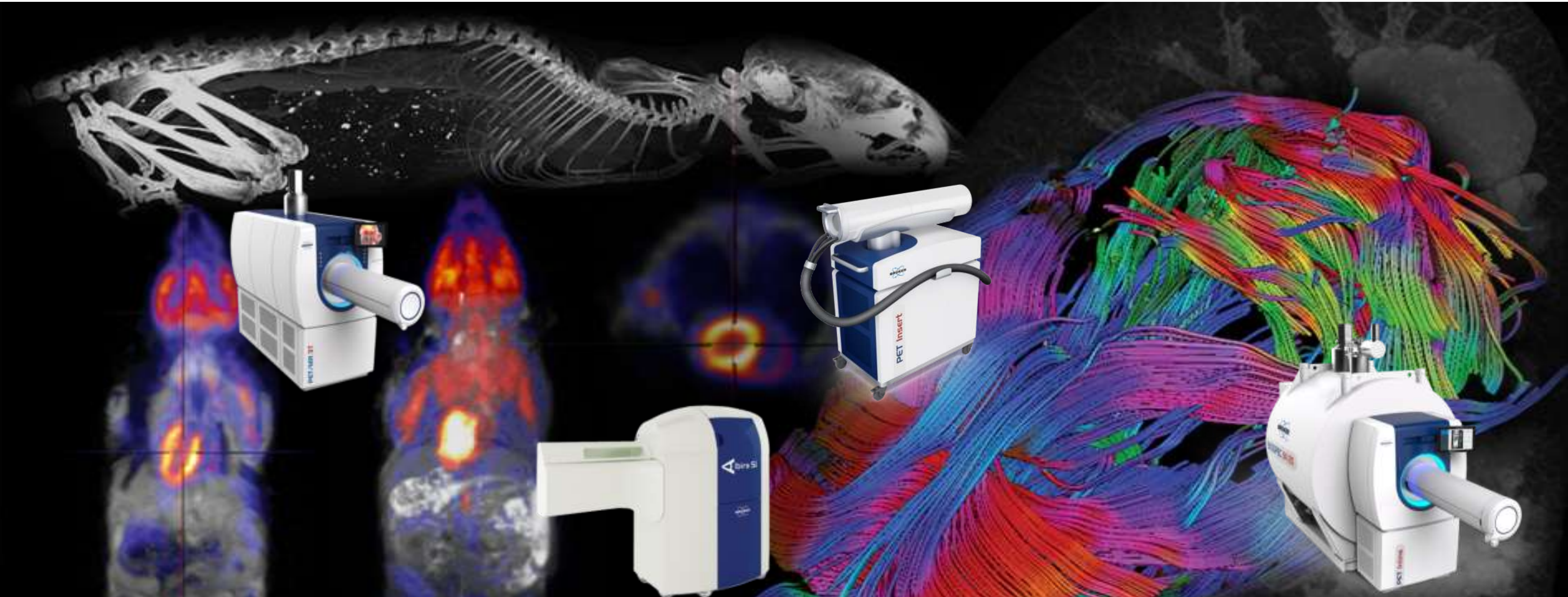
Adding color to your shades of grey: How PET/MR will level up your research

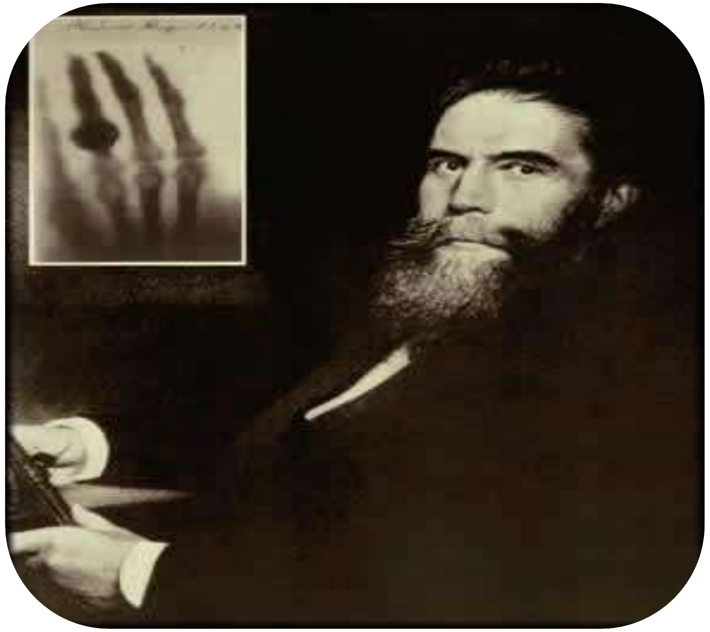
МЕЖДУНАРОДНАЯ КОНФЕРЕНЦИЯ
РЕАЛЬНЫЙ ПУТЬ ОТ НАУЧНЫХ РАЗРАБОТОК ДО ЛЕКАРСТВЕННЫХ СРЕДСТВ

Dr. Jens Waldeck
Bruker BioSpin Preclinical Imaging



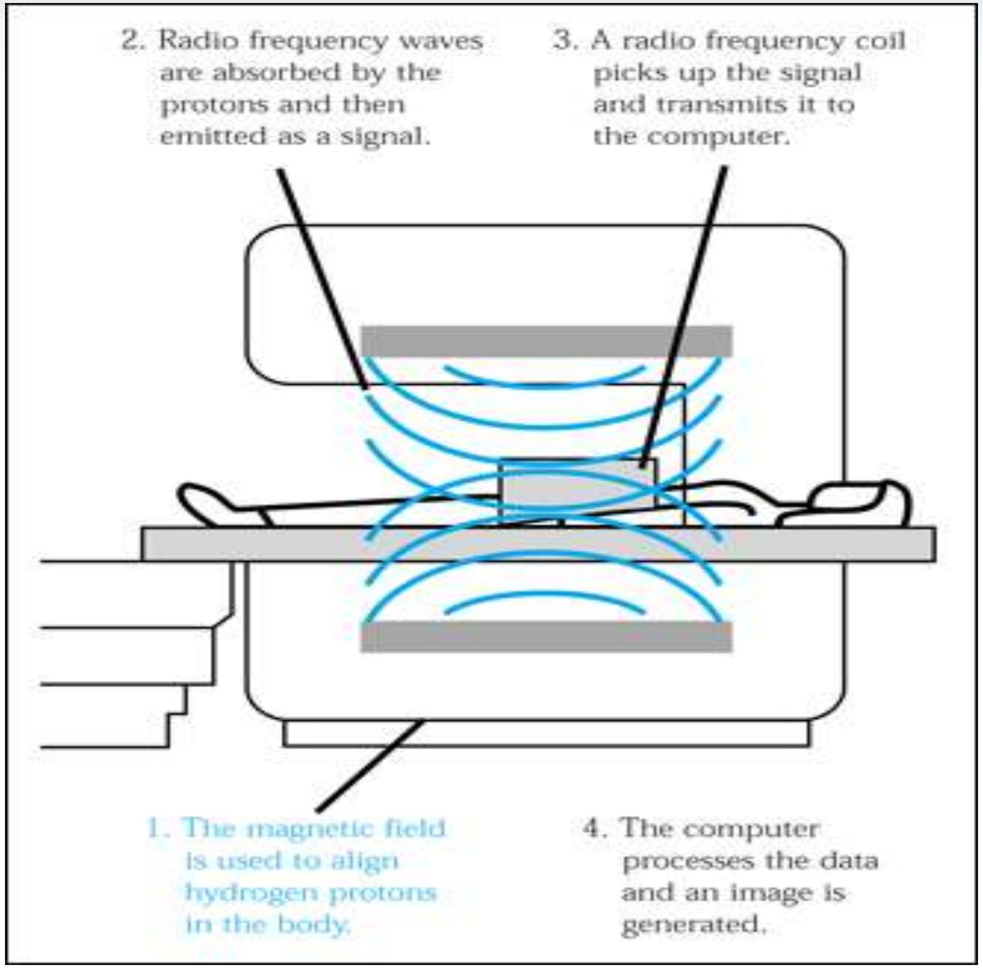
The long way to Preclinical Imaging

- 1895 Wilhelm Conrad Röntgen discovered the **X-rays**
- 1950 Brownell & Sweet identify brain tumor via backprojection of radioactiv signals
- 1969 First CT prototype by G. Houndsfield (scanning time: 9 days)
- 1969 CCD was developed
- 1973 first MRIs under development, e.g. by Bruker based on NMR knowledge
- 1974 first cross-sectional image of a living mouse using MRI
- 1975 M.E. Phelps and M. Ter-Pogossian publish first PET
- 1995 first transgenic GFP mouse
- 1997 first transgenic bioluminescent mouse
- 2001 first clinical PET/CTs
- 2007 first clinical PET/MRI prototypes
- 2010 first commercial clinical PET/MRI installations
- 2014 **first silicon PM based (Si) PET: Albira Si & sequential PET/MR**
- 2016 **first high field Si PET-Insert**
- 2018 ultra-low dose PET/CT – Si78

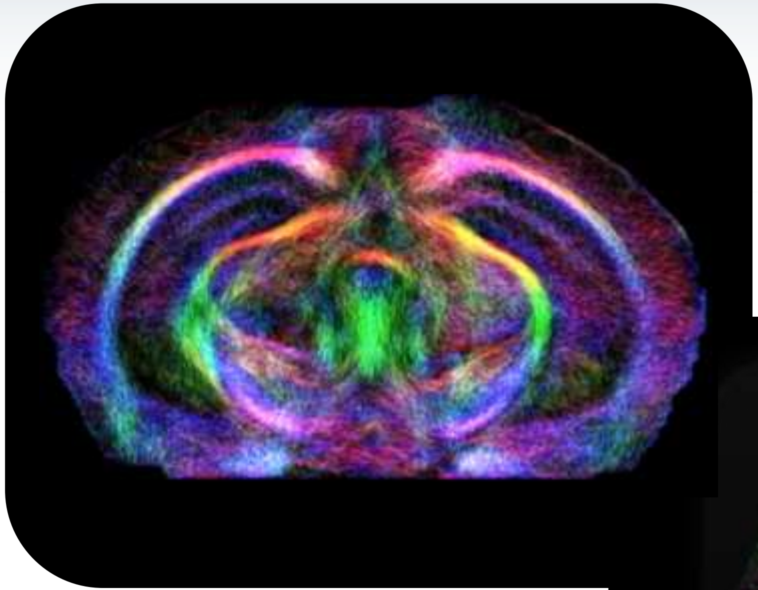


Micro-CT
SkyScan 1278 & Barium contrast agent

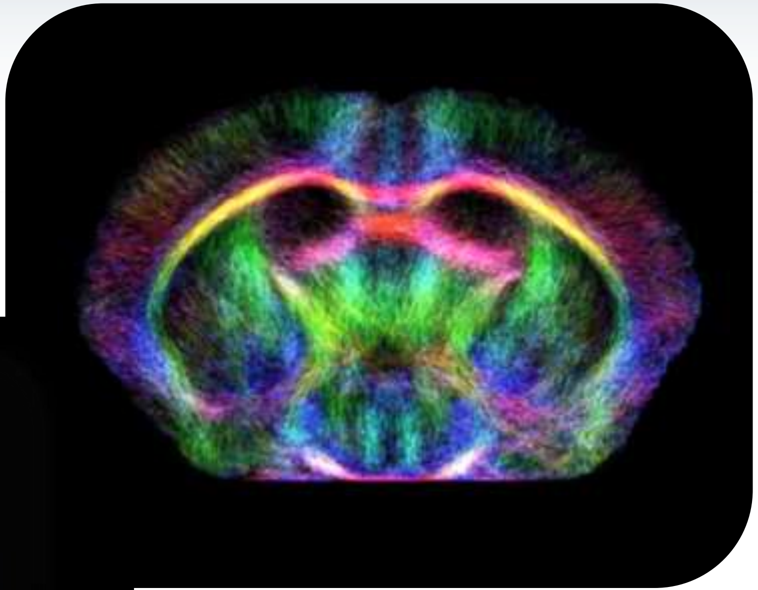
Magnetic Resonance Imaging (MRI)

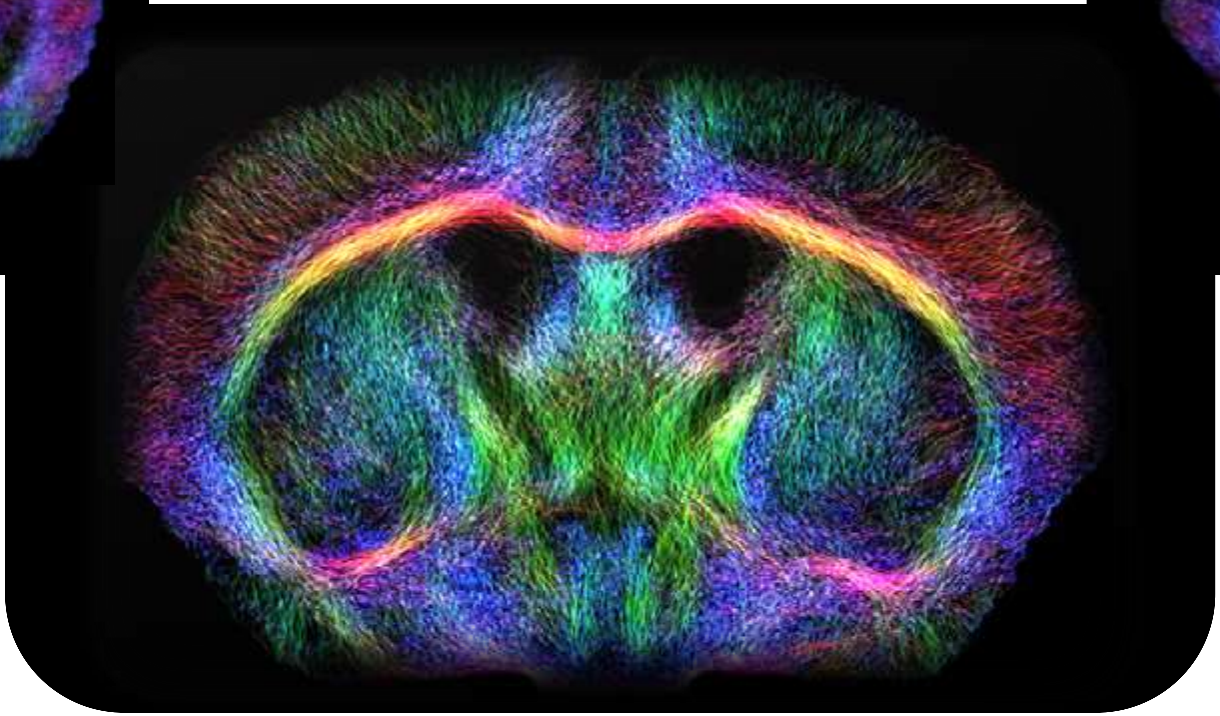


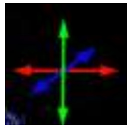
MRI High Resolution Fiber Tracking



Less than 16 μm in plane resolution yields excellent fiber tracking images



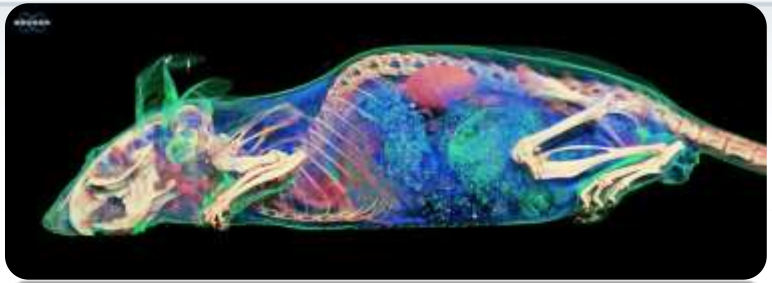


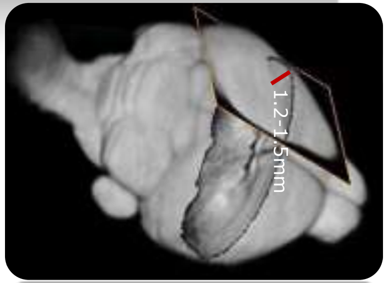


BioSpec® 70/20 USR, *MRI CryoProbe™*
Animal: mouse
Acquisition details: DTI-EPI,
diffusion directions: 30,
resolution: (12.5 × 15.5 × 50) μm^3,
scan time: 25 min
Courtesy: L.-A. Harsan, D. von Elverfeldt et al.,
University Medical Center Freiburg, Freiburg, Germany

MRI/CT

Excellent soft/hard tissue contrast, but limited sensitivity



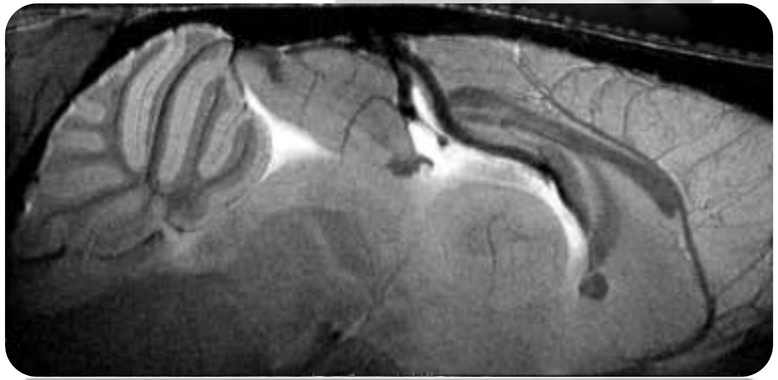


Advantages:

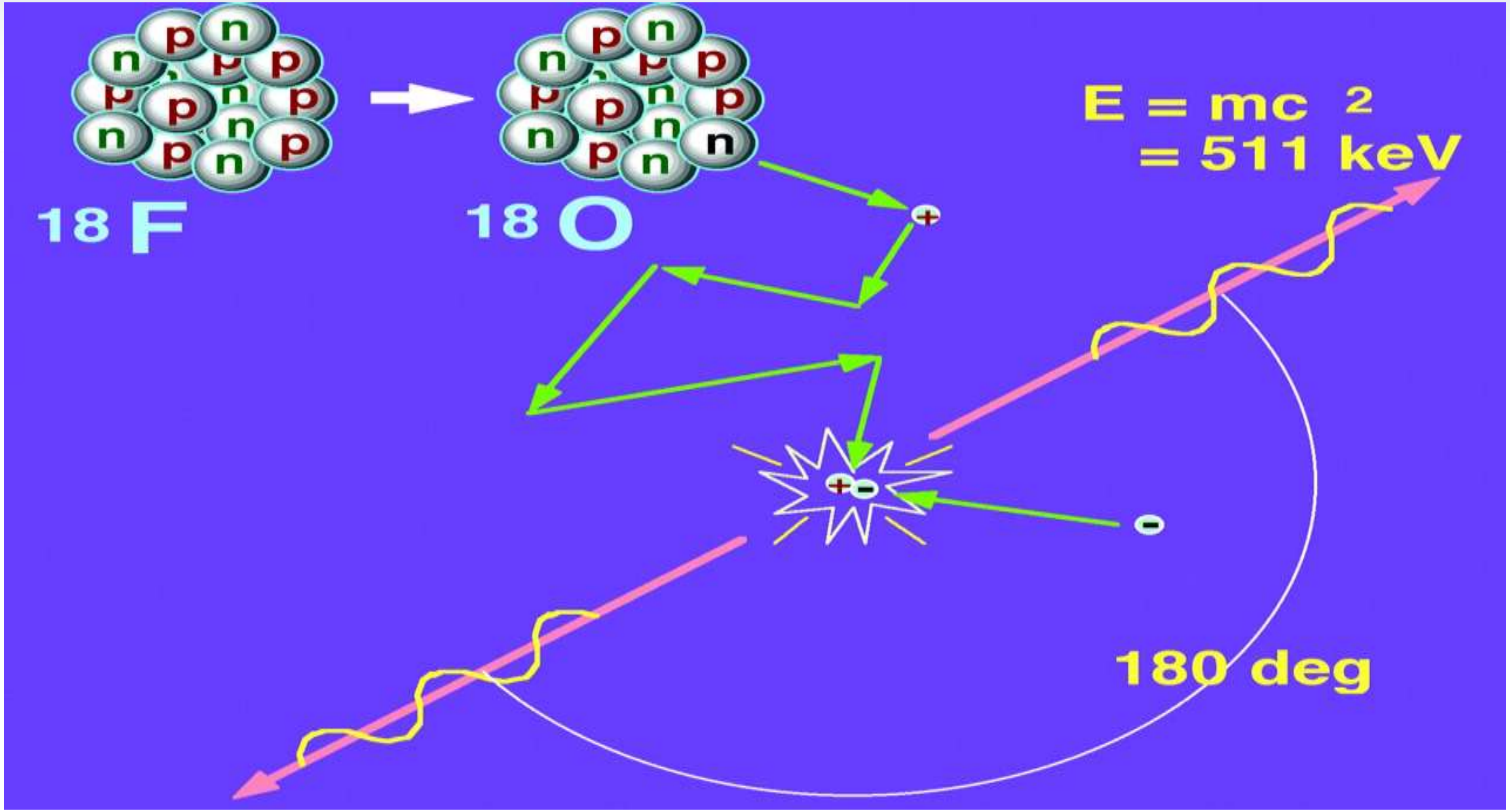
- high-resolution and anatomical information details
- excellent MRI soft/ CT hard-tissue contrast
- MRI: ability to measure a variety of physiological, metabolic and biochemical parameters.
- Semi-quantitative(MRI)/quantitative (CT)

BUT:

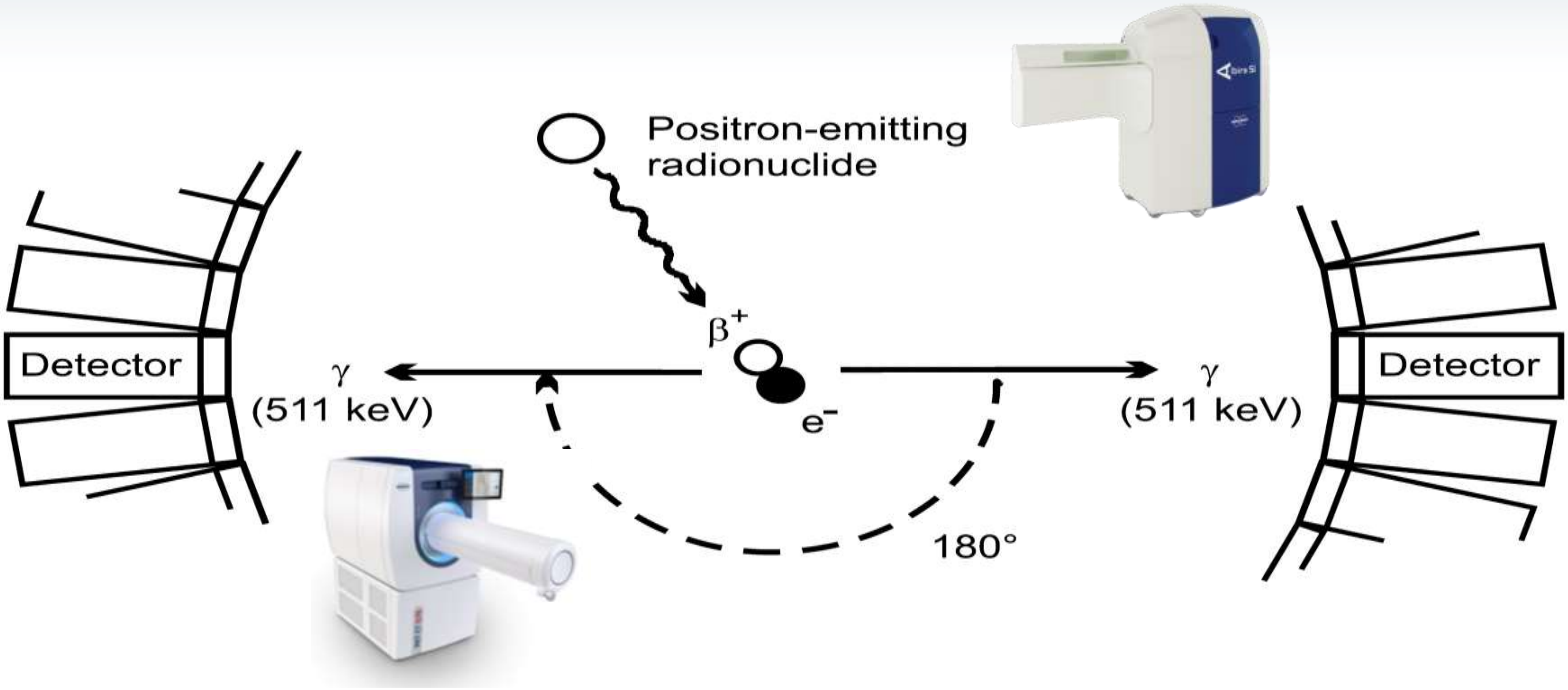
- low (molar) sensitivity of MR
- limited number of probes (MRI: Gd, Fe; CT: Iodine, Ag)



In vivo **PET** Imaging



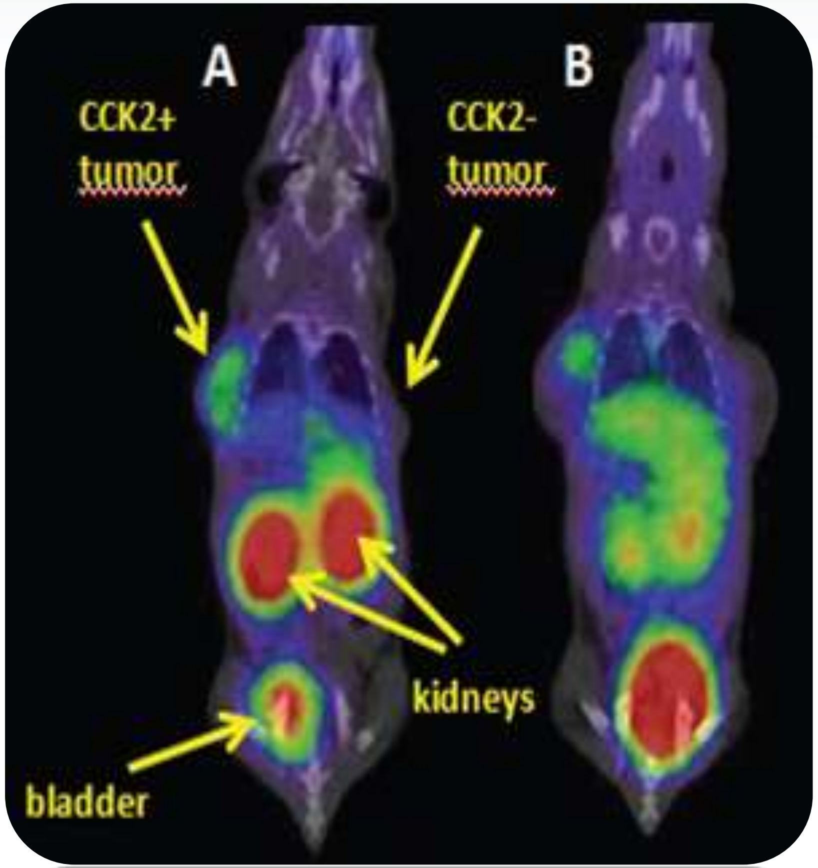
In vivo **PET** Imaging



PET
Excellent Sensitivity, but limited Anatomy

Advantages:

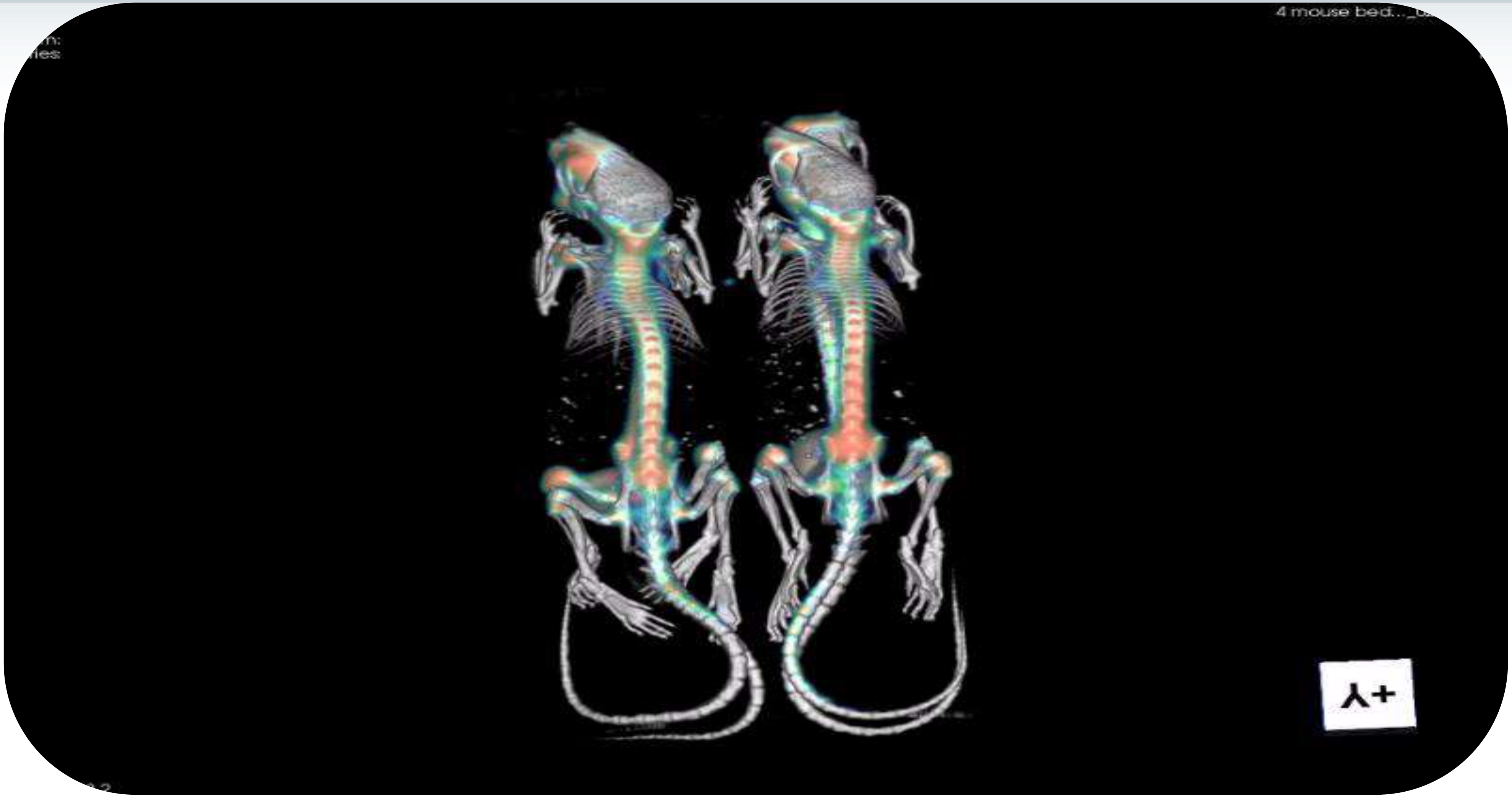
- High sensitivity
- Wide variety of tracers/probes (contrast agents)
- excellent soft tissue contrast
- Metabolic, kinetic and molecular information
- Quantitative



BUT:

- Limited resolution (e.g. ^{18}F: 0.7 mm)
- No hard and soft tissue information / anatomy

PET/CT



Is simultaneous PET/MRI (always) needed?

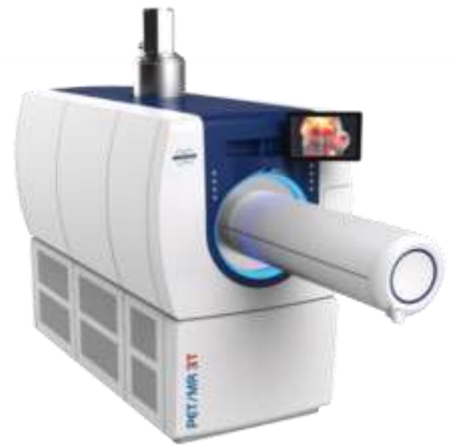
No:
- Classic single parameter scans
- "quick & dirty" evaluations
- Well established models, e.g. for treatment response studies

Maybe:
- Need for each method to help each other (e.g. attenuation correction, motion correction, partial volume…)

Yes:
- Multiparametic Imaging: cardiac perfusion; Metabolomics
- Need to reduce the anesthesia duration while acquiring complex data (severe disease models)
- dynamically evolving physiological/pathological conditions, e.g. brain activation/stroke
- Onco-omics
- …

The **PET/MR** Combinations
inline (sequential) or insite (simultaneous)

PET/MR 3T



- Clinical MR Field Strength
- compact
- high-performance imaging
- sequential PET/MR
- translational PET/MR

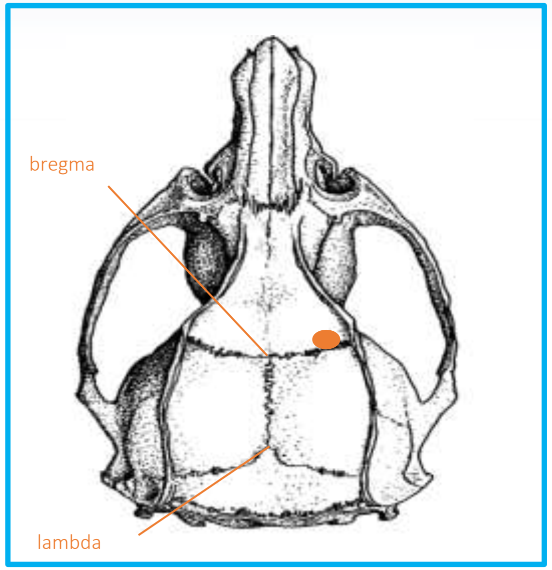
PET/MR Inline

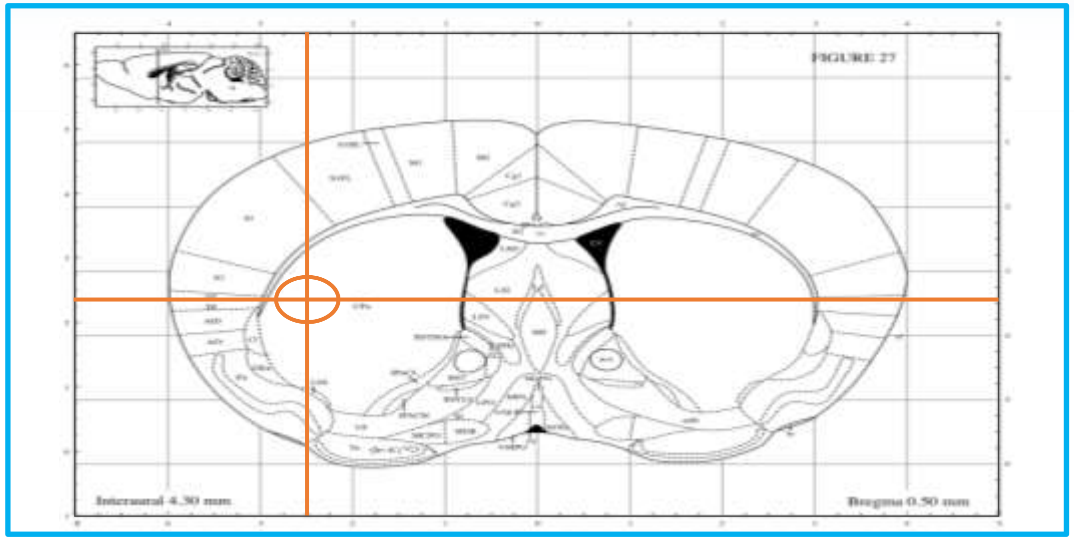
- high-field PET module
- for existing/new high field MR installations
- sequential PET/MR
- tested up to 15 Tesla

PET/MR Insert

- PET/MR insert for 4D correlation
- simultaneous
- for existing/new high field MR installations
- tested up to 15 Tesla

Murine glioma model





C57BL/6 mice; 12 weeks of ages

Cells = CT-2A murine high grade glioma cells

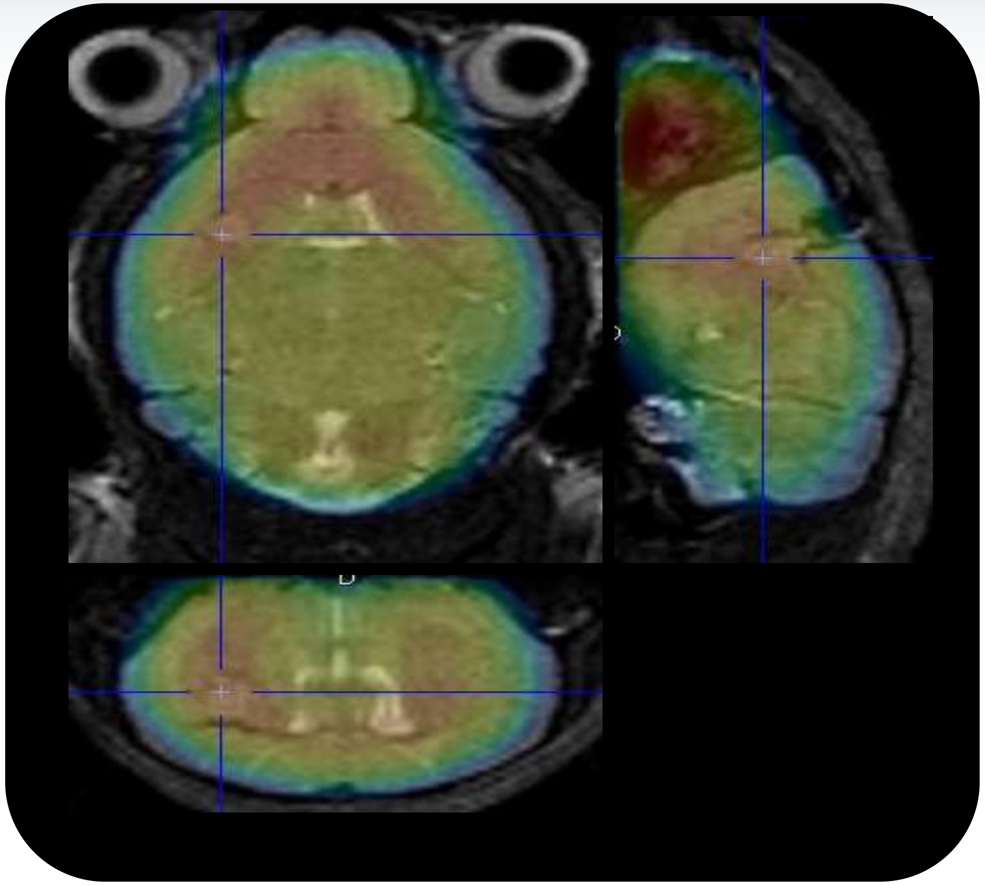
Challenge (seeing the implanted cells 8 days after implantation):

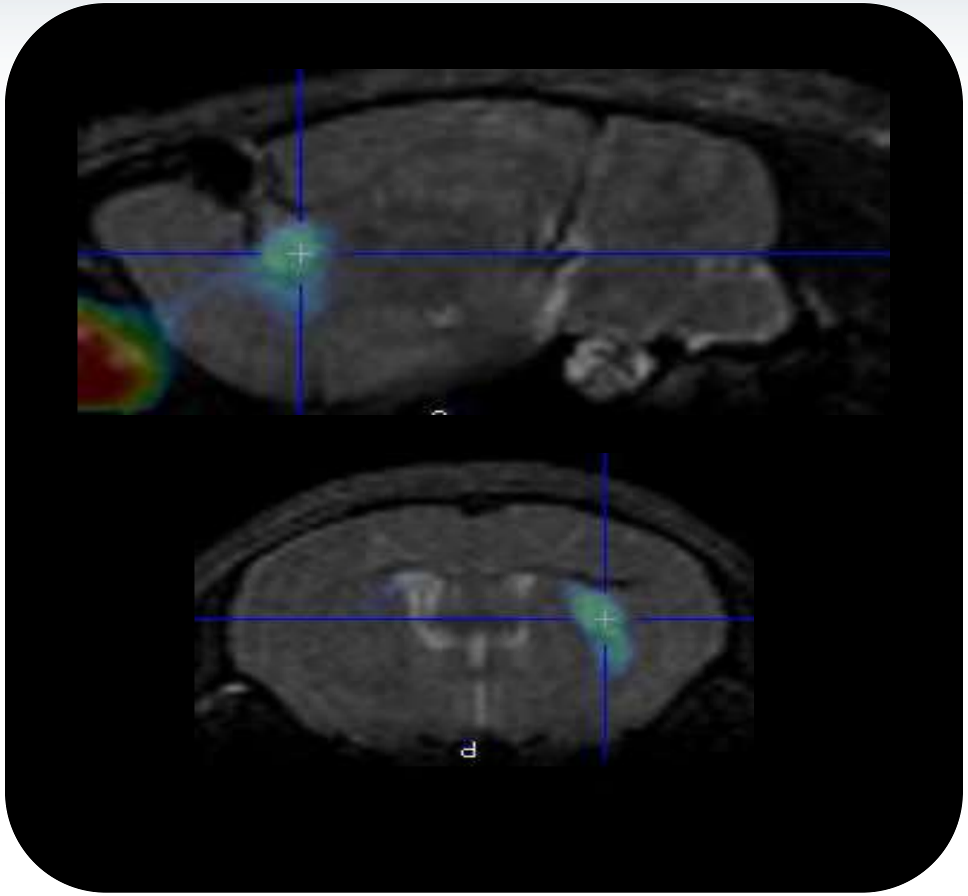
- small tumor = 5.000 cells

Anesthesia: 60 mg/kg ketamine + 0.8 mg/kg medetomidine i.p.

Courtesy of Matteo Riva, MD. matteo.riva@kuleuven.be

Glioma PET/MRI

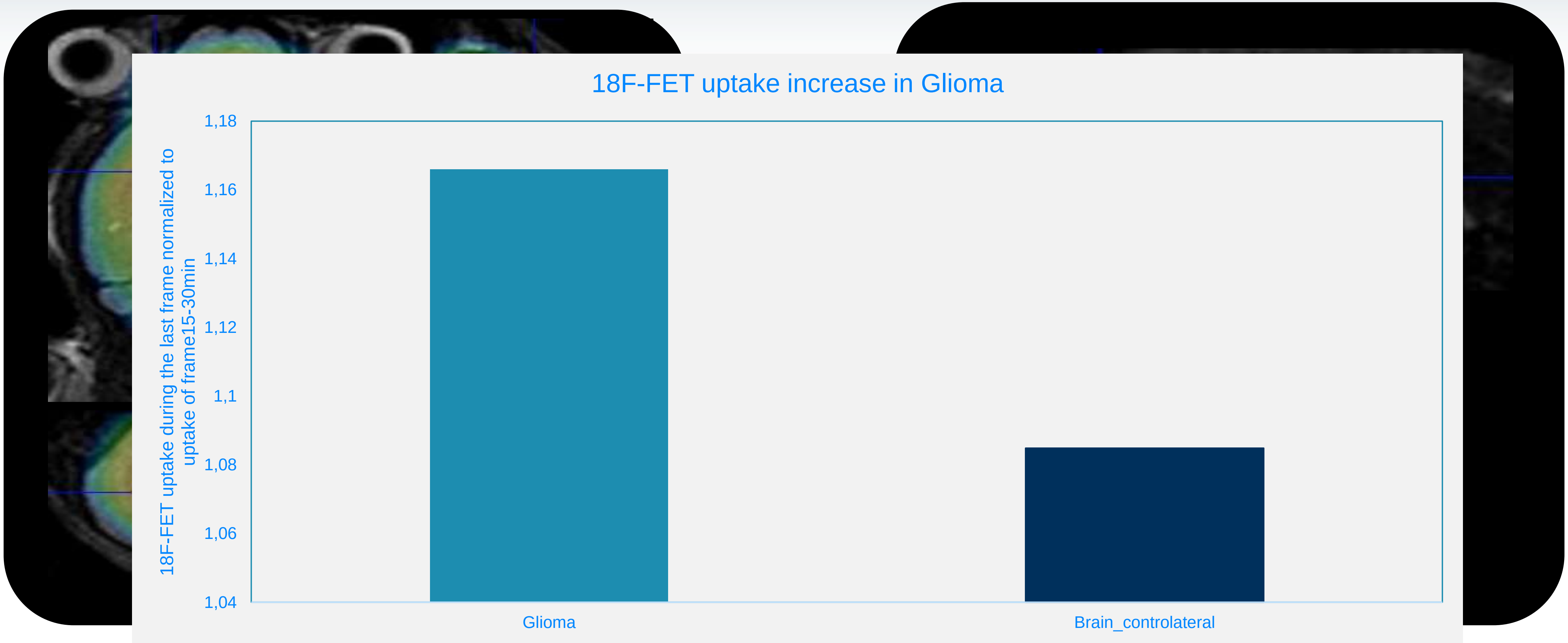




left: Registration between 3D T2w MRI and PET-FDG
right: visualization of FDG uptake by the glioma on the MRI overlay

Courtesy of Matteo Riva, MD. matteo.riva@kuleuven.be

Glioma PET/MRI

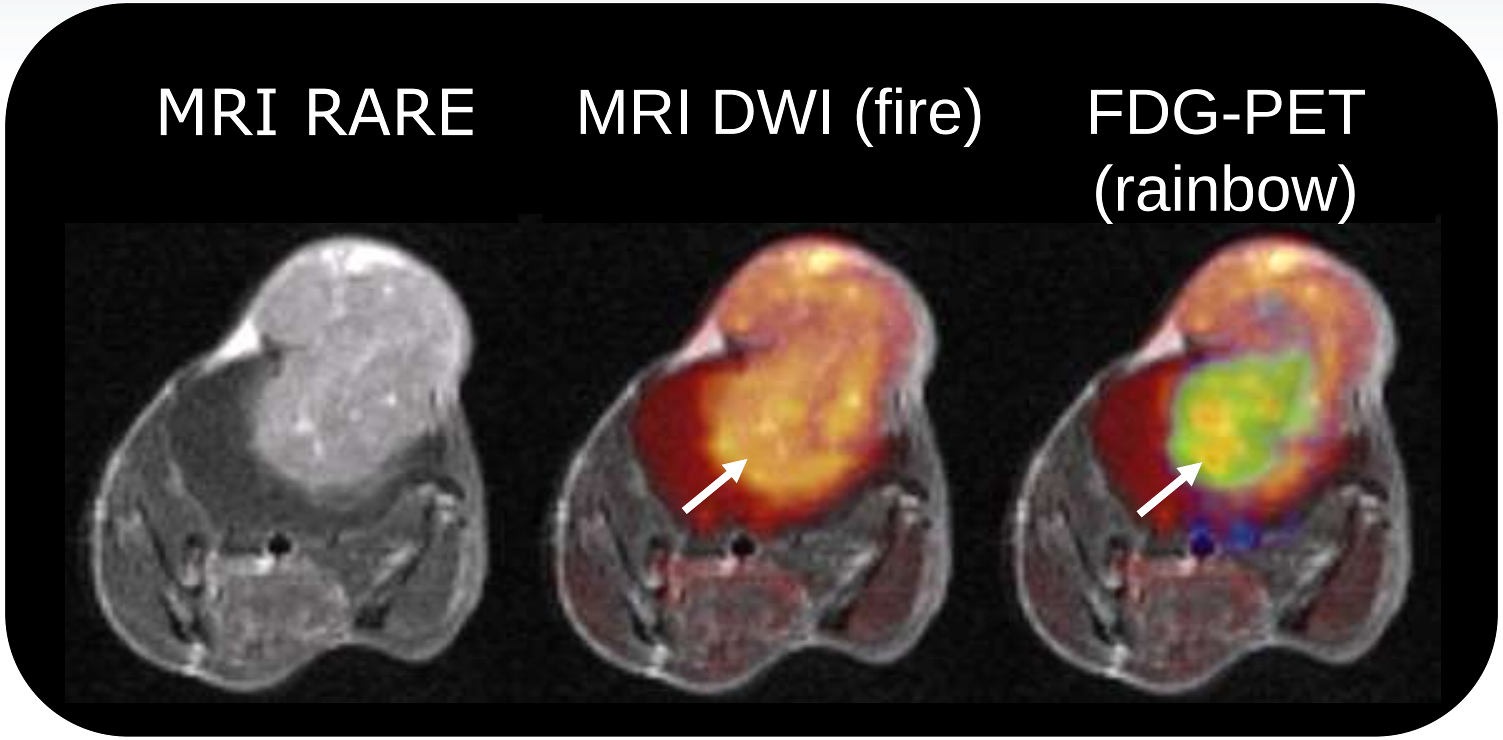


left: Registration between 3D T2w MRI and PET-FDG
right: visualization of FDG uptake by the glioma on the MRI overlay

Courtesy of Matteo Riva, MD. matteo.riva@kuleuven.be

Tumor Multiparametric - **Onco-omix**

- End stage glioma mouse model (50,000 CT-2A cells, 8 days post injection)
- Triple-overlay of FDG-PET, diffusion weighted images (DWI), and RARE MRI benefits from precise inherent co-registration
- FDG uptake showed heterogeneity in the tumor corresponding to regions with low diffusion suggesting loci of high cellular division (white arrow)

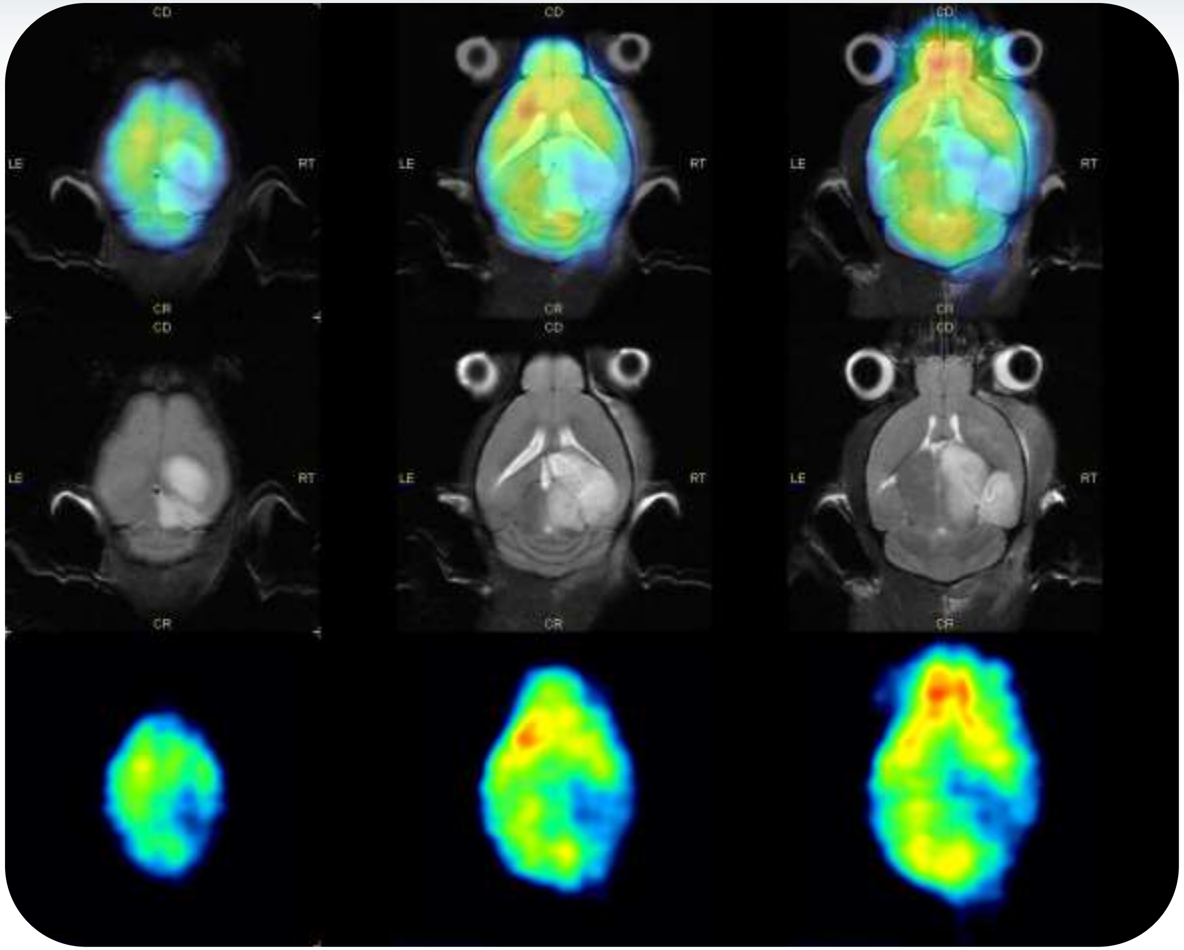


Acquisition details: MRI: T1-RARE, resolution: (195 × 195) μm², scan time: 1 min 17 s, DTI_SE, scan time: 10 min 40 s, 5 b-values: 5-1000 s/mm²
PET: 10.4 MBq ^{18}F-FDG, 10 min scan, 2 h after injection

Courtesy: Dr. Uwe Himmelreich, Dr. Willy Gsell, Dr. Cindy Casteels and Dr. Matteo Riva, Molecular Small Animal Imaging Center (MoSAIC), University hospital of Leuven, Belgium

Middle **C**erebral **A**rtery **O**cclusion (MCAO) PET/MR

- Ischemic MCAO mouse model (intraluminal transient MCAO, 24 h post occlusion / reperfusion)
- High resolution MR enables the location of the lesion including the vasogenic edema corresponding to the low FDG uptake (core of the lesion)

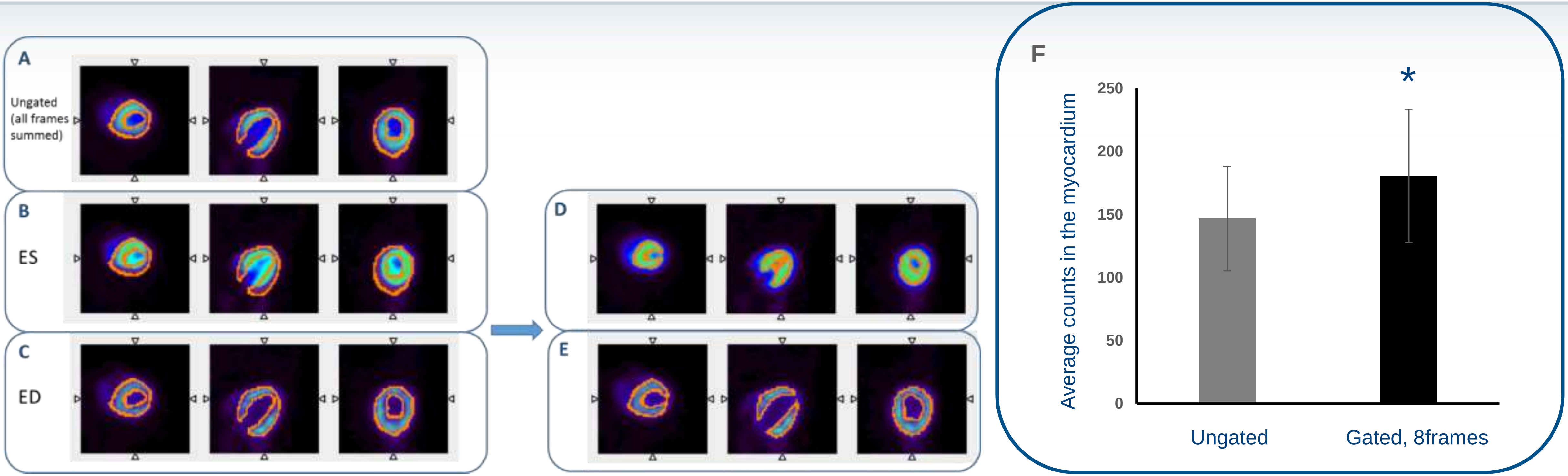


Acquisition details: MRI: Turbo-RARE, resolution: (86 × 86) µm^2, PET: 13.6 MBq ^{18}F-FDG, 45 min scan, performed 20 min post injection

PET technology developed in cooperation with ONCOVISION and i3M

Courtesy: Dr. Uwe Himmelreich, Dr. Willy Gsell, Dr. Cindy Casteels, Molecular Small Animal Imaging Center (MoSAIC), University hospital of Leuven, Belgium

Gated vs. non-gated PET



Error estimation in myocardial FDG uptake. A: 3D isocontour determined from ungated FDG scan (summation of all cine frames). B and C: corresponding views of the same region of interest on the end systole (ES) and end diastole (ED). D and E: refined region of interest for ES and ED extracted from gated scan. The difference between gated and ungated estimation of myocadial FDG uptake resulted a significant underestimation of 22 $\pm$ 6 % in the ungated evaluation compare to gated scan (P<0,05 paired t-test, N = 7).*

Can MRI improve PET gating?

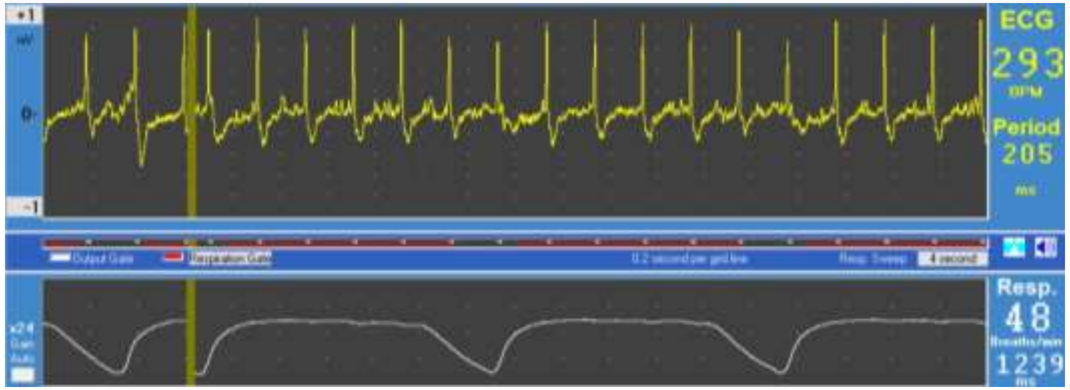
Problem:
ECG might not be possible especially when using MRI or severe infarcted animals.

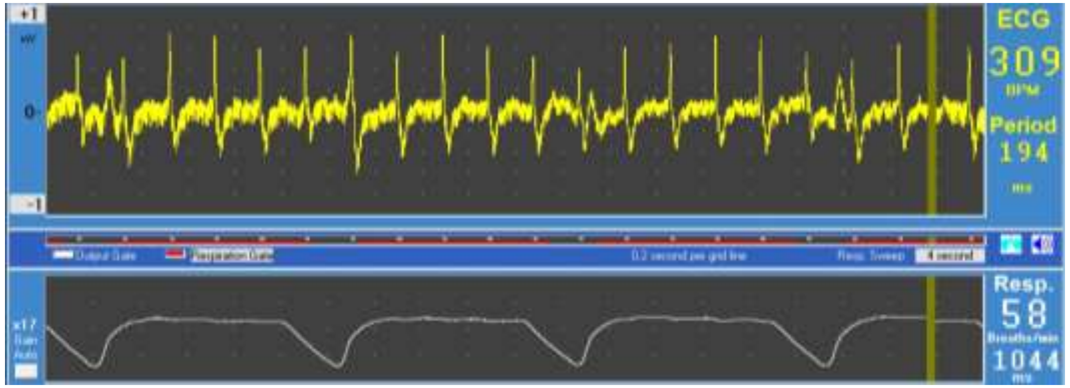
Solutions?

- Use of navigator based self-gated (Intragate) MRI sequence?

- Intragate provides accurate measurement of ejection fraction (Bovens et al., NMR Biomed. 2011; 24: 307–315).

- Simplify the animal handling and the potential attenuation caused by ECG electrodes



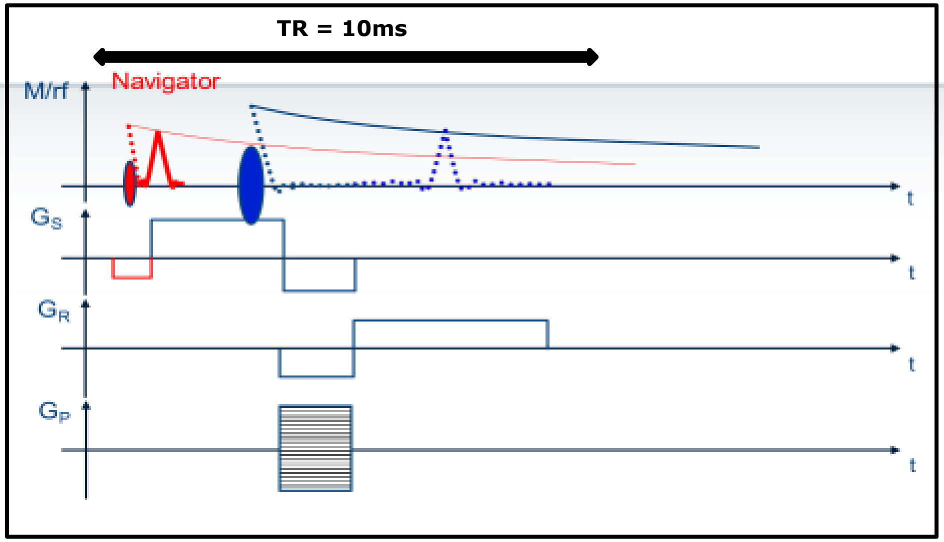


… so to say…

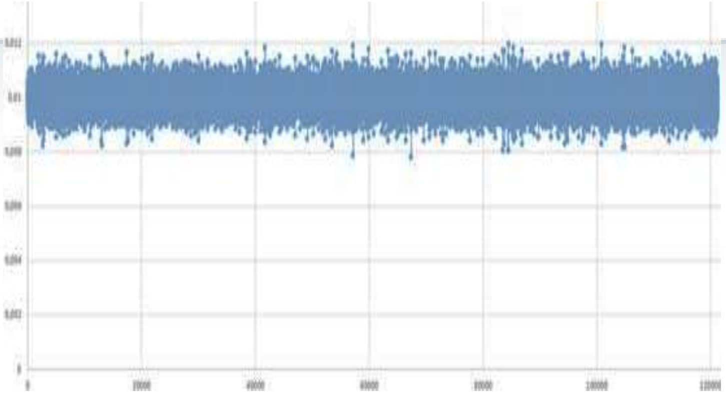
non-gated

gated

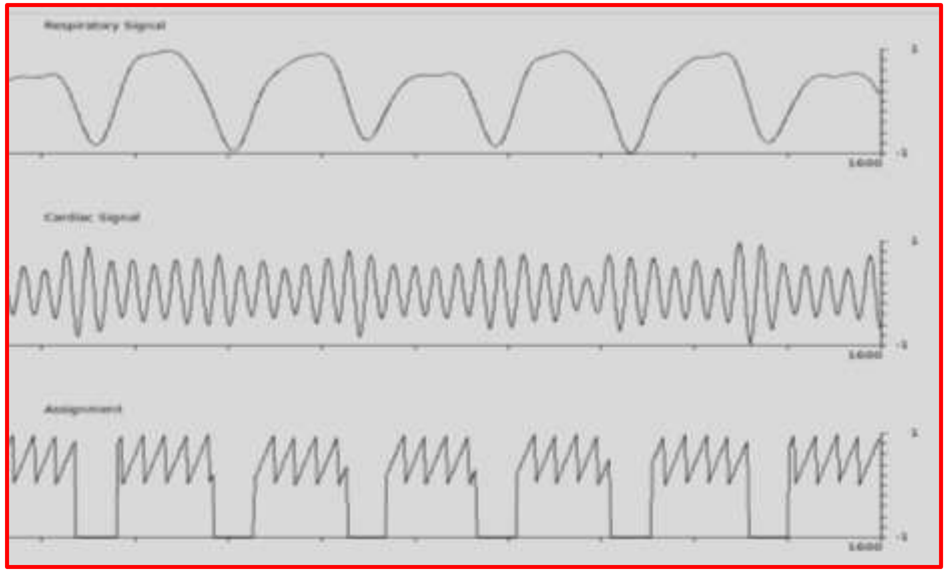
Methods

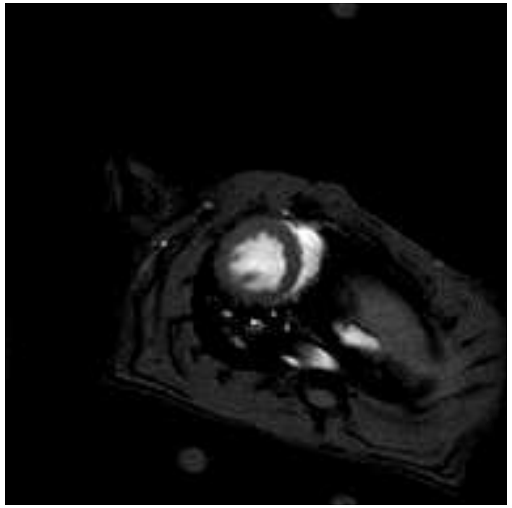


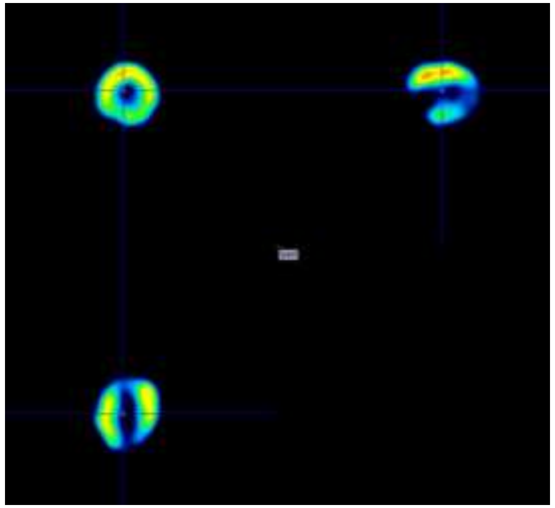
TTL signal generated by MRI for each TR



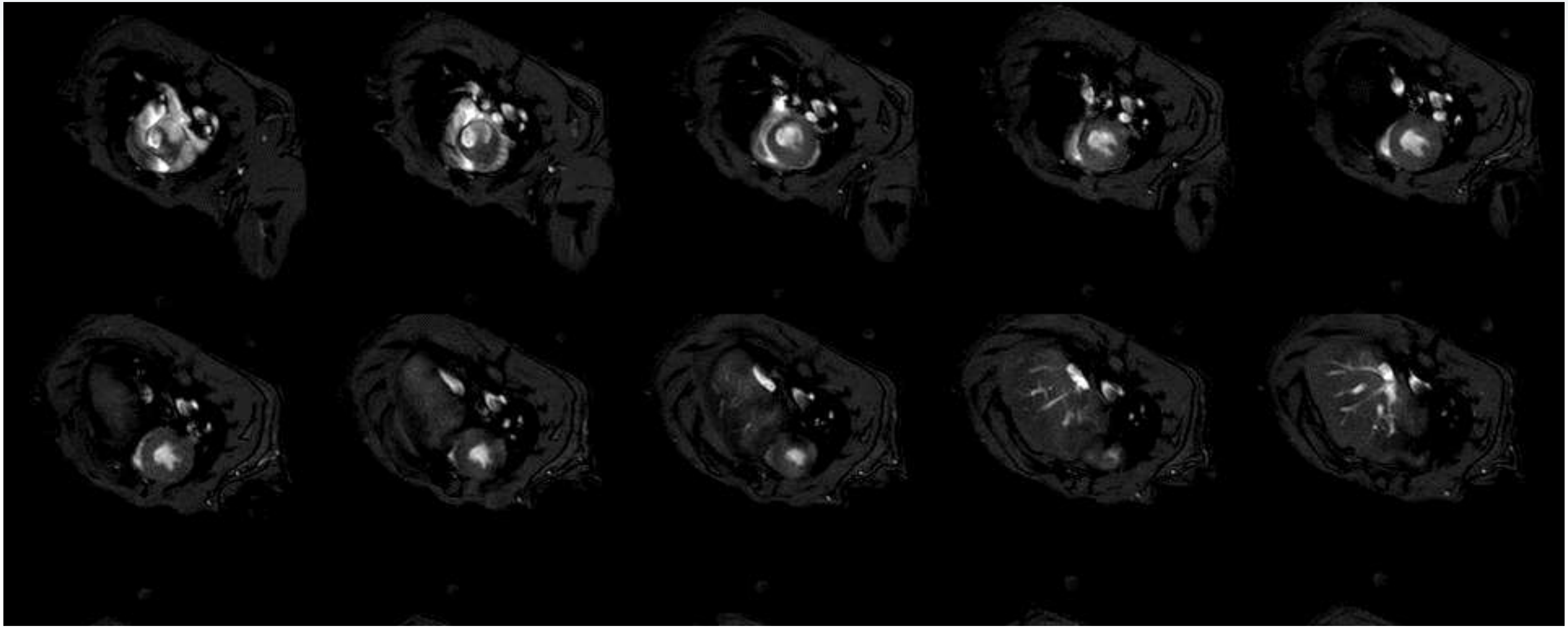
Listmode rebinning with frame duration equivalent to MRI repetition time (10ms) and sorting according to the MRI intragate information





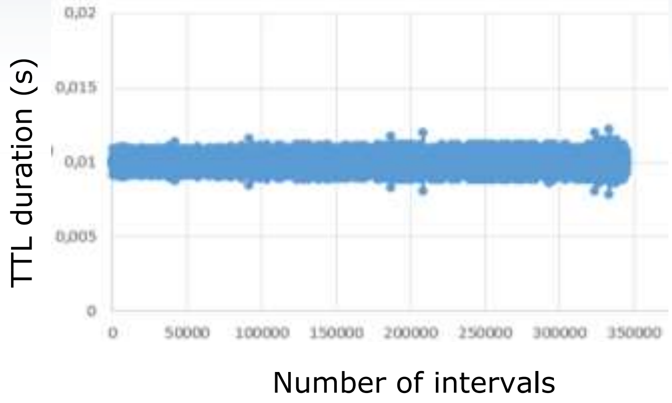


IntraGate MRI Results

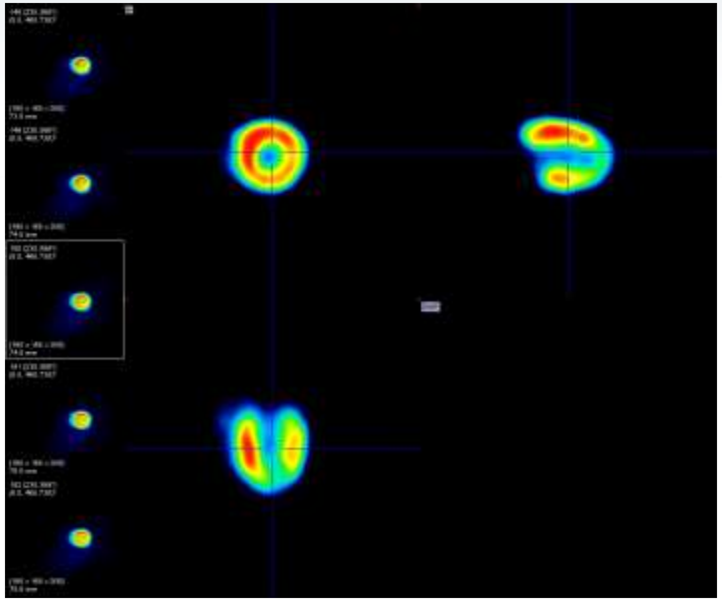


PET gating via *a priori* MRI Intragate Data

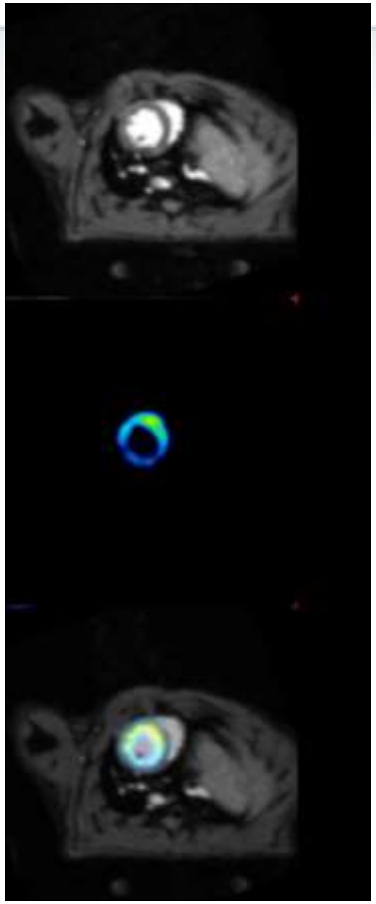
PET TTL detection



- PET TTL detection: 345600 intervals with an average of 10,0002677ms duration
- MRI intragate: 345600 loop with TR of 10ms



PET data are then sorted by combining both PET gatelist and intragate files



Results: Image quality

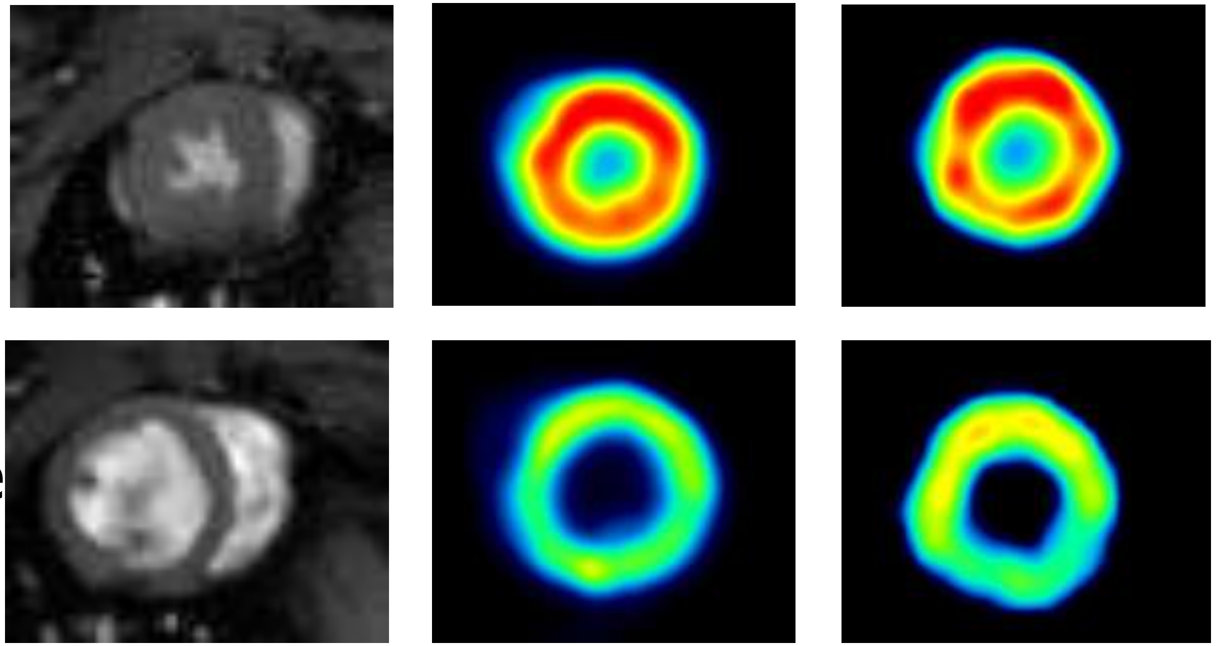
MRI
(n = 4)

ECG-PET
(n = 4)

IntraGate
PET/MRI
(n = 4)

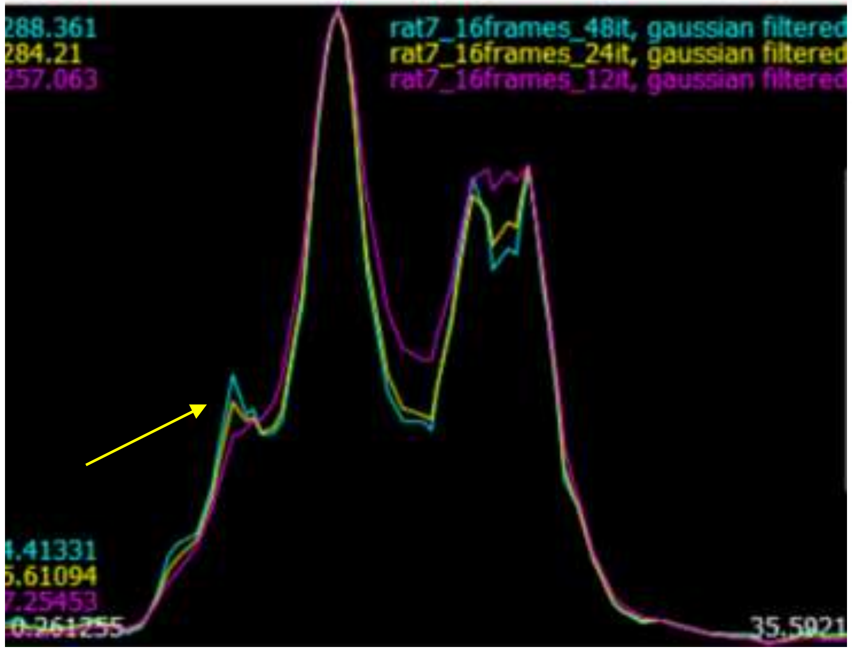
End systole

End diastole

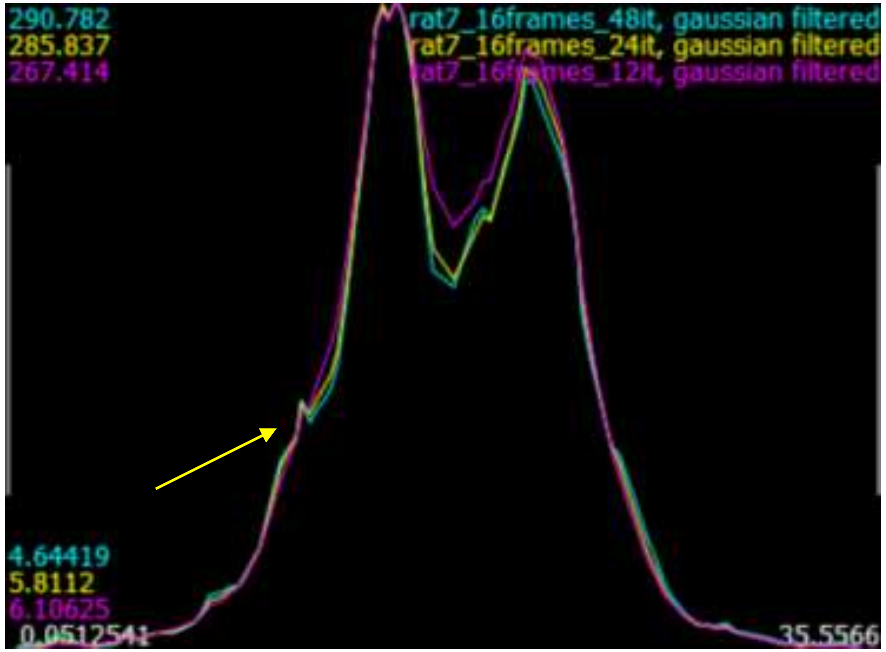


ED/ES IntraGate Data

ED



ES

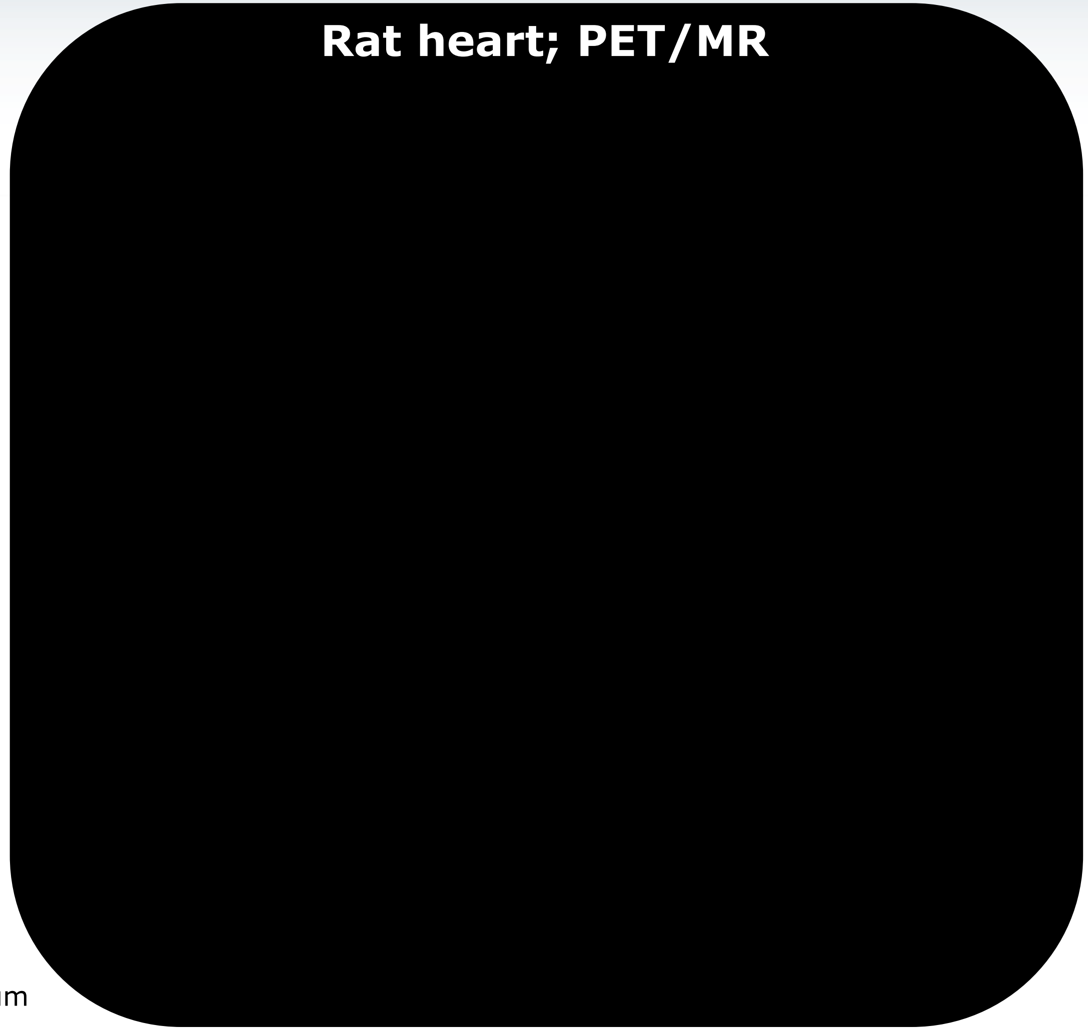


Line profile accross the mycardium in short axis view. Data reconstructed with 12, 24 and 48 iterations. Note the right myocardium visible at end diastole and end systole with 48iterations

Cardiac PET

- **IntraGate-PET:** Unmatched cardiac PET imaging based on MRI Self-Gating
- **4D Real Time** combination of PET tracer kinetics and functional MRI

→ **Unique** applications and improved PET imaging



Courtesy: Dr. Uwe Himmelreich, Dr. Matteo Riva, Dr. Willy Gsell, Dr. Cindy Casteels,
Molecular Small Animal Imaging Center (MoSAIC), Katholieke Universiteit Leuven,, Belgium

Conclusion

MRI

- Offers superior tissue contrast
- High resolution
- AT correction
- Helps in analysing the PET
- IntraGate movement correction
- A priori information

PET

- Overcomes MRI semi-quantitativenes
- Adds high sensitive molecular, kinetic, pharmacodynamic and/or metabolic info
- Offers cross-validation
- Most flexible and dedicated in terms of (clinical) tracers

…

Innovation with Integrity

Acknowledgements

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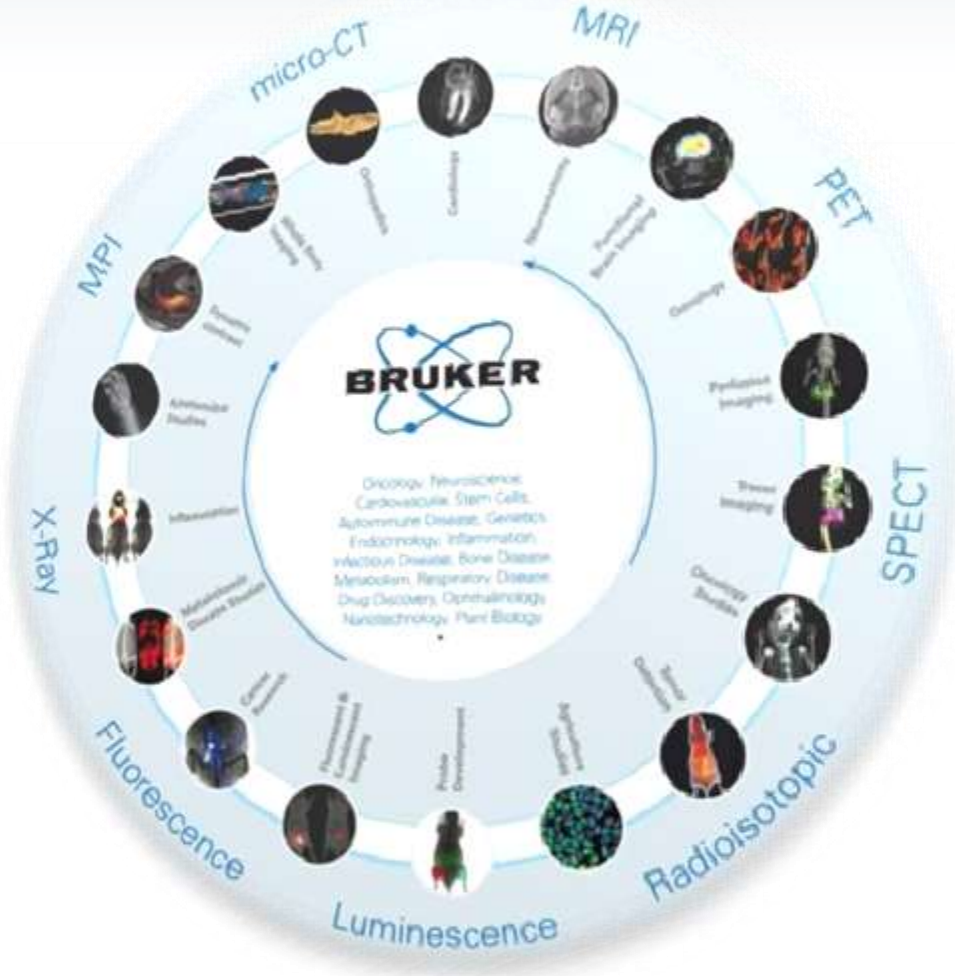

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"We are looking forward to boosting our imaging capabilities with the 9.4T Bruker BioSpec. The integrated PET module will help us to gain new and exciting insights into our preclinical cancer models."

Mark Ladd, DKFZ, Heidelberg, Germany

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"We are very delighted to upgrade our existing BioSpec® 94/30 with the PET Insert from Bruker to enable cutting edge simultaneous PET/MR applications"

Prof. T. Helbich, Preclinical Imaging Lab., Medical University of Vienna

PET Insert for simultaneous PET/MR on Bruker BioSpec® 30 cm systems

PET Insert for High Field MRI
Pioneering Preclinical PET/MR

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"The combination of high resolution molecular information and exquisite anatomical contrast will bring oncological small animal imaging to a whole new level. We will extensively explore the system's possibilities in oncology and also improve cardiological and neurological imaging"

Christophe Deroose, KU Leuven, Belgium

Bruker PET Insert for High Field MRI

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"Theranostics is a growing oncological field allowing nuclear medicine physicians and scientists to quantify the presence of cellular and molecular targets in a given patient first with a diagnostic radioisotope, before treating the disease with the same radiopharmaceutical but labelled with a therapeutic radioisotope.

The multimodal capabilities of our Albira Si PET/SPECT/CT are playing a key role in pioneering our theranostics translational research programs"

— John Prior, PhD MD, Lausanne University Hospital and Swiss Cancer Center Lausanne, Switzerland

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