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Respiratory Motion and Gating in Whole-Body PET/CT Imaging

By Paul Kinahan, Ph.D.

LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

1. List two major roles of CT imaging in combined PET/CT scanners.
2. Explain the sources and effects of respiratory mismatch between PET and CT images.
3. Summarize the methods used to mitigate the effects of respiratory mismatch.
4. Describe the potential benefits of respiratory gating in whole-body PET imaging.

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PET radiotracer imaging with the labeled glucose analog F-18 fluorodeoxyglucose (FDG) is increasingly being used in oncology imaging due to its usefulness in detecting and staging cancer and metastatic disease.^{1,2} A promising new application of PET is tumor imaging for therapy monitoring, which constitutes a strong basis for individually tailored therapy for patients.^{3,4} Both respiratory motion and respiratory gating in whole-body PET/CT imaging can affect diagnosis and assessment of therapy response for oncology and cardiac imaging.

Awareness of the value of using PET/CT imaging to identify early response to therapy has been increasing. In January 2005, the National Cancer Institute sponsored a workshop on the role of FDG-PET in the evaluation of therapeutic response in cancer. One conclusion from the workshop was that improved quantitation is needed, including robust and accurate methods for performing PET/CT imaging.

The advent of the dual-modality PET/CT scanner has improved the ability to diagnose and stage cancer and to monitor response to therapy.⁵ PET/CT has become the most comprehensive diagnostic tool in oncology imaging by providing improved lesion identification and localization.⁶ PET/CT scanners are now also being used for cardiac imaging, as an integrated scanner offers a single-study noninvasive technique for the diagnosis of coronary artery disease. PET imaging provides functional measurement of myocardial perfusion and metabolism, while contrast-enhanced CT angiography offers

structural assessment of coronary anatomy and atherosclerotic burden.

The primary purpose of combining CT and PET systems in a single scanner is the precise anatomic localization of regions identified on PET images showing radiotracer uptake. Although it is possible to use nonrigid image registration to align separately acquired whole-body PET and CT images, challenges remain in the practical implementation and validation of software-based methods.⁷

A secondary benefit, but an important synergy, of dual-modality imaging is the use of CT for attenuation correction of PET emission data.⁸ Compensating PET emission data for the effects of photon attenuation by the patient is an essential step for generating quantitatively accurate PET images. If attenuation correction is not performed, the resulting PET image is strongly distorted in a complex spatially varying manner. In earlier PET-only scanners, attenuation correction factors were measured by an orbiting positron transmission source acting much like an x-ray CT scanner, albeit one that produced an extremely noisy attenuation image.

All manufacturers of PET/CT scanners now incorporate x-ray CT-based attenuation correction (CTAC) algorithms in their systems. For most PET/CT scanners, such an algorithm is the only option offered. The CT data have much lower statistical noise and can be acquired in a shorter time than a standard PET transmission scan. CT transmission scans can also be acquired after the PET tracer is injected, which provides unbiased postinjection transmission scanning, reducing image

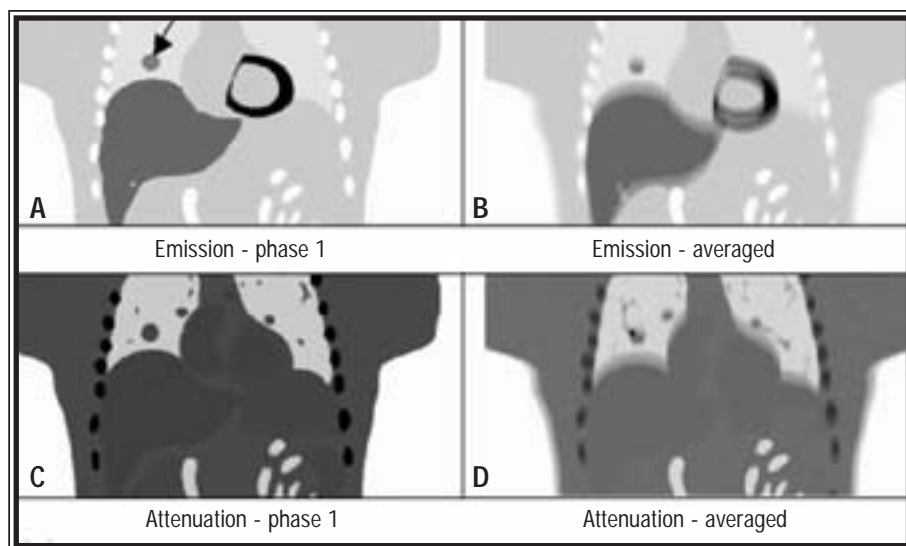


Figure 1. Noiseless computer simulation shows effects of respiratory motion on PET emission and attenuation images. Top row shows emission object (tracer uptake), while bottom row shows linear attenuation coefficients that will reduce the PET emission data. These must be corrected.

bias while shortening the time spent by a patient on the scanner bed and providing more efficient use of scanner time.

The use of CT-based attenuation correction, however, can potentially introduce errors into the PET image, which is undesirable in quantitative assessment of response to therapy. There are two major sources of error in CT-based attenuation correction: scaling of attenuation coefficients and positional mismatches between the PET and CT acquisitions.⁸

To be used for attenuation correction, the CT data must be transformed to an estimate of the attenuation coefficients at 511 keV. The so-called bilinear scaling method is used on PET/CT scanners to convert CT images for attenuation correction of PET data. In this method, different scaling factors (for water and air, and for water and bone, respectively) are used to calculate the attenuation values for CT numbers H for which $-1000 < H < 0$, and for $H > 0$. The bilinear scaling method has been shown to give reasonable results for biological materials in practice. With materials such as contrast agents, however, errors in PET image standardized uptake values (SUVs) can be introduced by using the bilinear scaling method. While these errors may not significantly affect diagnostic utility in many cases, they can affect decisions or therapies that depend on accurate estimation of tracer uptake.

RESPIRATORY MOTION

Positional mismatches between PET and CT acquisitions can occur in two ways:

large-scale patient motion (e.g., shifting on the scanner couch) and respiratory motion.⁸ The spatial blurring and effect on image contrast caused by respiratory motion is illustrated in Figure 1 using a computer simulation of a torso with a 2-cm lesion (arrow).

The respiratory motion in this study was divided into 10 phases, or segments. The left column of Figure 1 shows the emission and attenuation images for just the first phase of the respiratory cycle, corresponding to end-expiration. Since this represents one-tenth of the respiratory cycle, little or no respiratory blurring effect is visible. The right column of Figure 1 shows the equivalent images averaged over all 10 phases of the respiratory cycle. In this case, considerable blurring and reduction in contrast at the edges of objects are visible.

The full effect of respiratory motion in PET/CT imaging is more complicated than Figure 1B implies. The figure illustrates a case in which attenuation correction is not needed. In fact, attenuation correction is needed to recover either Figure 1A, which would be obtained if respiratory gating is used, or Figure 1B, which corresponds to standard whole-body PET imaging (respiratory averaged). In earlier PET-only scanners with an orbiting transmission source, a respiratory-averaged attenuation image similar to Figure 1D was measured, since the transmission acquisition lasted several minutes. This image could be used to correct the respiratory-averaged PET emission data corresponding to Figure 1B.

This correction procedure using emission and attenuation data that were already respiratory averaged does not strictly follow protocol, as attenuation correction should be applied before any respiratory averaging. Nonetheless, this procedure, which is still used in PET-only scanners, generally provides acceptable results, likely because the noise in the PET transmission scan tends to mask any errors caused by applying attenuation correction after the respiratory averaging of the emission and attenuation data.

With CT-based attenuation correction, the CT-image is acquired much more quickly, leading to an attenuation image that can look more like Figure 1C than 1D. Diagnostic CT imaging protocols typically call for a helical CT scan to be acquired during a breath-hold, reducing well-known artifacts that appear if respiratory motion occurs. Unfortunately, the breath-hold is usually at maximum inspiration, which leads to a poor spatial match with the PET emission data. This spatial mismatch can then lead to errors in attenuation correction, and thus incorrect PET image values, and spatial misalignment between the PET and CT images.

Most PET/CT imaging centers therefore rely on a helical CT scan acquired during minimal tidal breathing for attenuation correction. This practice reduces the most severe artifact but often leads to mismatches between the PET and CT images in the diaphragm region, where there is a sharp boundary between the attenuation values for the liver and lung, as shown in Figure 1C. PET/CT scanners are particularly sensitive to this error, as the acquisition direction of the PET and CT scans are roughly parallel to the surface of the diaphragm. Mismatches in PET and CT scans of the diaphragm region due to respiratory motion lead to so-called banana artifacts in the PET image similar to that shown in Figure 2A. For cardiac imaging, respiratory misalignment between PET and CT scans of the lateral myocardial wall and the air of the lung space often lead to clinically significant artifacts that can falsely indicate reduced perfusion in the lateral myocardial wall.

Several methods can potentially minimize the banana artifact and other artifacts resulting from respiratory motion during CT scanning. Various groups have explored the option of performing the CT scan during breath-hold at an optimized lung volume, such as at midexpiration, to minimize potential mismatches.⁹ Our clinical experience has found that asking a

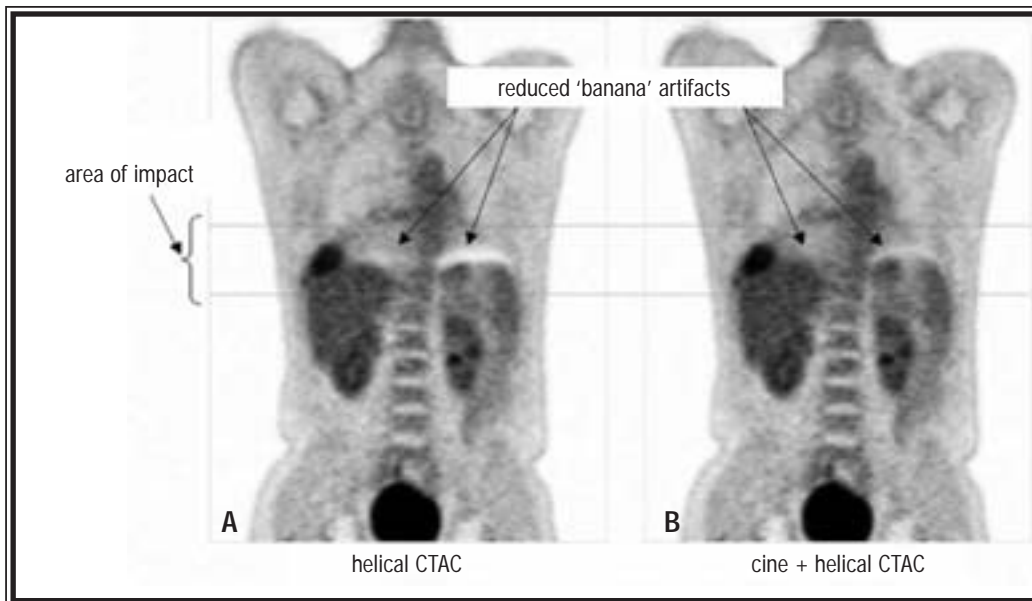


Figure 2. Banana artifacts arise from respiratory mismatch of emission (PET) data and CT attenuation correction images. Image on left is typical of artifacts that occur when a single helical scan is used for CT-based attenuation correction. Image on right demonstrates the significant reduction in banana artifact that can be obtained when a series of cine CT scans over the diaphragm region are added to provide a respiratory-averaged CT scan, similar to that shown in Figure 1D.

patient to hold his or her breath at a certain point in the respiratory cycle causes highly variable and often undesirable results. Even with breath coaching, such as that used in radiation therapy, it is difficult to state the optimal breath protocol applicable for all patients (midexpiration versus full expiration versus shallow expiration versus constant shallow breathing). Finally, even if the CT scan is performed at the optimal location, it will not perfectly match the PET scan acquired over many full respiratory cycles.

An alternative approach is to acquire cine CT scans over the diaphragm region for a duration of at least one respiratory cycle.¹⁰ These images can be added together to form a respiratory-averaged attenuation image similar to Figure 1D, which approximates the behavior of an orbiting transmission source in a PET-only scanner. With newer PET/CT scanners, it is possible to simply add the cine CT scans to the helical CT scan. The effect of this cine+helical CTAC procedure is illustrated in Figure 2B, which shows a significant reduction in the banana artifacts.

A simpler approach, and one that can be combined with the cine+helical CTAC procedure, is acquisition of the PET scan before the CT scan. Essentially, all current PET/CT protocols follow a pattern: First, a scout projection view is used to define the PET and CT scan ranges; next, a helical CT scan over the prescribed range that lasts approx-

imately 30 seconds is performed; and, finally, a PET scan that lasts from 10 to 30 minutes is performed. The rationale for the PET-first protocol is that patient motion is likelier in the first few minutes of the scanning procedure. After the much longer PET scan, the patient will have settled into a quiescent state, thus more closely matching a CT scan that follows immediately afterwards. Initial clinical experience indicates that the PET-first protocol, when combined with the cine+helical CTAC procedure, almost completely removes the appearance of banana artifacts.

RESPIRATORY GATING

Even if respiratory-induced artifacts are minimized using the methods described above, patient respiration during a PET/CT scan degrades contrast and quantitative accuracy. Figure 1B illustrates this motion blurring effect. Respiratory gating can avoid motion blurring by sorting the data from the PET scan into a predefined set of respiratory phase segments analogous to cardiac-gated imaging. Respiratory gating assumes that the periodic breathing pattern is essentially unchanged for the duration of the patient scan.

Adding data from different times but from the same segment of the periodic pattern does not introduce bias. A trigger signal is used to mark a consistent reference point, such as maximum inspiration, within each respiratory cycle. This allows the PET data from each respiratory cycle to be divided into predefined segments, typically fixed percentages of the phase or amplitude between sequential trigger signals. In cardiac gating, the trigger signal is typically generated from an ECG monitor, which provides a reliable timing reference.

Getting a reliable timing reference is more difficult in respiratory gating, however, due to the possible methods of breathing: diaphragm versus rib cage motion or some combination of the two. The two most common methods are optical tracking

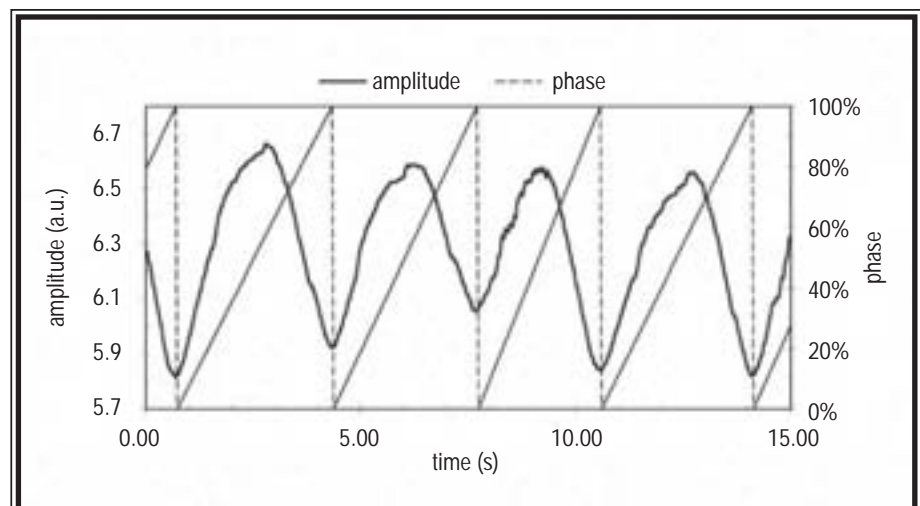


Figure 3. Example of a respiratory amplitude trace from an optical tracking system. Amplitude signal shows vertical motion of a small reflector placed on patient's torso.

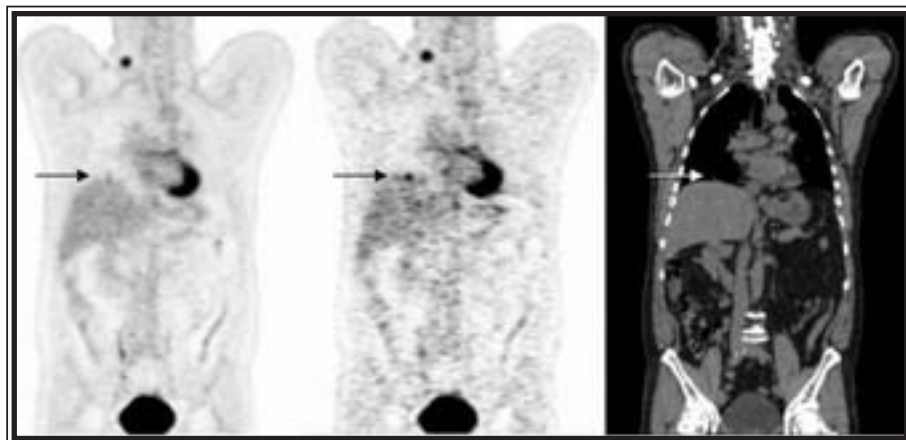


Figure 4. Example of the effect of respiratory gating on whole-body PET imaging. A: Standard whole-body PET image. B: One phase of the same study gated into seven respiratory phases. C: Corresponding CT image. Arrows indicate lesion with a volume of less than 1 cc.

of a small reflector placed on the patient's chest or abdomen and the use of a stretchable belt with pressure transducers placed around the torso. Both approaches have been shown to yield similar results in controlled studies used for radiation treatment planning and/or radiation therapy.¹¹ In routine clinical diagnostic scans, however, the vagaries of patient respiratory patterns can make these systems somewhat unreliable.

Figure 3 shows an example of a respiratory amplitude trace from an optical tracking system. In this example, the respiratory period is approximately four seconds, but it is also variable, as can be seen by comparing the width of the amplitude signal of the last two full respiratory cycles. By using the percentage phase signal, however, even variable width respiratory cycles can be divided up properly into consistent phases.

Once respiratory-gated PET images are acquired, the resolution and contrast within each phase image is increased compared with the standard respiratory averaged, or static, image. This is illustrated by comparing Figures 4A and 4B (and 1A and 1B). The increase in noise for each phase of a respiratory gated study is readily apparent in Figure 4. This noise increase, however, is mitigated by viewing the sequence of respiratory phase images as a cine or movie loop.

There are still some technical issues to resolve in respiratory gating of PET data. The use of a single CT image for attenuation correction of respiratory-gated PET scans will introduce artifacts into the reconstructed PET emission images. One solution is to acquire low-dose respiratory-gated CT scans to match the respiratory-gated PET data to perform phase-matched attenuation correction.

This procedure, however, is still under development.

Figure 4 is a dramatic example of the potential impact of respiratory gating. It should be noted, however, that this level of improvement in lesion detection is rare. A more common effect of respiratory gating is an increase in the measured SUV for a lesion, which is otherwise reduced by respiratory blurring. This is of particular importance considering the increasing role of PET in assessing patient response to therapy.

CONCLUSION

The introduction of PET/CT scanning has significantly enhanced the physician's armamentarium for the diagnosis and staging of cancer as well as for therapy planning and response monitoring. PET/CT imaging also has tremendous potential for integrated diagnosis of coronary artery disease by combining images of myocardial perfusion and metabolism with contrast-enhanced CT angiography.

Use of the CT scan for attenuation correction, however, has raised the importance of respiratory motion, which was overlooked in the previous generation of PET-only scanners. Recent technological advances can mitigate the effects of respiratory mismatch between the PET and CT scans, and the use of whole-body respiratory gating can restore contrast and resolution, albeit at the expense of increased noise. The most likely application of respiratory gating will be in improving the accuracy of PET images used to assess response to therapy, where accurate quantitation is of paramount importance.

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REFERENCES

- Czernin J, Phelps ME. Positron emission tomography scanning: current and future applications. *Ann Rev Med* 2002;53:89-112.
- Rohren EM, Turkington TG, Coleman RE. Clinical applications of PET in oncology. *Radiology* 2004;231:305-332.
- Mankoff DA, Muzi M, Krohn KA. Quantitative positron emission tomography imaging to measure tumor response to therapy: what is the best method? *Molec Imag Biol* 2003;5:281-285.
- Stahl A, Wieder H, Piert M, et al. Positron emission tomography as a tool for translational research in oncology. *Molec Imag Biol* 2004;6:214-224.
- Beyer T, Townsend DW, Brun T, et al. A combined PET/CT scanner for clinical oncology. *J Nucl Med* 2000;41:1369-1379.
- Wahl RL. Why nearly all PET of abdominal and pelvic cancers will be performed as PET/CT. *J Nucl Med* 2004;45:82S-95S.
- Slomka PJ. Software approach to merging molecular with anatomic information. *J Nucl Med* 2004;45(Suppl 1):36S-45S.
- Kinahan PE, Hasegawa BH, Beyer T. X-ray-based attenuation correction for positron emission tomography/computed tomography scanners. *Semin Nucl Med* July 2003;33(3):166-179.
- Beyer T, Antoch G, Blodgett T, et al. Dual-modality PET/CT imaging: the effect of ACF-artifact, respiratory motion on combined image quality in clinical oncology. *Eur J Nucl Med* 2003;30(4):588-596.
- Pan T, Mawlawi O, Nehmeh SA, et al. Attenuation correction of PET images with respiration-averaged CT images in PET/CT. *J Nucl Med* 2005;46(9):1481-1487.
- Li XA, Stepaniak C, Gore E. Technical and dosimetric aspects of respiratory gating using a pressure-sensor motion monitoring system. *Med Phys* 2006;33(1):145-54.



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