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Beyond stillness: the importance of tackling patient's motion for reliable parametric imaging

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Positron emission tomography (PET) is currently going through a technological revolution marked by the introduction of long axial field of view (LAFOV) PET systems, advanced processing tools based on artificial intelligence, and the implementation of kinetic models directly within the scanner console for dynamic acquisitions [1–4]. The combination of these technologies is now opening new transformative possibilities in the field of nuclear medicine enabling researchers to glean more insightful information about physiological processes, interconnection between organs, and the differentiation of healthy, inflamed, and tumoral tissues [5, 6]. The significance of these emerging areas for clinical practice is further demonstrated by numerous studies that explore the feasibility and reliability of kinetic applications for tumour prognosis, particularly when employing [¹⁸F] FDG [7–9].

Despite the advantages of kinetic analysis and the development of LAFOV PET, the extended acquisition protocol inevitably implies various forms of patient motion, which can exert a significant influence on the quality and reliability of parametric PET images [10–12]. In the context of reduction of its effects, extensive efforts have been dedicated on addressing cardiac and respiratory motion [13–16]. In addition, the spatial mismatch of the time-frames is another likely source of error for parameter estimation as it first causes a misalignment among the PET frames and the CT image for attenuation correction (CTAC) and second it can generate inconsistencies when applying kinetic modelling at voxel level which leads to artefacts in quantification. Given

the potential role of parametric imaging in clinical decision-making, it becomes imperative to acknowledge how motion may impact dynamic PET analysis and the need to introduce robust and reliable methods to solve this issue.

A recent Image-of-the-Month publication underlines the urgency of solving this aspect for clinical applications illustrating the case of a LAFOV PET image affected by patient respiratory motion, and the effects of this motion on the evaluation of the Patlak net influx rate (K_i) image [17]. In this study, the authors investigated the motion artefacts in the context of lymph node lesions and found that within the acquisition window, the displacement of lymph nodes covered approximately 6–7 mm, a relatively small magnitude but significant enough to severely disrupt the Patlak analysis in the region of interest. While PET image resolution is about 3.5 mm, a lesion movement more than twice this measure was sufficient to introduce inaccuracies in the K_i images. Notably, such impactful consequences were obtained even if the dynamic acquisition was shortened to only 15 min by using a population IF — a situation that is expected to be less susceptible to motion than in traditional dynamic PET.

Nevertheless, some worrying effects can be distinguished on parametric images caused by the spatial inconsistencies of lesion position over time. Firstly, motion can lead to a reduced volume of the lesion exhibiting a positive net influx rate. Secondly, the K_i image can assume negative values, primarily observed in the region of the lesion most susceptible to motion effects. These findings suggest that the impact of uneven patient motion can differ across various regions of the body resulting in a variable distribution of artefacts within the parametric images and most importantly in erroneous quantification. Therefore, motion needs to be considered carefully when kinetic analysis is applied.

In the context of dynamic image analysis, the consequences of patient motion can further lead to an inaccurate definition of the image-derived input function (IDIF) significantly impacting the estimation of the kinetic parameters.

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Whether the IDIF is generated manually from PET frames, or automatically segmented from CT images, the presence of thoracic motion risks to compromise the accurate assessment of blood activity curve. When generated manually, an average of the earlier PET frames is typically used to define a volume of interest (VOI) in a large blood pool. However, if substantial patient motion occurs during the image acquisition, the VOI defined in earlier frames will be misplaced in later frames, leading to incorrect measurement of blood activity. Alternatively to the manual definition, the VOI used to extract the IDIF can be defined automatically in the CT images. In this case, inaccuracies in IDIF definition can arise from both the mismatch between PET and CT, as well as from motion occurring during the acquisition. When it comes to the particular case of K_i estimation with Patlak analysis, it has been shown that subject motion during scanning will affect the area under the curve of the IDIF and thus lead to erroneous K_i values [18].

The correction for motion requires the following steps:

- (1) alignment of CTAC with all PET frames,
- (2) reconstruction of all PET frames, and
- (3) co-registration of all PET frames in one position which could be the CT position.

Any image manipulations are not trivial and require a specific image treatment that should be done carefully for avoiding the introduction of other sources of error. The key limitation is that direct parametric reconstruction requires the incorporation of motion information and this is something not available at the current clinical systems [19]. Therefore, caution needs to be taken when direct parametric reconstruction is applied in the console of the scanners.

The results reported in literature reinforce the importance of motion correction to achieve greater accuracy and reliability for appropriate parametric analysis and avoid possible misjudgements at the clinical level. In fact, the possible changes in net influx values, attributable to patient motion, carry significant clinical implications. For example, the fluctuations in K_i values induced or reduced by motion have the potential to produce erroneous assessments of tumour metabolism, obscure quantitative differences, and lead to overestimation or underestimation of disease severity. This, in turn, can result in misdiagnoses, suboptimal treatment planning, and inadequate monitoring of therapeutic responses.

The integration of tools within the standard clinical practice capable of directly addressing patient motion is both timely and critical. This urgency is underscored by the fact that most scanner vendors now offer software for parametric image reconstruction directly from the scanner's console. However, a notable gap exists concerning the implementation of processing methods to mitigate the impact of motion

within the tomographic image reconstruction procedures [15]. The unsupervised generation of parametric images and the potential inaccuracy due to patient motion represent a serious concern for the advancement of the field: it may have highly relevant implications for the reliability of the results, thereby invalidating even fundamental tasks, such as tumour delineation and precise determination of quantitative values. Considering the expanding role of parametric analysis in clinical practice, the ability to accurately produce parametric imaging data is a central challenge in the translation of parametric imaging into clinical application. Therefore, it is about time that robust solutions to correct for any type of body motion became available in the clinical systems.

Declarations

Competing interests Author J. S. and C. T. declare collaboration and funding from Siemens Healthineers. C. T. also declares funding from Positrono and General Electric Healthcare. All the other authors declare they have no financial interests.

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