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Introduction

Attenuation correction (AC) has become necessary in myocardial perfusion imaging (MPI) due to the likelihood of photon attenuation artefacts. In addition to a general reduction of photon counts in larger patients, localised photon attenuation artefacts typically caused by diaphragmatic attenuation in larger males and breast attenuation in larger females (1,2) can cause difficulties in interpretation. Misinterpretation could lead to unnecessary invasive intervention, such as coronary angiography. This type of error is clinically unacceptable, and a high-quality attenuation map is recommended to correct for these patient induced artefacts (3). For these reasons AC is recommended by the American Society of Nuclear Cardiology and Society of Nuclear Medicine for MPI studies (4).

AC was initially performed using radionuclide based transmission images but has been superseded by an x-ray computed tomography (CT) based technique (5-7) In comparison to a radioactive line source, CT based AC has improved the quality of the attenuation map due to better spatial resolution, increased photon flux and no cross-talk from different radionuclide gamma ray energies. As a result MPI studies have seen improvements in diagnostic accuracy (8,9).

While the usefulness of CT based AC is clear there is controversy regarding what must be done about the incidentally produced low-resolution CT images that are the basis of AC.

In the United Kingdom (UK), regulations dictate that a clinical evaluation and record must be made for every exposure (10). The implication here is that all image information should be reviewed, regardless of the reason for exposure (i.e. AC and not a diagnostic quality scan). However, the typically low quality of images produced for AC in single photon emission computed tomography/computed tomography (SPECT/CT) means that it is not clear whether this could be counterproductive. To further complicate this, the diagnostic quality of these images is also liable to significant variation due to the diversity of CT parameters used for an AC acquisition in different SPECT/CT systems. Despite variation in the acquisition, the reliability of attenuation maps provided by CT units has been found to be independent of both tube charge (mAs) (11) and tube rotation speed (12). Furthermore a static phantom study of the low-resolution CT images produced by a single SPECT/CT system for AC has reported that mAs had no impact on an observer's ability to detect certain simulated lesions (13).

Some retrospective clinical work has been done to evaluate the diagnostic suitability of these low-resolution images; Goetze et al (14) studied 200 consecutive patients undergoing attenuation corrected MPI using CT based AC in a single SPECT/CT system. The review of these coincidentally acquired low-resolution images revealed 234 extracardiac abnormalities in 119 patients; 15 previously undiscovered incidental findings were categorized as having major significance, requiring either further testing or follow-up. An expert in CT and a resident in nuclear medicine with no formal CT training completed this retrospective review and the results described the consensus opinion. Based on the consensus opinion the authors recommended routine assessment of these low-resolution images. However, no receiver operating characteristic (ROC) study was completed and their study was confined to a solitary SPECT/CT system while in practice there is considerable variation in acquisition parameters and other device characteristics between SPECT/CT systems in clinical use. The current study investigates the impact of the CT acquisition parameters used in five SPECT/CT systems in the UK.

Materials and Methods

Image Acquisition

Since it would not be desirable from ethical and practical considerations to image enough patients in all five modalities to generate sufficient numbers of normal and abnormal cases for the observer study, a phantom study was indicated. Phantom simulation allows the production of reliable system-matched images without concerns over radiation dose.

Spherical simulated lesions with diameters 3, 5, 8, 10 and 12mm, and densities -800, -630 and +100 Hounsfield Units (HU), for a total of 15 inserted lesions (some diameter-density combinations were repeated) which were manually inserted in 17 trans-axial slices in an anthropomorphic chest phantom (*Lungman N1 Multipurpose Chest Phantom, Kyoto Kagaku Company Ltd, Japan*) representing a 70Kg male. The lesions were composed of urethane (-800 and -630HU) and a combination of polyurethane, hydroxyapatite and a urethane resin (+100HU). This resulted in 17 abnormal image slices, each containing 1-3 simulated pulmonary lesions, and 9 normal slices, i.e., containing no lesions. The phantom was scanned on a dedicated diagnostic quality multi-detector CT (MDCT) scanner, not to be confused with CT units in the SPECT/CT systems, which were the subject of the comparison study. The MDCT images provided a lesion reference map that would act as the truth (gold-standard) for the observer performance study. The high-resolution MDCT scan was repeated at the end of the SPECT/CT imaging, described next, to ensure that lesion positions had not changed.

All images for the observer study were produced from a single CT acquisition of the phantom from each SPECT/CT system using site-specific CT acquisition protocols, Table 1, appropriate to a 70Kg male. The variation in CT acquisition parameters and estimated CT Dose Index (CTDI) listed in this Table is representative of general practice in the UK. The variation in slice thicknesses gave rise to a differing number of axial CT slices but each acquisition covered the full length of the phantom. Four SPECT/CT systems (labelled 1-4) used low-resolution CT systems from the same manufacturer, and the fifth (labelled 5) used a CT system capable of producing diagnostic quality images from a different manufacturer, which was used as a backup to the dedicated diagnostic CT system in that imaging facility.

Figure 1, which shows two representative slices imaged using each SPECT/CT system, is arranged in 5 rows (labelled with numbers 1-5 corresponding to the 5 SPECT/CT systems) and two columns: the first labelled (a) corresponds to the abnormal slice (the arrow points to the location of the simulated lesion) and the second labelled (b) corresponds to the normal slice. Since the slices were not viewed in three-dimensional volumetric mode, care had to be exercised in choosing the central locations of the chosen slices so that sets of five “matched” slices, for example, those corresponding to each column in Figure 1, corresponded to the same physical region of the phantom. For normal slices this was achieved using anatomical landmarks (simulated major vessels and bony structures) visible on the high-resolution MDCT images. For abnormal slices this was achieved by selecting that slice that maximized the visual contrast of the contained lesion.

Observer Performance Study

Each CT acquisition produced 26 image slices for the observer performance study. Twenty-one professionals working in nuclear medicine (0-4 years CT experience, mean 1.2±1.2) each completed the study in a single session lasting approximately 90 minutes. No time restriction was enforced. All selected Images, 26 from each of the 5 SPECT/CT systems were pooled together and displayed in a different randomised order for each observer. The observer was unaware of the SPECT/CT system used to generate each image. Observers were informed they would be interpreting 17 abnormal image slices, each containing 1-3 simulated pulmonary lesions, and 9 normal slices, imaged in five modalities. They were required to localise all suspicious areas precisely using mouse clicks. Additionally, an individual confidence score rendered on a 10-point integer (1-10) rating scale, was required for each localisation (mark); this was implemented using a slider bar. Image evaluations were conducted using ROCView (15) (*Bury St Edmunds, UK, www.rocview.net*) on identical monitors (*iiyama ProLite B2206WS 22 inch widescreen LCD, iiyama, Netherlands*) (1680x1050 pixels, 1.8 megapixel resolution), satisfying the standards set by The Royal College of Radiologists (16). Observations were completed in low ambient light environments.

Lesion visibility was maximised using a lung window setting (width 1500, level -500) which was held fixed for all observers.

Each localisation (mark) was classified (scored) as lesion localisation (LL) or non-lesion localisation (NL) using a 20-pixel radial diameter acceptance radius (AR) centred on each lesion. To test for effects of varying the acceptance radius, the data was also analysed using a 40-pixel acceptance radius. The analysis was repeated for two subgroupings of readers according to experience: 7 readers with no CT experience and 14 readers with CT experience.

Statistical Analysis

Multi-reader multi-case (MRMC) FROC ratings corresponding to 2730 (26 cases X 21 observers X 5 SPECT/CT systems) individual slice observations were analysed using the jackknife alternative FROC (JAFROC) method (17) (*JAFROC 4.2, www.devchakraborty.com/downloads*). The outcome analysed was the unweighted JAFROC figure of merit (FOM), which is the empirical probability that a lesion is rated higher than any mark on a normal case (equal weighting was employed). The software also outputs the numbers of LL marks per slice and the average numbers of NL marks per normal slice, and the corresponding number per abnormal slice.
The DLL module used for the significance testing was developed at the University of Iowa (18-24). The relevant statistics provided by the software are the F-statistic and p-value for testing the null hypothesis that all SPECT/CT systems have identical performance, the individual and observer averaged FOMs for each SPECT/CT system, the FOM differences between pairs of SPECT/CT systems, and 95% confidence

intervals for the FOMs and the paired differences. Since the results are specific to the particular phantom and slices used in the study, random-reader fixed-case results reported by the software are used. Analyses using the software were conducted separately for the four subsamples corresponding to the two values of acceptance radius (AR) and the two levels of CT experience. Since cases are treated as fixed, the observer FOMs, averaged across the five SPECT/CT systems are independent. Therefore we apply a two-independent-group t-test to the observer averaged FOMs (where CT experience is the grouping variable), providing a confidence interval. If the global test is significant, then we follow it by individual within-system confidence intervals. Type I error is controlled as follows. Consider the family of tests consisting of the five global tests: four tests for identical system performance and one test of identical experience performance. For this family the maximum type I error rate (probability that we will incorrectly conclude that there are any differences for any of the five groups) is limited to 0.05 by performing each of the five tests at the Bonferroni corrected level of alpha = 0.01. Follow-up 95% confidence intervals and corresponding hypotheses tests (alpha = 0.05) for pair-wise differences are reported only if the corresponding global test is significant; in this way, for a particular global test the overall type I error for follow-up tests (i.e., the probability that we will incorrectly observer any differences) is limited to .05 if there are no real differences. Thus, in order for a statistically significant difference to be declared, the p-value of the overall F-test had to be smaller than 0.01 and the 95% confidence interval for the paired difference between FOMs had to exclude zero.

Plotting free-response data

Single rating per image ROC data is usefully visualized via the receiver operating characteristic (ROC) curve. Free-response data, consisting of mark-rating pairs, can be visualized in 3 ways. (1) The highest rating of all marks on a slice (or zero if the slice has no marks) is the highest rating inferred ROC rating of the slice; this can be used to construct inferred ROC curves (true positive fraction, TPF, vs. false positive fraction, FPF). (2) The FROC (free-response ROC) is the plot of lesion localization fraction (LLF = fraction of lesions correctly localized) vs. non-lesion localization fraction (NLF = number of non-lesions divided by the total number of slices). (3) The AFROC (alternative free-response ROC) is the plot of LLF vs. FPF: a linear interpolation from the uppermost operating point to (1,1) is included in the area under the AFROC, which is the JAFROC figure of merit.

Empirical ROC/FROC/AFROC curves were produced for each SPECT/CT system. For the AFROC, linear interpolation was used to estimate the lesion localization fraction (LLF) for all observers at 200 abscissa values between operating points (0.005 increments between 0 and 1) and these were averaged to yield the reader-averaged plot.

Results

Table 2 summarizes the results of the four analyses conducted (for AR = 20, 40, CT experienced and no CT experience): it lists the F statistic, and in parenthesis the numerator and denominator degrees of freedom, the P-value, the average number of NL marks per normal slice, the corresponding number per abnormal slice, and the average number of LL marks per abnormal slice. For 20-pixel acceptance radius and all 21 readers, Figure 2a displays the JAFROC FOMs and 95% confidence intervals for the five SPECT/CT systems; the FOM values were 0.602, 0.639, 0.372, 0.475 and 0.719 respectively. Figure 2 (a) shows that system 3 had the lowest FOM, while system 5 had the highest, 1 and 2 were similar, and slightly below 5, while 4 was intermediate between 3 and 5. Differences between pairs of SPECT/CT system and corresponding confidence intervals are shown in Figure 2b. A statistically significant difference in FOMs (confidence interval not including zero) was found between all but one pair of SPECT/CT systems (the 1-2 pairing difference was not significant – these systems only differed in mAs values, Table 1). SPECT/CT system 5 was significantly superior to all other SPECT/CT systems. The significance of differences in SPECT/CT system pairings were unchanged for the other three analyses (AR = 40, CT experienced, no CT experience) with one difference: the SPECT systems 1 vs. 2 difference became significant (with 2 superior) for AR = 20 for the CT experienced readers – i.e., the higher mAs system was significantly superior for the experienced readers provided the tighter acceptance radius criterion was adopted.

Figure 3 shows reader averaged inferred ROC, FROC and AFROC curves for AR = 20 and all 21 readers. The AFROC/FROC curves for AR = 40 are visually identical to those shown in Figure 3; the small increments in FOM are not visually apparent. Since localization specific scoring is not performed in ROC analysis, the ROC curves are independent of AR. Figure 4 compares the reader averaged FOMs of the CT experienced, n = 14; and no CT experience, n = 7. Despite a trend towards higher FOMs for the experienced group (modality averaged value = 0.596 for experienced group vs. 0.492 for the inexperienced group), the Welch’s 2-sample t-test of the modality-averaged JAFROC FOMs between the two experience based reader groups revealed no significant difference in lesion detection performance on the basis of CT experience (p = 0.0539, subgroup difference 0.105 (95% CI -0.002, 0.211).

Discussion

This study evaluated lesion detectability in the low-resolution CT images acquired for attenuation correction as part of the SPECT/CT myocardial perfusion imaging technique. The diagnostic value of these images has been in question, but the work of Goetze et al (14) has suggested that there is value in reporting interpretations from these images. Legislative pressures in the UK also require a formal record of each exposure to be created.

The statistically significant differences observed in this study, which were especially large for SPECT/CT system 5 compared to the others, suggest that there may be some clinical implications of the differences in image acquisition parameters between clinical centres. We believe this is the first work to assess the influence of the CT protocol on the diagnostic potential of the attenuation corrected images in patients undergoing myocardial perfusion imaging.

Previous work (13) with 20 readers on the detection of simulated lesions on CT images acquired for AC using a free-response study was unable to demonstrate statistically different performance when changing mAs over the range 15.8 to 39.5. The current work was likewise unable to detect a mAs effect if all observers were included (n=21; AR = 20 and 40 pixels). However, when we restricted to CT experienced observers (n=14) and a tight acceptance radius (AR = 20 pixels) the mAs effect (SPECT systems 1 vs. 2) became significant. The ability to demonstrated significance is likely due to two factors: (i) using the more lax acceptance radius (AR = 40) is expected to confuse perceptual NLs (incorrect decisions) as LLs (scored correct decisions) (25), and (ii) using experienced observers is expected to reduce inter-reader variability. Both of these effects are expected to increase statistical power.

From examination of Figure 2 (b), and focusing on the differences with the largest magnitudes, it appears that the axial (z-axis) resolution (i.e., reconstructed slice thickness) and matrix size appear to be the main factor in determining lesion detection performance, with smaller slice thickness and larger matrix sizes contributing to higher performance. The comparatively higher performance of system 2 (6.1 mm thick slices) relative to system 3 (10mm thick slice) is consistent with the slice thickness effect, as is the superiority of system 5 (5 mm thick slices) to all other systems. The superiority of system 4 to 3 is attributable to the larger matrix size of the former. SPECT/CT system 5, the only system with diagnostic capability, showed the highest observer performance, being statistically better than all other systems. System 5 uses a lower kilovolt potential and a smaller pixel size to offer improved image contrast and spatial resolution respectively. The reconstructed slice thickness is also smaller, thus providing improved axial resolution.

Initially we had concerns that a larger reconstructed slice thickness may favour lesion detection, when using single axial images vs. three-dimensional display, due to less noise being present in the image. However lesion detection improved as the reconstructed slice thickness decreased, suggesting that the partial volume effect has a greater impact on lesion detection than image noise.

While lesion detection performance for the CT experienced group was somewhat higher than for the inexperienced group, Figure 4, the difference was not statistically significant. However, this subgroup analysis may have relevance to the nuclear medicine community, where CT interpretation skills can vary broadly due to the training pathway of those reporting myocardial perfusion imaging studies (i.e. radiologist vs. nuclear medicine physician). It has been suggested that further training might be required for clinicians with less experience in CT to recognise extra-cardiac findings and establish the need for follow-up (26). More specifically, it has been recommended (27) that nuclear medicine physicians without CT training should report only the functional data (SPECT) with radiologists involved to report the anatomical data (CT), therefore providing a collaborative report.

This laboratory study reflects the variation in CT protocols used for AC in the UK. However, limitations are evident in this type of phantom study. Respiratory motion was not simulated and this is likely to have effect in a patient population. In this study, tube rotation times ranged from 1.5 seconds (treatment 5) to 23.1 and 30 seconds (treatments 1-4) which could allow 4-5 normal breathing cycles to occur, thus allowing greater potential for respiratory motion artefacts (28). Respiratory motion artefacts are evident with slow and fast tube rotation speeds, with greater impact on slow rotations (29).

Conclusion

Protocol variations in operation for CT based AC have a significant impact on lesion detection performance. The results imply that z-axis resolution and matrix size had the greatest impact on lesion detection, with a weaker but detectable dependence on the mAs product.

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Figure Captions

Figure 1: An abnormal slice (left column, labelled a) containing a 12mm and -630 HU simulated lesion (arrowed), and a normal slice (right column, labelled b) for each of the five SPECT/CT systems (numbered 1 - 5) used in this study.

Figure 2a: JAFROC figures-of-merit (FOM) and 95% confidence intervals for the 5 SPECT/CT systems (AR = 20).

Figure 2b: FOM difference (AR = 20) for all SPECT/CT system pairings (labelled on the x-axis; e.g., 1 – 2 means FOM for system 1 minus that for system 2) and 95% confidence intervals. Confidence intervals that do not include zero demonstrate a significant difference between the corresponding treatments.

Figure 3: Empirical reader averaged ROC, FROC and AFROC curves for all SPECT/CT systems using an acceptance radius of 20-pixels.

Figure 4: Illustrating the effect of CT experience. Shown are reader averaged JAFROC figures-of-merit and 95% confidence intervals. CT experience: 14 readers; no-CT experience: 7 readers.

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