The clinical dilemma of incidental findings on the low-resolution CT images from SPECT/CT MPI studies

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A review of incidental findings on low-resolution CT images during SPECT myocardial perfusion imaging: A clinical dilemma

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Abstract

Incidental findings are common in medical imaging. There is a particularly high prevalence of incidental findings within the thorax, the most frequent being pulmonary nodules. Whilst pulmonary nodules have the potential to be malignant, the vast majority will be benign, resulting in a high number of false-positive findings. Low-resolution CT images produced during attenuation correction (AC) during single-photon emission tomography (SPECT) are essentially a by-product of the process. The high number of false-positive incidental findings detected on CTAC images causes a reporting dilemma. Early detection of cancer can be beneficial but false-positive findings and over diagnosis can be detrimental to the patient. CTAC images are not diagnostic quality and further diagnostic tests are usually necessary for definitive diagnosis to be reached. Given the high number of false-positive findings, the psychological effects and harms to the patient should be given consideration. This review recommends that caution should be taken when routine reporting of CTAC images occurs.

Introduction

Medical imaging employs a range of modalities that yield both anatomical and functional information *(1).* Visual correlation of images from separate imaging modalities can provide more information than images from a single modality alone, though there is an inevitable risk of mis-registration between images that have been acquired during different imaging sessions. The development of hybrid imaging has led to the integration of two modalities in one machine, allowing co-registration of images that have been acquired in a single session *(1),(2)*. This allows direct correlation of anatomical and functional information, increasing sensitivity and specificity whilst adding clarity to indeterminate cases *(3).* SPECT-CT offers an excellent example of hybrid imaging, combining the functional ability of single photon emission computed tomography (SPECT) with the anatomical ability of x-ray computed tomography (CT).

In this article we discuss the concept of incidental findings on low-resolution CT images utilised in SPECT, with particular emphasis on myocardial perfusion imaging (MPI).

The strength of SPECT lies in gaining pathophysiological detail in a minimally invasive way *(4).* Pathological processes can be identified by the uptake of radiopharmaceuticals but the precise location is often difficult to ascertain due to lack of anatomical landmarks and low image resolution. Moreover, uptake on some scans is often non-specific, revealing abnormalities without specific

cause. CT can provide a useful means of localisation, also enabling additional characterization by virtue of providing a site-specific correspondence between anatomical and physiological information.

SPECT images are susceptible to artifact as a result of attenuation deficits due to scatter and absorption of photons *(5),(6),(7)*. In order to improve image quantification and reduce attenuation artifacts, a low-dose CT acquisition can be performed allowing attenuation correction (AC) of the SPECT images. CT attenuation correction (CTAC) is now commonly used because this often improves image quality and increases overall diagnostic accuracy *(5).*

There are therefore three distinct reasons why CT may be combined with SPECT:

1. CT can be used to characterise an abnormality seen on the SPECT images. This will usually require a diagnostic quality (high resolution) CT scan.
2. CT can be used for localisation of an abnormality seen on the SPECT images.
3. CT can be used for AC of the SPECT images. This only requires a low resolution CT acquisition, typically using a much lower ionising radiation dose than that required for diagnostic quality CT. Although the images are considered to be non-diagnostic, they often reveal incidental findings.

Incidental Findings

An incidental finding can be defined as an unsuspected finding that is not related to the clinical reason for performing the diagnostic test *(8),(9).* Table 1 summarises some typical examples of incidental findings that can be identified on CTAC images of the chest.

Incidental findings may or may not already be known from previous diagnostic tests. Findings that are already known to the clinician are likely to have a management strategy in place and so often do not require further investigation. Previously unknown incidental findings are termed new incidental findings and are likely to fall into one of three categories: clinically significant, clinically insignificant or indeterminate. Clinically significant incidental findings have a high suspicion of underlying pathology that could impact negatively on patient wellbeing, requiring further investigation *(9).*

Table 1 – Examples of incidental findings on SPECT-CT images of the chest

The frequency of incidental findings on CTAC images is particularly high within the thorax *(10)*, possibly due to the inherent contrast resolution and low attenuation of the x-ray beam through this area. Lung cancer shares co-morbidities with heart disease; the clinical reason that these patients are being scanned. It is, therefore, not surprising that extra-cardiac pathology is frequently detected.

The high number of incidental findings identified on CTAC images causes a dilemma. The acquisition was intended for attenuation correction alone and not for evaluation, and the relatively low-resolution of the CTAC images means that characterization of findings is often not possible. Additionally, unlike diagnostic quality CT examinations of the chest and abdomen, there is likely to be breathing artifact on CTAC images because patients are not required to breath-hold. The cranio-caudal range of the CTAC acquisition is also limited to the cardiac area only; detection of incidental findings is therefore also restricted.

Incidental findings on CTAC images from SPECT during myocardial perfusion imaging (MPI)

The number of incidental findings on the CTAC images produced during SPECT MPI is noteworthy and the number of clinically significant and indeterminate findings can often be as high as 10% *(10).*

A high proportion of findings on chest CT are pulmonary nodules *(11).* Whilst the majority of lung nodules are benign, there is potential for them to develop into lung cancer *(12).* CTAC images, which often reveal lung nodules as well as other pathologies, were never intended for radiological reporting but there is growing evidence to suggest that they should be *(10).*

Lung cancer is the leading cause of death in most countries including the United States *(12),(13).* Early lung cancer is often asymptomatic and

symptoms only arise when the disease is at an advanced stage; the prognosis for lung cancer is consequently poor *(13).* However, the prognosis for non-small cell lung cancer (NSCLC) improves significantly if it is detected at an early stage when surgical resection is possible *(12),(13).* This is not the case with small cell lung cancer (SCLC). Recommendations for the management of pulmonary nodules have been developed from lung cancer screening trials, suggesting a necessary balance between early intervention to reduce mortality from lung cancer, and the risks of early morbidity and mortality from intervention of false-positive findings and over diagnosis *(11).*

The high prevalence of lung nodules on CT of the chest is of particular concern during SPECT-CT MPI because any such findings will be incidental and may signpost a patient to an alternative or additional care pathway. Although there is an argument for early treatment of lung cancer, the detection of lung nodules on CTAC images does not necessarily result in reduced mortality from lung cancer. A high proportion of lung nodules are ultimately found to be benign and the patient might not benefit, and might actually be harmed, from these being followed up.

This sentiment is echoed by the outcomes of lung cancer screening trials; mortality must be reduced and the benefits to the patient must outweigh the risks for a screening programme to be effective *(12).* The National Lung Screening Trial (NLST) has demonstrated that it is possible to reduce mortality from lung cancer by using low-dose CT screening in place of chest x-ray and sputum tests *(14).* However, in doing so, there is a high rate of

false-positive findings and over diagnoses as well as an increased radiation burden to the patient *(15).* Over diagnosis of indolent tumours that would not have become symptomatic in a patient's lifetime have cost implications as well as raising patient anxiety and morbidity in the same way that false-positive findings might *(16).* Consequently, several organisations have made the decision not to implement screening programmes. Where screening programmes have been implemented, they are focused specifically to the population at high risk *(17).*

This adds to the dilemma of whether clinicians should review the CTAC images. Reviewing them and providing a report could possibly enable early diagnosis of pathology and potentially a better prognosis. However, identifying incidental findings could increase risk to the patient without necessarily providing any benefit. Further diagnostic examinations are often associated with an increase in ionising radiation dose and possibly invasive procedures that can carry physical risk and psychological harm to the patient *(9),(18),(19)*. Furthermore, only a very small percentage of these incidental findings are significant at definitive diagnosis *(9),(20),(21).*

Exclusion of intravenous contrast use in CTAC

There is often poor inherent contrast resolution between organs and soft tissues within the body due to relatively small differences in density. The use of contrast agents artificially improves contrast resolution between soft tissue structures. The iodination of the contrast agent increases the density within

the organs and so will affect the extent of attenuation of the x-ray beam that occurs. The different organs take up contrast at different rates and this results in an increase in contrast resolution on the CT images. Similarly, pathological tissue can demonstrate selective uptake of contrast agents; tumours that are highly vascular tend to enhance avidly whereas ischaemic tissue tends not to enhance. This improves demonstration of pathology in relation to normal tissue and aids characterisation of the pathology. It is unusual to perform diagnostic CT of the chest, abdomen and pelvis without the use of intravenous contrast for this reason.

The use of intravenous contrast with SPECT-CT is not without problems. Contrast agents will attenuate gamma rays in the same way that they attenuate x-rays. The result is degradation of the quality of the SPECT images. Contra-indications relating to the use of iodinated intravenous contrast agents also exist.

CTAC images are not considered to be diagnostic because of the acquisition parameters used along with the lack of intravenous contrast to enhance contrast resolution.

Image quality

The image quality of CTAC images is directly related to how the images have been acquired, typically with a low tube current (mA) and a wide slice width. This enables attenuation correction to be performed with the production of co-

incidental low-resolution CT images. The long acquisition time results in motion artifact from breathing on the CTAC images. The nature of incidental findings can be difficult to determine, resulting in a high number of false-positive findings.

As technology has progressed, multi-detector CT (MDCT) scanners have been utilised in some hybrid systems. MDCT offers increased technological capabilities with the potential to produce CT images of a superior quality than CTAC images typically associated with the earlier systems. The potential to utilise narrow slices, reduce imaging time and utilise a higher mA has provided the option to improve image quality that, in some cases, is comparable to diagnostic CT. This has inevitably led to a variation in CTAC image quality in different departments that is related not only to the capability of the CT scanner but also to the way in which parameters have been optimised *(20).* There are ethical considerations when CT image quality is improved in this way because there will be an inevitable increase in ionising radiation dose to the patient, for an uncertain gain.

CT parameters relating to patient dose and image quality

CT image quality is dependent upon how the data is acquired and also how it is reconstructed and viewed. Ideally, we would choose the best image quality possible but this would involve changing the acquisition parameters in a way that would greatly increase the radiation dose to the patient. Therefore, it is necessary to use a technique called optimisation, *(22)* the aim of which is to

produce the required image quality for the least radiation dose. This does not necessarily mean the best image quality or the lowest radiation dose but is a compromise so that the images produced are tailored to the purpose for which they are acquired.

Diagnostic CT results in images that are of sufficient quality that a diagnosis can be made. It is usually necessary for images to have good spatial and contrast resolution and be free from artifacts. This is not true for the CTAC acquisition for MPI. The acquisition is merely for attenuation correction purposes and so the acquisition parameters can be significantly reduced.

The mA used for CTAC is much lower than that used for diagnostic quality CT enabling the radiation dose to the patient to be reduced. Resultant CT images will be noisy and have poor contrast resolution. The slice width for CTAC is usually considerably wider than that of diagnostic CT. This also has an effect on image quality and will reduce the spatial resolution (ability to determine fine detail) but it will improve contrast resolution. The long rotation time, frequently associated with some of the older SPECT-CT systems, results in a longer overall scan time. This renders the CTAC images susceptible to motion artifact, especially within the thorax and abdomen. Whilst this has no significance for CTAC purposes, it does become relevant when the intent is to make a diagnosis from images.

Table 2 – Examples of how diagnostic CT Chest acquisition parameters might differ for CTAC MPI

‘Diagnostic’ value of CTAC MPI images acquired with different image qualities

Lesion detection performance studies, using the Free-response Receiver Operating Characteristic (FROC) method, have been conducted to investigate the influence of different CTAC image qualities on detection of nodules on chest phantoms. FROC is a method to assess observer performance and captures the observer’s ability to say where the lesion is and assign a confidence rating to their decision.

In a lung phantom study, variation of mA values (1, 1.5, 2 and 2.5) on one SPECT-CT system, with all other parameters remaining unchanged, had no statistically significant difference in performance in lesion detection at the different mA values *(23).* In a further lung phantom study involving a range of SPECT-CT systems there was a difference in lesion detectability relative to the capability of the CT unit *(24).* These results were reproduced in a study using the same chest phantom on two different SPECT-CT systems. Here, lesion detection was found to be more reliable on one system than the other and was related to the reconstruction algorithms used on one CT unit rather than the acquisition parameters *(25).* It is worth noting that the phantom was stationary in all studies and so did not truly represent the clinical situation

where motion artifact from breathing would cause degradation of the CTAC images.

A 2-year multi-centre study that took place in four nuclear medicine departments in the UK, was granted local approval from each participating hospital and ethical approval from the University of Salford, following advice from the Health Research Authority (26). Positive findings were identified on the CTAC images of 962 (28%) of 3485 patients undergoing SPECT MPI. Of these findings, 824 (24%) were new findings. Eighty-four (2.4%) patients had findings that were thought to be clinically significant at the time of the imaging and had not been known about previously, but only 10 (0.29%) patients had findings that were confirmed to be clinically significant at definitive diagnosis. In this study 74 out of 84 patients had false-positive findings that involved follow up diagnostic tests and possibly intervention before a definitive, negative outcome was reached. This has the implication of increased physical and psychological risk to the patient and raises the question about whether the CTAC images should be reported.

The positive predictive value (PPV) across all the centres was low and this finding resulted in one centre stopping reporting CTAC images. Statistically there was no significant difference between the PPV for CTAC images acquired using low resolution and better resolution machines. The study concluded that routine reporting of CTAC images was not beneficial. The information from this study appears to be novel and no similar clinical studies were identified.

Whether to report CTAC images is a common dilemma as the detection of early pathology can lead to an improved prognosis. However, further investigations for characterisation can be costly and increase the radiation burden and other risks to the patient *(27).*

Patient Perspective

False-positive incidental findings or findings that result in an over diagnosis can lead to increased patient anxiety. Whilst malignancies diagnosed at an early stage might potentially result in reduced patient mortality, only a very small percentage of findings on CTAC images have been found to be malignant or detrimental to the patient at definitive diagnosis *(28).*

The literature surrounding the psychological effects of patients who have incidental findings during SPECT-CT examinations is limited. There is, however, an abundance of literature relating to the psychological effects of patients who have been recently diagnosed with cancer or who are awaiting definitive diagnosis, and some parallels can be drawn to patients with incidental findings.

Patients who have incidental findings as part of a screening examination or are being investigated for a suspected cancer will usually have a care pathway and support structure in place. Support structure typically involves nursing, medical and other professionals being available to help the patient

and their families. This is often not the case for patients who have incidental findings during SPECT-CT. They will receive limited support due to the unexpected nature of the findings.

Pulmonary nodules are one of the most frequent incidental findings on CT of the thorax *(29),(19).* These can be single or multiple and can be of unknown significance. Most nodules are benign but if they are indeterminate, they will require surveillance, which can take 2 to 3 years *(30).* Almost all patients who are told that they have a pulmonary nodule assume that they have cancer *(16).* Just raising the possibility of cancer can be threatening *(17)* and can lead to distress up until, and possibly beyond, definitive diagnosis *(18).*

Pulmonary nodules are of particular clinical relevance*(8),* as they do have the potential to become malignant, although the majority will be benign *(31).* Further management of pulmonary nodules is based upon size, the likelihood of malignancy increasing with the size of the nodule *(32),(33).* The indeterminate nature of pulmonary nodules frequently leads to follow up CT imaging over a period of time to monitor any change in size of the nodule. If its size remains stable over a period of 2 years then it is considered to be benign. This inevitably increases the radiation burden to the patient along with anxiety levels. Biopsy of pulmonary nodules, which would give a more definitive answer, is often not possible due to their small size and location within the lung *(32).* Despite reassurance, the patient might believe that they have cancer in the absence of a definitive diagnosis.

Lung cancer screening involves harm as well as benefit and in some circumstances, the harm could outweigh the benefit *(33).* This also applies to patients with incidental findings on CTAC images. The harms from over treatment of false-positive findings should be considered when considering the benefits of reviewing these images *(34).* Whilst patients may gain some reassurance from a negative screening examination, this cannot be applied to CTAC due to the limited range of the chest MPI imaging. Therefore, a normal CT MPI CTAC scan does not exclude pathology that falls outside this limited range.

Early detection of lung cancer does not necessarily mean improved outcome. Approximately 25-30% of patients will present with potentially curable disease *(35),* but lung cancers develop quickly and metastasise early, often leading to a poor prognosis *(19).* Metastases are frequently present at the time of initial presentation. This also needs to be balanced against the high rate of benign pathology that is also be detected *(19).*

The psychological effects of patients who are diagnosed with false-positive findings can discourage patients from attending screening or diagnostic procedures in the future *(33).* If they have had a significant mis-diagnosis then they are likely to lose trust in diagnostic procedures. Psychological effects can be transient or more persistent. At initial diagnosis the patient is more likely to suffer anxiety but over time this tends to develop into depression. Both anxiety and depression can persist before and after treatment *(35).*

Financial and time implications when reporting CTAC findings

The financial impact and time aspects need to be taken into consideration when routine reporting of CTAC images occurs. A radiological report takes time to construct and in the case of clinically significant findings, is likely to affect future management of the patient. This is justifiable when there is a net patient benefit. However, this appears not to be the case when reporting CTAC images that demonstrate a high yield of false-positive findings. Similarly, follow up examinations that are performed to assist definitive diagnosis will inevitably have cost and time implications that will not necessarily benefit the patient and might, in fact, be a potential cause of patient harm *(36).* The cost-effective nature of reporting CTAC images is brought into question along with the benefit and harms related to the patient.

Conclusion

CTAC yields low-resolution images that are not considered to be diagnostic. Whilst they can demonstrate pathology and incidental findings are common, there is increased potential for pathology to be missed or wrongly diagnosed when compared to diagnostic quality CT images.

Incidental findings can be numerous on SPECT-CT MPI AC images and, regardless of definitive diagnosis, they can cause psychological distress to the patient. One study has called into question the practice of producing a routine report for CTAC images from SPECT-MPI studies *(28)*. If these images are

reported, this should be done with caution and possibly with the use of a rider in the written report stating that the images are low-resolution and not intended for diagnosis. Careful consideration should be given to the potential impact that an abnormal report could have on the patient.

If the CTAC images are reported, a support structure and appropriate educational advice similar to those found in screening programmes might help patients who have a clinically significant incidental finding to understand their diagnosis.

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Table 1 – Examples of incidental findings on SPECT-CT images of the chest

Incidental Finding
Coronary vessel calcification
Vascular anomalies
Valve replacement
Pacemaker
Atelectasis
Effusion
Consolidation
Lobar collapse
Nodules
Mass
Pulmonary metastases
Ground glass opacities
Aortic aneurysm

Source: Adapted from (Coward et al, 2014)

Table 2 – Examples of how diagnostic CT Chest acquisition parameters might differ for CTAC MPI

Parameter	Diagnostic Value	CTAC MPI Value
kV	120	120
mA	Automated (300-400 approx.)	1.5-33
Rotation Time (s)	0.33	1.5-30
Effective mAs	100-130 (dependent on automated mA)	24-50
Acquired slice thickness (mm)	0.5-1	5-10
Reconstructed slice thickness (mm)	3	5-10
Pitch	0.75-1	1-2