Experience with the First Integrated Whole-Body PET/MR

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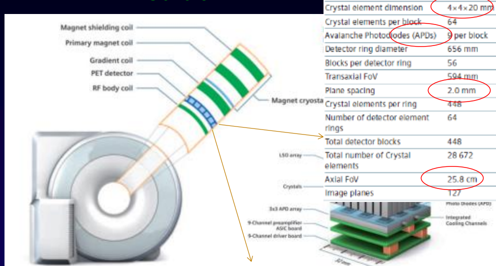
AAPM July 2015

New Technology: Simultaneous PET/MR

Siemens mMR



Crystal material	LSO
Crystal element dimension	4×4×20 mm
Crystal elements per block	64
Avalanche Photodiodes (APDs)	9 per block
Detector ring diameter	656 mm
Blocks per detector ring	56
Transaxial FoV	594 mm
Plane spacing	2.0 mm
Crystal elements per ring	448
Number of detector element rings	64
Total detector blocks	448
Total number of Crystal elements	28 672
Axial FoV	25.8 cm
Image planes	127

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8 detector cassette encased in Cu for magnetic field shielding

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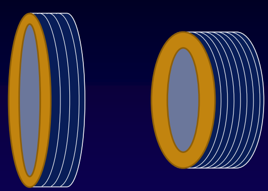
PET Scanner Design Considerations

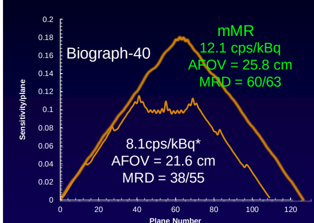
MR bore has limited diameter but longer of axial length

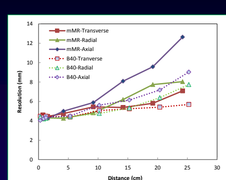


Crystal size is the same but should we expect the same performance as PET/CT?

PET/CT	PET/MR
82 cm diameter	65.6 cm diameter
21.6 cm length	25.8 cm length
13x13 blocks	8x8 blocks

Sensitivity Profile Comparison B40 - mMR



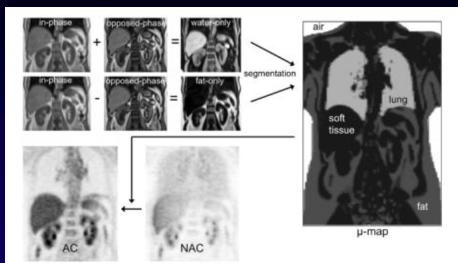


The longer scanner axis and increased maximum ring difference contribute to 50% increased sensitivity of mMR compared to Biograph-40.
Resolution measurements with a point source; The spatial resolution is nearly identical between mMR and Biograph-40 **up to 10 cm** in all directions.

*From Jakoby et al., IEEE-2006 NSS-MIC Conference Record.

Biograph mMR in Oncology

Attenuation Correction in PET/MR



DIXON sequence: 20 sec
dual echo 3D-VIBE: TR/TEs=2.3ms/1.23,2.46ms

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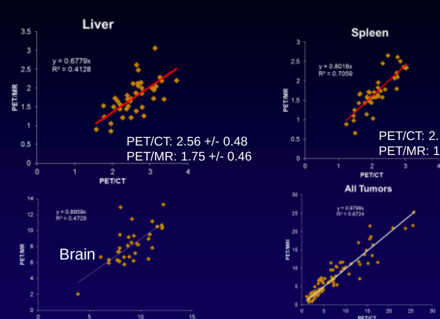
PET/MR vs PET/CT SUV comparison: ~50 patients



- No difference in lesion detectability
- Similar organ and lesion SUV (except bones)

Besa, Laforest et al. RSNA 2012

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First Clinical Experience with Integrated Whole-Body PET-MR: Comparison to PET-CT in Patients with Oncologic Diseases

- Drzezga, et al. JNM, 2012
- 32 patients w/ oncologic diagnoses
  - Single injection of ^{18}F-FDG underwent PET-CT (2 min/bed position), followed by PET-MRI (4 minutes/bed position).
- No significant difference in numbers of lesions detected.
- Qualitative evaluation: high correlation between mean SUVs (ρ = 0.93)
- Bone SUVs underestimated by 10-20% in PET/MR

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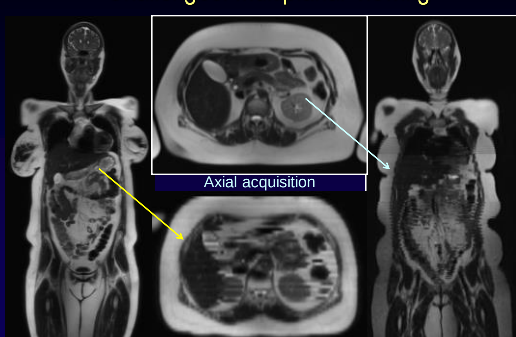
Whole-Body PET/MR Workflow Issues

- General considerations
  - Sequences acquired: **goal is to provide added value over PET/CT or MR alone**
    - General whole-body examination
    - Whole-body plus locally-focused examination
      - Pelvic neoplasm protocol
      - Liver/pancreas neoplasm protocol
  - Length of whole-body examination: PET/MR studies should ideally not exceed 20-30 min (duration of standard PET/CT exam)
    - Additional time for locally
    - Patient comfort/complian
    - Economic viability is dete
    - Possible benefit of integra

Sequences	Acquisition Time
PET: 4-5 stations for vertex-thighs	~120-180 sec/station
2-point DIXON 3D breath-hold T1-weighted sequence (MR-AC)	~20 sec/station (simultaneous to PET)
T2-weighted single-shot turbo spin echo sequence (e.g., HASTE)	~60-90 sec/station (simultaneous to PET

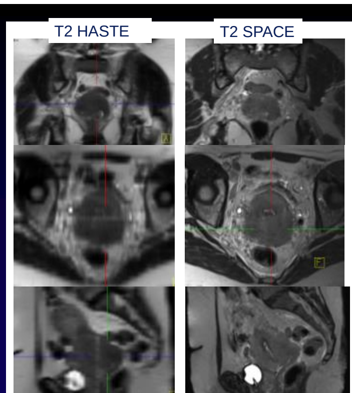
Slide courtesy Kathy Fowler, MD

Challenges: Multiplanar viewing



T2 coronal acquisition

SPACE = VISTA = CUBE



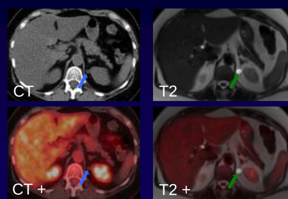
T2 space allows for near isotropic acquisition and no loss of resolution in MPR images

Case 1: incidental lesion characterization (breast cancer)

- PET/MR demonstrates superiority over PET/CT in characterizing certain incidental lesions

50 y/o M with history of breast cancer status-post mastectomy and tamoxifen in 2006, now with abdominal distension concerning for disease recurrence

- PET/CT shows exophytic hypometabolic lesion arising from medial left kidney with attenuation higher than simple fluid
- PET/MR definitively identifies this lesion as a simple cyst
- No evidence of metastatic disease on either study



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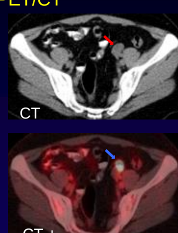
Slide courtesy Kathy Fowler, MD

Case 2: ovary-lymph node discrimination (cervical cancer)

- Many soft tissue FDG-avid lesions cannot be definitively characterized by non-contrast PET/CT

42 y/o F with newly diagnosed cervical adenocarcinoma

- Initial staging PET/CT shows misregistered FDG-avid focus that appears to correspond to a soft tissue nodule
- Differential included:
  - Nodal metastasis
  - Ovarian metastasis
  - Physiologic ovarian uptake
  - Misregistered activity from subjacent bowel



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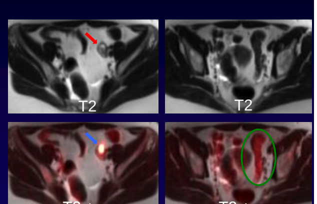
Slide courtesy Kathy Fowler, MD

Case 2: ovary-lymph node discrimination (cervical cancer)

- In same patient, superior soft tissue resolution of PET/MR allows differentiation of ovary from lymph node

42 y/o F with newly diagnosed cervical adenocarcinoma

- With improved registration and soft tissue detail, PET/MR identifies ovary as site of FDG-avidity, distinct from subjacent bowel activity
- Differential included:
  - Ovarian metastasis
  - Physiologic ovarian uptake
- Surgical pathology showed benign ovarian tissue only; uptake was physiologic
- In this case, PET/MR better-delineated potential sites of metastatic disease for preoperative planning, compared to PET/CT



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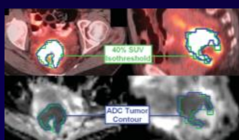
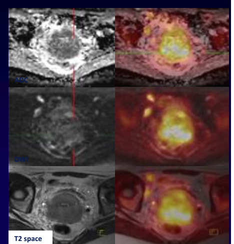
Slide courtesy Kathy Fowler, MD

Cervical Cancer

FDG-PET/MR

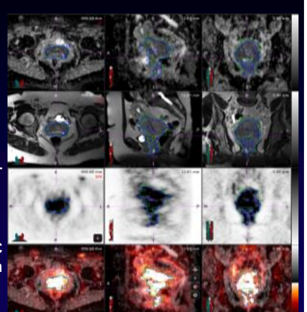
- ADC correlates with SUV max
- Olsen J, et. al. Washington University squamous cell





76 year old woman with FIGO IIIA squamous cell carcinoma of the cervix

PET/MR provides accurate registration for pelvic imaging



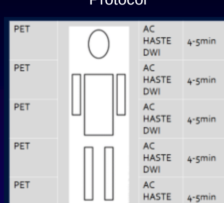
Radiation Reduction: Pediatric Imaging

- WU Experience:
  - 9 peds cases (age 12-18)
  - Various tumor types
  - All patients tolerated examination
- Our Current protocol:
  - FDG @ 0.15 mCi/Kg FDG injection

    CT Protocols: Adult: 120 kVp, 110 mAs eff.

    Pediatric: 80-100 KVp, 35-70 mAs eff.
- CT account for approximately ½ the radiation dose
- PET/MR allows for dose reduction by 50% or more
- However, due to the longer scan time in PET/MR (due to MR sequences) a much more aggressive PET dose reduction protocol can be employed by using longer scan time per bed position (3-4 min vs 1-2 min) without affecting total procedure time

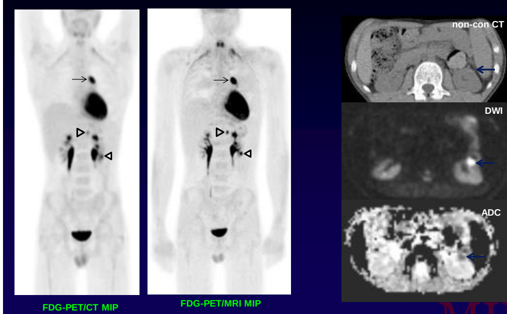
Pediatric WB PET/MR Protocol



PET	**8.0 +/- 0.9 mSv**
CT	5.8 +/- 3.3 mSv

Slide courtesy of Kathy Fowler, J. McConathy

16 yo boy with large B-Cell lymphoma PET/MR better characterized stage IV disease



Slide courtesy of Kathy Fowler, J. McConathy

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PET Listmode Motion Corrected Images in Pancreas PET/MR imaging

- ~80% of patients develop disease recurrence after surgery. Improved up-front identification would better select patients for appropriate treatment. Second, we found that *34% have positive margins* rate in final pathology.
- Imaging the Pancreas by FDG PET is difficult due to typically low uptake
- A comprehensive PET/MR protocol for imaging the Pancreas consists of T1-, T2-weighted (w or w/o Fat Sat) and ADC-DWI and many of them are taken *at breath-hold*
- There is plenty of time for a lot of PET acquisition!

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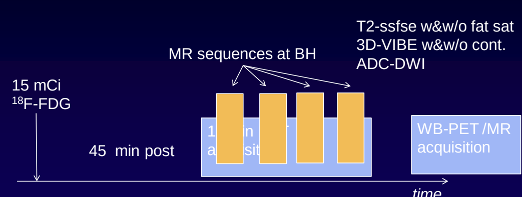
Data Driven Breath-hold PET

Pancreatic Cancer patients involved in a comprehensive mMR study



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Coronal T2-SSFSE @ Breath-hold

From a very collaborative patient!

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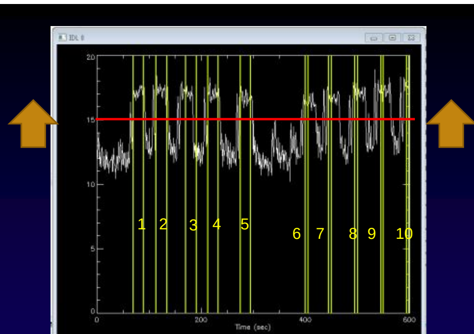
SSFSE = HASTE



Axial Center of Mass of all the PET events in bins of 0.5 sec. The first breath-hold period started at ~70 seconds from the start of the listmode acquisition.

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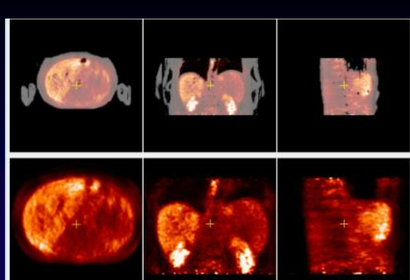
COM technique proposed by Buther et al. JNM 50 (2009)



The initial attenuation correction was taken at normal inspiration. Here the T2-HASTE taken at breath-hold was segmented to produce a mu-map attenuation file which removed all breathing artifacts.

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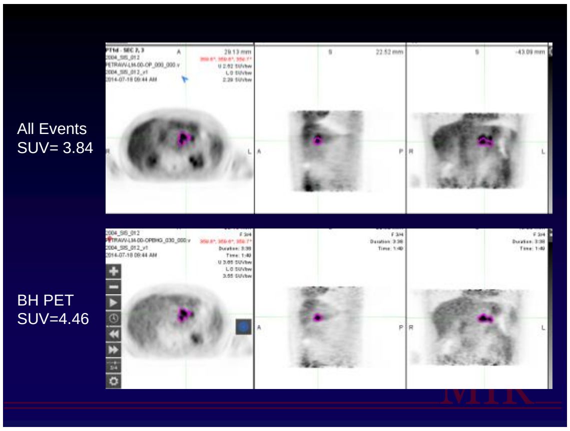
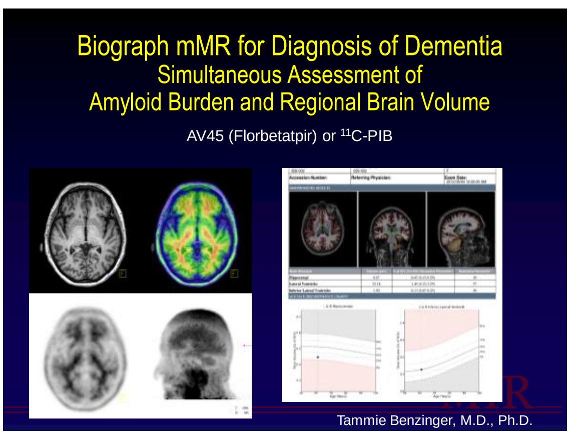
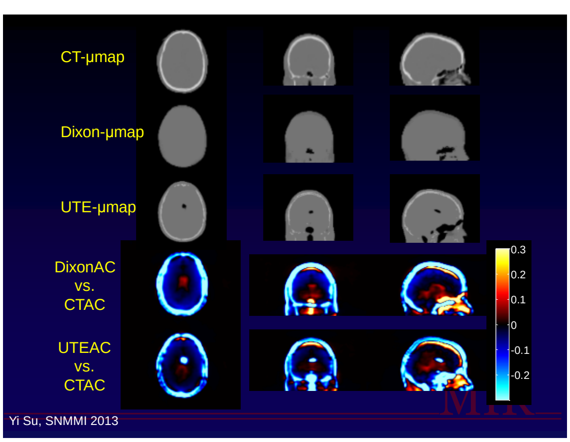
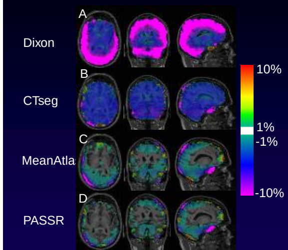

All Events
SUV= 3.84
BH PET
SUV=4.46


Biograph mMR for Diagnosis of Dementia
Simultaneous Assessment of
Amyloid Burden and Regional Brain Volume
AV45 (Florbetatpir) or 11C-PIB
Tammie Benzinger, M.D., Ph.D.


CT-μmap
Dixon-μmap
UTE-μmap
DixonAC
vs.
CTAC
UTEAC
vs.
CTAC
0.3
0.2
0.1
0
-0.1
-0.2
Yi Su, SNMMI 2013

PASSR MRAC Evaluation



MAPE	Whole Brain	Gray Matter	White Matter
Dixon	12.74±2.16% ***	15.8±2.42% ***	10.33±1.22% **
CTseg	4.87±1.04% ***	5.26±0.91% ***	4.84±1.75% **
MeanAtlas	2.67±1.08% **	3.6±1.02% **	2.37±1.87%
PASSR	2.42±1.0%	3.28±0.93%	2.16±1.75%
%Voxels	Within ± 2% PE	Within ± 5% PE	Within ± 10% PE
Dixon	2.7±0.1% ***	16.2±7.8% ***	54.1±12.3% ***
CTseg	8.2±2.5% ***	68.3±20.2% ***	94.6±3.6%
MeanAtlas	63.9±17.2% **	84.3±14.6% ***	95.2±2.7% ***
PASSR	68.0±16.5%	85.8±12.9%	96.0±2.5%

PASSR: Probabilistic Air Segmentation and Sparse Regression Estimated Pseudo CT for PET/MR Attenuation Correction

Chen, An H. et al., Radiology 2014

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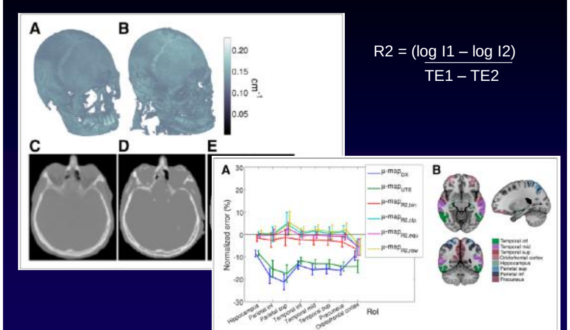
Yi Su, Washington University

Bone segmentation from R2 mapping



$$R2 = \frac{(\log I1 - \log I2)}{TE1 - TE2}$$

Cabello et al. JNM 2015

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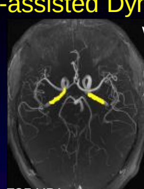
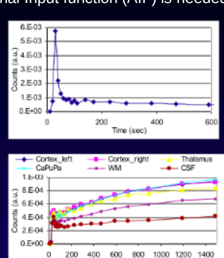
MR-assisted Dynamic PET Data Analysis

Where Arterial Input function (AIF) is needed!





Arterial input function (top) and time activity curves (bottom) in structures of interest segmented from the simultaneously acquired MR data.

- ✓ Cerebral blood flow (CBF)
- ✓ Cerebral blood volume (CBV)
- ✓ Oxygen extraction fraction (OEF)
- ✓ Cerebral oxygen metabolic rate ($CMRO_2$)
- ✓ Cerebral glucose metabolic rate (CMRglu)
- ✓ Oxygen-glucose index (OGI)

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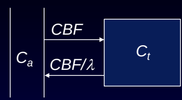
Tammie Benzinger, M.D., Ph.D., Yi Su, Ph.D.

Image Derived AIF Technique – O^{15}-H_2O



$$\frac{dC_t}{dt} = CBF \cdot C_a - \frac{CBF}{\lambda} \cdot C_t$$

⇩

$$C_a = \frac{1}{CBF_1}\frac{dC_{t1}}{dt} + \frac{C_{t1}}{\lambda}$$

$$C_{t2} = CBF_2 \bullet C_a \otimes e^{-\frac{CBF_2}{\lambda}t}$$

$$C_{t3} = CBF_3 \bullet C_a \otimes e^{-\frac{CBF_3}{\lambda}t}$$

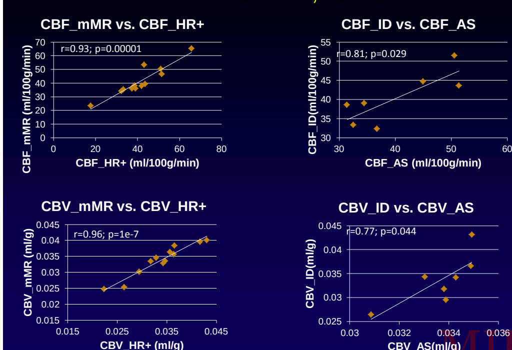
$$C_{art} = f_1 \cdot C_a + f_2 \cdot CBF_b \bullet C_a \otimes e^{-\frac{CBF_b}{\lambda}t}$$

$$Q(\mathbf{p}) = \sum_{i=1}^{N}\left[w_{1i}(C_{t1}(t_i) - PET_{1,i})^2 + w_{2i}(C_{t2}(t_i) - PET_{t2,i})^2 + w_{3i}(C_{art}(t_i) - PET_{art,i})^2\right]$$

f_1, f_2 from TOF MRA; Ca, CBF1, CBF2, CBF3, CBFb from modeling

Yi Su, see also PlosONE April 2015 for AIF derived in ^{11}C-PIB

mMR vs. HR+, vs AS



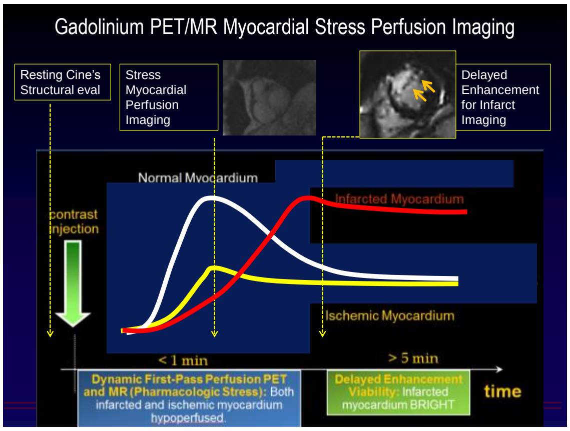
Yi Su, Washington University

Myocardial Imaging -- Potential Benefits of PET/MR

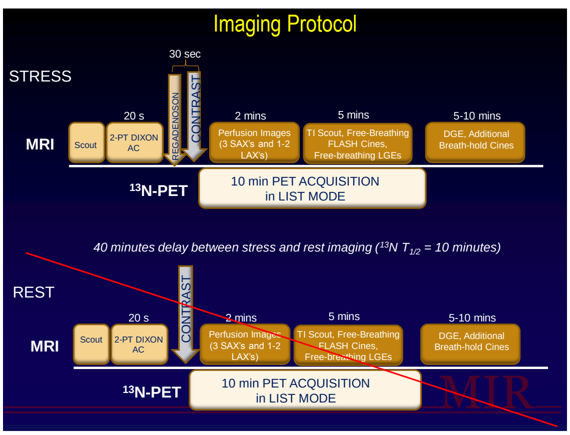
PET
- Noninvasive reference standard for myocardial Stress/Rest perfusion and viability
- Whole heart volumetric coverage

MRI
- Delayed Gadolinium enhancement definitive for infarct depiction
- Option for MR angiography of the coronaries

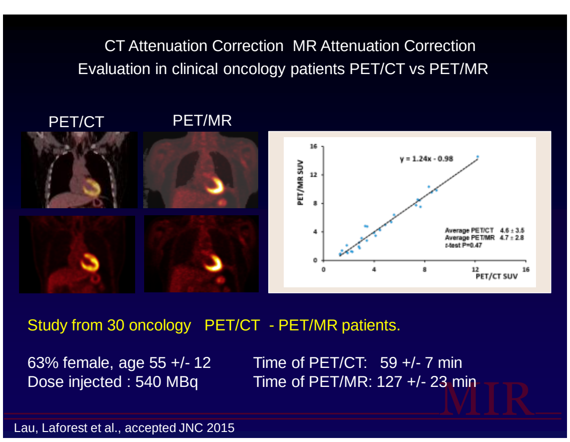
Together:
- Highly robust examination
- Shorter exam time (potentially < 1 hour)
- Lower radiation dose than standard myocardial PET or SPECT
- Elimination of breast or other attenuation artifacts
- Internal validation between PET and MR
- Absolute myocardial blood flow quantification by PET and MR
- Detection of other cardiac findings otherwise missed by SPECT or other standalone stress imaging modalities
- Simultaneous response to a single physiological stimulus
  Simultaneous PET and MR perfusion



Gadolinium PET/MR Myocardial Stress Perfusion Imaging
Resting Cine's Structural eval
Stress Myocardial Perfusion Imaging
Delayed Enhancement for Infarct Imaging
Normal Myocardium
Infarcted Myocardium
contrast injection
Ischemic Myocardium
< 1 min
> 5 min
Dynamic First-Pass Perfusion PET and MR (Pharmacologic Stress): Both infarcted and ischemic myocardium hypoperfused.
Delayed Enhancement Viability: Infarcted myocardium BRIGHT
time



Imaging Protocol
30 sec
STRESS
REGADENOSON
CONTRAST
20 s
2 mins
5 mins
5-10 mins
MRI
Scout
2-PT DIXON AC
Perfusion Images (3 SAX's and 1-2 LAX's)
TI Scout, Free-Breathing FLASH Cines, Free-breathing LGEs
DGE, Additional Breath-hold Cines
13N-PET
10 min PET ACQUISITION in LIST MODE
40 minutes delay between stress and rest imaging (13N T1/2 = 10 minutes)
REST
CONTRAST
20 s
2 mins
5 mins
5-10 mins
MRI
Scout
2-PT DIXON AC
Perfusion Images (3 SAX's and 1-2 LAX's)
TI Scout, Free-Breathing FLASH Cines, Free-breathing LGEs
DGE, Additional Breath-hold Cines
13N-PET
10 min PET ACQUISITION in LIST MODE
MIR



CT Attenuation Correction MR Attenuation Correction
Evaluation in clinical oncology patients PET/CT vs PET/MR
PET/CT
PET/MR
y = 1.24x - 0.98
PET/MR SUV
PET/CT SUV
Study from 30 oncology PET/CT - PET/MR patients.
63% female, age 55 +/- 12
Dose injected : 540 MBq
Time of PET/CT: 59 +/- 7 min
Time of PET/MR: 127 +/- 23 min
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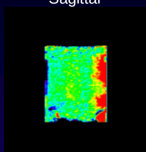
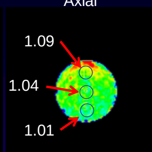
Lau, Laforest et al., accepted JNC 2015

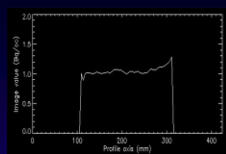
Effect of Attenuation from the phased array body coil. Test with uniform ^{68}Ge-cylinder.

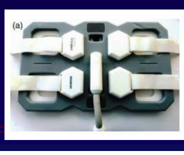
Sagittal



Axial







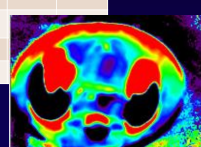
Vertical Profile

Ratio of 2 hr scans w/o and with phased array coil

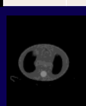
Effect of Phased Array Coil with Cardiac Phantom

^{18}F Phantom with 5:1 heart wall to background ratio

Region	PA Coil	Without PA coil	%	B40
Background	1.00	1.03	2.5	1.00
1cm lesion	2.67	2.52	-6.0	2.59
Heart Wall	3.34	3.44	3.0	3.70
Heart Cavity	0.42	0.33		
Lungs	0.05	0.03		
Bone	0.23	0.17		



Attenuation from CT-AC without PA coil.



Effect of the Lung Segmentation Value

In mMR, lungs are uniformly segmented at 0.0224 cm^{-1}.

	Average	Max	Min
RUL	-733	+70	-853
	-804	+16	-892
	-766	+15	-877
	-765	-353	-873
	-766	-71	-953
RLL	-719	+45	-797
	-735	-85	-918
	-721	-218	-872
	-706	-247	-866
	-673	-312	-889
LUL	-637	+45	-797
	-821	-85	-918
	-779	-218	-872
	-764	-245	-866
	-788	-312	-889
LLL	-670	-146	-855
	-684	-88	-820
	-730	-284	-846
	-679	-276	-803
	-733	-106	-862

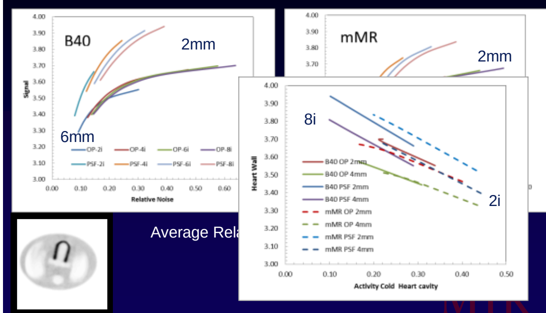
Observed lungs CT HU from 5 consecutive PET/CT patients

Scaled to 511 keV ATN: corresponds to a range of 0.0175 to 0.0289 cm-1

Region	PET +/- % change
Liver	2.0
Myocardium	2.2
Left Ventricle	0.6
Vertebral Body	2.5
Lungs	14.8
Aorta	1.5

Lau, Laforest, Woodard et al., accepted JNC 2015

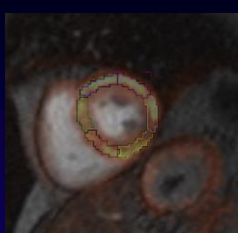
Systematic Signal/Noise Evaluation



Average Rel

60 million events (trues+scatter) for each dataset

Evaluation of MBFs from ^{13}N-NH3



10 min Listmode ^{13}N-NH3 PET data sorted on 20 frames: 2x5s, 11x10s, 2x30s, 3x60s and 2x120s.

OSEM 3D: 3it/24subsets-G4mm

ROIs drawn on 16 segments from NH3 PET fused on Gd-perfusion MRI.

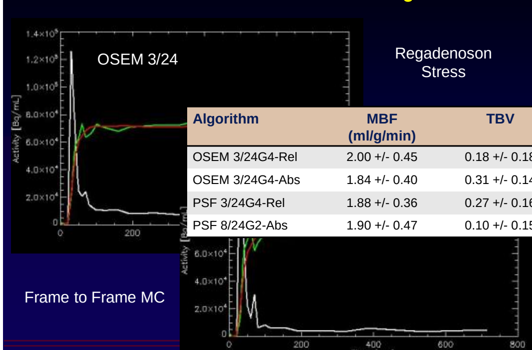
ROIs drawn on 1-3 min PET.

The 2-compartment 4-parameters model of Hutchins et al.

MIR

Evaluation of Reconstruction Algorithms

Regadenoson Stress



Algorithm	MBF (ml/g/min)	TBV
OSEM 3/24G4-Rel	2.00 +/- 0.45	0.18 +/- 0.18
OSEM 3/24G4-Abs	1.84 +/- 0.40	0.31 +/- 0.14
PSF 3/24G4-Rel	1.88 +/- 0.36	0.27 +/- 0.16
PSF 8/24G2-Abs	1.90 +/- 0.47	0.10 +/- 0.15

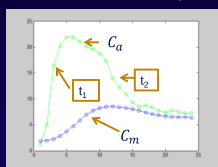
Frame to Frame MC

Estimation of arterial input function (AIF) in cardiac magnetic resonance

- Bolus injection of a large dose of gadolinium contrast media results in a saturation of AIF signal in blood pool
- "Real" AIF (($\overline{C_a}$) can be reconstructed from "truncated" AIF (C_a) and myocardial signal (C_m) by minimizing a cost function*

$$E = \|\nabla_t C_m - S(S^T S)^{-1} S^T \nabla_t C_m\|^2$$

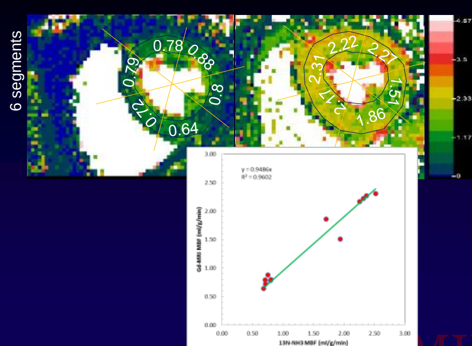
- MBF is calculated via a conventional Fermi model (with manual rigid registration for motion correction)



t_1 and t_2 are the cutoff points for the saturation zone. Every point in between is replaced during fitting calculation

*Wang H & Cao Y, JMRI 36(2012)p411-21

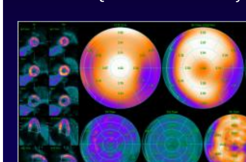
Jie Zheng, Ph.D.

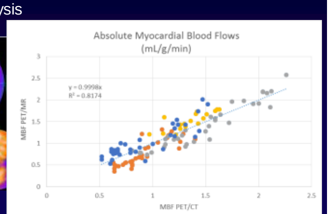


Jie Zheng, Ph.D.

MBF Comparison PET/CT – PET/MR

- 4 Patients underwent REST/STRESS ^{13}NH3 on PET/CT(B40) and mMR
- ~10 mCi injections, 1hr apart, STRESS then REST.
- PET/CT – mMR on consecutive days
- Dynamic LISTMODE acquisition for 10min
- CTAC on PET/CT
- DIXON on PET/MR
- Cedars QPET Software analysis



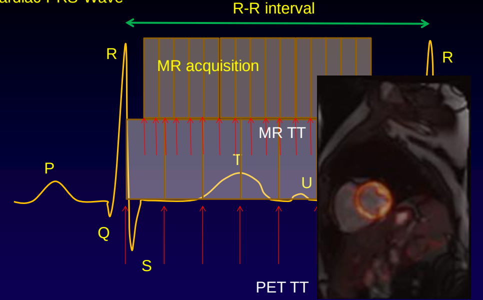


Does mMR provide TRULY SIMULTANEOUS acquisition?

- Although data acquisition are done simultaneously, PET and MR data acquisitions are done independently and therefore are not truly simultaneous and also not synchronous.
- For example, a physiologically triggered acquisition from MR will not be synchronous with its PET counter part. The trigger times for MR are independent of the PET trigger times in gated acquisition.

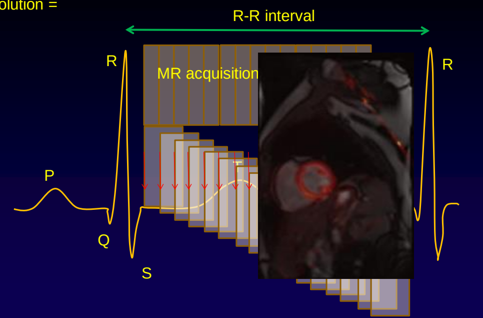
Since PET data is acquired in LISTMODE, we propose to use the trigger time information from the MR acquisition for the PET data listmode sorting and therefore to create *SYNCHRONOUS* PET/MR images.

Cardiac PRS-Wave

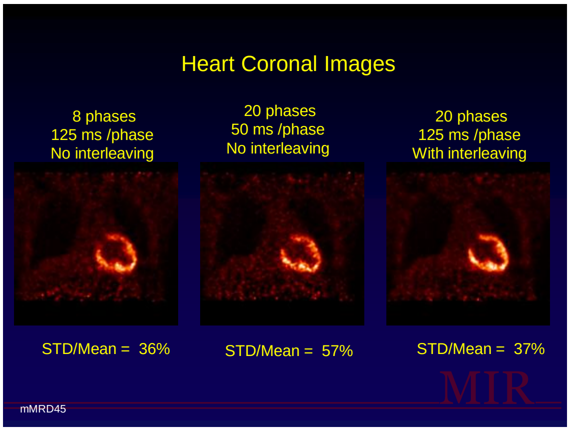


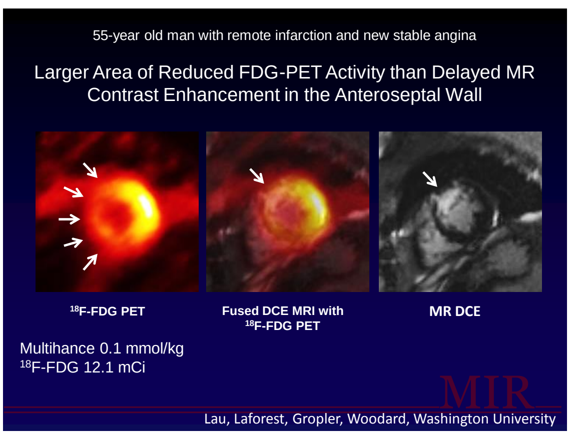
The PET and MR trigger times (TT) generally do not match.
Trigger time = start of each phase image

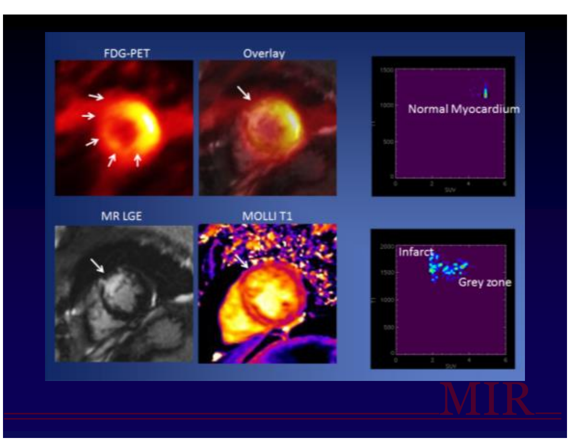
Solution =



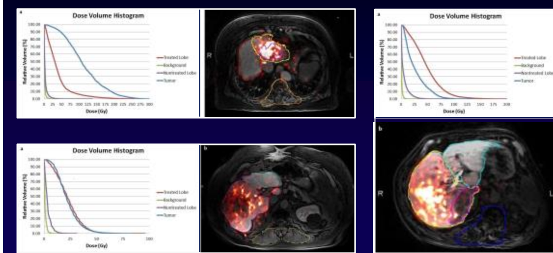
We propose to use the MR trigger times to sort the PET listmode data. In our approach we also use an adjustable phase width to provide for improved statistics.
Therefore, we obtain *Synchronicity* and temporal *interleaving* of the PET gated images.


Heart Coronal Images
8 phases
125 ms /phase
No interleaving
20 phases
50 ms /phase
No interleaving
20 phases
125 ms /phase
With interleaving
STD/Mean = 36%
STD/Mean = 57%
STD/Mean = 37%
MIR
mMRD45


55-year old man with remote infarction and new stable angina
Larger Area of Reduced FDG-PET Activity than Delayed MR Contrast Enhancement in the Anteroseptal Wall
18F-FDG PET
Fused DCE MRI with 18F-FDG PET
MR DCE
Multihance 0.1 mmol/kg
18F-FDG 12.1 mCi
MIR
Lau, Laforest, Gropler, Woodard, Washington University


FDG-PET
Overlay
Normal Myocardium
MR LGE
MOLLI T1
Infarct
Grey zone
MIR

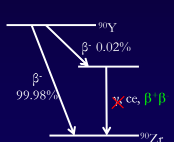
Assessing Dose Deposition in ^{90}Y Radioembolization

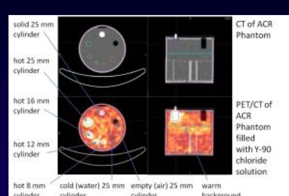


Nikki Maughan, SU-D-201-5

Phantom Experiment

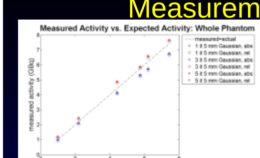
- β^- decay of ^{90}Y decays into ^{90}Zr
- Tissue penetration (2.5 mm mean, 11 mm max)
- Energy: 0.9367 MeV
- Half-life: 64.2 hrs
- Positron emission via internal pair production: 32 ppm



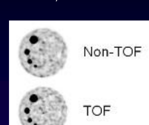


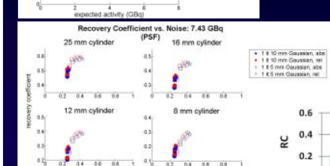
Nikki Maughan, SU-D-201-5

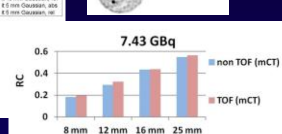
Measurements in mMR



Optimal parameters: 3 iterations, 21 subsets, 5 mm Gaussian post-reconstruction filter, with PSF







Nikki Maughan, SU-D-201-5
mCT experiment and data analysis, Mootaz Eldib, Mt. Sinai, NY

Summary and Opportunities

- Simultaneous PET/MR Works!
- PET/MR has shown to be non-inferior to PET/CT in lesion detectability and provide accrued diagnostic information for oncology applications
- PET/MR provides better characterization of certain incidental lesions. Superior soft tissue resolution of PET/MR facilitates local staging.
- Offers an excellent opportunity for dose reduction which will be especially beneficial for the pediatric population
- Achieves the goal of simultaneous PET/MR acquisition of added value over PET/CT or MR alone
- Early experience demonstrates utility of integrated PET/MR in the diagnosis and management of various malignancies
- PET/MR offers an unprecedented opportunity for motion correction to improve PET. Many sites have reported significant progress.
- The work has just begun.

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