Potential Applications of PET-Based Novel Quantitative Techniques in Pediatric Diseases and Disorders

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KEYWORDS

• PET • Pediatrics • Quantitative imaging

KEY POINTS

- Hybrid PET imaging has significantly expanded the applications of this imaging modality.
- Semi-quantitative PET/CT imaging has been the predominant technique for assessment of PET images due to its simplicity and practicality.
- Respiratory motion has degrading effect on quantitative PET and its correction improves the image accuracy.
- By combining the metabolic and volumetric information from the PET images, global metabolic activity has been shown to be a better predictor of disease.

INTRODUCTION

The progress made in hybrid PET imaging during the last few decades has significantly expanded the role of this modality in both clinical and research applications.[1–3] When computed tomography (CT) and magnetic resonance imaging are combined with PET imaging, structure and function are mapped in one image, and the quantitative accuracy of the data is improved. The role of PET/CT pediatric oncological and non-oncological disorders has been widely discussed in the literature.[4,5] In this correspondence, we will briefly review different quantitative techniques which could potentially improve PET/CT imaging of the pediatric diseases.

SIMPLIFIED PET QUANTIFICATION OF UPTAKE THROUGH STANDARDIZED UPTAKE VALUES

In an ideal setting, PET quantification should adopt tracer kinetic models. However, this approach has substantial limitations because it requires dynamic data acquisition and continuous arterial blood sampling. Therefore, over the past 2 decades, a simple semiquantitative method has been adopted. This method is practical and can be done in the clinic.

Standardized uptake value (SUV) was developed to measure radiotracer concentration in a specified region of interest at various time points after the injection of the compound.[6] Validation studies show a linear correlation between SUV and kinetic modeling.[7–9]

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PET Clin 15 (2020) 281–284
https://doi.org/10.1016/j.cpet.2020.03.010

SUVs are expressed as maximum SUV (SUV_{max}), representing the single highest voxel/pixel in a defined region/volume of interest, or as mean SUV (SUV_{mean}), which provides the average SUV in all voxels/pixels in the assigned location or volume of interest. The specific factors that can influence the accuracy of SUV assessment include extravasation at the site of administration of radiotracer, residual activity in the syringe, and discrepancy between the time recorded in the dose calibrator and the PET acquisition and injection times.[10,11] High blood glucose levels lead to suboptimal SUV measurements.

ADVERSE EFFECT OF RESPIRATORY MOTION ON QUANTITATIVE PET DATA

Respiratory motion is a major factor adversely affecting the accuracy of PET measurements. This factor is most significant when the structure of interest is in the chest or upper abdomen. Correction for misalignment between PET and CT scans caused by respiratory motion has been challenging and is therefore an area of current investigations.[12,13]

PARTIAL VOLUME EFFECT AND ITS IMPACT ON PET QUANTIFICATION

Partial volume effect (PVE) is caused by the suboptimal spatial resolution of PET and results in degradation of the images generated and also underestimation of the true levels of the administered compound at the targeted sites. Respiratory or cardiac motions lead to pronounced effects caused by movement of the structures.

Over the years, attempts have been made to correct for PVE by using several data acquisition strategies.[14,15] Partial volume correction (PVC) is a necessity and should not be ignored in the clinical setting. Studies of patients with lung lesions have shown that PVC leads to an increase the accuracy of SUV estimates from 55% to 89% in lesions smaller than 2 cm.[16]

GLOBAL DISEASE BURDEN: ASSESSING GLOBAL METABOLIC ACTIVITY

The concept of global metabolic activity assessment was introduced in 1993 for quantifying overall metabolic activity in patients with Alzheimer disease compared with age-matched controls.[17] This innovative approach revealed substantial differences between the 2 populations and led to a new beginning in PET quantification. This idea was based on combining volumetric and metabolic data into a single parameter, named global disease burden. In the late 1990s, the concept of total lesion glycolysis (TLG) was introduced to measure the overall metabolic response of the lesion to cancer treatment.[18]

Studies show that this approach correlates with other PET response parameters and is reproducible. Thus, global disease measurement gives information that is complementary to that of conventional SUV and its variants and further enhances the role of PET.

With the advances made in medical image segmentation of various structures, global disease assessment has become more powerful. Commercial image analysis software now provides schemes for the generation of highly reproducible and accurate data with excellent agreement with manual measurements.

Recent publications indicate the feasibility of the global assessment methods for assessing malignant mesothelioma,[19] lymphoma,[20] sarcoidosis,[19] Crohn disease,[21] radiation pneumonitis,[22,23] brain disorders,[24,25] and atherosclerosis.[26–28] By adopting commercially available software, 18F-fluorodeoxyglucose (FDG)–avid abnormalities can be segmented to generate the metabolically active volume (MAV) and the partial volume corrected SUV_{mean} ($pvcSUV_{mean}$). These values permit the calculation of the partial volume corrected metabolic volume product (pvcMVP), which leads to $pvcMVP_{mean} = MAV \times pvcSUV_{mean}$. In addition, global disease activity score can be obtained by summing pvcMVPs in all FDG-avid lesions in the body. One review of metabolic tumor volume and total glycolysis in solid tumors concluded that "both metabolic tumor volume and TLG have the potential to become valuable as prognostic biomarkers for survival outcome, clinical staging, and response to both neoadjuvant and concurrent therapies."[29] Therefore, the authors anticipate the development of more sophisticated and automated software schemes that will permit the generation of these quantitative parameters for assessing disease activity. Such measurements may provide clinicians with a single number summing up the overall disease activity throughout the body for monitoring and evaluating treatment response which can be potentially used in pediatric imaging.[30]

SUMMARY

The introduction of hybrid PET/CT has allowed clinicians to combine structural and molecular data at the same setting, and this has brought about a paradigm shift in diagnostic imaging. At present, molecular imaging with PET is at the forefront of patient management in many disciplines, including pediatrics. This powerful combined modality can be used in the initial diagnosis and later phases

of the disease, and following various interventions. Adopting PET/CT spares patients from futile and costly therapies as well as considerable risks. The application of novel quantitative methods described in this article will enhance the impact of modern imaging modalities in variety of clinical settings. This modality will further improve the outcome from many serious diseases and disorders and will also result in reducing health care costs.

ACKNOWLEDGMENTS

The content of this article was adapted from a previous publication on the same topic by the same authors.[9]

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