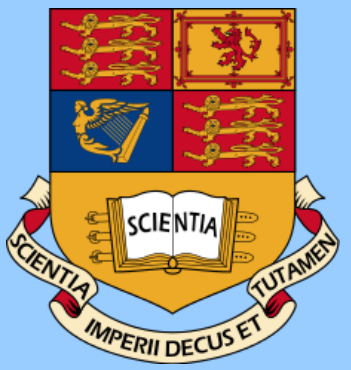
2nd Divonne Brainstorming meeting on
CERN Medical Applications

# Overview of Imaging- Current status from medical perspective

Pat Price

Imperial College London


# Current status from medical prospective

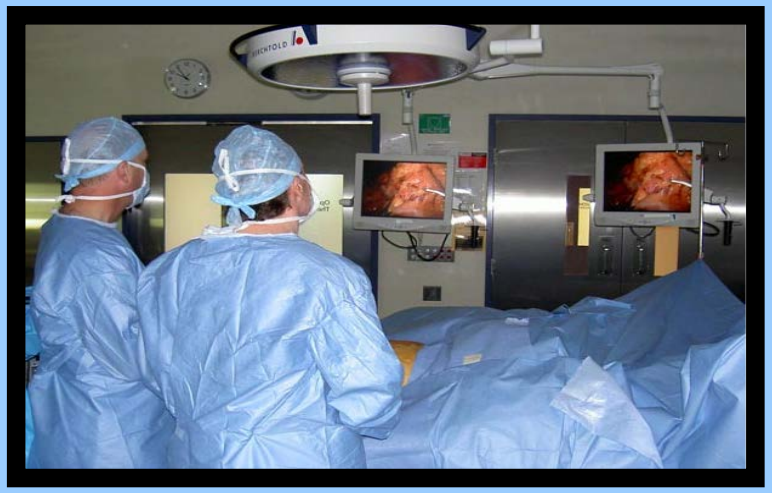
**Current clinical use**

- Anatomical-invasive/real time (RT)
- Diagnostic
- Functional
- Ex-vivo

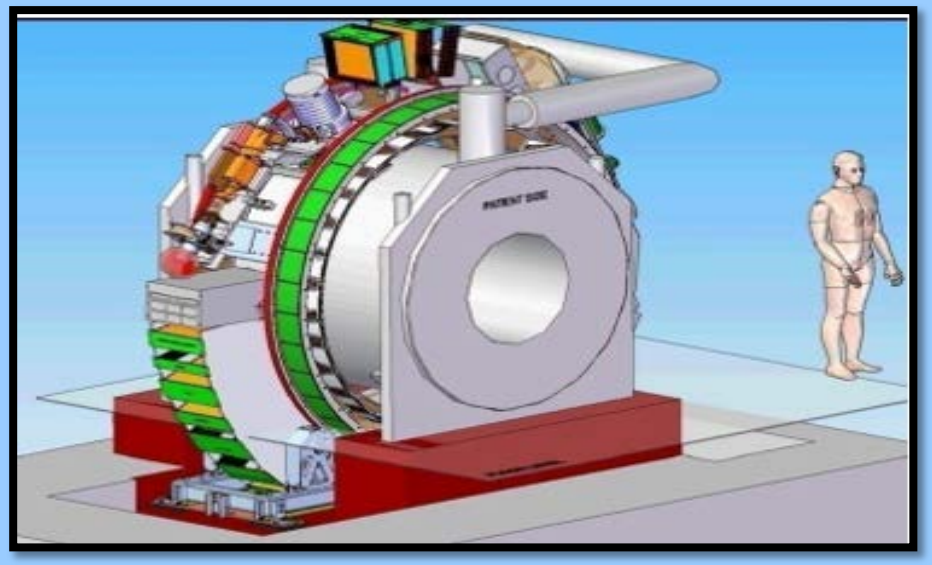
**All need**

- Increased sensitivity/resolution
- Increased specificity
- Increased biological information

# Imaging in Development of surgery

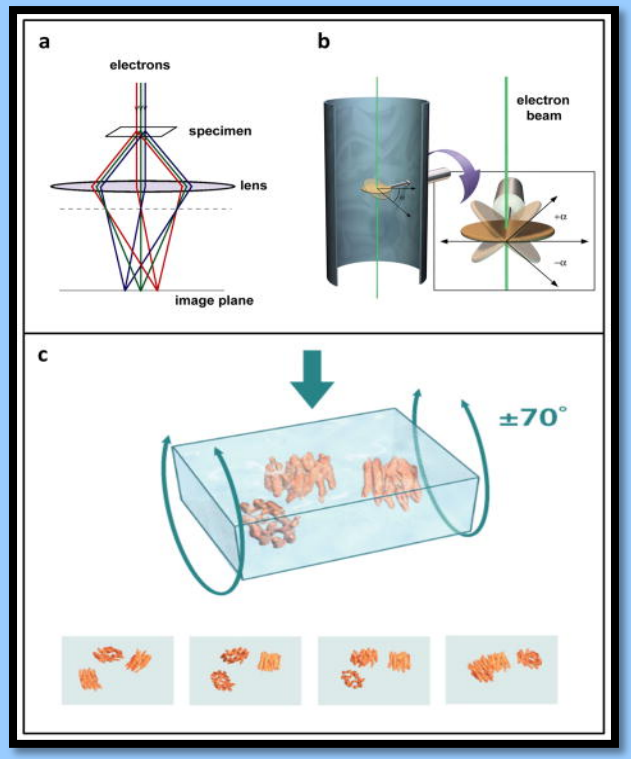



# The Magnetic Resonance Imaging–Linac System



Jan J.W. Lagendijk, et al Seminars in Radiation Oncology,
Volume 24, Issue 3, 2014, 207–209

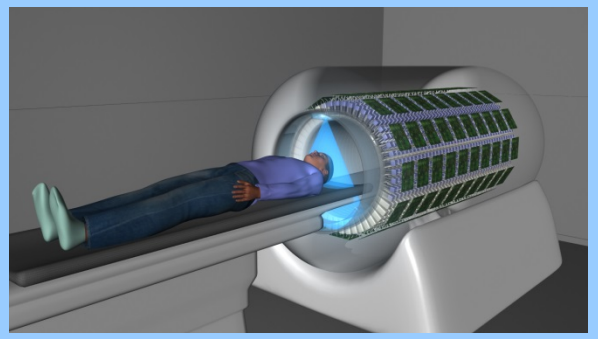
# Cryo-electron microscopy




- Cryogenic Transmission Electron microscope for high-resolution single particle analysis
- Cryo-tomography of biological samples

# Total body PET
# Transformative areas of investigative medicine:

- **Detecting occult low density multi-system disease**
  - Ultra-staging of micro-metastases
  - Plaques in atherosclerosis
  - Inflammation
  - Infection.
- **Providing total body kinetics**
  - Drug delivery /extended time courses /physiologically based PK models
  - Translational pipe line for new radio-labelled imaging biomarkers
  - Toxicology.
- **Enabling Low radiation dose studies**
  - Repeat studies
  - Normal subjects
  - Young patients
  - Maternal-Fetal
- **Studying interactive regional pathologies brain: body**
  - Anxiety/Depression
  - Alzheimer's Disease
  - Metabolic syndrome/Obesity.
- **-- Studying the interactions between the body's organs**
- **Expanding the commercial future**
  - New applications
  - Higher clinical throughput.



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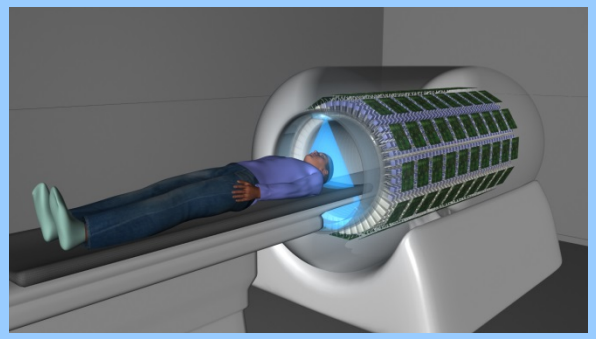
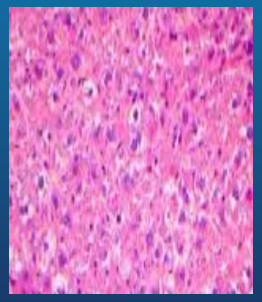
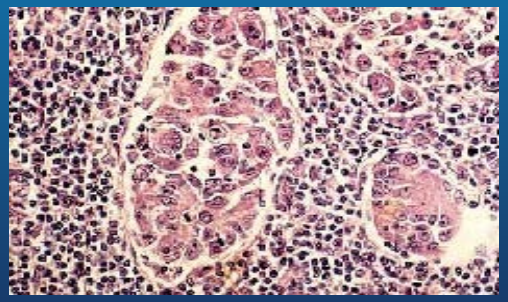


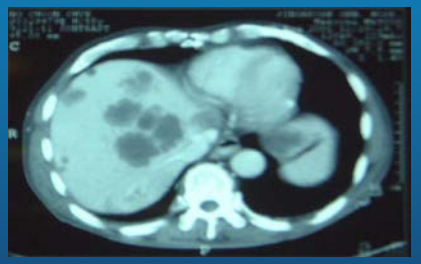
# Detecting Micro-Metastatic Cancer- The Challenge

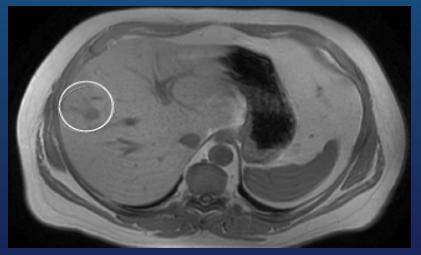
| No Mets | ITC 1cell-<0.2mm | Micro Mets 0.2-6mm | Subclinical 6-9mm | Clinical >1cm |
|---|---|---|---|---|

| PET Ultra-staging | PET | MRI | CT | USS |
|---|---|---|---|---|









# Current cancer imaging with $^{18}$FDG

# The challenge micro-metastases

# Economics of Better Selection for Adjuvant Chemotherapy

- In the USA alone 140,000 patients diagnosed with colorectal cancer per year. 60% late stage receive adjuvant chemotherapy after surgery
- 44% of post surgical patient do not need adjuvant chemotherapy as do not have micrometastases
- Clinical trials of novel adjuvant therapy based on 5 years survival so long and expensive
- Similar challenges in Neoadjuvant therapy
- Similar issues with breast/lung/prostate etc

# Hypothesis
# For ultra-staging in cancer*

The total body Ultra PET scanner will be 40 times more sensitive than conventional scanners for whole body imaging

&

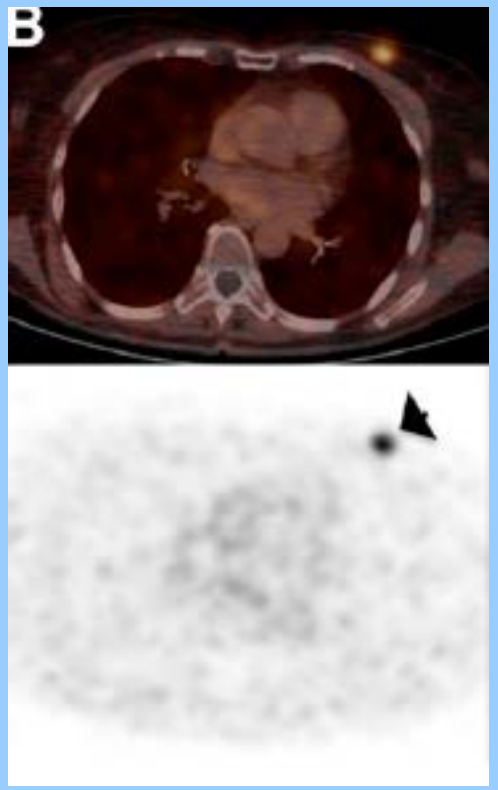
By waiting 3 half lives; 330 minutes post administration of $^{18}$FDG, the enhanced contrast will make it possible to measure raised levels of activity in organs which correspond to the presence of microscopic cancer

*Price P M, Badawi R D, Cherry S R , Jones T.
Journal of Nuclear Medicine 2014;55:696-697

# Phase I Study of $^{68}$Ga-HER2-Nanobody for PET/CT Assessment of HER2 Expression in Breast Carcinoma

Marleen Keyaerts*[1,2], Catarina Xavier*[2], Johannes Heemskerk[1], Nick Devoogdt[2,3], Hendrik Everaert[1], Chloé Ackaert[3], Marian Vanhoeij[4], Francois P. Duhoux[5], Thierry Gevaert[6], Philippe Simon[7], Denis Schallier[8], Christel Fontaine[8], Ilse Vaneycken[1,2], Christian Vanhove[9], Jacques De Greve[8], Jan Lamote[4], Vicky Caveliers[1,2], and Tony Lahoutte[1,2]

J Nucl Med 2016; 57:27–33

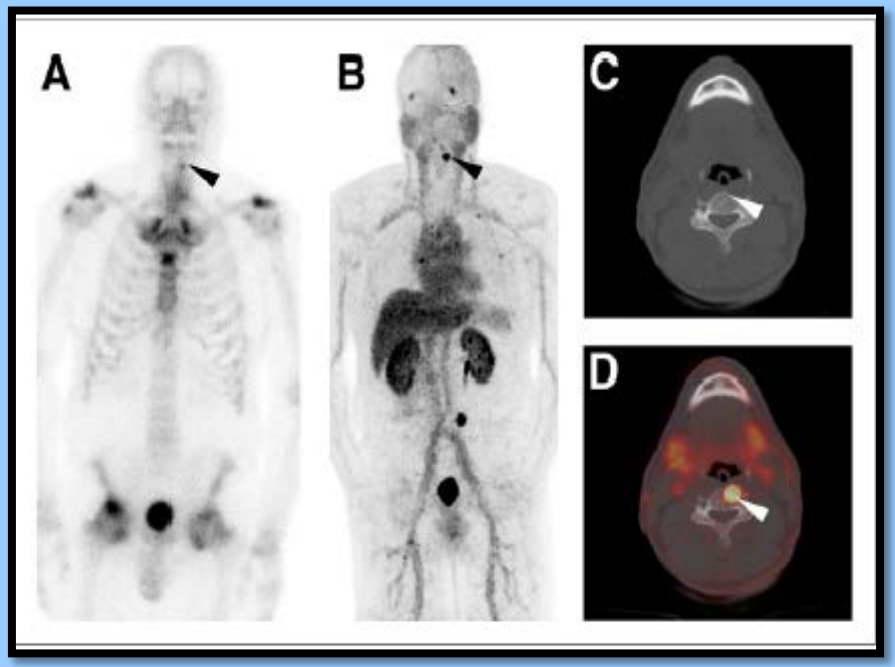



90 mins after injection

# Comparison of Prostate-Specific Membrane Antigen–Based $^{18}$F-DCFBC PET/CT to Conventional Imaging Modalities for Detection of Hormone-Naïve and Castration-Resistant Metastatic Prostate Cancer

Steven P. Rowe[1], Katarzyna J. Macura[1–3], Anthony Ciarallo[1], Esther Mena[1], Amanda Blackford[2], Rosa Nadal[2], Emmanuel S. Antonarakis[2], Mario A. Eisenberger[2], Michael A. Carducci[2], Ashley E. Ross[3], Philip W. Kantoff[4], Daniel P. Holt[1], Robert F. Dannals[1], Ronnie C. Mease[1], Martin G. Pomper[1], and Steve Y. Cho[1]

J Nucl Med 2016; 57:46–53



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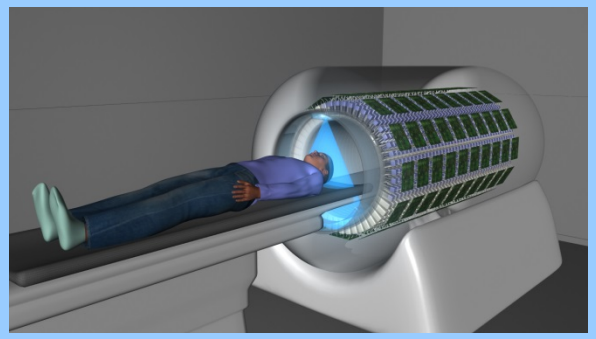
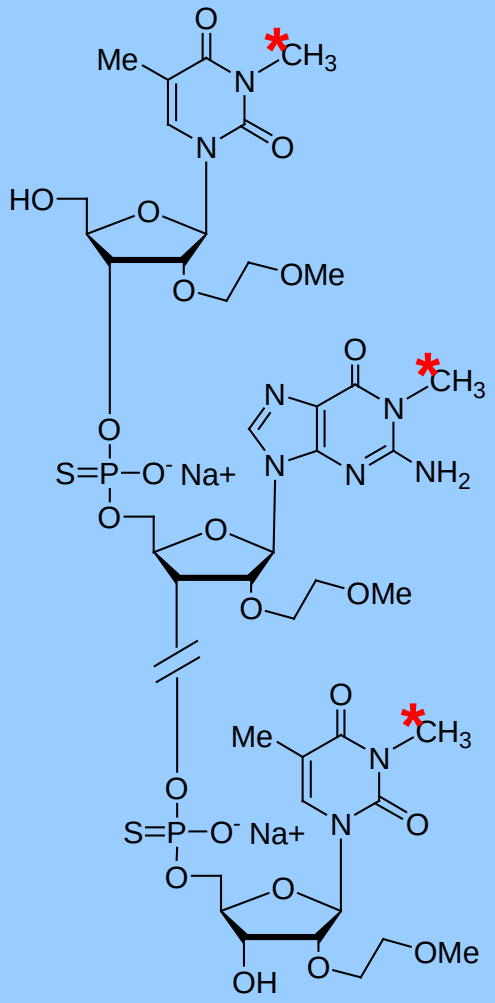
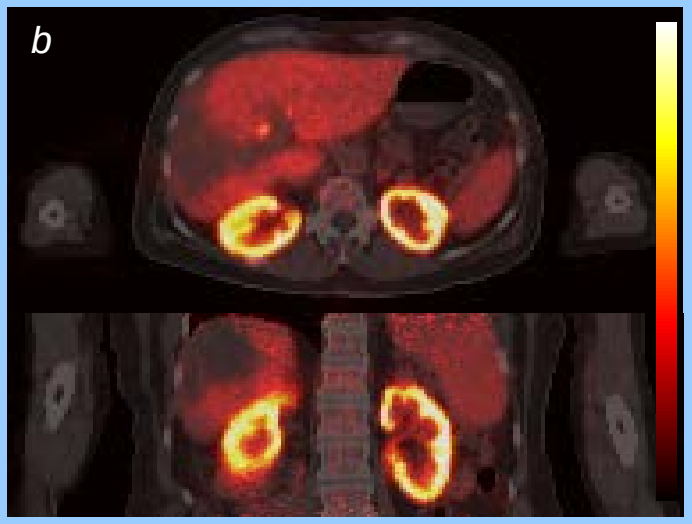
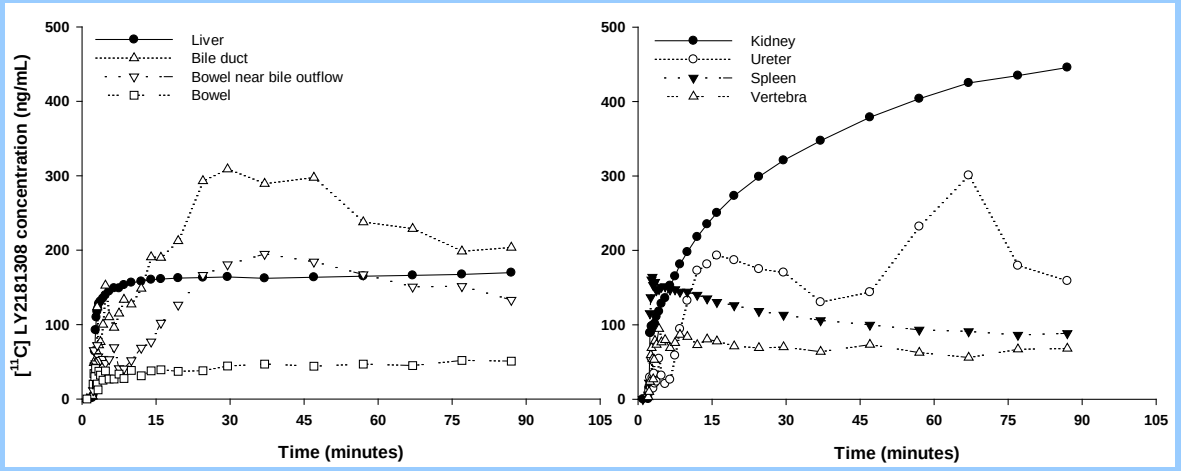


# Antisense Oligonucleotide Carbon-11-LY2181308 Uptake

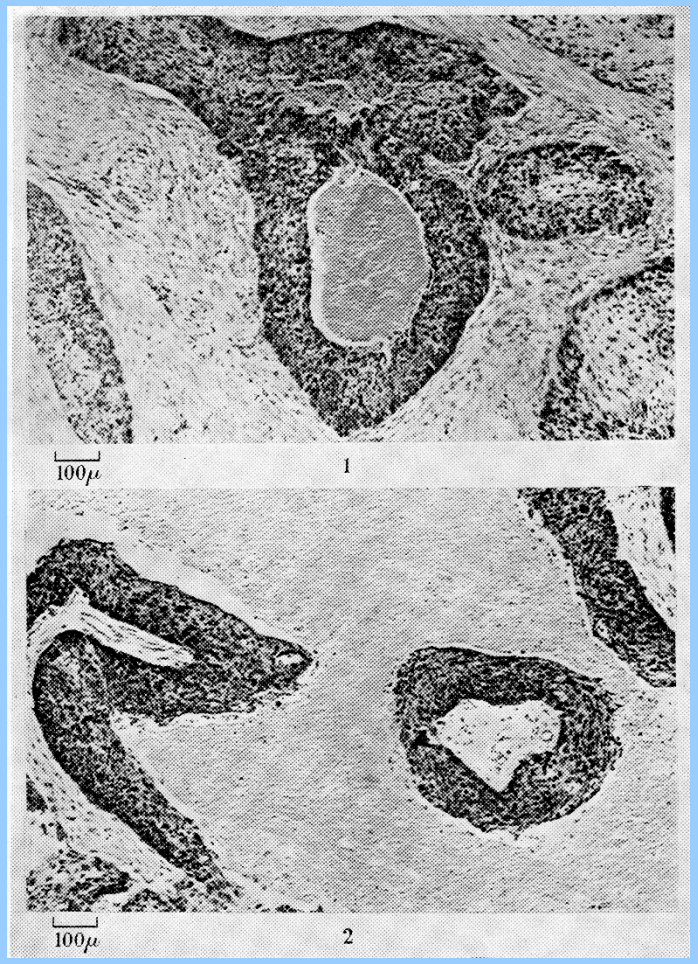


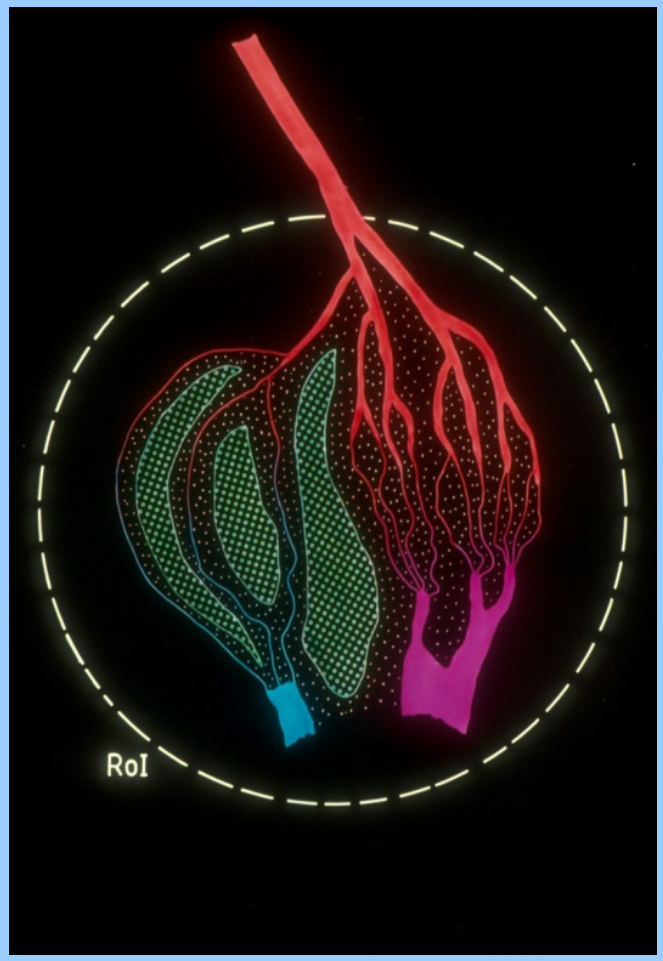







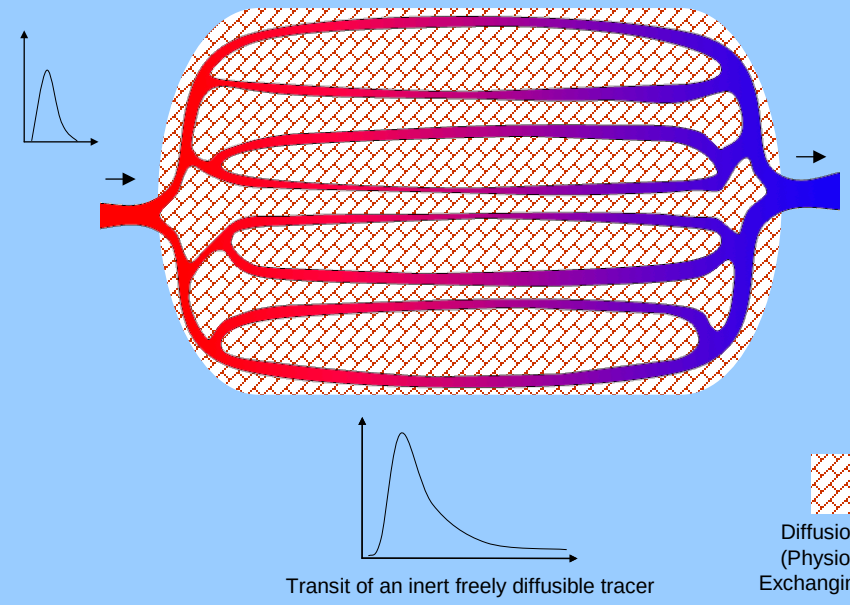
# Perfusion Dependant Drug Delivery Due to Tumour Microscopic Heterogeneity



# Measuring Tumour Heterogeneity with High sensitivity PET

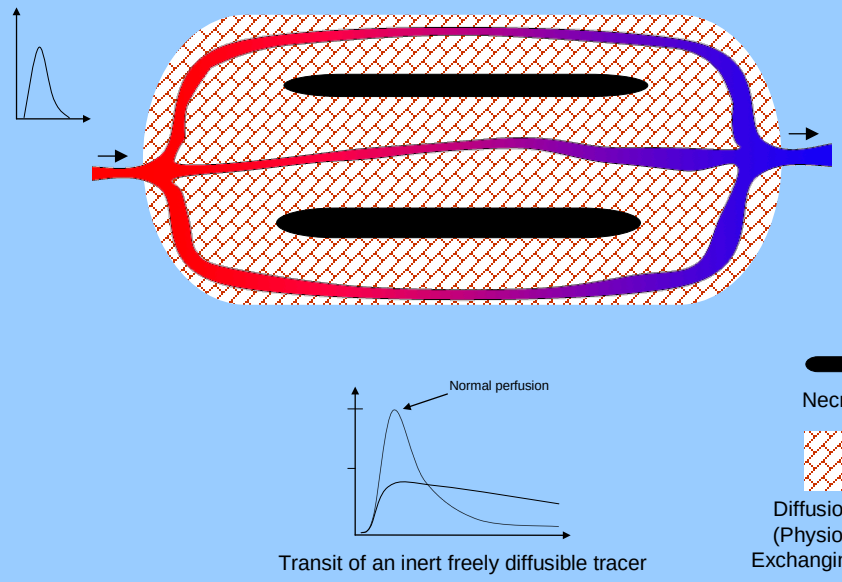
## Uniform Perfusion



Transit of an inert freely diffusible tracer

Diffusion space (Physiologically Exchanging Space)

## Heterogeneous Perfusion




Transit of an inert freely diffusible tracer

Necrosis

Diffusion space (Physiologically Exchanging Space)

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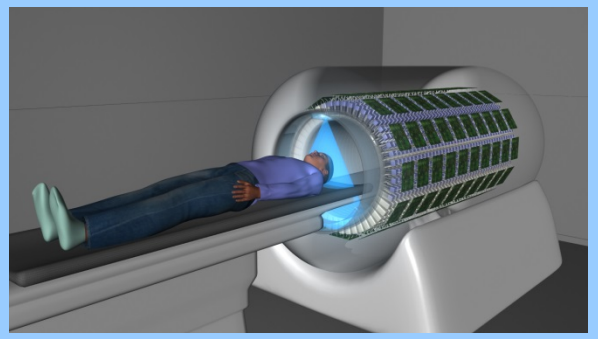
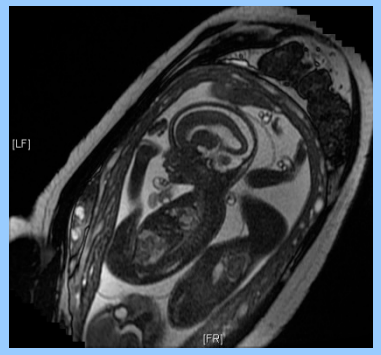


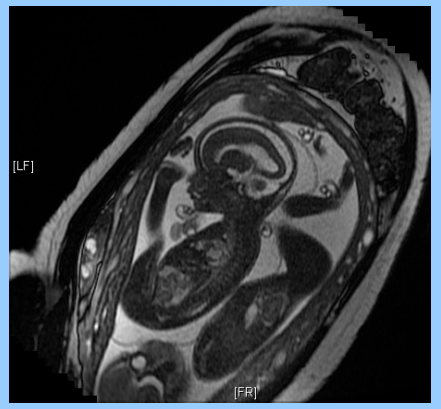
# Maternal-Fetal Health



- 15M babies/year are born pre-term (<37 weeks) “born too soon”
- 1.1M babies die/year because of pre-term complications
- Many surviving pre-term babies are disabled
- 3M still born babies per year
- Intrauterine growth restriction (IUGR) is due to abnormal placenta function

# Intrauterine Growth Restriction is associated with

- Raised neonatal mortality and morbidity
- Diabetes in adulthood
- Hypertension in adulthood
- Ischemic heart disease in adulthood
- Metabolic syndrome (obesity)



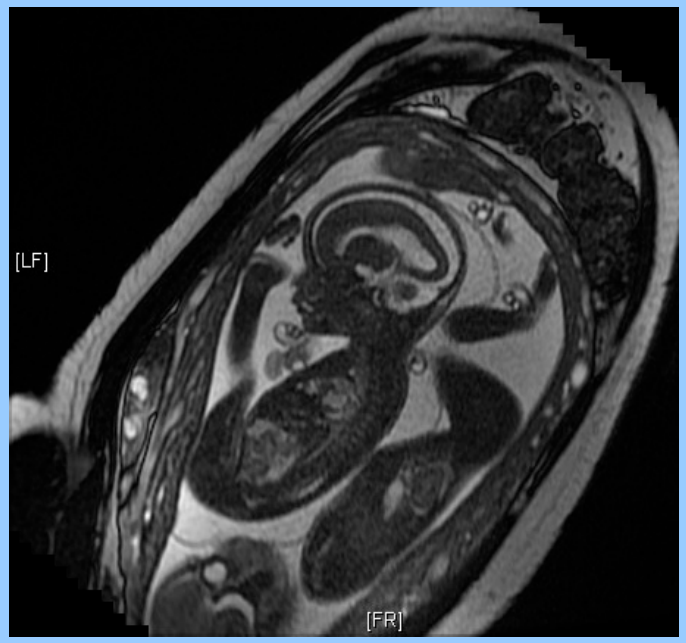
# The Case for Maternal-Fetal PET

Tracing nutrient from the mother to the fetus
(Placenta transport  e.g. Oxygen, glucose, amino acids)

Placenta transporters

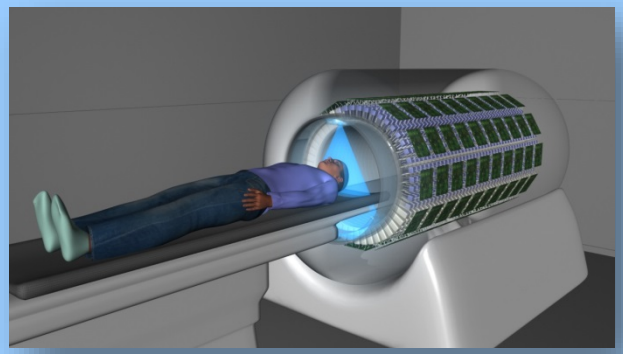
Metabolic health of the fetus

Schizophrenia
Autism
Cognitive impairment
Inflammation/infection




Drugs and toxins distribution between mother to fetus

Maternal cardiovascular physiology



# Maternal-Fetal PET

## Cost (radiation dose)

## vs

## Benefit (immediate & lifetime impact)

## Imaging at the beginning of life and not just at the end

The potential for low dose functional studies in maternal-fetal medicine using combined PET and MRI Terry Jones and Thomas F. Budinger. Journal of Nuclear Medicine 2013, 54: 2017-2018

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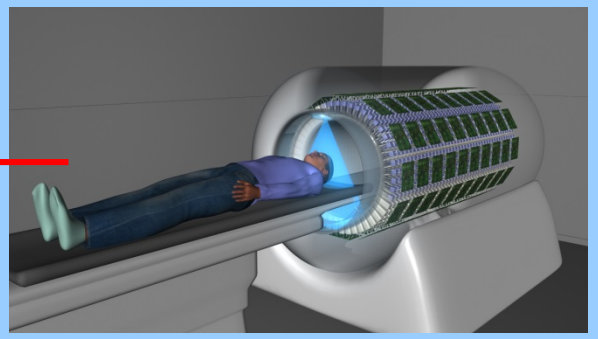
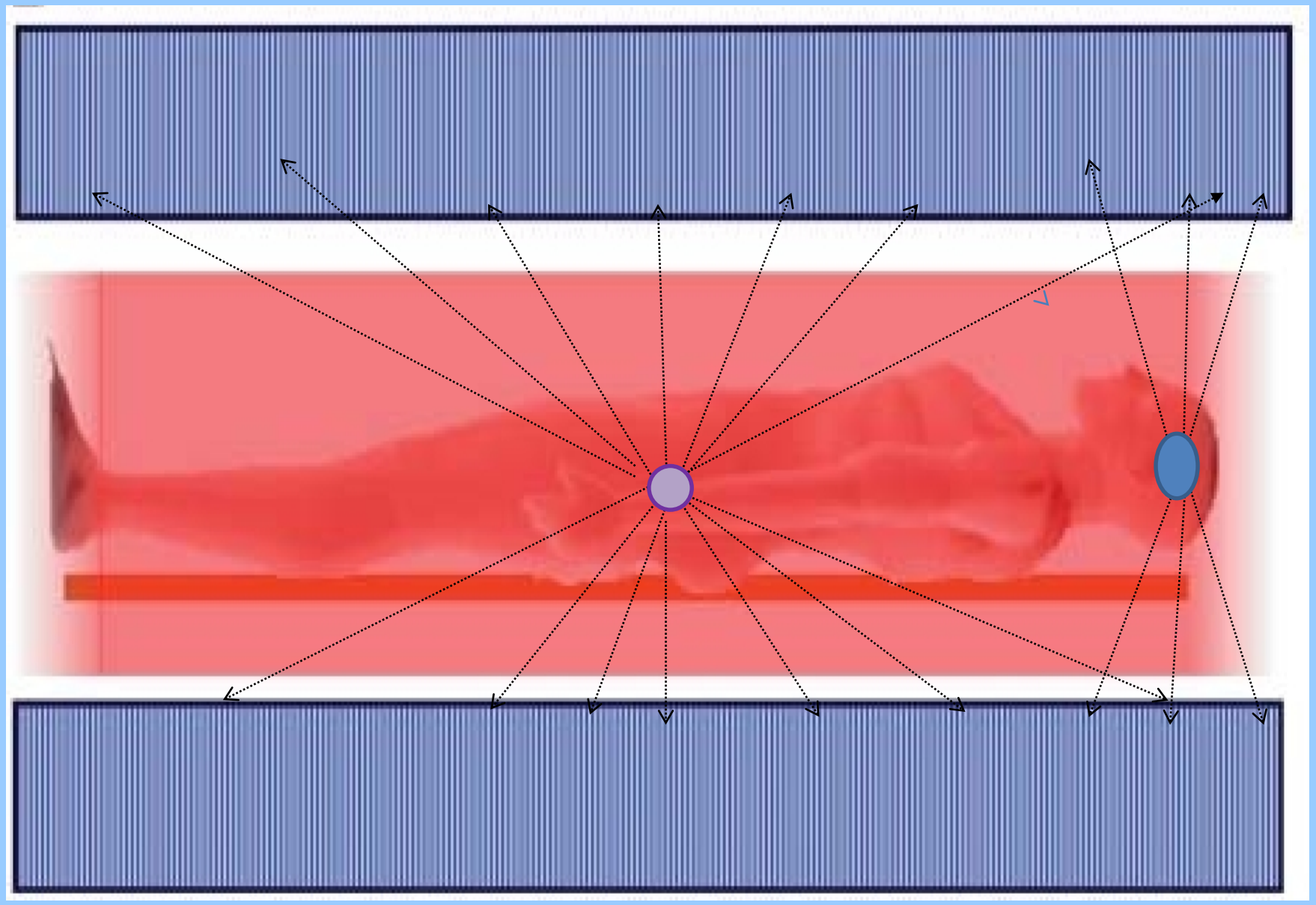
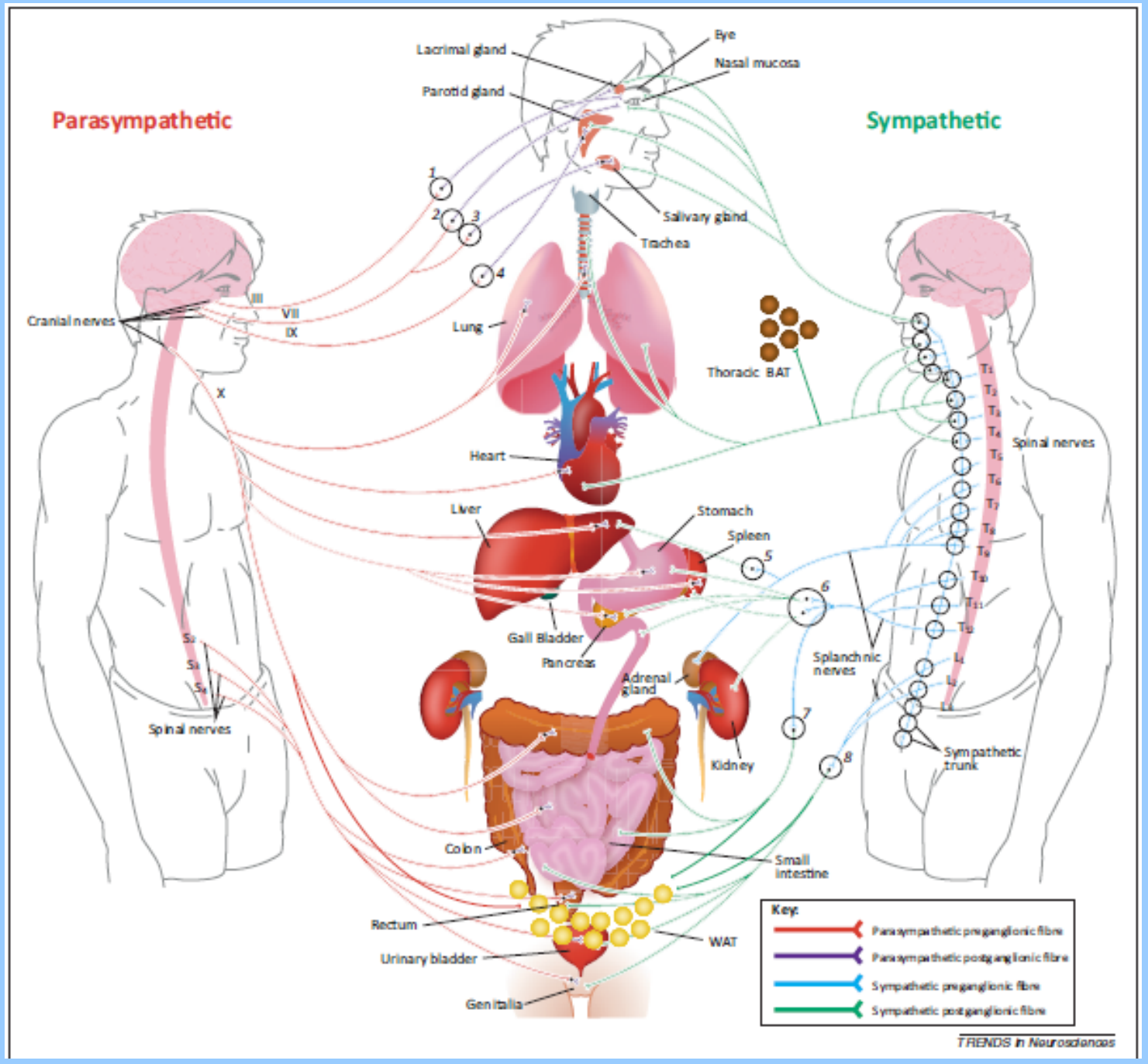




# Brain-Body Positron Emission Tomography

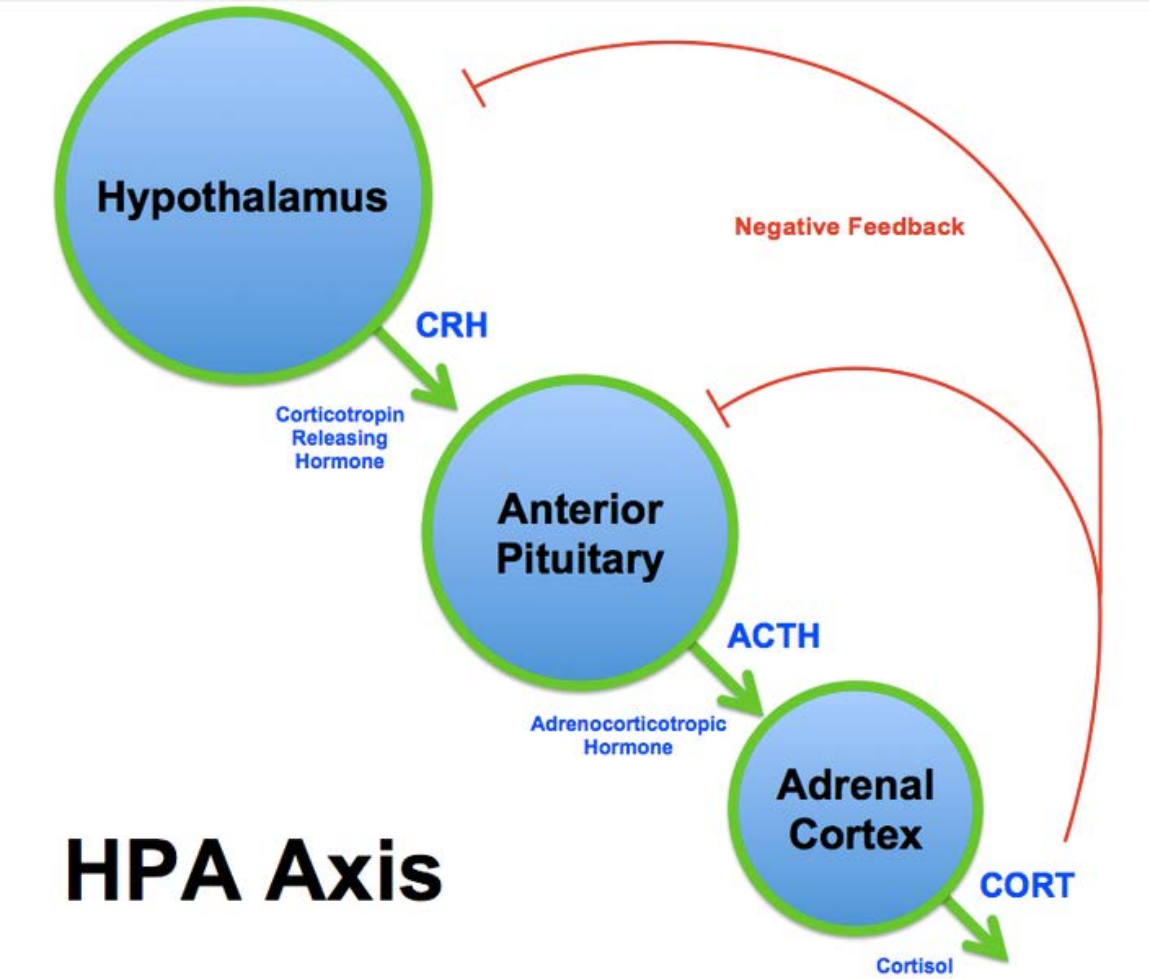

Parasympathetic
Sympathetic
Lacrimal gland
Eye
Nasal mucosa
Parotid gland
Salivary gland
Trachea
Lung
Thoracic BAT
Cranial nerves
III
VII
IX
X
Spinal nerves
Heart
Liver
Stomach
Spleen
Gall Bladder
Pancreas
Adrenal gland
Kidney
Splanchnic nerves
Sympathetic trunk
Spinal nerves
Colon
Small intestine
Rectum
Urinary bladder
Genitalia
WAT
Key:
Parasympathetic preganglionic fibre
Parasympathetic postganglionic fibre
Sympathetic preganglionic fibre
Sympathetic postganglionic fibre
TRENDS in Neurosciences

# Stress and disease

Major Depressive Disorder, Irritable Bowel Syndrome, Borderline Personality Disorder,

Bipolar Disorder

ADHD




Anxiety Disorder

Insomnia

Alcoholism

Fibromyalgia

Posttraumatic Stress Disorder,

Burnout, Chronic Fatigue Syndrome

# The 10 Year Vision

# Using Total Body PET: Molecular/Functional Imaging of the total body with high sensitivity "Systems Biology" in Clinical Research

# Health Care