PET / MR in Diagnosis , Therapy and Response Assessment

Georges El Fakhri, PhD, DABR

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Gordon Center for Medical Imaging

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

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Rationale for Integrated PET-MR

PET	MR
• High sensitivity	• Exquisite high resolution, excellent soft tissue contrast
• Absolute quantitation	• Non ionizing
• Good Time resolution	• Excellent time resolution
• Poor spatial resolution • Limited anatomic information	• Poor sensitivity • Absolute quantitation challenging

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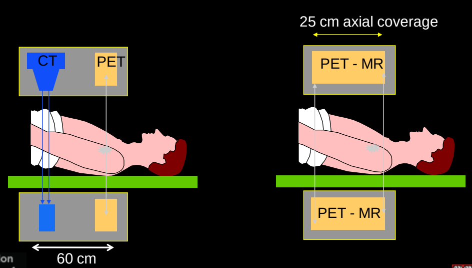
Integrated Whole-Body MR-PET

Sequential PET-CT *vs* Simultaneous PET – MR



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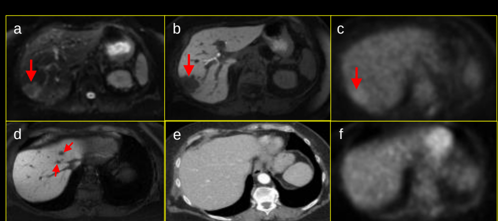
Clinical value of PET-MR in detecting small liver lesions



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).

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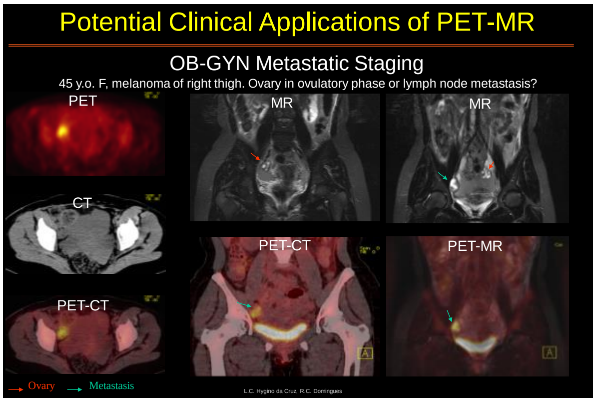
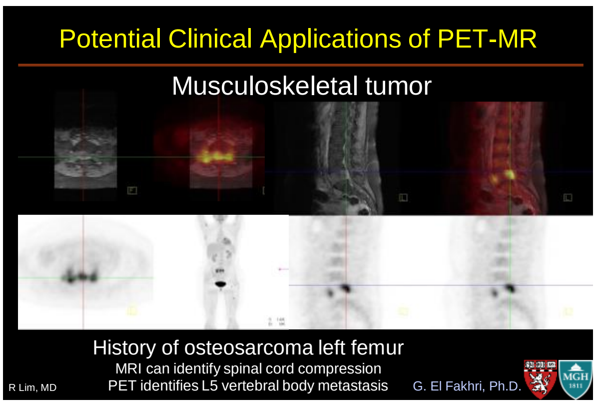

Potential Clinical Applications of PET-MR
OB-GYN Metastatic Staging
45 y.o. F, melanoma of right thigh. Ovary in ovulatory phase or lymph node metastasis?
PET
MR
MR
CT
PET-CT
PET-MR
PET-CT
Ovary
Metastasis
L.C. Hygino da Cruz, R.C. Domingues


Potential Clinical Applications of PET-MR
Musculoskeletal tumor
History of osteosarcoma left femur
MRI can identify spinal cord compression
PET identifies L5 vertebral body metastasis
R Lim, MD
G. El Fakhri, Ph.D.
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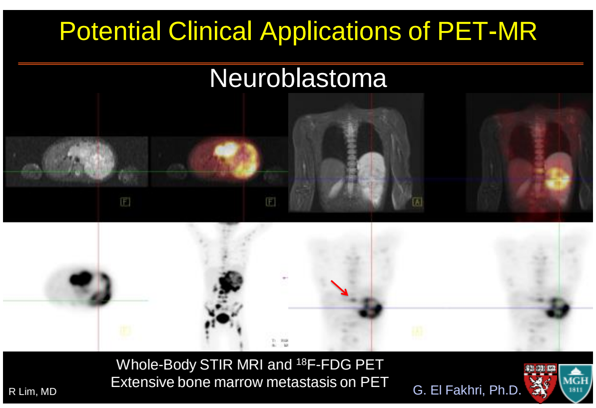
Potential Clinical Applications of PET-MR
Neuroblastoma
Whole-Body STIR MRI and 18F-FDG PET
Extensive bone marrow metastasis on PET
R Lim, MD
G. El Fakhri, Ph.D.
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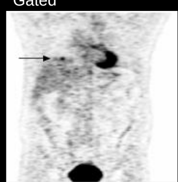
Rationale : Motion deteriorates PET & CT image quality

- Blurring
- Lower Noise

Uncorrected

- Using all PET data at *all* motion phases *without* motion correction

Gated



- Using some PET data only at *one* motion phase

- Freezing Motion
- Higher Noise

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

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Methods: Motion Corrected OSEM

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

$$a_{ni}(f) = \sum_{j=1}^{M} a_{nj} \times m_{ji}(f)$$

Static system matrix: a_{nj}

Motion interpolation matrix (i.e., contribution of pixel i in the ref. frame to pixel j in the deformed frame): $m_{ji}(f)$

$$\rho_i^{(a+1)} = \frac{\rho_i^{(a)}}{\sum_{f=1}^{F} s_i(f)} \sum_{n=1}^{N} \frac{a_{ni}(f_n)}{\sum_{j=1}^{M} a_{nj}(f_n)\rho_j^{(a)}}$$

Number of counts in list-mode: N

Motion dependent system matrix: $a_{ni}(f_n)$

- Attenuation correction using deformed attenuation maps at each frame:

Attenuation map in the reference frame

Transformation using measured motion fields from tagged MR

Attenuation maps in the deformed frames

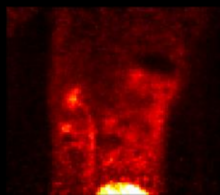
Ouyang J., Petibon Y., El Fakhri G.

Primate Results: Acquisition

- Motion Correction with *Primate* in simultaneous PET-MR

Gated tagged MR

Gated PET



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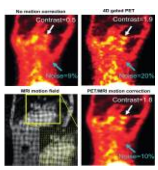
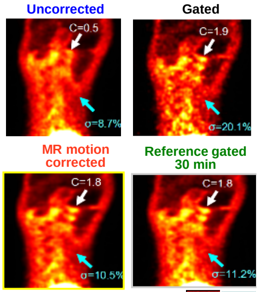
Chun et al. J. Nucl. Med. 2012

Nonhuman Primate Results

JNM The Journal of Nuclear Medicine



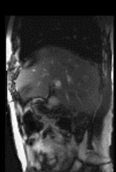


SNMMI Society of Nuclear Medicine and Molecular Imaging

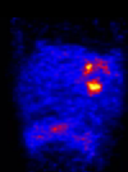
Chun S.Y., Reese T., Guerin B., Catana C., Zhu X., Alpert N., El Fakhri G.
Tagged MR-based Motion Correction in Simultaneous PET-MR. *JNM* 2012; 1284-1291

Liver patient study

Cine MRI (TrueFISP)



Respiratory Gated PET



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

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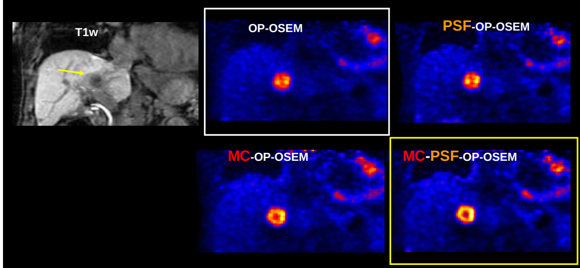
Petibon, Huang, Ouyang, Reese, Li, Syrkina, Chen and El Fakhri.
Relative role of MR-based motion and PSF corrections in WB PET-MR. Med. Phys., 2014

Hepatic Cancer Study



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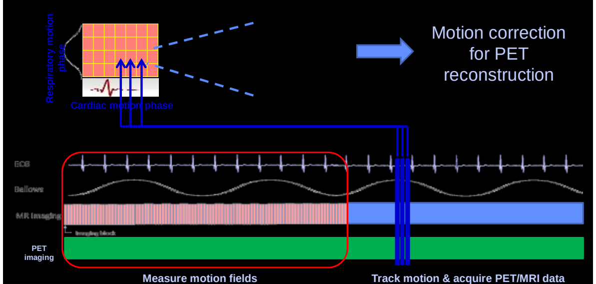
Petibon, Huang, Ouyang and El Fakhri.
Role of MR-based motion and PSF corrections in WB PET-MR. Med. Phys., 2014; 41

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 concensus 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 preop RT clinical target volume using PET-MRI?

Chen Y.L., Lim R., El Fakhri G.

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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 GTV ?

Chen Y.L., Lim R., El Fakhri G.

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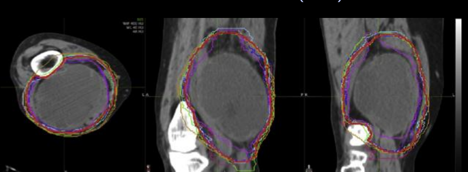
PET-MR in Radiation oncology treatment planning

Soft Tissue Sarcoma (STS)



Chen Y.L., Lim R., El Fakhri G.

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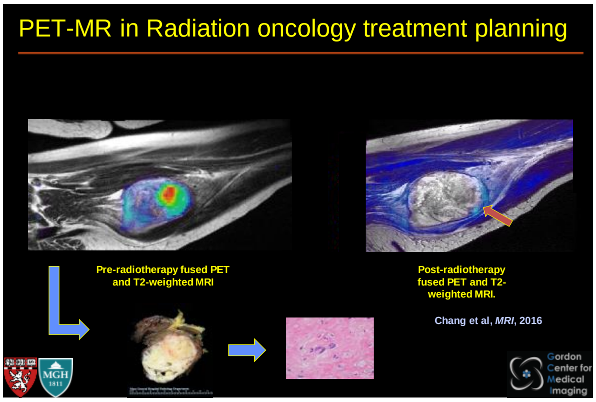
PET-MR in Radiation oncology treatment planning
Pre-radiotherapy fused PET and T2-weighted MRI
Post-radiotherapy fused PET and T2-weighted MRI.
Chang et al, MRI, 2016
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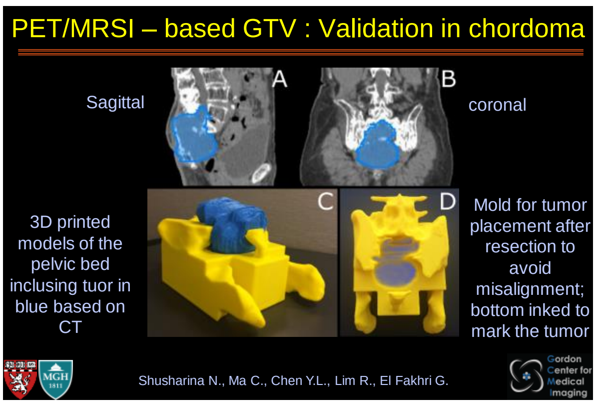
PET/MRSI – based GTV : Validation in chordoma
Sagittal
A
B
coronal
3D printed models of the pelvic bed inclusing tuor in blue based on CT
C
D
Mold for tumor placement after resection to avoid misalignment; bottom inked to mark the tumor
Shusharina N., Ma C., Chen Y.L., Lim R., El Fakhri G.
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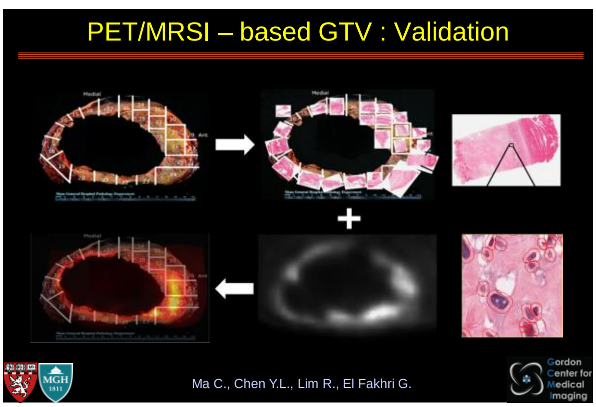
PET/MRSI – based GTV : Validation
Ma C., Chen Y.L., Lim R., El Fakhri G.
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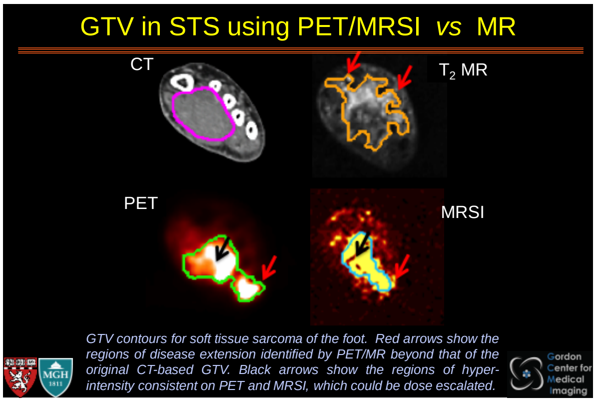
GTV in STS using PET/MRSI vs MR
CT
T2 MR
PET
MRSI
GTV contours for soft tissue sarcoma of the foot. Red arrows show the regions of disease extension identified by PET/MR beyond that of the original CT-based GTV. Black arrows show the regions of hyper-intensity consistent on PET and MRSI, which could be dose escalated.
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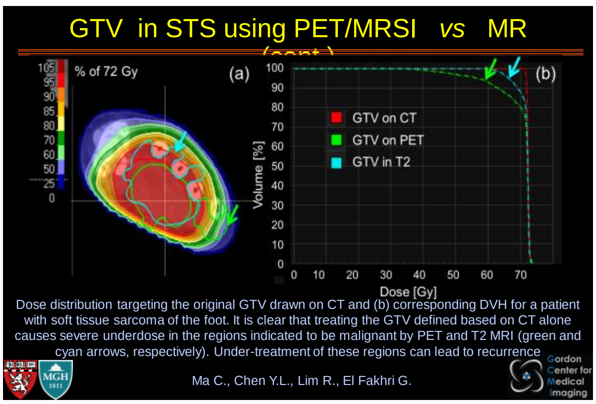
GTV in STS using PET/MRSI vs MR
% of 72 Gy
(a)
(b)
GTV on CT
GTV on PET
GTV in T2
Volume [%]
Dose [Gy]
Dose distribution targeting the original GTV drawn on CT and (b) corresponding DVH for a patient with soft tissue sarcoma of the foot. It is clear that treating the GTV defined based on CT alone causes severe underdose in the regions indicated to be malignant by PET and T2 MRI (green and cyan arrows, respectively). Under-treatment of these regions can lead to recurrence
Ma C., Chen Y.L., Lim R., El Fakhri G.
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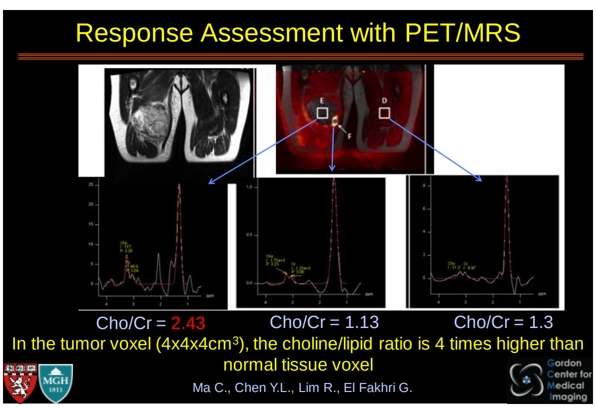
Response Assessment with PET/MRS
Cho/Cr = 2.43
Cho/Cr = 1.13
Cho/Cr = 1.3
In the tumor voxel (4x4x4cm³), the choline/lipid ratio is 4 times higher than normal tissue voxel
Ma C., Chen Y.L., Lim R., El Fakhri G.
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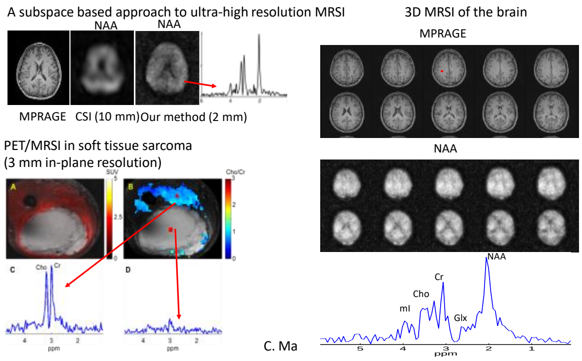
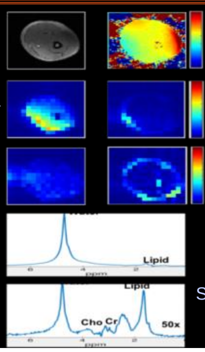
Ultra-high resolution MR spectroscopic imaging



Response Assessment with PET/MRS



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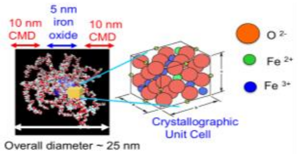
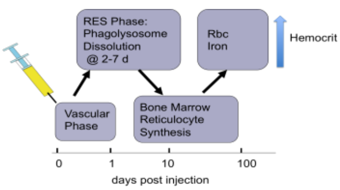
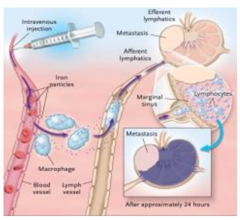
Background on Feraheme (FH)



Clinical and research applications of FH





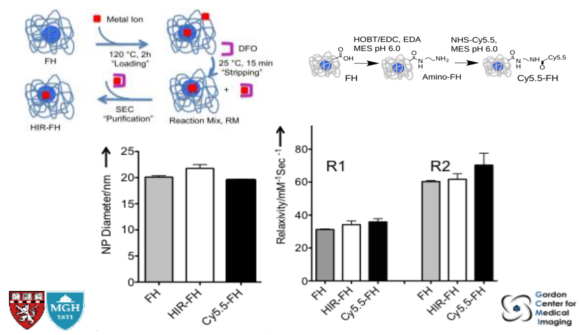
Harisinghani et al., *NEJM* 2003

Clinical trials using MRI of macrophages with FH

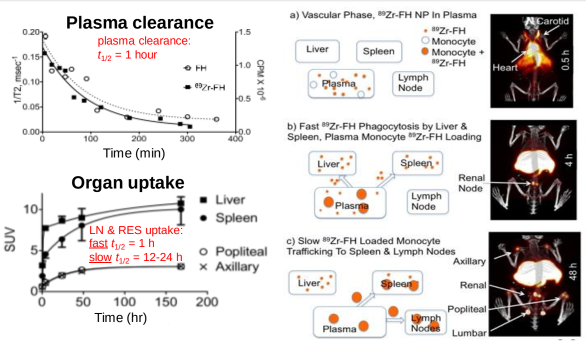
Clinical trials imaging FH uptake by macrophages using MRI

- Diabetes Inflammation (Type I Progression) NCT01710072/Gaglia
- Carotid Inflammation NCT01674257/Newby
- Brain Tumor Uptake NCT00103038 & NCT00660543/Neuwelt
- Lymph node metastases: Pancreatic, prostate breast, thyroid NCT00920023/Weissleder, NCT00087347/Harisinghani, NCT01927887/Harisinghani
- Myocardial Infarction NCT01323296/Newby
- CNS Inflammation: Stroke, Mult. Scler., Surgery, Aneursym NCT00659776/Neuwelt NCT01710072/Hasan

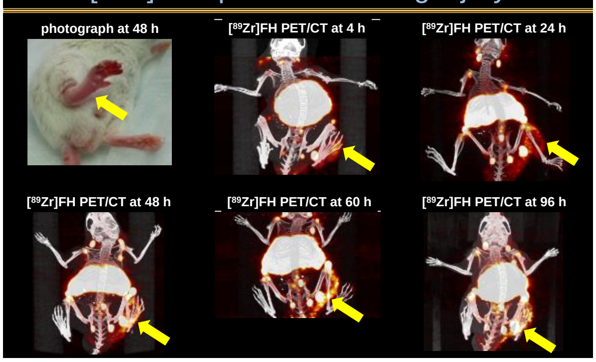
Heat-induced radiolabeling (HIR)

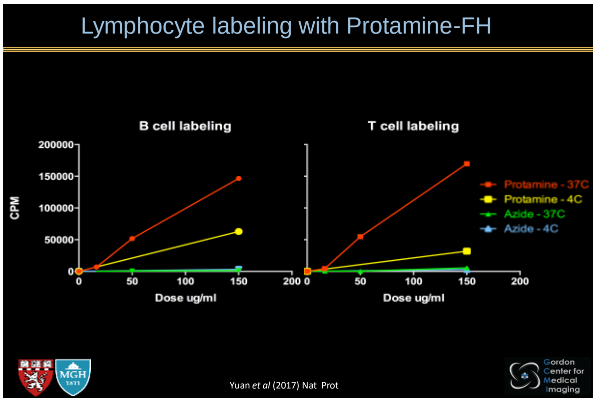


[89Zr]FH kinetics and proposed trafficking model



[89Zr]FH uptake in hind leg injury




Lymphocyte labeling with Protamine-FH
B cell labeling
T cell labeling
CPM
200000
150000
100000
50000
0
0
50
100
150
200
Dose ug/ml
Protamine - 37C
Protamine - 4C
Azide - 37C
Azide - 4C
Yuan et al (2017) Nat Prot
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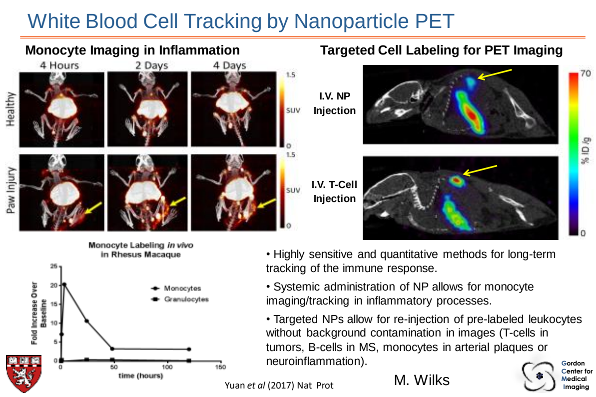
White Blood Cell Tracking by Nanoparticle PET
Monocyte Imaging in Inflammation
4 Hours
2 Days
4 Days
Healthy
Paw Injury
SUV
Targeted Cell Labeling for PET Imaging
I.V. NP Injection
I.V. T-Cell Injection
70
0
% ID /g
Monocyte Labeling in vivo in Rhesus Macaque
Fold Increase Over Baseline
Monocytes
Granulocytes
time (hours)
• 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-labeled leukocytes without background contamination in images (T-cells in tumors, B-cells in MS, monocytes in arterial plaques or neuroinflammation).
Yuan et al (2017) Nat Prot
M. Wilks
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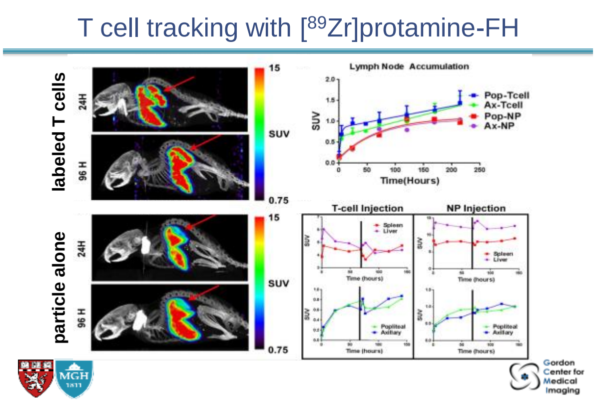
T cell tracking with [89Zr]protamine-FH
labeled T cells
particle alone
24H
96 H
15
SUV
0.75
Lymph Node Accumulation
SUV
Time(Hours)
Pop-Tcell
Ax-Tcell
Pop-NP
Ax-NP
T-cell Injection
NP Injection
Spleen
Liver
Popliteal
Axillary
Time (hours)
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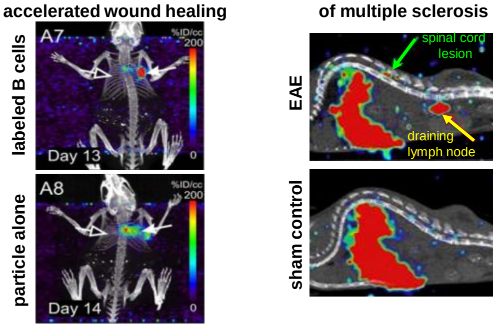
B cell tracking with [^{89}Zr]protamine-FH



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