Small Animal Imaging Techniques

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Faculté de biologie et de médecine

Overview

- Small animal imaging
- Particularities of small animal imaging
- Examples of application
- Image processing & analysis

Small animal imaging

- Non invasive, longitudinal study
- (semi-)quantitative, spatial and temporal information
- Embrace all physiological factors
- Systemic disease

Small animal imaging

- Fundamental research
- Drug development
- Translational research
- Bench to bedside ↔ bedside to bench

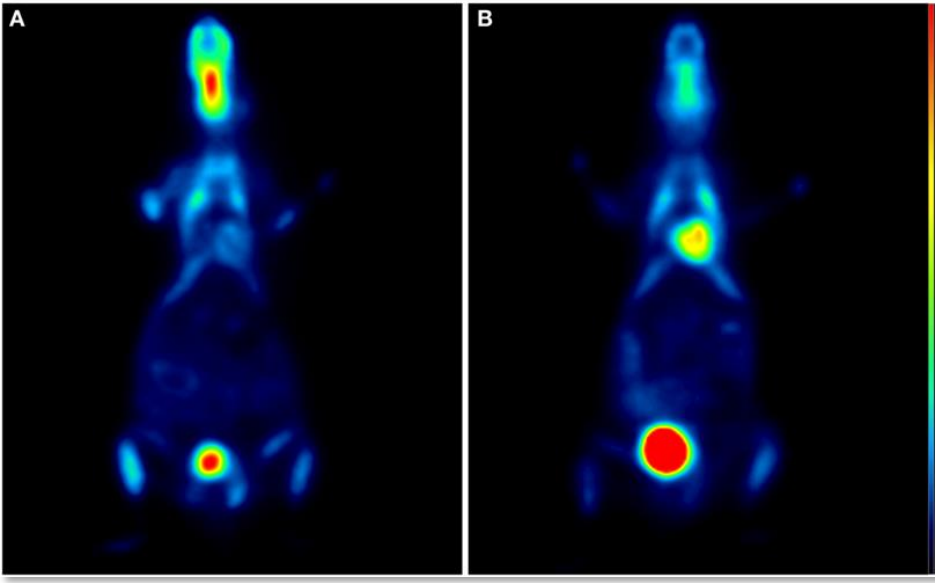
Physiology of small animal

	Mouse	Human
Blood Volume	1.7 ml	5 L
Resp. frequency [per min]	60-230	12-20
Heart Frequency [per min]	300-800	60-90
Anaesthesia	Yes	No
Hypothermia	Yes	No

Physiology of small animal

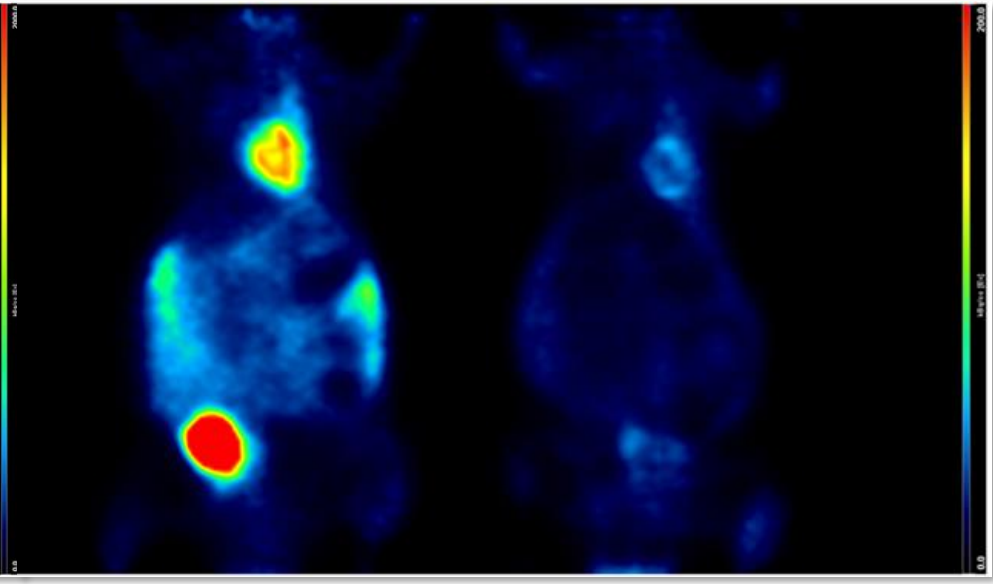
Influence of anesthetic drug on cardiac ^{18}F-FDG uptake.

Ketamine/xylazine **Isoflurane**



Influence of length of anesthesia on cardiac uptake.

Whole procedure **Only acquisition**



Small Animal Imaging techniques


Bioluminescence

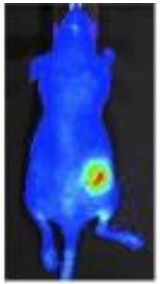
- ✓ Convenient
- ✓ nM sensitivity
- ✗ 5 cm imaging depth
- ✗ 1-5 mm resolution


Ultrasound

- ✓ 50 µm resolution
- ✗ 3 cm imaging depth
- ✗ Operator dependent

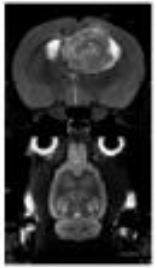

PET/CT

- ✓ No limit of depth
- ✓ pM sensitivity
- ✓ quantitative
- ✗ 1-2 mm resolution
- ✗ Radioactivity

Fluorescence

- ✓ Convenient
- ✓ nM sensitivity
- ✗ 1 cm imaging depth
- ✗ 2-3 mm resolution

MRI

- ✓ 10-100 µm resolution
- ✓ Soft tissue contrast
- ✗ Expensive

SPECT/CT

- ✓ No limit of depth
- ✓ pM sensitivity
- ✗ 0,3-2 mm resolution
- ✗ Radioactivity

microPET/SPECT/CT

Animal Management System

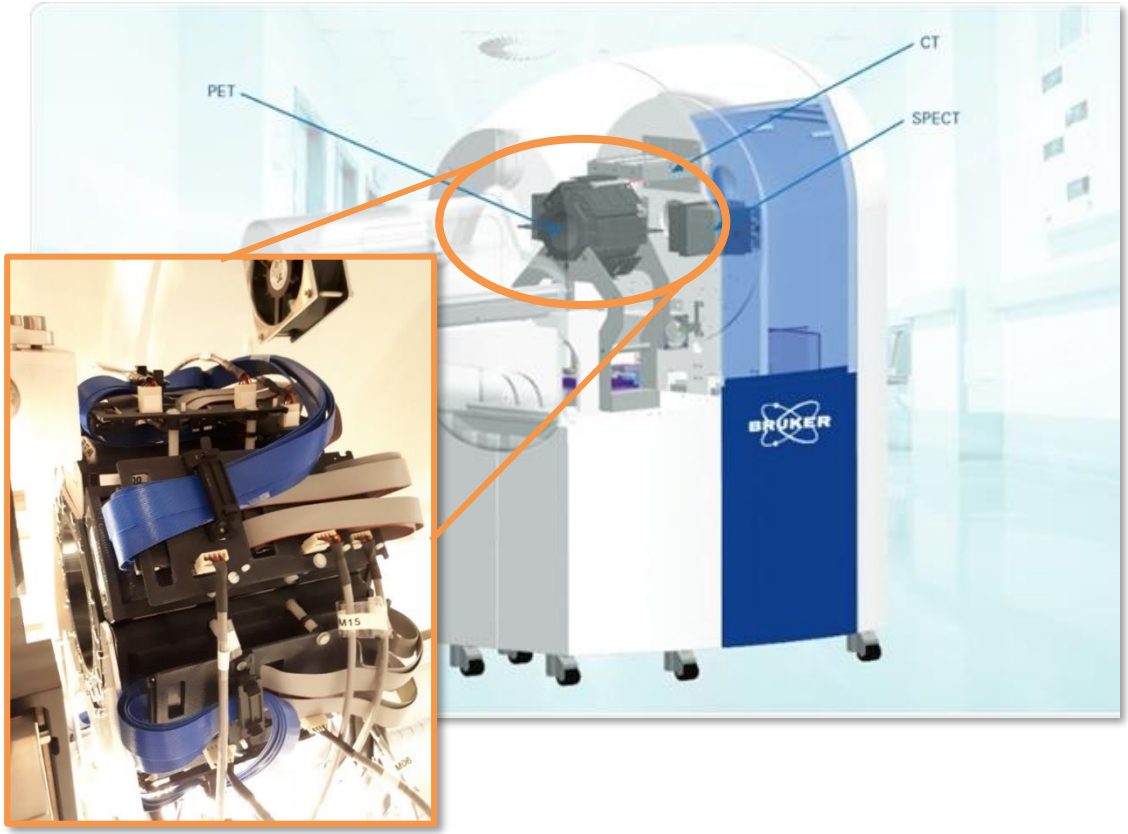
- ✓ Temperature regulated environment for mice & rats
- ✓ Gas ports for use with anesthesia
- ✓ Live color webcam for monitoring of animals
- ✓ ECG/respiratory gating
- ✓ 800 Kg
- ✓ Auto shielded
- ✓ Turn-key system

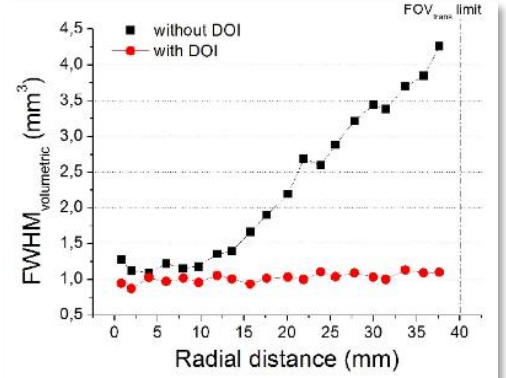
microPET/SPECT/CT

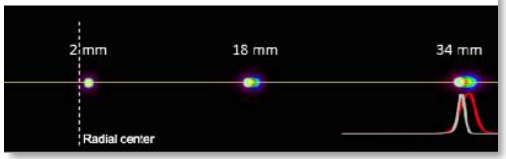
PET modality

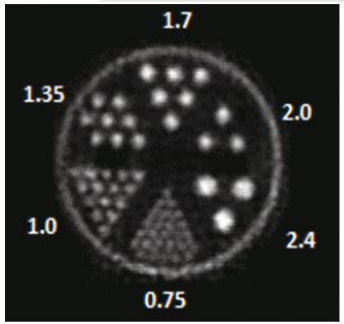
- ✓ Exclusive, proprietary PET detectors
  - ✓ Single LYSO crystal
  - ✓ 12x12 SiPM
- ✓ High spatial resolution over all the FOV
- ✓ Sensitivity 4.5 %
- ✓ Average energy resolution 17 %
- ✓ 8 detectors per ring, 3 rings
- ✓ Large FOV 148 mm x 80 mm
- ✓ Reconstruction MLEM

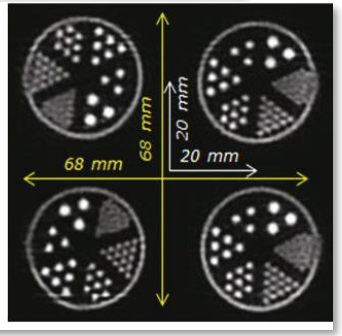
microPET/SPECT/CT



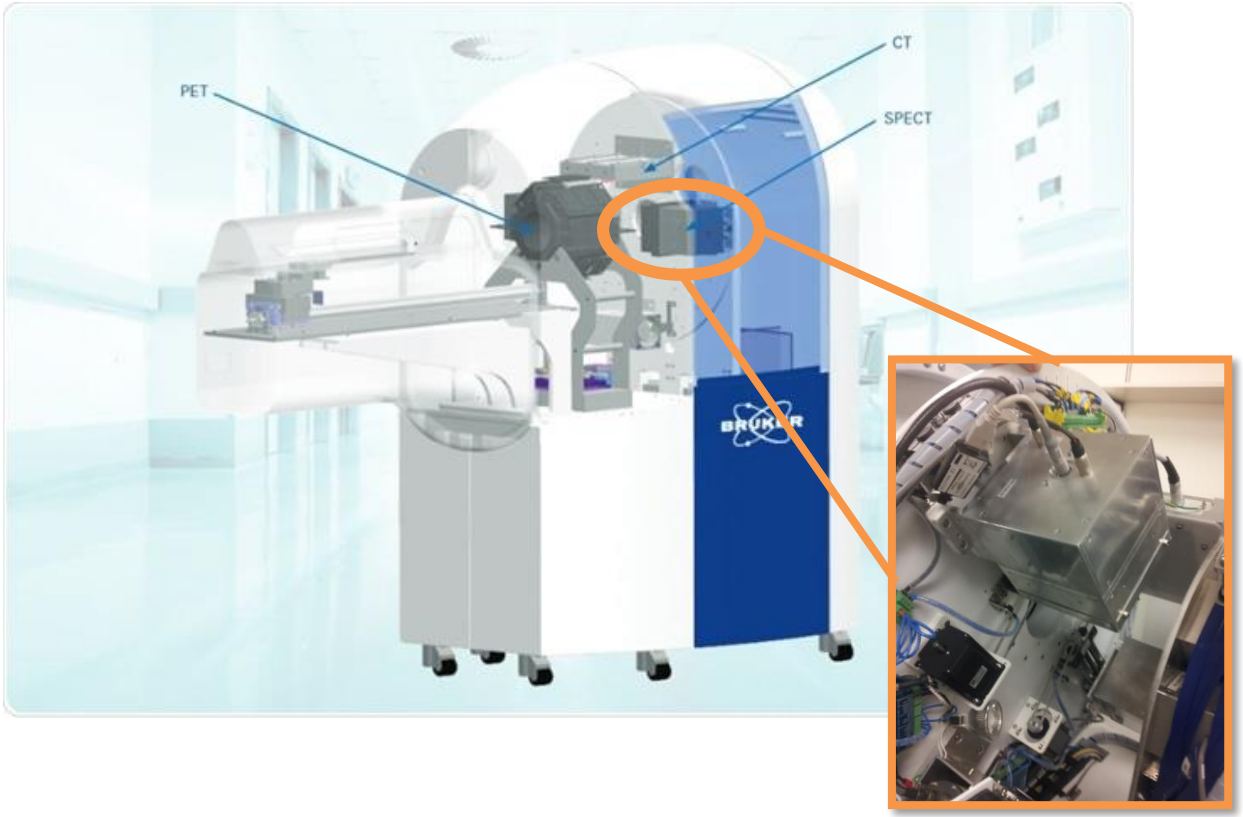








microPET/SPECT/CT



SPECT modality

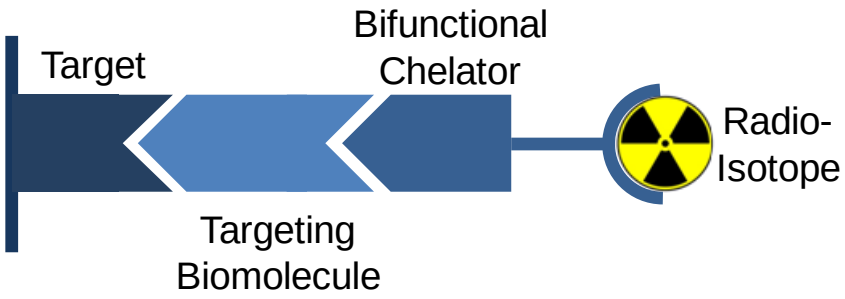
- ✓ Dual head camera
- ✓ CsI(Na) single crystals
- ✓ Sensitivity 1800 CPS/Mbq
- ✓ Energy resolution: 0.18
- ✓ Energy range 30-400 keV
- ✓ FOV 25 – 120 mm
- ✓ Spatial resolution 0.5 mm
- ✓ Single and multi-pinhole collimators

microPET/SPECT/CT

CT system

- ✓ Spatial resolution 90 µm
- ✓ X-ray source 10-50 kVp with 35 um X-ray spot size
- ✓ Two-dimensional 12 cm x 12 cm, 2400 x 2400 pixel detector
- ✓ FOV 7 cm
- ✓ Rapid acquisition and reconstruction
- ✓ Safe fully shielded cabinet X-ray system with interlocks

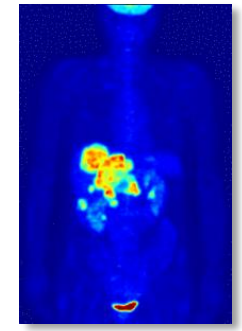
Radiotracer

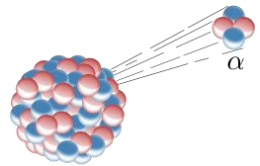


Theranostic approach

« Diagnostic » radio-isotopes
Tb-152, Ga-68, Lu-177, …

« Therapeutic » radio-isotopes
Tb-149, Y-90, Lu-177, …





Selection of currently investigated targeting biomolecules :

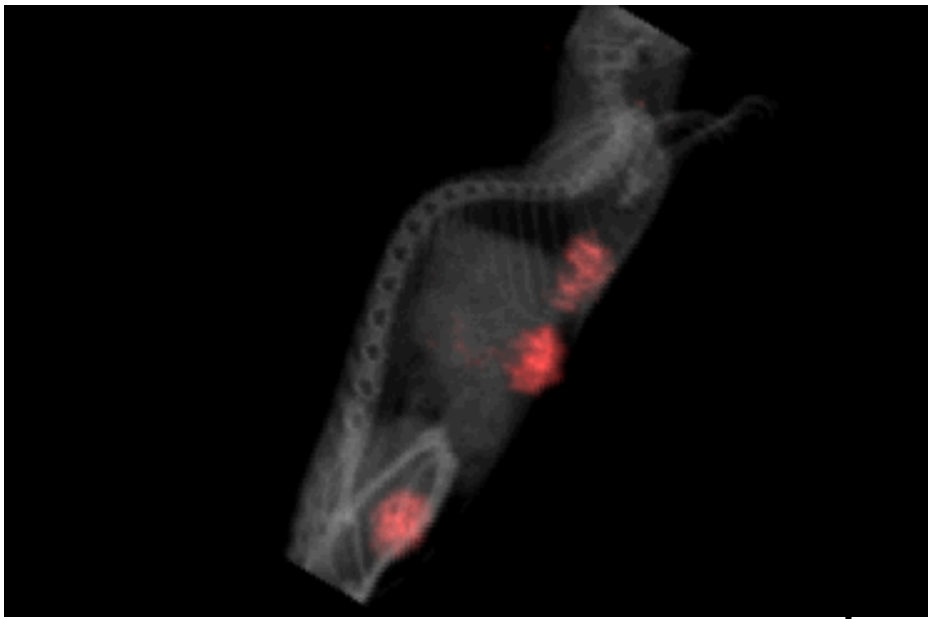
- FEPPA → small molecule
- Neurotensin derivatives → peptide
- Bombesin derivatives → peptide
- TEM-1 → antibody
- 3BNC117 → antibody
- Others in development…

Small animal radionuclide imaging workflow

Small animal radionuclide imaging workflow

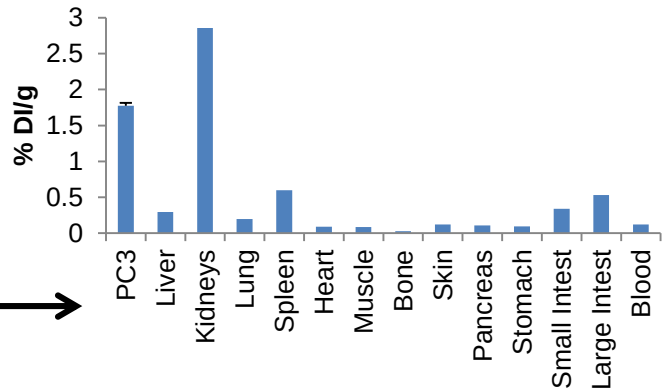
PET/CT acquisitions of ^{68}Ga bombesin and neurotensin analogs in human prostate cancer xenografts

^{68}Ga-DOTA-NT20.3-Ile
Neurotensin

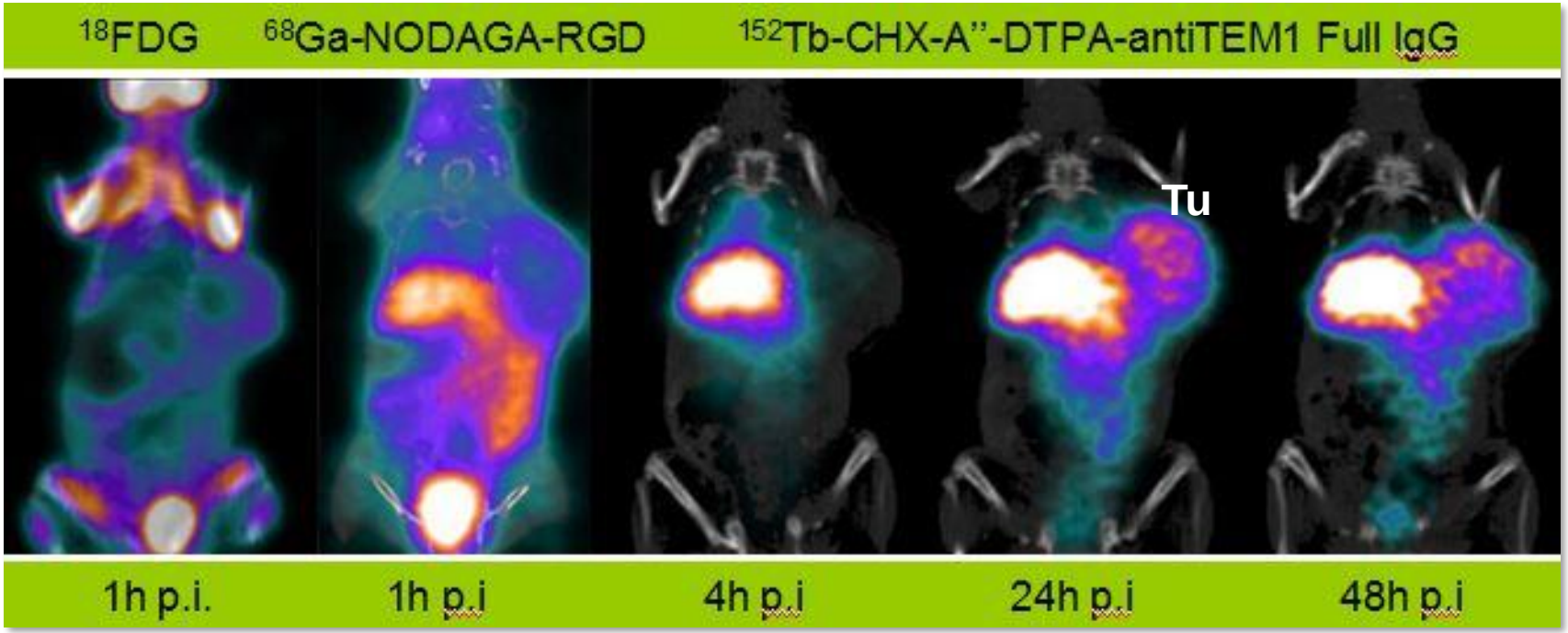


Female SCID grafted with PC3
Injection of 2.5 MBq ^{68}Ga -NODAGA-MJ9-Bombesin and 3.7 MBq ^{68}Ga -DOTA-NT20.3-Ile
Acquisition 180 minutes post-injection

Biodistribution

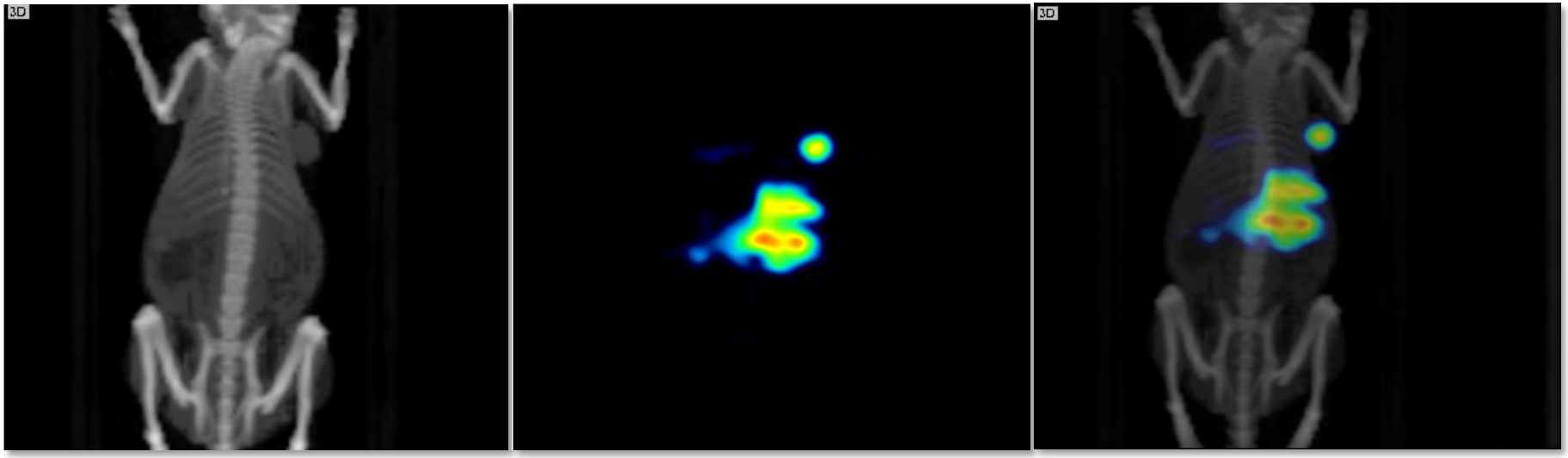


First PET images of ^{152}Tb-CHX-A''-DTPA-Full IgG



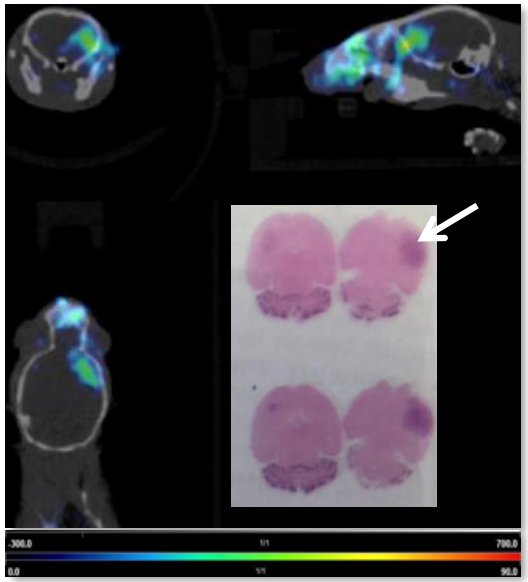
PET/CT acquisition over 48h post-injection of 7 Mbq of ^{152}Tb-CHX-A''-DTPA-Full IgG in mice bearing RD-ES Ewing Sarcoma compared to ^{18}F-FDG and ^{68}Ga-NODAGA-RGD

First SPECT imaging of ^{111}In-CHX-A”-DTPA-ScFv78Fc

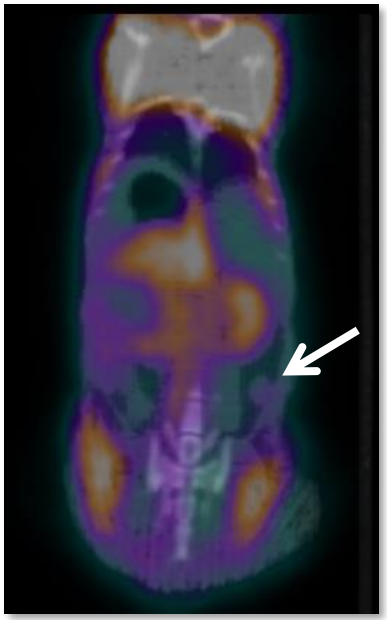


^{111}In-CHX-A”-DTPA-ScFv78Fc in mouse bearing A673 Ewing sarcoma tumor
1.88 MBq / 33 µg 20 h post injection
FOV dual head SPECT 360°, 60 projections, 45 sec/proj
CT 45 keV 200 µA

PET/CT mice acquisitions of orthotopic glioblastoma and spontaneous colon cancer

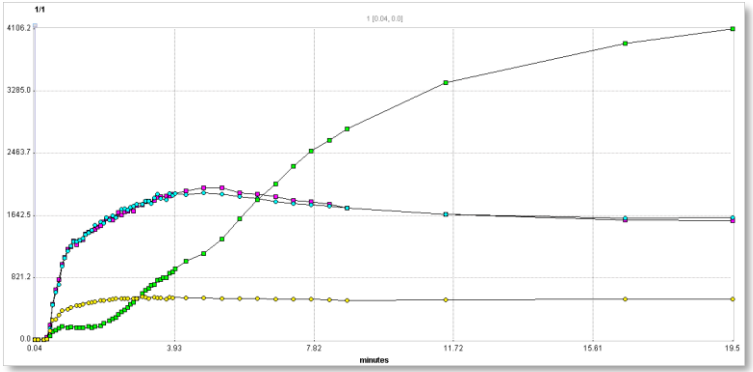


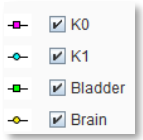
Representative PET/CT acquisition 90-min post-injection of 8.0 ± 1.6 MBq ^{68}Ga-MJ9 in mice bearing MGH4 primary glioblastoma 90 post injection of 10’000 cells. Tumor-to-normal brain ratio was 2.4 ± 0.8 (n=3)

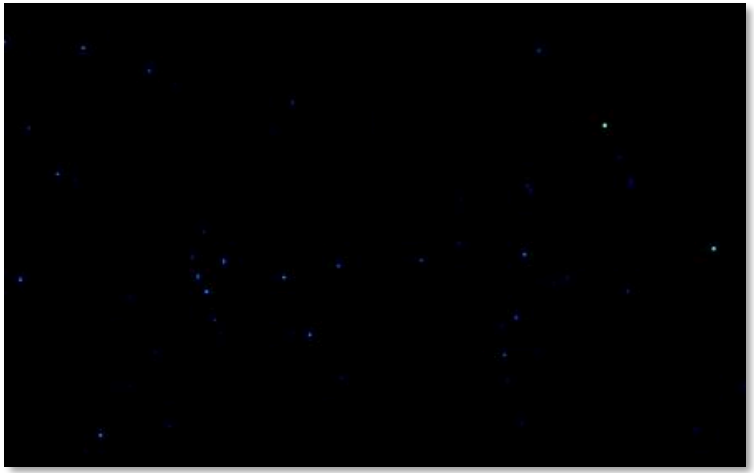


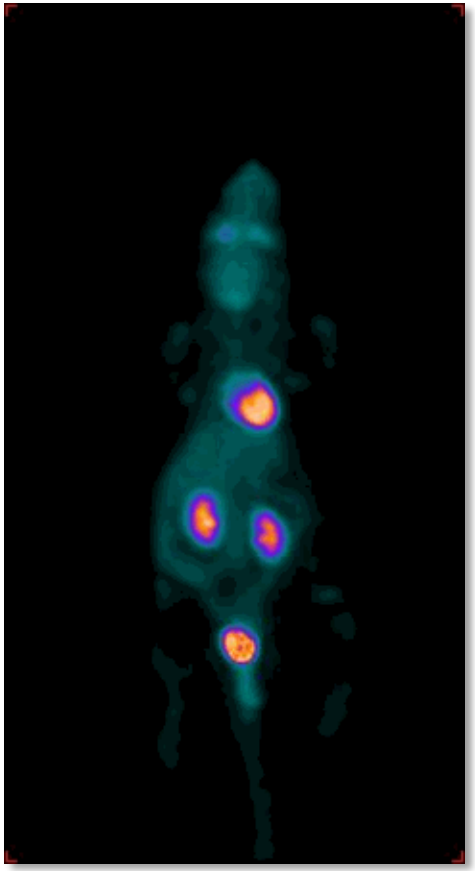
Representative PET/CT acquisition 60 min post-injection of 7 MBq ^{18}F-FDG in a mouse with spontaneous colon cancer

Pharmacokinetics PET acquisition of 18F-FDG

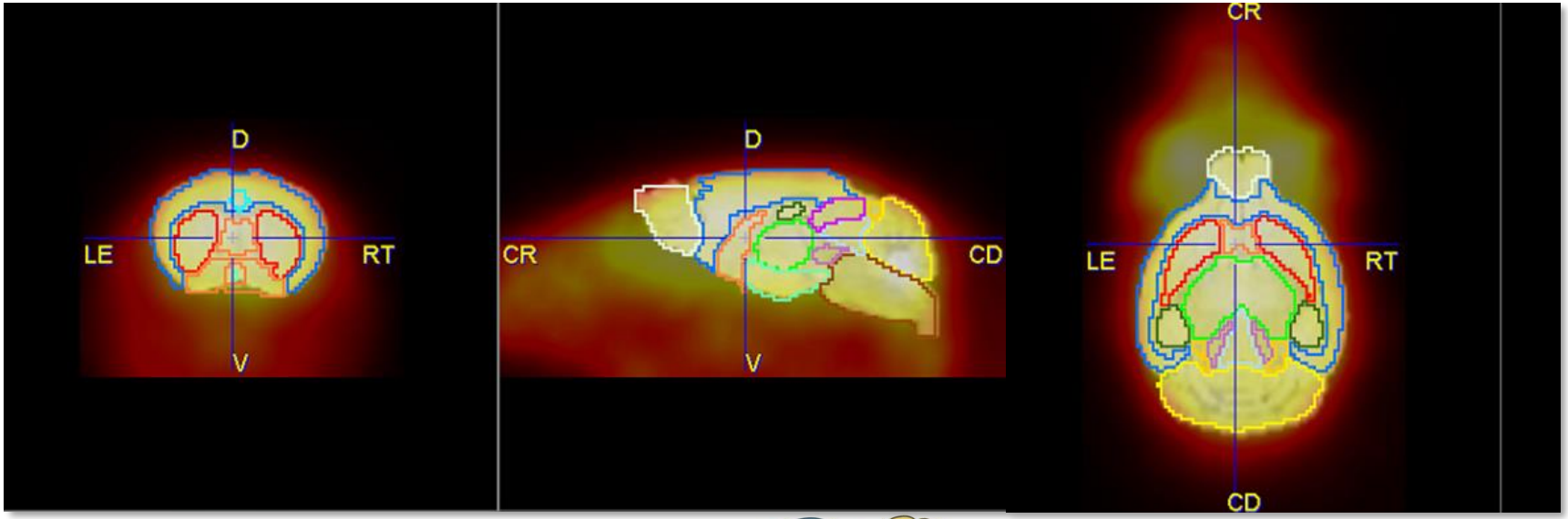


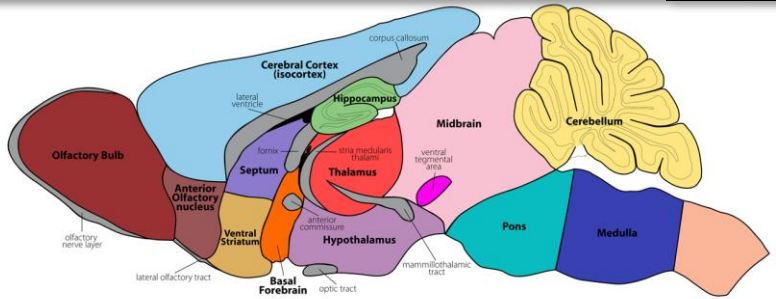




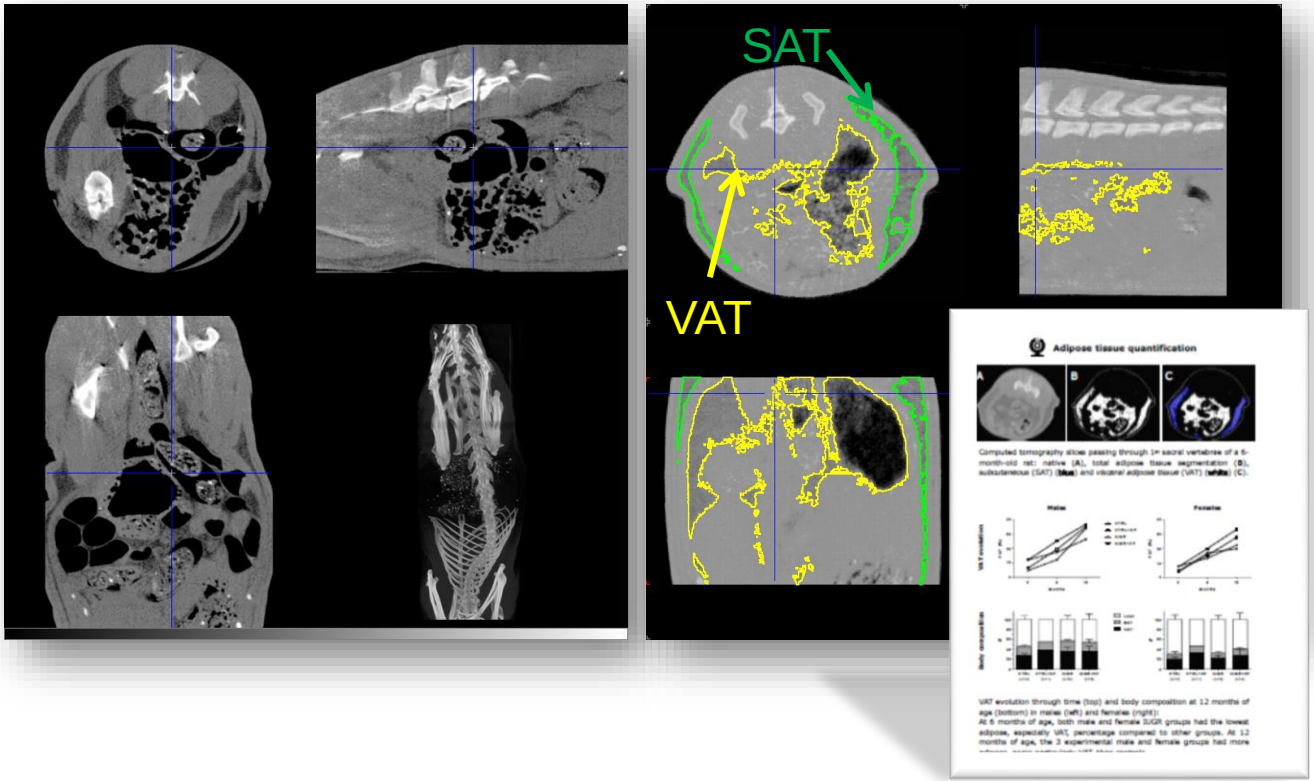


Brain mapping in LPS induced neuroinflamation detected by 18F-FEPPA





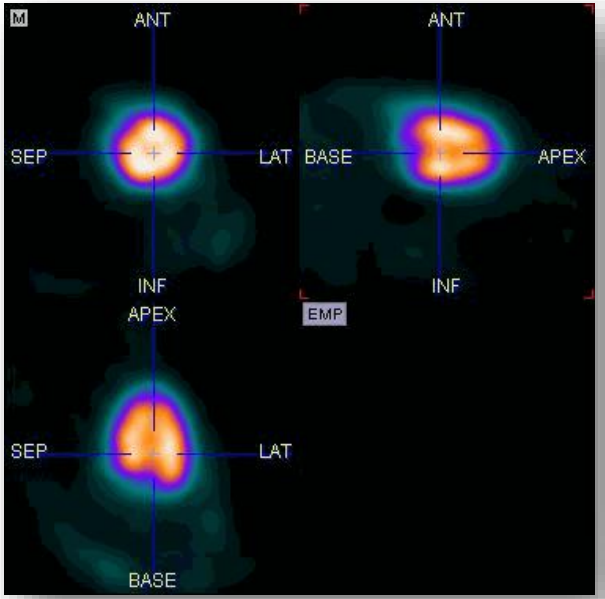
Quantification of adipose tissue in rats with in intrauterine deprivation by computed tomography

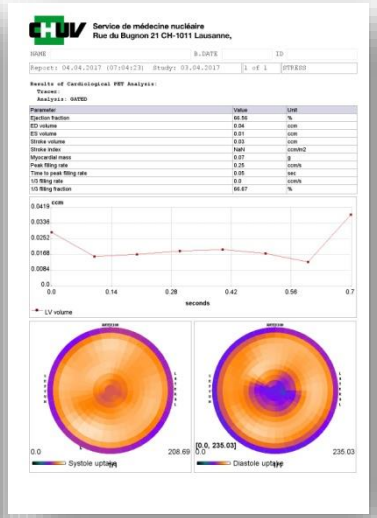


CT images of rats and semi automatic segmentation lean mass, subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) have shown that as age increases rats born with intrauterine deprivation gain more VAT than control which may predispose them to cardio metabolic disorders thereafter

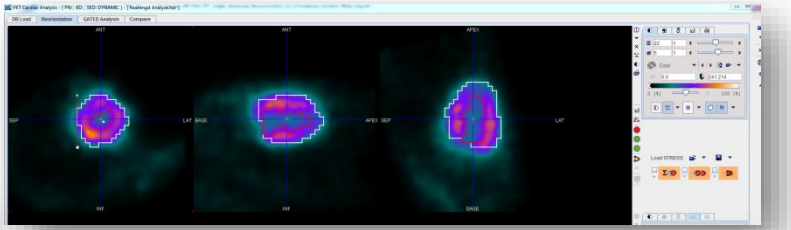
PET Gated Heart Study in Mouse

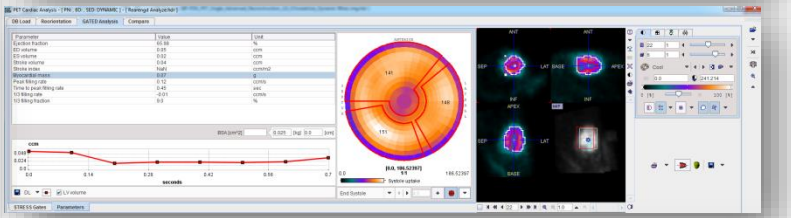
Twenty minutes PET cardiac gated acquisition of a mouse injected iv with 15 Mbq ^{18}F-FDG 45 minutes post-injection

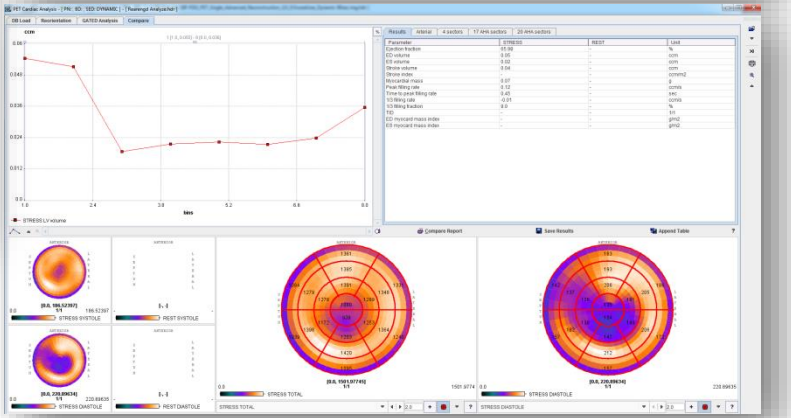




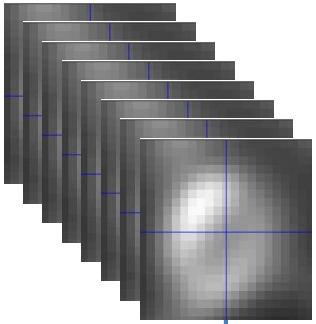
LVEF=67%







PET Heart Study in Mouse Image Processing

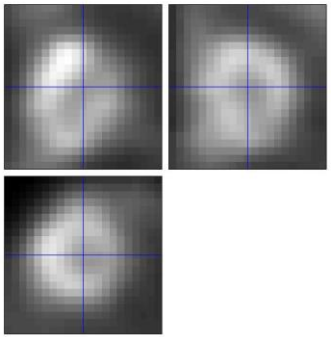


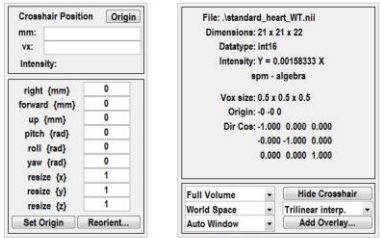
Realignment

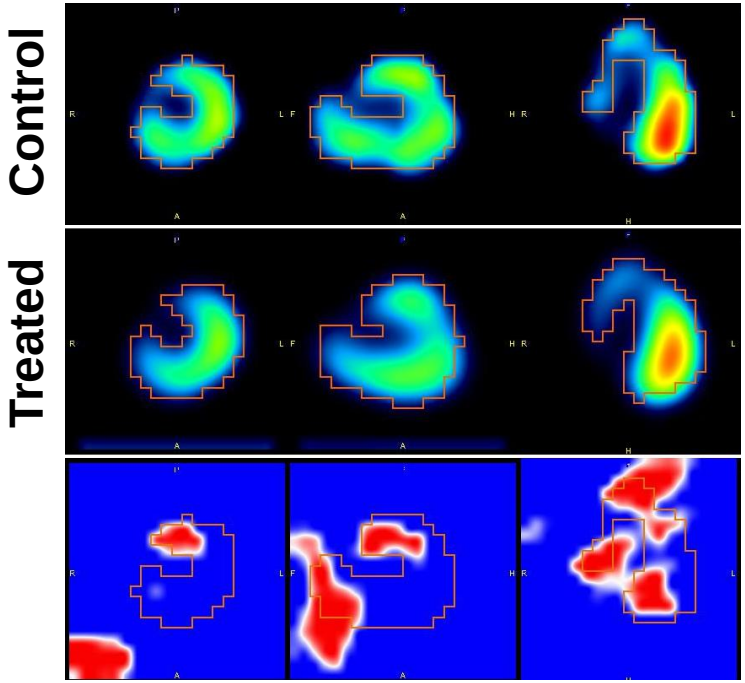
Normalisation

Coregistration

Pooled data set



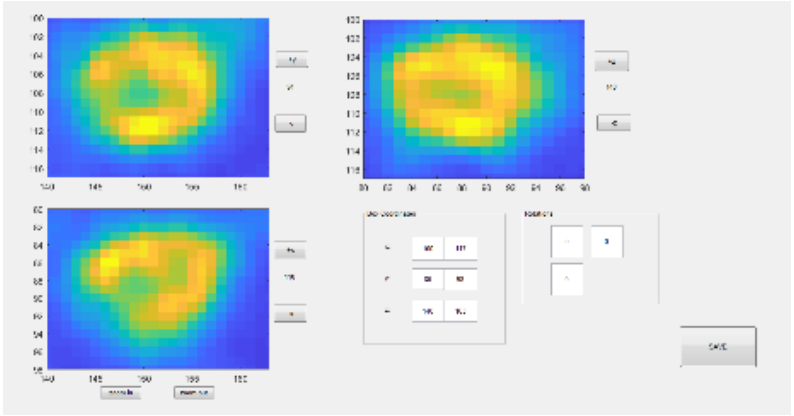




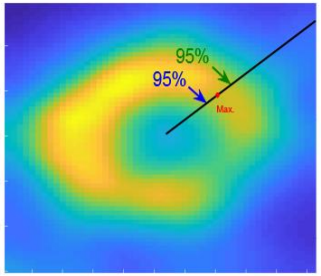
"Red" higher 18F-FDG uptake in control group than treated groups

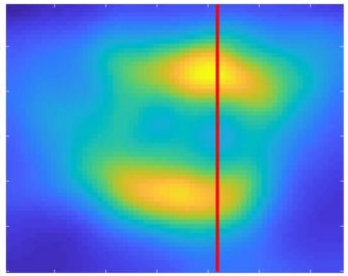
PET Gated Heart Study in Mouse Image Processing

Semi automatic orientation and delimitation

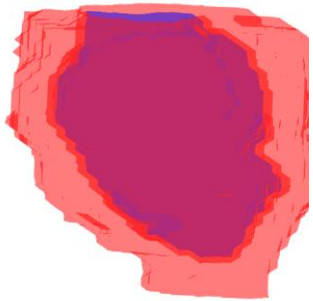


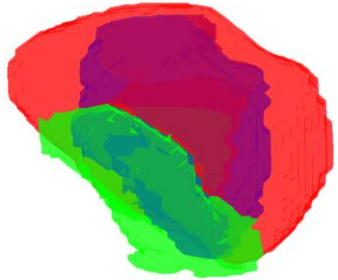
Automatic segmentation of VOI



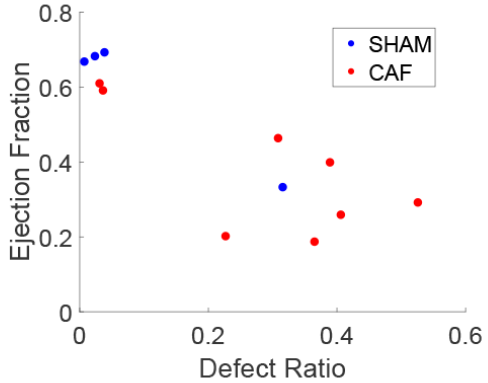


Automatic volume rendering





Statistical analysis



Conclusion

- State of the art imaging devices taking advantage of the latest technical developments
- Longitudinal study
- Translational tool (bench to bedside ↔ bedside to bench)
- Bring together experts from different fields

Thank you

Collaborators:
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