THE FRONTIERS OF MEDICAL IMAGING

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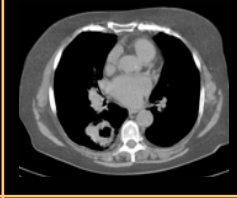
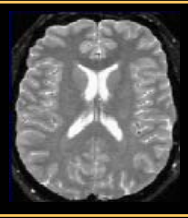
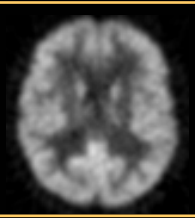
MEDICAL IMAGING

TECHNIQUE		YEAR	ENERGY	PHYSICAL PROPERTY	IMAGING
RADIOLOGY	X RAYS IMAGING	**1895**	X RAYS	ABSORPTION	
ECHOGRAPHY	ULTRASOUND IMAGING	1950	US	REFLECTION TRANSMISSION	
NUCLEAR MEDICINE	RADIOISOTOPE IMAGING	1950	γ RAYS	RADIATION EMISSION	

COMPUTERIZED TOMOGRAPHY

TECHNIQUE		YEAR	ENERGY	PHYSICAL PROPERTY	IMAGING	
X RAYS COMPUTERIZED TOMOGRAPHY	**CT**	**1971**	X RAYS	ABSORPTION		MORPHOLOGY
MAGNETIC RESONANCE IMAGING	MRI	1980	RADIO WAVES	MAGNETIC RESONANCE		MORPHOLOGY /FUNCTION
POSITRON EMISSION TOMOGRAPHY	PET	1973	γRAYS	RADIATION EMISSION		FUNCTION

PHYSICAL PERFORMANCE

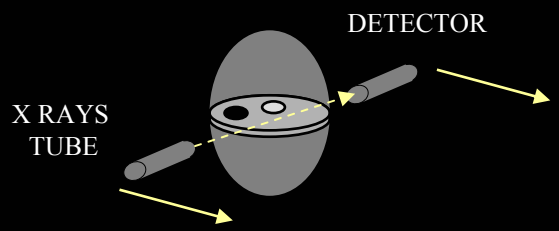
COVERAGE: to collect data from an entire organ in a single scan

SPATIAL RESOLUTION: to see tiny structures in 3D volumes
high spatial resolutions in plane and in z-direction (slice thickness)

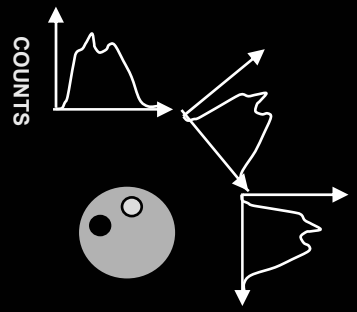
TEMPORAL RESOLUTION: to perform a scan in a very short time

CONTRAST RESOLUTION: to resolve small structures despite the similarity to surrounding tissues
high intrinsic contrast, high spatial resolution, high sensitivity and low noise

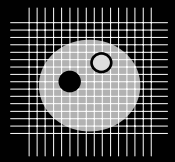
X RAYS COMPUTERIZED TOMOGRAPHY (CT)



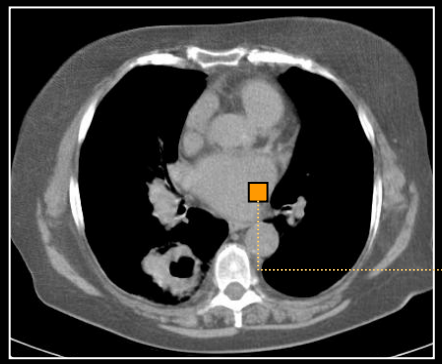
A – LINEAR SAMPLING



B – ANGULAR SAMPLING



C - RECONSTRUCTION

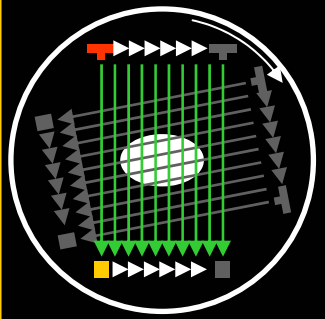
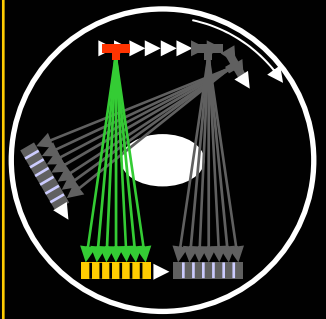
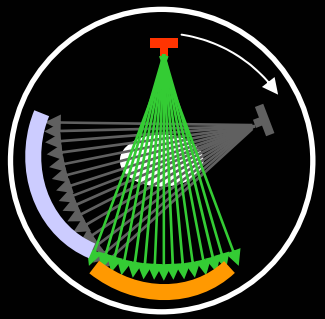
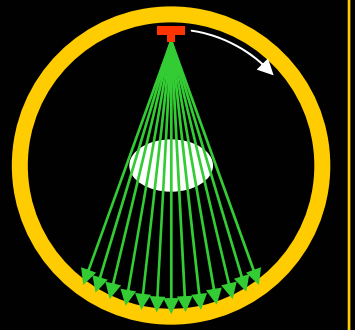
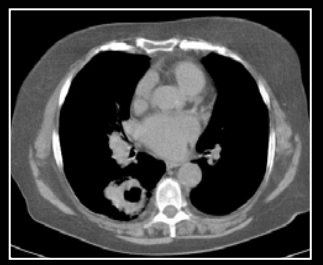
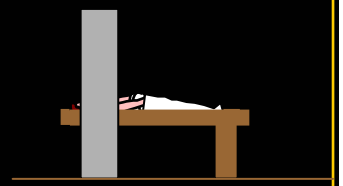


HOUNSFIELD UNIT

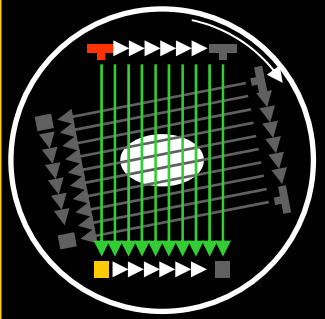
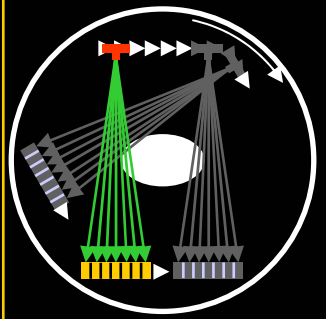
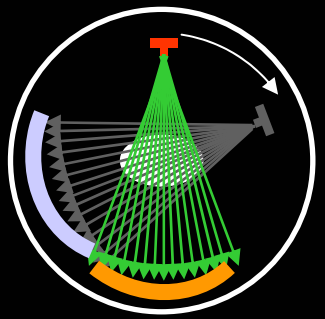
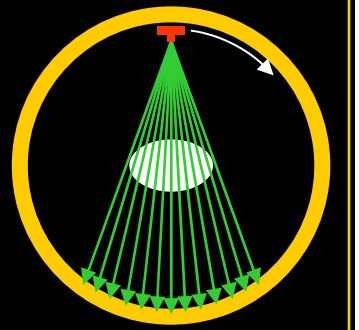
$$HU = \frac{\mu - \mu_w}{\mu_w} 1000$$

X RAYS
COMPUTERIZED TOMOGRAPHY

CT SCANNERS

GENERATION	I 1972	II 1974	III 1976	IV 1977
				
SOURCE-DETECTOR MOTION	TRANSLATION ROTATION	TRANSLATION ROTATION	ROTATION	ROTATION
DETECTORS NUMBER	1	~ 3-30	~ 400-500	~ 600-4800
SCAN (ROTATION) TIME	5 min	~ 10-60 sec	~ sec	~ sec
SLICE Number Thickness Pixel size	1 13 mm ~ 5 x 5 mm	1	1 1 mm 0,5 x 0,5 mm	1 1 mm 0,5 x 0,5 mm
				STEP AND SHOOT 

CT SCANNERS

GENERATION	I 1972	II 1974	III 1976	IV 1977
				
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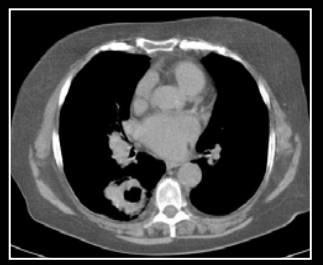
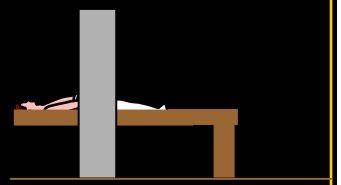
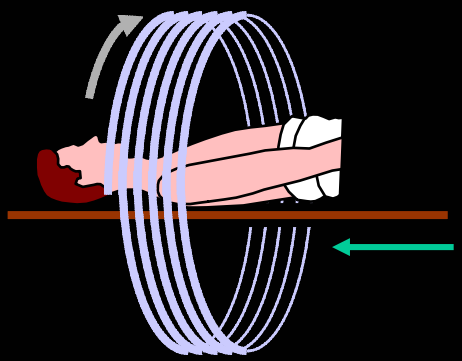
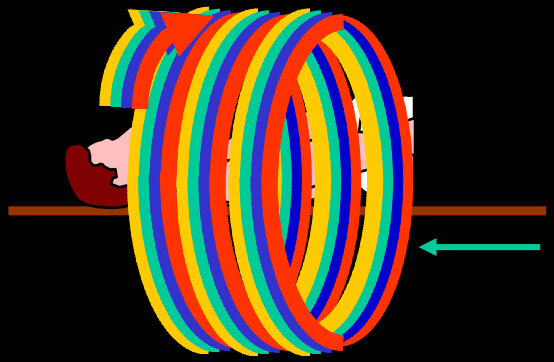
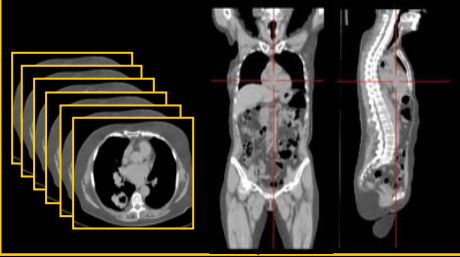
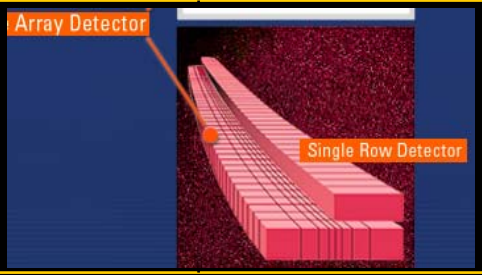
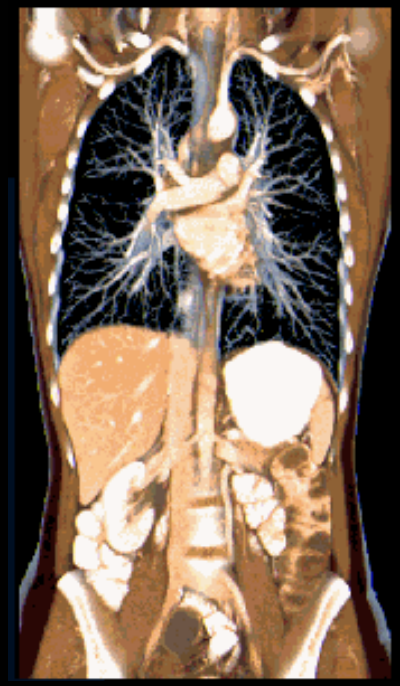
				STEP AND SHOOT 

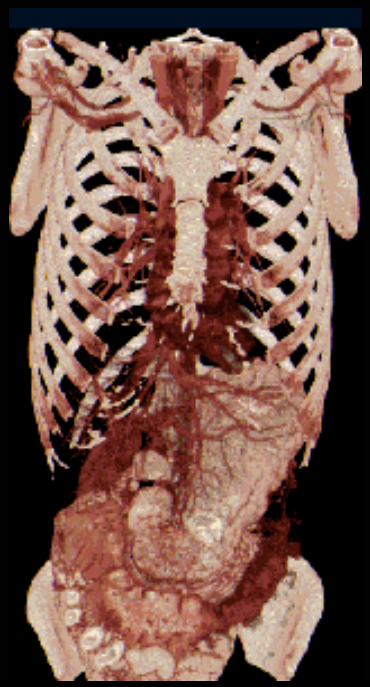
CT SCANNERS

GENERATION	SPIRAL CT		MULTI SLICE SPIRAL CT		
	1989	1994	1998	2002	2004
					
DETECTOR MOTION	Continuous volume acquisition		Continuous volume acquisition		
ROTATION TIME	1 sec	0,75 sec	0,5 sec	0,4 sec	< 0,4 sec
SPEED	24 sec / 24 cm PITCH=1	100 sec / 130 cm PITCH=1			
SLICES Number min Thickness	1 2 mm	1 1 mm	4 1 mm	16 0,6 mm	64 < 0,4 mm
					

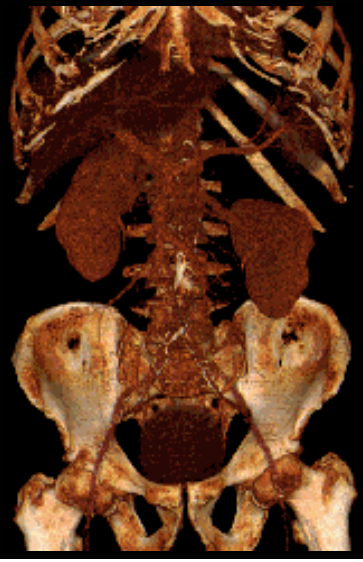
PITCH = TABLE FEED PER ROTATION/COLLIMATION

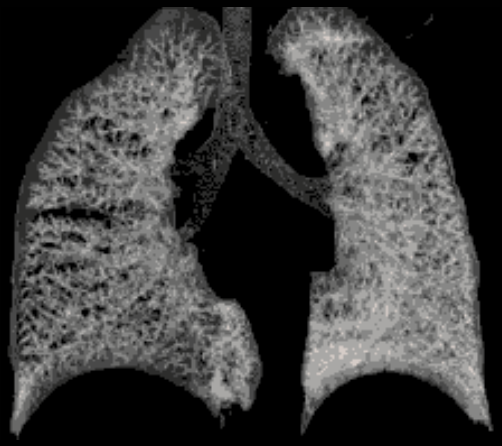
VOLUMETRIC CT





< 0,4 sec/ rotation
Organ in a sec (17 cm/sec)
Whole body < 10 sec





TECHNOLOGICAL DEVELOPMENTS

- SLIP RING TECHNOLOGY
  continuously rotating gantry
- X RAYS TUBE
  up to 100 KW generator, 80-140 mV, 800 mA peak power, fast heat dissipation
- ULTRA FAST DETECTORS
  e.g. Ceramics
- COMPUTER and SOFTWARE
  reconstruction parallel to scan acquisition
  processing of thousands of images

VIRTUAL COLONOGRAPHY CT

VIRTUAL ENDOSCOPY

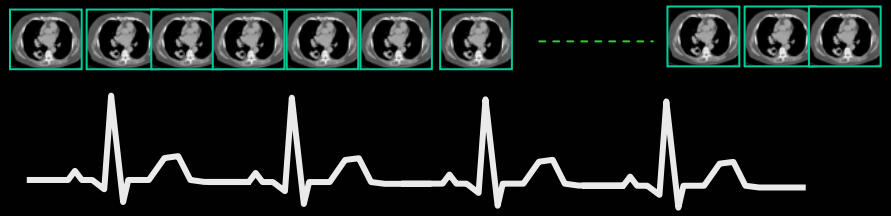
TRANSAXIAL

SAGITTAL

CORONAL

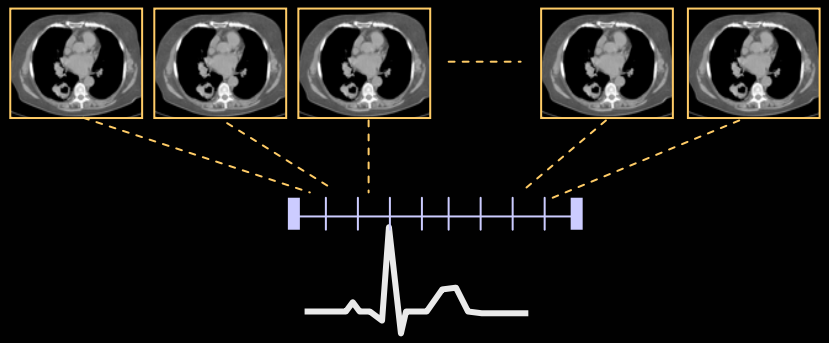
G.E MEDICAL SYSTEMS

CARDIAC CT

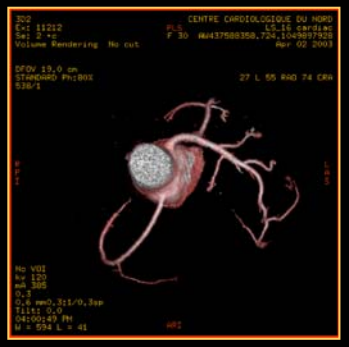


DYNAMIC CT ACQUISIION

ECG

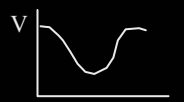


PHASES OF A CARDIAC CYCLE



VOLUME RENDERED IMAGE OF HEART AND VESSELS

- EJECTION FRACTION
- CARDIAC OUTPUT
- REGIONAL WALL MOTION
- ..



FUNCTIONAL PARAMETERS

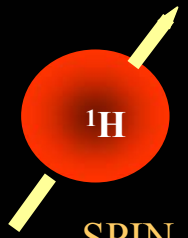
THE FRONTIERS OF CT IMAGING

INCREASED COVERAGE SPEED
(combining the increased coverage and decreased scan time)

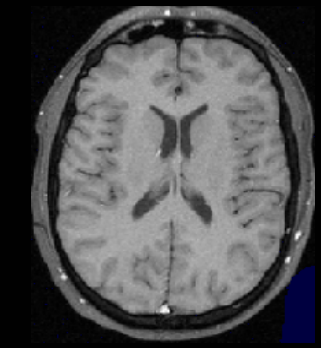
- WHOLE BODY STUDIES IN LESS THAN 10 SEC
- CAPTURING OF MOVING ORGANS
- PHYSIOLOGIC (NOT ONLY MORPHOLOGIC) IMAGING

MAGNETIC RESONANCE IMAGING (MRI)

MAGNETIC FIELD: 1.5 – 3Tesla



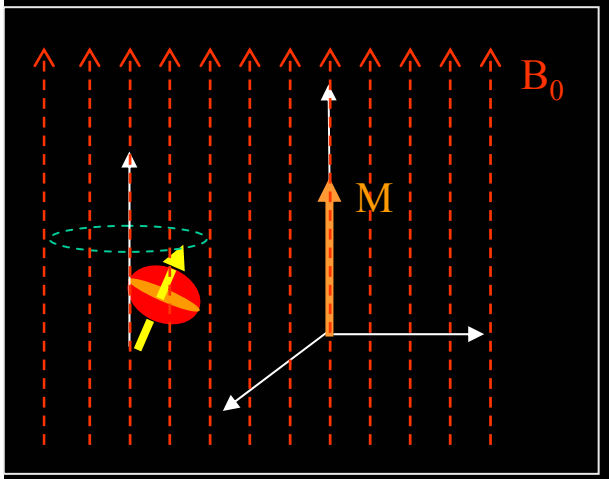
SPIN

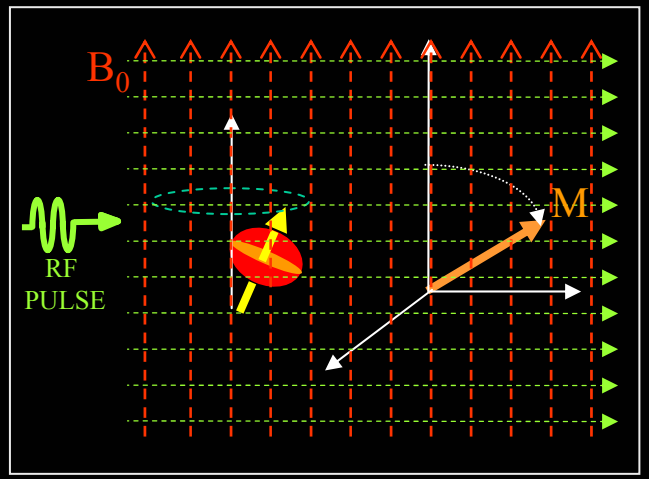


H_2O

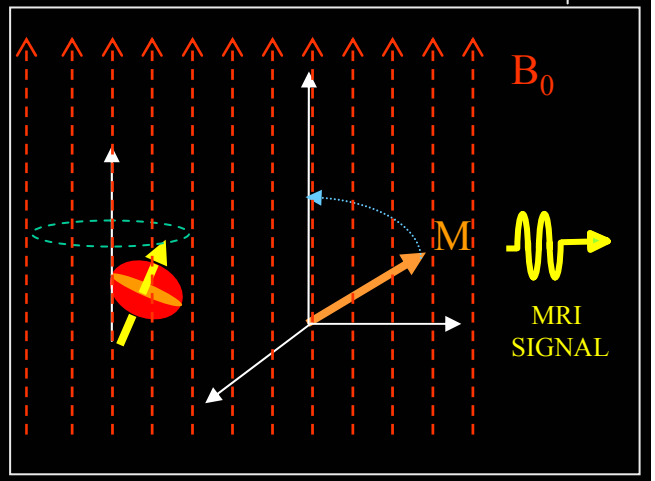
LARMOUR FREQUENCY

$\nu_0 = [\gamma / 2\pi] B_0$



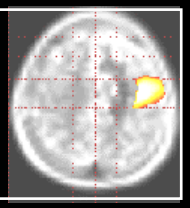
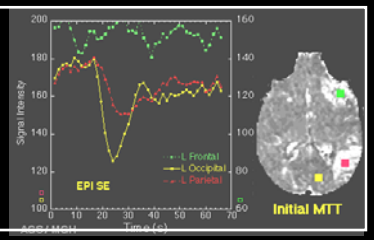


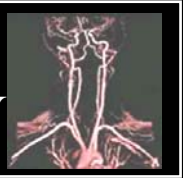
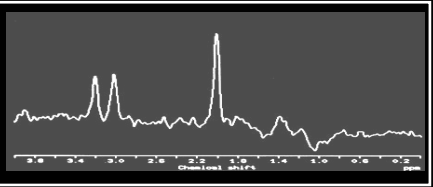
EXCITATION



RELAXATION

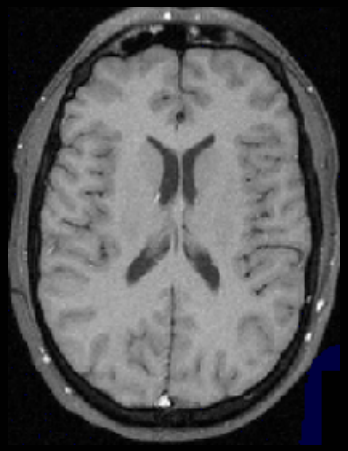
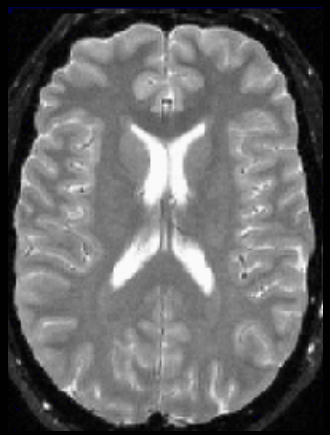
NMR

- MORPHOLOGY 
- FUNCTION
  - BOLD 
  - Gd PERFUSION 

  - DIFFUSION/ PERFUSION 
- FLOW → MR ANGIOGRAPHY 
- CHEMICAL CONTENT
  - MR SPECTROSCOPY *in vitro*
  - MR SPECTROSCOPY *in vivo* 

MAGNETIC RESONANCE IMAGING (MRI)

MORPHOLOGY

		
T1	T2	PD

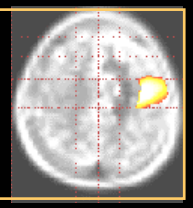
SCAN TIME to cover an entire organ:	~ min
SPATIAL RESOLUTION:	~ mm
CONTRAST RESOLUTION:	very high for soft tissues

NMR

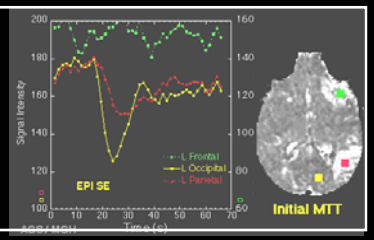
MORPHOLOGY

FUNCTION

BOLD



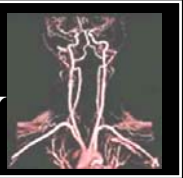
Gd PERFUSION



DIFFUSION/
PERFUSION

FLOW

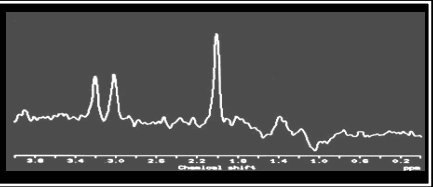
MR
ANGIOGRAPHY



CHEMICAL
CONTENT

MR SPECTROSCOPY
in vitro

MR SPECTROSCOPY
in vivo



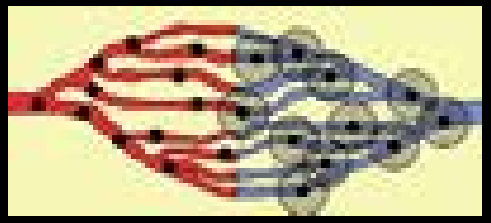
fMRI BOLD

Blood

Oxygenation

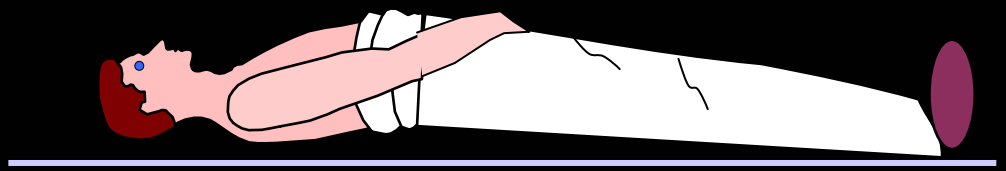
Level

Dependent

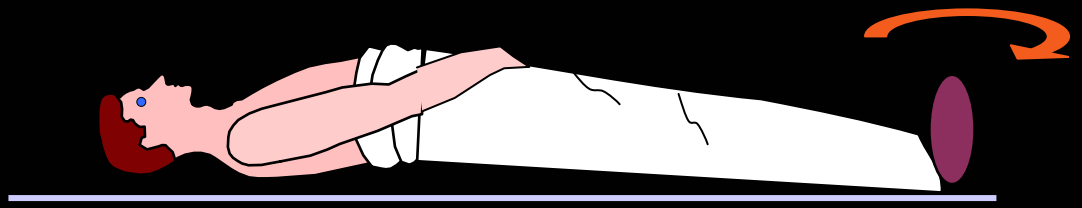


- Oxyhaemoglobin in the arterial blood is diamagnetic
- Deoxyhaemoglobin in the draining veins is strongly PARAMAGNETIC
- Deoxyhaemoglobin can serve as an intrisic paramagnetic contrast agent

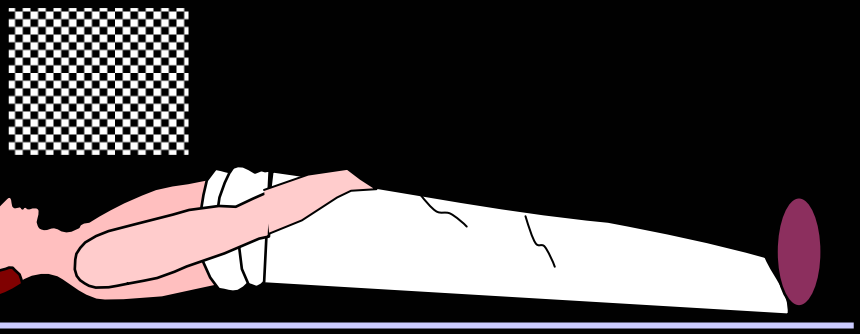
ACTIVATION STUDIES

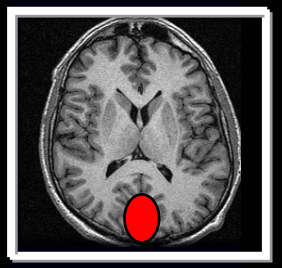


Control condition

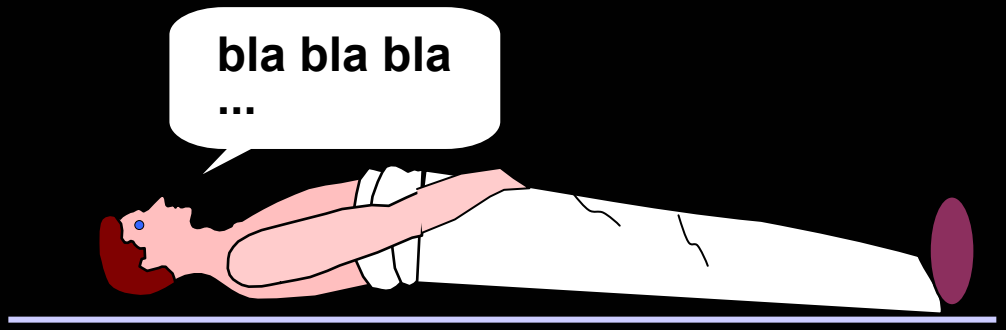


Motor stimulation



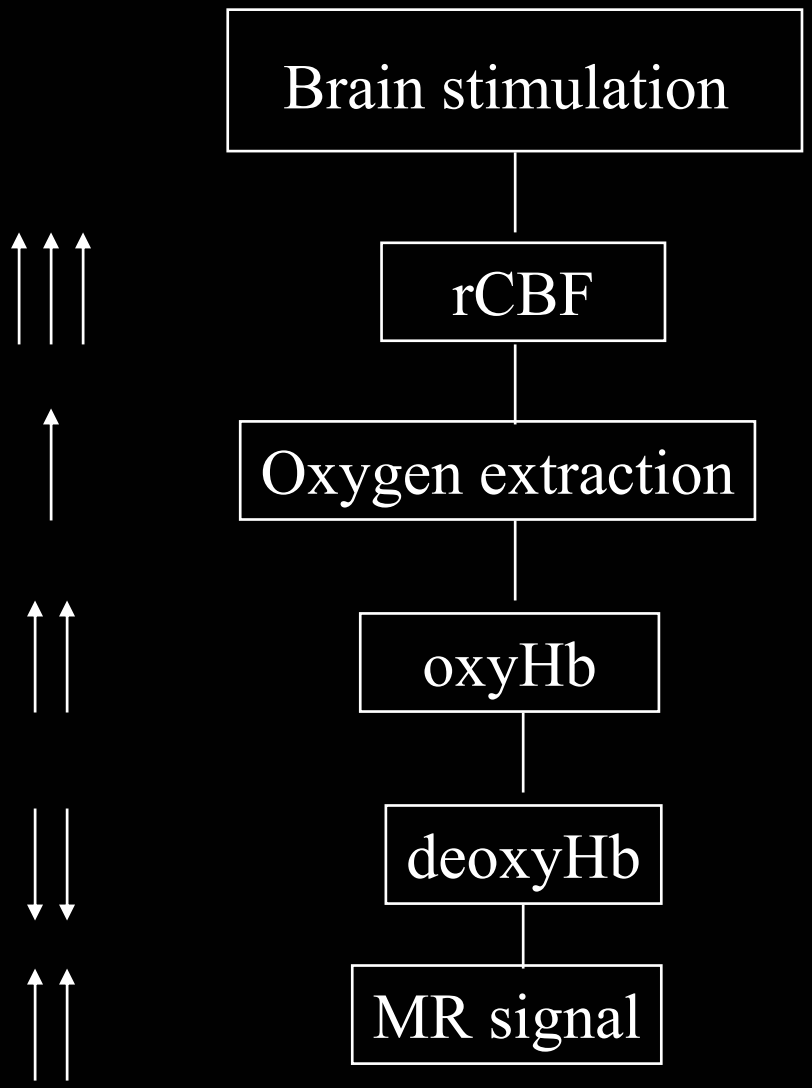


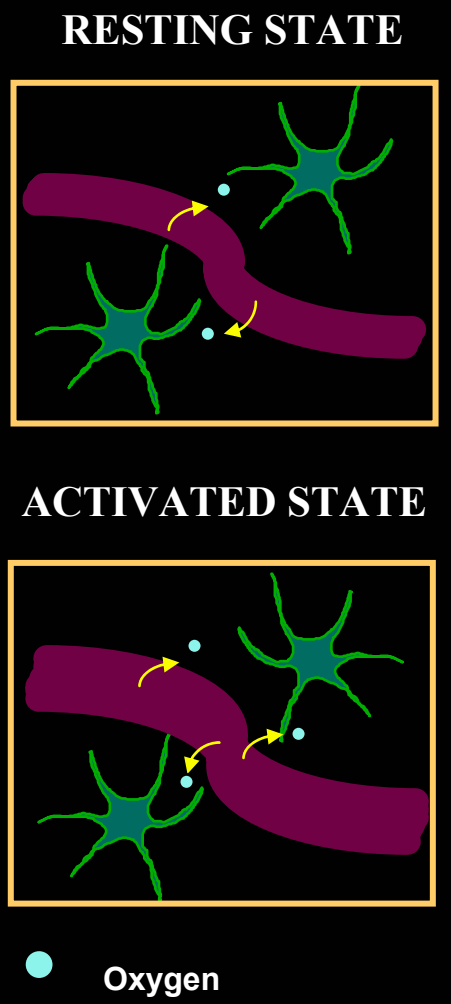
Visual stimulation



Cognitive stimulation

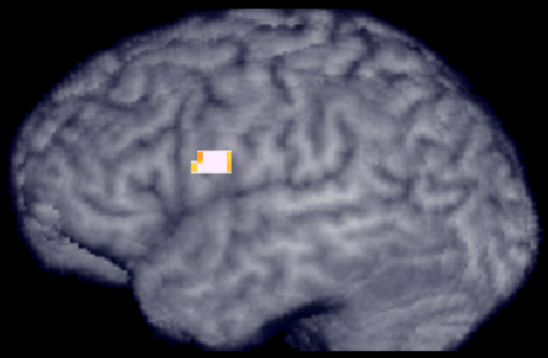
fMRI BOLD ACTIVATION STUDIES



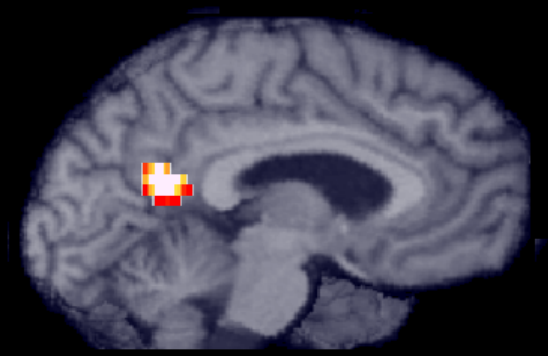


fMRI BOLD

COGNITIVE ACTIVATION
VERBAL FLUENCY



PHONEMIC



SEMANTIC

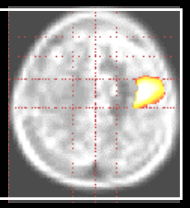
E. Paulesu et al, Neuroreport, 1997, 8(8):2011-7.

NMR

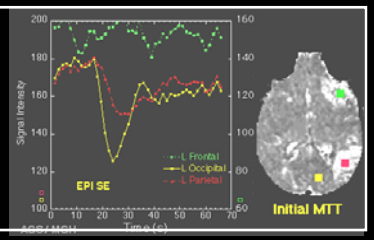
MORPHOLOGY

FUNCTION

BOLD



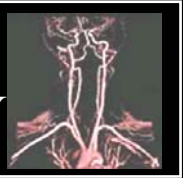
Gd PERFUSION



DIFFUSION/
PERFUSION

FLOW

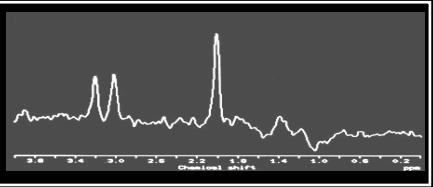
MR
ANGIOGRAPHY



CHEMICAL
CONTENT

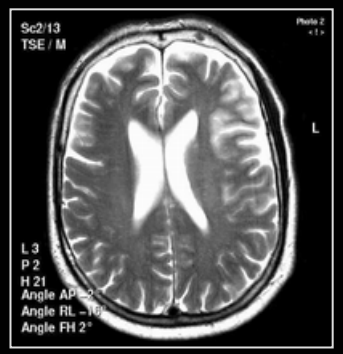
MR SPECTROSCOPY
in vitro

MR SPECTROSCOPY
in vivo



DIFFUSION WEIGHTED MRI

DW-MRI: measure of the effect of H_2O molecules diffusion on tissues MR signal



T2

weighted image

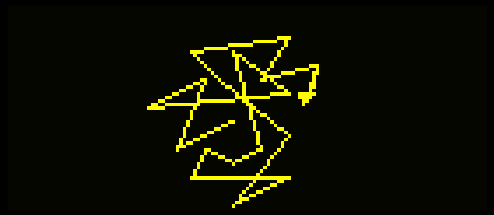
DIFFUSION

weighted image

Acute trombosis of the left carotid artery.

DIFFUSION WEIGHTED MRI

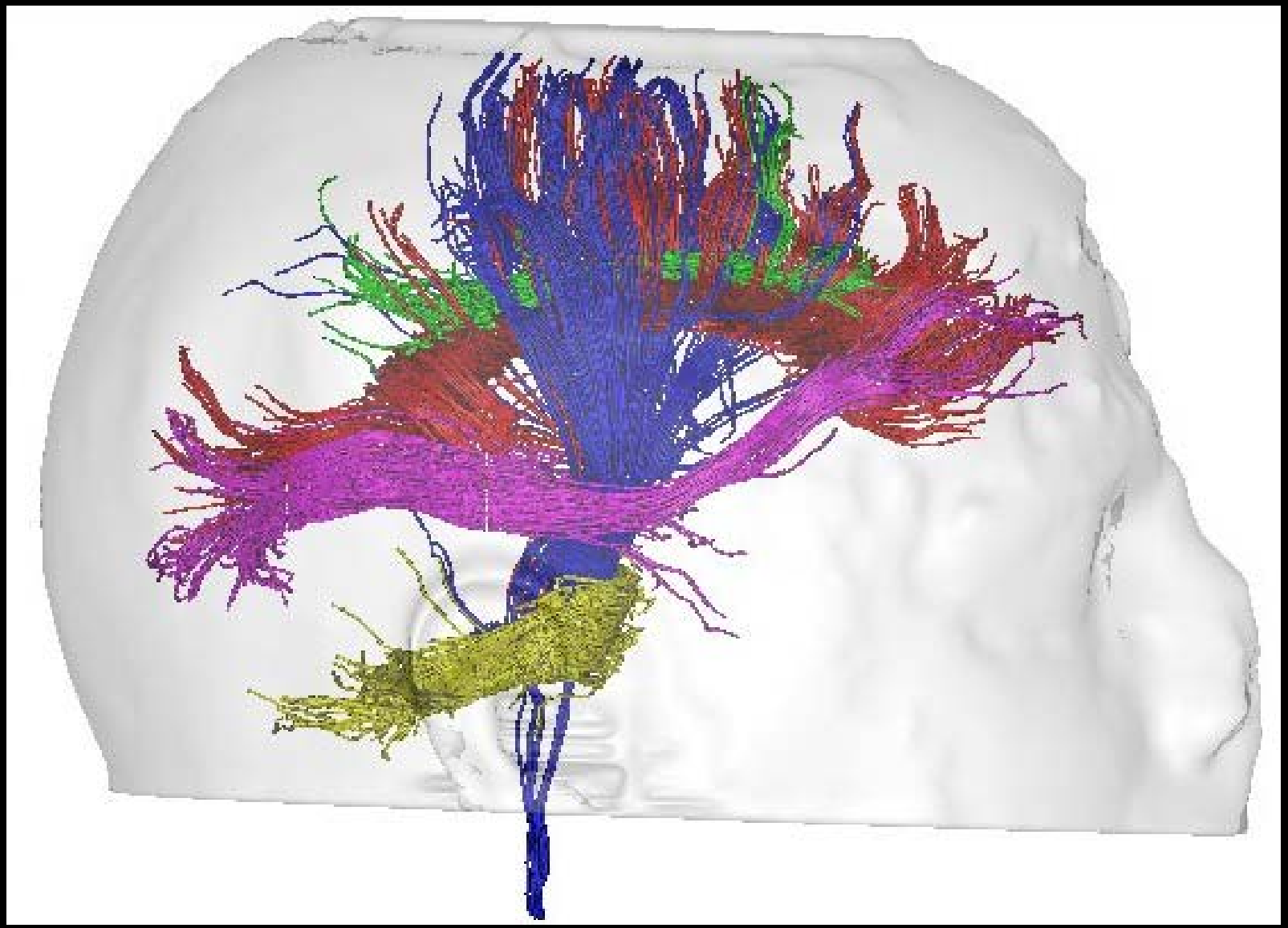
- Diffusion anisotropy resulting from the presence of obstacles limiting the molecular movements in some directions can be detected and tracked
- Anisotropy can be observed in white matter in the brain as a result of its organization in bundles of fibers



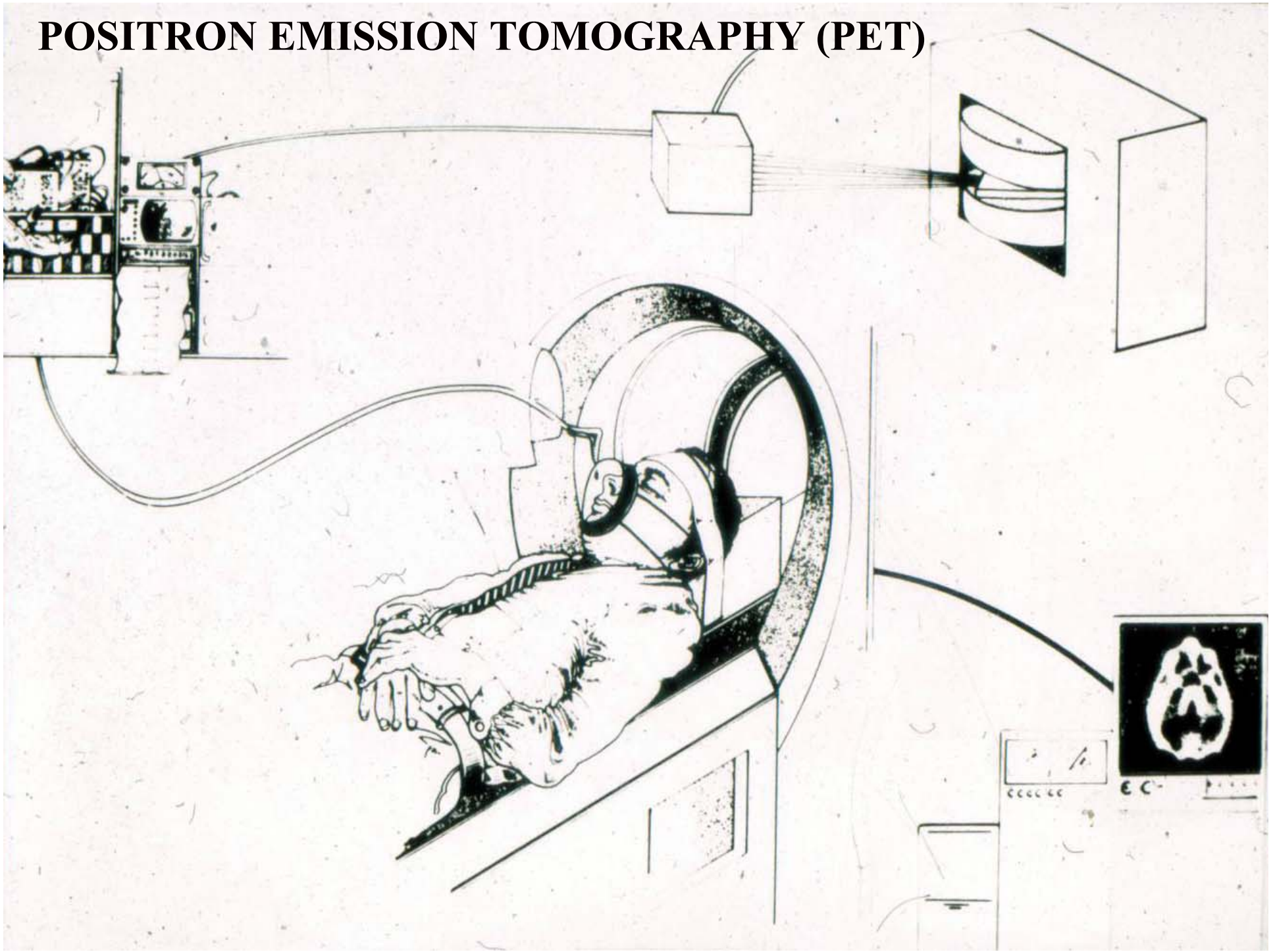
Free Diffusion

Restricted Diffusion

DIFFUSION IMAGING – FIBER TRACKING



POSITRON EMISSION TOMOGRAPHY (PET)



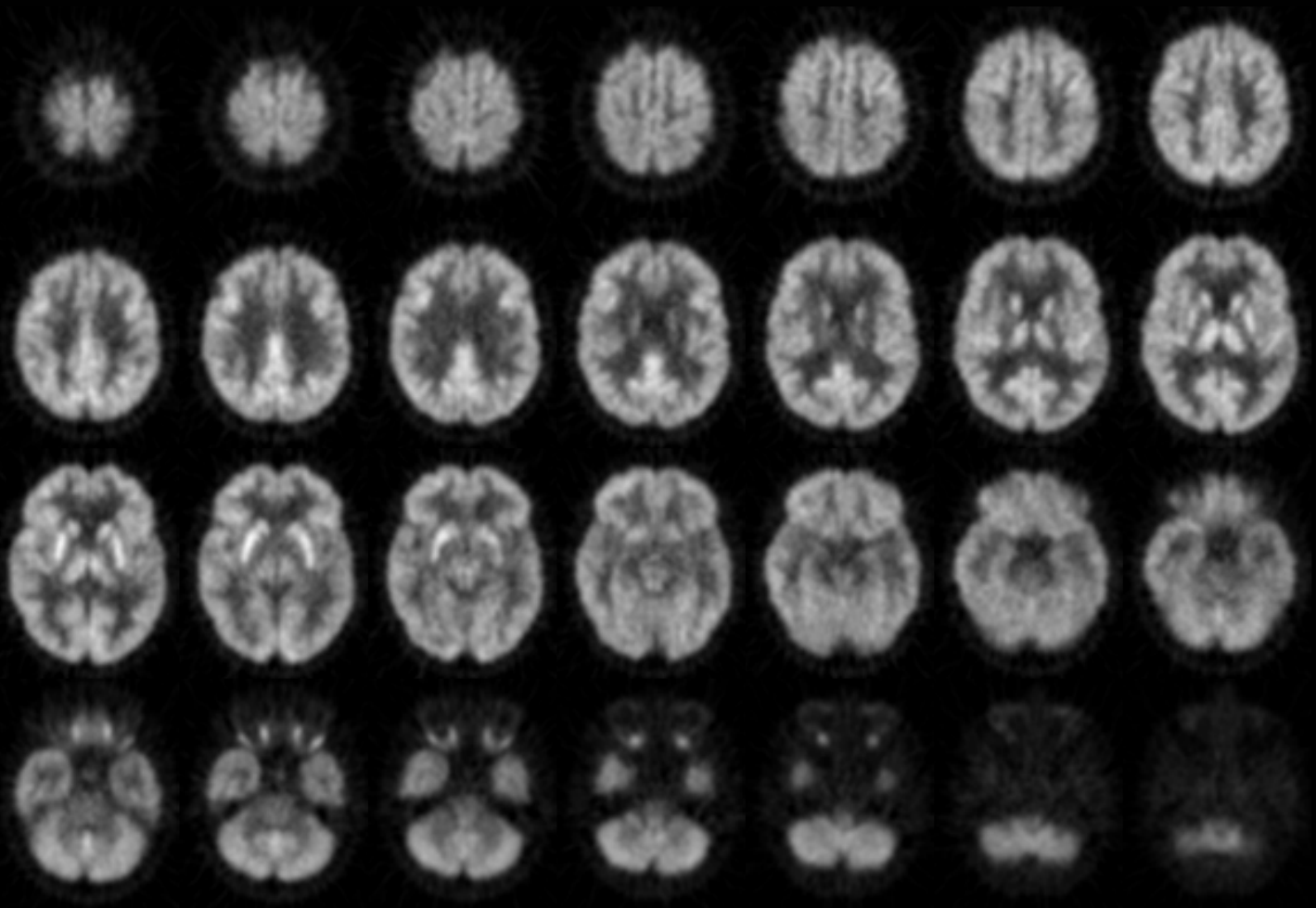
POSITRON EMISSION TOMOGRAPHY (PET)

ISOTOPES	$T_{1/2}$	
^{11}C	20.4 min	“natural”
^{13}N	10.0 min	“natural”
^{15}O	2.0 min	“natural”
^{18}F	109.8 min	“pseudo-natural”

RADIOTRACERS PREPARED AT HSR

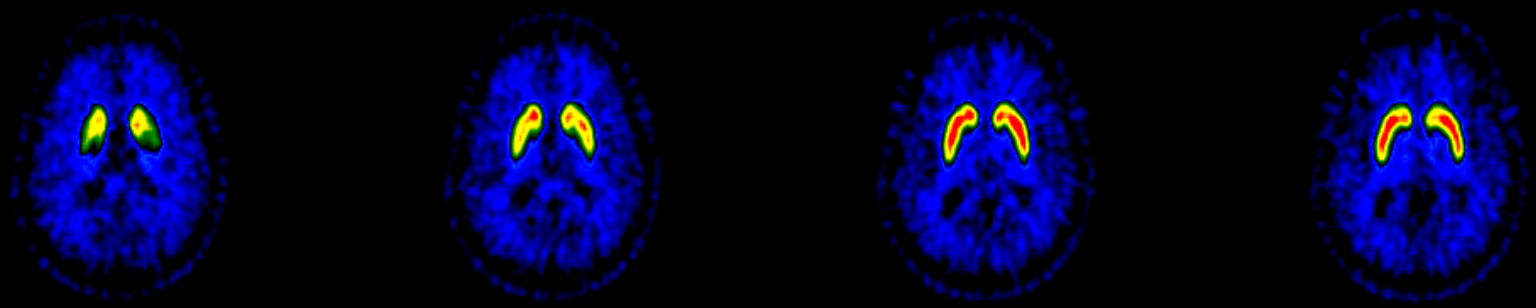
[18F]FDG	Glucose metabolism
[18F]FESP	D2 and 5-HT_2 receptor antagonist
[15O]H2O	Cerebral flow, Functional activation studies
[13N]AMMONIA	Myocardial flow
m-[11C]hydroxyefedrine	Adrenergic antagonist
[11C]FLUMAZENIL	Benzodiazepine receptor antagonist
[11C]RACLOPRIDE	Dopamine D2 receptor antagonist
[11C]FE-β-CIT	Dopamine reuptake inhibitor
[11C]SCH23390	Dopamine D1 receptor antagonist
[11C]CARAZOLOL	Adrenergic β1/β2 receptor antagonist
[11C]MCN5652	Serotonin reuptake inhibitor
[11C]MDL100907	Serotonin 5-HT2A receptor antagonist
[11C]methylcoline	Prostate Cancer
[11C]FLUVOXAMINE	Serotonin reuptake inhibitor
[11C]CGP62349	GABAB antagonist
[11C]isovaleroil-L-carnitine	Cerebral metabolism
[^{11}C]PNU167760	Serotonin 5-HT_{1A} receptor antagonist
[^{11}C] BISOPROLOL	Adrenergic β1 antagonist
[^{11}C] ICI118551	Adrenergic β_2 receptor antagonista
[^{11}C] OLANZAPINE	Atypical Antipsychotic
[^{11}C] SB235753	Dopamine D4 receptor antagonist
[^{11}C] E2020	Muscarinic M_2 receptor antagonist
[^{11}C] SCH442416	Adenosine A_{2A} receptor antagonist
[^{11}C] PALMITATE	Fatty acids metabolism
[^{11}C] A 84543	Nicotine $\alpha_2\beta_4$ antagonist
[^{11}C] VC195	Peripheral Benzodiazepine
[^{11}C] VC193M	Peripheral Benzodiazepine
[^{11}C] VC198M	Peripheral Benzodiazepine
[^{11}C] WAY100635	Serotonin 5-HT1A receptor antagonist
[^{11}C]RN5	Adrenergic α1 receptor antagonist
[^{11}C] VA100	Opioid K1 receptor antagonist
[^{11}C] CARFENTANIL	Opioid μ receptor agonist
[^{11}C] ZOFENOPRIL	ACE inhibitor
[^{18}F]FLUORO CAPTOPRIL	ACE inhibitor
[^{11}C] CNR1	α1 adrenergic antagonist
[^{11}C] PK1113195	Peripheral Benzodiazepine
[^{11}C] F167	σ_2 receptor antagonist
[^{11}C] PD60	dopamine D_3 antagonist
[^{11}C] PD78	dopamine D_3 antagonist

PET – CEREBRAL GLUCOSE METABOLISM

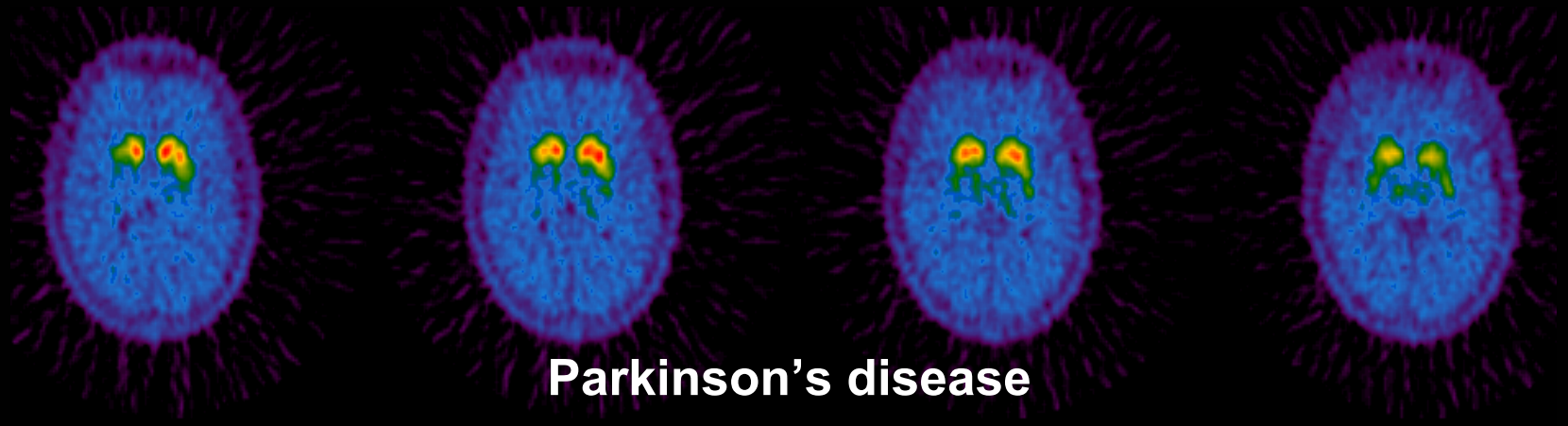


^{18}F-FLUORYDEOXYGLUCOSE (^{18}FDG)

PET FUNCTIONAL RECEPTOR IMAGING



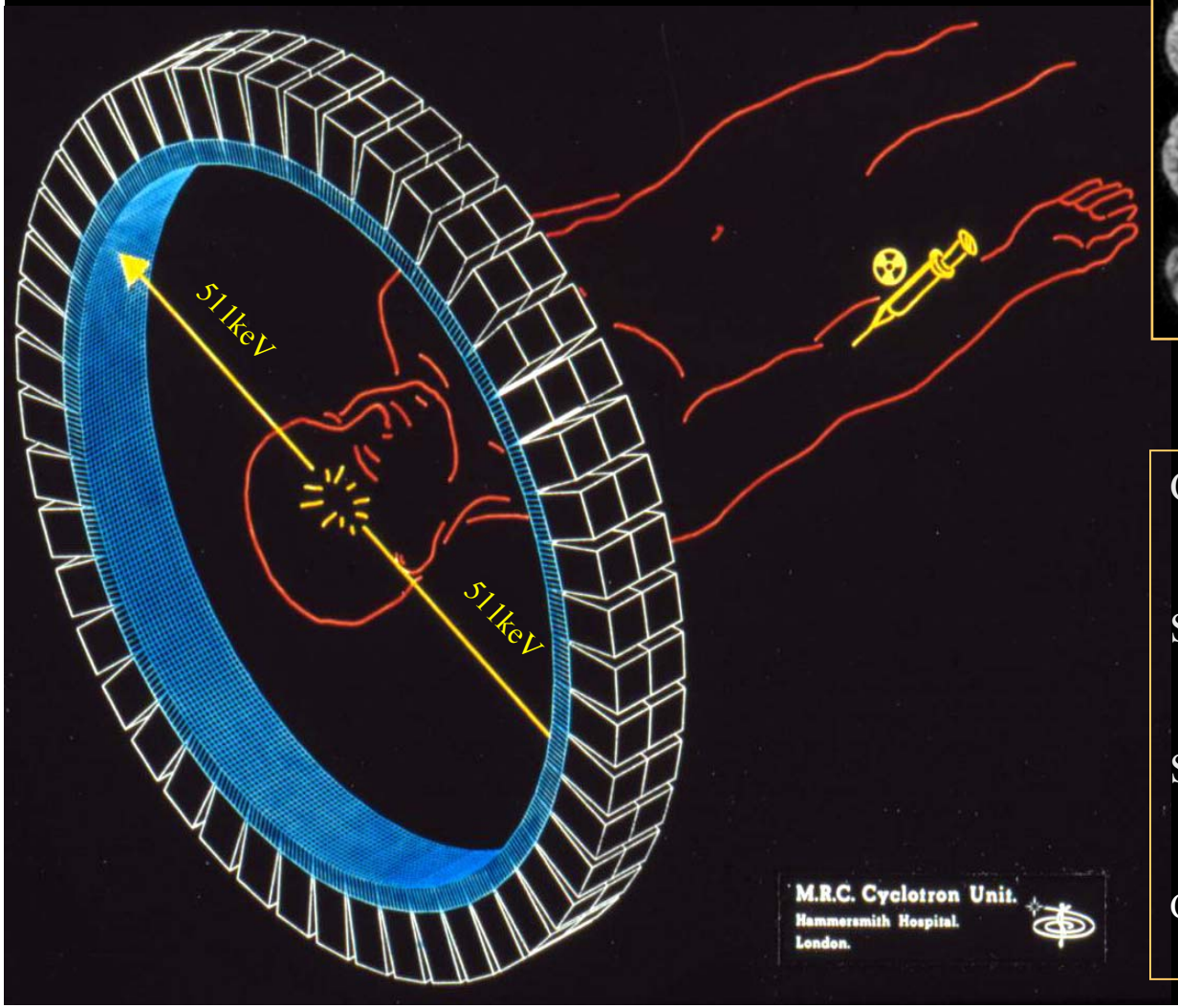
Normal Subject

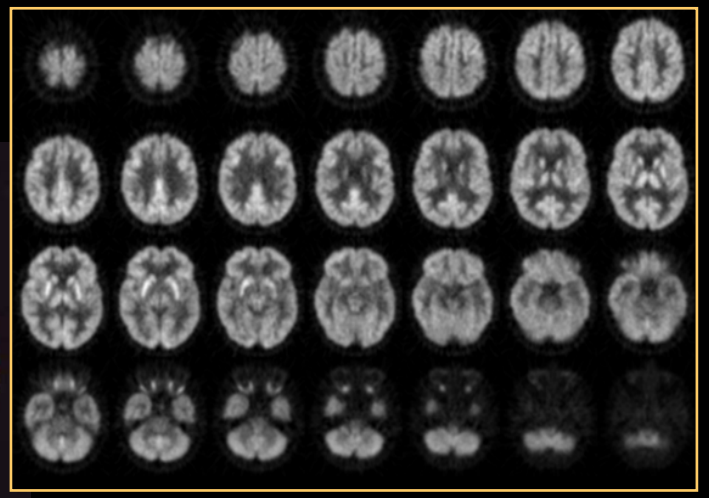


Parkinson's disease

[^{11}C] FE-CIT

POSITRON EMISSION TOMOGRAPHY (PET)





COVERAGE:
~ 15-20 cm

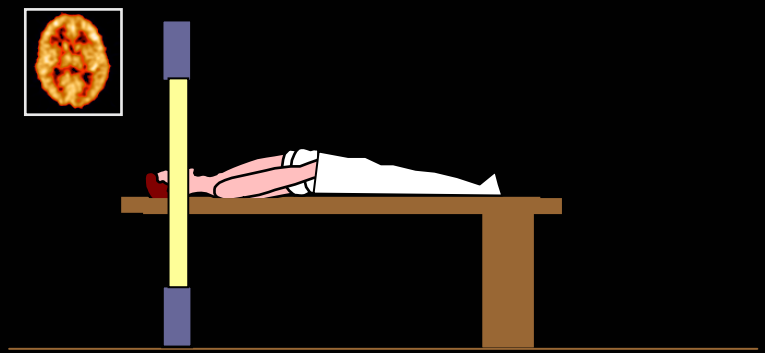
SPATIAL RESOLUTION:
~ 5 mm

SCAN TIME to cover an entire organ:
~ 5 min

CONTRAST RESOLUTION:
depends on the radiotracer

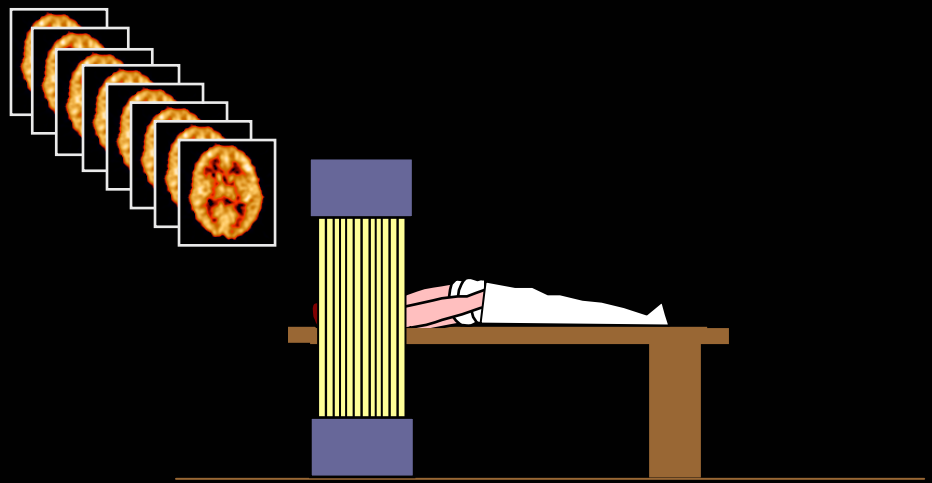
PET
COVERAGE AND AXIAL SAMPLING

FIRST GENERATION PET



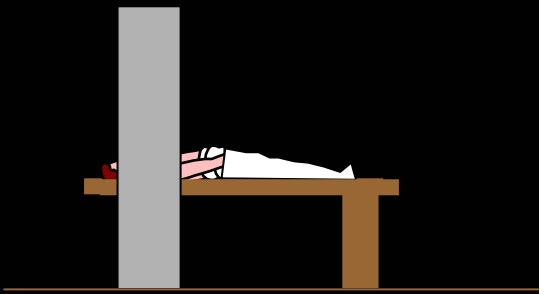
1 SLICE – 2 cm

CURRENT GENERATION PET

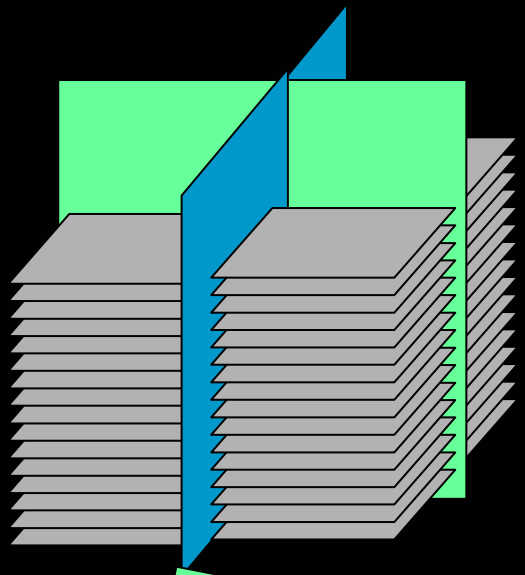


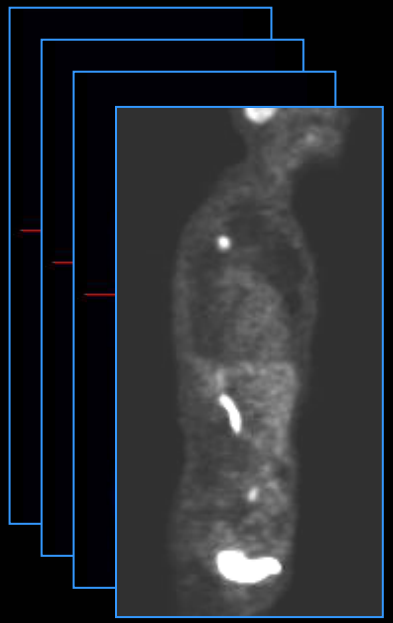
> 40 SLICES – 6 mm
Axial FOV: 15 –20 cm

TOTAL BODY STUDIES



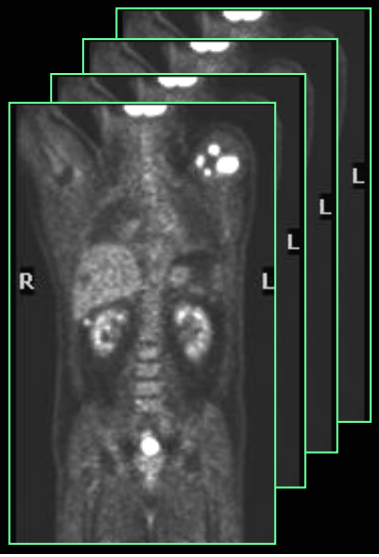
TRANSAXIAL IMAGES



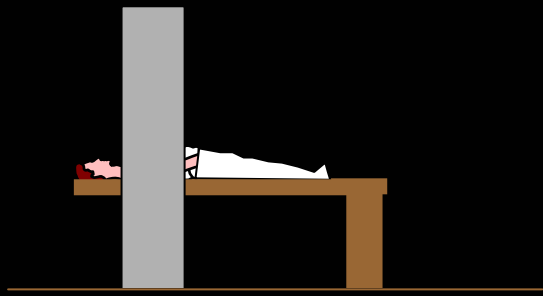


SAGITTAL

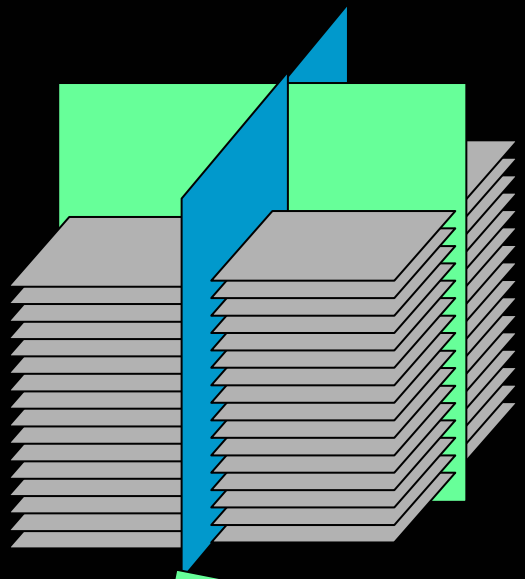
CORONAL

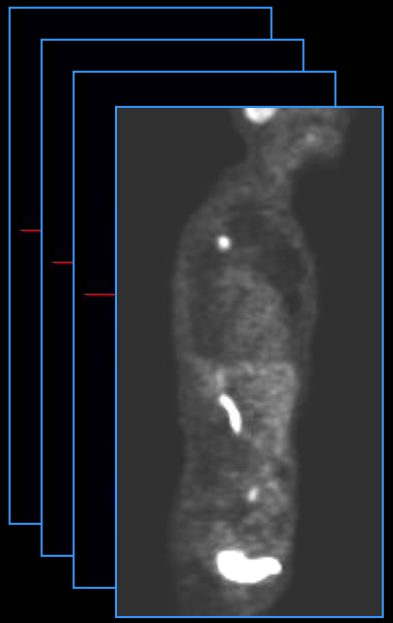


TOTAL BODY STUDIES



TRANSAXIAL IMAGES





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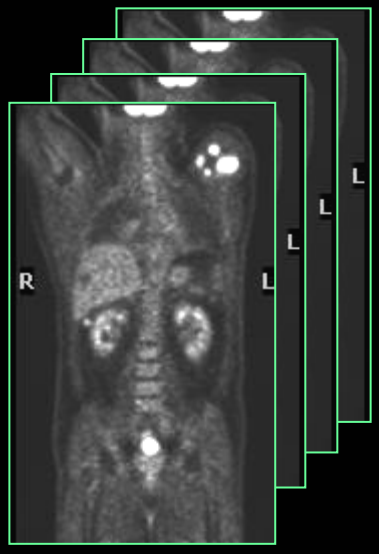
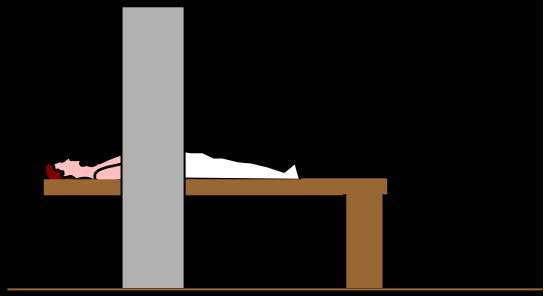
CORONAL



TOTAL BODY STUDIES



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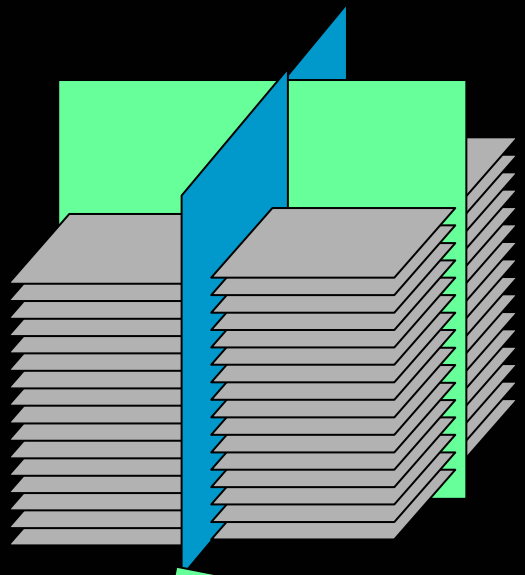

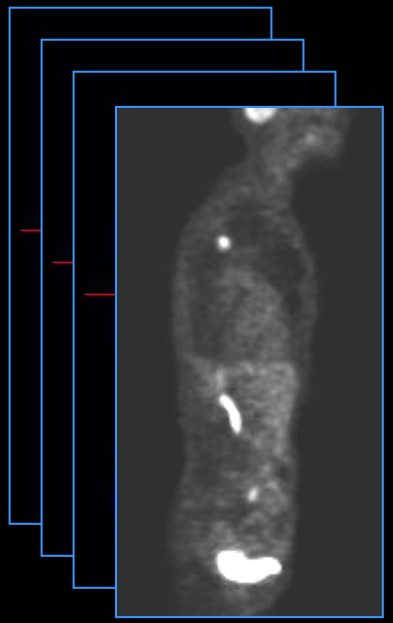

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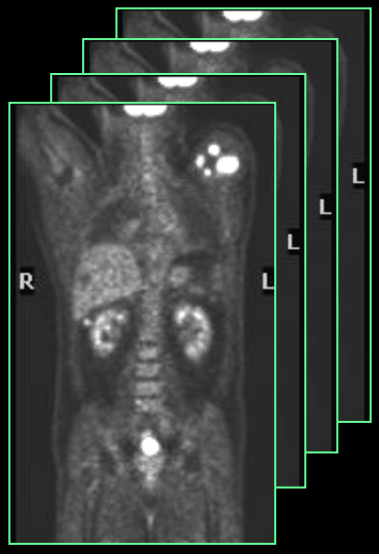
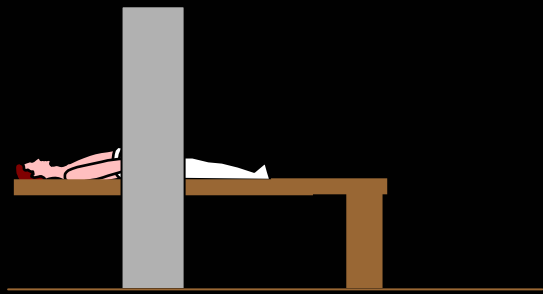
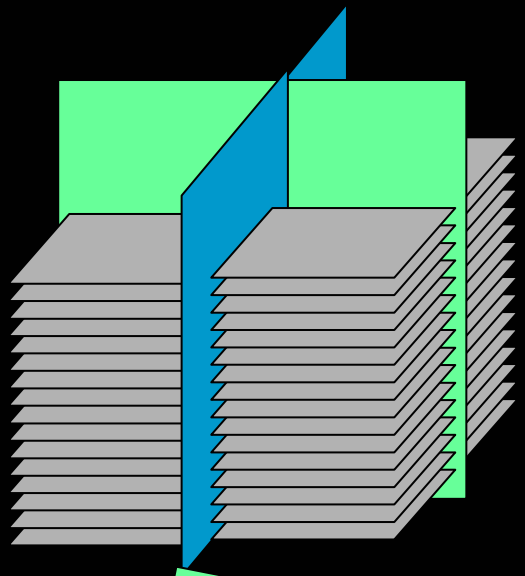
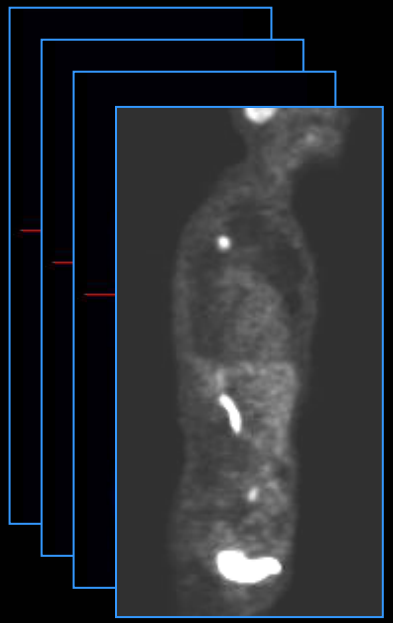


TOTAL BODY STUDIES



TRANSAXIAL IMAGES





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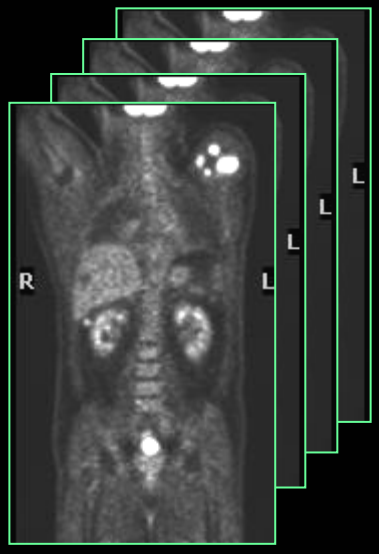
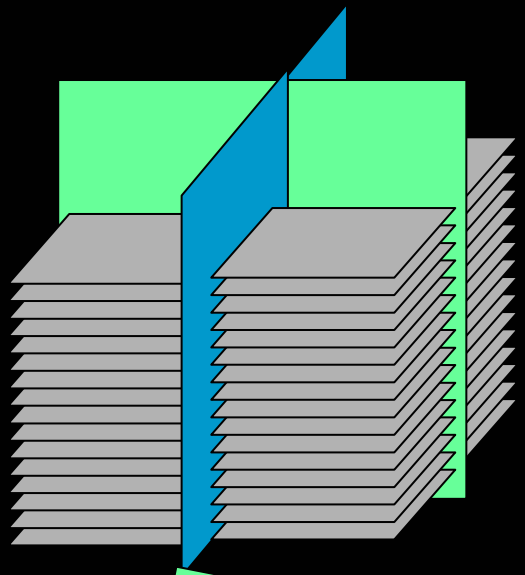
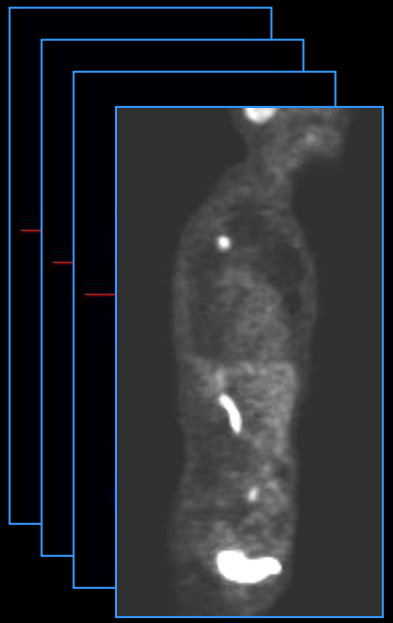
CORONAL



TOTAL BODY STUDIES – ^{18}FDG

TRANSAXIAL IMAGES





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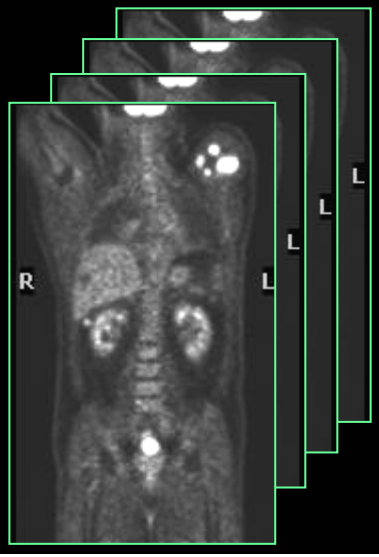
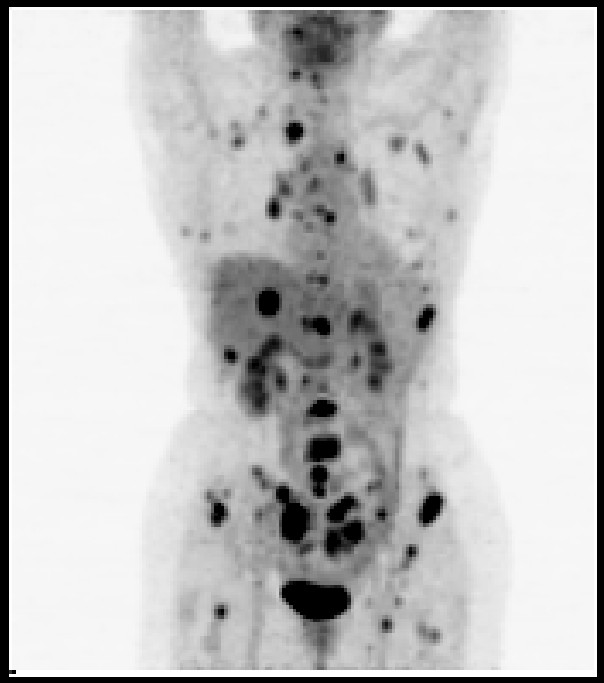
CORONAL

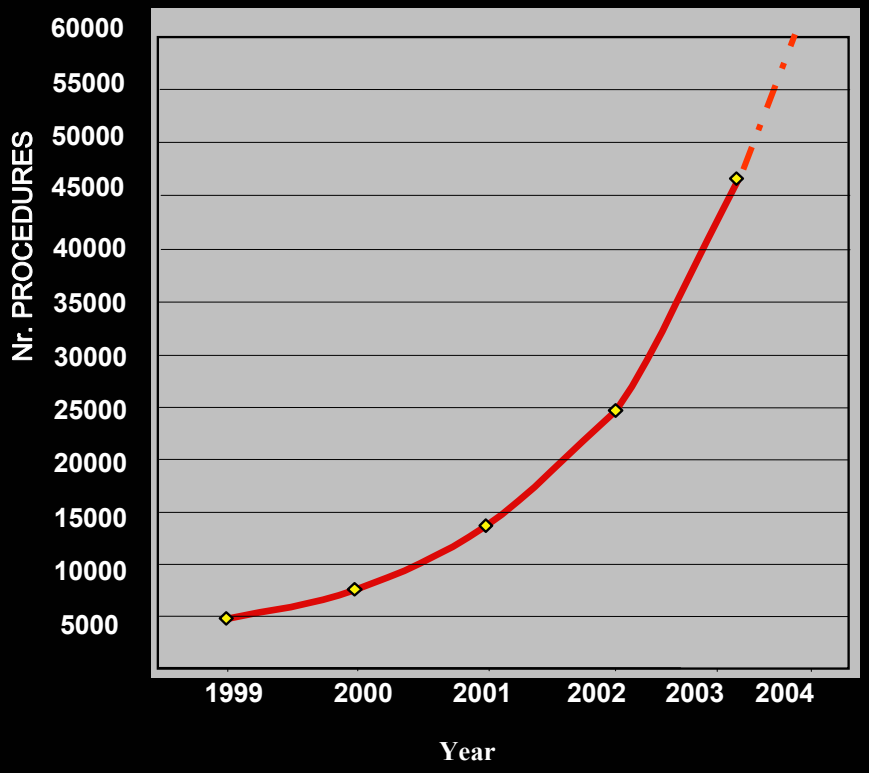


^{18}F-FDG WHOLE BODY PET

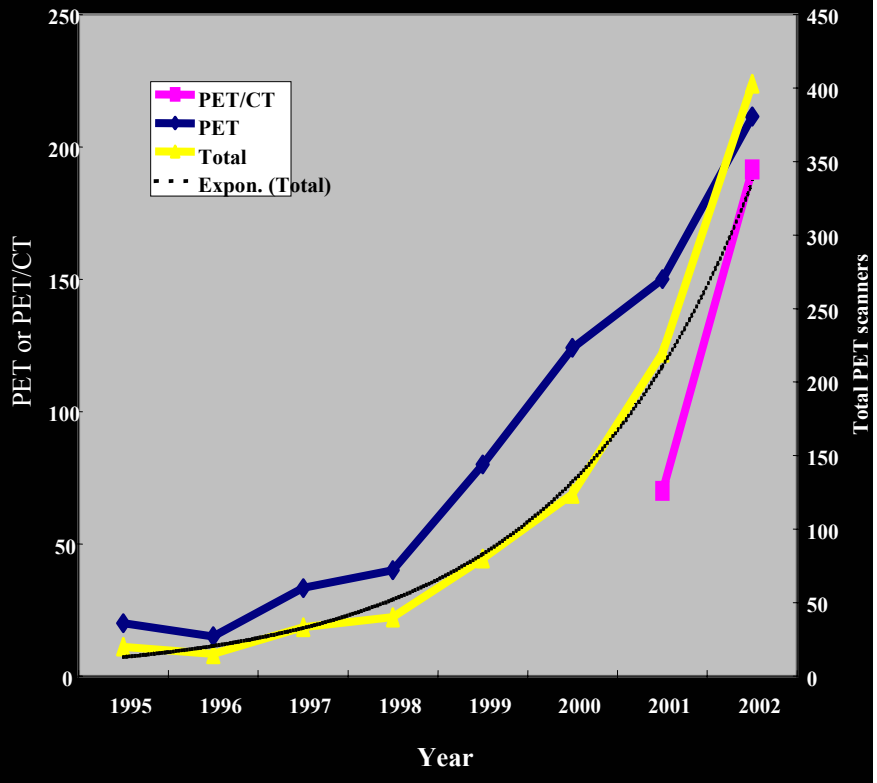
- DIAGNOSIS
- STAGING
- RE-STAGING AND FOLLOW-UP
- RADIOTHERAPY



CLINICAL PET IN ITALY
TOTAL EXAMS/YEAR



ESTIMATED
PET - PET/CT
SCANNER UNITS WW



ADVANCES IN PET IMAGING

RADIOCHEMISTRY — NEW TRACERS PET

INSTRUMENTATION HW/SW
- NEW SCINTILLATION CRYSTALS
- PET/CT

TRACERS for TUMOR CHARACTERIZATION

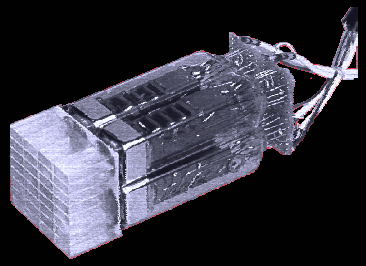
• Glucose metabolism	[^{18}F]FDG
• Membrane function	[^{11}C]Choline
• Proliferation	[^{18}F]FLT
• Oxygenation	[^{18}F]FMISO
	[^{18}F]FAZA
	[^{64}Cu]ATSM
• Apoptosis	[^{18}F]Annexin V
• Angiogenesis	[^{18}F]NGR-peptide
• Neuroendocrine tumors	[^{110}In]Octreotate

ADVANCES IN PET IMAGING

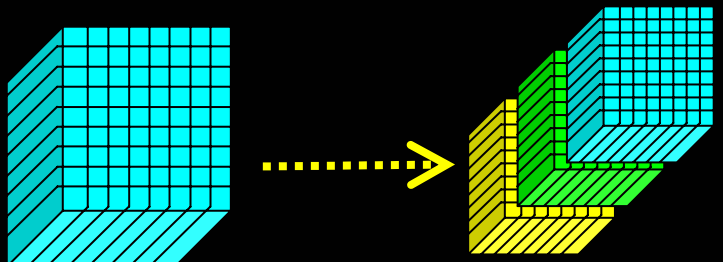
RADIOCHEMISTRY — NEW TRACERS PET

INSTRUMENTATION HW/SW
- NEW SCINTILLATION CRYSTALS
- PET/CT

FUTURE DEVELOPMENTS IN PET



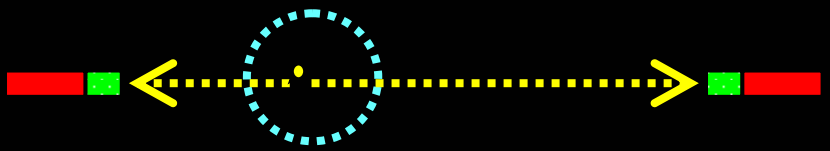
CURRENT DETECTORS: BGO, GSO, LSO



SANDWICH OF DETECTORS

NEW DETECTORS with:

- SMALLER SIZE (2-3 mm)
- GOOD ENERGY RESOLUTION
- DEPTH OF INTERACTION INFORMATION



FASTER DETECTORS for

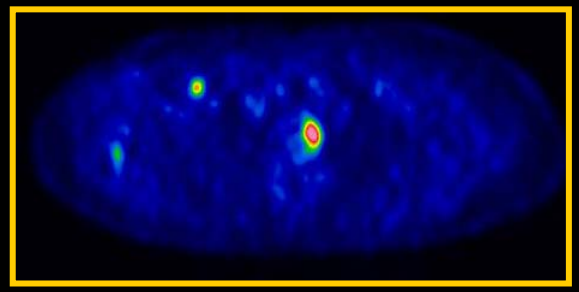
- HIGH COUNT RATE CAPABILITY
- TIME OF FLIGHT INFORMATION

ADVANCES IN PET IMAGING

RADIOCHEMISTRY — NEW TRACERS PET

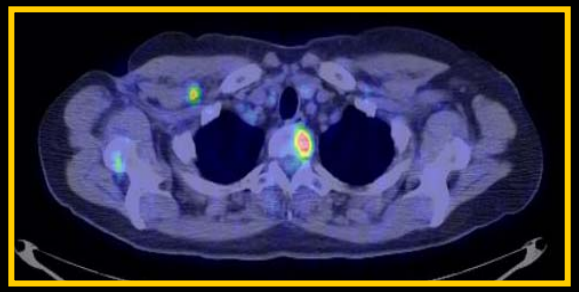
INSTRUMENTATION HW/SW
- NEW SCINTILLATION CRYSTALS
- PET/CT

PET – [^{18}F]FDG



PET

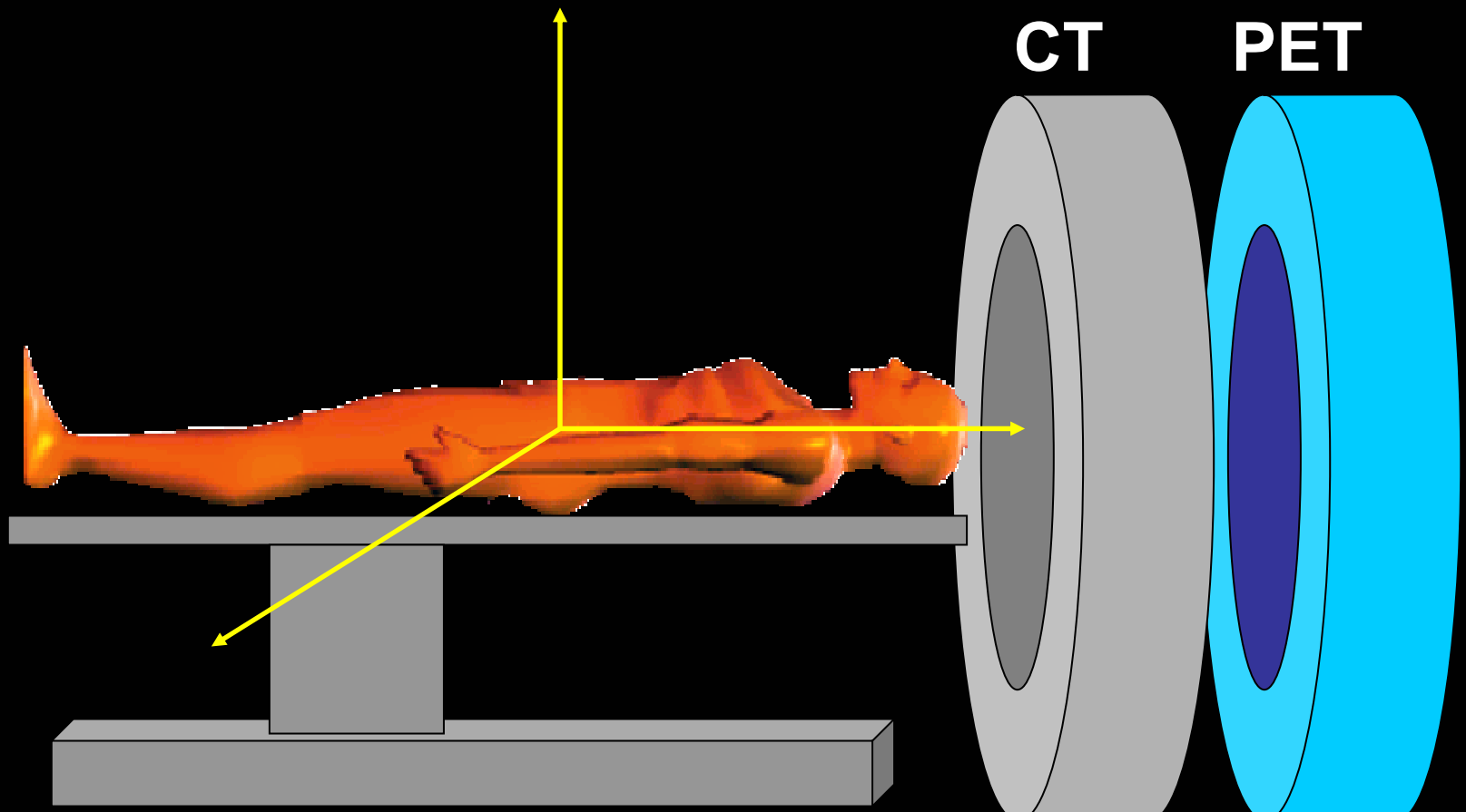
CT



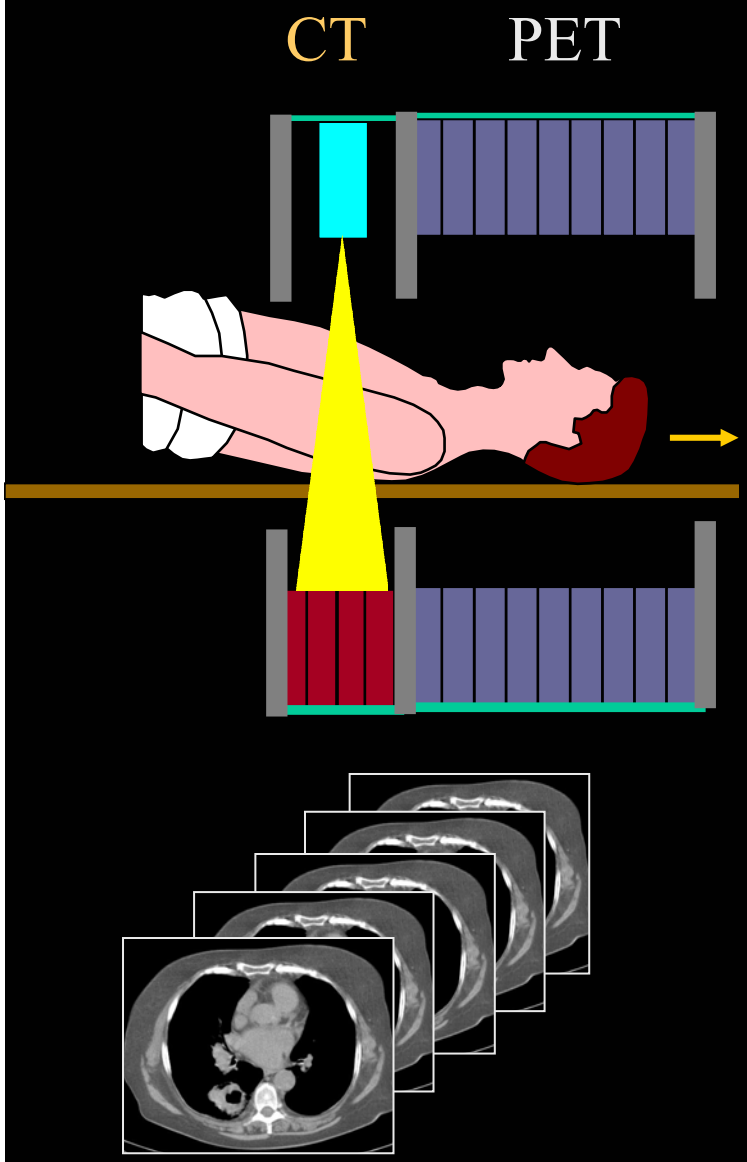
PET/CT

LACK OF ANATOMICAL INFORMATION

PET/CT

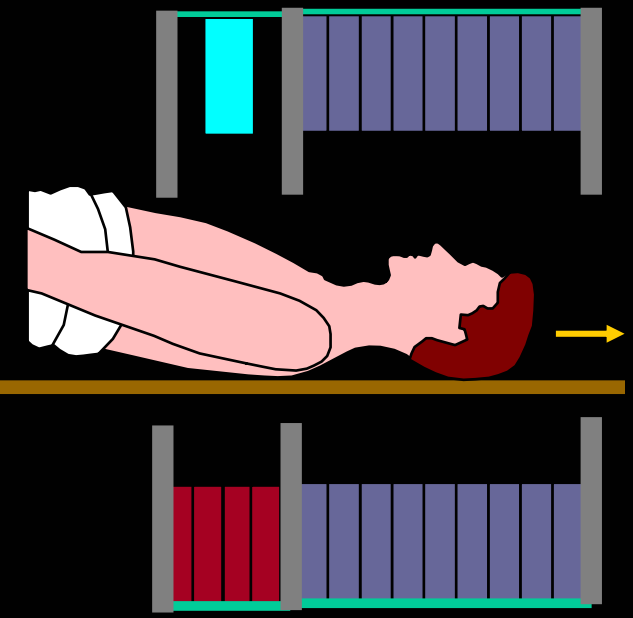


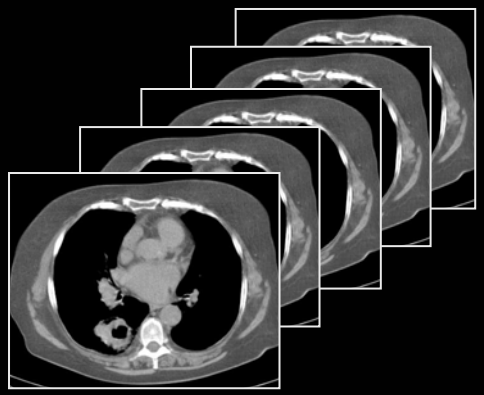
PET/CT



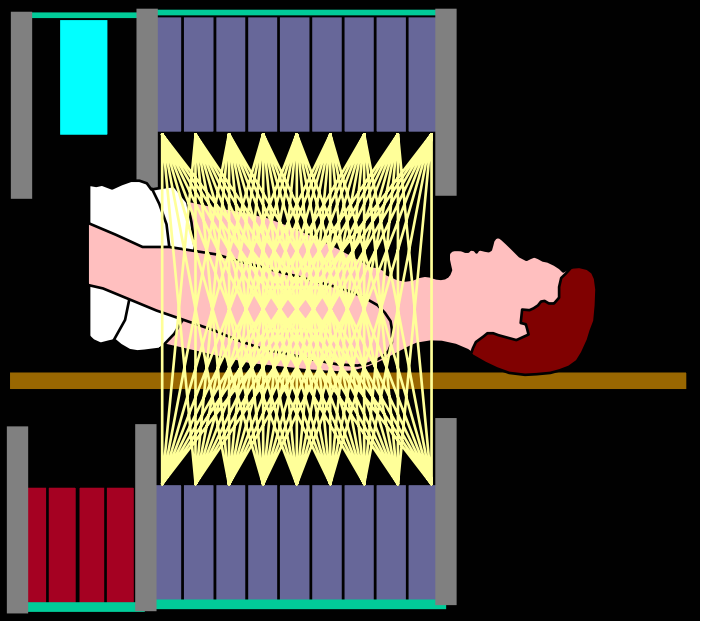
PET/CT

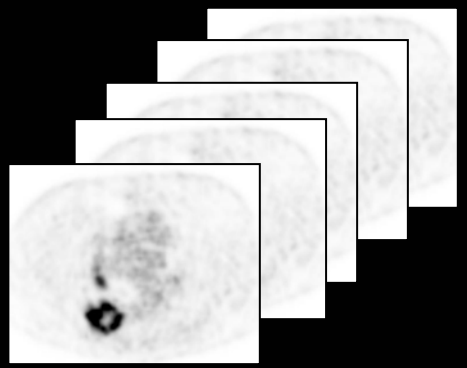
CT PET



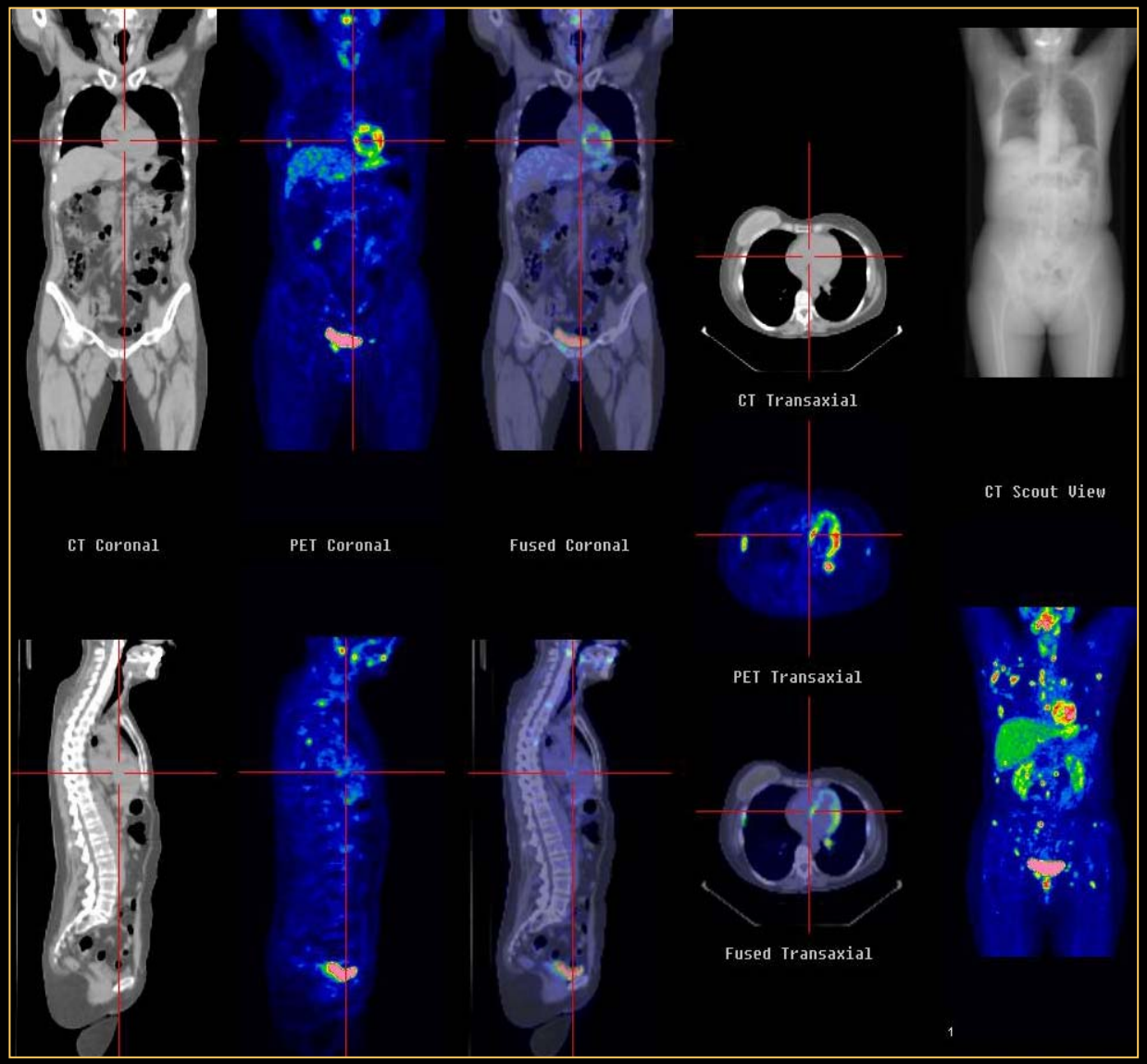


CT PET

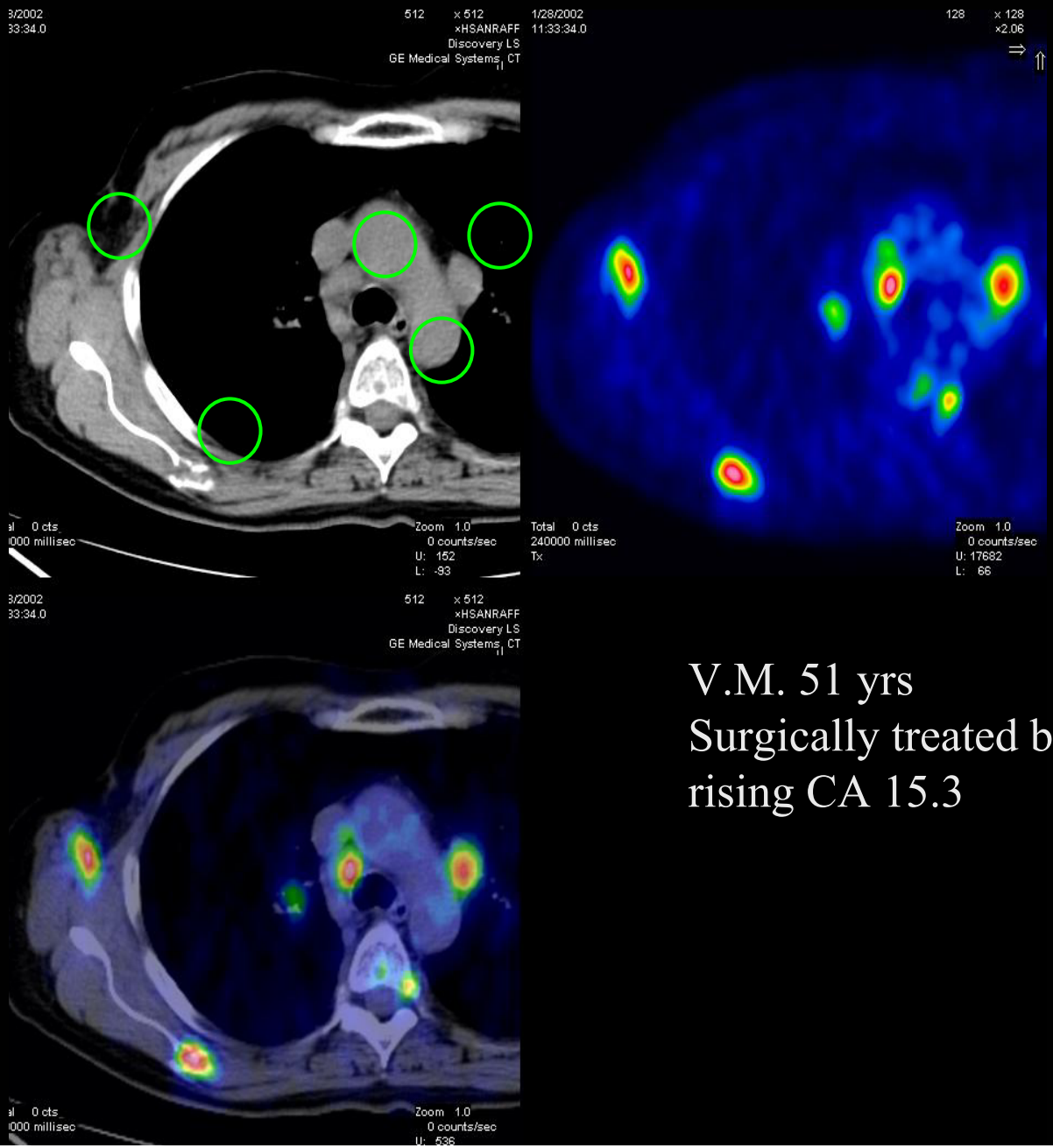




^{18}F-FDG PET/CT



CT/PET UNAMBIGUOUS TISSUE LOCALIZATION



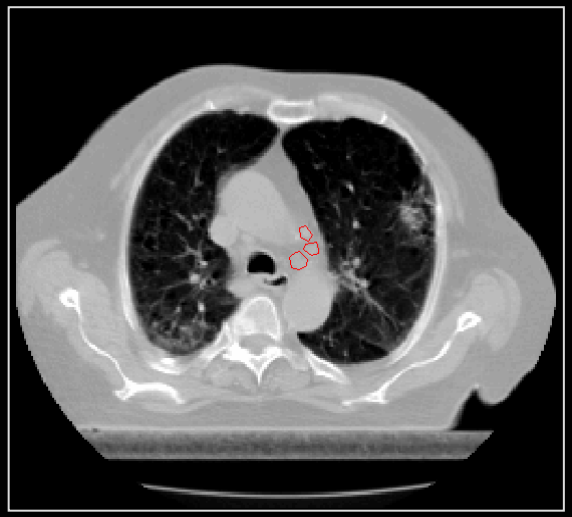
V.M. 51 yrs
Surgically treated breast cancer
rising CA 15.3

HSR Milan

PET/CT - APPLICATIONS

- ANATOMICAL LOCALIZATION OF PET FUNCTIONAL IMAGES
- PET/CT GUIDED RADIOTHERAPY TREATMENT PLANNING

PET/CT BASED RADIOTHERAPY



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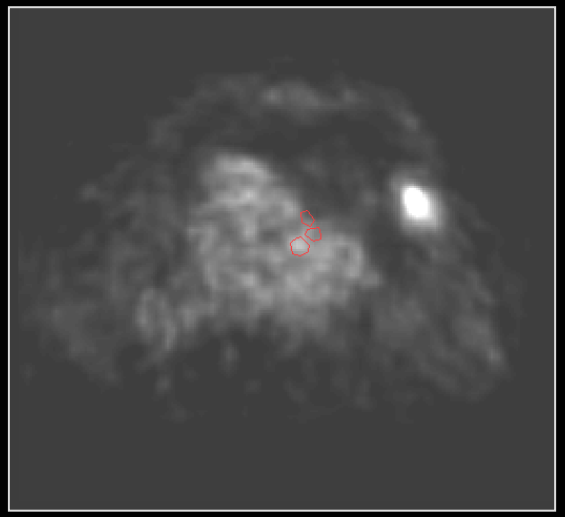
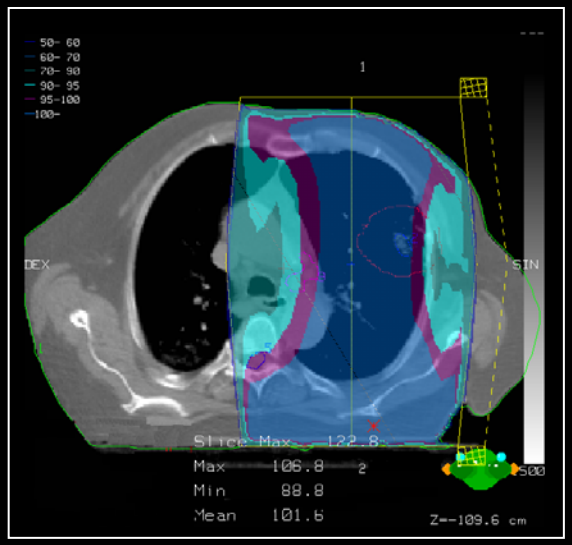


PET



CT BASED

PET/CT BASED

TREATMENT PLAN

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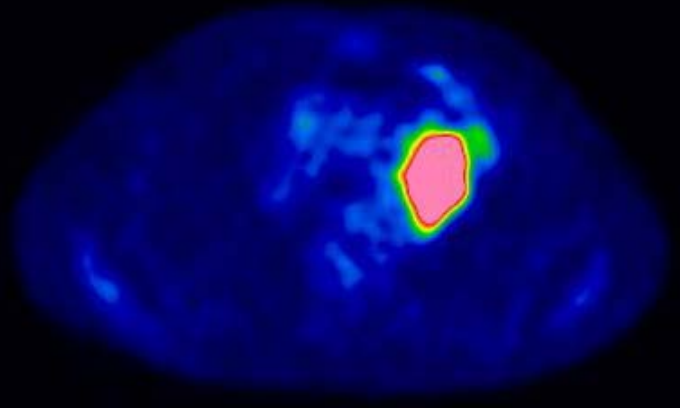
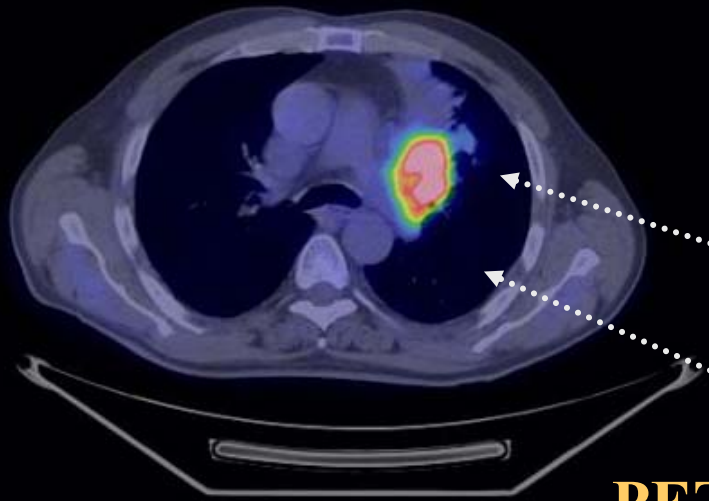
DECREASED TARGET VOLUME

PRIMARY TUMOR(T) CHARACTERIZATION

CT



[^{18}F]FDG PET



PET/CT

ATELECTASIC AREA

VIABLE TUMOR

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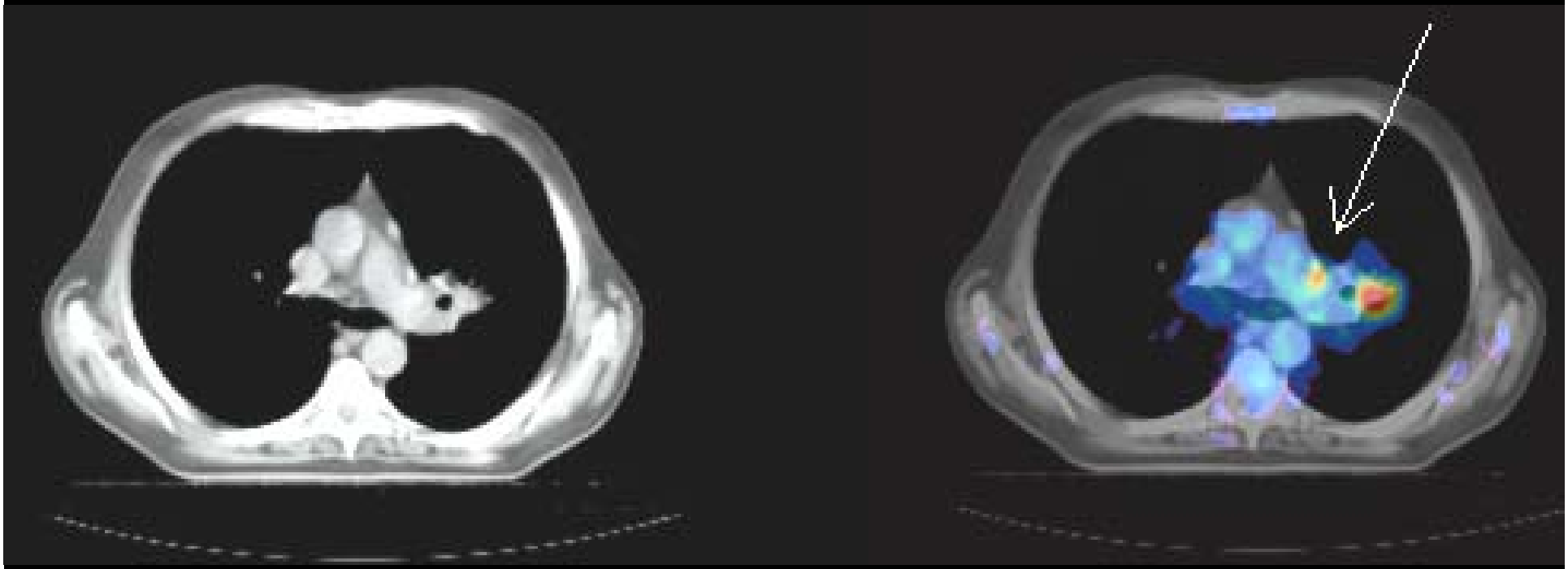
INCREASED TARGET VOLUME

LYMPH NODES CHARACTERIZATION



CT

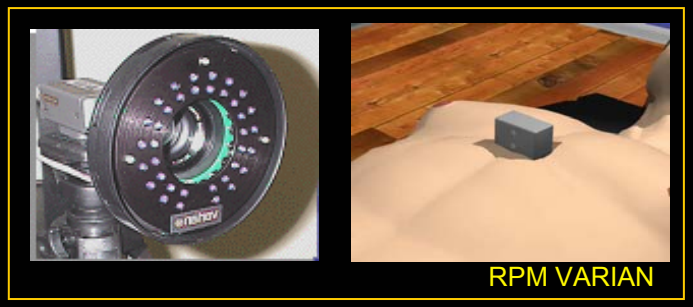
LYMPH-NODES WITH DIAMETER < 10 mm

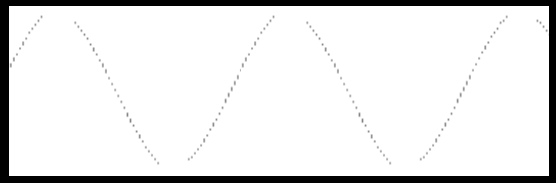
PET/CT:

PATHOLOGICAL LYMPH-NODAL UPTAKE

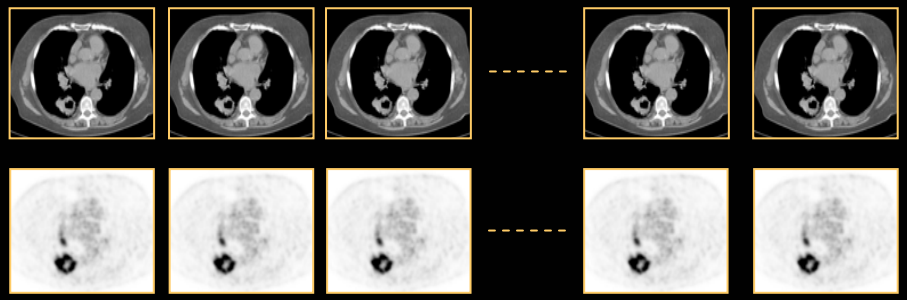
4D PET/CT

Respiration control during PET/CT



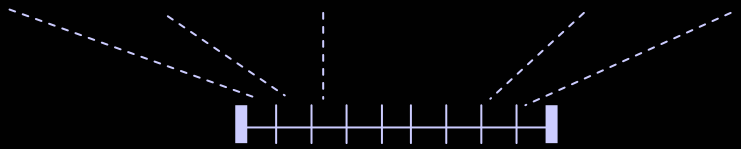


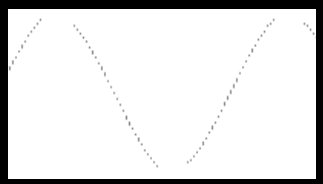
RESPIRATORY CURVE



CT

PET





RESPIRATORY CYCLE

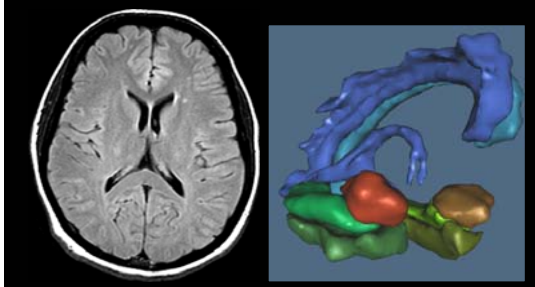
MOLECULAR IMAGING

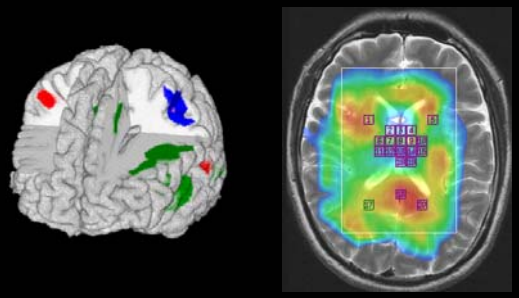
Visual representation, characterization and quantification of biological processes at the cellular and sub cellular level within living organisms.

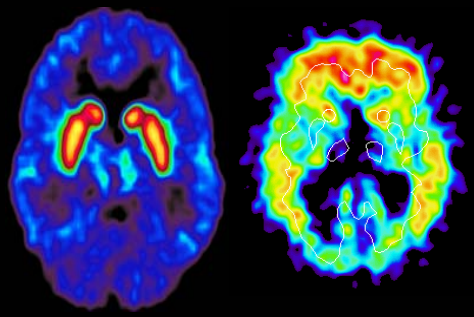
- multiple imaging capture techniques (Nuclear medicine/PET, MRI, MRS, Optical,…)
- basic cell/molecular biology
- medical physics
- biomathematics
- bioinformatics
-

TOWARDS MOLECULAR IMAGING

ANATOMICAL IMAGING → **PHYSIOLOGICAL IMAGING** → **MOLECULAR IMAGING**







- Morphology
- Morphometry

- Haemodynamics
- Vascular permeability
- Tissue oxygenation/hypoxia
- CNS activity
- Metabolites
- pH

- Target-specific contrast agents
- Functional receptor imaging
- PharmacoKinetics

STRUCTURE → **MECHANISM** → **TARGET**

MACROSCOPIC

MICROSCOPIC

L.Faas GEMS