



Pitfalls on PET/CT Due to Artifacts and Instrumentation

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PET/CT has become a preferred imaging modality over PET-only scanners in clinical practice. However, along with the significant improvement in diagnostic accuracy and patient throughput, pitfalls on PET/CT are reported as well. This review provides a general overview on the potential influence of the limitations with respect to PET/CT instrumentation and artifacts associated with the modality integration on the image appearance and quantitative accuracy of PET. Approaches proposed in literature to address the limitations or minimize the artifacts are discussed as well as their current challenges for clinical applications. Although the CT component can play an important role in assisting clinical diagnosis, we concentrate on the imaging scenarios where CT is used to provide auxiliary information for attenuation compensation and scatter correction in PET.

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Introduction

The introduction of PET/CT allows the acquisition of both functional and anatomical information in a single imaging session.^{1,2} It not only reduces the potential setup errors between separate CT and PET scans but also improves patient experience and throughput.^{3,4} In current practice, PET/CT has been intensively applied in oncology, cardiology, and neurology. Its application is expected to expand further with the development of novel radioactive tracers.

Benefits of applying the integrated PET/CT in clinical practice have been evaluated in literature.⁵ In terms of diagnostic accuracy, it has been demonstrated that PET/CT outperforms subsequent PET and CT studies viewed side-by-side.^{6,7} The improvement is resulted from that both the image quality and quantitative accuracy of PET are improved as better attenuation correction⁸ and scatter estimation⁹ are achieved by incorporating information of the subject captured by CT.

This also encourages the exploration of potential clinical applications, such as disease followup,¹⁰⁻¹³ therapy monitoring,¹⁴⁻¹⁸ and receptor occupancy,^{19,20} which rely on accurate

quantification and object delineation on PET images. However, challenges emerge inevitably with the introduction of PET/CT in both clinical and research environment as well. The aim of this review is to provide a general overview on the current limitations with respect to PET/CT instrumentation and the image artifacts observed in PET/CT imaging. The possible solutions proposed in literature to address the limitations or eliminate the artifacts are discussed as well. Although, with the advancement of technology, the CT component of state-of-the-art PET/CT scanners is able to meet the clinical diagnostic merit and be used as a stand-alone CT scanner, this review focuses on discussion in imaging scenarios where CT is used to provide auxiliary information for PET.

Physics and Instrumentation of PET/CT

PET scanners are designed especially for positron-emitting radioactive tracers. When interacting with matter, the positron loses its kinetic energy and annihilates with an electron, creating two 511 keV photons emitted almost back-to-back. The travel range for a positron before it undergoes annihilation, named positron range, varies with the positron emitter applied. To capture these two photons, coincidence detectors positioned in opposite directions are used. Since one or both the photons may be scattered by any object along their travel to/in the detector, an energy discriminator can be used to

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prevent them being accepted in a wrong coincidence detector pair when the energy loss caused by the direction change is large enough. Given the annihilation can occur closer to one detector than the other, depending on the timing resolution of the detectors, two photons arriving a coincidence detector pair within a certain time window are registered as an event. The location of the annihilation can then be traced along the straight line defined by the paired coincidence detectors (line of response, LOR). For detectors with fine timing resolution, the difference in arrival time for the pair of annihilation photons (time-of-flight, TOF information) can be used to further reduce the location uncertainty of the event along the LOR.²¹

Current PET scanners usually adopt stationary detectors arranged in a ring shape to achieve 360-degree acquisition. Most PET detectors consist of scintillation crystals (scintillators) coupled with photosensors, such as photo-multiplier tubes and Silicon photo-multipliers for converting the energy of photon to electrical signals. To increase the efficiency of the conversion, thick scintillators can be chosen. However, due to the ring shape arrangement of detectors, this increases the probability of photons hitting on the side of scintillators, especially for annihilations occurring off the center of the field-of-view (FOV). These events can be slight mispositioned while estimating their location along the LOR when information regarding the depth of interaction in scintillators is not available.²²

As annihilation photons can be absorbed (attenuated) by the imaging subject before interacting with the detector, the registered events will not reflect the true activity distribution in the subject. The attenuation rate depends on the photon energy as well as the distance and material that these photons have to travel through. In addition to provide anatomical information, CT can be used to estimate the attenuation as it is based on the variable absorption of x-rays by different tissues. A CT scanner consists of a donut-shape gantry, on which an x-ray tube and detectors positioned diametrically opposite to the tube are mounted. In contrast to the stationary geometry of PET, CT x-ray tube and detectors rotate simultaneously around the subject to achieve multiple angle acquisition. The voxel value in a CT image represents the linear attenuation coefficient of a given tissue in relation to that of water in Hounsfield Unit (HU). The noise level of a CT image is affected by the x-ray tube current and voltage. When a higher tube current or voltage is applied, more photons are generated and collected by the detectors hence a lower image noise level can be observed. The change of x-ray tube voltage also changes the CT image contrast as the attenuation rate of x-ray photon varies with its energy determined by the tube voltage. Since a typical CT x-ray tube generates photons with energy between 20 and 150 keV, the derived attenuation coefficients from a CT image have to be converted for photon energy of 511 keV for PET attenuation correction.²³

Limitations With Respect to PET Instrumentation

As the purpose of the CT acquisition in most cases is to provide auxiliary information for PET, limitations with respect

to PET/CT instrumentation can be focused on the system sensitivity and spatial resolution of PET scanners. The former quantifies the total efficiency of PET scanner to detect photons emitted from the subject while the later measures the capability of PET to distinguish close structures. It is well accepted that the diagnostic accuracy of PET is highly affected by these two factors as they determine the image quality and quantitative accuracy of the final PET images. In particular, low sensitivity of PET leads to high noise level in the images. This not only interferes the visual interpretation but also results in overestimation in applications based on quantitative analysis.²⁴ The image appearance is degraded in terms of object delineation by low spatial resolution as well. Since it is hard to obtain reliable regions-of-interests on the blurred images, the quantitative results derived from them can be biased.^{25,26}

By increasing the system sensitivity, one can also achieve a higher patient throughput by shortening the imaging time²⁷ or a lower radiation exposure to both staff and patients by reducing the administered activity.^{28,29} In terms of advanced application, it enables the performance of dynamic imaging with short time frames as well.^{28,29} Many studies have shown that more information regarding the underlying physiological processes can be revealed by analyzing dynamic datasets.³⁰⁻³⁵ Moreover, the increase of sensitivity also helps relieve the constraints on pursuing high resolution PET imaging.³⁶ For example, imaging configurations, such as narrow energy window, can be chosen to exclude small-angle scattering while maintaining reasonable count statistics.

In the past few decades, intensive efforts have been made in geometry and detector design to improve the sensitivity and resolution of PET scanners. For example, scanners with an extended axial FOV are developed to achieve ~5 to 40 times higher sensitivity than current commercial scanners for human whole-body studies^{29,37-39} (Fig. 1). The introduction of detectors with small crystals and the ability of providing depth of interaction discrimination improves the localization of the pair of annihilation photons, which in turn improve the spatial resolution from ~3-5 mm to ~2-3 mm for ¹⁸F-labeled human brain studies.³⁹ The system resolution can also be improved by adopting detectors with fine timing and energy resolution as a more accurate localization of photons and rejection of scattered events can be achieved. The innovations in PET instrumentation with respect to system and detector design are recently reviewed.⁴⁰

Although advanced technical approaches, such as extremely long axial FOV and small crystals, are able to provide fundamental improvements in PET imaging, the implications to economics have limited most of their current applications within research purposes. Instead of pursuing high system spatial resolution of PET scanners, the effectiveness of incorporating TOF information and point spread function (PSF) that models the positron range of the applied positron emitter into a reconstruction algorithm to improve the spatial resolution and qualitative accuracy in the image domain has been demonstrated in literature.⁴¹⁻⁵¹ However, since the modeling may involve high computational demand, the patient throughput could be affected accordingly.⁵² In

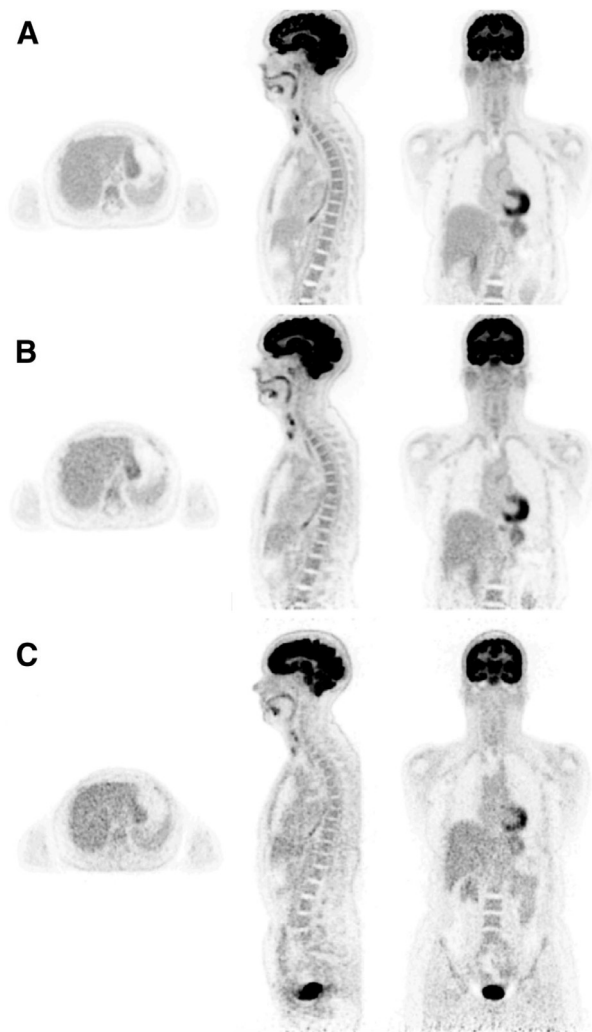


Figure 1 Representative axial (left), sagittal (middle) and coronal (right) views for a healthy subject imaged on the (A) PennPET Explorer (axial FOV = 64 cm) and (C) clinical Philips Ingenuity TF PET/CT (axial FOV = 18 cm) for 20 minutes. The PennPET Explorer data were down sampled by 87.5% to represent a 2.5 minutes scan (B). The subject was injected with 555 MBq of ^{18}F -FDG and scanned at 1 and 1.5 hours after the injection on the Philips Ingenuity TF PET/CT and PennPET Explorer, respectively. An imaging protocol with 10 bed positions was conducted for the Philips Ingenuity TF PET/CT acquisition. Since the system sensitivity is improved as the axial FOV increases, the visual noise level for images in (B) is even lower than that for images in (C). (Adapted with permission from Ref 37.)

addition, it has been shown that PSF reconstruction could lead to edge artifacts at feature boundaries. For small lesion quantification, such artifacts could merge and form a “peak”, resulting in overestimation of maximum standardized uptake value (SUV_{max}).⁵³ To modulate the influence of low system sensitivity on image noise level, a post filtering on the reconstructed images is often applied at the expense of image spatial resolution.^{54,55} In recent years, deep learning based methods for image noise reduction have gained attention in research and clinical communities.⁵⁶⁻⁶⁰ Although effective noise reduction can be achieved efficiently, images generated from these methods usually represent resolution loss.

Moreover, the performance of the networks could depend on the noise level of the images used for training and vary with applications.⁶¹

Artifacts in PET/CT Imaging

Depending on the role of CT in PET data processing, different artifacts could emerge⁶²⁻⁶⁴ Most artifacts observed in PET/CT imaging can be attributed to the misalignment between PET and CT data, errors in the CT-derived attenuation coefficients or CT image truncation.

Misalignment Between PET and CT Data

As the PET and CT data are usually obtained sequentially in practice, misalignment between these two datasets could happen due to motion of the subject between the acquisitions, and/or within either/both of the acquisitions. Even with careful positioning, good alignment between them could still be difficult to achieve as the time spans of the acquisitions is quite different.

The presence of misalignment between PET and CT images can lead to over/under estimation of regional activity distribution when the CT images are used for attenuation correction in PET⁶⁵⁻⁷² (Fig. 2). In the case where the CT data are utilized for scatter estimation, erroneous scatter estimation resulted from the misalignment could degrade the image quality significantly, rendering up the diagnostic value of PET^{73,74} (Fig. 3). Literatures also show that deficiencies in scatter estimation can decrease the convergence rate of the applied iterative image reconstruction algorithm.⁷⁵ The

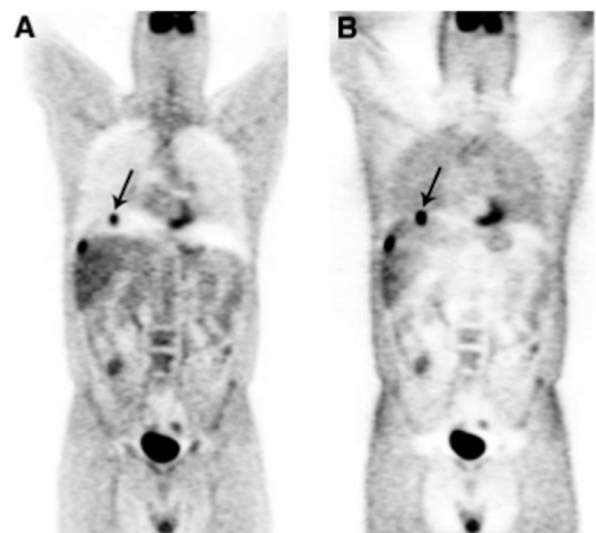


Figure 2 Representative coronal views for a subject with colon cancer. The PET data were reconstructed with (A) and without (B) applying the CT-based attenuation correction. The misalignment between PET and CT due to respiratory motion leads to curvilinear cold artifact around the lower lung and liver dome regions. The lesion at liver dome (indicated with an arrow) is mislocalized to right lung when the misaligned CT is used for attenuation correction. (Adapted with permission from Ref 64.)

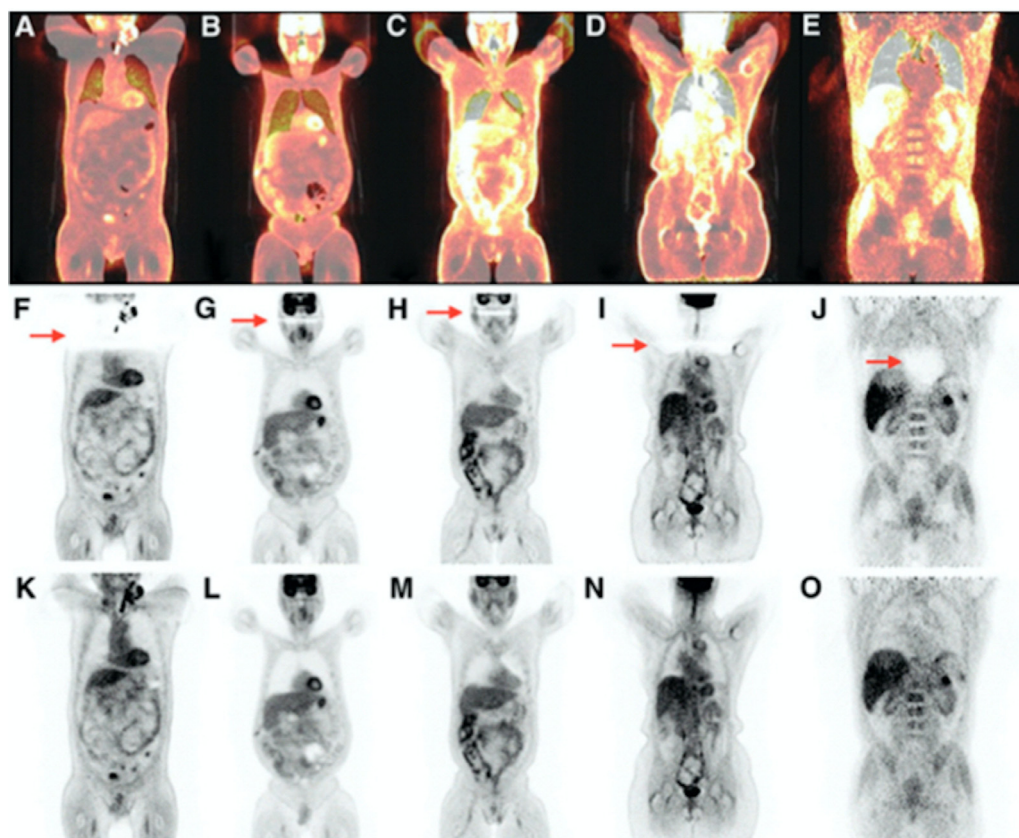


Figure 3 Representative coronal (right) views for five different patients showing artifacts resulted from arm motion. Each column shows data from different patient. First 4 columns show PET data obtained with ^{18}F -FDG (61 ± 16 minutes of uptake and 635 ± 67 MBq). Last column shows PET data obtained with ^{11}C -acetate (28 minutes of uptake and 639 MBq). The first row displays nonattenuation and scatter corrected PET images superimposed on the corresponding CT images to highlight the misalignment between PET and CT due to arm motion. PET images with CT-based attenuation and scatter correction are shown in the second row. Cold artifacts (indicated with red arrows) can be observed at the level of arm motion. The artifacts are substantially reduced (bottom row) by not applying scatter correction. (Adapted with permission from Ref 73.)

image quality and quantitative accuracy hence the diagnostic accuracy of PET can therefore be hampered by the over/under compensation for attenuation, erroneous scatter correction, slow algorithm convergence rate or any combination among them.

Although the diagnostic accuracy of PET can also be affected by the image blurry introduced by motion, this review concentrates on the image degradation factors resulted from the integration of PET and CT. In general, the motion effects that cause the misalignment issues in PET/CT can be categorized into two groups, voluntary motion and involuntary motion. The definition for each group of motion and the possible compensation strategies as well as their challenges in clinical applications will be discussed in this section.

Voluntary Motion

Voluntary motion refers to gross patient motion during and/or between the data acquisitions. In practice, the presence of voluntary motion can be limited by providing clear instruction to the patient. Cushions or holders that restrict movement of the patient can be applied as well.^{62,72}

To tackle the misalignment caused by voluntary motion, software that performs image co-registration can be used to align the CT images with the PET images reconstructed without applying the CT-based attenuation correction. The outcome of the co-registration can then be utilized to transform the CT images which will later be incorporated into a final PET image reconstruction for attenuation correction and scatter estimation.^{76,77} This two-step approach is straightforward and requires minimum changes to the applied reconstruction algorithm. However, it decreases the patient throughput due to the need of performing an additional PET reconstruction.

One strategy around the issue is to apply algorithms that simultaneously estimate the activity distribution and attenuation map from the PET data, leading to perfectly aligned attenuation correction as the attenuation map is derived from PET emission data.⁷⁸⁻⁸¹ The CT images are usually used to provide a priori knowledge regarding the intensity distribution of the attenuation map for the joint estimation as the problem is very ill-conditioned. The scattered events can be calculated based on the estimated attenuation map during the optimization as well. By exploring the information

contained in multiple energy windows, algorithms that allow joint estimation of activity distribution, attenuation map and scattered events are also proposed.⁸² Although the influence of the misaligned CT images in PET reconstruction can be eliminated, the performance of these algorithms is sensitive to the data noise level and the availability of TOF information. In recent years, deep learning based methods are proposed to generate aligned attenuation maps⁸³⁻⁸⁵ or directly the attenuation corrected PET images.⁸⁶ Networks that are able to achieve simultaneous attenuation and scatter correction are proposed as well.^{87,88} This type of approaches is of great interest for clinical applications as it is able to generate the desired results much more efficient than other approaches once the network is trained. However, in addition to having access to powerful computation setups, a large scale PET/CT data collection is also essential for training the deep learning networks. Moreover, although promising results have been shown in literature, a thorough demonstration and evaluation for their reliability in different imaging applications are required.⁸⁹

Involuntary Motion

Misalignment between PET and CT images induced by involuntary motion, including respiratory motion and cardiac contraction, is a well-known problem in PET/CT studies in the thorax region. Articles dedicating to the issue and its potential influence in practice can be found in literature.⁹⁰⁻⁹⁵

Given the time span of PET and CT acquisitions in practice, the reconstructed PET images represent the average position over multiple respiratory and cardiac cycles while the CT images acquired with only a few seconds typically under breath holding are snap shots capturing a nearly static position in the cycles. To eliminate the mismatch in position, CT scanning protocols that aim to obtain CT images representing the average respiratory/cardiac position can be employed.⁹⁶⁻¹⁰⁰ As opposed to finding the averaged CT, methods based on respiratory/cardiac gating on both the CT and PET datasets are developed as well.¹⁰¹⁻¹⁰³ Depending on the applied gating techniques, the data are sorted into several gates according to the phase or displacement of the motion recorded using an external device or derived from the data themselves.¹⁰⁴ The gated CT and PET data are then paired up accordingly and either reconstructed individually and registered to a reference gate¹⁰⁵ or incorporated into 4-dimensional (4D) reconstruction algorithms.^{106,107} Although satisfactory results are shown in literature, clinical applications of these methods are limited by the potential increase of patient total dose and decrease of patient throughput due to the need of special scans to obtain the averaged or gated CT images.

Assuming a finer phase or displacement sampling is applied and negligible motion effects in each gate of PET is observed, the misalignment problem between CT and each gate of PET can be treated as that caused by voluntary motion. Therefore, methods introduced in the previous section can also be utilized to achieve alignment between CT and each gate of PET.¹⁰⁸ Although sharing the same limitations as applied to voluntary motion, these approaches do not rely on the availability of the averaged or gated CT images. However, as only a portion of counts is included in

each gate of PET, an additional image registration between a predefined reference gate and every other gate may be necessary to achieve preferable image noise level for visual interpretation. Instead of seeking the activity distribution and the corresponding attenuation map directly from the PET data, a different joint estimation algorithm incorporates a warp matrix into the objective function to take into account the smooth deformation between different gates induced by respiration and cardiac contraction.¹⁰⁹⁻¹¹¹ Since the whole set of gated PET data is used for the optimization, this algorithm shows the potential to provide aligned attenuation map for each gate without increasing noise level. Similarly, the estimated scattered events can be updated using the deformed attenuation map during the optimization. Although the algorithm is less sensitive to data noise level, it is computationally expensive and shows dependency on the availability of TOF information.

In practice, respiratory motion is a more complicated issue than cardiac motion as the breathing pattern of the patient can change during and/or between the acquisitions. The performance of methods based on gated PET/CT datasets is therefore subject to the breathing variability and applied gating technique.¹¹²⁻¹¹⁴ Although the dependency can be reduced by offering breathing coaching or controller during the scans,¹¹⁵⁻¹¹⁸ regular breathing pattern throughout the data acquisitions is still hard to achieve, especially for patients with compromised lung function. To adapt to irregular breathing patterns, one strategy is to derive individual motion model from the nonattenuation corrected PET images to deform the CT images.¹¹⁹ However, this approach requires initial PET reconstructions and shows performance dependence on tracer distribution and data statistics. The motion model can also be derived from CT images,¹²⁰⁻¹²² with the need of performing respiratory gated CT scans and risk failing when inconsistency in breathing pattern between the CT and PET acquisitions is observed. Although both the implications to imaging protocol and sensitivity to data statistics can be eliminated by using population-based motion models,^{123,124} demonstrations on their usefulness in a clinical context are required. A thorough review on respiratory motion model development can be found in Ref 125.

Errors in CT-Derived Attenuation Coefficients

Contrast Medium

In practice, the conversion from CT numbers to attenuation coefficients for PET data correction is achieved by applying multilinear scaling methods. These methods generally work well with soft tissues and bone structures but could result in overestimation of attenuation for applications involving CT contrast agents.¹²⁶⁻¹³¹ This is because of that the contrast agents usually are designed to have high absorption rate for CT photon energies such that the underlying pathology can be enhanced in CT images. However, considering the difference in photon energies between PET and CT, the increase in

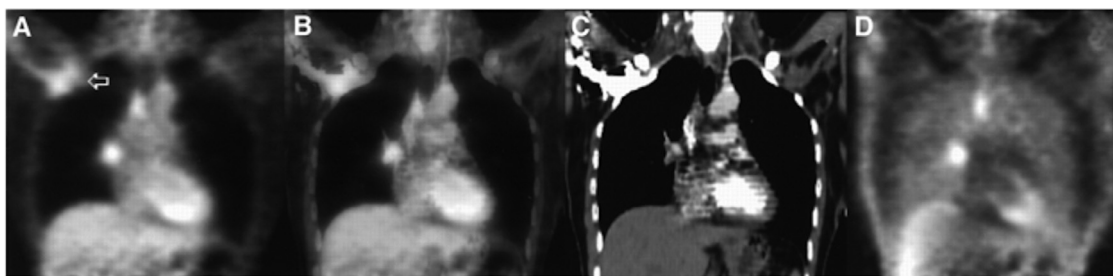


Figure 4 Representative coronal views for a subject with centrally located non-small cell cancer of right lung and mediastinal lymph node metastasis. Attenuation corrected PET image (A), PET/CT fusion image (B), CT image (C) and PET image uncorrected for attenuation (D) are given from left to right. The presence of highly concentrated contrast agent in right subclavian vein on CT image leads to erroneous attenuation correction in right axillary region (indicated with an arrow) on attenuation corrected PET. The hot spot is not detectable on PET image uncorrected for attenuation. (Adapted with permission from Ref 126.)

CT numbers caused by contrast agents may not correspond to a stronger attenuation effect in PET imaging. Therefore, the attenuation could be overestimated around the presence of contrast agent, leading to regional elevation of PET activity (Fig. 4). In addition to conducting a separate noncontrast CT for PET attenuation correction, scaling methods accounting for the influence of CT contrast agent^{132,133} or photon energy difference between PET and CT²³ are proposed. The overestimation of attenuation can also be avoided by using negative oral contrast agents.¹³⁴ For applications where positive contrast agents are necessary, the injection concentration and protocol of the agent can be adjusted to reduce its influence on the derivation of attenuation coefficients.¹³⁵

Metallic Implant

The other cause that leads to erroneous CT-derived attenuation coefficients is the presence of metal implants. Since the x-rays are mostly attenuated by the metallic objects, not much data are recorded in the projection bins intercepted

with the implants. This results in dark and bright streaking artifacts after reconstruction of the data. Application of such CT images for PET attenuation correction introduces over/under estimation of tracer uptake in regions where the artifacts are observed (Fig. 5). This in turn biases quantification and visual interpretation of PET images. Various methods aiming to eliminate the streaking artifacts in CT images have been proposed. The majority of them involve distinguishing the values affected by the metallic objects and replacing them by appropriate estimates in the projection or image domain. There have also been approaches that incorporate estimation and correction of the artifacts into an image reconstruction algorithm. With potential increase of patient total dose, several studies suggest to eliminate the influence of the metallic implants by increasing the tube voltage of the CT scanner or employing a dual-energy CT scan. More details as well as the strengths and limitations of these strategies have been discussed in literature.¹³⁶⁻¹³⁸ Recently, deep learning networks operating in the projection¹³⁹⁻¹⁴¹ or image domain¹⁴¹⁻¹⁴⁷ are also explore for achieving efficient metal artifact reduction.

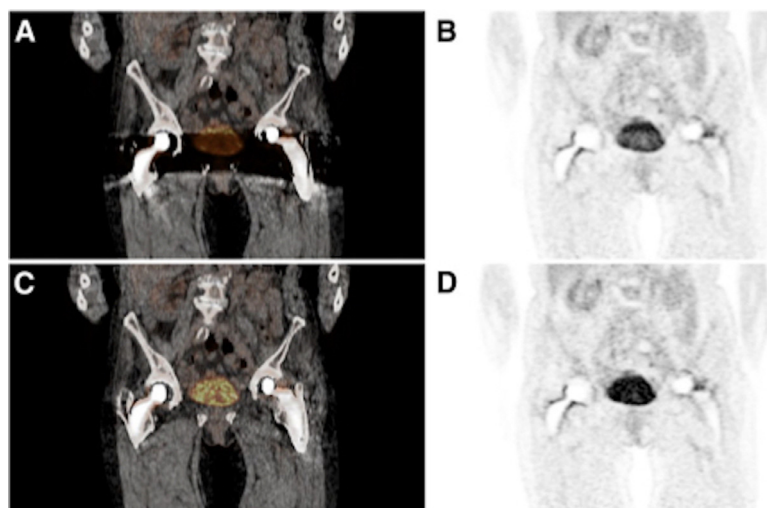


Figure 5 Representative coronal views for a subject with possible malignant cyst in right ovary. The metallic implants lead to a dark band in hip region on CT image (A). The artifact is substantially reduced by applying an iterative metal artifact reduction algorithm (C). PET images using CT without and with applying metal artifact reduction for attenuation correction are given in (B) and (D). The artifact in CT leads to lower activity in the corresponding regions on PET image. (Adapted with permission from Ref 149.)

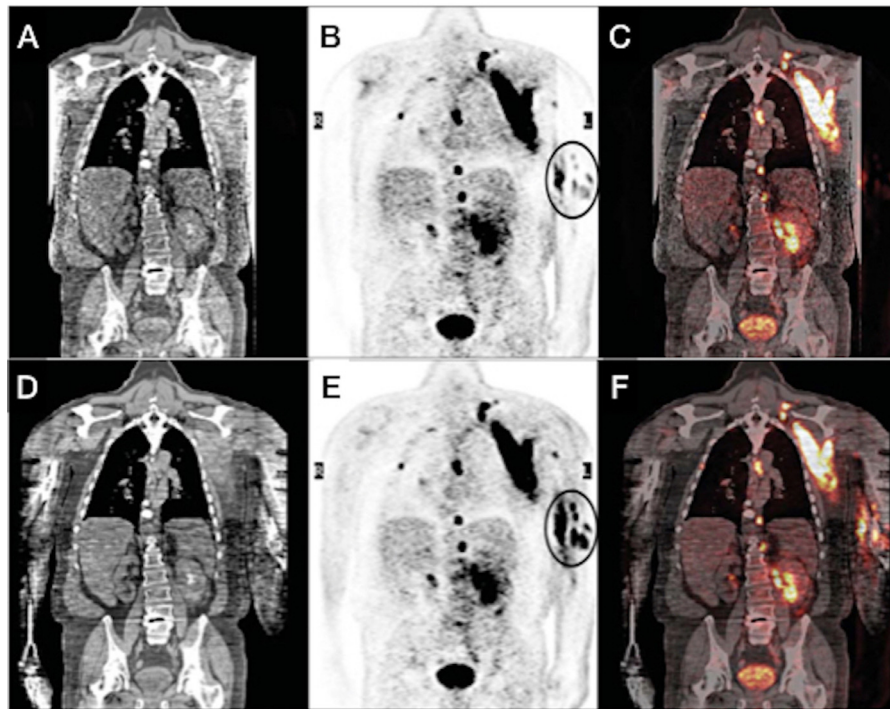


Figure 6 Representative coronal views for a subject with history of diffuse large B-cell lymphoma. The first row displays CT image with truncation of arms (A), PET image using the truncated CT for attenuation correction (B) and PET/CT fusion image. The corresponding results with truncation correction on CT are shown in the second row (D)-(F). The contrast of lesions within the truncated region becomes higher after applying the correction. In terms of quantification, an average difference of 328% in maximum standard uptake value (SUV) for four measurements of ^{18}F -FDG-avid tumor (within ellipse) was recorded. (Adapted with permission from Ref 153.)

Although most of the above mentioned methods are developed for diagnostic CT imaging, several studies have shown the effectiveness of considering metal artifact reduction techniques for PET/CT systems to prevent potential quantitative errors and false interpretation of PET images.¹⁴⁸⁻¹⁵¹

CT Image Truncation

Since the transaxial FOV of CT is usually smaller than that of PET for commercial PET/CT systems, the anatomy covered in PET imaging could be truncated in CT, especially for large patients.¹⁵² Different patient positioning in PET and CT acquisitions, for instance the arms of the patient are placed over the head in one scan but at the side in the other scan, can also lead to anatomy mismatch between PET and CT images. The lack of corresponding information from CT for attenuation correction can cause over-/underestimation of tracer concentration in PET⁶⁴ (Fig. 6). Although not being removed completely, issues induced by anatomy mismatch in PET and CT can be largely reduced by applying CT data extrapolation based on the assumption that the total attenuation of each projection should be a constant.¹⁵³⁻¹⁵⁸ With small modifications, the algorithm proposed to estimate the attenuation map and activity distribution simultaneously can be used to estimate the missing attenuation information as well as the activity distribution.¹⁵⁸⁻¹⁵⁹ However, as it requires an initial PET reconstruction and a priori information

regarding the location of the affected regions, the algorithm shows potential implications to the patient throughput for clinical applications. Although further demonstration is required, a recently proposed machine learning based method can also be a possible solution.¹⁶⁰

Conclusion

The introduction of combined PET/CT scanners has improved the diagnostic accuracy and patient throughput significantly in various fields. With decades of physics and instrumentation developments, potential clinical applications that rely on accurate lesion delineation and quantification have become possible. However, there are still technical challenges hence opportunities to make further improvement in PET/CT imaging to ensure that the best interests of both the health care providers and public are upheld.

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