Measurement of higher brain function in humans

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Higher Brain Functions, Mariella De Biasi, Course Director
April 26/28, 2011

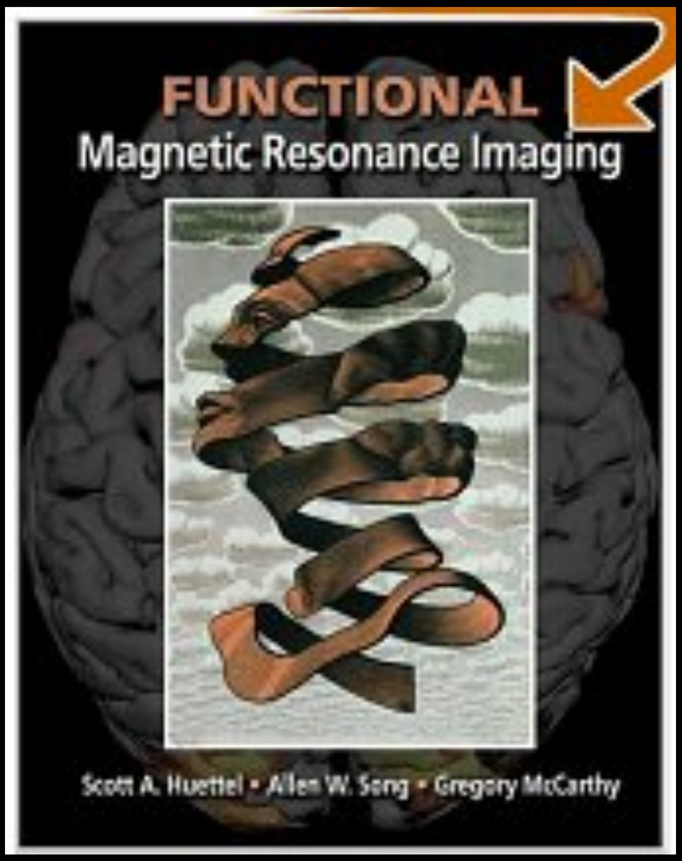
Introduction to fMRI

Cross-listed as:

Rice Psychology 671

BCM GS-NE-439

Textbook



Functional Magnetic Resonance Imaging by Scott A. Huettel, Allen W. Song, and Gregory McCarthy (Hardcover - April 1, 2004)

Why is neuroimaging difficult?

Palpation/Sensation

-skull: can't feel much from outside (sorry, ultrasound)

-no nerves in brain: can't feel much from inside

Alphabet Soup

CT

MRI

SPECT

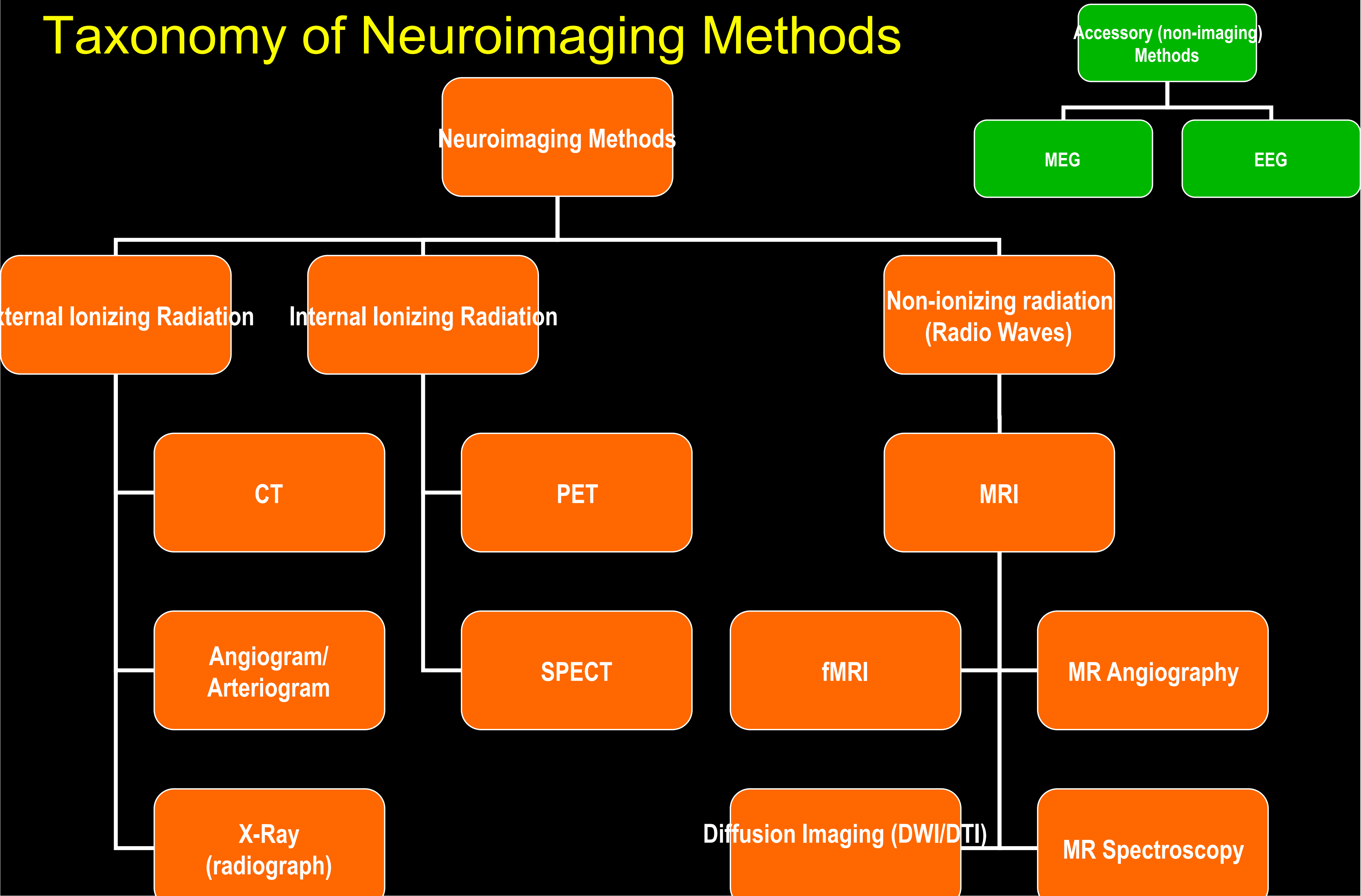
PET

MEG

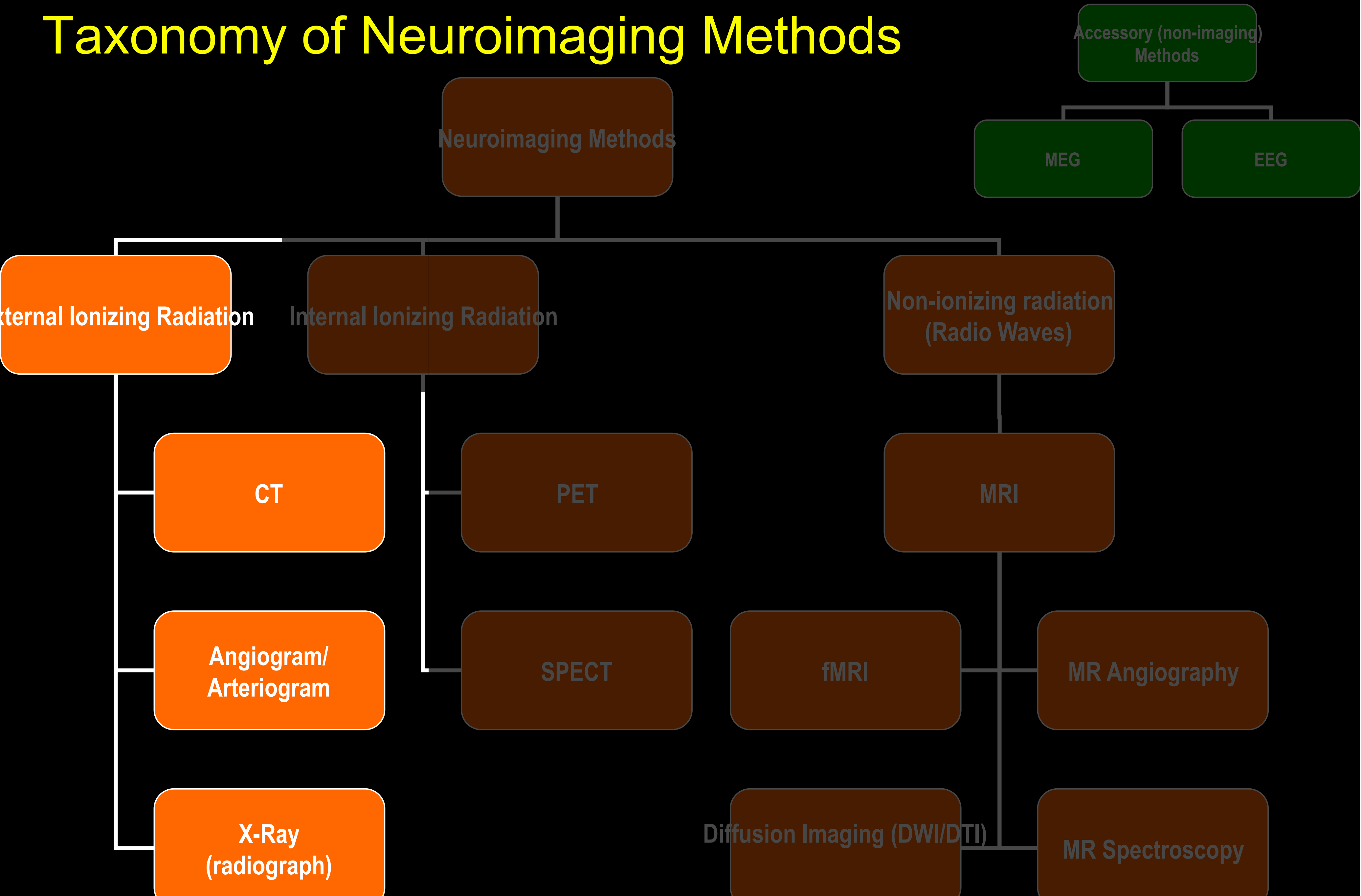
EEG

fMRI

Taxonomy of Neuroimaging Methods



Taxonomy of Neuroimaging Methods



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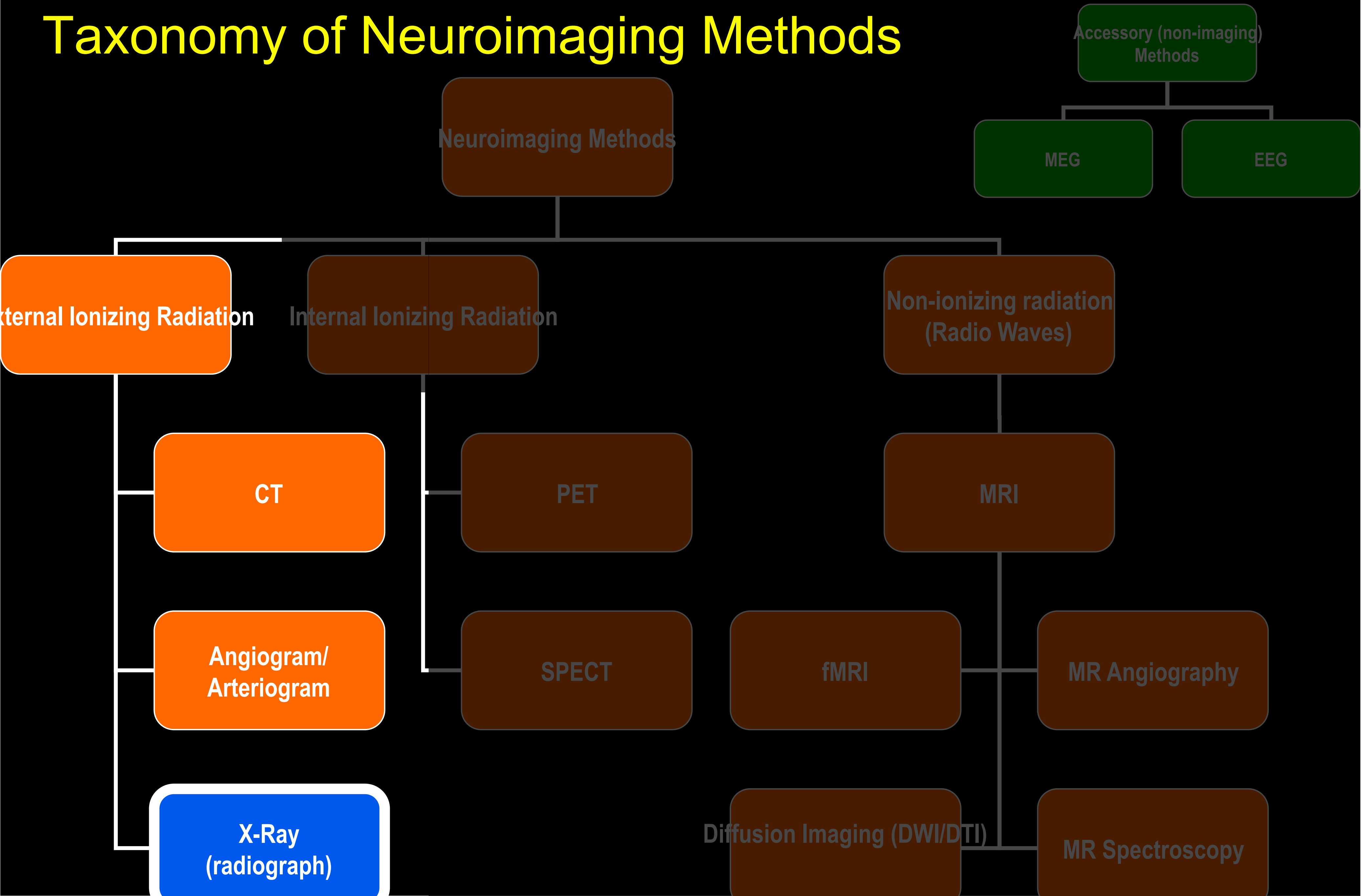
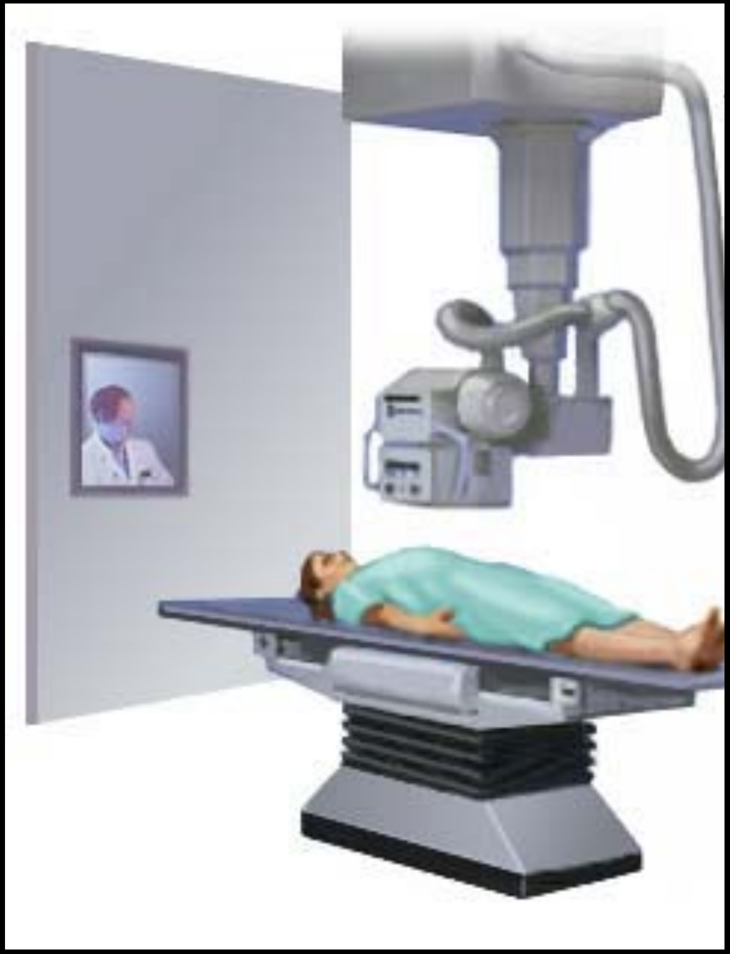


X-Ray (radiograph)—bones, not brain!
(tissue density)



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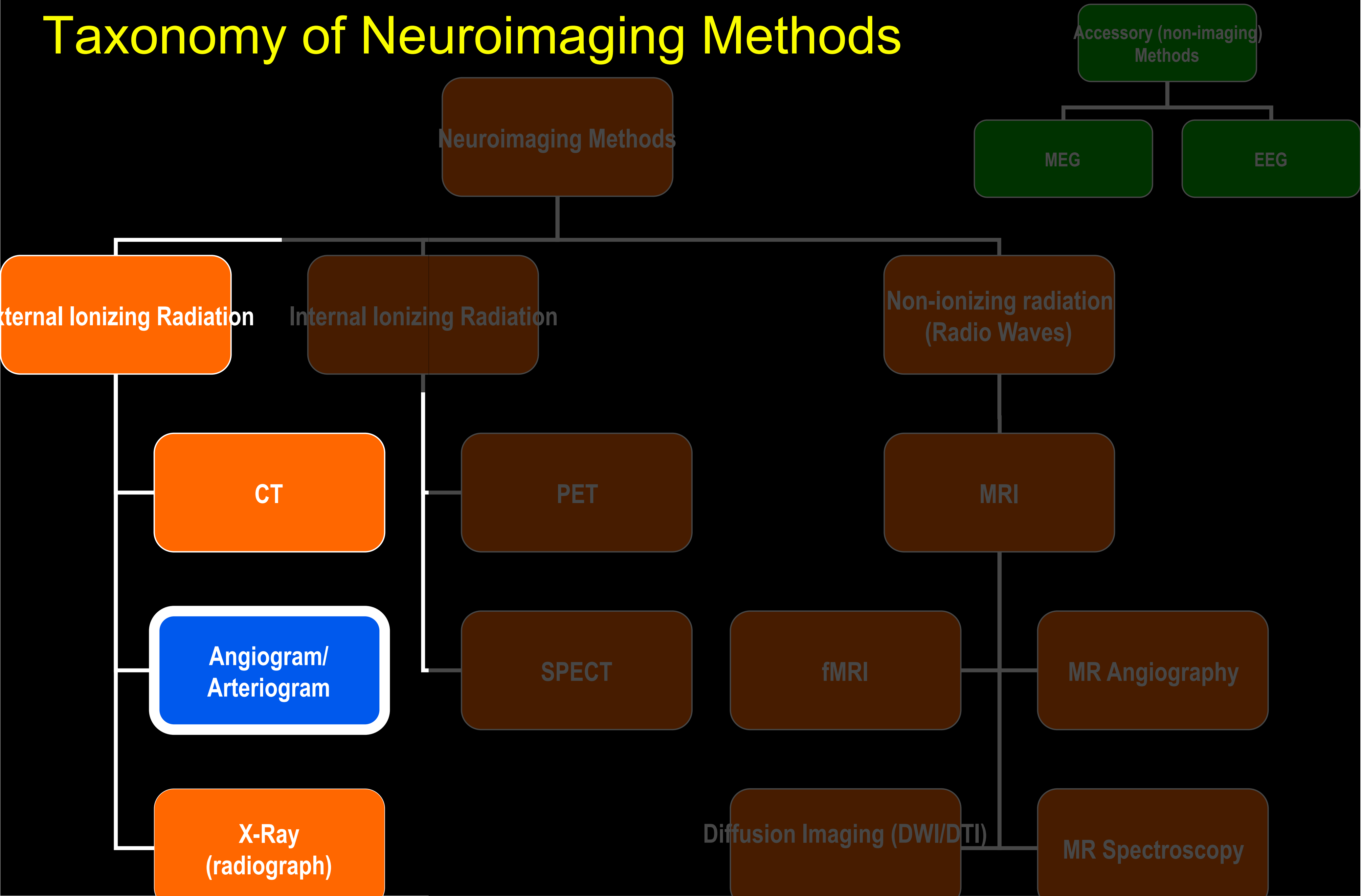
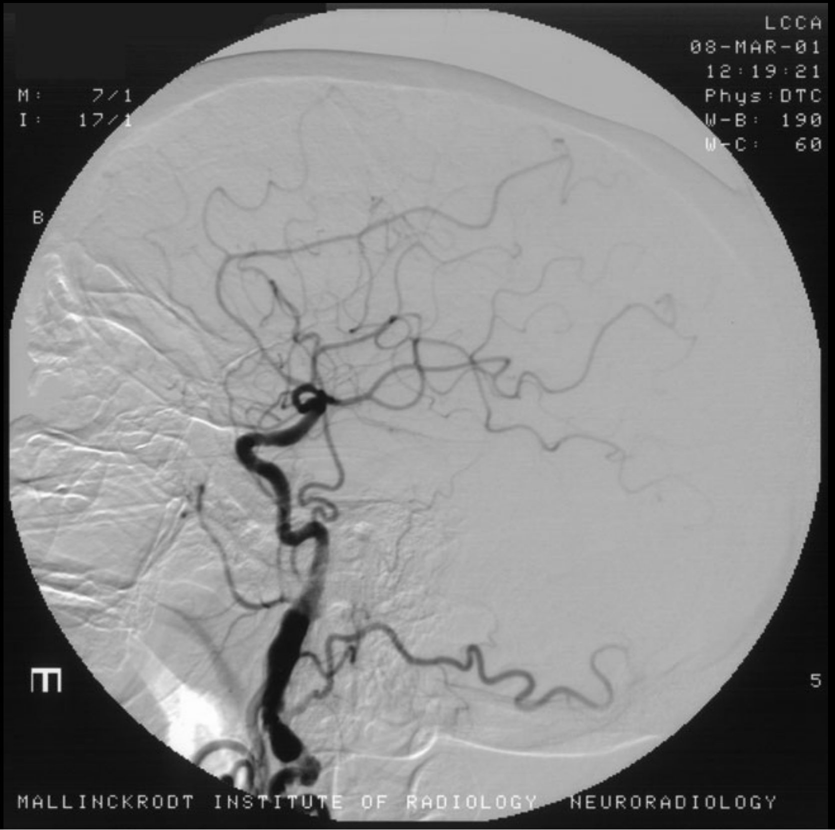


Arteriogram (a.k.a. Angiogram)

Basic principle: Inject contrast agent (dye) that is radio-opaque i.e. iodine containing agents



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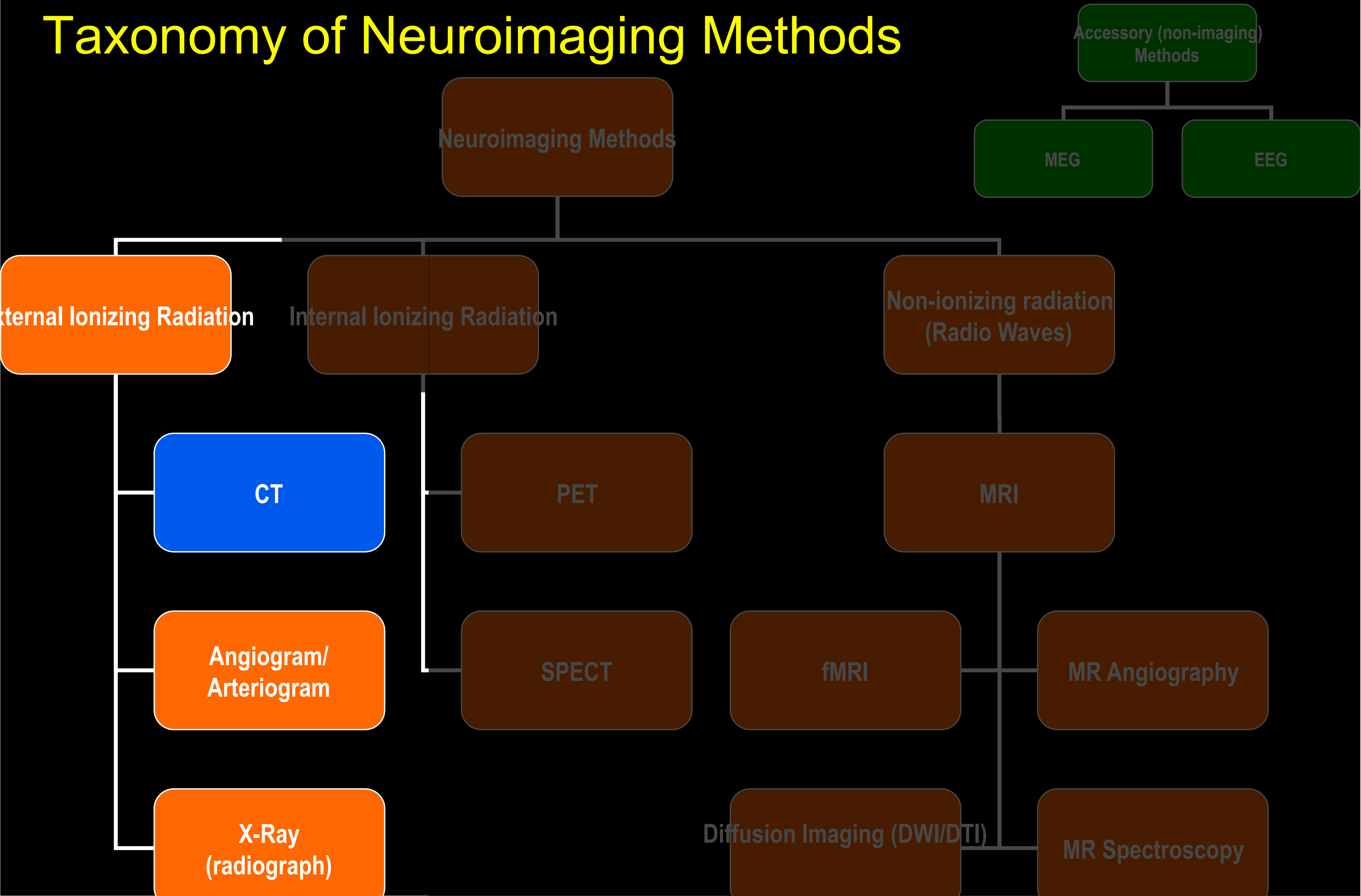
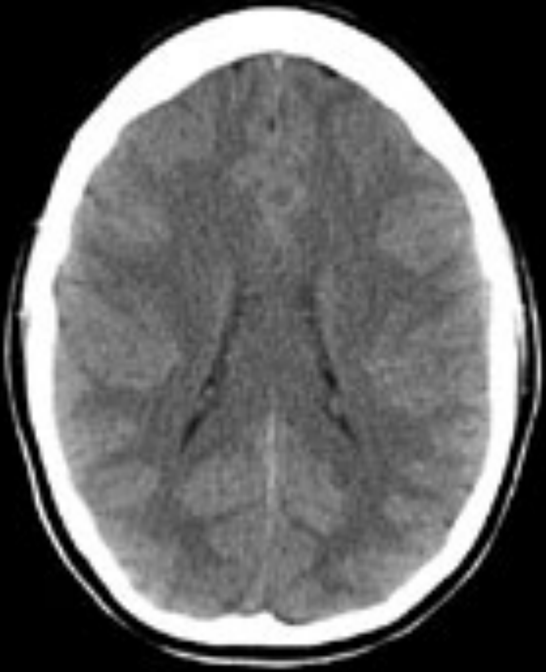


CT (computed tomography)



CT (computed tomography)

Pros:
Widely available

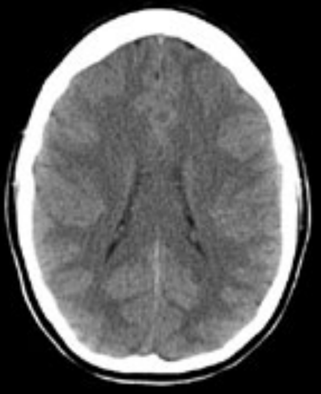
Very fast to collect whole-head images
(one slice in < 1 ms; whole head in ~ seconds; whole exam in 10 minutes)

Somewhat cheaper than MRI
(~$500 vs ~$1000 for MRI)

Less hassle (few contraindications)

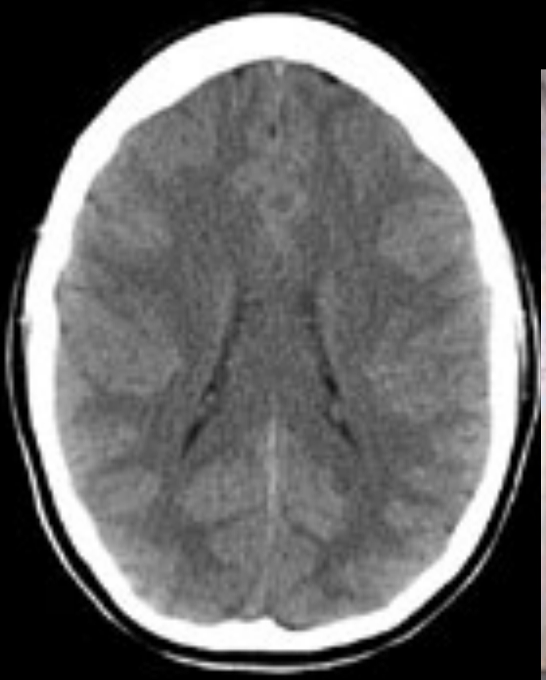
Best for an emergency

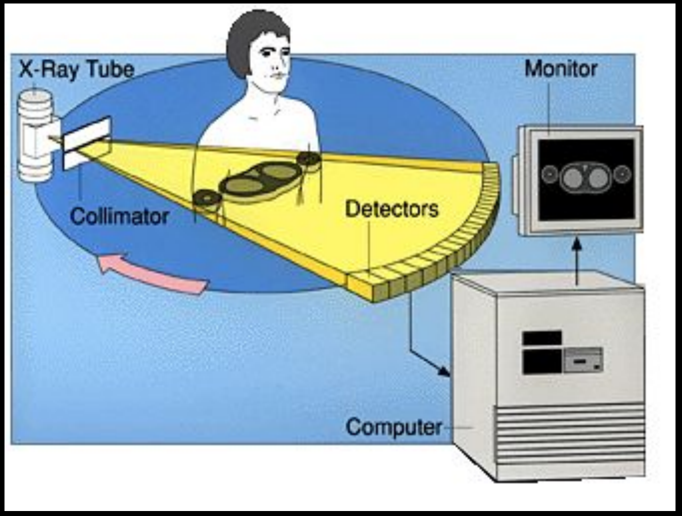
Cons:
Exposure to ionizing radiation (increased risk of cancer)
can require a contrast agent—for brain, injectable iodine compound
Poor tissue contrast
not versatile



CT (computed tomography)

Basic Principle: rotate machinery to take multiple x-rays with different paths through the body





Common clinical use: stroke

Patient presents with stroke

80%

ischemic

Give tPA, dissolve clot,
Blood flow restored,
Patient recovers

20%

hemorraghic

Give tPA, prevent clotting,
Patient dies of massive bleed

Common clinical use: stroke

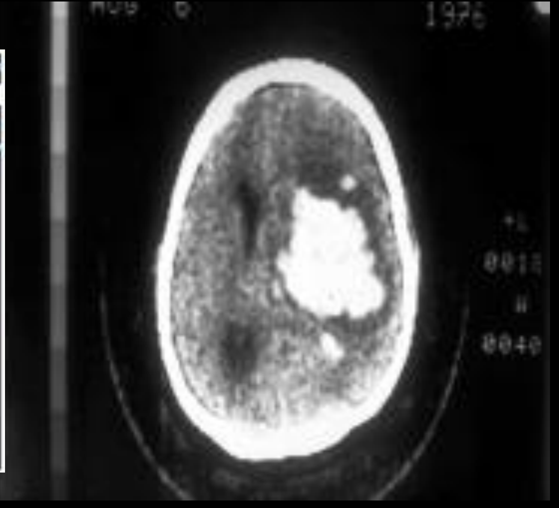
Patient presents with stroke

80%

ischemic

20%

hemorraghic



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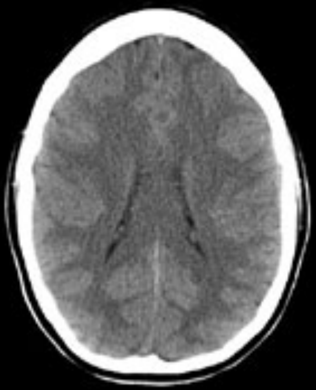
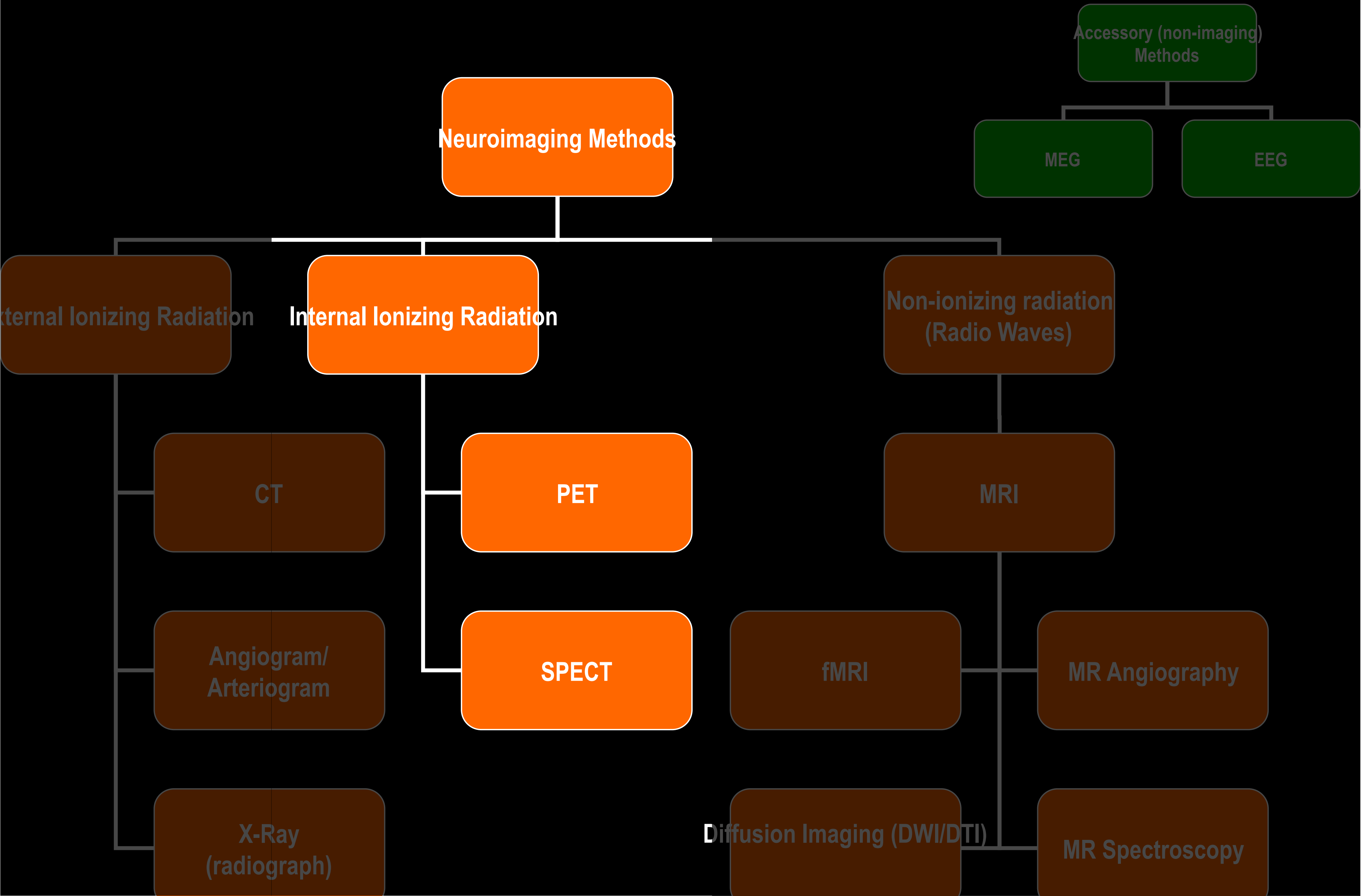
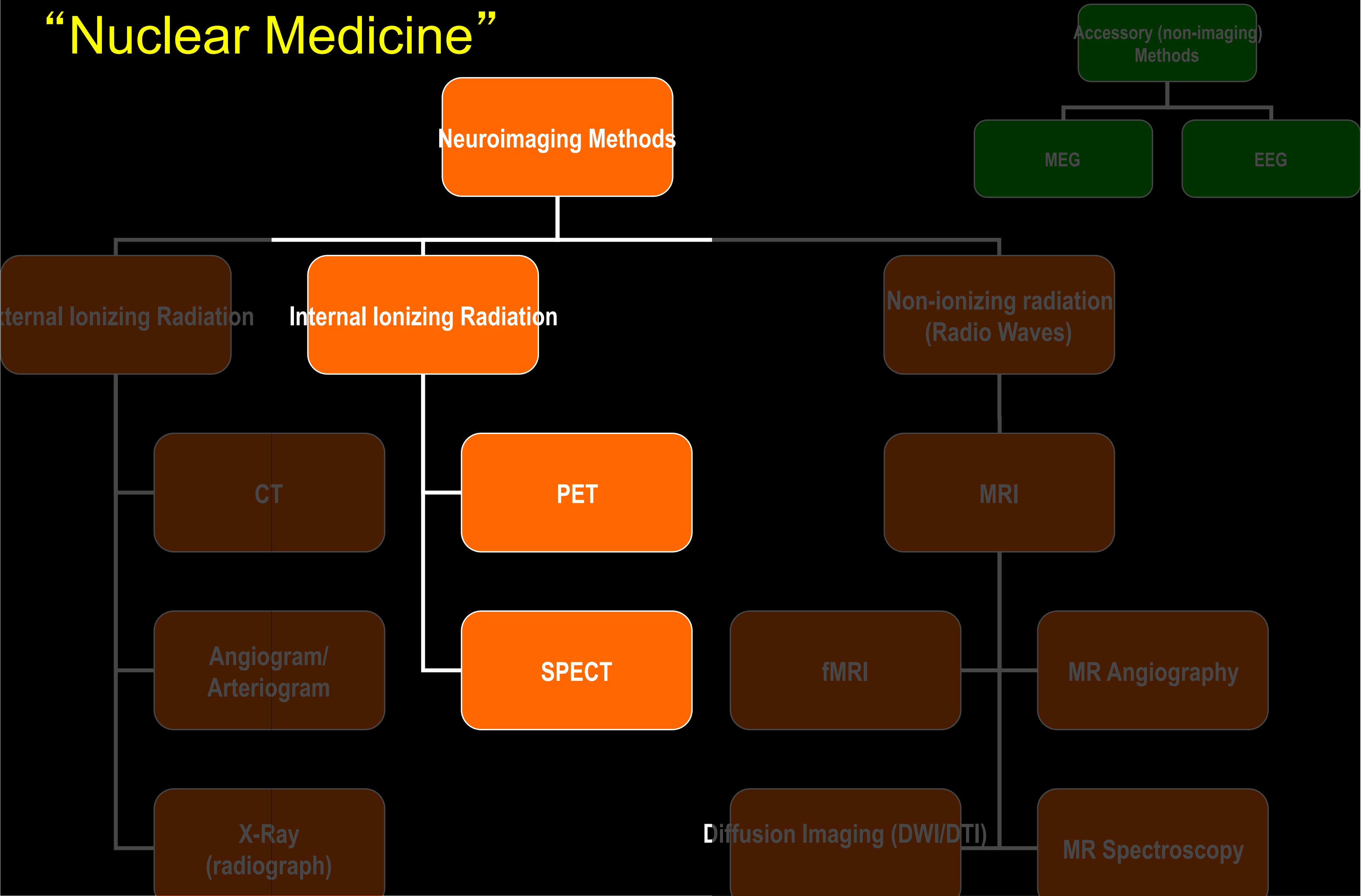
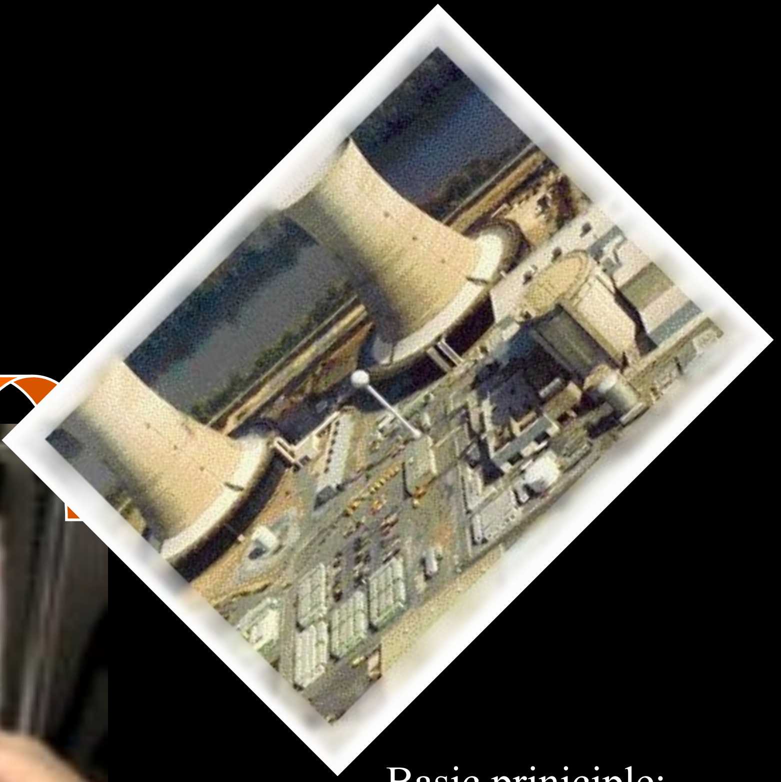



Accessory (non-imaging) Methods
MEG
EEG
Neuroimaging Methods
xternal Ionizing Radiation
Internal Ionizing Radiation
Non-ionizing radiation (Radio Waves)
CT
PET
MRI
Angiogram/ Arteriogram
SPECT
fMRI
MR Angiography
X-Ray (radiograph)
Diffusion Imaging (DWI/DTI)
MR Spectroscopy

"Nuclear Medicine"



“Nuclear Medicine”: PET/SPECT



Basic priniciple:

Inject radioactive isotope attached to metabolic compound (Oxygen, Glucose, etc.)

Wait for it to decay, look for radioactive decay products

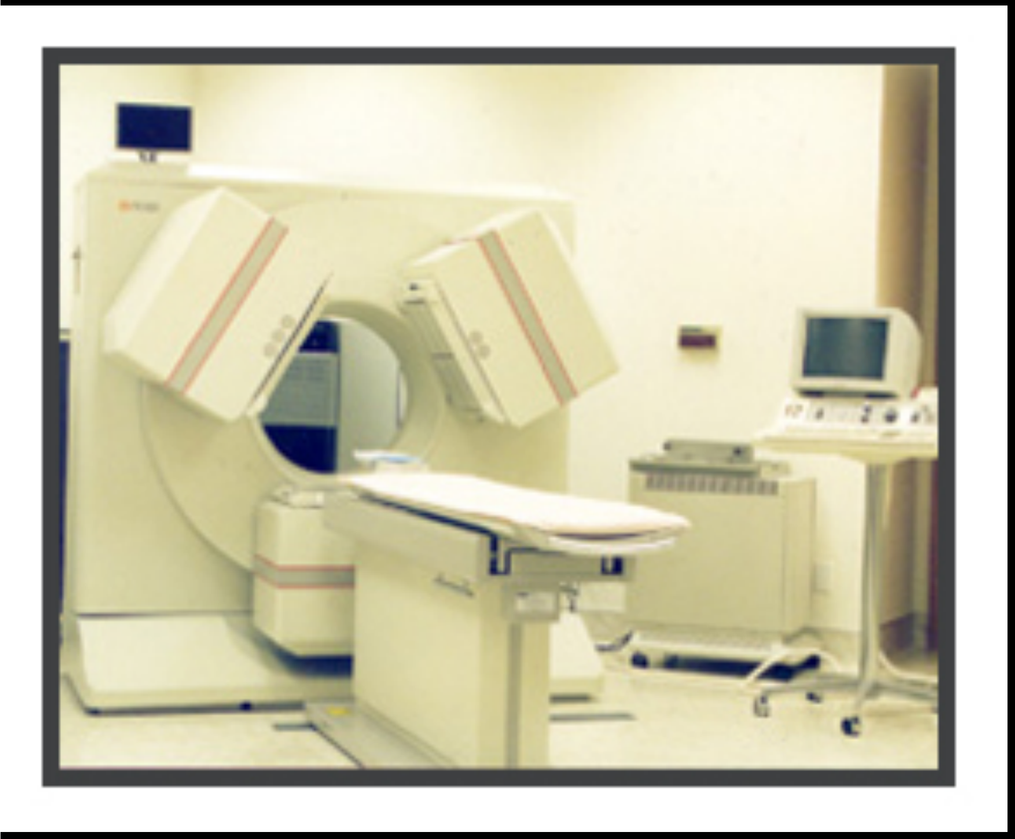
PET/SPECT

Pros:
Fairly cheap (~ $1000)

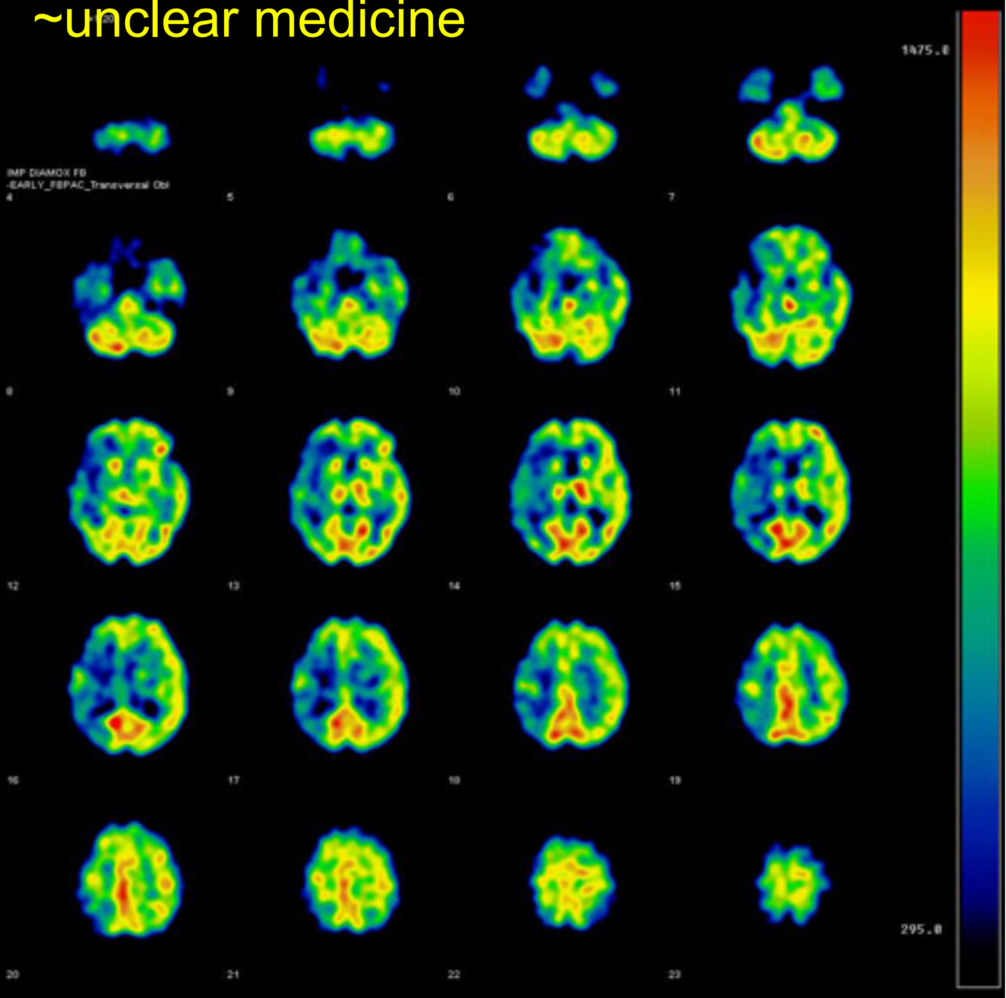
Shows function
(metabolism)

Cons:
Exposure to ionizing radiation (increased risk of cancer)
~1 year of background radiation
Low-resolution
Slow to very slow
not versatile

SPECT
Single Photon Emission Computed Tomography



"Nuclear Medicine":
~unclear medicine



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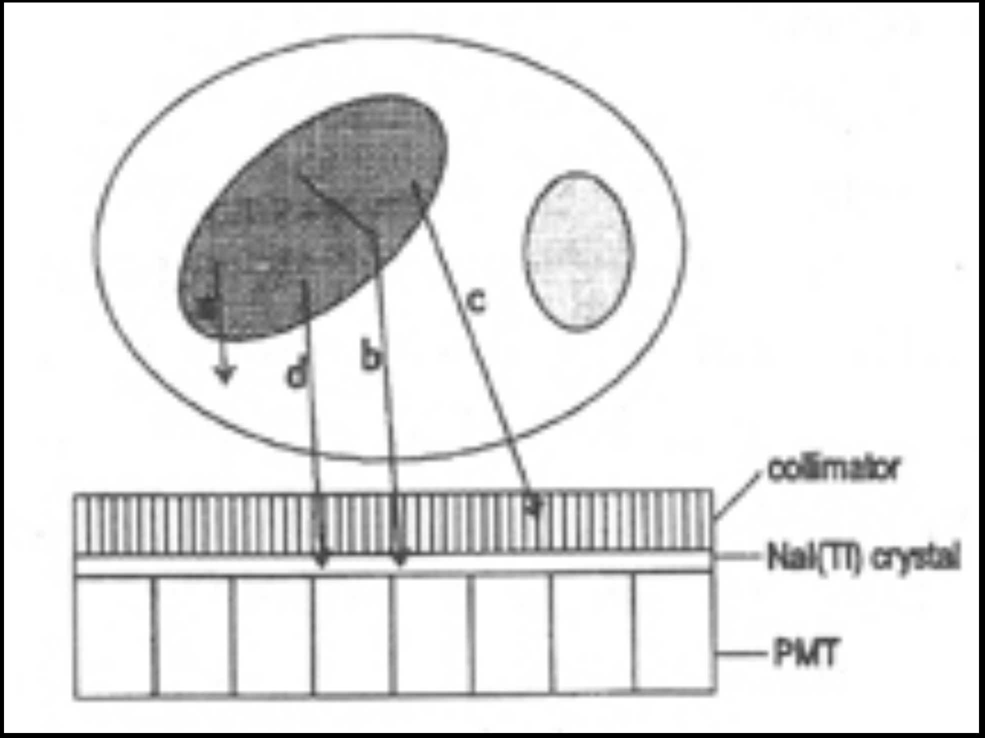


Radionuclides

Single-Gamma emitting

99mTc, 123I, 67Ga, 111In

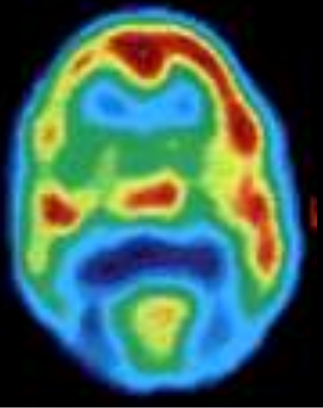
PET: Positron Emission Tomography

Basic priniciple:

Inject radioactive isotope attached to important metabolic compound (Oxygen, Glucose)

Wait for it to decay.

Pick up **two** particles going in opposite directions—improves spatial resolution



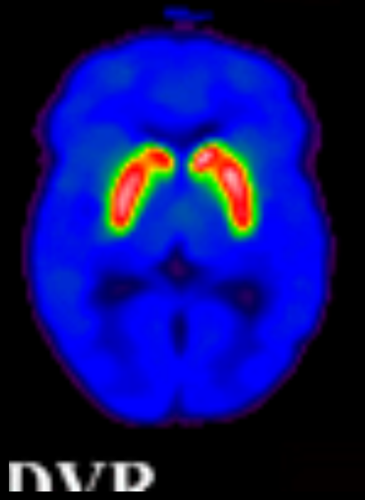
- PET uses beta-plus-emitting radionuclides such as C-11, N-13, O-15, and F-18 which annihilate into two 511-keV photons that travel in opposite directions.

Developments in PET

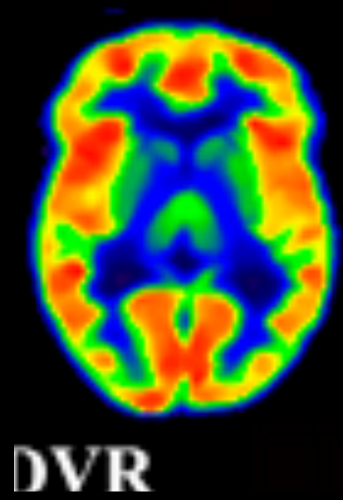
- Development of new radiotracers

[11C]DTBZ

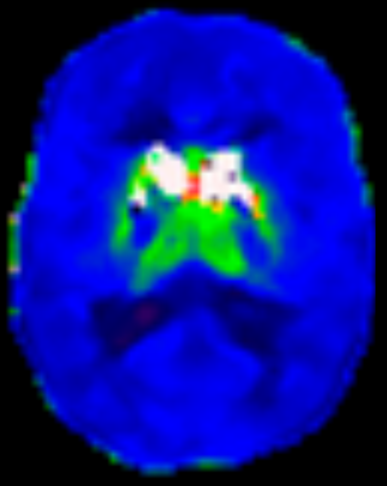
VMAT2
~dopamine,serotonin



[11C] Flumazenil
(benzodiazepine receptor antagonist
~ GABA-A)

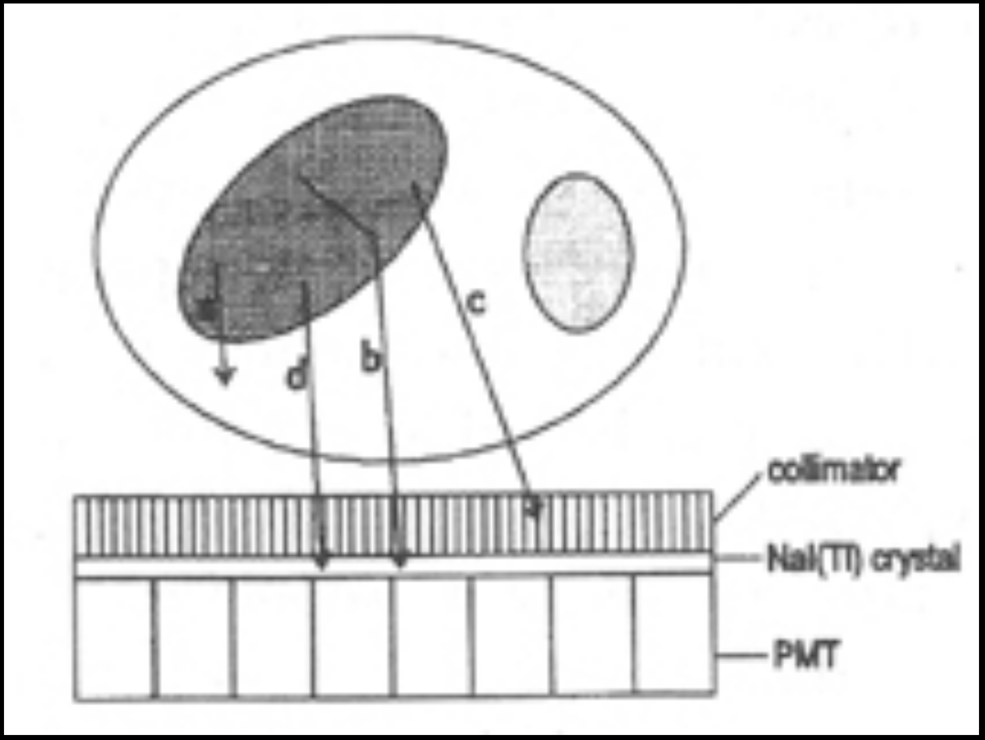


[11C]PMP
Substrate for AChE

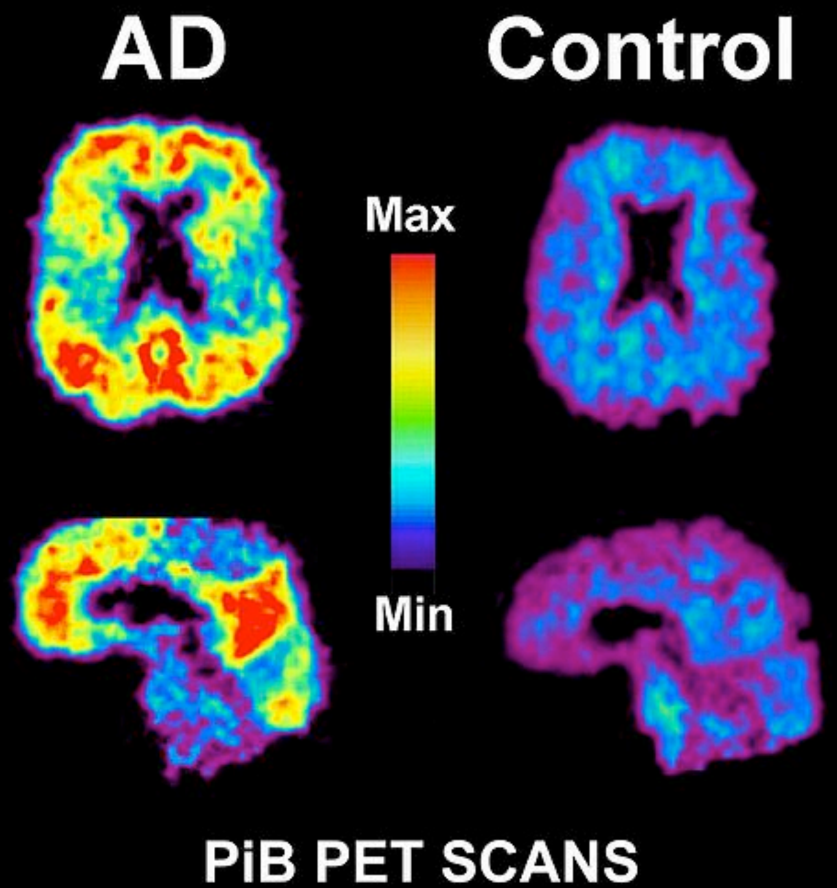


Joshi et al., JCBFM 2009

2 –photons instead of one → better resolution

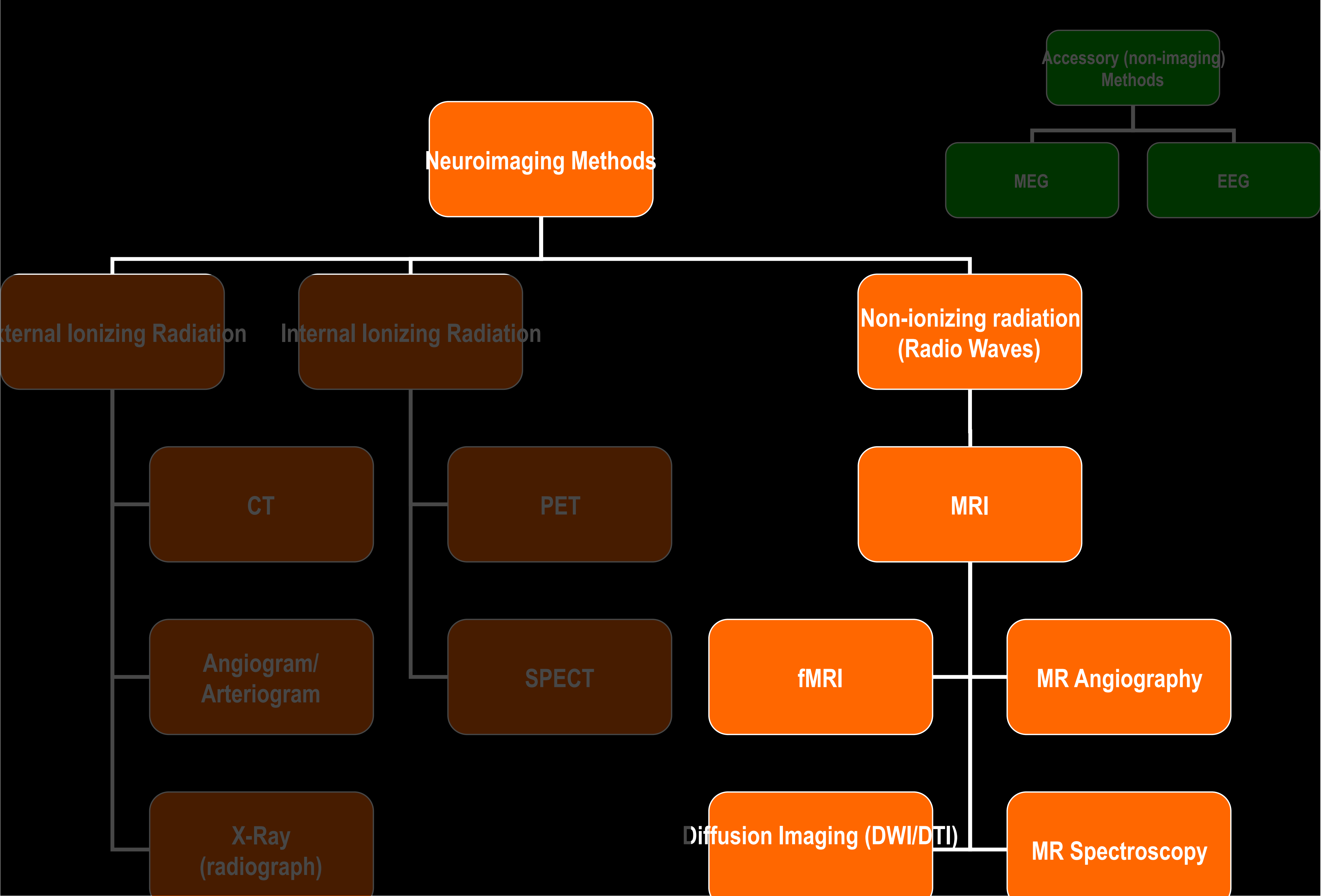


Sample Clinical Application: Alzheimer's Diagnosis



University of Pittsburgh
PET Amyloid Imaging Group

- Compounds that bind to AD plaques
- Conditional approval by FDA (Jan 2011)
- C. M. Clark et al. J. Am. Med. Assoc. **305,** 275–283; 2011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MR Angiography
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Diffusion Imaging (DWI/DTI)
MR Spectroscopy

MRI: Magnetic Resonance Imaging

Pros:

incredible images

advancing very rapidly

extremely high resolution

extremely versatile

NO ionizing radiation

Cons:

moderately expensive (~ $1000)

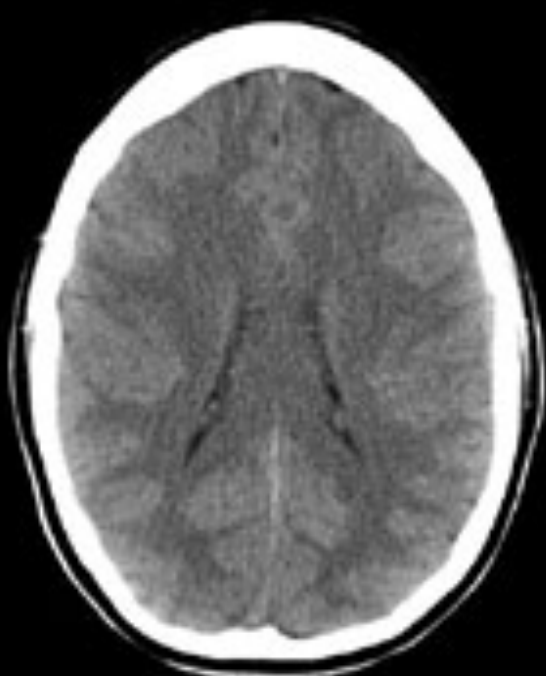
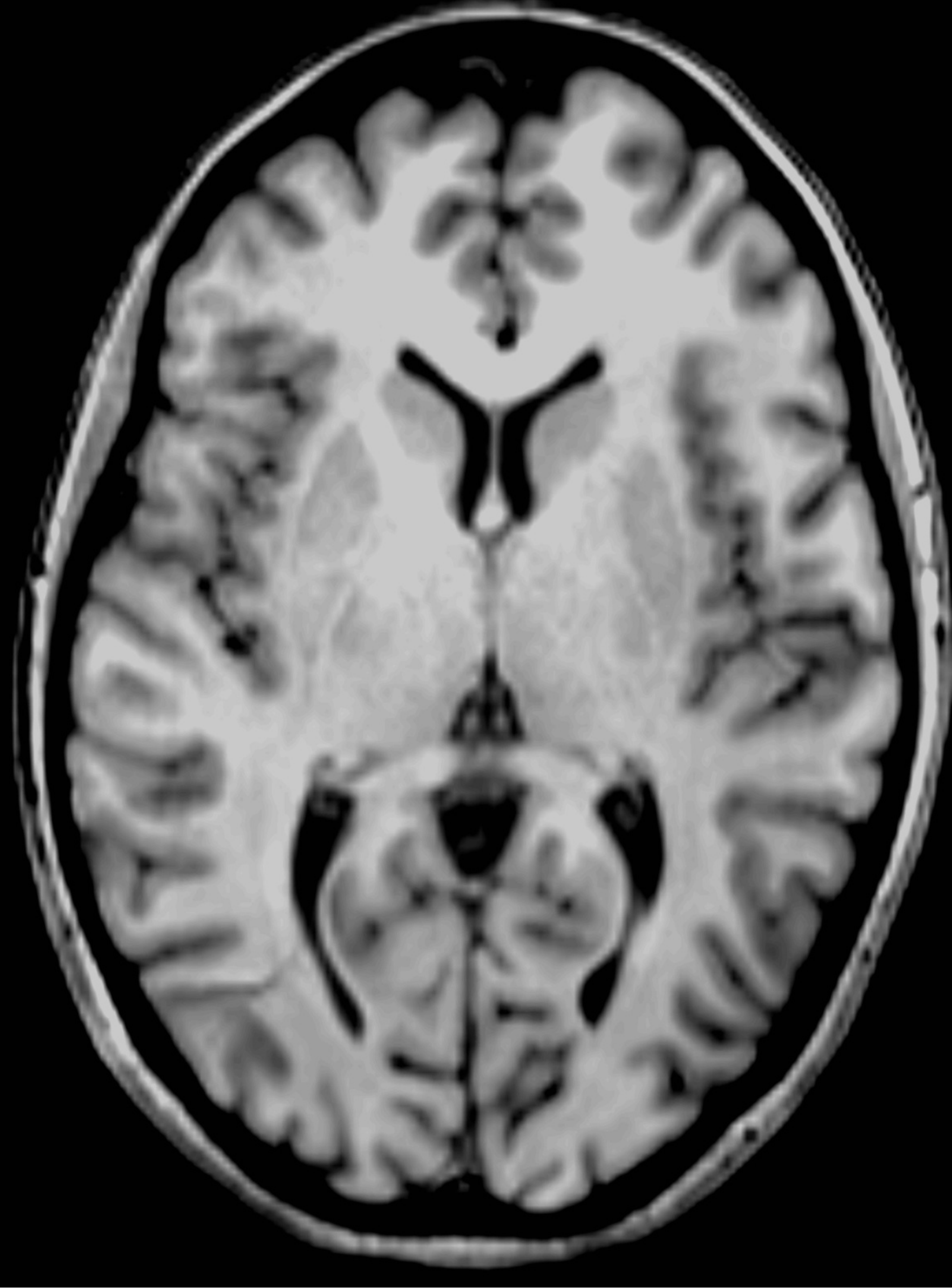
complex

some contraindications

Can require injection of contrast agents (Gadolinium/ Iron compounds)

Imaging Techniques: MRI

- the MR scanner is a giant magnet: 1.5T, 3T, 7T, 9T

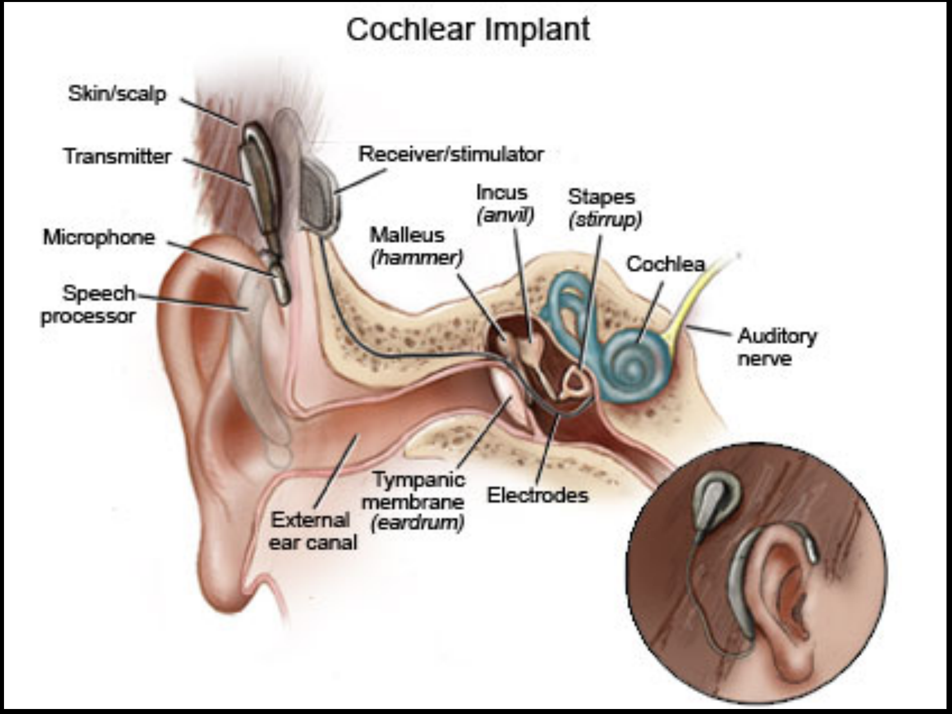



Contraindications I

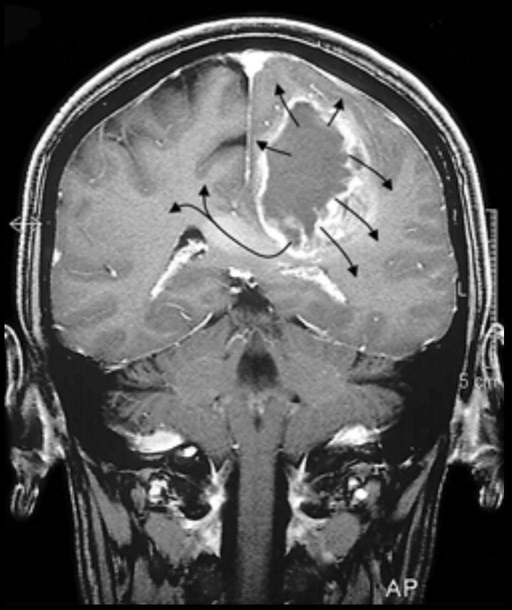
- Ferrous metal in body

Contraindications II

- Cochlear implants (always)
- Maybe: pacemakers, vagal nerve stimulators, old (> 20 year) surgical implants



Clinical Applications



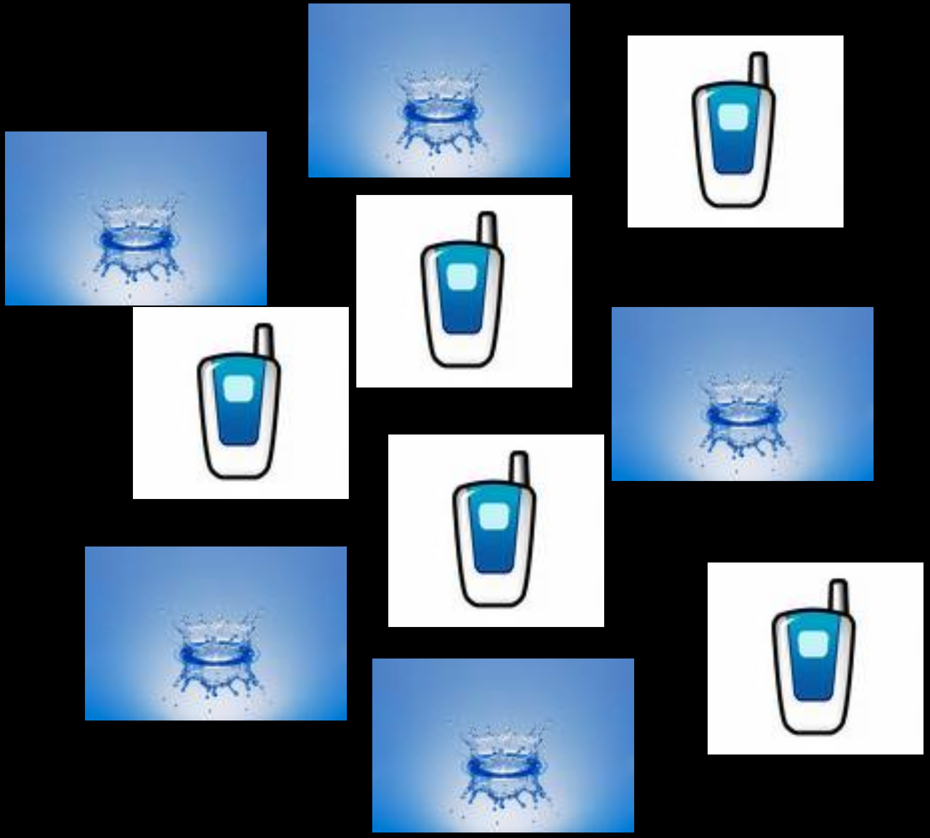
BCM HNL

-- 5 research-dedicated 3 tesla scanners made by Siemens

--2 head-only, 3 full-body

MRI (Magnetic Resonance Imaging)

Basic principle: uses radio waves to interrogate protons in water molecules in the brain



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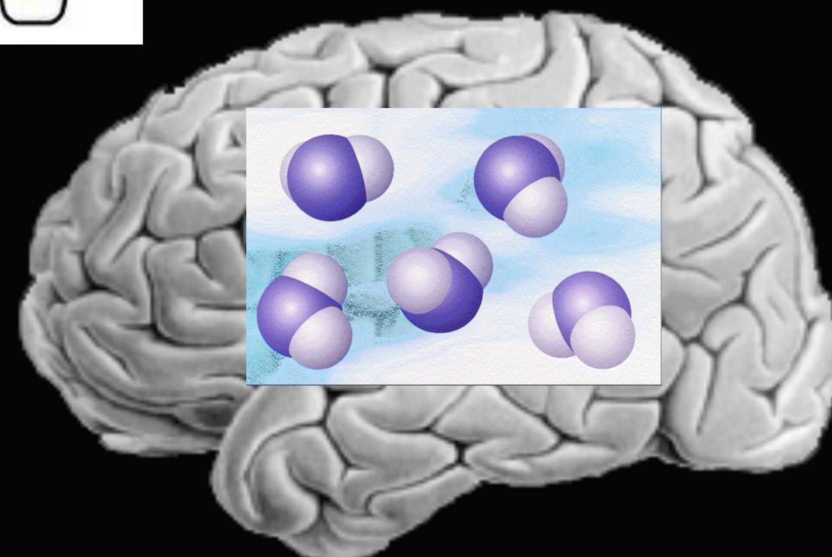
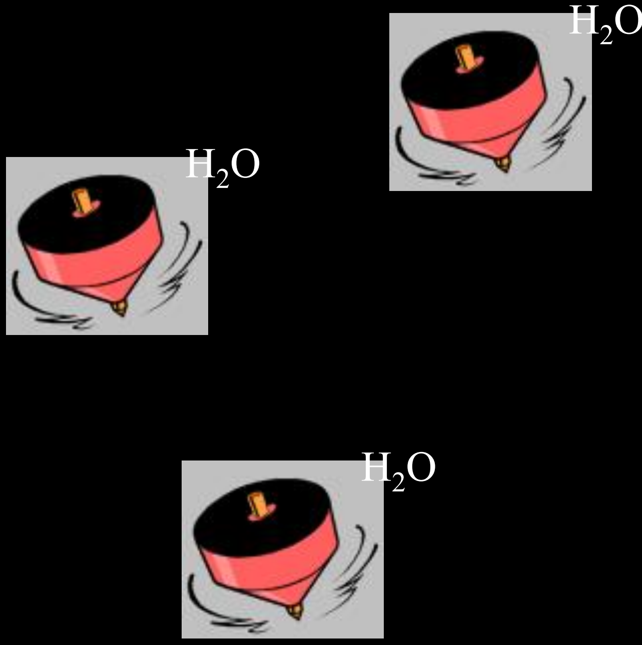


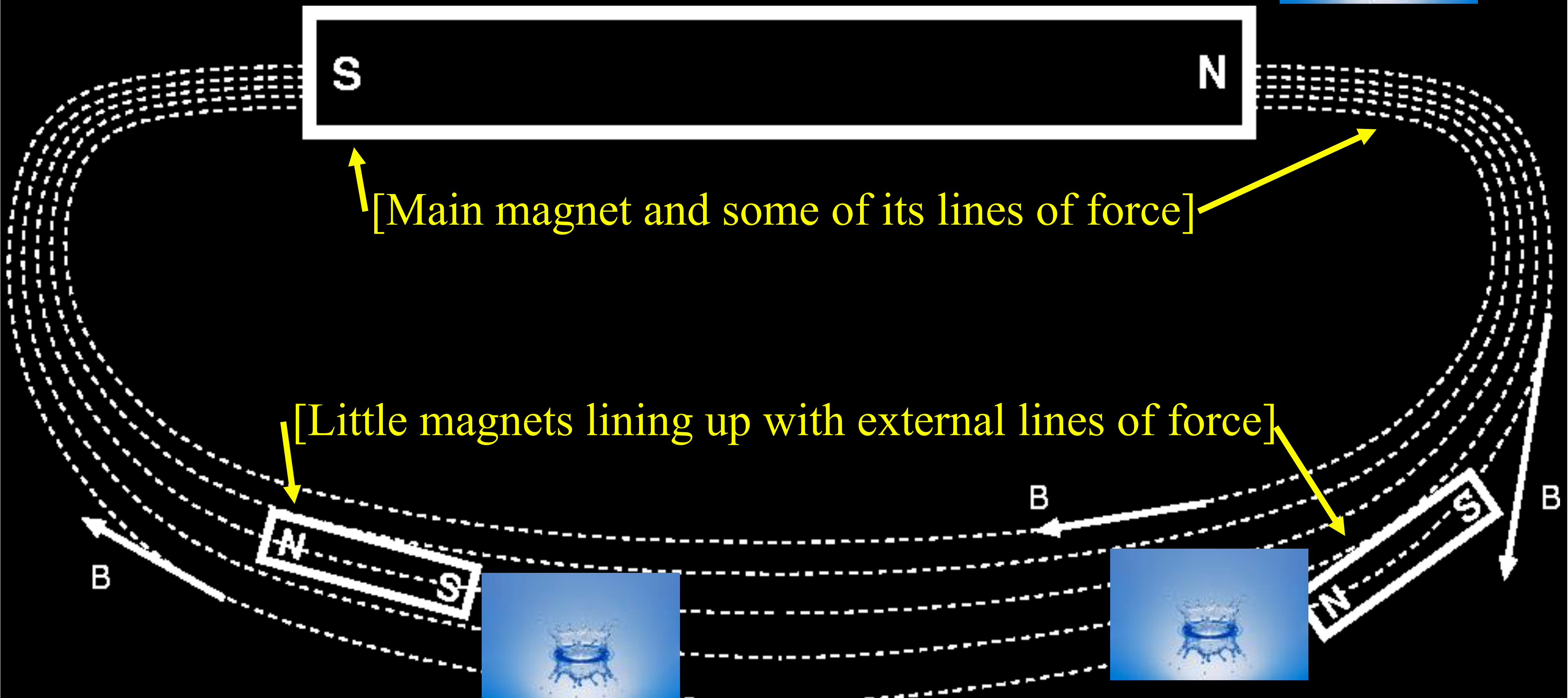
128 MHz at 3T (~ FM Radio)

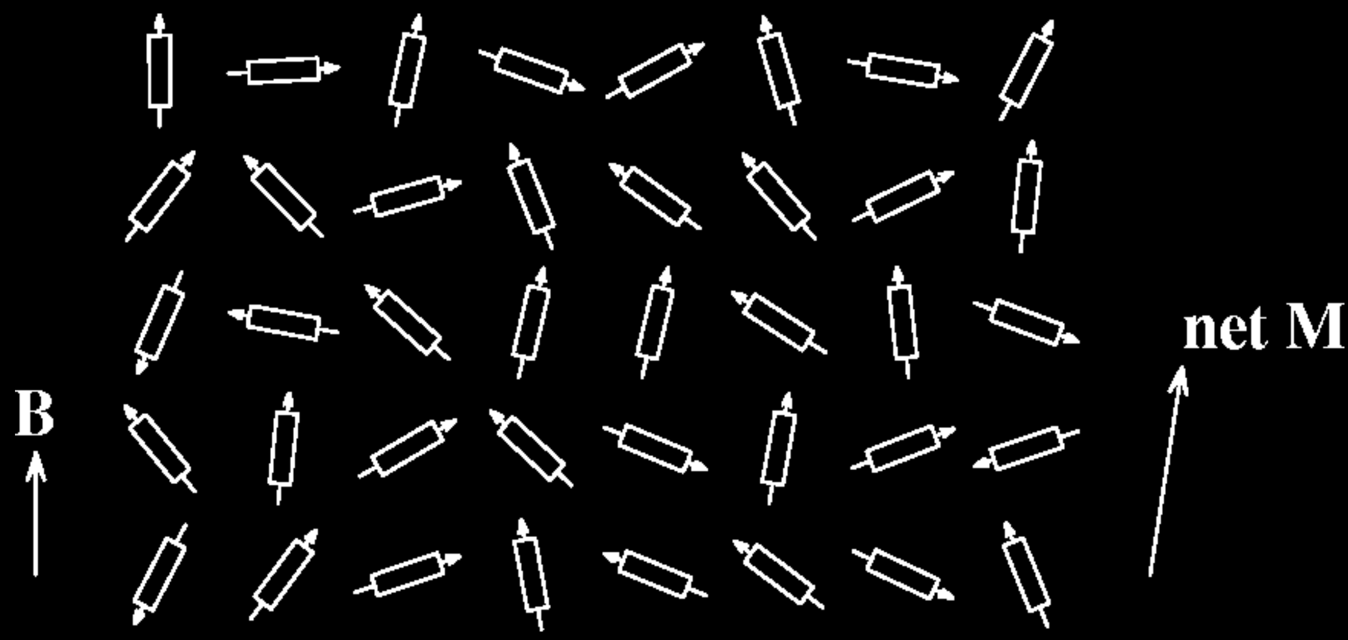
We listen to these radio waves with an "RF coil" (radio antenna)



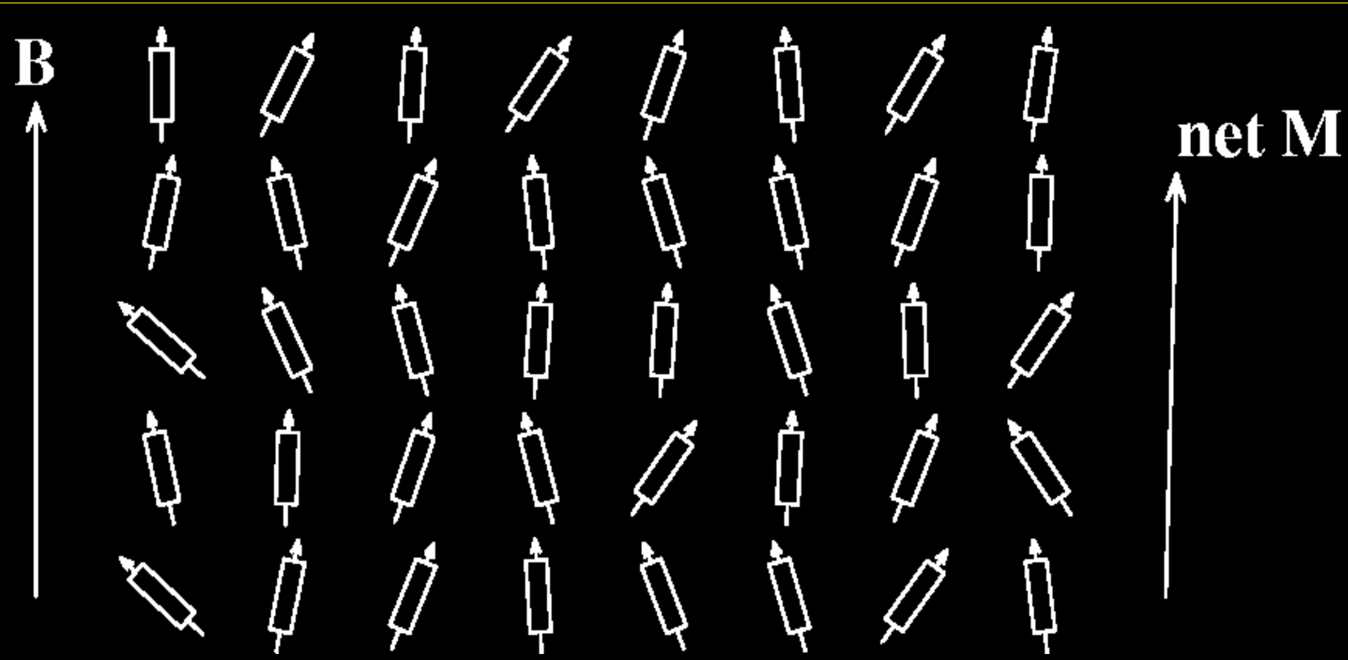
B_0 = Giant Field Produced by Giant Magnet

- Purpose is to align H protons in H_2O (little magnets)





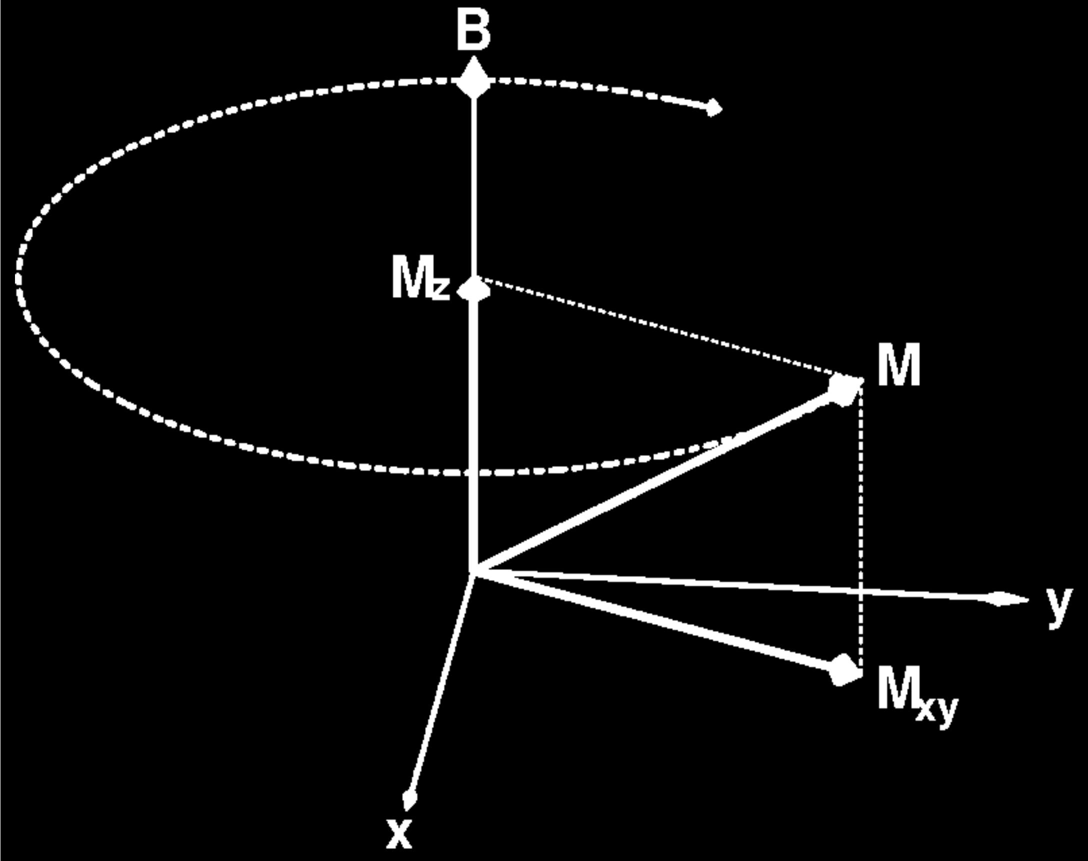
- Small B_0 produces small net magnetization M
- Thermal motions try to randomize alignment of proton magnets

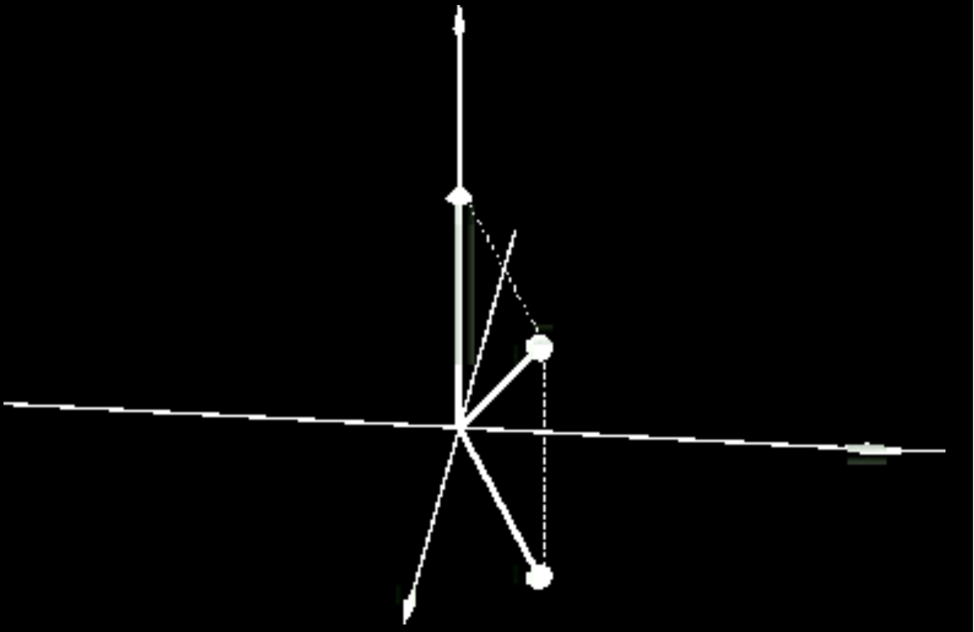


- Larger B_0 produces larger net magnetization M, lined up with B_0
- Reality check: 0.0003% of protons aligned per Tesla of B_0

Precession of Magnetization *M*

- Magnetic field causes *M* to rotate (or ***precess***) about the direction of *B* at a frequency proportional to the size of *B* — 42 million times per second (42 MHz), per Tesla of *B*

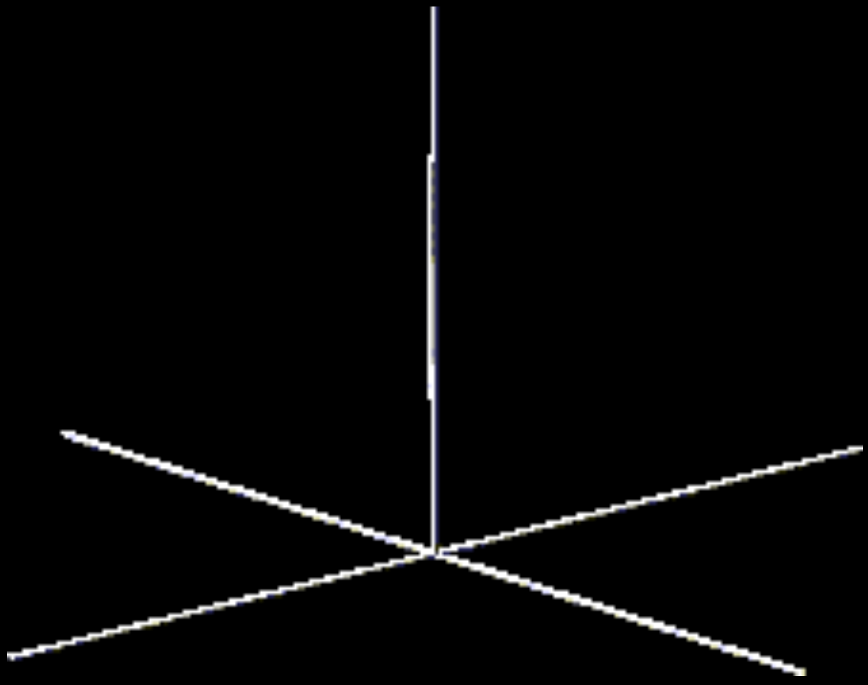




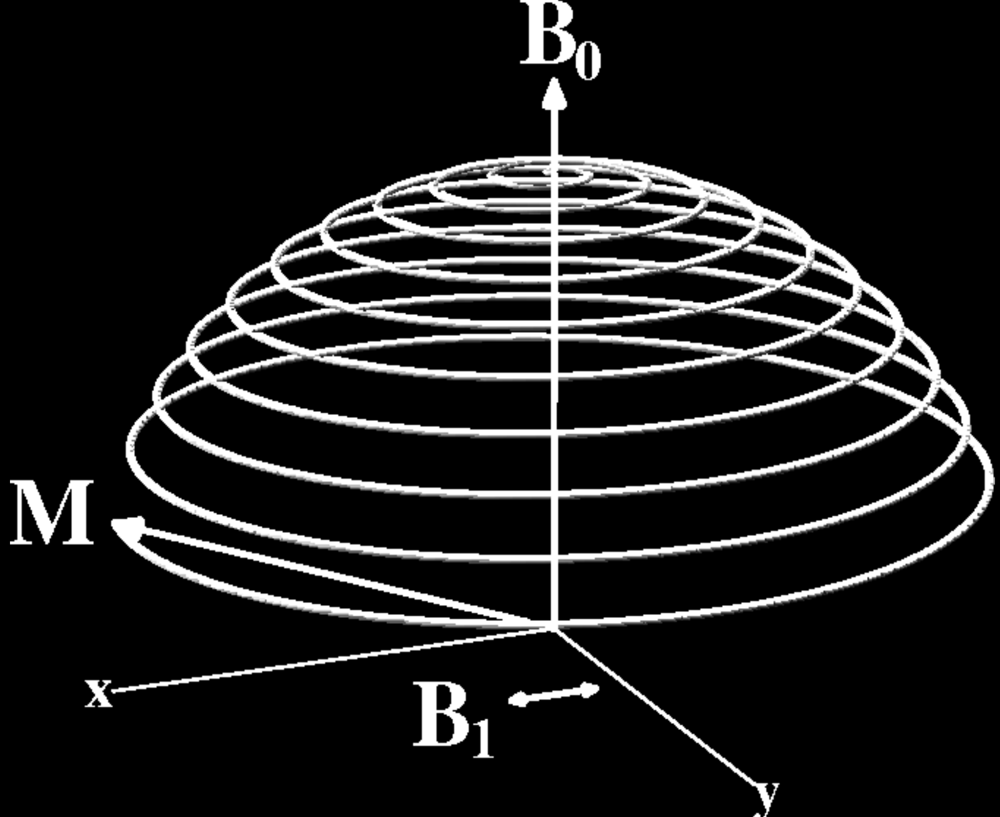
- N.B.: part of *M* parallel to *B* (M_z) does not precess

B_1 = Excitation (Transmitted) Radio Frequency (RF) Field

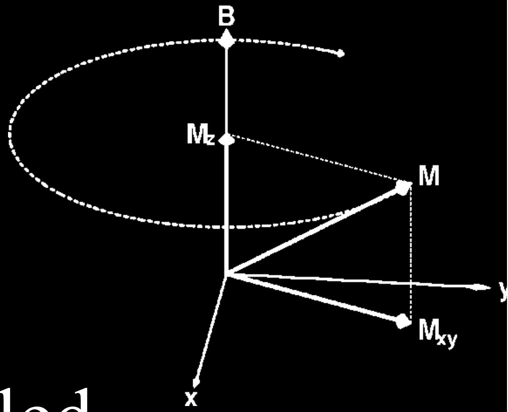
- Left alone, M will align itself with B in about 2–3 s
- <u>So don't leave it alone</u>: apply (transmit) a magnetic field B_1 that fluctuates at the precession frequency and points perpendicular to B_0



Time = 2–4 ms

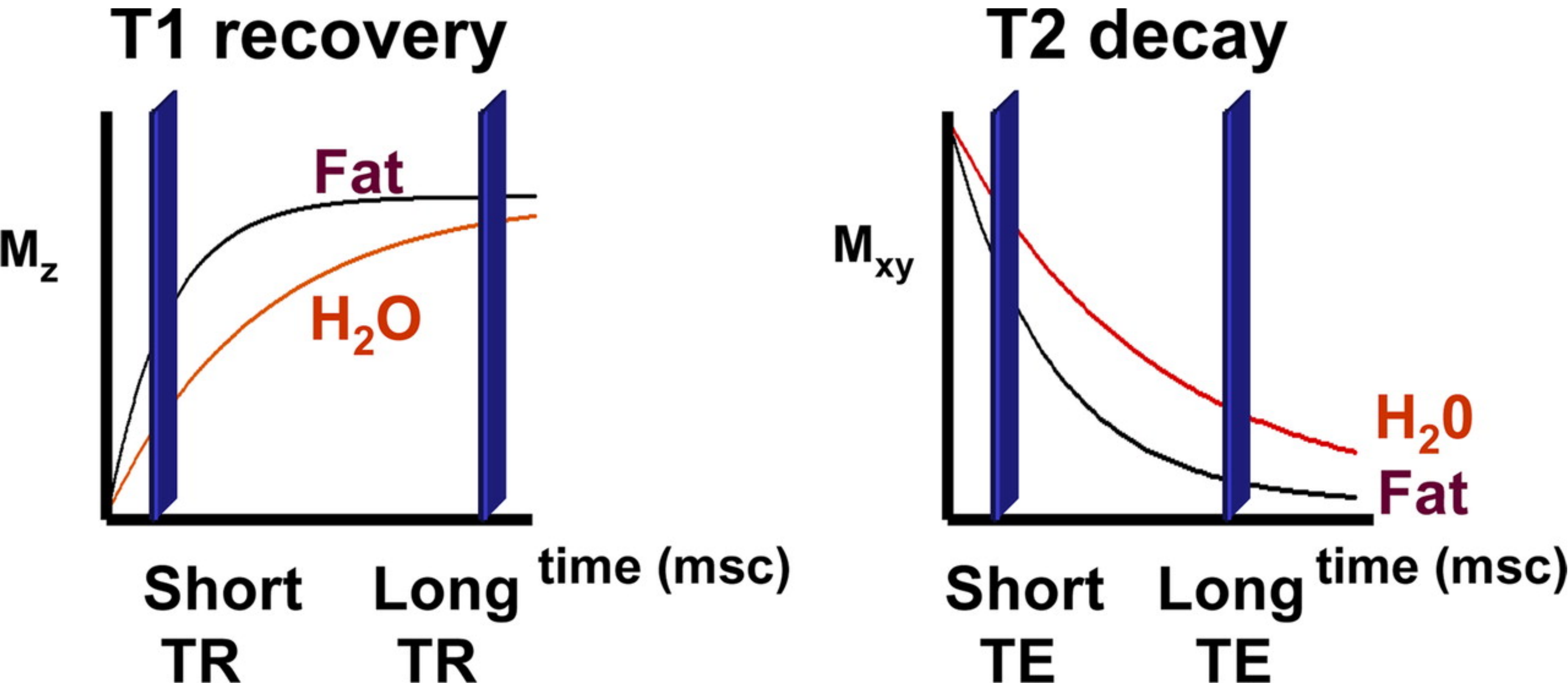


Relaxation: Nothing Lasts Forever



- In absence of external B_1, M will go back to being aligned with static field B_0 — this is called *relaxation*
- T2: Part of M perpendicular to B_0 shrinks [M_{xy}]
  - This part of M is called *transverse magnetization*
  - It provides the detectable RF signal
- T1: Part of M parallel to B_0 grows back [M_z]
  - This part of M is called *longitudinal magnetization*
  - Not directly detectable, but is converted into transverse magnetization by externally applied B_1

Ants on a Pole analogy—two different physical properties



Bitar, R. et al. Radiographics 2006;26:513-537

T1WI

Dark
Air, mineral rich tissue (cortical bone, stones), fast-flowing blood

Low
Collagenous tissue (ligaments, tendons, scars), high free water tissue (kidneys, gonads, edema, fluids [urine, bile], simple cysts, bladder, gallbladder, spleen, CSF), high bound water tissues (liver, pancreas, adrenals, hyaline cartilage, muscle)

Intermediate
Proteinaceous tissue (abscess, complex cysts, synovial fluid)

Bright
Fat, fatty bone marrow, blood products (methemoglobin [metHb]), slow-flowing blood, radiation change, paramagnetic contrast agents

T2WI

Dark
Air, mineral rich tissue (cortical bone, stones), fast-flowing blood

Low
Collagenous tissue (ligaments, tendons, scars), bone islands

High bound water tissues (liver, pancreas, adrenals, hyaline cartilage, muscle)

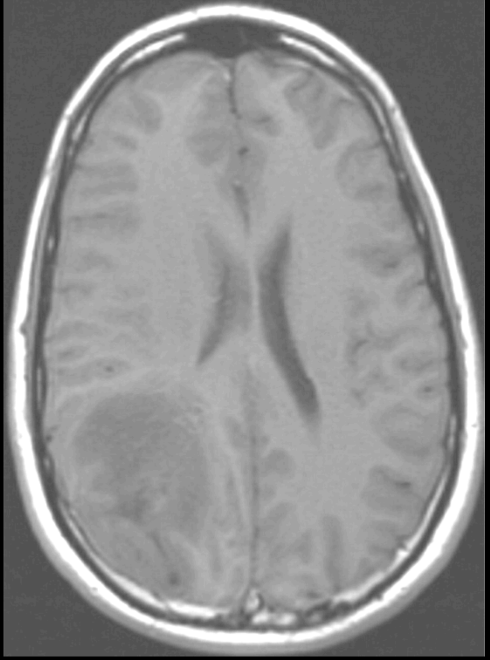
Intermediate
Fat, fatty bone marrow

Bright
High free water tissue (kidneys, gonads, edema, fluids (urine, bile), simple cysts, bladder, gallbladder, spleen, CSF), proteinaceous tissue, blood products (oxyhemoglobin, extracellular metHb)

Basics of MR

- T1 ~ Longitudinal Magnetization/Relaxation

"hi-resolution, normal anatomy"

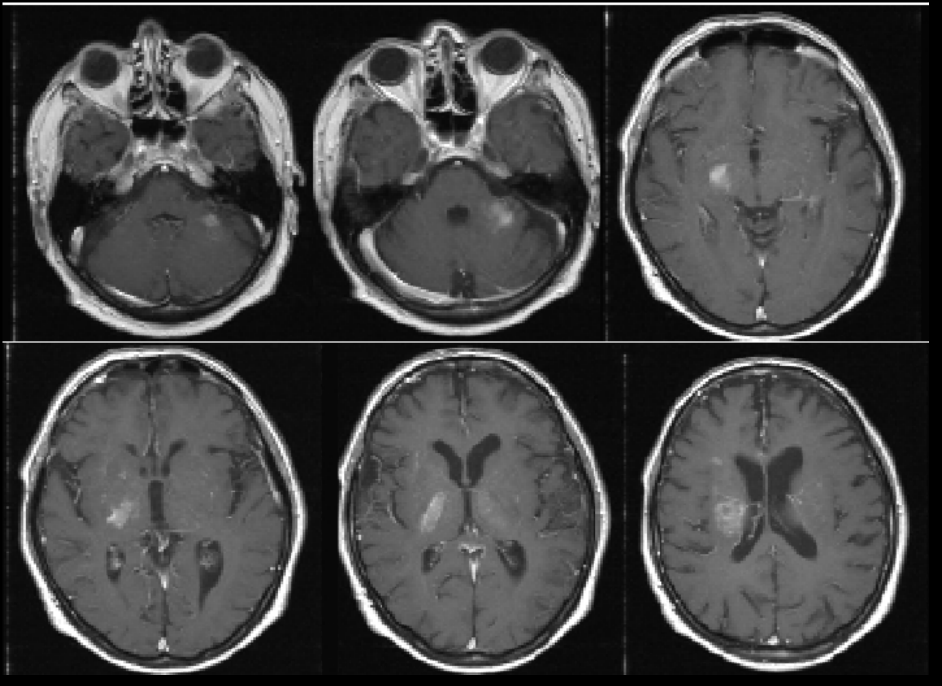


T2 ~ Transverse Magnetization/ Relaxation

"pathology"—water content

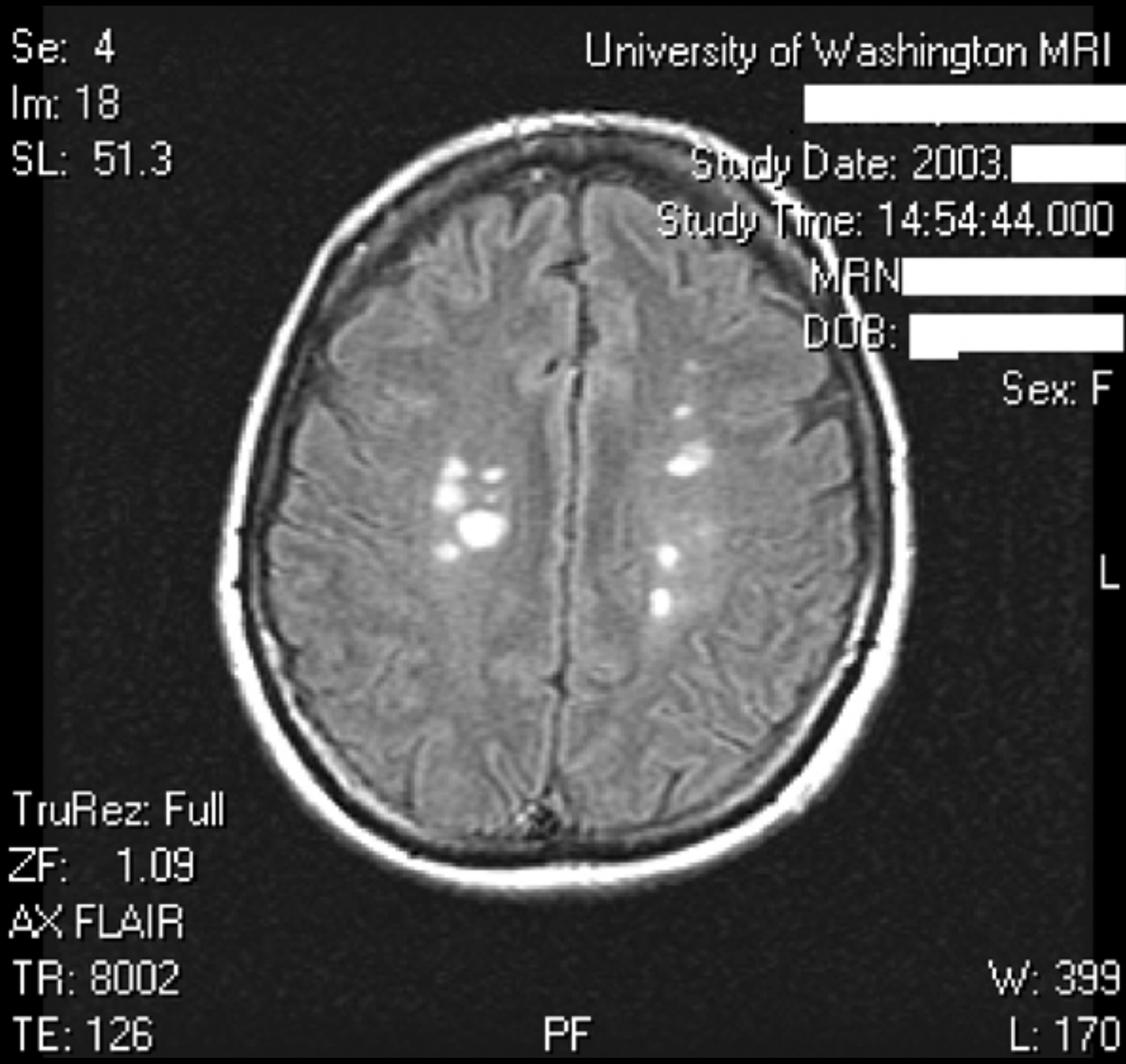
Basics of MR—contrast agents

- Gadolinium
- can be injected to enhance contrast (usually in T1 images); hastens T1 recovery making image brighter



Clinical Applications: Multiple Sclerosis

- T2 is best for seeing white matter abnormalities

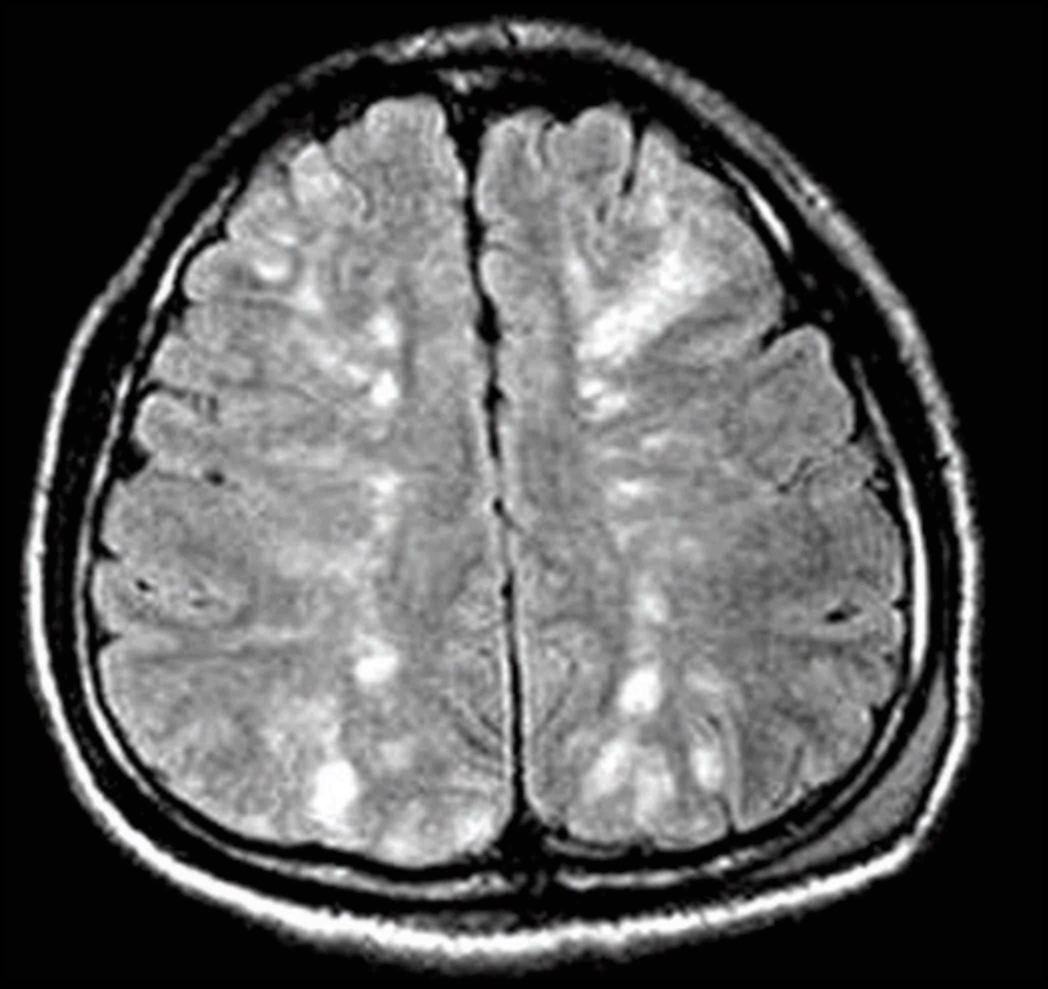


Bonus—Shelf Exam Question

A 53-year-old woman dies 4 days after an automobile collision. She sustained multiple injuries including a femoral fracture. Widespread petechiae are found in the cerebral white matter at autopsy. Which of the following is the most likely cause of these findings?

(A) Acute respiratory distress syndrome
(B) Contrecoup injury
(C) Fat embolization
(D) Septicemia
(E) Subdural hematoma

Fat emboli (FLAIR T2)



Scanner as computer…

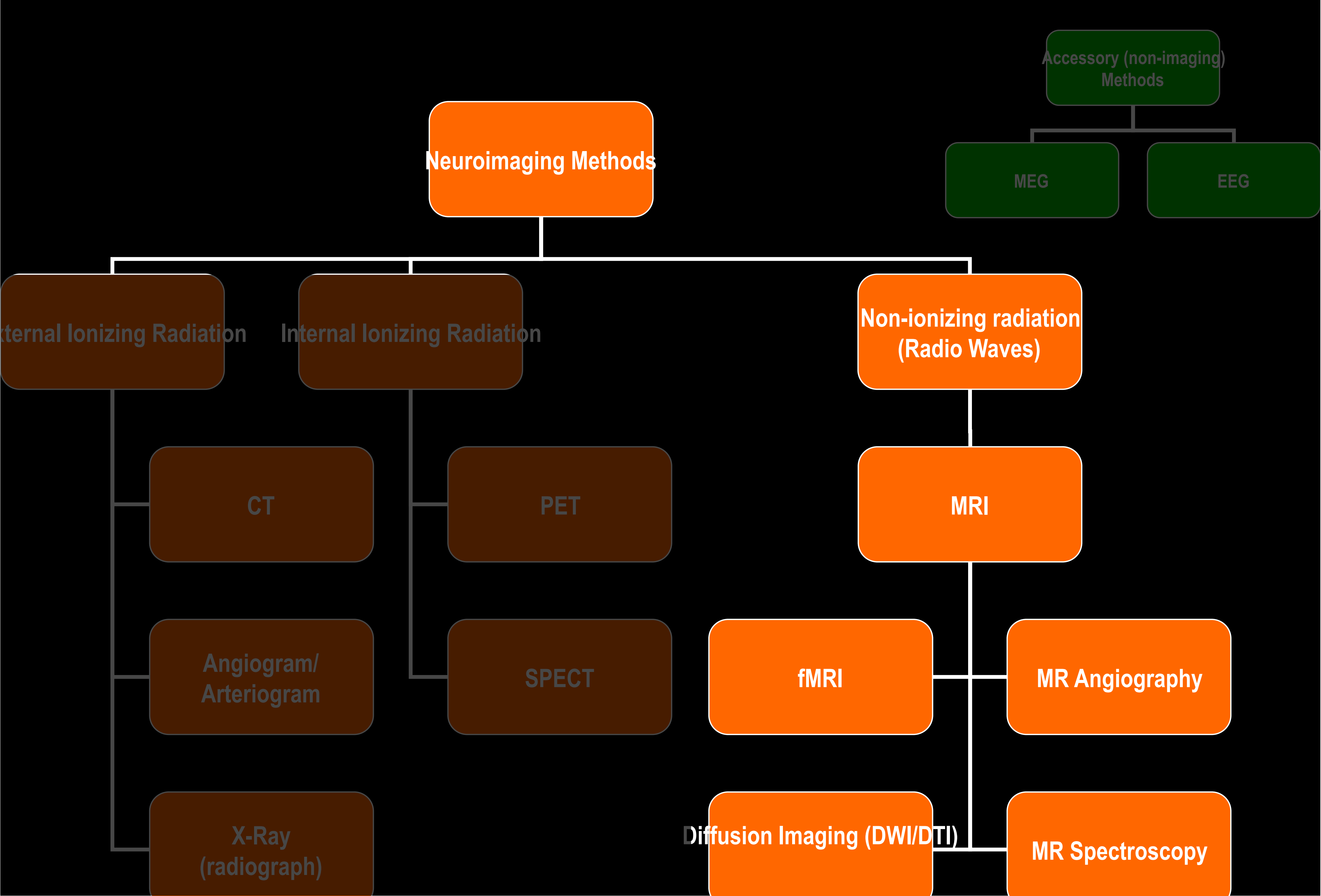
- pulse sequences are software

CT vs MRI

TV with one channel (not that much good on)

vs.

Computer that can run lots of programs (takes longer to boot up, but get more for it)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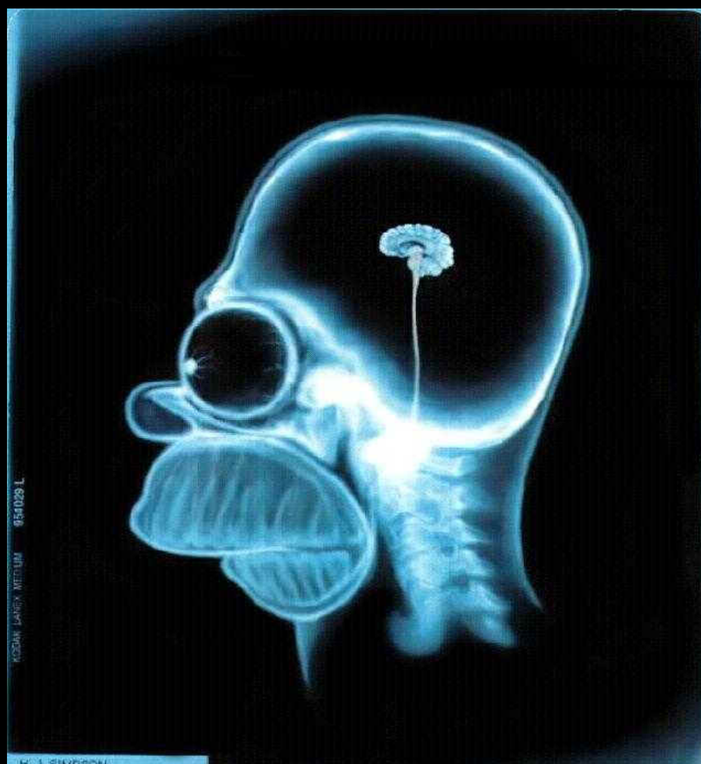
MRI vs. fMRI

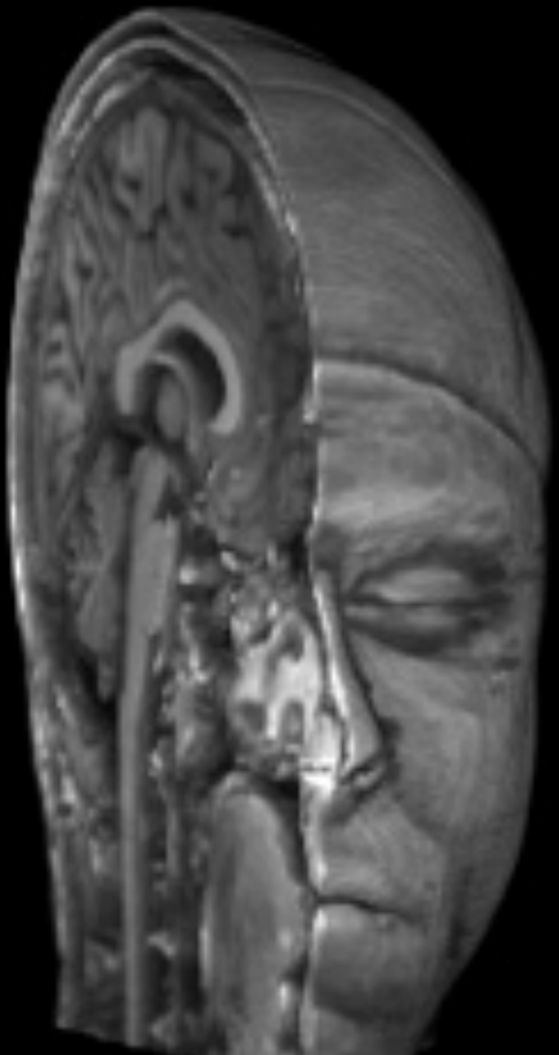
MRI studies brain anatomy.



Functional MRI (fMRI) studies brain function.

fMRI for Dummies

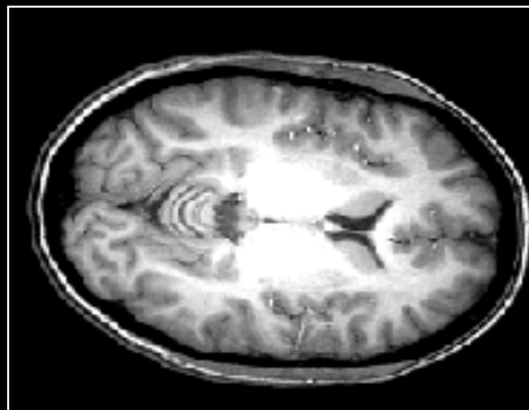
An “anonymous” grad student



MRI vs. fMRI

MRI

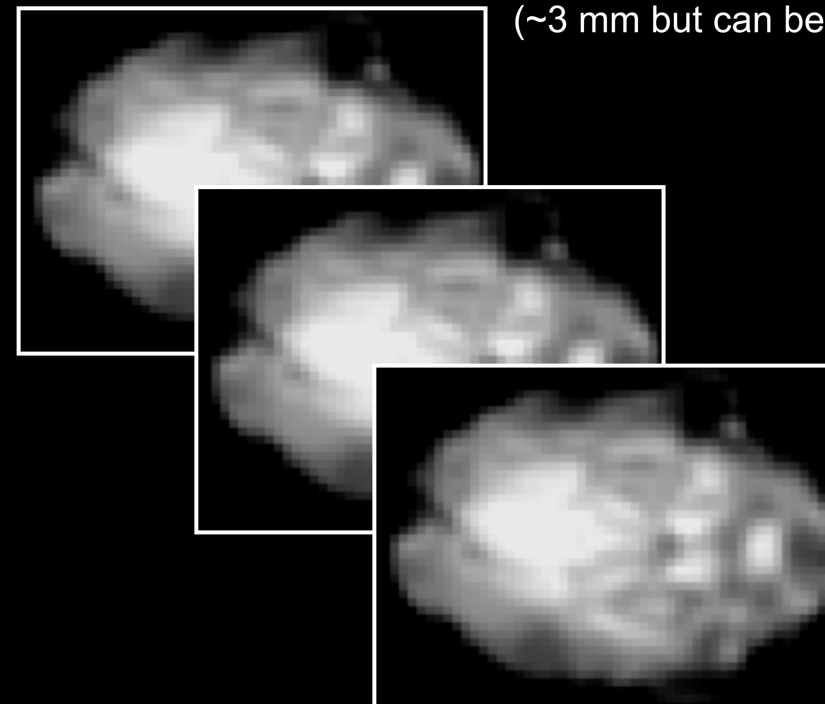
high resolution
(1 mm)



one image

fMRI

low resolution
(~3 mm but can be better)



many images
(e.g., every 2 sec for 5 mins)

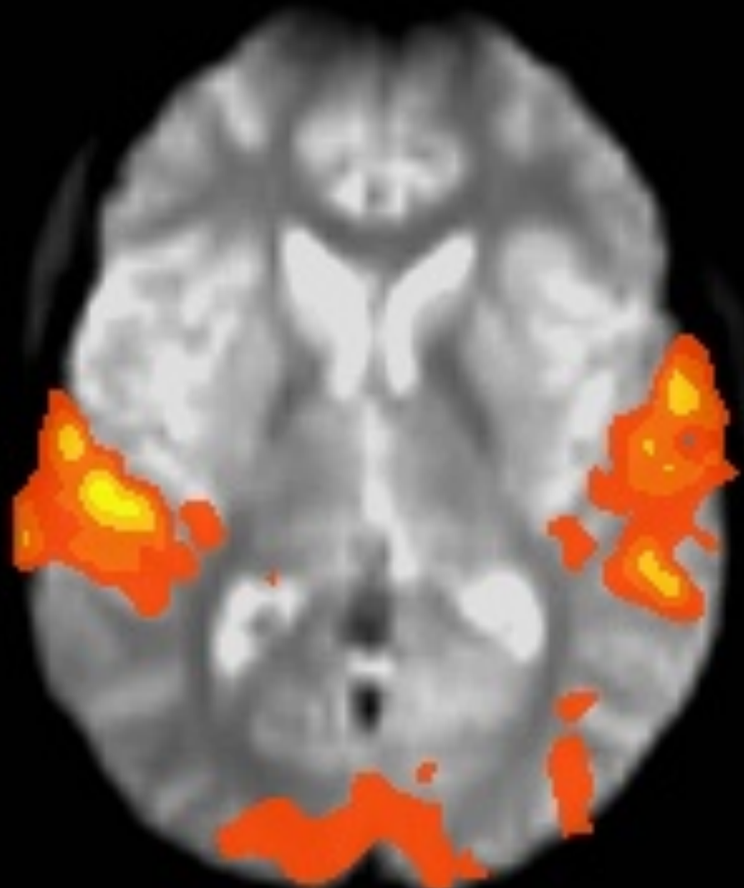
fMRI

Blood Oxygenation Level Dependent (BOLD) signal
indirect measure of neural activity

↑ neural activity → ↑ blood oxygen → ↑ fMRI signal

fMRI for Dummies

An “anonymous” M3



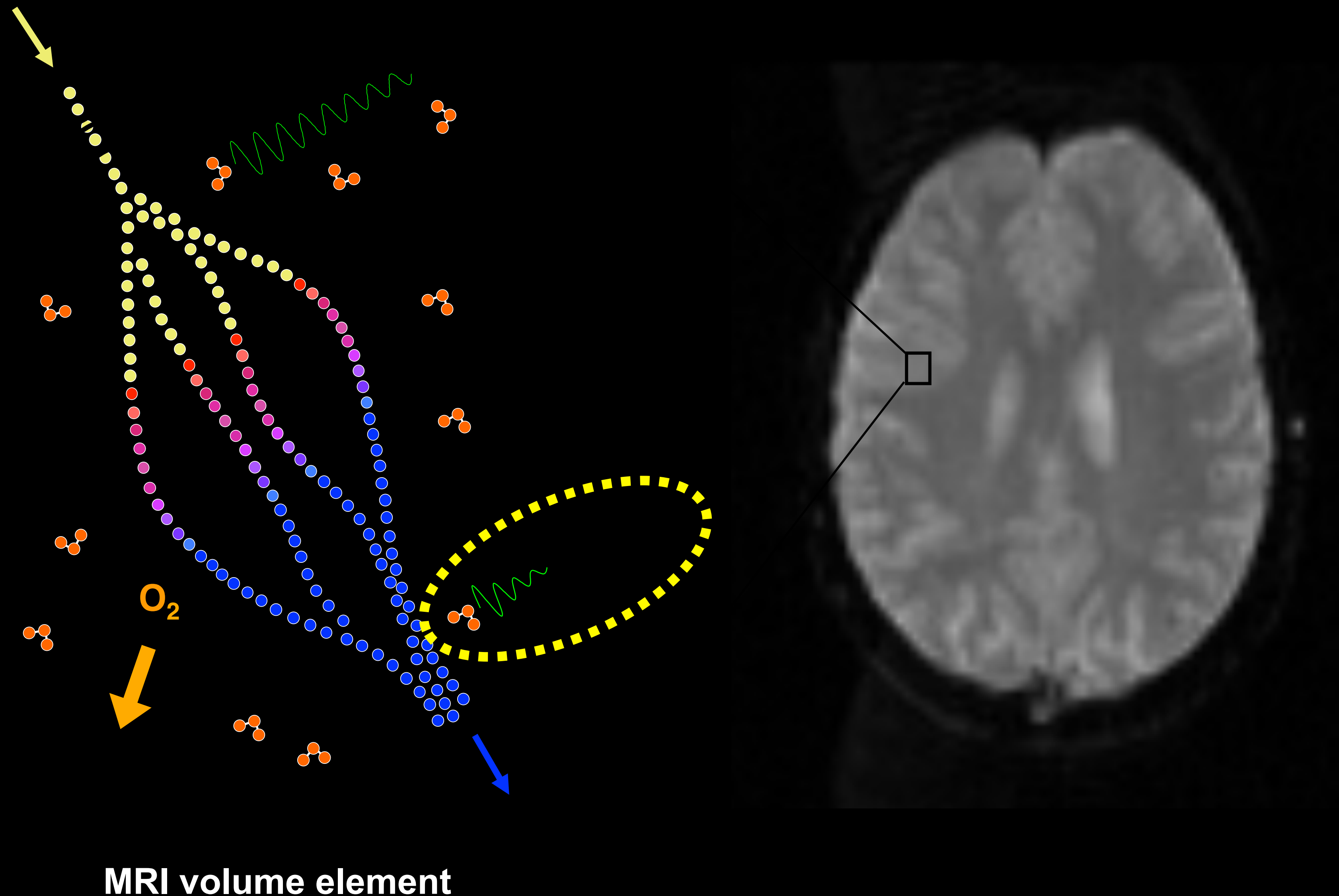
Metabolism

- Brain uses ~20% of total body oxygen

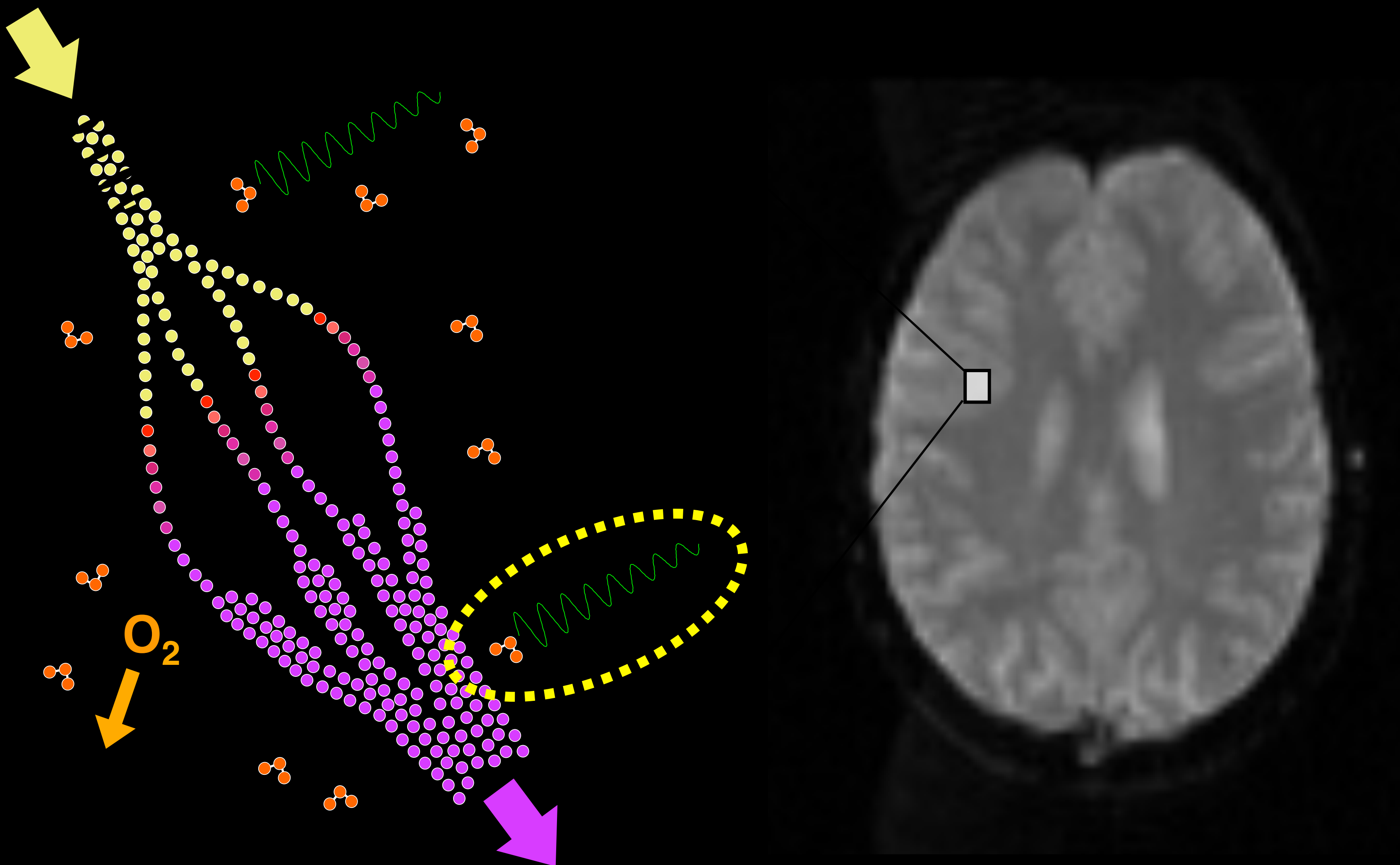
(even though only 1-2% of total body mass)

Complex mechanism for regulating cerebral blood flow to ensure adequate oxygen supply

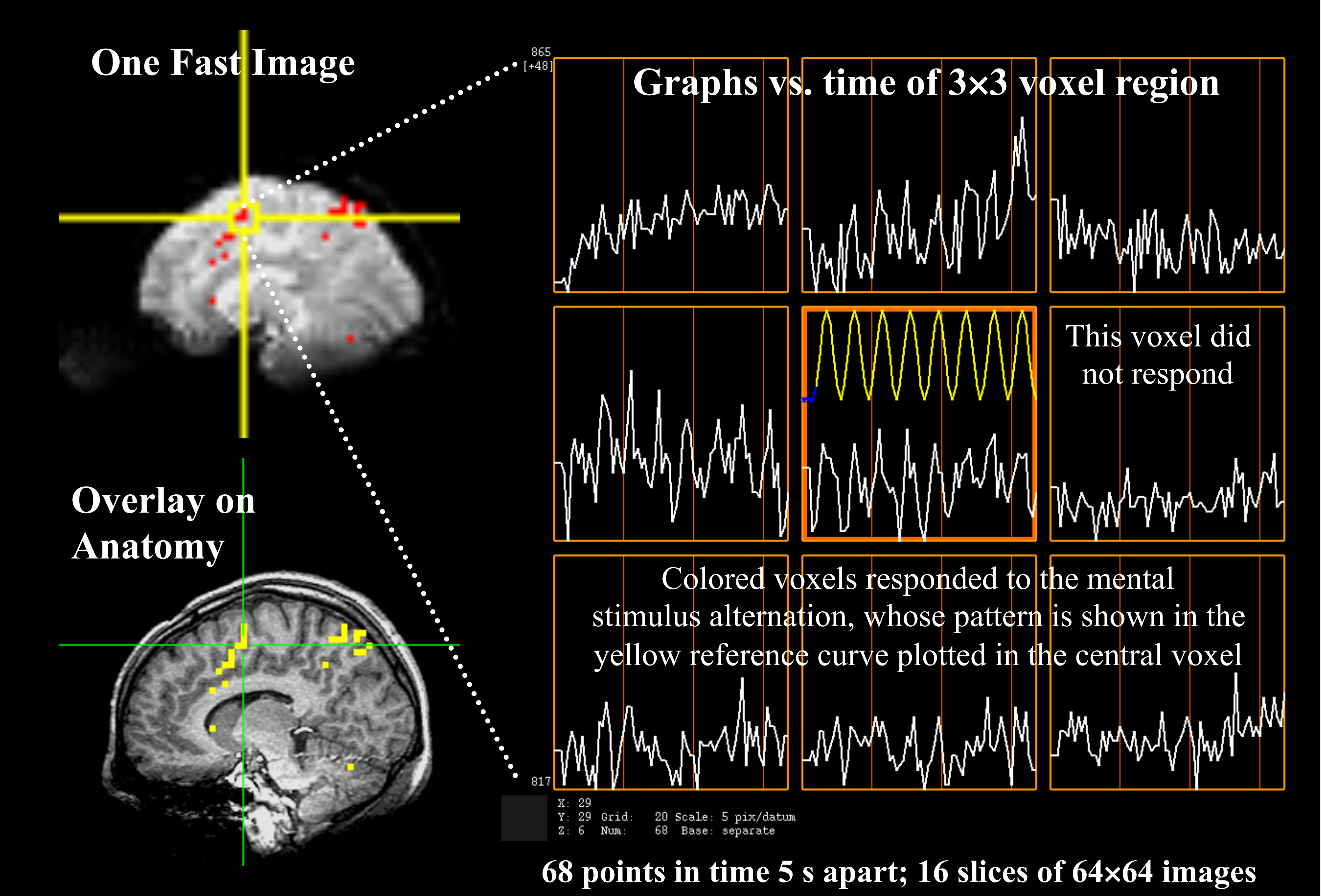
Deoxygenated blood attenuates T_2^*-weighted MR images



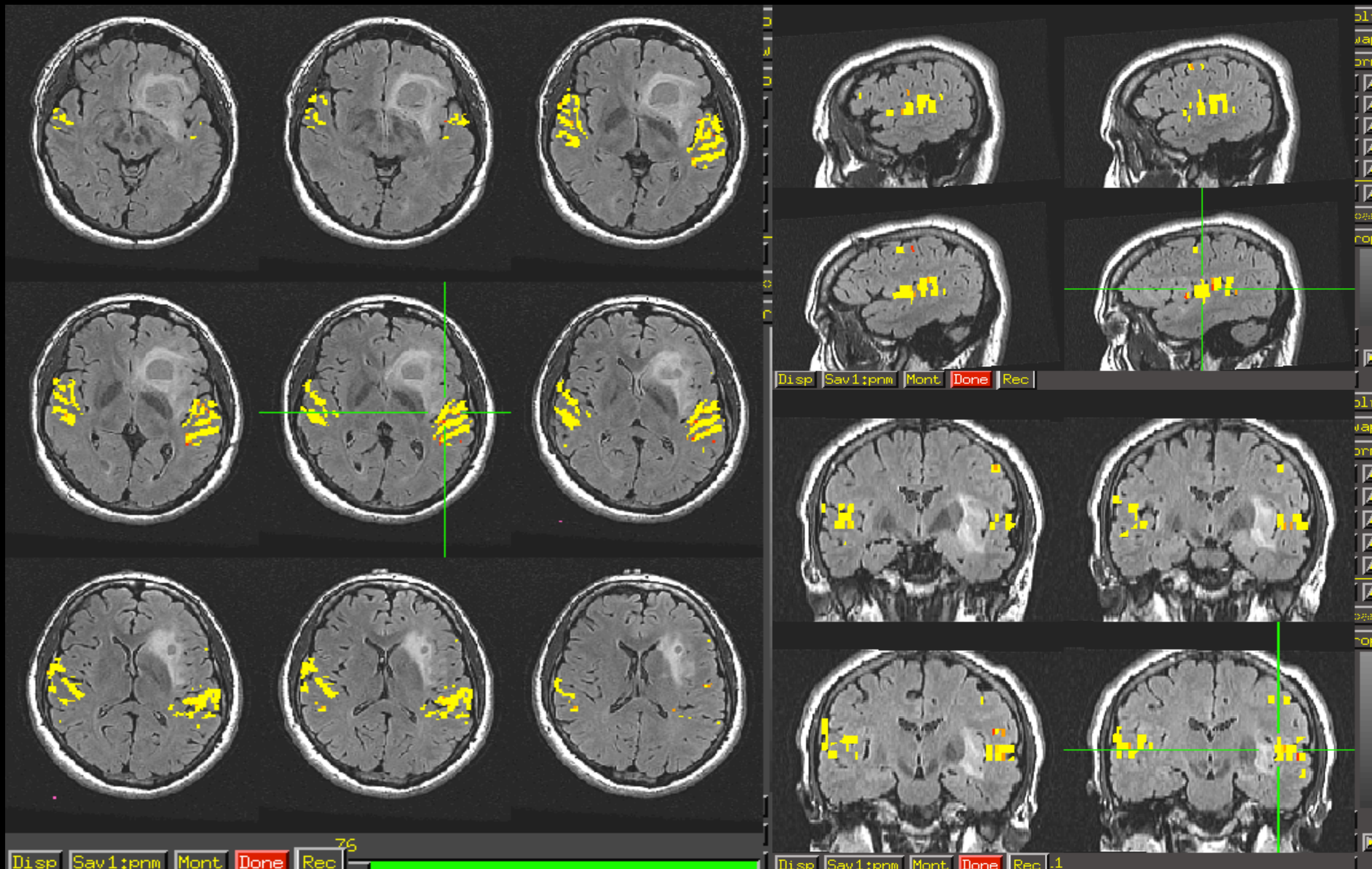
decrease of venous dHb during increased perfusion:

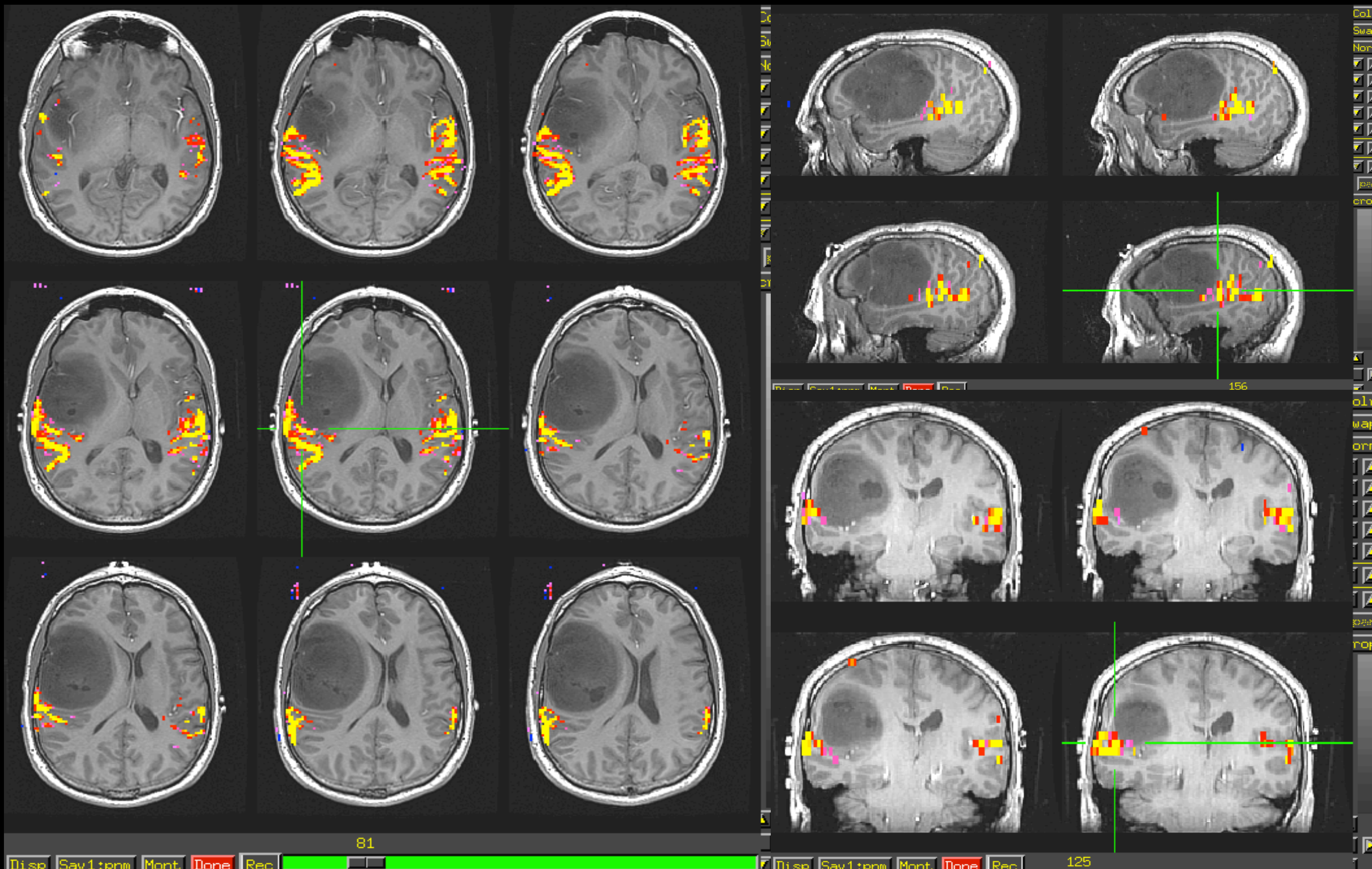


Human 3T used for BOLD fMRI

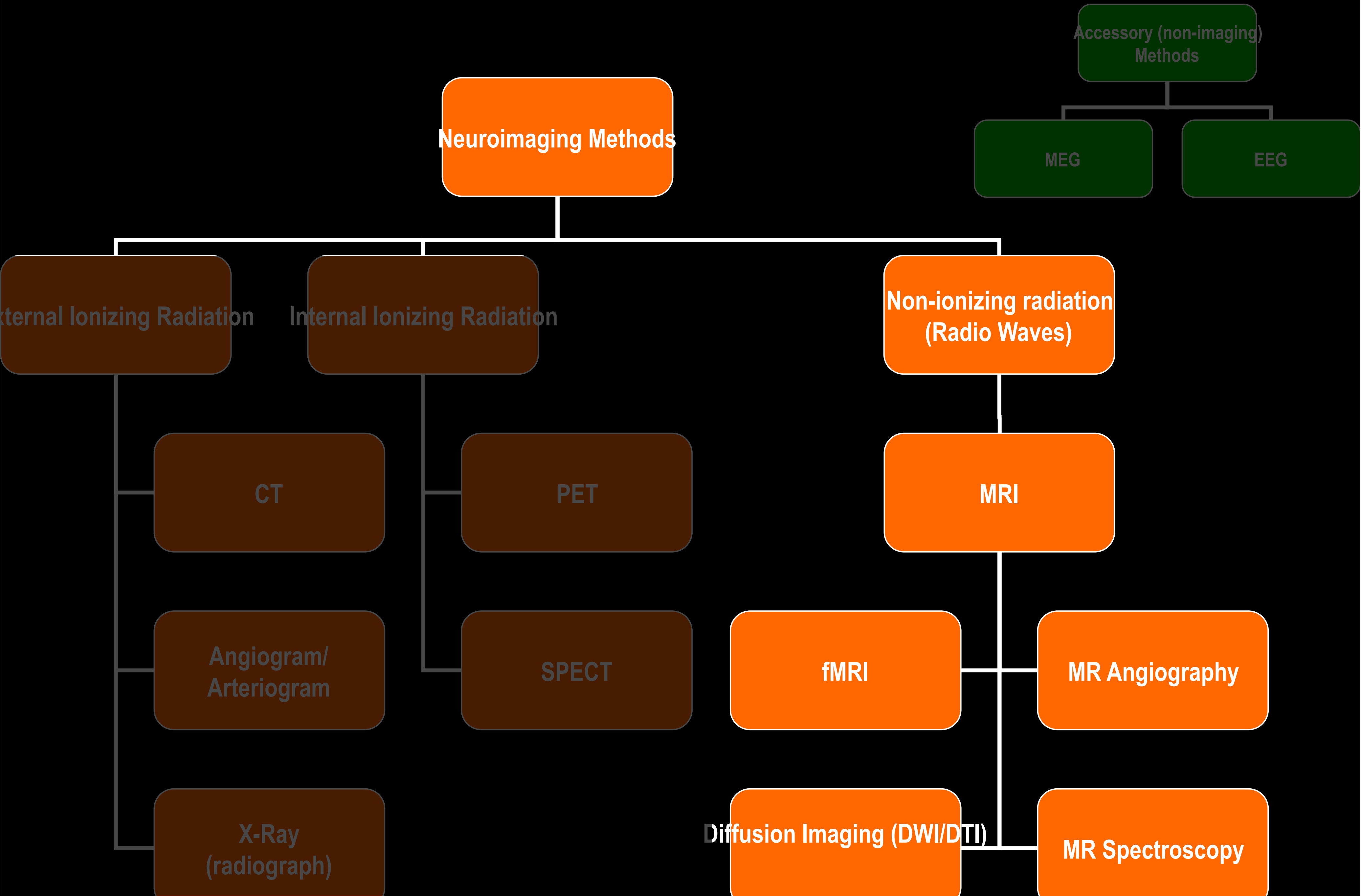


One Fast Image
Overlay on Anatomy
865
[+48]
Graphs vs. time of 3×3 voxel region
This voxel did not respond
Colored voxels responded to the mental stimulus alternation, whose pattern is shown in the yellow reference curve plotted in the central voxel
817
X: 29
Y: 29 Grid: 20 Scale: 5 pix/datum
Z: 6 Num: 68 Base: separate
68 points in time 5 s apart; 16 slices of 64×64 images

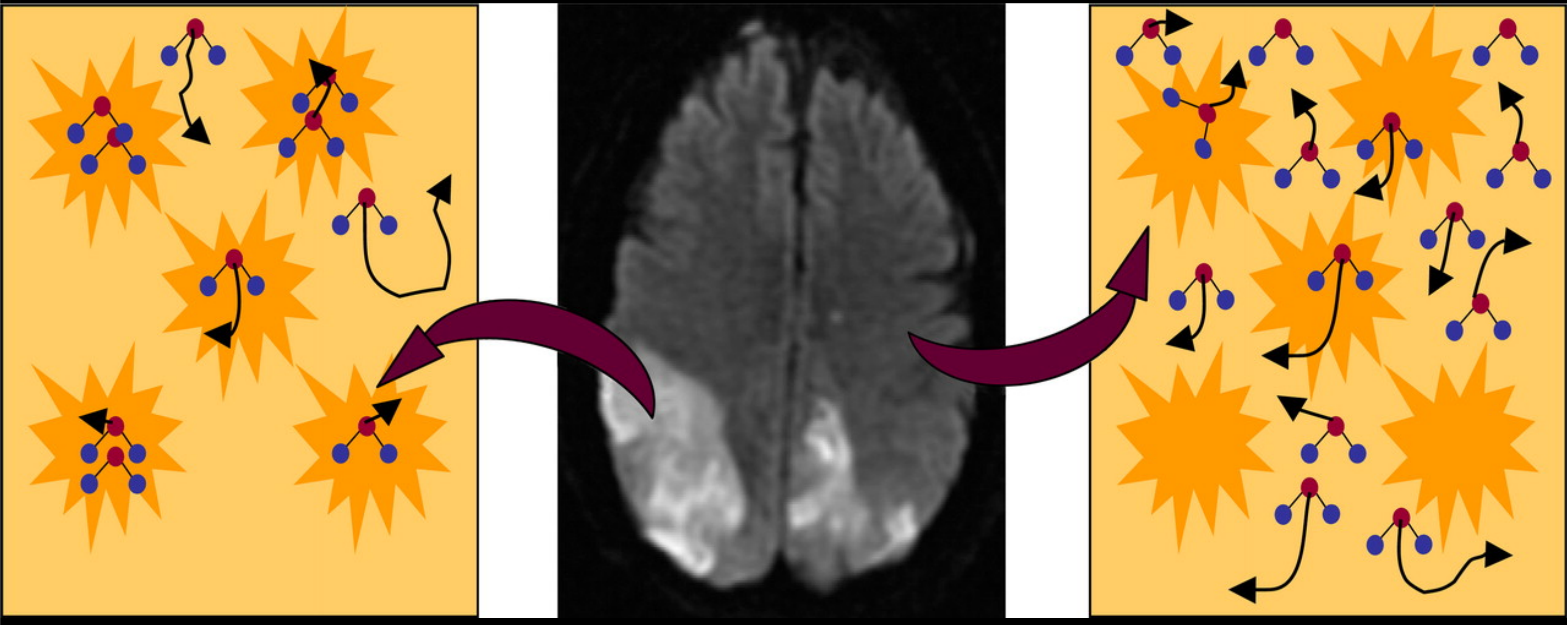

Disp
Sav1:pnm
Mont
Done
Rec
76



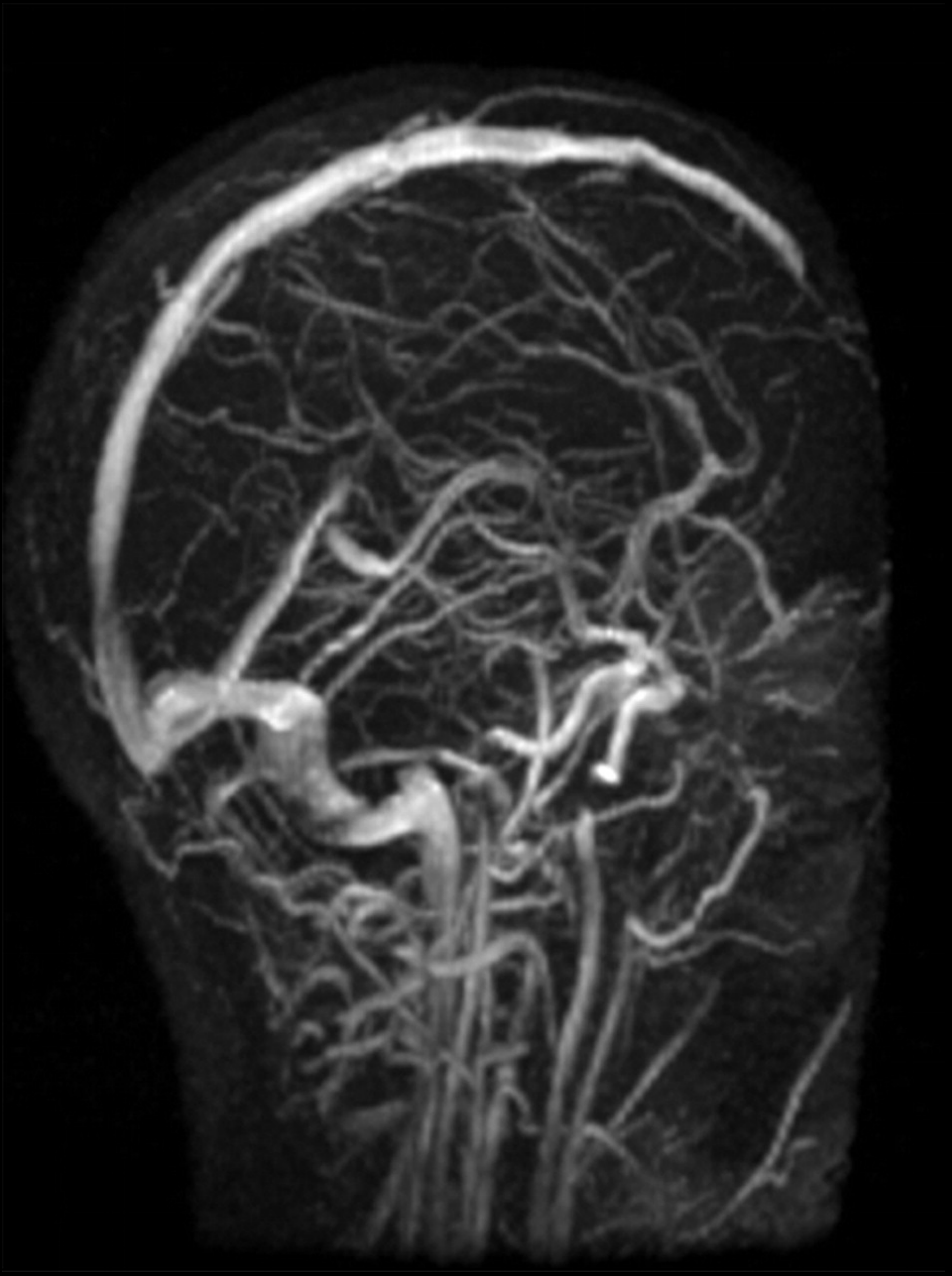
Colr
Swap
Norm
crop
156
81
Disp
Sav1:pnm
Mont
Done
Rec
125
Disp
Sav1:pnm
Mont
Done
Rec


Accessory (non-imaging) Methods
MEG
EEG
Neuroimaging Methods
xternal Ionizing Radiation
Internal Ionizing Radiation
Non-ionizing radiation (Radio Waves)
CT
PET
MRI
Angiogram/ Arteriogram
SPECT
fMRI
MR Angiography
X-Ray (radiograph)
Diffusion Imaging (DWI/DTI)
MR Spectroscopy

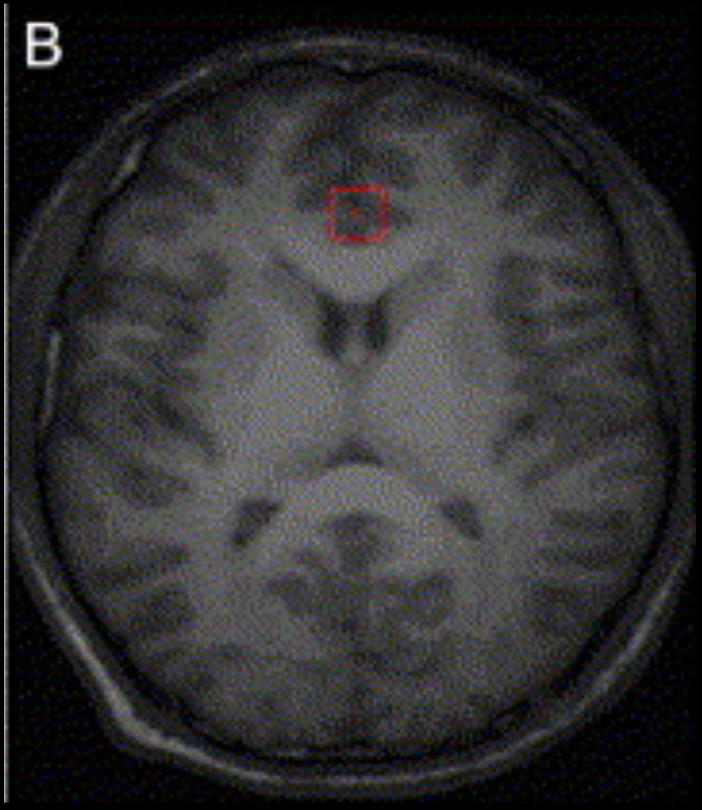
Diffusion Weighted Imaging—earliest post-stroke diagnosis

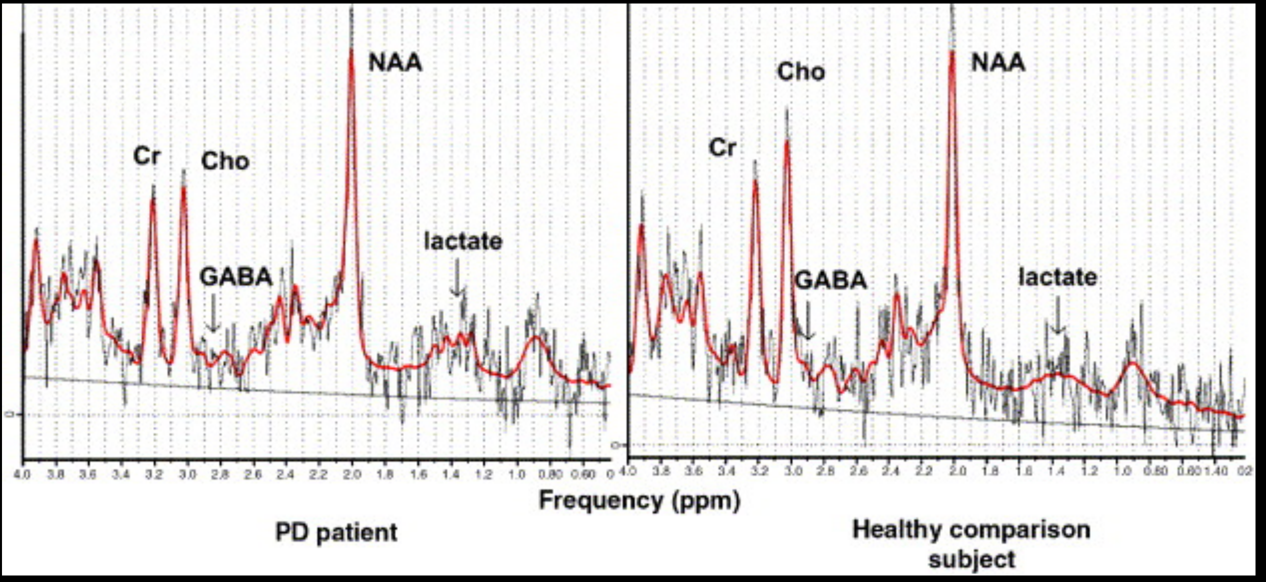


MR Angiography



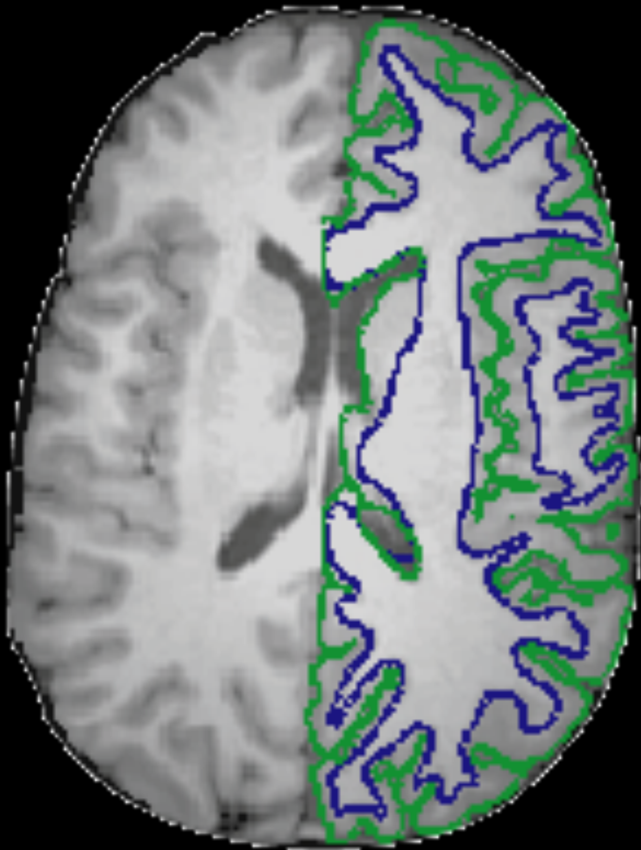
Magnetic Resonance Spectroscopy

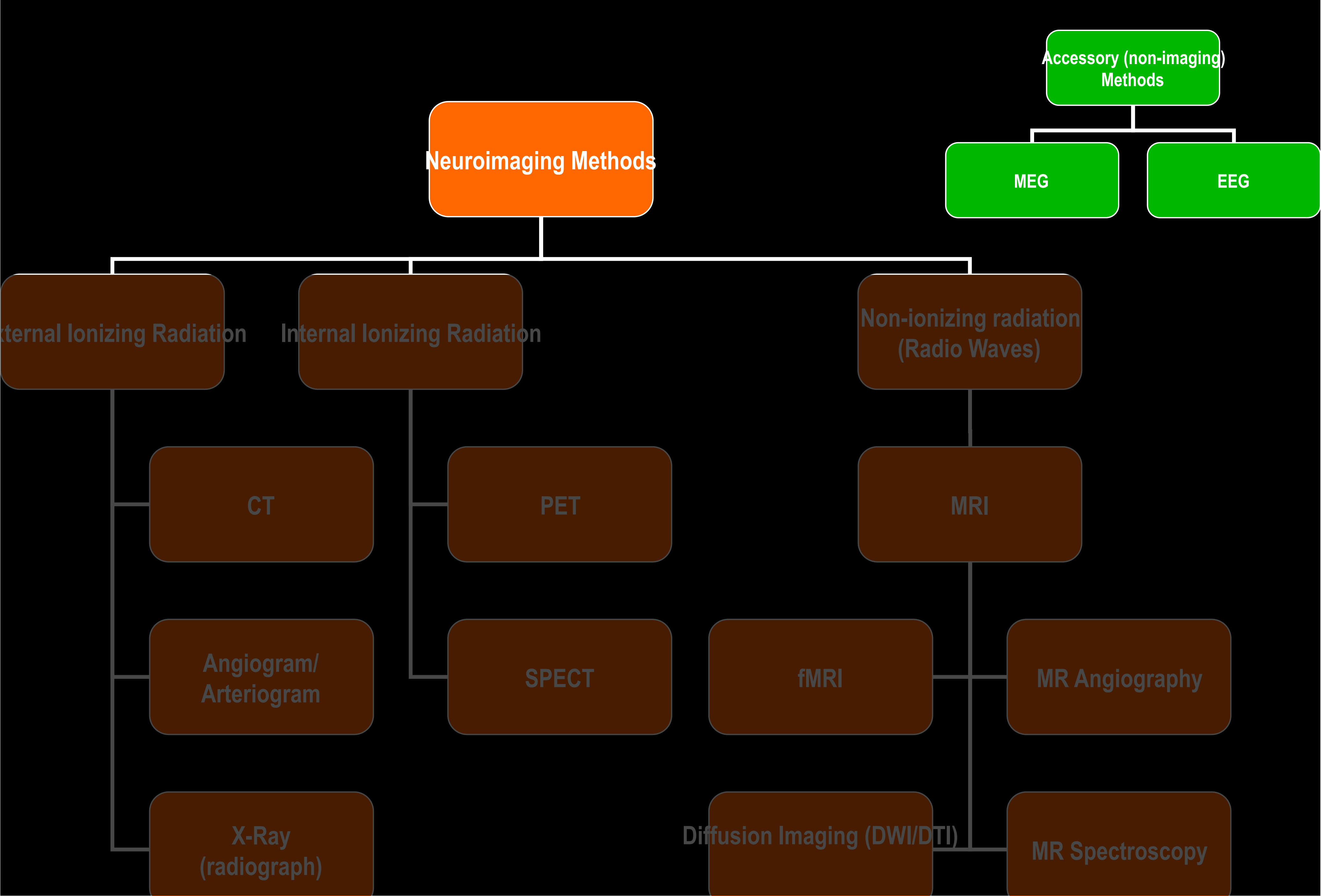




reduced GABA in panic disorder

Cortical Surface Models—AD/PD




Accessory (non-imaging) Methods
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Internal Ionizing Radiation
Non-ionizing radiation (Radio Waves)
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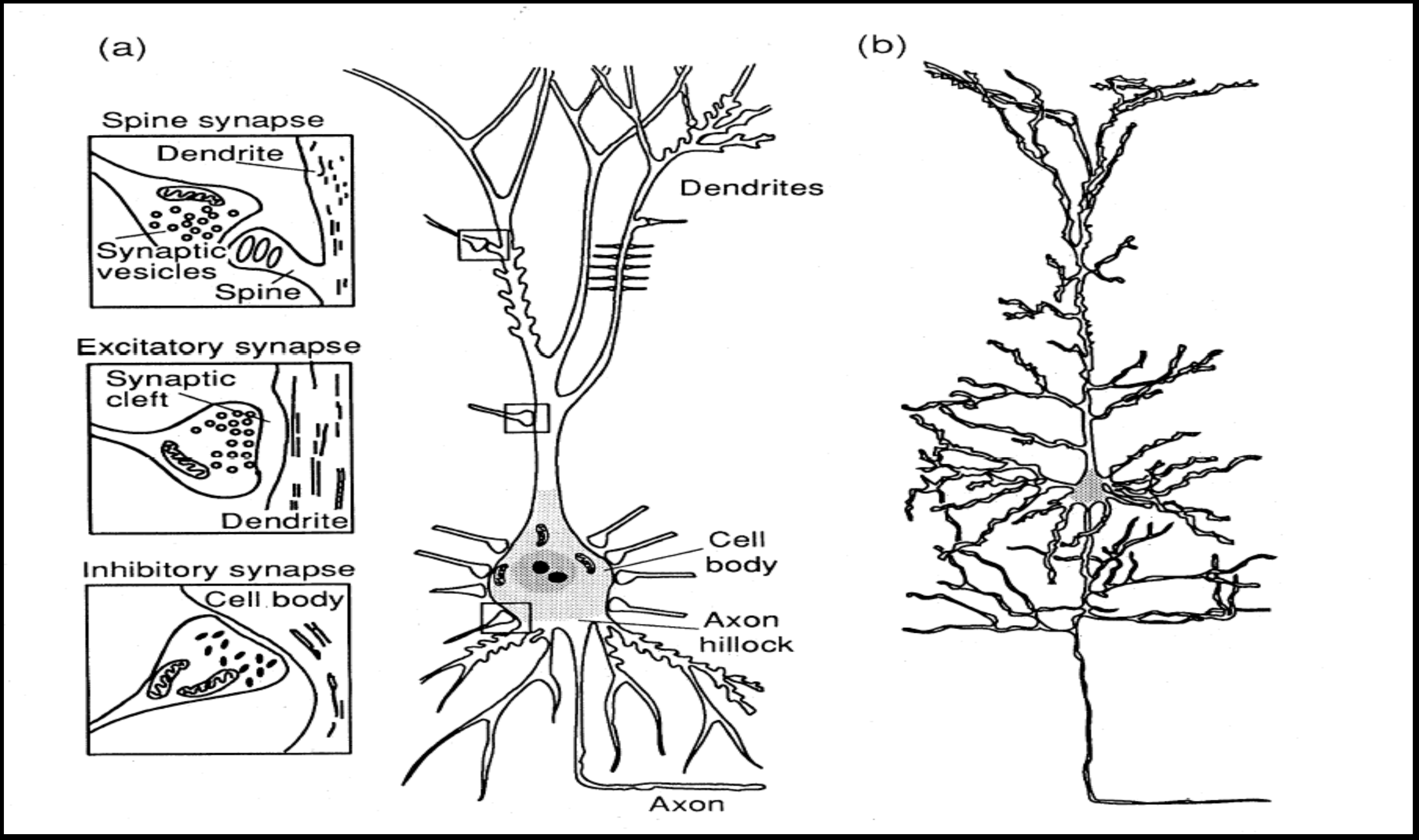
Angiogram/ Arteriogram
X-Ray (radiograph)
PET
SPECT
MRI
fMRI
MR Angiography
Diffusion Imaging (DWI/DTI)
MR Spectroscopy


(a)
Spine synapse
Dendrite
Synaptic
vesicles
Spine
Excitatory synapse
Synaptic
cleft
Dendrite
Inhibitory synapse
Cell body
Dendrites
Cell
body
Axon
hillock
Axon
(b)

EEG/MEG

Pros:

Completely non-invasive—**only modality that NEVER requires injection of a contrast agent**

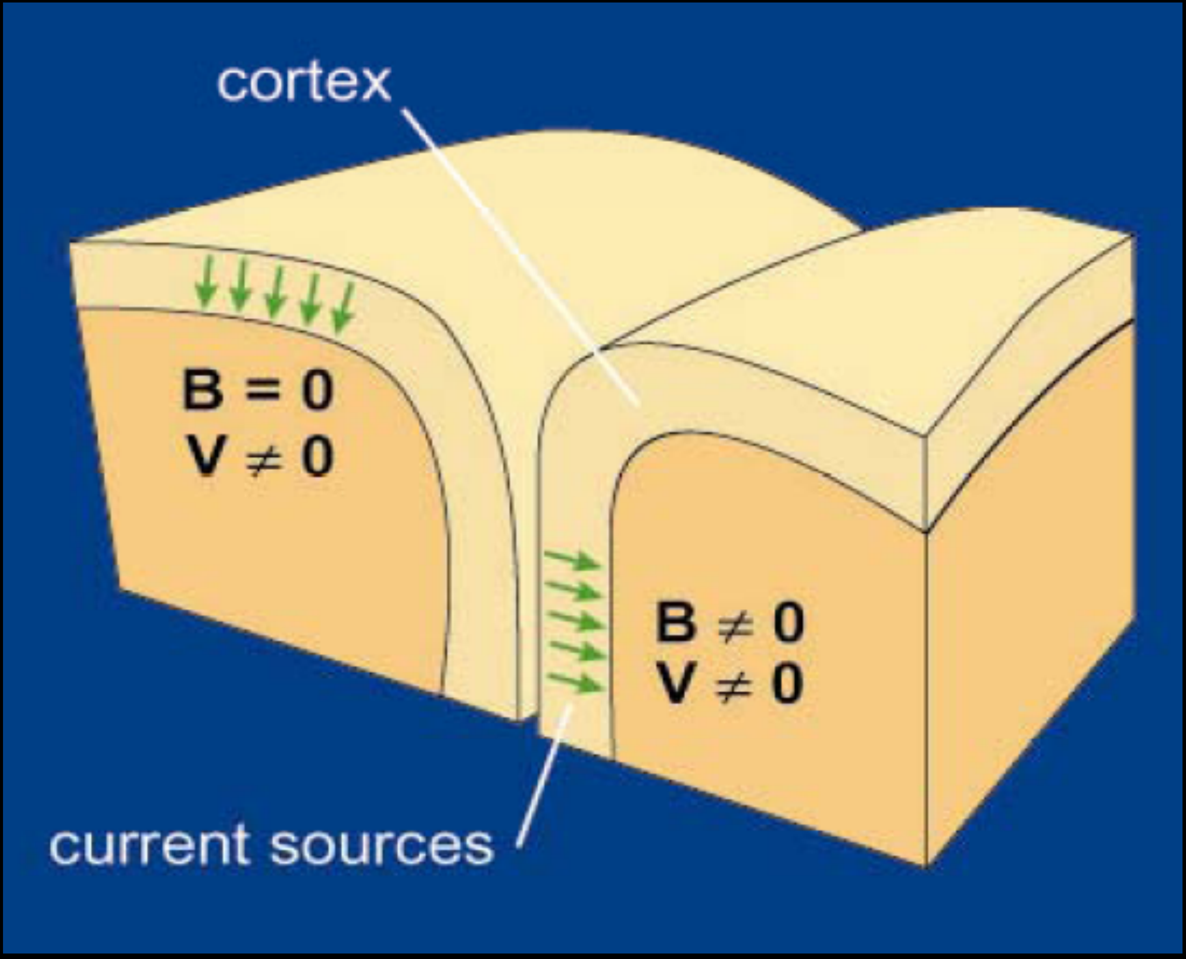
no ionizing radiation

direct measurement of neuronal activity

Cons:

not really neuroimaging

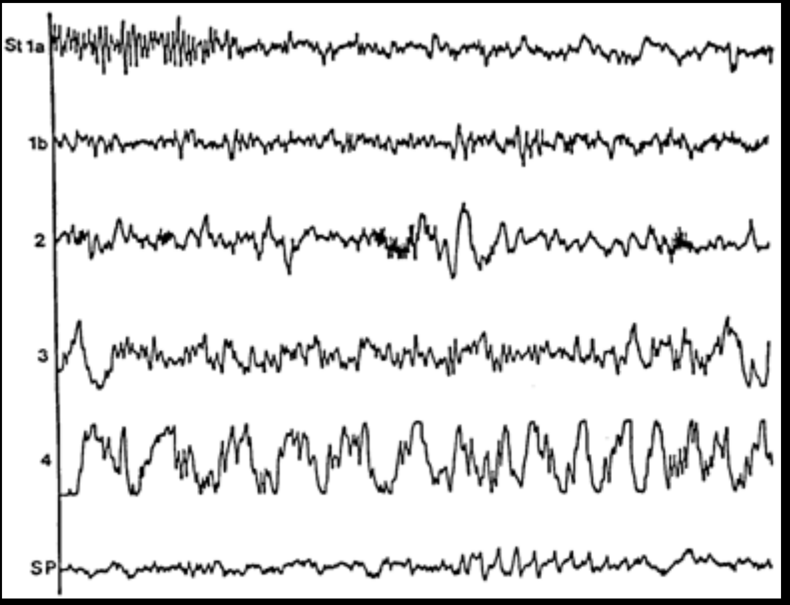
Limited clinical utility:
EEG—sleep studies
MEG--epilepsy



cortex
B = 0
V ≠ 0
B ≠ 0
V ≠ 0
current sources

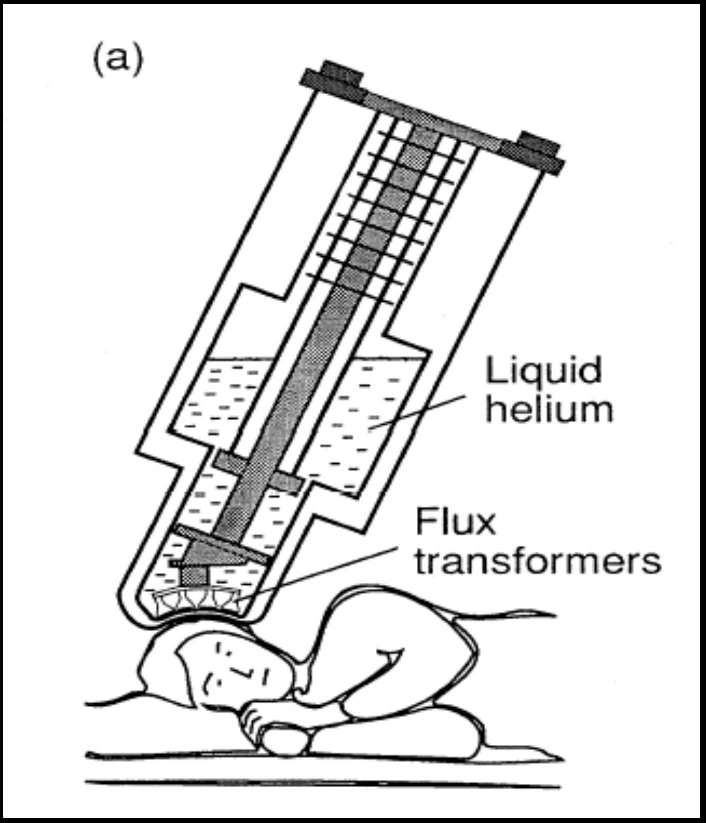
EEG

basic priniciple: electrodes on scalp surface record summed electrical activity (mainly synaptic) of many neurons



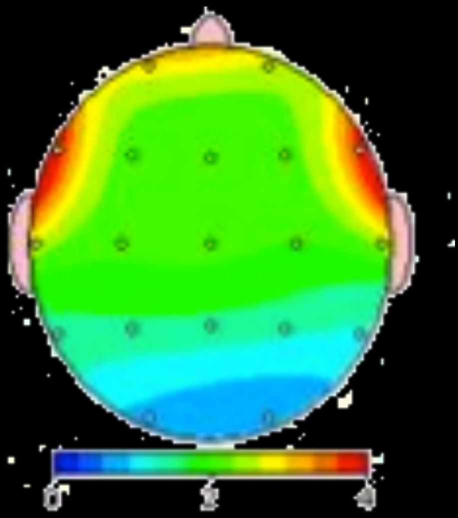
MEG Scanner

basic priniciple: sensors near scalp surface record summed magnetic field resulting from electrical activity (mainly synaptic) of many neurons

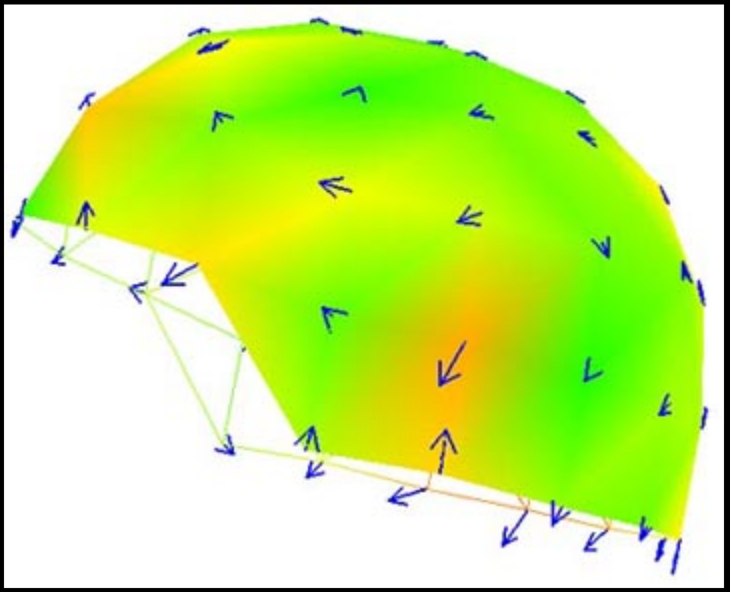


EEG/MEG Results

EEG Activation Map



MEG Activation Map



Taxonomy of Neuroimaging Methods