Molecular Imaging: Dream or Reality

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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
Molecular Imaging in Medicine

Structure
- Physiology
- Metabolism
- Drug distribution
- Receptors

MRI
- PET
- CT
- US
- SPET
- MEG

PET
- PET
- MRS

MRI
- PET
- SPET
- MRS

Gene expression
- Receptors
- Molecular pathways
- Drug distribution
- Metabolism
- Physiology

Turku PET Centre
In vitro and Ex vivo tissue imaging
In vivo preclinical imaging

Mouse $[^{18}\text{F}]$FDG heart
- Ax
- Cor
- Sag

Rat $[^{18}\text{F}]$CFT brain

Rat whole-body PET and MRI

Mouse $[^{18}\text{F}]$FDG whole-body PET/CT

PET
CT
PET/CT
Clinical Applications of PET and PET/CT
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 microdosage
- Phase I-III trials
- Efficacy
- Safety
- Human PK
- Dose Selection
- Bioavailability
- Patient selection
- Surrogate endpoints

Early identification of failure or success
- Phase IV
- Safety
- Diagnosis & staging
- Patient selection
- Treatment planning
- Molecular therapy and imaging package for clinical application
Challenges in Molecular Imaging

- Disease Models
- Tracers
- Imaging tools
In Vivo Molecular Imaging

- Definition of *in vivo* molecular imaging
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In Vivo Imaging Modalities

- Positron Emission Tomography (PET)
- Single Positron Emission Tomography (SPECT)
- Computer Tomography (CT)
- Magnetic Resonance Imaging (MRI)
- Optical Imaging (OI)
- Ultrasound (US)
Comparison of Relative Strengths of Different Imaging Modalities

Complementary!
# Comparison between different imaging modalities

<table>
<thead>
<tr>
<th>Modality</th>
<th>Spatial resolution</th>
<th>Depth</th>
<th>Temporal resolution</th>
<th>Sensitivity</th>
<th>Molecular probe</th>
</tr>
</thead>
<tbody>
<tr>
<td>PET</td>
<td>1-2 mm</td>
<td>No limit</td>
<td>10 s-min</td>
<td>pmol-fmol</td>
<td>ng</td>
</tr>
<tr>
<td>SPECT</td>
<td>0.5-1.5 mm</td>
<td>No limit</td>
<td>min</td>
<td>pmol</td>
<td>ng</td>
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<tr>
<td>Bioluminescence</td>
<td>3-5 mm</td>
<td>1-2 mm</td>
<td>sec-min</td>
<td>fmol</td>
<td>µg-mg</td>
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<tr>
<td>Fluorescence</td>
<td>2-3 mm</td>
<td>&lt;1 mm</td>
<td>sec-min</td>
<td>pmol-fmol</td>
<td>µg-mg</td>
</tr>
<tr>
<td>MRI</td>
<td>25-100 µm</td>
<td>No limit</td>
<td>min-hrs</td>
<td>mmol</td>
<td>µg-mg</td>
</tr>
<tr>
<td>CT</td>
<td>50-200 µm</td>
<td>No limit</td>
<td>min</td>
<td>-</td>
<td>N/A</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>50-500 µm</td>
<td>mm-cm</td>
<td>sec-min</td>
<td>-</td>
<td>µg-mg</td>
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</tbody>
</table>
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 infrastructure in the Turku PET Centre Imaging Platform
Turku Biol maging

Nanoscopic

In vitro tissue

In vivo non-clinical

Cell

Ex vivo

Clinical
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
### Tracers at Turku PET Centre

<table>
<thead>
<tr>
<th>F-18 Tracers</th>
<th>C-11 Tracers</th>
<th>O-15 Tracers</th>
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</thead>
<tbody>
<tr>
<td>[18F]FTHA</td>
<td>[11C]Choline</td>
<td>Cu-64 Tracers</td>
</tr>
<tr>
<td>[18F]FEMPA</td>
<td>[11C]MP4A</td>
<td></td>
</tr>
<tr>
<td></td>
<td>[11C]NMSP</td>
<td></td>
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<tr>
<td>Ga-68 Tracers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ga-DOTATOC</td>
<td>[11C]NNC756</td>
<td></td>
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<tr>
<td>Ga-Bombesin</td>
<td>[11C]Palmitic acid</td>
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</tr>
<tr>
<td>DOTAVAP-PEG-P2</td>
<td>[11C]Raclopride</td>
<td></td>
</tr>
<tr>
<td>Ga-[(3-EtOsal)₂Me₄BAPEN]⁺</td>
<td>[11C]SCH39166</td>
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<tr>
<td>Ga-[(3-MeOsal)₂BAPDMEN]⁺</td>
<td>[11C]WAY100635</td>
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<tr>
<td>Ga-[(3-MeOsal)₂Me₄BAPEN]⁺</td>
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<td>Ga[(sal)₂BAPDMEN]⁺</td>
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<td>Ga-ATSM</td>
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<td>[11C]PK 11195</td>
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<td>Ga-DOTA-Bombesin</td>
<td>[11C]ORMA</td>
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<tr>
<td>Ga-NOTA</td>
<td>[11C]Deuterium deprenyl</td>
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</tr>
<tr>
<td>Ga-NOTAVAP-Ab</td>
<td>[11C]TMSX</td>
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<tr>
<td>Ga-oligo (22mer)</td>
<td>[11C]PE21</td>
<td></td>
</tr>
</tbody>
</table>
In Vivo Molecular Imaging

- Definition of \textit{in vivo} molecular imaging
- Molecular imaging methodology
- \textit{Translational aspects}
- Examples of applications
Models of human diseases

From phantoms....
Models of human diseases

...to small animals....

LDL receptor- and ApoB48 -deficient mouse

Aorta

Plaqua

Longitudinally opened aorta

stenotic aortic valve region
Models of human diseases

...to larger animals....

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

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

The model has been adopted from NCVC Osaka
Models of human diseases

...to human carotid...

MRI-PET (18F-FDG)
Models of human diseases

...to human coronaries.

Acute LAD plaque rupture

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


Turku PET Centre, Finland
In Vivo Molecular Imaging

- Definition of *in vivo* molecular imaging
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- Translational aspects
- *Examples of applications*
Analysis of Cardiac PET 15-O-water study

A difference image of a heart [15O]-water study

The reoriented image

The mathematical model has been developed and transferred from NCVC Osaka

The polar plot

Transaxial slices

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

<table>
<thead>
<tr>
<th>Method</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDCT</td>
<td>76</td>
<td>94</td>
<td>91</td>
</tr>
<tr>
<td>PET</td>
<td>77</td>
<td>98</td>
<td>93</td>
</tr>
<tr>
<td>MDCT-PET hybrid</td>
<td>96</td>
<td>99</td>
<td>98</td>
</tr>
</tbody>
</table>

Kajander et al. Circulation 2010
Perfusion quantitation using MRI

Saturation-recovery Turbo fast low angle shot (FLASH)

Pärkkä et al, MRM 2006

The model has been developed and transferred from Mie University
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 m²
  - Clinical and preclinical imaging laboratories
- Research
  - Neurotransmission, cardiometabolic research, preclinical imaging and drug research, radiochemistry
  - >40 different tracers in routine use

www.pet.fi
Turku PET Centre
Publications per year

Thesis
In Finnish
IF < 1
IF 1.0-2.9
IF 3.0-4.9
IF 5.0-