Molecular Imaging: Dream or Reality

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Turku PET
Centre

Funding organisations

University of Turku, Turku, Finland

Åbo Akademi University, Turku, Finland

Hospital District of Southwest Finland

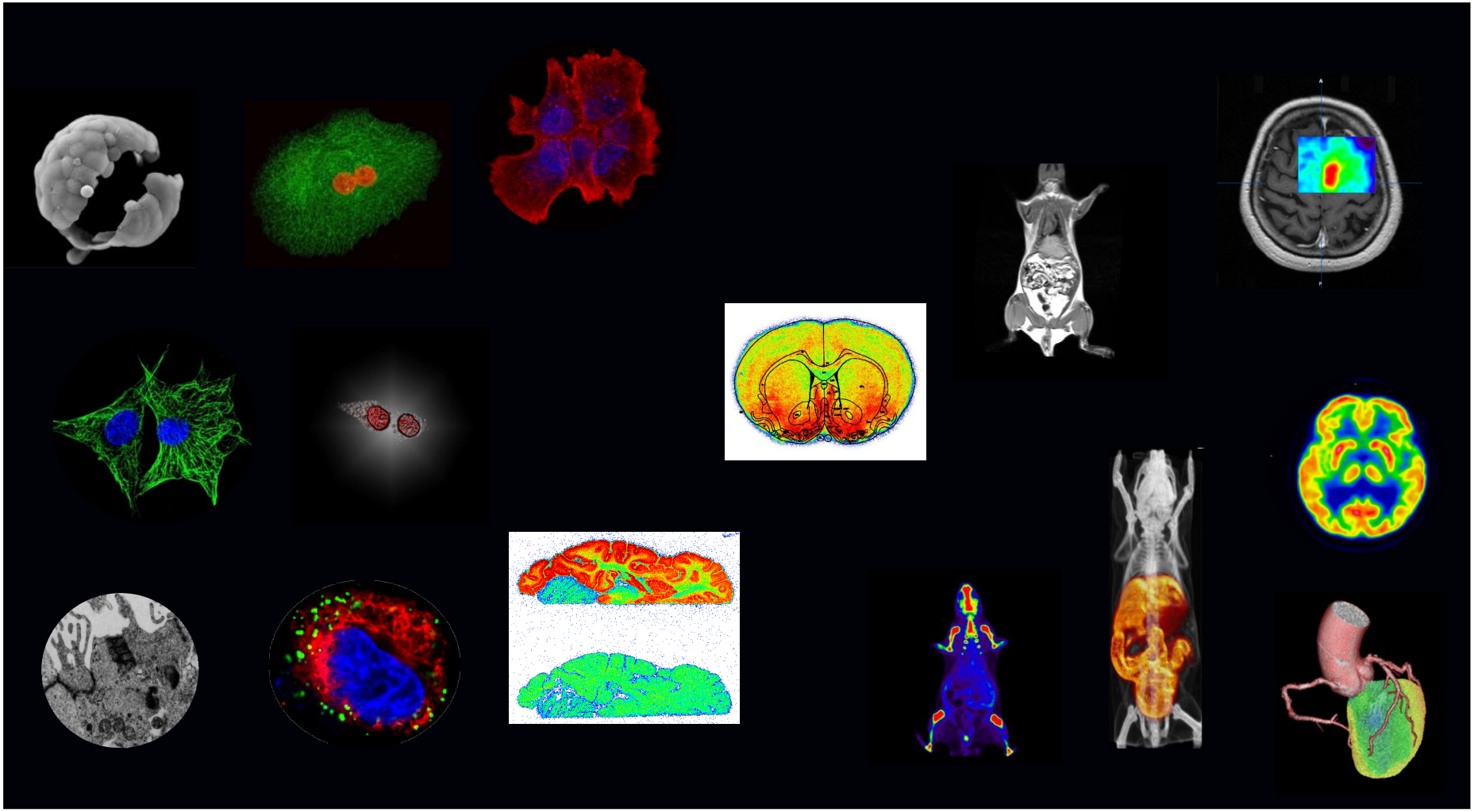
Center of Excellence on Molecular Imaging in Cardiovascular and Metabolic Research 2008 - 2013

IMAGE-HF (Finland-Canada)
TEKES-CIHR funded multicentre project about imaging in heart failure

In Vivo Molecular Imaging

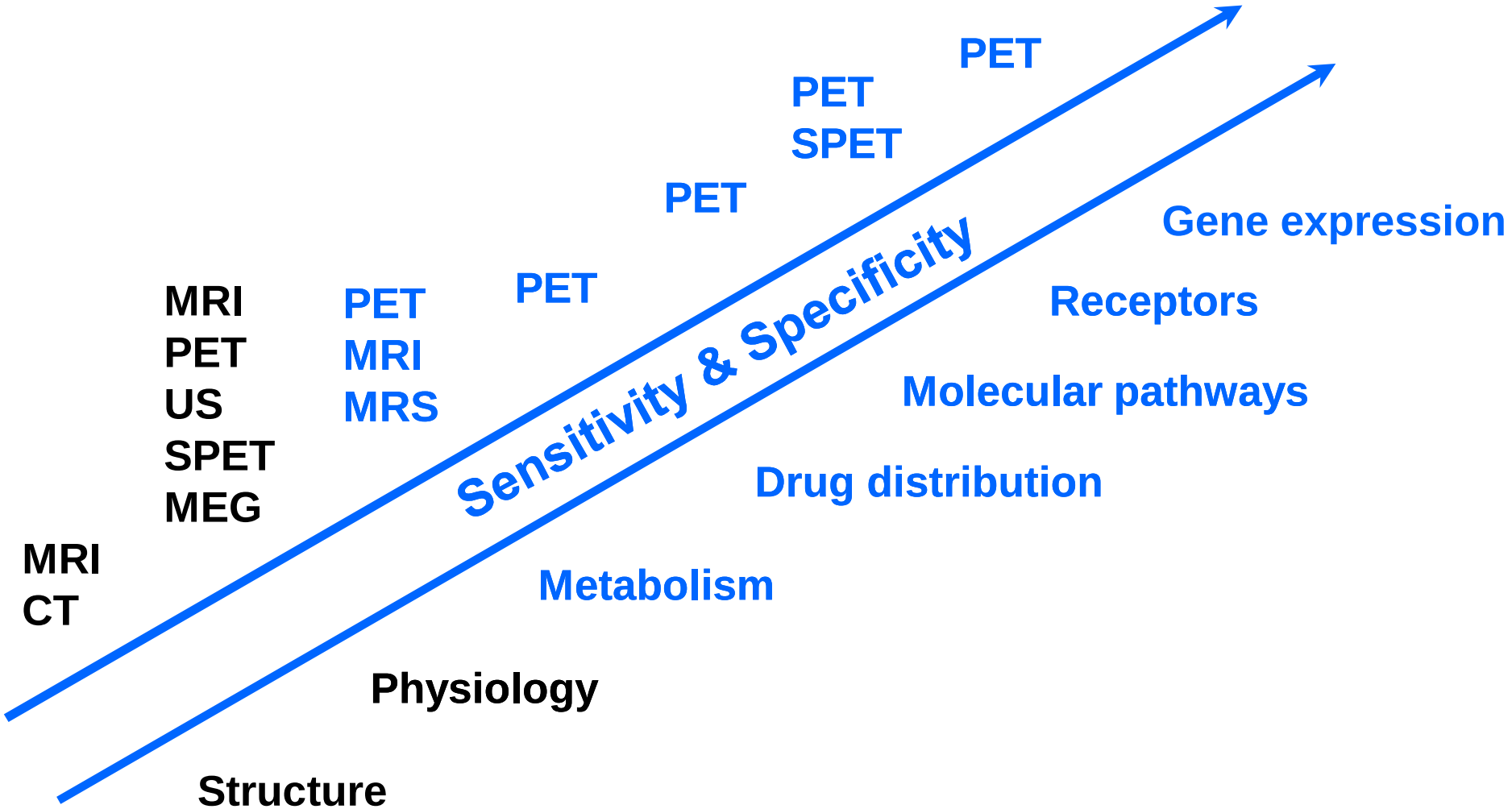
- Definition of *in vivo* molecular imaging
- Molecular imaging methodology
- Translational aspects
- Examples of applications

Biomedical Imaging



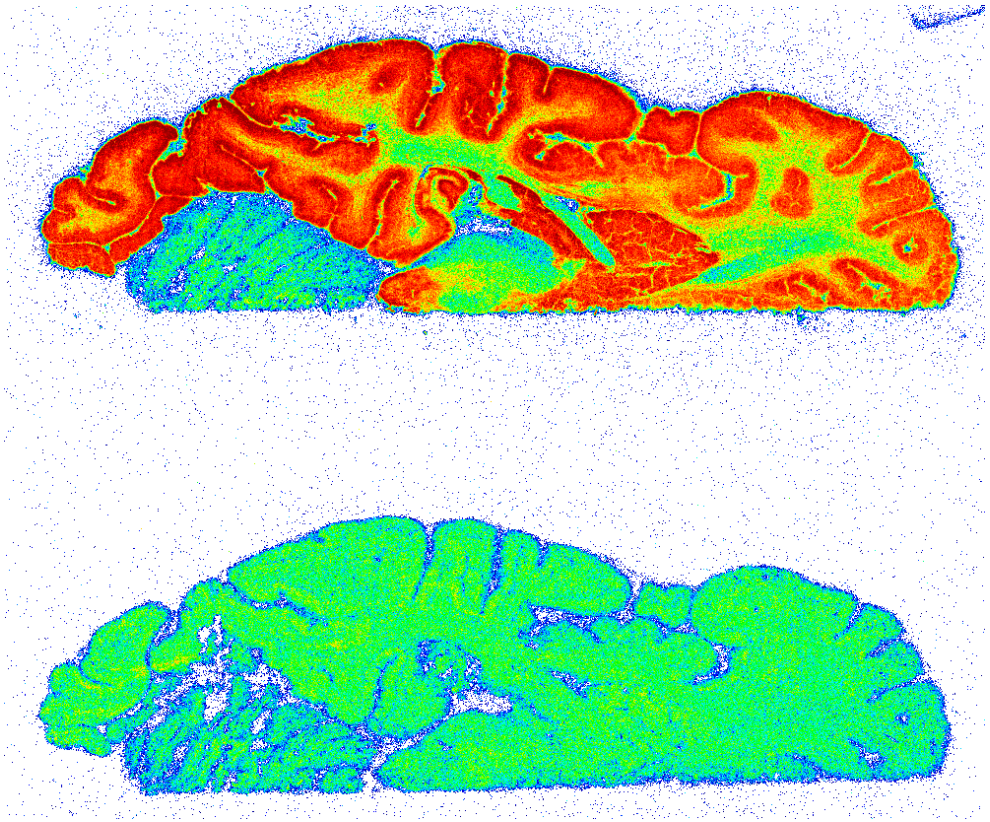
Nanoscopic **Cell** ***In vitro* tissue** ***Ex vivo*** ***In vivo* non-clinical** **Clinical**

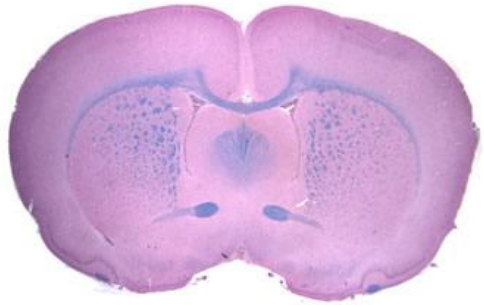
Molecular Imaging in Medicine



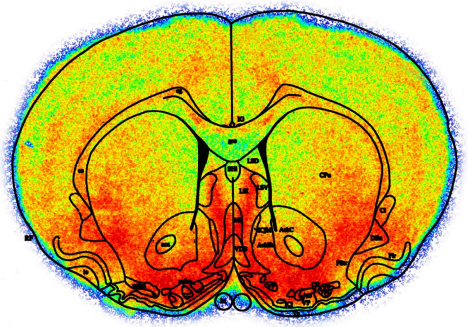
Turku PET Centre

In vitro and Ex vivo tissue imaging

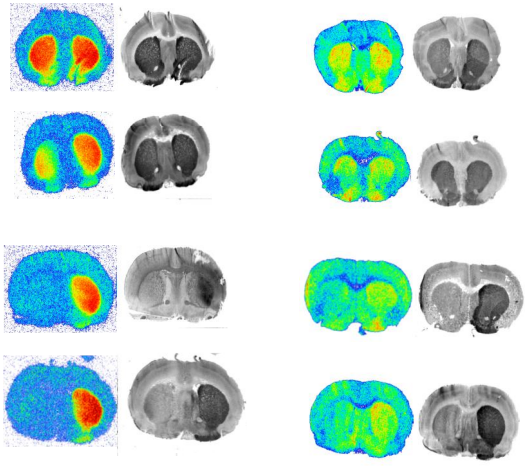




Immunohistologia



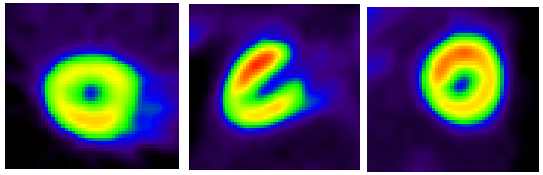
Autoradiografia



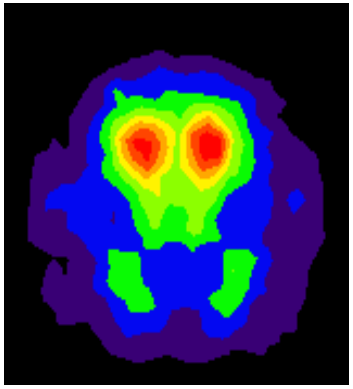
In vivo preclinical imaging

Mouse [^{18}F]FDG heart

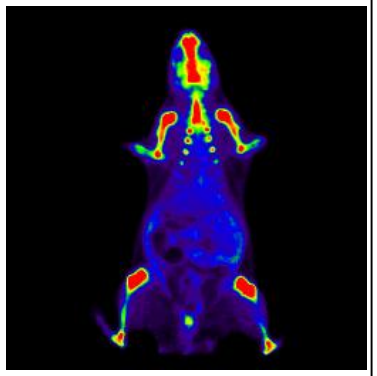
Ax Cor Sag

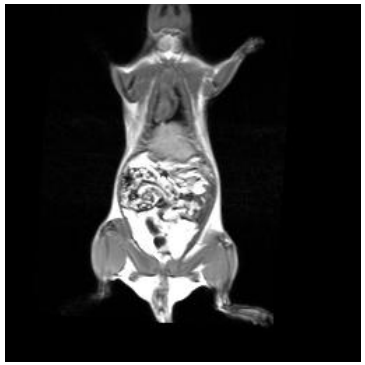


Rat [^{18}F]CFT brain



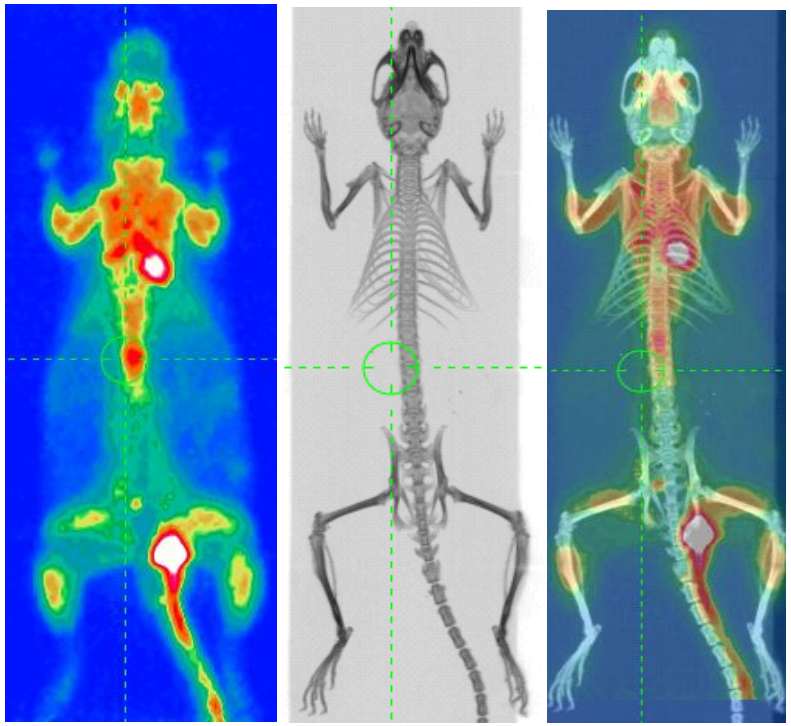
Rat whole-body PET and MRI



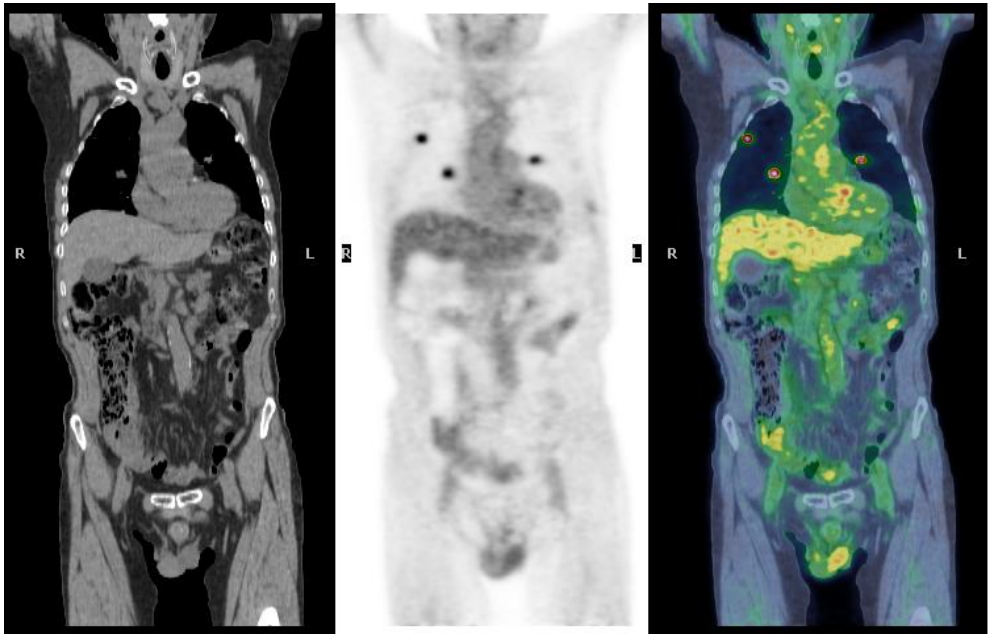


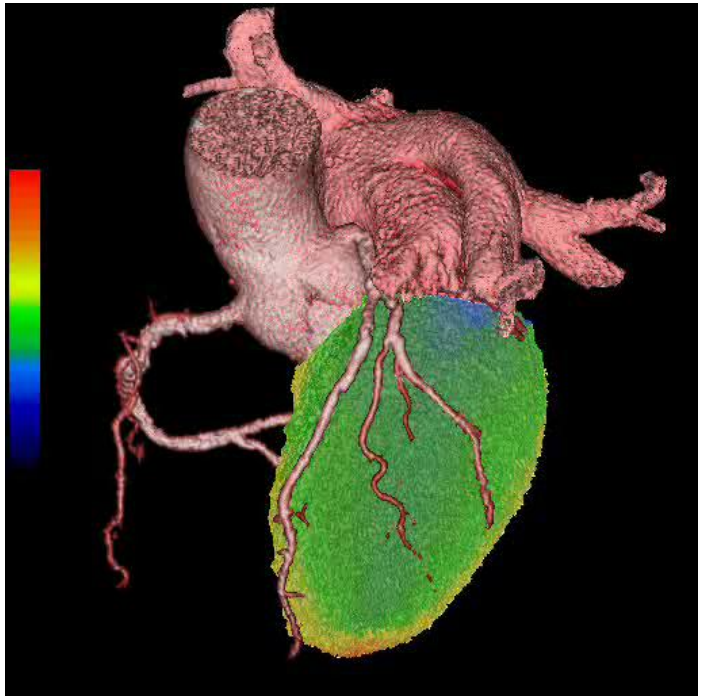
Mouse [^{18}F]FDG whole-body

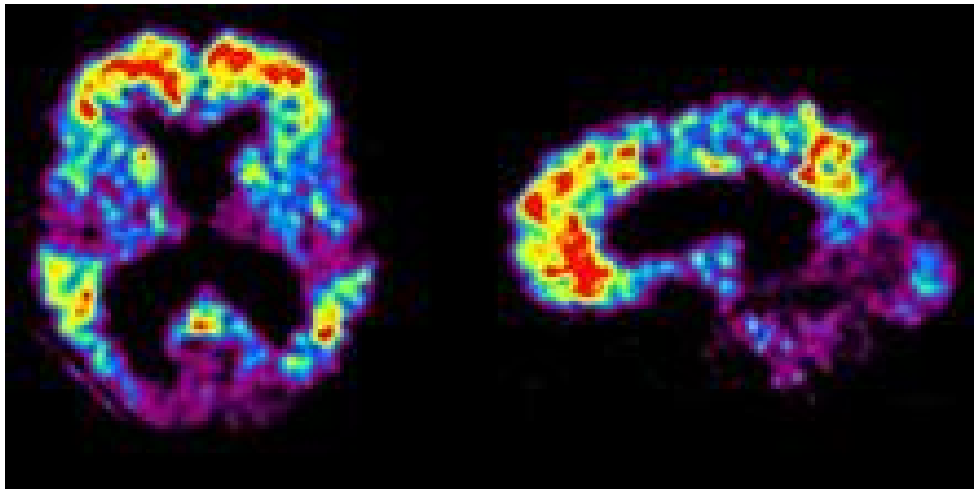
PET CT PET/CT



Clinical Applications of PET and PET/CT







Turku PET Centre, Finland

Imaging in 2020

- Individualized therapy requires individualized diagnostics
  - Non-invasive imaging
  - Molecular Imaging
  - Fusion imaging
- Prevention of disease requires early detection
  - Imaging for screening

PET imaging applications in drug discovery and development

Enhance pathway and target identification in living systems

Proof of mechanism
Species differences
PK/PD
ADME
Safety
Dose ranging
Drug delivery
Efficacy

Enhance the quality of lead compound selection in living systems

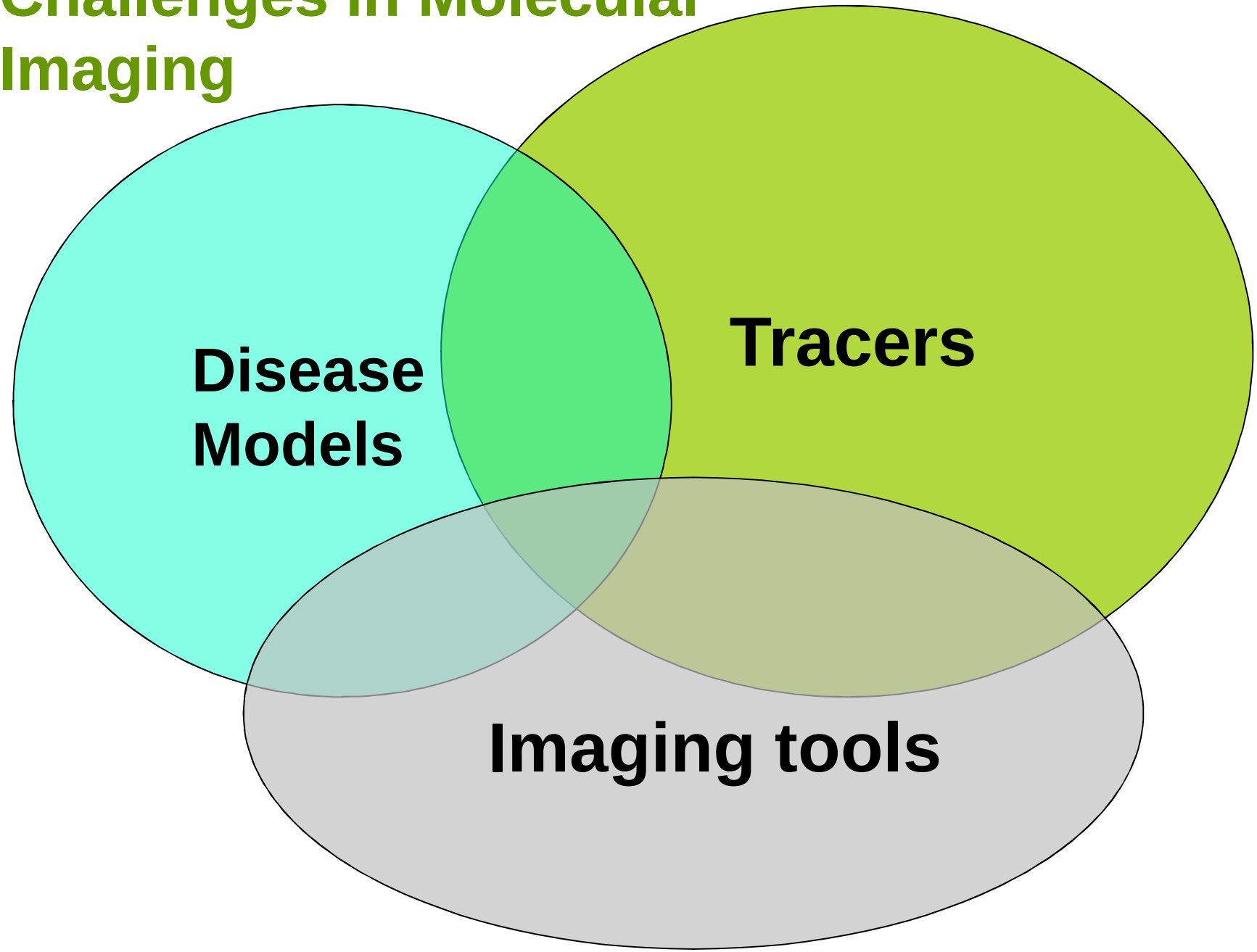
Phase 0 microdosing
Phase I-III trials
Efficacy
Safety
Human PK
Dose Selection
Bioavailability
Patient selection
Surrogate endpoints

Early identification of failure or succes

Phase IV
Safety
Diagnosis & staging
Patient selection
Treament planning

Molecular therapy and imaging package for clinical application

Challenges in Molecular Imaging



In Vivo Molecular Imaging

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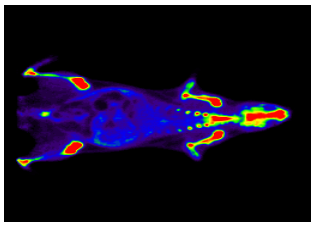
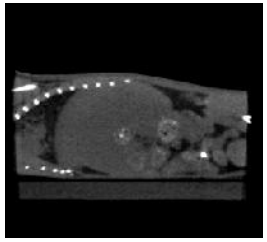
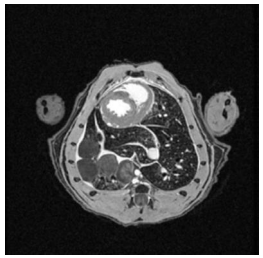
In Vivo Imaging Modalities



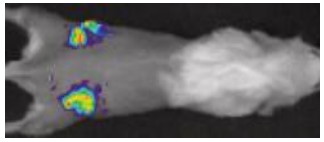
Positron **E**mission **T**omography (**PET)**
Single **P**ositron **E**mission **T**omography (**SPECT)**



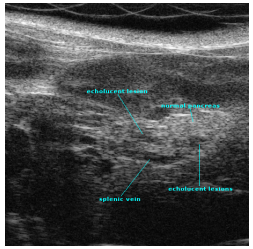
Computer **T**omography (**CT)**



Magnetic **R**esonance **I**maging (**MRI)**

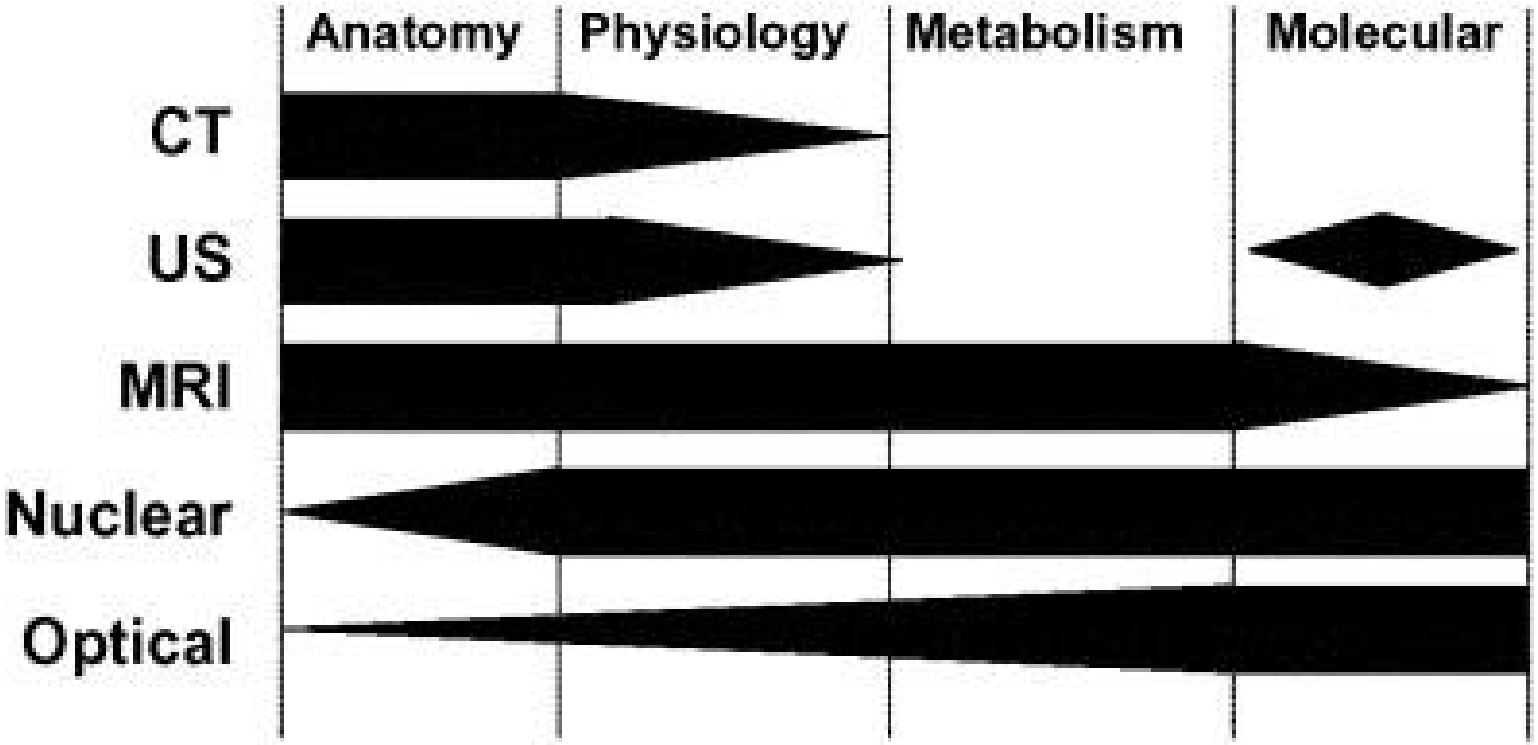


Optical **I**maging (**OI)**



Ultra**S**ound (**US)**

Comparison of Relative Strengths of Different Imaging Modalities



Complementary!

Comparison between different imaging modalities

Modality	Spatial resolution	Depth	Temporal resolution	Sensitivity	Molecular probe
PET	1–2 mm	No limit	10 s-min	pmol-fmol	ng
SPECT	0.5–1.5 mm	No limit	min	pmol	ng
Bioluminescence	3–5 mm	1–2 mm	sec-min	fmol	µg-mg
Fluorescence	2–3 mm	<1 mm	sec-min	pmol-fmol	µg-mg
MRI	25–100 µm	No limit	min-hrs	mmol	µg-mg
CT	50–200 µm	No limit	min	–	N/A
Ultrasound	50–500 µm	mm-cm	sec-min	–	µg-mg

Molecular imaging laboratory

- Autoradiography
- Micro CT
- Animal MRI
- Micro PET
- Optical imaging
- Multimodality systems (PET/CT/SPECT/MRI)
- Human scanners (SPECT, PET, MRI, CT, US)

Imaging –
Requirements for international success

- Imaging infrastructure
- Expertise
- Critical mass of skills → Networking

Special expertise in small animal imaging in Finland

❑ Micro CT	Turku
❑ Animal MRI	Kuopio
❑ Micro PET(CT)	Turku
❑ Micro SPECT	Kuopio, Helsinki
❑ Optical imaging	Helsinki, Turku

Special expertise in human imaging research in Finland

❑ SPECT	Kuopio
❑ CT	Turku
❑ MRI	Turku, Helsinki, Kuopio
❑ PET	Turku
❑ Ultrasound	Turku, Helsinki, Tampere
❑ MEG	Helsinki
❑ Multimodality	Turku

Biomedical *in vivo* Imaging infrastruture in the Turku PET Centre Imaging Platform

Micro-CT

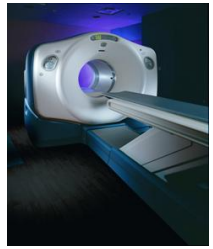
Optical imaging system

Animal US

3T MRI/PET

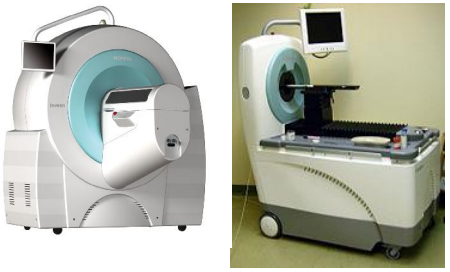
Philips 1,5 T MRI

GE VCT PET/CT 64-slice CT

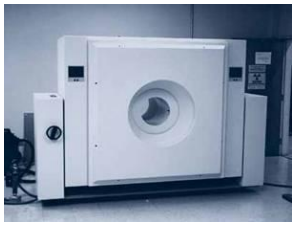


Fuji FLA-7000 Phosphor imaging device

Siemens Inveon multimodality Animal PET/CT



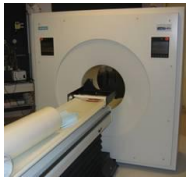
Animal/human PET HRRT



GE D690 PET/CT

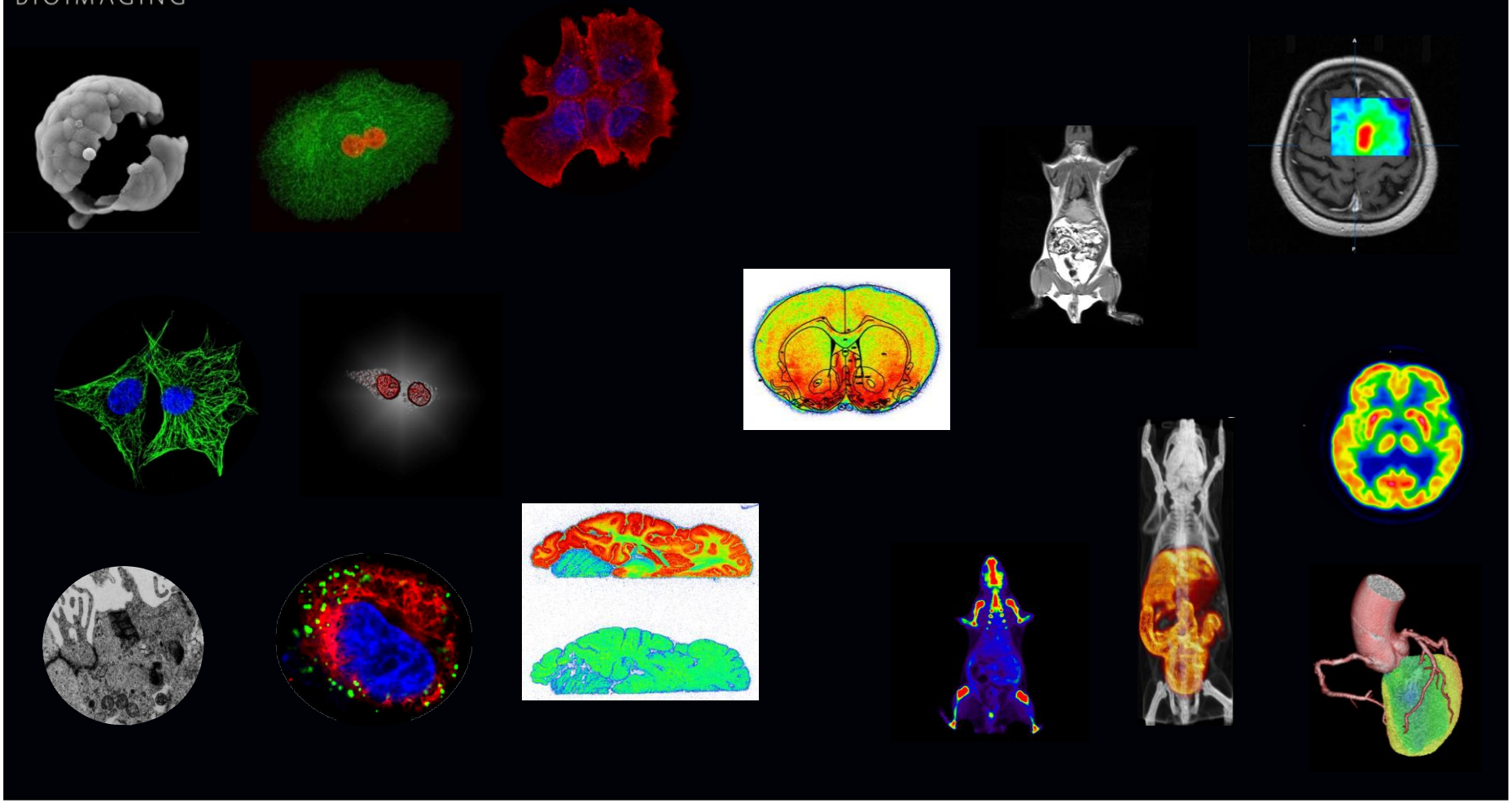
Human Digital US

SIEMENS PET HR+



Ex vivo | ***In vivo* non-clinical** | **Clinical**

Turku BioImaging

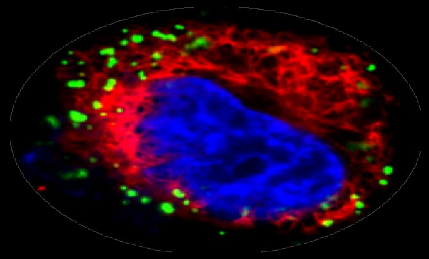


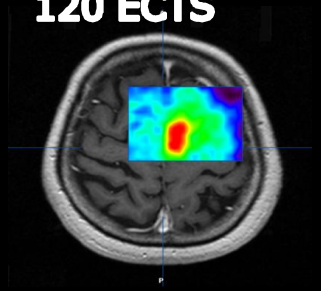
Nanoscopic | ***In vitro* tissue** | ***In vivo* non-clinical**

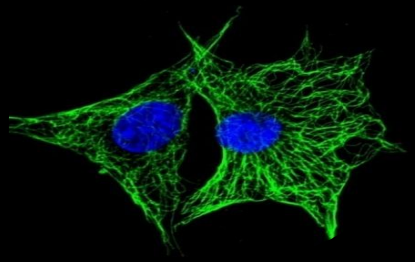
Cell | ***Ex vivo*** | **Clinical**

Master´s Degree Programme in Biomedical Imaging

120 ECTS







A NEW INTERNATIONAL PROGRAMME IN BIOMEDICAL IMAGING LEADING TO A M.Sc. DEGREE (120 ECTS, 2 years)

- **A Joint Degree Programme of the Department of Biosciences at Åbo Akademi University and the Medical Faculty at the University of Turku, Finland**
- **The programme covers a broad spectrum of diverse imaging technologies and provides the students with cutting-edge knowledge and good practical skills in a wide range of imaging methods**
- **The Master´s programme is intended for students with a B.Sc. degree, equivalent to a Finnish B.Sc. degree, in the Life Sciences or applicable areas of biomedical sciences, engineering, physics, or chemistry**
- **Language of instruction: English**

www.abo.fi/bioimaging
www.med.utu.fi/bioimaging

TURKU BIOIMAGING

Tracers are the critical elements for molecular imaging

Partnering with
- Academic centers
- Industry

Tracers at Turku PET Centre

F-18 Tracers
[18F]FDG
[18F]FDOPA
[18F]CFT
[18F]FTHA
[18F]F^-
[18F]L165
[18F]FETNIM
[18F]FBPA
[18F]FDA
[18F]AH110691
[18F]EF5
[18F]DPA
[18F]FEMPA
[18F]Flutematamol

Ga-68 Tracers
Ga-DOTATOC
Ga-Bombesin
DOTAVAP-PEG-P2
Ga- PAPP-A-NOTA
Ga-[$(3\text{-EtOsal})_2Me_4BAPEN]^+$
Ga-[$(3\text{-MeOsal})_2BAPDMEN]^+$
Ga-[$(3\text{-MeOsal})_2Me_4BAPEN]^+$
Ga[$(sal)_2BAPDMEN]^+$
Ga-ATSM
Ga-DOTA
Ga-DOTA-Bombesin
Ga-NODAGA-Exendin
Ga-NOTA
Ga-NOTAVAP-Ab
Ga-oligo (22mer)
Ga-PAPP-A-NOTA

C-11 Tracers
[11C]Acetate
[11C]Carfentanil
[11C]CFT
[11C]Choline
[11C]CIT
[11C]Deprenyl
[11C]DOPA
[11C]FLB457
[11C]Flumazenil
[11C]MeAIB
[11C]Methionine
[11C]MHED
[11C]MP4A
[11C]MTO
[11C]NMSP
[11C]NNC756
[11C]Palmitic acid
[11C]Raclopride
[11C]SCH23390
[11C]SCH39166
[11C]WAY100635
[11C]MP4B
[11C]PIB
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[11C]PK 11195
[11C]ORMA
[11C]Madam
[11C]Deuterium deprenyl
[11C]TMSX
[11C]PE21
[11C]ORMB

O-15 Tracers
O-15-water
O-15-CO
O-15-O2

Cu-64 Tracers
Cu-64-Exendin

In Vivo Molecular Imaging

- Definition of *in vivo* molecular imaging
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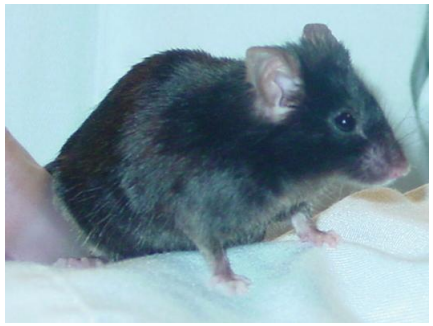
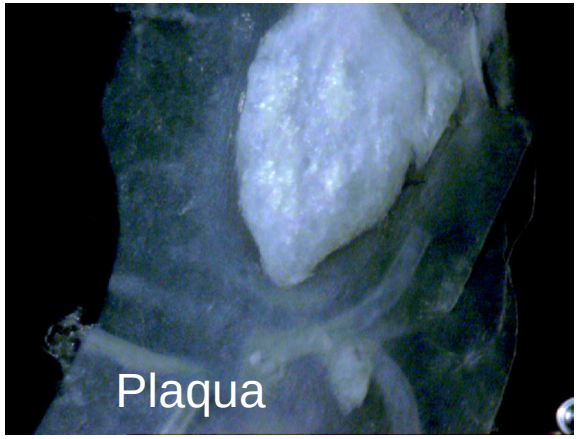
Models of human diseases

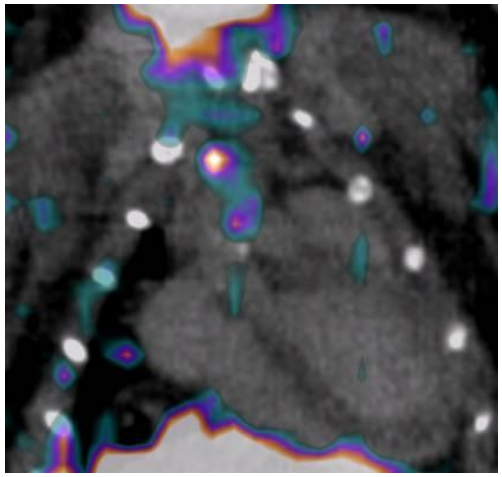
From phantoms….

Models of human diseases

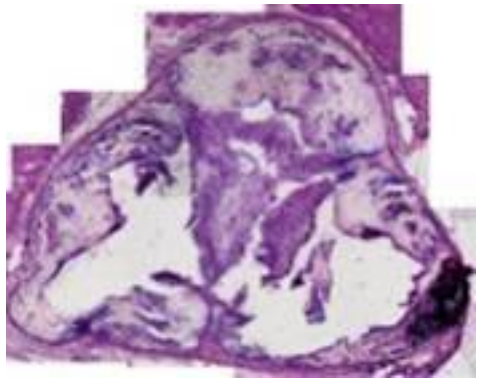
…to small animals….







LDL receptor- and ApoB48 -deficient mouse

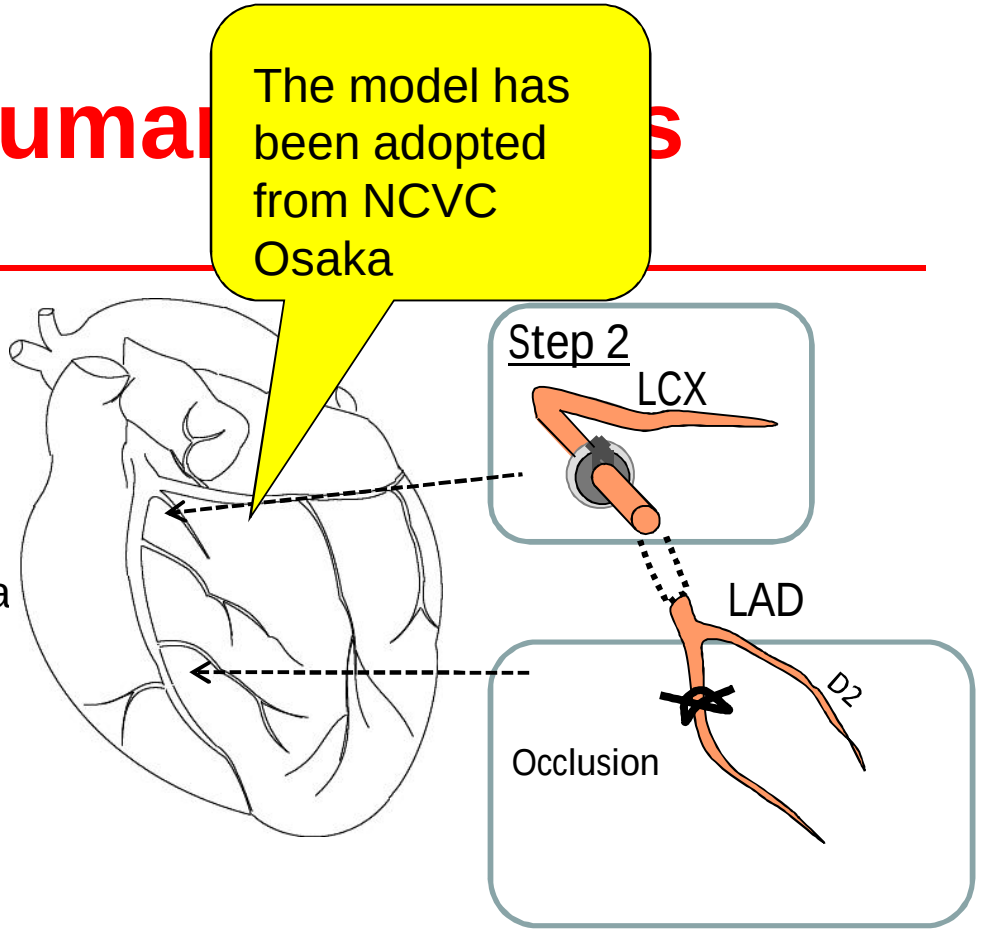


stenotic aortic valve region

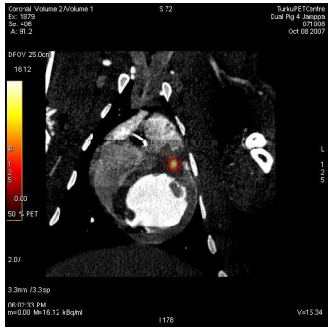
Models of human…s

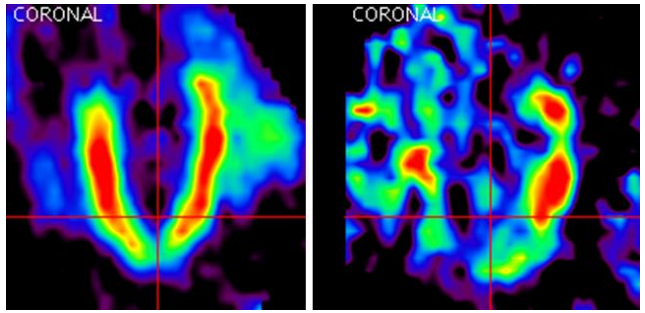
…to larger animals….

- Pig models
  - CAD
    - Diabetes and hypercholestolemia
  - Heart Failure
    - Post-MI 2 step LAD occlusion
  - Plaque
    - Catheter introduced targets



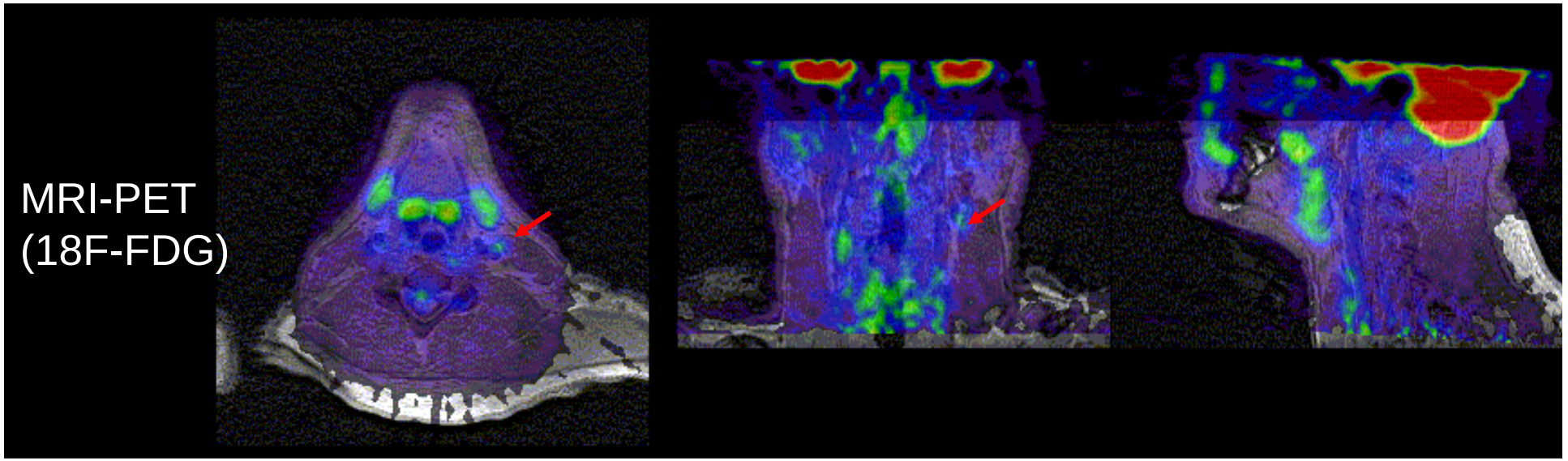
- Validation of models
  - Molecular imaging
  - Perfusion
  - Function
  - Histology





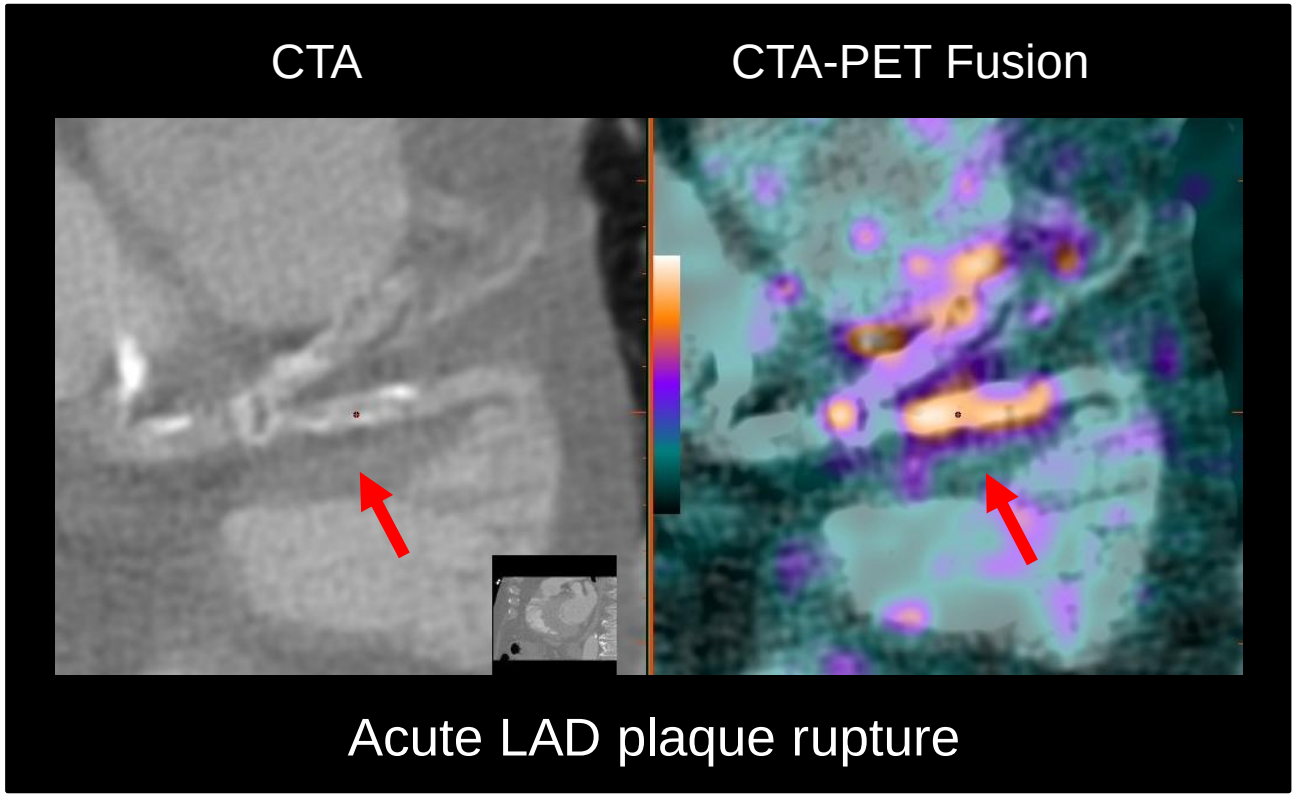
Models of human diseases

…to human carotid…



Models of human diseases

…to human coronaries.



Myocardial FDG uptake supressed by low carbohydrate, high fat diet
Dual gated PET/CT

Teräs et al. Eur J Nucl Med Mol Imaging 2009

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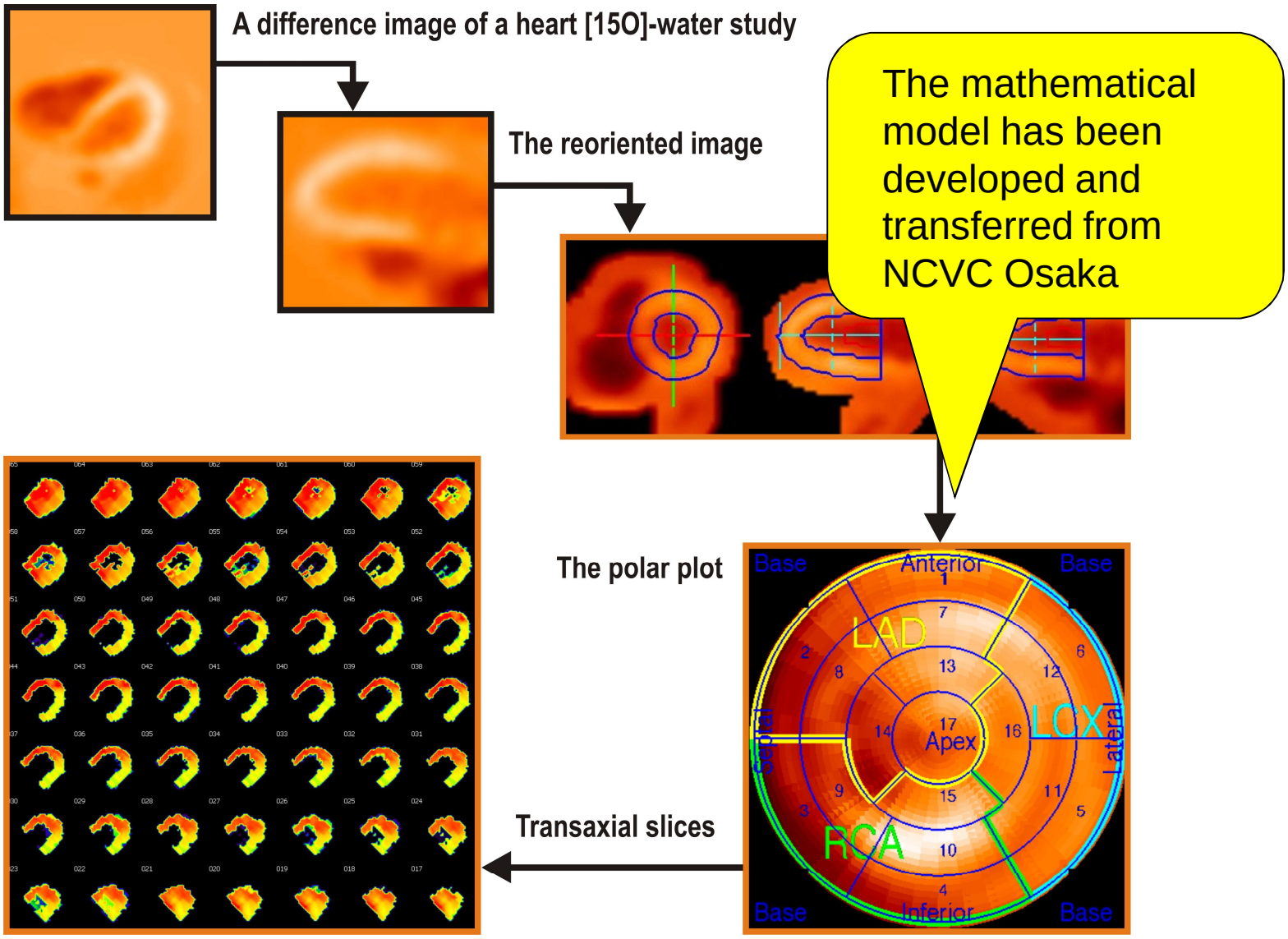
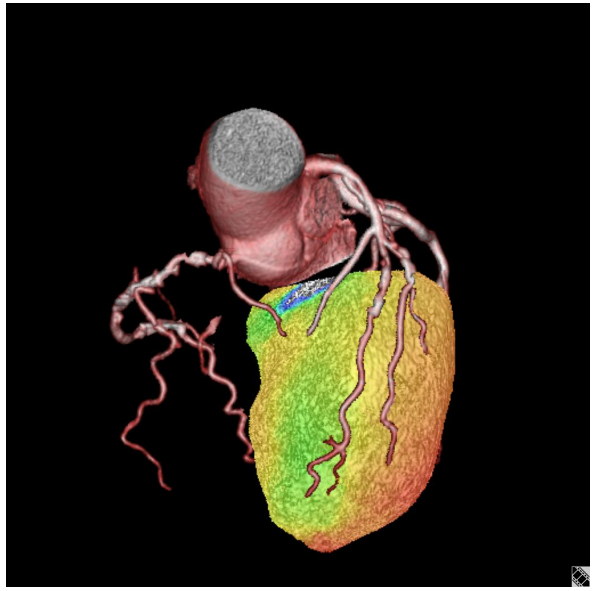
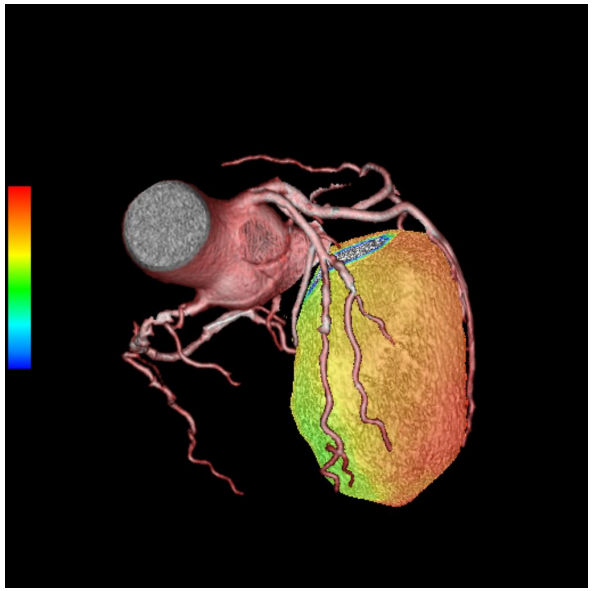
Analysis of Cardiac PET 15-O-water study

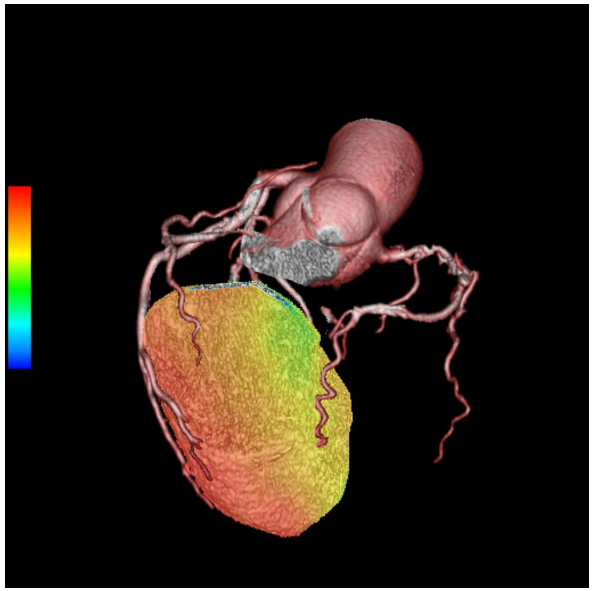


Carimas ™ software developed by Turku PET Centre

Hybrid PET/CT stress images







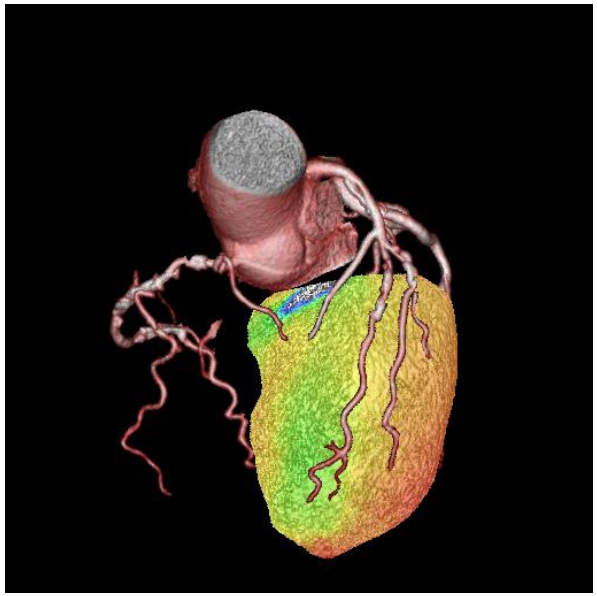
Perfusion in ml/g/min

LAD septal 2.0

ant. 2.4-2.6

LCX 2.9-3.2

RCA 2.0



Criteria:

Perfusion in ml/g/min

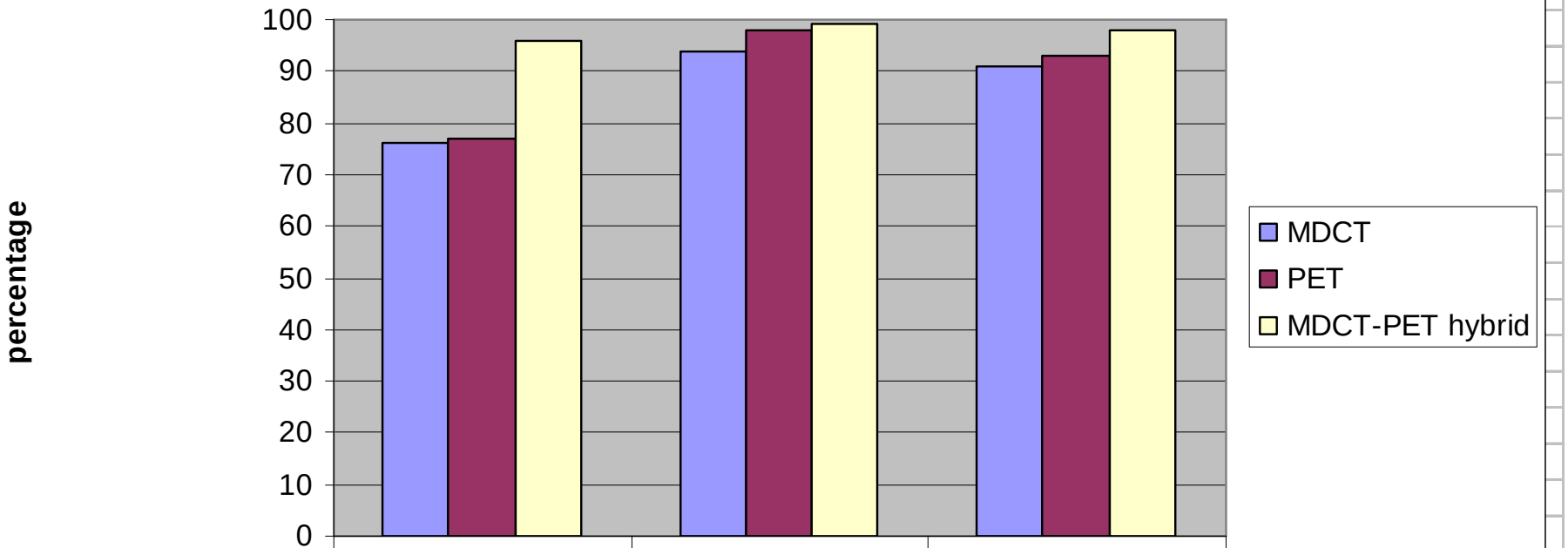
Normal > 2.5

Mildly abnormal 2.0-2.5

Clearly abnormal ≤2.0

Hybrid PET/CT vs. ICA + FFR

Vessel analysis in patients with intermediate likelihood of CAD, N=107



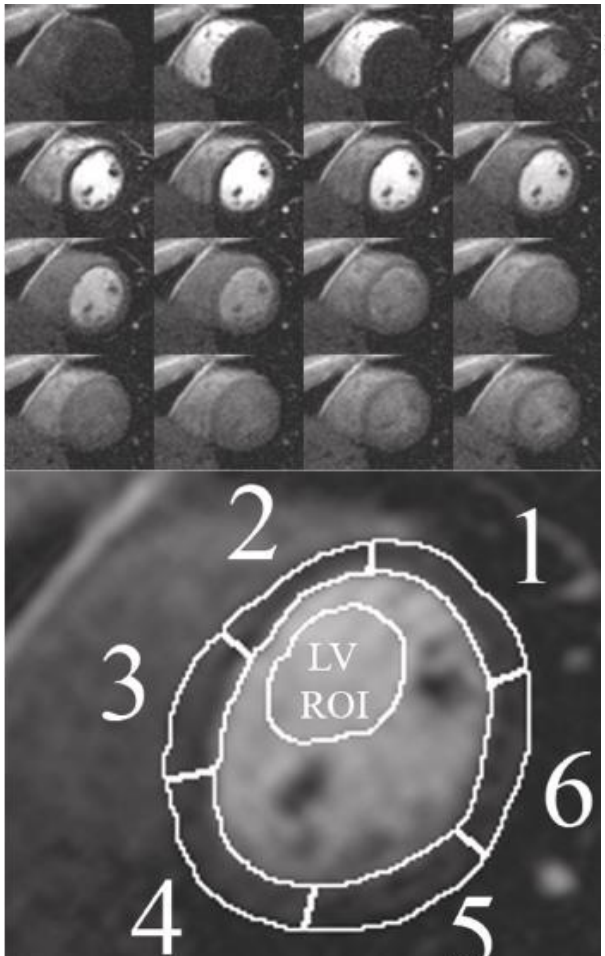
	PPV (%)	NPV (%)	Accuracy (%)
MDCT	76	94	91
PET	77	98	93
MDCT-PET hybrid	96	99	98

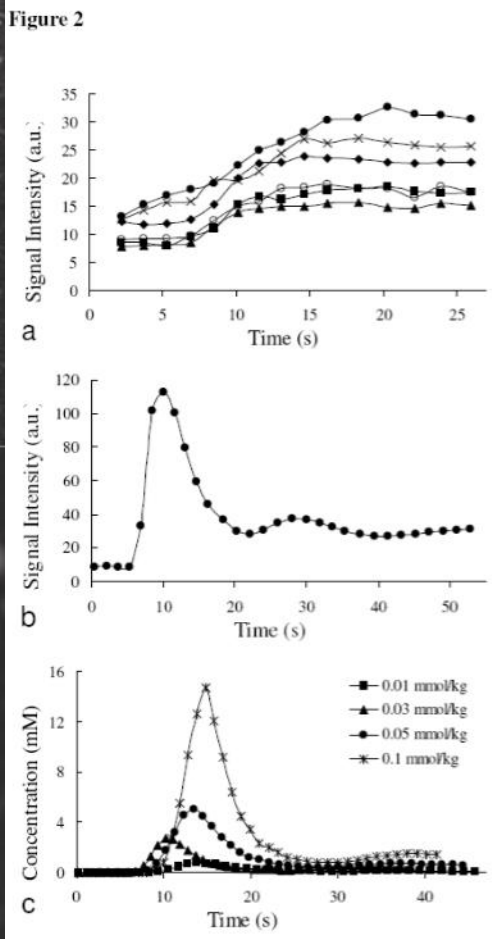
Kajander et al Circulation 2010

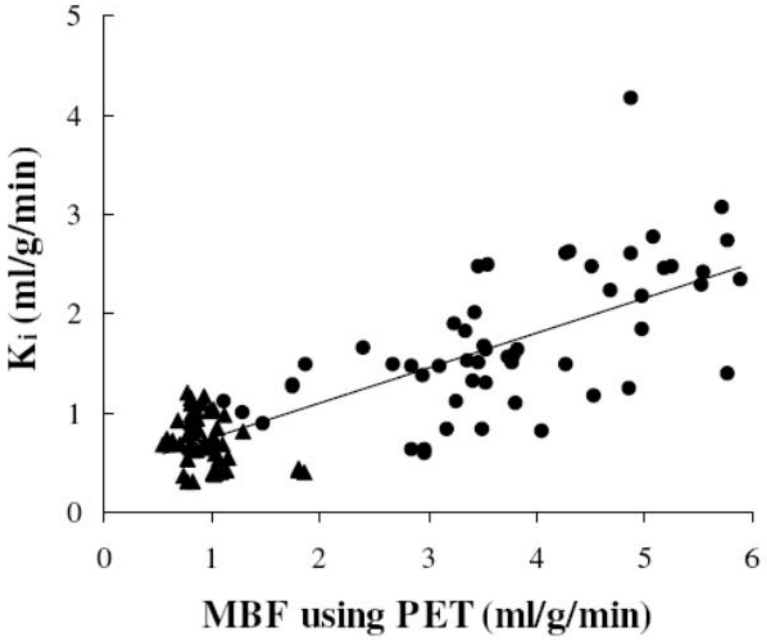
Perfusion quantitati RI

The model has been developed and transferred from Mie University

Saturation-recovery Turbo fast low







Pärkkä et al, MRM 2006

Thank you

Turku PET Centre today

- A National Research Institute for imaging
  - University of Turku, Åbo Akademi University and Turku University Hospital
- 110 persons in staff and investigators
- Imaging devices
  - 6 PET/CT
    - GE Discovery VCT (whole-body PET/CT)
    - GE D690 (whole-body PET/CT)
    - Siemens HR+ (whole-body PET)
    - HRRT (brain/animal PET)
    - 2 Siemens Inveon (small animal PET/CT)
  - 1 PET/MRI 3.0T
  - 1 MRI: Philips 1.5T
  - 3 Ultrasound scanners
    - 2 Acuson (Doppler echocardiography)
    - VisualSonics Vevo (small animal ultrasound)
- Radiochemistry laboratory
  - 3 cyclotrons, 2 ^{68}Ge/^{68}Ga generators
  - 19 hot cells (13 in GMP)
- Facilities
  - 3000 m^2
  - Clinical and preclinical imaging laboratories
- Research
  - Neurotransmission, cardiometabolic research, preclinical imaging and drug research, radiochemistry
  - >40 different tracers in routine use

Åbo Akademi

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Publications per year