# 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.

A comparison of a person's body

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# Material and methods

## Data Preparation

Our study aimed to evaluate the performance of our model across different scenarios, including various external scanners and radiotracers. Multiple hospital imaging centres in five different places were used as a primary dataset for training and initial model validation. The dataset contained Gallium PET/CT scans. To test the model's adaptability, a secondary dataset was incorporated, distinct in both the imaging centres (external to the primary dataset) and the type of radiotracer used (18F-FDG PET scans from two different hospitals). Additionally, a specialised set of images presenting artefacts was included to assess the model's capability to identify and correct for image quality issues. The Ethics Committee of the Geneva University Hospital approved this retrospective study, which spans across several institutions.

### Gallium PET/CT dataset

A cohort of more than 1000 patients underwent 68Ga-prostate-specific membrane antigen (PSMA)/DOTA-TATE (TOC). PET/CT imaging across five centres located in different countries. To ensure the integrity of the data for model training, an expert in nuclear medicine evaluated all the scans, identifying 184 images of optimal quality without artefacts from the total pool. Detailed information on the datasets collected from the various locations is outlined in Table 1. The method of CT-based attenuation and scatter correction (CT-ASC) was applied to amend PET images for accurate correction of attenuation and scatter effects in the images.

Table 1: Data information in 5 different imaging centers.

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Center** | **No** | **Train** | **Validation** | **Test** | **Scanner** | **Reconstruction** | **Matrix size × Z\*** |
| Center 1 | 56 | 43 | 11 | 2 | Siemens Biograph 6 | 3D-OSEM | 168 × 168 |
| Center 2 | 31 | 25 | 4 | 2 | GE Discovery IQ | 3D-OSEM | 192 × 192 |
| Center 3 | 45 | 35 | 8 | 2 | Siemens mCT | 3D-OSEM | 200 × 200 |
| Center 4 | 40 | 28 | 10 | 2 | Siemens Biograph 6 | 3D-OSEM | 168 × 168 |
| External Center | 12 | - | - | 12 | Siemens Horizon | PSF+TOF+3D-OSEM | 180 × 180 |
| **Total** | **184** | **131** | **33** | **20** | - | - | - |
| \*  Z' representing the number of slices in the axial view, depends on body length, scanner resolution, scan protocol, and patient positioning. So, it is different patiently. | | | | | | | |

#### Normalization of PET Imaging Data

In PET imaging, the standardised uptake value (SUV) is a crucial quantitative measure that normalises the detected radiotracer concentration in a way that allows comparison between patients and scans. It corrects for the injected dose of the radiotracer and the patient's body weight. This conversion is essential as it factors in variations due to patient size and the amount of radiotracer administered. The SUV is typically calculated using the formula:

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| --- | --- |
|  | ( 1) |

To turn the voxel values into standardised uptake value (SUV) metrics, this conversion was done the same way on all of our MAC and NAC images.



To achieve uniformity across all images, the voxel intensities were normalised by dividing by a constant factor. In particular, MAC images underwent a factor of 5 scaling, while NAC images underwent a factor of 2. By applying a uniform scale adjustment across the dataset, this method of normalisation by a constant factor makes the process easier while keeping the relative differences in radiotracer uptake between different areas within and across the images.



This method ensures that the data remains quantitatively comparable while being computationally straightforward. By scaling the intensity values in this manner, we were able to preserve the quantitative nature of PET imaging, which is vital for accurate diagnosis and assessment of metabolic activity. The histogram of the images post-normalisation illustrates the effect of this scaling on the distribution of voxel intensities, confirming the consistency of intensity levels across the processed images.

#### Data Transformation and Augmentations:

For training data preparation, each PET image was initially trimmed to fit the body's outline, followed by the addition of zero-padding to standardise the dimensions to a uniform bounding box size of 168×168×Z (with 'Z' representing the count of slices), as illustrated in figure 2a, ensuring the retention of original image resolution and anatomical structure.

This ensured the preservation of the original resolution and the fidelity of the anatomical representation. To ensure uniformity and enhance the training process's efficiency, all PET images were re-scaled to a voxel size of 4.07 × 4.07 × 3.0 mm3, the most common resolution across the collected data and crucial for consistent image analysis. This standardisation was crucial for achieving consistent image quality throughout the dataset. Details regarding the initial voxel spacing are provided in Figure 2b.

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| Figure 1: Distribution of maximum intensity values for NAC and MAC images, displaying variations pre- and post-normalization to highlight data scaling effects. non-ASC images were scaled down by a factor of 2, and CT-ASC images by a factor of 5. |

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| Figure 2: **A)** Distribution of initial PET image dimensions across sagittal, coronal, and axial planes. Each bar represents the frequency of occurrence for specific dimension sizes within the dataset. **B)** Proportion of different voxel spacings utilized in PET image preprocessing. The donut charts depict the percentage of images corresponding to each voxel spacing dimension in millimeters across sagittal, coronal, and axial views. |

### Generation of Anatomy-Dependent Correction Maps (ADCM)

In exploring advanced techniques for PET image correction, we examine a decomposition-based deep learning approach previously outlined in the literature (52). From NAC to MAC (model-based attenuation correction), the complex end-to-end generation was broken down into two parts: anatomy-independent textures (related to tracers and diseases) and anatomy-dependent correction.

In other words, this method involves dividing the MAC image into these two key component maps. Anatomy-independent information, which correlates with tracer type and disease pathology, and another component, anatomy-dependent factors necessary for image correction.

The conditional equation that captures the ratio of the MAC intensity to the NAC intensity defines the anatomy-dependent correction map (ADCM) at each voxel:

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|  | ( 2) |

The threshold ε ensures that division by zero is avoided, defaulting to the MAC intensity where necessary.

In the evaluation phase, our trained model predicts the DL-ADCM for a given NAC. We then employ the following transformation (equation 2) to achieve the DL model-based attenuation correction (DL):

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| --- | --- |
|  | ( 3) |

Sample cases are visualised in Figure 3.

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| --- | --- | --- | --- | --- | --- | --- |
|  | | NAC-PET MAC-PET ADCM | | | NAC-PET MAC-PET ADCM | |
| **a)** | A comparison of a body scan  Description automatically generated with medium confidence | | | A comparison of a body scan  Description automatically generated with medium confidence | |
| **b)** | A several images of a person's body  Description automatically generated | | | A comparison of a body scan  Description automatically generated with medium confidence | |
| **c)** | A close-up of several images of a person's body  Description automatically generated | | | A comparison of x-ray images of a human body  Description automatically generated | |
|  | | | Figure 3: the middle slice of the coronal view for NAC, MAC, and ADCM images. Color bar unit: SUV | | | |

#### Normalization

As we already mentioned, famous normalisation methods were not used to calibrate ADCM in order to protect the quantitative accuracy of SUV metrics, which is necessary for accurate clinical interpretations. We came up with an empirical normalisation factor just for ADCM values. This factor was carefully chosen to bring the dataset's wide range of values into a more manageable range that is good for deep learning applications. This factor ensures the broad spectrum of data, ranging from minimal to several thousand units, is normalised in a way that permits later recalibration into their original SUV metrics. Notably, extreme values that could bias the model (such as outliers with values of 28180 and 7300) were carefully excluded to align the focus with the representative range critical for analysis. Then, voxel intensities were normalised using a factor of 50 to maintain relative, comparable, and manageable values for training. The resultant histograms, illustrating the distribution of maximum values both pre- and post-normalisation, are depicted in Figure 4.

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Figure 4: shows the range of highest intensity values for NAC and MAC images as well as ADCM metrics, showing changes before and after normalization to show how data scaling affects the images. Scaling down non-ASC images by a factor of 2, CT-ASC images by a factor of 5, and ADCM by a factor of 50.

### FDG Datasets

To assess the model's performance with various radiotracers, our study incorporated a dataset of 20 whole-body 18F-FDG PET scans originating from two distinct hospitals, representing our external radiotracer dataset. During the preprocessing phase, the intensities of voxels in both MAC (CT-based attenuation corrected) and NAC (non-attenuation scatter corrected) images were standardised to SUVs. This made the dynamic range of intensities more uniform so that network training would work better. Empirical scaling factors, 9 for MAC and 3 for NAC images, were applied to further constrain the dynamic range.

To achieve homogeneity across the dataset, we standardised the voxel spacing to 1.92 mm for both coronal and sagittal planes, with an axial dimension set to 3.0 mm, which aligns with 52% of the existing data. These standardised spacings ensure uniformity across all scans in preparation for model training. Further details on the imaging parameters are presented in Table 2.

Table 2: "Overview of External Radiotracer Dataset Specifications.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Center** | **Test** | **Scanner** | **Reconstruction** | **Matrix size × Z** |
| Center 6 | 10 | ? | ? | 272 × 200 |
| Center 7 | 10 | ? | ? | 272 × 200 |
| Total | 20 | - | - | - |

### Artifact dataset

In this study, a secondary test set was utilised to rigorously evaluate the performance of the developed model under more challenging conditions. This set consisted of imaging data from 198 patients, each displaying various types of artefacts. The artefacts in this dataset were chosen to test how well the model can handle and correctly interpret images that are distorted by common problems seen in clinical Ga imaging, like motion and Halo artefacts.

## Deep neural network

For final implementation, we leverage the Dyn-UNet architecture, renowned for its adaptability and efficiency in processing biomedical images (Isensee et al., 2019). This model is particularly chosen for its dynamic configuration and deep supervision, enabling precise results tailored to the specific requirements of our dataset.

The Dyn-UNet model's initialization is specially made to find the best kernel sizes and strides based on the size and spacing of the input patches in our dataset. By evaluating the spatial dimensions and resolution of the input data, these parameters were determined, ensuring the network architecture is directly aligned with the inherent characteristics of our medical images.

The Dyn-UNet model is specified with supervision heads, which ensure that intermediate layers are optimised for accurate prediction, enhancing learning efficiency and model robustness. Deep supervision ensures that intermediate layers are also optimised for accurate prediction, not just the final output layer. This strategy boosts the learning efficiency and enhances the robustness of the model, making it adept at segmenting complex anatomical structures with high fidelity.

For the Gallium dataset, the computed kernel sizes and strides are set to four layers of [3, 3, 3] kernels, with strides transitioning from [1, 1, 1] in the initial layer to [2, 2, 1] in the deeper layers. Thereby ensuring a balanced focus on capturing both high-resolution details and broader anatomical structures. Additionally, the implementation of deep supervision, with two supervision heads, was a critical decision aimed at enhancing the learning process by optimising both the final and intermediate layers of the network. This comprehensive approach to selecting hyperparameters underscores our commitment to leveraging the Dyn-UNet's full potential for achieving precise and robust segmentation results, tailored specifically to the complexity and variety of our imaging data. By adjusting the ReLU activation function in the last layer, we can get the non-zero value from the concept of the PET image.

Our deep learning network was designed to process NAC images as inputs with the objective of generating MAC images. For certain scenarios, which will be elaborated upon later, the output included the anatomy-dependent correction maps (ADCM), derived from the MAC images.

Network training involved using 3D patches sized at 168x168x16 and 20 sample patches per patient. The key training parameters were as follows: a learning rate of 0.001, and the optimisation of the mean squared error (MSE) loss function—also referred to as the squared L2 norm. The MSE loss function was employed to measure the deviation of the network's output from the MAC ground truth.

The optimisation of the network was conducted using the Adam algorithm, with the aim of minimising the loss function effectively. The beta coefficients, set at 0.5 and 0.999, governed the moment estimates' exponential decay rates. The architecture of our network is detailed in Supplemental Material 1.

To enhance the robustness of our model, we implemented specific data augmentations. These included adding rotations of ±15 degrees and increasing the number of samples per patient from 4 to 20.

To maintain the integrity of the model, only artefact-free datasets were used during the network's training and validation stages. We trained the network over 400 epochs to ensure adequate convergence and comprehensive learning from the dataset. An epoch represents a complete iteration over the entire training dataset. The validation set, separate from the training set, was used solely to assess the network's performance and was not involved in fine-tuning any hyperparameters. To prevent data leakage and ensure data integrity, there was no overlap of patients across the training, testing, and validation datasets, maintaining the independence of each dataset.

Details on alternative models tested, including those that did not meet our criteria for inclusion in the final report, are documented in Supplementary Material 2 for transparency and completeness.

## Training approaches for deep learning models:

#### Integrated multi-Center model:

A Dyn-Unet deep learning model was developed using a combined dataset from four different centres, all utilising gallium-based tracers. This model was initially trained on a collective dataset and subsequently tested on an external centre's data to evaluate its generalisation capabilities. It was also tested within the originating dataset from each centre. This approach aims to overcome the limitations of models trained on data from single centres, which may struggle with generalizability to new, unseen cases.

#### 2- Tune TL model:

To address the challenges encountered with different radiotracers, the model underwent tuning through transfer learning (TL). This method involves modifying the deep learning model by integrating learning from decentralised data sources without requiring direct data sharing. This refinement was aimed at enhancing the model’s performance and adaptability across different tracer types, providing a more robust solution that could potentially handle variability more effectively.

#### Decomposition Model:

This methodology adopts a new approach by decomposing the transformation from non-attenuation corrected PET (NAC-PET) to model-based attenuation corrected PET (MAC-PET) into two distinct components. Specifically, the model targets anatomy-independent features associated with tracers and diseases and anatomy-dependent corrections that are crucial for accurate image interpretation. This decomposition enables a more targeted and efficient handling of the data during the deep learning process.

The previous network was employed to focus exclusively on estimating the anatomy-dependent correction maps (ADCM). This model's effectiveness is evaluated through its ability to generalise across different centres and tracers, testing its robustness in a variety of clinical settings.

## Quantitative evaluation:

The model's efficacy was rigorously quantified using a range of statistical metrics, calculated by comparing the DL-predicted PET images against the ground truth CT-based attenuation/scatter corrected images. These voxel-wise metrics computed as follows:

* **Mean Error (ME):** This reflects the average deviation across all voxels.

( 4)

* **Mean Absolute Error (MAE):** Measures the average magnitude of errors without considering their direction.

( 5)

* **Relative Error (RE%):** Provides a percentage error relative to the true values, indicating the proportion of the deviation.

( 6)

* **Absolute Relative Error (ARE%):** Captures the absolute percentage difference, ensuring that all deviations are treated equally regardless of their direction.

( 7)

Where tot refers to the total number of voxels, and and indicate the predicted image via DL model and the ground truth image, respectively.

* **Peak Signal-to-Noise Ratio (PSNR):** Evaluates the ratio of the maximum possible signal to the corrupting noise.

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|  | ( 8) |

In Eq. 8, Peak represents the maximum intensity value in the image.

* **Structural Similarity Index (SSIM):** Assesses the perceptual quality of the predicted images relative to the reference images.

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|  | ( 9) |

where: and are the averages of the pixel intensities in the predicted PET images () and the CT-attenuation corrected PET images (), respectively. and are the variances of the pixel intensities in the predicted and CT-attenuation corrected PET images, respectively. is the covariance of the predicted and CT-attenuation corrected PET images.

and are constants to stabilize the division with a weak denominator; L is the dynamic range of the pixel values (typically ). = 0.01 and =0.03 are default values for the stabilization constants.

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