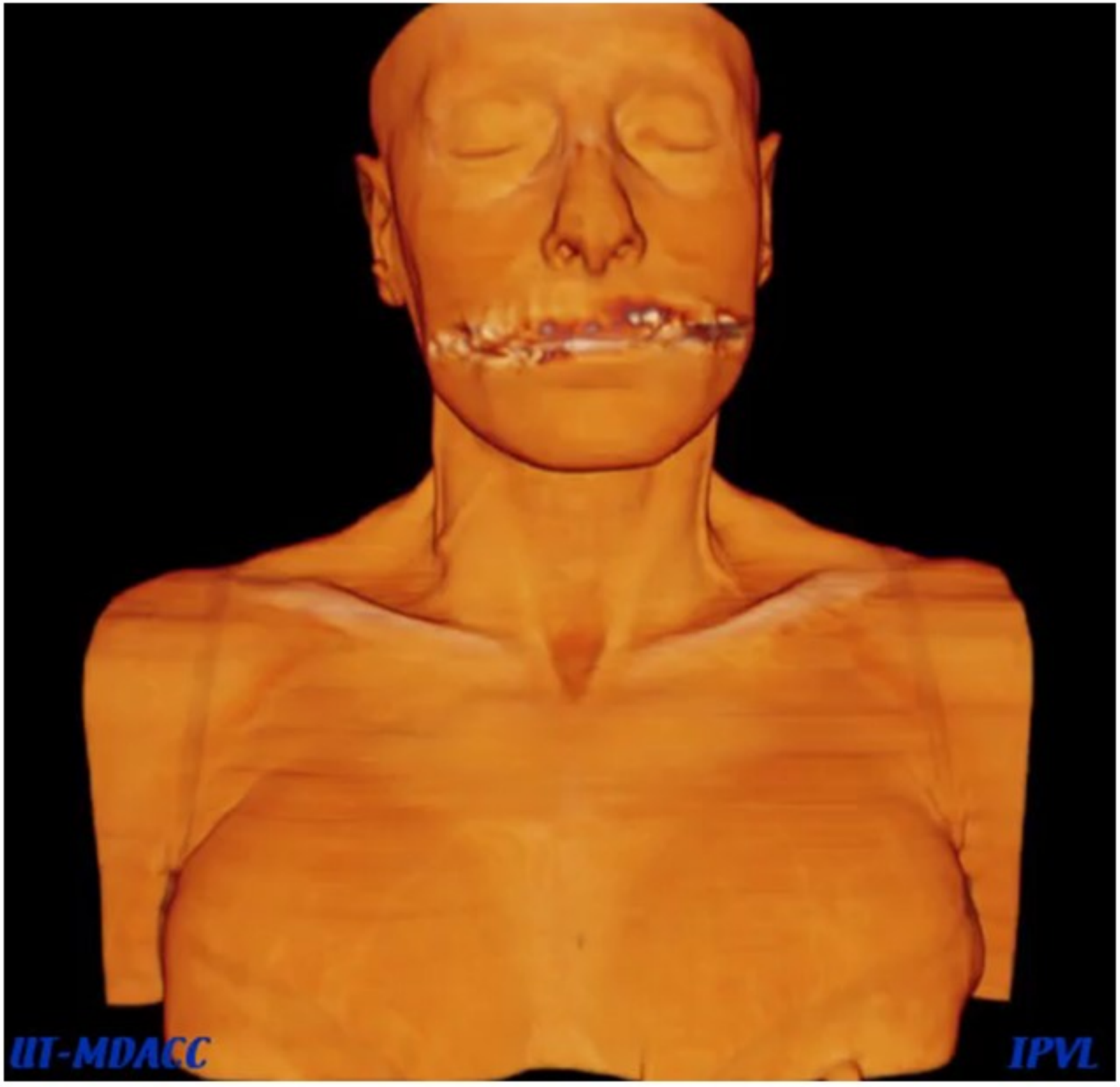
Parathyroid adenoma (KK; Tc-99M-sestamibi SPECT/CT)

(source data MDACC; post-proc./visu. LMB)



Parathyroid adenoma (KK; Tc-99M-sestamibi SPECT/CT)

(source data MDACC; post-proc./visu. LMB)



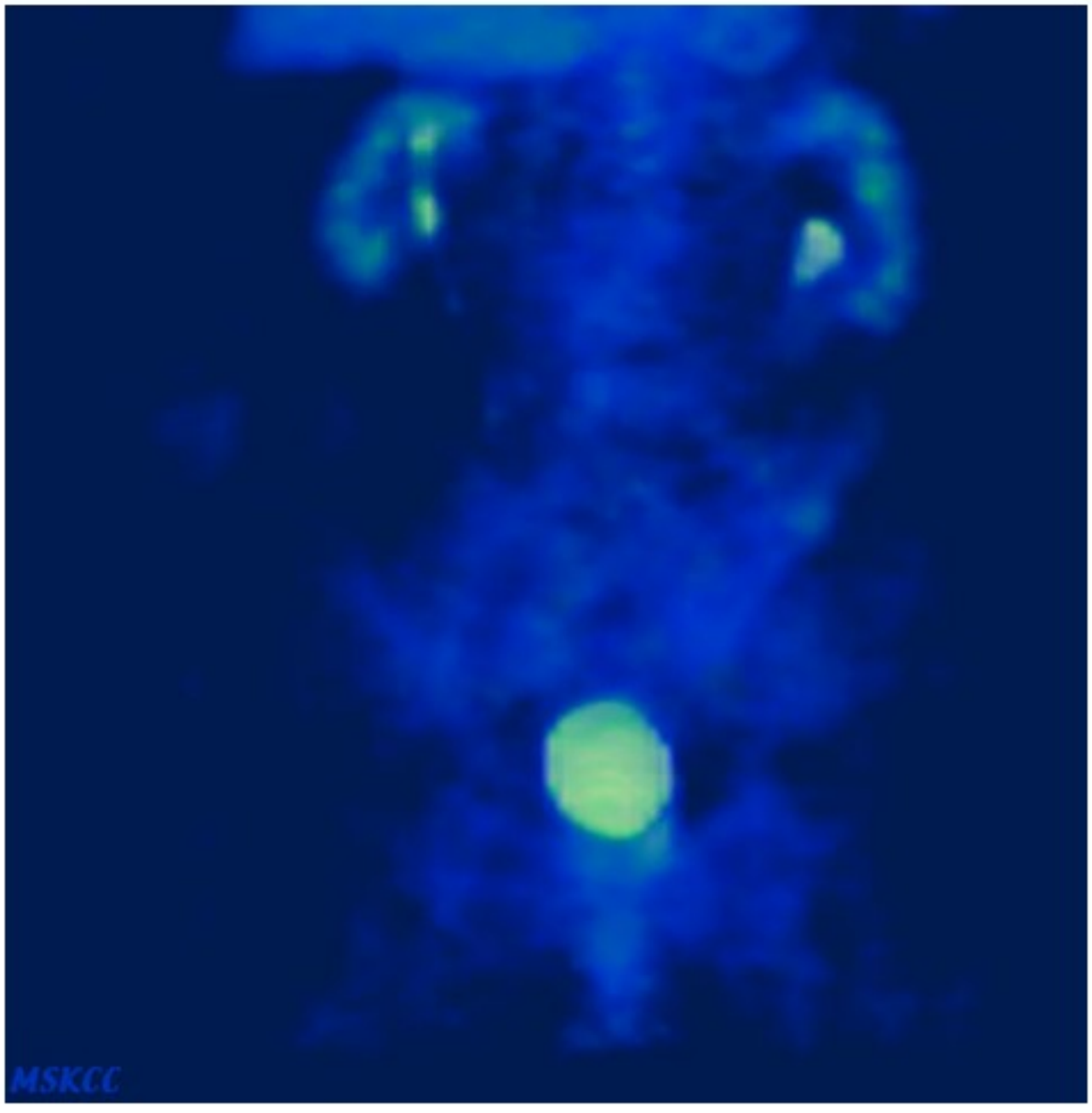
mip

vrRot

nav

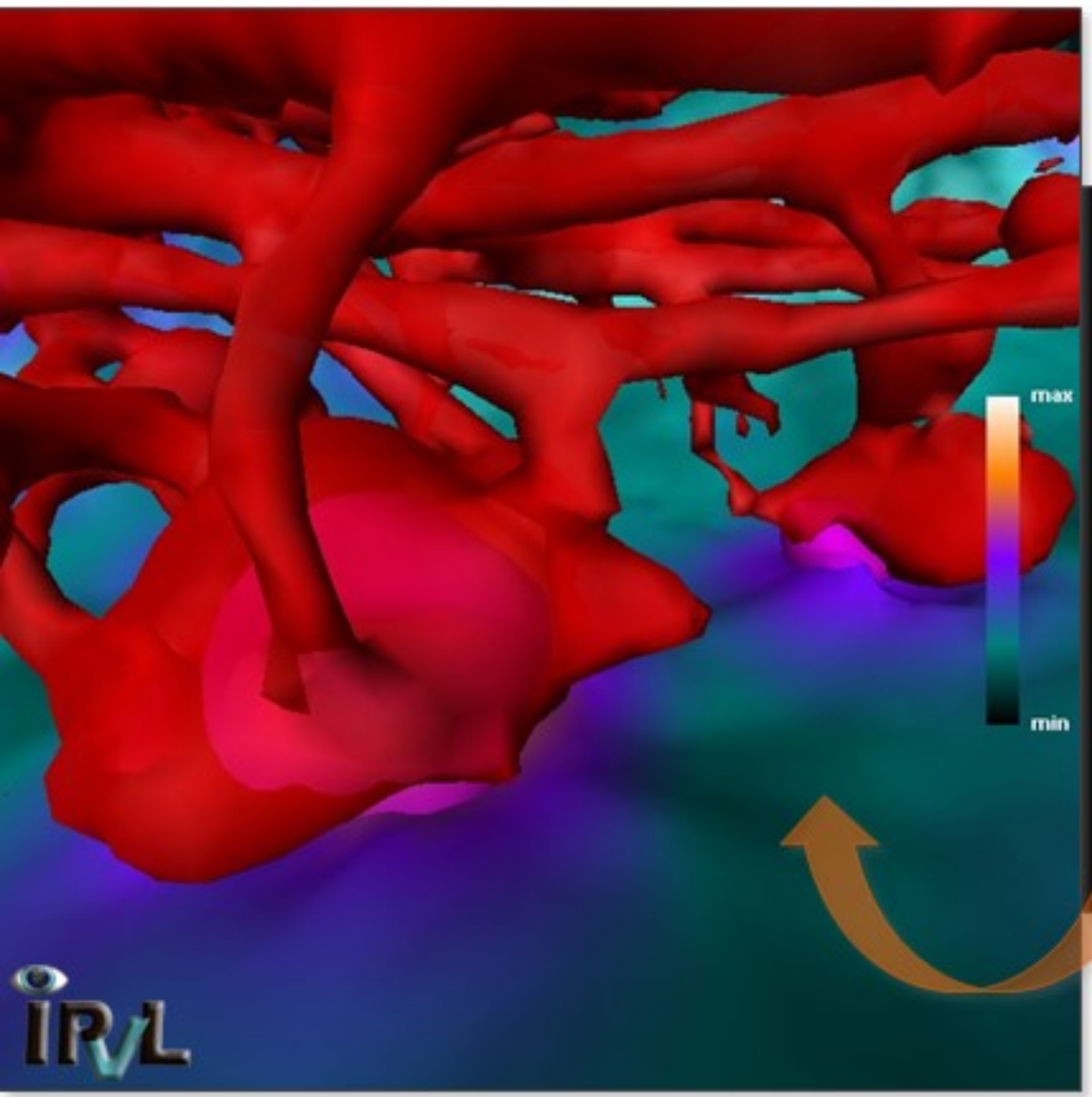
PET/CT: very first combined VR (prostate cancer with FDG)

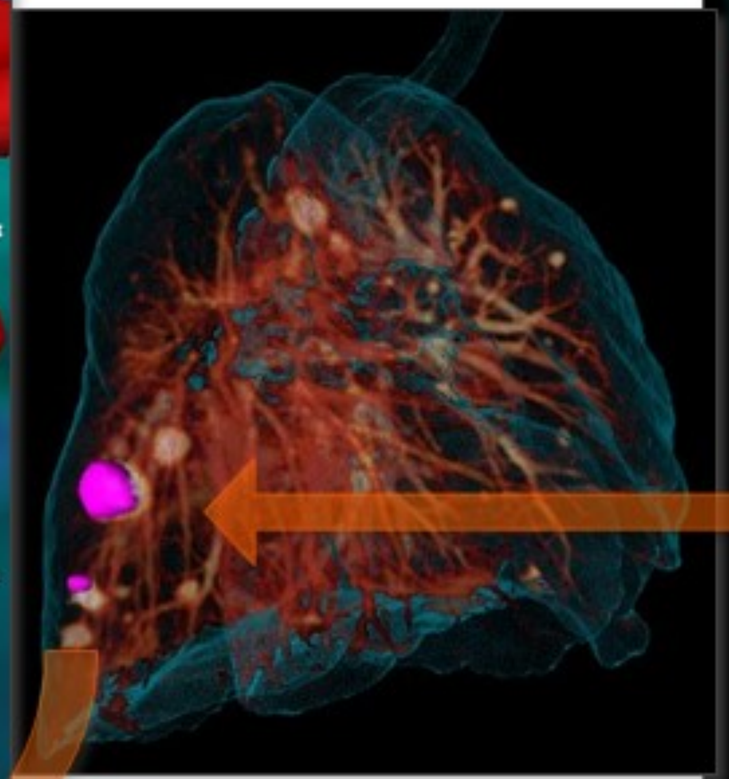
(source data SKCC; post-proc./visu. LMB)

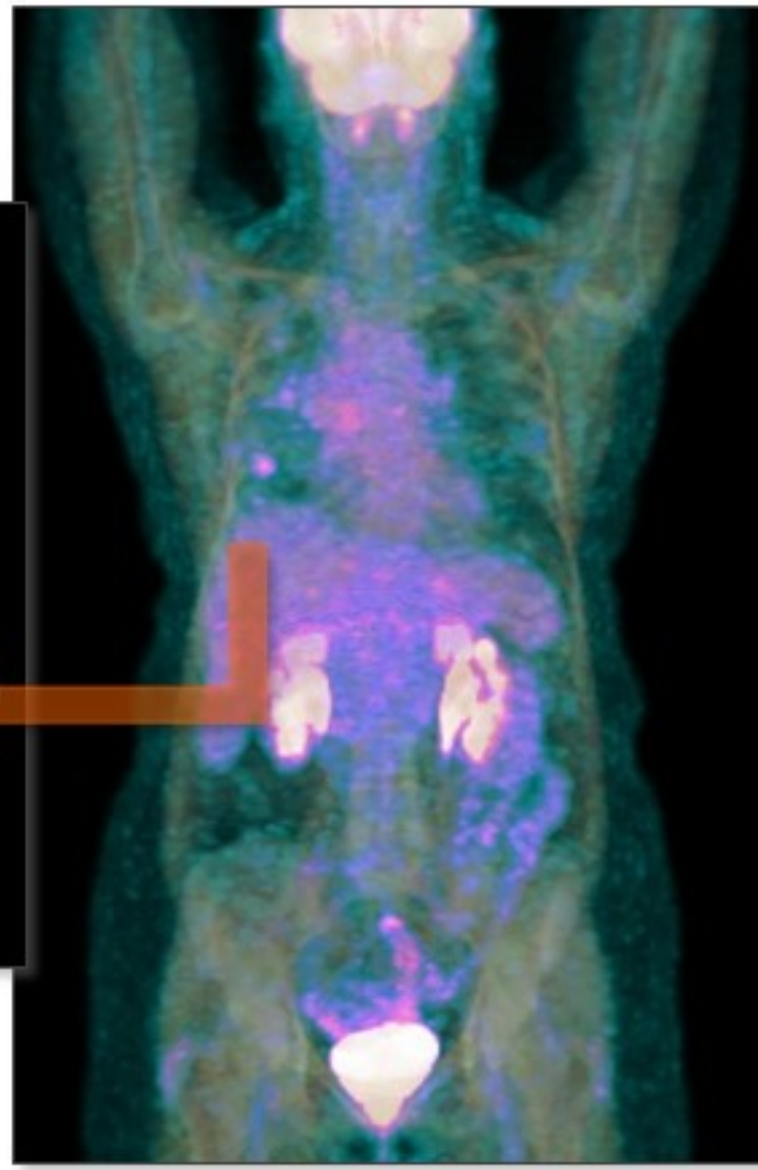


PET/CT in lung tumors

(source data MDACC; post-proc./visu. LMB)







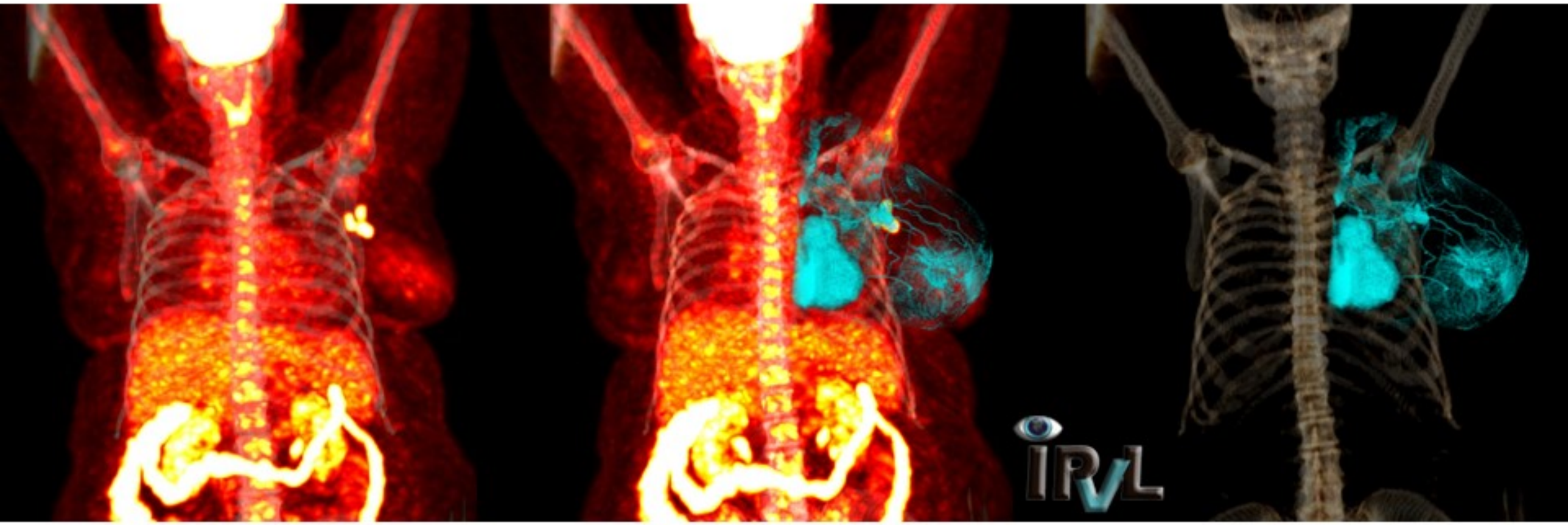
"...vessel co-option as a mechanism of acquired resistance to anti-angiogenic therapy and could have important implications including the potential therapeutic benefits of targeting vessel co-option in conjunction with vascular endothelial growth factor receptor signaling."

(from E.A. Kuczynski et al, J Natl Cancer Inst 108(8), 2016)

Organ (breast, etc.) specific (hybrid) imaging and fusion:

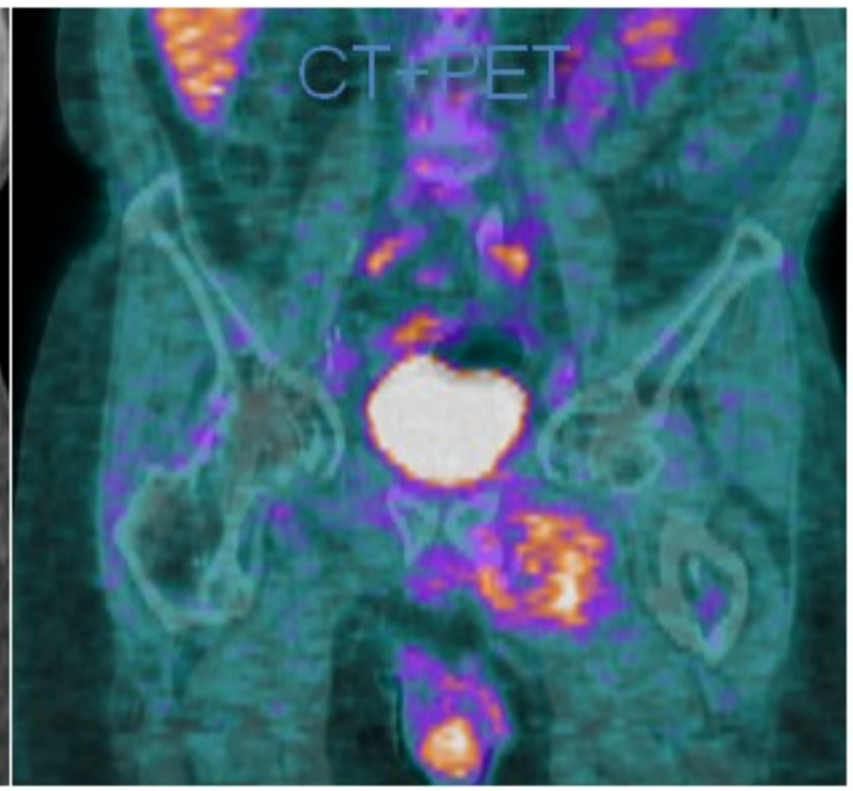
PET/CT + MR DCE

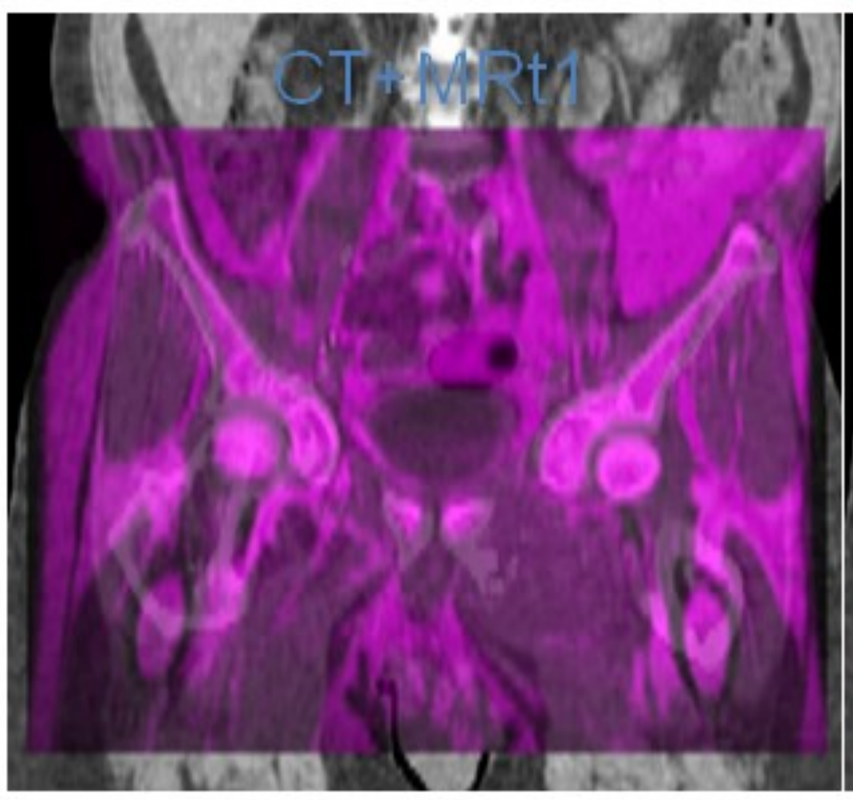
(source data MDACC; post-proc./visu. LMB)

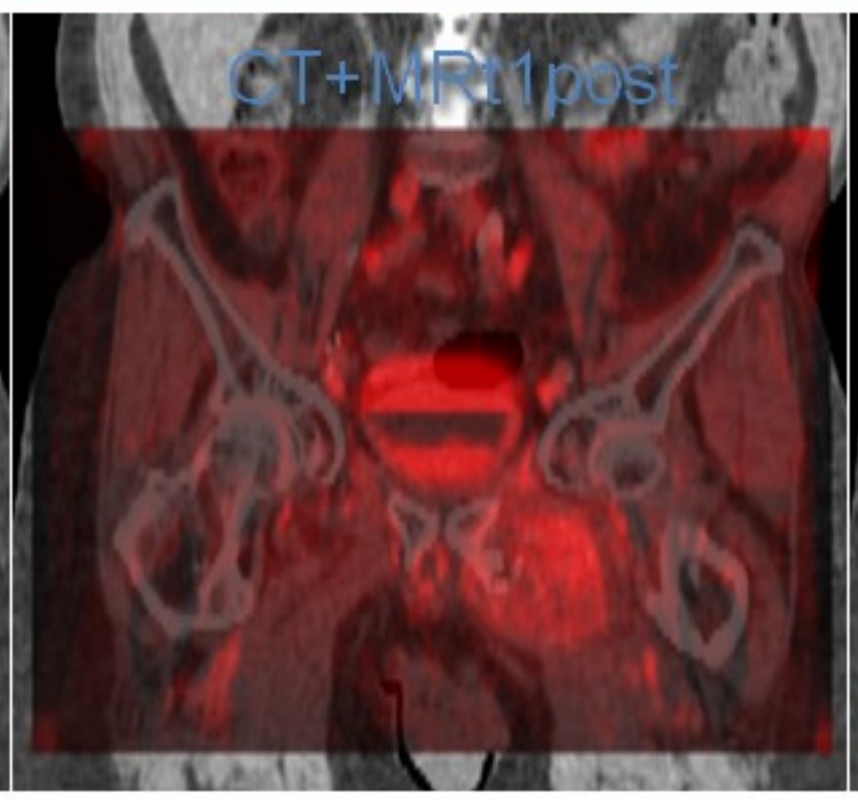


Suppress biopsies? (fr; osteosarcoma) - PET ; MR: T1, T1post, T2 ⇔ biopsy

(source data MDACC; post-proc./visu. LMB)







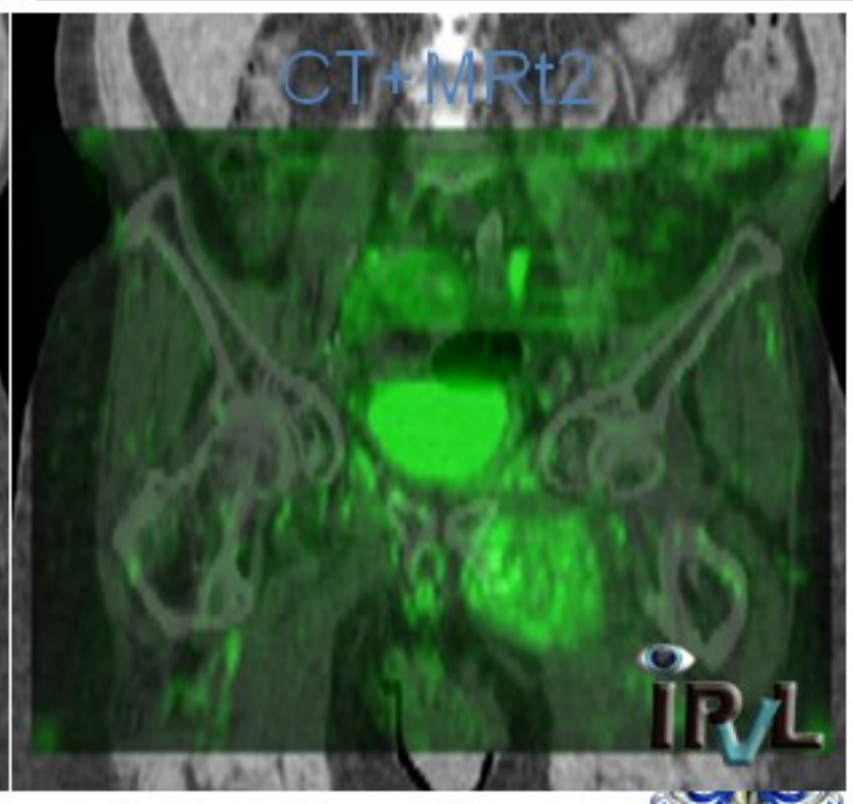
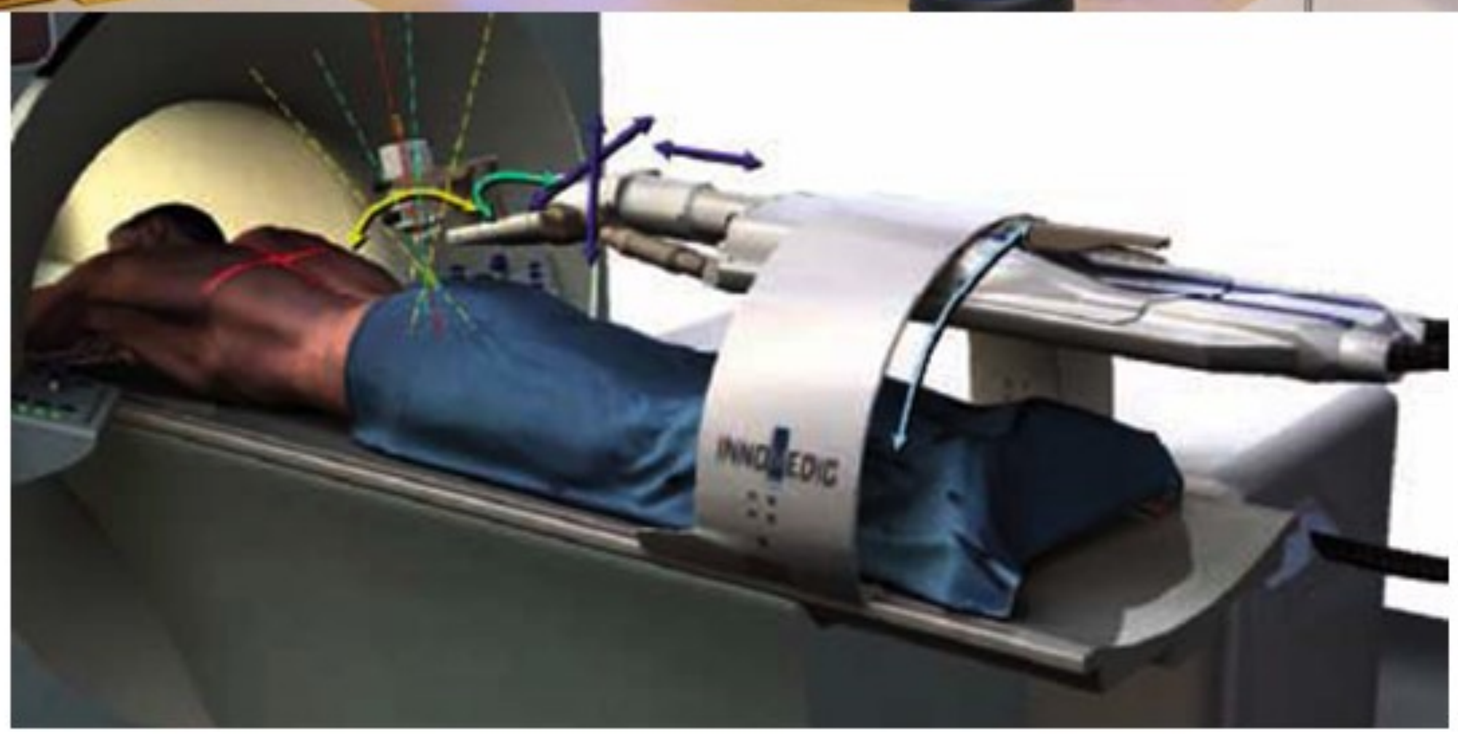
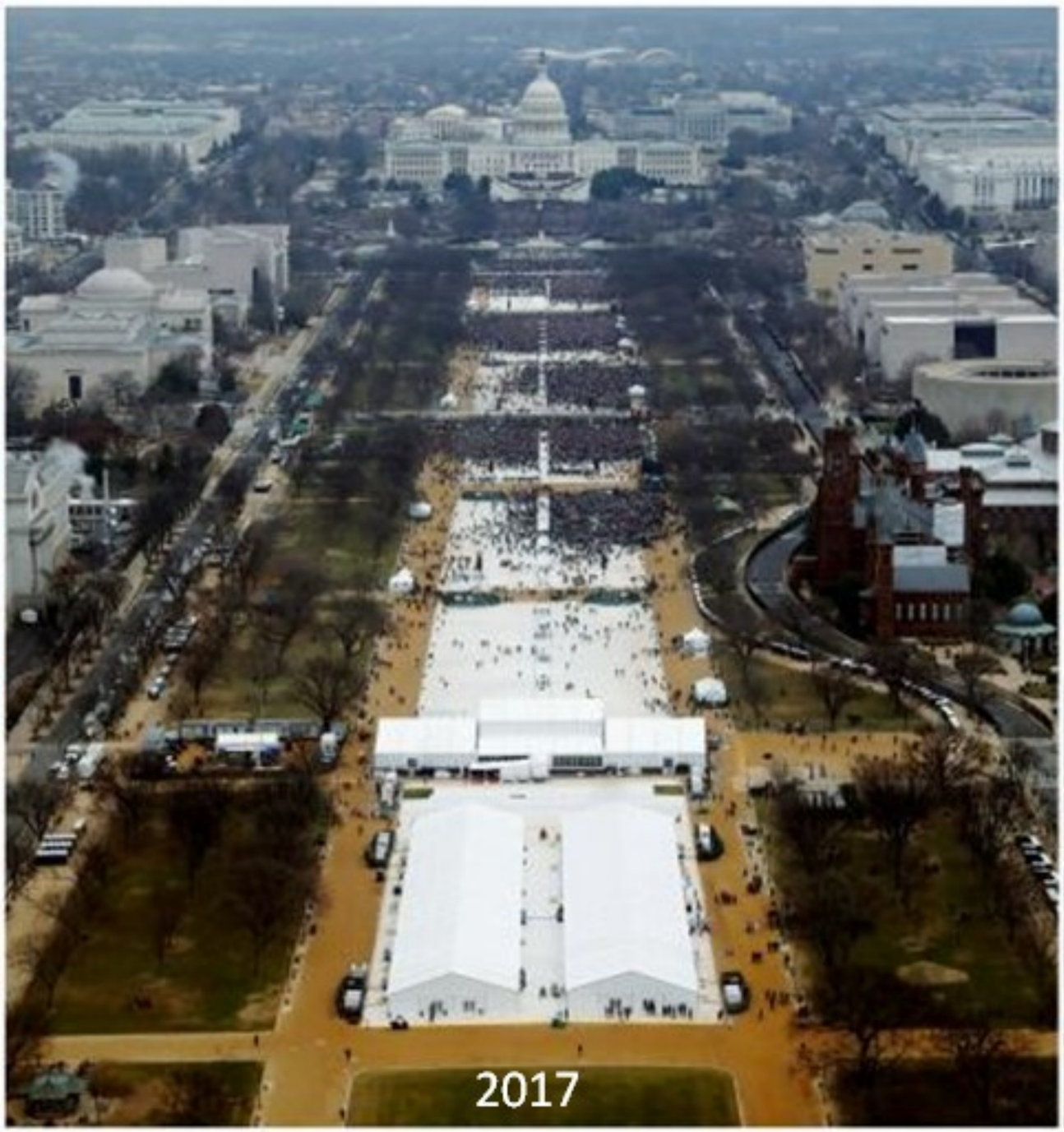


Image guidance: integrated navigation and "robots" + intra-op MM imaging
+ "real-time" monitoring of therapy (surgery, ablation, RT, etc) ⇔ one-stop-shops



Subjectivity...



... now ok in politics (aka "AltFacts"), but **to be avoided in clinical settings**...

=> Imaging as a biomarker!...

can we use imaging to better characterise disease and/or guide and assess therapy?

Imaging biomarkers for cancer ... in a nutshell ... V2

(LMB)

Physical, structural measurements: (CT, MR, U/S) *texture*

-"Direct": stereology, BMD, HU; DWI, ADC, DTI; elasto.

-Segmentation: shape, size (RECIST, WHO , volume), content

Physiology/function: (*CT, MR,* PET, SPECT)

-Motion (respiratory, cardiac, motility, etc.)

-Static uptake: contrast (CT,MR), SUV(PET)

-Dynamic uptake:

-multiphase imaging (CT, MR)

-DCE (MR, CT)

-PK (PET, MR)

relevant structures

PERCIST

contrast agent, tracer transport and evaluation, PK/PD model

Imaging + derived information

Visualisation

other (meta)data,

disciplines (bio, physio, histo, chem, physics, math,...),

species/models (preclinical)

translation

Radiomics Fingerprinting

Multimodality/sensor: (incl. time: motion and sequential/follow-up)

-CT, MR, PET, SPECT, U/S, *PA*

multi -Parametric maps

clincial application

Diagnosis, characterization

Prognosis, management

expertise/knowledge base, predictive model

Treatment planning, delivery, monitoring, follow-up

vector/payload transport, delivery, devices

simulation

TRA...

+ constant evolution & innovation...

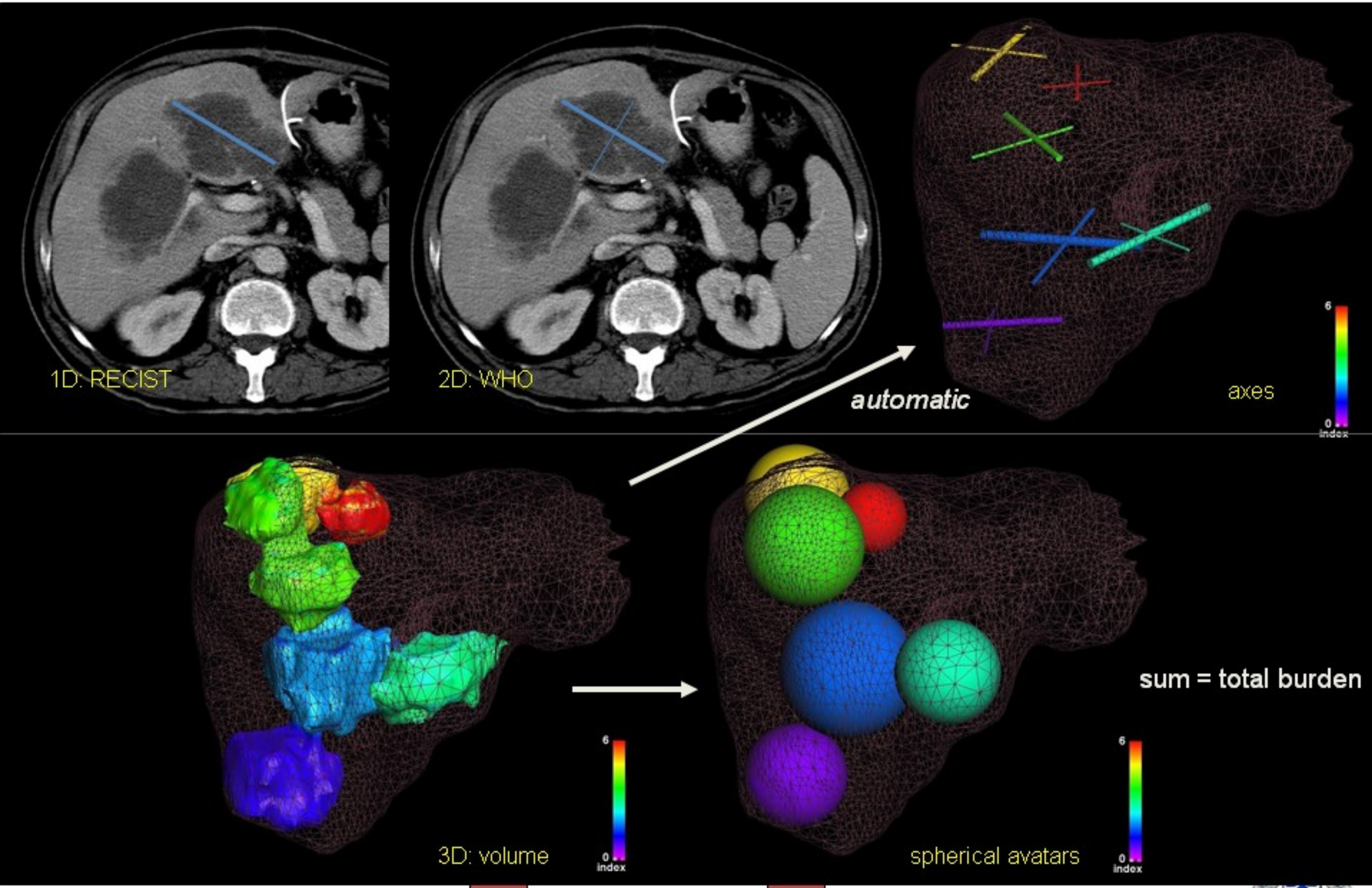
for every new approach and paradigm:

R&D, implementation, trials (evaluation, validation), exploitation

Therapy Response Assessment: morphological (baseline+follow-up)

(source data MSKCC; post-proc./visu. LMB)

(colorectal cancer + liver metastases) ***(RECIST: Response Evaluation Criteria In Solid Tumors)***



Therapy Response Assessment: morphological (baseline+follow-up)

(source data MSKCC; post-proc./visu. LMB)

(colorectal cancer + liver metastases) ***(RECIST: Response Evaluation Criteria In Solid Tumors)***

% change
shrinkage: max to min

RECIST
1D: -33 to -26

WHO
2D: -54 to -46

volume
3D: -74 to -55

baseline

follow-up (+65 days)

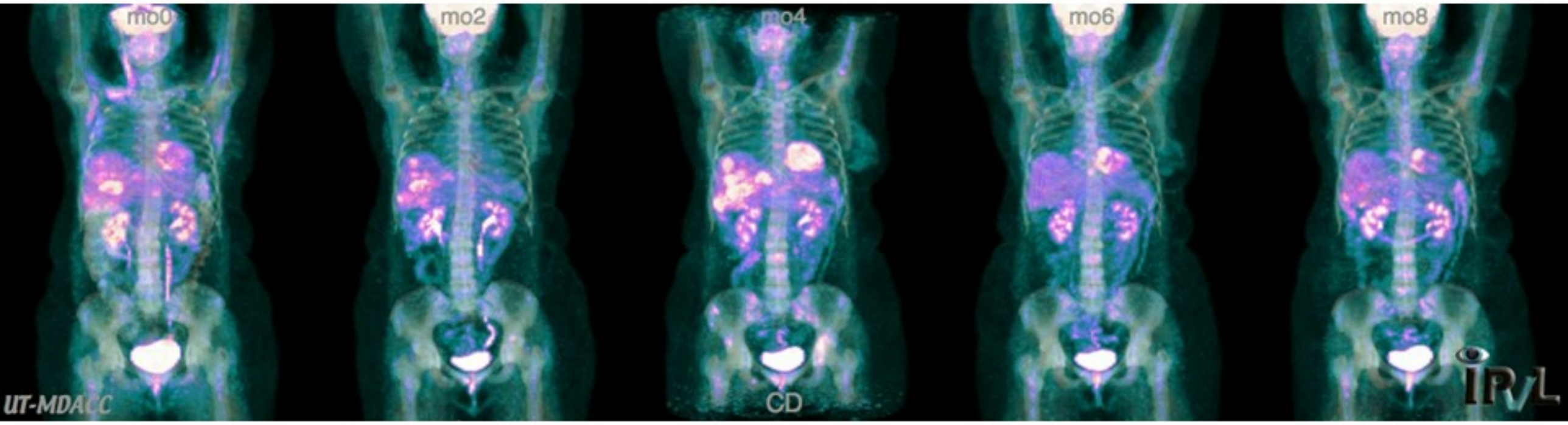
doubling time (days)
shrinkage: min to max 3D: -56 to -34

Therapy response: functional (breast cancer mets and chemoT)

(source data MDACC; post-proc./visu. LMB)

no response
=> change of regimen

therapy A *therapy B*



time + therapy

"Q"AI: Standard Uptake Value (or SU Ratio)

(cf Ludwig Strauss, 80's)

$$SUV = \frac{\text{mean activity within a ROI (mCi/ml)}}{\text{injected dose (mCI)/body mass (kg)}}$$

variations: use *body surface area* or *lean body (mass)weight*

PERCIST
(cf Richard Wahl, 2009)

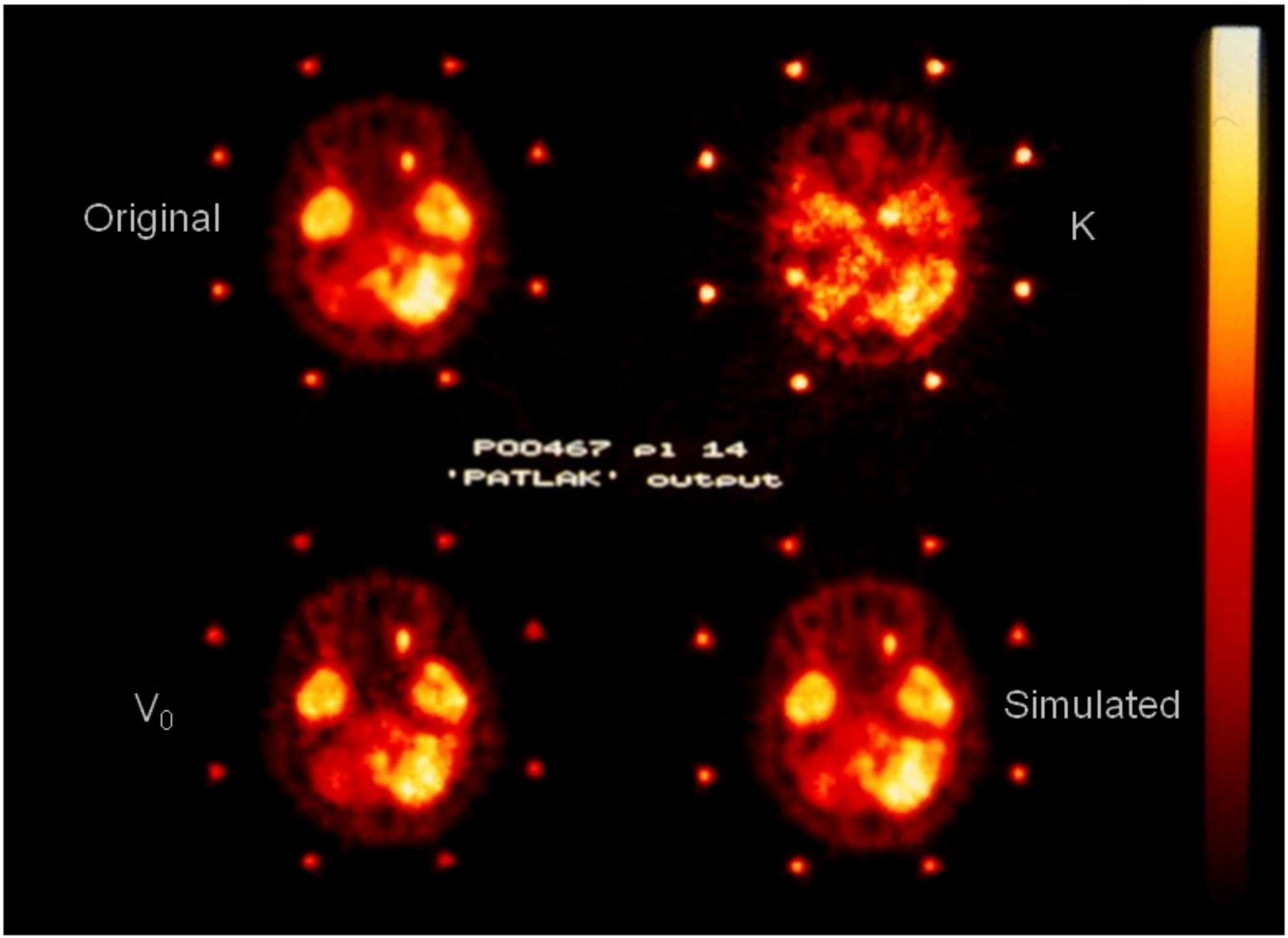
SUV is affected by:

- plasma glucose levels
- time between administration and acquisition
- body weight or surface area
- size of ROI
- resolution of scanner and patient motion
  (<=> blurring and PVE)
- actual definition

SUV < 2.0 ≈> benign lesion
> 2.0 ≈> malignant lesion
(2.0 ≈ blood pool activity)

QAI: parametric imaging - FDG PET (Patlak: $R(t) = K \int_0^t C_p(\tau)\, d\tau + V_0 C_p(t)$)

k4=0 => K≈k2k3/(k2+k3)



but still seldom implemented in the clinic (logistics, throughput, …)

except for MR-DCE

(source data ULB; post-proc./visu. LMB)

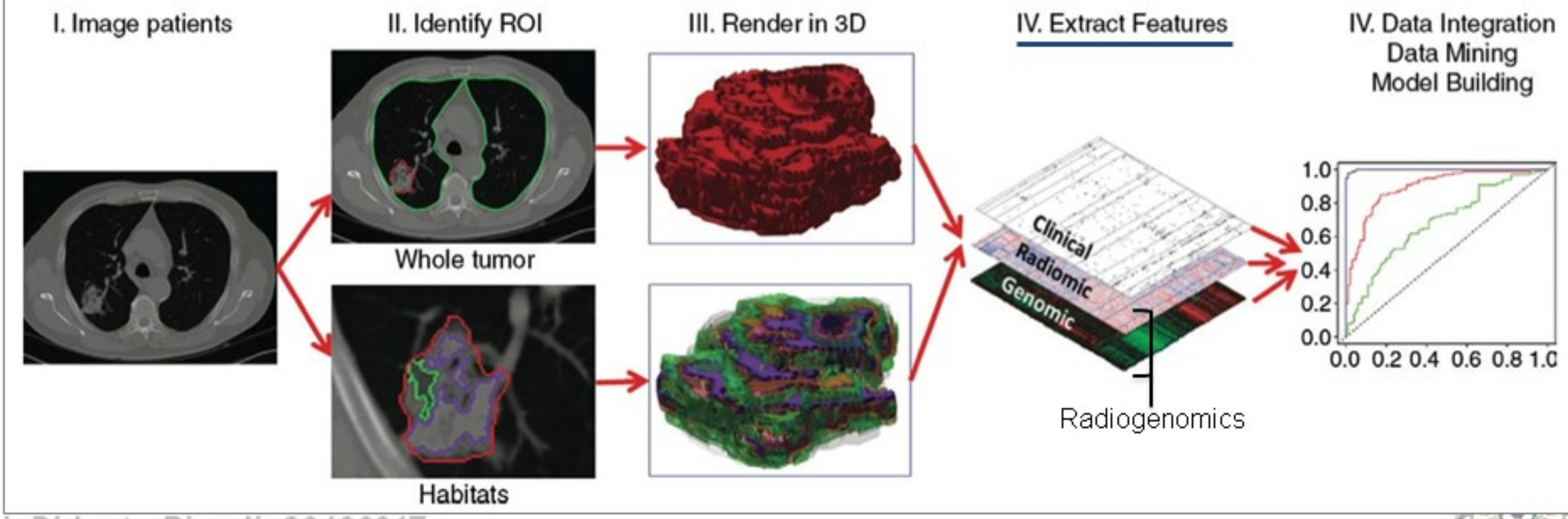
Radiomics: definition, principle

(from R. Gillies et al, Radiol 278(2), 2015)

"Radiomics" = extraction and analysis of large amounts of **advanced quantitative imaging features** from medical images, including standard-of-care images ⇔ very large potential subject pool.
Radiomics data are in a mineable form that can be used to build **descriptive and predictive models** relating image features to **phenotypes** or gene–protein signatures. The core hypothesis of radiomics is that these models, which **can include biological or medical data**, can provide valuable **diagnostic, prognostic or predictive information**. *(adapted from V. Kumar et al, 2012)*

- **semantic:** through radiologist's visual assessment
- **agnostic:** mathematically derived

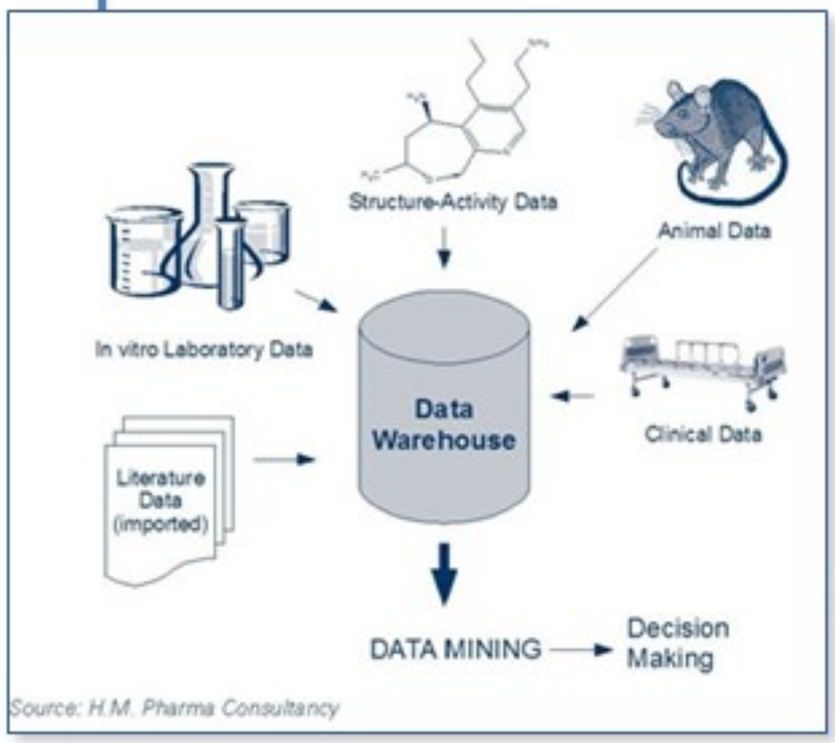
Semantic	Agnostic
Size	Histogram (skewness, kurtosis)
Shape	Haralick textures
Location	Laws textures
Vascularity	Wavelets
Spiculation	Laplacian transforms
Necrosis	Minkowski functionals
Attachments or lepidics	Fractal dimensions



Biomedical translation: the case of drug discovery and development...

target discovery | target validation | lead discovery | lead validation | lead optimization | preclinical proof of concept | preclinical development | clinical trials

Basic — Translational — Clinical



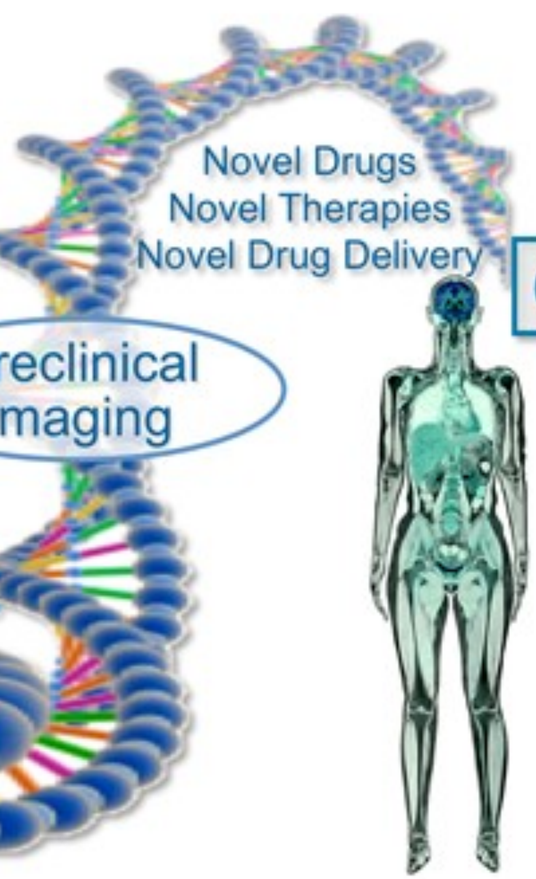
Source: H.M. Pharma Consultancy

Fundamental Biological Research

Animal Models
Pathology
Biochemical Analysis
Modelling and Bioinformatics
DMPK
Genetics

Preclinical Imaging

Novel Drugs
Novel Therapies
Novel Drug Delivery

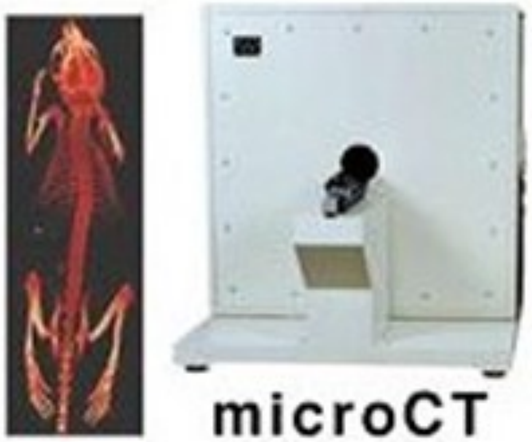


Clinic

©SD-LB

MM (structural and molecular) animal imaging

(courtesy CIMI)



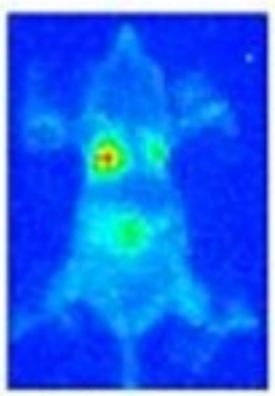
microCT

microPET

microSPECT

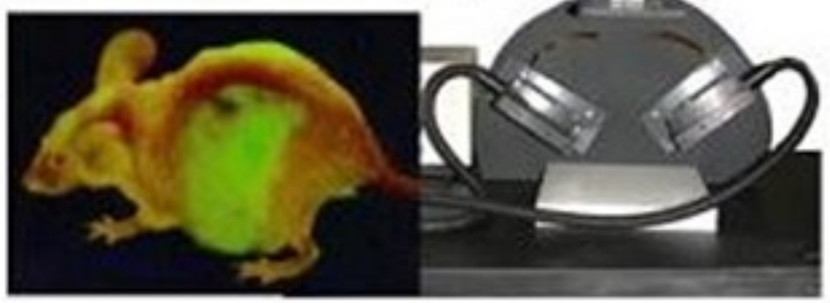
Animal MRI

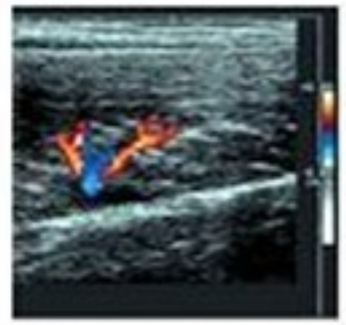
Autoradiography



Bioluminescence

Fluorescence



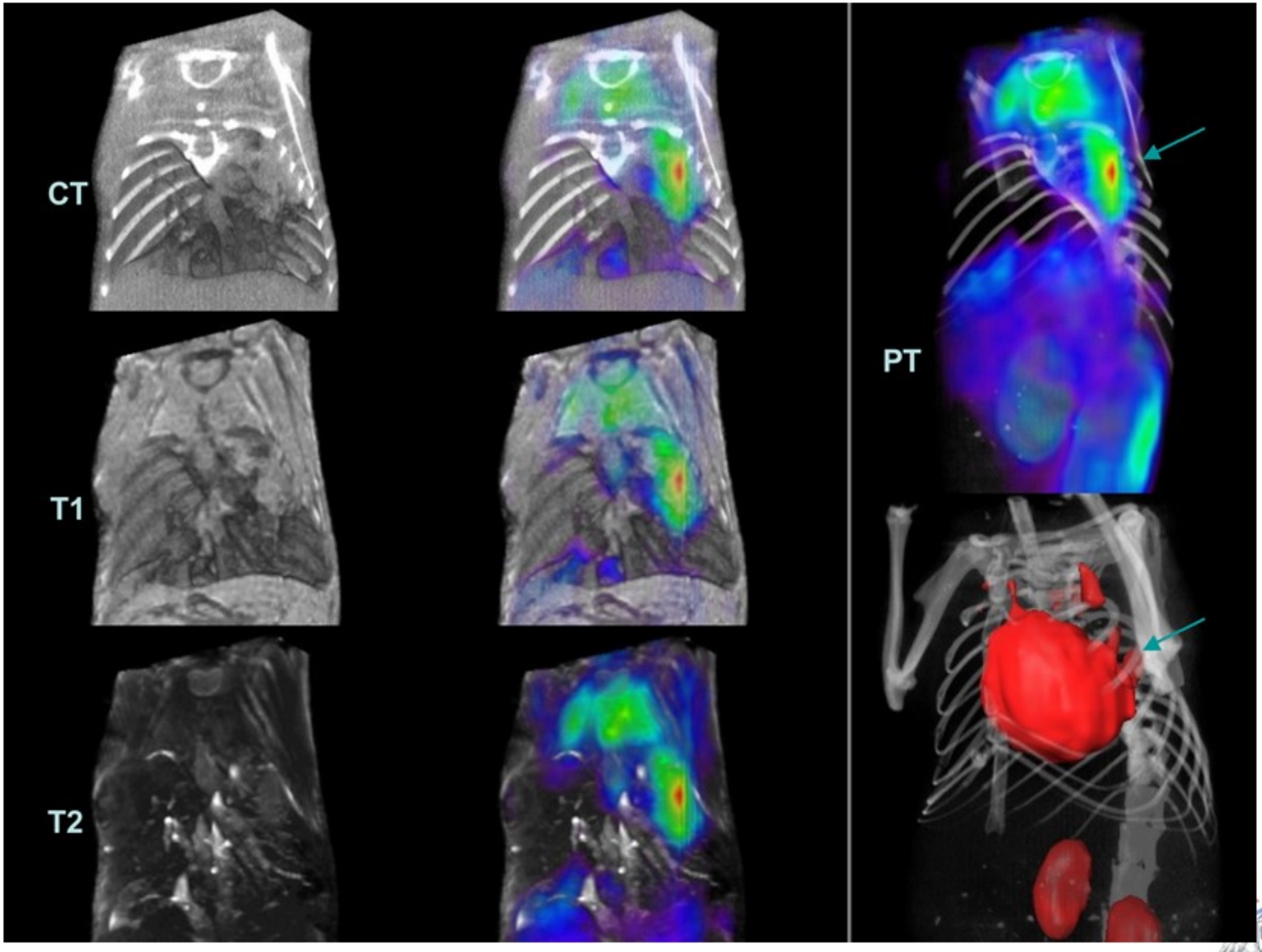


Ultrasound

(+ PhotoAcoustic, etc)

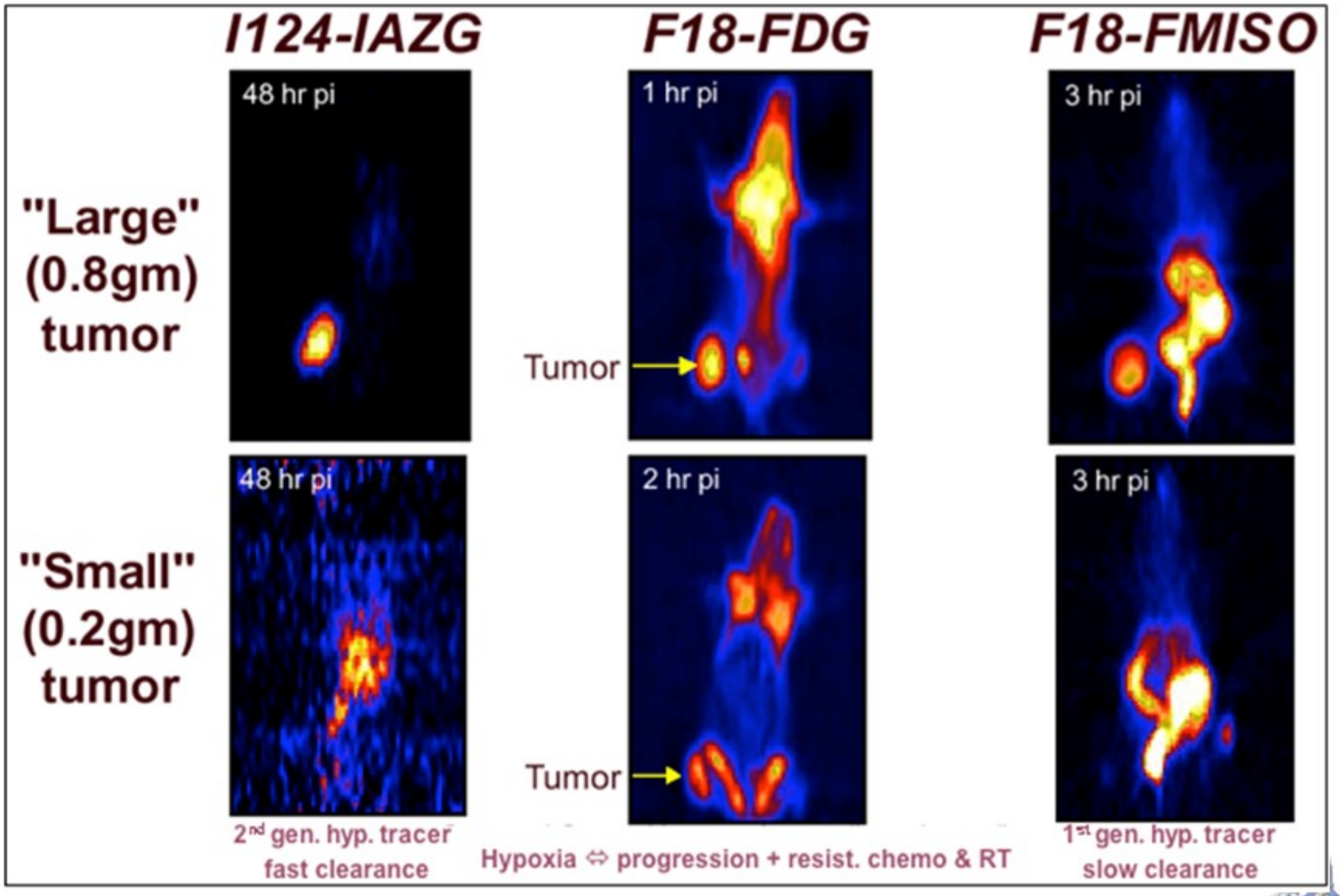
µMM (CT, MR and PET) of a mouse lung tumor

(source data + collab. J. Kurie, MDACC; post-proc./visu. LMB)



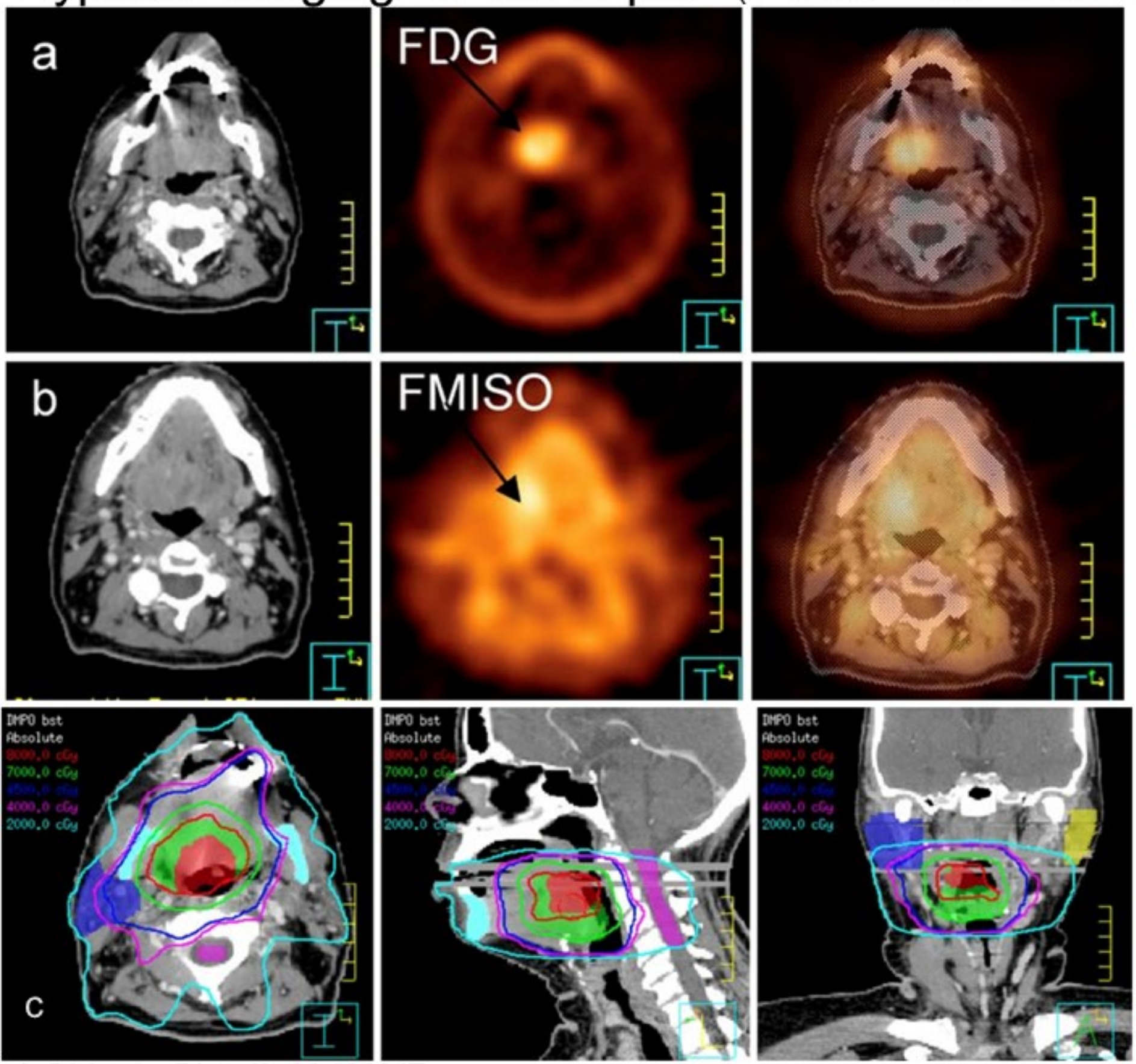
µPET mouse imaging: multiple hypoxia tracers ⇔ contenders

(courtesy SKI-MSKCC)



radioactive half life: ^{18}F: 109.8min; ^{124}I: 4.2d

Hypoxia imaging for IMRT plan (F-MISO = 18F-misonidazole)



From: J.G. Rajendran et al. Eur J Nucl Med Mol Imaging, 2006. 33:S44–S53

CT/PET: (a) FDG uptake of primary tumor, (b) FMISO uptake (hypoxic subvolume of primary tumor)

(c) MPR of isodose map (IMRT plan) superimposed to CT.

Primary FDG PTV (green) was treated to 70 Gy.

FMISO PTV (red) was treated with an additional 10-Gy boost in a consecutive plan.

Ipsilateral parotid gland (blue) receives <40 Gy to 40% of its volume.

Contralateral parotid gland (yellow) receives <20 Gy to 20% of its volume.

Mandible (sky blue) constrained to <70 Gy.

Cord (pink) constrained to <45 Gy

The future?...

"The future is here. It's just not widely distributed yet."
William Gibson, writer

...will likely build on the past and present...

"The best way to predict the future is to create it."
Abraham Lincoln, former US President

Dual(multi)-energy CT: => material decomposition => virtual (un)enhanced, monochromatic (to minimize pseudo-enhancement) and iodine map images

C's 14HU < B's 31HU ⇔ B's pseudoenhancement minimized => **cyst**

A+B => initial cyst diagnosis; but C's iodine enhancement > **cystic RCC**

(from A. Mileto et al, AJR 204, 2015)

More/better probes (PET tracers for cancer as exemple, etc.)

System	Ligand
Glucose metabolism	18F-FDG
Lipid metabolism	11C-acetate
Nucleic acid metabolism	18FUdR (uridine)
Amino acids	11C-Methionine
	11C-Tyrosine
	18F-FMT
	18F-FET (fluoro ethyl tyrosine)
Hypoxia	18F-FMISO (fluoro misonidazole)
	64Cu-ATSM
	124I-IAZG
	18F-FAZA
Proliferation	18F-FLT (fluoro deoxy thymidine)
	11C-Thymidine
	18F-FMAU
Bone mets	18F-NaF

also: 11C-Leucine, Monoclonal AntiBodies (mAb's), etc.

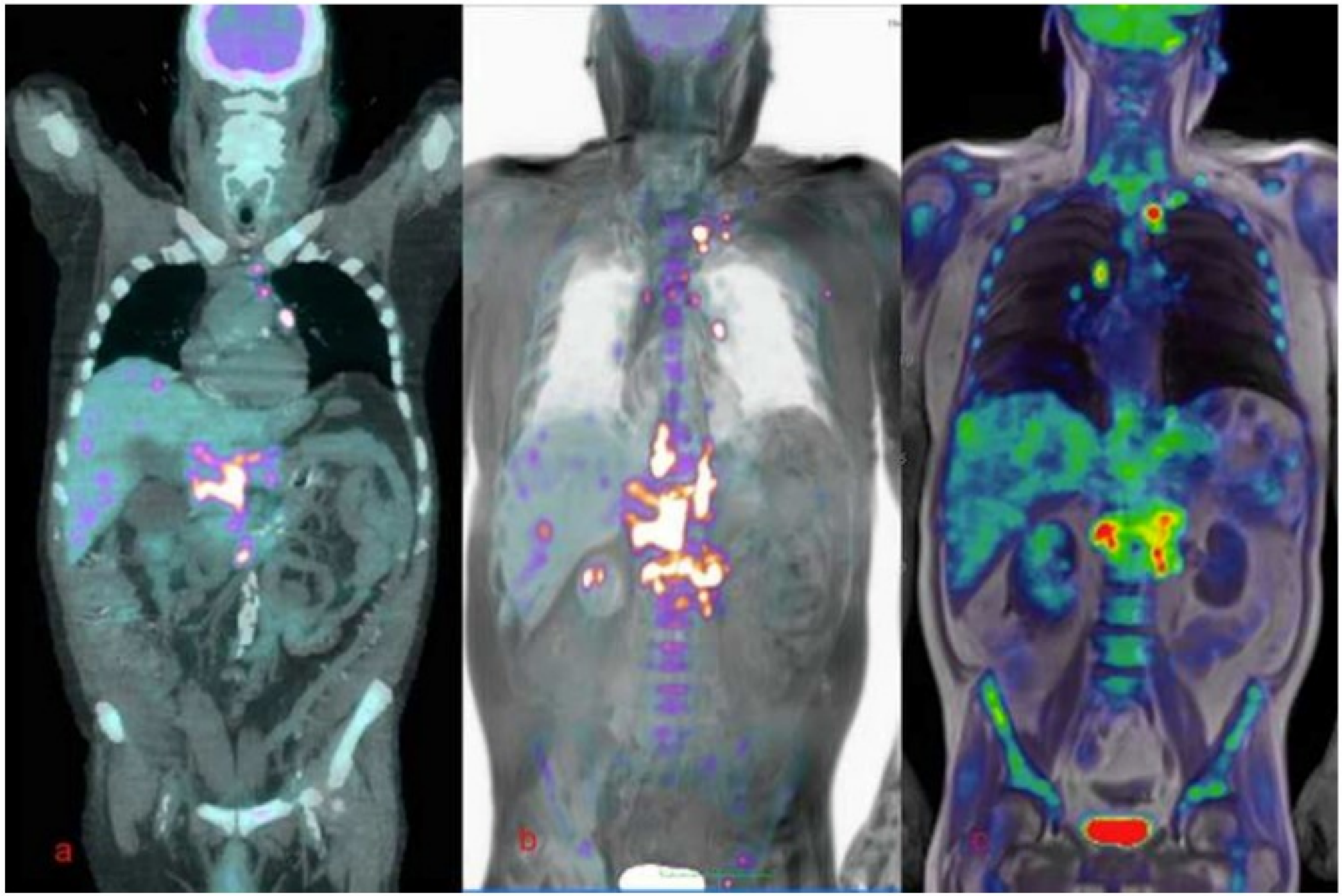
radioactive half life: 11C: 20.4min; 18F: 109.8min; 64Cu: 12.7h; 124I: 4.2d

"The future of PET and NM is in probes, not instrumentation"

Mike Phelps, famous PET pioneer

More/better integration via hybrids and exploitation thereof

PET/CT & PET/MR (also SPECT/CT, etc.)

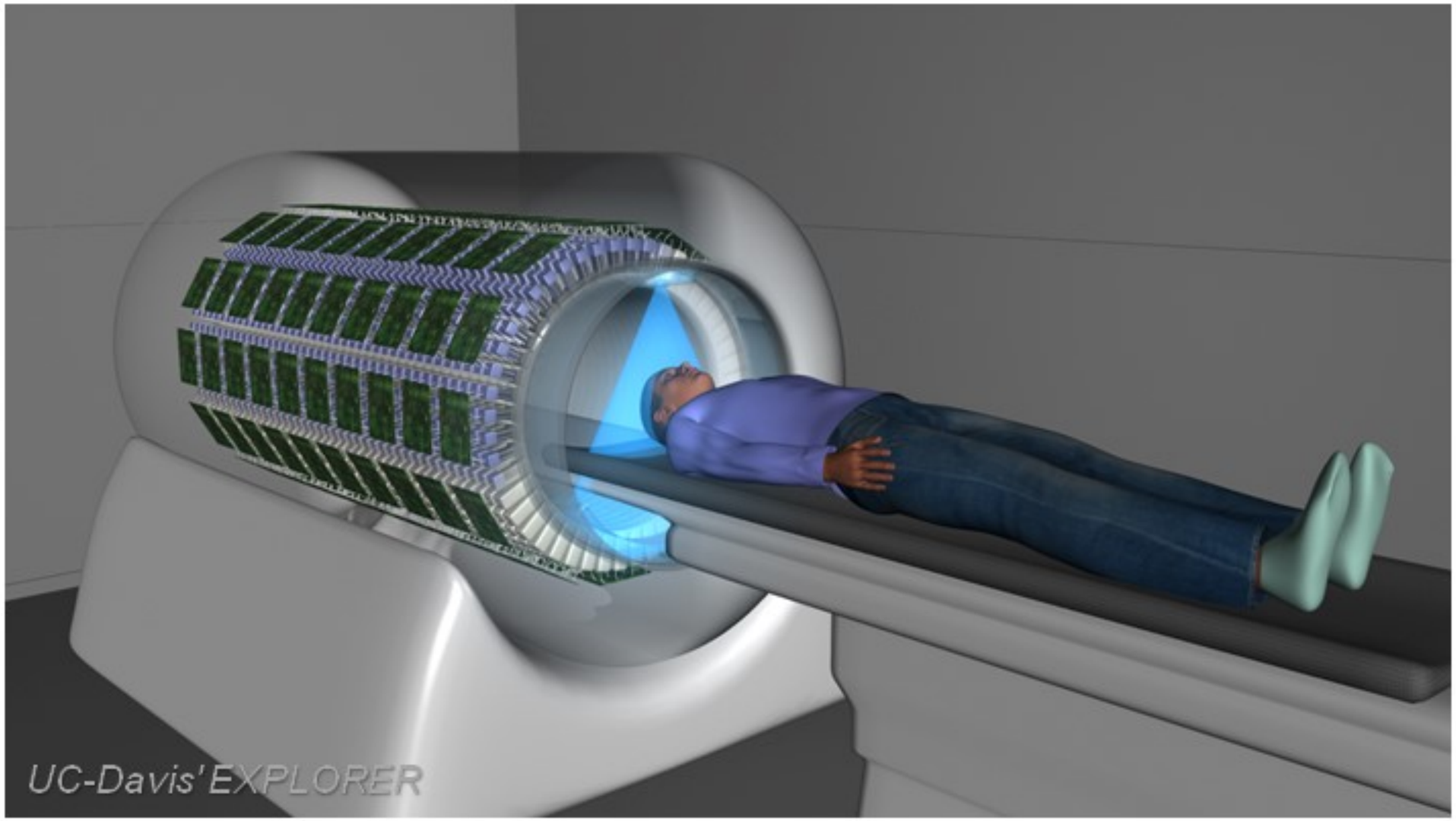


18F-FDG PET CT scan (thick MPR) (a) shows multiple confluent nodes above and below the diaphragm. Multiple liver lesions are also seen. Cross sectional PET-MRI (b) MIP and (c) volume rendered reconstruction show similar appearances.

(from F. Fraioli et al. The British Institute of Radiology, Nov 2013)

Truly whole body (and beyond…)

=> opportunity/challenge of new metrics & paradigms



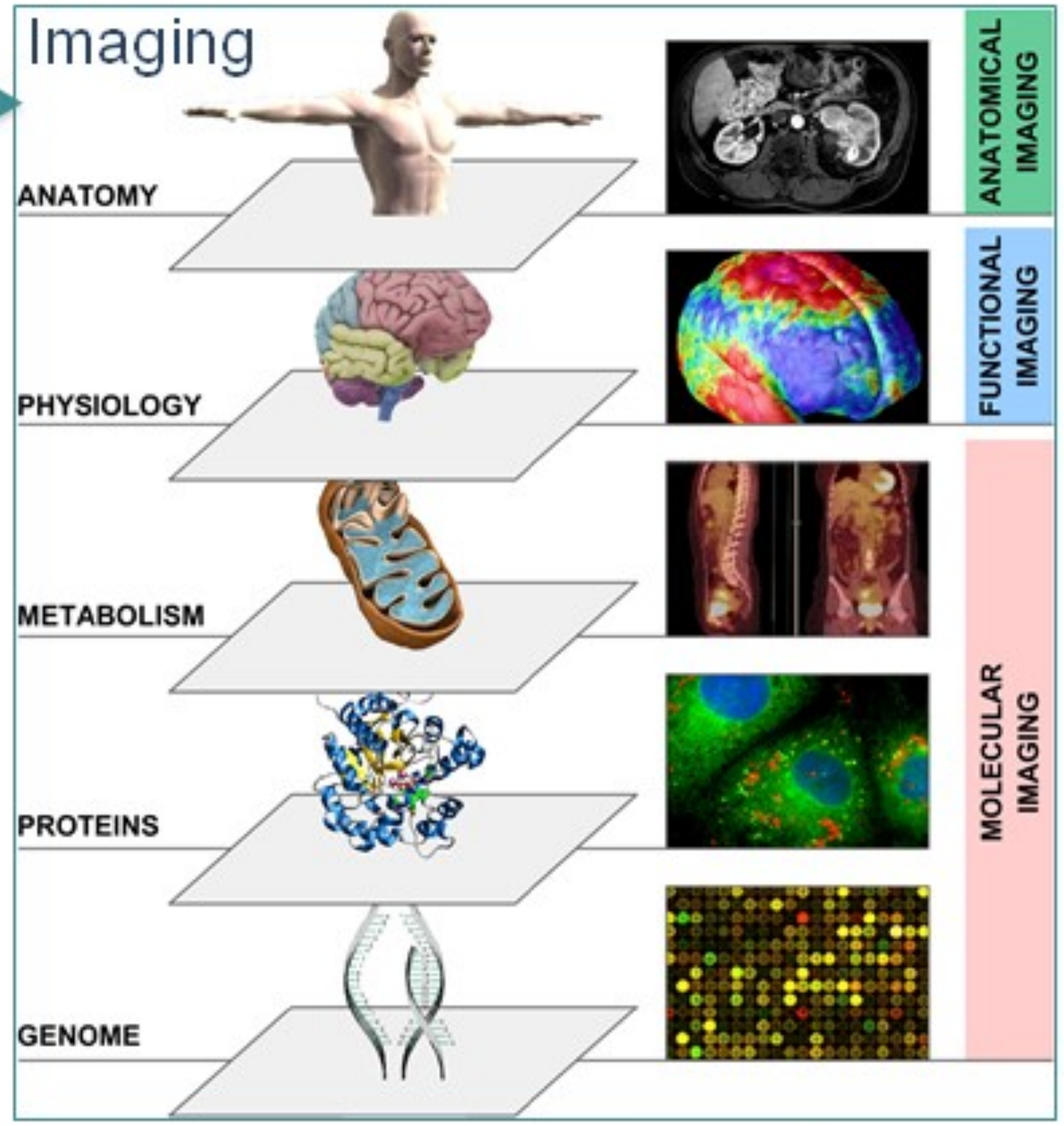
also: industrial,
backscatter,
muons, …

Whole-body (PET/CT melanoma): of the forest and the trees…

(source data CRIF; post-proc./visu. LMB)

More/better metrics and integration

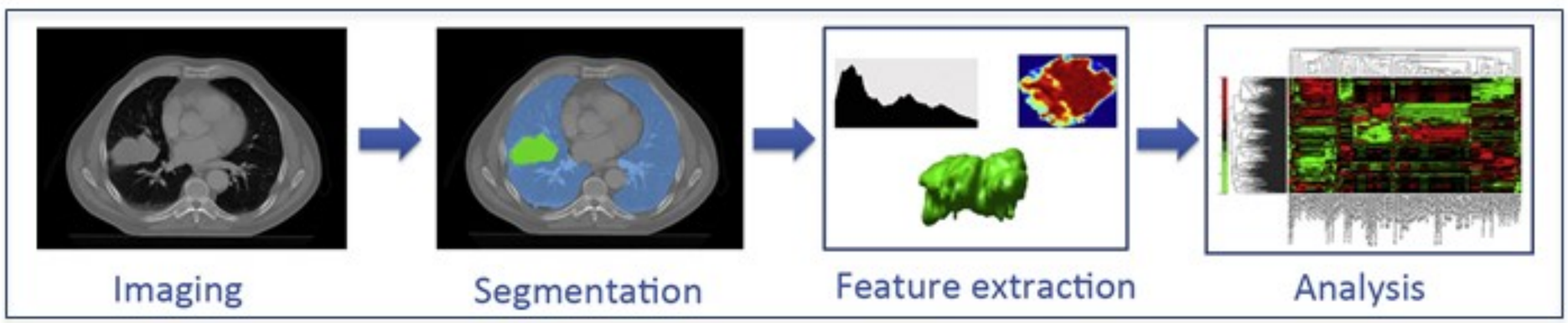
(in part from P. Lambin et al., Eur J of Cancer, 48(4), 2012)



appearance, size, RECIST, WHO, volume, motion, texture, DWI, shape, etc.

4D, DCE, PK, fMRI, MRS, mpMR, etc.

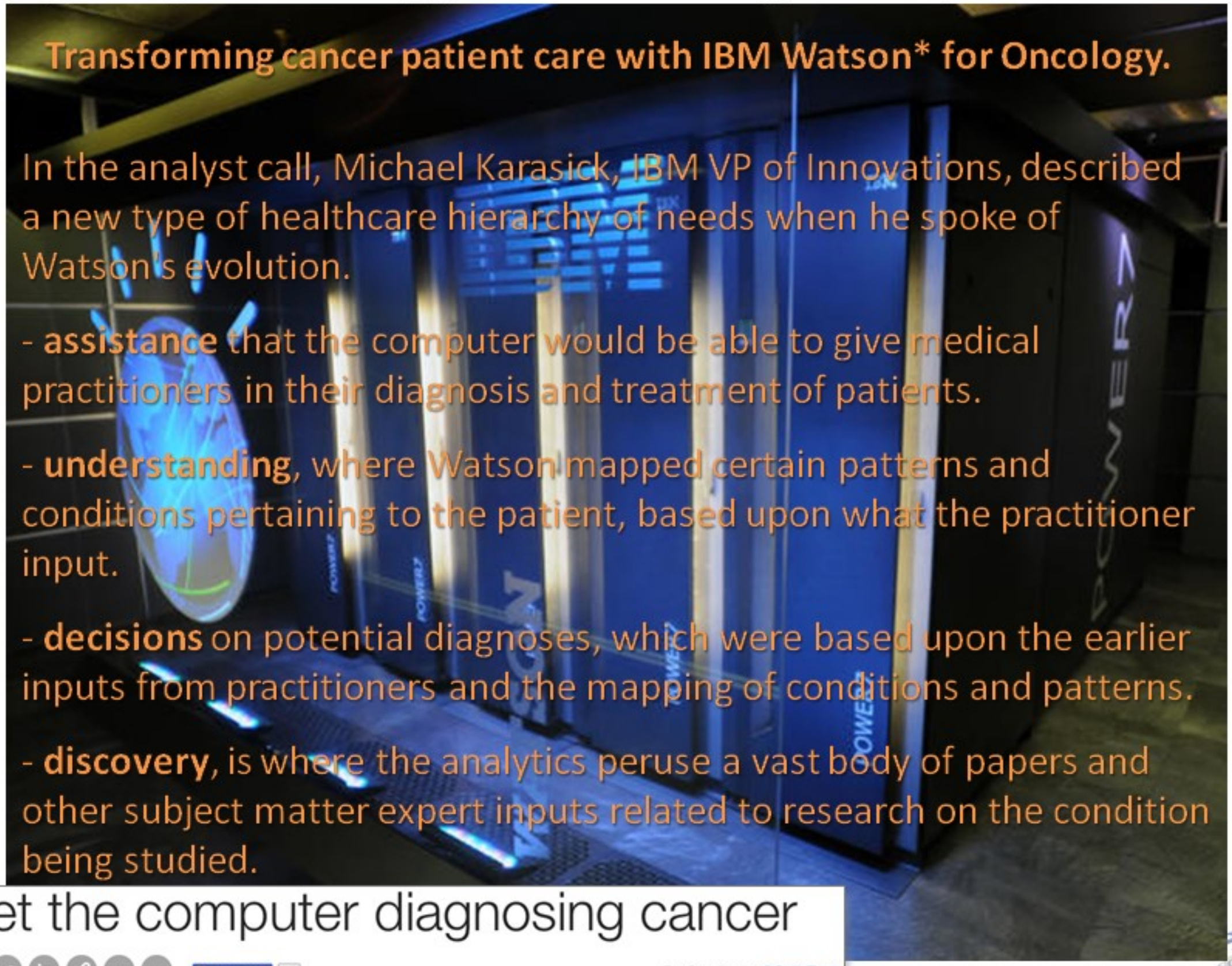
SUV, PERCIST, 4D, PK/PD, probe pathway, mpMR, etc.



radiomics pipeline

Extracting more information from medical images using advanced feature analysis ⇔ "advanced CAD"

"Imaging" as part of a bigger whole... "Big Data" *(+ M & D Learning...)*



Meet the computer diagnosing cancer

Recommend 112

By @loufoglia @CNNTech

* also Oracle, Enlitic, Apple etc.

End goal: personalised/precision medicine: imaging bits

Data Collection

Multimodal Images

MRI

PET

Other modalities

CT

SPECT

Ultrasound

Optical

Other information sources

Biopsies & body fluids

Histology, IHC

Molecular data

Reference data

Atlas

Image banks

Data Analysis

Image quality enhancement

Multimodal Images registration

Brain segmentation

Features extraction

Patterns recognition

Quantification

Images data analysis

DNA/RNA/ Prot/Metab. data integration

Systems models

Interaction networks

Database searches

Statistical analysis

'omics' data analysis

Historical / Reference data Integration

Data Mining Data Discovery

Composite Biomarkers Inference

Pharmacokinetic modeling

Predictive modeling

Virtual / Augmented Reality

Artificial Intelligence

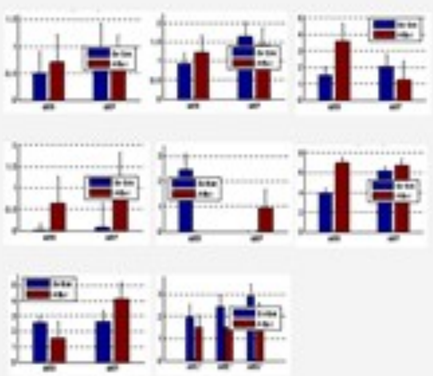
Visualization Techniques

Decision Support Systems

Advanced information processing techniques

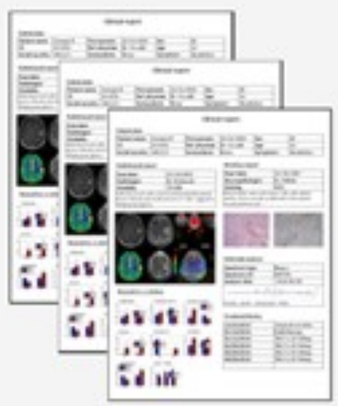
Data Presentation

Disease relevant biomarkers



- Receptors, mutations
- Proliferation,
- Metabolic activity
- Angiogenesis, hypoxia
- Inflammation, Infiltration
- Cell death

Patient management support



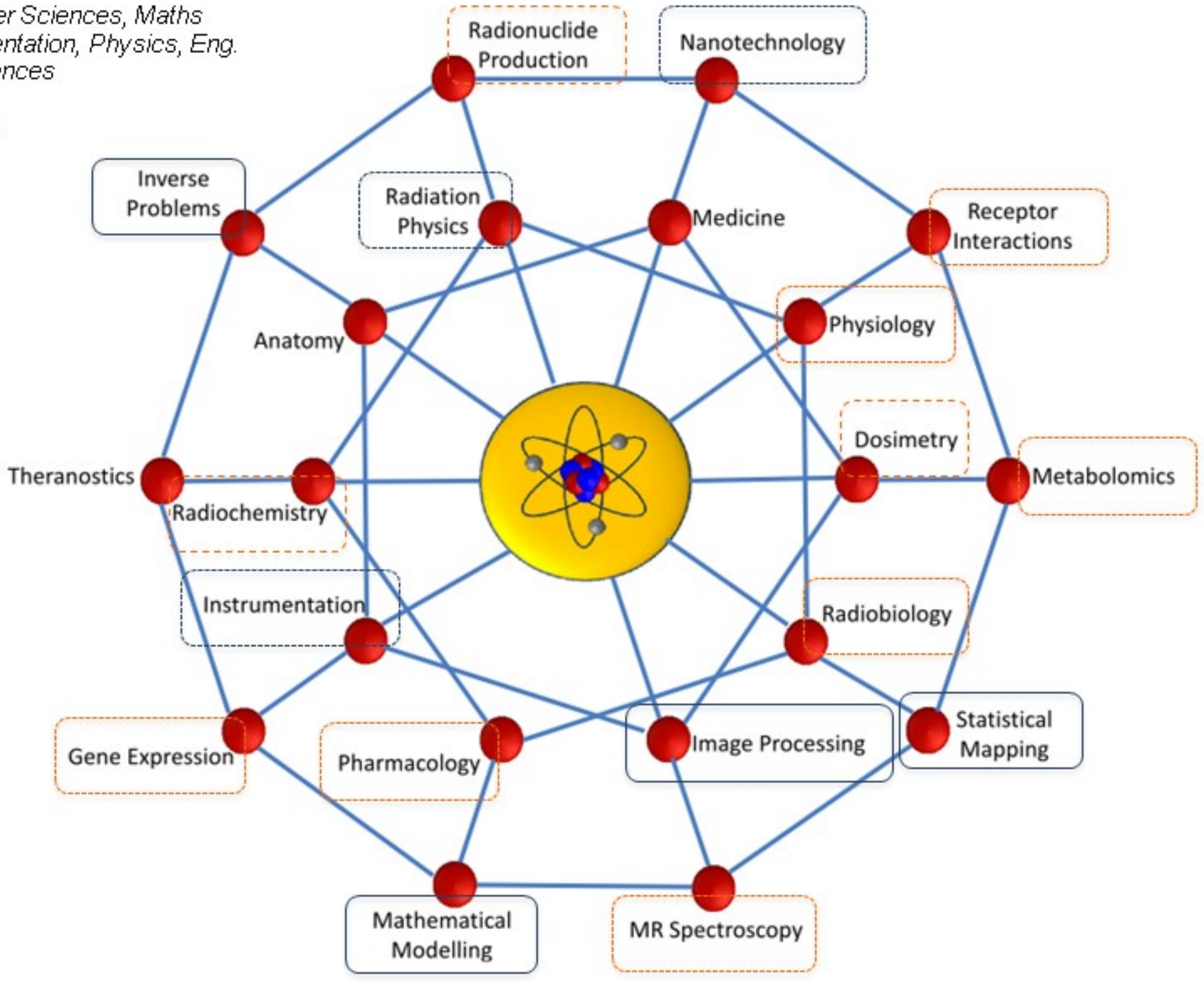
- Diagnostic, prognosis
- Patient stratification
- Treatment planning
- Therapy monitoring

(from O. Keunen et al, Adv Drug Deliv Rev, 2014. 76(30):96-115)

Biomedical imaging: inherently multidisciplinary

(derived from D. Bailey, EJNMMI Physics 2014, 1:4)

Computer Sciences, Maths
Instrumentation, Physics, Eng.
Life Sciences
Probes
others: Clinical



Conclusions:

Software registration isn't dead and remains a key component of modern* imaging and protocols (*incl. hybrids*)

Much is happening on the advanced* imaging and translational* sides of things

Personalized/precision medicine is imminent*...

**moving targets...*

Acknowledgments:

➢Most examples and thoughts from work and time spent at:

- Service Hospitalier Frédéric Joliot (SHFJ) *(Instrumentation & Computing Head a.i.)*
  CEA, Orsay, F
- Biophysics & Nuclear Medicine *(Research & Computer Scientist)*
  UCLA, Los Angeles, USA
- PET & Biomedical Cyclotron Center *(founding co-Director; Instrum. & Comp. Head)*
  ULB, Brussels, B
- Laboratory of Functional and Multidimensional Imaging (LFMI) *(founding Director)*
  HUG, Geneva, CH
- Departments of Radiology & Medical Physics *(AIL founding Technical Director)*
  MSKCC, New York, USA
- Image Processing & Visualization Laboratory (IPVL) &
  Scientific Computing Resource (SCR) *(founding Director)*
  Dept of Imaging Physics; MDACC, Houston, USA
- Centre for Oncology and Molecular Medicine - DMS *(Imaging Head)*
  Clinical Research Imaging Facility (CRIF) *(founding Head)*
  Division Imaging & Technology *(founding co-Head)*
  University & Ninewells Hospital, Dundee, UK
- School/Dept. of Computer Science *(Prof. of Medical Imaging, Head)*
  University of Lincoln, UK

➢Other contributions as credited; past, present and ***future*** collaborations and partners