Challenges towards simultaneous PET-MRI

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On behalf of Hyperimage collaboration

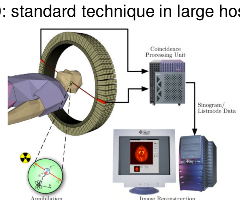
CERN physics for health workshop, February 2010

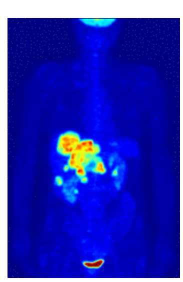
Overview:

1. Why do we want PET-MRI ?
2. Concepts for small animal, brain and whole body PET-MRI
3. The Hyperimage project
4. Attenuation and motion correction for PET-MRI
5. Future prospects

Positron Emission Tomography

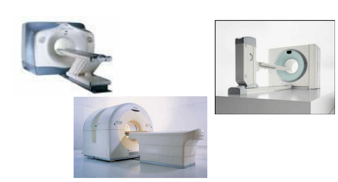
- During 80 and 90s mostly a research tool
- Since 2000: standard technique in large hospital in EU/US for diagnosis of cancer

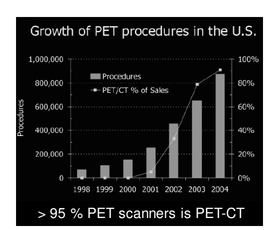




- Provides functional information:
  - Blood flow
  - Oxygen use
  - Glucose metabolism

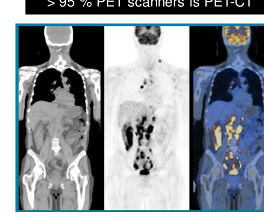
PET-CT is the new standard





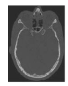
Why PET-CT instead of PET ?

- FDG-PET shows tumors and CT helps in localization
- Higher specificity/sensitivity versus separate PET and CT
- Hardware based image fusion is easier
- Faster acquisition, CT for attenuation correction

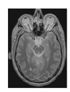
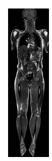


Why hybrid MR-PET ?

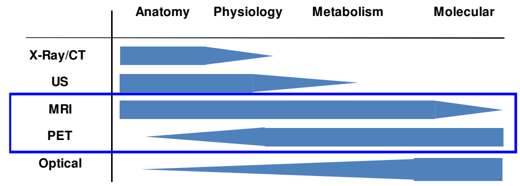
- **Sequential PET-CT** technically simple
  - 90 % oncology (whole body PET-CT)
  - CT low contrast in soft tissue (brain)
  - Sequential scanning (motion inbetween scans)
  - Radiation dose of CT is high (70-80 % of PET-CT study)

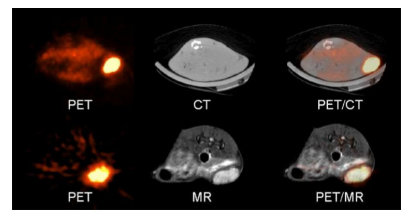



- **Simultaneous MR-PET** technically challenging, but large potential
  - Clinical indications
    - Neuro: Alzheimer, epilepsy, tumors,...
    - Mammography
    - Pediatric scans
    - Combination of PET and fMRI, MR spectroscopy, diffusion tensor MR
  - Additional advantages compared to CT
    - MR based motion correction
    - Lower radiation dose for follow up studies

Role of Imaging Modalities





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Source: Ralph Weissleder

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1. Why do we want PET-MRI ?
2. **Concepts for small animal, brain and whole body PET-MRI**
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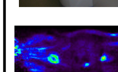
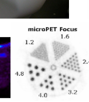
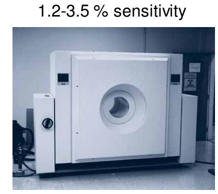
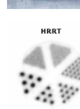
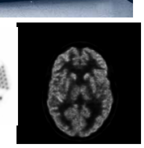
Small animal PET
1-2 mm resolution
4-12 cm FOV
2-10 % sensitivity

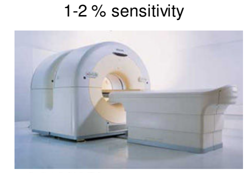
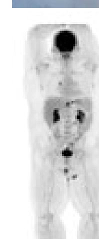
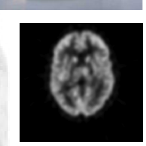




Brain PET
2-3 mm resolution
30 cm FOV
1.2-3.5 % sensitivity

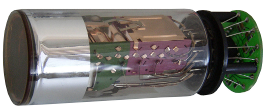


Whole body PET-CT
4-6 mm resolution
50-60 cm FOV
1-2 % sensitivity

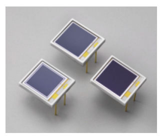




*Lammertsma et al.

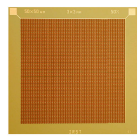
Different Sensor Technologies



PMT
Reliable
Cheap but bulky
used in all whole body scanners



APD
Temperature sensitive
Used in some brain and small animal systems

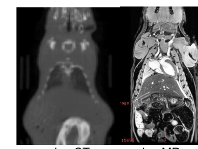


SiPM
Very new technology
Only in small prototypes

Type	PMT	APD	SiPM
MR compliant	no	yes	yes
ToF compliant	yes	no	yes

*Schulz et al.

What do we want in near future ?

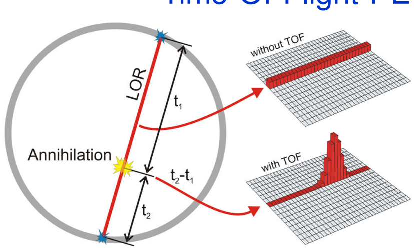


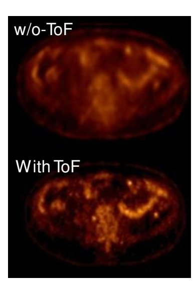
Next generation small animal PET
- Smaller detector pixels --> spatial resolution below 1 mm
- Depth of interaction improve uniformity of spatial resolution
- Larger axial FOV --> scan complete mouse or rat in one position
- PET-MR --> a lot better soft tissue contrast than PET-CT

Next generation brain PET
- Improved energy resolution --> reduce scatter
- Small coincidence window reduce randoms
- Depth of interaction --> improve uniformity of spatial resolution
- In some cases PET-MRI is very interesting

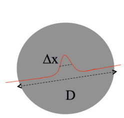
Next generation whole body PET
- Improved energy resolution --> reduce scatter
- Small coincidence window --> reduce randoms
- Time-of-Flight PET below 500 ps --> improve image quality for same counts
- PET-MR or PET-CT

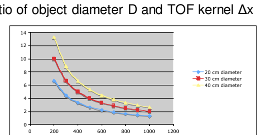
Whole body imaging benefits most from Time-Of-Flight-PET





TOF gain proportional to ratio of object diameter D and TOF kernel Δx





*Karp et al.
* Egger et al.

Design issues: PET

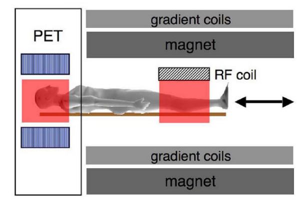
- Sensitivity to magnetic field
  - Static field (1.5 – 11.7 T)
  - Gradient fields (20 – 100 mT/m)
  - Radiofrequency pulses (64 – 500 MHz)
  - RF interference in electronics
  - Generation of eddy currents in electronics
- Geometric constraints
  - Fit inside the bore of MR
- Attenuation correction for PET-MRI

Design issues: MRI

- Magnetic field inhomogeneity
- Gradient nonlinearity
- Susceptibility artefacts

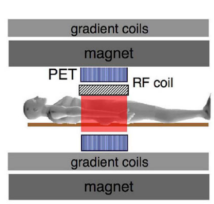
Design: “tandem”

- Minimal interference
- No geometric constraints
- Use existing systems
- Not simultaneous



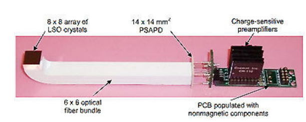
Design: “integrated”

- True simultaneous
- Higher throughput
- Temporal correlation
- Space for PET/enough FOV for whole body

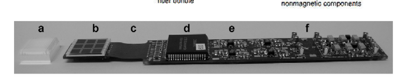


Detector Concepts for Simultaneous PET/MR

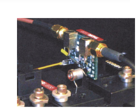
- Optical Light-Guides
  UC Davis / Simon Cherry



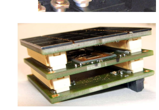
- Analog readout of APDs/SiPMs
  SIEMENS and Tubingen/ Pichler



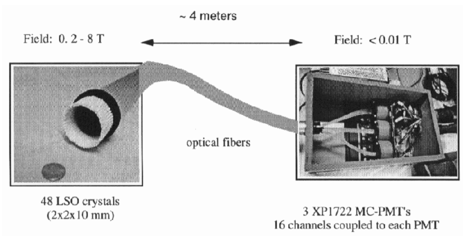
- Optical coupled readout of APDs/SiPMs
  Stanford University/ Craig S. Levin



- ASIC readout of analog SiPMs



First PET inserts



Issues with early systems

Very low PET sensitivity (only 48 scintillators)
Optical fiber attenuation
Reduced energy resolution
Reduced timing resolution

- 3.8 cm bore size
- 48 LSO scintillators
- Optical fibers => PMTs

Y. Shao et al., "Simultaneous PET and MR imaging," Phys. Med. Biol., vol. 42, pp. 1965–1970, 1997.

Split magnet MRI

- Radial optical fibers
- More scintillators
- 3D PET
- Time, energy resolution
- Low field strength

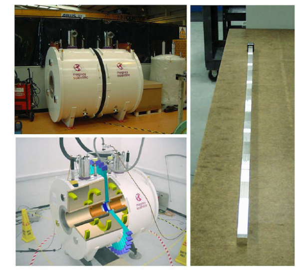
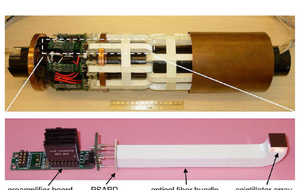


Fig. 4. *(a) Split magnet design for combined PET/MRI. (b) The PET detectors will be located in the gap with the optical fibers emanating radially as shown. (c) View of (front) a single PET detector module with scintillator array connected to (back) a position-sensitive PMT by optical fibers. Adapted with permission from [23].*

[23]: A. J. Lucas et al., "Development of a combined microPET(R)-MR system," Tech. Cancer Res. Treat., vol. 5, pp. 337–341, 2006.

PET/MRI with APDs: preclinical

- 1024 LSO scintillators
- PSAPDs inside bore but outside FOV
  - still uses optical fibers
- FOV = 35 x 35 x 12 mm³
- No significant interference between PET and MRI
- PET spatial resolution = 1.2 mm



C. Catana et al., "Simultaneous acquisition of multislice PET and MR images: Initial results with a MR-compatible PET scanner," J. Nucl. Med., vol. 47, pp. 1968–1976, 2006.

Small animal MR-PET Prototype *

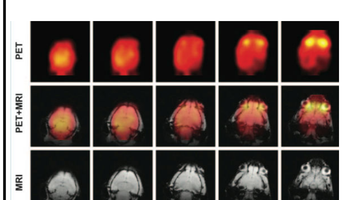
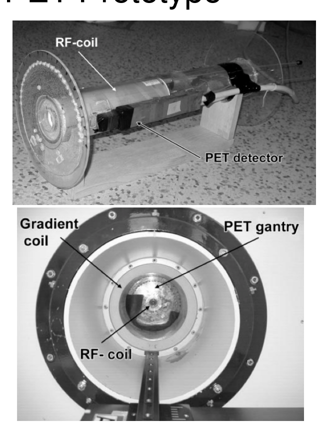


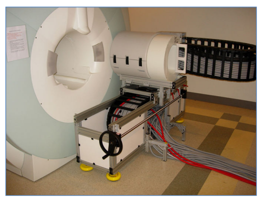
Figure 6: Simultaneously acquired PET (filtered back projection, 2.5-mm Gaussian postsmoothing filter) and coronal unenhanced fast low-angle shot MR (394/5.9, 40° flip angle, six signals acquired, 1-mm section thickness, 256 × 256 pixels) images of a mouse head injected with FDG. The fused PET/MR images show good alignment of images acquired with the two imaging modalities. The increased uptake of the PET images correlates with the location of the Harderian glands behind the eyes in the MR images.

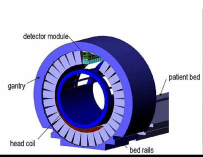


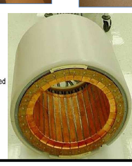
* Judenhofer, Pichler, university of Tuebingen

Brain MR-PET Prototype scanner*

Siemens BrainPET prototype scanner installed inside the MAGNETOM TIM Trio MR scanner (left); BrainPET withdrawn from the MR scanner for stand alone MR operation (right)



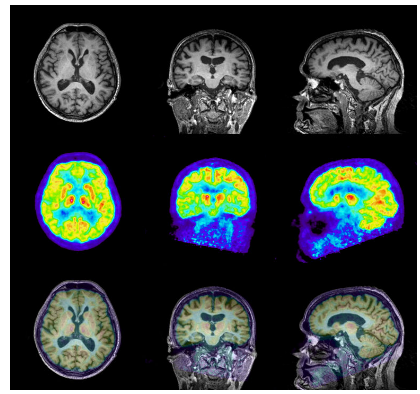




- 23040 LSO scintillators
- 1440 PSAPDs
- axial FOV = 19 cm
- PET spatial resolution = 2.5 mm

*Catana et al. Mass General Hospital

Simultaneously recorded MR-FDG-PET Images



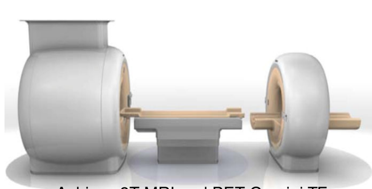
T1-MPRAGE
10 min

FDG-PET:
Recorded 20-50 min p.i., attenuation corrected, not scatter corrected, reconstructed with PRESTO, a fully 3D-OSEM program developed at Jülich, (no point spread modeling)

Fusion

Herzog et al. JNM 2009, Suppl2, 310P

Sequential whole body PET-MR for determining clinical potential of PET-MRI



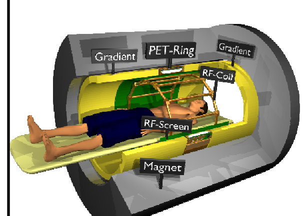
Achieva 3T MRI and PET Gemini TF

+	-
Easier for service and production	Not simultaneous
Standard technology	2 acquisitions
No performance loss for MR and PET	Large room
No interference	No motion correction

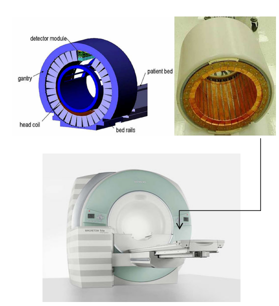
Installed in Mount Sinai NY dec 2009

23

Towards simultaneous whole body PET-MR



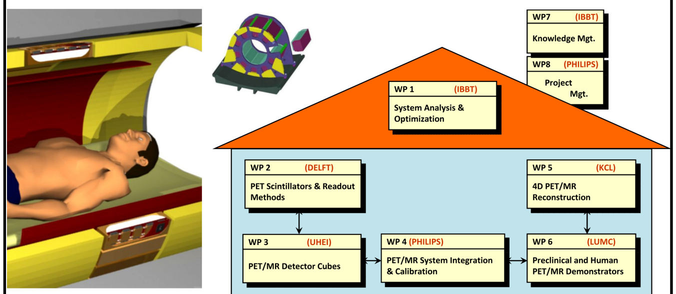
Philips research EU-FP7 collaboration
MR design based on linac MRI (Utrecht)
PET SiPM based
Timing first prototype to be determined



Siemens Healthcare Knoxville (USA) –Tuebingen group (Pichler/Clausen): first full-body PET-MRI prototype built during 2009/2010, ready in 2011. PET APD based

Study cumulative effect of whole imaging chain in simultaneous PET/MR in EU-FP7 Sublima project

Aim: Truly simultaneous, fully integrated, solid-state PET/MR technology for concurrent functional and anatomical imaging with unsurpassed image quality. Determine best systems and built first basic units for preclinical, brain and whole body PET-MRI



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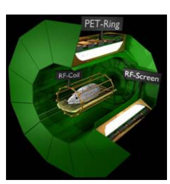
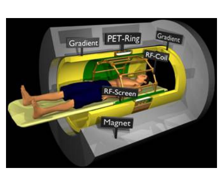
2. Concepts for small animal, brain and whole body PET-MRI
3. **The Hyperimage project**
4. Attenuation and motion correction for PET-MRI
5. Future prospects

HYPERImage

Main Objectives:

1. **Development of MR-compatible detector technology with ultra-high time resolution**
2. **Development of hybrid PET/MR test systems with dramatically improved effective sensitivity**
3. **Development of 4D PET/MR motion, attenuation, and functional data acquisition techniques**
4. **PET/MR test and validation in preclinical studies in cancer and CVD**
5. **First clinical whole body PET/MR investigations of breast cancer**

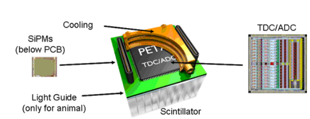




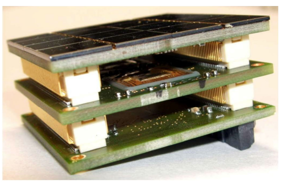
WP1-Objectives

Novel ToF-PET Detector Module Development

- **SiPM-Array Development:**
  - Optimization of SiPM-arrays for time-of-flight PET (increase PDE, improve energy resolution and packaging)
- **TDC/ADC ASIC Development:**
  - Performance Improvement
  - Interfacing and Packaging
  - Reduction of Power Consumption
- **ToF-PET Module:**
  - Design of MR-compatible ToF-PET module
  - Test and optimization



Status of hardware developments



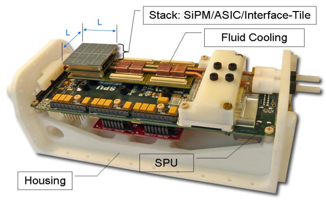
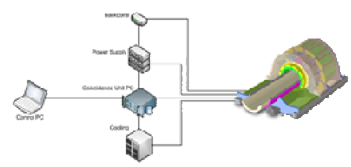
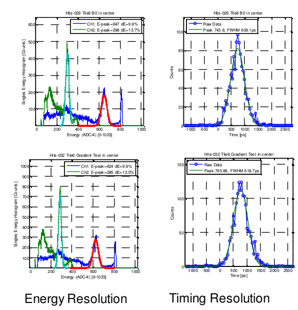


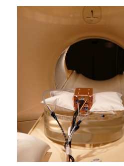
Fig. 1.6: Detector stack with SiPM board (top), ASIC board (middle) and control board (bottom)



Influence of MR on PET: PET Timing and Energy resoution



PET Module in MR-center



MR gradient test in MR-center

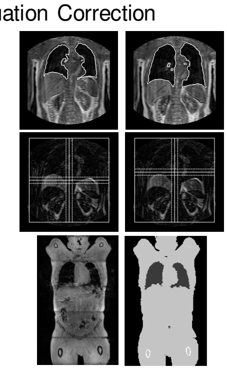
Status:

- No visible change in PET energy and timing resolution

WP3-Objectives

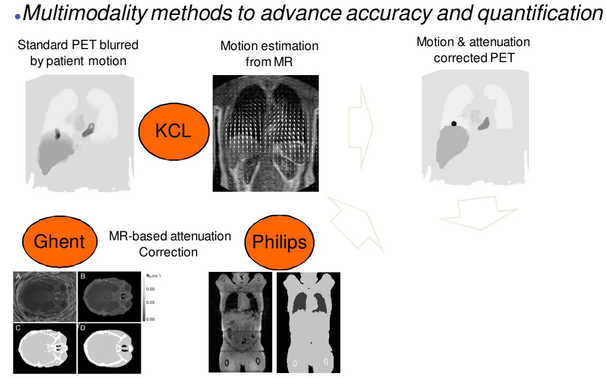
Novel Algorithms for Motion and Attenuation Correction

- Improvement of the PET image quality by using concurrently acquired **MR image data for patient motion correction**
- Itegration of **motion correction** with the acquisition of complementary **functional information from PET and MR**
- Investigation of robust **PET attenuation correction** methods based on **MR** data
- Development of data analysis and visualization for **multidimensional PET/MR data**



Overview

- *Multimodality methods to advance accuracy and quantification*



Problem of attenuation correction in PET-MR:

PET-CT: CT-based attenuation correction

Rescaled CT HU => PET 511 keV ACF

+ : Fast
  - Good contrast
- : Radiation dose
  - Scaling mismatch (?)

PET: Transmission-based attenuation correction

Rotating rod source (Cs)

+ : Correct absolute ACF factors
  - Lower radiation dose
- : Slow
  - Noisy data

\>> Both methods unusable in PET-MR

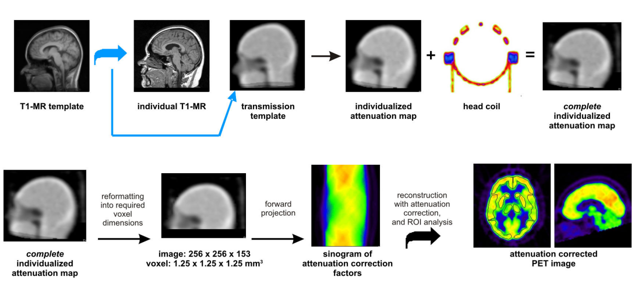
Problem: MR-based attenuation correction

Derive attenuation map from MR images?

Attenuation ~ Tissue (electron) density
MR intensity ~ Proton density & Relaxation properties

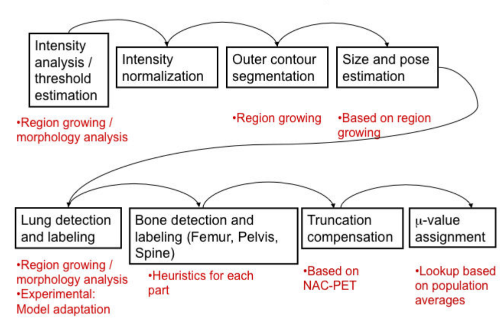
=> No direct correlation between MR intensity and attenuation
=> Most methods use segmentation into different tissue classes and then assign corresponding attenuation coefficients

Template-Based attenuation correction in MR-PET



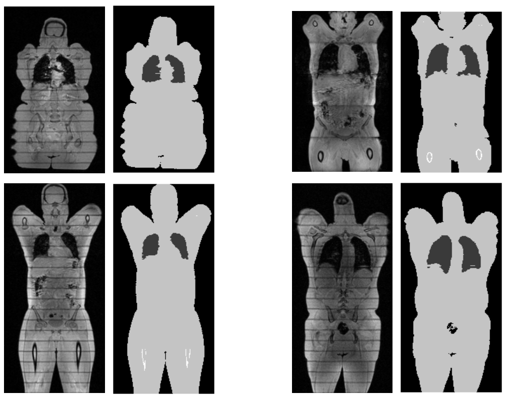
Rota Kops, E. et al. IEEE NSS-MIC Conf. Rec. 2007, 4327–4330.

The fast and practical approach for whole body MRAC
PET attenuation map generation from MR



Philips Medical/Research Volkmar Schulz, IEEE MIC

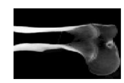
Segmentation and μ-value-assignment- examples



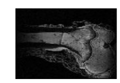
Problem: MR-based attenuation correction

Extra problem: bone – air contrast in MR

- Cortical bone has a very short relaxation time
  - => Signal disappears before it can be acquired with normal MR sequences
  - => Low signal intensity in cortical bone = comparable to air



CT



MRI

Proposed solution: UTE R_2-maps

Proposed solution: Visualizing bone: UTE sequence

Ultrashort Echo Time (UTE) sequence

- Dual-echo sequence:
  - First "echo": FID, very fast after excitation (< 100 μs)
  - Second echo: gradient echo (≈ 1.7 ms)
- Contrast between both echo's is used for detection of 3 tissue types:

MR intensity	**Echo 1**	**Echo 2**
Air	Low (zero)	Low (zero)
Soft tissue	High	Medium-High
Bone	Medium	Low

Proposed solution: Visualizing bone: UTE sequence

Ultrashort Echo Time (UTE) sequence
- Dual-echo sequence:
  - First "echo": FID, very fast after excitation (< 100 µs)
  - Second echo: gradient echo (≈ 1.7 ms)
- Contrast between both echo's is used for detection of 3 tissue types:


T_{E1} = 0.072 ms


T_{E2} = 1.747 ms

Proposed solution: Quantitativity / Stability

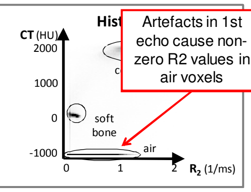
Image intensity is not a stable, quantitative parameter
- Dependent on e.g. MR receiver gain, ...

Quantitative parameter: $R_2 = 1/T_2$
- Calculated voxel-by-voxel from both echo's: $$R_2 = \frac{\ln I_1 - \ln I_2}{T_{E2} - T_{E1}}$$

Proof of concept:

Segment of bovine femur bone containing cortical bone and soft bone

=> Compare CT with R_2-map



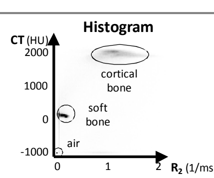
Proposed solution: Detecting air

Air mask: derived from first echo image
- **Region growing** for external air
- **Thresholding** for internal air cavities (e.g. sinuses)

=> Set all voxels containing air to zero

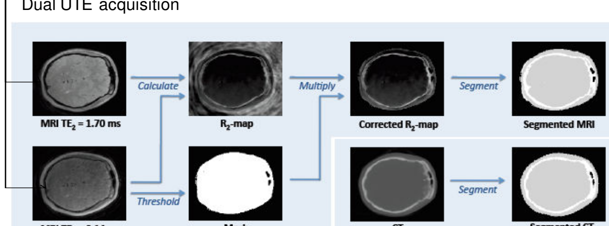
Proof of concept:

Same methodology as above



Proposed solution: Image processing workflow

Dual UTE acquisition



Results

Modeling of the PRISM 3000 XP+

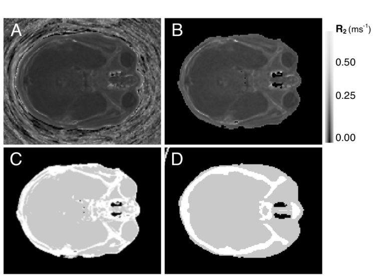
Results: Clinical results

Test of algorithm on clinical brain PET-CT-MRI data sets

- 5 patients from epilepsy trial
- ^{18}F-FDG PET
  - Philips Gemini TF PET-CT
  - Acquisition time = 7 min
  - Voxelsize = 2 mm
- Low-dose CT
  - Philips Gemini TF PET-CT / 50 mAs, 120 kVp
  - In-plane resolution = 1.17 mm
  - Slice thickness 5 mm
- UTE MR
  - Philips Achieva 3T, Head coil
  - T_{E1} = 0.14 ms, TE2 = 1.80 ms
  - Acquisition time = 6 min
  - Voxelsize = 1.3 mm

Results: Clinical results

Derivation of segmented attenuation maps from MR and CT:

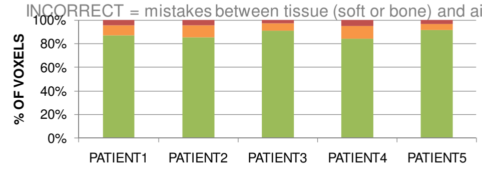


A = R_2-map, B = corrected R_2-map, C = segmented MR, D = segmented CT

Results: Clinical results

Voxel-by-voxel comparison of segmentation with CT:

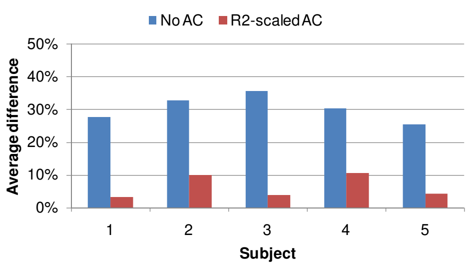
ALL CORRECT = correct class was selected
TISSUE/AIR CORRECT = mistakes between bone and soft tissue
INCORRECT = mistakes between tissue (soft or bone) and air



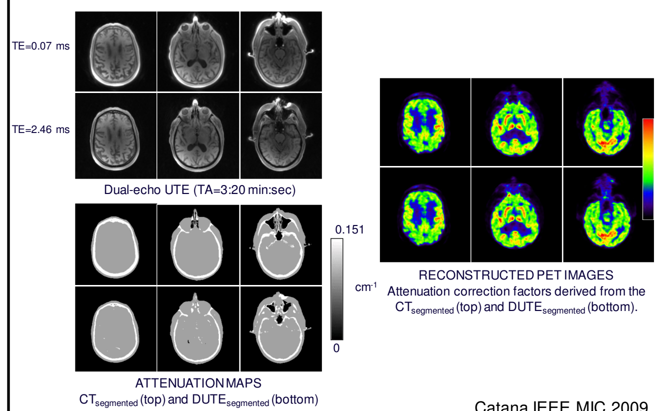
Results: Clinical results

Comparison of reconstruction with CTAC and MRAC

Calculation of average percent difference from CTAC over the complete brain



MR-based Attenuation Correction



Catana IEEE MIC 2009

Results: Clinical results

Test of algorithm on preclinical SPECT-CT-MRI data sets*

- 5 rats from stroke trial (pre-infarct)
- HPMAO SPECT
  - Siemens e.cam dual-head / 1.5 mm pinholes
  - Acquisition time = 30 min
  - Voxelsize = 0.6 mm

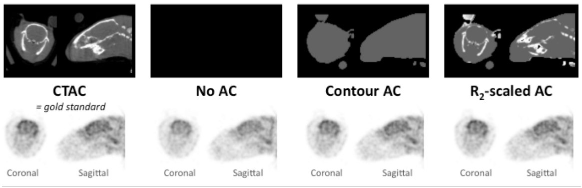
- µCT
  - Skyscan 1178 /
  - Acquisition time = 2 min
  - Voxelsize = 0.083 mm

- UTE MR
  - Philips Achieva 3T, Wrist coil
  - T_{E1} = 0.15 ms, TE2 = 2.40 ms
  - Acquisition time = 35 min
  - Voxelsize = 0.5 mm

Collaboration Ugent-VUB (Lahoutte-Vanhove)

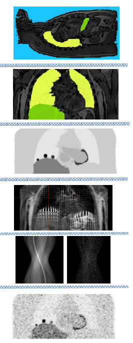
Results: Preclinical results

Reconstruction with 4 attenuation maps:



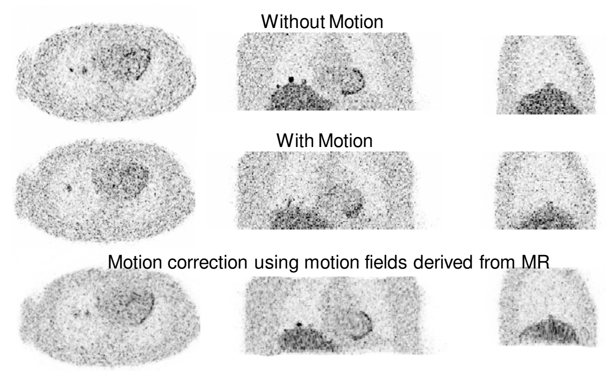
Motion correction Fast simulation of 4D PET data

1. High resolution MR scans
2. MR segmentation
3. Assign PET tracer values
4. Apply MR derived deformation fields
5. Simulate projection data with Poisson noise
6. Reconstruction



KCL-UGENT Planned submission to *IEEE Transactions on Nuclear Science* in Jan 2010

Results: Example of motion correction procedure- (post-reconstruction correction on simulated data)



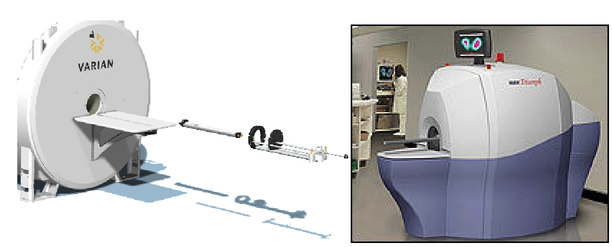
Planned submission to *Physics in Medicine and Biology* in May 2010

Overview:

1. Why do we want PET-MRI ?
2. Concepts for small animal, brain and whole body PET-MRI
3. The Hyperimage project
4. Attenuation and motion correction for PET-MRI
5. **Future prospects**

Small animal PET-MRI

Simultaneous PET-MR very interesting tool for research
For workflow reasons and mostly anatomical MRI
a Sequential PET-MRI close to each other is also an option



7T MRI

APD PET, CZT SPECT
Flat panel micro CT

Brain PET-MRI

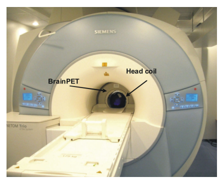
MR is the standard imaging technique for brain imaging
MRI is already 'multimodal': DTI,fMRI, T1, T2

Most brain PET now on whole body PET-CT (no commercial brain PET) and registered to MRI.

Brain PET-MRI has only added value if it is simultaneous.

Brain PET can become an insert option for a 3T, but not very practical in daily research (cables, calibration).

Brain PET on whole body simultaneous PET-MR



Whole body PET-MRI

Still debate about best future multimodality system for whole body

PET-CT	PET-MRI
Fast Reliable Quantitative (AC)	Soft tissue contrast Less dose (follow up studies) Motion correction Research tool

PET-CT in most centers
PET-MRI and PET-CT in research centers

Whole body PET-MRI

What is the best concept ?

	Scanners in 2 rooms + shuttle	Sequential	Full integration
+	Optimal performance	Optimal performance	Simultaneous
+	Cost efficient	Easier for service	Motion correction
-	Patient motion	Some motion	Interference Lower performance
-	AC for PET	Room size	Very expensive

Attenuation correction

Different options but nothing as good as PET-CT
best compromise between speed and reproducibility will be used

	MR based attenuation	Transmission PET	Template based
+	No dose	511 keV	Fast
+	Can be combined with scout scan	Works for any object	
-	Loss of MR scan time	Motion of source	How do we deal with implants ?
-	Artefacts from MR will propagate	Blurry	Difficult for whole body
-	Smaller FOV, truncation		

Acknowledgements

Hyperimage: Vincent Keereman, Paul Marsden, Tobias Schaeffer ,Volkmar Schulz,…

Harvard/Mass general hospital: Ciprian Catana

Juelich: H.Herzog, E.Kops

Questions ?

A new magnetic resonance imaging (MRI)-compatible positron emission tomography (PET) detector design is being developed that uses electro-optical coupling to bring the amplitude and arrival time information of high-speed PET detector scintillation pulses out of an MRI system. The electro-optical coupling technology consists of a magnetically insensitive photodetector output signal connected to a nonmagnetic vertical cavity surface emitting laser (VCSEL) diode that is coupled to a multimode optical fiber.

Modeling of the PRISM 3000 XP+

Oncology

- Multimodal tumor response monitoring
  - MRI: size, heterogeneity, growth rate
  - PET: metabolic activity (FDG), proliferation (FLT)
- MRI tumor response monitoring
  - Based on correlation of MR determinations with PET results
- Multimodal tumor detection
  - PET: highly sensitive detection of very small lesions
  - MRI: high-resolution imaging of detected lesions

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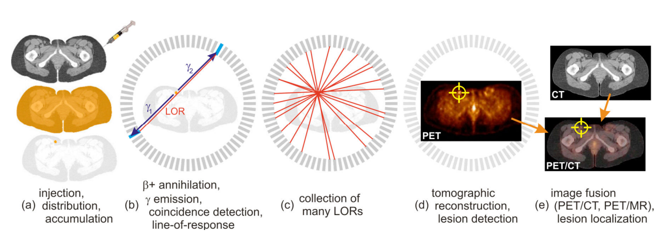
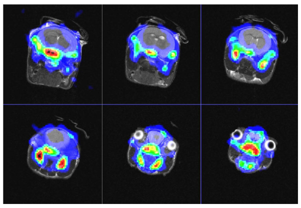
Multidisciplinary



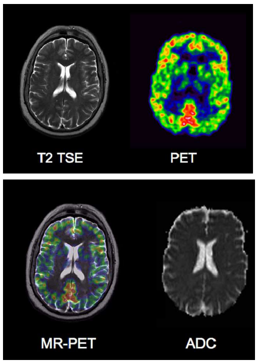
Anatomical context

- Automatic registration
- Clinical
- Multilabeled compounds
  - ^{11}C / ^{13}C
  - ^{18}F / ^{17}F



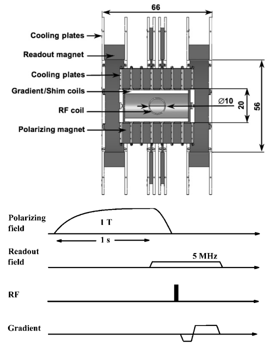
Brain function

- Spatial + temporal correlation
- Cerebral blood flow
  - PET: $H_2{}^{15}O$
  - MRI: IV contrast agent bolus
- Activation
  - PET: FDG
  - MRI: BOLD-effect



Field-cycled MRI

- Interleaved acquisition
- Time, energy resolution
- Effective sensitivity
- Low field strength



K. M. Gilbert et al., "Design of field-cycled magnetic resonance systems for small animal imaging," Phys. Med. Biol., vol. 51, pp. 2825–2841, 2006.