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Repeatability of Quantitative Whole Body ^{18}F-FDG PET/CT Uptake Measures in NSCLC Patients: Dynamic versus Test-Retest Design.

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TO THE EDITOR: In the September issue of *the Journal of Nuclear Medicine,* Kramer et al. comprehensively investigated repeatability (R) of various quantitative ^{18}F-FDG uptake metrics in lung cancer patients, including SUV_{max}, SUV_{mean}, SUV_{peak}, metabolically active tumor volume (MATV) and total lesion glycolysis (TLG)*(1)*. A test-retest study was performed within 3 days, involving double baseline whole-body ^{18}F-FDG PET/CT at 60 and 90 minutes post-injection (p.i.). Results were compared to those of some previously published studies performed in various oncologic diseases, such as ovarian cancer, lung cancer (NSCLC), esophageal cancer, and liver metastases for TLG in particular.

However, a previous study regarding TLG variability in lung cancer patients, involving that of SUV_{mean} and MATV, was not included in Kramer et al.'s comparison *(2)*. In that study, R was differently assessed from a dynamic acquisition involving 10 frames within 60–110 min p.i. over 13 lesions, instead of a test-retest acquisition within 3 days over a total of 60 lesions in Kramer et al.'s study. Moreover, SUV_{peak} repeatability was obtained from a further dynamic

study involving 20 lung cancer lesions *(3)*. We thought of interest to compare the two methods, i.e. dynamic and test-retest design.

Values for dynamic R obtained within 60–110 min p.i. *versus* test-retest R obtained at 90 min p.i. for all lesions by Kramer et al. (R is reproducibility coefficient in Table 3) are the following: 19.6 vs 23.3%, 14.1 vs 17.8%, 13.2 vs 15.8%, 31.6 vs 23.7%, 36.4 vs 30.7% for SUV_{max}, SUV_{mean}, SUV_{peak}, TLG and MATV (95% reliability), respectively *(1-3)*. Although the parameter range and the 50% of the SUV_{max} thresholding method (used for assessing SUV_{mean}, MATV, and hence TLG) were not exactly similar, the dynamic R percentages are consistent with the test-retest ones, as much as R estimate uncertainty is not provided.

Let us further discuss the comparison between the two designs. The dynamic design involved ten 2.5-min frames, leading to a ±12.5-min time window around a mean uptake time, in comparison with the test-retest one that reported a maximal range of 7 min for uptake time (scan 1 in Table 1 by Kramer). We suggest that reducing the acquisition time for bed positions, i.e. < 2.5-min that is possible with modern PET-CT systems, and reducing the number of dynamic frames, may bridge the two designs. In the framework of assessing response to treatment, it is noteworthy that the dynamic design does not take into account some origins of parameter variability such as changes in plasma glucose level (within normal range), injected dose and differences in uptake time. However, Kramer et al. reported that glucose correction does not improve R performance (and even deteriorates it) and the relative uncertainty about the injected dose is usually very low *(1)*. Regarding differences in uptake time, Kramer et al. showed that the correction proposed by van den Hoff et al. significantly reduced differences between 60-min and 90-min data *(4)*. We would like to emphasize that (i) the time window of the dynamic design includes a variability of ±12.5-min around a mean uptake time that may take into account differences in uptake time usually met in current clinical practice, and alternatively (ii) simply

removing the ^{18}F physical decay-correction can reduce differences between 60-min and 90-min SUVs *(5)*. Finally, the dynamic design involving several frames reduces the number of lesions to be investigated (and hence that of patients to be recruited) for reliably determining R, in comparison with the test-retest study, since, for the same number of lesions, the greater the number of dynamic frames the lower the R estimate uncertainty. We thus suggest that the dynamic design takes into consideration both the patient radiation dose and a busy clinical practice.

In conclusion, the comprehensive study of Kramer et al. about repeatability of various ^{18}F-FDG uptake measures will be very useful to the nuclear physicians in their current practice *(1)*. It has been achieved by using a test-retest design, and we would like to emphasize that the tool box for assessing measurement uncertainty in quantitative PET imaging fortunately offers different designs, each involving pros and cons. An alternative dynamic design is available that may be particularly suitable when the role of technical parameters in this uncertainty is investigated in an arbitrary PET-CT system. Nevertheless, whatever the design, it clearly appears that guidelines should recommend that any quantitative outcome be accompanied with its measurement uncertainty, which should be specifically determined for each PET-CT system as soon as commissioning.

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