Introduction

Positron Emission Tomography (PET) is a key molecular imaging modalities used during in vivo studies for the assessment of various diseases in a non-invasive manner (1–3). The use of PET is important in the clinical oncology field, including diagnostic, staging, restaging, assessment of therapeutic response, and radiation therapy planning (4–6). Artefact minimization and high-quality imaging are, therefore, imperatives for the role they play in the qualitative interpretation and quantitative analysis of PET scans (7, 8).

Artefacts in PET imaging are anomalies in the final images that do not correspond to the true distribution of the radiotracer within the body. These can be caused by a variety of factors, including patient motion, improper scanner calibration, and physiological processes that interfere with signal acquisition. Artefacts can lead to misinterpretations in clinical diagnosis, making it essential to identify and correct them to enhance the accuracy of PET scans (9–12).

Still, artefacts in medical imaging is a recurring challenge that can lower the quality of images and make them less reliable. This can lead to erroneous interpretations that could adversely influence clinical decisions (13, 14).

Scatter correction is a technique used to enhance the quality of PET images by removing scatter radiation that can blur images and obscure details. During a PET scan, photons emitted by the radiotracer can scatter as they collide with other particles before reaching the detectors (15–17). This scatter distorts the image by introducing signals from incorrect locations. Scatter correction algorithms estimate the number of scattered photons and subtract them from the detected signals, thereby improving image clarity and contrast (15).

Attenuation correction is another critical process in PET imaging, which compensates for the loss of signal intensity due to the absorption of photons within the body. Different tissues absorb photons at varying rates, which can lead to underestimation of tracer concentration in areas like bones or organs with higher densities. Attenuation correction uses information from a transmission scan (using either a radioactive source or a CT scan) to accurately map the absorption properties of various tissues and adjust the PET signal accordingly (18,19). This correction is crucial for providing quantitatively accurate images that reflect the true distribution of the radiotracer (13, 14, 20–23).

Attenuation and scatter correction (ASC) are critical during PET image reconstruction, primarily aimed at enhancing image clarity and accuracy Despite the implementation of these corrections, artefacts can still occur, particularly under complex scenarios such as high radiotracer activity or patient movement (7, 9, 11, 12). Common artefacts encountered in PET imaging can be categorised as follows: (i) those associated with the distribution of the tracer, such as halo artefacts; (ii) those that arise from the alignment of PET with CT or MR images, including mismatch, misregistration, or motion artefacts; and (iii) those transmitted from CT or MRI to PET images, such as errors caused by metals, contrast agents, and image truncation (9, 10, 24, 25).

Halo artefacts are very common in PET imaging, especially with compounds that are labelled with gallium-68 (68Ga). They make it hard to correctly interpret high-activity regions adjacent to organs. In fact, these are a type of radiopharmaceutical artefact that happens when too much radiopharmaceutical builds up and makes it harder to see what's going on in nearby tissues (26, 27).

These artefacts are primarily induced by incorrect scatter correction during image reconstruction, where negative values near regions of intense radiopharmaceutical accumulation—such as the bladder or kidneys due to urinary excretion of the tracer—lead to the assignment of zero values to these voxels due to the non-negativity constraint in statistical reconstruction algorithms. This phenomenon results in the formation of a "halo" or photogenic area around these high-activity zones, potentially obscuring faint abnormalities and impacting the diagnosis, staging, and treatment planning for cancer patients. When halo artefacts are present on PET images, especially near primary tumours or areas where pelvic cancers tend to come back locally, they can lead to a wrong diagnosis because they hide or change how the images are seen and interpreted quantitatively. Trying to get rid of these artefacts, like giving diuretics, often makes the patient more uncomfortable and increases the chance of motion artefacts, which makes the image quality and readability even worse (26, 28).

Most PET acquisition settings are performed with arms up (to decrease photon scatter). As arm raising is uncomfortable for patients, this will cause arm motion during sequential PET and CT/MRI scans. This is one example of the mismatch effect (29–31).

Mismatch artefacts constitute a significant challenge in PET imaging, particularly when discrepancies arise between PET and anatomical scans such as CT or MRI. These discrepancies can stem from both voluntary and involuntary movements of organs, potentially leading to the misidentification, mislocalization, and inaccurate quantification of lesions. This issue is critical as it can result in misdiagnoses and, subsequently, inappropriate patient management (32–34). Techniques such as deformable image registration have been developed to mitigate these effects, though they cannot always eliminate the problem. Mismatched artefacts mean that PET imaging needs to be done in a more complex way, using different CT acquisition protocols and other techniques to reduce the chance of misalignments (35, 36).

Truncation artefacts in PET imaging emerge primarily due to the disparities in the trans axial fields of view (FOVs) between PET and CT/MRI modalities. These artefacts are particularly prevalent in scenarios involving obese patients or when patients have their arms down during the scanning process, as well as in cases where PET/CT or PET/MR scans are utilised for treatment planning (37–39). Truncation artefacts happen when there aren't any matching parts of the attenuation map for structures that go beyond the CT/MR images. This makes standardised uptake value (SUV) estimates wrong, usually giving too high of an estimate around the edges and too low of an estimate in the middle of the image. The issue is compounded when anatomical images truncate parts of the patient's body, leading to artefacts and distorted activity quantification in PET images. Optimally positioning the patient in the centre of the FOV with arms-up can decrease such artefacts, yet specific conditions, like scanning for melanoma or head-neck cancer, necessitate arms-down positioning. To fix or lessen truncation artefacts, different methods have been tried, such as extended FOV CT scans, extrapolation of CT projections, specialised MR sequences, and manual or semi-automatic in-painting algorithms. Despite these efforts, it is still hard to deal with truncation artefacts, especially in obese patients where more photons are attenuated and scattered, making the image quality and quantitative accuracy even worse (38–40).

Halo and mismatch artefacts are notably frequent in PET imaging using gallium-68 (68Ga)-labeled radiopharmaceuticals. These artefacts might be overlooked if they are subtle, yet when pronounced, they can significantly degrade the image quality, necessitating additional scans. However, even repeated scanning often fails to correct these artefacts, as they are sometimes inherent and unavoidable in specific situations (11, 12, 41, 42).

Attenuation and scatter correction techniques are necessary for making reconstructed and quantitative PET images, but they also cause some artefacts, which means that PET imaging needs to be done in a more nuanced way. Understanding the limitations and potential pitfalls of these techniques is crucial for radiologists and clinicians to interpret PET images accurately. Ensuring meticulous calibration, considering patient-specific factors, and using advanced correction algorithms are essential steps in minimising the impact of these artefacts on clinical outcomes.

Integration into CT or MRI is necessary for quantitatively accurate and visually readable PET images. Attenuation and scatter correction (ASC) are required to make PET images that are both quantitatively accurate and easy to read visually (13, 43). Typically, an unenhanced, low-dose CT scan is conducted alongside PET/CT scans for ASC, and occasionally, a diagnostic CT scan with a contrast agent may serve the same function (44, 45). Elimination of the CT component could be particularly beneficial for patients requiring repeated PET/CT scans, notably paediatric patients, as even marginal reductions in cumulative radiation exposure are of significance (46, 47).

The integration of computed tomography (CT) in PET/CT imaging, while invaluable for attenuation correction (AC) and precise anatomical localization, significantly contributes to the total ionising radiation dose received by patients. Innovations such as long axial field of view (LAFOV) total-body PET scanners have markedly improved image resolution and quantification while reducing the need for high radiopharmaceutical doses (16–18, 21–22). Nonetheless, the aspiration for entirely CT-free PET imaging methodologies is driven by the imperative to diminish radiation exposure in vulnerable populations and during repeated examinations or longitudinal studies (48).

Historically, the field has seen progress through magnetic resonance (MR)-based strategies and algorithmic advances such as the maximum likelihood estimation of activity and attenuation (MLAA), further refined with time of flight (TOF) enhancements (49–51). Despite these developments, the interplay between activity distribution and attenuation remains a challenging frontier, compounded by scanner-specific noise and resolution discrepancies (23).

Deep learning (DL) has emerged as a groundbreaking approach in PET imaging, revolutionising attenuation correction and artefact reduction (52–57). DL-based methods have been developed for a variety of applications, including the synthesis of pseudo-CT images from MRI or uncorrected PET data, prediction of scatter maps from emission data (36, 39, 58–61), and direct generation of ASC PET images from uncorrected inputs (53, 57, 62). These advancements not only demonstrate the vast potential of DL in enhancing the safety and efficacy of PET imaging but also highlight its capability to improve image quality significantly and reduce errors caused by metal artefacts and truncation effects in both PET/CT and PET/MRI modalities (37, 63).

Deep learning presents a promising paradigm capable of transcending traditional challenges in PET imaging, such as the activity-attenuation crosstalk and the noise inherent in the imaging process (36, 55). However, the success of DL critically hinges on its adaptability to the dynamic nature of PET tracers, particularly Ga-68, and the variability across imaging platforms. This includes dealing with differences in scanners, creating new tracers that have specific biodistributions, and the fact that PET imaging domains are naturally diverse (35, 64).

Furthermore, the use of federated learning (FL) addresses critical challenges such as data privacy and limited dataset sizes in medical imaging. FL lets DL models be trained in different places without compromising data privacy. This makes the models more stable and able to adapt to differences in data and imaging protocols (11, 12, 42, 65). This approach is invaluable in environments where data sharing is restricted by ethical and regulatory considerations.

Yet, the quest for CT-free PET imaging avenues, particularly beneficial in paediatric scans, repetitive examinations, and pharmaceutical research, underscores the need for novel correction techniques devoid of additional radiation risks. However, there are still some problems with how well DL approaches work in PET imaging. This is why we need to create a DL model that doesn't depend on the centre or tracer used, so it can be used for all Ga-68 PET imaging problems. As the technology progresses, further research is necessary to address the emerging challenges, particularly in adapting DL models to handle the rapid advancements in imaging technologies and tracer development. The ongoing refinement of these innovative methodologies will be crucial for achieving widespread clinical acceptance and enhancing the diagnostic capabilities of PET imaging (52).

One significant challenge for deep learning methods in PET imaging is the struggle to adapt to the inherent heterogeneity across various domains. Variations in spatial resolution and sensitivity among scanners, coupled with the ongoing changes in biodistributions of new tracers, pose challenges in developing a comprehensive training dataset. This diversity can compromise the consistency and reliability of deep learning approaches for attenuation correction, making it challenging to capture the full range of variables in real-world situations.

Studies in the past have shown that direct ASC frameworks can help fix artefacts in 18F-FDG PET/CT images. However, gallium-based PET images often exhibit lower quality and resolution, potentially due to their unique characteristics and interactions within the body. As a result, these images require more nuanced approaches to ensure accurate interpretation and analysis (36, 65).

This thesis will try to take a step into the problematic field of correction in PET imaging artefacts, with especially high-prevalence ones: mismatch and halo artefacts in 68Ga PET imaging. The aim of this paper is to look at several deep learning models and methodologies to design a multi-centre model that allows semi- and un-direct data sharing at each centre due to some demerits of conventional deep learning techniques. This is made possible by the use of a novel deep learning architecture called Dyn-Unet with a sophisticated 3D convolutional capability, allowing for precise disentangling and correction of artefacts.

We will use our approach to estimate and compare the performance of models under both strategies within different levels of tracer dynamics and multi-centre data environments. In particular, we will integrate domain expertise into our deep learning framework in order to detect and correct artefacts more efficiently in multi-centre studies.

This research will aim to be a demonstration of the possibility, as well as the superior performance, of the deep learning models for real clinical settings, which will potentially set a new standard of CT-free PET imaging that enhances diagnostic accuracy while minimising radiation exposure and procedural complexity.

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