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COMMENTARY

Correction for Partial Volume Effect Is a Must, Not a Luxury, to Fully Exploit the Potential of Quantitative PET Imaging in Clinical Oncology

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Abstract
The partial volume effect (PVE) is considered as one of the major degrading factors impacting image quality and hampering the accuracy of quantitative PET imaging in clinical oncology. This effect is the consequence of the limited spatial resolution of whole-body PET scanners, which results in blurring of the generated images by the scanner's response function. A number of strategies have been devised to deal with partial volume effect. However, the lack of consensus on the clinical relevance of partial volume correction and the most appropriate technique to be used in the context of clinical oncology limited their application in clinical setting. This issue is debated in this commentary.

Key words: PET, Partial volume effect, Partial volume correction, Quantification, Clinical oncology

PET is without any doubt the imaging modality of choice for the *in vivo* quantitative assessment of molecular targets in a wide range of oncologic malignancies. However, its quantitative potential is still hampered by a number of physical degrading factors including partial volume effect, which results from the limited spatial resolution of current generation whole-body PET scanners. Although the total number of counts is preserved, partial volume effect spreads them over a larger region, thus making tiny malignant lesions appear greater but with less tracer uptake [1, 2]. A number of partial-volume-correction (PVC) strategies have been devised and applied with a certain degree of success in research studies, albeit without reaching the level of maturity needed for implementation in the clinic, predominantly in oncological, cardiovascular, and neurological imaging where it is expected to open new avenues in disease understanding and management [3].

The systematic review and meta-analysis by Cysouw et al. about the impact of PVC in quantification of malignant lesions is an important contribution to the field [4]. The authors have made an effort in reviewing the existing literature reaching a conclusion that the role of PVC on a routine basis in daily clinical practice of PET is at present still uncertain given the many uncertainties involved in PVC methodology. We wish to point out that regardless of the outcome of this meta-analysis, which intrinsically bears a number of limitations and pitfalls [5, 6], the authors of the article above recognized in a previous article that ignoring such an important element in PET quantification may adversely affect the impact of this most powerful modality in managing patients with cancer and other serious disorders [7]. This study assessed the influence of PVC combined with several volumes of interest (VOI) techniques on the accuracy

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and precision of PET quantification. In line with the meta-analysis, the authors suggest that PVC is beneficial but that several challenges prevent its use in clinical setting. A comprehensive discussion of the limitations of meta-analysis is beyond the scope of this communication. Still, we would like to express our opinion that "*the assumption that a meta-analysis routinely represents the final and accurate viewpoint in an area of research is not warranted*" [8].

Initial applications of tomographic imaging either with SPECT or PET primarily dealt with assessment of central nervous system and cardiac disorders. However, compared to SPECT, PET imaging has had a far-reaching impact in investigating a multitude of maladies throughout the body. Significant improvement in spatial resolution of PET instruments over the past two decades has allowed visualizing small lesions in many organs. Unfortunately, this has given the impression that images generated by PET can be used without further refinement, assuming they represent the ultimate results for both research and clinical purposes. One of the early observations made when combining PET images with those of CT and MRI to determine the complementary roles of structural and molecular imaging was the impact of unavoidable and unexpected effects of structural abnormalities on quantitative measurements made by PET. Our group noted cortical atrophy as seen on CT or MRI results in significant underestimation of metabolic activity as calculated by PET [9]. This observation led to employing somewhat primitive approaches to segment the brain and the cerebral spinal fluid (CSF) to correct partial volume effects of brain activity and improve the quantification of the imaging data with PET. Soon thereafter, the introduction of novel segmentation techniques with MRI further enhanced the impact of PVC in assessing abnormalities in various organs [10]. This phenomenon is particularly true for abnormalities that are located in mid-trunk regions where the body size, juxtaposition of different tissue classes, and motion are major offenders for accurate quantification with PET.

Segmentation, although a major issue facing PET quantification, is a challenge in itself that is outside the scope of this comment. The basic physics of PET supports the idea that PVC of PET data contributes to the improvement of the quantitative accuracy of image-derived PET metrics and interpretive certainty. We agree that there is a way to go before the clinical significance of PVC is clearly documented. However, this does not justify explaining a way or minimizing the crucial influence that PVC has upon quantitative PET measurements. PVC is strongly needed to obtain reliable numbers for accumulated tracer activity in the body, not only in single PET scans, but particularly when repeat scans are required, because then, all measurement errors contribute twice, which puts even greater demand on measurement certainty and its critical role in assessing response to treatment when significant shrinkage and reduction in tumor size is expected [11]. This might probably also apply to differentiation and better characterization of suspicious small focal uptake.

Ignoring PVC has resulted in advocating the view that lung lesions with uncorrected SUV less than 2.5 are benign and should not be investigated by surgery or biopsy for determining the true nature of such abnormalities. Unfortunately, this poorly conceived concept led to underdiagnosing this lethal cancer in many patients and its serious consequences [12–15]. These investigators were unaware that spatial resolution of PET in clinical imaging (lung) is substantially lower than what is measured when characterizing the performance of PET scanners using phantom studies [16, 17]. While the spatial resolution of PET as measured using point sources is approximately 4–6 mm, its true value in the trunk is substantially worse in organs such as the lungs and the liver, and as such, lesions that are smaller than 1 cm may pose a serious challenge with this technology. This is particularly true in lesions that are located in the lower lungs and in the liver where respiratory motion substantially blurs PET images [18, 19]. Unfortunately, respiratory motion correction is suboptimal for correcting this physiological artifact and has not been able to adequately address this major issue in the clinical setting.

The major advantages of PET over conventional imaging techniques including CT and MRI are its extraordinary sensitivity and potential accurate quantification of disease activity at various stages of the disease. Therefore, improvements in accurate quantification and efforts to perform global assessment of disease activity throughout the body in patients with cancer or other disorders have become a necessity for both diagnostic and therapeutic purposes [20]. Such measurements will require partial volume-corrected values along with accurate measurement of the size of the abnormalities visualized by PET [21]. This will allow for quantification of global disease activity in each lesion as well as the overall disease burden throughout the body. These measurements will heavily depend on PVC, and therefore, ignoring this important element in PET quantification will undermine the impact of this incredibly powerful technology [22–24].

In recent years, great interest in assessing cardiac calcification in the coronary arteries has resulted in adopting measurement techniques that are suboptimal for detection and quantification of calcification in arteries that are only 1–2 mm in diameter and are subject to cardiac and respiratory motion [25, 26]. We believe every effort should be made to avoid such approaches in the future. Therefore, there is a dire need to employ methodologies that can overcome these unavoidable physical and physiological obstacles for accurate performance of PET imaging in certain organ disorders.

We agree with the authors about the difficulties that we are facing in accurate partial volume correction with the existing modalities used by practicing PET specialists. But we believe that what is currently being done is not adequate

enough for optimal utilization of the information that is provided by PET for managing the most serious disease of mankind. Therefore, we would recommend major efforts be made towards standardization and harmonization of imaging protocols, consensus on which PVC and consequent segmentation technique to be used for each specific application and localization, assessment of their characteristics, and clinical value on the way to their implementation on software supplied by scanner manufacturers for routine management of patients with cancer and other serious diseases.

Compliance with Ethical Standards

Conflict of Interest

All authors declare that they have no conflict of interest.

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