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Relationship between ^{18}F-FDG PET SUV with Partial Volume Correction and Histology in Gastric and Gastro-Oesophageal Cancer

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ABSTRACT

In vivo molecular imaging techniques is increasingly used in the management of oncological patients, allowing different aspects of oncological pathologies to be assessed (e.g. metabolism, hypoxia) non invasively. The possibility to extract indexes of disease from *in vivo* biomedical images and to associate them with their biological drivers opens new prospective on the role of *in vivo* molecular imaging and expedites the translation of novel biomarkers from the bench to the clinical environment. In this work we investigate the relationship between ^{18}F-FDG uptake measured by Body-Weight Standardized Uptake Value (SUV_{BW}) as index of cell glucose metabolism, and histological indices for gastric and gastro-oesophageal cancer. For this purpose, Partial Volume Effect Correction (PVC) has been properly compensated prior to the measurement of the PET index (PVC-SUV_{BW}). The correlation of ^{18}F-FDG PVC-SUV_{BW} with histology data was evaluated by bivariate and multivariate statistical analysis. Although obtained in a limited number of patients, our results suggest that correlations can be found when PVC is applied to SUV_{BW} and that ^{18}F-FDG PET can provide information on biological characteristics of gastric and gastro-oesophageal cancer lesions.

Keywords: ^{18}F-FDG PET; SUV; Gastric Cancer

1. Introduction

In vivo disease biomarkers are increasingly demanded by clinicians in order to characterize a disease, to make prognosis and to predict response to treatment non invasively.

Body-Weight Standardized Uptake Value (SUV_{BW}), measured by Fluorodeoxyglucose and Positron Emission Tomography (^{18}F-FDG PET), has been extensively used as semi-quantitative index accounting for altered glucose metabolism of an oncological lesion. In order to obtain an accurate measurement of ^{18}F-FDG SUV_{BW}, a Correction for Partial Volume Effect (PVC) has been proved mandatory, since this effect causes severe underestimation of SUV_{BW} (up to 80% - 90% for small lesions) [1,2].

Aim of this work was to evaluate the metabolic impact of PVC on SUV_{BW} as potential *in vivo* prognostic biomarker of gastric and gastro-oesophageal cancer, reflecting *ex vivo* histo-pathological characteristics.

2. Materials and Methods

Fourty-nine patients (31 men, 18 women; mean age 63 ± 13 years; age range: 33 - 83 years) with biopsy-proven gastric and gastro-oesophageal cancer underwent a basal ^{18}F-FDG PET-CT study. ^{18}F-FDG PET/CT sensitivity was assessed. Patient weight, and injected/residual dose were measured in order to calculate PVC-SUV_{BW} on primitive gastric and gastro-oesophageal lesions detected on ^{18}F-FDG PET images.

Patients fasted for twelve hours before the exams and were intravenous injected with ^{18}F-FDG (1 mCi/10 kg). The PET-CT protocol began 60 minutes after the injection. All PET-CT studies were performed according to the oncological clinical protocol implemented on the discovery STE scanner, including a SCOUT scan at 40 mA, a CT scan at 140 keV and 150 mA (10 s) and 3D PET scans (2.5 min/scan) for adjacent bed positions. PET images were reconstructed by a 3D ordered subset expectation maximization algorithm (OSEM, 28 subsets, 2 iterations, 5.14 mm Gaussian post-smoothing) with corrections for random, scatter and attenuation incorporated into the iterative process.

An Operator Independent technique using an auto-

matic threshold was used to define Regions of Interest (ROIs) on PET images [2] and quantitative analysis was performed by calculating mean SUV_{BW} for each primitive gastric and gastro-oesophageal lesions. The RC-based correction methods developed in [2] was used to correct in order to account for Partial Volume Effect.

Both SUV_{BW} and PVC-SUV_{BW} were obtained by Touch-SUV software [3,4].

Correlation tests (Mann-Whitney and Kruskal Wallis tests for univariate analysis and hierarchical clustering combined with a pre-processing k-means analysis for multivariate analysis) were performed in order to evaluate the relationships between ^{18}F-FDG PVC-SUV_{BW} and biopsy-evaluated histotype (signet ring cell carcinoma (SR), squamous cell carcinoma (S) and other adenocarcinoma (ADK) subtype) and grade (G1, G2, G3) (according to WHO and Lauren classifications).

3. Results

^{18}F-FDG PET/CT was able to detect gastric and gastro-oesophageal cancer with a sensitivity of 82%: ^{18}F-FDG PET/CT images of 9 (18%) biopsy-proven gastric cancers were classified as negative, showing no ^{18}F-FDG uptake in the primitive lesions. Negative PET images were not quantified and were excluded by correlation analysis.

Mean primitive lesion diameter (sphere-equivalent diameter) was 2.15 ± 1.17 cm, ranging from 0.99 cm to 6.25 cm. Lesion size confirmed the need of PVC for accurate PET quantification for more than 75% of lesions [2].

Signet ring cell carcinomas showed a lower ^{18}F-FDG PVC-SUV_{BW} compared to squamous cell carcinomas and to other adenocarcinoma subtypes (PVC-SUV_{BW}: 5.57 ± 3.22 g/cc vs 9.90 ± 1.91 g/cc vs 9.32 ± 4.26 g/cc; Mann-Whitney test, $p < 0.05$). No correlation was found when PVC was not applied to SUV_{BW}.

No correlations were found between grade and ^{18}F-FDG PVC-SUV_{BW} or ^{18}F-FDG SUV_{BW} (Kruskal Wallis test, $p > 0.05$).

Figure 1 shows the results for univariate analysis.

The pre-processing k-means cluster analysis allowed to stratify patients in three different groups on the basis of PVC-SUV_{BW} (PVC-$SUV_{BW} \leq 6.25$ g/cc; 6.25g/cc < PVC-SUV_{BW} < 11.60 g/cc; PVC-$SUV_{BW} \geq 11.60$ g/cc). Using these groups, the hierarchical cluster analysis performed on PVC-SUV_{BW}, histotype and grade showed that poorly differentiated (G3) signet ring cell carcinomas were significantly associated with ^{18}F-FDG PVC-$SUV_{BW} \leq 6.25$ g/cc ($p < 0.05$), while moderately differentiated (G2, G1) squamous cell carcinoma were significantly associated with ^{18}F-FDG PVC-SUV_{BW} > 11.6 g/cc; ($p < 0.05$).

Figure 2 shows the results of the hierarchical cluster analysis.

4. Discussion

The role of ^{18}F-FDG PET in staging gastric and gastro-esophageal cancer is controversial. Some works showed a good sensitivity (94%) in the detection of primary gastric and gastro-oesophageal lesions [5], while other studies softened the impact of ^{18}F-FDG PET [6] highlighting in particular its low sensitivity for signet-ring cells carcinomas [7].

In current clinical practice, the election modalities for gastric and gastro-oesophageal cancer remains Endoscopic Ultrasound (EUS) and Computerized Tomography (CT), even if ^{18}F-FDG PET has been suggested in the work-up of patients with incomplete staging as obtained by EUS [5,6] and for detection of distant metastases.

Although obtained in limited population of patients with gastric and gastro-oesophageal cancer, our results show that PVC-SUV_{BW} can have a prognostic role for those lesions detected by ^{18}F-FDG PET.

In literature, few works have been devoted to investigate the relationship between ^{18}F-FDG uptake, as detected

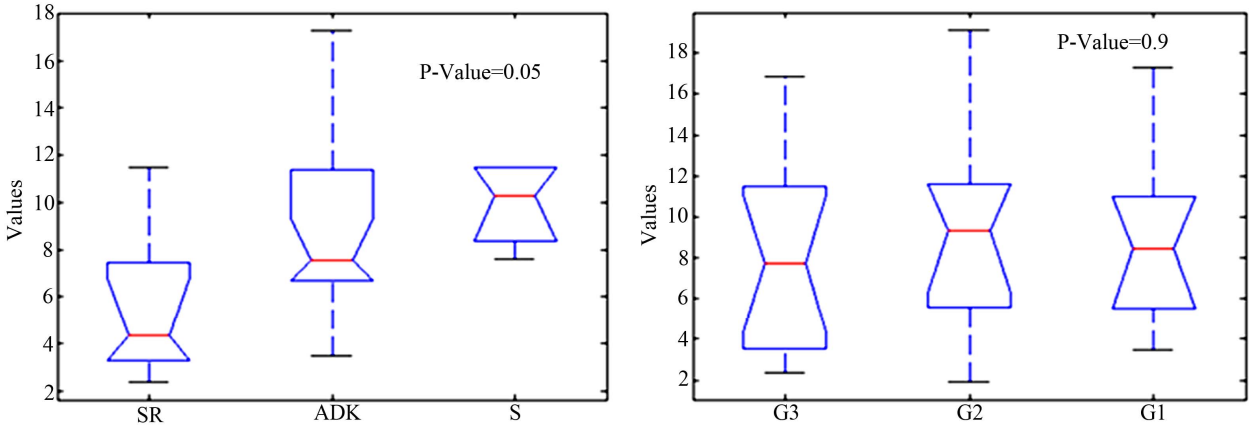

Figure 1. Results of bi-variate tests on histological type and grade.

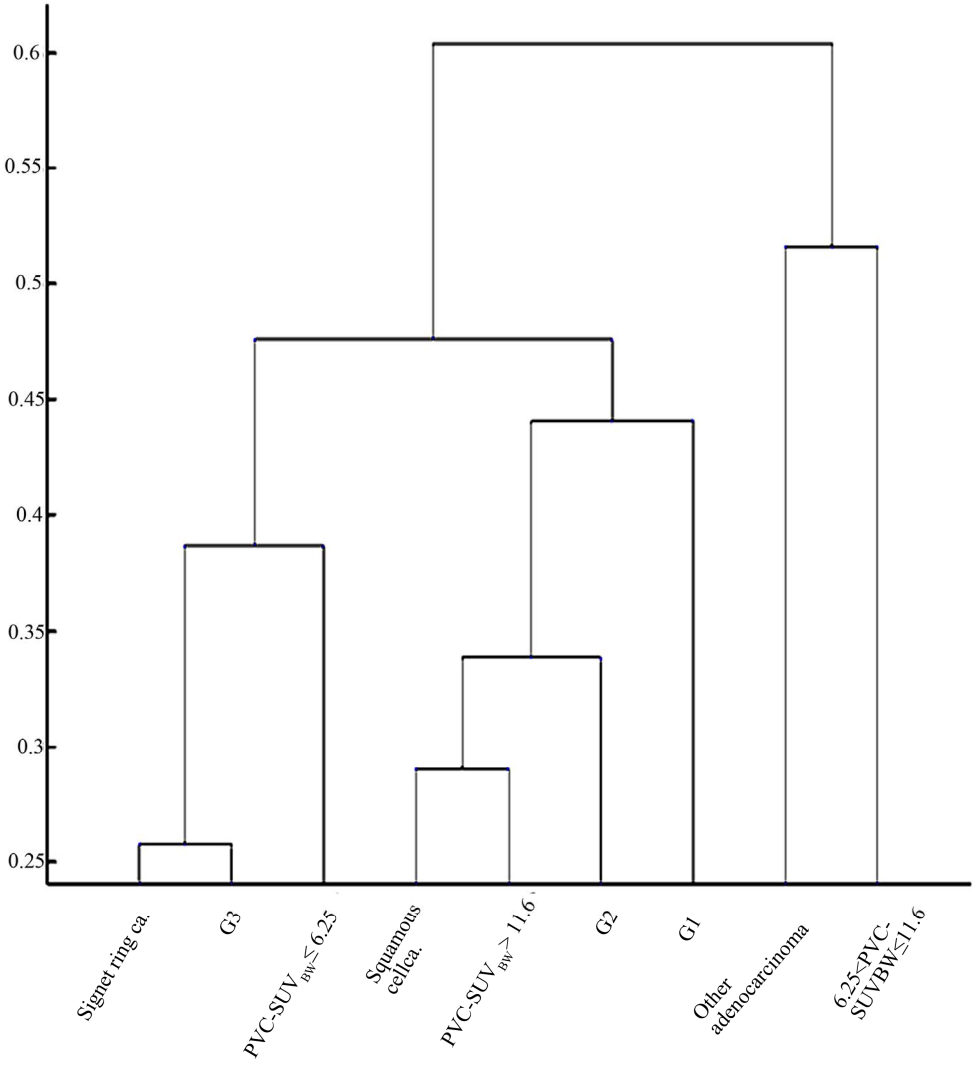

Figure 2. Results of hierarchical cluster analysis.

and measured by PET, and tumour biological characteristics of gastro-oesophageal lesions [8,9]. In published studies no correction for PVC has been used prior to the measurement of ^{18}F-FDG uptake. No correlation was found between ^{18}F-FDG uptake and the differentiation grade [9], neither between ^{18}F-FDG uptake and histological type [8], as obtained in our work when PVC was not applied to SUV_{BW}.

Results of our work suggest that correlations can be found when PVC is applied.

Our work gives added value to current evidences on the role of ^{18}F-FDG in gastric and gastro-oesophageal cancer in adopting, for the first time at our knowledge, two strategies: 1) the application of PVC for the accurate measurement of ^{18}F-FDG SUV_{BW} of small lesions and 2) the use of a multivariate hierarchic cluster analysis combined to a k-means pre-clustering approach for multiple correlations.

Our results need to be validated on a larger cohort of patients.

5. Conclusion

^{18}F-FDG PET can provide information on biological characteristics of gastric and gastro-oesophageal cancer by means of ^{18}F-FDG SUV on condition that partial volume correction is properly applied prior to the measurement of PET quantification indexes.

REFERENCES

[1] M. Soret, S. L. Bacharach and I. Buvat, "Partial-Volume Effect in PET Tumor Imaging," *Journal of Nuclear Medicine*, Vol. 48, No. 6, 2007, pp. 932-945. doi:10.2967/jnumed.106.035774

[2] F. Gallivanone, A. Stefano, C. Canevari, L. Gianolli, C. Messa, M. C. Gilardi and I. Castiglioni, "PVE Correction

in PET-CT Whole-Body Oncological Studies from PVE-Affected Images," *IEEE Transactions on Nuclear Science*, Vol. 58, No. 3, 2011, pp. 736-747. doi:10.1109/TNS.2011.2108316

[3] I. Castiglioni, F. Gallivanone and A. Stefano, "TOUCH SUV, SIAE Registration No 007449-D006667," 2009.

[4] A. Stefano, F. Gallivanone, E. Grosso, G. Russo, C. Messa, V. Tripoli, M. C. Gilardi and I. Castiglioni "TOUCH-SUV: A Touchscreen-Assisted Tool for Quantitative, Reproducible, Clinically Feasible and Collaborative Diagnostic Reporting of Whole-Body PET-CT Studies," *Software Engineering*, Vol. 1, No. 1, 2011, pp. 1-8.

[5] W. L. Wong and R. J. Chambers, "Role of PET/PET CT in the Staging and Restaging of Thoracic Oesophageal Cancer and Gastro-Oesophageal Cancer: A Literature Review," *Abdominal Imaging*, Vol. 33, No. 2, 2008, pp. 183-190. doi:10.1007/s00261-007-9241-1

[6] G. Lucignani, "Oesophageal Cancer: Can Imaging Improve Its Assessment?" *European Journal of Nuclear Medicine and Molecular Imaging*, Vol. 35, No. 10, 2008, pp. 1921-1927. doi:10.1007/s00259-008-0884-0

[7] T. K. Ha, Y. Y. Choi, S. Y. Song and S. J. Kwon, "F18-Fluorodeoxyglucose-Positron Emission Tomography and Computed Tomography Is Not Accurate in Preoperative Staging of Gastric Cancer," *Journal of the Korean Surgical Society*, Vol. 81, No. 2, 2011, pp. 104-110. doi:10.4174/jkss.2011.81.2.104

[8] H. Miyata, Y. Doki, T. Yasuda, M. Yamasaki, I. Higuchi and Y. Makari, "Evaluation of Clinical Significance of 18F-Fluorodeoxyglucose Positron Emission Tomography in Superficial Squamous Cell Carcinomas of the Thoracic Esophagus," *Diseases of the Esophagus*, Vol. 21, No. 2, 2008, pp. 144-150. doi:10.1111/j.1442-2050.2007.00743.x

[9] M. Westerterp, G. W. Sloof, O. S. Hoekstra, F. J. T. Kate, G. A. Meijer and J. B. Reitsma, "18FDG Uptake in Oesophageal Adenocarcinoma: Linking Biology and Outcome," *Journal of Cancer Research and Clinical Oncology*, Vol. 134, No. 2, 2008, pp. 227-236. doi:10.1007/s00432-007-0275-0

