Deutsche Gesellschaft für Nuklearmedizin e.V.

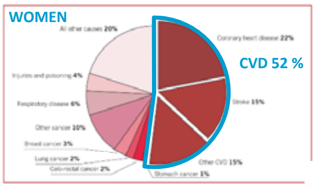
SUMMER SCHOOL 2016

Molecular Imaging in Preclinical Cardiovascular Research

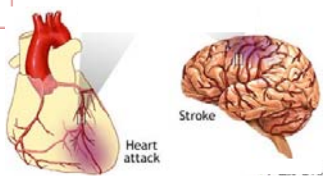
Lisa Honold
European Institute for Molecular Imaging, Münster

European Institute for Molecular Imaging

Cardiovascular Disease – A Challenge Worldwide



European Heart Network 2012

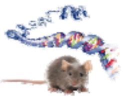


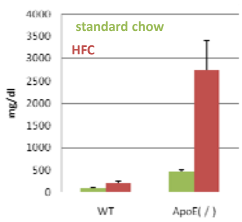
Cardiovascular Disease Models

Small animals do typically not present with cardiovascular diseases

Animal Models of Atherosclerosis

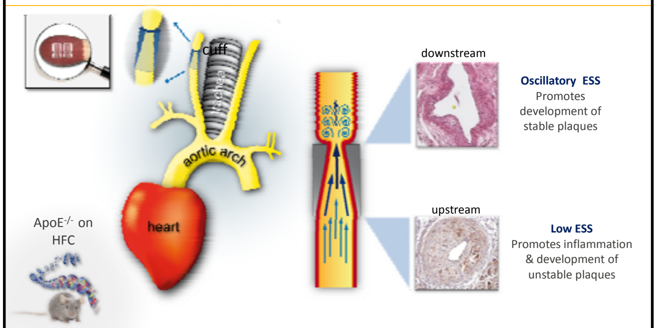
ApolipoproteinE $^{-/-}$ mouse





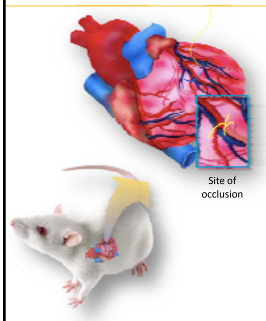
Nakashima, ATVB 1994

Cuff Model – shear-stress induced local atherosclerosis



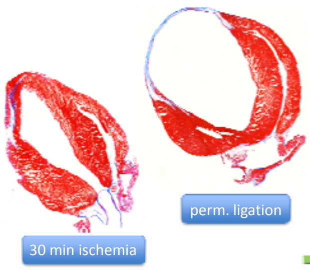
Kuhlmann et al., JoVE 2011

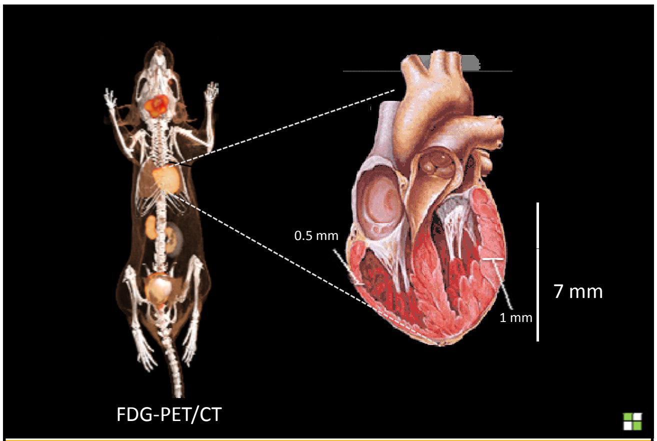
Induction of Myocardial Infarction



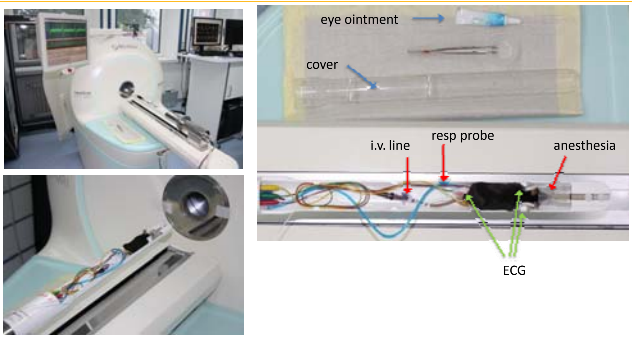
scar formation

3 weeks after induction of MI



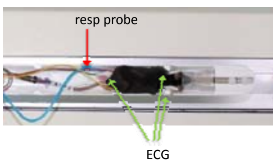


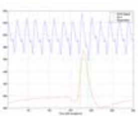
Imaging: Monitoring of bio signals



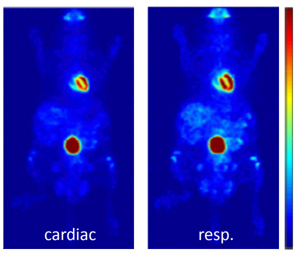
Imaging: Movement Correction

Mouse: 26 g, heart rate, ~ 500 bpm





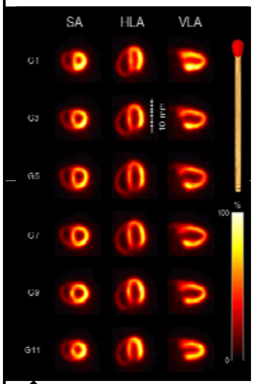
Reconstructed Gates: 8

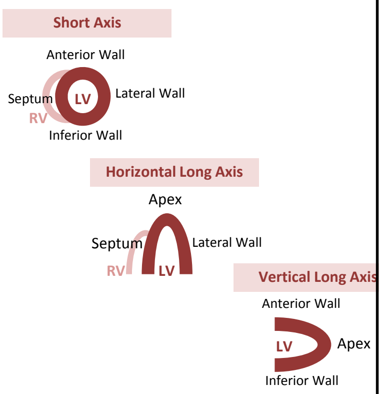


List mode acquisition:
60-90 min p.i. 12 MBq F-18-FDG

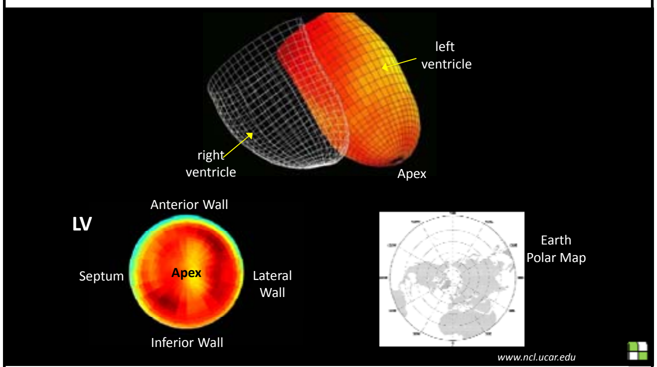
Schäfers K, Z Med Phys 2006

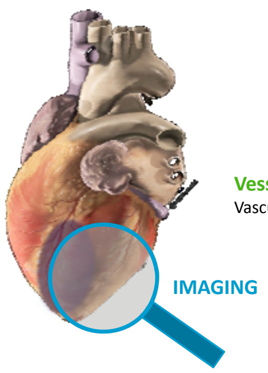
Visualization





Segmentation / Quantitative Analysis





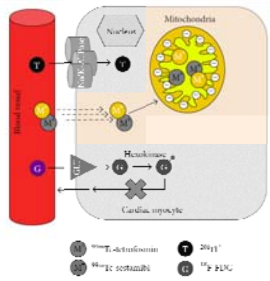
Vessels
Vascular Inflammation

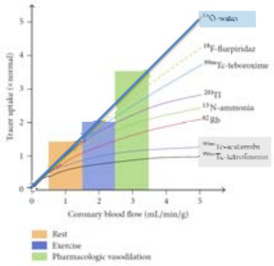
IMAGING

Myocardium
Perfusion
Viability

Myocardial Perfusion Imaging

Blood Cardiomyocyte

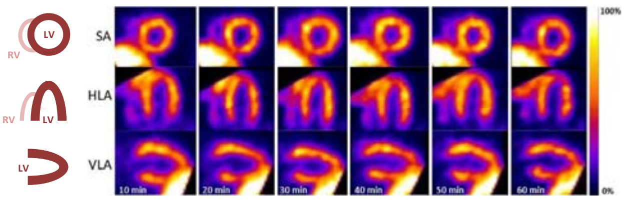




Sogbein, Biomed Res Int. 2014

Myocardial Perfusion Imaging

Healthy mouse, 26g



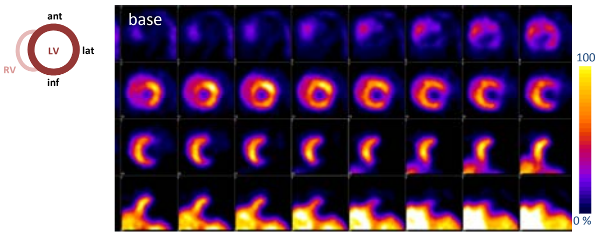
10 20 30 40 50 60 min

time after injection

Vrachimis A, EJNMMI Res. 2012

Myocardial Perfusion Imaging

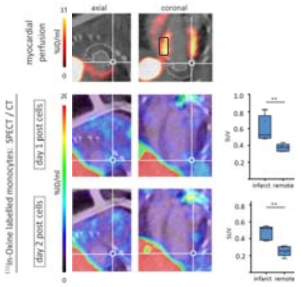
Mouse, 24g Ischemia !



apex

Perfusion Imaging: Application

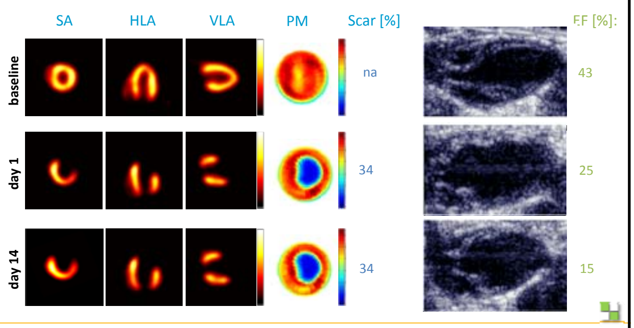
Monocyte migration



Honold L, Gran S, Roth J, Schäfers M, in preparation

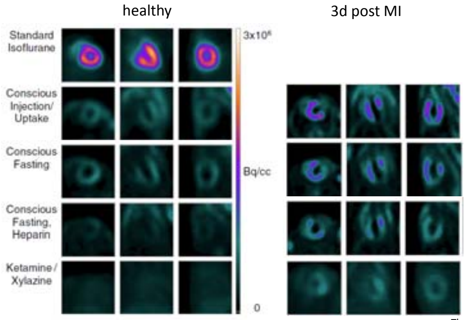
Viability

Mouse, 24g, permanent MI ^{18}F-FDG-PET ultrasound



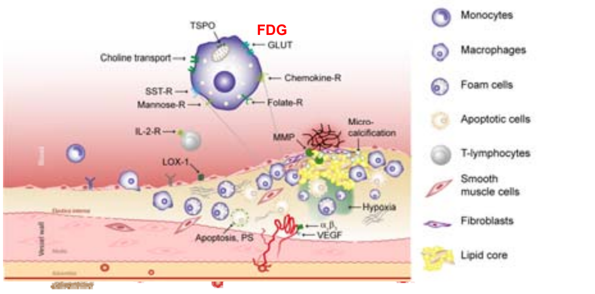
Influence of anesthesia on cardiac ^{18}F-FDG uptake

~8MBq FDG i.v.
Acq. 50-60min p.i.



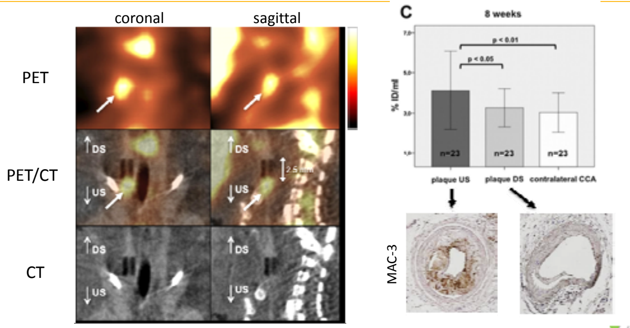
Thackeray et al., EJNMMI 2015

Atherosclerosis – targets



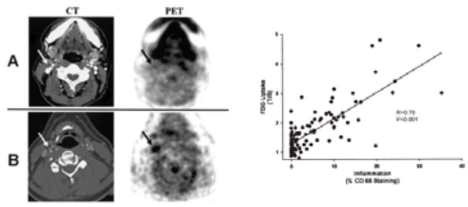
Vrachimis et al. QJNM 2016

FDG-PET/CT in Carotid Cuff Model



Wenning et al., Atherosclerosis 2014

FDG-PET in patients

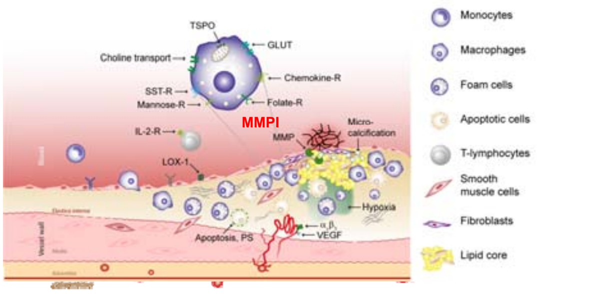


→ FDG signal correlates with macrophage density in excised carotid samples

But: true nature of FDG signal is still unclear (macrophages vs. surrounding fat vs. ???)

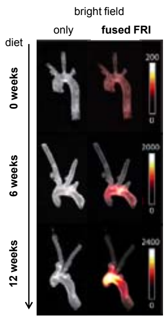
Tawakol et al. J.Am.Coll.Cardiol. 2006

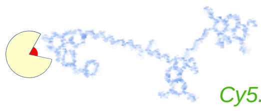
Atherosclerosis – targets



Vrachimis et al. QJNM 2016

MMP Imaging





Cy5.5-MMPI

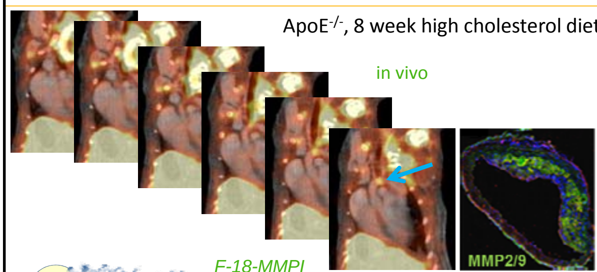
Faust A. Bioconjug Chem 2008
Faust A. Contrast Media Mol Imaging 2013

Waschkau B

MMP Imaging

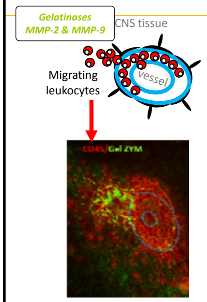
ApoE$^{-/-}$, 8 week high cholesterol diet

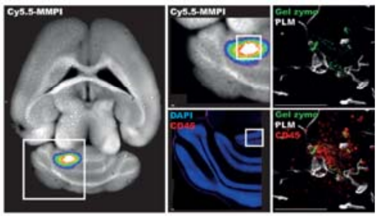
in vivo



F-18-MMPI

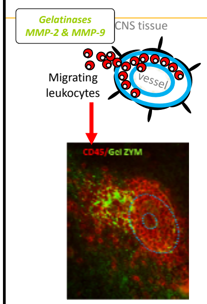
Translational MMP Imaging in MS



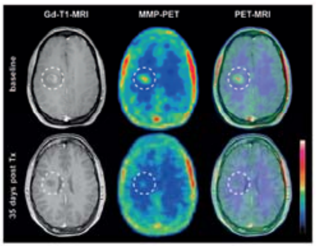


Gerwien H, Hermann S, Schäfers M, Sorkin L, in revision

Translational MMP Imaging in MS



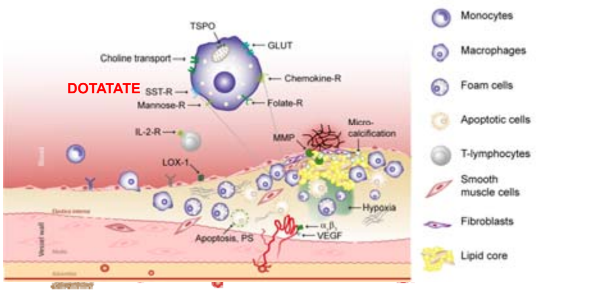
^{18}F-MMPI-PET and Gd-T1-MRI of patient with acute attack of relapsing remitting MS at baseline and 35 days after treatment (methylprednisolone)



30-60 min p.i. of 250 MBq MMP radiotracer ^{18}F-BR351

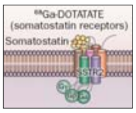
Gerwien H, Hermann S, Schäfers M, Sorkin L, in revision

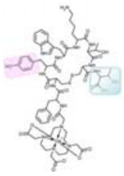
Atherosclerosis – targets



Vrachimis et al. QJNM 2016

Somatostatin-receptor imaging with DOTATATE





Somatostatin (SST): Circulating peptide with neuroendocrine, immunomodulatory and cell-regulatory functions

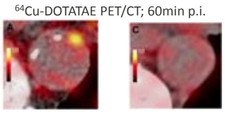
SSTRs: Overexpressed in a number of diseases, particularly neuroendocrine tumors

DOTATATE: SST analog with SSTR2 specificity
^{68}Ga or ^{64}Cu labeled

Tarkin et al. Nat. Reviews Card., 2014

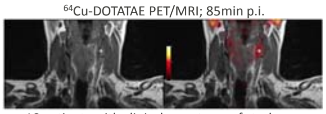
DOTATATE PET in patients

^{64}Cu-DOTATAE PET/CT; 60min p.i.



Framingham risk score: 30 Framingham risk score: 2

^{64}Cu-DOTATAE PET/MRI; 85min p.i.



10 patients with clinical symptoms of stroke or transient ischemic attack

In vivo imaging and gene expression analysis of plaque regions after carotid endarterectomy

Several retrospective studies report DOTATATE PET (^{68}Ga or ^{64}Cu) signal to correlate with presence of plaques and cardiovascular risk factors

Strong correlation between *in vivo* signal and *ex vivo* markers of activated macrophages (CD163)

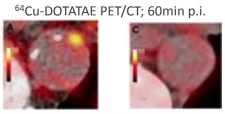
→ Detection of vulnerable plaques?

Rominger et al. 2010, JNM; Li et al. 2012, EJNMMI; Malmberg et al. JNM 2015

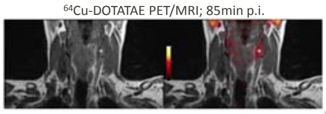
Pedersen et al. Arterioscl. Throm. Vas. 2015

DOTATATE PET in patients

^{64}Cu-DOTATAE PET/CT; 60min p.i.



^{64}Cu-DOTATAE PET/MRI; 85min p.i.



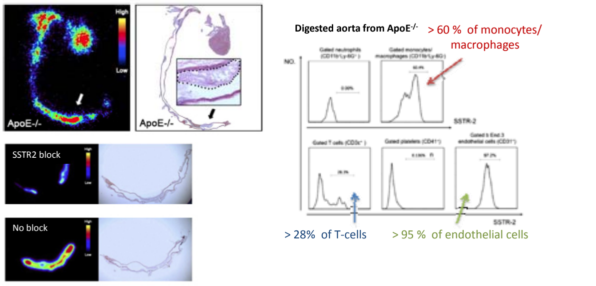
VISION study
(Vascular Inflammation imaging using Somatostatin receptor psitron emissION tomography)

50 subjects with atherosclerosis,
sequential PET/CT imaging with ^{68}Ga-DOTATATE and ^{18}F-FDG,
contrast angiography of carotid and coronary arteries,
autoradiography and immunohistochemistry of excised carotid plaques

US National Library of Medicine. ClinicalTrials.gov, http://clinicaltrials.gov/show/NCT02021188 (2013)

SSTR2 imaging – bedside to bench - to bedside?

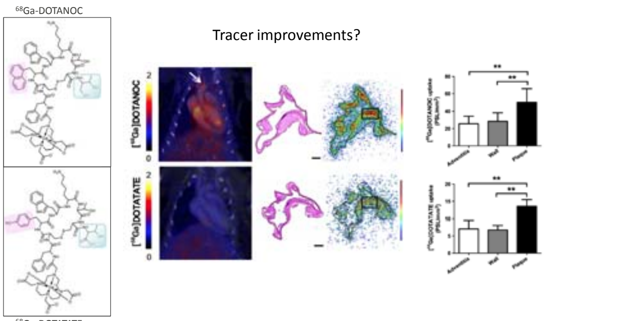
Specific tracer uptake on tissue level? What cells in the plaque express SSTR2?



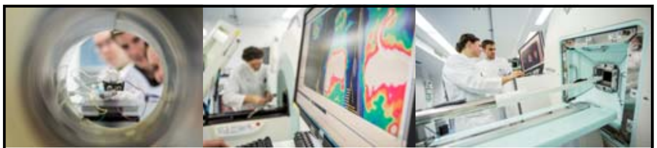
Li et al. Atherosc l., 2013

SSTR2 imaging – bedside to bench - to bedside?

Tracer improvements?



Rinne et al. MOL IMAGING BIOL, 2016



European Institute for Molecular Imaging

CRC 656 Molecular Cardiovascular Imaging

UKM Klinik für Nuklearmedizin

Cells in Motion Cluster of Excellence

Mouse Imaging Workshop
14-18 November 2016

Topics

- **Animal handling:** i.v./i.p. injection, tail vein catheter, anaesthesia, surgery
- **µPET/µSPECT:** static and dynamic scanning, CT fusion
- **µCT:** *in vivo* scans +/- contrast agents, respiratory gating
- **µMRI:** *in vivo* scans +/- contrast agents, cardiac & respiratory gating
- **Ultrasound:** hands-on scanning +/- contrast agents
- **Optical imaging:** fluorescence, bioluminescence
- **Multimodal imaging:** PET/CT, PET/MRI, SPECT/CT
- **Image analysis:** methods, coregistration, quantification (VisualLab)

http://www.uni-muenster.de/EIMI/teaching/mia/