PET / MR in Diagnosis, Therapy and Response Assessment

Georges El Fakhri, PhD, DABR

Outline: PET/MR in Diagnosis and Therapy

- Rationale for PET / MR
- PET/MR for Motion Compensation
- PET/MR guidance in Radiation Therapy
- Novel directions in Immunotherapy
**Rationale for Integrated PET-MR**

**PET**
- High sensitivity
- Absolute quantitation
- Good Time resolution
- Poor spatial resolution
- Limited anatomic information

**MR**
- Exquisite high resolution, excellent soft tissue contrast
- Non ionizing
- Excellent time resolution
- Poor sensitivity
- Absolute quantitation challenging

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**Integrated Whole-Body MR-PET**

**Sequential PET-CT vs Simultaneous PET – MR**

- 25 cm axial coverage

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**Clinical value of PET-MR in detecting small liver lesions**

66 year old woman with inflammatory bowel disease and an incidentally-discovered liver lesion. Axial T2 and axial postcontrast (Eovist) images demonstrate an indeterminate suspicious dominant hepatic lesion (Fig 2a-b). Lesion was biopsied and found to be cholangiocarcinoma, and was FDG-avid on PET-CT staging exam (Fig 2c). Many smaller lesions were also seen on MR (Fig 2d), but were not confidently identified on PET or CT (Fig 2e-f).
Potential Clinical Applications of PET-MR

OB-GYN Metastatic Staging

45 y.o. F, melanoma of right thigh. Ovary in ovulatory phase or lymph node metastasis?

PET-CT

CT

PET

PET-CT

PET-MR

L.C. Hygino da Cruz, R.C. Domingues

History of osteosarcoma left femur

MRI can identify spinal cord compression
PET identifies L5 vertebral body metastasis

G. El Fakhri, Ph.D.
R Lim, MD

Musculoskeletal tumor

PET-CT

PET

PET-CT

PET-MR

R Lim, MD

G. El Fakhri, Ph.D.

Neuroblastoma

Whole-Body STIR MRI and 18F-FDG PET

Extensive bone marrow metastasis on PET

R Lim, MD

G. El Fakhri, Ph.D.
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Rationale: Motion deteriorates PET & CT image quality

- Blurring
- Lower Noise

Solution 1: Using all PET data with MR-based motion correction

Methods: Motion Corrected OSEM

- List-mode MLEM reconstruction algorithm with motion modeled in the system matrix:

\[ \alpha^{(m)}(f) = \sum \beta^{(m)}(f) \]

Data system matrix

- Attenuation correction using deformed attenuation maps at each frame:

Ouyang J., Petibon Y., El Fakhri G.
Primate Results: Acquisition

- Motion Correction with Primate in simultaneous PET-MR

Gated tagged MR  Gated PET


Nonhuman Primate Results

Liver patient study

Cine MRI (TrueFISP)  Respiratory Gated PET

Respiratory motion amplitude in the dome of the liver (~0.7-1.5cm).

Hepatic Cancer Study

Petibon, Huang, Ouyang and El Fakhri. Role of MR-based motion and PSF corrections in WB PET-MR. Med. Phys., 2014; 41:

Measure Motion Fields and Track Motion Phases

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PET-MRI for clinical target definition in RT planning for Soft Tissue Sarcoma

- Peritumoral edema for STS can extend up to 4 cm from the T1 gross tumor
- Current RTOG consensus for STS clinical target volume for high grade STS
  - 3.5 cm longitudinally
  - 1.5 cm radially
- Additional T2 suspicious edema would be added to the expansion
- However, some lesions are associated with very extensive T2 abnormalities
- Can we better define the amount of suspicious peritumoral edema to include for pre-op RT clinical target volume using PET-MRI?

PET-MRI for clinical target definition in RT planning for Sarcoma (cont)

- While for both bone and soft tissue sarcoma, en bloc resection results in best local control, there is significant associated morbidity and functional consequences of multimodality therapy including wound healing complications, pathologic fractures, etc.
- Local control rate with definitive RT is 50-70% for STS and spine/pelvic bone sarcomas compared to >90% using (neo)adjuvant RT with en bloc resection
- Can multi-modality functional imaging provide guidance for better CTV definition and outlining intra-tumoral radio-resistant areas for dose escalation within CTV?

PET-MR in Radiation oncology treatment planning
Pre-radiotherapy fused PET and T2-weighted MRI
Post-radiotherapy fused PET and T2-weighted MRI
Chang et al., AJR, 2016

PET/MRSI – based GTV : Validation in chordoma
Sagittal coronal
3D printed models of the pelvic bed including tumor in blue based on CT
Mold for tumor placement after resection to avoid misalignment; bottom inked to mark the tumor
Shusharina N., Ma C., Chen Y.L., Lim R., El Fakhri G.

PET/MRSI – based GTV : Validation
Ma C., Chen Y.L., Lim R., El Fakhri G.
GTV in STS using PET/MRSI vs MR

GTV contours for soft tissue sarcoma of the foot. Red arrows show the regions of disease extension identified by PET/MR beyond that of the original CT-based GTV. Black arrows show the regions of hyperintensity consistent on PET and MRSI, which could be dose escalated.

GTV in STS using PET/MRSI vs MR (cont.)

Dose distribution targeting the original GTV drawn on CT and the corresponding DVH for a patient with soft tissue sarcoma of the foot. It is clear that treating the GTV defined based on CT alone causes severe underdose in the regions indicated to be malignant by PET and T2 MR (green and cyan arrows, respectively). Under-treatment of these regions can lead to recurrence.

Response Assessment with PET/MRS

In the tumor voxel (4x4x4cm³), the choline/lipid ratio is 4 times higher than normal tissue voxel.

Ma C., Chen Y.L., Lim R., El Fakhri G.
Ultra-high resolution MR spectroscopic imaging

A subspace based approach to ultra-high resolution MRSI

MPRAGE

NAA

PET/MRSI in soft tissue sarcoma
(3 mm in-plane resolution)

NAA

Cr

Cho

mI

Glx

3D MRSI of the brain

MPRAGE

NAA

PET/MRSI in soft tissue sarcoma
(3 mm in-plane resolution)

NAA

Cr

Cho

mI

Glx

Response Assessment with PET/MRS

GRE

B0 map

Water

lipid image obtained using a sinc pulse

Water

lipid image with spectral-spatial pulses (20x)

Representative spectrum using sinc pulse

Spectrum at same voxel (50x) with spectral-spatial

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Background on Feraheme (FH)

Clinical and research applications of FH

Clinical trials using MRI of macrophages with FH
Heat-induced radiolabeling (HIR)

[89Zr]FH kinetics and proposed trafficking model

[89Zr]FH uptake in hind leg injury
Lymphocyte labeling with Protamine-FH

Yuan et al. (2017) Nat Prot

White Blood Cell Tracking by Nanoparticle PET

Monocyte Imaging in Inflammation

- Highly sensitive and quantitative methods for long-term tracking of the immune response.
- Systemic administration of NP allows for monocyte imaging/tracking in inflammatory processes.
- Targeted NPs allow for re-injection of pre-labelled leukocytes without background contamination in images (T-cells in tumors, B-cells in MS, monocytes in arterial plaques or neuroinflammation).

Targeted Cell Labeling for PET Imaging

M. Wilks

T cell tracking with [89Zr]protamine-FH

M. Wilks
B cell tracking with $[^{89}\text{Zr}]$protamine-FH

- Topical application in B cell accelerated wound healing
- I.v. B cells in EAE model of multiple sclerosis

Labeled B cells

Particle alone

Day 13

Day 14

EAE

Sham control

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THANK YOU!