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EDITORIAL

Is radionuclide transmission scanning obsolete for dual-modality PET/CT systems?

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Background

With the introduction of dual-modality PET/CT imaging, the nuclear medicine community is witnessing a revolution in its daily clinical practice. The hope is that this technology will alleviate the complexity of the clinical decision-making process and improve patient management [1]. Even though combined PET/CT units have been accepted commercially, the clinical benefits of and the need for these systems remain controversial [2] and are still being debated [3]. For example, PET alone provides enough information to resolve clinically relevant metabolic problems for many malignant diseases, offering a sensitivity and specificity in excess of 90%; some argue that an incremental improvement in specificity or sensitivity beyond that point probably cannot justify the cost of performing image fusion systematically for all patients on a routine basis. The marketing strategy of vendors (supported by many scientists) aiming to achieve wider diffusion of hybrid PET/CT technology in clinical practice is that the added value of combined units is well established and represents the ultimate solution for image co-registration, allowing appropriate combination of imaging technologies to yield useful fusion of functional and anatomical images [1]. It appears that more than 90% of last year's PET sales were PET/CT; this is leading almost all scanner manufacturers to entirely replace PET-only scanners by combined PET/CT, a questionable choice according to some active researchers in the field [2]. Whereas combined PET/CT has many interesting features and offers many advantages compared with software approaches to image co-registration for patient diagnosis and image-guided radiation therapy, it is often argued that combined PET/CT is not the ultimate solution for image co-registration and will most likely not be considered a major breakthrough that revolutionised the paradigm of medical imaging [3].

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It is the role of medical physicists providing physics support to clinical PET facilities and involved in today's biomedical imaging research enterprise to debate important issues related to design aspects of this technology and optimal data acquisition and processing protocols with the aim of improving image quality and obtaining accurate quantitative measures. Among many other issues, the important role of attenuation correction (AC) in PET has been discussed in a number of review papers [4–6] and debated in editorials [7, 8] and point/counterpoint papers [9–11].

Clinical significance of attenuation correction

There is no doubt that incorporation of AC in PET data processing protocols contributes in improving image quality, interpretive certainty and diagnostic accuracy. The extent to which it can be shown to have a decisive impact upon the goal for which the image is to be utilised is a much more tricky issue, as very few studies have addressed the clinical consequences for reporting. For example, it was reported that AC in myocardial perfusion imaging instigated a change in diagnosis in approximately 10% of patients, corresponding to one-fifth of the abnormal studies [12]. Nevertheless, the added value provided by AC is no longer the subject of debate in myocardial perfusion imaging [13] or even in oncology studies, where it remained controversial [7, 14, 15] until it was shown fairly conclusively that AC almost always facilitates tumour detection [16].

Functional brain imaging can be regarded as a special case since many simple and sophisticated transmissionless AC methods can be used; as a consequence it would be irrational to attempt to justify the use of non-corrected images even in a busy clinical department or in facilities lacking expert physics support [17]. Whether the use of sophisticated transmission-based methods is required in daily practice or justified only in research studies, where there is greater emphasis on accurate quantitative measurements, is another issue that is still being debated [9–11].

Pros and cons of radionuclide transmission-based attenuation correction

Before the advent of combined PET/CT units, measured AC using external positron-emitting (^{68}Ge/^{68}Ga) or single-photon emitting (^{137}Cs) radionuclide sources was the most commonly used procedure (gold standard) in both clinical and research settings. Transmission-based scanning is expected to yield the best attenuation map as a result of matched energy and spatial resolution. Scaling for the difference between 662-keV (for ^{137}Cs sources) and 511-keV energies is less of an issue compared with scaling low-energy polyenergetic X-ray beams for CT and can be easily performed by normalisation to a slab phantom scan and correction for scatter and cross-section variation using a log-linear transformation of the attenuation factors [18]. Single-photon emitting transmission sources have the further advantage that, in order to reduce the interference, radionuclides can be chosen that emit photons at an energy different from the 511 keV of annihilation photons. Various strategies have also been proposed to eliminate contamination of emission data by transmission photons (for simultaneous scanning) and to reduce spillover of emission data into the transmission energy window (for post-injection transmission scanning) [5]. For example, combining non-uniform emission contamination subtraction with transmission image segmentation was proven to successfully compensate for emission contamination in transmission measurements on the high-resolution research tomograph (HRRT) PET scanner [19]. Furthermore, substantial reduction of emission data contamination by transmission photons, allowing achievement of good transmission image quality, was reported on a prototype simultaneous emission–transmission scanning system [20] through the use of a fast, dedicated, lutetium oxyorthosilicate-based reference detector placed close to the collimated coincidence point source used to produce the transmission data.

The most important drawbacks of radionuclide transmission scanning are the extra complexity of the PET camera design and the data acquisition and processing protocols and the extra cost resulting from the periodic requirement to replace expensive sources. Other known limitations already observed during the early stages of PET development include registration problems caused by patient- or motion-induced misalignment between transmission and emission scans, which can result in erroneous estimation of regional tissue activity concentrations, noise propagation from the transmission scan to the emission scan [21], particularly for lines of response that pass through the thickest parts of the body and larger bony structures, and the time required to perform a statistically reliable transmission scan. The filtering of transmission scans aiming at noise reduction results in a difference in spatial resolution between the transmission and the emission data to which it is applied since emission data are not usually smoothed at this stage. This causes bias at the interfaces between regions of high and low tissue density [22] and is a far greater challenge in whole-body PET owing to the more complex juxtapositions of media with different attenuating properties, e.g. lung/soft tissue/bone in the thorax. This can be tackled by using more sophisticated approaches such as anisotropic diffusion filtering [23]. To avoid lengthy transmission scans, techniques using transmission image segmentation and tissue classification have been proposed to reduce noise propagation from transmission to emission scans by delineating different anatomical regions of uniform attenuation followed by assignment of known tissue-dependent attenuation coefficients using weighted averaging. The adverse effect is the increased bias introduced by segmented AC when assessing absolute or semi-quantitative indices, the magnitude of which is difficult to predict in clinical studies. One should note that, except the registration problem, most of these limitations have been overcome through research, with the development of rod-windowed transmission devices, reliable simultaneous and post-injection transmission scanning methodology and robust transmission image segmentation algorithms [5].

Pros and cons of CT-based attenuation correction

Dual-modality imaging offers a critical advantage over separate PET and CT imaging units in correlating functional and anatomical images without moving the patient (other than table translation). The use of CT also generates a high-resolution noise-free attenuation map, allowing noise propagation to PET emission data to be reduced significantly and overall scanning time to be decreased; this in turn improves patient comfort and throughput and reduces operating costs as there is no need for regular replacement of transmission radionuclide sources.

Notwithstanding the success and widespread clinical adoption of PET/CT, there are several challenges confronting the use of dual-modality imaging that may represent inherent limitations to this technique. In addition to a much higher absorbed dose to the patient, there are many physical and physiological factors that hamper the accurate registration of both imaging modalities and the accurate quantitative analysis of PET data following CT-based AC (CT-AC). These include: the inherent difference between CT and PET image matrix size and resolution; polychromaticity of X-ray photons (30–140 keV) requiring transformation to monoenergetic 511-keV photons and creating beam-hardening artefacts; misregistration between CT and PET images owing to, for instance, respiratory motion; truncation artefacts due to the discrepancy between fields of view in a combined PET/CT scanner; the presence of oral and intravenous contrast medium; metallic implants; X-ray scatter in CT images for future generation cone-beam geometries; and other CT artefacts from any source.

Patient motion (either voluntarily or involuntarily) between or during the anatomical and functional image acquisitions remains a major challenge for PET/CT imaging protocols. Patient motion also occurs due to respiration, cardiac motion, peristalsis and bladder filling, all of which can lead to motion blurring or misregistration errors between the PET and CT image acquisitions [24]. It is frequently suggested that, owing to the different time resolution and respiratory patterns between PET and CT scanning, the diaphragm is displaced or occupies different positions in the CT images (usually captured during a single position) and the PET images (usually averaged over several respiratory cycles). This misregistration may induce mislocalisation of abnormalities and, more importantly, produce incorrect AC maps leading to typical cold artefacts on approximately 84% of studies at the lung/diaphragm interface [25]. It has also been reported that liver metastases not detectable on PET images obtained through CT-AC are clearly seen on radionuclide transmission-based attenuation-corrected images [26]. Even if this has been recognised as a rare pitfall, false negative interpretation of liver dome lesions may result from erroneous CT-AC. It has also been reported that radionuclide scanning-based AC would be a more reliable approach to AC for ungated cardiac PET studies because it has similar temporal characteristics to the PET scan, and thus provides consistent data for AC [27].

It is still a matter of controversy whether the use of contrast medium in dual-modality PET/CT imaging produces medically significant artefacts. Some studies have corroborated while others have contradicted the hypothesis that the presence of contrast medium can be a source of errors and artefacts when the CT data are used for AC of PET images, depending on the route of administration and the phase protocol of CT imaging [28]. The optimal quantity and route of administration of contrast medium and potential correction schemes are still open questions which require further research and development efforts [29].

The progress in CT-AC methodology has been immense in the past few years, the main opportunities having arisen from the development of both optimised scanning protocols and innovative and faster image processing algorithms. This has permitted the implementation of much more ambitious algorithms that tackle the challenges of whole-body PET/CT imaging. Some recently proposed solutions to the aforementioned problems have now been used successfully in clinical and research settings. These include optimised contrast-enhanced CT protocols, tracking and correction of respiratory motion, metal artefact reduction, truncation artefact correction, and beam hardening and x-ray scatter compensation. It should be pointed out that the majority of methods and algorithms described in the literature have been applied primarily to computer-simulated images and simplified experimental arrangements. Some solutions to the problems associated with AC are less suitable for routine application in patients than in phantom simulations. These hot topics undoubtedly require further research and development efforts.

Comparison of attenuation correction methodologies

Within the context of whole-body imaging, the problems associated with the use of CT-AC and the complexity inherent to transmissionless AC have spurred the further development of transmission-based AC methodologies, which remain an active research area. Some scanner manufacturers have decided to preserve radionuclide transmission scanning devices on new-generation hybrid PET/CT units, such as the Sceptre P3 (Hitachi Medical Systems America, Inc., Twinsburg, OH, USA), the Gemini (Philips Medical Systems, Best, The Netherlands) and the first units of the Discovery LS PET/CT series (GE Healthcare Technologies, Waukesha, WI). This allows the combination of both CT- and radionuclide scanning-based AC to permit effective imaging of patients with metal implants and prosthetics. A limited number of studies reported in the literature have offered detailed comparative assessment between CT-AC and radionuclide scanning-based AC, including ^{68}Ga versus CT-AC [27, 30–33] and ^{137}Cs versus CT-AC [26, 34]. Clinical and scientific data are required to impartially establish whether the advantages and clinical benefits of transmission scanning-based AC are sufficient to offset its additional running costs, or whether CT-AC should be the only option on hybrid PET/CT units.

Summary

It is undisputable that CT-AC has several virtues and should be targeted for further research. However, it should be recognised that its clinical benefits have not been unequivocally demonstrated and need to be carefully documented by investigators before wider acceptance. The key point is that many PET procedures do not require a diagnostic quality CT and radionuclide-based transmission scanning would be a better option than low-dose CT protocols. It is still too early to claim that transmission scanning devices are obsolete for PET/CT, and that CT-AC should be the gold standard on these systems. My opinion is that transmission scanning still has a genuine role and remains an appealing alternative until all the problems associated with CT-AC are resolved through research.

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