



Correlation Between FDG Hotspots on Pre-radiotherapy PET/CT and Areas of HNSCC Local Relapse: Impact of Treatment Position and Images Registration Method

Blandine Truffault, David Bourhis, Anne Chaput, Jérémie Calais, Philippe Robin, Romain Le Pennec, François Lucia, Jean-Christophe Leclère, Dorothy Gujral, Pierre Vera, et al.

► To cite this version:

Blandine Truffault, David Bourhis, Anne Chaput, Jérémie Calais, Philippe Robin, et al.. Correlation Between FDG Hotspots on Pre-radiotherapy PET/CT and Areas of HNSCC Local Relapse: Impact of Treatment Position and Images Registration Method. *Frontiers in Medicine*, 2020, 7, pp.218. 10.3389/fmed.2020.00218 . hal-02922556

HAL Id: hal-02922556

<https://hal.science/hal-02922556>

Submitted on 22 Dec 2023

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may



Correlation Between FDG Hotspots on Pre-radiotherapy PET/CT and Areas of HNSCC Local Relapse: Impact of Treatment Position and Images Registration Method

Blandine Truffault¹, David Bourhis^{1,2}, Anne Chaput¹, Jeremie Calais^{3,4}, Philippe Robin^{1,2}, Romain Le Pennec¹, François Lucia⁵, Jean-Christophe Leclère⁶, Dorothy M. Gujral^{7,8}, Pierre Vera⁴, Pierre-Yves Salaün^{1,2}, Ulrike Schick⁵ and Ronan Abgral^{1,2*}

¹ Department of Nuclear Medicine, Brest University Hospital, Brest, France, ² European University of Brittany, Brest, France, ³ Department of Medical and Molecular Pharmacology, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, United States, ⁴ Department of Nuclear Medicine and Radiology, Henri Becquerel Center, Quantif (LITIS EA 4108 – FR CNRS 3638), Rouen University Hospital, Rouen, France, ⁵ Department of Radiotherapy, Brest University Hospital, Brest, France, ⁶ Department of Oto-rhino-laryngology, Brest University Hospital, Brest, France, ⁷ Clinical Oncology Department, Imperial College Healthcare NHS Trust, Charing Cross Hospital, Hammersmith,

position. Comparison of registration method demonstrated OF and $A_{xN}R_x/R_x$ indices ($x = 30\%$ to 50% SUVmax) were significantly higher with ER vs. RR in NTP ($p < 0.03$), but not in TP. For patient position, the OF and $A_{xN}R_x/R_x$ indices were higher in TP than in NTP when RR was used with a trend toward significance, particularly for $x=40\%$ SUVmax (0.50 ± 0.22 vs. 0.31 ± 0.13 , $p = 0.094$).

Conclusion: Our study suggested that PET/CT acquired in TP improves results in the localization of FDG hotspots in HNSCC. If TP is not possible, using an ER method is significantly more accurate than RR for overlap estimation.

Keywords: FDG-PET/CT hotspots, local relapse, HNSCC, images registration, radiotherapy treatment position

INTRODUCTION

Head and neck squamous cell cancer carcinomas (HNSCC) are the sixth most common cancer (1, 2) with around 800,000 new cases worldwide in 2015. These tumors have a poor prognosis, with a 5-year survival rate $< 50\%$ (3), particularly because two thirds of patients are unfortunately diagnosed at advanced stage. In addition to

was 70Gy (2Gy/fraction/day, 5 sessions/week) over 7 weeks +/- concomitant systemic treatment: Cetuximab, Cisplatin or Carboplatin.

Follow-Up

Clinical follow-up was performed as recommended by the National Comprehensive Cancer Network (30). Patients with persistent disease on FDG-PET/CT 3 months after RT completion, and those who, after initial complete response, relapsed within the radiation field during follow-up were pooled together to comprise the LR group. Histological evidence was highly recommended; otherwise evidence of progression on imaging was used to define LR.

The following clinical characteristics were obtained for each patient and considered as variables in univariate analysis: age, sex, tumor location, AJCC stage, systemic treatment modality, RT dose and RT duration.

FDG-PET/CT Imaging

The first FDG-PET/CT (PET_A) was performed for initial staging. The post-therapeutic PET_R was defined as either the PET performed at the time of the first evaluation (3 months) in patients showing persistent/progressive disease, or the first PET performed during follow-up (suspected recurrence or systematic surveillance) that demonstrated LR. All indications for FDG PET/CT were reviewed according to guidelines (15, 30) by a multidisciplinary team.

All FDG-P

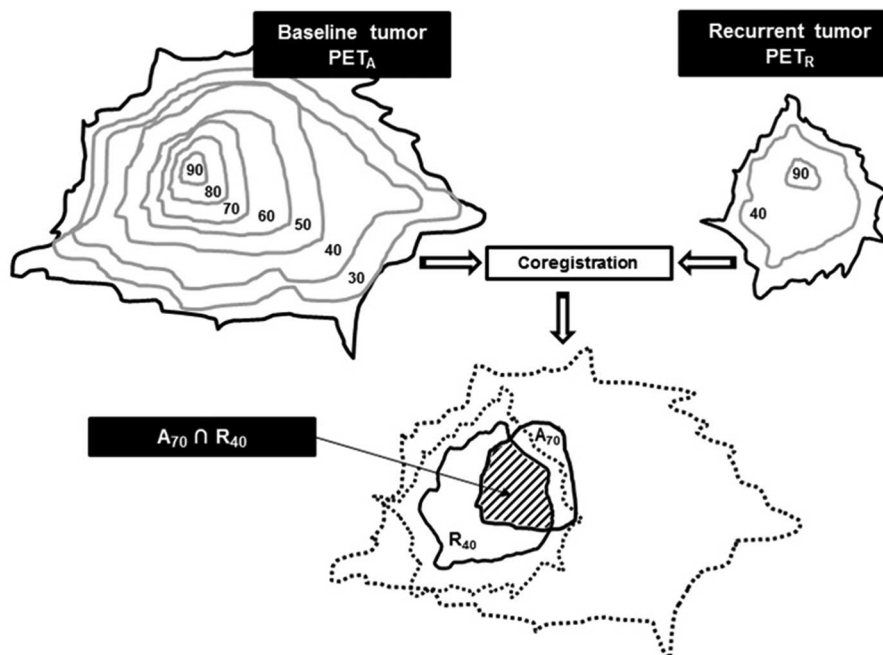


FIGURE 1 | Typical A_{70} and R_{40} sub-volumes overlap estimation after co-registration and reports. Use with permission of Calais et al. (27).

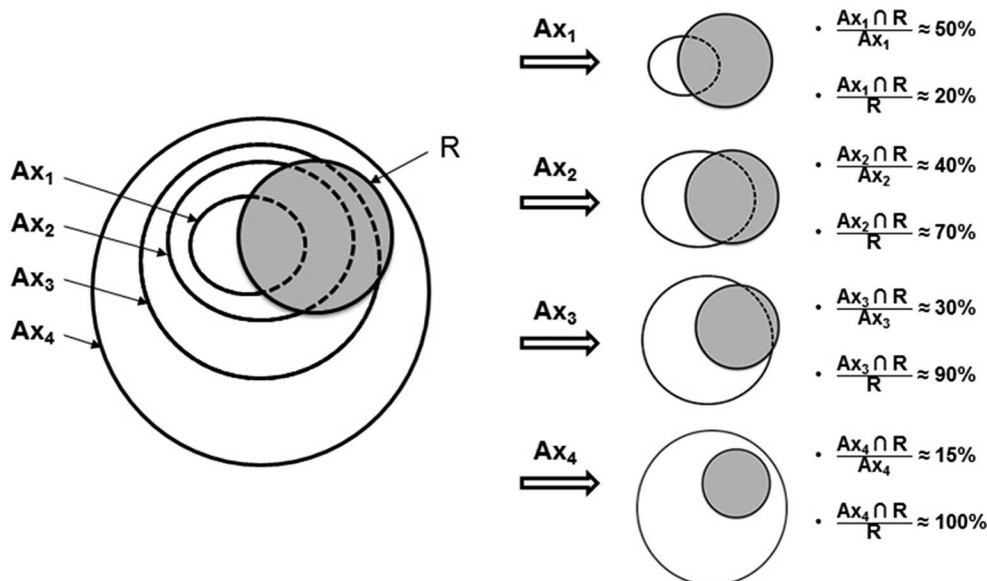


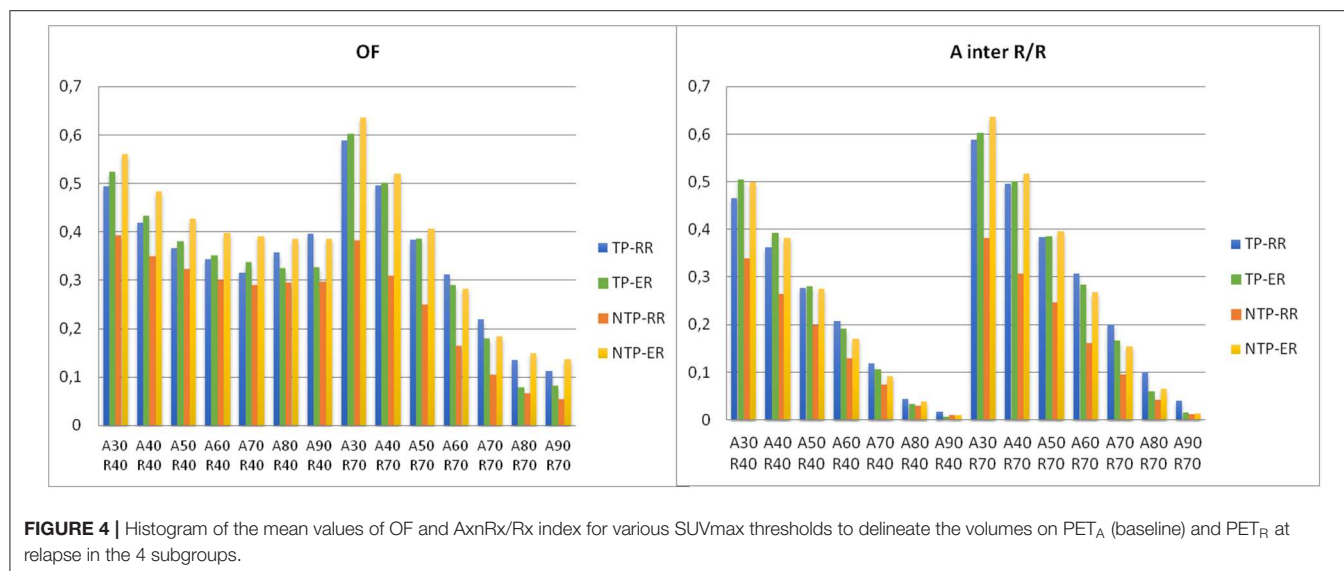
TABLE 1 | Characteristics of the 199 patients included in the study.

	TOTAL (n = 199)	CR (n = 120)	DR (n = 36)	LR (n = 43)
Age, yo $\pm$ SD	62.5 $\pm$ 10.2	61.3 $\pm$ 8.9	64.0 $\pm$ 10.2	64.7 $\pm$ 12.7
Gender, n (%)				
Male	142(71.4)	85(70.8)	26(72.2)	31(72.1)
Female	57(28.6)	35(29.2)	10(27.8)	12(27.9)
Tumor location, n (%)				
Rhinopharynx	7(3.5)	5(4.2)	1(2.8)*	1(2.3)*
Oropharynx	124(62.3)	70(58.3)	26(72.2)*	28(65.1)*
Hypopharynx	24(12.1)	14(11.7)	5(13.9)*	

TABLE 2 | Metabolic parameters on baseline PET/CT.

	TOTAL (n = 199)	CR (n = 120)	DR (n = 36)	LR (n = 43)	GR (n = 79)
SUVmax	20.0 ± 9.6	19.2 ± 9.5	20.1 ± 6.1	21.2 ± 8.2	20.7 ± 7.3
SUVmean	12.0 ± 5.6	11.3 ± 5.7	12.3 ± 3.8	12.5 ± 4.8	12.4 ± 4.3
MTV (cc)	7.7 ± 7.8	6.4 ± 7.1	9.8 ± 8.4*	9.1 ± 7.2*	9.4 ± 7.7*
TLG (g)	90.6 ± 101.8	75.2 ± 98.4	120.7 ± 111.4*	105.9 ± 80.6*	112.7 ± 95.5*

*Significantly different from CR. MTV = A₄₀.



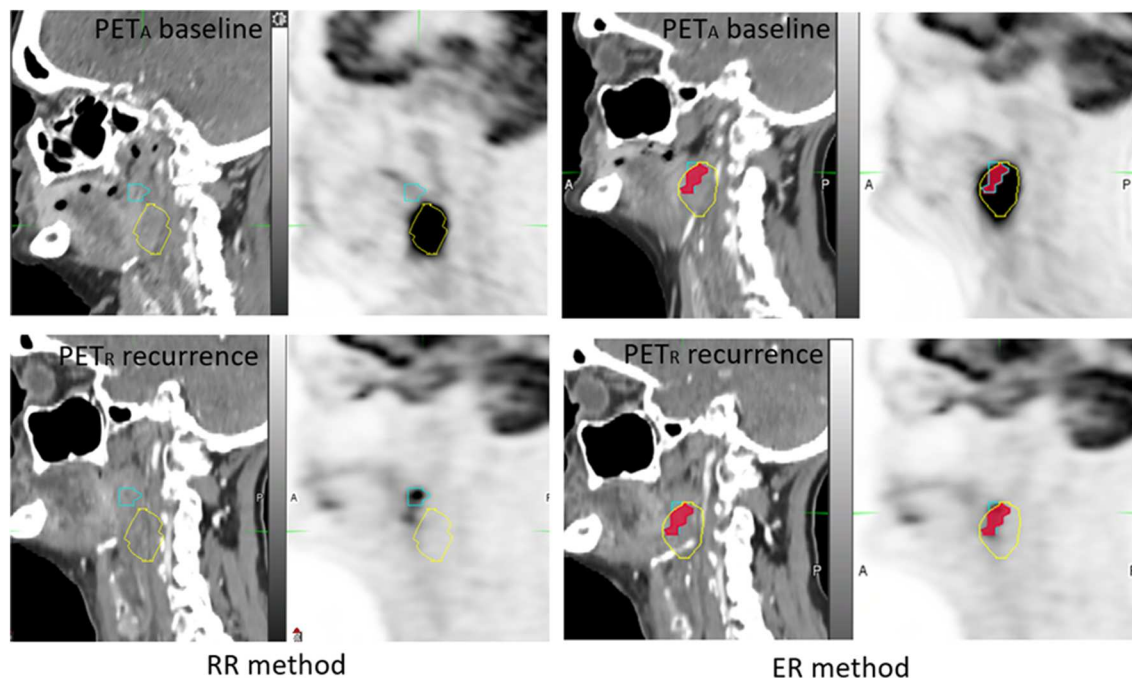


FIGURE 5 | Example of 65 year-old woman, with T3N1M0 oropharyngeal squamous cell carcinoma. Before the emergence of reflex otalgia and neck pain, a PET-CT was performed 2 months after radiotherapy and showed a local persistent disease. PET_A (images on the top) and PET_R (images on the bottom) were not scanned in treatment position (NTP) and coregistered with RR method (on the left) and ER method (on the right). A₄₀ subvolume (yellow line), R₄₀ subvolume (blue line) and A₄₀ ∩ R₄₀ (red area). The OF (A₄₀, R₄₀) index was calculated respectively at 0 and 0.80 for RR and ER registration methods.

the obtained OF(A₅₀nR₈

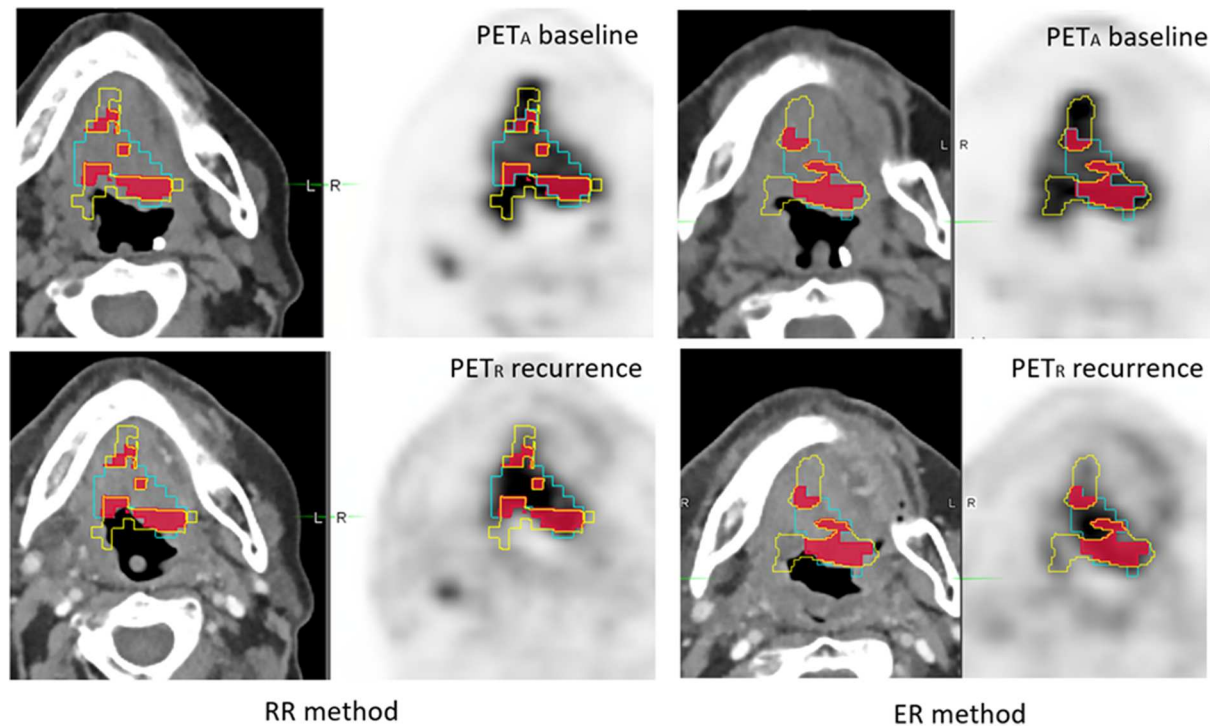
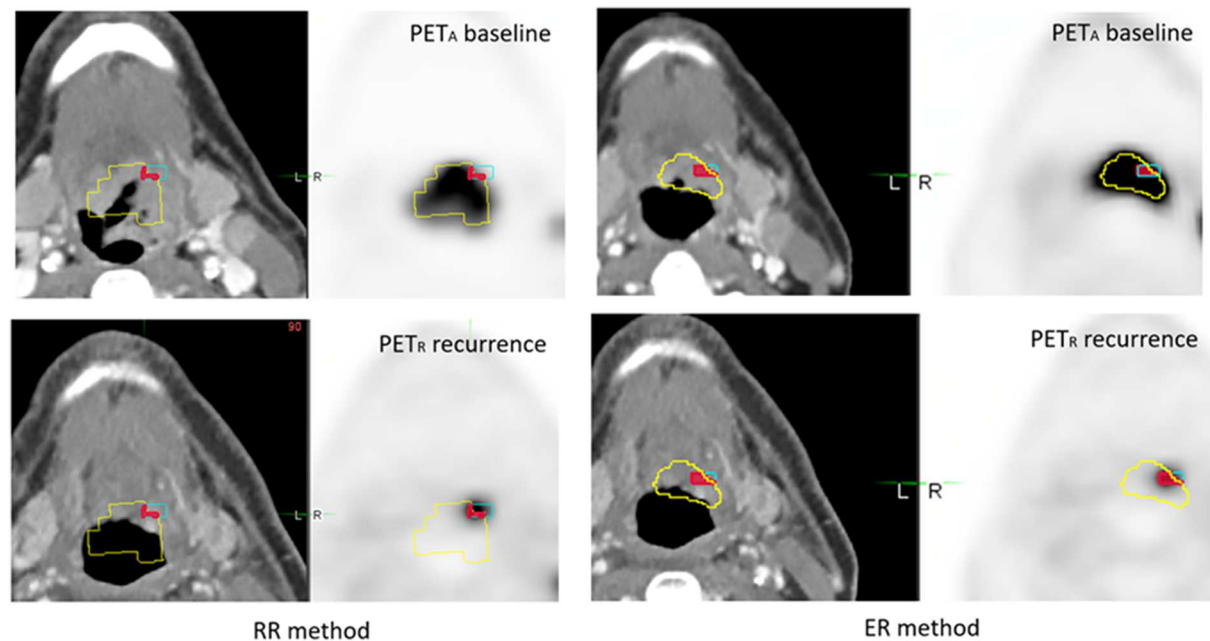


FIGURE 6 | Example of 56 year-old woman with T4N2M0 oropharyngeal squamous cell carcinoma. A therapeutic response assessment by PET/CT was performed 3 months after chemo-radiotherapy, showing persistent disease. PET_A (images on the top) and PET_R (images on the bottom) were scanned in treatment position (TP) and coregistered with RR method (left) and ER method (right). A₄₀ subvolume is represented as a yellow line, R₄₀ subvolume as a blue line and A₄₀ ∩ R₄₀ in red area. The OF (A₄₀, R₄₀) index was calculated, respectively at 0.50 and 0.51 for RR and ER registration methods.



FDG-avid tumor subvolumes. They demonstrated that $MTV > 4.4cc$ and $TLG > 34.6g$ were associated with a better 3-year overall survival ($p = 0.006$ and $p = 0.01$, respectively) in a series of 41 patients (39). These results are concordant with our findings.

Textural analysis on pre-RT FDG-PET/CT, already recognized as a prognostic factor for survival (40), could be an interesting approach to predict HNSCC local recurrence sites. Beaumont et al. showed that 15 parameters extracted from a voxel to voxel analysis, combining radiomics and spatial location, allowed better prediction of local failure than a regional analysis, with a median area under the receiver-operating curve of 0.71 (41). The published literature to date mainly underlines methods in assessing tumor hypoxia, a well-known factor for RT resistance (42, 43). Thureau et al. reported that IMRT dose-painting with pre-RT 18F-misonidazole (F-MISO) PET/CT provided NSCLC radiotherapy plan matching with dose/volume (D/V) objectives and organs at risk (OAR) tolerance (36). Patients with F-MISO positive scans who received an RT boost (70 to 86Gy) tend to have a better overall survival (median 26.5 vs. 15.3 months, $p = 0.71$) (44).

Our study has some limitations. First, although larger than previous series, the number of included patients (43 LR) is relatively low, contributing to the lack of power and the inability to confirm superiority of TP when the RR method was used

5. Tejpal G, Jaiprakash A, Susovan B, Ghosh-Laskar S, Murthy V, Budrukkar A. IMRT and iGRT in head and neck cancer: have we delivered what we promised? *Indian J Surg Oncol.* (2010) 1:166–85. doi: 10.1007/s13193-010-0030-x
6. Tobias JS, Monson K, Gupta N, Macdougall H, Glaholm J, Hutchison I, et al. Chemoradiotherapy for locally advanced head and neck cancer: 10-year follow-up of the UK Head and Neck (UKHAN1) trial. *Lancet Oncol.* (2010) 11:66–74. doi: 10.1016/S1470-2045(09)70306-7
7. Leeman JE, Li J-G, Pei X, Venigalla P, Zumsteg ZS, Katsoulakis E, et al. Patterns of treatment failure and postrecurrence outcomes among patients with locally advanced head and neck squamous cell carcinoma after chemoradiotherapy using modern radiation techniques. *JAMA Oncol.* (2017) 3:1487–94. doi: 10.1001/jamaoncol.2017.0973
8. Leclerc M, Maingon P, Hamoir M, Dalban C, Calais G, Nuyts S, et al. A dose escalation study with intensity modulated radiation therapy (IMRT) in t2N0, t2N1, t3N0 squamous cell carcinomas (SCC) of the oropharynx, larynx and hypopharynx using a

- radiotherapy in lung cancer. *Radiat Oncol.* (2018) 13:208–7. doi: 10.1186/s13014-018-1147-2
37. Abgral R, Keromnes N, Robin P, Le Roux P-Y, Bourhis D, Palard X, et al. Prognostic value of volumetric parameters measured by 18F-FDG PET/CT in patients with head and neck squamous cell carcinoma. *Eur J Nucl Med Mol Imaging.* (2014) 41:659–67. doi: 10.1007/s00259-013-2618-1
 38. Abgral R, Valette G, Robin P, Rousset J, Keromnes N, Le Roux P-Y, et al. Prognostic evaluation of percentage variation of metabolic tumor burden calculated by dual-phase (18) FDG PET-CT imaging in patients with head and neck cancer. *Head Neck.* (2016) 38 Suppl 1:E600–. doi: 10.1002/hed.24048
 39. Mapelli P, Broggi S, Incerti E, Alongi P, Kirienko M, Fiorino C, et al. FDG-PET/CT predicts outcome in oropharyngeal carcinoma patients undergoing intensity modulated radiation therapy with dose escalation to fDG-avid tumour volumes. *Curr Radiopharm.* (2017) 10:102–10. doi: 10.2174/1874471010666170413151108
 40. Guezennec C, Robin P, Orlhac F, Bourhis D, Delcroix O