DW-MRI and PET correlation in Lymphoma

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Outline

I. Diffusion-weighted magnetic resonance imaging (DW-MRI) in Oncology

II. DW-MRI in Lymphoma

III. DW-MRI and PET correlation in Lymphoma
DW-MRI

• Probes diffusion of water molecules in
  – Extra- and intracellular spaces
  – Intravascular space

• Reflects tissue cellularity and cell membrane integrity

• Qualitative and Quantitative information
**DW-MRI**

Stejskal and Tanner (1965)

Apparent Diffusion Coefficient: ADC

- **b (s/mm²)** determines diffusion-weighting
- ADC can be calculated with ≥ 2 data points with different **b** values = \( \frac{1}{b_1-b_0} \ln \left( \frac{S[b_1]}{S[b_0]} \right) \) mm²/s

Koh DM et al. AJR 2007

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Separation of Diffusion and Perfusion in Intravoxel Incoherent Motion MR Imaging

Radiology 1988; 168:497-505
No restriction

Restriction (tumor)
No restriction: ADC is high

Restriction: ADC is low
DW-MRI in Oncology: T stage

Lin G et al. *Radiology* 2009
DW-MRI in Oncology: N stage

Vandecaveye V et al. Radiology 2009
Abstract

On May 3, 2008, a National Cancer Institute (NCI)-sponsored open consensus conference was held in Toronto, Ontario, Canada, during the 2008 International Society for Magnetic Resonance in Medicine Meeting. Approximately 100 experts and stakeholders summarized the current understanding of diffusion-weighted magnetic resonance imaging (DW-MRI) and reached consensus on the use of DW-MRI as a cancer imaging biomarker. DW-MRI should be tested as an imaging biomarker in the context of well-defined clinical trials, by adding DW-MRI to existing NCI-sponsored trials, particularly those with tissue sampling or survival indicators. Where possible, DW-MRI measurements should be compared with histologic indices including cellularity and tissue response. There is a need for tissue equivalent diffusivity phantoms; meanwhile, simple fluid-filled phantoms should be used. Mono-exponential assessments of apparent diffusion coefficient values should use two b values (100 and between 500 and 1000 mm²/sec depending on the application). Free breathing with multiple acquisitions is superior to complex gating techniques. Baseline patient reproducibility studies should be part of study designs. Both region of interest and histogram analysis of apparent diffusion coefficient measurements should be obtained. Standards for measurement, analysis, and display are needed. Annotated data from validation studies (along with outcome measures) should be made publicly available. Magnetic resonance imaging vendors should be engaged in this process. The NCI should establish a task force of experts (physicists, radiologists, and oncologists) to plan, organize technical aspects, and conduct pilot trials. The American College of Radiology Imaging Network infrastructure may be suitable for these purposes. There is an extraordinary opportunity for DW-MRI to evolve into a clinically valuable imaging tool, potentially important for drug development.

Neoplasia (2009) 11, 102–125
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DW-MRI in Lymphoma

• Lymphoma: high cellularity and high nuclear-to-cytoplasm ratio

• Lower ADC values than other tumors

Nakayama T et al. *J Magn Reson Imaging* 2004
King AD et al. *Radiology* 2007

DLBCL: H&E stain
ADC = 0.504 x 10^{-3} \text{ mm}^2/\text{s} \\
T cell lymphoma

ADC = 1.115 x 10^{-3} \text{ mm}^2/\text{s} \\
WD SCC

D/D Malignant cervical lymphadenopathy

ADC ($\times 10^{-3}$ mm$^2$/sec)

King AD et al. Radiology 2007
Monitoring response to chemotherapy of non-Hodgkin’s lymphoma xenografts by $T_2$-weighted and diffusion-weighted MRI

Ming Q. Huang, Stephen Pickup, David S. Nelson, Hui Qiao, He N. Xu, Lin Z. Li, Rong Zhou, E. James Delikatny, Harish Poptani and Jerry D. Glickson*

Molecular Imaging Laboratory, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA
H & E/mitosis  |  Ki-67/proliferation index  |  FITC/apoptosis index

(a) control  |  (c)  |  (e) treated
(b) control  |  (d)  |  (f)

Huang MQ et al. *NMR Biomed* 2008
Whole-body DW-MRI

• Lack of ionizing radiation
• High spatial resolution
• Excellent soft tissue contrast (extranodal)
• Quantitative parameters on a whole-body scale
Free breathing
Thin sections (4mm/-1mm overlapping) allows 3D MPR and MIP
\( b = 0, 1000 \text{ s/mm}^2 \)
Inverse gray → PET-like
No ADC mapping

Kwee TC et al. *Eur Radiol* 2008
WB MRI/DWI vs. CECT

- First study with pure lymphoma patients
- Mixed HL n = 7/NHL n = 23 (different grades)
- Pretreatment staging vs. CECT
- MRI (T1w and T2w) ± DWIBS
- Reference: PET/BM biopsy/CT F/U

Kwee TC et al. *Invest Radiol* 2009
WB MRI/DWI vs. CECT

62 y/o, DLBCL

T1w/T2w CT DWIBS FDG-PET

PET/CT fusion T1w/T2w F/U

False negative on T1/T2w, CT & blind iliac crest biopsy later proven with image-guided biopsy

Kwee TC et al. *Invest Radiol* 2009
WB DW-MRI (our experience)

- Whole-body protocol using only DW-MRI
- $b$ values = 50, 400, 800 s/mm$^2$
- Respiratory gating for slice co-registration
- Whole-body ADC mapping
- No 3D reconstruction
- FOV as CECT
WB DW-MRI (our experience)

Surface coils to increase SNR
Skull base to Groin 30~45min

Smallest $b$ at 50 reduces perfusion effect and eliminates signal from vessels

Materials & Methods

• Image interpretation and analysis directly on native axial images

• Combine good T2-weighted morphological/size and DW-MR functional information

✓ A 79 year-old patient with concomitant DLBCL and follicular lymphoma
Outline

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Whole-body diffusion-weighted magnetic resonance imaging with apparent diffusion coefficient mapping for staging patients with diffuse large B-cell lymphoma

- 15 DLBCL patients, in 2 with concomitant follicular lymphoma
- Lesion detection on b50 DW images (equivalent to T2w)
- FDG-PET/CT as reference standard

Visual analysis of ADC map and quantitative ADC measurement on > 1cm LN
Patient 79y, concomitant DLBCL and follicular lymphoma.
Lymph node involvement

- IWG Cheson’s size criteria (> 1 cm)
- DWI and PET/CT matched in 277 (94%) out of 296 lymph node regions
- 73 (89%) of the 82 regions, positive on both DWI and PET – restricted diffusion (black) on ADC maps – ADC = $0.752 \times 10^{-3} \pm 0.210$ mm$^2$/s
- Size criteria alone: Se 90% and Sp 94%
- Size plus visual ADC analysis: Se 81% and Sp 100%

Lin C et al. *Eur Radiol* 2010
Patient 24y, Gastric DLBCL regional LN+ 15-mm lymph node (arrow), negative on FDG-PET

• Positive on DWI according to size criteria (no abnormal FDG uptake), but no restricted diffusion on ADC map
• This node did not show size/signal change after chemotherapy
Similar cellularity; Comparable ADC values
Organ involvement

- 20 organs recorded positive
- Concordance 100%
- DW-MRI more sensitive for the detection of renal and hepatic involvement
- Finally, Ann Arbor stages agreed in 14 (93%) patients

Lin C et al. *Eur Radiol* 2010
Patient 42y, DLBCL renal involvement

- On PET/CT, lesions might be masked by normal FDG excretion, which would depend on the color scale adjustment.
Patient 57y, concomitant DLBCL and follicular lymphoma

Hepatic involvement

- DWI helped to confirm hepatic involvement in case of small focal lesions
- On PET/CT, FDG uptake of liver was within normal range
Same patient, concomitant DLBCL and follicular lymphoma bone marrow involvement

- Focal lesions stay white on $b_{800}$ images and show restricted diffusion on ADC map
- Fracture of left sacral ala $\rightarrow$ no restricted diffusion
WB MRI/DWI vs. PET/CT

Staging

- van Ufford HM and Kwee TC et al. *AJR* 2011
  - Mixed HL and NHL (aggressive and indolent)
  - Long acquisition time (T1w/T2w + DWIBS)
  - Moderate agreement (HL, DLBCL)
  - Discordance mainly in indolent patients
Response assessment

FDG-PET: reference standard

Revised Cheson’s response criteria *J Clin Oncol* 2007


![](image)

Probability of Event-Free Survival

FDG-PET (-)  n = 54

FDG-PET (+)  n = 36

median follow-up: 24mo

p < 0.0001
Whole-Body Diffusion-Weighted Imaging With Apparent Diffusion Coefficient Mapping for Treatment Response Assessment in Patients With Diffuse Large B-Cell Lymphoma

Pilot Study

Chieh Lin, MD, PhD,*†† Emmanuel Itti, MD, PhD,‡§ Alain Luciani, MD, PhD,*†† Benhalima Zegai, MD,*
Shih-jui Lin, PhD,** Frédérique Kuhnowski, MD,† †† Frédéric Pigneur, MD,* Isabelle Gaillard, MD,† ††
Gaetano Paone, MD,‡§ Michel Meignan, MD, PhD,‡§ Corinne Haioun, MD,† ††
and Alain Rahmouni, MD, PhD*‡

• Same 15 DLBCL patients as staging study
• Lesion detection on b50 DW images
• FDG-PET/CT as reference standard

Size, Visual ADC analysis and ADC change following 4 chemotherapy cycles (R-CHOP in 13 and R-ACVBP in 2)

Lin C et al. Invest Radiol 2011
Response assessment in DLBCL

• Residual nodes > 1cm in 26 regions

ADC : $0.658 \times 10^{-3} \pm 0.153 \text{ mm}^2/\text{s} \rightarrow 1.501 \times 10^{-3} \pm 0.307 \text{ mm}^2/\text{s}$

(paired $t$ test, $P < 0.0001$)
Patient 23y, mediastinal DLBCL

- After four cycles, residual mass 8 x 1 cm persisted → CR uncertain (Cheson 1999) but PET (-) → CR (Revised Cheson/Juweid 2007).
- No restricted diffusion on ADC map after treatment.
**TABLE 2.** Per-Region Comparison of Diagnosis of Residual Lymph Node Involvement on Whole-Body DWI and Integrated FDG PET/CT

<table>
<thead>
<tr>
<th></th>
<th>PET/CT</th>
<th>PET/CT</th>
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<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
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<tr>
<td>DWI criteria</td>
<td>Size criteria alone</td>
<td>Size plus visual ADC analysis</td>
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<tr>
<td>Positive</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Negative</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

Decrease false positives combining size and visual ADC analysis

Lin C et al. *Invest Radiol* 2011
DW-MRI vs. FDG-PET/CT

- Punwani S et al. ADC vs. SUV in HL. *Cancer Biomark* 2010 Jan.
- Wu X et al. ADC vs. SUV in DLBCL. *Eur J Radiol* 2011 May [Epub]
Early response in DLBCL

- 8 patients

- Baseline (E1), 1 week (E2) and 2 cycles (E3)

- ADC \(0.71 \times 10^{-3} \text{ mm}^2/\text{s} (\text{E1})\) → increase by 77% at E2 (p<0.05); total increase 106%

- Baseline ADC correlated inversely with SUVmax and active tumor burden on PET/CT (p<0.05)

Wu X et al. *NMR Blomed* 2011
Conclusions

• Lesion detection
  – DW-MRI (± T2w) shows more lesions than CT
  – DW-MRI more sensitive for extranodal sites except diffuse splenic involvement

• Response assessment
  – Significant ADC changes on a whole-body scale

• Prospective study with larger cohort is required

• Technical challenges…
Patient 49y, mediastinal DLBCL, partial response at 4 cycles, progression at the end of treatment.

- Tiny right pulmonary nodule (arrow) showed persistent FDG uptake (positive)
- This nodule was also clearly identified on DWI (arrow)
Patient 68y, DLBCL, 71.5% SUVmax reduction at 4 cycles (R-CHOP)

Nov. 2009  SUVmax = 27

Aug. 2010  SUVmax = 10
After 4 cycles (R-GEMOX)
Three months later, mass decreased in size → false positive of PET and DWI
Hybrid PET/MRI: new era?

Simultaneous 3T PET/MRI system

Cell density complementary to tissue metabolism
Monochromatic imaging

One test
One answer

Many tests
Many answers

One test
Many answers

Multi-parametric data
Hyperpolarized $^{13}$C MRI and PET: In Vivo Tumor Biochemistry

Injected hyperpolarized $[^{13}\text{C}]$pyruvate

$[^{13}\text{C}]$lactate produced from injected hyperpolarized $[^{13}\text{C}]$pyruvate

$^{18}$F-FDG

DNP: dynamic nuclear polarization

Nat Med 2007 A murine lymphoma model
Ask right question for each scenario with well designed study.

Continuously improve DW-MR technology before it can be applied in daily practice.
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"AREN'T THERE ENOUGH PROBLEMS IN THE WORLD ALREADY?"