Menton 2011

DW-MRI and PET correlation in Lymphoma

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Outline

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

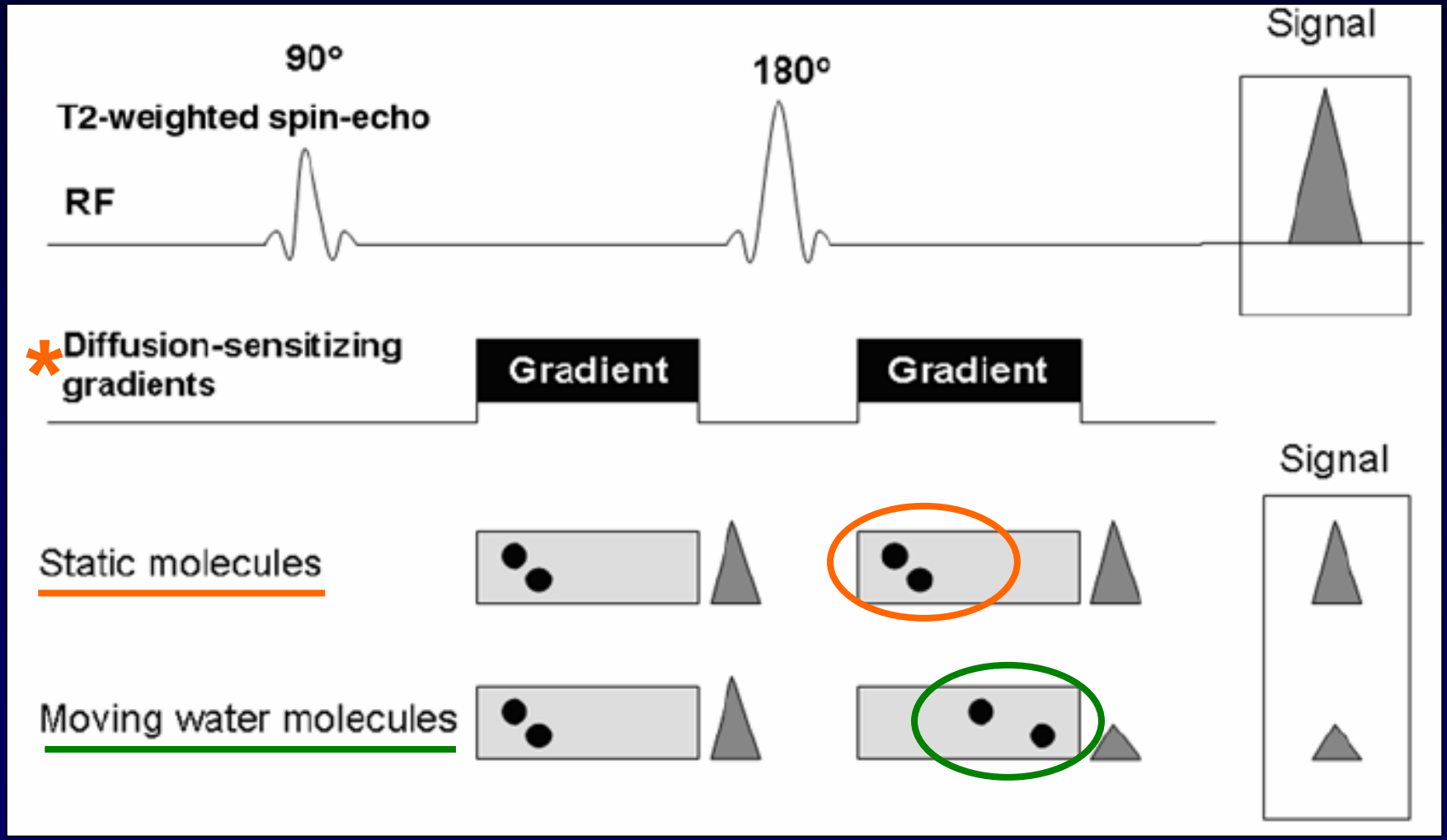
II. DW-MRI in Lymphoma

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)

Koh DM et al. ***AJR*** 2007

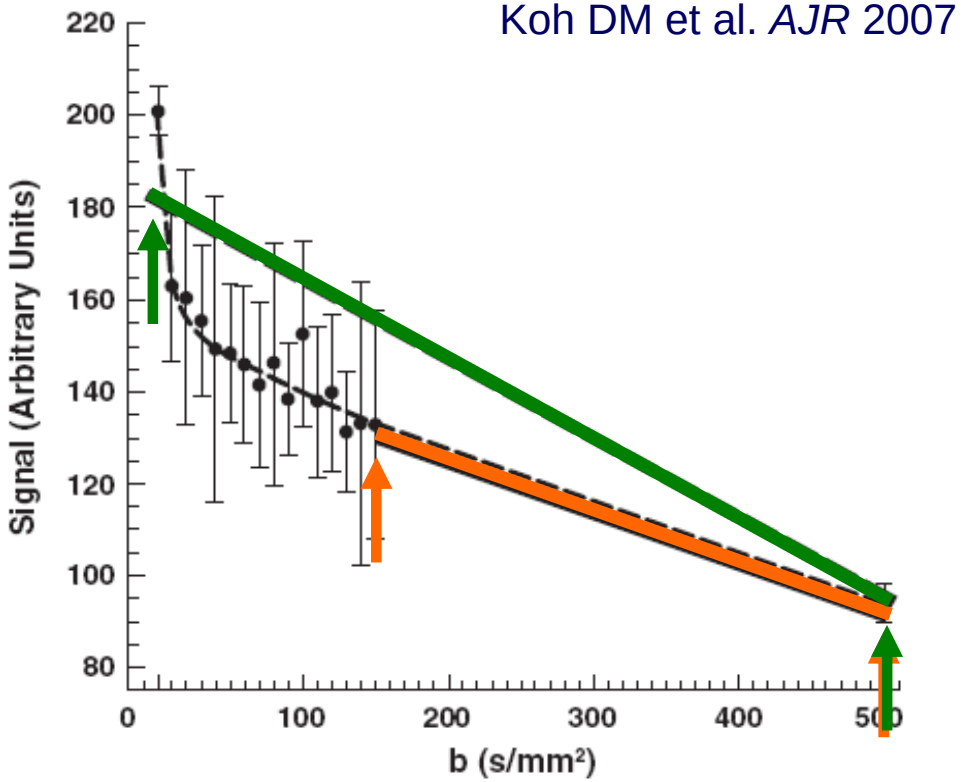
Apparent Diffusion Coefficient: **ADC**

Denis Le Bihan, MD, PhD • Eric Breton, MS • Denis Lallemand, MD
• Marie-Louise Aubin, MD • Jacqueline Vignaud, MD • Maurice Laval-Jeantet, MD

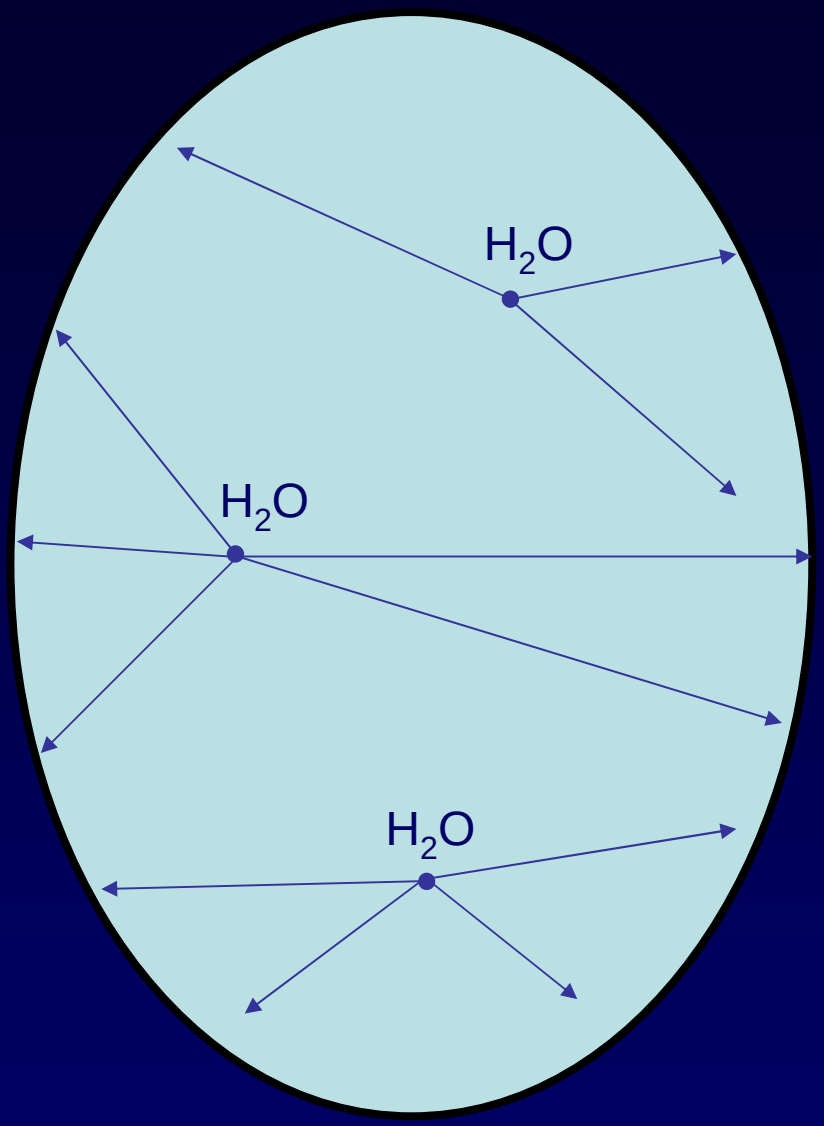
Separation of Diffusion and Perfusion in Intravoxel Incoherent Motion MR Imaging[1]

Radiology 1988; 168:497-505

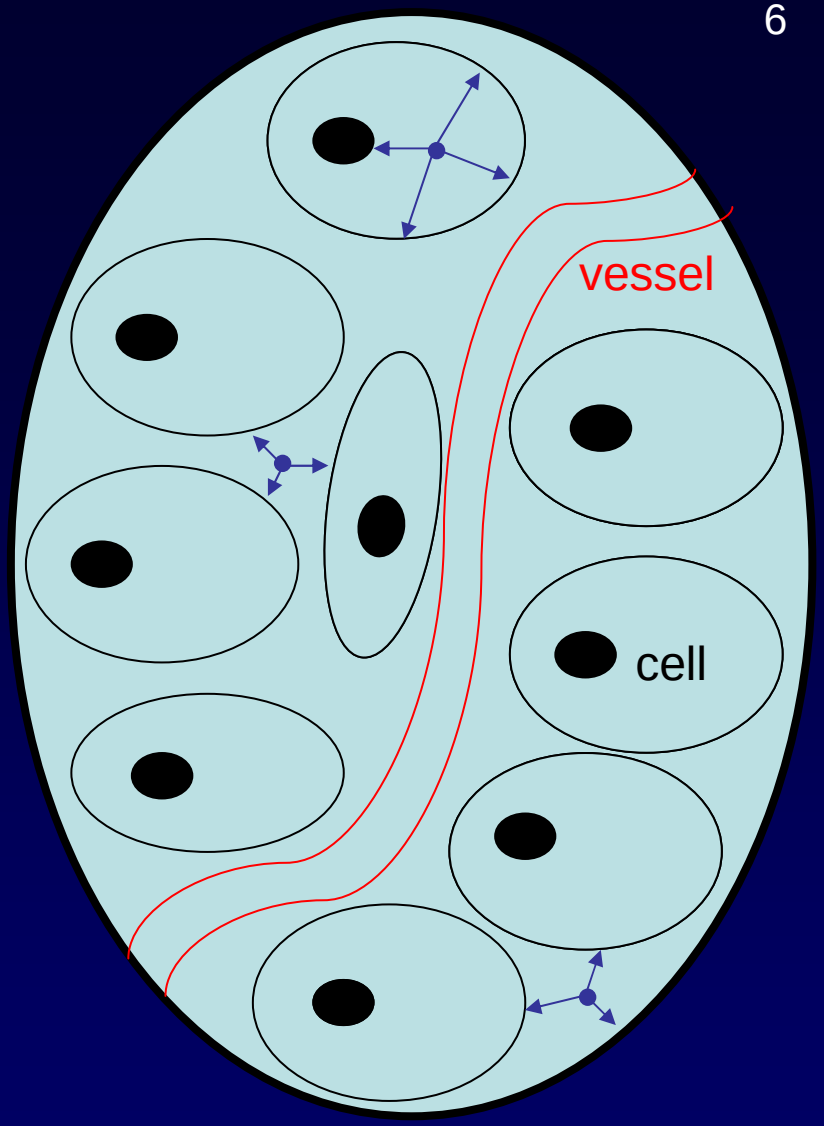
Koh DM et al. *AJR* 2007



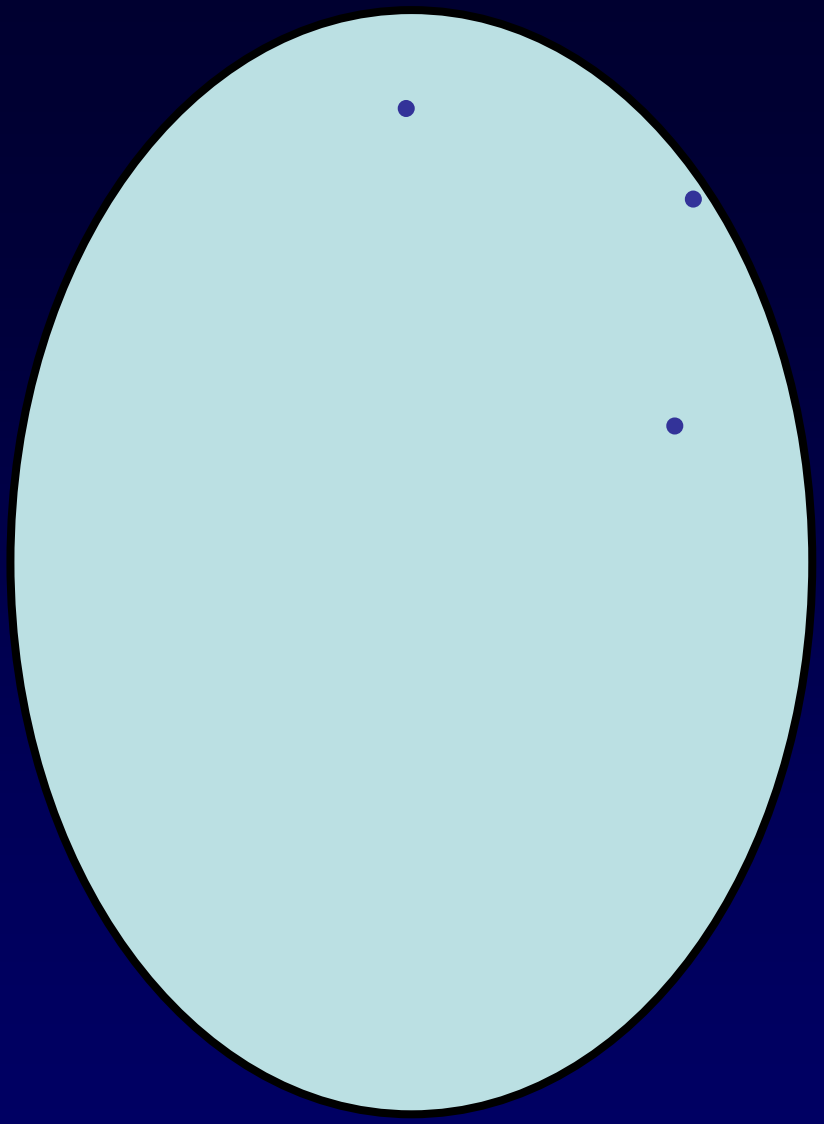
- ***b*** (s/mm^2) determines diffusion-weighting
- ADC can be calculated with ≥ 2 data points with different ***b*** values = $(1/b_1\text{-}b_0)$ ln $(S[b_1]/S[b_0])$ mm^2/s



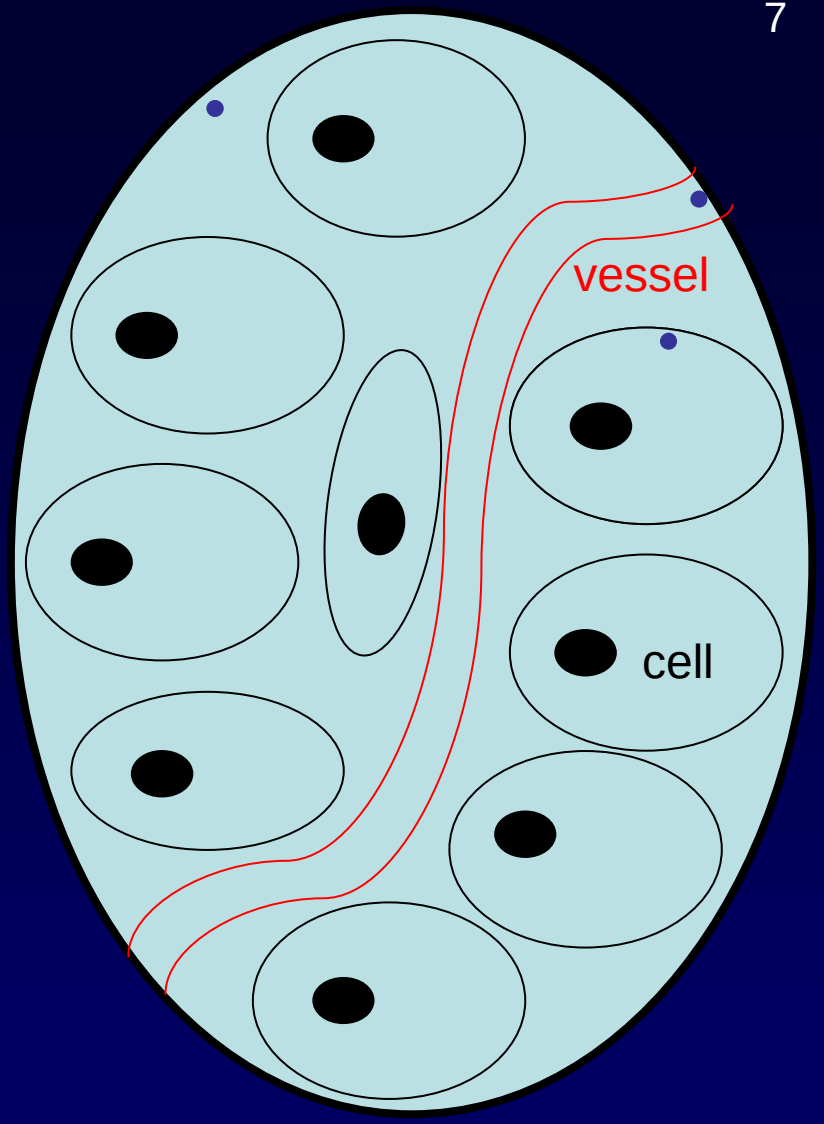
No restriction



Restriction (tumor)

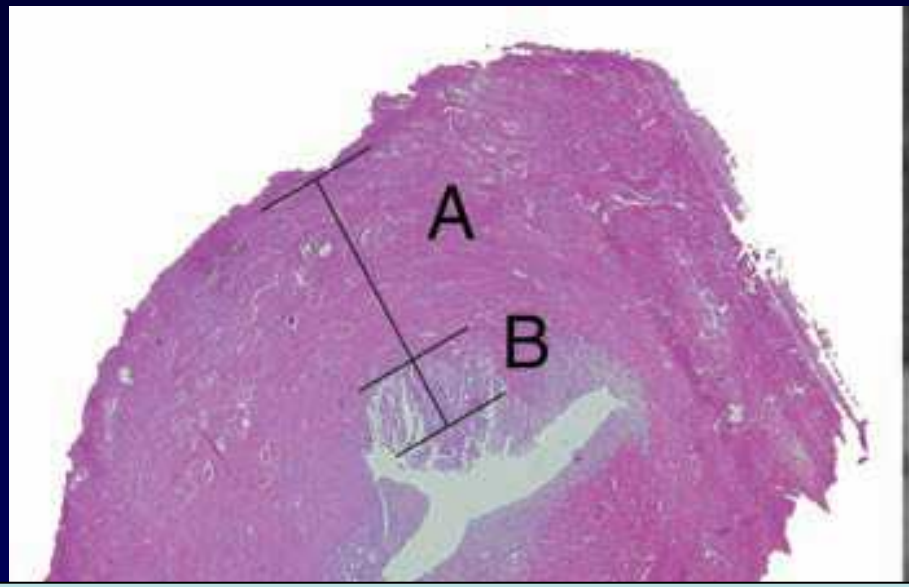


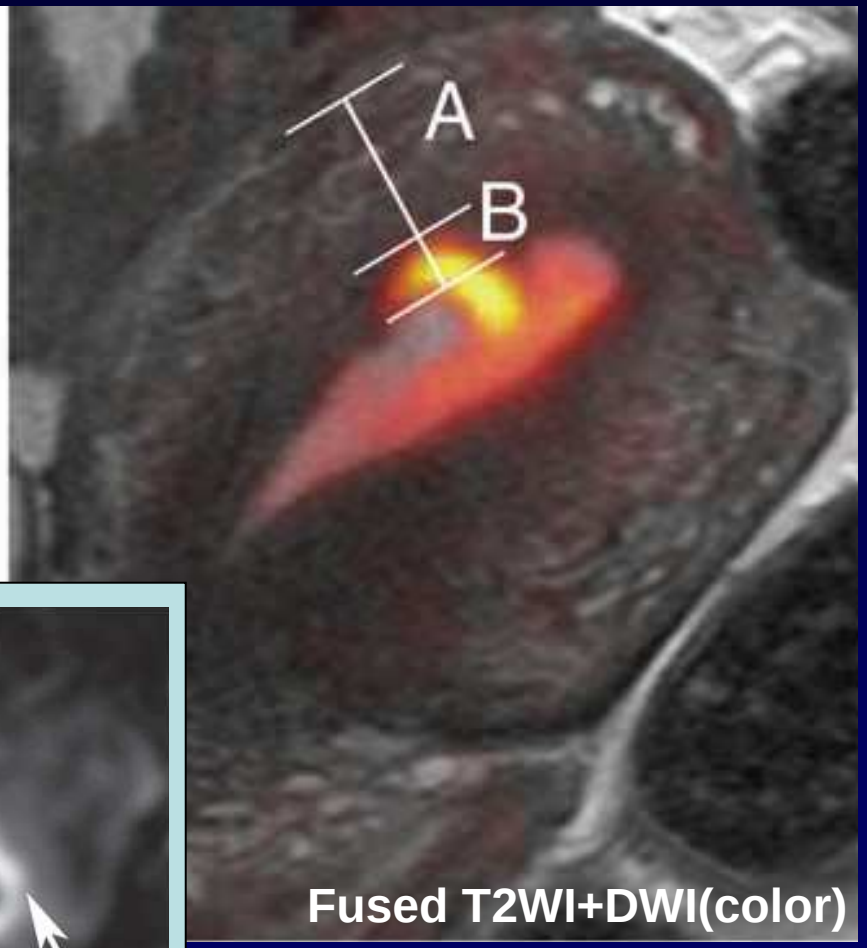
No restriction: ADC is high

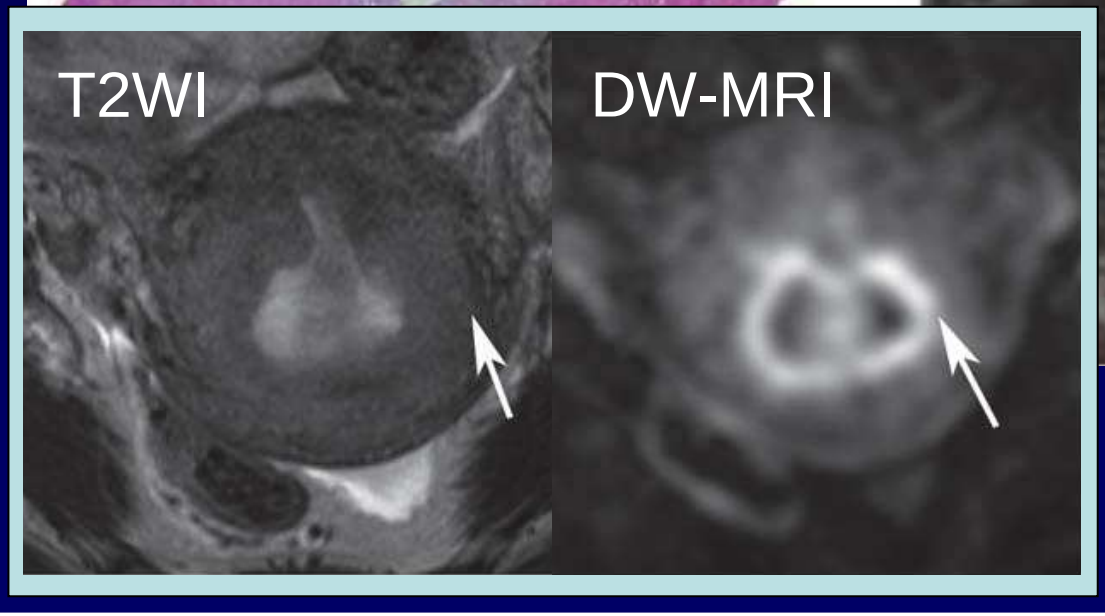


Restriction: ADC is low

DW-MRI in Oncology: T stage

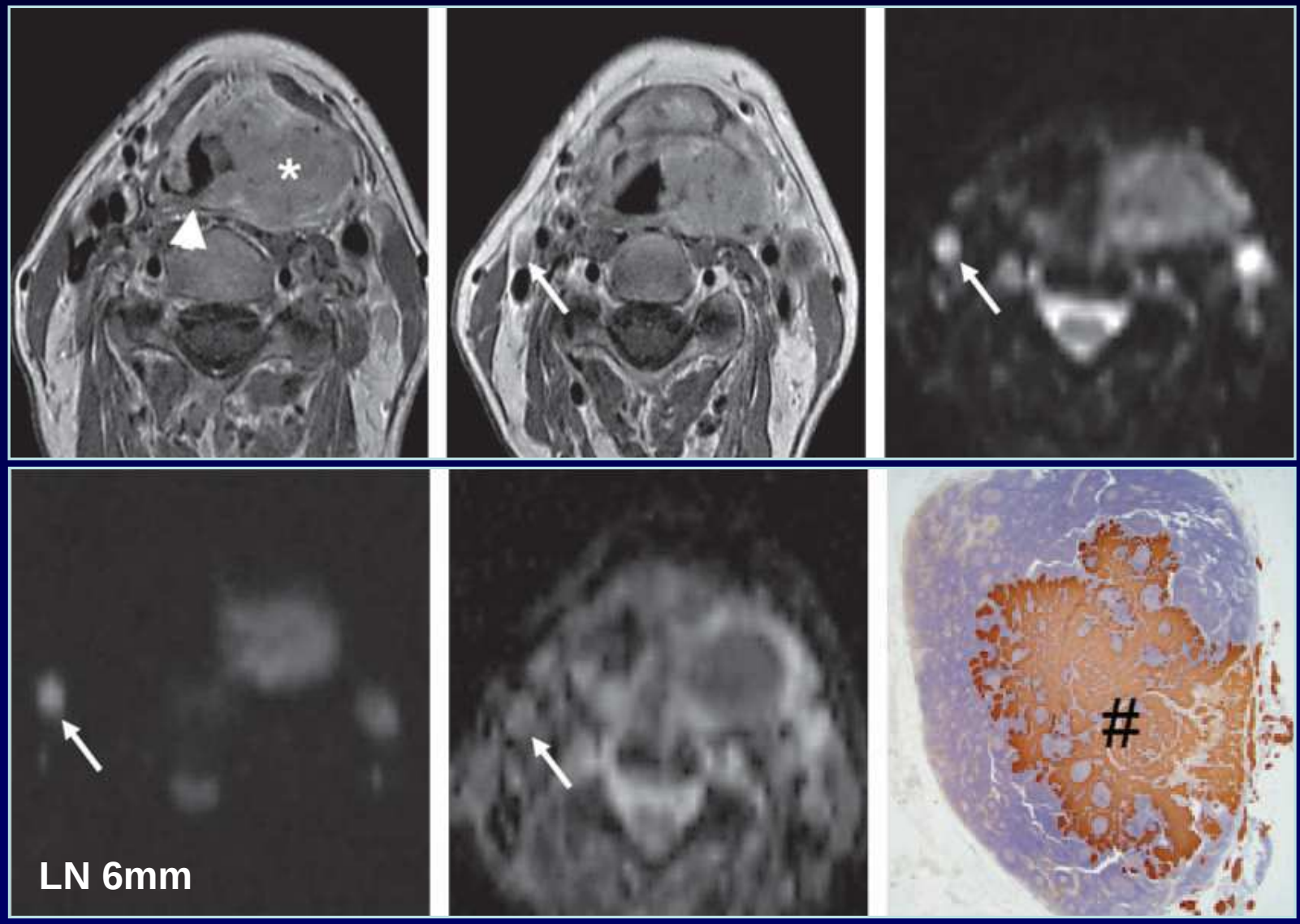






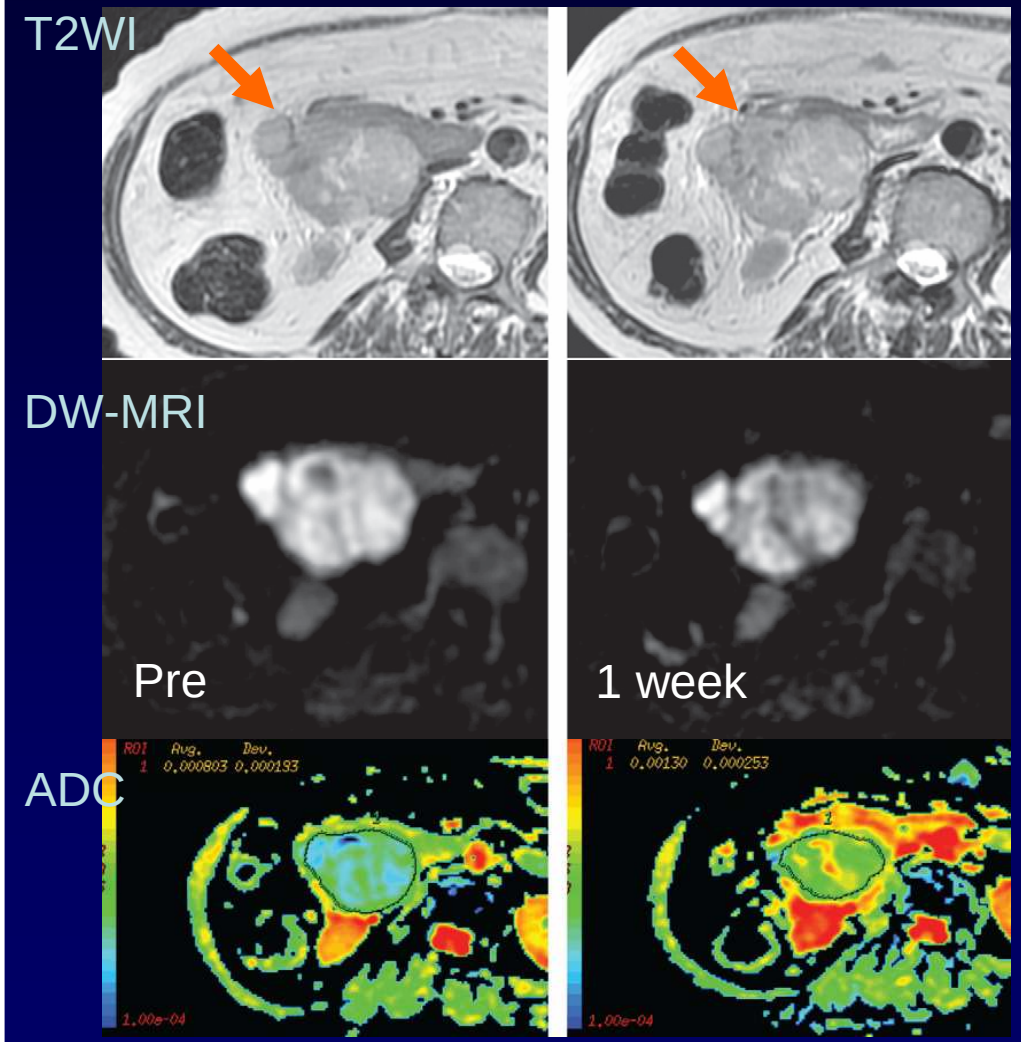
Lin G et al. ***Radiology*** 2009

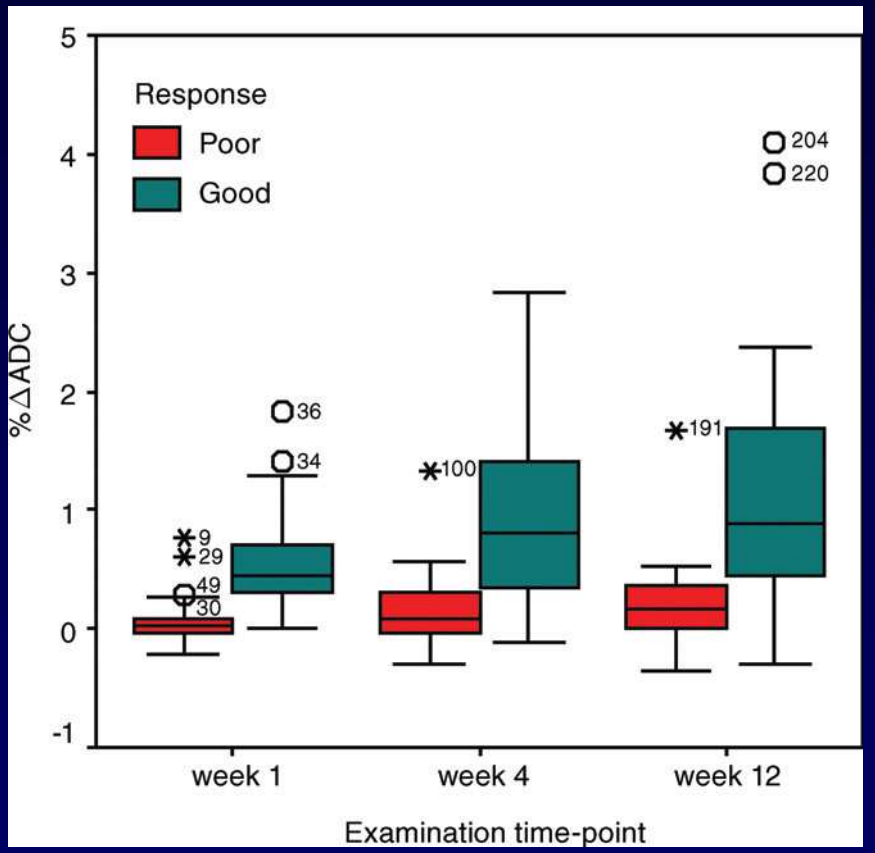
DW-MRI in Oncology: N stage



Vandecaveye V et al. ***Radiology*** 2009

DW-MRI in Oncology: Response





Tang L et al. ***Radiology*** 2011

NEOPLASIA
www.neoplasia.com
Volume 11 Number 2 February 2009 pp. 102–125 102

Meeting Rep

Diffu
Resc
Canc
and

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. Monoexponential assessments of apparent diffusion coefficient values should use two *b* values (>100 and between 500 and 1000 mm^2/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

Outline

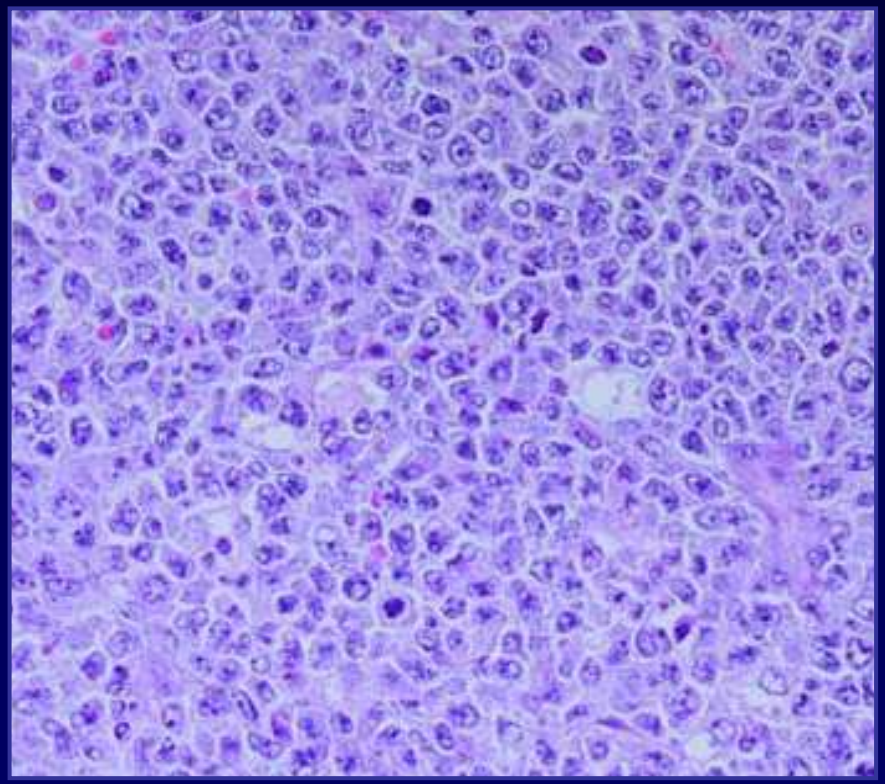
I. Diffusion-weighted magnetic resonance imaging (DW-MRI) in Oncology

II. DW-MRI in Lymphoma

III. DW-MRI and PET correlation in Lymphoma

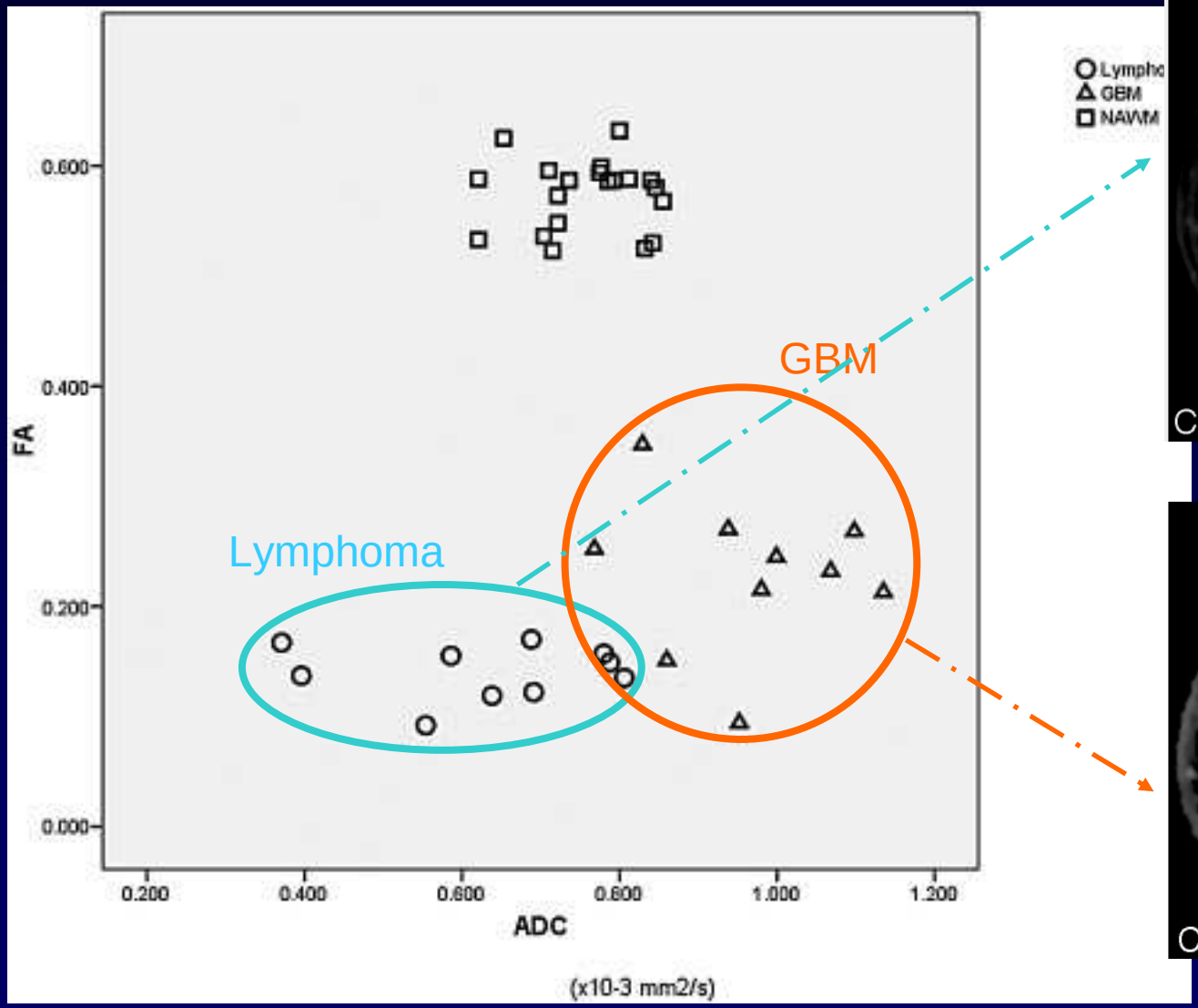
DW-MRI in Lymphoma

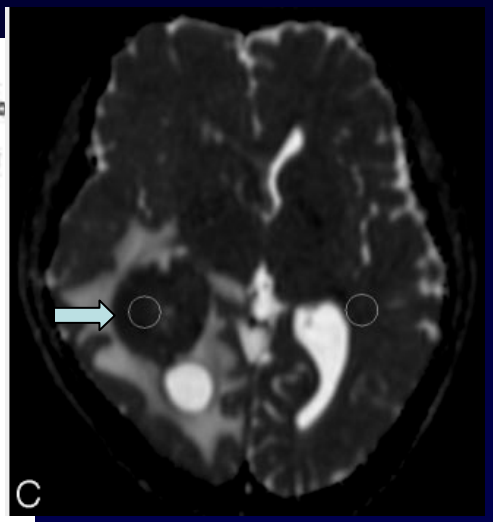
- Lymphoma: high cellularity and high nuclear-to-cytoplasm ratio
- Lower ADC values than other tumors

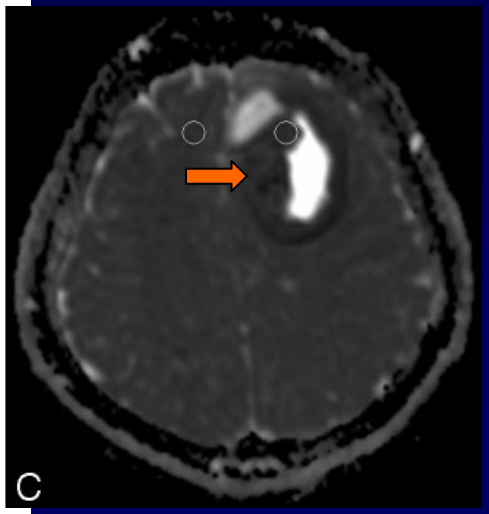


DLBCL: H&E stain

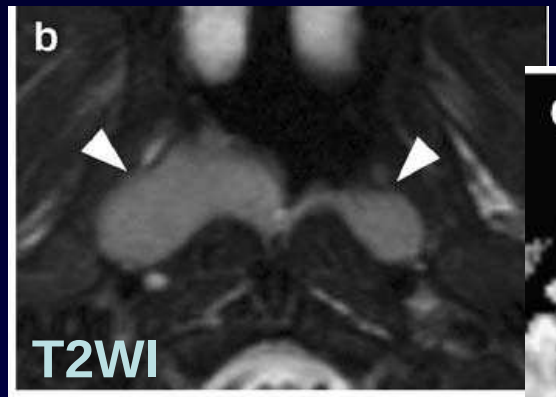
Nakayama T et al. ***J Magn Reson Imaging*** 2004
Sumi M et al. ***Eur Radiol*** 2007
King AD et al. ***Radiology*** 2007
Toh CH et al. ***AJNR Am J Neuroradiol*** 2008

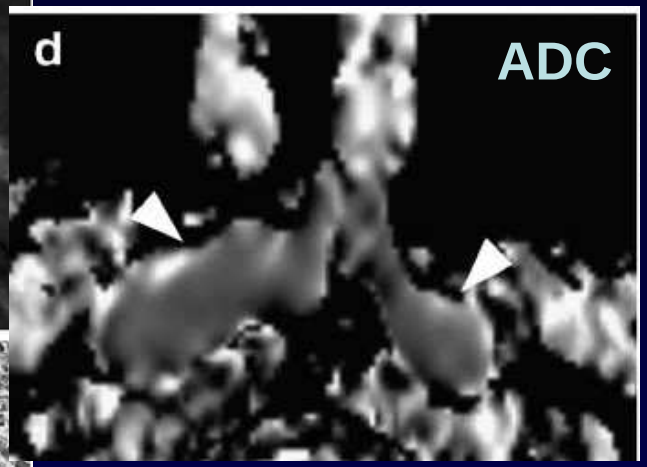


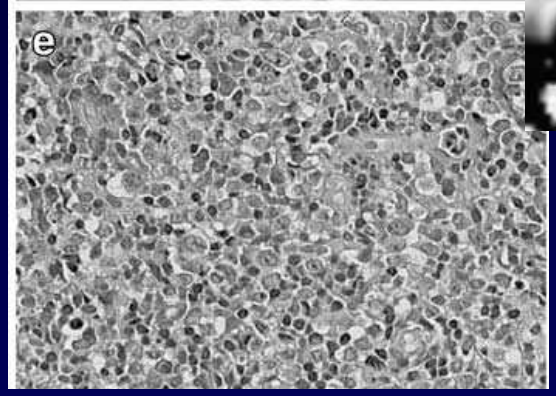




Toh CH et al. ***AJNR*** 2008

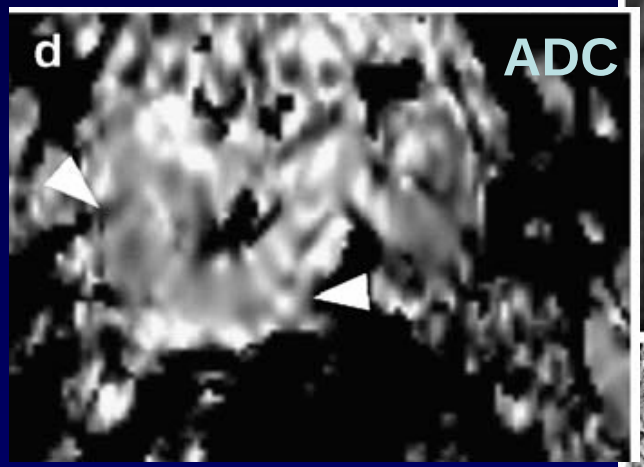


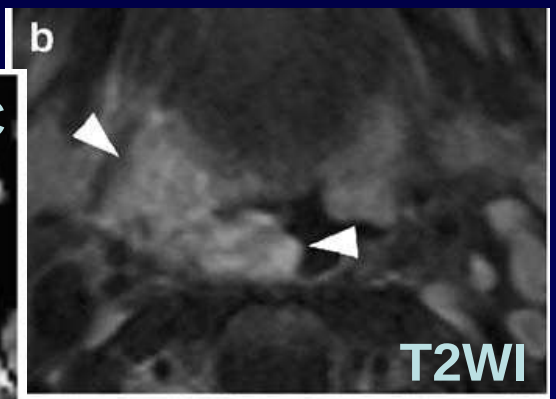


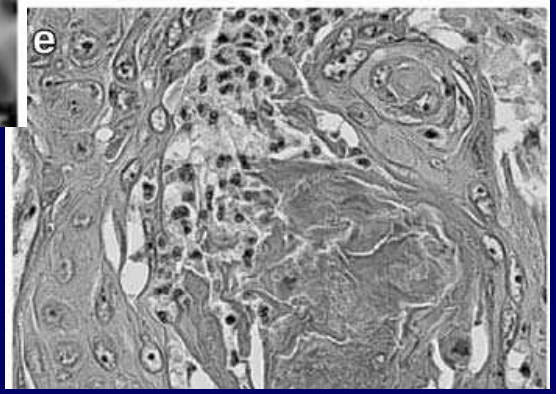


ADC = 0.504 x 10^{-3} mm^2/s

T cell lymphoma





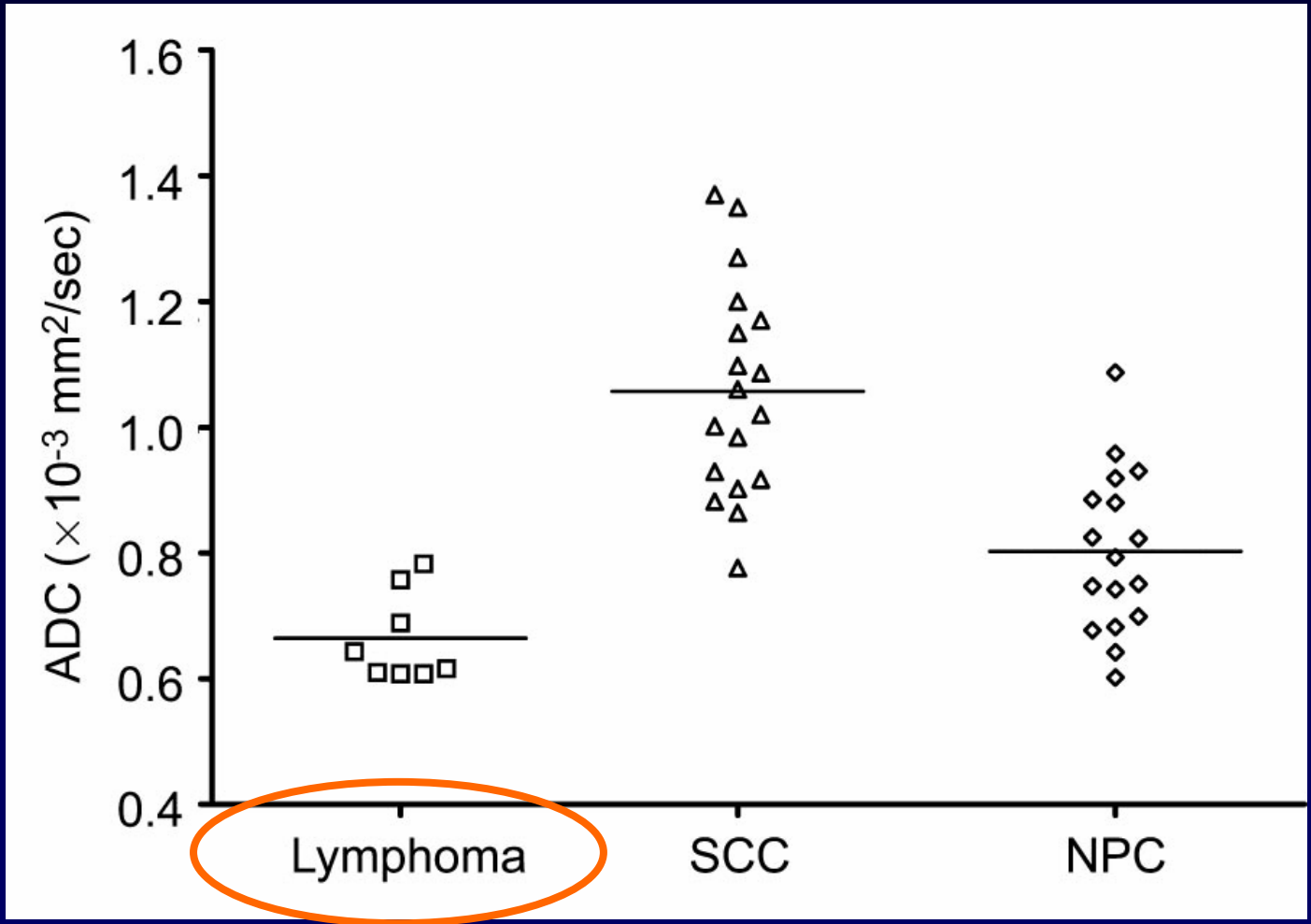


ADC = 1.115 x 10^{-3} mm^2/s

WD SCC

Sumi M et al. ***Eur Radiol*** 2007

D/D Malignant cervical lymphadenopathy



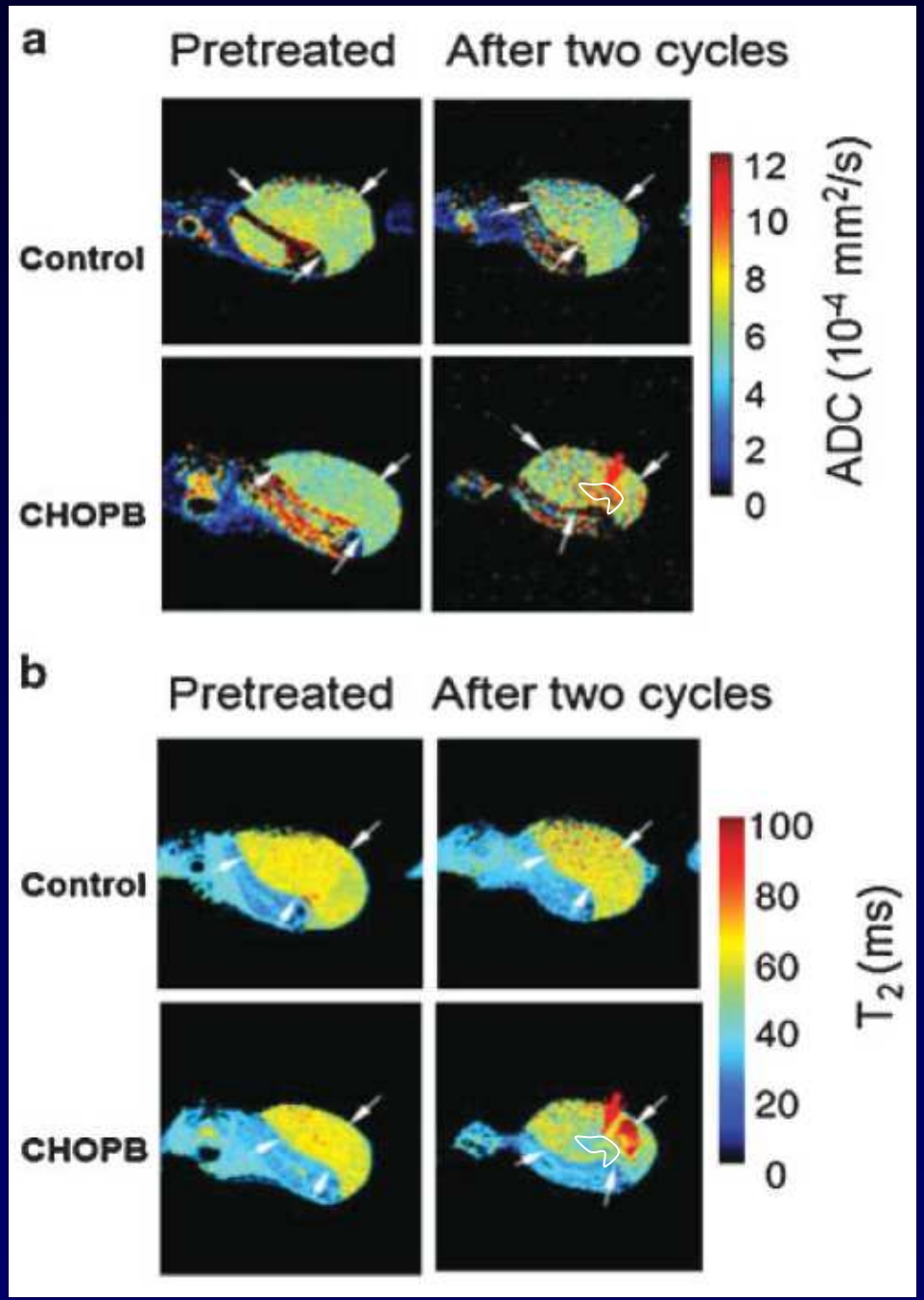
King AD et al. ***Radiology*** 2007

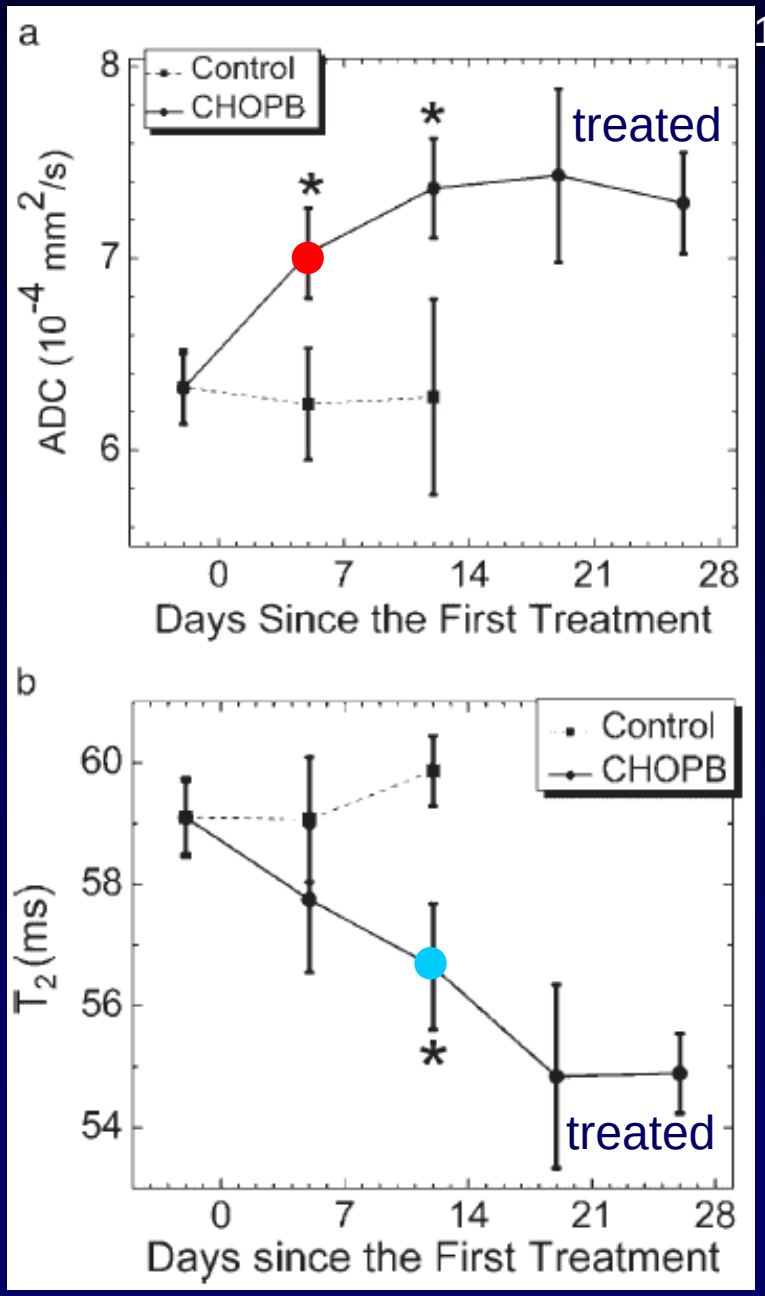
NMR IN BIOMEDICINE
NMR Biomed. (2008)
Published online in Wiley InterScience
(www.interscience.wiley.com) DOI:10.1002/nbm.1261

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*

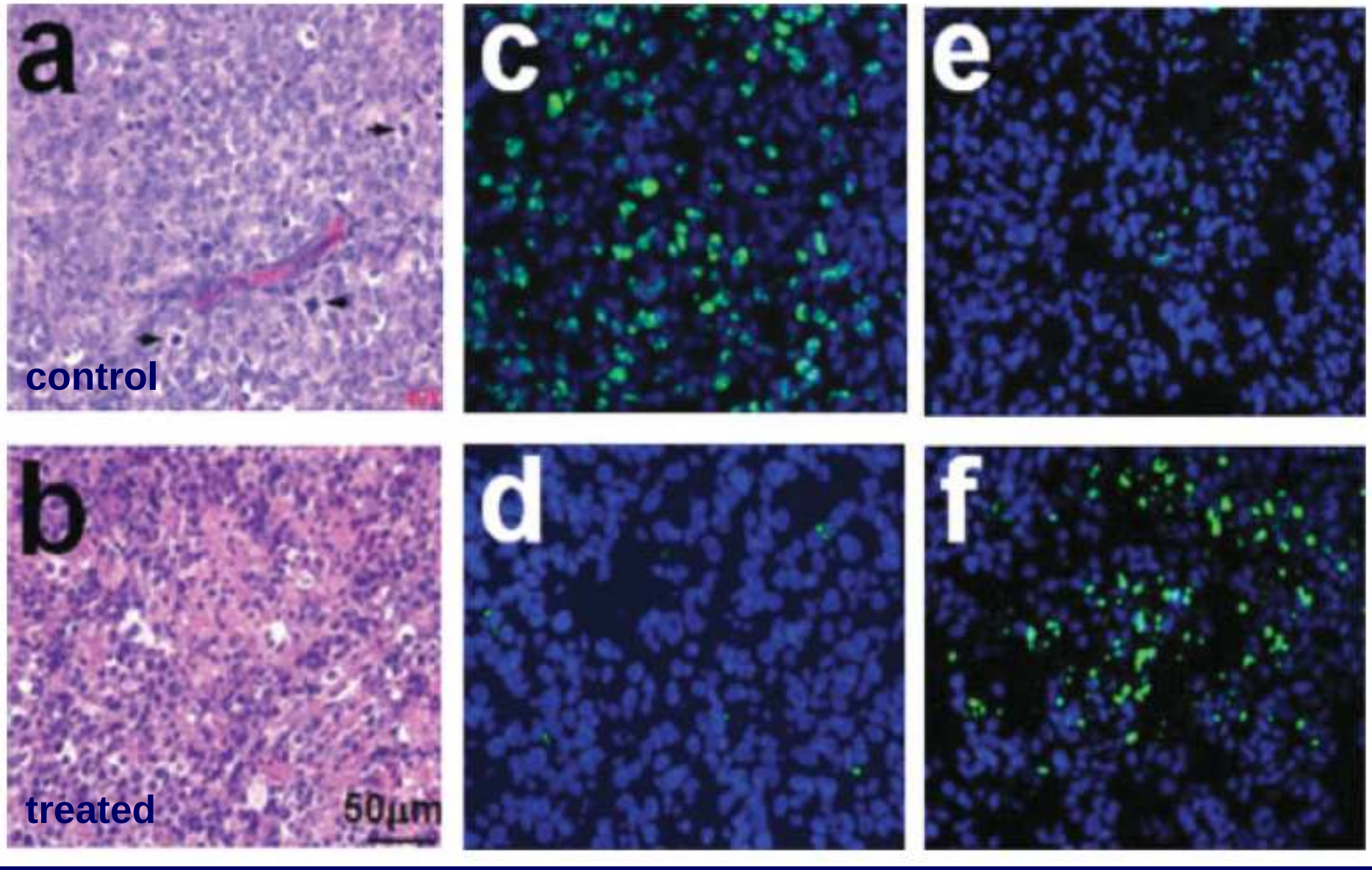
Molecular Imaging Laboratory, Department of Radiology, University of Pennsylvania, Philadelphia, PA, USA





Huang MQ et al. ***NMR Biomed*** 2008

H & E/mitosis | Ki-67/proliferation index | FITC/apoptosis index



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

TECHNICAL NOTE

Radiation Medicine: Vol. 22 No. 4, 275–282 p.p., 2004

Diffusion Weig
with Background Bo
Technical Improvem
and High

Taro Takahara,* Yutaka Im
Seiji Nasu,*

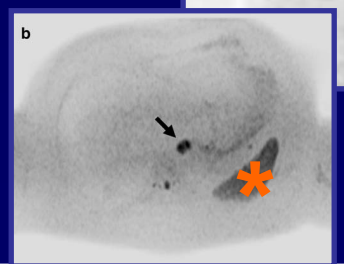
Free breathing

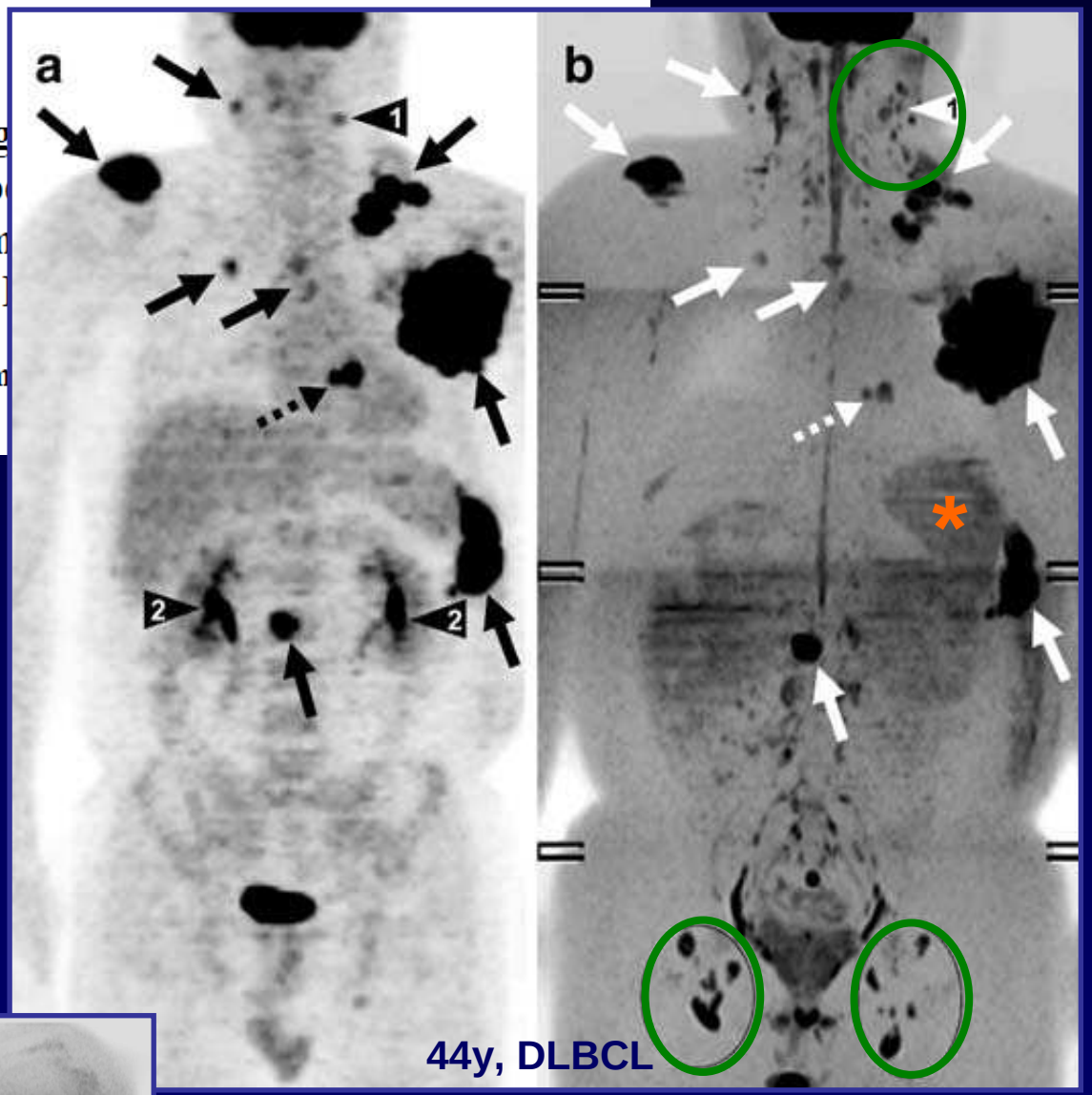
Thin sections (4mm/-1mm overlapping) allows 3D MPR and MIP

b = 0, **1000** s/mm^2

Inverse gray → **PET-like**

No ADC mapping





44y, DLBCL

PET **DWIBS *b* = 1000**

Kwee TC et al. ***Eur Radiol*** 2008

WB MRI/DWI vs. CECT

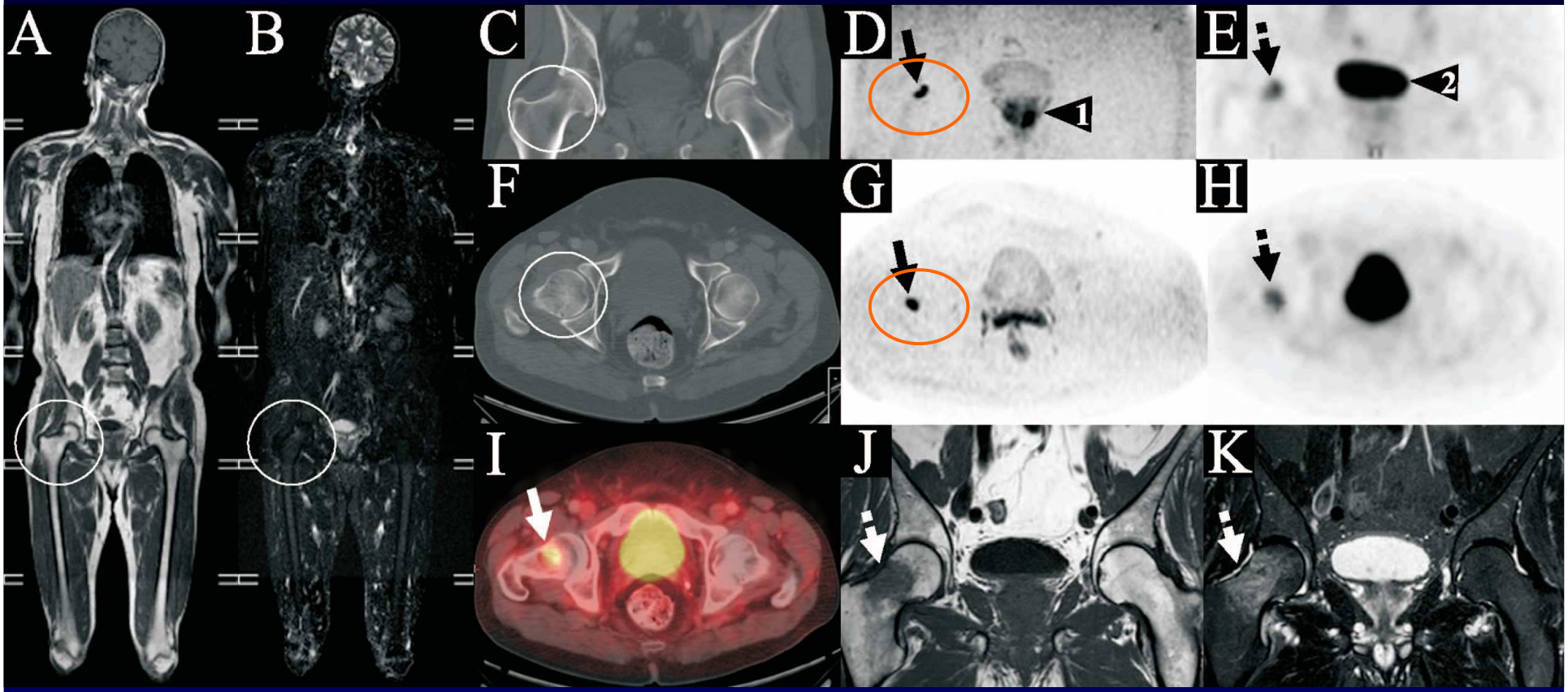
- First study with pure lymphoma patients
- Mixed HL n = 7/NHL n = 23 (different grades)
- Pretreatment staging vs. CECT
- MRI (T1w and T2w) ± DWIBS
- Reference: PET/BM biopsy/CT F/U

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

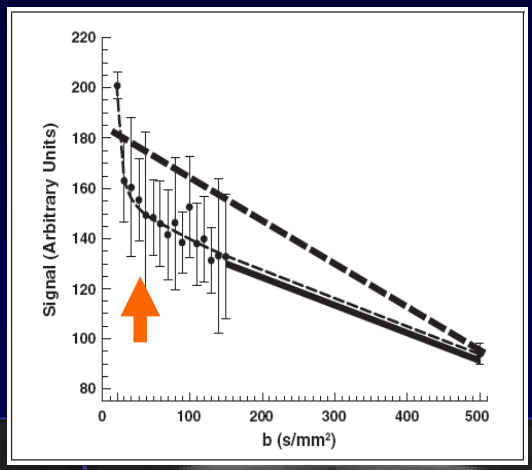
Kwee TC et al. ***Invest Radiol*** 2009

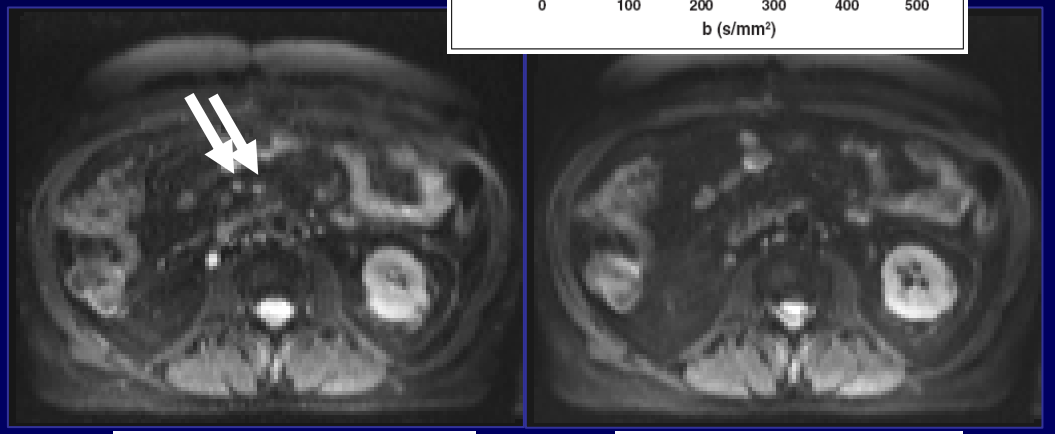
WB DW-MRI (our experience)

- 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





b = 0 s/mm²

b = 50 s/mm²

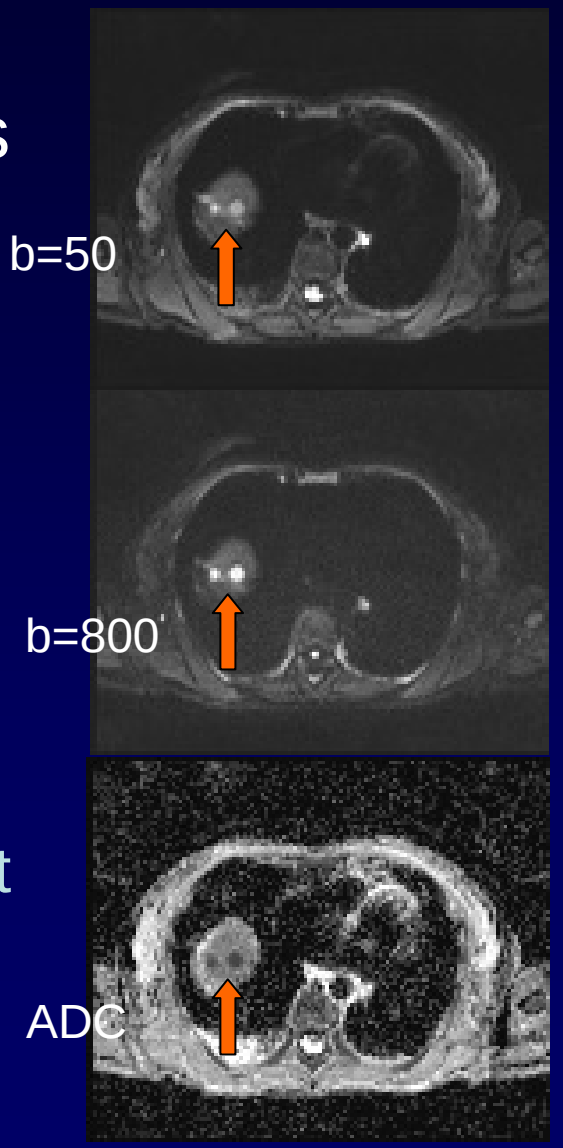
Smallest *b* at 50 reduces perfusion effect and eliminates signal from vessels

Nguyen TD et al. ***J Magn Reson Imaging*** 2008

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



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Eur Radiol (2010) 20: 2027–2038
DOI 10.1007/s00330-010-1758-y

MAGNETIC RESONANCE

Chieh Lin
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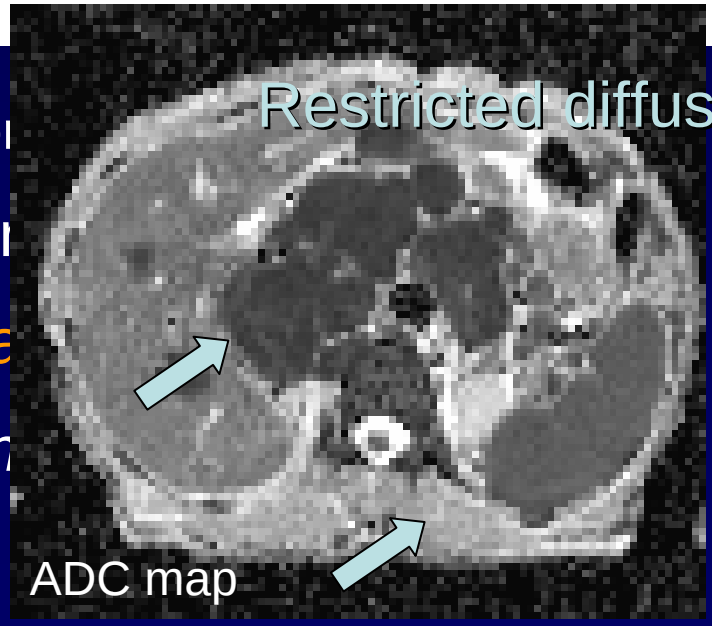
Alain Rahmouni

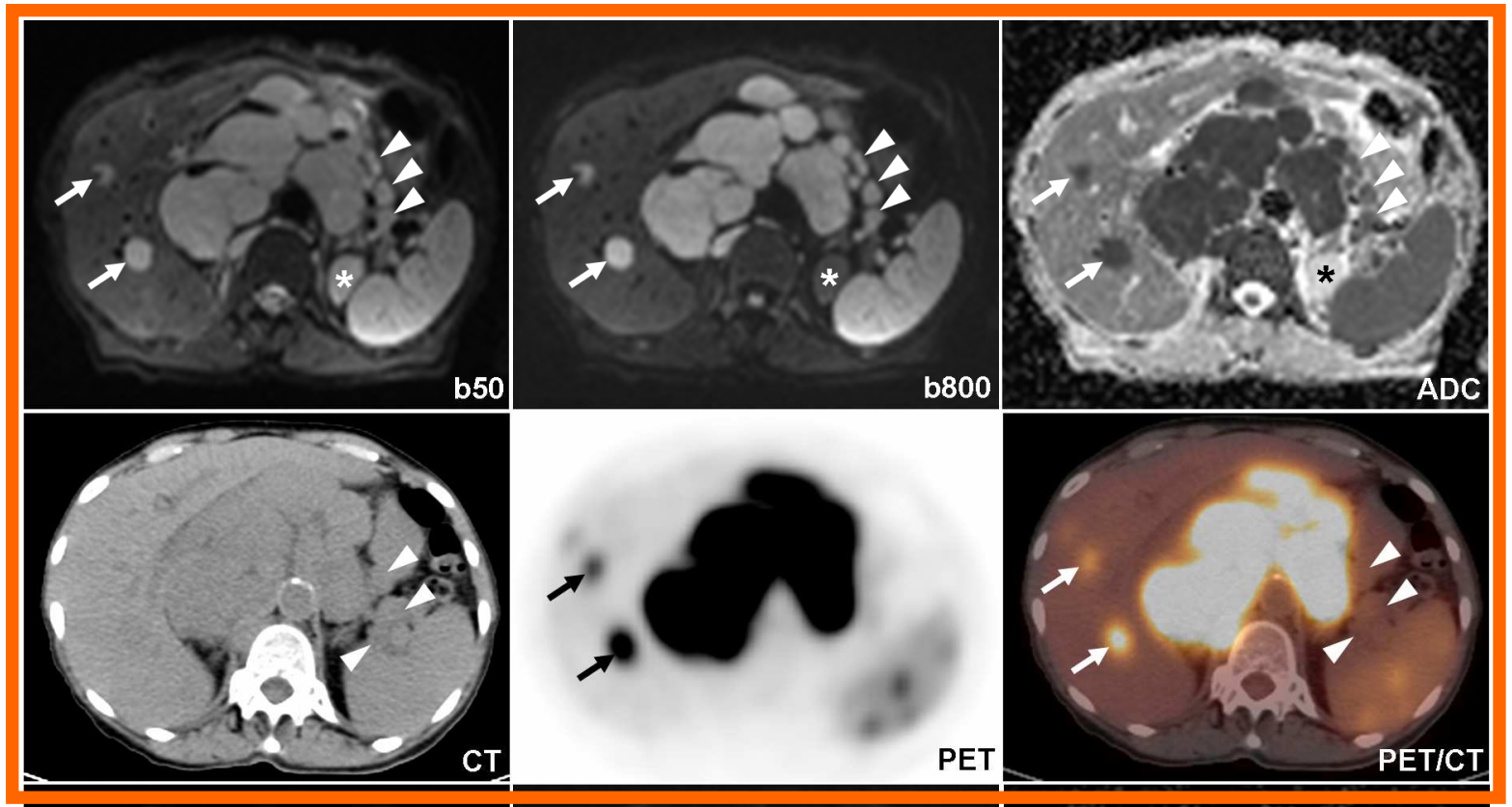
Whole-body diffusion-weighted magnetic resonance imaging with apparent diffusion coefficient mapping for staging patients with diffuse large B-cell lymphoma

- 15 DLBCL patients, in 2 with co
- Lesion detection on b50 DW i
- FDG-PET/CT as reference sta

Visual analysis of ADC map ar

measurement on > 1cm LN



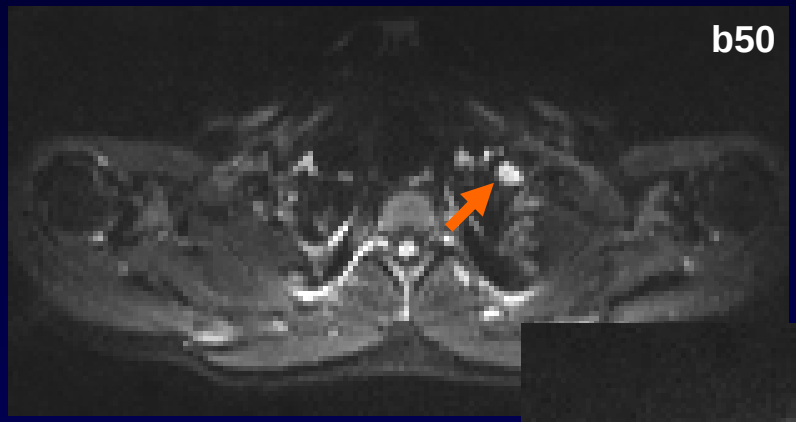

b50
b800
ADC
CT
PET
PET/CT
b50
b800
ADC

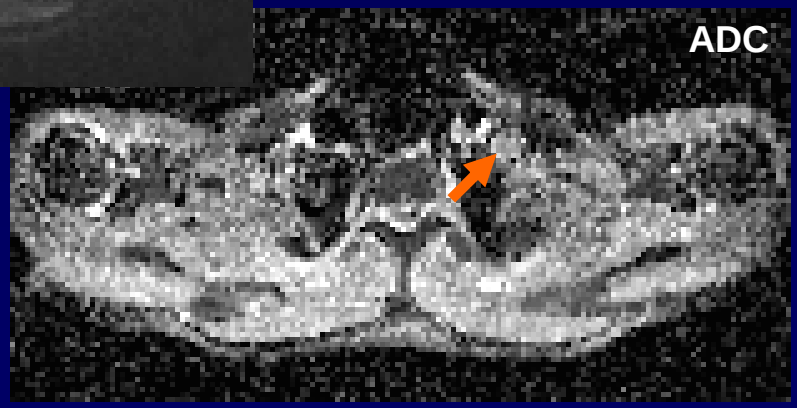
Lymph node involvement

- 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%**

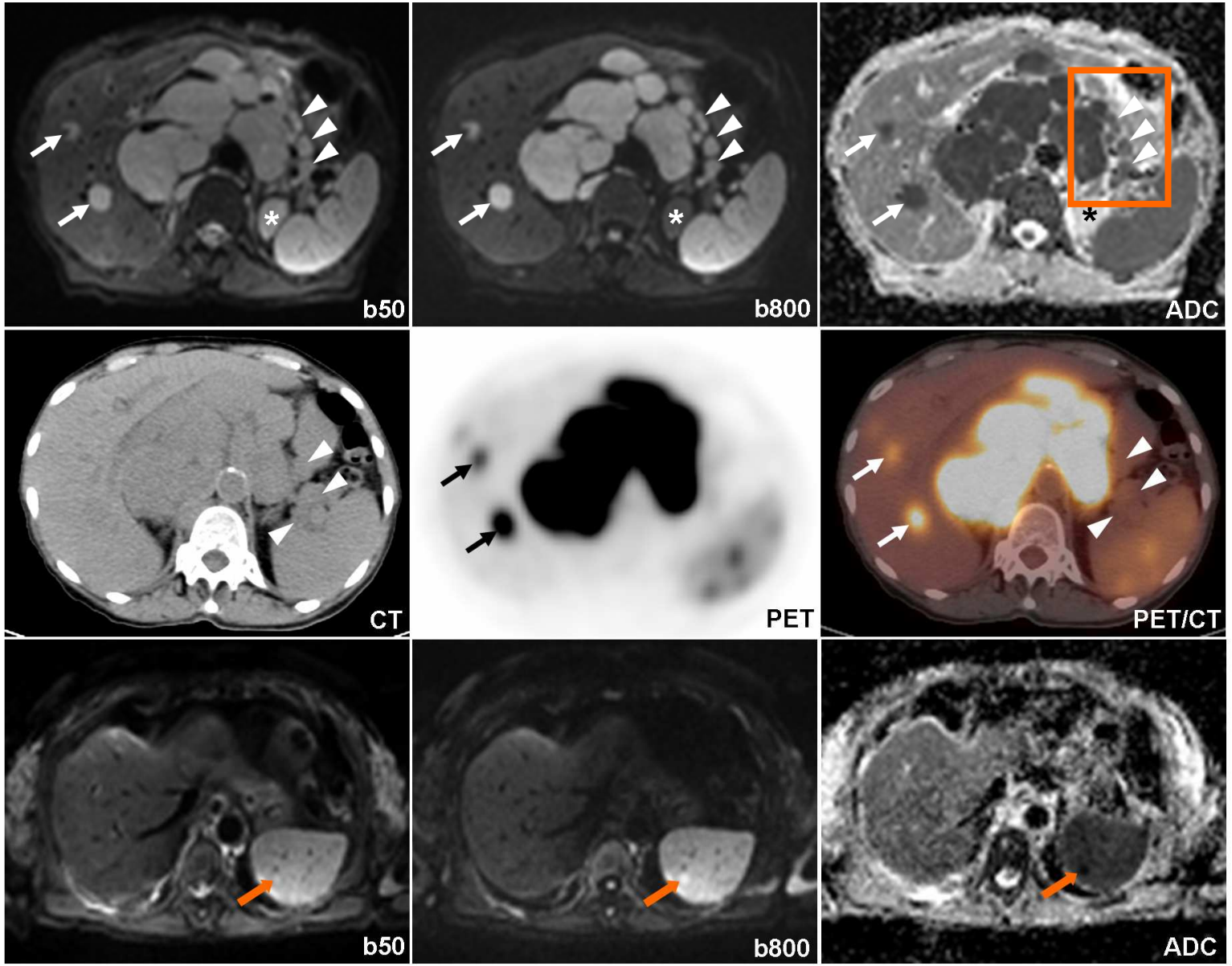
Lin C et al. ***Eur Radiol*** 2010

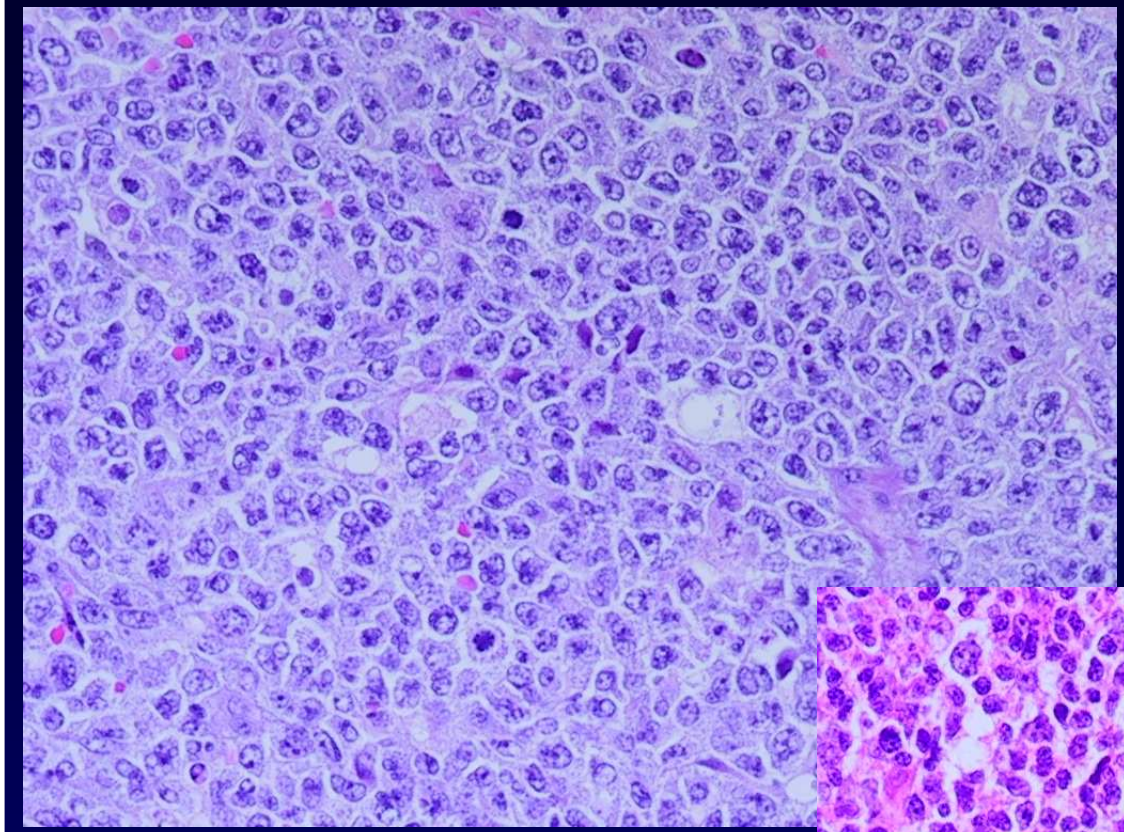
Patient 24y, Gastric DLBCL regional LN+
15-mm lymph node (arrow), negative on FDG-PET





- 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

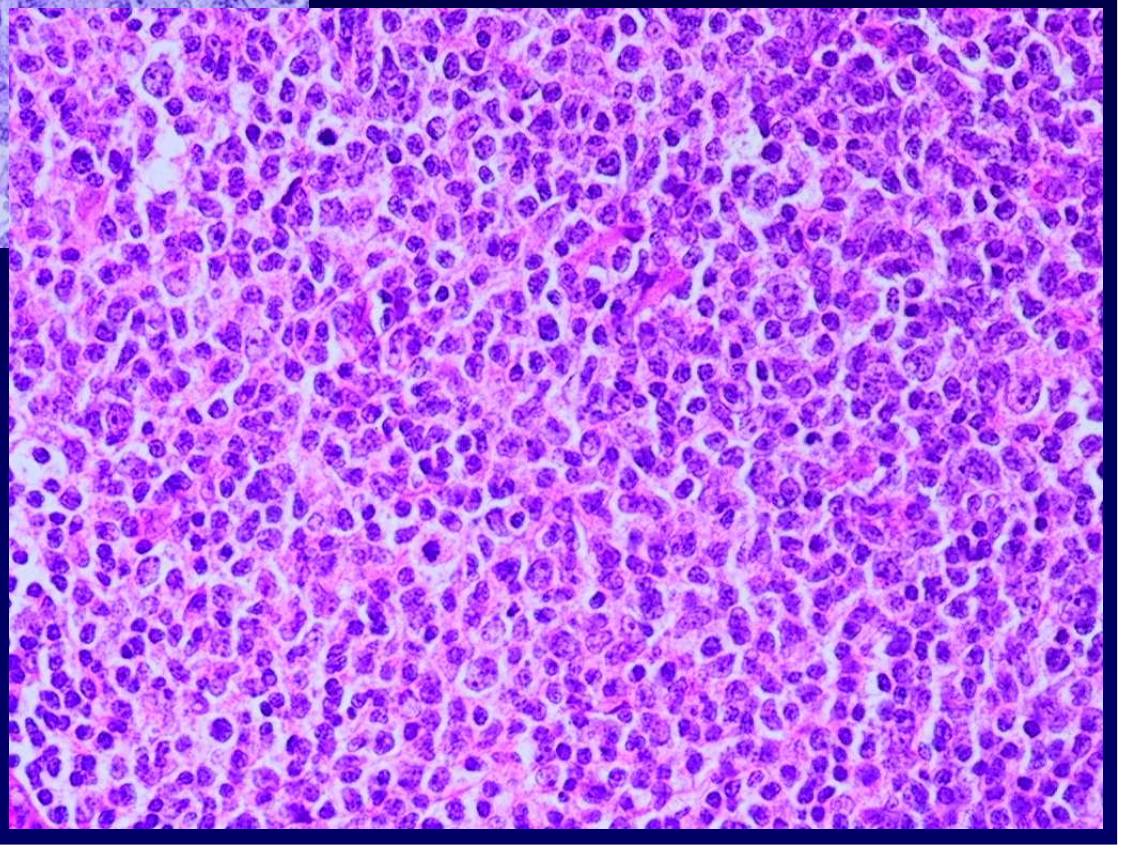

b50
b800
ADC
CT
PET
PET/CT
b50
b800
ADC



DLBCL

Similar cellularity;

Comparable ADC values



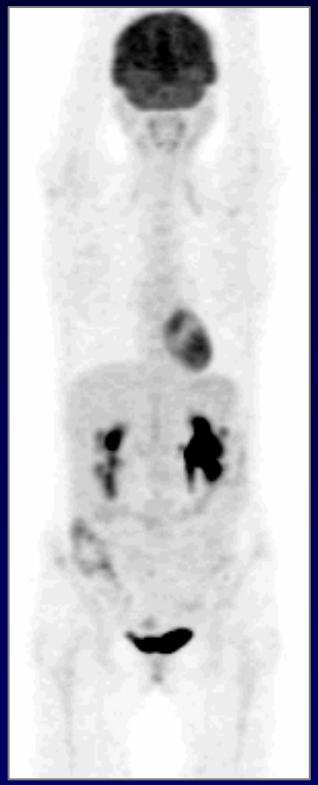
Follicular lymphoma

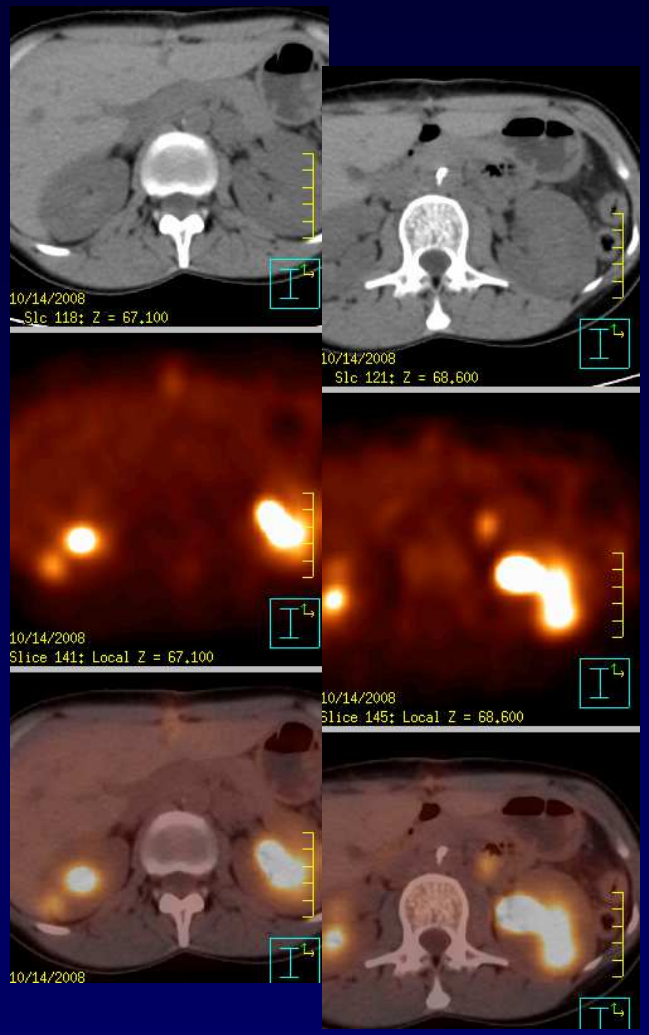
Organ involvement

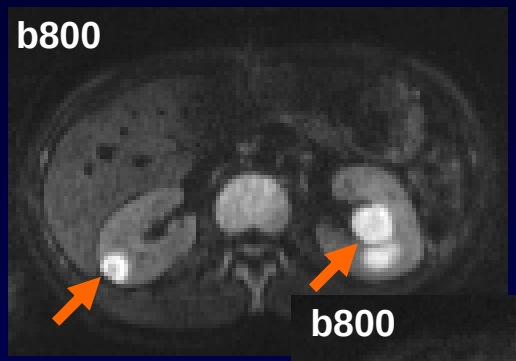
- 20 organs recorded positive
- Concordance 100%
- DW-MRI more sensitive for the detection of renal and hepatic involvement
- Finally, Ann Arbor stages agreed in 14 (93%) patients

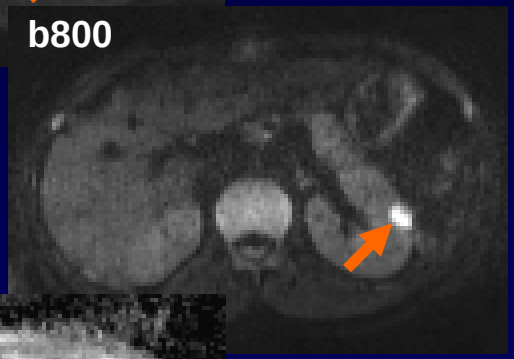
Lin C et al. ***Eur Radiol*** 2010

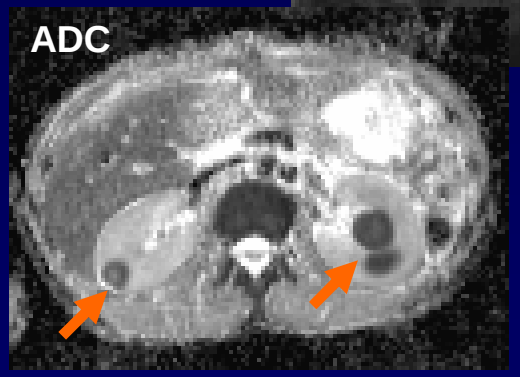
Patient 42y, DLBCL **renal involvement**





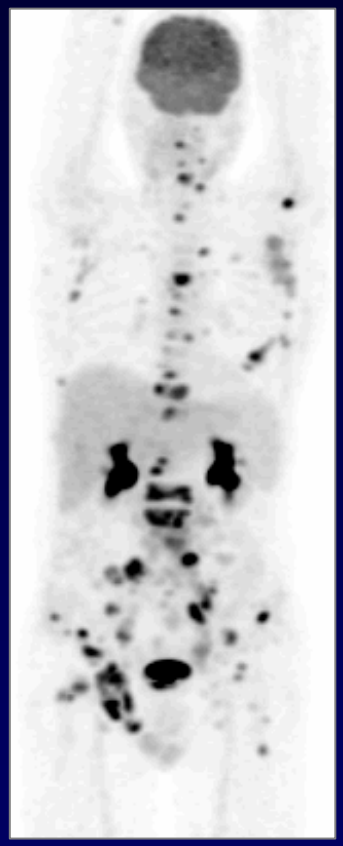


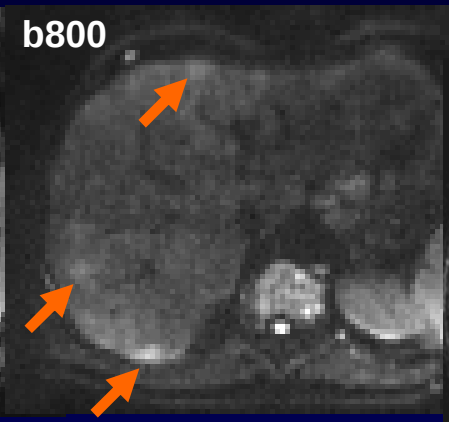


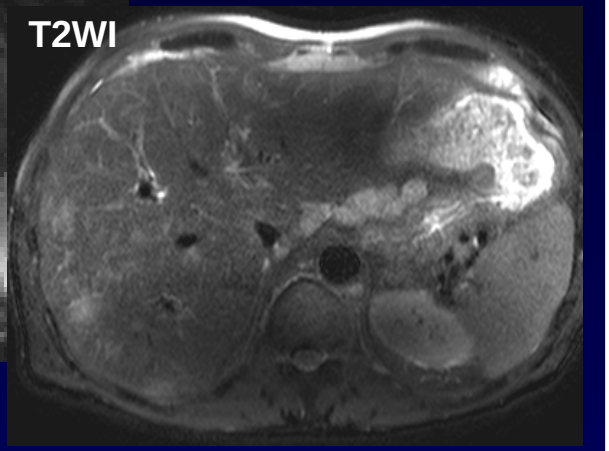


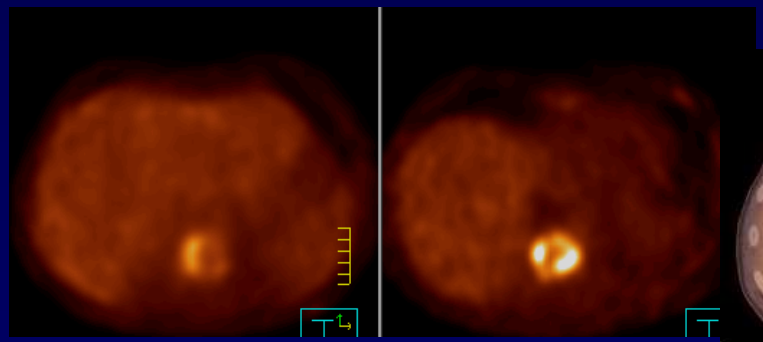
• On PET/CT, lesions might be masked by normal FDG excretion, which would depend on the color scale adjustment.

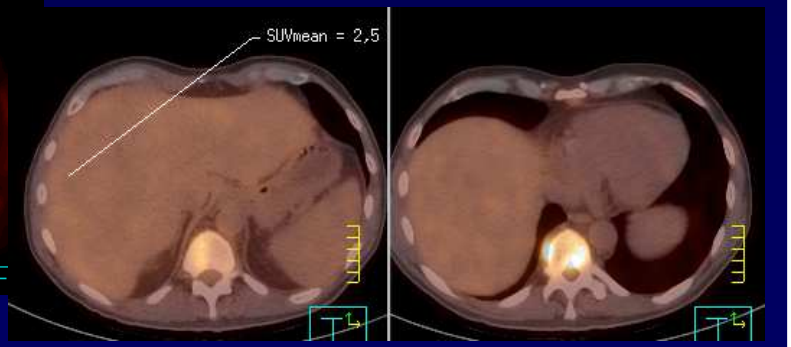
Patient 57y, concomitant DLBCL and follicular lymphoma
Hepatic involvement





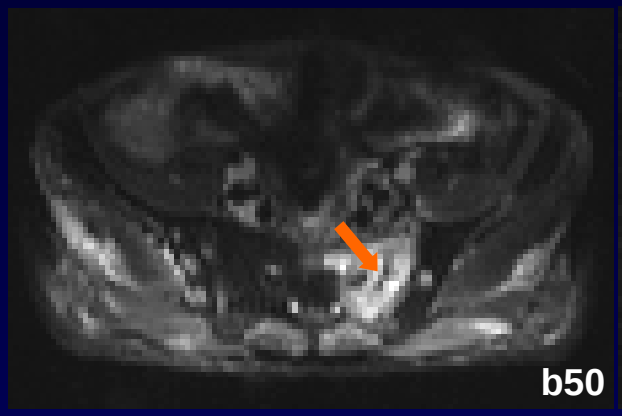


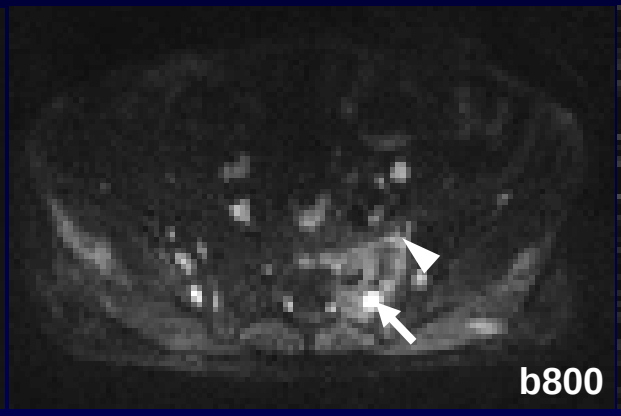


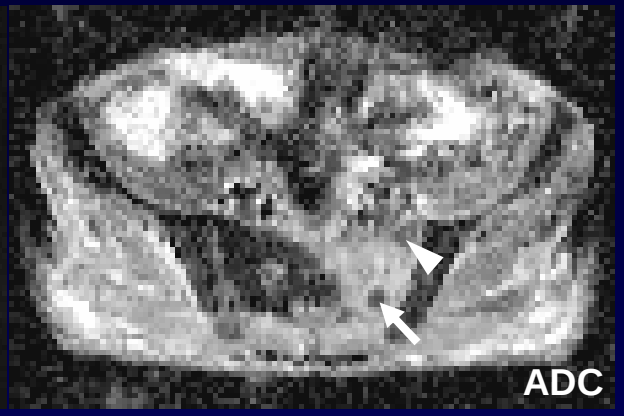


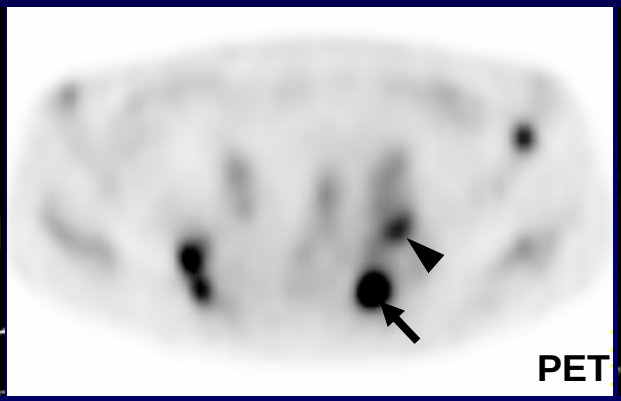
- DWI helped to confirm hepatic involvement in case of small focal lesions
- On PET/CT, FDG uptake of liver was within normal range

Same patient, concomitant DLBCL and follicular lymphoma **bone marrow involvement**

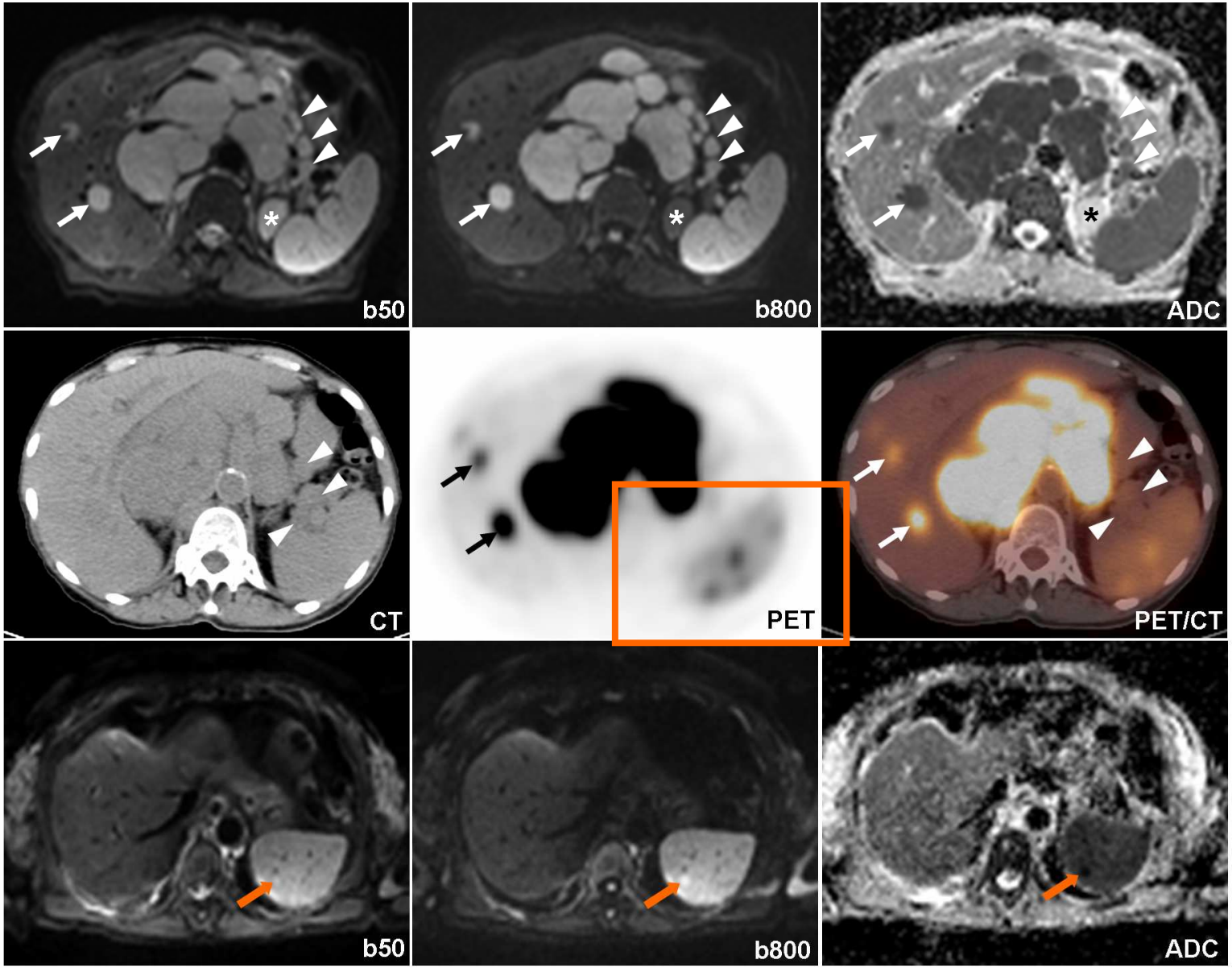








- Focal lesions stay white on *b*800 images and show restricted diffusion on ADC map
- Fracture of left sacral ala → no restricted diffusion


b50
b800
ADC
CT
PET
PET/CT
b50
b800
ADC

WB MRI/DWI vs. PET/CT

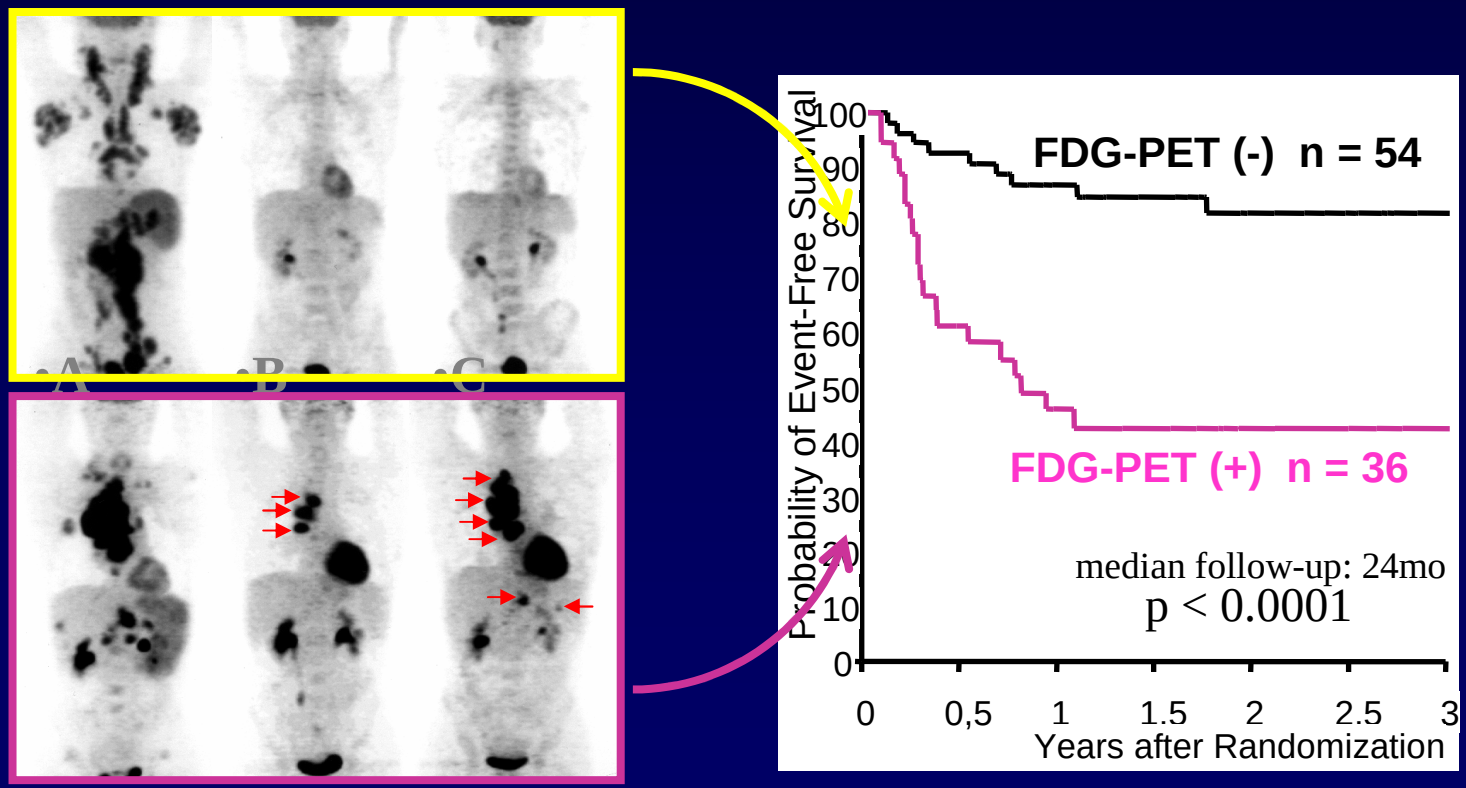
Staging

- van Ufford HM and Kwee TC et al. ***AJR*** 2011
- Abdulqadhr G et al. ***Acta Radiol*** 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



Haioun C & Itti E, Rahmouni A, et al. ***Blood*** *2005*

ORIGINAL ARTICLE

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*†*

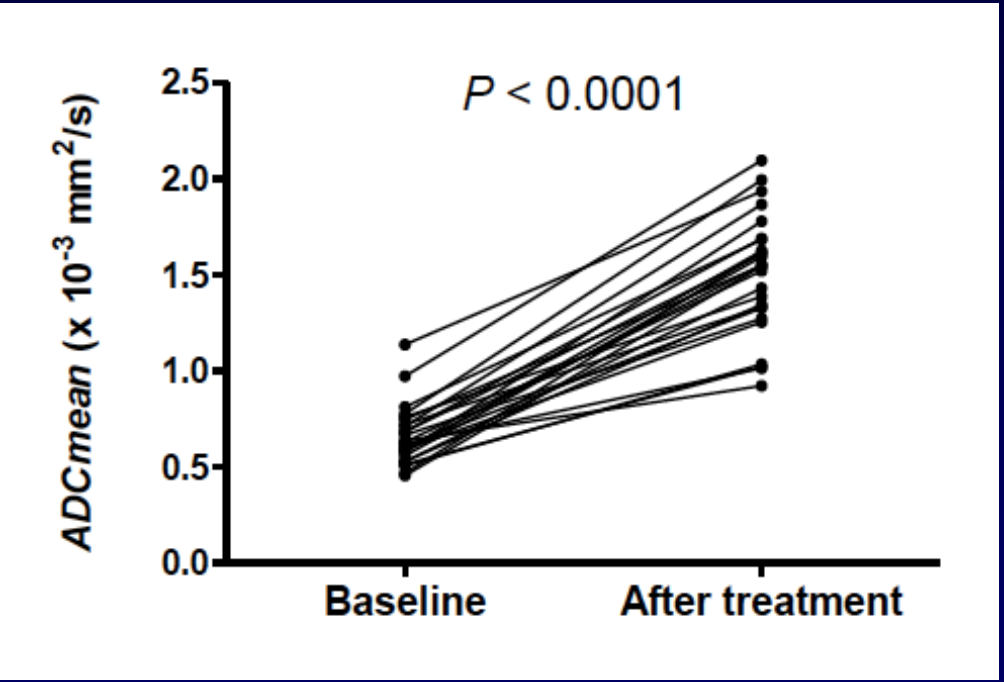
- Same 15 DLBCL patients as staging study
- Lesion detection on b50 DW images
- FDG-PET/CT as reference standard

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

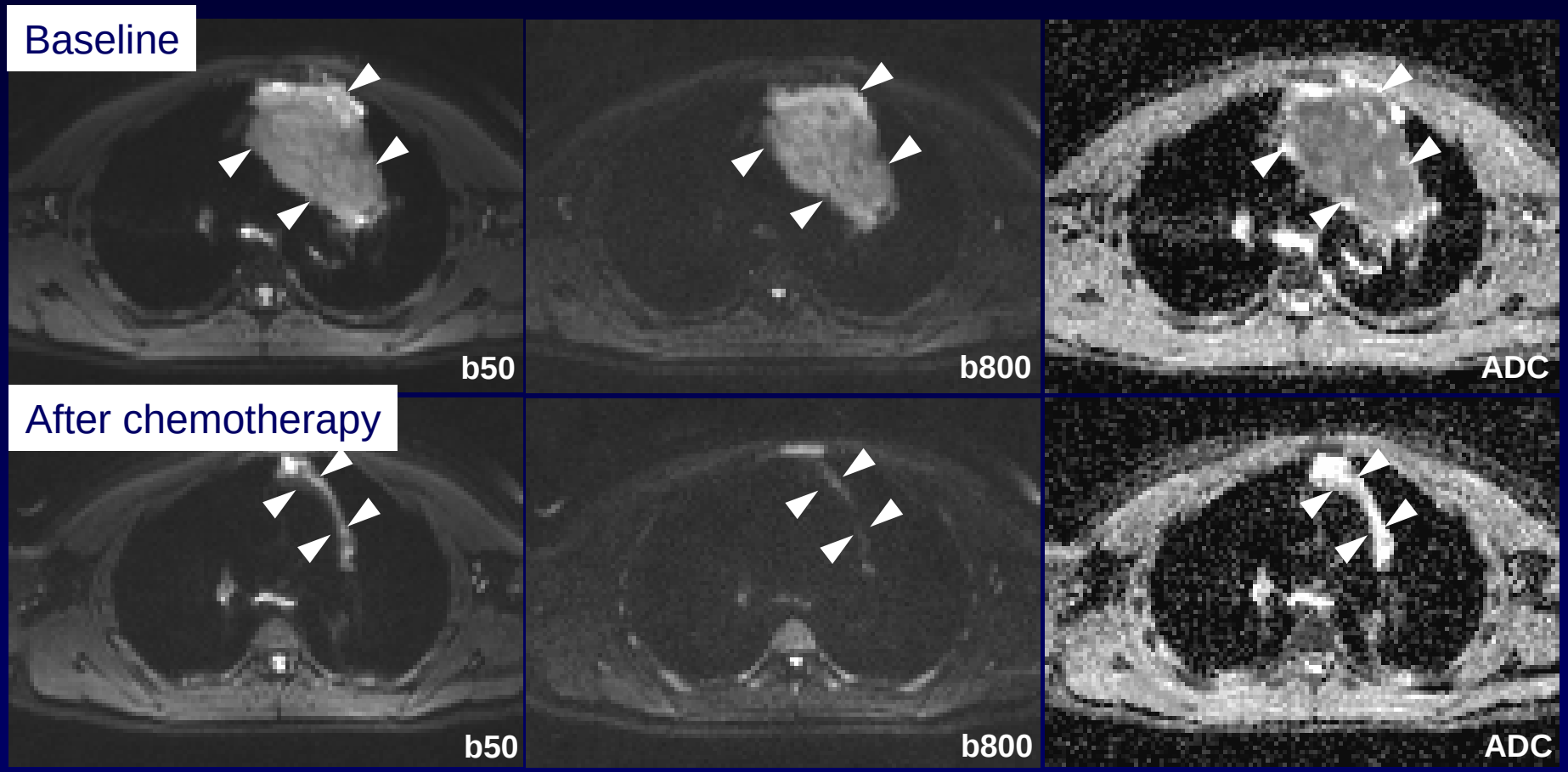
- Residual nodes > 1cm in 26 regions



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

	PET/CT		PET/CT	
	Positive	**Negative**	**Positive**	**Negative**
DWI criteria	Size criteria alone		Size plus visual ADC analysis	
Positive	6	20	2	2
Negative	0	59	4	77

Decrease false positives combining size and visual ADC analysis

Lin C et al. ***Invest Radiol*** 2011

DW-MRI vs. FDG-PET/CT

- Lin C et al. DLBCL staging. *Eur Radiol* 2010 Aug.
- van Uffort HM et al. Lymphoma staging. *AJR* 2011 Mar.
- Abdulqadhr G et al. Lymphoma staging. *Acta Radiol* 2011 Mar.
- Wu X et al. DLBCL early response evaluation. *NMR Biomed* 2011 Mar.
- Lin C et al. DLBCL response assessment. *Invest Radiol* 2011 May.
- 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 0.71×10^{-3} mm^2/s (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 Biomed*** 2011

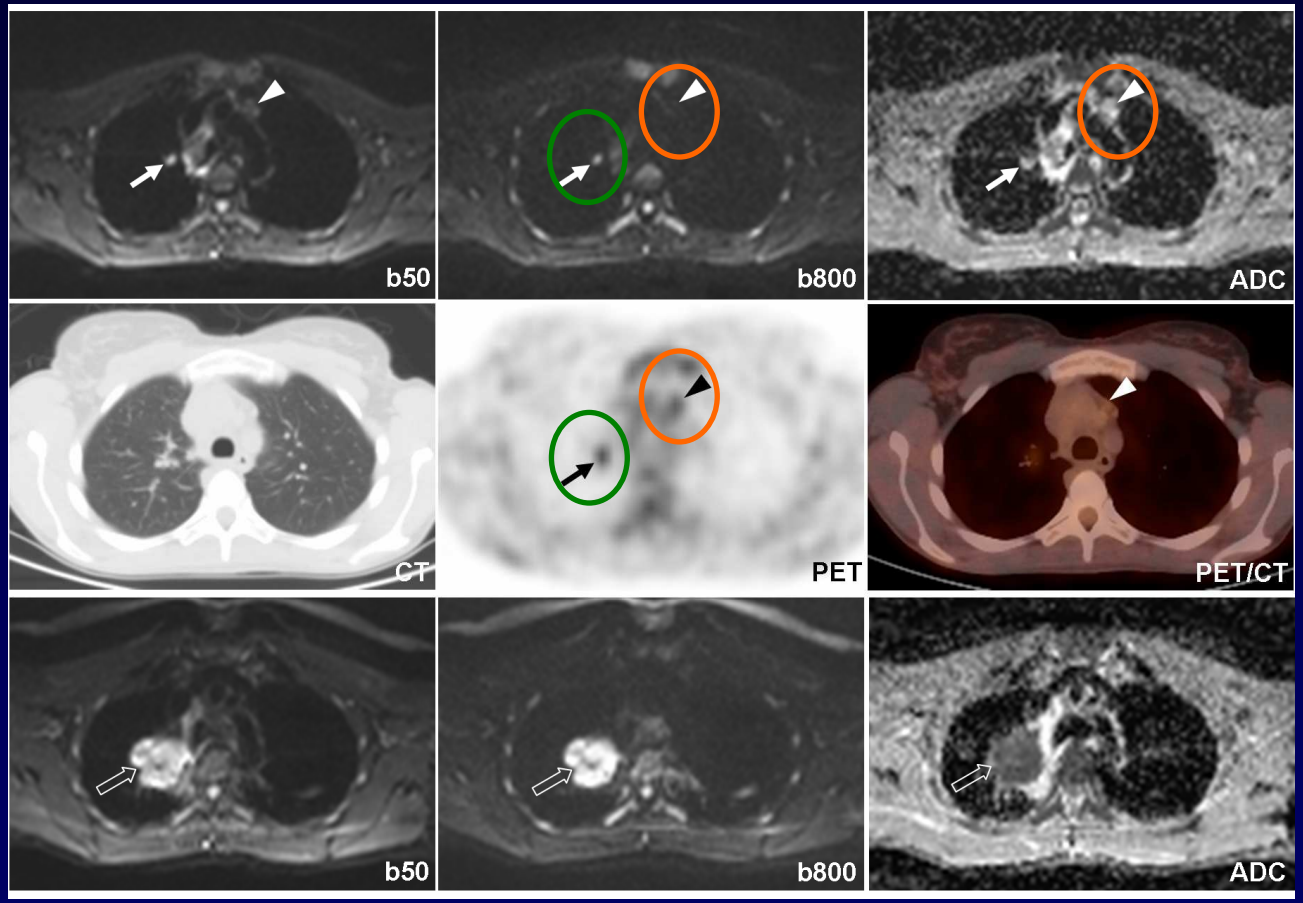
Conclusions

- 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.

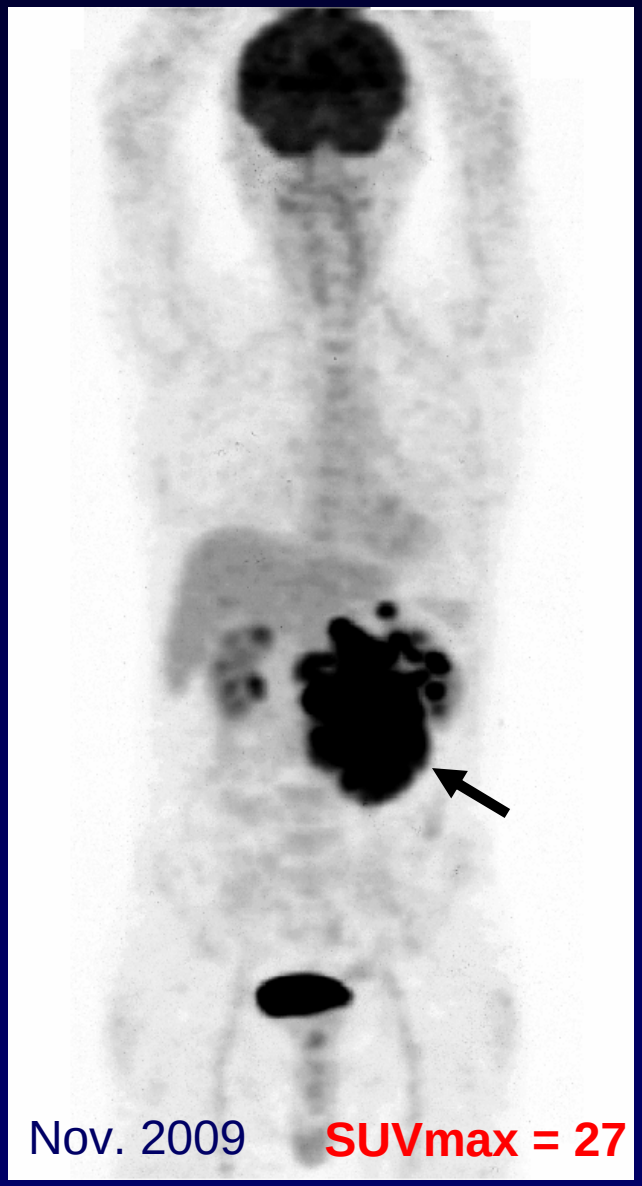
4 cycles

End of tx



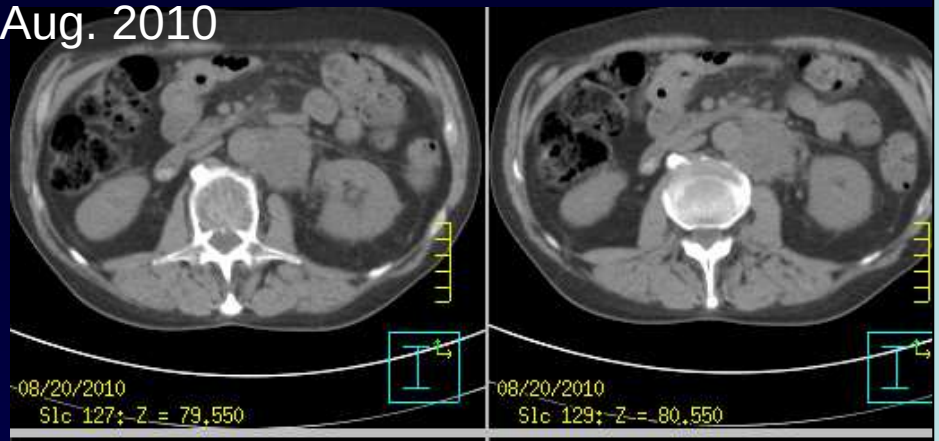
- Tiny right pulmonary nodule (arrow) showed persistent FDG uptake (positive)
- This nodule was also clearly identified on DWI (arrow)

Patient 68y, DLBCL, 71.5% SUVmax reduction at 4 cycles (R-CHOP)

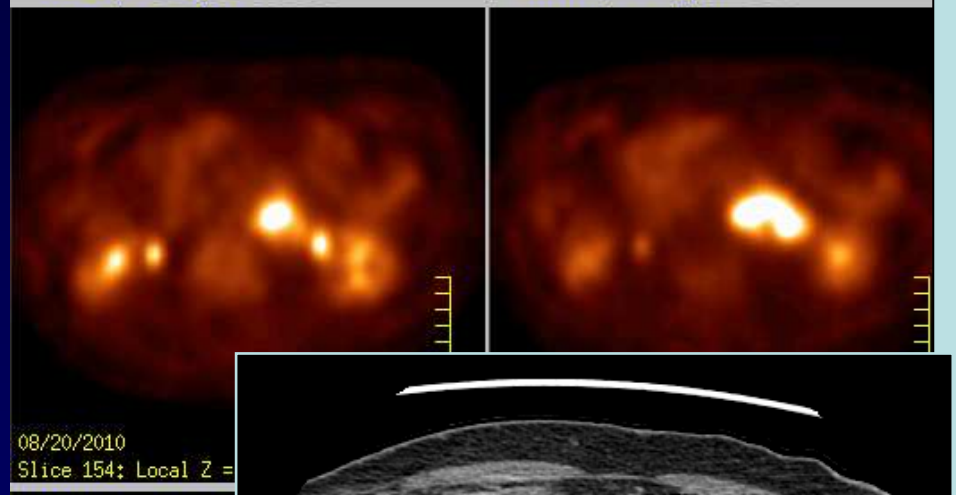


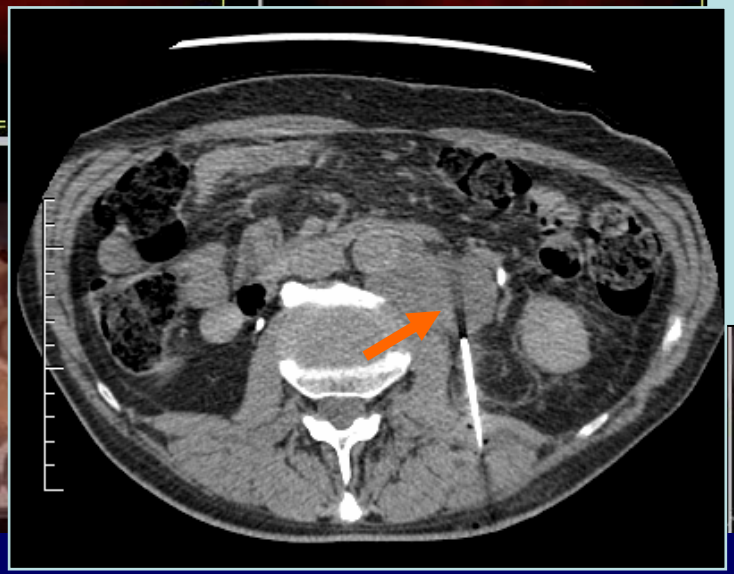
After 4 cycles (R-GEMOX)

Aug. 2010

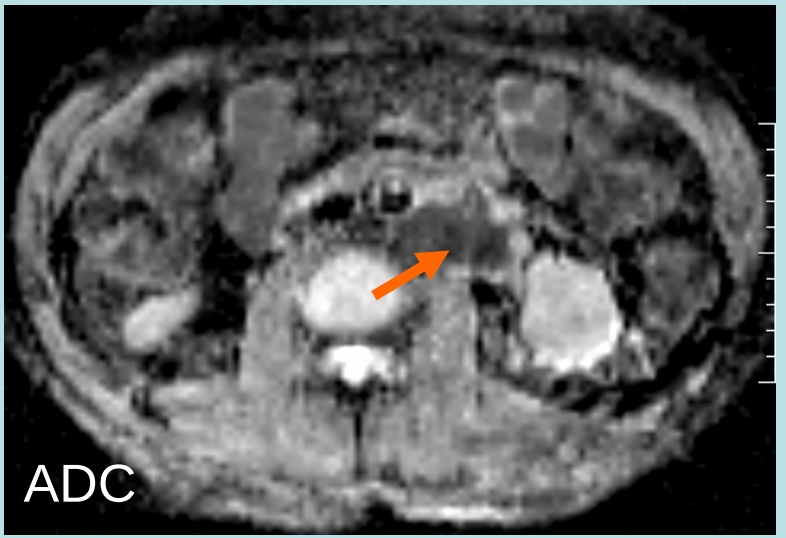

08/20/2010
Slc 127; Z = 79.550

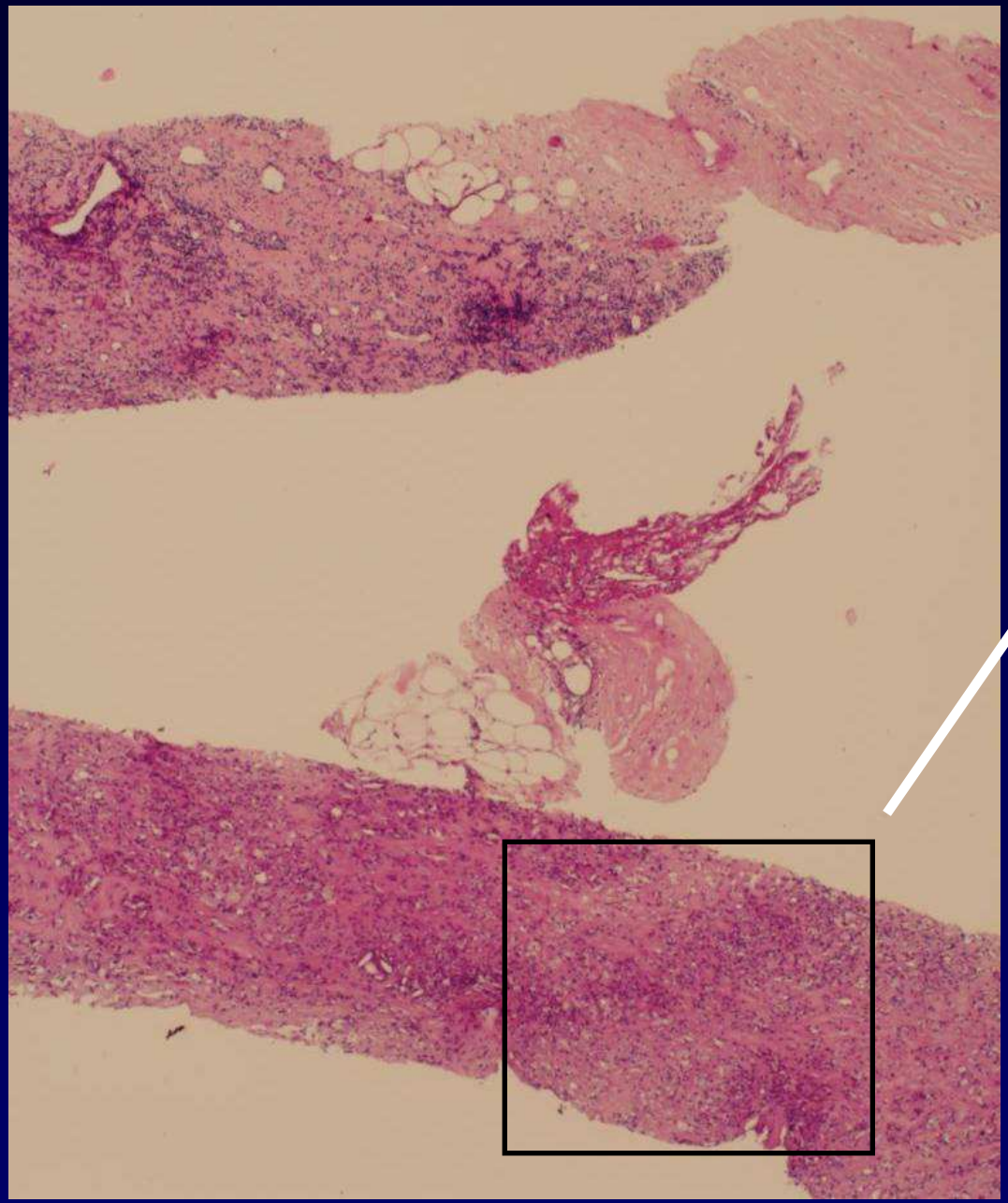
08/20/2010
Slc 129; Z = 80.550

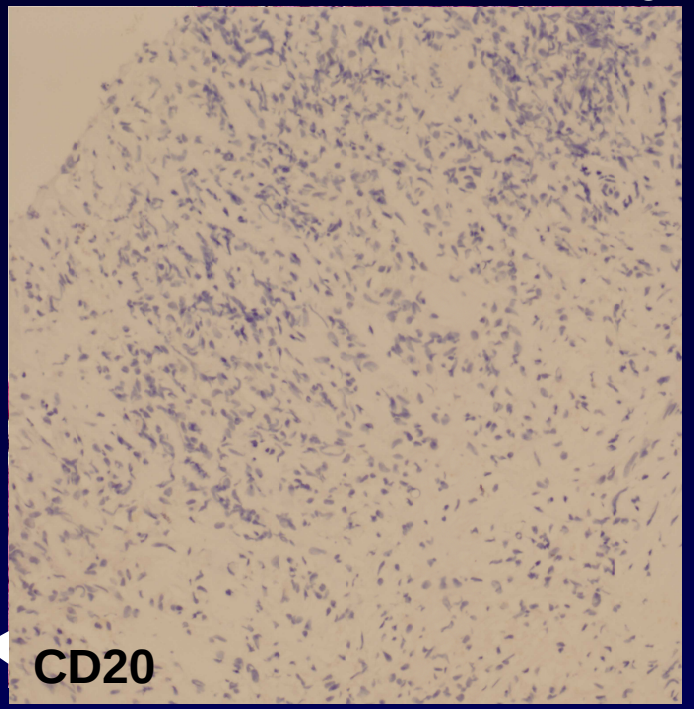

08/20/2010
Slice 154; Local Z =

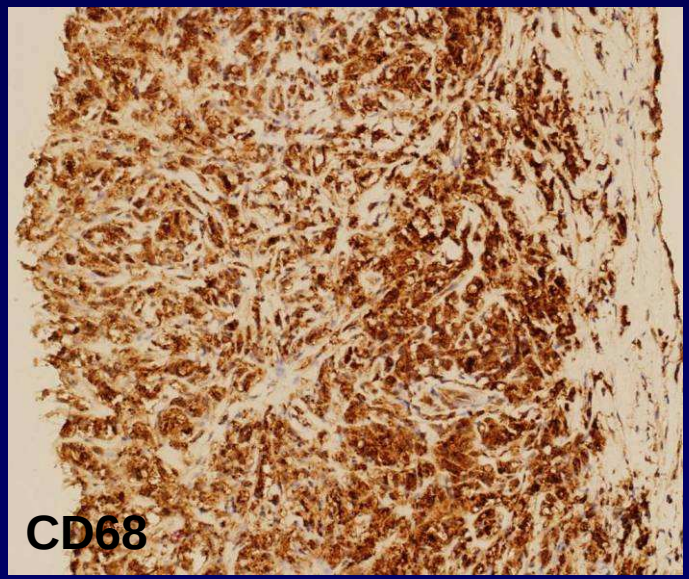



b50


ADC



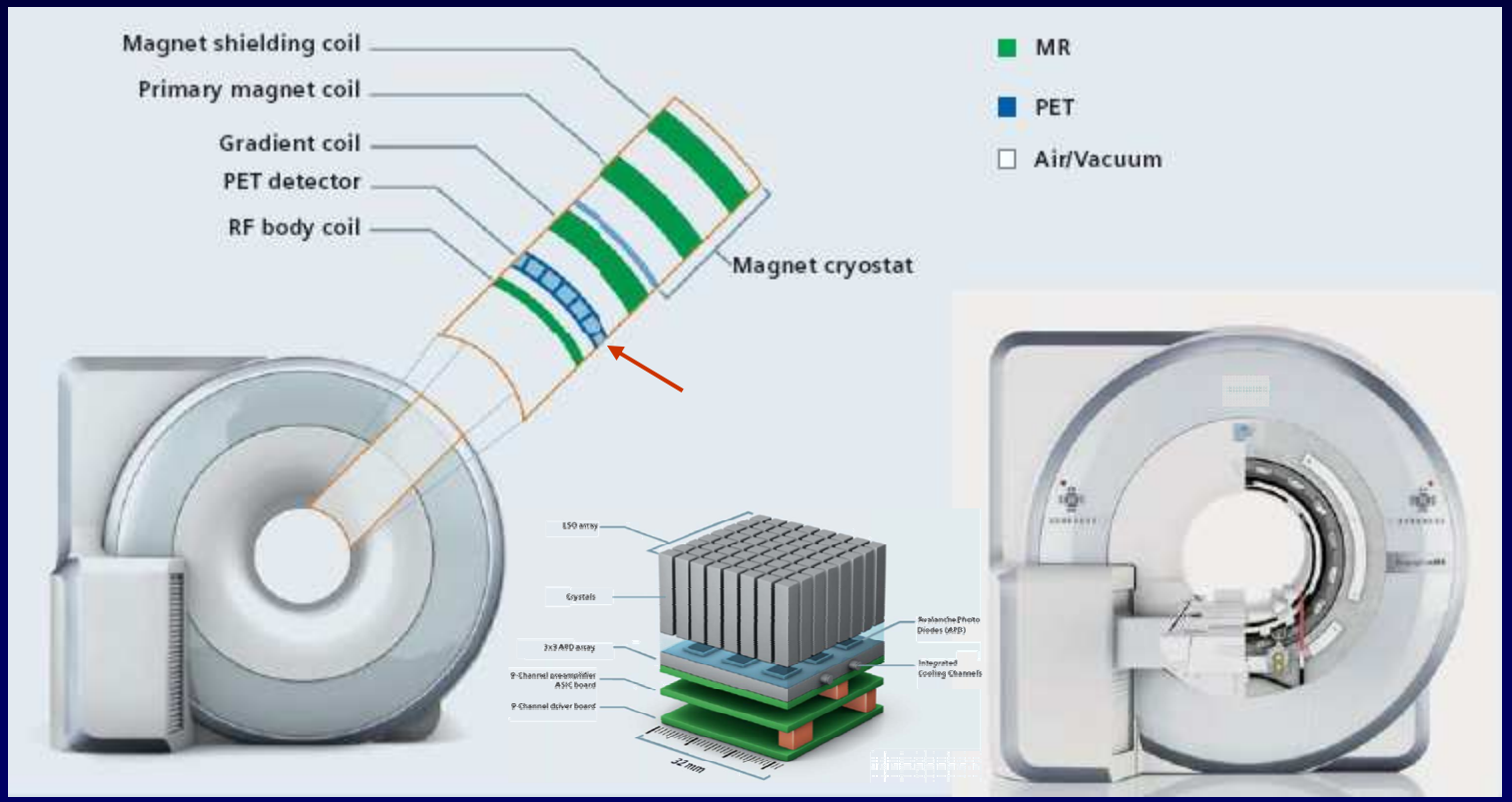

CD20


CD68

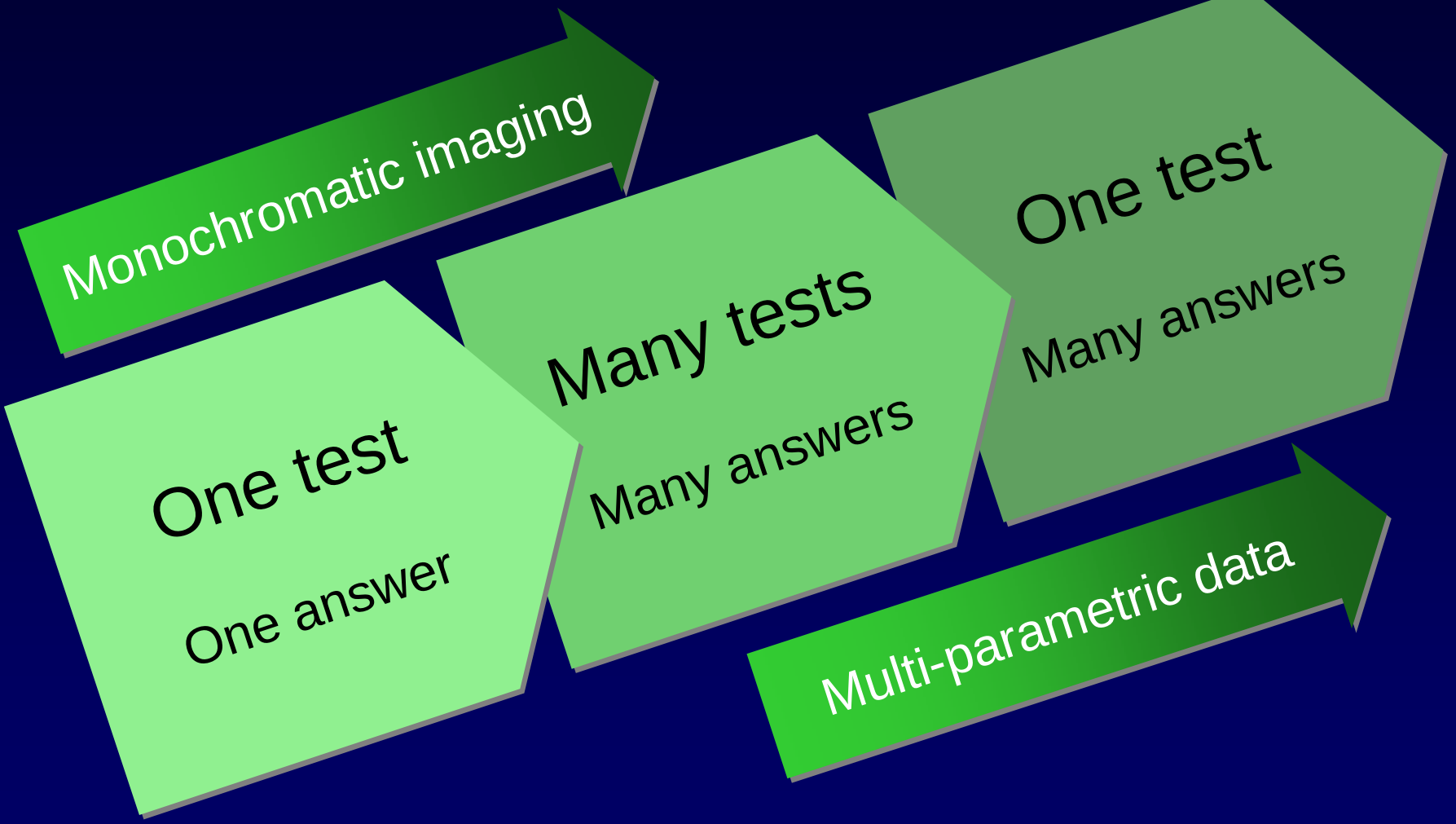
Three months later, mass decreased in size → false positive of PET and DWI

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

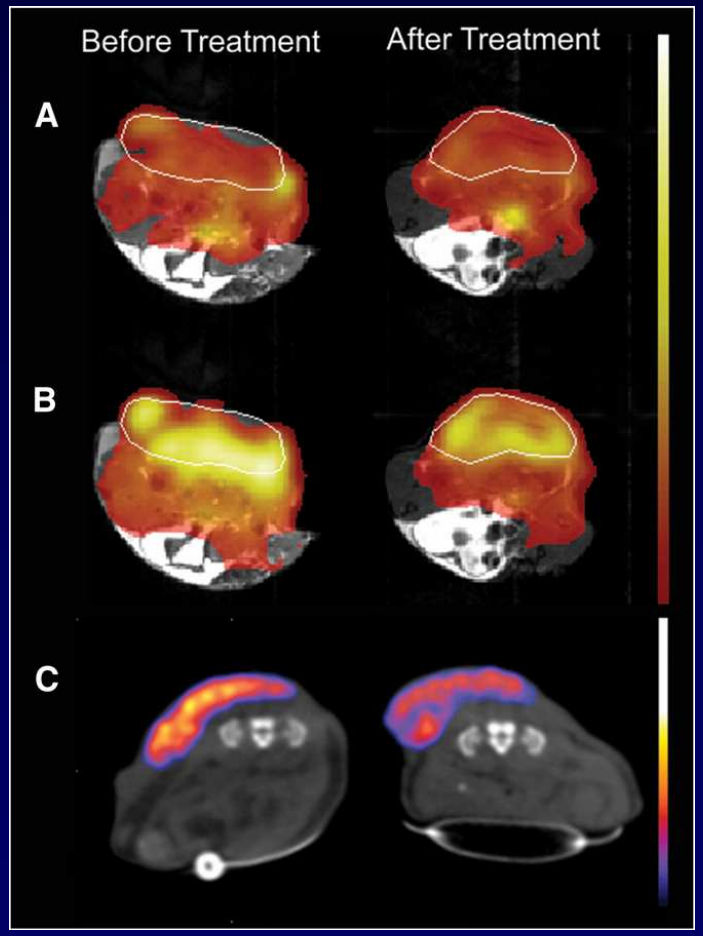
Journal of Nuclear Medicine, published on August 17, 2011 as doi:10.2967/jnumed.110.085258

Hyperpolarized ^{13}C MRI and PET: In Vivo Tumor Biochemistry

DNP-MRSI

DNP-MRSI

PET/CT



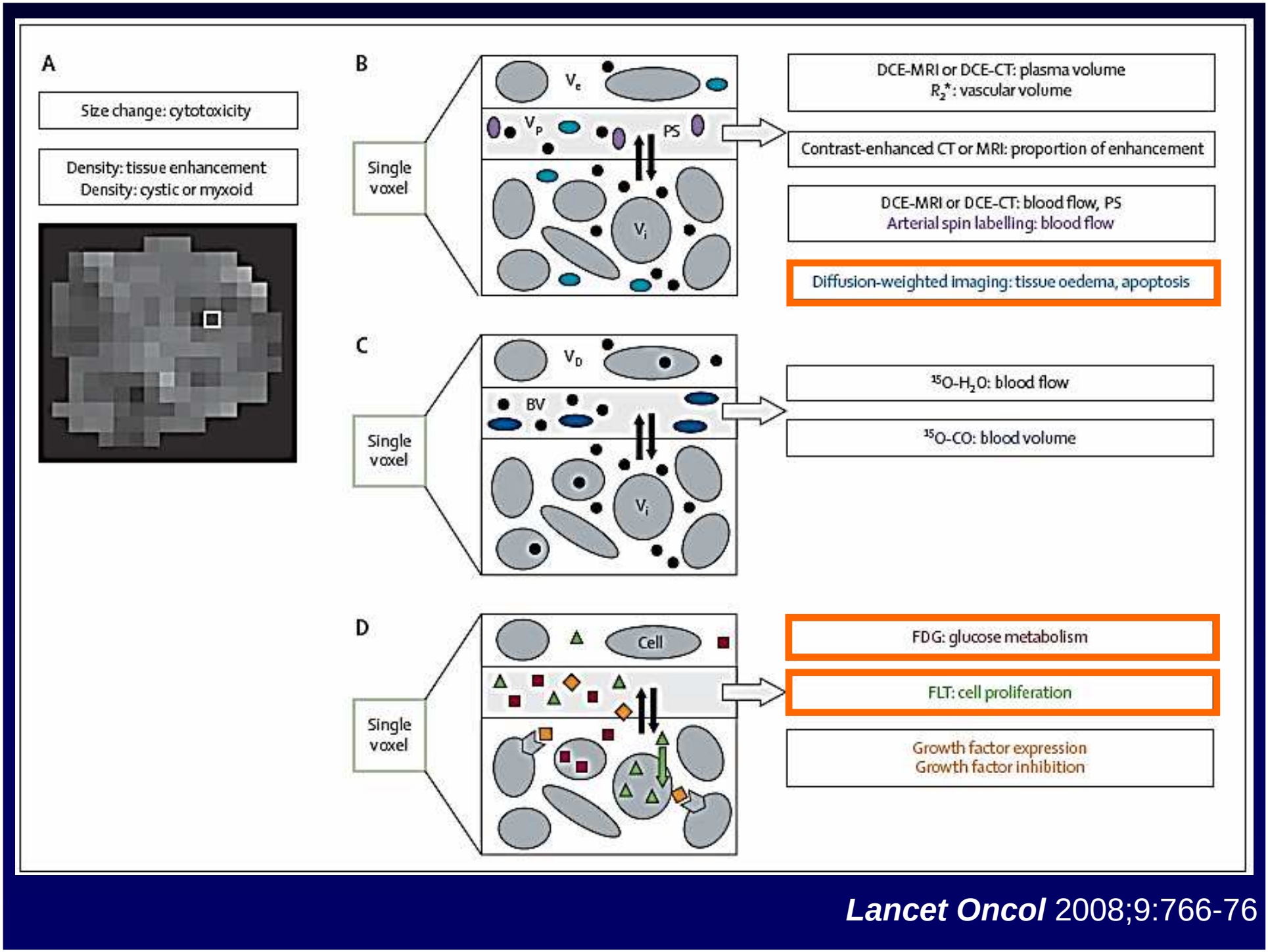
Injected hyperpolarized [^{13}C]pyruvate

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

^{18}F-FDG

Nat Med 2007 A murine lymphoma model

DNP: dynamic nuclear polarization



Lancet Oncol 2008;9:766-76

Eur Radiol (2011) 21:555–558
DOI 10.1007/s00330-010-2035-9

EDITORIAL

From multislice CT to whole-body biomarker imaging in lymphoma patients

Cédric de Bazelaire · Eric de Kerviler

?

- Ask right que
- Continuously
applied in daily

Acknowledgements

- CHU Henri Mondor

  Dept. of Radiology/Nuclear Medicine/Hematology/Pathology

  – Prof. Alain Rahmouni
  – Prof. Alain Luciani
  – Prof. Michel Meignan
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  – Prof. Corinne Haioun
  – Prof. Phillipe Gaulard
  – Dr. Julien Moroch etc.

- CGMH

  Molecular Imaging Center & Dept. of Nuclear Medicine

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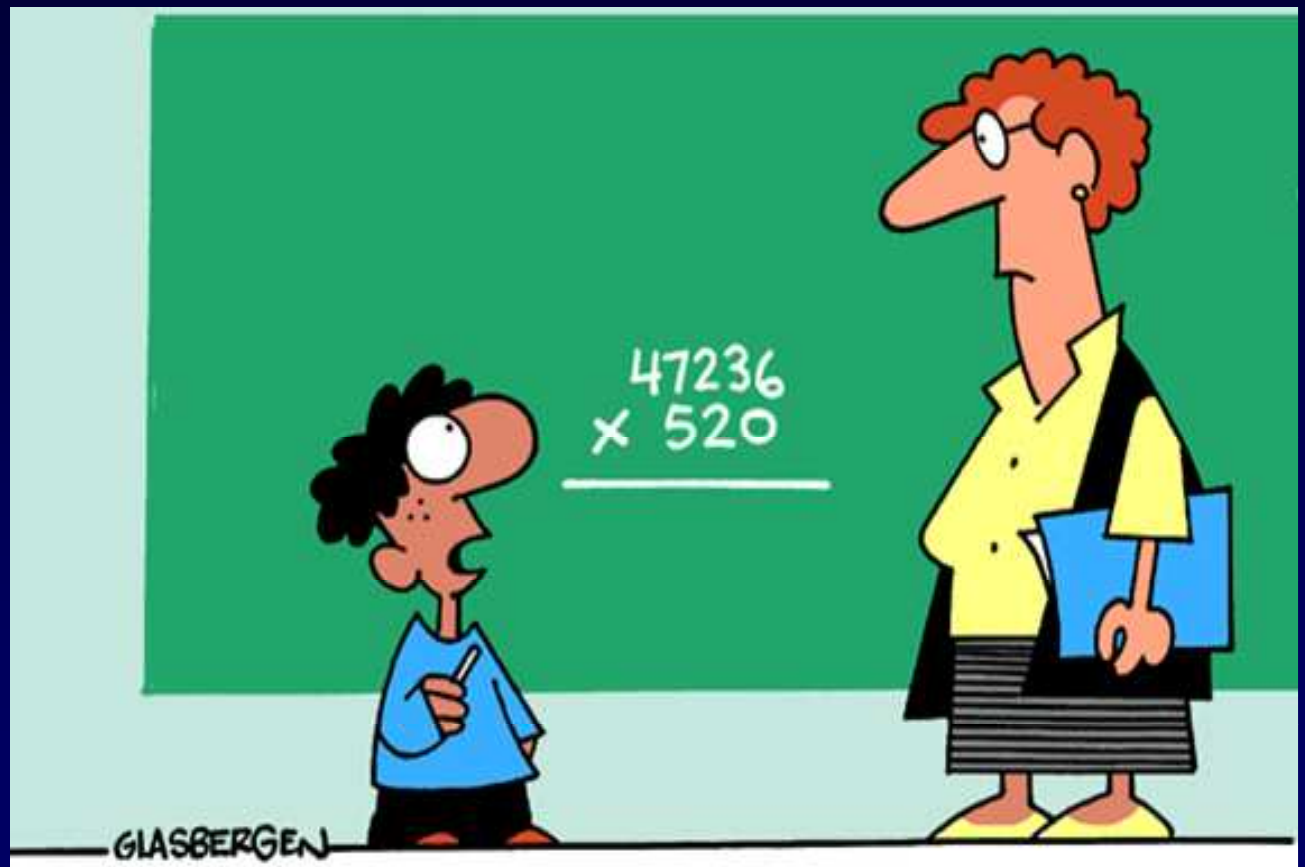
- Siemens, France

  Research & Development

  – Dr. Alexandre Vignaud

Thank you!


47236
x 520
GLASBERGEN
"AREN'T THERE ENOUGH PROBLEMS IN THE WORLD ALREADY?"