Journal of Nuclear Medicine, published on January 10, 2020 as doi:10.2967/jnumed.120.241778

SUV_{max-V} for assessing treatment response in FDG-PET Imaging of Patient-Derived Tumor Xenografts involving Triple-Negative Breast Cancer

Eric Laffon [1,2,3*], Roger Marthan [1,2,3].

[1]CHU de Bordeaux - F-33000 Bordeaux, France.

[2]Univ. Bordeaux, Centre de Recherche Cardio-Thoracique de Bordeaux, F-33000 Bordeaux, France.

[3]INSERM U-1045, Centre de Recherche Cardio-Thoracique de Bordeaux F-33000 Bordeaux, France.

*Correspondence: Eric Laffon, Service de Médecine Nucléaire, Hôpital Haut-Lévèque, avenue de Magellan, 33604 Pessac, France. elaffon@u-bordeaux.fr

TO THE EDITOR:

In the preclinical arm of a co-clinical trial, Dr Savaikar et al. recently optimized ^{18}F-FDG-PET imaging biomarkers of response to a combined docetaxel/carboplatin therapy in patient-derived tumor xenografts (PDX) involving triple-negative breast cancer (TNBC)(*1*). Twenty one necrotic-core phenotype tumors as well as 13 solid tumors were examined. Besides a preclinical µPERCIST paradigm, 43 imaging metrics were evaluated, both in the whole tumor and in a single highest-intensity tumor slice. These metrics included (i) mean standard uptake values (SUV) obtained from various fixed percentages of the maximal-SUV thresholds (SUV_{Th}), and mean SUVs obtained from the voxels involved in a sphere centered at the maximal-SUV voxel (SUV_{Peak}). The following spherical volumes of 4 – 14 – 33mm^3 (radius of 1 – 2 – 3voxels) were considered, leading to SUV_{P4} – SUV_{P14} – SUV_{P33}, respectively. In particular, Bland-Altman plots of test-retest data allowed us to estimate SUV_{25} reproducibility (also called repeatability) percentage (R; 95%-confidence) of about 20 / 25% for solid / necrotic tumors (from Figure 3C / G, respectively). Finally, a coined quantitative response assessment score favored SUV_{25} followed by SUV_{P14} as optimal metrics of response to therapy in PDX models.

We would like to stress the central role of R in assessing treatment response for any investigated SUV metrics, that is, the minimal relative change between two SUVs assessed from two successive examinations that is required to consider a significant difference *(2)*. In this

connection, we suggest that a further SUV metrics, i.e., the $SUV_{max\text{-}V}$, might be particularly suitable in the current context involving 21 tumors with a necrotic-core phenotype (and with varying tumor dimensions), thus exhibiting a low ^{18}F-FDG uptake at the core and well-separated ^{18}F-FDG-positive areas (Figure 2 by Savaikar et al.). Indeed, it has been previously shown, in lung cancer patients, that R of $SUV_{max\text{-}N}$, which is an average SUV computed from the N hottest voxels regardless of their location within a ^{18}F-FDG-positive lesion, was significantly lower for N = 30 than that of SUV_{Peak} obtained from maximal SUV and its 26 neighboring voxels *(3)*. In a subsequent study, $SUV_{max\text{-}40}$ was found to more likely represent the most metabolically-active portions of tumors than SUV_{Peak} that was obtained from the voxels involved in a 1-mL sphere centered at the maximal-SUV voxel, with close R performance *(4)*. Finally, the $SUV_{max\text{-}N}$ procedure for treatment-response assessment has been described in a Takayasu-arteritis patient, emphasizing that the greater the N value, the lower the $SUV_{max\text{-}N}$ R and, hence, the more efficient the metrics (Table 1 in *(5)*). Noteworthy, since the voxel volume may depend on the PET system, instead of the $SUV_{max\text{-}N}$, one could alternatively use the $SUV_{max\text{-}V}$ defined as an average SUV computed from an arbitrary total hottest volume (V), regardless of the location within the ^{18}F-FDG-positive lesion of the hottest voxels included in it. When comparing baseline / after-treatment scan, V should be set in the scan showing the lowest total ^{18}F-FDG-positive volume, but at the greatest possible value since the greater the V value, the lower the $SUV_{max\text{-}V}$ R.

To conclude, Savaikar et al. addressed the important issue of reaching a consensus on reproducibility of imaging metrics for assessing response to therapy in oncology animal models *(1)*. We suggest that the $SUV_{max\text{-}V}$ metrics may have a place in this toolbox, with V set at the greatest possible value in the scan showing the lowest tumor uptake (that is expected to be the post-treatment one). Finally, in the current series, whether R of $SUV_{max\text{-}14mm3}$ or $SUV_{max\text{-}33mm3}$ might be lower than R of SUV_{25}, SUV_{P14mm3} and SUV_{P33mm3} remains to be assessed.

REFERENCES

1. Savaikar MA, Whitehead T, Roy S, et al. SUV25 and μPERCIST: precision imaging of response to therapy in co-clinical FDG-PET imaging of triple negative breast cancer (TNBC) patient-derived tumor xenografts (PDX). *J Nucl Med.* 2019 Nov 22. doi: 10.2967/jnumed.119.234286. [Epub ahead of print]
2. Bland JM, Altman DG. Statistics notes: measurement error. *BMJ.* 1996;313:744–746.

3. Laffon E, Lamare F, de Clermont H, Burger IA, Marthan R. Variability of average SUV from several hottest voxels is lower than that of SUVmax and SUVpeak. *Eur Radiol.* 2014;24:1964–1670.
4. Laffon E, Burger IA, Lamare F, de Clermont H, Marthan R. SUVpeak performance in lung cancer: comparison to average SUV from the 40 hottest voxels. *J Nucl Med.* 2016;57:85–88.
5. Caubet O, Meunier V, Marthan R, Laffon E. Early assessment of treatment response in Takayasu arteritis: an 18FDG PET procedure. *Clin Nucl Med.* 2016;41:743–745.