Positron Emission Tomography (PET) is a pivotal 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). Artifacts 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).

Artifacts 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. Artifacts can lead to misinterpretations in clinical diagnosis, making it essential to identify and correct them to enhance the accuracy of PET scans (9–12).

However, the presence of artifacts in medical imaging still is a recurring challenge that may impair image fidelity and quantitative reliability, potentially leading 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 density. Attenuation correction uses data 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, artifacts can still occur, particularly under complex scenarios such as high radiotracer activity or patient movement (7,9,11,12). Common artifacts encountered in PET imaging can be categorized as follows: (i) those associated with the distribution of the tracer, such as halo artifacts; (ii) those that arise from the alignment of PET with CT or MR images, including mismatch, misregistration, or motion artifacts; 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 artifacts in PET imaging notably prevalent with gallium-68 (68Ga)-labeled compounds, represent a significant challenge in accurately interpreting high-activity regions adjacent to organs. In fact, these are a Radiopharmaceutical-related artifact category which arise from excessive radiopharmaceutical accumulation and complicate the evaluation of adjacent tissues (26,27).

These artifacts 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. The presence of halo artifacts, particularly near primary tumours or areas prone to local recurrences in pelvic cancers, poses a risk of misdiagnosis by masking or altering the visual and quantitative interpretation of PET images. Efforts to mitigate these artifacts, such as the administration of diuretics, often result in increased patient discomfort and the potential for motion artifacts, further complicating the image quality and interpretability (26,28).

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

Mismatch artifacts represent 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, mis localization, 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 completely eliminate the problem. The occurrence of mismatch artifacts necessitates a nuanced approach to PET imaging, incorporating strategies like different CT acquisition protocols to minimize potential misalignments (35,36).

Truncation artifacts in PET imaging emerge primarily due to the disparities in the trans axial fields of view (FOVs) between PET and CT/MRI modalities. These artifacts 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 utilized for treatment planning (37–39). The essence of truncation artifacts lies in the absence of corresponding parts of the attenuation map for structures that extend beyond the CT/MR images, leading to inaccuracies in standardized uptake value (SUV) estimations—typically, an overestimation at the periphery and an underestimation towards the center of the image. The issue is compounded when anatomical images truncate parts of the patient's body, leading to artifacts and distorted activity quantification in PET images. Optimally positioning the patient in the centre of the FOV with arms raised can mitigate such artifacts, yet specific conditions, like scanning for melanoma or head-neck cancer, necessitate arms-down positioning. Various strategies, including extended FOV CT scans, extrapolation of CT projections, specialized MR sequences, and manual or semi-automatic in-painting algorithms, have been explored to address or alleviate truncation artifacts. Despite these efforts, managing truncation artifacts remains a complex challenge, especially in overweight patients where increased photon attenuation and scattering further degrade image quality and quantitative accuracy (38–40).

Halo and mismatch artifacts are notably frequent in PET imaging using gallium-68 (68Ga)-labelled radiopharmaceuticals. These artifacts 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 artifacts, as they are sometimes inherent and unavoidable in specific situations (11,12,41,42).

While attenuation and scatter correction techniques are indispensable for producing reconstructed and quantitative PET images, their role in the occurrence of certain artifacts necessitates a nuanced approach to PET imaging. Understanding the limitations and potential pitfalls of these techniques is crucial for radiologists and clinicians in interpreting PET images accurately. Ensuring meticulous calibration, considering patient-specific factors, and using advanced correction algorithms are essential steps in minimizing the impact of these artifacts 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 for the production of quantitative accurate and visually readable PET images demanding effective attenuation and scatter correction (ASC) (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 ionizing 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, revolutionizing attenuation correction and artifact 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 artifacts 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 addressing scanner variability, evolving tracers with unique biodistributions, and the heterogeneity inherent in PET imaging domains (35,64).

Furthermore, the use of federated learning (FL) addresses critical challenges such as data privacy and limited dataset sizes in medical imaging. FL allows for the decentralized training of DL models across multiple institutions without compromising data privacy, enhancing model robustness and adaptability to local variations 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 pediatric scans, repetitive examinations, and pharmaceutical research, underscores the need for novel correction techniques devoid of additional radiation risks. Despite these strides, the efficacy of DL approaches in PET imaging faces limitations which necessitates the development of a DL model that transcends center-specific and tracer-specific constraints, offering a universally applicable solution for Ga-68 PET imaging. 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 of the significant challenges faced by deep learning methods in PET imaging is their struggle to adapt to the heterogeneity inherent across various domains. Differences in spatial resolution and sensitivity across scanners, along with the continually evolving biodistributions of new tracers, complicate the creation of a comprehensive training dataset. This diversity can undermine the consistency and reliability of deep learning approaches for attenuation correction, as it becomes increasingly difficult to represent the full spectrum of variables encountered in real-world scenarios.

Previous studies have shown the effectiveness of direct ASC frameworks for artifact correction in (18F-FDG) PET/CT imaging. 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 make a step into the problematic field of correction in PET imaging artifacts, with especially high-prevalence ones: mismatch and halo artifacts in 68Ga PET imaging. The aim of this paper is to look at several deep learning models and methodologies to design a multi-center model that allows semi- and un-direct data sharing of each center due to some demerits of conventional deep learning techniques. This is made possible by the use of the novel deep learning architecture called Dyn-Unet with a sophisticated 3D convolutional capability, allowing for precise disentangling and correction of artifacts.

We will use our approach to estimate and compare the performance of models under both strategies within conditions of different levels of tracer dynamics and multi-center data environments. In particular, we will integrate domain expertise in our deep learning framework in order to detect and correct artifacts more efficiently in multi-center 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 minimizing radiation exposure and procedural complexity.

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