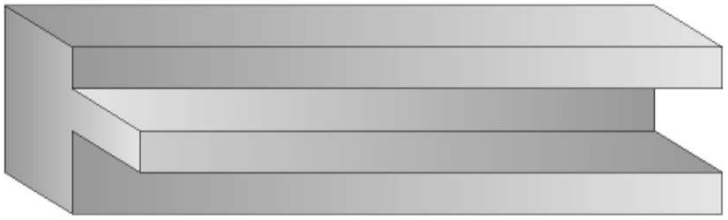
MRI in lymphoma: where are we in 2016



www.ilusaodeotica.com

Alain Rahmouni

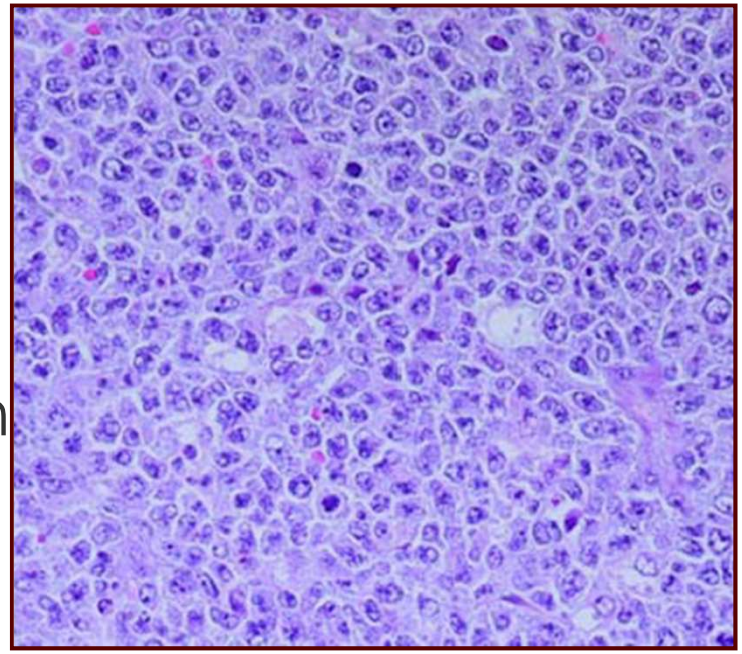
Henri Mondor Academic Hospital
Paris Est Créteil University, France

Plan

- Requirements
  - DWI signal in lymphoma
  - ADC measurement
  - SNR:
    - Surface coils
    - 1.5 T and 3T
  - Moving table and stations
  - EPI sequence design
- Imaging findings
- Pitfalls and limitations
- What's new?

DW signal in lymphoma

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



DLBCL: H&E stain

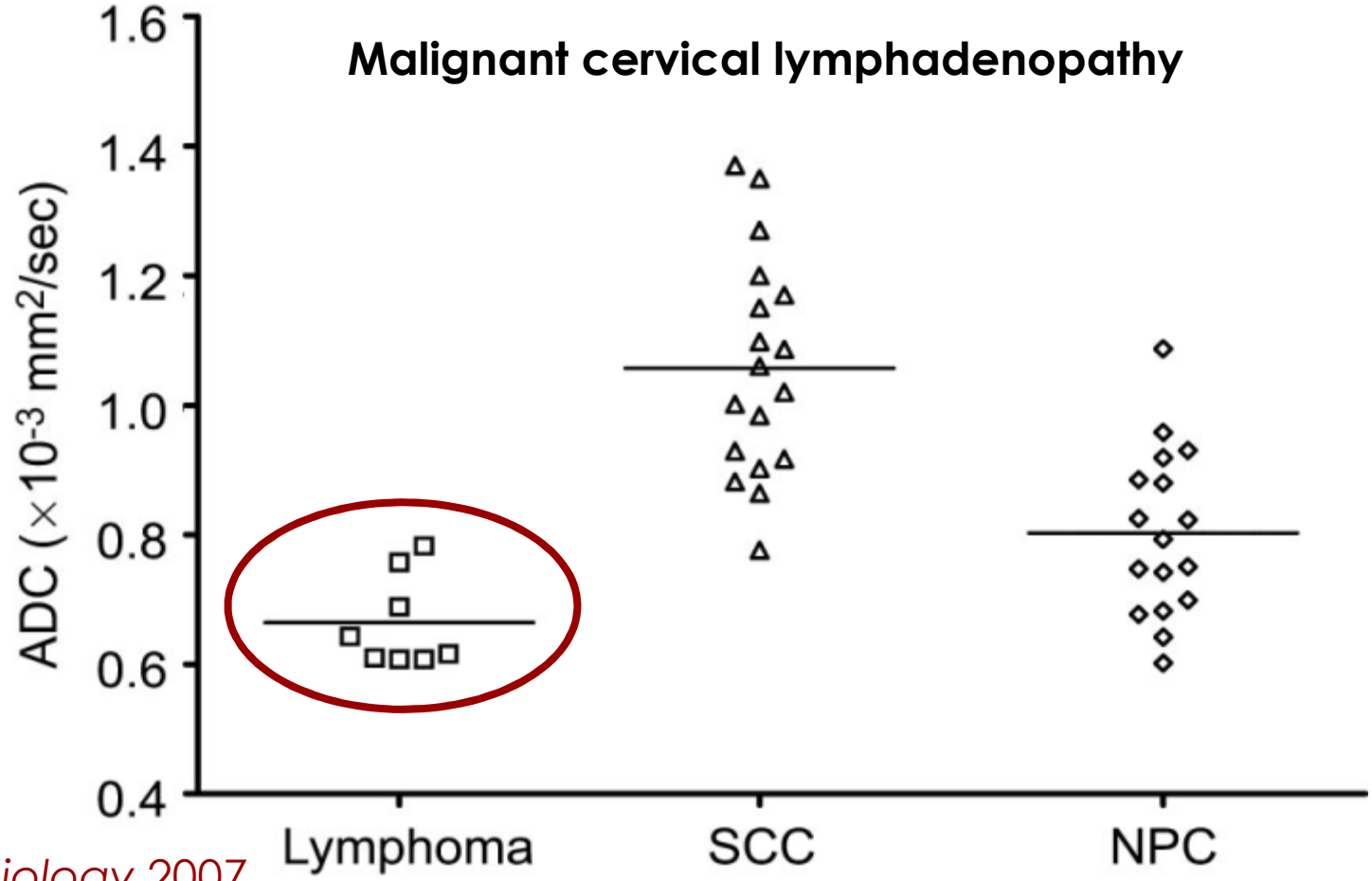
Nakayama T et al. J Magn Reson Imaging 2004

Sumi M et al. Eur Radiol 2007

King AD et al. Radiology 2007

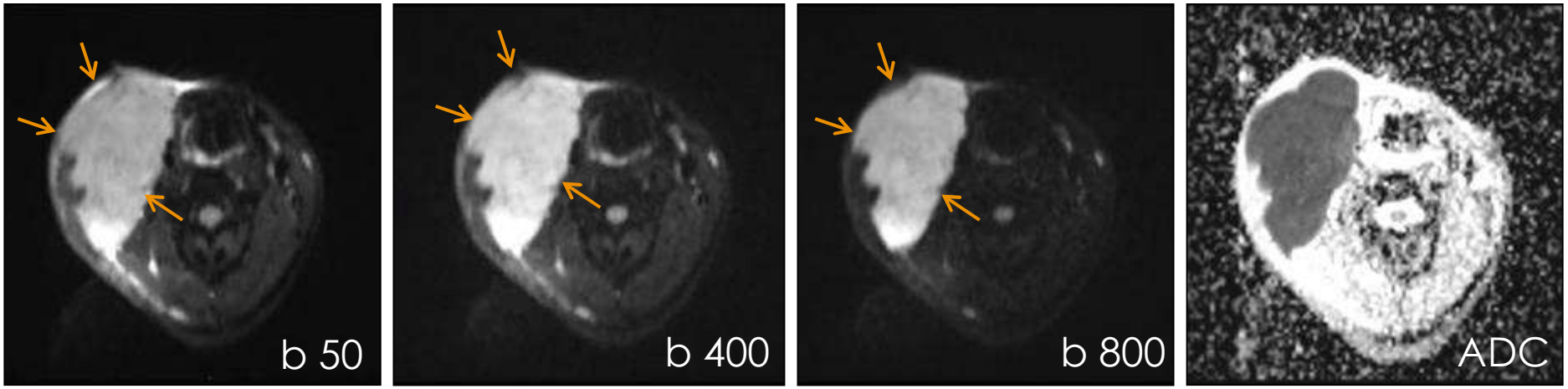
Toh CH et al. AJNR Am J Neuroradiol 2008

DW signal in lymphoma



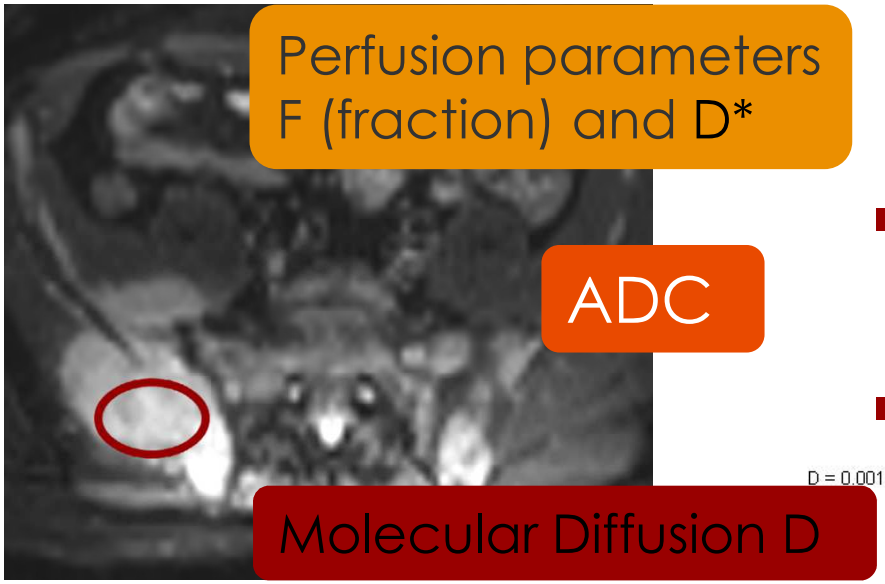
King AD et al. *Radiology* 2007

DW signal in lymphoma

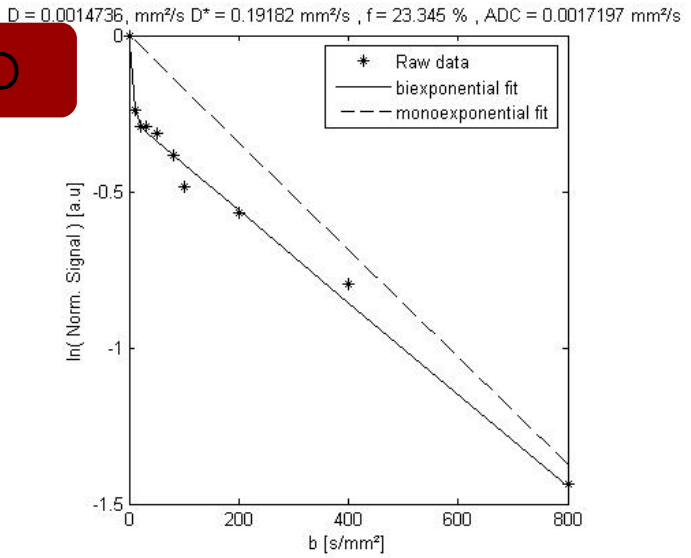


- 44 y/o, DLBCL stage IV, right cervical mass. High signal on b50, b400, b800 EPI images. Low ADC (compared to muscle). 3 T images

ADC measurement



- To obtain ADC, at least 2 b values: low b<50, and high b> 800 s/mm2
- When b increases, the signal decrease is complex
- $S=S_0[(1-f).exp^{(-b.D)}+f.exp^{-b(D+D^*)}]$



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

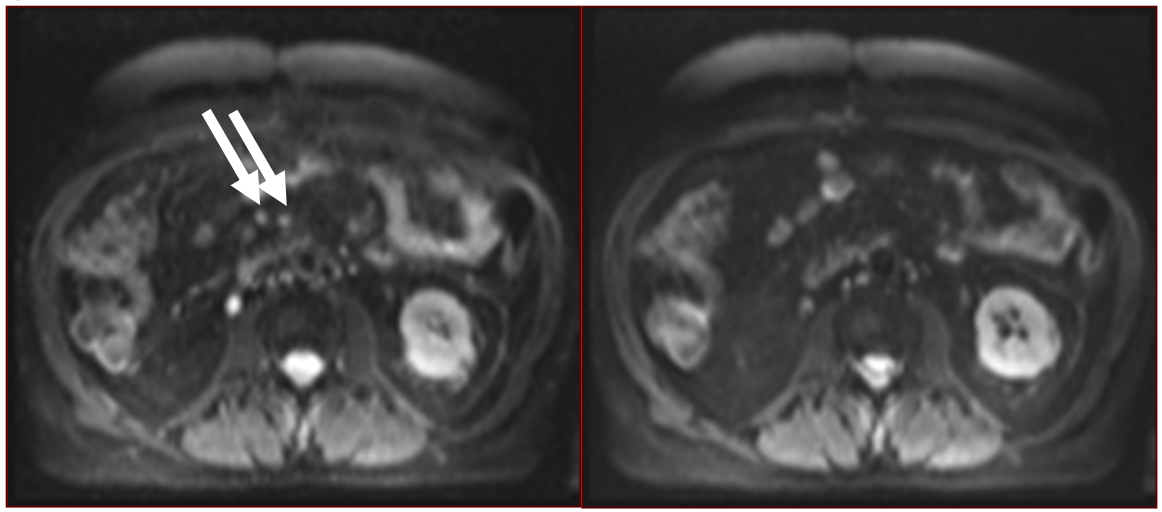
Separation of Diffusion and Perfusion in Intravoxel Incoherent Motion MR Imaging[1]

Radiology 1988

ADC measurement, b value selection

- EPI axial image combines T2 weighted morphological/size analysis and functional information
- Small b acts as a velocity filter and limits « perfusion » effect; detection of nodes is easy as small b eliminates signal from vessels

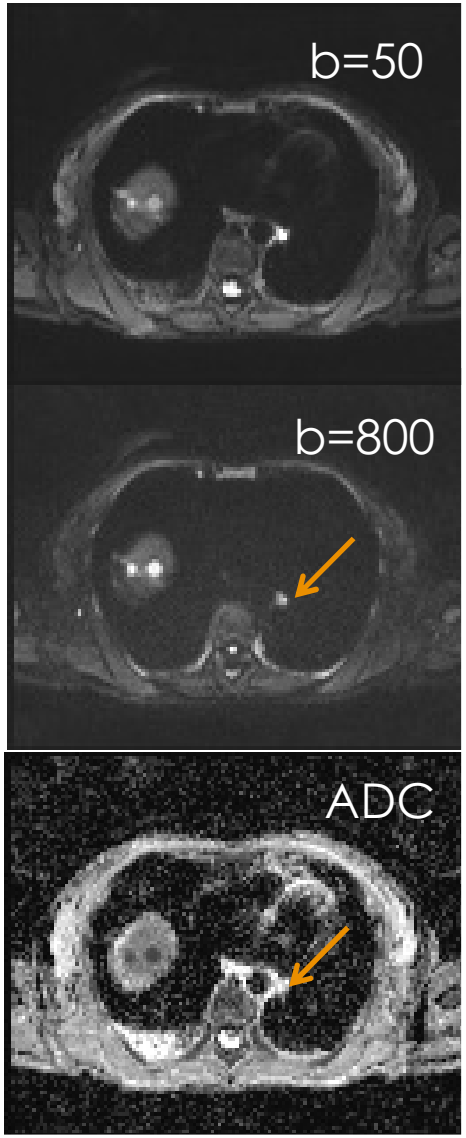
Nguyen TD et al.
J Magn Reson Imaging 2008



b = 0 s/mm^2 ***b*** = 50 s/mm^2

Combining morphological analysis and ADC measurement

- EPI axial image is a T2 weighted image allowing morphological/size analysis and
- In the same acquisition, functional information can also be obtained from b images and ADC analysis

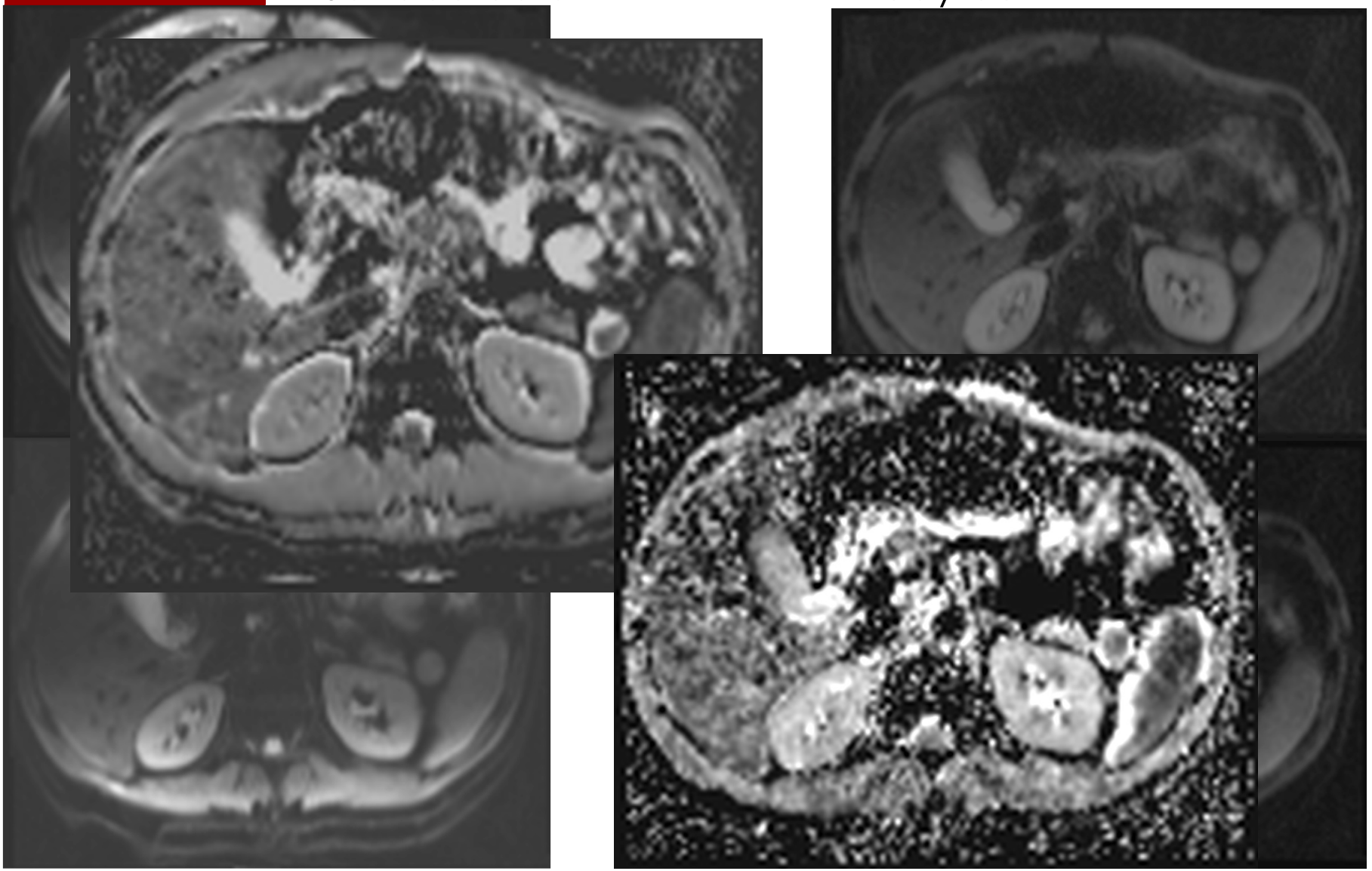


- 79 y/o, DLBCL Ann Arbor stage IV. 1.5T
  - High signal of liver lesions at b 50 and b 800. Low ADC (compared to muscle).
  - High signal of 1 cm para aortic node still present at b 800 but decreasing. High ADC
  - Intermediate signal of right pleural effusion (motion of free pleural effusion) not present at b800. High ADC

SNR, surface coils

Surface coils

Body coil



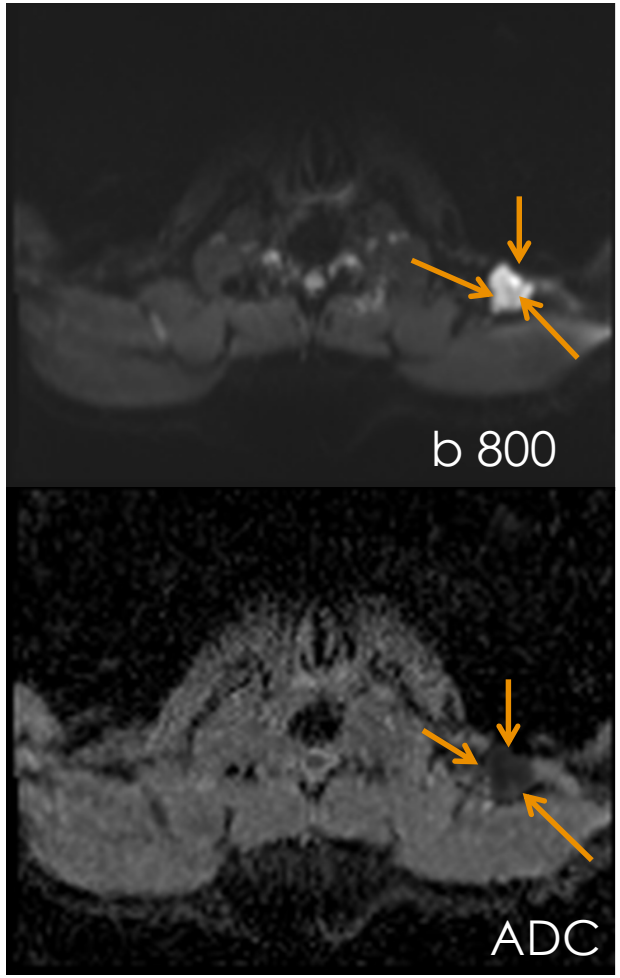
SNR, surface coils

- Head Coil : 12 elements
- Cervical Spine Coil : 4 elements
- Thoracic-Lumbar Spine : 24 elements
- Body coils (anterior) : 2x6 elements
- Total = 52 elements Phased

SNR, 1.5 T vs 3 T

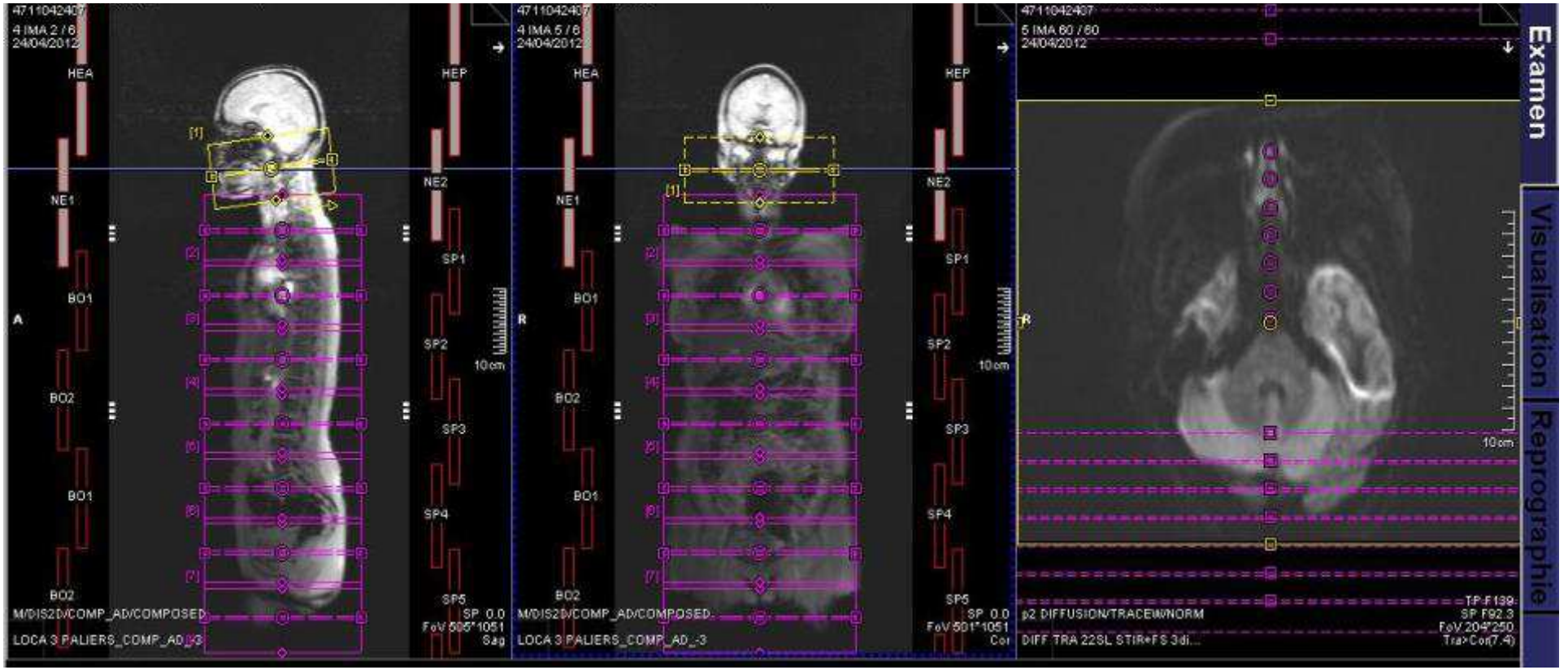
- Acquisition Time : decreased number of acquisitions at 3T
- Susceptibility artifacts in clinical situations

- 26 y/o. Hodgkin disease. 3T DWI Supraclavicular 1.5 cm node; no artifact in this difficult area (interface air-tissue)

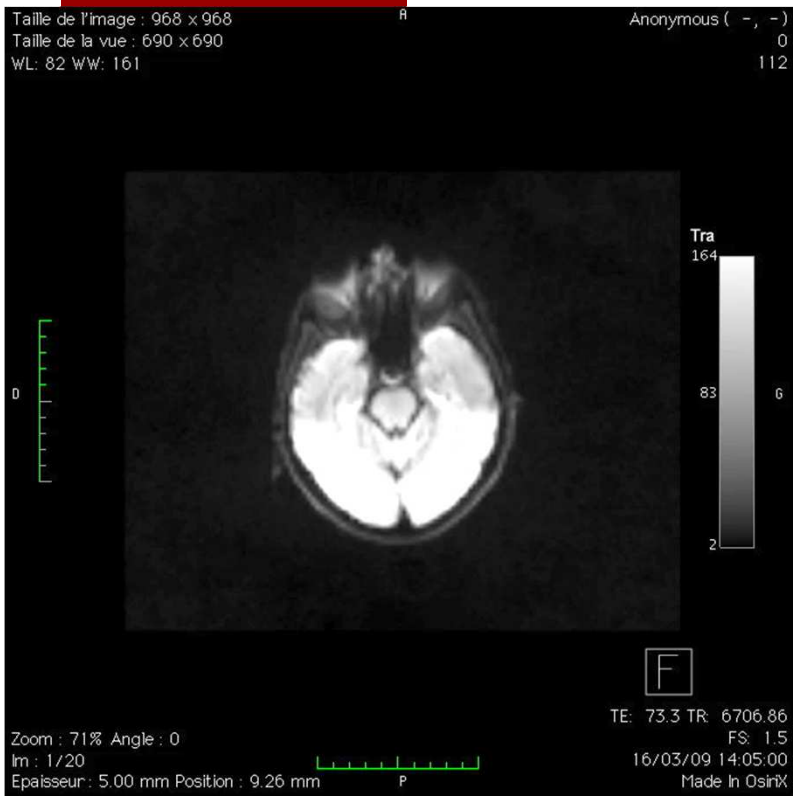


Moving table and stations

- 7 to 8 stacks, 11-cm thickness, 22 slices, 5 mm thickness
- Only 11-cm to get each slice close to the center of the magnet



EPI sequence



- Fat suppresion-water excitation or STIR
- Reduced TE (50 msec) using parallel acquisition : acceleration factor of 2
- Respiratory gating for accurate ADC measurements in moving regions, *Lee.Y, et al. Radiology sep 2014*
- In our experience, acquisition time at 1.5T with 4 nex : 50 to 60 mn. At 3T, 2 nex, 25 to 30 mn.

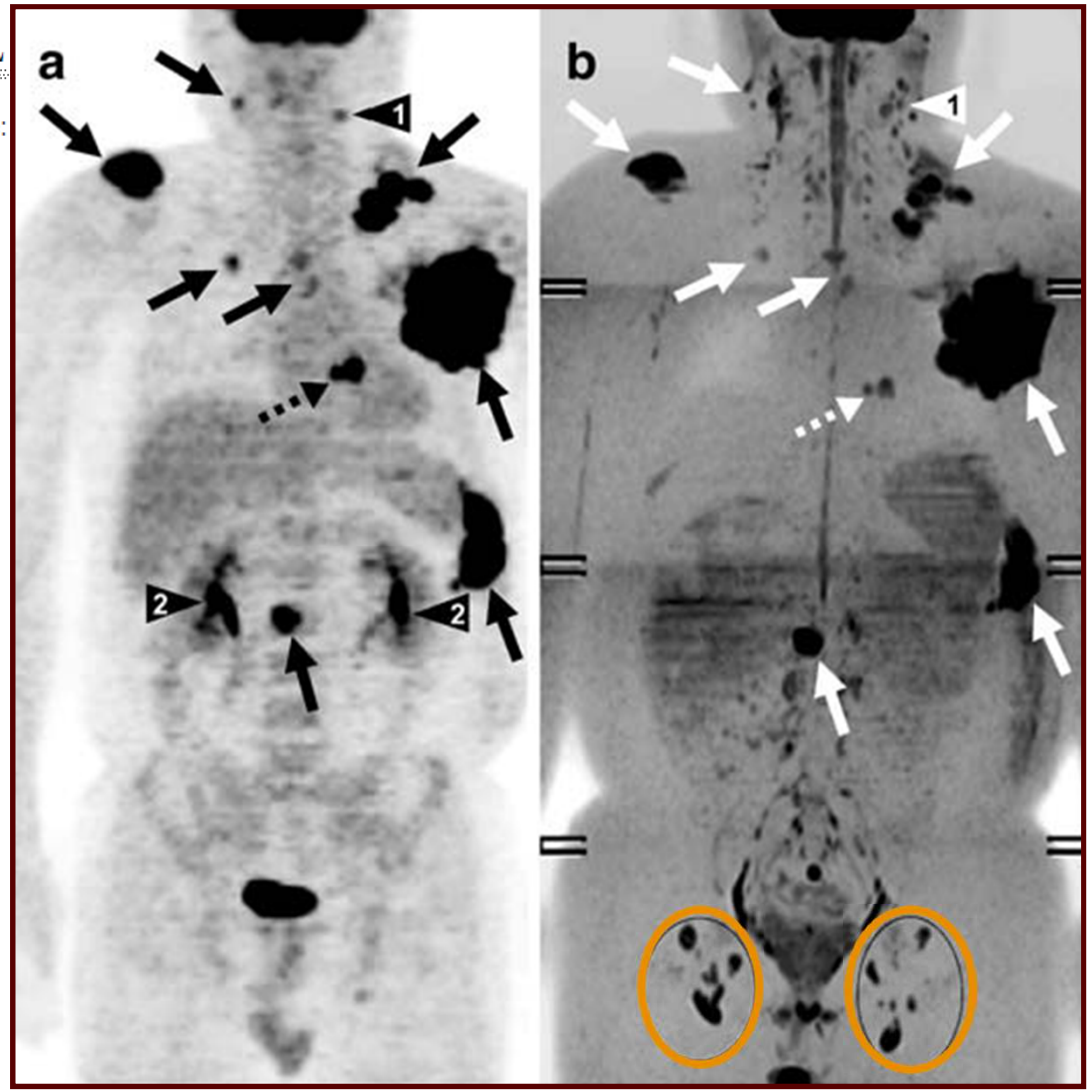
Lin C et al, Rahmouni A. Eur Radiol 2010
Lin C et al, Rahmouni A. Invest Radiol 2011
Toledano et al, Rahmouni A. Radiographics 2015

PET and DWIBS

- No respiratory gating
- b 1000 STIR EPI images
- Inverted gray and MIP in order to obtain pseudo-PET

TECHNICAL

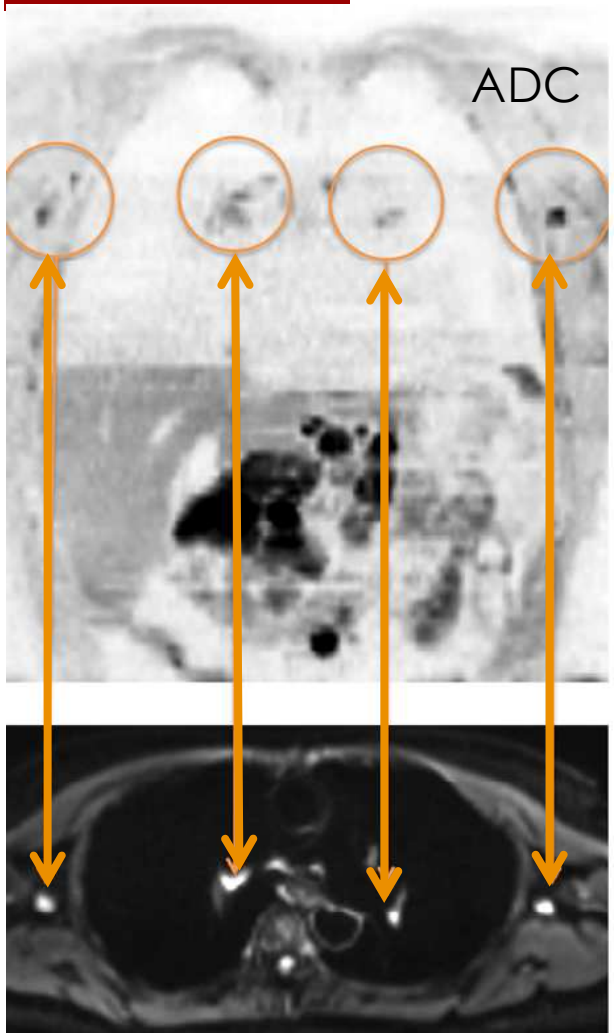
Radiation Medicine:

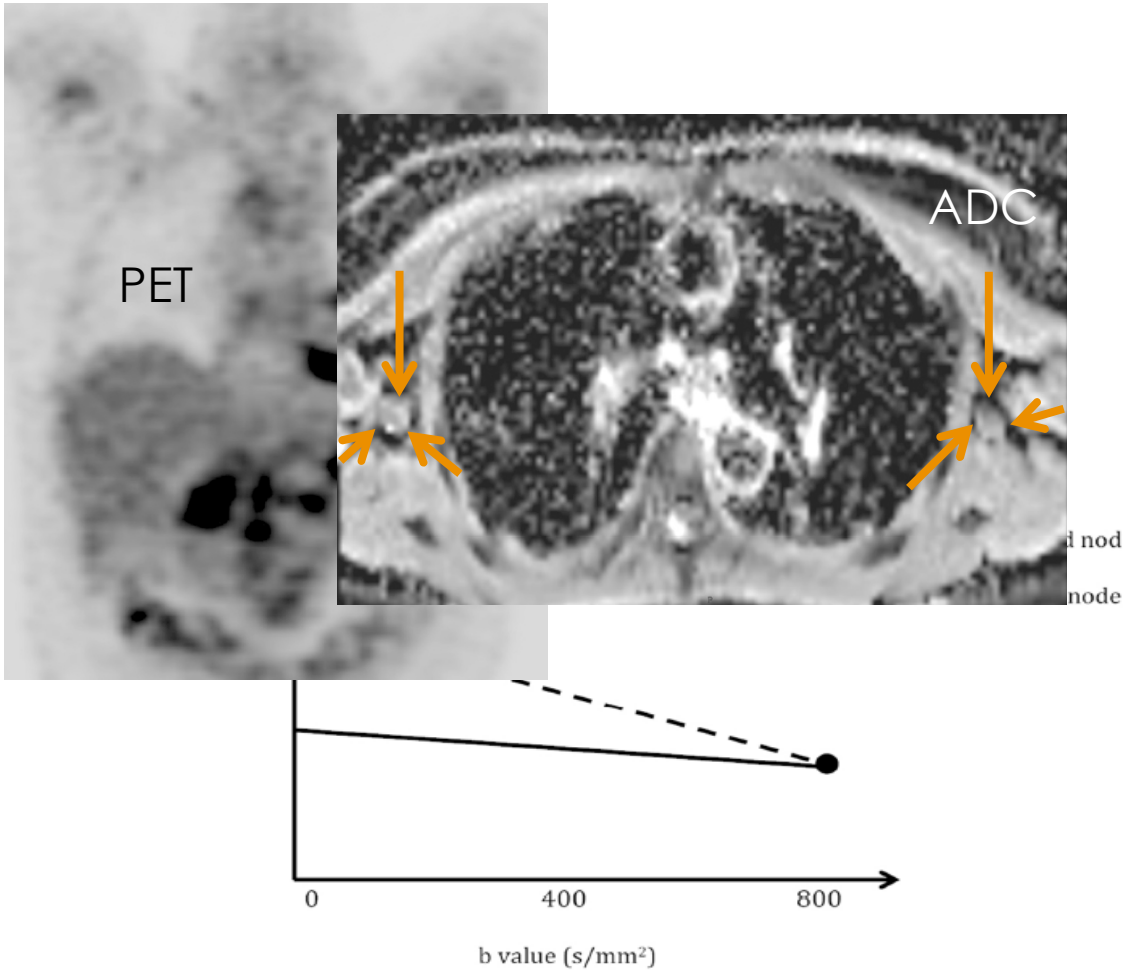


PET DWIBS

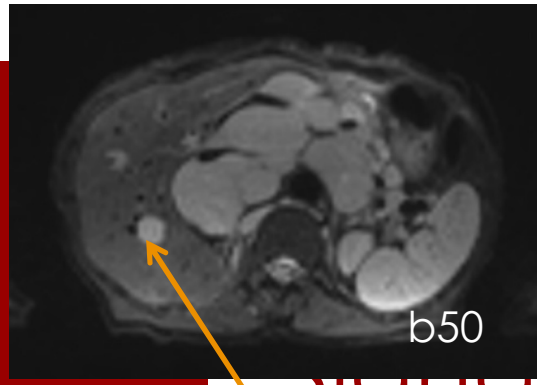
Kwee TC et al. Eur Radiol 2008

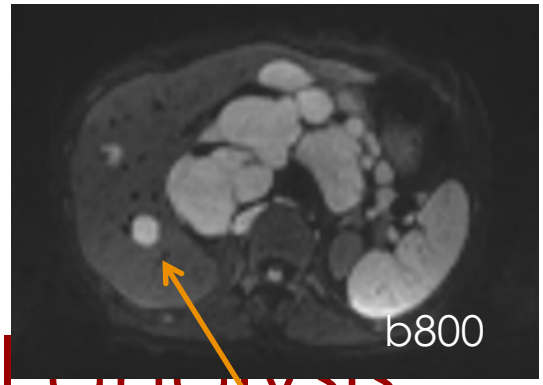
DWIBS versus ADC mapping

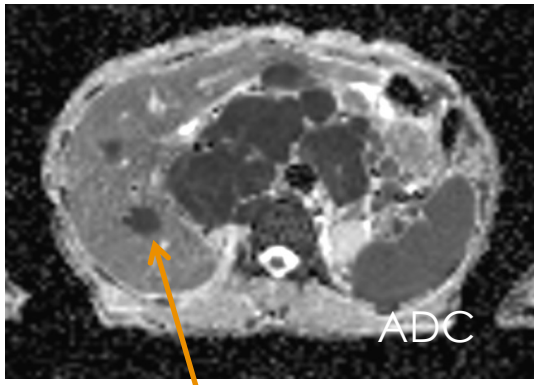


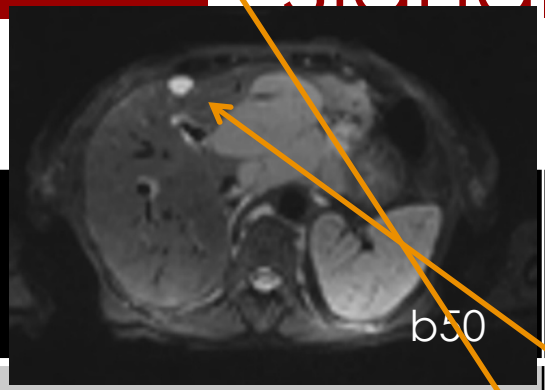


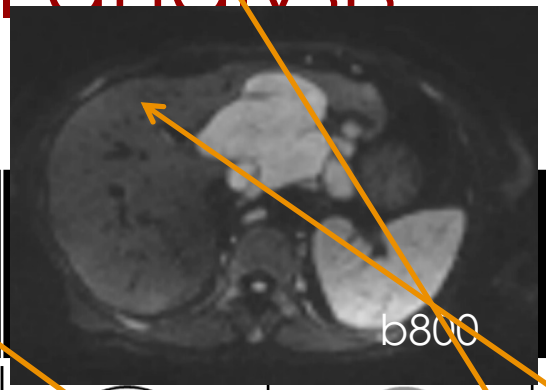
b 800: high signal node: restriction of diffusion ?

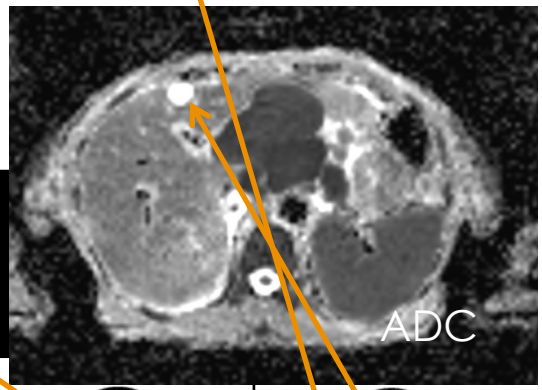












Benign lesions				
Lymphoma lesions				
T2 « shine through » effect				

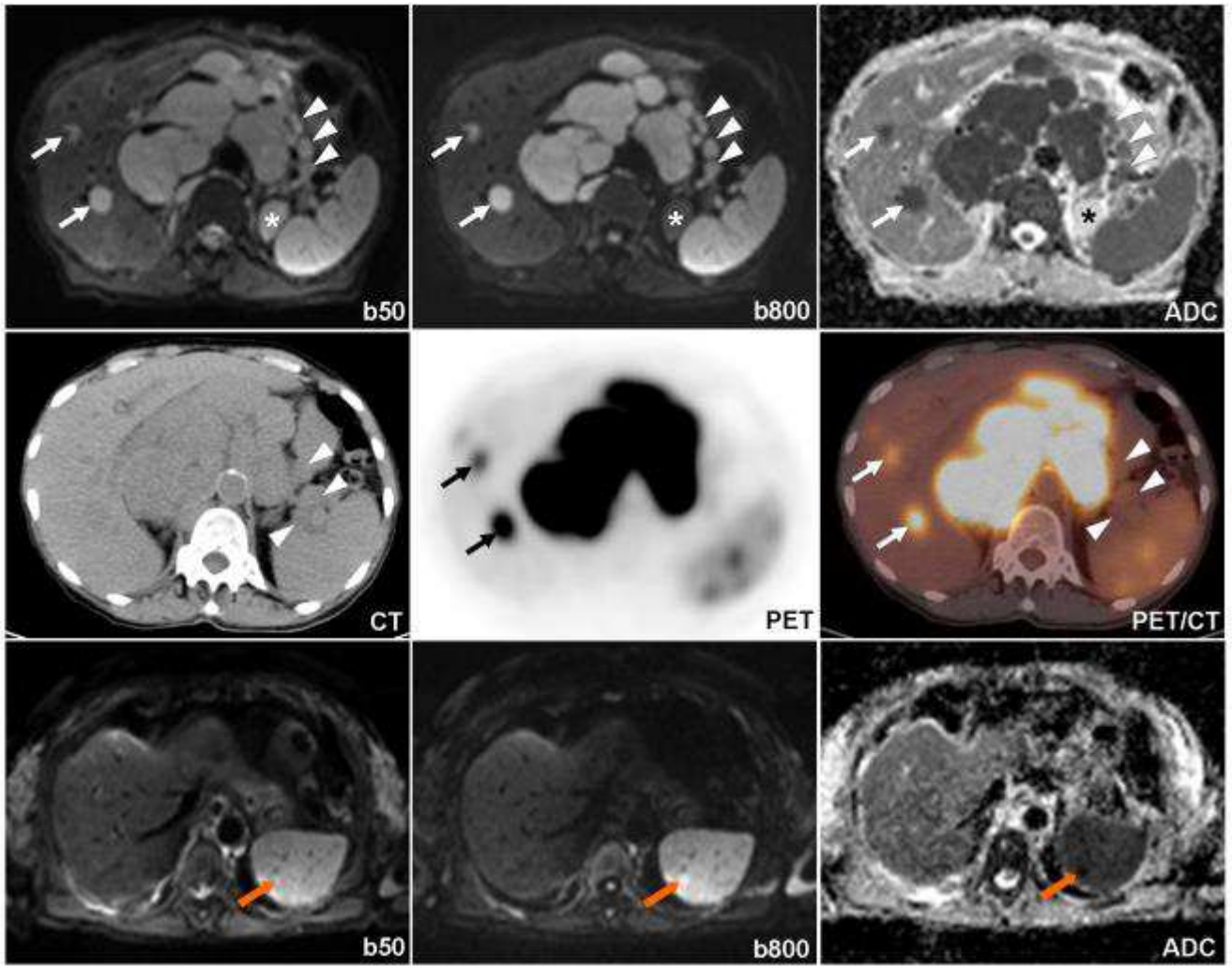
Staging-WB-DWI-MRI versus PET

- In our experience based on patients with DLBCL, DWI and PET/CT matched in 94% lymph node regions.
- All organs involved on PET/CT were detected on DWI; DWI detected some additional organ lesions. Eur Radiol 2010
- Concordance Kappa test DWI / PET varied between 0.7 and 0.94 among published studies

Tsuji. K, et al. JMRI 2014
Littooij. A, et al. Eur Radiol 2014
Mayerhoefer. ME, et al. Clin Cancer Res 2014
Including 140 patients. Sensitivity 100% for extra-Nodol involvement. Sensitivity slightly less than PET/CT For nodal involvement due to artifacts

Staging

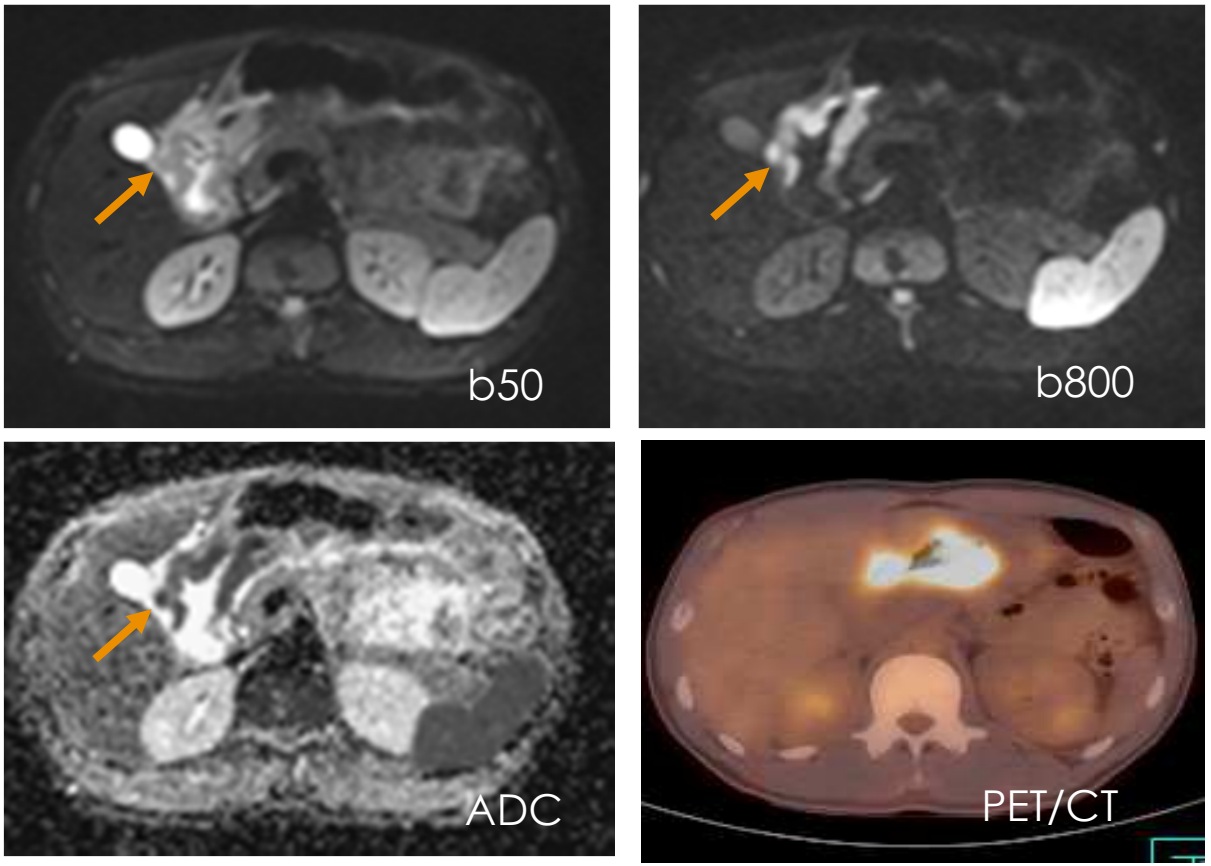
- Almost concordant staging: additional nodes of the splenic hilum: indolent lymphoma?



79 y/o, DLBCL stage IV. 1.5T

Staging

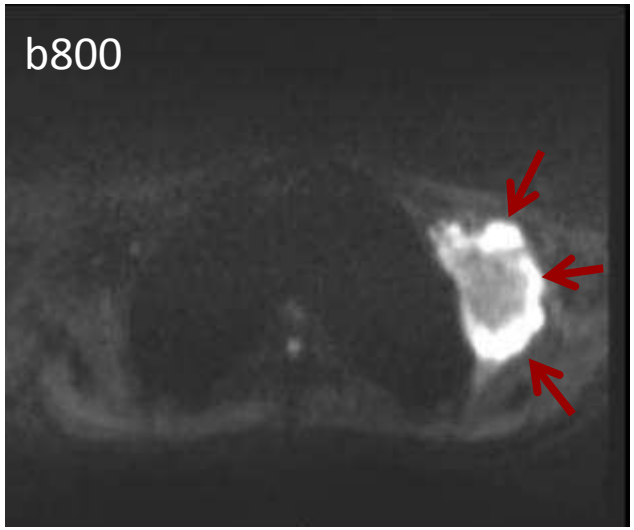
- Almost concordant staging: stomach involvement, low ADC. Detection on DWI of an additional node

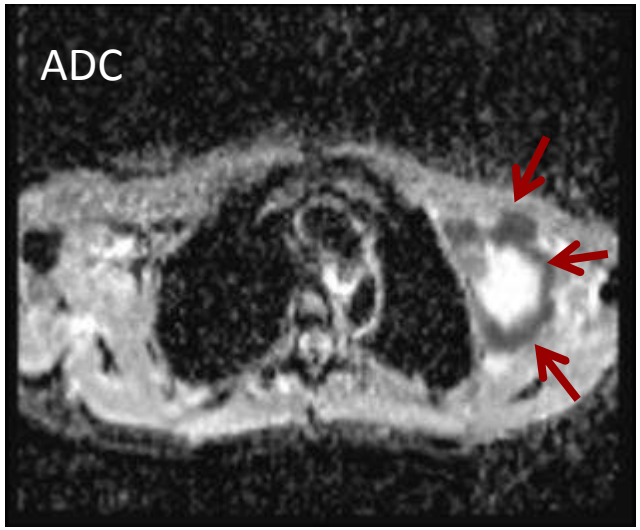


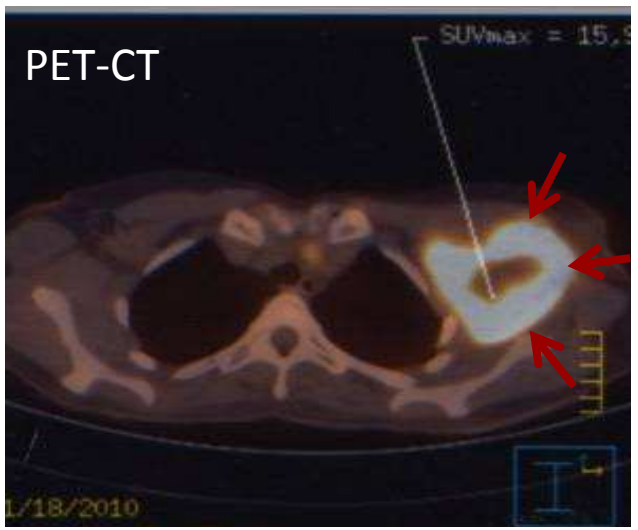
44 y/o. DLBCL. 1.5T

Staging

- 55 y/o female patient, DLBCL before treatment
- Necrotic Axillary mass with concordant FDG-PET-CT findings

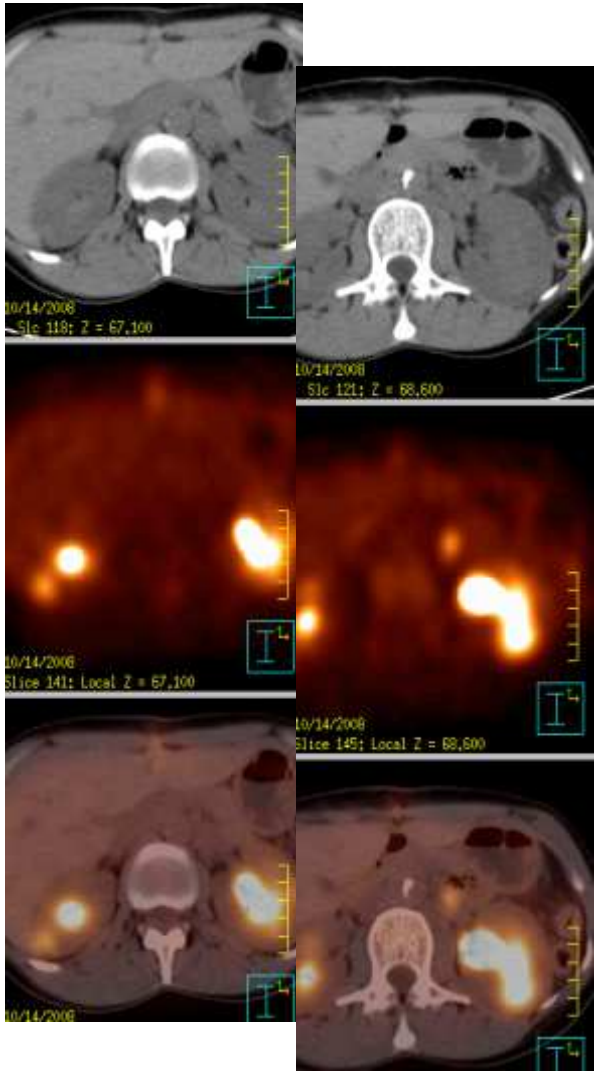


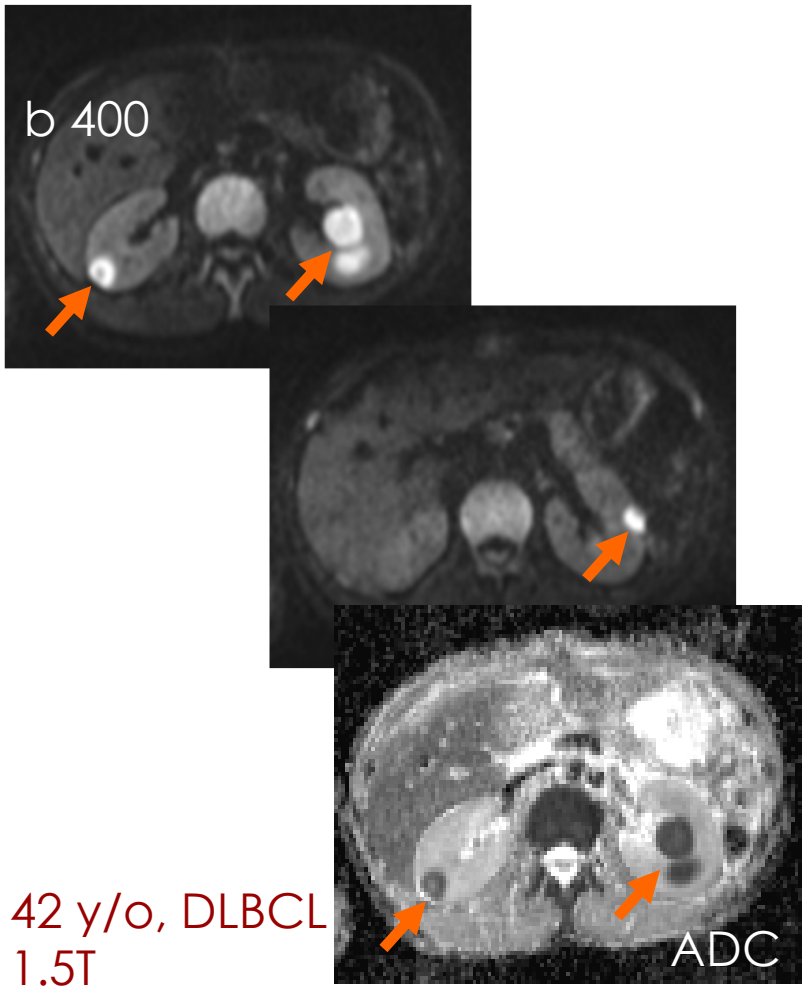




Staging

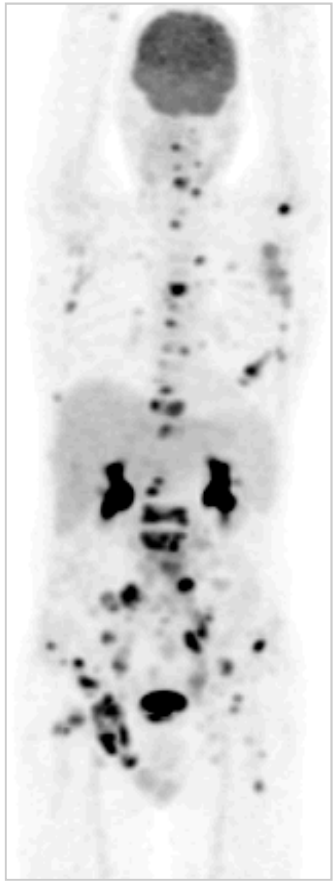
- On PET/CT, lesions might be masked by normal FDG excretion, which would depend on the color scale adjustment. 1.5T



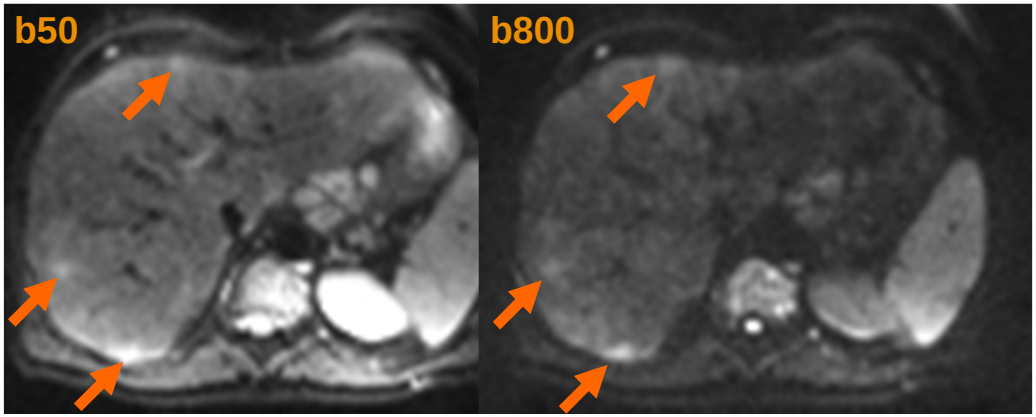


42 y/o, DLBCL
1.5T

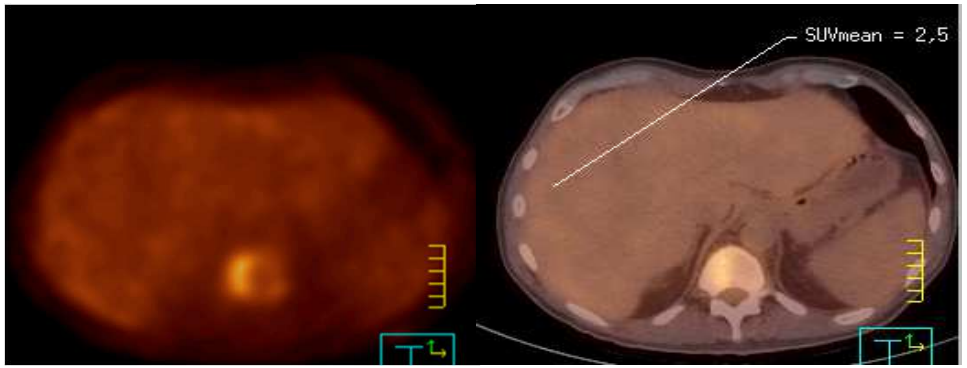
Staging - discordances



- DWI showed hepatic involvement with small focal lesions



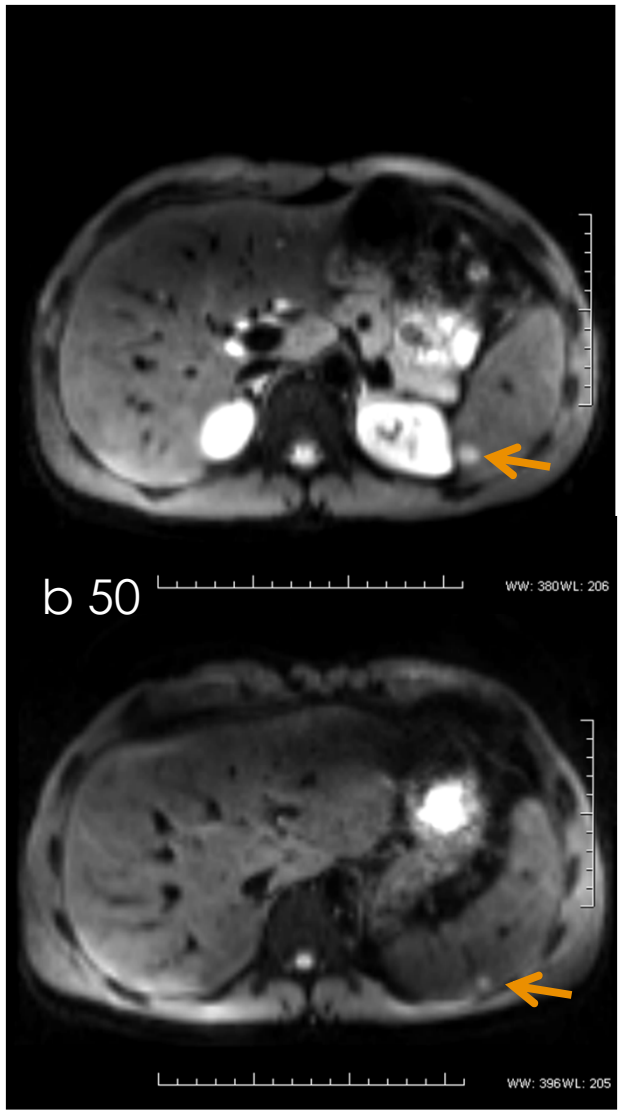
- On PET/CT, FDG uptake of liver was within normal range



57 y/o associated DLBCL and follicular lymphoma. 1.5T

Staging - discordances

- 23 y/o HL, stage 2 on PET/CT and enhanced CT with no spleen nodule
- High signal sub-centimetric nodules on EPI. 3T
- DW-MRI after treatment was normal: specific HL nodules?



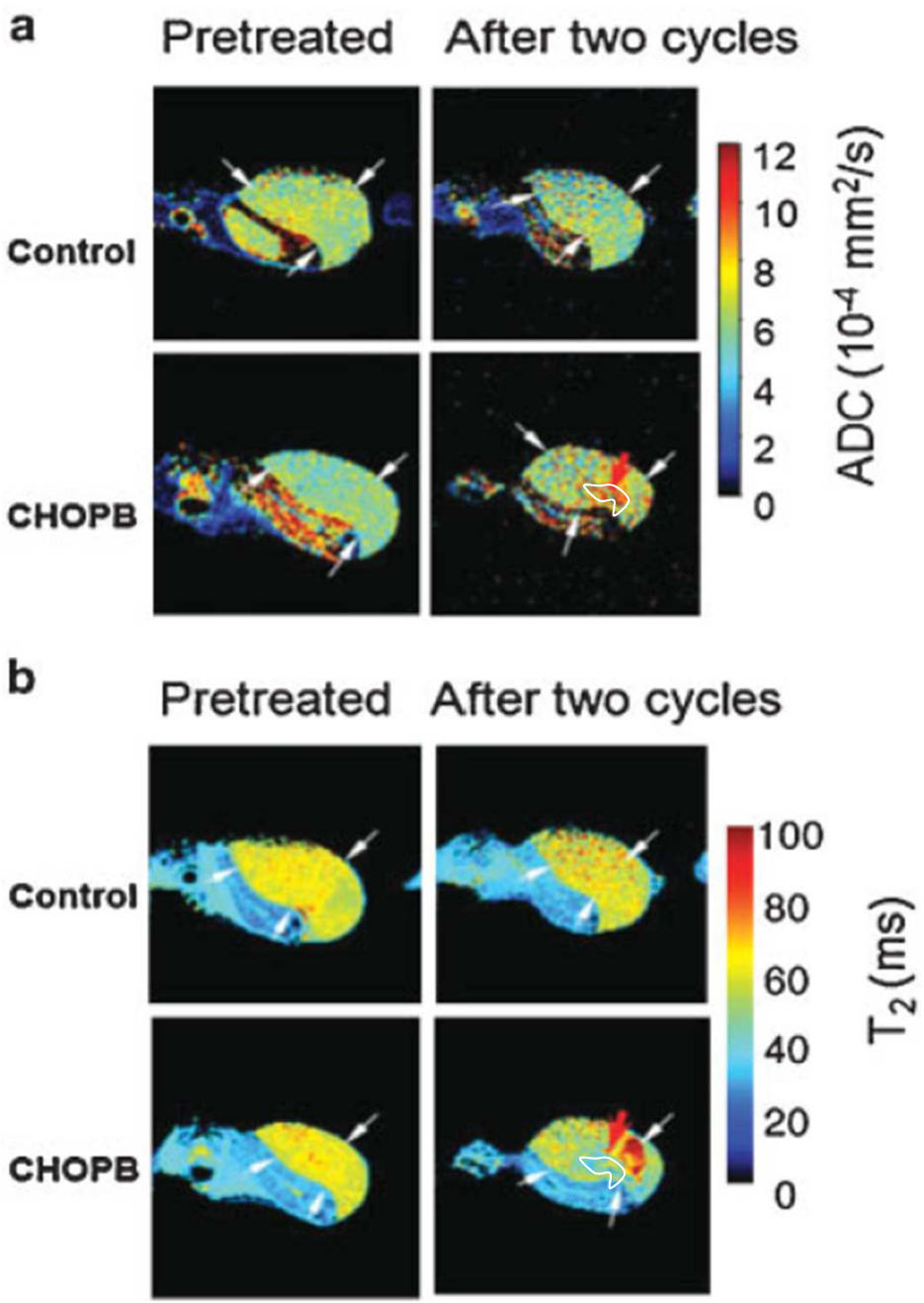
Response to treatment experimental data

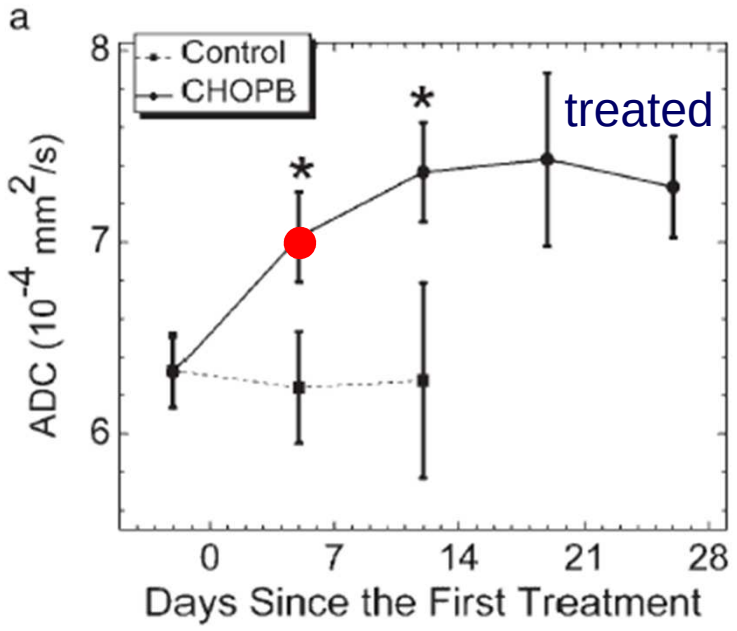
NMR IN BIOMEDICINE
NMR Biomed. (2008)
Published online in Wiley InterScience
(www.interscience.wiley.com) DOI:10.1002/nbm.1261

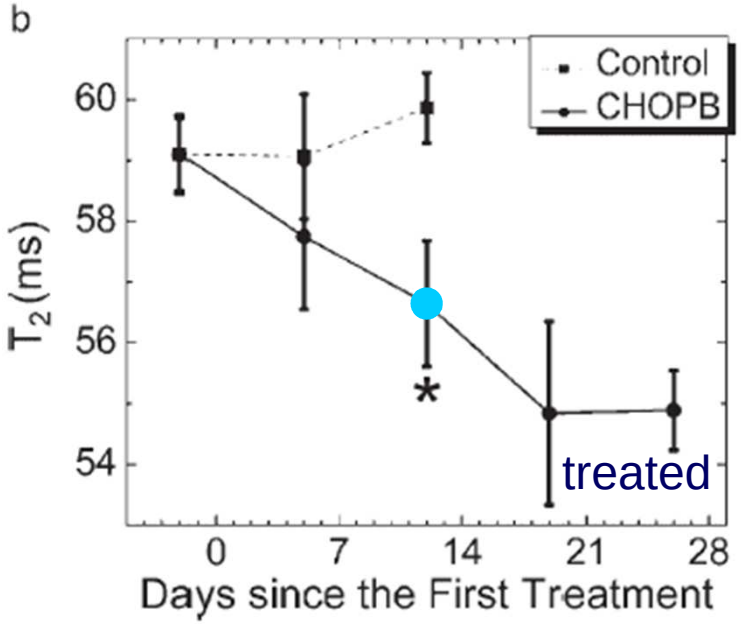
Monitoring response to chemotherapy of non-Hodgkin's lymphoma xenografts by T_2-weighted and diffusion-weighted MRI

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


a
Pretreated
After two cycles
Control
CHOPB
12
10
8
6
4
2
0
ADC (10-4 mm2/s)
b
Pretreated
After two cycles
Control
CHOPB
100
80
60
40
20
0
T2 (ms)

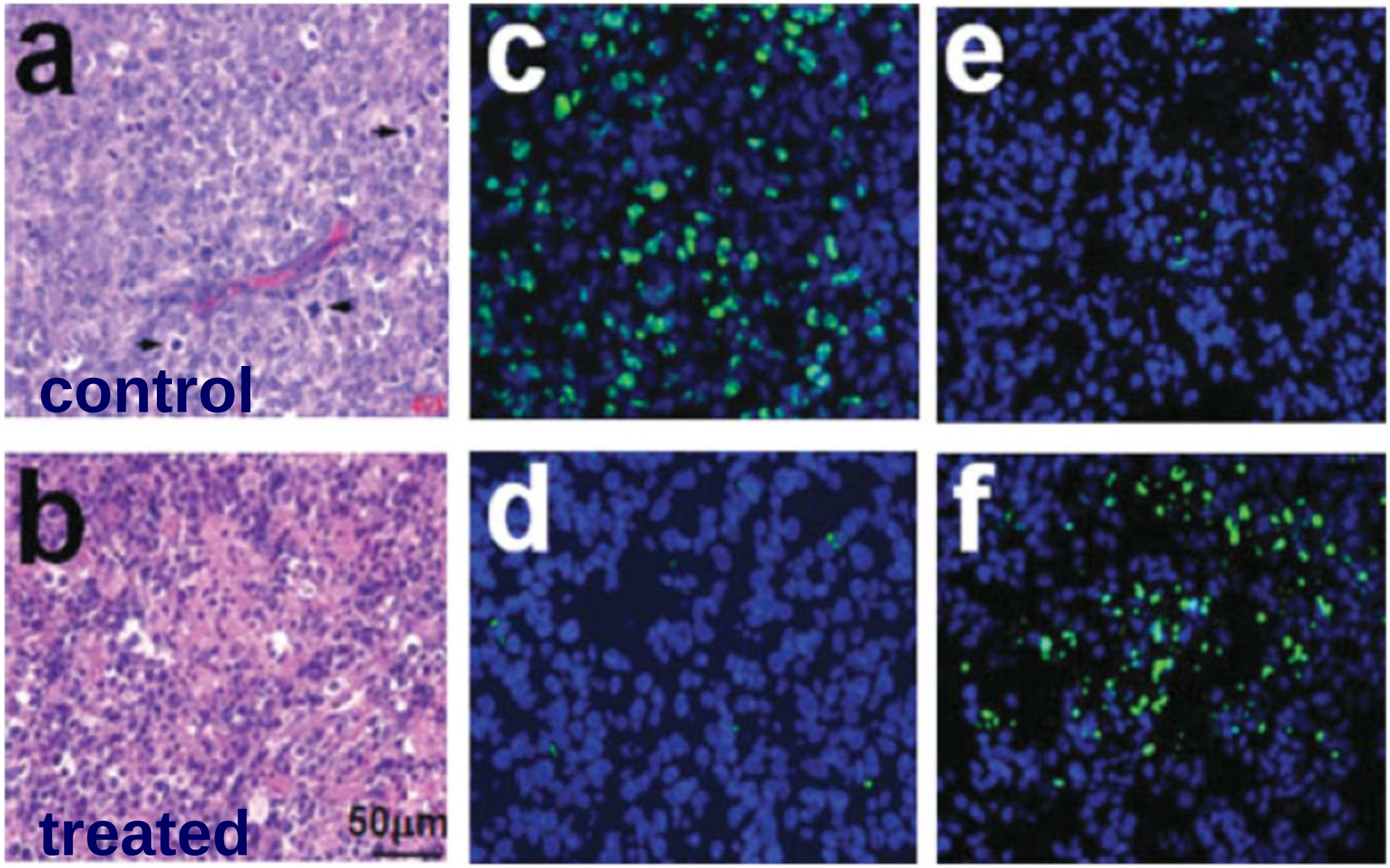

a
Control
CHOPB
treated
8
7
6
ADC (10-4 mm2/s)
0
7
14
21
28
Days Since the First Treatment


b
Control
CHOPB
60
58
56
54
T2 (ms)
treated
0
7
14
21
28
Days since the First Treatment

H & E/mitosis

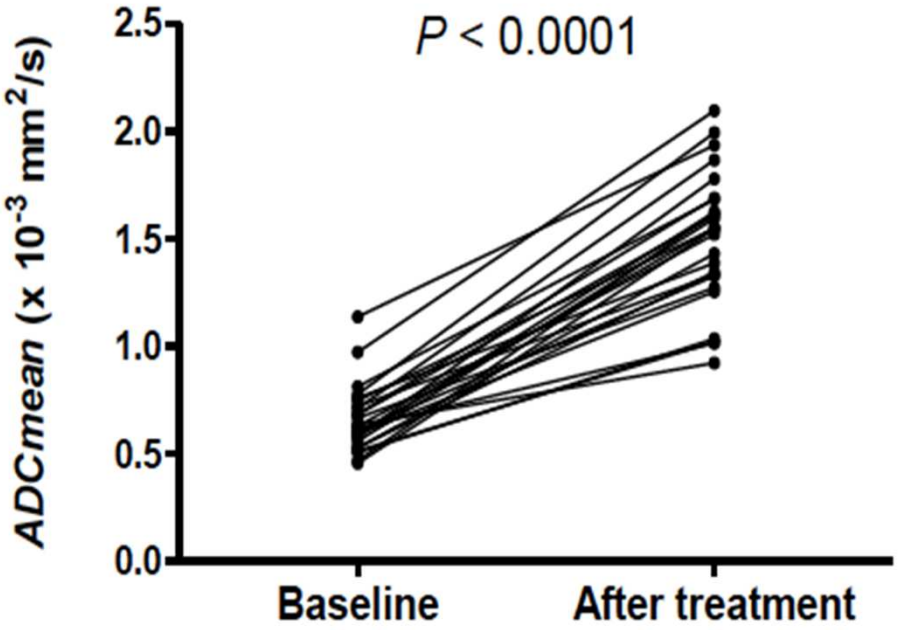
Ki-67/proliferation index

FITC/apoptosis index



Response to treatment, patients

- In good responders, ADC increased



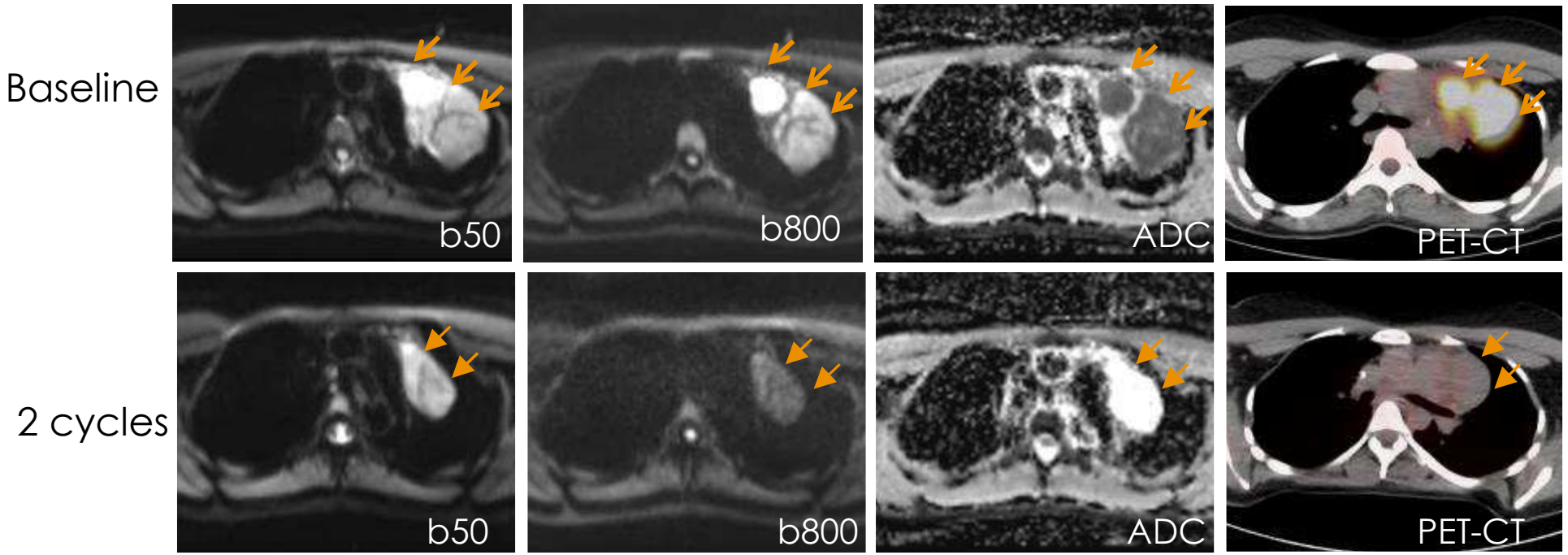
Lin C et al, Rahmouni A. Invest Radiol 2011

Response to treatment

	Mean ADC before treatment	Mean ADC after/during treatment
Lin et al Invest Radiol 2011	0.658 x 10^{-3} mm^2/s	1.501 x 10^{-3} mm^2/s
Chen et al Magn Reson Imaging 2012	0.595 x 10^{-3} mm^2/s	1.169 x 10^{-3} mm^2/s
Wu et al NMR Biomed 2011	0.710 x 10^{-3} mm^2/s	1.462 x 10^{-3} mm^2/s
Wu et al NMR Biomed 2013	0.680 x 10^{-3} mm^2/s	1.285 x 10^{-3} mm^2/s
Horger et al European journal of Radiology 2194	0,79 x 10^{-3} mm^2/s	1,295 x 10^{-3} mm^2/s
Siegel et al NMR biomed 2014	0,772 x 10^{-3} mm^2/s	1,428 x 10^{-3} mm^2/s

Response to treatment

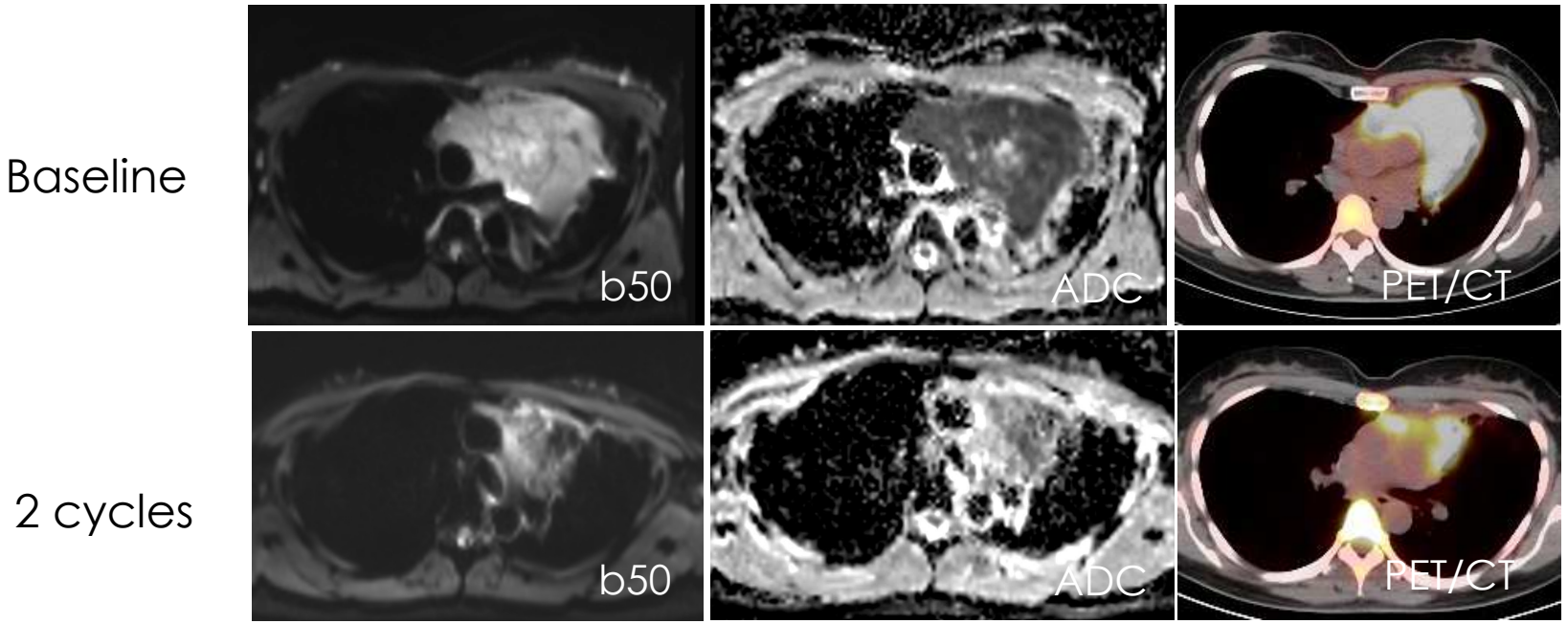
- Good responder



29 y/o HL. Mediastinal mass at baseline. Low ADC; SUV9. Residual mass after 2 cycles of chemotherapy. High ADC; no FDG uptake. According to 1999 Cheson size criteria, the patient is in partial response (PR), but in complete response (CR) according to Cheson 2014 criteria and ADC. 3T.

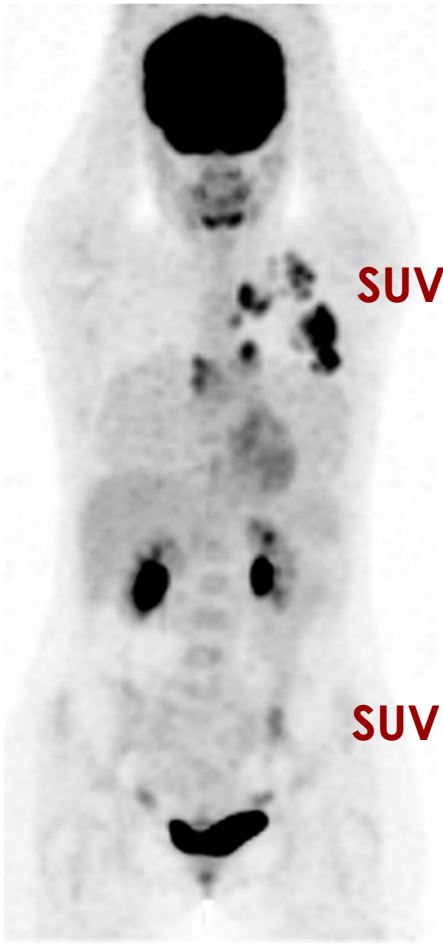
Response to treatment

- Partial response



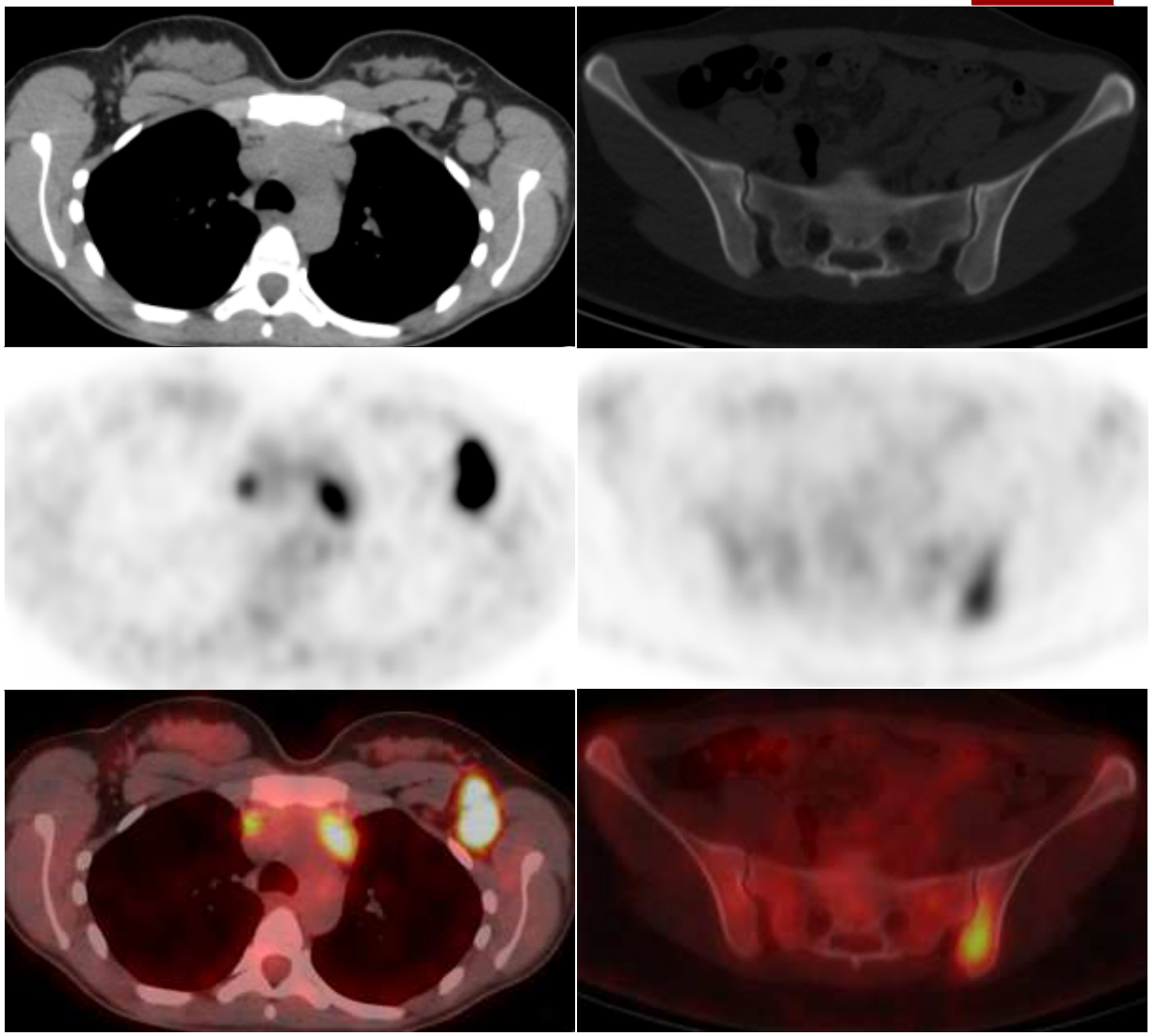
51 y/o patient, DLBCL. Mediastinal mass at baseline. Low ADC; SUV16. After two cycles of chemotherapy, the anterior mediastinal mass is heterogeneous, with main regions showing restricted diffusion. Persistent low ADC and SUV 6. According to Cheson size criteria, the patient is in partial response (PR) as well as on PET/CT (Cheson 2014) and ADC.

Response to treatment

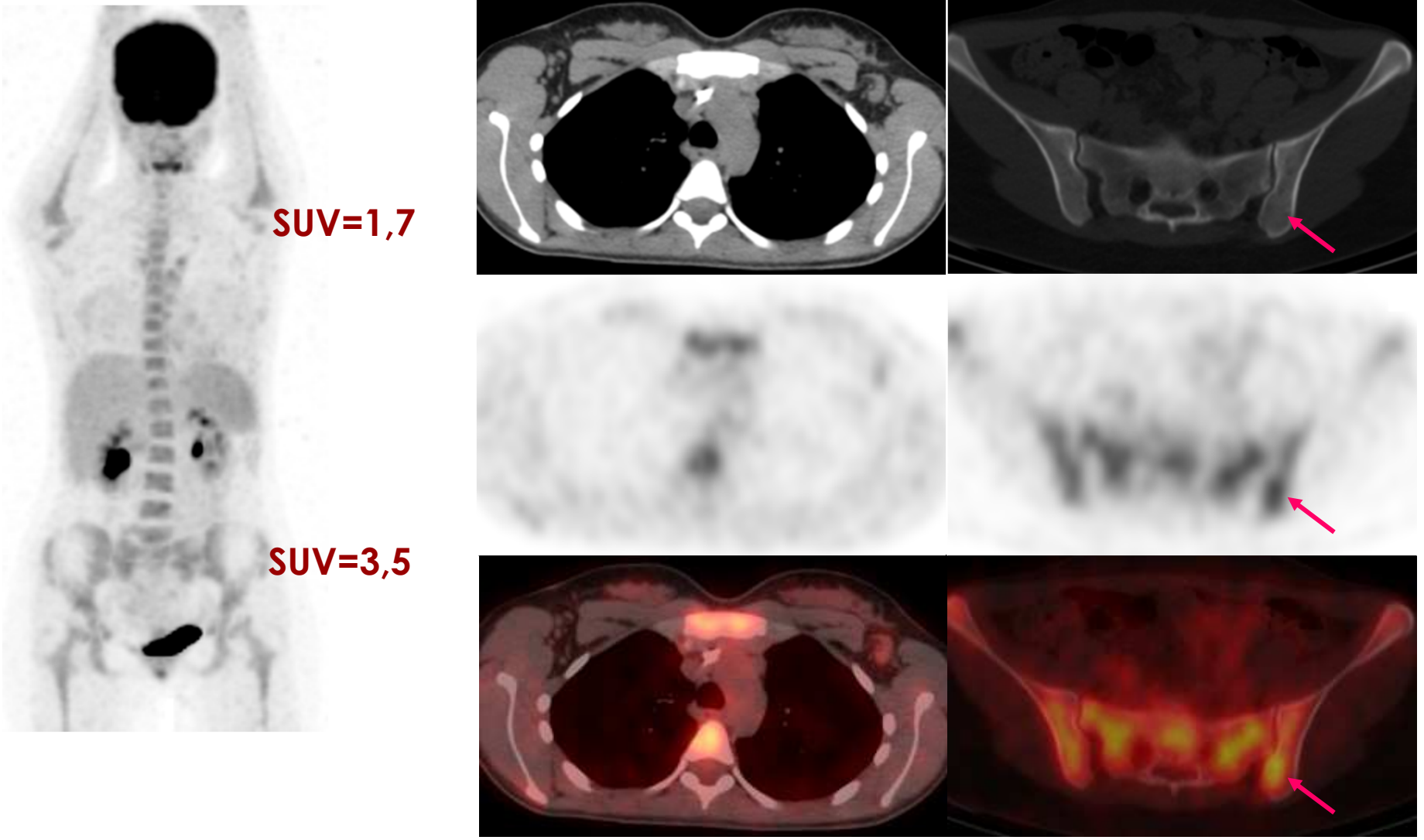


SUV=10,8

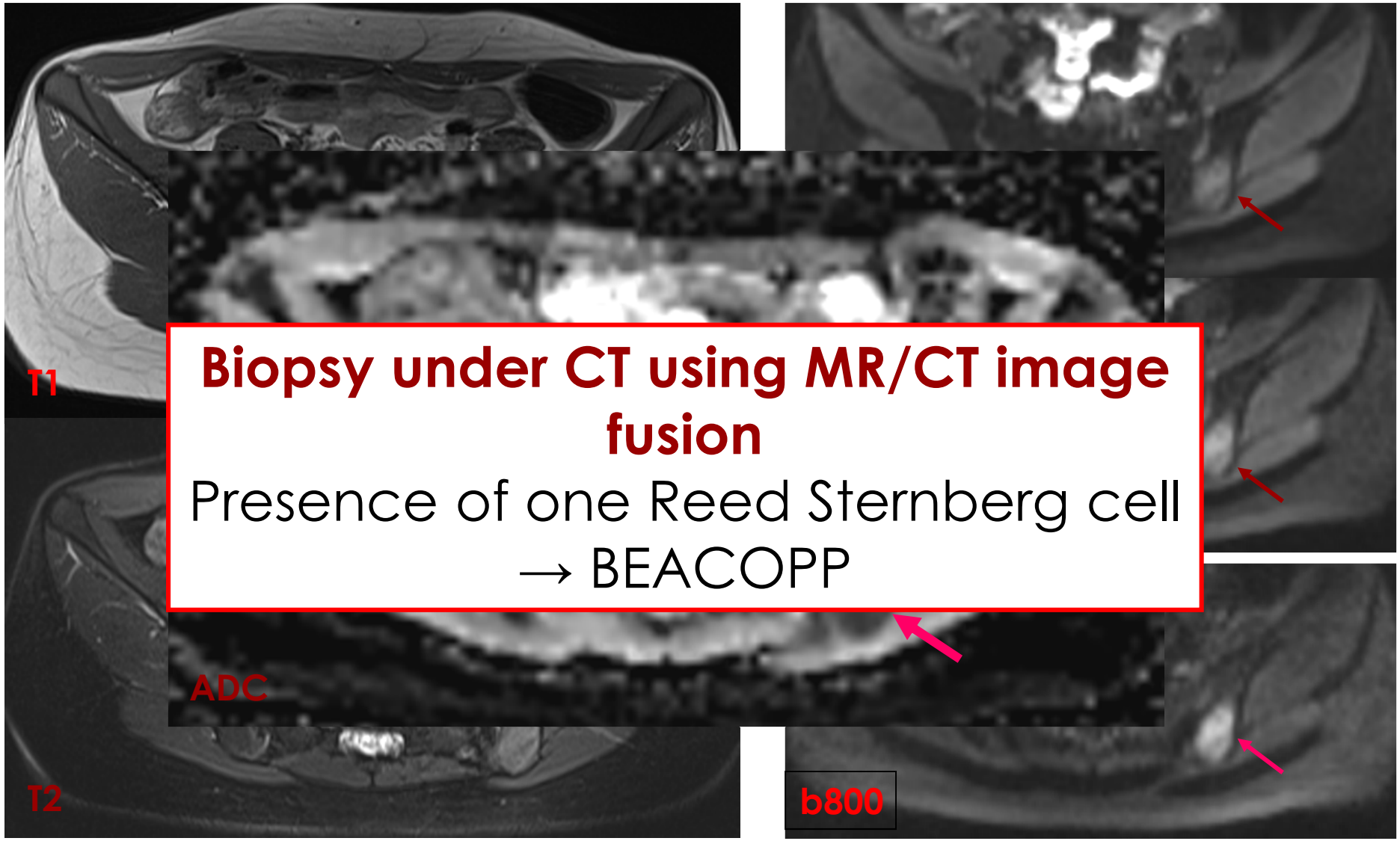
SUV=3,4



51 y/o patient, Hodgkin L on axillary biopsy
Single and low bone marrow uptake of left ilium → Stage IV



After 2 BEACOPP, Deauville 3 but a doubtful ilium uptake is still present in the same SUV range than bone marrow hyperplasia



Biopsy under CT using MR/CT image fusion

Presence of one Reed Sternberg cell

→ BEACOPP

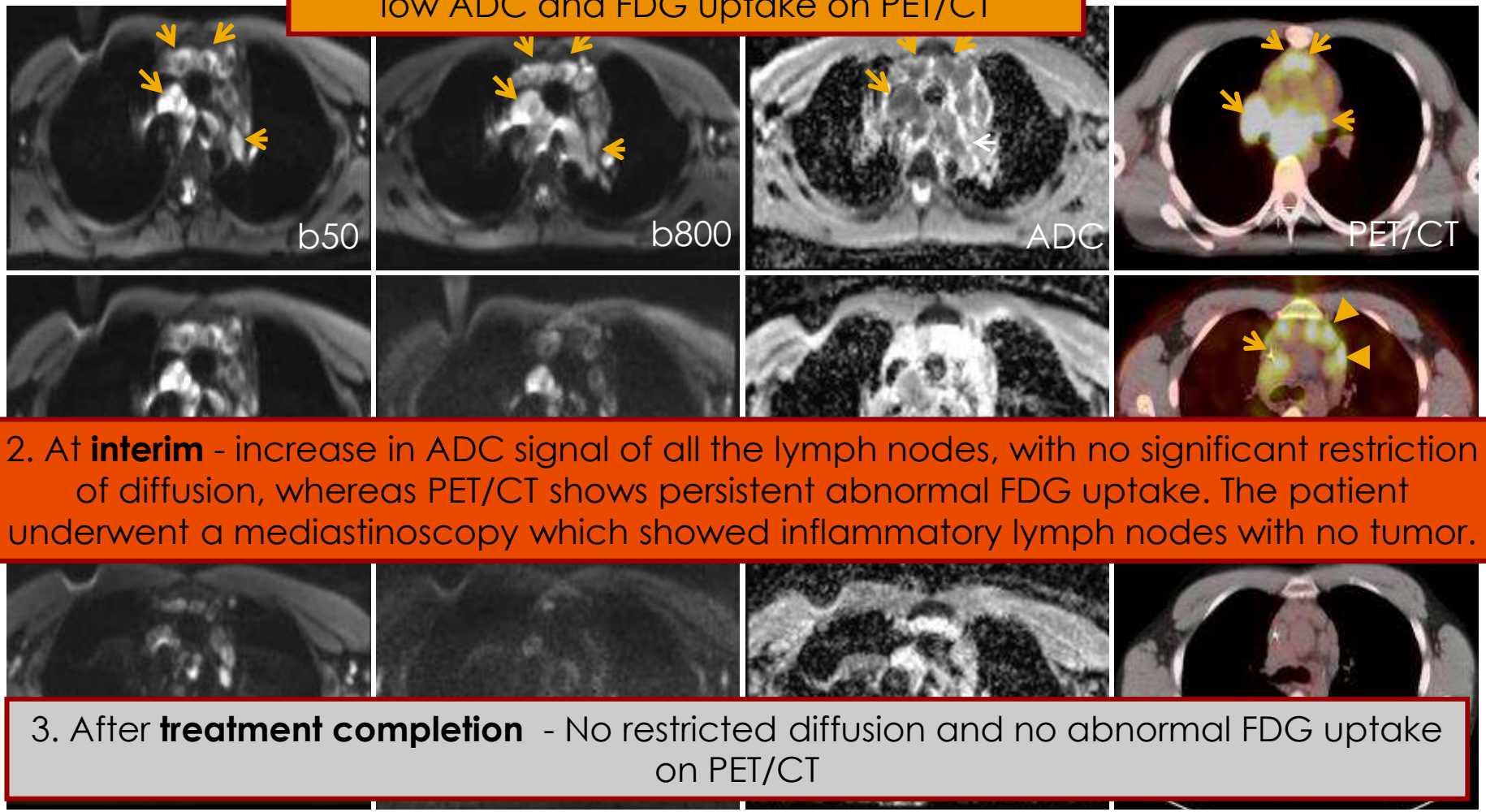
MR before and after 2 cycles treatment was unchanged

- Signal does not change from b 50 to b 800
- ADC is restricted compared to muscle at 0.6

Response to treatment - discordances

1. **Baseline** - Mediastinal lymph nodes with low ADC and FDG uptake on PET/CT

34 y/o HL stage 2 . 3T



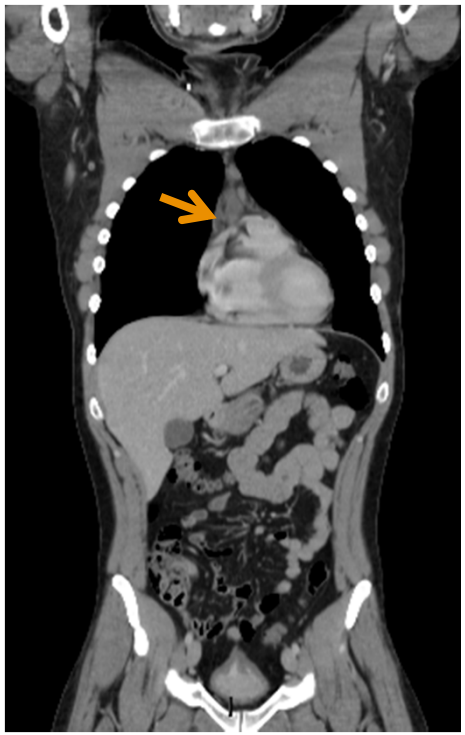
2. At **interim** - increase in ADC signal of all the lymph nodes, with no significant restriction of diffusion, whereas PET/CT shows persistent abnormal FDG uptake. The patient underwent a mediastinoscopy which showed inflammatory lymph nodes with no tumor.

3. After **treatment completion** - No restricted diffusion and no abnormal FDG uptake on PET/CT

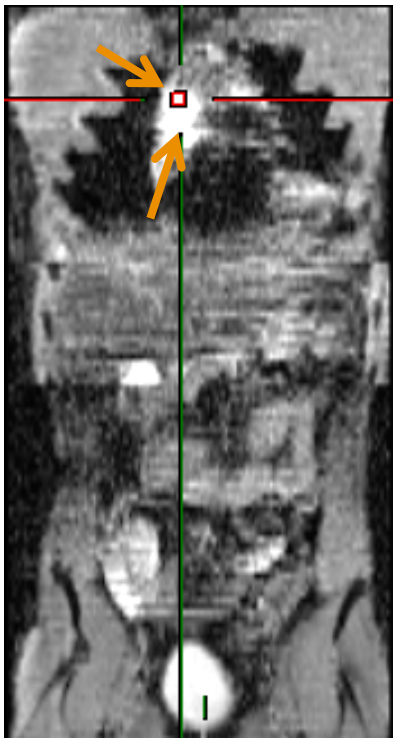
Response to treatment - discordances

- 25 y/o HL. 3T
- End of treatment, 6 cycles BEACOPP
- Residual mediastinal enlarged node
- No FDG uptake
- High ADC
- CT follow-up

PET



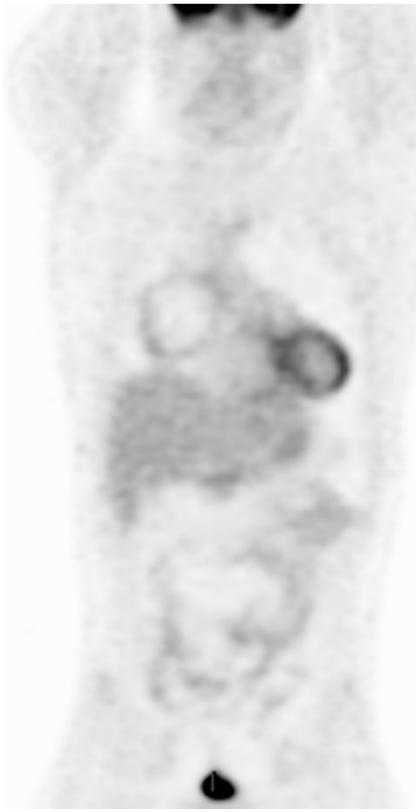
Post-contrast-CT



ADC

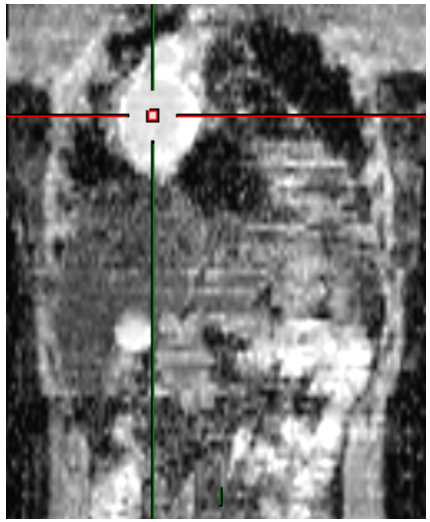
Response to treatment - discordances

- 3-months later, mass increased
- On CT, low attenuation mass
- Increased FDG peripheral uptake, SUV 2.2 Deauville 2/3
- High ADC in the center but low/intermediate ADC at the periphery

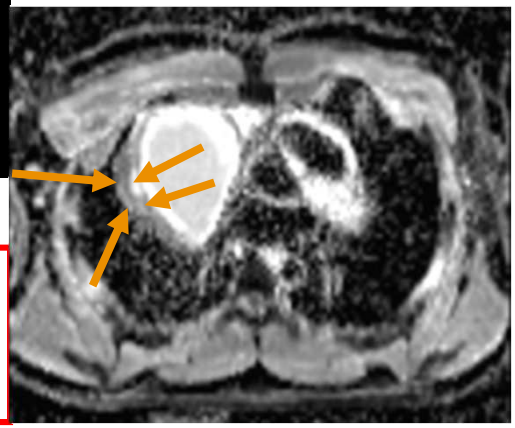


PET

Post-contrast-CT

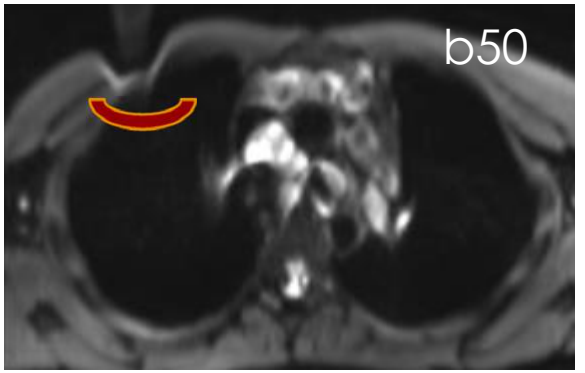


ADC

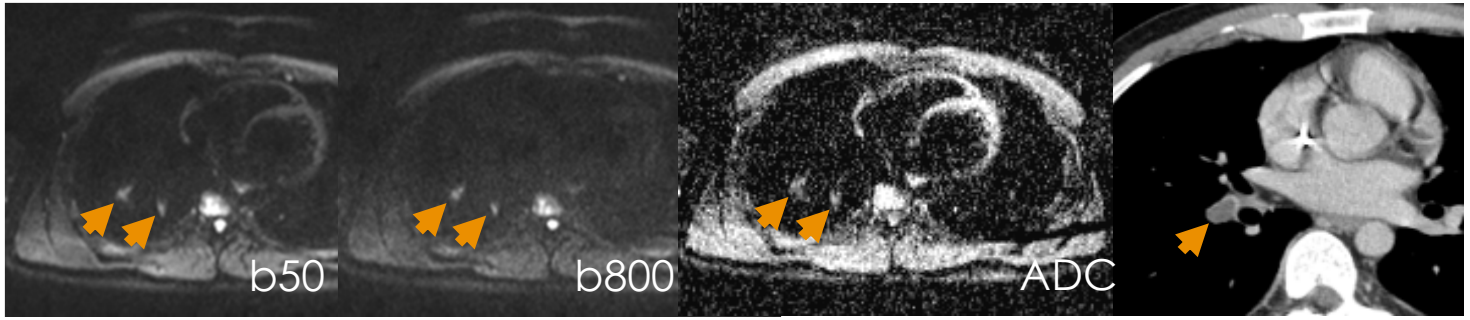


Sugery → fibrosis,
no tumoral cell

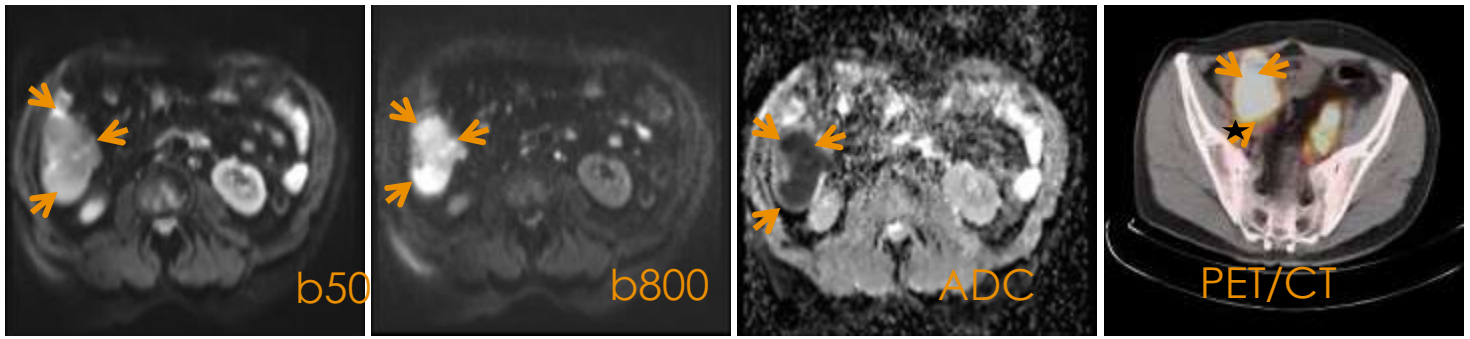
Artifacts and pitfalls – patient related



- Metal artifact
- Pulmonary embolism mimicking lung nodules

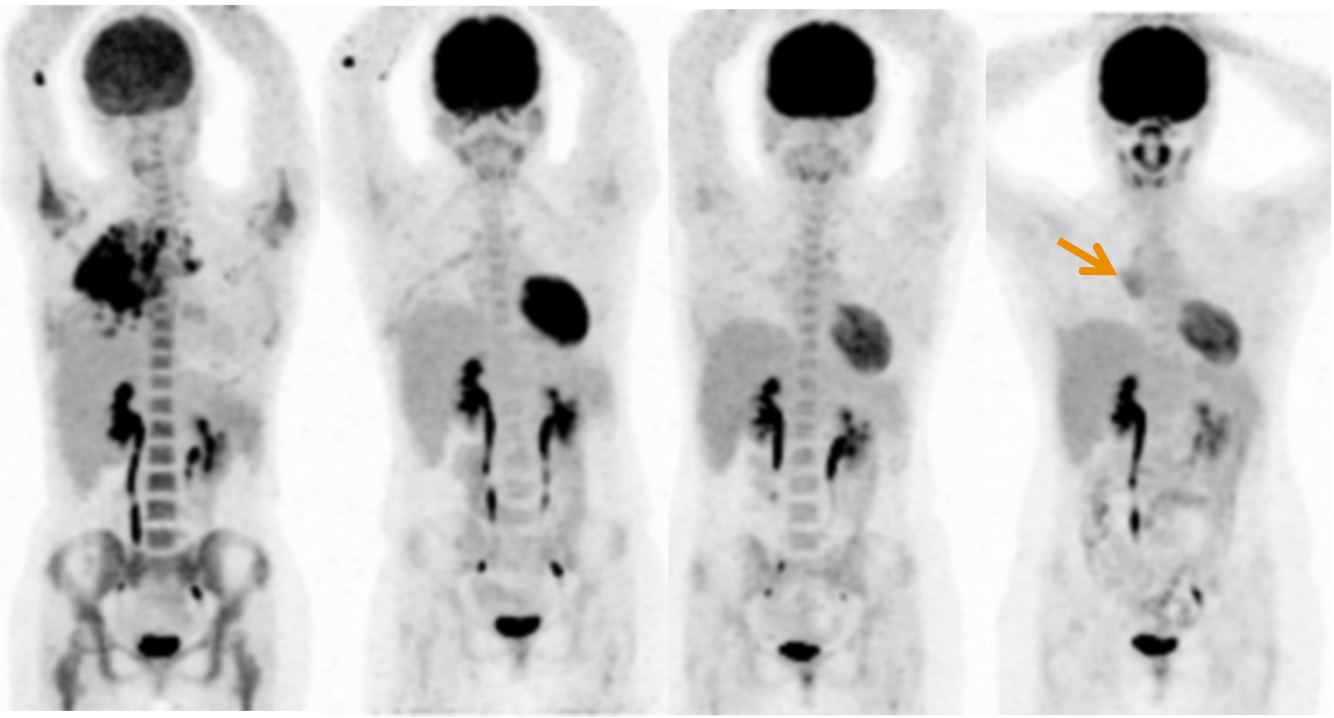


- 55 y/o, DLBCL. Right colic mass appearing in different positions on MRI and PET/CT, due to bowel movement



Pitfalls

- 28 y/o DLBCL stage IV
- At the end of the treatment, complete remission Deauville 2; no significant FDG uptake
- On CT follow-up, after 3 months, increased focal mediastinal mass: relapse?



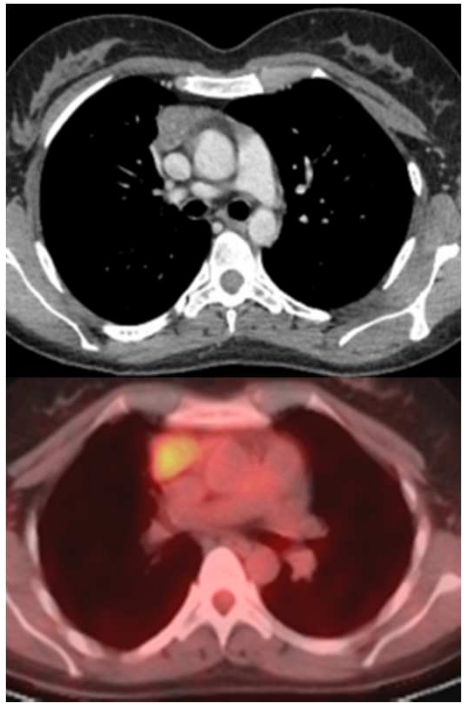
PET at staging SUV11

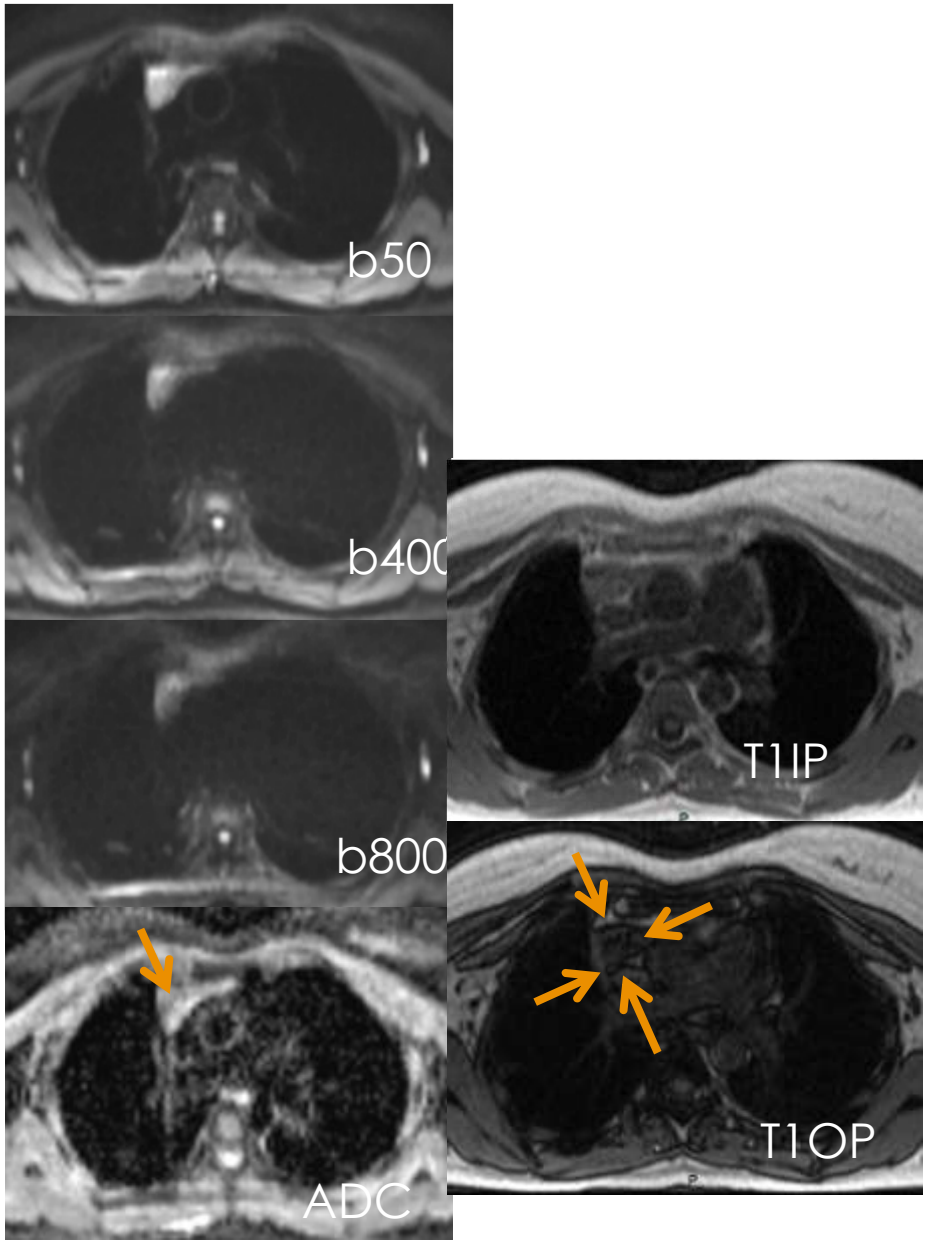
4 cycles SUV 1.8

End of treatment SUV1.7

Follow-up at 3 months SUV 3.5

Pitfalls

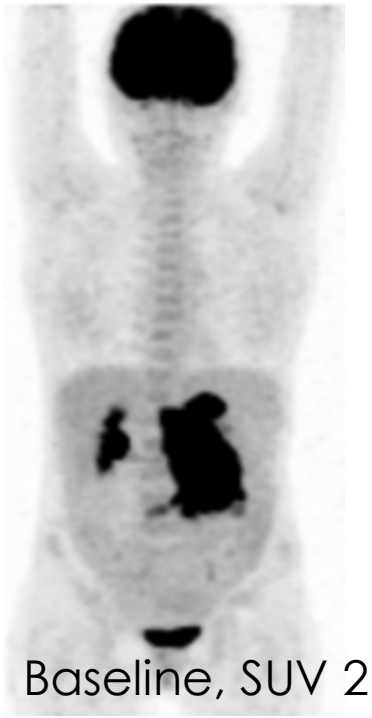




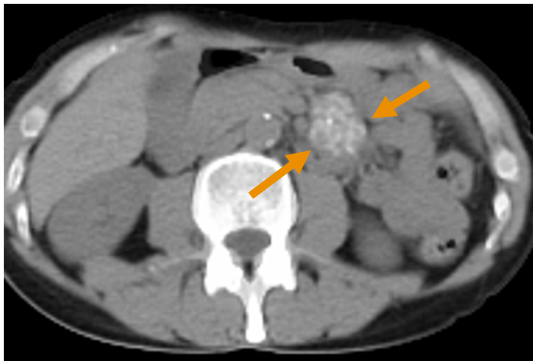
- ADC is high
- Comparison of T1-w in phase and T1-w out of phase images demonstrates the presence of fat: Thymic rebound

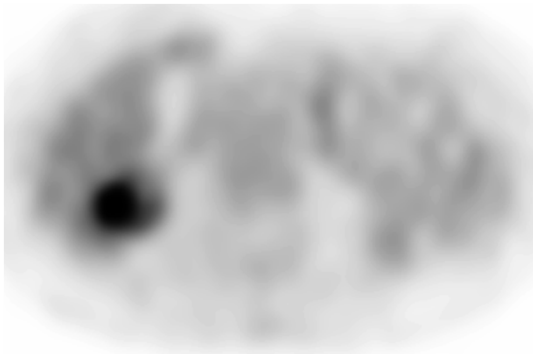
Pitfalls, calcium

- 49 y/o. DLBCL, stage IV in CR after treatment.
- Low signal of the mesenteric mass due to calcifications

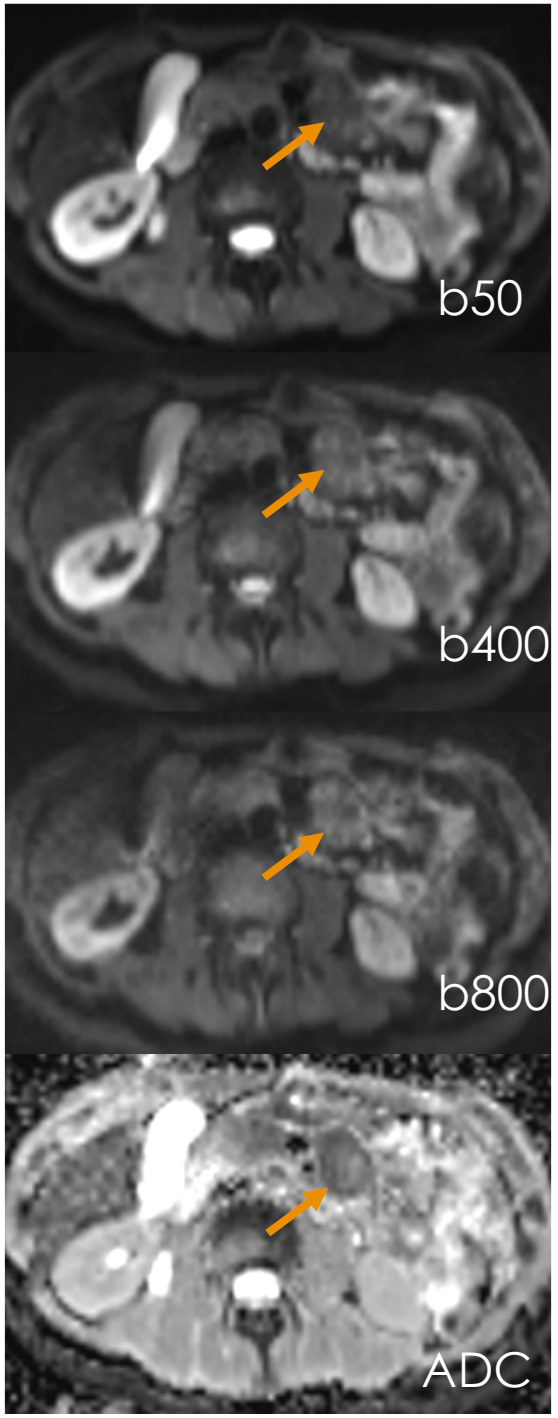


Baseline, SUV 21





End of treatment, SUV 2



Conclusion 1

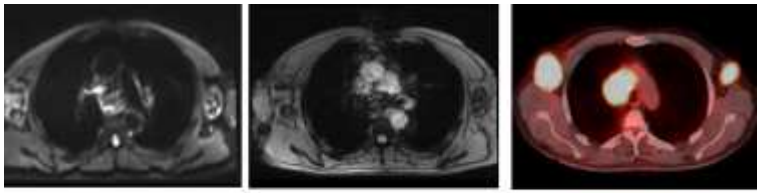
- WB DWI MR imaging is a good technique for lesion detection comparable to PET-CT at staging
- Potential interesting technique for response assessement but small series

- Limitations due to patient: motion-calcified masses
- Limitations due to technical problems: homogeneity of B0 and B1 especially for air-tissue interfaces: nodes-lung nodules

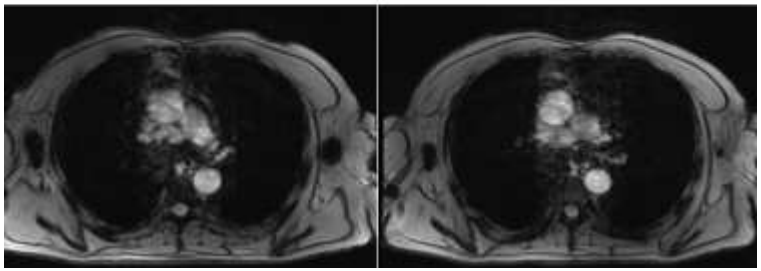
What's new? iron

- Some authors have described low signal of lymphoma lesions on DWI in some patients before treatment
- Our preliminary results of complementary T2* GRE sequences showed that MR was able to detect Iron deposits in some lymphoma lesions (no calcium on CT); See Cottereau AS poster
- Dumont AE, Ford RJ, Becker FF: Siderosis of lymph nodes patients with Hodgkin's disease. *Cancer* 1976

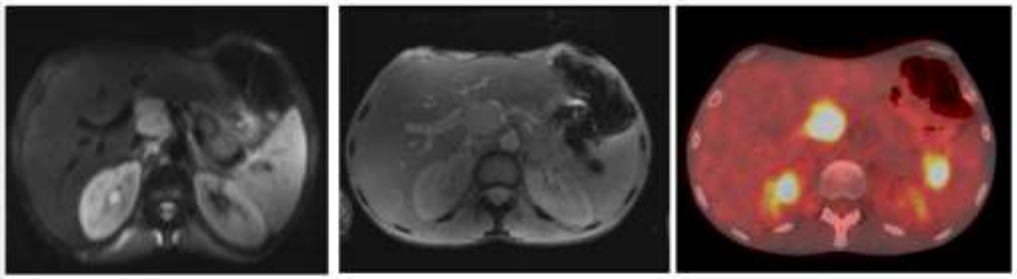
Baseline



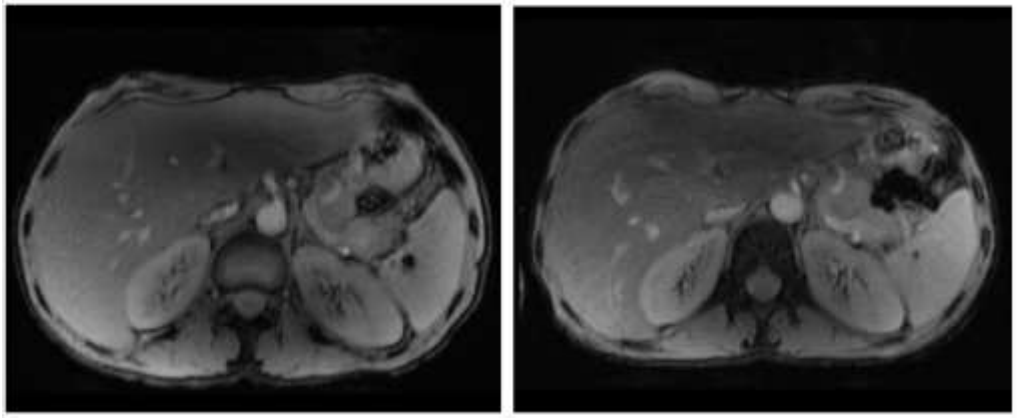
2 Cycles and End treatment



What's new?



Baseline

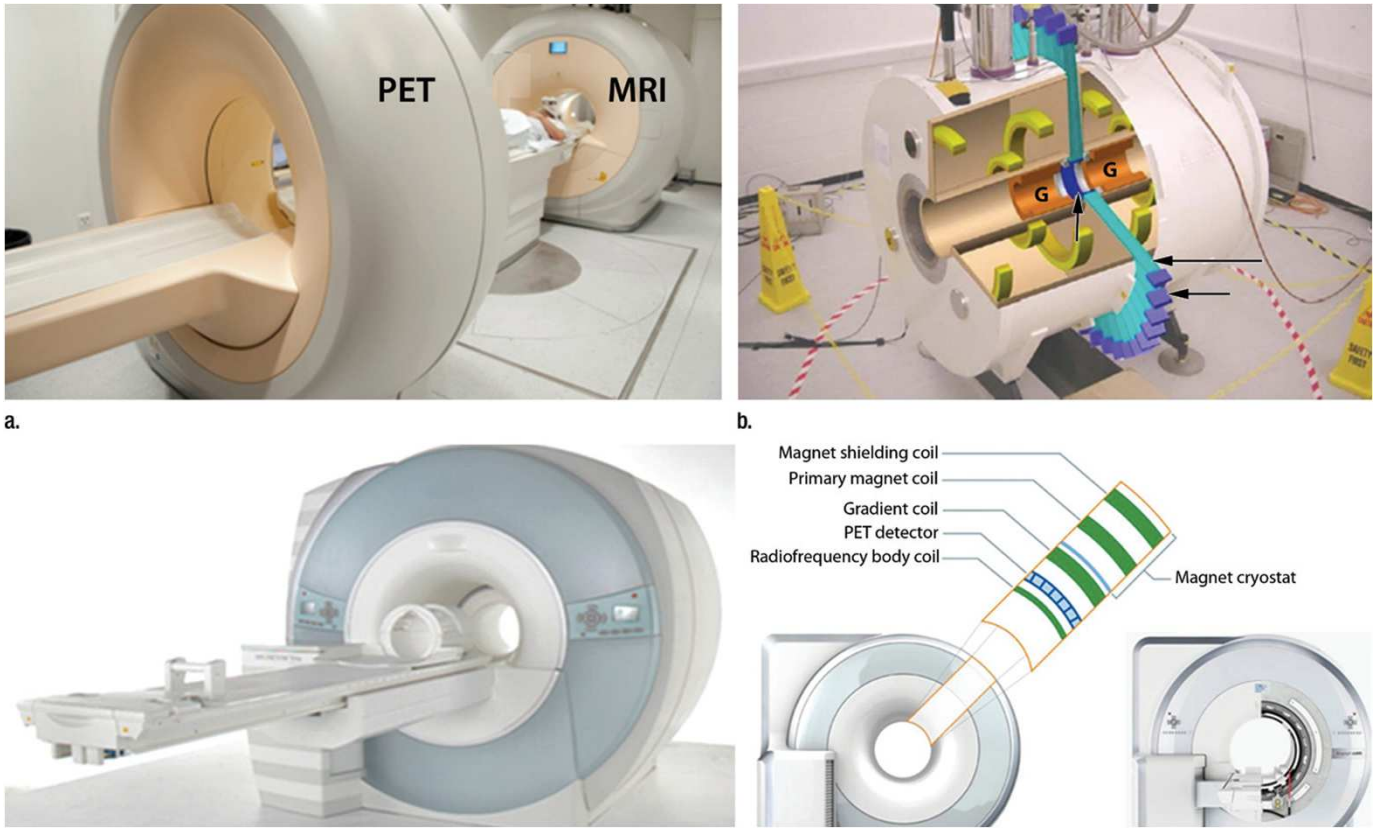


2 Cycles and End treatment

What's new? Iron

- Relationship:
  - To HL ++ and DLBCL+
  - To FDG uptake (all cases)
  - To inflammatory syndrom
- On the prediction of HL treatment response. EJ de Andreas-Galiana et al. Clin Transl Oncol 2015.
  No imaging studies; « Serum ferritin turned to be the most discrimatory variable in predicting treatment response »

What's new? Simultaneous PET-MR



PET/MR vs PET/CT

- Afaq A et al. Clin Nucl Med 2016: comparison of PET/MR and PET/CT in 66 patients with HL and NHL presenting 95 nodal and 8 extranodal lesions.
  - Additional 3 nodal and 1 extra nodal sites on PET/MRI
  - Negative correlation of ADC and SUVmax ?

- Ponisio MR et al. Pediatr Radiol 2016: 9 PET/MRI in 8 children undergoing PET/CT. « PET/MRI performance is comparable to PET/CT for lesion detection and SUV measurements »

Conclusion on WB-DWI MRI

- Morphological and functional information at a Whole body scale allowing for lesion detection and response assessment
- Can be Fast (<30mn), Routine, and Reliable but limitations exist : respiratory artifacts, calcium overload, magnetic susceptibility artifacts…
- Although WB-DWI seems appropriate for lymphoma, its role is not defined: studies with larger cohort required

Un grand merci

- Dr Chieh LIN, Taipei, Taiwan
- Pr Alain LUCIANI, Dr MULE Sébastien, Dr Frederic PIGNEUR, Dr Sarah TOLEDANO, Medical Imaging Department
- Pierre ZERBIB, Chief MRI Technologist
- Dr COTTEREAU Anne-Ségolène, Pr Emmanull ITTI, Pr Michel MEIGNAN, Nuclear Medicine
- Pr Corinne HAIOUN, MD, PhD, Dr Karim BELHADJ, Hematology
- Alexandre VIGNAUD, PhD, CEA, Neurospin, Saclay, France