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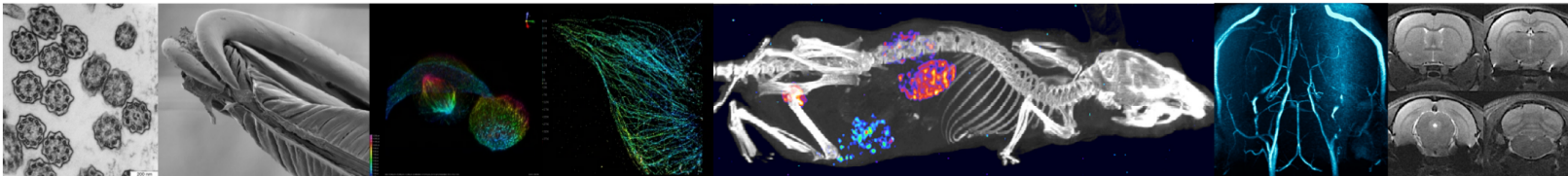
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BIOIMAGING CENTRE



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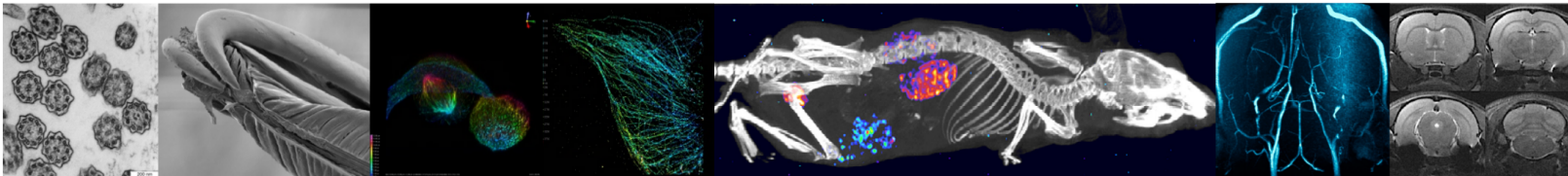
- Infrastructure within the Medical Faculty
- Started 2008
- Our mission is to establish a major **translational bio-imaging center at Lund university**, combining knowledge in the fields of medical physics, preclinical and clinical medicine, chemistry, technology and applied mathematics in order to develop imaging methods for the advanced study of human morphology, cellular metabolism and physiological function in health and disease.



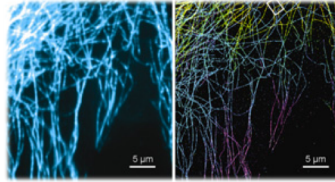
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LBIC from micro to macro

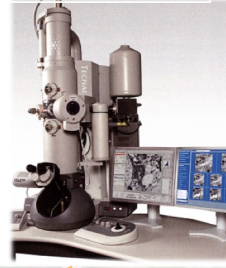
- Microscopy
 - Advanced light microscopy
 - Electron microscopy
 - VR and 3D visualisation
- Preclinical MR
 - 9.4T
- Preclinical NM
 - PET/CT
 - SPECT/CT
 - CT
 - Radiochemistry
- Clinical MR
 - 1.5T
 - 3T
- National 7T facility



Mikroskopi
Avancerad ljusmikroskopi



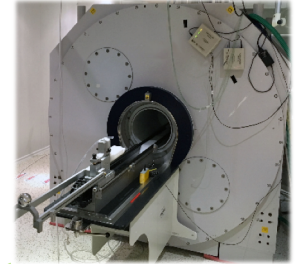
TEM/SEM



PET/CT, SPECT/CT, µCT



9.4T MR



Administration,
labbutrymme,
IT, bildanalys

3T, 1.5T MR



Cyklotron 1-2 och
hotlab



Skånes universitetssjukhus, Lund

7T MR



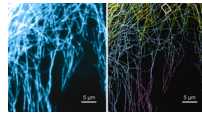
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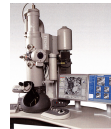
Microscopy

Center Staff, laboratory space, image analysis

Optical



TEM/SEM



Lina Gefors

Research Engineer Platform coordinator -
Microscopy

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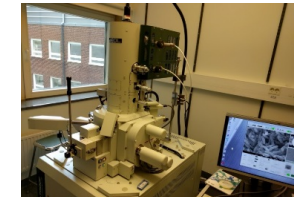
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Microscopy

- Electronmicroscopy, enlarging up to 10.000x (TEM/SEM)
- STORM, Stochastic Optical Reconstruction Microscopy
- TIRF, total internal reflection fluorescence
11.000 images/s of fast processes in living cells
- Confocal, optical filtration of laser to
reconstruct 2D images into 3D



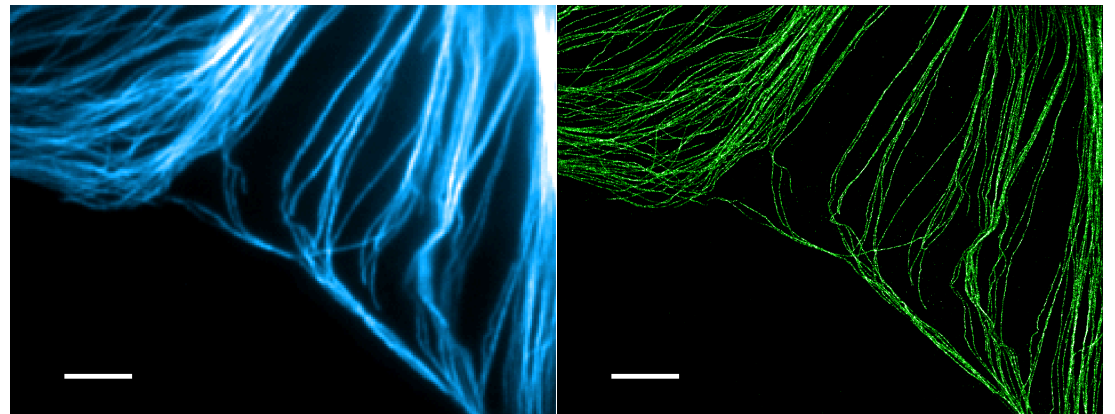
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Microscopy

- TEM & SEM



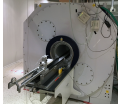
- STORM



Preclinical MR

Center Staff, laboratory space, image analysis

9.4T MRI



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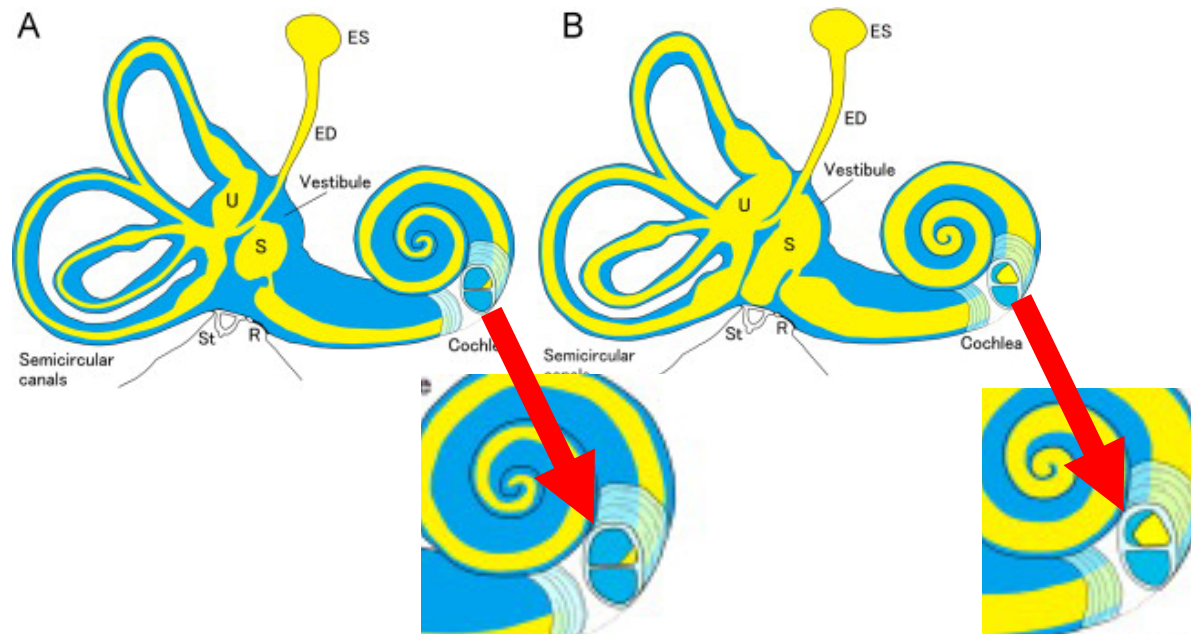


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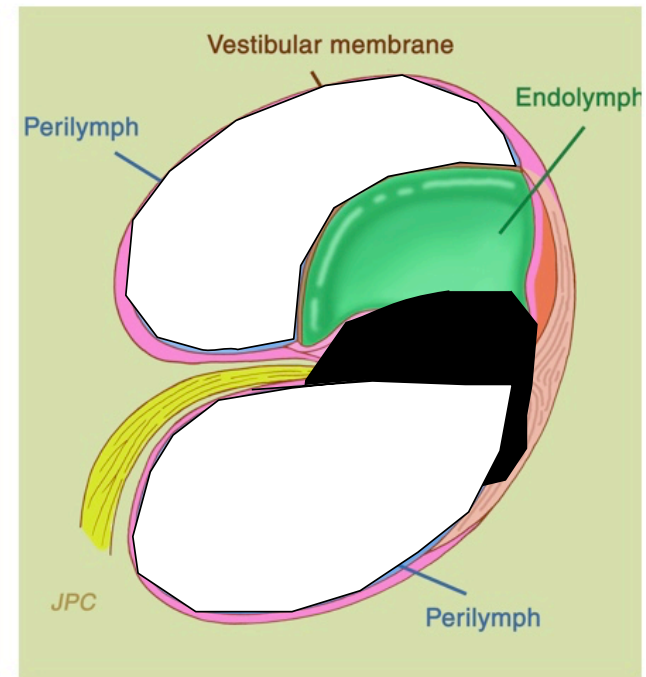
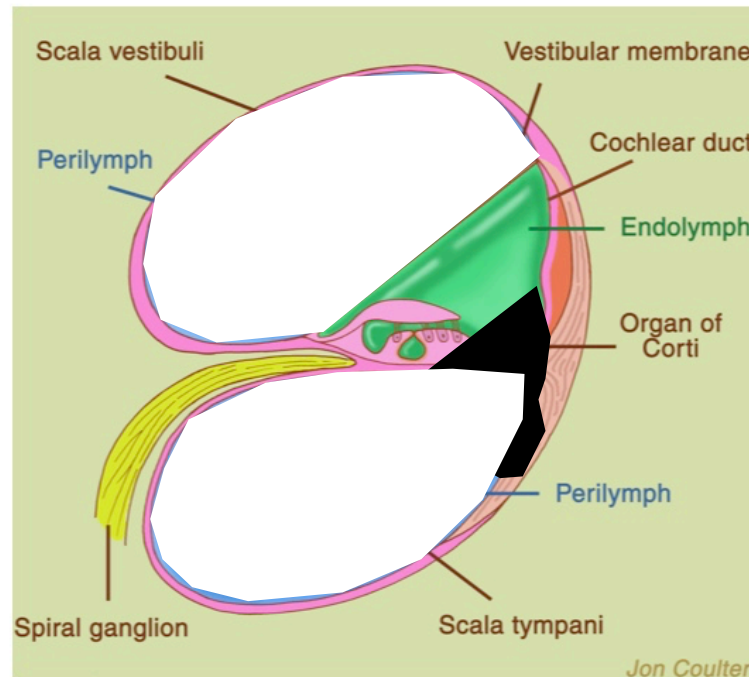
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Preclinical MR

- Endolymphatic hydrops in human innerear

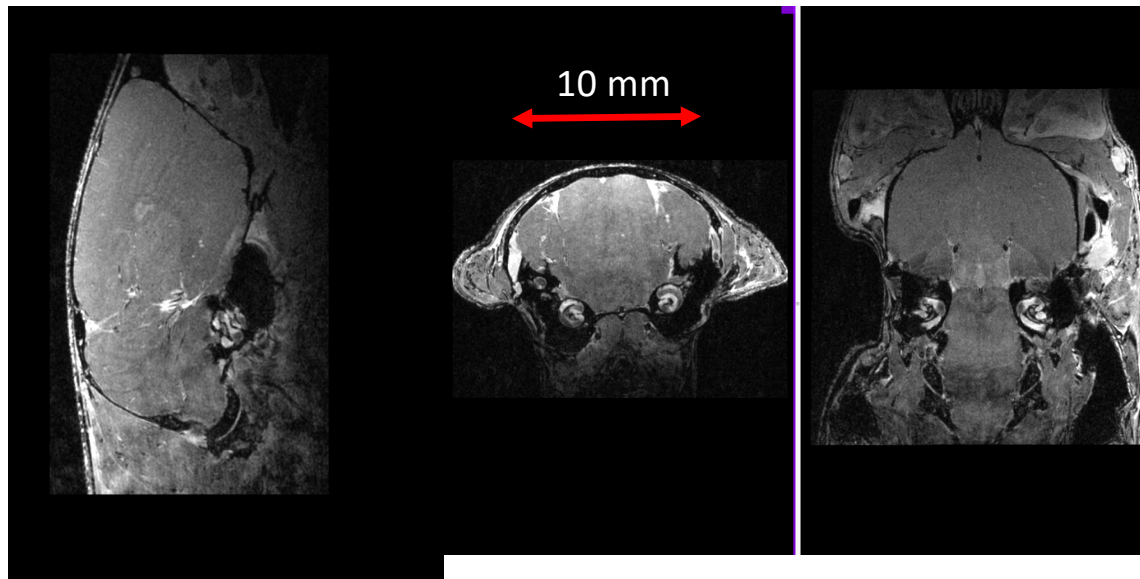


Contrast enhancement of the perilymphatic volume using MRI

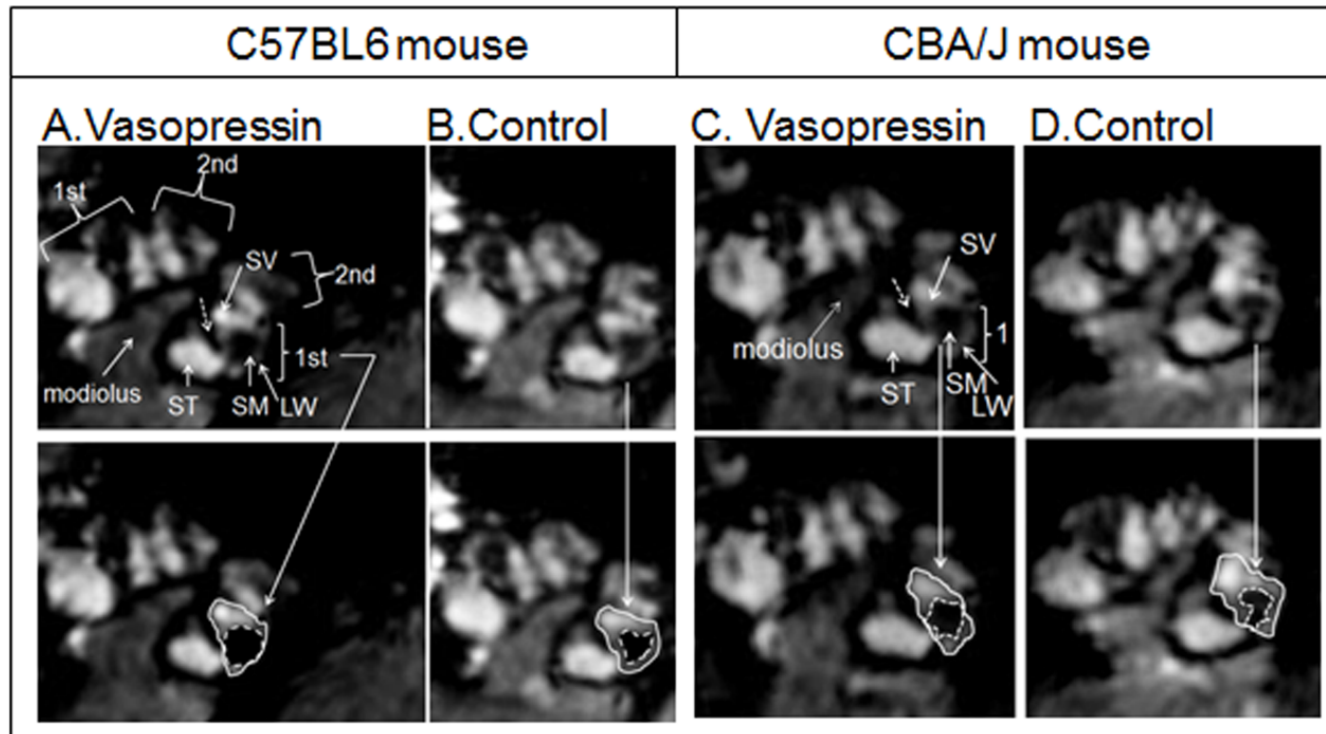


Preclinical MR

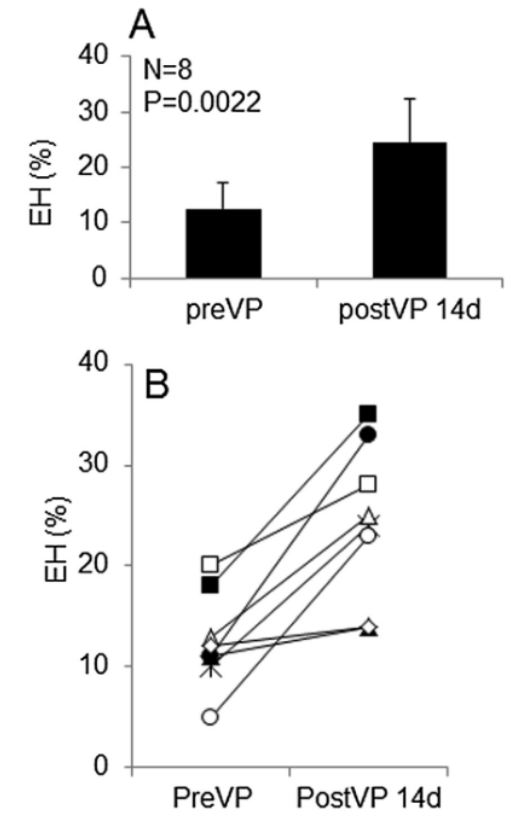
- Mouse inner ear 3D-imaging in vivo at 9.4T after injection of a clinical approved MRI contrast agent



MR Imaging before and after Vasopressin



Evaluation of scala Media vs scala Vestibuli+Media



Preclinical Nuclear Medicine

- text

Center Staff, laboratory space, image analysis

PET/CT, SPECT/CT



Cyclotron 1-2 and hot laboratory space



Ritha Gidlöf, Ph.D.

Laboratory Researcher / Radiochemist
Platform responsible - Preclinical Nuclear
Medicine

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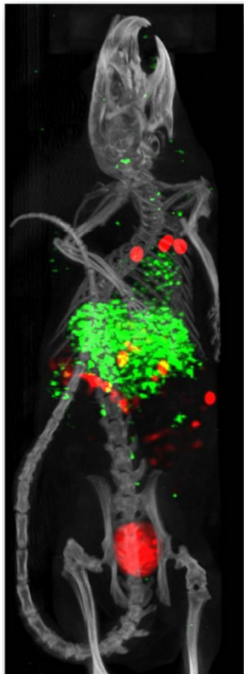


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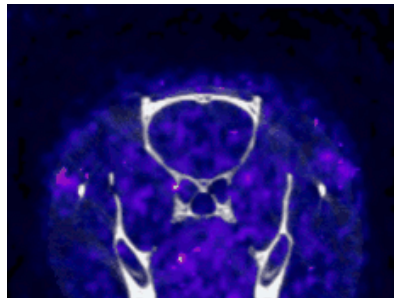
Biodistribution of two radiolabelled targeting agents in an ovarian cancer xenograft (NanoSPECT/CT)
Jonas Ahlstedt, Infektionsmedicin

Preclinical NM

A CT X-ray image of the head of a hip joint from a mouse.
 $\varnothing = 1.3 \text{ mm}$
Gustav Grafström, LBIC



Rat images showing striatal dopamine, detected with the NanoPET/CT using [18F]-FEPE2I, along the transversal plan
Deniz Kirik, BRAINS unit





Pia Sundgren

Co-Director LBIC, Professor in
Radiologi/MD.Ph.D./Plattform responsible -
Clinical MR

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Clinical MR/ 7T National Facility



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3T WB MR



7T WB MR

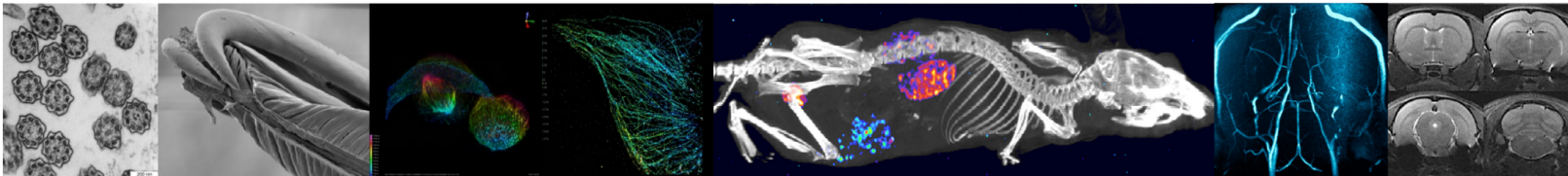


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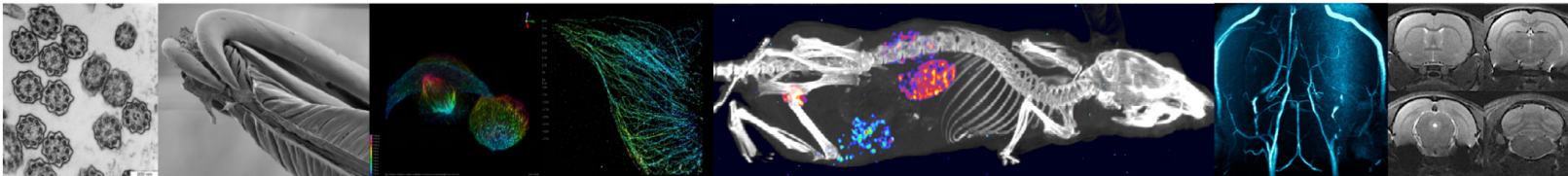
- We help researcher to produce images for
 - **Research**
 - Education
 - Quality control
- Method development
- Education



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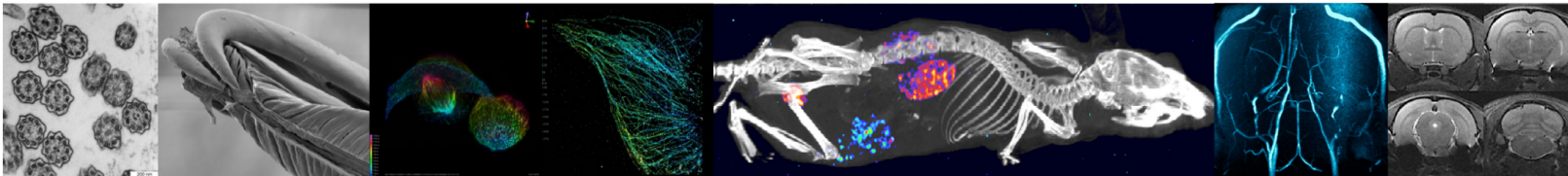
LBIC projects

- Contact platform leader for desired technique
- Research Board application
- Researcher performs the study, with support from LBIC personnel
- Analysis on LBIC computer, or transfer of raw data
- Help with visual presentation if necessary



LBIC events

- Preclinical imaging course
 - March 2020
- Confocal microscopy course
 - October/November 2020
- 7T-meeting
- Preclinical MR meeting



Preclinical Nuclear Medicine

Preclinical Nuclear Medicine



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Associate Researcher/Radiation physicist

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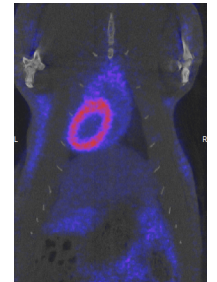
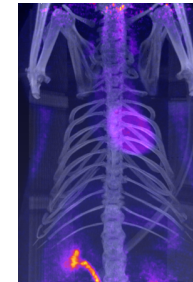
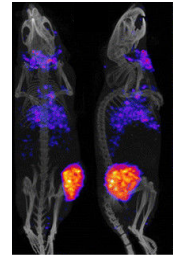
Marie.Sydoff@med.lu.se



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PET/SPECT/CT

- nanoSPECT/CT
 - Uses radionuclides with long half-life to look at biological processes
 - Exemplified by antibodies in a subcutaneous tumour
- nanoPET/CT
 - Uses radioactivity with short half-lives to look at faster processes
 - Glucose uptake in the heart
- μ CT
 - Uses density differences to take 2D x-rays reconstructed into 3D volumes
 - Mouse femur with 10 μ m resolution




Preclinical Nuclear Medicine

- Radiochemistry
 - Chemical structure with a radioactive element attached to it
- PET and SPECT
 - Generalisation: using radioactive substances as a contrast to study biological phenomena
- CT
 - 3D xray providing a morphological volume for the radioactive signal



Basic Methodology

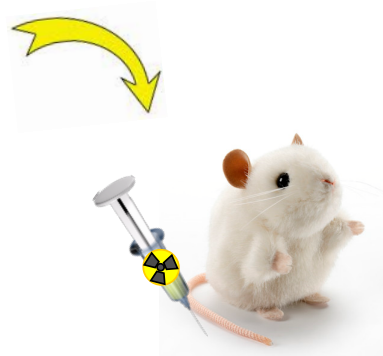
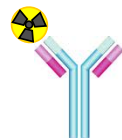
- 
- Molecule of interest**
- Ligand
 - Antibody fragment
 - Antibody
 - Small molecules

- 
- Radioisotope**
- Shortlived (min-hours)
 - Longlived (days-months)

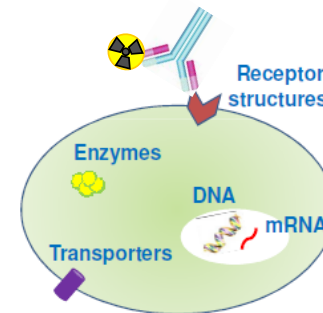


PET/SPECT Scan

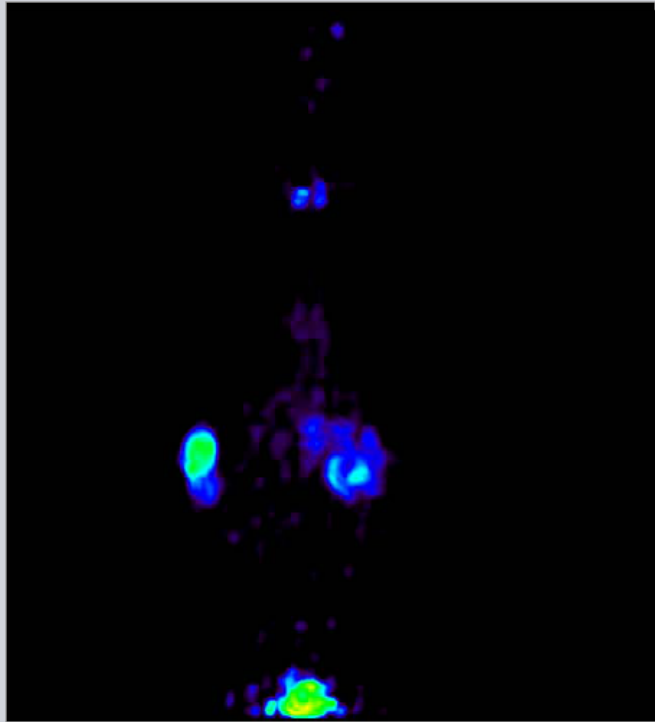
- Customized tracer/probe**
- specific
 - targeting to a biomarker



Inject into animals
(mouse, rats)



What are we looking at?



- Human colon cancer xenograft
- 100 μCi I-124
- Labeled anti-CEA engineered antibody fragment (tunable pharmacokinetics)
- **Where is the activity located?**
- **What are we looking at?**



Rat CT scan

PET and CT-fused image



- Human colon cancer xenograft
- 100 μCi I-124
- Labeled anti-CEA engineered antibody fragment (tunable pharmacokinetics)
- Screening CT scan (200 μm)

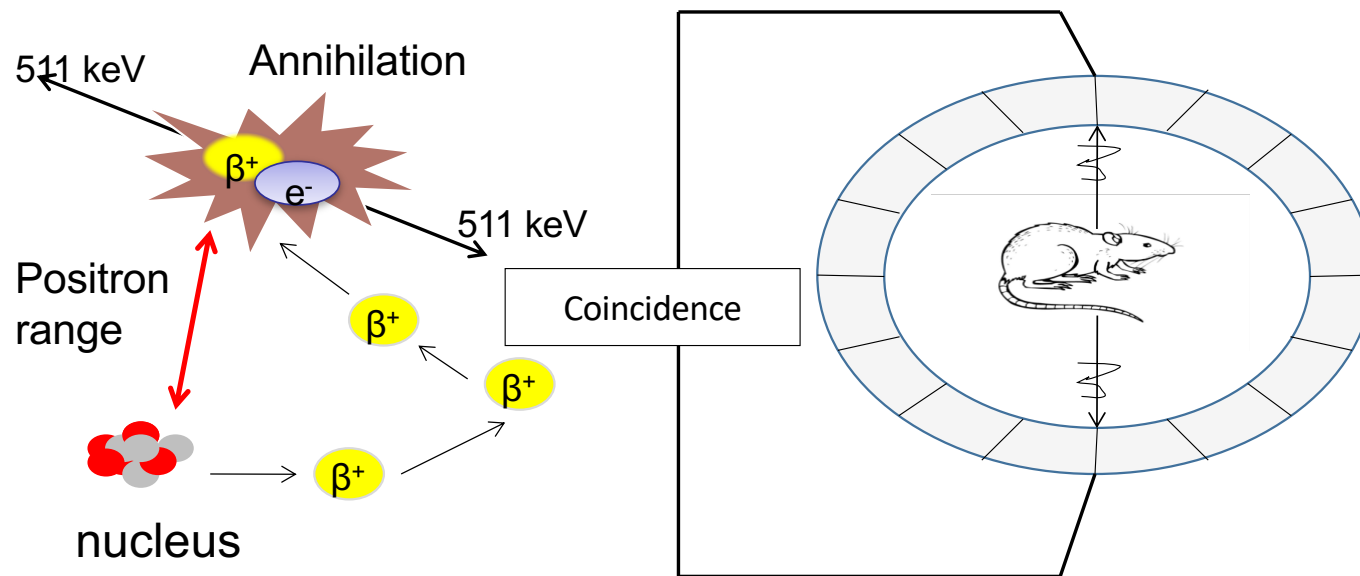
Adding the anatomical information makes the image understandable.

Radioactivity & Decay

- α decay
 - Emission of an α particle (helium)
 - paper
- β decay
 - β ray (electron or positron) and a neutrino
 - foil
- γ decay
 - Ionizing radiation
 - Lead or tungsten blocks



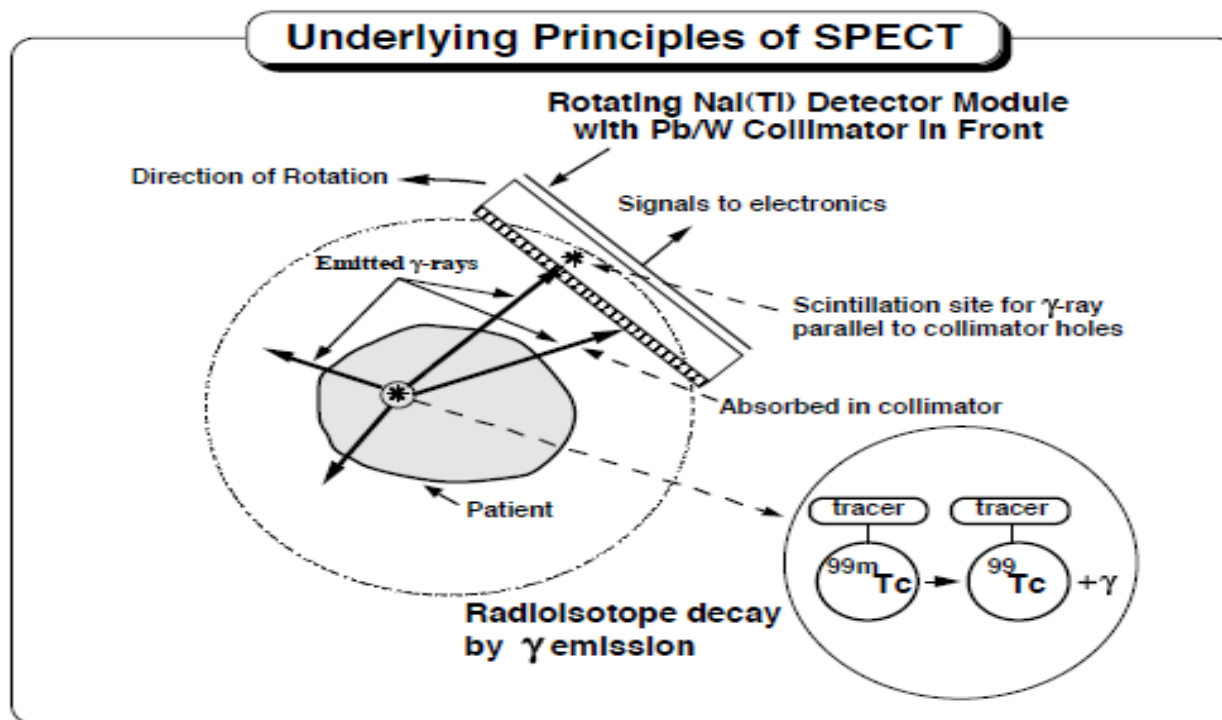
What is PET?



- Positron emission tomography
- 2 photons simultaneously detected
- Rings of detectors
- No collimator
- Usually have to be produced onsite due to short half-life

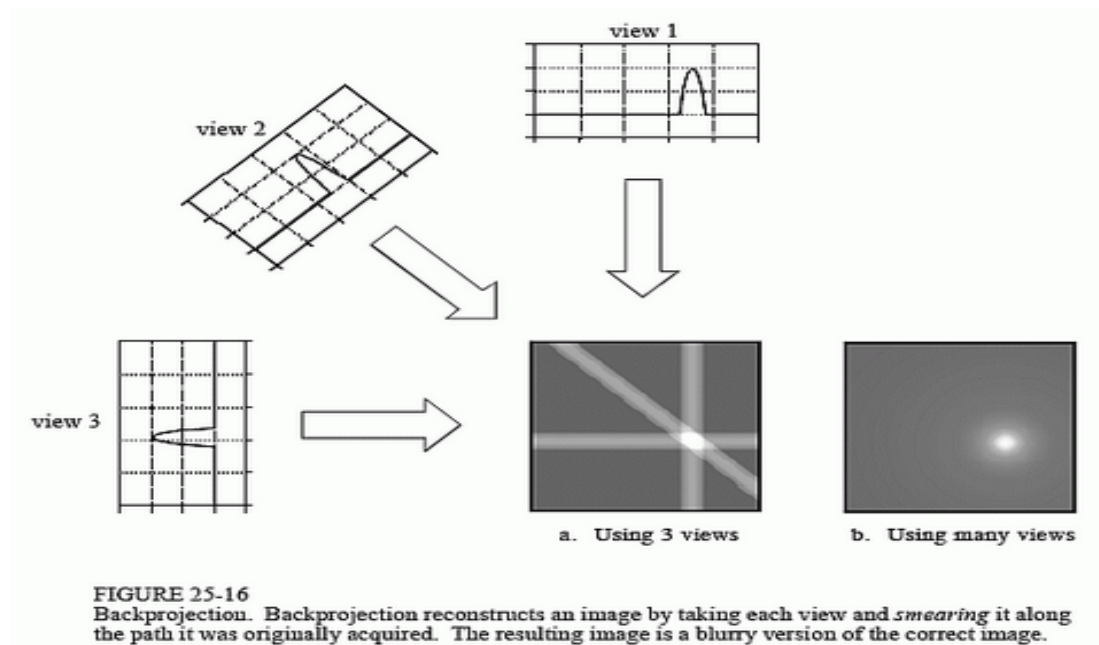
A positron ejected from the nucleus of a radioactive isotope travels in tissue. Annihilation with an electron creates two 511 keV gamma rays in opposite directions. By detecting these gamma rays, an image can be determined

What is SPECT?

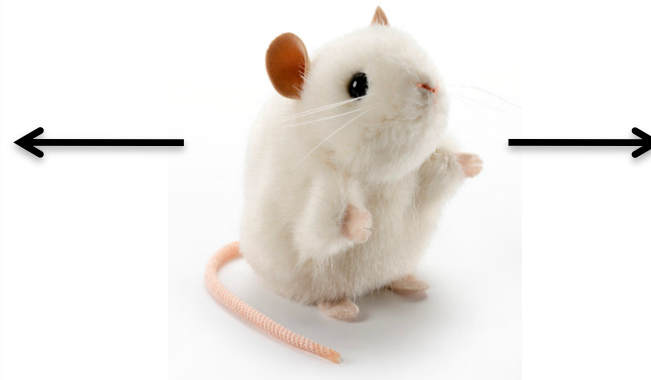


- Single Photon Emission Computed Tomography
- A single photon is produced
- Needs one or more photon detectors
- Collimator
- Tracer decays slower
- Tracers don't have to be produced onsite

What is SPECT?



PET vs SPECT



Preclinical PET		Preclinical SPECT
511 keV	Form of energy used	Gamma rays
1 mm	Resolution	0.5 mm
sec – min	Acquisition time	min
Medium – high	Availability of Radionuclides	high
Medium – high	Sensitivity	high
High	Cost	Medium - high

Benefits

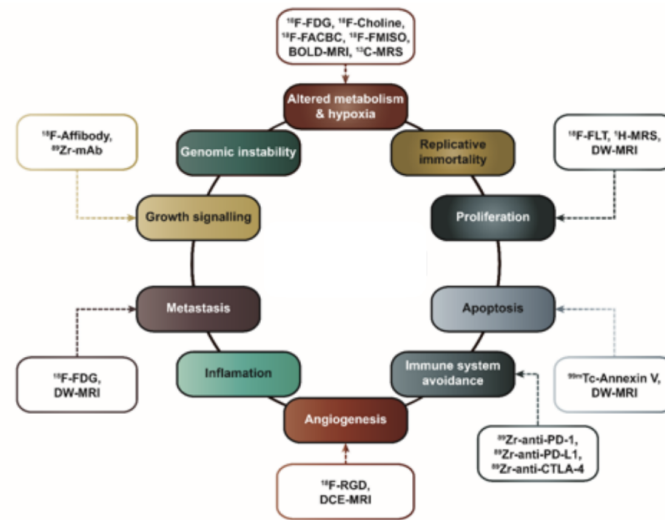
- Noninvasive
- High sensitivity (10^{-9} mol – 10^{-15} mol)
- Physiological phenomena
- Tissue function
- Cellular functions
- Biochemical processes



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Preclinical Nuclear Medicine

Connections Between Tumour Biology and Imaging



Adapted from Hanahan and Weinberg, *Cell*, 144:646-74, 2011

From Bruker webinar: "Monitoring Cancer Treatments with Immuno-PET", Gabriela Kramer-Marek, The Institute of Cancer Research, London, 14th of March 2019



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Projects

- **Oncology**
 - Cancer therapy
 - Diabetes
 - **Bone imaging**
 - ECV cardiac
 - Inflammation
 - Evolutionbiology
 - Gastrointestinal passage
- Biodistribution
 - Neuro
 - Instrument evaluation
 - Quality control for production of isotopes



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Dynamic imaging of kidney function in mice

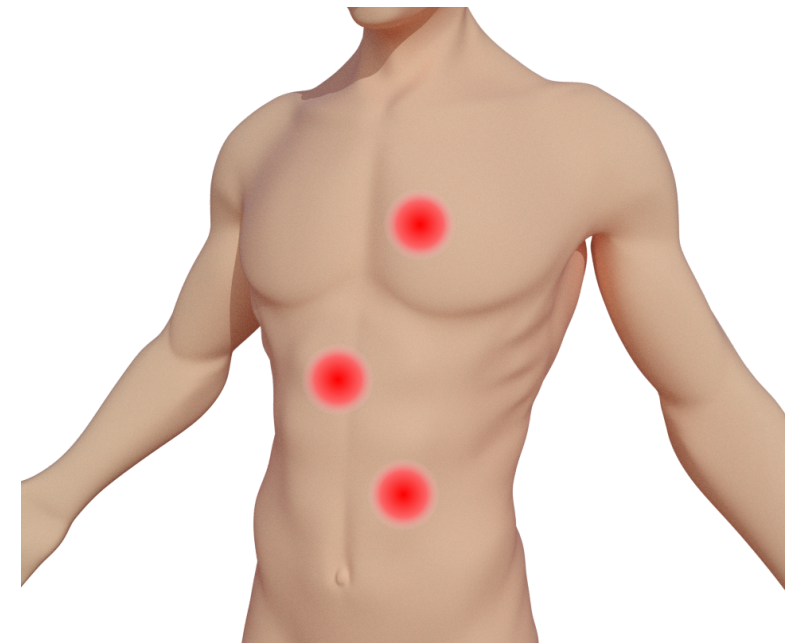
Ahlstedt/Johansson/Sydooff/Karlsson/ Thordarson/Gram/Eriksson , Neuroendocrinology, DOI: 10.1159/000500473 (2019-04)



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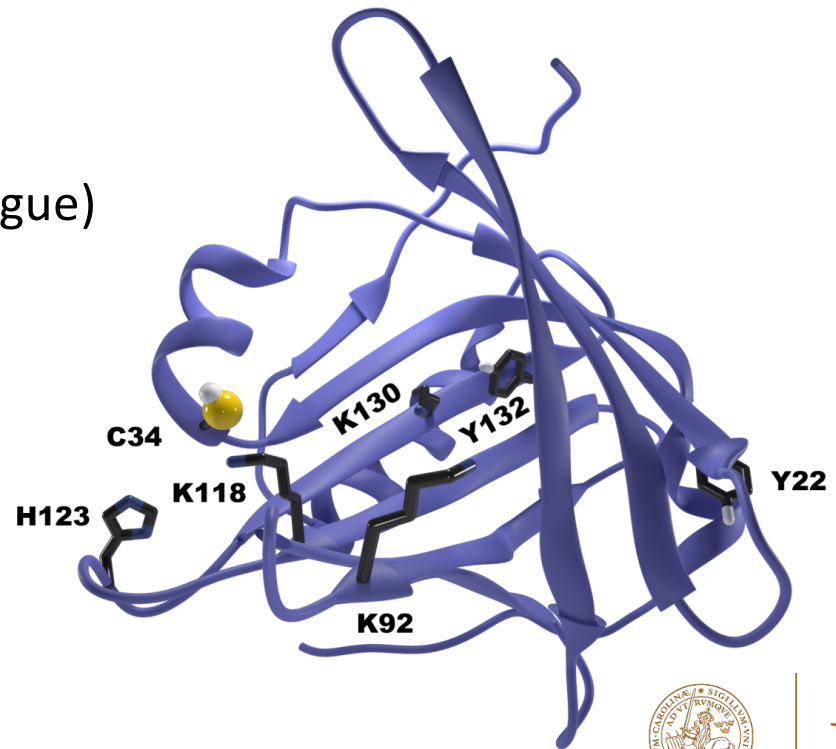
PRRT and A1M (alpha-1-microglobulin)

- NETs and nephrotoxicity
 - Relatively rare
 - Lu-177-DOTATATE (somatostatin analogue)
 - Glomerular and tubular damage
 - Bone marrow
- A1M
 - Endogenous radical scavenger
 - Redox properties
 - Co-localizes with somatostatin analogues



PRRT and A1M (alpha-1-microglobulin)

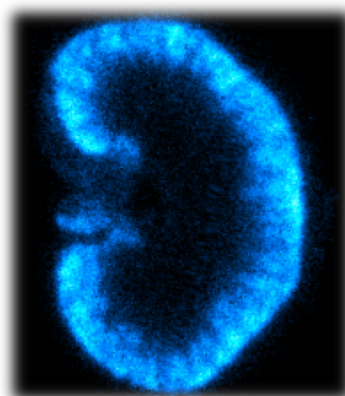
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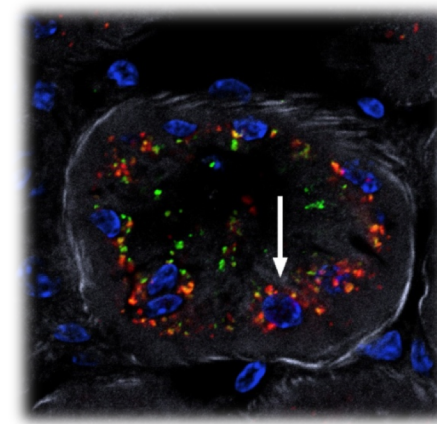
SPECT/CT



AUTORADIOGRAPHY



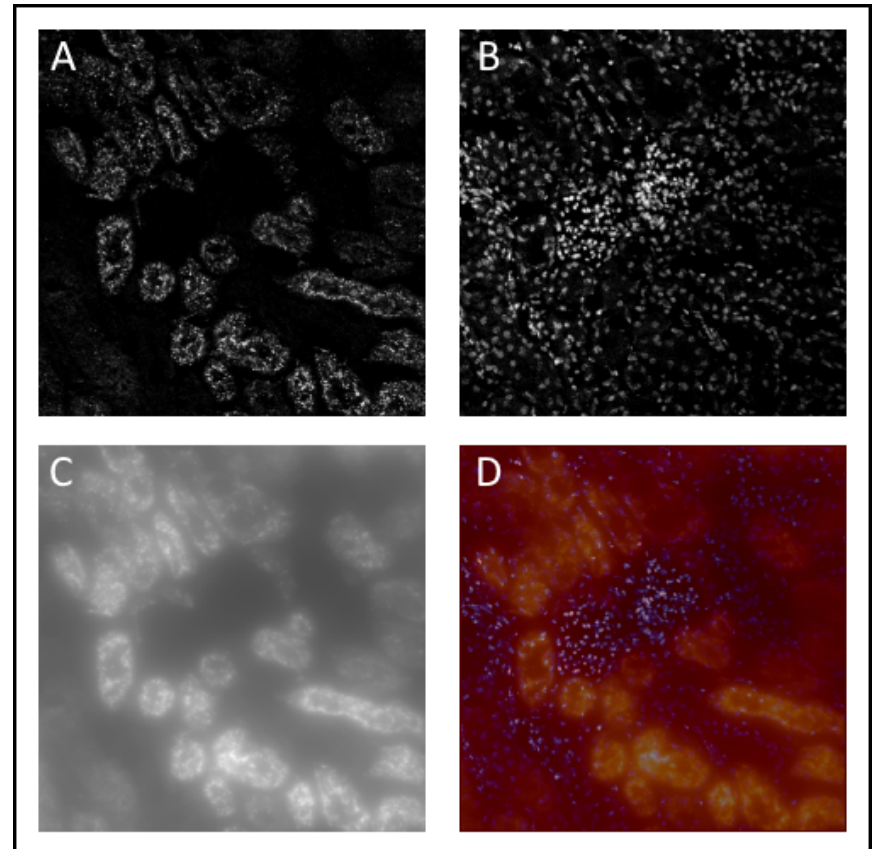
MICROSCOPY



PRRT and A1M

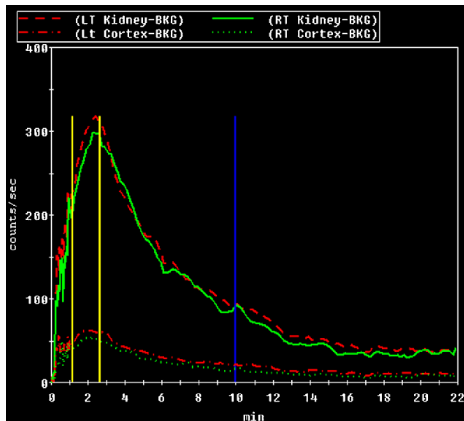
- High absorbed dose rate in tubules compared to glomeruli
- Kidney damage relatively easy to show, however...

...Clinically relevant tracers are important!

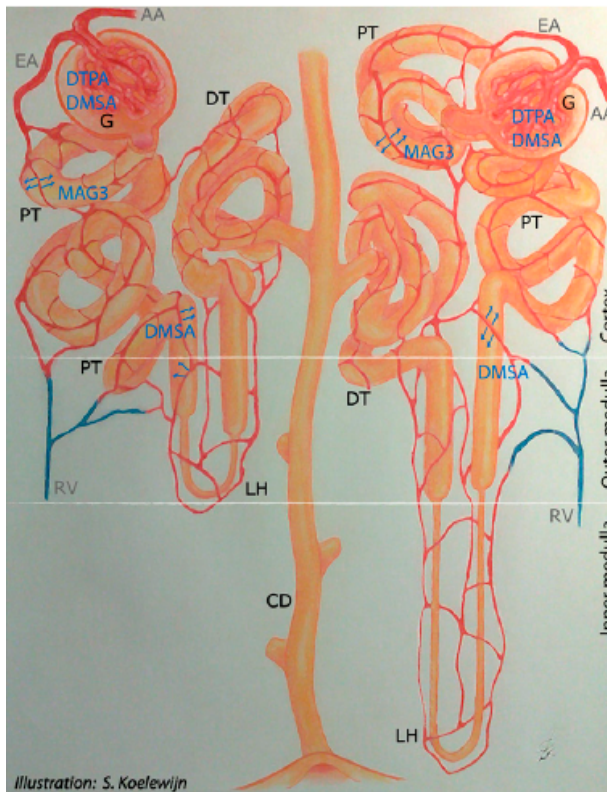


Project planning

- Choice of radiopharmaceutical (radionuclide + tracer)
- Choice of imaging system
- Planning of measuring methodology



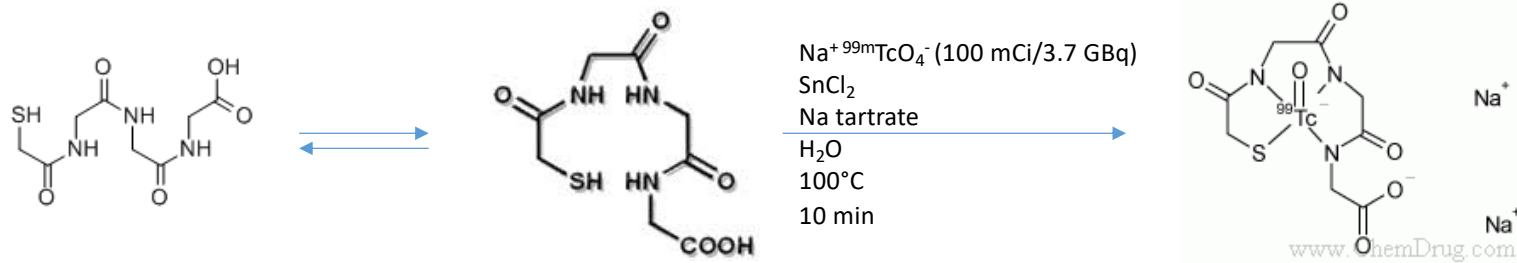
Choice of radiopharmaceutical



- ^{99m}Tc -labeled mercaptoacetyltriglycine; ^{99m}Tc -MAG3
- Can be used as an independent measure of kidney function
- Extraction via proximal tubules



Radiochemistry

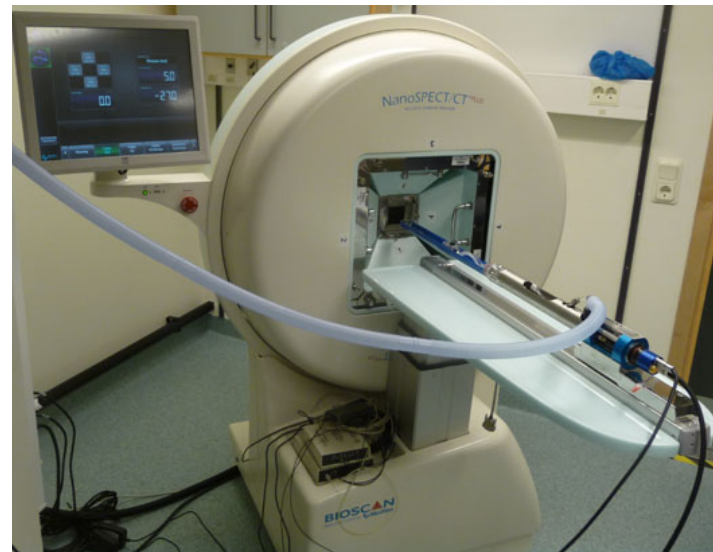
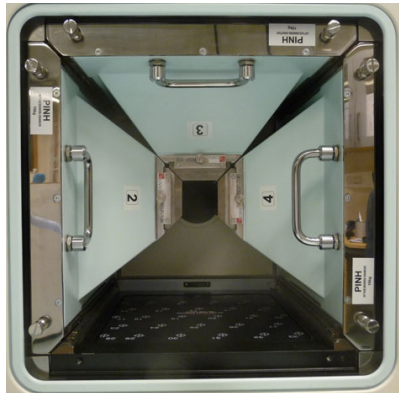
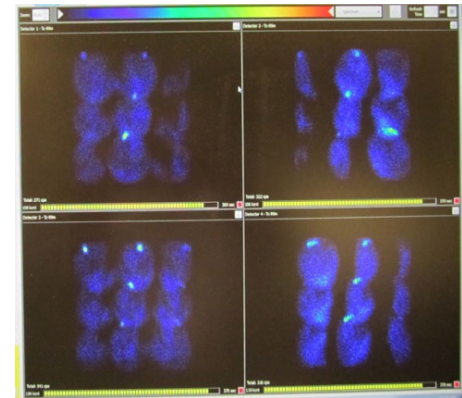


1 mg = 0,0038 mmol

100 mCi = 19,23 nanogram = 0,19 nanomol

Imaging with SPECT

- Single Photon Emission Computed Tomography
- Good for low energy photons (^{99m}Tc : 140 keV)
- Multi pinhole; 4 x 9 projections for each time frame



Ahlstedt/Johansson/Sydooff/Karlsson/ Thordarson/Gram/Eriksson , Neuroendocrinology, DOI: 10.1159/000500473 (2019-04)



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Dynamic imaging with ^{99m}Tc -MAG3

Renogram; shows the uptake and extraction of the radiopharmaceutical over time.

Measuring protocol: 5s/frame, 60 frames

Detectors not revolving due to short time span

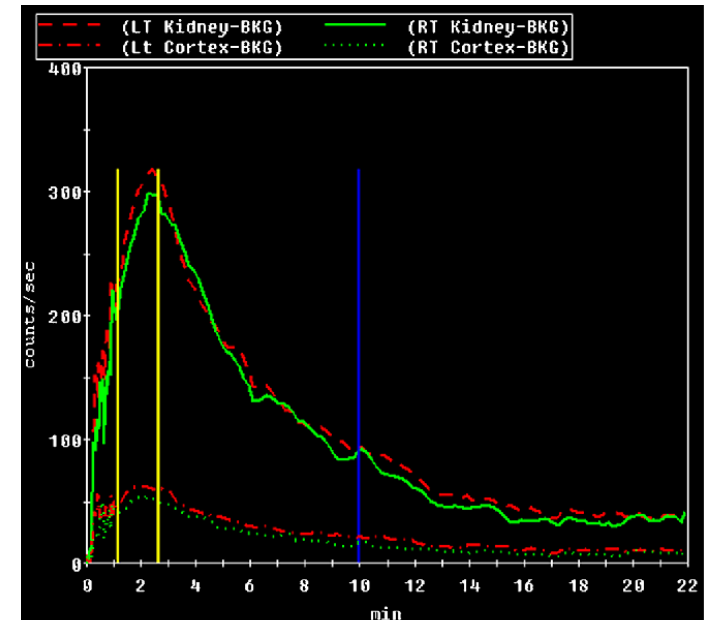
Difficulties

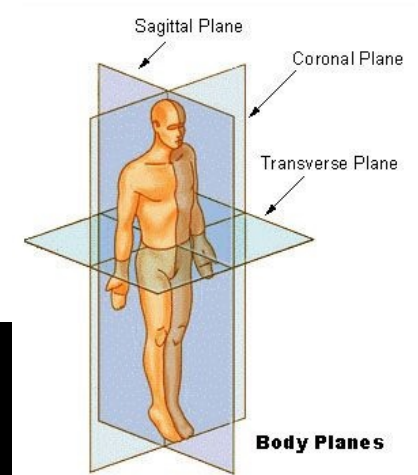
Small FOV – CT needed for localization; one kidney in FOV

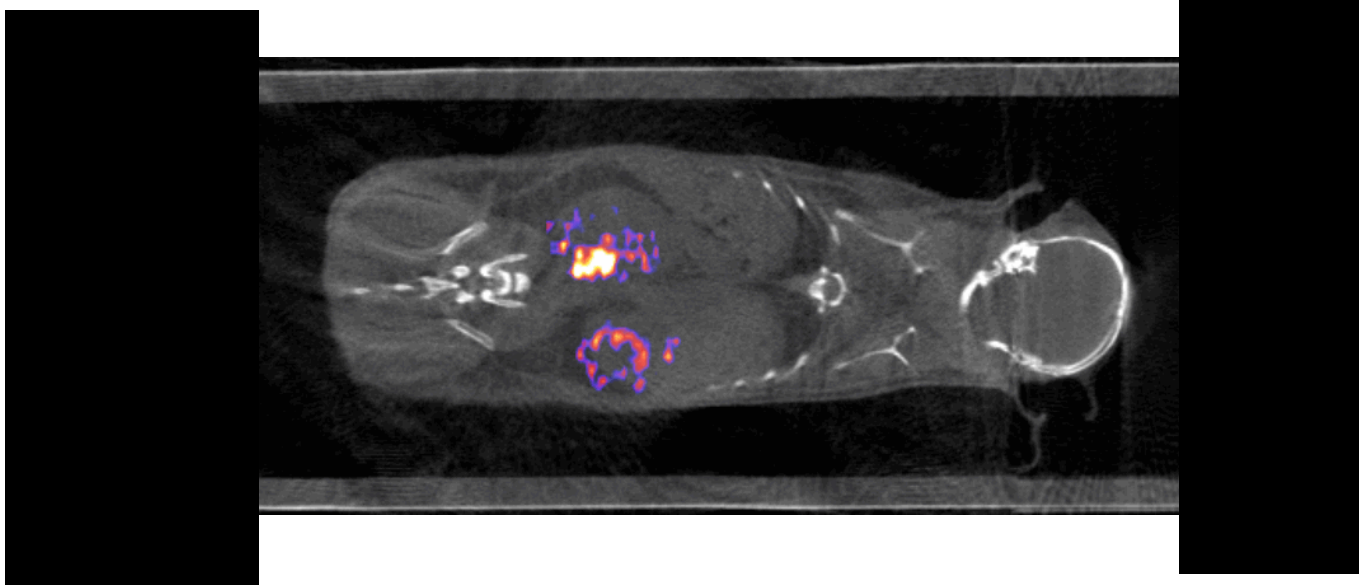
Fast process – ~20 s to peak uptake in renogram

Infusion of radiopharmaceutical while the animal is in the camera

Two persons needed for measurement, infusion and monitoring of animals





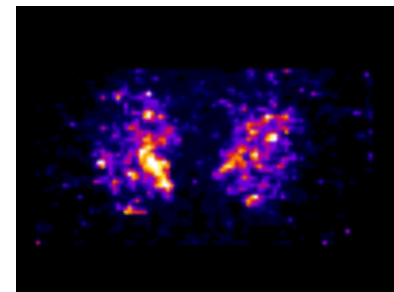
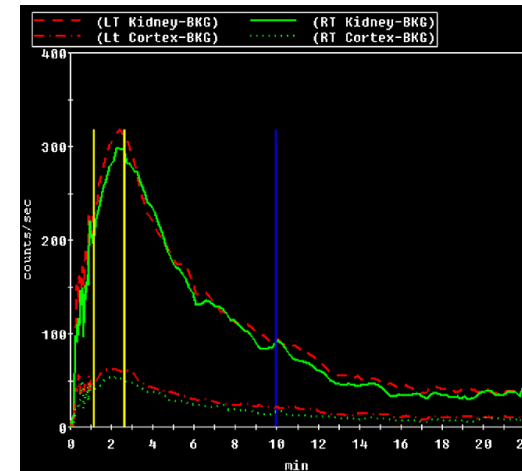
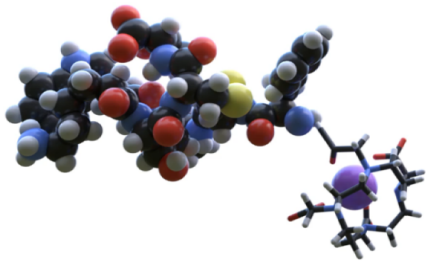


Ahlstedt/Johansson/Sydooff/Karlsson/ Thordarson/Gram/Eriksson , Neuroendocrinology, DOI: 10.1159/000500473 (2019-04)



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Outcome of measurements



Non-Invasive Imaging Methodologies for Assessment of Radiation Damage to Bone Marrow and Kidneys from Peptide Receptor Radionuclide Therapy

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Eddie Thordarson^a Magnus Gram^a Olof Eriksson^{b, d}

^aA1M Pharma AB, Lund, Sweden; ^bAntaros Medical AB, Mölndal, Sweden; ^cLund University Bioimaging Center, Lund University, Lund, Sweden; ^dScience for Life Laboratory, Department of Medicinal Chemistry, Uppsala, Sweden



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