Added Value of Computed Tomography Attenuation Correction and

Prone Position in Improvement of Breast and Subdiaphragmatic

Attenuations in Myocardial Perfusion Imaging

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Abstract:

Soft tissue attenuation of gamma photons is the most common source of artifacts and remains an intricate problem for myocardial perfusion imaging (MPI) by single-photon emission computed tomography (SPECT) imaging. Breast and Sub-diaphragmatic artifacts are the most frequent causes of false-positive images in female patients. Many ways are introduced to overcome the attenuation artifacts, including the prone position to avoid breast attenuation or by using hybrid SPECT/ computed tomography (CT) systems. The purpose of the study is to evaluate the role of prone images in attenuation correction comparing to CT attenuation correction in MPI. Material and Methods; Forty-four patients were initially included in the study. Statistical analysis was done for thirty patients with suspected or confirmed ischemic heart disease (IHD). All the patients underwent the ordinary supine stress/rest SPECT myocardial perfusion imaging (MPI) then; additional stress/rest prone SPECT as well as stress/rest SPECT/CT images were acquired, each study was interpreted separately and their results were compared. Results; It was found that 58% (31/53) of the depicted defects were attributed to attenuation artifacts; the computed tomography attenuation correction (CT-AC) imaging technique was able to correct 52% versus 49% for prone imaging. The sensitivity, specificity, and diagnostic accuracy were 100%, 90.3%, and 94% for CT AC respectively versus 100%, 83.8%, and 91% for prone imaging. Inferior wall defects were more common in males (95%) and CT AC provided better performance than prone imaging for them (i.e. 92.9% in CT AC versus 90.9% in prone imaging). On the other hand, anterior wall defects were more common in females (83.3%) in which prone imaging was better than CT-AC for them. Conclusion; both CT and prone imaging increased the specificity and diagnostic accuracy of myocardial perfusion imaging without affecting the sensitivity.

Keywords: SPECT/CT; attenuation correction; prone imaging; MPI

1. Background

Single photon emission computed tomography (SPECT) myocardial perfusion imaging is considered a useful non-invasive imaging modality in the evaluation of suspected or established coronary artery diseases. Moreover; it has an important role in risk assessment, management decisions, and prognosis of patients with ischemic heart diseases. Radionuclide myocardial perfusion scintigraphy (MPS) has become established as one of the main functional cardiac imaging technique for ischemic heart disease (IHD), constituting approximately one-third of all nuclear medicine procedures done annually in the United States, with substantial growth annually. The increasing use of MPS for the diagnosis of clinically important coronary artery disease (CAD) is the direct result of its strengths; MPS is a robust and highly validated technique, widely available, with a clear role in the assessment of patients investigated for CAD as stated by internationally published guidelines (1).

However, imaging artifacts could limit the utility of the study. These artifacts could be technical or patient related. Therefore, many additive techniques were used to overcome this drawback.

Patient motion and soft tissue attenuation are the two most common sources of artifacts in MPI. However, researches are focusing on attenuation artifacts and how to overcome them in order to improve diagnostic accuracy and certainty of the final report by reading physicians. Patient related artifacts remain an issue of concern. The location of the attenuation artifact depends on the position of the soft-tissue attenuator in relation to the left ventricle. The severity of the artifact depends on the size and density of the attenuator in relation to adjacent tissue. Within the acquired SPECT image, the artifact may appear as a fixed or reversible defect depending on whether the attenuator is in a constant or variable position in stress and rest image acquisitions (2). Several methods were added to the conventional SPECT imaging for attenuation correction. Additional prone SPECT images, as well as upright (erect) imaging, were described for sub-diaphragmatic attenuation to differentiate attenuation artifacts from true hypo-perfusion defects thus, improving the quality, increasing the specificity and accuracy of myocardial perfusion imaging.

Now with the era of hybrid imaging, SPECT/CT devices were used to produce an integrated CT attenuated corrected image in order to discriminate between true perfusion defects and artifacts. The instrumentation, radiopharmaceuticals, and methodology used for myocardial perfusion scintigraphy have evolved over the years. Multi-view planar imaging was followed by single-photon emission tomography (SPECT), gated SPECT, SPECT/CT, and PET/CT. However, the underlying physiological principles that make myocardial perfusion imaging an important diagnostic tool remain unchanged (3). Although, SPECT imaging of myocardial perfusion provides a sensitive means of detecting and localizing CAD and assessing left ventricular (LV) function. The method suffers from the potential for poor specificity due to image artifacts related to both patient and technical factors (2). Technical artifacts include; Patient motion, Gating problems, and Reconstruction and processing errors. On the other hand; Soft-Tissue Attenuation, Breast attenuation, Diaphragmatic attenuation, and subdiaphragmatic activity, and Lateral Chest-Wall Fat Attenuation are among Patient-related artifacts.

Attenuation correction methods

Attenuation within the body is not uniform, therefore; accurate attenuation correction requires a precise estimate of the patient specific attenuation distribution (3).

For this reason, many attempts have been established to overcome the attenuation artifacts. Acquiring prone position SPECT was one effective costless method. Also, attenuation maps were generated to be sequential on simultaneous acquisition of emission and transmission images, this was achieved using the Gadolinium source as well as the hybrid SPECT/CT devices (2).

Low dose CT; preferred AC method done sequentially after the emission but may cause misregistration artifact due to motion during emission scan and different breathing patterns between the long emission and very short CT AC scan.

Also, the **<u>D-SPECT cameras</u>** have high diagnostic accuracy for the detection of CAD and it increases the confidence of interpretation compared to stress-only supine MPI in a group of obese patients, thus reducing the physician-perceived need for rest imaging (4). Use of D-SPECT (ultra-high sensitive CZT crystals with solid-state technology) must be in two position comparison (upright and supine) to be effective.

Prone position: additional non-gated and non-AC, but not every patient is possible due to physical limitations, despite shorter acquisition time than the supine imaging. It yields more accurate scintigraphic interpretations without any additional cost, it is inexpensive and it does not deliver any extra radiation to the patient. It is associated with increased inferior and septal wall counts, less patient motion (2). Patient discomfort, being less suitable for females with large breasts and obese patients should be considered as a limiting factor for this additional acquisition protocol (2).

The addition of the prone position to stress supine myocardial scintigraphy could decrease the false positive rates and leads to more accurate results. Furthermore, it was postulated that it increases specificity without compromising sensitivity for the diagnosis of CAD. It has a key benefit of reducing the number of unnecessary rest studies performed, whilst minimizing radiation exposure, investigation time, and costs (5).

Transmission line source (Gd-153); emission and transmission done simultaneously for better registration between the two but needs transmission source QC done separately and need to replace the source every 18 months, which is not billable revenue. In addition, occasional mechanical issues with the line sources could cause the camera downtime.

Evaluating wall motion and wall thickening (with or w/o myocardial contours) from the gated images could also help distinguish the attenuation artifacts from true defects on perfusion image.

<u>SPECT/CT and attenuation correction</u>

The advent of hybrid SPET/CT technology gave rise to the potential for computed tomography (CT) images to serve as transmission maps for the AC of SPET data. Images produced by CT hold many advantages: they are obtained in seconds or a few minutes (depending on the CT device) and generally provide high quality transmission maps, there is no radioactivity cross-talk with emission images and the life of the x-ray tube is very long. The additional radiation dose to the patient varies considerably between scanners and different protocols but is generally low; with low-dose CT devices used in the first generation. Hybrid SPET/CT systems, in particular, the effective dose is about 1mSv or less (6).

Low dose CT AC allows reviewing the chest CT image (non-diagnostic quality) for incidental findings (cardiac or non-cardiac) and assess the presence of calcium (with or w/o score). If CT rings > 4-slices, able to add diagnostic coronary artery calcium (CAC) scoring to improve diagnostic certainty, especially in equivocal MPI study with 0 score vs extensive calcium score. If CT rings > 64-slices, able to add coronary CT angiography as well.

Common factors that may degrade CT maps are patient movement during CT acquisition and excessive beam hardening created by selective low-energy x-ray attenuation in bone structures or metallic implants. Also, in hybrid systems with a CT field of view smaller than that of SPECT, exclusion of part of the thorax from CT slices, the so called "body truncation", inevitably impacts on the accuracy of AC in patients with large body habitus. Motion artifacts are common when using slow-CT devices. Fast multi-detector CT scanners acquire images of the chest within a few seconds while the patient is holding his breath, thereby avoiding such artifacts (6). Misregistration of emission-transmission slices can result from a software misalignment error or, more frequently, from patient motion between SPECT and CT acquisition, a change in the breathing pattern between acquisitions, axing of the examining table as it moves inside the gantry and upward creeping of the heart after the cessation of vigorous stress (7). Single photon emission tomography-CT misregistration of some degree is unavoidable with fast CT scanners which take frozen images of the chest, because SPECT acquisition is much slower including several respiratory cycles and representing an average of the chest motion during respiration (8). Actually, misregistration of emission and transmission slices is quite common in MPI SPECT/CT studies (9, 10). This misalignment may introduce false defects in MPI images and give rise to interpretation errors if left uncorrected. This is considered case-specific and thus hardly predictable (11). Software tools for the manual correction of misregistration have been developed by gamma-camera manufacturers. After the implementation of CT-AC, the reconstructed SPECT slices look somehow different from those of the uncorrected study (non-AC). Apart from the elimination of attenuation artifacts, other common features of corrected images include apical thinning, apical defects frequently create interpretation uncertainties, particularly when these extend to the apical portion of the anterior wall or appear as partly or fully reversible at rest. Also, more intense delineation of the right ventricular wall and accentuation of extra-cardiac subdiaphragmatic activity are included in the common features of CT attenuation. Also, the myocardial wall of the left ventricle appears thicker and the cavity is smaller. These normal patterns should be kept in mind when interpreting AC studies (12).

In addition, true perfusion defects, particularly in the inferior and inferolateral wall, usually appear smaller in corrected compared with uncorrected images. CT-AC is a valuable innovation, particularly helpful in males and obese patients. Moreover, the inspection of non-diagnostic CT images may reveal unsuspected concurrent pathology and thereby foster further investigation. Nevertheless, CT-AC studies should be interpreted with caution, side-by-side with non-AC images and in the context of clinical data.

2. Methods

Patients demographic data: This prospective control study was performed in the Nuclear Medicine Unit (NEMROCK center), Cairo University during the period from January 2017 till June 2017. The institutional review board (IRB) approved this retrospective study and the requirement to obtain informed consent was waived. It included **30** patients [20 males (66.67%) & 10 females (33.33%)] with mean age 53 ± 12 years after excluding 14 patients did not benefit from the additional images 4 patients were interpreted as normal in the Non-AC, CT-AC, and the prone-AC (with no perfusion defect) and 10 patients were proved to have multi-vessel disease in the three study sets (they had Non-AC defect not corrected by either CT-AC or prone-AC). All the patients underwent the conventional ECG-gated single-photon emission computed tomography (*SPECT*) Technetium-99m SestaMIBI myocardial perfusion imaging (^{99m}Tc SestaMIBI). Then additional CT attenuation images, as well as prone single-photon emission computed tomography (SPECT), were added.

The selection process included identifying those patients who fulfilled the criteria given below, and it was approved by the *ethical committee*.

Inclusion criteria, all patients referred for myocardial perfusion scan of different age groups. *Exclusion Criteria*, *n*o volunteers were included in this study, Patients who underwent pharmacological stress study, Patients with LBBB, and Patients underwent or who are candidates for CABG.

All patients underwent the two days protocol (rest & exercise stress) of myocardial perfusion SPECT with intravenous injection of 15 to 25 mCi (555 to 925 MBq) of 99mTc SestaMIBI according to body weight for each study.

Cardiac medication including beta blockers, theophylline derivatives, nitrates, and calcium channel blockers were stopped 48 hours prior to the study. Patients were instructed to fast for 4 to 6 hours before the test.

Rest/stress gated images were acquired with a commercially available dual-head gamma camera equipped with an integrated x-ray transmission system (Seimens). Emission data were acquired by the use of parallel hole low-energy high-resolution collimators, with the patient in the supine and prone positions. The acquisition orbits were body contour over a 180° arc, via 30 stops and 30 seconds per stop. The image acquisition matrix was 128 X 128. Images were acquired on the 140-keV photopeak with a 20% symmetric window. Resting SPECT images were acquired in the supine position 45 to 60 minutes after administration of the radiopharmaceutical then prone images were acquired. Stress SPECT images were acquired first in the supine position and then in the prone position 30 to 45 minutes after exercise and after administration of the radiopharmaceutical. The resting and stress SPECT images were gated via 8 frames per cycle, and the RR time acceptance window was 20%. The stress and supine SPECT images were corrected for attenuation by the use of a low-dose CT-based transmission scan acquired at a slice step 1mm. a current of 80 mA and v. the total SPECT/CT time was approximately 25 minutes.

All raw data sets were corrected with the isotope decay factor and checked for patient motion by reviewing a rotating cine display.

The projection data from the ECG-gated SPECT scan were summed and perfusion images were reconstructed with 3D ordered subsets expectation maximization (OSEM) algorithm and built-in processing that preserved the linearity between photon counts in projection data and pixel values in reconstructed images. Cardiac SPECT software Cedars cardiac suite (QPS/QGS) reconstructed cross-sectional cardiac images along the short and long axes of the heart to form: short axis (from apex to base), horizontal long axis (inferior to anterior wall), and vertical long axis (from septum to lateral wall).

Statistical Analysis

The statistical analysis was done using the Excel 2016 as well as the SPSS. The quantitative data was summarized as mean and standard deviation, whereas the frequency data was summarized as percentage.

Agreement was tested using kappa statistic. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

3. Results

The study included initially 44 patients coming with suspected or confirmed myocardial ischemia. After interpreting the MPI images and correlating them with clinical risk and other available diagnostic modalities (stress ECG, stress echocardiography, cardiac catheterization); 4 patients were interpreted as normal in the Non-AC, CT-AC and the prone-AC (with no perfusion defect) and 10 patients were proved to have multi-vessel disease in the three study sets (they had Non-AC defect not corrected by either CT-AC or prone-AC). These 14 patients did not benefit from the additional images hence; they were excluded from the statistical analysis. (**Table 1**)

The remaining 30 patients included 20 males (67%) & 10 females (33%) with mean age of 53 ± 12 years (**Table 2**).

In each of the 30 patients, left ventricular myocardial wall as a whole was divided into 5 walls (i.e. Apex, anterior, inferior, lateral and septal walls).

The total number of hypoperfusion defects elicited in the non-corrected images in different myocardial walls was 53 defects. After correlating the scan findings with the final diagnosis (i.e. attenuation artifact versus true hypoperfusion defect), 31 (58%) defects were finally interpreted as attenuation artifact and 22 (42%) defects were finally diagnosed as true ischemic defects (**Table 3**).

Using the two attenuation correction techniques (CT-AC and prone images), it was found that among the 31 Non-AC attenuation artifacts, CT-AC corrected 28 artifacts while 26 artifacts were corrected in prone images (Figure 1).

In CT-AC images, 50 out of 53 defects were correctly diagnosed representing 94.3%, as 28 (52.8%) defects were correctly diagnosed as attenuation and 22 (41.5%) were correctly diagnosed as true defects. However, 3 defects (5.7%) were mismatched between the final diagnosis and CT-AC interpretation as CT-AC failed to correct the attenuation artifacts with high statistical agreement (p<0.001) between CT-AC and final diagnosis in number of corrected artifacts as shown in (**Table 4**).

On the other hand, in prone images 48 out of 53 defects were correctly diagnosed representing 91%, as 26(49%) defects were correctly diagnosed as being attenuation and 21(42%) defects diagnosed as true ischemic defects. 5 defects (9%) showed mismatch between the final diagnosis and the prone interpretation because prone images failed to correct the attenuation artifact (Figure 2). Prone imaging showed statistical agreement with the final diagnosis with P value <0.001

Although the sensitivity of the study was almost not affected with the additional CT-AC or the prone images, the calculated specificity for detection of true defects in the CT-AC study was 90.3% and that of the prone images was 83.8% as shown in **Tables 5** and 6.

Figure 3, A 41-year-old male patient who is neither diabetic nor hypertensive complaining of tachycardia and chest pain for 2 months, EF: 61%. Showing hypoperfusion defect in the inferior wall and the normalization of the defect with CT_AC and Prone images.

Figure 4, A 50-year-old female patient who is neither hypertensive nor smoker but she has recent history of diabetes presenting with atypical chest pain for 4 months. EF63%, the coronary angiography showed atherosclerotic vessels with no significant stenosis. Showing hypoperfusion defect in the antero-septal wall and the improvement of the defect with CT_AC and Prone images.

Figure 5, represents the differences in polar maps of attenuated versus prone processing, as well as the non-corrected images for a 51-year-old male patient who is neither diabetic nor hypertensive complaining of chest pain for 2 months, EF: 58%. Showing hypoperfusion defect in the inferior wall and the normalization of the defect with CT AC and Prone images.

4. Discussion

Soft tissue attenuation is considered one of the main limitations of myocardial perfusion imaging. Therefore, additional techniques were proposed to overcome this problem. In our study, we evaluated the role of prone and CT attenuation corrected imaging in attenuation correction and we tried to postulate which technique is collectively better.

As previously said; statistical analysis was performed for 30 patients which include 20 males ($\approx 67\%$) and 10 females ($\approx 33\%$). All of these patients underwent the conventional Stress/rest No_AC; then, CT-AC images as well as stress/rest prone images were added. An experienced physician with ≥ 15 years experience in nuclear cardiology interpreted the stress/rest No_AC images, stress/rest CT_AC images and the stress/rest prone images separately. The final diagnosis (i.e. whether the elicited hypo-perfusion defect was attributed to attenuation artifact or true defect) was concluded taking in consideration the patient's risk and the available investigations including the Echocardiography and the coronary angiography.

In our study, we elicited 53 hypoperfusion defects in different myocardial walls preferentially the inferior wall followed by the anterior wall representing 39.6% and 22.6% respectively. 31 out of the depicted 53 hypoperfusion defects were attributed to attenuation artifacts representing 58%. In other words, more than > 50% of the elicited hypoperfusion defects would have been falsely interpreted as positive ones in the absence of additional attenuation correction techniques. On comparing the role of prone imaging

to the CT_AC imaging in attenuation correction, we found that prone imaging corrected 26 out of the 53 defects representing 49% whereas the CT_AC corrected 28 out of the 53 defects representing 52%. Also, the overall accuracy of the prone imaging was 91% compared to 94.3% for the CT_AC imaging.

Mathur et al found that 581/1383 (42%) of the initial stress myocardial perfusion imaging to be normal, whereas subsequent use of CT_AC increased the percentage of normal rate to 90% (1247/1383). According to our results, CT_AC imaging was statistically significant p<0.001; however, the results were comparable to that prone imaging to a great extent (13).

Malkerner et al compared supine stress/rest No_AC with supine stress/rest CT_AC and stress/rest prone imaging in 334 patients (14). They found that the percentages of patients yielding normal study were 61.4%, 82.9% and 90.4% in the No_AC, prone and CT_AC respectively. It proved that the combination of supine No_AC/CT_AC images is superior to that of supine No_AC/prone images (p=0.01) (14). It also postulated that the addition of prone imaging does not significantly alter the number of equivocal interpretation compared to the CT_AC results. However; in the absence of CT_AC images, prone imaging provides significantly fewer equivocal results than the standard supine No_AC imaging (14). And this conclusion coincides with our results to a great extent but it should be noted that although CT_AC was better than prone imaging (i.e.kappa value -0.869 versus -0.817 for CT_AC and prone imaging respectively), both techniques showed statistical significance (P<0.001), Also, the agreement between the CT_AC and prone techniques was p<0.001.

Stathaki et al showed comparable results proving that prone imaging improved the specificity and normalcy rates in anterior wall defects where 63.1% of the defects disappeared in the prone imaging (15).

Furthermore, our study revealed that the sensitivity, specificity and diagnostic accuracy were 100%, 90.3% and 94.3% respectively for CT_AC imaging versus 100%,

83.8% and 91% in the prone imaging. Actually, the reason behind the 100% sensitivity is attributed to the small sample size; moreover, we did not encounter any false negative results for either the CT_AC or prone imaging. In fact, many papers revealed an increase in the specificity and diagnostic accuracy without affecting the sensitivity. *Slomka et al;* which evaluated the value of quantitative supine/prone imaging in detection of coronary artery diseases and normalcy rates in women, indicated that the verity which combined prone/supine quantification has the effect of increasing the specificity and normalcy rate without altering the sensitivity (16). It also reported that the CT_AC technique improved the sensitivity, specificity and diagnostic accuracy for detection of coronary artery diseases (16).

On the other hand, *Shamra et al* referred to the role of CT_AC and its advantages to rule out significant coronary artery diseases and reduce the false positive results. Nevertheless, its use might compromise the sensitivity of the study (17). This was truly different from our study for the aforementioned reasons. Also, *Raza et al* showed that Sensitivity, specificity and diagnostic accuracy for detection of coronary artery disease were found to be 100%, 11% and 79% respectively for No_AC images and 66%, 78% and 68% for CT_AC implying that the CT_AC decreased the sensitivity as well as the diagnostic accuracy which is totally different from our results (18).

The main limitation in our study was the small sample size. Also, the prone position was not comfortable for many females and for extremely obese patients. Moreover, all the included patients were derived from one center. Eventually, quantification data were not statistically analyzed but they were taken in consideration while interpreting the cases.

5. Conclusion

Additional SPECT/CT and prone imaging as attenuation correction techniques increased the specificity and diagnostic accuracy of myocardial perfusion imaging through their role in attenuation correction this in return could raise the possibility of stress only study.

Prone images as attenuation correction method was relatively better in correction of anterior wall attenuation than CT, with both having good agreement with the final diagnosis.

CT as attenuation correction method was relatively better than prone images in correction of inferior wall attenuation, with both having good agreement with the final diagnosis.

Declarations

-Ethics approval and consent to participate

All procedures performed in the study involved human subject's data, were obtained without patients' information other than age and sex. Approval was obtained from the Institutional Review Board at NEMROCK. The study protocol was in accordance with the ethical standards of the institutional and national research committees and with the tenets of the 1964 Declaration of Helsinki and its later amendments.

-Conflict of Interest

The authors declare that they have no conflicts of interest.

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Figure 1: Corrected and non-corrected artifacts using CTAC and prone imaging



Figure 2: Matching between technique of correction and final diagnosis



Figure 3; The difference between **a):** NO_AC images showing mild reversible inferior wall hypoperfusion defect. **b):** stress/rest CT_AC images showing normalization of the inferior wall hypoperfusion defect. **c):** stress/rest prone images showing normalization of the inferior wall hypoperfusion defect.







Figure 5; Variation between a) No_AC showing hypoperfusion defect in the inferior wall. b) CT_AC images shows a partial improvement of the inferior wall defect is noted in the stress/rest. c) prone images showing a complete resolution of the inferior wall defect is noted in the stress/rest.

	Number of patients	Non-AC	CT-AC	Prone-AC
Negative for myocardial ischemia	4	No perfusion defect	No perfusion defect	No perfusion defect
Multi-vessel diseases	10	Positive for perfusion defect	Positive for perfusion defect	Positive for perfusion defect

Table 1: Presence or absence of myocardial ischemia in 14 excluded cases.

Gender	Number	Percentage	Age (Mean ± SD)	
Male	20	67%	54.7 ± 12.5	
Female	10	33%	49.8 ± 11	
Total	30	100%	53 ± 12	

Table 2: age and sex distribution in 30 patients of study population

Final diagnosis		*CT-AC	*Prone images
True defect (N=22)		22	22
Attenuation artifact	Corrected	28	26
(N=31)	Non-corrected	3	5
Total (N=53) 53			53
*P<0.001			

 Table 3: Agreement between different correcting techniques in relation to non-corrected images in all walls' defects.

Tashniqua of	Final			
correction	matched diagnosis	Mismatched diagnosis	Total	
CT-AC	50	3	53	
number (%)	(94%)	(6%)	(100%)	
Prone-AC	48	5	53	
number (%)	(91%)	(9%)	(100%)	

Table 4: Matching between technique of correction and final diagnosis

	Wall defects (CT_AC)	Wall defects in Prone	True defects	Total
Corrected	28 (90.32%)	26 (83.8%)	None	26 (49.1%)
Non-Corrected	3 (9.68%)	5 (16.2%)	22 (100%)	27 (50.9%)
Total	31 (100%)		22(100%)	53 (100%)

Table 5: Correlation between wall defects (Prone & CT_AC) and final diagnosis (Correction)

	Specificity	Sensitivity
CT_AC	90.3%	100%
Prone images	83.8%	100%

Table 6: Specificity and sensitivity