CHIEF SCIENTIST OFFICE

CODE: CAF/22/20

RESEARCH PROJECT BRIEFING

Quantification and Standard Uptake Values in Dual Radiopharmaceutical Parathyroid SPECT-CT Imaging

AIMS

Introduction – In Nuclear Medicine, a gamma camera is used to acquire 3D-SPECT/CT images (single photon emission computed tomography) which combines two types of imaging – the SPECT image shows tissue function, and the CT shows corresponding anatomy. SPECT/CT imaging involves the injection of a radiopharmaceutical – this is a radioactive tracer that is taken up by the tissues of interest and there are many different radioisotopes and tracers that can be used in Nuclear Medicine to look at different areas in the body. Recent advancements in SPECT imaging include quantification which gives us the ability to measure the uptake of a radiopharmaceutical in the body, providing more information about the function of that tissue.

Parathyroid SPECT/CT imaging is performed to localise any abnormal parathyroid glands before surgery. The parathyroid glands are in the neck, positioned behind the thyroid gland. There are four in total and these are small pea sized glands that work as part of the endocrine system and their main function is to manage calcium and vitamin D levels. There are three main parathyroid pathologies which include parathyroid adenoma (a benign soft tissue mass that usually affects one gland), hyperplasia (when multiple parathyroid glands become enlarged and overactive) and carcinoma (malignant cancer tissue in the parathyroid glands). It can be difficult to tell the difference between parathyroid adenoma and parathyroid hyperplasia in imaging due to the small size of these glands. It is useful for surgeons to know if the patient is likely to have single or multiple surgical targets, therefore, it would be beneficial if SPECT/CT imaging could better determine disease type and the number of glands involved which would therefore provide the number of surgical targets.

In parathyroid SPECT/CT imaging, two different radioactive tracers are injected, allowing us to see the function of two different tissues at the same time – the thyroid and parathyroid glands. Dual-tracer imaging is possible as the radioisotopes have different energies so the gamma camera can collect this data in different energy windows, however, imaging can be technically challenging. Higher radioisotope energies may scatter into lower energy windows making them difficult to distinguish – this is called downscatter which can significantly degrade image quality. There are few publications on the correction of downscatter and its impact on SPECT quantification.

Previous research from our centre found that our department's parathyroid imaging procedure which utilises 3D SPECT/CT and subtraction imaging is highly efficient in detecting parathyroid disease, however, there remains a small risk of repeat surgery due to failure in detecting multiple overactive glands within imaging. The main aim of this PhD was to assess the addition of SPECT quantification in parathyroid imaging and determine if it can be used to identify different disease types and decide the best treatment for the patient, giving the best possible clinical outcome. This work also included assessing all aspects that may impact SPECT quantification such as downscatter and image artefacts. Therefore, the aims of this work included:

- For SPECT quantification to measure the amount of radioactivity in the body, it requires a calibration factor for each gamma camera and radioisotope. The first aim of this work was to measure and confirm the calibration factors for two radioisotopes - [Tc^{99m}] and [I^{123}] which are both used for parathyroid nuclear medicine imaging.
- An investigation was carried out to assess a SPECT artefact that was observed within patient images (an artefact is an area of radioactivity seen in imaging that doesn't represent true uptake in the body, as seen in figure 1). The aim of this work was to assess the cause of the artefact, the severity of the artefact in two different gamma camera setups (L-shaped and H-shaped) and the impact the artefact had on image quality and SPECT quantification.

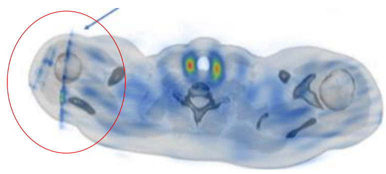

Figure 1: Artefact (circled) in parathyroid SPECT/CT image.

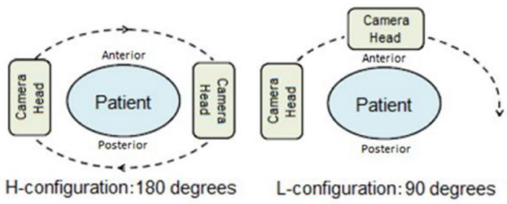

Figure 2: Gamma camera in H and L-shaped setup.

- A previous departmental audit published in 2017 compared patients' parathyroid imaging results to surgical results. Since then, several gamma cameras have been replaced so this project aimed to extend this audit to include more recent patient datasets on the newer systems and to collect data from additional nuclear medicine departments in NHS Greater Glasgow and Clyde.
- An anonymised physician observer study was carried out to assess the potential of using SPECT quantification in parathyroid imaging to develop a pre-surgical method to identify different parathyroid disease types, including adenoma, hyperplasia, multiple gland disease or parathyroid cancer.

- The final aim of the PhD was to compare two correction techniques for downscatter in parathyroid imaging and assess the impact on SPECT quantification and image quality.

KEY FINDINGS

- The calibration factors used for SPECT quantification are highly dependent on two set up parameters - energy window size and the type of gamma camera collimator (a lead filter that blocks unwanted radiation).
- The artefact identified when the camera was in an L-shaped setup was found to impact the [Tc^{99m}] image visually but had minimal effect on SPECT quantification. The artefact did, however, impact the visual assessment and quantification of [I^{123}]. The artefact was improved qualitatively and quantitatively when using a H-shaped camera setup (see figure 2).
- As part of this research, an additional 385 patients were added to the retrospective audit and it was found that 11.3% of all patients that had surgery had different results between imaging and surgery.
- It was also found that patients with a higher pre-surgical parathyroid hormone (PTH) measure were more likely to have parathyroid hyperplasia or carcinoma rather than adenoma.
- The observer study found that SPECT quantification measures cannot be used to predict the type of parathyroid disease but may be a useful guidance tool alongside biochemical measures such as PTH.
- Assessment of two downscatter correction methods - triple energy window (TEW) and full collimator modelling (FCM) found FCM more successful in reducing downscatter and recreating the true radioactive uptake within SPECT images, therefore, improving quantification.

WHAT DID THE STUDY INVOLVE?

To obtain the calibration factors (CFs), a uniform phantom was used to measure gamma camera sensitivity (a measure of how efficient the gamma camera is at detecting radiation). The CFs can then covert the SPECT image counts to a measure of radioactive concentration. To validate the CFs, another imaging phantom was used with known radioactivity concentration in a range of sphere sizes. These phantom studies were

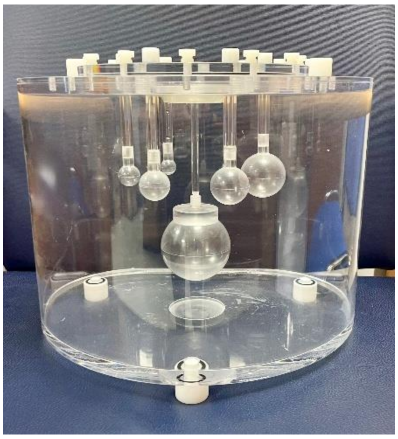

Figure 3: Uniform phantom (left) and validation phantom with a range of sphere sizes. (right)

performed on five gamma cameras for [Tc^{99m}] and [I^{123}] using a parathyroid protocol.

Additional parathyroid/thyroid phantom studies were performed to investigate the imaging artefact with two different camera setups: L-shaped and H-shaped. The artefact was observed in SPECT images of large patients, resulting in radioactivity being out with the field of view (FOV); therefore, the phantom was acquired with and without non-specific background activity extending out with the imaging FOV to mimic the artefact.

A previous departmental audit was performed using data from two nuclear medicine sites from 2012 – 2014. As part of this PhD, this audit was extended to include data from 2019 - 2023 for five nuclear medicine departments in NHS GGC, ensuring the raw patient data was available. This was carried out due to the replacement of several gamma cameras since the previous audit and to extend the audit to include all the nuclear medicine sites in NHS GGC. This research project required a large dataset of parathyroid SPECT/CT images to identify cases where imaging differed from surgical pathology results. The patient data was categorised into the following groups: concordant cases (same result between imaging and surgery), discrepant cases (different result between imaging and surgery), patients awaiting surgery and no surgery or being managed with medication. From the audit, a collection of 30 datasets were used in an anonymised observer study to obtain SPECT quantification measures for different disease types.

The assessment of downscatter involved additional phantom studies with known radioactivity. Triple energy window correction uses multiple energy windows alongside the main emission window and performs a subtraction technique that aims to remove the contribution of downscatter from the main energy windows. Another method, full collimator modelling (FCM) was also assessed and is a technique that uses Monte Carlo modelling to simulate radiation and correct for downscatter between [Tc^{99m}] and [I^{123}]. Single and dual-radioisotope phantom studies were performed and compared before and after these corrections were applied.

WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Calibration factors (CFs) varied with different energy windows which indicated the importance of standard acquisition protocols between sites and ensuring appropriate and matching CFs for the patient data being used. It was also found that the CFs varied significantly with different gamma camera collimators which can impact on the gamma camera's ability to detect radiation.

The imaging artefact identified in retrospective patient SPECT/CT parathyroid images was caused by truncation which is when part of the patient or radioactivity lies out with the imaging field of view. For larger, overweight patients, the gamma camera rotation is limited in an L-shaped setup. The artefact impacted on SPECT quantification, especially around the area of the artefact which could be the location of an abnormal ectopic gland (an ectopic gland is positioned in a non-typical location such as lower in the neck or in the chest). Further investigation found that the artefact was not produced when acquiring images in the H-shaped camera setup and this resulted in a change to the local protocol following clinician review.

The retrospective patient audit assessed a total of 543 patient cases, of which 385 were collected as part of the extended audit. The categorisation of all patient data and pathology surgical results found that 46.5% were concordant cases (same result between imaging and surgery), 11.3% were discrepant (different result between imaging and surgery), 7.2% of patients were awaiting surgery and 32.6% had opted for no surgery and to be managed with medication.

The discrepant patient cases were further assessed to compare their parathyroid hormone (PTH) biochemical results pre and post-surgery. It was found that patients with higher pre-surgical PTH (greater than 50 pmol/L) were more likely to have parathyroid hyperplasia or carcinoma as compared to adenoma cases (as shown in figure 4).

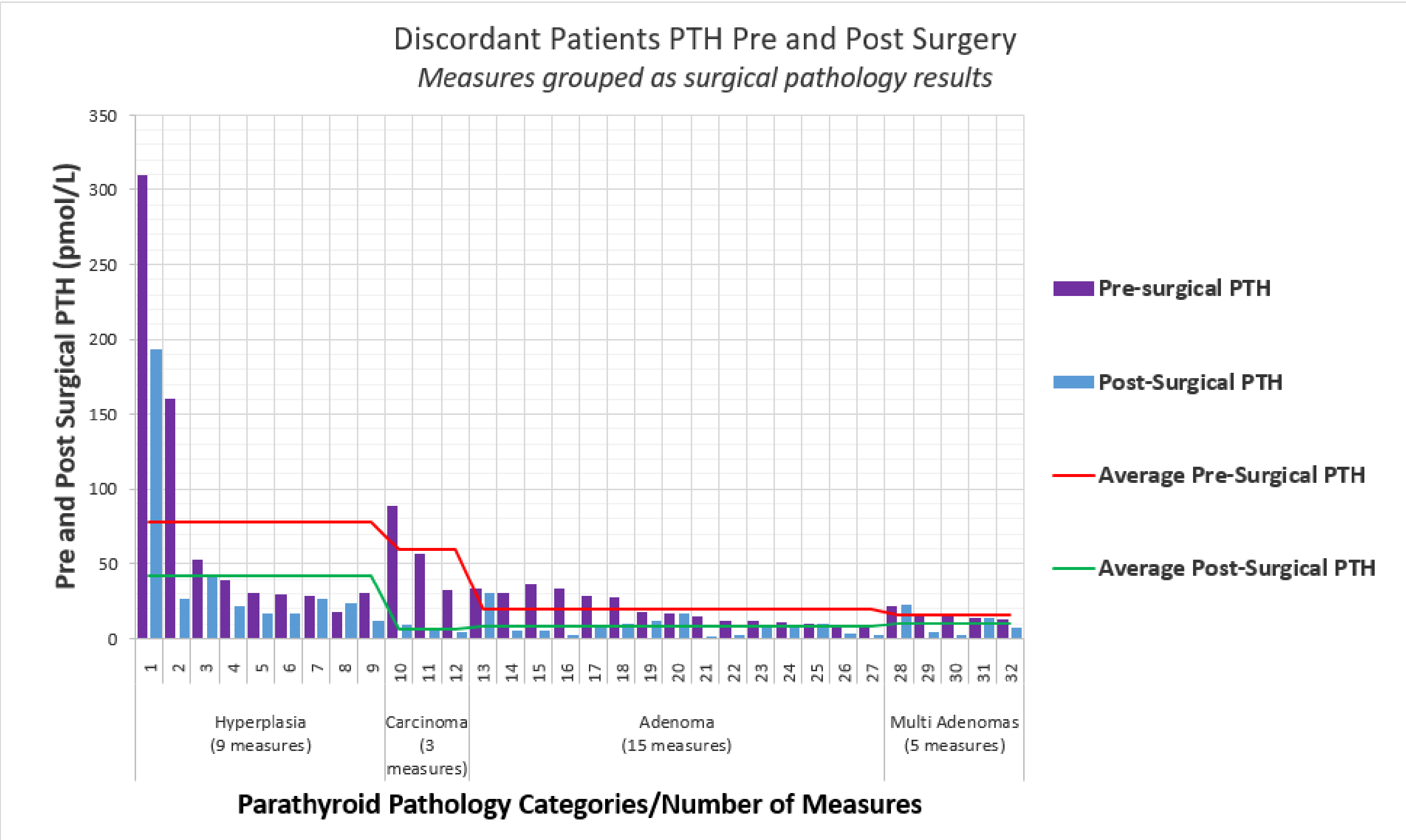

Figure 4: Parathyroid hormone pre and post-surgery with pathology results for the discordant patient group.

There is an overlap in pre-surgical PTH measures for all pathologies so this cannot be used as a predictor of pathology type.

Figures 5 and 6 show the results of the anonymised clinical observer study and the spread of quantification measures across two different parathyroid pathologies – parathyroid adenoma (24 patients) and hyperplasia (7 patients). The SPECT quantification measures are called SUVmean and SUVmax – this is the average and maximum standard uptake value and is quoted in figure 5. Statistical t-tests highlight that there was a significant difference between the quantification of parathyroid adenoma and hyperplasia. Figure 5 also highlights two outlier values within each pathology group. Figure 6 shows he overlap in quantification measures for both pathologies, although the differences are considered significant.

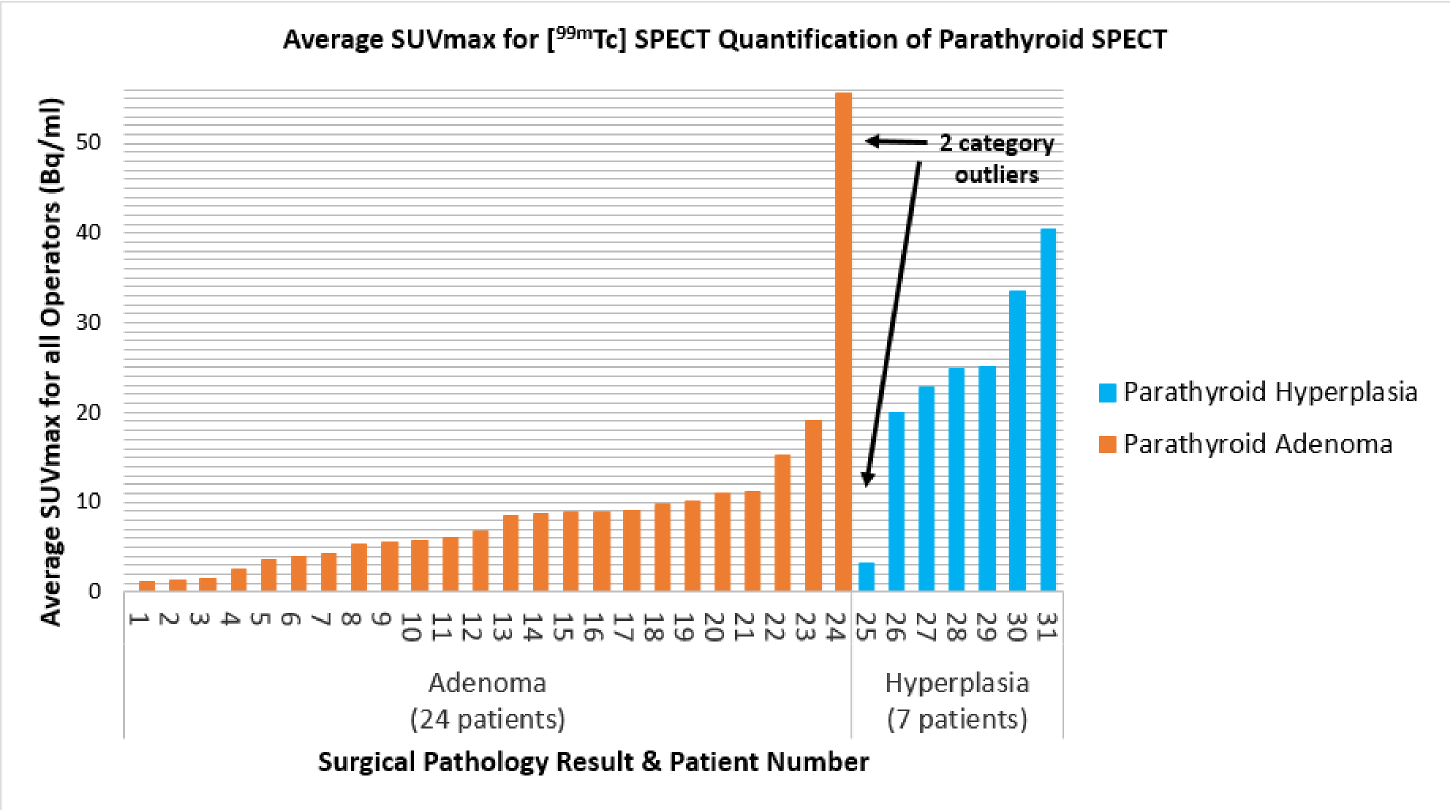

Figure 5: Observer study results and comparison of different parathyroid pathologies.

Linear regression analysis was performed and found that quantification cannot be used as a sole predictor of parathyroid pathology, however, can be used as a guidance tool alongside biochemical results.

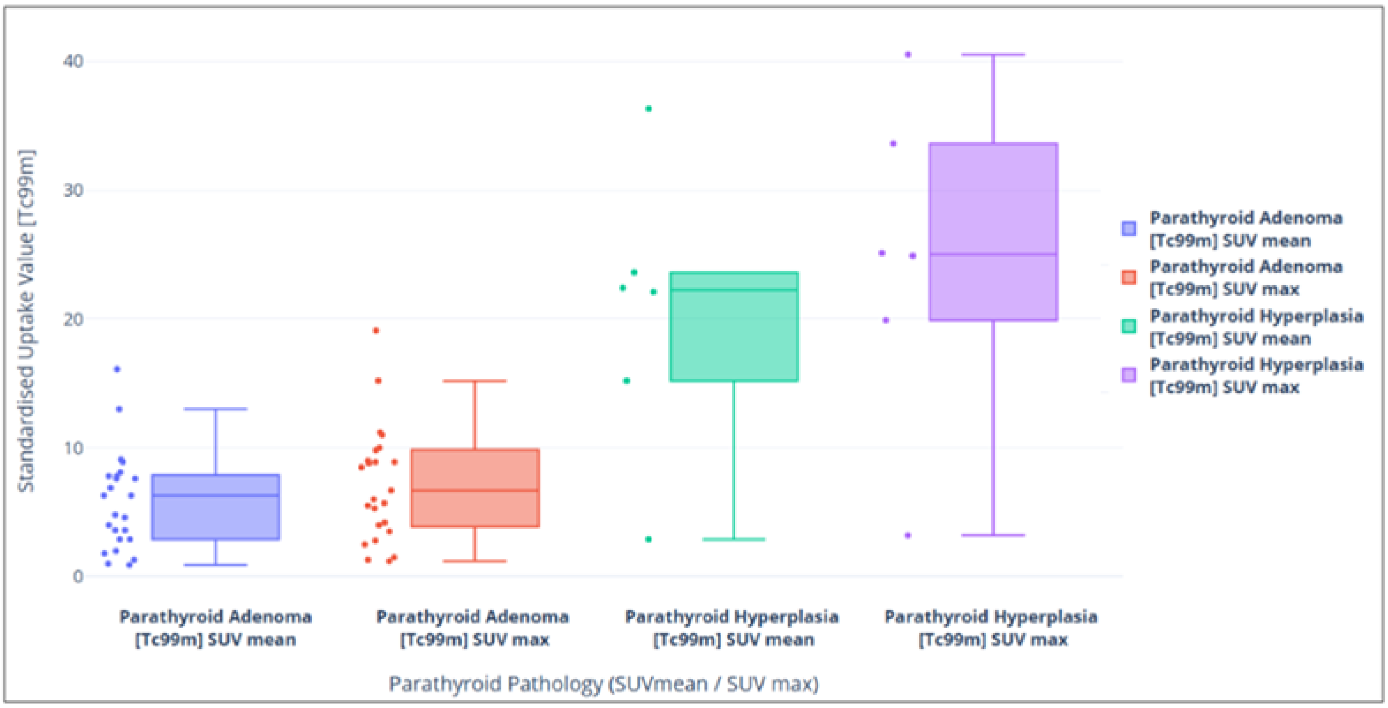

Figure 6: Boxplots for parathyroid adenoma and hyperplasia SUV mean and max for [Tc99m] and [I123].

The assessment of two downscatter correction techniques found that full collimator modelling (FCM) was more successful in reducing downscatter from the high energy emissions of [I^{123}] into [Tc^{99m}]. This work compared the true radioactivity to the imaged/measured radioactivity before and after the applied correction. FCM was able to recreate the true activity concentration of [Tc^{99m}] within SPECT images (as shown in figure 7).

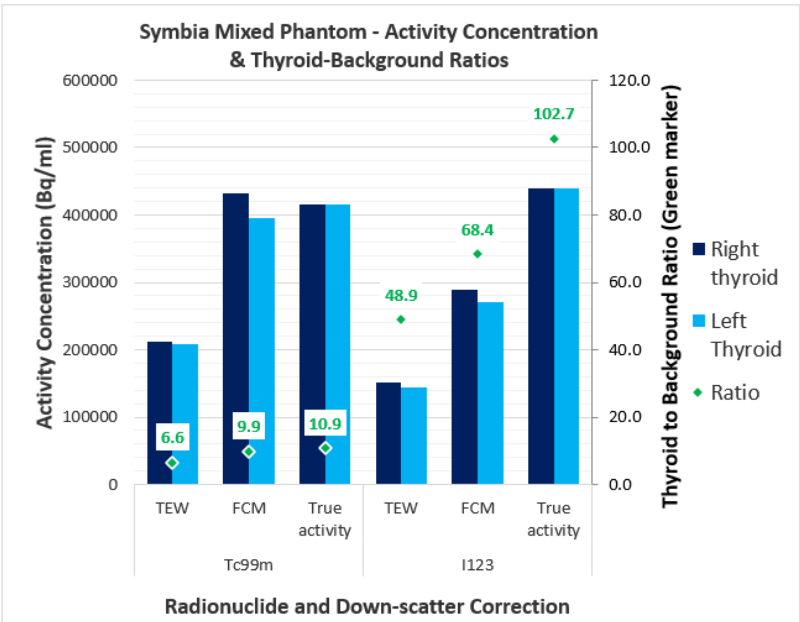

Figure 7: Radioactivity measures for left and right thyroid lobe for the true radioactivity, the measured radioactivity after triple energy window (TEW) correction and the measured radioactivity after full collimator modelling (FCM) correction for two radioisotopes - [Tc^{99m}] and [I^{123}].

WHAT IMPACT COULD THE FINDINGS HAVE?

- The calibration factors measured as part of this work could be used in future implementation of SPECT quantification for multiple clinical procedures, therefore, having a wider benefit on all nuclear medicine studies.
- A change to the local protocol was applied during the research project following the findings of the imaging artefact and that the L-shaped camera setup was not recommended as the limited gamma camera rotation caused the artefact – the standard protocol locally and across NHS GGC is to now use H-shaped camera setup for parathyroid imaging and the findings have been disseminated in a 2025 publication in NM Communications.
- The findings of the observer study suggest that introduction of SPECT quantification for parathyroid imaging could aid in differentiating between parathyroid adenoma and parathyroid hyperplasia. This would improve surgical guidance about potential multi-gland disease prior to minimally invasive surgery – improving the reporting clinicians confidence, guidance to the surgeon and patient outcomes.
- SPECT quantification and downscatter correction for parathyroid imaging have not been routinely introduced into clinical practice as there is ongoing work required before clinical implementation.

HOW WILL THE OUTCOMES BE DISSEMINATED?

Publications - The findings of the imaging artefact investigation were published as a technical note in Nuclear Medicine Communications in October 2025 and I am aiming for two future publications for the observer study and downscatter correction work.

National and International Conferences - This research work has been showcased in multiple poster and oral presentations at national and international conferences including:

- Virtual Hermes User Group Meeting, oral presentation, April 2021
- British Nuclear Medicine Society Spring Meeting, Harrogate, oral presentation, May 2023
- British Institute of Radiology H&N Imaging, poster presentation, Leeds, February 2024
- NHS GGC Clinical Physics and Bioengineering, Symposium, presentations in 2022, 2023 and 2024.
- European Association of Nuclear Medicine Annual Congress, Hamburg, Germany, poster presentation, October 2024
- NHS GGC Clinical Physics and Bioengineering, Seminar sessions, oral presentations in 2024 and 2025.

I was invited to participate and contribute to the NHS GGC optimisation and standardisation group to discuss the parathyroid SPECT/CT protocol with a multi-disciplinary team of clinical technologists, clinical scientists and nuclear medicine physicians. The group assessed available guidance, legislation, performed clinician observer studies and compared protocols, resulting in an agreed standard NHS GGC protocol for parathyroid imaging.

Throughout the PhD, I have participated in monthly multi-disciplinary team meetings alongside Endocrinologists and Surgeons within NHS GGC discussing complex thyroid and parathyroid patient cases. This has given me the opportunity to share my research aims, gather the details of patient cases and network with colleagues involved in diagnosis and treatment of parathyroid pathology. I have also regularly attended and presented at an Advances in Research meeting within the School of Cardiovascular and Metabolic Health, University of Glasgow.

CONCLUSION

This research study, alongside others carried out within NHS GGC has initiated discussions about routine SPECT quantification for multiple clinical procedures which will improve diagnostic reporting and clinician confidence. The work assessing calibration factors established what aspects of acquisitions can significantly impact CFs. A change of local practice was put in place following the investigation of a SPECT imaging artefact to improve parathyroid SPECT/CT images qualitatively and quantitatively. A local observer study determined that SPECT quantification can be used as a guidance tool in the diagnosis and differentiation of parathyroid pathologies and routine clinical implementation will be explored. The patient audit work found that of all patients that had surgery, 11.3% had discrepant results between imaging and surgery. Finally, the assessment of different downscatter correction techniques has determined that full collimator modelling is the more accurate technique in correcting for downscatter between [Tc^{99m}] and [I^{123}] for parathyroid imaging. Further work will establish if this additional correction step can be optimised as currently this correction method is computationally expensive and can take hours to apply making it impractical for routine clinical use.

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