



Dynamic whole-body FDG-PET imaging for oncology studies

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Received: 30 October 2021 / Accepted: 4 January 2022 / Published online: 20 January 2022
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Abstract

Introduction Recent PET/CT systems have improved sensitivity and spatial resolution by smaller PET detectors and improved reconstruction software. In addition, continuous-bed-motion mode is now available in some PET systems for whole-body PET imaging. In this review, we describe the advantages of dynamic whole-body FDG-PET in oncology studies.

Methods PET–CT imaging was obtained at 60 min after FDG administration. Dynamic whole-body imaging with continuous bed motion in 3 min each with flow motion was obtained over 400 oncology cases. For routine image analysis, these dynamic phases (usually four phases) were summed as early FDG imaging. The image quality of each serial dynamic imaging was visually evaluated. In addition, changes in FDG uptake were analyzed in consecutive dynamic imaging and also in early delayed (90 min after FDG administration) time point imaging (dual-time-point imaging; DTPI). Image interpretation was performed by consensus of two nuclear medicine physicians.

Result All consecutive dynamic whole-body PET images of 3 min duration had acceptable image quality. Many of the areas with physiologically high FDG uptake had altered uptake on serial images. On the other hand, most of the benign and malignant lesions did not show visual changes on serial images. In the study of 60 patients with suspected colorectal cancer, unchanged uptake was noted in almost all regions with pathologically proved FDG uptake, indicating high sensitivity with high negative predictive value on both serial dynamic imaging and on DTPI. We proposed another application of serial dynamic imaging for minimizing motion artifacts for patients who may be likely to move during PET studies.

Discussion Dynamic whole-body imaging has several advantages over the static imaging. Serial assessment of changes in FDG uptake over a short period of time is useful for distinguishing pathological from physiological uptake, especially in the abdominal regions. These dynamic PET studies may minimize the need for DTPI. In addition, continuous dynamic imaging has the potential to reduce motion artifacts in patients who are likely to move during PET imaging. Furthermore, kinetic analysis of the FDG distribution in tumor areas has a potential for precise tissue characterization.

Conclusion Dynamic whole-body FDG-PET imaging permits assessment of serial FDG uptake change which is particularly useful for differentiation of pathological uptake from physiological uptake with high diagnostic accuracy. This imaging can be applied for minimizing motion artifacts. Wide clinical applications of such serial, dynamic whole-body PET imaging is expected in oncological studies in the near future.

Keywords Whole-body PET · ¹⁸F-FDG · Dynamic acquisition · Cancer

Introduction

¹⁸F-FDG-PET/CT is now widely used as a valuable imaging modality in clinical oncology. This is commonly used for tumor characterization, staging, restaging, and therapy monitoring [1–5]. FDG-PET imaging has been used as surrogate for assessment of tumor glycolytic activity, which is an important marker of tumor biology. Current FDG whole-body PET/CT imaging is performed at a predefined time point, usually 60 min after tracer administration. PET/CT images are reviewed qualitatively for FDG uptake (positive

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or negative) and semi-quantitative measure of glucose uptake by the standardized uptake value (SUV) [6–8]. On the other hand, FDG uptake is also seen in physiological tissues. Thus, it is often difficult to differentiate pathological ^{18}F -FDG uptake from physiological ^{18}F -FDG uptake in routine static PET imaging [9–15].

Present study summarizes advantages of serial dynamic whole-body PET imaging and introduces several clinical values of assessing dynamic FDG uptake changes in oncology studies.

Methods

Most PET systems use step-and-shoot imaging for whole-body imaging, in which dynamic PET study may be confined to a single-bed position. Some new PET camera systems have continuous-bed-motion mode for whole-body imaging using flow-motion system [16–18]. This dynamic whole-body imaging has several advantages over the conventional step-and-shoot bed motion (Fig. 1). Actual field of view is

the area of detector field of view in step-and-shoot motion which may show low sensitivity in peripheral areas of view. Thus, some overlap imaging is needed for each step for whole-body imaging. In continuous bed motion, on the other hand, the sensitivity over the axial range is uniform with requiring no overlap [16–18]. Therefore, the whole-body imaging with continuous bed motion permits better uniformity, reproducibility, and higher sensitivity than the conventional whole-body imaging with step-and-shoot motion. In addition, FDG uptake change and motion may be visually assessed using various sequential analysis (Table 1).

In our PET centers, each patient fasted for > 4 h, and their blood glucose levels were below 200 mg/dl prior to FDG injection. FDG-PET/CT imaging was obtained at 60 min after administration of 2–5-MBq/kg body weight of ^{18}F -FDG. We performed serial dynamic whole-body imaging with continuous bed motion at varying speeds (6 mm/s from the head to the pelvis and 14 mm/s for the lower limbs in our hospital) to acquire each whole-body phase in ~ 3 min in list mode using Biograph Horizon with flow motion (Siemens Medical Solutions) [19, 20].

Fig. 1 Actual field of view on step-and-shoot imaging and continuous-bed-motion imaging. Since sensitivity is low in the peripheral areas of view, and thus, some overlap imaging is needed for whole-body imaging in step-and-shoot imaging. On the other hand, actual field of view is uniform without need for overlap imaging in continuous bed motion. Thus, the sensitivity is higher and uniform for whole-body imaging in the continuous bed motion

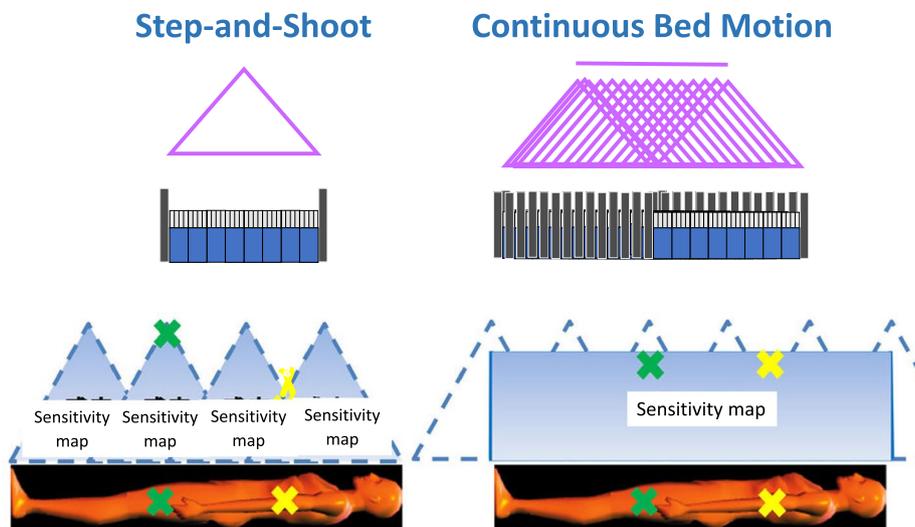


Table 1 Advantages of dynamic whole-body imaging using continuous bed motion

Physical advantages

- Better uniformity and reproducibility
- Higher sensitivity (no need for overlap imaging)
- Dynamic whole-body imaging available

Clinical advantages

- High-quality images available after summation for routine image analysis
- Dynamic assessment of serial changes in shape and uptake (differentiation of pathological uptake from physiological uptake)
- Select suitable images for summation without motion artifact
- Quantitative analysis of FDG uptake using appropriate kinetic models (parametric imaging available such as K_i , DV)
- Potential applications of kinetic studies in whole body with new PET tracers

For the purpose of routine image interpretation, these dynamic phases (usually four phases) were summed in a reconstruction equivalent to a 12-min whole-body acquisition for routine image interpretation. The dynamic whole-body PET images and the summed whole-body PET image were reconstructed using attenuation-corrected ordinary Poisson three-dimensional ordered-subset expectation maximization (3D-OSEM) reconstruction with a 4-mm post-reconstruction Gaussian filter, using a 180×180 -pixel matrix [19, 20],

Image interpretation was performed by two board-certified nuclear medicine physicians and the final judgment was decided by consensus [19, 20].

Results

Image quality

We have acquired over 400 cases of this dynamic whole-body FDG-PET imaging as a part of routine procedures, particularly for patients suspected with abdominal areas. Two board-certificated nuclear medicine physicians performed image interpretation and assessed the image quality of the serial dynamic whole-body and summed images [19, 20]. All of the 3-min serial dynamic whole-body PET images were of acceptable image quality. Most of 12-min summed whole-body images provided high-quality images which are commonly used for routine image interpretation [19, 20]. In addition, dynamic whole-body imaging has been used for various clinical purposes as described in Table 1.

Differentiation of pathological uptake from physiological uptake

It is often difficult to differentiate pathological ^{18}F -FDG uptake from physiological ^{18}F -FDG uptake on routine static PET imaging. Dynamic distribution of ^{18}F -FDG uptake may hold a promise to differentiate pathological uptake without change from physiological uptake with change (Table 1). Accordingly, we performed dynamic whole-body imaging to assess the serial change of ^{18}F -FDG uptake in various anatomical regions. Areas of high ^{18}F -FDG uptake were identified in dynamic images and summed image. In dynamic image evaluation, if an area of high uptake disappeared in any phase, or if more than half of the area of uptake showed morphologic change, these were defined as areas of “changed uptake”.

In dynamic image evaluation, physiological changed uptake was found in 9/19 areas in gastric region (47%), 32/39 areas in small intestine (82%), 17/33 areas in colon (52%), and 60/63 areas in ureter (95%) (Fig. 2). On the other hand, most of benign and malignant lesions showed no visual change in serial images, suggesting high diagnostic value for differentiating physiological FDG uptake from pathological FDG uptake based on presence of uptake change on serial dynamic imaging [19].

A number of studies indicate that malignant lesions often show a gradual increase of FDG accumulation from an early phase to a delayed phase, and therefore, dual-time-point imaging (DTPI) may provide increased ability to detect malignant lesions and facilitate differentiation of malignant lesions from benign lesions [21–27]. Thus, delayed (90–120 min after FDG administration) PET imaging is often applied to compare the FDG uptake with that on conventional early (60 min after FDG administration)

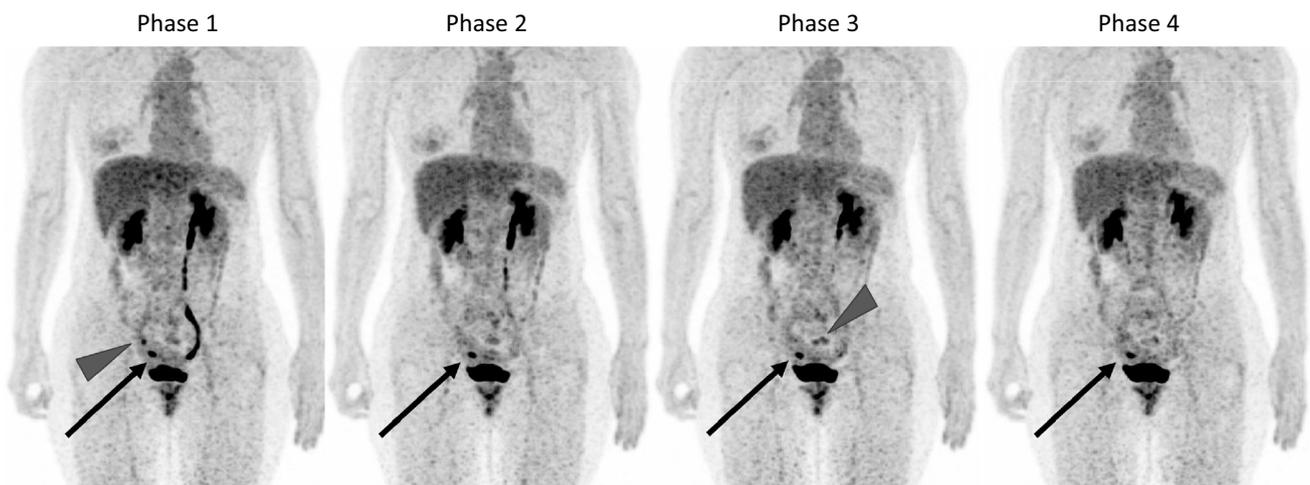


Fig. 2 Four serial whole-body dynamic PET images (3 min each) of a patient with rectal cancer. FDG uptake in the rectal cancer does not move (arrows) but other FDG uptakes in ureter and sigmoid colon move (arrow heads)

PET imaging. This early delayed imaging (dual-time-point imaging; DTPI) plays a valuable role for the differentiating FDG take lesions [21–27]. However, such delayed imaging is cumbersome for patients who have to wait to come back to PET room for separate delayed imaging. In addition, such imaging requires additional machine time and another radiation burden to each patient by additional CT for attenuation correction.

We assessed the frequency of change observed in colorectal uptake shape by dynamic PET imaging as compared to DTPI, to differentiate pathological uptake from physiological uptake in 60 patients with suspected colorectal cancer [20]. Particularly, when changed FDG uptake was seen on serial dynamic imaging as well as DTPI, such lesion was highly likely to represent physiological FDG uptake. Among 73 histologically proven pathological FDG uptakes, unchanged uptake was noted in almost all regions with high sensitivity on both serial dynamic imaging and on DTPI (Fig. 3). In addition, most of the changed FDG uptake on either serial dynamic imaging or DTPI was physiological

uptake, indicating very high negative predictive value. These results indicated that high focal FDG uptake was highly likely to be physiological uptake when the focal FDG uptake showed changes on serial dynamic imaging and DTPI, as well [20]. Our results also indicated slightly but significantly higher diagnostic accuracy of serial dynamic imaging for such differentiation than DTPI.

Similar results were obtained with other abdominal cancer, such as gynecological tumors (Fig. 4). Based on these results, serial dynamic imaging permits assessment of sequential changes in uptake shape within a short period without any additional imaging time.

Minimizing motion artifact

Typical patient motion has several types, including periodic respiratory and cardiac motion, non-periodical motion of the stomach and bowel system, and bulk body motion [28–30]. The most straightforward correction method is to perform respiratory and electrocardiographic gated

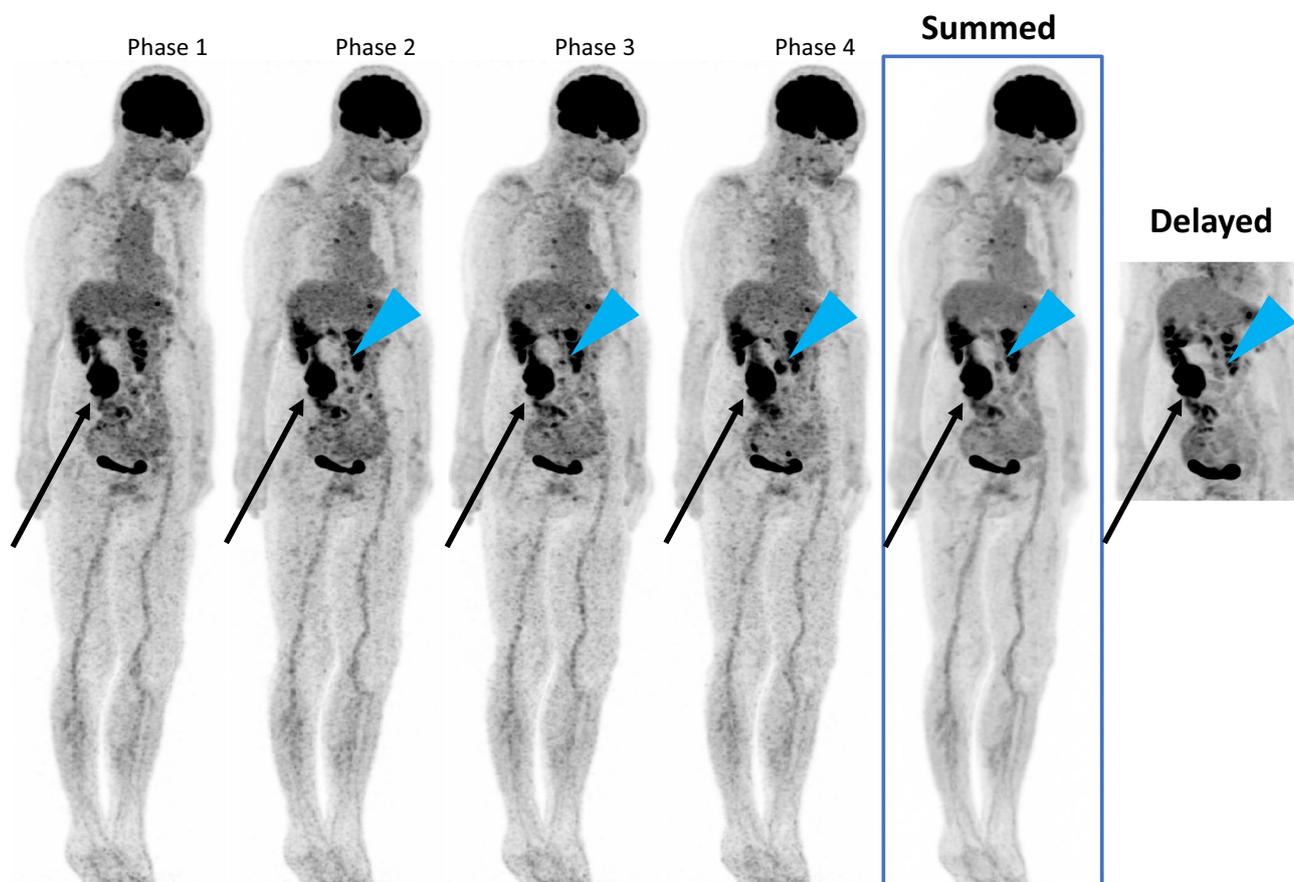


Fig. 3 Four serial whole-body dynamic PET images (3 min each), the summed image (12 min), and the delayed image of a patient with colon cancer. High FDG uptake in the ascending colon does not move (arrows), but adjacent FDG uptake in colon changes in shape (arrow

heads) on serial dynamic imaging. The FDG uptake change is also noted on summed early and delayed imaging, but such FDG uptake change is better identified by serial dynamic imaging

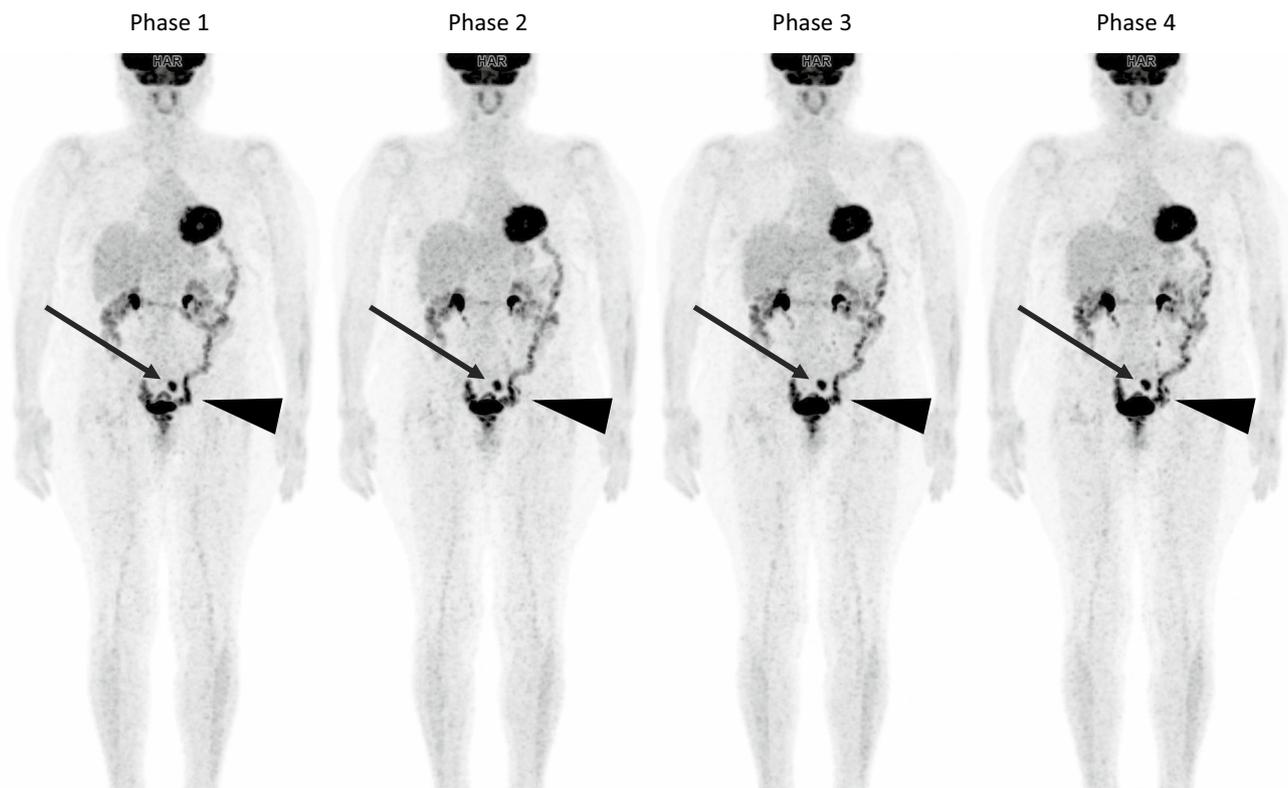


Fig. 4 Four serial whole-body dynamic PET images (3 min each) of a patient with endometrial cancer. FDG uptake in the endometrial cancer does not move (arrows) but other FDG uptakes in sigmoid colon slightly move (arrow heads)

acquisition, to accept only data from the end-expiration phase of the breathing cycle or end-diastolic phase of the cardiac cycle. The motion noise may be minimized with short PET acquisition. However, medication may reduce bowel motion for imaging.

Actual patient motion should seriously be considered for appropriate PET imaging. Since most FDG-PET-CT studies are performed for oncology patients, many of them may have difficulty in staying still without motion during PET/CT imaging due to pain. It is also difficult to ask young child or demented person to stay still for imaging. Patient motion may often create detrimental motion artifacts causing difficulty in image interpretation. When the patient motion is simple, such motion may be corrected by use of anatomical information for suitable reconstruction [31]. However, complex motion may cause difficulties in motion correction in many cases.

We have proposed another application of serial whole-body dynamic imaging for minimizing motion artifacts. Figure 5 shows serial 3-min dynamic whole-body images of 82-year-old patient with lung cancer. The Phase 3-to-Phase 5 images suggested arm motions. While summation of Phase 1 through Phase 5 images showed striking motion artifacts in chest and arms, such motion artifacts were minimized by summation of Phase 1 and Phase 2 images. In addition, the

image quality was high with these summation as compared to the individual 3-min whole-body images [32].

Potential roles for quantitative assessment

PET has a great advantage for quantitative analysis of tracer concentration and metabolic alterations using suitable tracer kinetic models. FDG uptake and clearance depend on the time interval between intravenous FDG administration and imaging. On sequential image analysis after FDG administration, tissues with high glycolysis may have continuously increasing amounts of FDG trapped in cells in the form of FDG-6-phosphate, while FDG uptake may decrease over time in tissues with high glucose-6-phosphatase. In many PET studies, standardized uptake (SUV) value of FDG at the time of FDG-PET imaging is quantitatively analyzed and displayed. In addition, SUV uptake change over time is analyzed over 30–60 min using DTPI in various oncology fields [33–40]. On the basis of the concept of differences in glucose metabolism, FDG uptake tends to increase or remain high in many malignant lesions as compared to benign lesions including infection and inflammation. Such differences may be nicely assessed by sequential FDG imaging. However, a number of other studies have demonstrated significant overlap of FDG uptake patterns between benign and

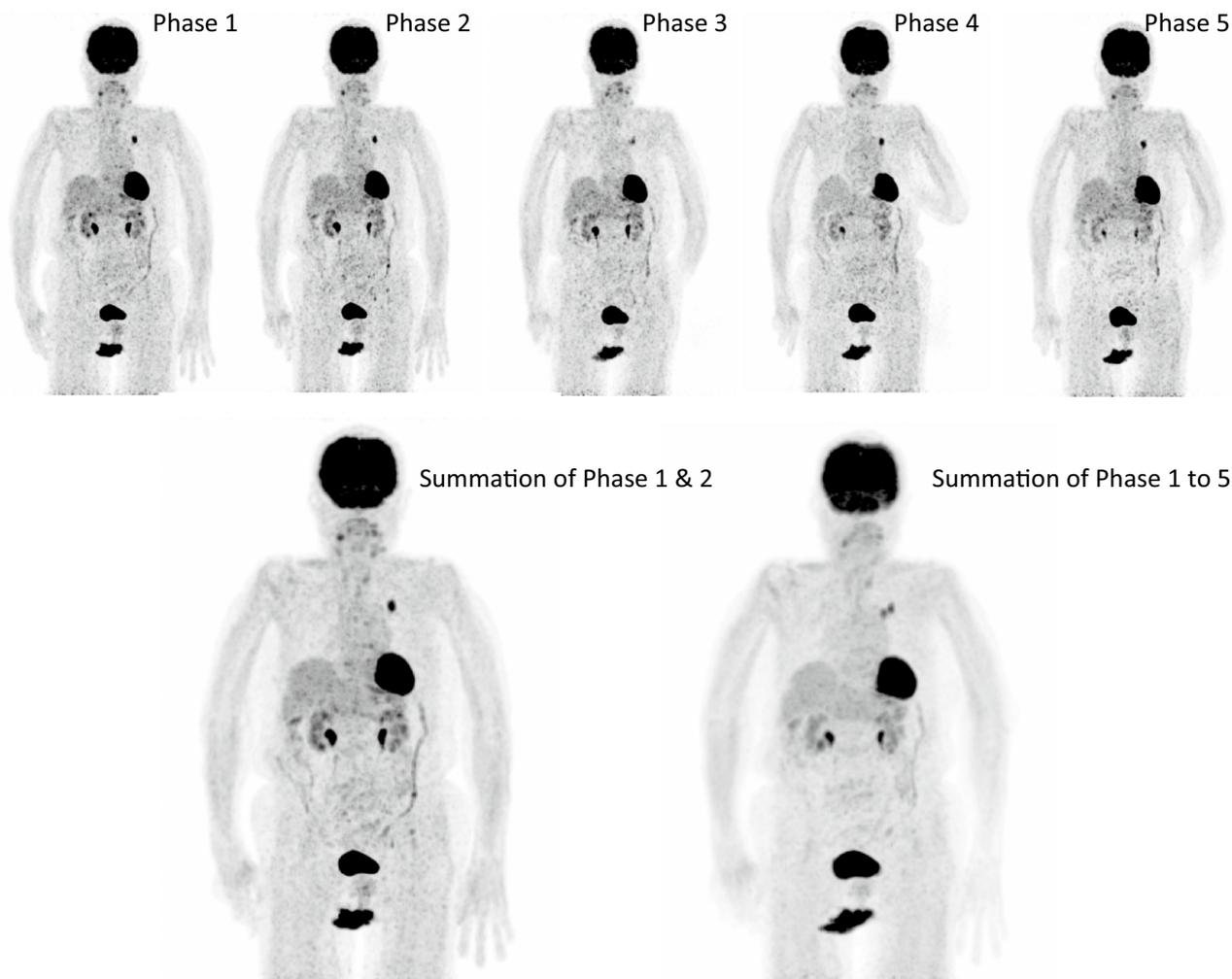


Fig. 5 Five serial dynamic whole-body PET images (3 min each) (top) of 82-year-old patient with lung cancer. This patient moved during Phase 3 through Phase 5 images. The summed-up FDG image (from Phase 1 to Phase 5) (bottom right) shows motion artifact,

including pulmonary lesion. However, the motion artifact is minimized with better image quality on the selected summed-up image (Phase 1 and Phase 2) (bottom left)

malignant lesions even on DTPI [33, 41]. Serial dynamic whole-body PET also enables semi-quantitative analysis of FDG uptake changes similarly with DTPI (Fig. 6) [18]. Serial imaging has advantages for more reliable assessment of FDG uptake change using multiple points as compared to the two-point analysis with DTPI (Table 1).

Discussion

Dynamic whole-body imaging has several advantages over a single static imaging. Serial assessment of changes in FDG uptake over a short period of time is useful for distinguishing pathological from physiological uptake. It is effective in distinguishing pathological from physiological uptake, especially in the abdominal region [19].

These dynamic PET studies may minimize the need for DTPI [20]. In addition, continuous dynamic imaging has the potential to reduce motion artifacts in patients who are likely to move during PET imaging. The total acquisition time for this dynamic whole-body imaging ($3 \text{ min} \times 4\text{--}5$) is same as conventional single whole-body imaging (12–15 min). The major differences are that this dynamic imaging may require small additional time for reconstruction and data management as compared a single whole-body imaging.

These conclusions were obtained for those suspected with colorectal cancer and other abdominal cancer, as shown in Fig. 4. This new imaging is particularly useful to differentiate para-aortic or para-iliac lymph-node involvements from physiological FDG uptake in ureter, colon, or ovaries. Furthermore, this new imaging may be able to minimize

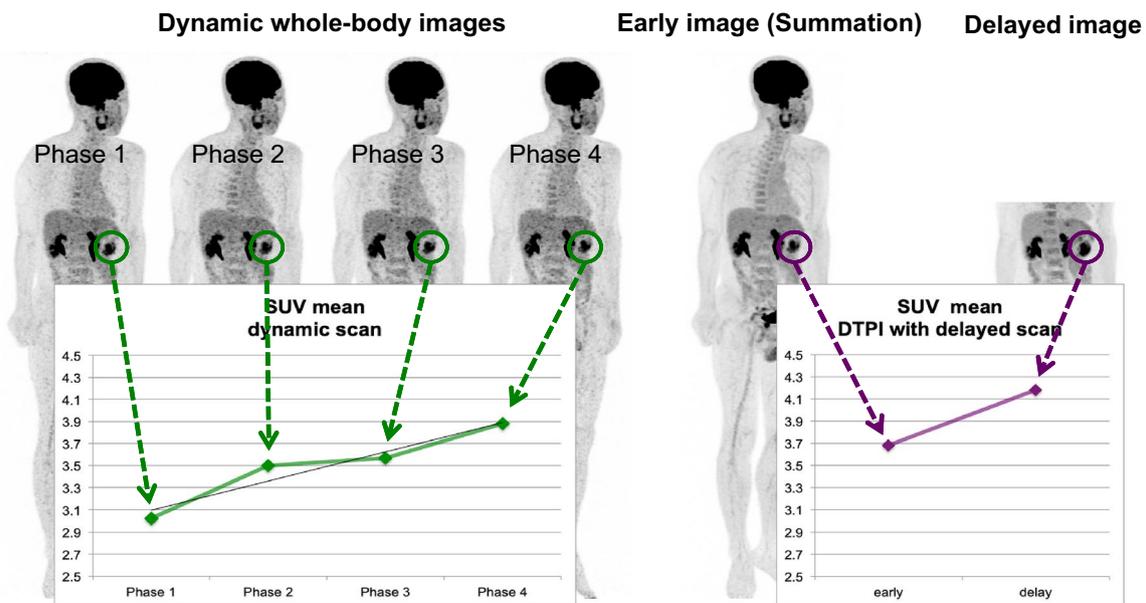


Fig. 6 Four serial dynamic whole-body PET images (left) and early (summation)/delayed images (right) of a patient with colon cancer. High and persistent FDG uptake is noted (circles) with FDG count

increase in the lesion on dynamic images. Such FDG uptake increase is also noted on dual-time-point imaging (DTPI)

the need of delayed imaging for assessment of FDG uptake change.

There are several reasons why the serial dynamic imaging showed a better FDG uptake in motion than DTPI. FDG may accumulate in the wall of the GI tract but may also be secreted inside the GI tract, resulting in to-and-fro motion in the GI tract [42, 43]. Dynamic whole-body imaging has the additional advantage of enabling the assessment of uptake change over time on multiple serial images (sometimes with cine-mode display) as compared to only two images on DTPI.

There seems to be rather rare to show significant artifacts due to patient motion during PET study. In addition, a striking patient motion may stop the image acquisition to reset the PET camera for another imaging. However, such serial dynamic imaging is particularly useful in reducing mild but significant motion artifacts for patients who may be likely to move during PET studies (Table 1).

Another important aspect of this dynamic imaging is for semi-quantitative analysis of FDG uptake changes. We analyzed count change in SUV mean by making small region of interest (ROI) in abnormal uptake areas as compared to the early delayed imaging, as shown in Fig. 6.

New strategies are developed for the generation of parametric images (pixel-by-pixel analysis), ranging from graphical analysis, such as Patlak method [44, 45]. The graphical analysis is a simple, robust, and enables the direct estimation of the primary kinetic macro-components of the tracer uptake across multiple fields of views. The serial dynamic

whole-body PET imaging is considered as a suitable method for this purpose. Recently, there are a number of reports which indicate clinical feasibility of dynamic FDG-PET/CT applied on a pilot cohort of oncology cases [46–48]. One of the preliminary studies indicates that multi-pass whole-body PET K_i parametric imaging utilizing robust Patlak graphical analysis may achieve equivalent or, potentially, superior lesion detectability than standard-of-care SUV imaging with reduced false-positive rates in routine oncology applications [48]. K_i parametric imaging seems to be particularly valuable to differentiate abnormal uptake lesions with gradual increase in FDG uptake from physiological uptake areas with gradual decrease in uptake such as liver and vessels. K_i may reflect count change, and, therefore, has a potential to enhance detection of abnormal FDG uptake lesions in high background areas [48, 49].

The Patlak model is valid after some time when the free tracer has reached a steady state between blood and tissue. This model estimates the Patlak slope (K_i) which is the rate of irreversible uptake, and the Patlak intercept (DV), which is the apparent distribution volume of non-metabolized tracer (Table 1). Accordingly, the metabolic rate of FDG is estimated as follows: $\text{MRFDG} = K_i \times \text{blood glucose}$ [49, 50].

One of the major issues for kinetic analysis is how to obtain suitable input function for graphic analysis. Arterial or arterialized venous blood sampling is commonly performed particularly for brain studies, but this is quite invasive [44, 51–53]. Image-based input function can be obtained by serial dynamic PET imaging which covers large

arterial blood regions such as the left ventricle and aorta [54]. Recently, standardized input function was proposed as a surrogate which may facilitate such parametric studies, as compared to the actual measurement of input function on rapid dynamic imaging in the cardiac areas [55–58]. Such precise FDG kinetic analysis seems rather complicated and remains investigative. However, serial dynamic FDG-PET imaging may hold a new promise for quantitative analysis of glucose metabolism with suitable kinetic models for precise tissue characterization in variety fields, including oncology area.

Conclusions and future directions

Recent advances of PET camera system permit dynamic whole-body imaging. This new imaging has significant advantages over the conventional step-and-shoot bed motion. Serial assessment of FDG uptake changes within short time interval is valuable in differentiating pathological uptake from physiological uptake, particularly in abdominal areas. Such serial dynamic imaging is useful to reduce possible mild but significant motion artifacts for patients who may highly likely to move during PET studies. Furthermore, more precise assessment of tissue characterization is possible in oncological studies. Such dynamic tracer kinetic studies are needed in the whole-body areas using new PET tracers (Table 1). Since such elegant image acquisition and analysis will become available with new and high-performance PET systems, wide clinical applications of such imaging are expected in the near future.

Acknowledgements We appreciate Siemens Medical Systems for strong technical support for imaging and reconstruction.

Declarations

Conflict of interest All authors declare that there has no conflict of interest.

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