Joint Symposium ESMO-EANM: Impact of molecular imaging on management of lymphoma

Potential and pitfalls in PET-imaging of lymphoma

Luca Ceriani

Nuclear Medicine and PET-CT Centre
Oncology Institute of Southern Switzerland – Bellinzona (CH)

luca.ceriani@eoc.ch

Disclosure slide

- I declare no conflict of interest.

Fields of further development

- PET Technology
- New techniques of hybrid imaging
- New metabolic biomarkers
- Radiotracers
- PET «culture»

Evolution of the PET technology

2000 → **2014**

CT attenuation correction

Iterative protocols

Lutetium oxyortho-silicate (LSO)

Ultra-fast detector electronics (3D)

Time-of-flight (TOF)

Resolution recovery (PFS)

Increase of axial FOV

Continuous motion of the cradle

Sensitivity
Resolution
Image Quality

PET-imaging potential in lymphoma

Technological developments improved the diagnostic accuracy

↑ **sensitivity:** ↑ detection rate of lesions with low uptake
i.e. in FDG non-avid lymphoma

↓ radioactivity injected
(reduction of effective dose ~ 25%)

↓ time of PET images acquisition (15-20 min.)

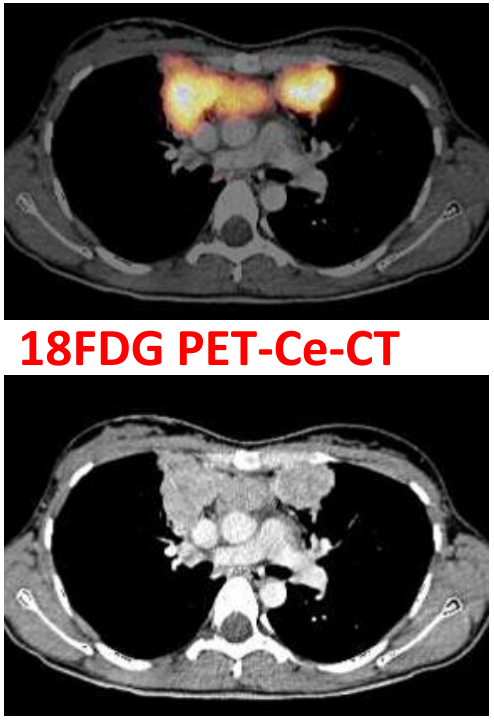
↑ **resolution:** ↑ detection rate of smaller lesions (4-5 mm)

↑ accuracy of measurement (quantification)

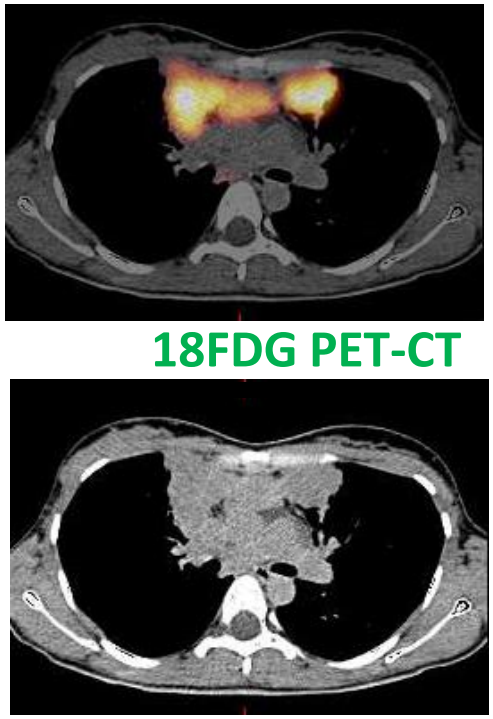
New techniques of hybrid imaging

- **PET- CT** **(low dose)**
- **PET- CeCT** **(contrast enhanced – full dose)**
- **PET- MRI**

New techniques of hybrid imaging: **PET-CeCT**



18FDG PET-Ce-CT



18FDG PET-CT

More anatomical details
More precision in measurement
No impact on PET findings.

Higher exposure to radiations

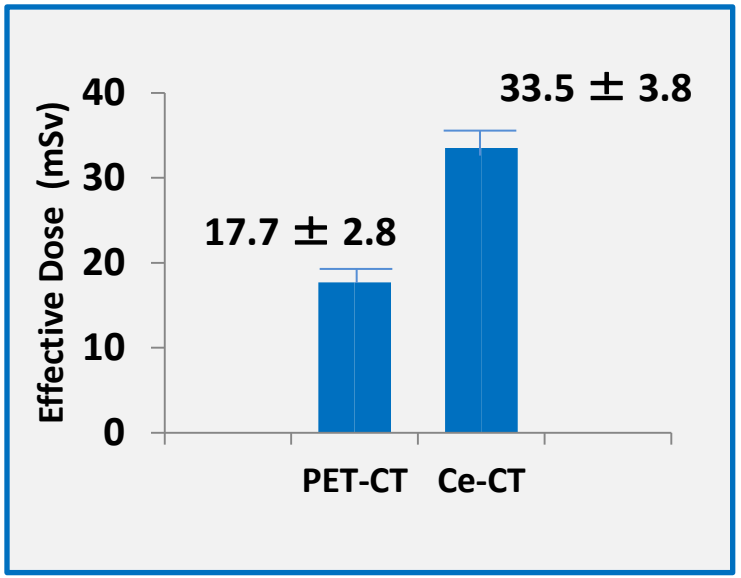
PET-CT (low dose) 10-15 mSv
PET-CeCT (full dose) 25-30 mSv

PET-imaging potential in lymphoma

Clinical impact of CeCT combined with low-dose 18F-FDG PET-CT on routine lymphoma management.

N=237

- **No CeCT impact** **219 (92%)**
- **clear CeCT impact** **7 (3%)**
  (upstaging in 2, DVT detection in 5)
- **debatable CeCT impact** **11 (5%)**
  (additional investigations with no treatment change in 10)



Chalave J et al. Leuk Lymphoma 2014

PET-imaging potential in lymphoma

Can full-dose Contrast-enhanced CT be omitted from an FDG-PET/CT staging examination in newly FDG-avid lymphoma?

N=29

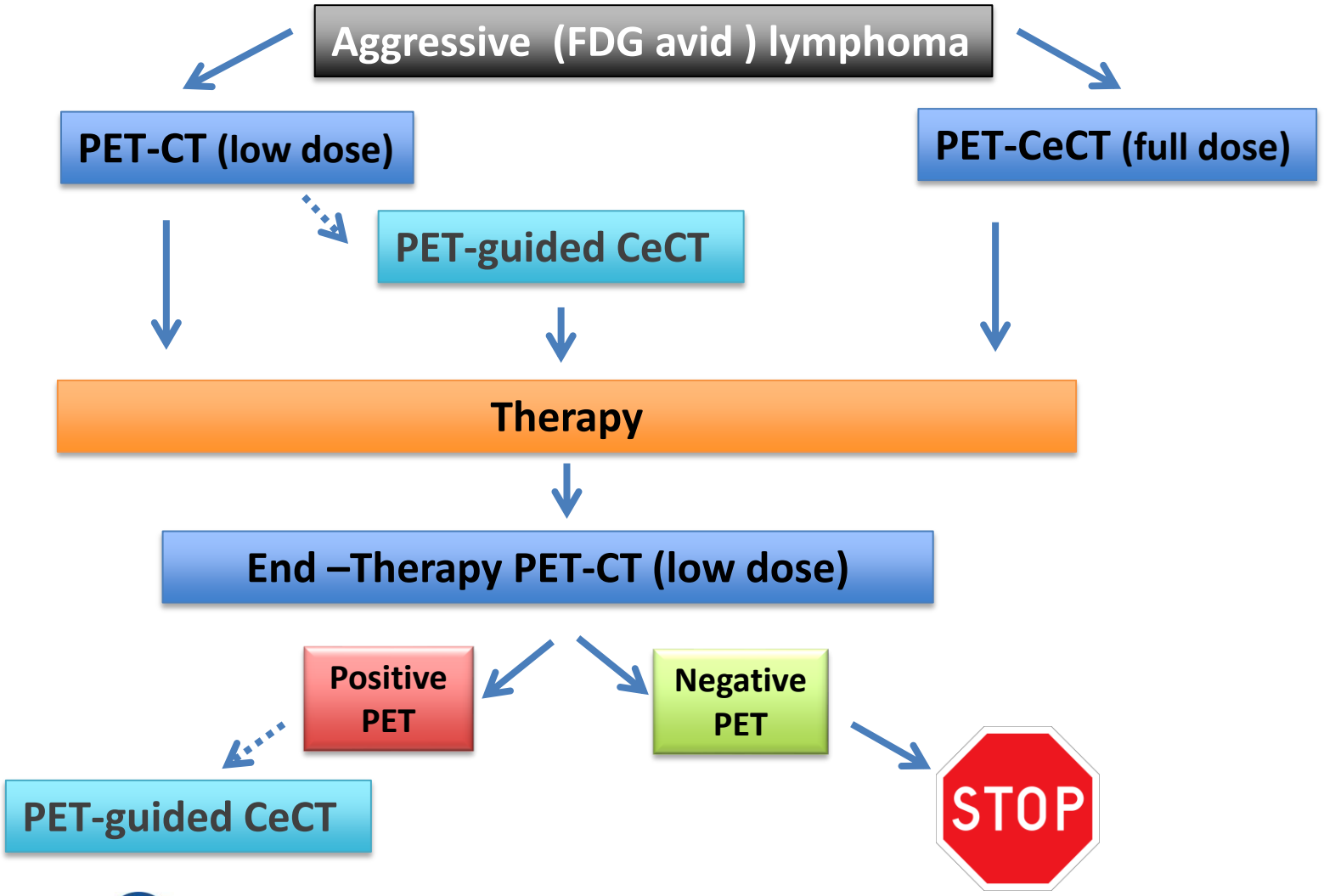
- **No CeCT impact** **27 (93%)**
- **upstaging** **2 (7%)**

Authors' conclusions

unenhanced low-dose FDG-PET/CT should be the modality of choice at least in younger patients and in those at increased risk of CT contrast-induced allergic reactions or nephropathy

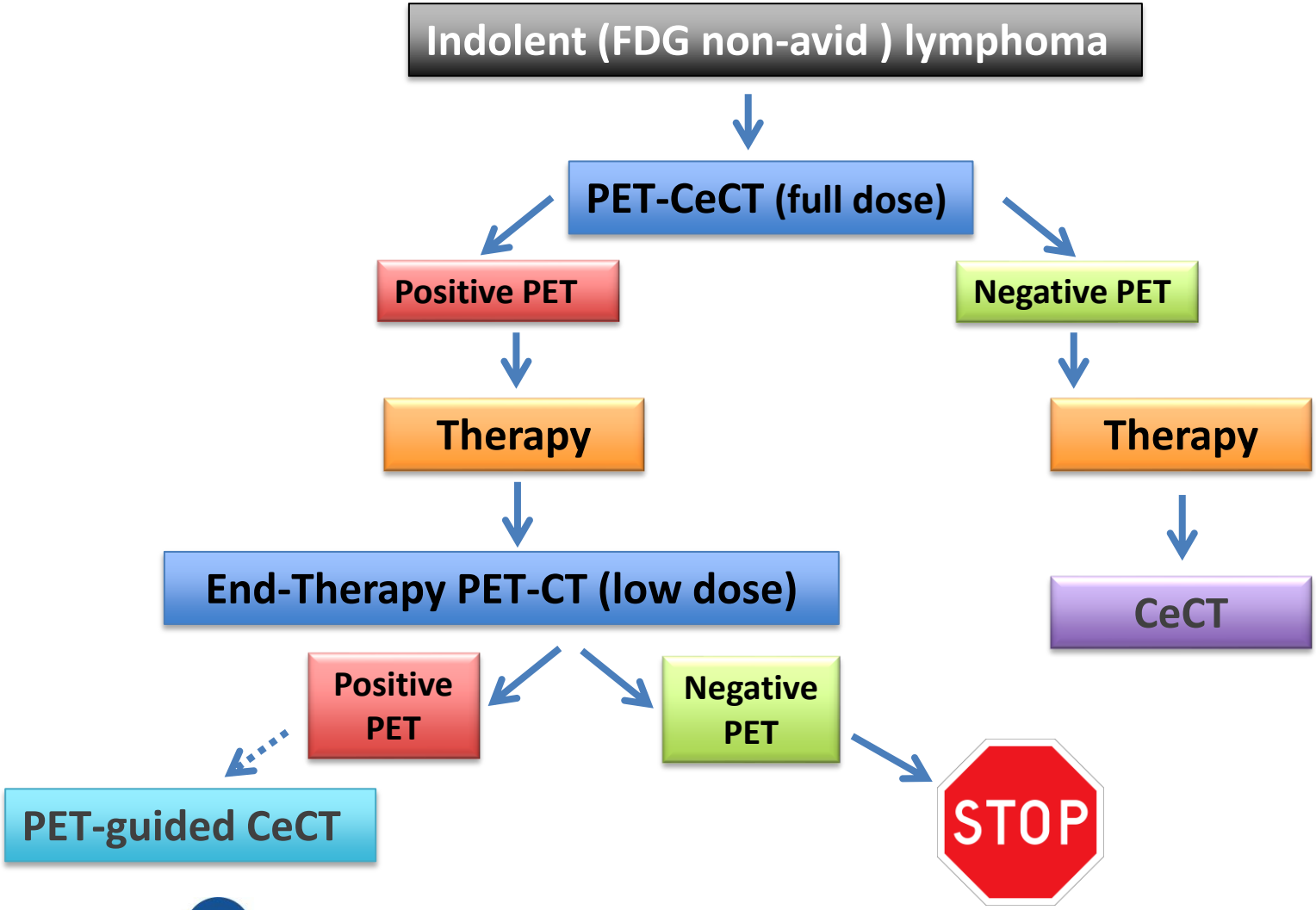
Van *Hamersvelt* HP et al. J Comput Assist Tomogr 2014

PET-imaging potential in lymphoma

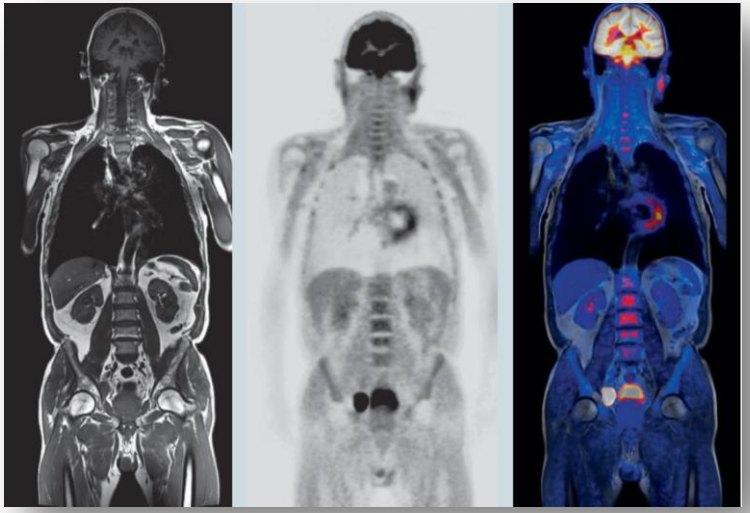


Modified from *Kostakoglu L. et al. EJNMMI 2014*

PET-imaging potential in lymphoma



New techniques of hybrid imaging : **PET- MRI**



Work in progress -
No clinical role today.
Complementary to PET-CT

Potential advantages

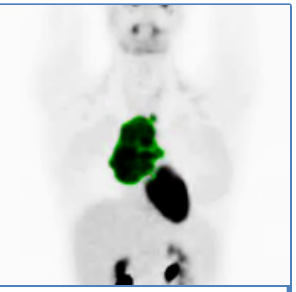
- **Reduction of Exposure to radiations**
- **Complementary/superior diagnostic value of MRI compared to CT**
- **Indications : bone marrow, soft tissues, spleen, liver.**

Open problems

- **Attenuation correction**
- **MR-specific diagnostic limitations**
- **Workflow**
- **Design of suitable imaging protocols**

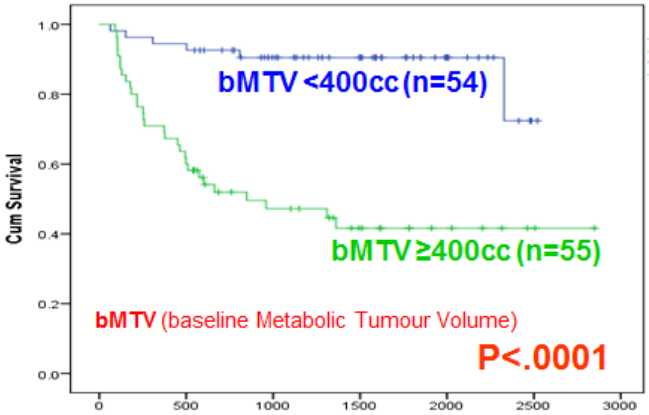
New metabolic biomarkers

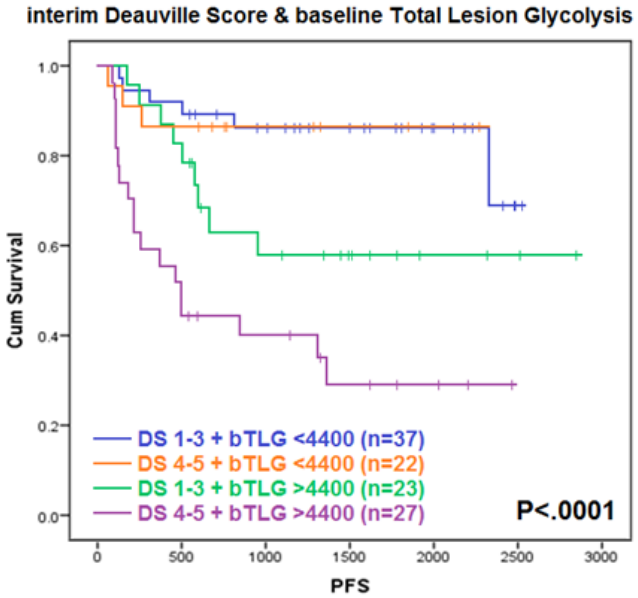
- **MTV : metabolic tumor volume**
  (Tumor burden)



- **TLG : total lesion glycolysis**
  (morpho-metabolic marker - **MTV x Standard Uptake Value (SUV) mean**)
  (metabolic burden)

Prognostic role of metabolic PET biomarkers in DLBCL

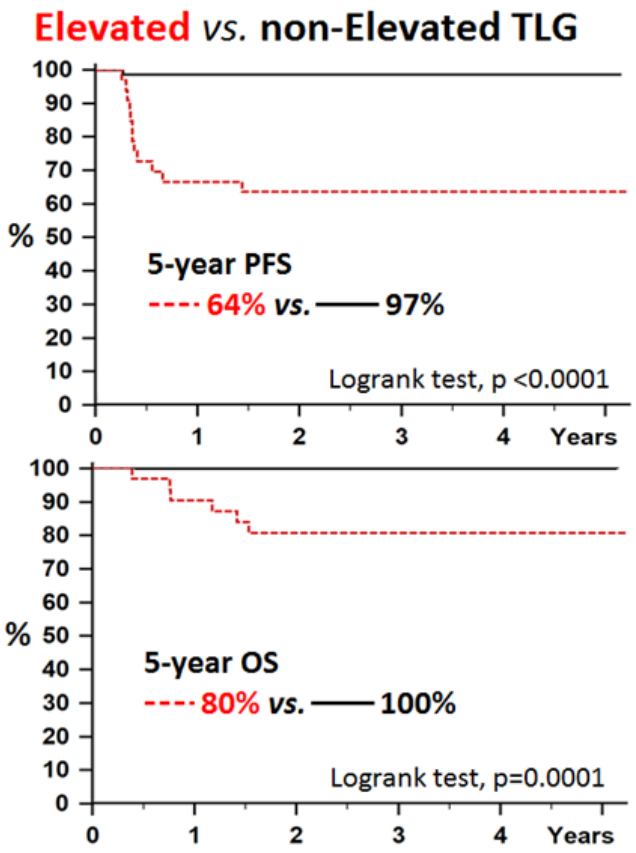




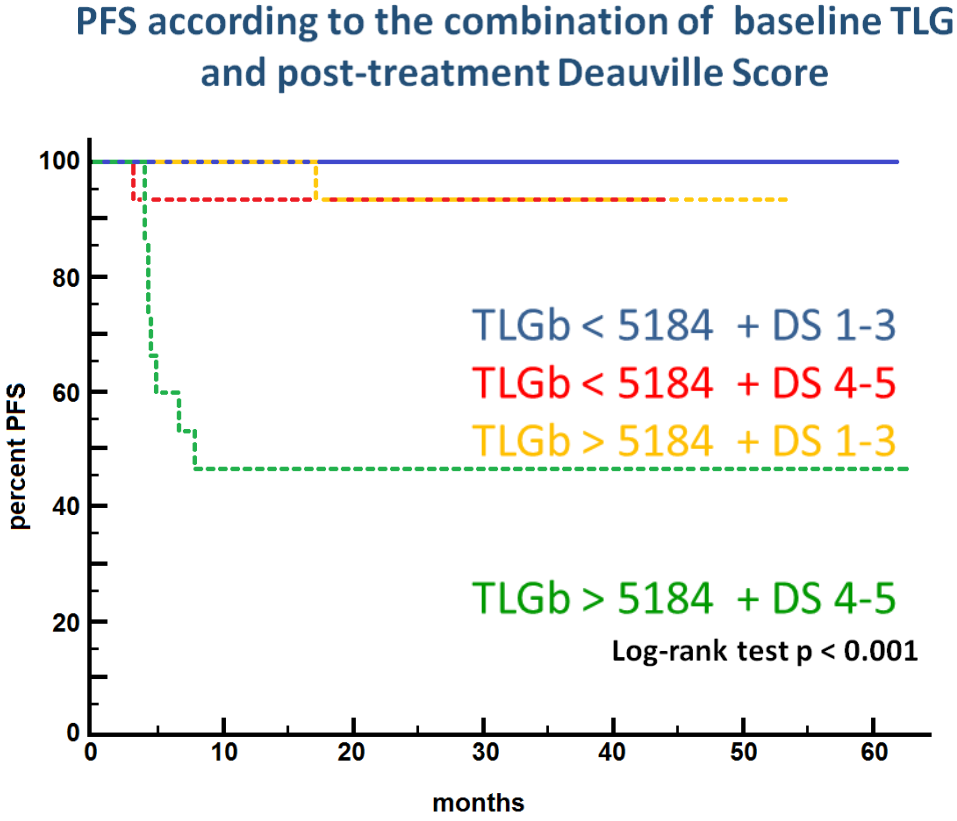
- Baseline MTV and TLG strongly predictive of prognosis but on multivariate analysis only Deauville score after 2 cycles & baseline TLG were significant
- A model combining these 2 parameters can predict a group with significantly low PFS

N.G. Mikhaeel, Hematol Oncol 2013. 31(s 1):100.

Prognostic role of metabolic PET biomarkers in PMLBCL



Ceriani L. et al. Hematol Oncol 2013. 31(s1):187-8



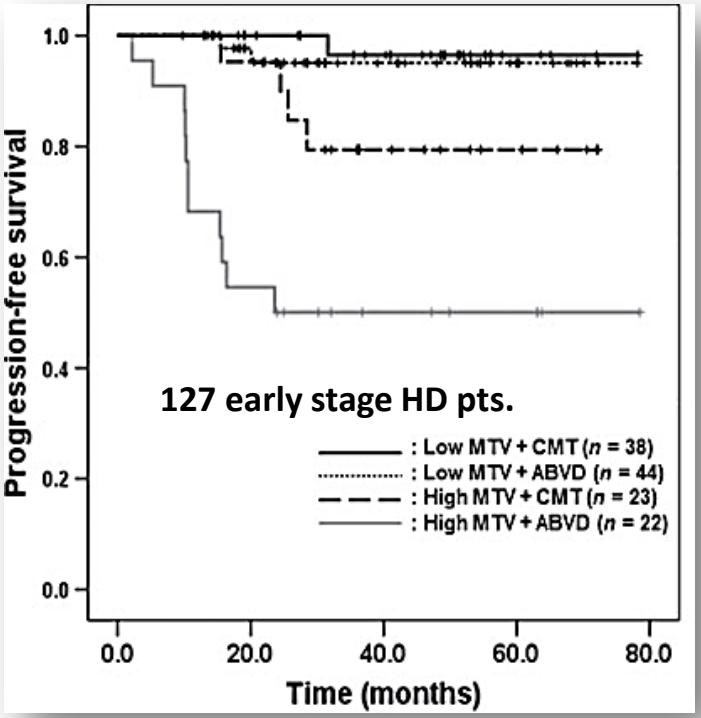
Zucca E. et al. Hematologica. 2014. 9(s1):524-525

Prognostic role of metabolic PET biomarkers in HD

Summary of Cox proportional hazards analysis c

Parameter	PFS *p*-value	OS *p*-value
Pre-treatment PET Metrics		
SUV max	NS	NS
SUV mean	NS	NS
MTV	NS	NS
Interim PET Metrics		
SUVmax	0.01	< 0.01
MTV	NS	NS
iSUV TLG	NS	NS
SUV mean	NS	NS
Calculated PET Metrics		
$MTV_{int/pre}$	0.01	< 0.01
$SUVmean_{int/pre}$	NS	< 0.05
$SUVmax_{int/pre}$	0.02	0.01
$iSUV_{int/pre}$ TLG	0.01	< 0.01

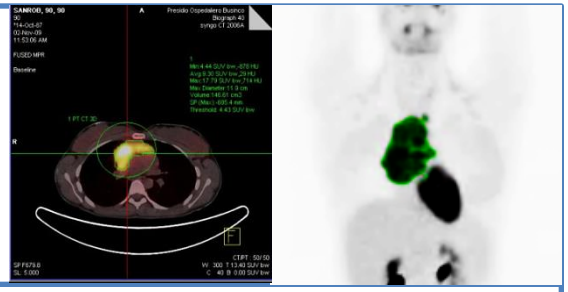
Tseng D et al. *Radiat Oncol. 2012*



Song MK et al. *Cancer Sci. 2013*

New metabolic biomarkers

- **MTV : metabolic tumor volume**
  (Tumor burden)



- **TLG : total lesion glycolysis**
  (morpho-metabolic marker - **MTV x Standard Uptake Value (SUV) mean)**
  (metabolic burden)

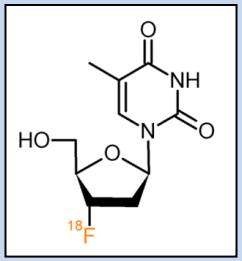
Open problems:

- **Lack of standardization**
- **Time expensive procedure**

New radiotracers

3'-deoxi-3'-18F- fluoro-thymidine (FLT) : marker of proliferative activity.

^{18}FLT uptake < ^{18}FDG in tumor lesions



^{18}FLT

- **Promising probe to determine therapy response and to distinguish between tumors and inflammatory masses**

  FLT uptake not affected by the temporary intralesional rise in the inflammatory cells (lower false positive rate).

- **Predictive marker of response, early during the treatment**
- **Prognostic marker baseline**

New « cultural» approaches

- **Common language and standard criteria**
- **Collect data (metanalysis and multicentre trials)**
- **Share experiences**

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

J Clin Oncol 32. © 2014

Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification

Bruce D. Cheson, Richard I. Fisher, Sally F. Barrington, Franco Cavalli, Lawrence H. Schwartz, Emanuele Zucca, and T. Andrew Lister

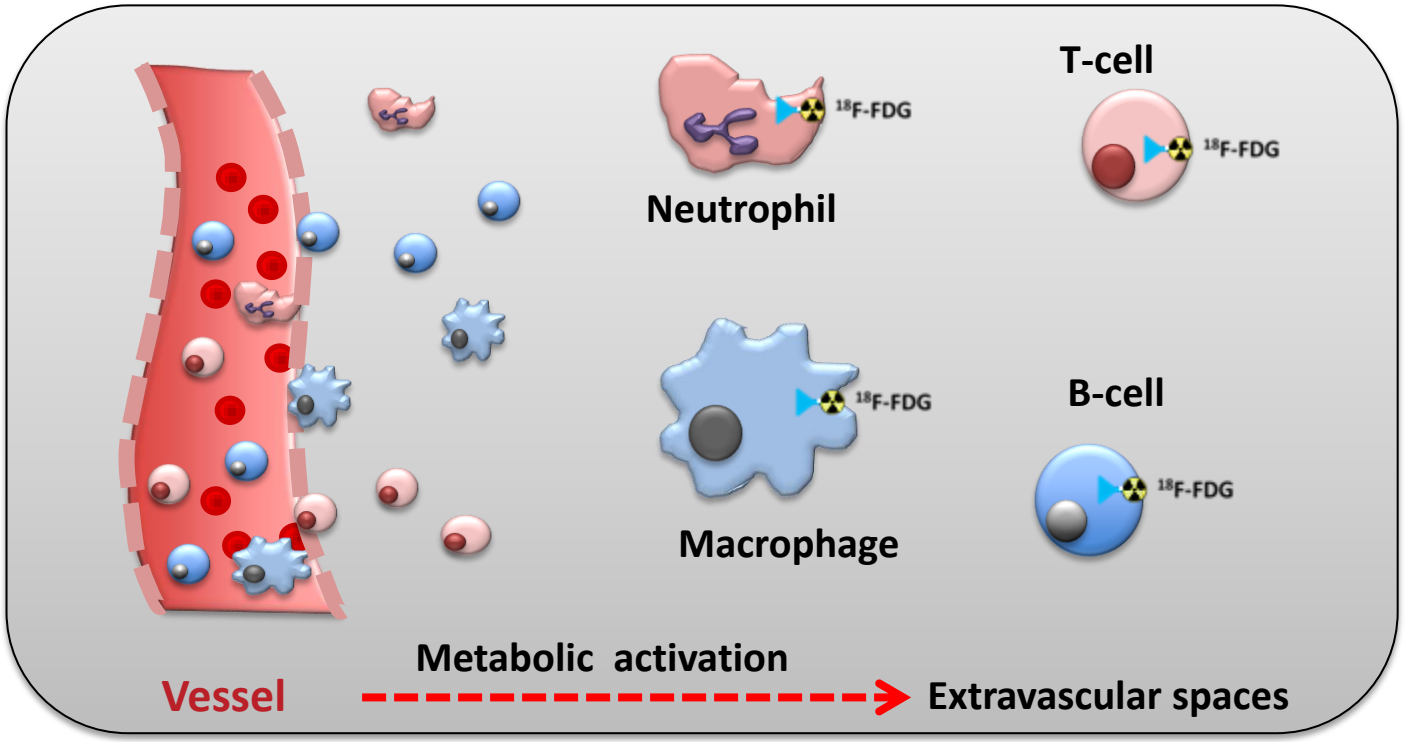
Role of Imaging in the Staging and Response Assessment of Lymphoma: Consensus of the International Conference on Malignant Lymphomas Imaging Working Group

Sally F. Barrington, N. George Mikhaeel, Lale Kostakoglu, Michel Meignan, Martin Hutchings, Stefan P. Müeller, Lawrence H. Schwartz, Emanuele Zucca, Richard I. Fisher, Judith Trotman, Otto S. Hoekstra, Rodney J. Hicks, Michael J. O'Doherty, Roland Hustinx, Alberto Biggi, and Bruce D. Cheson

Common causes of false-positive FDG PET findings

- Inflammation
- Infections

↓ specificity



PET-imaging pitfalls in lymphoma

Inflammation : **- related to the therapy**

intra-lesional (Immuno- /chemo- therapy)
intra and peri-lesional (radiotherapy)
organs (side effects /drug toxicity/ reaction)

- due to cronic inflammatory diseases

i.e. sarcoidosis , tubercolosis..

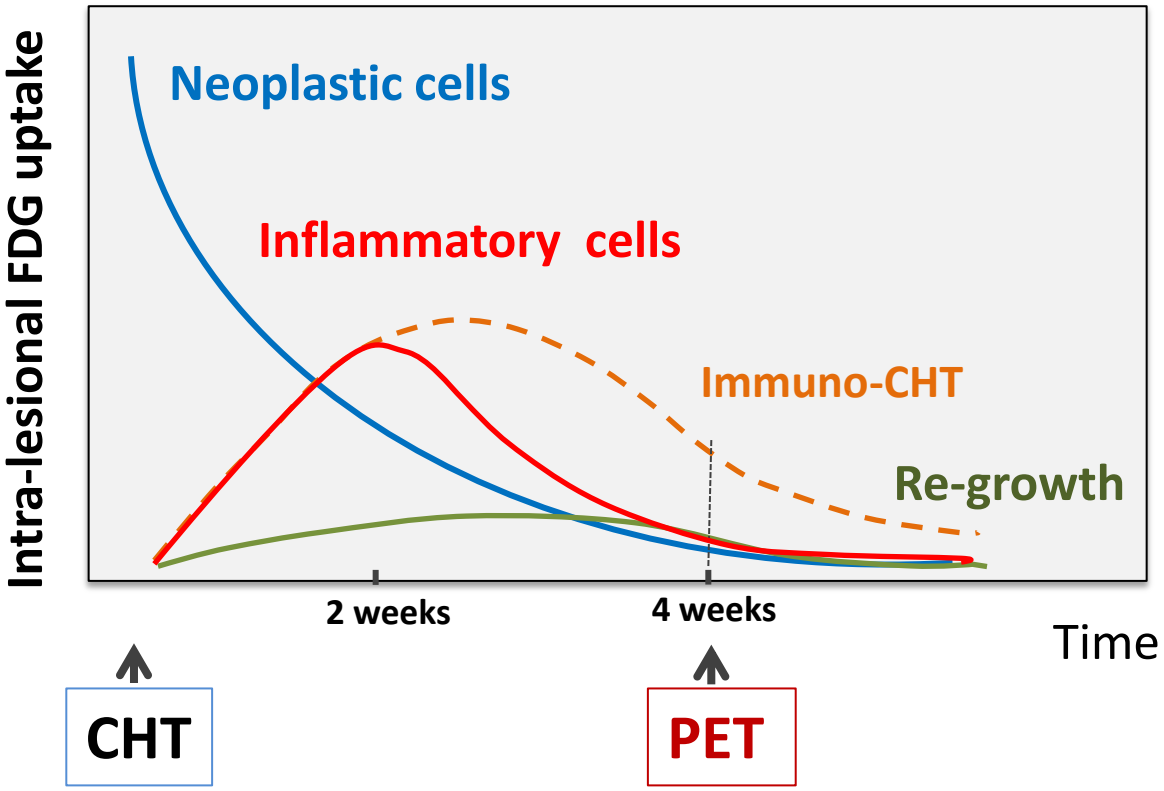
Infections : **- secondary to leucopenia**

(pneumonia, enterocolitis, urinary infections ..)

- relapse of known diseases (HIV+ pts.)

Common causes of false-positive FDG PET findings

Intra-lesional inflammation



PET-imaging pitfalls in lymphoma

High incidence of false-positive PET scans in patients with aggressive non-Hodgkin's lymphoma treated with rituximab-containing regimens.

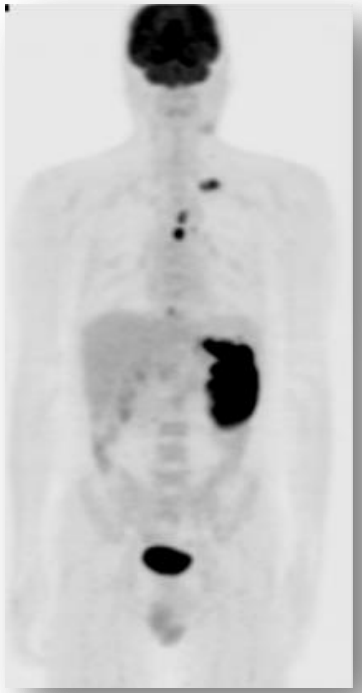
Han H. S. et al. *Annals of Oncology 2009*

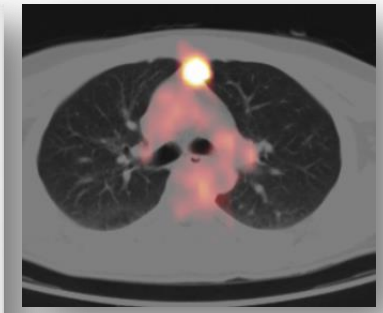
Authors' conclusions

Compared with previous reports in pre-rituximab era, **addition of rituximab resulted in reduced PPV** and sensitivity of mid- and post-therapy PET in pts with aggressive B-cell NHL.

Change of the definition of the metabolic CR:
Deauville Score 3 : residual uptake ≤ liver uptake

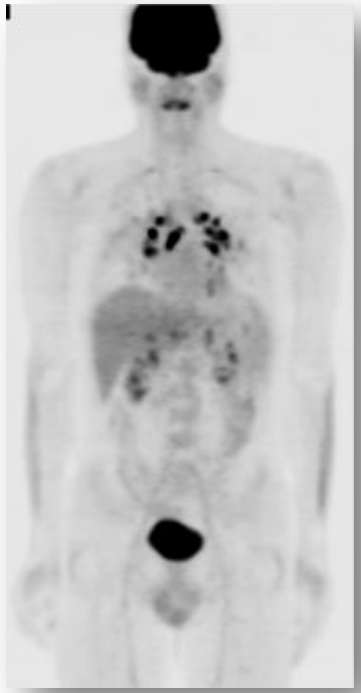
Cronic inflammatory diseases

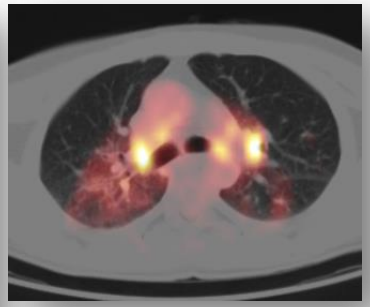




Basal staging

Follicular lymphoma

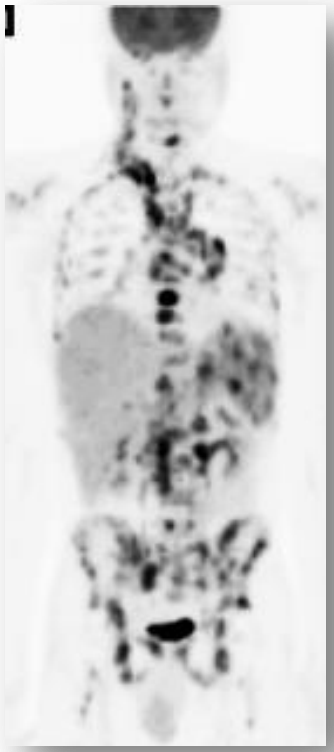




End-treatment

Biopsy : sarcoidosis

PET-imaging pitfalls in lymphoma



^{18}FDG PET-CT

11/2007

HD
HIV +

05/2008

CR

02/2010

Biopsy : follicular hyperplasia
Reactive adenopathy

PET-imaging pitfalls in lymphoma

Differentiation of HIV-associated lymphoma from HIV-associated reactive adenopathy using quantitative FDG PET and symmetry.

Metric	HIV-associated lymphoma (N=19)	HIV-associated reactive adenopathy (N=22)	P value[a]
Single SUL-Max	15.9±6.8	2.9±2.4	<0.0001
TLG			
Mean±SD	2,146.5±2,778.5	30.6±53.8	<0.0001
Median (range)	1,766 (1.97 – 12,660)	1.0 (1.0 – 153.3)	
Single SUL-Peak	12.6±5.7	2.0±2.0	<0.0001
Glycolytic volume/MTV	409.8±611.5	9.6±14.5	<0.0001
Sum SUL-Peak	69.3±54.5	7.2±9.1	<0.0001
Sum SUL-Max	104.3±88.9	16.3±20.2	<0.0001
Summed CT nodal size	104.5±73.5	61.8±48.5	0.06
Single nodal visual score[b], reader 1			
Median (range)	4 (0 – 4)	4 (0 – 4)	0.24
Sum nodal visual score, reader 1			
Median (range)	24 (0 – 60)	11.5 (0 – 66)	0.41
Nasopharyngeal region SUL-Max	3.5±3.2	3.7±2.9	0.54

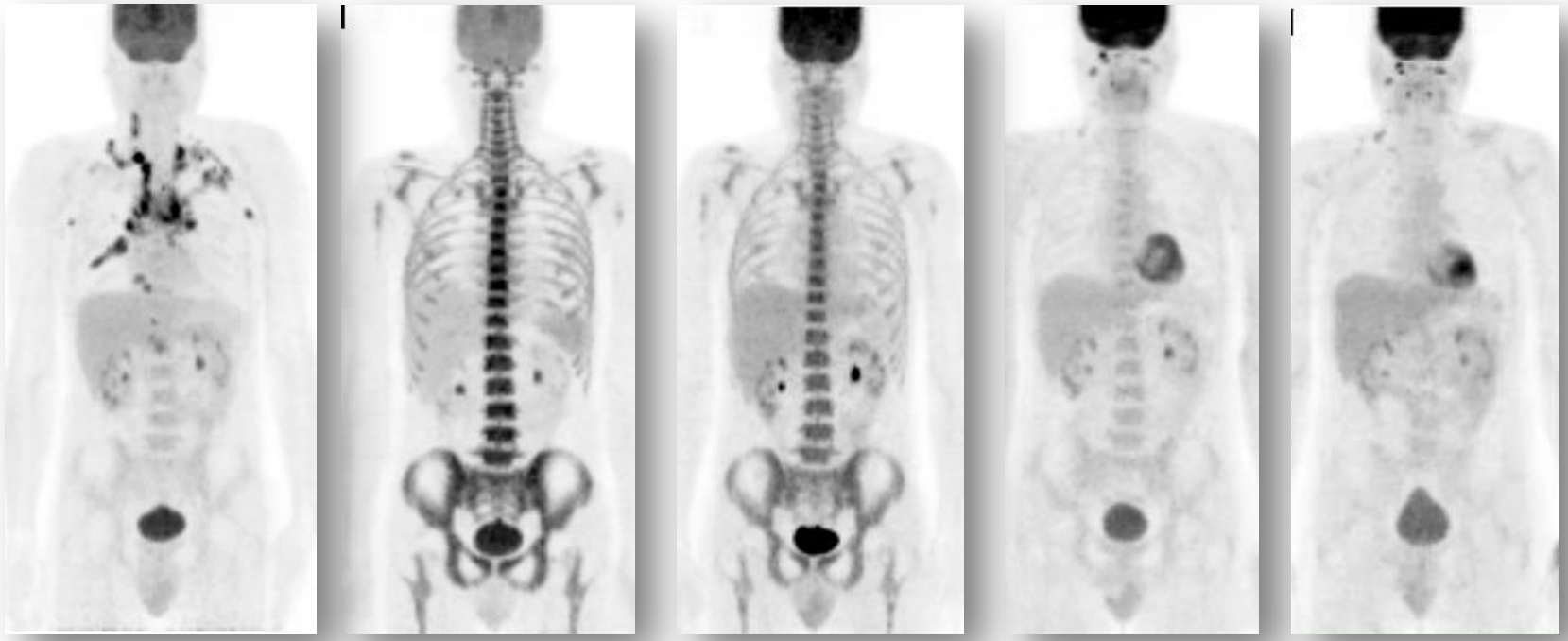
Mhlanga JC et al. EJNMMI 2014

Gold standard : Biopsy or cytologic assessment

PET-imaging pitfalls in lymphoma

DLBCL

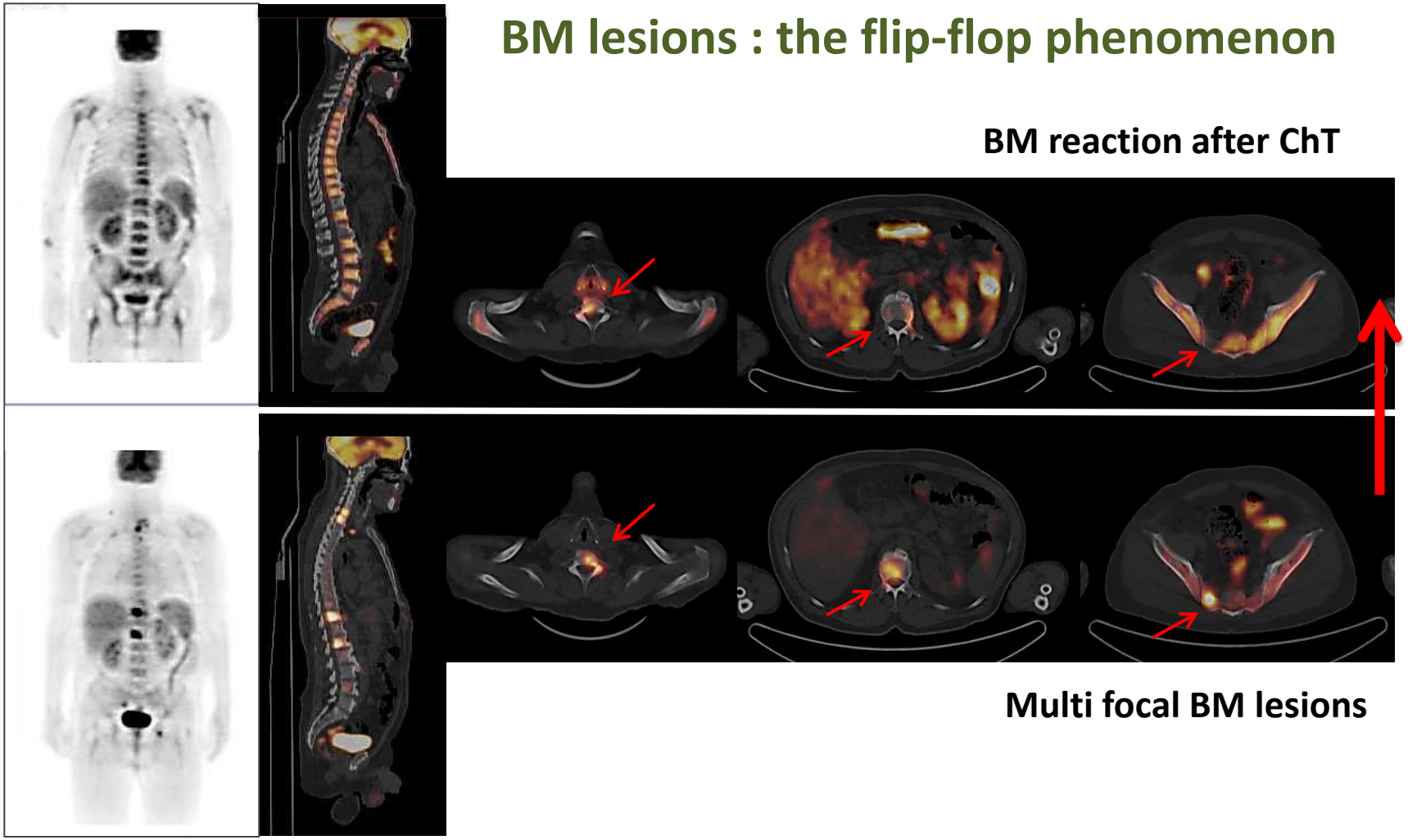
Bone marrow reaction



07/08	09/08	10/08	01/09	04/09
basal staging	after 2nd cycle CHT and G-CSF	after 3dt cycle CHT		

PET-imaging pitfalls in lymphoma

BM lesions : the flip-flop phenomenon



BM reaction after ChT

Multi focal BM lesions

PET-imaging pitfalls in lymphoma

The interpretation of the PET-CT findings can be further optimized by a bidirectional communication between oncologist and nuclear physician.

MADRID 2014 ESMO congress

Thank you

for attention !