Uptake heterogeneity quantification in lung cancer: impact on image features variability of 3D- and 4D-PET/CT protocols.

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AIM: To evaluate the impact of different static (3D) and dynamic (4D) PET/CT protocols on PET image features variability.

INTRODUCTION

- The use of image features for prognosis and response monitoring requires an additional level of reproducibility, beyond what is needed for diagnostic imaging.
- In lung cancer, the evaluation of the lesion with FDG-PET/CT imaging presents additional challenges due to respiratory movement.

How significant is the **impact of the compensation of motion** implied by 4D PET/CT **on image features (IF) ?**

Is this **effect on IF** more significant than the **voxel size** of image **reconstruction** or image **post-resampling**?

MATERIALS & METHODS

31 Lung cancer patients

(Non-) small cell lung cancer (73 ± 8 y):

14 females and 17 males.

Scans performed during the same session:

- Static (3D-)
- Retrospectively respiratory gated (4D-) PET/CT with 10 phases.

36 lesions (minimum diameter 3FWHM):

- 42% in low region,
- 13 % in the middle and
- 43% in the upper region of the lobes.

Image Protocols

Philips System GEMINI TF (64)

Protocol	Δt PET(CT)	Reconstruction	Reconstruction Voxel (mm)	Resampled Voxel (mm)
4D	15 min (33 s)	BLOB-OSEM-TOF	4x4x4	-
3D	1.5 min (3.5 s)	BLOB-OSEM-TOF	2.11x2.11x4	-
3D−4	1.5 min (3.5 s)	BLOB-OSEM-TOF	4x4x4	-
3D−R	1.5 min (3.5 s)	BLOB-OSEM-TOF	2.11x2.11x4	4x4x4

BLOB-OSEM-TOF:3-dimensional blob based ordered-subset iterative time-of-flight with 2 iterations and 33 subsets.

The average scan starting times after the tracer administration:

68 ± 9 min for 3D-PET/CT

93 ± 11 min for 4D-PET/CT

Image Features (IF)

PET volume ($VOI_{40\%}$): fixed threshold of 40% of the lesion maximum intensity. Its use for heterogeneity quantification was validated in a previous study [1].

Standard uptake value (SUV) resampling method with a fixed number of bins (N=16, 32, 64).

3D version of the gray-level co-ocurrence matrix (GLCM), gray level run length matrix (GLRLM) and neighborhood gray tone difference matrix (NGTDM)

SUV-Histogram	Volume (**V**), Maximum SUV (**SUV_{max}**), Mean SUV (**SUV_{mean}**), Skweness (**S**), Coefficient of variance (**Cov**), Kurtosis (**K**), Energy(**E_H**) and Entropy (**Ent_H**),
GLCM	Local Homogeneity (**LH**), Correlation (**C_{CM}**), Contrast (**Con_{CM}**), Energy (**E_{CM}**), Entropy (**Ent_{CM}**), and Dissimilarity(**D**)
GLRLM	Short Run Emphasis (**SRE**), Long Run Emphasis (**LRE**), Low Gray-Level Run Emphasis (**LGRE**), High Gray-Level Run Emphasis (**HGRE**) , Short Run Low Gray-Level Emphasis (**SRLGE**), Short Run High Gray-Level Emphasis (**SRHGE**), Long Run Low Gray-Level Emphasis (**LRLGE**), Long Run High Gray-Level Emphasis (**LRHGE**) Gray-Level Non-uniformity (**GNU**), Run Length Non-uniformity (**RLNU**) and Run Percentage (**RP**)
NGTDM	Coarseness (**Coar**), Contrast (**Con_{NM}**), Complexity (**Comp**) and Texture Strength (**TS**)

Analysis

To compare two data samples :

Bland-Altman (BA) analysis

with significant difference determined based on the average of the differences relative to the mean and its 95% confidence interval (CI).

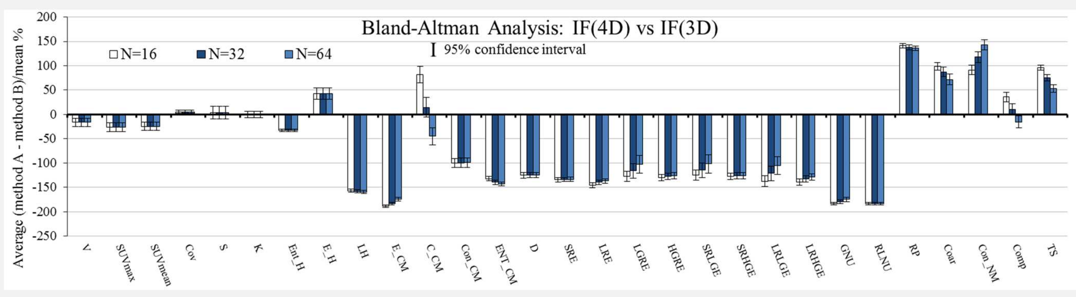
Correlations analysed in terms of:

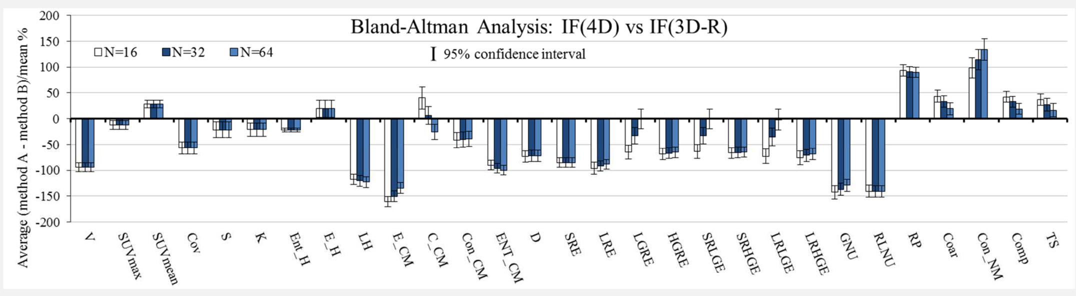
Spearman's and Pearson's correlation tests (p<0.05)

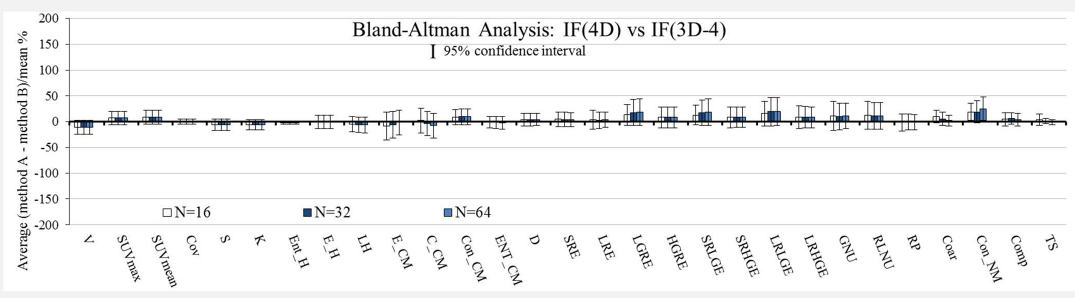
RESULTS

– **Comparison of PET IF derived from 4D- and three different 3D- PET/CT protocols:**

Bland – Altman Analysis







I. For the 3D- and 4D- PET/CT protocols employed in our clinical routine, most of the IF (except from S, K and E_{CM} with N=32) showed significant differences.

II. When 3D-PET image was post-resampled to the same voxel size of 4D-PET image (3D-R), differences were significant for most of the IF (except from LGRE, SRLGE and LRLGE for N=64 and C_{CM} for N=32)

III. When 3D-PET reconstruction was modified to comprise the same voxel size of 4D-PET image (3D-4), no significant differences were observed for most of the IF (except from Con_{NM} for N=32 and N=64)

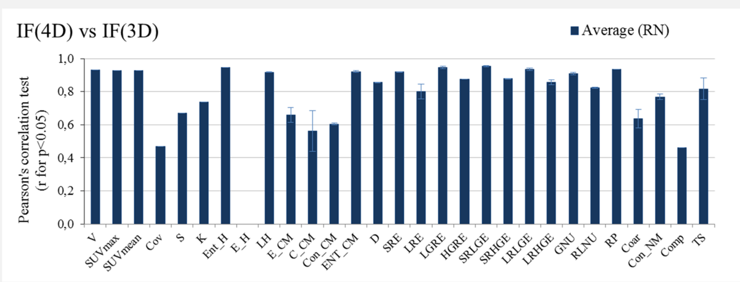
Correlation Test

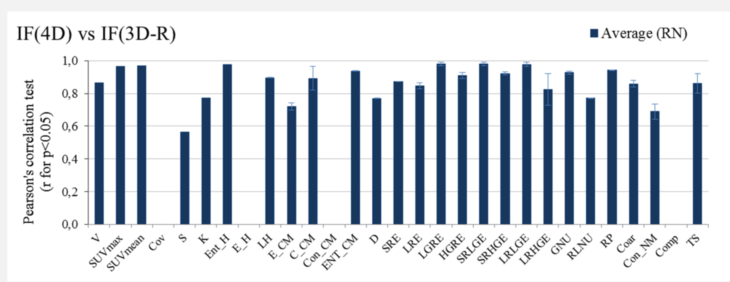
Some IF showed strong linear correlation (r>0.8, p<0.0001) independently of the protocol and the SUV discretization method.

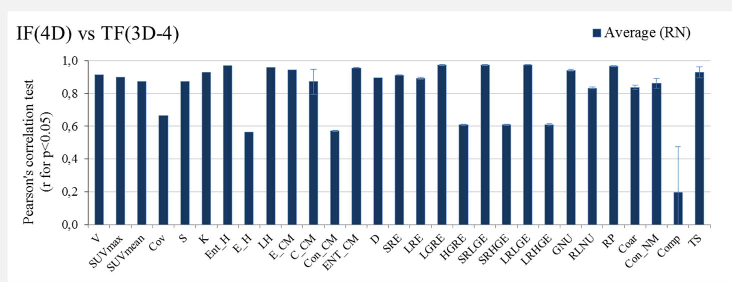
Ent_H,

SRE, LRE,LGRE, SRLGE, LRLGE,

GNU and RP







CONCLUSIONS

- For our patient cohort, **the compensation of tumor motion** implied by 4D-PET **had not significant impact on IF** (Results III).
- The **voxel size comprised in the image reconstruction** had **significant impact in IF** response (Results I & III).
  - In the comparison of IF derived from **3D vs 4D** PET, **image post-resampling effect** has to be taken into account to avoid **misinterpretation of the results** (Results II & III).
- Strong linear correlation observed for some IF suggested that the use of different protocols and resampling methods could not have a significant impact on their prognostic value. However, absolute values were sensitive to the protocol employed. Consequently, the **standardization of the protocol remains still a requirement when absolute IF quantification is involved**.

REFERENCES

[1] Carles. *et al*, "Evaluation of PET texture features with heterogeneous phantoms: complementarity and effect of motion and segmentation method" Phys. Med. Biol. **62** (2017) 652–668.