# 6th International Workshop on PET in Lymphoma

## Poster discussion

U. Duhrsen – T. Vander Borght

# A10. Is additional contrast-enhanced CT of any benefit to end-of-therapy PET/CT evaluation in follicular lymphoma

Gaetano Paone, Raditchkova-Sarnelli Mariana, Anastasios Stathis, Luca Giovanella, Emanuele Zucca, Luca Ceriani

Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

# Interim $^{18}$F-FDG PET/CT in aggressive lymphoma: assessment of interobserver agreement and impact of baseline PET or CT scan and disease localization

C.N. Burggraaff, A.C. Cornelisse, J.M. Zijlstra, O.S. Hoekstra, H.C.W. de Vet,
P.J. Lugtenburg, F. Celik, J.E. Huijbregts, A.I.J. Arens, B. de Keizer

**On behalf of the HOVON imaging Working Group**

## Aim:

To assess the interobserver agreement of interim $^{18}$F-FDG PET/CT (iPET/CT) using the Deauville 5-point scale (DS) in patients with aggressive lymphoma as a function of the baseline imaging modality ($^{18}$F-FDG PET/CT or CT only) and of the nodal- and extra nodal localizations with residual $^{18}$F-FDG uptake

## Methods:

- iPET/CT scans from HOVON 84 study (randomization: R-CHOP14 vs R2-CHOP14)
- DS 1-3: ‘negative’, DS 4-5: ‘positive’
- 2 reviewers/scan from a pool of 10 nuclear medicine physicians
- Statistics: Positive Agreement (PA)*  and Cohen’s Kappa

Poster A2

* Definition PA: given one reviewer scores positive, the probability that another reviewer scores positive as well.(de Vet et al. BMJ 2013).

## Results:

| | PA (%) | NA (%) | Kappa |
|---|---|---|---|
| **All iPET/CT scans (n=501)** | 73.0 | 92.0 | 0.65 |
| **Baseline CT (n=123)** | 60.9 | 91.0 | 0.52 |
| **Baseline PET/CT (n=378)** | 76.1 | 92.3 | 0.68 |

| | | Observer A | | |
|---|---|---|---|---|
| | | **DS 1-3** | **DS 4-5** | **Total scans** |
| **Observer B** | **DS 1-3** | 355 | 30 | 385 |
| | **DS 4-5** | 32 | 84 | 116 |
| | **Total scans** | 387 | 114 | 501 |

**Calculation NA & PA for main outcome:**

- NA= 92.0 %
- PA = 73.0 %

NA: 2x 355 / (2x355 + 30 + 32) *100% = 92.0 %

PA: 2x 84 / (2x84 + 30 + 32) *100% = 73.0 %

## Conclusion:

- Availability of a baseline $^{18}$F-FDG PET/CT seems to give a better interobserver agreement of iPET, although not statistically significant
- Despite reasonable kappas, the relatively low PA indicates that observer agreement needs to be improved before iPET can be used in treatment escalation trials in DLBCL patients

Poster A2

# Visual illusion

Michel Meignan©

# A quantitative approach to the interpretation of interim and final FDG-PET studies in Diffuse Large B Cell Lymphoma.

**Amanda Rotger [1], Montserrat Cortés [2], Xavier Setoain [3], Marc Simó [4], Ana Cristina Hernández [5], Pilar Sarandeses [5], Eva González-Balça [6], Dolores Caballero [7], Carlos García [5], Mónica Coronado [8].**

*[1] Hospital General Universitario Gregorio Marañón, [2] IDI PET-TAC Hospital de Bellvitge,[3] Hospital Clínic Barcelona,[4] Hospital Universitari Vall d´Hebron, [5]Hospital Universitario 12 de Octubre, [6] Hospital Duran i Reynals, [7]Hospital Universitario de Salamanca, [8] Hospital Universitario La Paz.*

**On behalf of the Spanish Group of Lymphoma (Grupo Español de Linfomas y Trasplante de Médula Osea, GELTAMO).**

## Background:

- The standard scale in evaluating treatment response in FDG-avid lymphomas relies on visual interpretation based on residual uptake related to a reference region 5-point score Deauville scale (DV). This may be a source of inter-rater discrepancy.
- ΔSUVmax has also been proposed as a predictor of response in interim PET in DLBCL patients.
- We used the data from DLBCL PET-CT studies included in a phase II randomized trial with central blinded review of images performed at baseline, and after 2-4-6 cycles of chemotherapy.

## Objectives:

- To establish a quantified continuous scale based on the ratio of:
  - target lesion maximum uptake / reference region medium uptake (liver or mediastinum).
    - rTMBP:ratio tumor-mediastinal blood pool
    - rTL: ratio tumor-liver
- Correlate it with:
  - DV scores
  - ΔSUVmax

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## Results:

- Each DV category translated to significantly different values in both ratios

| Deauville Score | Median rTMBP (iq range) | Median rTL (iq range) |
|---|---|---|
| **DV1** | 1,07 (0,62-1,50) | 0,71 (0,41-0,91) |
| **DV2** | 1,25 (1,00-1,54) | 0,90 (0,71-1,06) |
| **DV3** | 1,87 (1,60-2,17) | 1,30 (1,15-1,47) |
| **DV4** | 2,92 (2,47-3,92) | 2,12 (1,78-2,84) |
| **DV5** | 10,11 (6,43-17,92) | 7,07 (4,68-10,48) |

- The AUC was slightly higher for rTL (0,978) than for rTMBP (0,965);

| rTL cutoff | Sensitivity (%) | Specificity (%) |
|---|---|---|
| **0,7** | 90,9 | 92,5 |
| **2** | 78,2 | 99,4 |

- Both ratios proved strong significant inverse correlation with ΔSUVmax

## Conclusions:

- Target lesion /reference region uptake ratios prove to be significantly correlated with each score in the Deauville scale and with ΔSUVmax.
- This provides an additional easily measurable tool for image interpretation in difficult cases.
- Further studies can evaluate a potential prognostic value.

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# A5. Evaluating early interim FDG PET/CT with Peking criteria for predicting the outcome in DLBCL

Xuejuan Wang, Yang Fan, Yuewei Zhang, Zhi Yang , Nina Zhou, Chen Liu, Zhitao Ying, Jun Zhu

Peking University Cancer Hospital & Institute, Beijing, China

# A6. Can Peking Criteria accurately interpreting interim and end-of-treatment $^{18}$F-FDG PET/CT for prognosis of patients with diffuse large B cell lymphoma?

Uni-factor analysis of prognosis for patients with DLBCL using interim and end-of-treatment PET/CT (n=88, n=91)

| Risk factor | PET-4 | | PET-end | |
|---|---|---|---|---|
| | PFS | OS | PFS | OS |
| | HR | HR | HR | HR |
| Peking criteria | 11.714 | 38.139 | 38.139 | 12.005 |
| Deauville scale | 9.202 | 16.662 | 16.662 | 9.77 |
| $\Delta SUV_{max}$ | 3.793 | 6.794 | 6.794 | 5.03 |

Variables with influence on prognosis via multi-factor analysis

| | **PFS** | **OS** |
|---|---|---|
| **Risk factor** | **HR** | **HR** |
| **Interim PET/CT (n = 88)** | | |
| Stage (I, II vs. III, IV) | 4.818 | NA |
| LDH (normal vs. abnormal) | 1.544 | 2.635 |
| IPI (low vs. high) | 0.596 | NA |
| Bulky Disease (yes vs. no) | 1.036 | NA |
| Peking criteria (positive vs. negative) | 11.908 | 9.375 |
| **End-of-treatment PET/CT (n = 91)** | | |
| ECOG-PS (＜2 vs. ≥2) | 0.951 | NA |
| Stage (I, II vs. III, IV) | 2.704 | 5.628 |
| IPI (low vs. high) | 0.83 | NA |
| Peking criteria (positive vs. negative) | 29.731 | 15.084 |

# FDG PET/whole-body MRI, including diffusion-weighted imaging, for staging patients with classical Hodgkin lymphoma and diffuse large B-cell lymphoma: comparison with FDG PET/contrast-enhanced CT in a prospective study

R. Della Pepa[1], M. Picardi[1], E. Nicolai[2], A. Soricelli[3], C. Cerchione[1], N. Pugliese[1], F. Pane[1], M. Meignan[4], M. Salvatore[5]

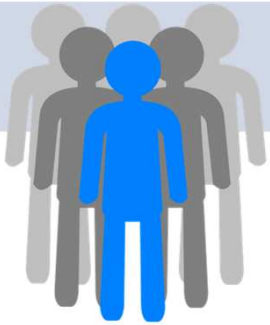
[1] Department of Clinical Medicine and Surgery, Hematology, Federico II University, via Sergio Pansini, 5, Naples, 80131, Italy; [2] Department of Nuclear Medicine, SDN IRCCS, Via Gianturco 113, 80143 Naples, Italy; [3] Department of Radiology, University of Naples Parthenope -SDN IRCCS, Via F. Acton 38, 80143Naples, Italy; [4] Centre Universitaire Hospitalier Henri Mondor, Lymphoma Study Association Imaging, Créteil, France; [5] Department of Radiology and of Nuclear Medicine, SDN IRCCS, Via Gianturco 113, 80143 Naples, Italy;

**BACKGROUND:** CT, together with FDG PET, are the crucial imaging tools for an accurate staging in Hodgkin lymphoma and non-Hodgkin lymphoma. Important disadvantages of diagnostic CT are the exposure of ionizing radiation and contrast-induced acute kidney injury.

Prevention of exposure to CT-related ionizing radiation and *i.v.* contrast medium is important. **Unenhanced whole-body magnetic resonance imaging is feasible and may be a good radiation-free alternative to CT for staging lymphoma.**

**AIM: The aim of this study was to compare staging obtained with fused FDG PET/MRI with staging obtained with FDG PET/CT for patients with newly diagnosed lymphoma.**

12 consecutive patients with newly diagnosed lymphoma were scheduled to receive imaging tools for staging




2/12 (16.6%) have failed to carry out MRI examination because of claustrophobia

10 patients were evaluable

## Patient characteristics

| Patient | Sex | Age (years) | Histological diagnosis | Ann Arbor staging (FDG PET/CT) | Organ involvement (FDG PET/CT) | Therapy (according to FDG PET/CT Ann Arbor staging) | Ann Arbor staging (FDG PET/MRI) | Organ involvement (FDG PET/MRI) | Therapy (according to FDG PET/MRI Ann Arbor staging) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 38 | cHL | IIA | - | ABVD X 4 | IIA | - | ABVD X 4 |
| 2 | M | 61 | cHL | IVSB | Liver, spleen, bone | ABVD X 6 | IVSB | Liver, spleen, bone | ABVD X 6 |
| 3 | M | 23 | cHL | IIB | - | ABVD X 6 | IIB | - | ABVD X 6 |
| 4 | F | 35 | cHL | IIA | - | ABVD X 4 | IIA | - | ABVD X 4 |
| 5 | F | 40 | DLBCL | IIEB | Bone (local infiltration) | R-CHOP X 6 | IIEB | Bone (local infiltration) | R-CHOP X 6 |
| 6 | F | 78 | DLBCL | IVB | Liver, bone | R-CHOP X 6 | IVB | Liver, bone | R-CHOP X 6 |
| 7 | F | 65 | cHL | IIIEB | Bone | ABVD X 6 | IIIEB | Bone | ABVD X 6 |
| 8 | M | 16 | cHL | IIEB | Bone | ABVD X 6 | IIEB | Bone | ABVD X 6 |
| 9 | F | 29 | cHL | IIB | - | ABVD X 6 | IIB | - | ABVD X 6 |
| 10 | M | 28 | cHL | IIA | - | ABVD X 4 | IIA | - | ABVD X 4 |

## CONCLUSIONS:

-**The agreement between FDG PET/MRI and PET/CT** for all nodal and extra-nodal regions **was 100%**, with a low inter-observer variability (Pearson's r=0.958; P <0.01);

- Ann Arbor stages according to FDG PET/MRI were concordant with those of FDG PET/CT in 100% (10/10) of patients. However, the average dose of ionizing radiation and of *i.v.* nonionic contrast medium (diagnostic CT) received by each patient was 19.9 mSv (range, 13.9-25.8) and 140 ml (range, 120-150), respectively.

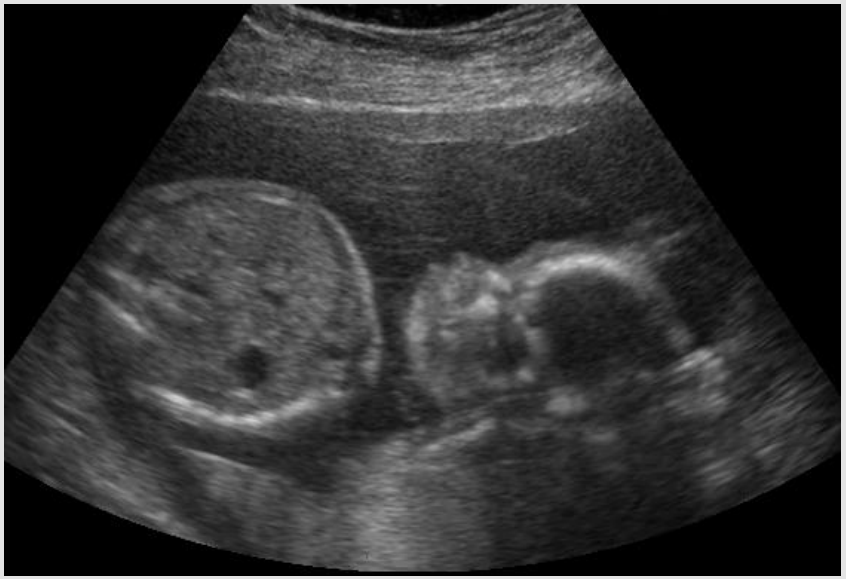
## C2. IRON DEPOSITS WITHIN UNTREATED LYMPHOMA LESIONS DETECTED ON DIFFUSION-WEIGHTED (DW) AND T2-WEIGHTED GRADIENT ECHO (GRE) MR IMAGING

Cottereau AS, Mule S, Lin Chieh, Belhadj K, Itti E, Tacher V, Pigneur F, Copie C,
Le Bras F, Haioun C, Luciani A, Rahmouni A

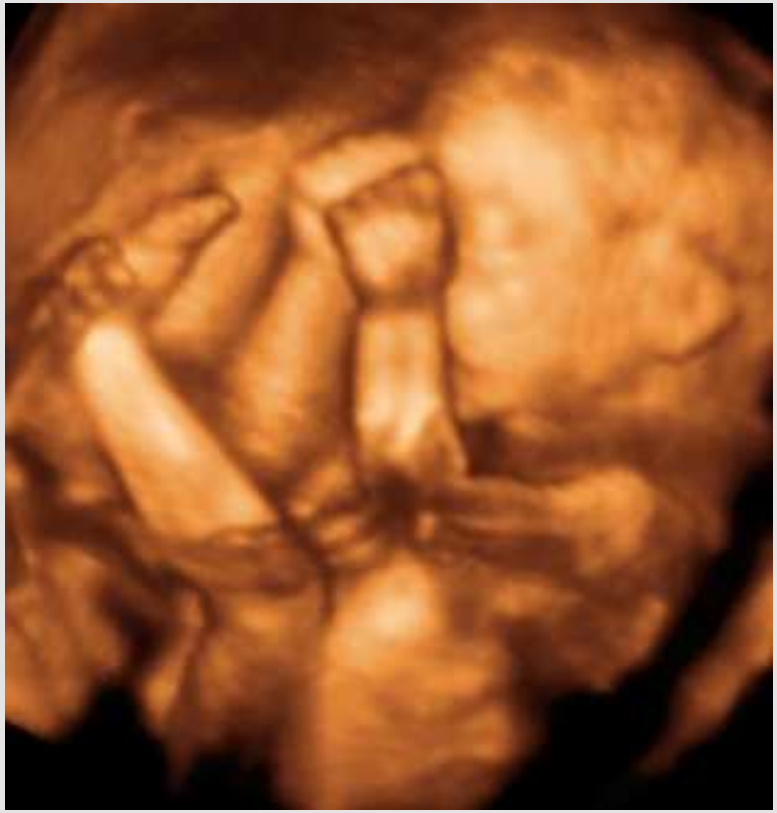
- Iron deposits compared with PET/CT and inflammatory biological findings
- 43 untreated patients (12 DLBCL, 20 HL, 11 FL)
- Low DW signal →T2 GRE sequence
- Iron deposits in 13 (40% HL, 33% DLBCL)
  Ann Arbor stage IV (77%)
  spleen, liver, nodes
  lesions with high FDG uptake
  when inflammatory biological markers
  (CRP, $\alpha$1- $\alpha$2-globulin, microcytic anemia)

## 2D



## 3D

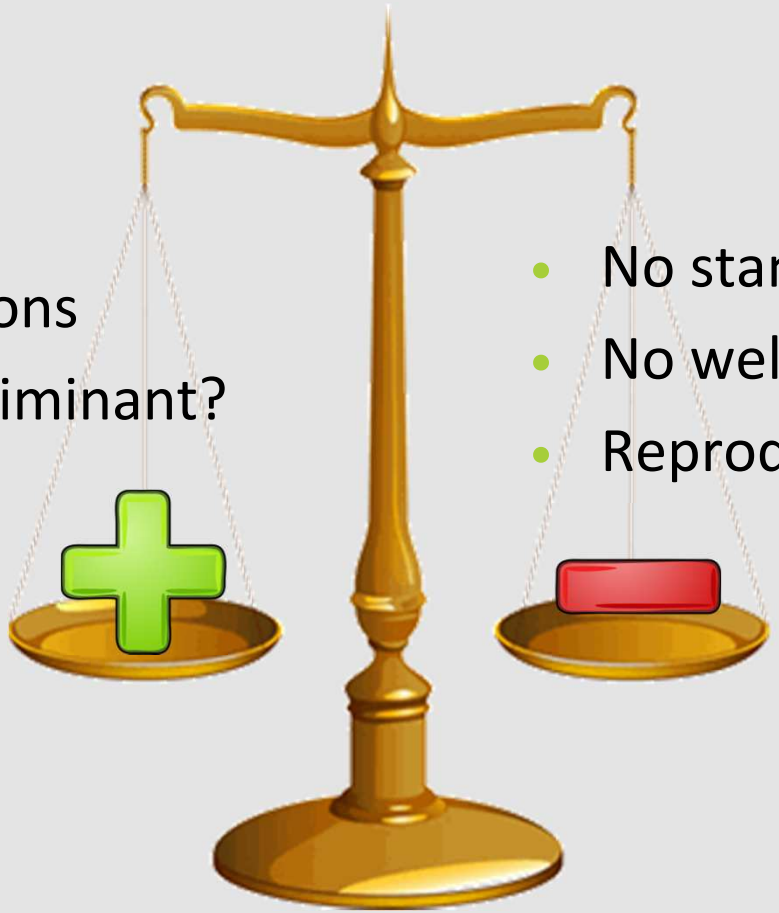


**Funny-looking picture OR really useful?**



# 3D *versus* 2D

- All the lesions
- More discriminant?

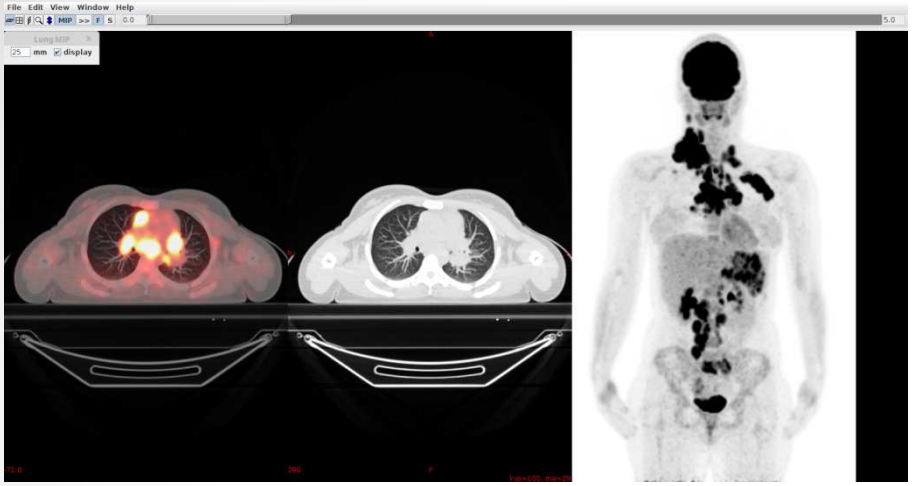


- No standardized method
- No well-defined threshold
- Reproducibility

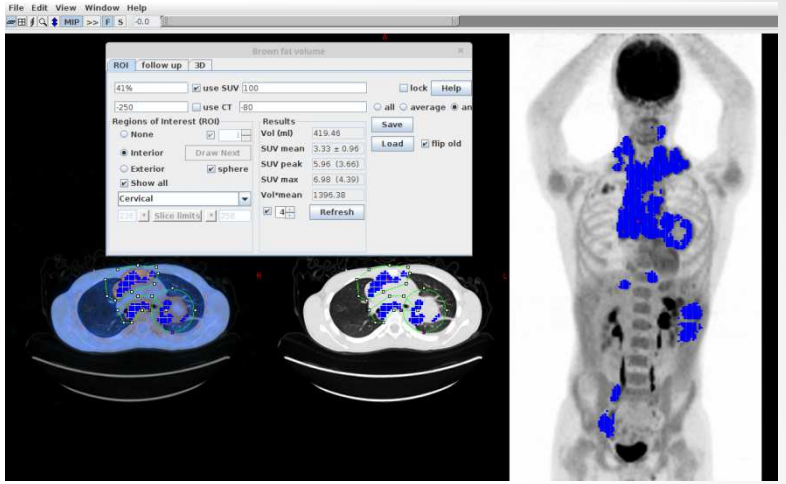


## G4. Beth Israel Plugin for FIJI:
## A free and open source software for PET/CT processing in research.

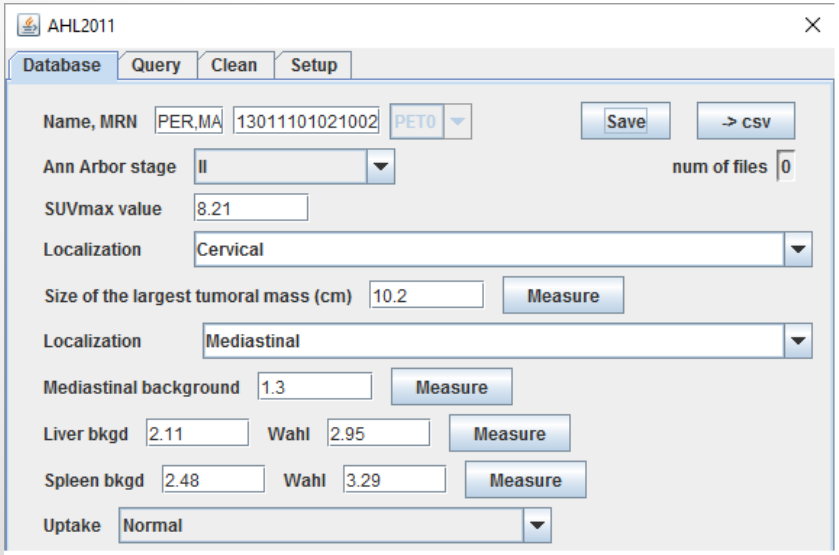
### Main view



### Quantification



### Dedicated per study form




Data are automatically filled with interaction in the viewer and sent to a personal central database across readers

Other features :

- Segmented tumor export writable into DICOM files (further tumor calculations or image mask for radiotherapy)
- Auto-segmentation (see E.Grossiord's poster)

http://www.petctviewer.org

# G2. Interobserver Reproducibility of Semi-Automated Assessment of MTV in DLBCL patients

Burggraaff CN , Kaßner I , Rahman F , Pieplenbosch S, Müller S, Barrington SF , De Vet HCW, Hoekstra OS, Zijlstra JM, Boellaard R

VU university medical center, Amsterdam, The Netherlands; University Hospital Essen, University of Duisburg-Essen, Germany; King's College London, United Kingdom; University medical center Groningen, The Netherlands

## E2. BASELINE TMV MEASURED WITH FIXED OR DIFFERENT ADAPTIVE THRESHOLDING METHODS EQUALLY PREDICTS OUTCOME IN PERIPHERAL T CELL LYMPHOMA

A-S. Cottereau, S. Hapdey, L.Chartier, O. Casasnovas, E. Itti, H. Tilly, P. Vera, M. Meignan, S. Becker

- 106 PTCL staged with a PET/CT
- TMTV computed with 41% SUVmax
  with adaptative threshold
  - Daisne (Da) modified based on signal/background ratio
  - Nestle (Ns) on tumor and background intensities
  - Fit including a 3D geometric model based on spatial resolution (Fit)
  - Black (Bl) based on mean SUVmax
- Different cut-off values, but similar prognostic values
- One single method easily applicable is mandatory for multicentric study

# G3. A new 3D full body lymphoma automated segmentation for PET images using machine learning multi-modality tumour characteristics

Eloïse Grossiord, Hugues Talbot, Laurent Najman and Michel Meignan

Université Paris-Est and Hôpital Henri-Mondor, Créteil, France

# PET-Based Textural Analysis Assessment in Early Stage Hodgkin Lymphoma Treated with Standard Combined Approach

Angelo Fama, Patrizia Ciammella, Massimiliano Casali, Natalia Villani, Marco Bertolini, Angela Ferrari, Elisa Barbolini, Ala Podgornii, Mauro Iori, Giacomo Feliciani, Stefano Luminari, Francesco Merli and Annibale Versari

Arcispedale Santa Maria Nuova, Istituto di Ricovero e Cura a Carattere Scientifico, Reggio Emilia,Italy

# G1. Association between textural and morphological tumor indices on baseline PET-CT and early metabolic response on interim PET-CT in malignant lymphomas with bulky mass

Yassine Al Tabaa, Fayçal Ben Bouallègue, Guillaume Cartron, Fabien Vauchot, Denis Mariano-Goulart

Department of Nuclear Medicine, Montpellier University, France

# F2. multiple myeloma CT scanning, reformatting and interpretation protocol

**Dr. Bart de Keizer, Dr. Jet Quarles van Ufford, Prof. Dr. Otto Hoekstra, Dr. Josée Zijlstra**

On behalf of the HOVON (Haemato Oncology Foundation for Adults in the Netherlands) imaging working group

Dutch-Belgian Cooperative Trial Group for Hematology Oncology • www.hovon.nl

# HOVON multiple myeloma CT scanning, reformatting and interpretation protocol

Dutch guideline on CT acquisition and interpretation

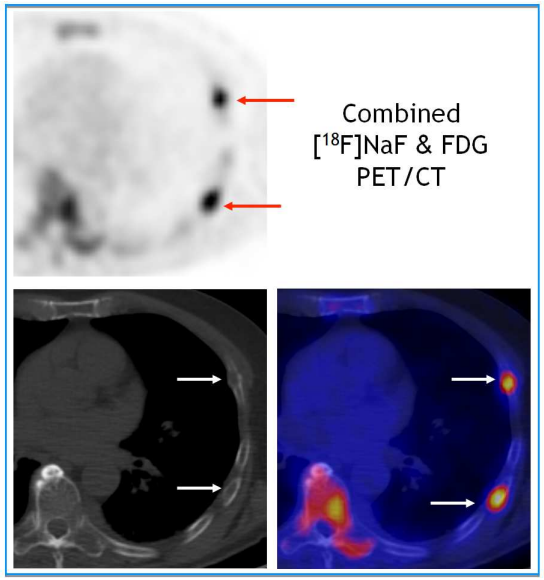
| | |
|---|---|
| **Scanning** | - Positioning with arms ventral of the body<br>- Low dose protocol<br>- Reconstruction with sharp / bone kernel<br>- Reconstructed slice thickness ≤1,5 mm |
| **Reformatting** | - axial, coronal and sagittal plane<br>- Slice thickness 3 mm<br>- Slice interval ≤3 mm<br>- Pixel size <1 x 1 mm |
| **Interpretation / positive lesions** | - Clear lytic lesions > 5mm<br>- Soft tissue lesions with destruction of cortical bone<br>- Extra-osseous soft tissue lesions adjacent to bone or extending outside of cortical bone |

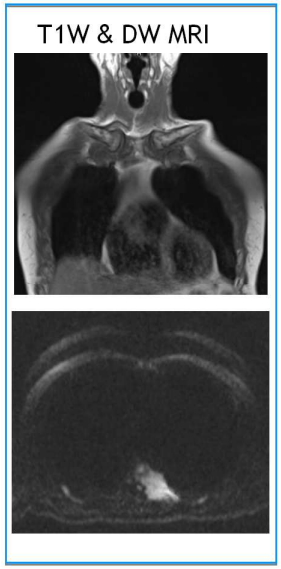
HOVON

# F4. Comparison of combined whole-body [$^{18}$F]NaF/[$^{18}$F]FDG PET/CT versus MRI for the detection of myeloma lesions

*N. Withofs, F. Cousin, T. Tancredi, P. Simoni, B. De Prijck, K. Hafraoui, C. Bonnet, V. Alvarez-Miezentseva, R. Hustinx, Y. Beguin, J. Caers*

| Feature | *n* = 13 patients |
|---|---|
| Age at diagnosis (median, range) | 65 y (46-83 y) |
| Sex: Male | 10 |
| Female | 3 |
| Isotype: IgG | 5 |
| IgA | 3 |
| IgA & IgG | 1 |
| Light chain | 4 |
| ISS stage 1 | 5 |
| 2 | 5 |
| 3 | 3 |
| Poor cytogenetics | 1 |

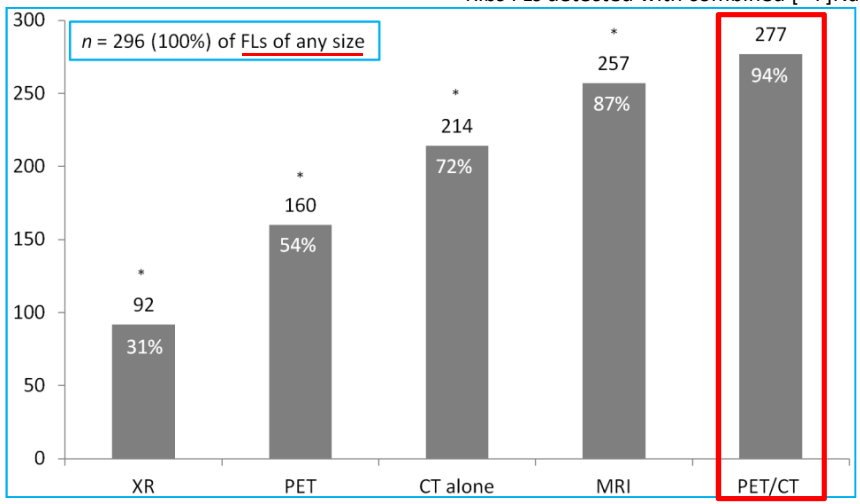


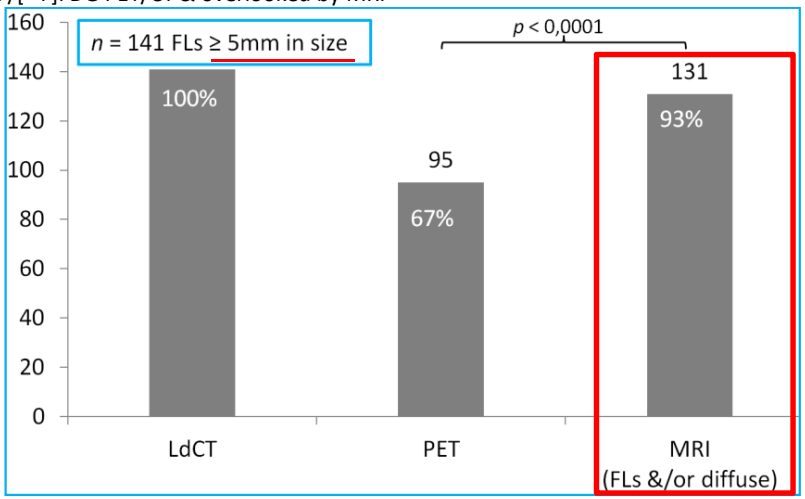




Ribs FLs detected with combined [$^{18}$F]NaF/[$^{18}$F]FDG PET/CT & overlooked by MRI

Whatever the **FLs** location, the detection rate of PET/CT and MRI was similar except for skull and rib MM lesions for which PET/CT was > MRI ($p < 0.05$).

Interestingly, for skull lesions, the detection rate of MRI was < XR.




* Detection rate significantly lower than PET/CT ($p < 0.05$)

## F1. $^{18}$F-FLUOROCHOLINE VERSUS $^{18}$F-FDG FOR PET/CT IMAGING IN PATIENTS WITH SUSPECTED RELAPSING OR PROGRESSIVE MULTIPLE MYELOMA: A PILOT STUDY

Thibaut Cassou-Mounat, Sona Balogova, Françoise Montravers, Valérie Nataf, Marie Calzada, Virginie Huchet, Khaldoun Kerrou, Jean-Yves Devaux, Mohamad Mohty, Jean-Noël Talbot, Laurent Garderet

- 21 MM PET/CT for suspected relapse or progression
- 2 readers' agreement: 0.81 for FDG and 0.89 for FCH
- Higher median SUVmax and T/NT for FCH *vs* FDG
- Almost all unmatched foci were FCH+ and FDG-, mostly in the head and neck region

# F1. $^{18}$F-FLUOROCHOLINE VERSUS $^{18}$F-FDG FOR PET/CT IMAGING IN PATIENTS WITH SUSPECTED RELAPSING OR PROGRESSIVE MULTIPLE MYELOMA: A PILOT STUDY

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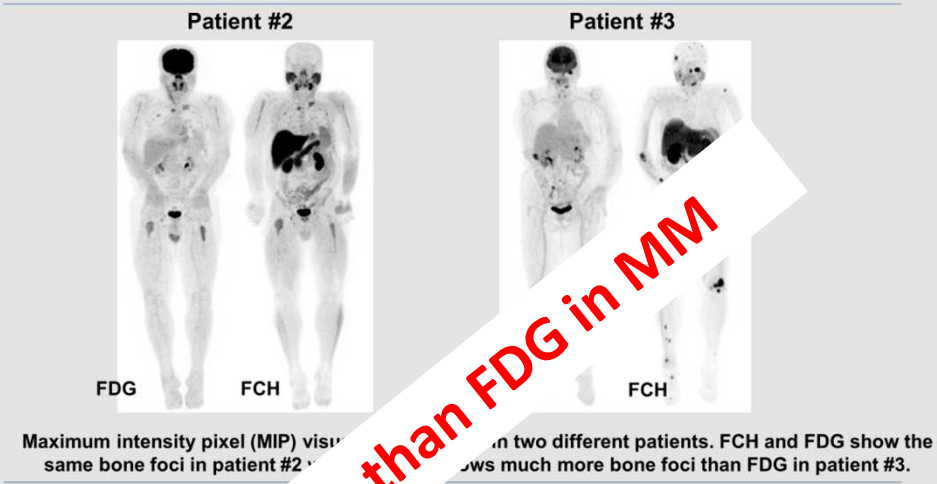
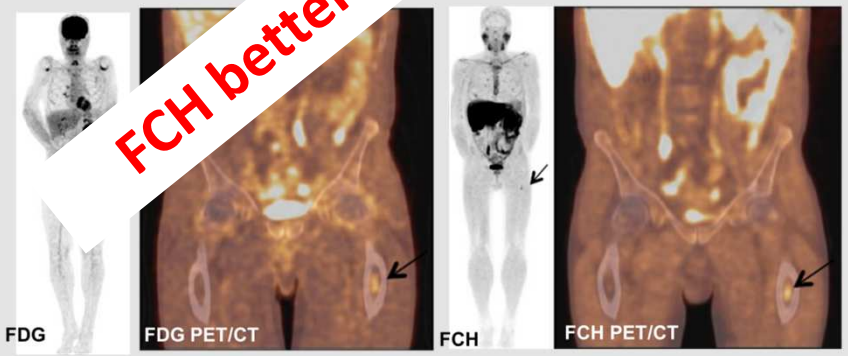



Maximum intensity pixel (MIP) visu… …n two different patients. FCH and FDG show the same bone foci in patient #2 … …ows much more bone foci than FDG in patient #3.




In patient #18, one single mild intraosseous focus was visible on FDG PET/CT in the left femoral shaft, SUVmax=2.5 according to both readers whereas SUVmax of the liver was 3.4. The focus was more easily detected on FCH PET/CT SUVmax=3.1.

# $^{89}$Zr-labeled-rituximab PET as an imaging biomarker to assess CD20 targeting:

## a pilot study in patients with relapsed/refractory diffuse large B cell lymphoma

Y.W.S. Jauw[1], M. C. Huisman[2], D. de Jong[3], D. J. Vugts[2], S. Zweegman[1], G.A.M.S. van Dongen[2], O.S. Hoekstra[2], J.M. Zijlstra[1]

Departments of [1]Hematology, [2]Radiology & Nuclear Medicine and [3]Pathology, VU University Medical Center, Amsterdam, The Netherlands

**Rationale:**

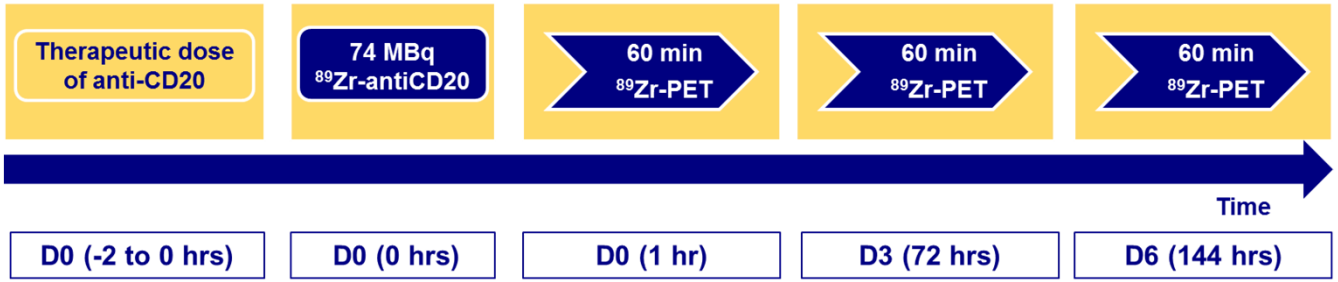
- Clinical benefit of repeated rituximab treatment might be limited by insufficient tumor targeting.
- Molecular imaging with $^{89}$Zirconium ($^{89}$Zr)-labeled rituximab PET provides a potential imaging biomarker to assess CD20 targeting

**Aim of the study:**

To explore the relation between tumor uptake of $^{89}$Zr-rituximab and CD20 expression in biopsies

**Methods:**

- Patients with relapsed/refractory DLBCL
- Tumor biopsies: CD 20 expression (ranking of immunohistochemistry)
- Tumor uptake of $^{89}$Zr-rituximab (in $SUV_{peak}$)




Poster A16

This research has been funded by DUTCH CANCER SOCIETY

# $^{89}$Zr-labeled-rituximab PET as an imaging biomarker to assess CD20 targeting:

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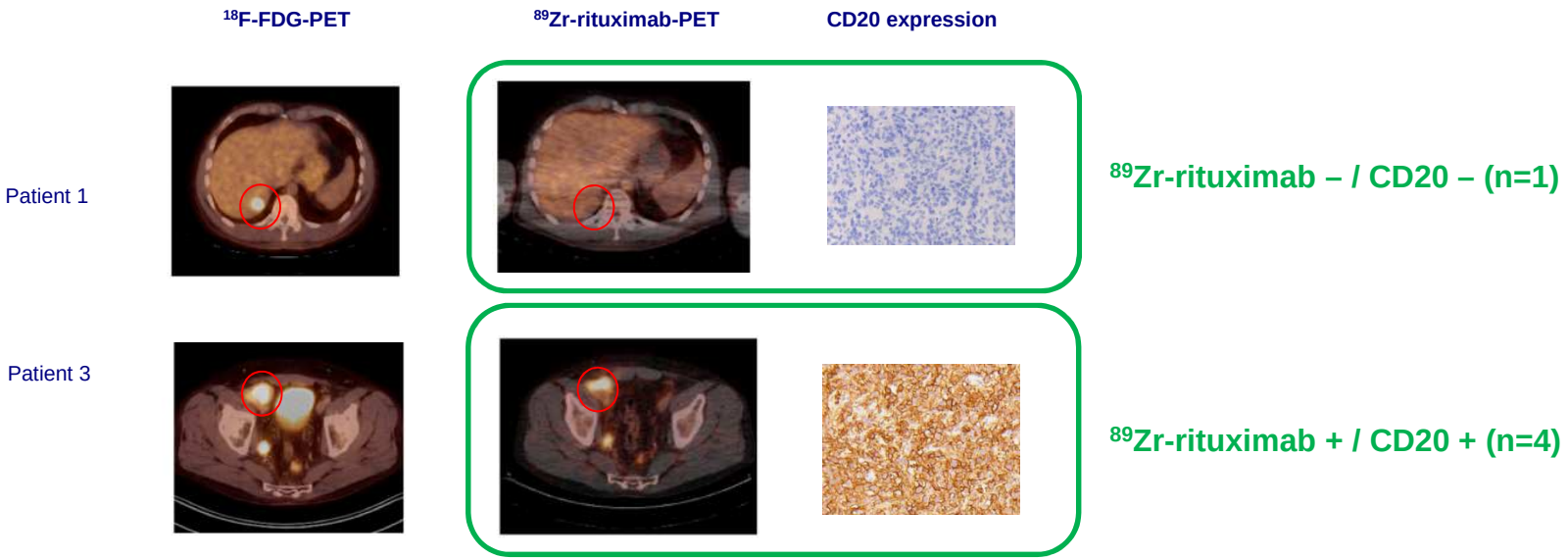
Departments of [1]Hematology, [2]Radiology & Nuclear Medicine and [3]Pathology, VU University Medical Center, Amsterdam, The Netherlands

## Results

Tumor uptake of $^{89}$Zr-rituximab and CD20 expression were concordant in 5 out of 6 patients.
Spearman's rank correlation coefficient ($r_s$) = 0.83, p=0.04




## Conclusions

1. Tumor uptake of $^{89}$Zr-rituximab **was correlated** with CD20 expression in biopsies.
2. Supports use of $^{89}$Zr-rituximab-PET as an imaging biomarker to assess CD20 targeting

Poster A16

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# In summary for the technical abstracts

- Baseline PET/CT more useful than CE-PET/CT
- Liver activity = the best reference?
- Sensitivity PET/DWI-MR = PET/CE-CT
- 3D parameters : software ? threshold ?
- Multiple Myeloma:
  - Standardization
  - Combined injection [$^{18}$F]NaF and [$^{18}$F]FDG > MRI
  - $^{18}$F-fluorocholine > $^{18}$F-FDG
- $^{89}$Zr-rituximab-PET = marker of immunochemosensitivity?