Enabling high quality, low dose myocardial perfusion imaging for nuclear cardiology

Philips BrightView XCT with Astonish

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Over the past 20 years, SPECT myocardial perfusion imaging (MPI) has become an important tool for assessing patients with known or suspected coronary artery disease (CAD). Despite the success of SPECT MPI, laboratories that are performing these procedures are under pressure to reduce costs, improve image acquisition efficiency, reduce absorbed radiation dose, and improve diagnostic accuracy. Philips Healthcare has recently developed two products to address these needs: BrightView XCT, which is well-suited to provide attenuation correction for cardiac imaging, and Astonish, an improved reconstruction method that makes more efficient use of acquired counts by incorporating imaging physics into the reconstruction process.

This paper describes the technical developments that Philips has made to advance nuclear cardiology by improving diagnostic accuracy, improving department efficiency, and reducing the radiation dose that patients receive in a practical way that can be implemented in most hospitals and clinics. It also presents clinical results demonstrating the value of these developments.

Philips BrightView XCT imaging system

BrightView XCT (Philips Healthcare, Cleveland, OH) is a compact, variable angle gamma camera with a high resolution flat panel X-ray detector system [1] for localization and attenuation correction of SPECT data that has many advantages for nuclear cardiology. The SPECT system uses Philips CloseUp technologies that are designed to improve SPECT image quality by keeping the detectors close to the patient. These include BodyGuard automatic body contouring and setup, a small cardiac dead space, an ultra-thin pallet, and CardioTrac roving field of view that also allows optimization of the pixel size without risk of truncation.

Another distinct feature of the SPECT system is the patented concurrent imaging technique that provides the ability to create multiple image sets from a single acquisition. Concurrent imaging can help nuclear cardiology by offering more flexibility in acquisition protocols and providing additional information without requiring additional imaging time. For example, gated and non-gated (perfusion) cardiac data can be acquired simultaneously. This is preferable to creating the perfusion data by summing the gated data, since all counts will be included in the non-gated data while some counts could be excluded from the summed gated data due to rejected beats. This could represent a significant

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sense and simplicity

loss of acquired counts in the perfusion image for patients with arrhythmias. Additionally, gated data could be acquired simultaneously with both 8-gated bins for better wall motion quality and 16-gated bins for more accurate ejection fraction calculation.

The flat panel X-ray detector system and the unique gantry design also offer several advantages for nuclear cardiology. The large gantry aperture enables imaging of obese patients and provides an open patient experience during the CT scan, as depicted in Figure 1. After the CT scan, the gantry automatically transitions into the SPECT imaging position for efficient workflow. Since the X-ray detector and the SPECT detectors are located on the same rotatable gantry, the emission and transmission images can be acquired with little or no table translation between scans. This co-planar design reduces the misalignment between the emission and transmission data since there is little opportunity for misalignment due to bed motion or differential table sag between the SPECT and CT imaging positions. This is important since misalignment between transmission and emission data is known to be a major source of artifacts in other integrated dual-modality imaging devices.[2] This design also reduces room size requirements and system weight compared to SPECT/CT systems utilizing spatially separated SPECT and CT gantries.

The flat panel X-ray detector system provides a low dose (0.12 mSv) CT image that can be used for attenuation correction of the cardiac SPECT data. A 47 cm diameter transverse field of view and a 14.4 cm axial length along the patient can be imaged with a single 360° rotation of the gantry. As a result, a transmission image of the entire heart can generally be obtained from a single 60-second spin while the patient is breathing. The transmission data is acquired as a volume, not as a series of slices like a conventional CT, which more closely matches the volumetric approach of the SPECT acquisitions. Furthermore, the free-breathing protocol enables acquisition of both the SPECT and the transmission data during tidal respiration; the attenuation data is averaged over multiple respiratory cycles to match the position of the heart during the SPECT acquisition. If the transmission data is acquired during a breath-hold there can be significant misalignment between the transmission and emission data which can lead to artifacts in the attenuation-corrected SPECT image.[2]

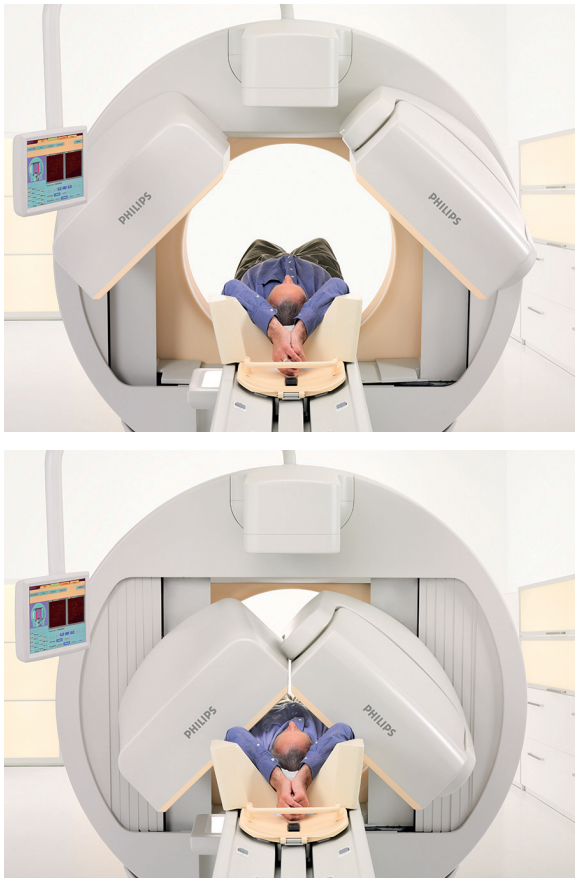

Figure 1. BrightView XCT system during the CT scan for cardiac attenuation correction (top) and during cardiac SPECT acquisition (bottom).

Figure 2 illustrates the differences in physiological states between free breathing and a breath-hold. It also illustrates the difficulties associated with patient compliance to breath-holding instructions. So acquiring the transmission data while the patient is free-breathing not only provides the best attenuation correction data, it's also easier for the patient and more efficient for the technologist.

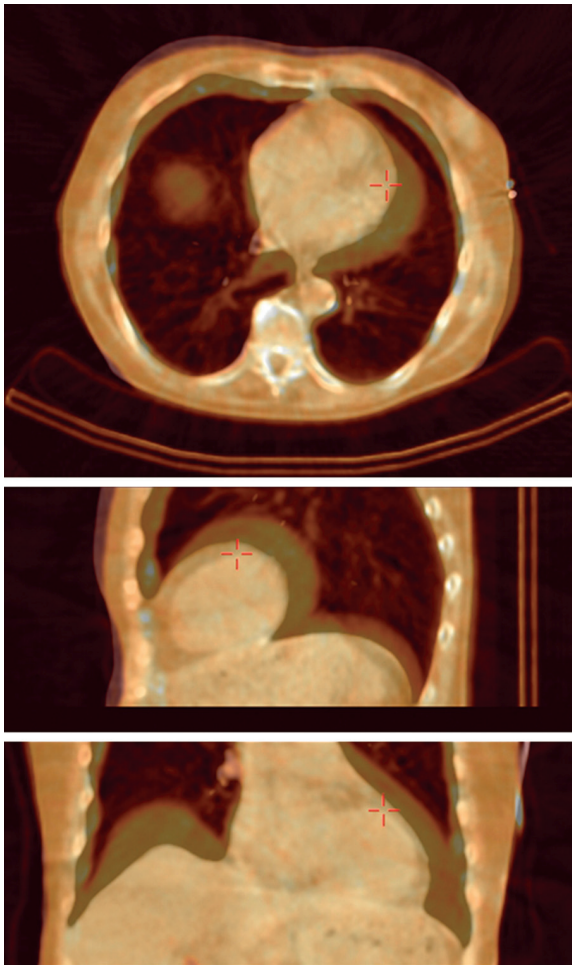

Figure 2. Transverse, sagittal, and coronal views of fused transmission images acquired over 60 seconds during tidal respiration (dark thermal image) and over 12 seconds during a breath-hold (grayscale images). For the breath-hold image, the patient was coached to hold their breath at end expiration. Even though this was a very cooperative patient, these images indicate that the patient inhaled prior to the breath-hold despite the coaching.

In order to verify that there is good registration between the emission and transmission data, the user is presented with a fused display of the SPECT and CT data within the reconstruction workflow. The user can scroll through the three orthogonal views illustrated in Figure 3 to verify that the images are correctly aligned. The brightness and background of each image can be adjusted independently and the amount of alpha blending can also be adjusted while assessing the registration of the two images. Because the SPECT and CT data are both acquired during free breathing with little or no table motion between the two acquisitions, the two images are generally well aligned. If there is any misalignment of the two data sets, however, due to patient motion between the two scans for instance, the position of the SPECT data can be adjusted relative to the CT data using manual shift and rotation tools. Any adjustments that are made to the SPECT position are incorporated into the attenuation map that is created and used for attenuation correction of the SPECT image.

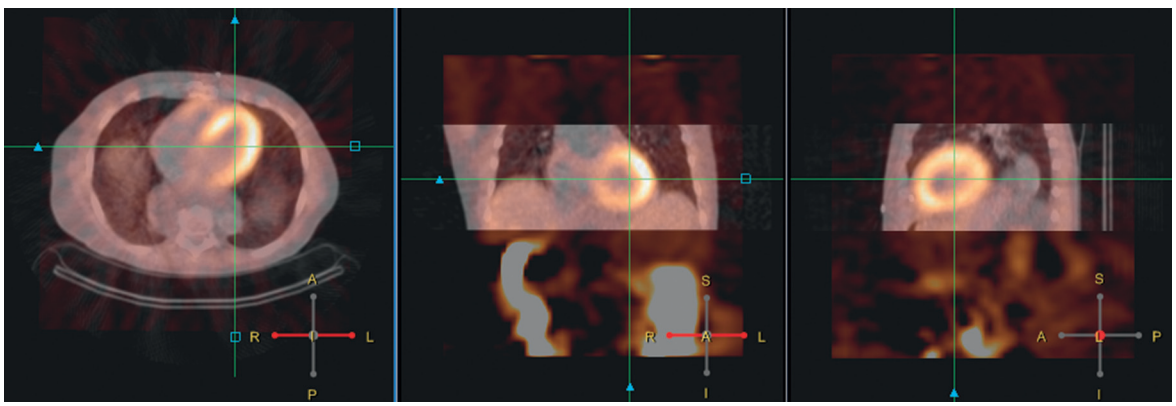

Figure 3. Fusion display of the SPECT and CT data presented to the user within the reconstruction workflow. If the alignment between the emission and transmission data is unacceptable, the registration can be adjusted prior to performing attenuation correction.

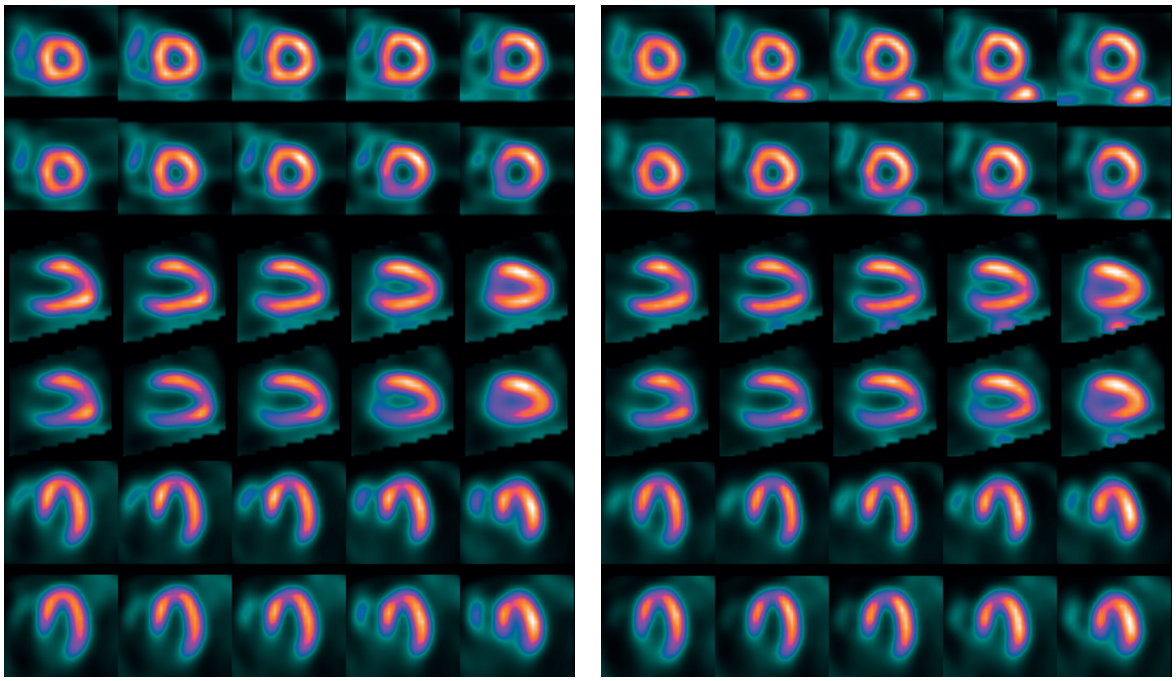

Figure 4. Short axis, vertical long axis, and horizontal long axis views of myocardial perfusion images acquired with BrightView XCT and reconstructed with attenuation correction (first row) and without attenuation correction (second row). In both the stress images (left) and rest images (right), attenuation correction fills in the inferior wall artifact seen without attenuation correction.

Because the CT scans for attenuation correction are acquired over 60 seconds with the patient breathing, there can be significant motion artifacts in the CT data. Additionally, since these CT scans are acquired at very low doses, there can be additional artifacts due to photon starvation. To overcome these artifacts, the software that converts the XCT image from Hounsfield unit (HU) values to linear attenuation coefficients first segments the XCT image so that values between -150 HU and +150 HU are treated as water. Furthermore, these scans are smoothed and down-sampled to match the SPECT voxel size during the generation of the attenuation map. As a result, the artifacts that may exist in the raw CT image do not impact the attenuation correction of the SPECT data and excellent results can be achieved as shown in by the example in Figure 4.

Astonish reconstruction

Iterative reconstruction methods enable resolution recovery, scatter correction, and attenuation correction to be incorporated into the reconstruction process. Astonish reconstruction uses a three-dimensional ordered subset expectation maximization (3D-OSEM) algorithm that models the Poisson noise for the counting statistics of the acquisition, similar to the maximum likelihood expectation maximization (MLEM) algorithm. The main advantage of using an OSEM algorithm rather than an MLEM algorithm is the computational time. Both algorithms start with an image estimate and then use the acquired data to update the image estimate in an iterative manner. In MLEM, the data from all projections are used to update the image estimate once per iteration. In OSEM, the data from each subset of projections are used to update the image estimate and one iteration is completed when all the projections have been used. In this manner, the image estimate is updated n times per iteration, where n is the number of subsets used. Since the image is updated more frequently with OSEM than MLEM, the reconstruction converges more rapidly and the overall computation time is less for OSEM reconstruction compared to MLEM reconstruction.

The three-dimensional implementation of Astonish allows for the incorporation of three-dimensional depth-dependent resolution recovery during image reconstruction. Astonish uses the convolution method [3] to model the varying resolution as a function of distance from the detector. During the acquisition of patient data, the distance from the collimator to the center of rotation is recorded for each projection angle. During the reconstruction process, the amount of blurring is calculated based on these measured distances and the collimator response function. The counts are spread over multiple pixels during both the forward- and back-projection steps of the iterative reconstruction with the degree of broadening determined by the collimator response function and the distance between the pixel and the collimator.

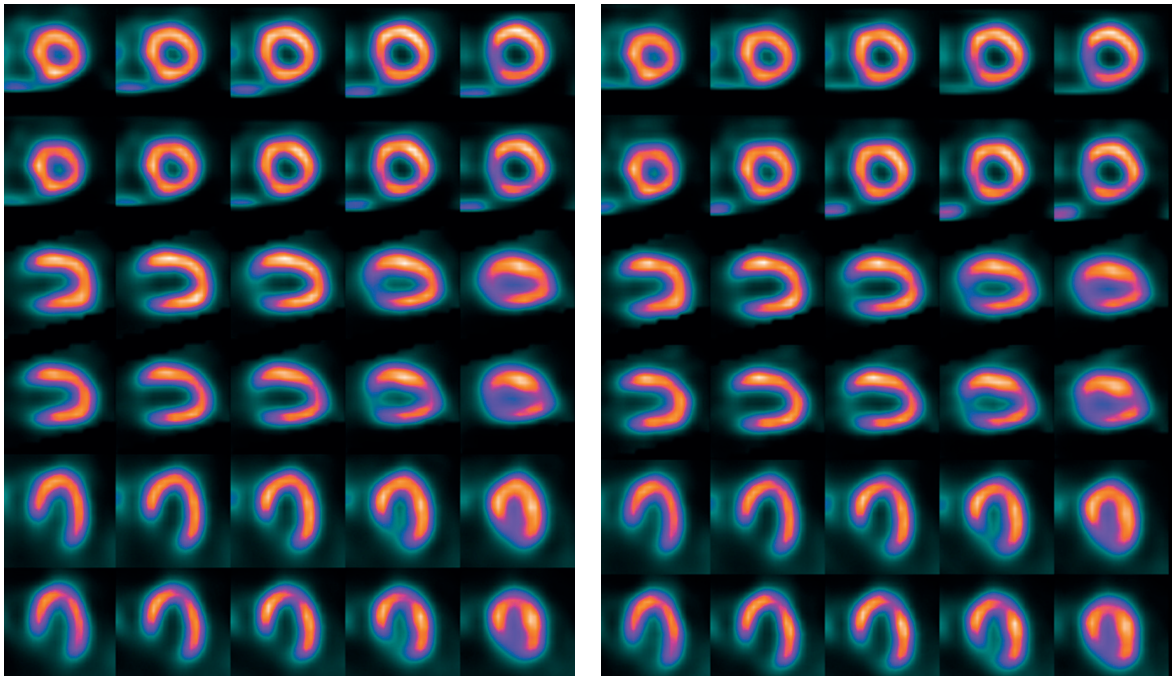

Figure 5. Full-count stress/rest images (left) compared to half-count stress/rest images (right) reconstructed with Astonish without attenuation correction. In all views, stress images are shown first, followed by rest images. Half-count images show no loss in image quality, enabling improved efficiency or lower dose imaging.

With many iterative reconstruction methods, the noise in the reconstructed images increases with the number of iterations. As a result, the noise in the image tends to be unacceptable by the time enough iterations have been used. To overcome this problem, Astonish incorporates a proprietary matched dual filter within the reconstruction process to control the accumulation of noise.[4] By performing the smoothing within the iterative process, Astonish can achieve superb noise suppression while preserving spatial resolution. It is this feature of Astonish, as well as the incorporation of the imaging physics into the reconstruction process, that enables half-count imaging, as illustrated in Figure 5. Additional details regarding the clinical performance of Astonish are included later in this paper.

When an attenuation map is present, the Astonish algorithm can perform attenuation correction and scatter correction in addition to resolution recovery. Throughout this paper, Astonish-AC will refer to Astonish reconstructions that incorporate attenuation and scatter corrections in addition to resolution recovery. For BrightView XCT, the attenuation map is generated from the X-ray CT image by converting the Hounsfield values to linear attenuation coefficients at 100 keV using a piecewise linear model.[5] The resulting attenuation map is a matrix of linear attenuation coefficients at 100 keV. The attenuation map is used to calculate the amount of attenuation from each point in the object through the body. This calculation is performed during the forward-projection process within the iterative reconstruction. Since the emission energy is typically not 100 keV, the linear attenuation coefficients in the attenuation map are scaled to the appropriate emission photon energy using the ratio of the linear attenuation coefficient of water at the emission energy to the linear attenuation coefficient of water at 100 keV.

Scatter correction is performed using the effective source scatter estimation (ESSE) method.[6] This method uses the concept of defining an effective source distribution of scatter and then calculating the expected scatter projection data from this effective source. With this approach, the estimate of the scatter is calculated from the emission image estimate, the attenuation map, and a pre-calculated three-dimensional scatter kernel that is specific to the emission photon energy and the target energy windows. This modeled scatter component is then added to the forward-projected current estimate before it is compared to the measured projection data in the iterative reconstruction process.

Clinical performance of Astonish

A multi-center clinical trial designed to test the performance of the Astonish algorithm for myocardial perfusion SPECT imaging was recently carried out.[7] Image quality, diagnostic confidence, and diagnostic accuracy for the detection of coronary artery disease were evaluated on data from 187 consecutive patients undergoing clinically indicated myocardial perfusion SPECT studies. The patients underwent subsequent cardiac catheterization (n = 132) or had a low likelihood of coronary artery disease (n = 55). In the first phase of the study, the clinical performance of Astonish with both full-count and half-count data was tested against filtered back projection (FBP) of full-count data. In this initial phase of the study, attenuation correction and scatter correction were not applied.

In comparison with traditional FBP with full-count data, Astonish significantly improved image quality for perfusion assessment of stress and rest images with both full-count and half-count data as shown in Figure 6. The quality of stress perfusion images was rated as excellent or good in 85% (n = 158), 98% (n = 183), and 95% (n = 178) of images using full-count FBP, full-count Astonish, and half-count Astonish, respectively ($p < 0.001$). Similarly, the quality of rest perfusion images was rated as excellent or good in 80% (n = 150), 95% (n = 177), and 92% (n = 172) of images using full-count FBP, full-count Astonish, and half-count Astonish, respectively ($p < 0.001$). This demonstrates the ability of Astonish to provide good image quality even with only half of the counts.

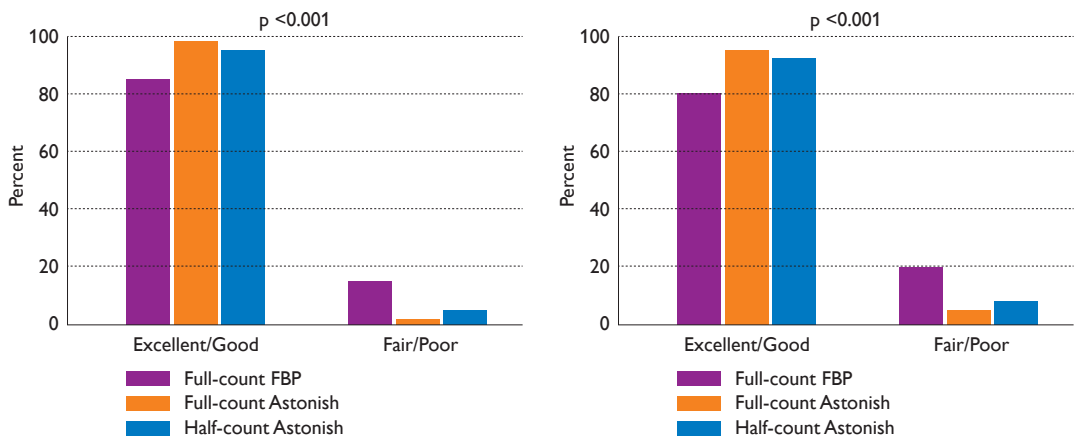

Figure 6. Comparison of perfusion image quality for stress images (left) and rest images (right) using full-count FBP, full-count Astonish and half-count Astonish.

Interpretive certainty of the perfusion images was not significantly different among the various processing methods. Studies were interpreted as definitely normal or definitely abnormal in 89% (n = 166), 83% (n = 155), and 88% (n = 165) of images using full-count FBP, full-count Astonish, and half-count Astonish, respectively ($p = 0.181$).

Similarly, there was no statistically significant difference in the diagnostic accuracy between the three processing methods as shown in Figure 7. The normalcy rate of low likelihood studies that were classified as definitely normal was 91% (n = 50), 76% (n = 42), and 76% (n = 42) for full-count FBP images, full-count Astonish images, and half-count Astonish images, respectively ($p = 0.079$).

The measured sensitivity, calculated using definitely abnormal interpretations, was found to be 76% (73/96), 75% (72/96), and 82% (79/96) for full-count FBP, full-count Astonish and half-count Astonish, respectively ($p = 0.422$). The measured specificity, calculated using definitely normal interpretations, was found to be 75% (68/91), 62% (56/91), and 63% (57/91) for full-count FBP, full-count Astonish and half-count Astonish, respectively ($p = 0.113$). None of these differences were statistically significant. This demonstrates the ability of Astonish to maintain diagnostic accuracy even with only half of the counts.

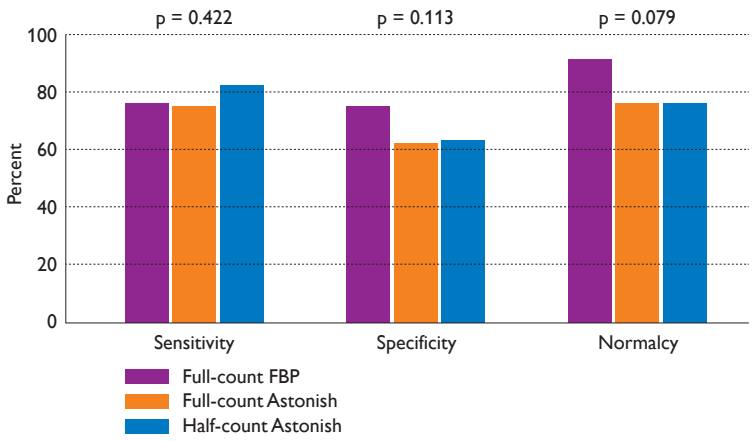

Figure 7. Comparison of diagnostic accuracy obtained with full-count FBP, full-count Astonish and half-count Astonish.

While this multi-center clinical trial only investigated the clinical performance of Astonish with Tc-99m-labeled agents, clinical performance of Astonish has been explored in smaller single-center studies with Tl-201 MPI. For example, Reyes et al. [8] concluded that with Tl-201 MPI, Astonish "improves parameters relating to image quality and increases confidence of interpretation without affecting the integrity of myocardial perfusion and left ventricular function data."

Clinical performance of Astonish with attenuation correction

In the second phase of the multi-center clinical trial carried out by Venero et al. [7], attenuation and scatter corrections were incorporated into the Astonish reconstructions and the clinical performance of Astonish with these corrections (referred to as Astonish-AC) were tested against Astonish without these corrections (referred to as Astonish) for both full-count and half-count data.

There was a statistically significant improvement in specificity and normalcy when myocardial perfusion data was corrected for scatter and attenuation. This was true for both full-count and half-count data as illustrated in Figure 8. The change in sensitivity was not statistically significant. It's also important to note that there were no statistically significant differences in the diagnostic indices for full-count Astonish-AC compared to half-count Astonish-AC ($p > 0.05$ for all comparisons). This demonstrates the ability of Astonish-AC to maintain diagnostic accuracy even when using only half of the counts.

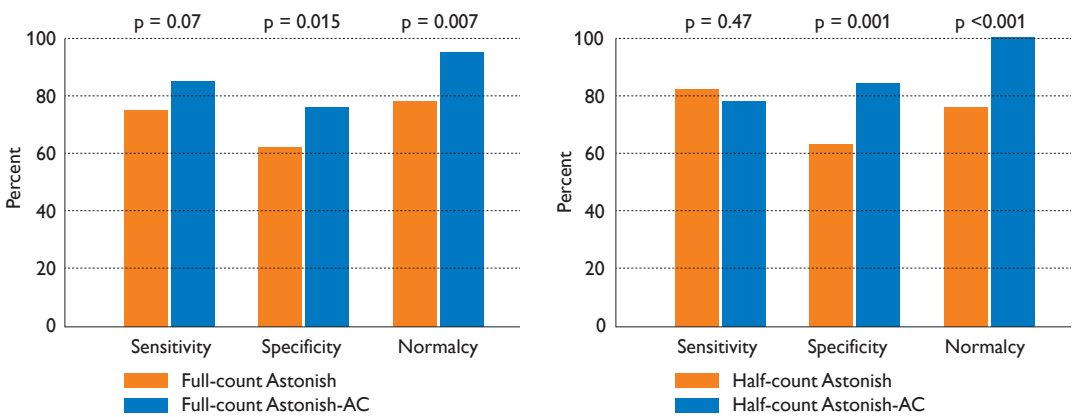

Figure 8. Comparison of diagnostic accuracy obtained with Astonish and Astonish with attenuation and scatter correction (Astonish-AC) for both full-count data (left) and half-count data (right).

Additional clinical benefits of attenuation correction

Because attenuation correction of SPECT MPI improves image quality, interpretive certainty, and diagnostic accuracy, the American Society of Nuclear Cardiology and the Society of Nuclear Medicine have jointly recommended the use of attenuation correction in addition to ECG gating for SPECT MPI studies.[9] More recent clinical studies have suggested that there may be additional clinical value of attenuation correction in SPECT MPI beyond the traditional improvements in image quality, interpretive certainty, and diagnostic accuracy.

Two recent single-center studies have indicated that attenuation correction can also provide incremental risk stratification. One such study consisted of a population of 7,382 consecutive patients who underwent attenuation-corrected ECG-gated sestamibi SPECT MPI at Hartford Hospital.[10] For each image, a summed stress score was calculated based on the attenuation-corrected image (AC-SSS) and the standard FBP reconstruction without attenuation correction image (SSS). Although patients with SSS of 0-3 are considered low risk, an AC-SSS of 1-3 was associated with a statistically significantly higher cardiac event rate compared to the low-risk group of AC-SSS = 0, thereby identifying a new at-risk group with AC-SSS of 1-3. A second study based on a single-center trial of 876 consecutive patients undergoing a one-day stress-rest Tc-99m-tetrofosmin SPECT MPI study for the evaluation of known or suspected CAD showed similar results.[11] In this study, CT-based attenuation correction (CT-AC) was used and, while a CT-AC-SSS of 0 was found to identify low risk patients with a warranty period of at least four years, a CT-AC-SSS of 1-8 was found to be associated with an intermediate risk of major adverse cardiac events. Both of these studies show that with attenuation correction, the prognostically relevant summed stress score cutoff for identifying low-risk patients is shifted towards lower values and a new at-risk group can be identified. This new risk stratification should be considered in patient management.

Stress-only imaging

An alternative strategy to the conventional stress/rest protocol used for MPI is a stress-only protocol where rest imaging is only performed in patients that have an equivocal or abnormal stress study. The advantages of such an approach are threefold. First, radiation exposure to the patient is significantly reduced by eliminating the resting exam. Second, laboratory costs can be reduced by eliminating unnecessary imaging time and radiopharmaceutical costs for resting studies. And third, laboratory efficiency can be improved by freeing up camera time to study additional patients.

A number of studies investigating the use of stress-only imaging have been performed over the years. Stress-only imaging paired with attenuation correction has been shown to be both diagnostically accurate [12] and to predict low risk for subsequent events when normal [13]. A recent study of 16,854 patients demonstrated that the prognostic value of a normal stress-only gated Tc-99m SPECT study performed with attenuation correction was equivalent to that obtained from a conventional rest/stress study.[14] The results of this study demonstrate that patients who have normal initial stress SPECT exams do not require additional rest imaging. Their results also demonstrate that this imaging strategy will significantly reduce radiation exposure in a substantial number of patients. A stress-only protocol was used in 8,034 patients (47.7%) whereas additional rest images were acquired in 8,820 (52.3%). The mean radiopharmaceutical dosage for the stress-only group was 21.3 ± 10.7 mCi, which was significantly lower than the 55.1 ± 11.9 mCi for the stress/rest group ($p < 0.001$). Furthermore, over half of the stress-only group ($n = 4,948$) received a low-dose stress-only study with a mean radiopharmaceutical dose of only 13.5 ± 2 mCi. This represents 29.4% of the total number of patients ($n = 16,854$) included in the study. The remainder of the stress-only group ($n = 3086$) received a high-dose stress-only study with a mean radiopharmaceutical dose of 33.8 ± 6.2 mCi.

Stress-only imaging with Astonish and attenuation correction

Another aspect of the multi-center Astonish clinical trial was the investigation of stress-only imaging with Astonish-AC.[15] In this portion of the trial, the data from 110 consecutive patients undergoing clinically indicated myocardial perfusion SPECT studies were retrospectively processed in three ways: conventional stress/rest processing with full-count FBP; stress-only imaging with full-count Astonish-AC; and stress-only imaging with half-count Astonish-AC. All images were interpreted in a blinded fashion and the gold standard was either a statistical low likelihood for coronary artery disease (n = 18) or the results of coronary angiography (n = 92).

This study found that there was no statistically significant difference in the diagnostic accuracy between the three processing methods as shown in Figure 9. By using Astonish-AC, the same diagnostic accuracy could be achieved despite using only a single image set (stress only) and with only half the counts compared to the conventional full-count stress/rest FBP. The perceived need for a rest image for half-count versus full-count stress-only images was 23% and 21%, respectively (p = 0.744).

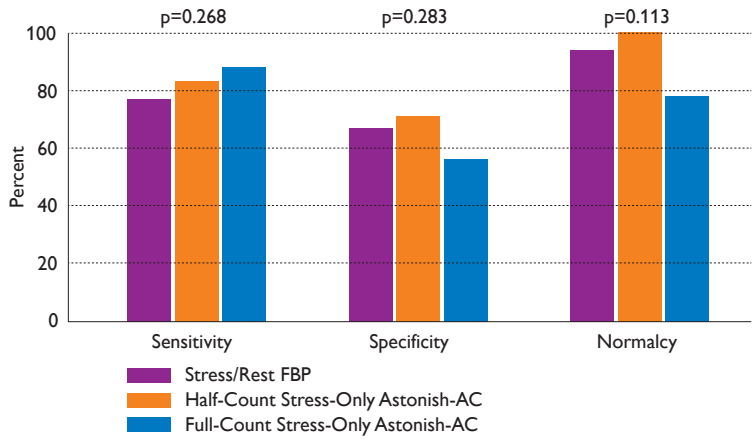

Figure 9. Comparison of diagnostic accuracy obtained with conventional Stress/Rest FBP, half-count stress-only Astonish-AC, and full-count stress-only Astonish-AC

Dose reduction

A recent ASNC Information Statement provides recommendations for reducing radiation exposure in myocardial perfusion imaging.[16] This document states that "Lowering the radiation dose while maintaining or improving image quality should be considered an improvement in quality of care." The results from the Astonish multi-center clinical cited previously [7] demonstrate that Astonish can be used effectively with half-count data. This provides sites the option of either reducing their imaging time by a factor of two or reducing the injected dose by a factor of two without a loss in image quality when using Astonish. This study further shows that by adding attenuation and scatter correction to Astonish, the diagnostic accuracy of the study can actually be increased despite the reduced dose.

The ASNC Information Statement goes on to state, "The use of stress-only imaging to exclude significant myocardial ischemia with Tc-99m-based tracers in appropriately selected patients provides the lowest radiation dose for SPECT. The accuracy of stress-only studies can be enhanced using attenuation correction." The stress-only results from the Astonish multi-center clinical trial cited previously [15] demonstrate that Astonish-AC permits reducing stress acquisition counts by one-half (which can be achieved by reducing the injected dose by one-half) while obviating the need for rest imaging in many patients referred for myocardial perfusion imaging.

And while attenuation correction may introduce additional radiation exposure, the benefits outweigh the potential risks provided this increased radiation exposure is minimal. The unique design of the BrightView XCT systems allows for very a low dose attenuation scan. The 0.12 mSv effective dose of the BrightView XCT attenuation scan is a negligible component of the radiation exposure received by the patient compared to the dose from the injected radiopharmaceutical and, as such, the use of attenuation correction is considered desirable.[16]

Table 1. Dose reduction capabilities available with BrightView XCT and Astonish.

	Tc-99m Sestamibi injected dose (mCi)	Absorbed dose (mSv)	Transmission dose (mSv)	Total absorbed dose (mSv)
Standard MPI (FPB) [16]	Stress – 27.5 Rest – 10	11.4*	0	11.4*
Half-dose Astonish	Stress – 13.8 Rest – 5	5.7*	0	5.7*
Half-dose Astonish-AC	Stress – 13.8 Rest – 5	5.7*	0.24*	5.9*
Stress-only half-dose Astonish-AC	Stress – 13.8	4.2	0.12	4.3

*Absorbed dose in mSv is the total due to both stress and rest procedures

Table 1 summarizes the dose reduction capabilities that BrightView XCT with Astonish can provide without compromising diagnostic accuracy. These doses are well below the average total radiation exposure of <9 mSv for SPECT MPI put forward by ASNC. [16]

Summary

BrightView XCT with Astonish provides multiple advantages for performing nuclear cardiology studies. The unique flat panel X-ray detector system provides a low dose (0.12 mSv) CT image that can be used for attenuation correction of the cardiac SPECT data. Moreover, the attenuation scan is acquired in a single 60-second rotation of the gantry with the patient breathing normally. This free-breathing protocol is well tolerated by patients, easy for technologists, and reduces misalignment between the transmission and emission data.

The ability of Astonish to process half-count data without compromising image quality gives the nuclear physician the option of improving laboratory efficiency by reducing the acquisition time using conventional dosing protocols, or reducing the patient radiation dose by injecting less radioactivity and using more conventional acquisition times.

Astonish with attenuation correction provides the physician with the ability to both reduce radiation doses and improve diagnostic accuracy. Furthermore, it enables stress-only imaging and the elimination of the resting portion of the exam, further reduces radiation exposures, increases patient convenience, and improves laboratory efficiency.

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