GE Healthcare

Q.Freeze

One image, Motion Eliminated, Quantitative Consistency, Low Dose.

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Respiratory motion presents significant challenges for PET/CT acquisitions that last several minutes in which breath holding is not an option. The induced motion artifacts may introduce significant image distortion, potentially leading to clinical misinterpretation involving apparent increase of lesion size and reduction of measured Standardized Uptake Value (SUV), and in many cases, potential miss of small lesions. Several techniques have been developed over the past years attempting to address these issues. While providing very interesting results, none of them addressed all the challenges simultaneously: image and quantification artifacts, high CT dose, and poor workflow.

Q.Freeze addresses each of these challenges by creating a single static image corrected for respiratory motion using a low dose CT technique. It uses 100% of the PET counts, in combination with a phase-gated low dose CT acquisition to remove PET/CT attenuation correction mismatch, to provide the best possible image quality. A robust and reliable non-rigid registration technique based on a multi-resolution optical flow methodology corrects PET data for respiratory motion. The resulting image has multiple benefits: frozen patient motion, reduced image noise and consistent quantitative accuracy.

MOTIONFREE PET/CT TECHNOLOGIES

One of the biggest clinical challenges for PET/CT imaging is patient respiratory motion. This motion leads to a blurring of moving features in static PET images. Blurring may in turn lead to lower detectability of tumors, inaccurate SUV measurements, and sub-optimal treatment planning volumes in radiation therapy. In addition, motion may lead to image artifacts due to respiratory displacement mismatch between CT and PET, since the CT is used for attenuation correction of the PET data.[1,2] Some of the documented benefits of motion correction include more precise fusion of PET and CT images, increased SUV accuracy, and improved volume measurement of small lesions.[4,5]

Several respiratory motion correction methods have been studied and are used by a few institutions in their day-to-day practice. Nevertheless limitations in workflow and dose of the current motion management techniques inhibit widespread adoption into routine clinical practice.

Deep inspiration breath hold technique

requires the patient to repeatedly hold their breath during the PET acquisition until enough data is acquired for good image quality and quantitative consistency.[6,7]

However, this technique requires a longer acquisition time and has workflow challenges as 40% to 60% of patients with lung cancer may be unable to tolerate breath holding.[8]

Quiescent period gating (QPG)

acquires data during free breathing, but only selects data from the nearly stationary period at the end of expiration to get the improved quality images.[9]

However, amplitude-based QPG is sensitive to respiratory baseline shifts and breathing irregularities that reduce its motion correction efficiency. In addition, mismatch between PET end of expiration and CT breath hold acquisition protocols may lead to PET and CT mismatch artifacts. Finally, QPG requires extra acquisition time to achieve the same number of counts as static.

4D phase-matched PET/CT (MotionMatch)

collects CT and PET data at each phase of the breathing cycle, and then matches the data for attenuation correction. Respiratory motion within each individual gate of this 4D data is reduced, thus leading to improved lesion quantitation and volume estimation. A recent retrospective clinical study of respiratory gating using MotionMatch technique showed that the "respiratory gated PET/CT technique is a valuable clinical tool in diagnosing lung lesions, improving quantification and confidence in reporting, reducing 3-D undetermined findings and increasing the overall accuracy in lung lesion detection and characterization".[10]

However, MotionMatch, primarily used in radiation therapy planning[11] to improve lesion contour segmentation, requires extra acquisition time for the 4D PET as well as extra CT dose for the 4D CT.

Q.FREEZE – A COMPREHENSIVE APPROACH TO MOTION

As described earlier, the major limitations to widespread clinical adoption of respiratory motion correction are:

- the need to use extra CT dose
- the need for additional acquisition time
- the sensitivity to irregular respiratory patterns.

Q.Freeze has been designed to overcome these challenges by using the entire acquired data to create a single 3D motion-corrected image, and to provide quantitative accuracy equivalent to 4D phase-matched PET/CT. Unlike conventional 4D PET imaging, Q.Freeze combines 100% of the PET counts into a 3D motion corrected image that has a comparable acquisition time and the equivalent image noise of a static acquisition.

Figure 1 and 2 represent the Phase gating and the Q.Freeze concepts. In order to reduce the image noise and improve quantification accuracy, Q.Freeze registers all phases to the predefined one; example phase 4 represents the quietest phase of the quiescent period.

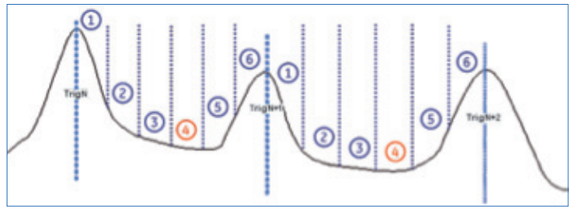


Figure 1: Theoretical patient respiratory cycle with 6 different gates. Phase 4 is the quietest phase of the quiescent period.

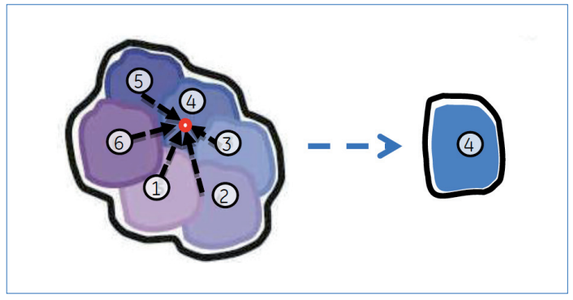


Figure 2: Conventional static PET volume that encompasses tumor motion (left) compared to the Q.Freeze 3D motion corrected images with reduced tumor volume (right). Q.Freeze registers all the gates to the user selected gate.

Figure 3 and figure 4 show typical patient respiratory curves with and without baseline shift and with and without irregularities. 40% of the population has been found to have irregular respiratory patterns.[12]

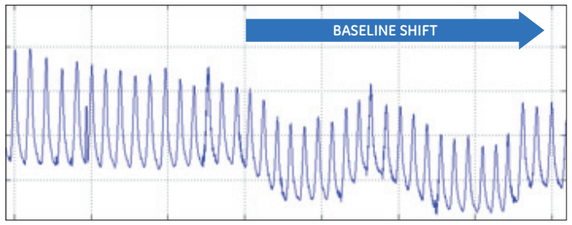


Figure 3: Typical patient respiratory curves showing baseline shifting during the patient 4D PET acquisition. Q.Freeze, based on phase gating, is not sensitive to baseline shift. The vertical axis represents the amplitude and the horizontal axis represents time.

Conventional amplitude-based gating combines counts into gates of preset amplitudes. In the case of a baseline shift, the respiratory curve may no longer be within the amplitude limits, thus losing counts and increasing image noise. Phase-based gating is not sensitive to baseline shift, and thus acquires all the counts.

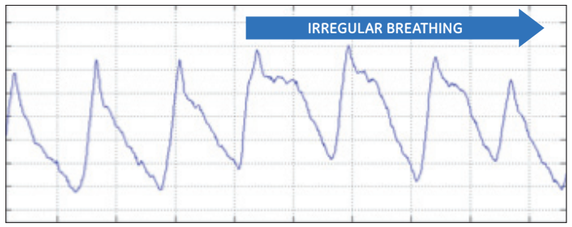
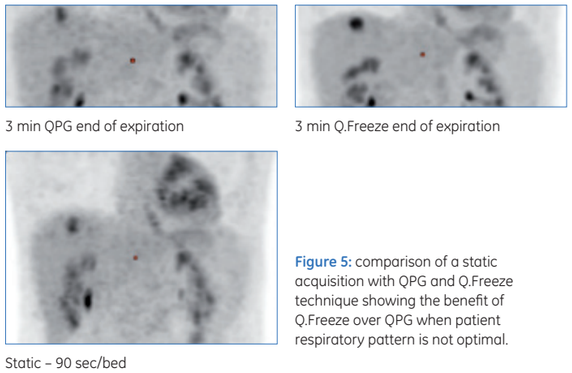


Figure 4: Typical patient respiratory curves showing an irregularity within the patient breathing pattern: This may add some blurring effect in one of the respiratory gates that Q.Freeze will be able to accommodate through the statistical median algorithm. The axes are defined the same as figure 3.

In addition, irregular patient breathing may add some blurring effect in QPG. Q.Freeze therefore gives the user the flexibility to select a reference gate for the registration as well as reduces the weighting factor of the most blurred gates within the end result using the Statistical Median Algorithm as demonstrated in figure 5.

Even with a regular patient breathing pattern, as shown in figure 1, the quiescent period represents about one third of the respiratory cycle. When the patient respiratory pattern is irregular the quiescent period may be even shorter and leads to image noise increase and quantification errors.



3 min QPG end of expiration

3 min Q.Freeze end of expiration

Static – 90 sec/bed

Figure 5: comparison of a static acquisition with QPG and Q.Freeze technique showing the benefit of Q.Freeze over QPG when patient respiratory pattern is not optimal.

Q.FREEZE TECHNOLOGY

Q.Freeze workflow leverages GE techniques to support low dose CT (Q.AC) similar to ultra-low dose techniques available in the literature,[13,14] simple workflow, full thorax coverage (ViP), and exceptional mismatch artifact free image quality (MotionMatch).

Q.Freeze is a global non-rigid registration technique (figure 6) incorporating additional PET specific constraints:

Multi-resolution

approach takes into consideration the low signal to noise ratio (SNR) PET images by focusing first on the global motion pattern and then refining the results with the details provided in the higher resolution levels of the image. It inhibits small size features from affecting the registration of the larger structures.[15]

Optical flow equation

Several approaches to motion estimation have been studied,[16-19] including PET sinogram-based motion estimation,[20] PET image-based motion estimation[21-23] and high resolution CT-based motion estimation.[25] The desired result of achieving fast convergence and excellent image quality and quantification accuracy is obtained by estimating the motion on gated PET images directly.

Viscosity and Elasticity regularizations.

This approach prevents motion over correction and provides a meaningful solution based on the environment of the feature. Model tissue viscosity and elasticity are used to take into consideration the anatomical environment of the feature.

Selection of the regularization settings requires a tradeoff between not removing enough motion blur and registering the noise. Two regularization schemes have been implemented within Q.Freeze to take care of the tissue elasticity and viscosity estimated from the surrounding area of the feature. Figure 7 illustrates motion vectors with and without regularization. While the regularized situation yields a field that is coherent and well-behaved spatially, the un-regularized case creates numerous over-estimates of the vectors and a generally incoherent behavior. It is clear that regularization is essential for the algorithm to produce meaningful solutions.

Statistical Median Algorithm.

Finally, the counts are combined into a 3D motion corrected image by using a statistical median algorithm. It generates the summation of gates into a single 3D motion correction image by analyzing the quality of the registration in each voxel of the image. As a result the image is cleared from registration noise and artifacts even in case of irregular breathing patterns.

The final equation for Q.Freeze can be described by the following:

$$\vec{V}_{i+1} = \left[\vec{V}_i + [I_R - I_g(\vec{V}_i)]\frac{\nabla I_g(\vec{V}_i)}{\|\nabla I_g(\vec{V}_i)\| + \alpha} \otimes \sigma_v\right] \otimes \sigma_e$$

where

- $\vec{V}_i$ is the displacement vector at i^{th} iteration initialized with $\vec{V}_0 = 0$
- I_R is the reference image to register to
- I_g is the gated image to be registered to the reference image
- σ_v and σ_e are regularization kernels

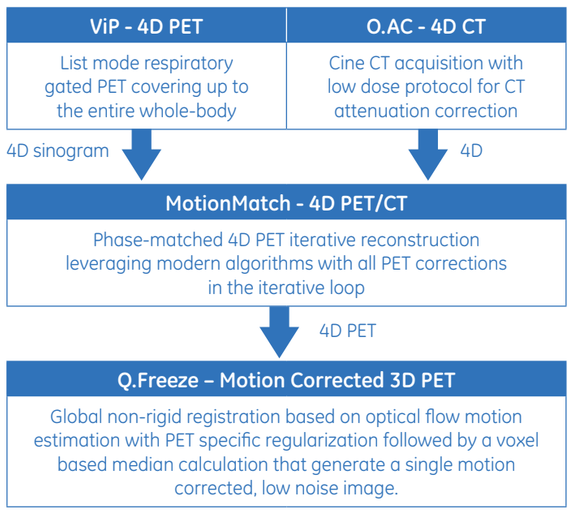


Figure 6: Q.Freeze starts with phase-matched 4D PET images, and then registers all the gated images together using a global non-rigid registration method.

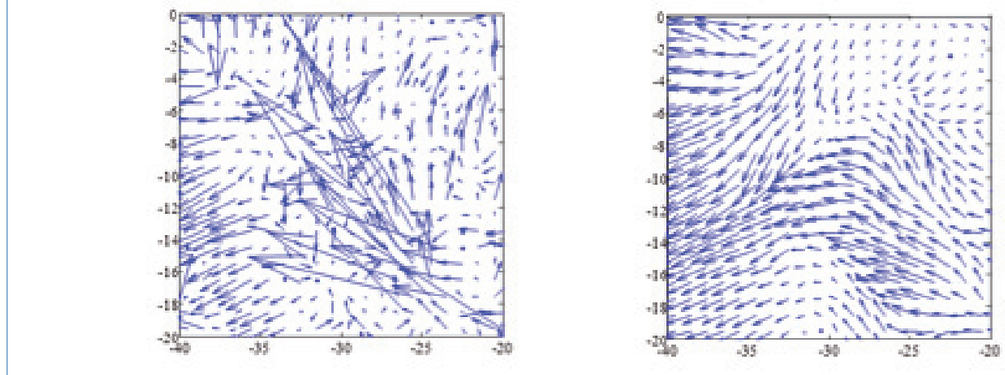


Figure 7: Motion vectors computed for a 2-D image using non-rigid registration with and without regularization. While the regularized situation yields a 2D field that is coherent and well-behaved spatially, the un-regularized case creates numerous over-estimates for the vectors in addition to a generally incoherent behavior. It is clear that regularization is essential for the algorithm to produce meaningful solutions.

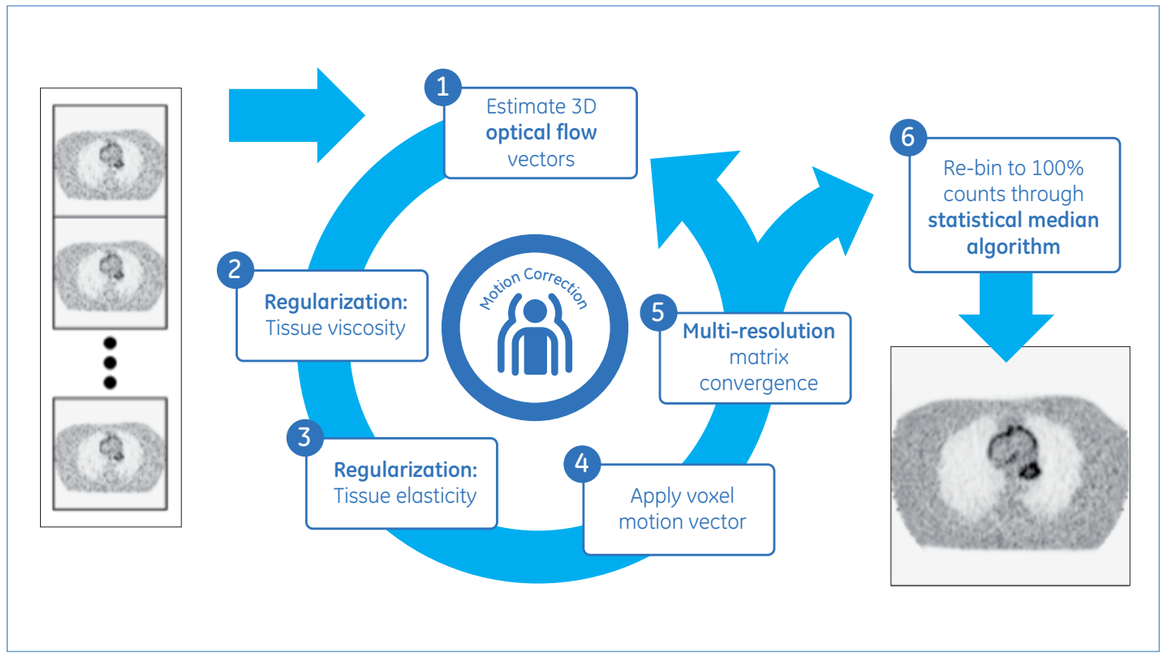


Figure 8: Q.Freeze's global non-rigid registration is an iterative algorithm that utilizes optical flow based motion methodology (1) with PET specific regularization (2 & 3) and is designed to provide fast, accurate and robust motion correction due to its multi- resolution strategy. It checks the convergence of the motion correction (5) before it is re-combined to a single high statistics 3D motion corrected image (6).

Q.FREEZE – QUANTIFICATION ACHIEVED CONSISTENTLY

Q.Freeze evaluation is based on the following metrics that represent the most clinical challenges of respiratory motion.

Center of mass difference

measures the distance from the lesion's center of mass in each gate to a reference gate. The center of mass difference provides a direct measurement of the registration accuracy. The smaller the difference, the better the registration.

Feature Volume

The visual blur in the static image resulting from respiratory motion generally appears stretched along the direction of the motion and can be quantified by tumor volume. The estimate of tumor volume obtained from a static image is usually higher than its value for individual gates. Comparing the tumor volume obtained from the Q.Freeze processing with that from the corresponding static image measures the extent of blur reduction.

SUV_{max}

The maximum SUV (within a region-of-interest) is often used to differentiate between malignant and benign tumors and to evaluate therapy effectiveness. Motion will blur the activity image, and hence reduce the measured activity concentration and corresponding SUV. Comparing the SUV obtained from the Q.Freeze processing with the SUV obtained from the corresponding static image measures the extent of quantitation recovery. In phantom studies, Maximum Activity Concentration (MAC) is used in lieu of SUV.

Phantom studies[26]

A phantom was constructed to evaluate the motion correction performance of Q.Freeze. The phantom used five 2 mL Ge-68 filled spheres suspended in a water-filled tank via lightweight fishing line as illustrated in figure 9. The spheres were set into motion using a QUASAR™ Programmable Respiratory Motion Phantom with a sinusoidal motion pattern. Three sets of experiments were performed with different motion amplitudes representing different patient respiratory cycle patterns. The motion of the QUASAR phantom was monitored by the

Varian® Real-time Position Management™ (RPM) to enable a gating signal into the GE Discovery PET/CT system during data acquisition.

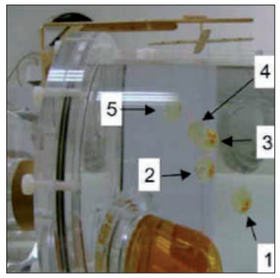
A three minute list mode PET acquisition was performed while the QUASAR phantom was motionless (benchmark). This data was used to form a single three minute dataset as well as six 30 second datasets as the benchmark. With the sources in motion, five replicate datasets of three minute phase-gated PET data were acquired in list mode. From each of these acquisitions, a three minute static scan was unlisted as well as a 6-bin (phase based) gated scan. PET images were formed using a fully 3D OSEM iterative reconstruction (VUE Point HD).

Figure 10 compares the PET benchmark images with conventional static and Q.Freeze image. The Q.Freeze image most closely resembles the benchmark image. The static image shows considerable blurring from the respiratory motion.

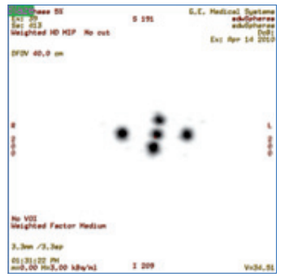
The maximum center of mass difference is reduced from a maximum of 23 mm to below 2 mm (sub-pixel proximity) with Q.Freeze, as shown in figure 11.

A comparison of sphere maximum activity concentration and sphere volume between conventional static and Q.Freeze shows Q.Freeze is on average 8.0% lower on sphere maximum activity concentration (figure 13) and 5.8% higher on sphere volume (figure 12) compared to the benchmark. Q.Freeze on average reduces the maximum activity error by 70% and reduces the volume error by 80% as compared to conventional static.

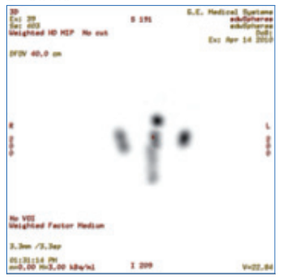
Figure 9: Side view of the phantom setup. The five spheres of Ge-68 are labeled 1 – 5 in the images. Image © 2012 IEEE (ref 26), used with permission.



a – Benchmark



b – STATIC



c – Q.Freeze

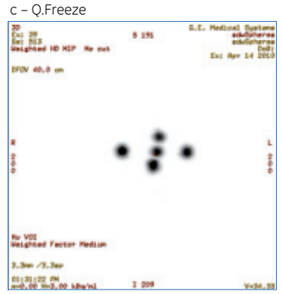


Figure 10: Comparison of PET benchmark, static and Q.Freeze images demonstrating the motion correction capability of Q.Freeze.

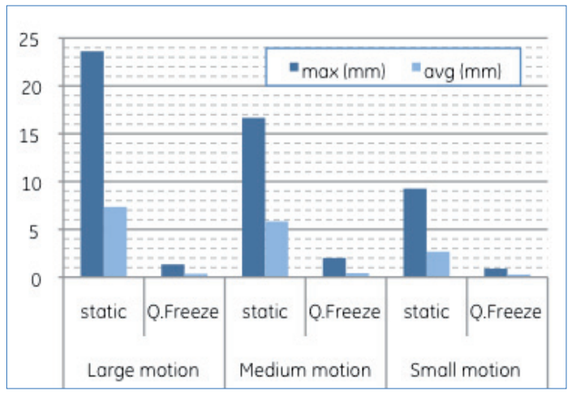


Figure 11: The maximum center of mass difference is reduced from a maximum of 23 mm to below 2 mm (sub-pixel proximity) with Q.Freeze. Max difference is the center of mass difference for the gate furthest from the reference gate.

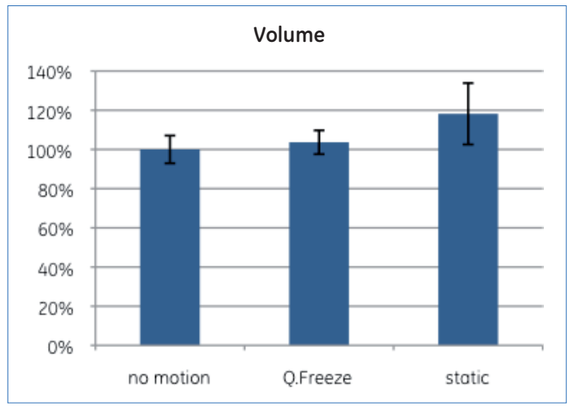


Figure 12: Comparison of sphere Volume, Static vs. Q.Freeze. Q.Freeze on average reduces sphere volume error by 80% compared to conventional static.

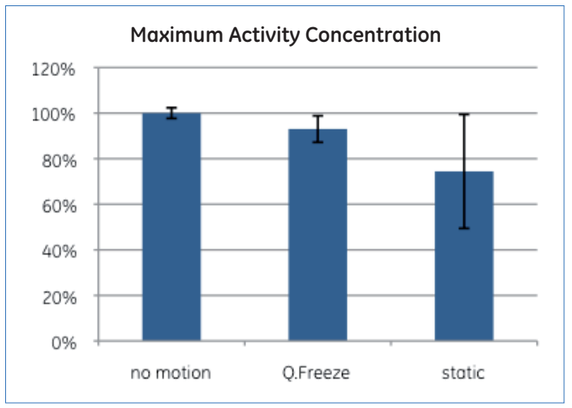


Figure 13: Comparison of spheres maximum activity concentration (MAC) Static vs. Q.Freeze. Q.Freeze on average reduces error 70% on sphere maximum activity concentration compared to conventional static.

Q.FREEZE – LOW DOSE CTAC FOR QUANTIFICATION ACCURACY CONSISTENCY

The success of Q.Freeze depends on the quality of the 4D PET data provided, including artifact free images and proper photon statistics. Mismatch between CTAC and PET, as seen in figure 14, leads to a degradation of the quantitative accuracy of PET images and can lead to image artifacts.[1,2] To avoid issues with attenuation mismatch, the gated PET images are reconstructed using gate-matched CT. However conventional low dose CT techniques are not intended for attenuation correction purpose and the extended duration of 4D CT scans results in a substantially higher radiation dose.

The GE-developed Q.AC technique addresses the low dose 4D CTAC requirements by drastically reducing the tube kVp and mA and therefore the dose to patient as shown in Table 1.

For Table 1, the Dose Length Product (DLP) for the 32 cm diameter CTDI 'body' phantom uses a scan length of 1000 mm from eyes to mid-thighs. Effective dose is estimated from the DLP using an adult chest-abdomen-pelvis factor of 0.015 mSv / (mGy × cm) as tabulated by Shrimpton.[27]

The new CTAC protocols with Q.AC provide CT data solely for attenuation correction at an effective dose of less than 0.5 mSv, compared to the previous CTAC protocols that gave an effective dose in the range 8 to 11 mSv. In this instance, a 20 X factor reduction in CT dose was achieved for attenuation correction.

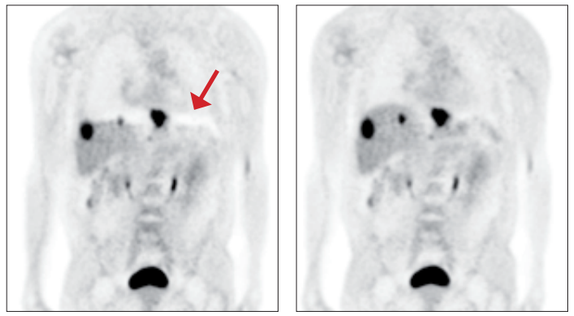


Figure 14: PET and CT mismatch artifact (left) corrected using MotionMatch PET/CT acquisition protocol (right)

16-slice CT protocol 100 cm scan length	Noise Index	Peak mA [a]	Effective Dose [b]
CONVENTIONAL - 140 kVp - 0.5 s - 0.938 pitch	28.5	79	8.4 mSv
Q.AC protocol - 120 kVp - 0.5 s - 1.675 pitch	140	10	0.4 mSv

64-slice CT protocol 100 cm scan length	Noise Index	Peak mA [a]	Effective Dose [b]
CONVENTIONAL - 140 kVp - 0.5 s - 0.984 pitch	28.5	102	11 mSv
Q.AC protocol - 100 kVp - 0.5 s - 1.531 pitch	170	10	0.4 mSv

Table 1: Dose comparison for selected PET/CT protocols

a. CT Peak mA is the maximum mA when scanning the thorax phantom and oval phantom used in this study

b. CT Effective dose estimated from DLP using a chest-abdomen-pelvis factor of 0.015 (Shrimpton)[6]

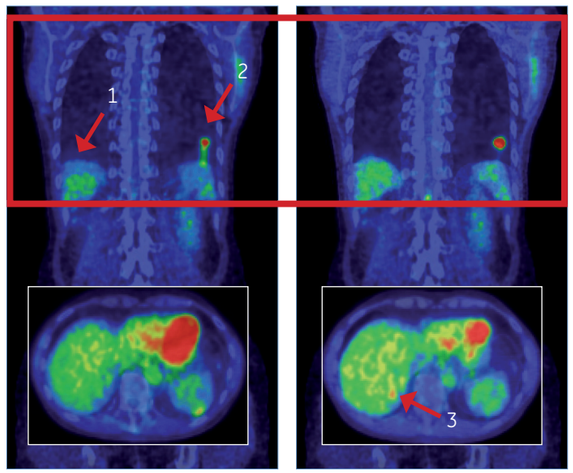
Q.FREEZE
100% COUNTS COLLECTED, EXCELLENT IMAGE QUALITY

Any motion reduction method that wastes counts will impair the PET image quality and the PET quantification accuracy, making it necessary to increase the acquisition time. Q.Freeze uses 100% of the counts collected by re-combining 100% of the counts into a single 3D motion corrected image.

A recent retrospective clinical study compared the performance between Q.Freeze and 4D PET/CT including 18 lung and 13 liver lesions among 28 patients. The scans were retrospectively rebinned to simulate shorter acquisition times, reprocessed and analysed with Q.Freeze. The results showed that the Q.Freeze algorithm can help to reduce the 4D PET/CT acquisition time by 50% while keeping the same outcome as a full 9 minute 4D PET scan[28]

▶ Case1: Motion corrected image

Courtesy of University of Milano–Bicocca, San Gerardo Hospital, Monza, Italy



STATIC - 10 min total WB

Q.FREEZE - 12 min total WB

Conventional static PET acquisition (left) shows respiratory motion artifacts:

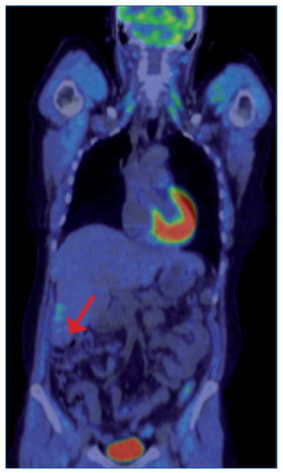
1. PET & CTAC mismatch artifact
2. Blurring artifact of the uptake

The acquisition of the typical 4D PET/CT study in list mode was originally 24 min. Q.Freeze helps to reduce the total acquisition time to 12 min, while the conventional static acquisition is about 10 min.

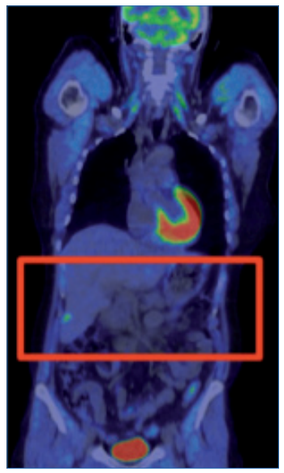
In this case, it was possible to confirm an additional uptake in the liver (3).

▶ Case2: Accurate quantification

Courtesy of Institut Curie Centre René Huguenin, Saint-Cloud, France



STATIC



Q.FREEZE

	SUVmax	Volume
Static - 1	3.19 g/mL	6.31 cm^3
Static - 2	2.90 g/mL	3.18 cm^3
Q.Freeze	3.36 g/mL	4.00 cm^3

The conventional static acquisition (left) shows two uptakes (L1 & L2) in the liver. Q.Freeze demonstrates its capability to correct for large displacement motion. The single uptake was confirmed in 4D CT and 4D PET.

SUMMARY

Successful respiratory motion management techniques need to be able to: demonstrate great image quality free of any artifacts; provide accurate quantitative imaging; handle robust workflow for any patient respiratory pattern; and use a low dose technique similar to an ultra-low dose CT acquisition protocol.[13,14]

Both phantom and retrospective clinical studies have demonstrated that Q.Freeze corrects for respiratory motion present in PET acquisitions, leading to superior image quality and increased quantitative accuracy (SUV & volume) in comparison to conventional static imaging. Phantom experiments showed a reduction of the center of mass difference to less than 2 mm with Q.Freeze. Q.Freeze also reduced the lesion volume error by 80% and reduced lesion maximum activity error by 70% compared to conventional static PET imaging.

The studies demonstrate that Q.Freeze provides an improvement in quantification measurement over static PET as provided by 4D PET/CT, but accomplishes this in even more challenging clinical situations and with shorter acquisition times.

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