An Evaluation of Direct Quantification using xSPECT Quant in Everyday Clinical Practice

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Background/Aims

xSPECT Quant™ was introduced in 2013 by Siemens Healthineers as a method of delivering absolute quantification of technetium tracer uptake in an arbitrary volume of tissue. Absolute quantification addresses many of the limitations of previous systems that provide relative quantification. This is done by accurately measuring the system physical characteristics and incorporating the imaging physics [1,2]. As several publications have shown advantages from quantification, we introduced this into our practice in August 2016 [3-5]. This pilot study set out to evaluate the clinical utility and practicality of direct quantification in everyday clinical practice.

Methodology and Data Collection

The scan technique we used has been described by us elsewhere [6]. The xSPECT Quant methodology has been described by Hans Vija [7]. xSPECT Bone reconstruction was the basis for direct quantification in Tc-HDP cases and xSPECT as the basis for Tc-PSMA. Image interpretation was primarily done on an Intelerad PACS system with fusion module capable of interrogating the quantification data. The clinical and specific quantitative data collection was done using a freely available database system (Memento™) that allows users to build specific databases for the Android operating system and populates a Google spreadsheet in the background. The advantage of this system is its ease of entry and that multiple users can enter data (technologists, clinician, and reporting physician or radiologist). Normal data can also be entered into the system. We maintained two databases –separately for general and oncology work. The oncology databases provided for both Tc-HDP and Tc-PSMA tracers and allowed for multiple studies per patient. For the general database, a thorough clinical history was undertaken using a comprehensive questionnaire that recorded patient conditions and/or injury, pain scores, pain frequency, type and location (using anatomical pain maps). A bone scan finding was considered relevant (MATCH) when the pain map, scan abnormality, and clinical findings were all consistent. For the oncology database, every patient's PSA results, surgery, radiation therapy and hormone therapy information were included in the database.

Database Interim Analysis

As of November 2017, we had 341 cases in the musculoskeletal database. There were referrals for 170 low back or buttock pain and 91 MATCHs (54%), i.e. a likely cause was found on bone scan (18 with more than one site). Where there was no abnormal uptake, or the pain distribution was inconsistent then the cause of the pain was considered unknown. The 91 MATCHs consisted of 86 degenerative or inflammatory lesions, 3 fractures, 1 metastasis, and 1 other. In these patients there was no significant correlation between SUVmax and pain scores (correlation coefficient = 0.23). Table 1 shows the SUVmax found in the symptomatic lesions. In terms of SUVmax the abnormal values in the MATCHs correlate well with the values of degenerative lesions in the study of Kuji et al [8]. That study was looking at scan differences between degenerative and metastatic lesions and did not consider whether the degenerative lesions were symptomatic, which may account for their much higher standard deviation. The MATCHs all have values well outside the normal range for lumbar vertebrae, previously found by Kaneta et al [9] and Cachovan et al [10]. Another previous study has shown that normal uptake in 50 females is an average bone tracer activity concentration of 48.15±13.66 kBq/ml, which corresponded to average SUV of 5.91±1.54 [10].

We also had 18 cases where the feet were considered normal to establish a tentative normal range for 3 locations in the feet (table 2).

As of February 2018 there were 82 patients (with up to 4 scans each) in our oncology database. The value of direct quantification in oncology is self evident (see clinical evaluation and Cases 1 and 2).

Table 1. Uptake Values in Patients with Symptomatic Low Back and Sacroiliac Pain

Clinical Group and Previous Studies	SUVmax	Standard Deviation	Number Cases
All low back pain MATCH	15.4	3.5	86
Facet Joint MATCH	15.4	4.2	42
Discogenic pain MATCH	15.6	2.9	15
Sacroiliac Pain MATCH	15.3	2.7	29
Kuji et al [8]: Degenerative lesions	16.7	6.7	101
Kaneta et al [9]: Normal lumbar vertebra	7.1	0.4	29
Cachovan et al [10]: Normal lumbar vertebra	5.9 (SUVave)	1.54	50

Table 2. Normal uptake in the feet in 18 patients with no significantly abnormal scan findings

	SUVmax	Range	SUVave	Range
Calcaneus	3.0+-1.2	1.0-3.8	1.3+-0.8	0.6-2.0
Second Metatarsal	3.1 +-1.2	1.7-4.4	0.9+-0.4	0.5-1.3
Navicular	3.2+-0.9	2.5-4.0	1.5 +-1.2	0.8-3.1

Table 3. Standard Uptake Windows (SUW) used in SPECT/CT imaging in our practice

Scan type	Lower Limit (SUV)	Upper Limit (SUV)
Bone xSPECT/CT Spine and Whole Body	1	16
Bone xSPECT/CT Feet	0.5	6
Bone xSPECT/CT Hands	0.5	10
PSMA xSPECT/CT Whole Body	1	5

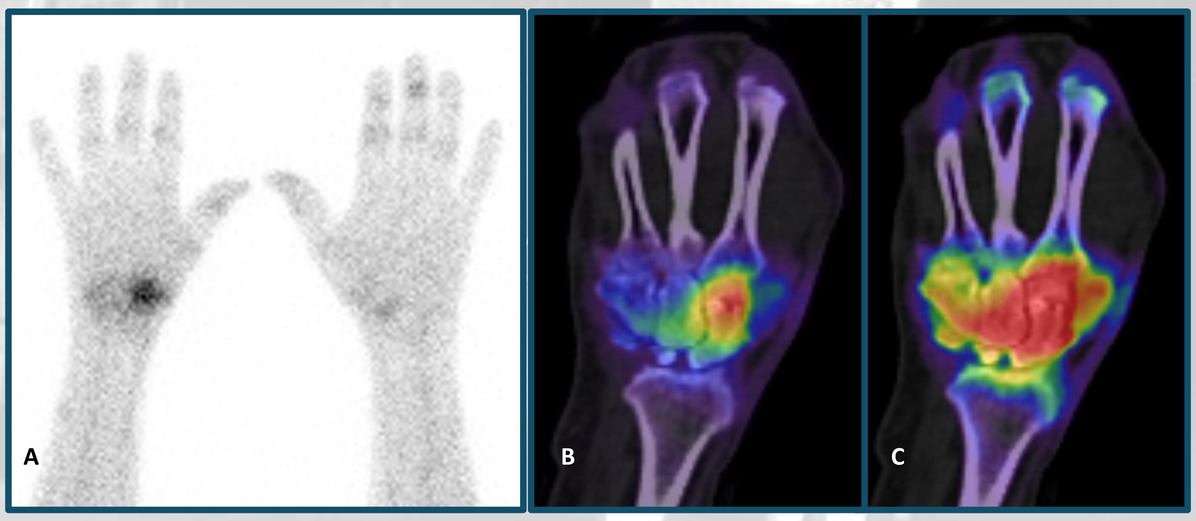
Clinical Evaluation

The greatest impact of the xSPECT Quant has been in oncology where both absolute and serial evaluation have become normal practice. In particular this provides an objective assessment of lesion uptake in a manner never before available. The study of Beck et al showed visual assessment alone shows inconsistent results (interobserver disagreement) in 42% of their series but high correlation (kappa =0.94) when using quantitative analysis[11]. It is now our routine to produce reports with tables outlining uptake values of specific lesions at diagnosis and serial values in follow-up scans. Clinically this is most important in metastatic breast cancer where the bone scan may be the only objective tool to assess chemotherapy. Cases 1 and 2 illustrate its use in Oncology.

Rather than measuring multiple lesions individually (in Oncology) we have developed several standard uptake windows (SUW) for image review, with upper and lower limits set by SUV rather than relative or software windowing that has been the conventional method (suggested windows see table 3). The windows are broadly based on the range of normal and abnormal uptake values in our database in each region. This ensures an accurate direct comparison between two scans (see case 2). We have now extended this concept to all our hybrid imaging so that all abnormalities that are outside the "normal" SUV range are naturally highlighted, but in a way that allows comparison across cases and over time. It also has helped us to efficiently review large number of hybrid slices and provides a "benchmark" for pattern recognition of bone and joint pathologies. It ensures that images are less affected by case specific factors such as bladder and kidney uptake, overall skeletal uptake, epiphyseal uptake, organ uptake (PSMA, Tc-pyrophosphate, pertechnetate and sestamibi scans), and where there is a wide range of tracer avidity in multiple lesions. Examples of how this is helpful are seen cases 2,3, and 4. Nevertheless, there are still many cases when the viewing windows need to be adjusted for clarity and display purposes. In particular the range of values seen in SPECT/CT of the hands is highly variable and the SUW concept cannot be reliably applied.

Our accumulated quantitative data has allowed us to more objectively assess and grade certain conditions such as osteoarthritis, sacroiliitis, and fractures (cases 3 and 4). While many joints can be windowed to look hotter or colder the measured SUV remains unchanged. Though clearly the presence of radiographic changes (sclerosis, erosions, ankyloses, etc.) and the pattern of tracer uptake influences the overall interpretation, the absolute uptake is now also an integral part of this. For example, we now consider uptake values in sacroiliitis (SUVmax) of 12-15 as mild, 15-20 moderate, and over 20 severe. Similarly, as normal ranges are developed grading systems based on lesion uptake can be developed for many specific structures: facet joints, fractures and even peri-prosthetic uptake. The final clinical value of this remains uncertain but xSPECT Quant provides a much more standardised and objective basis for lesion evaluation. Frequently the measured uptake value increases or reduces the perceived clinical importance of a lesion.

Fig 6 . Tc-HDP Bone scans (CASE 4): Planar delayed images (LEFT). xSPECT/CT bone images representative slice (RIGHT) showing two different windows: (B) Standard software window and (C) our SUW.



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Case 1

Mr WB is a 61 yr old male with a diagnosis of Gleason 9 prostate cancer after a biopsy in May 2017. His PSA was 20ng/ml at diagnosis. An xSPECT/CT PSMA scan showed abnormal lymph node uptake in paracaval, presacral, left common iliac lymph nodes as well as the right prostate and seminal vesicle. Only in the paracaval group were the size of the nodes increased at 22mm. No bone lesions were identified. He was subsequently commenced on androgen deprivation therapy and docetaxel in June 2017. In October 2017, his PSA was 0.25ng/ml. A follow-up PSMA scan was undertaken on 6/11/17 showed less uptake and reduced size of the enlarged lymph nodes. The presacral lymph node is shown Fig 2A and 2B. Though it is clear that there is no longer uptake in the presacral node, there is still persistent uptake in the prostate gland (Fig 2D). The latter is thus much better assessed by direct quantification. The SUVmax values declined by between 40% and 88% and correlated well with the 99% reduction in PSA (Fig 1). The size of the paracaval lymph nodes declined to 11mm.

Fig 1. Direct Quantification with Tc-PSMA demonstrating a response to therapy case 1. Y axis indicates SUVmax and PSA values.

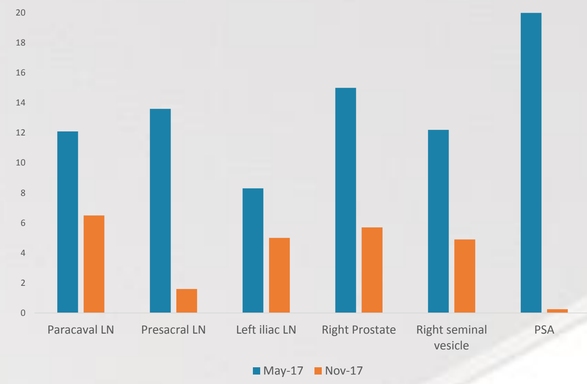


Fig 2 (below). Tc-PSMA uptake in presacral node (A)pre-therapy and (B)post-therapy, and prostate (C) pre-therapy and (D) post therapy.

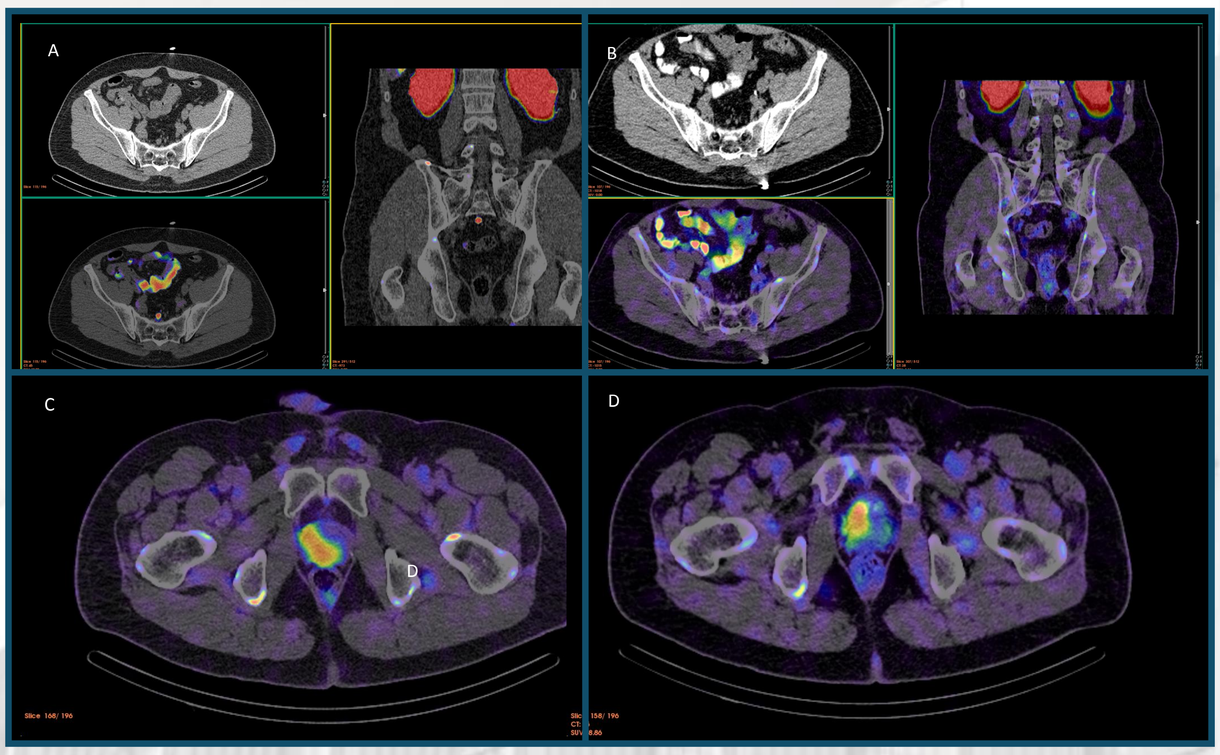
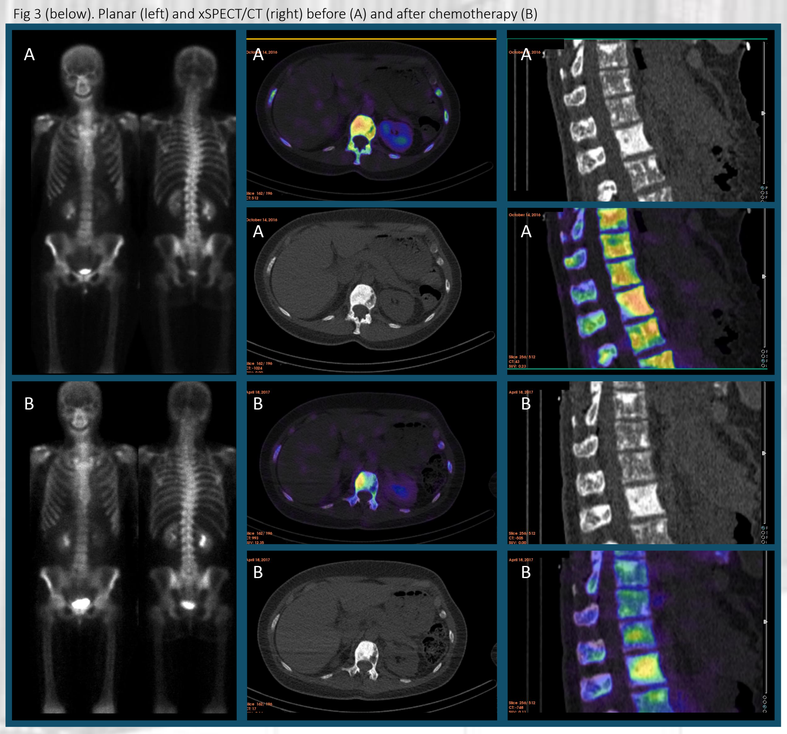


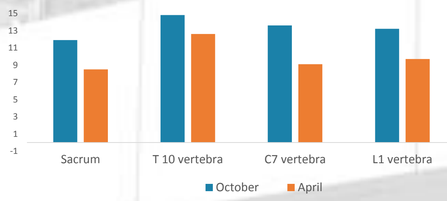
Fig 3 (below). Planar (left) and xSPECT/CT (right) before (A) and after chemotherapy (B)



Case 2

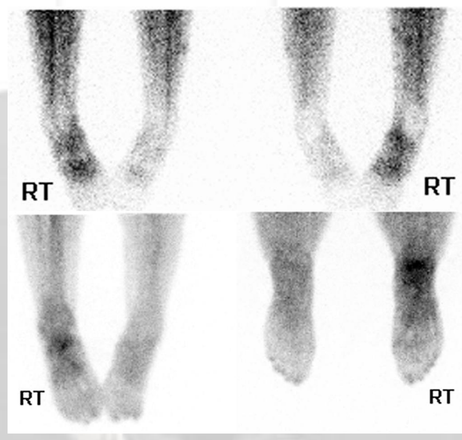
Ms LN is a 50yr old female with breast cancer and metastatic bone disease seen on CT, but essentially negative on a standard whole body planar scans (Fig 3), though overall skeletal uptake appears increased on the first scan. An xSPECT/CT in October 2016 showed widespread sclerotic metastases and she was subsequently commenced on chemotherapy. The follow-up whole body scan shows no meaningful difference. The xSPECT/CT scans (Fig 3) showed no significant change in the number and extent of bone lesions but using xSPECT Quant demonstrates reduced metabolic activity. Windowing on the xSPECT/CT is undertaken using SUW so that both pre-therapy (A) and post-therapy (B) can be easily compared, as standard windowing did not show a clear difference. Specific quantitative uptake in several lesions shows reduction of uptake of between 15% and 39%, interpreted as showing a response to therapy (Fig 4).

Fig 4. SUVmax before and after chemotherapy (CASE 2)



Case 3

Ms JW is a 42yr old female with longstanding left ankle pain, recently worse. A bone scan was undertaken looking for a stress fracture (Fig 5). Blood flow and planar images show asymmetric blood flow and delayed uptake of Tc-HDP tracer in the lower legs. Conventional imaging methods have no way of clearly defining normal uptake. Bone images are usually chosen to display the uptake variance across the chosen region (e.g. Fig 5A and 5B). However xSPECT/CT Quant bone images using an SUW can reflect absolute uptake and thus show the uptake is reduced in the left foot and normal in the right (Fig 5C), consistent with altered sympathetic tone. This can be confirmed with direct quantification. Uptake in the right hindfoot is SUVa=1.0 and CTa=221 which compares with the left foot SUVa=0.7 and CTa=248, confirming reduced tracer uptake but no loss of bone density in the left foot.



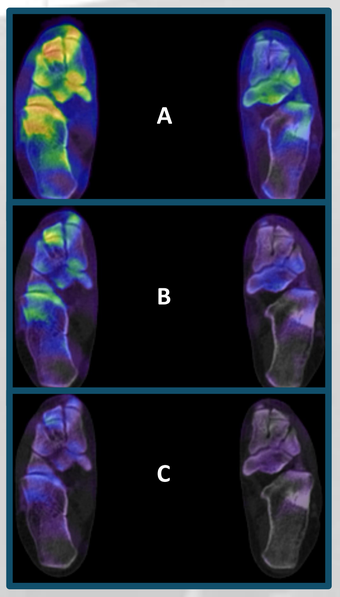


Fig 5 (above and right). Tc-HDP Bone scans (CASE 3).
Planar images above: Blood flow (top row) and planar delayed images (bottom row).
xSPECT/CT bone images (representative slice) shown right:
(A) The default software window (SUV 0-2.9),
(B) a user selected window (SUV 0.3-3.8)
(C) our SUW foot (SUV 0.5-6 SUV).

Case 4

Mr AK 57yr male was referred with a tender painful right wrist. He had a history of trapeziectomy 4 months ago and increased pain after a fall 6 weeks ago. Delayed planar (Fig 6A) and xSPECT/CT bone images are shown (Fig 6 B,C). The xSPECT/CT bone image (B) shows the default software window (0-25.9 SUV) and the image (C) shows our SUW (0.5-10 SUV). Depending on windowing the uptake in the wrist can be shown to be variable in extent. Image B might be interpreted as primarily showing a problem confined to the distal scaphoid and adjacent trapezoid, but image C suggests a more widespread process. The SUVmax overlies the scapho-trapezoid joint and measures 25.8. The advantage of standardised uptake windows (SUW) is that a high variation in uptake can be more objectively assessed, and allows the reviewer to develop consistency over time.

Discussion

xSPECT Quant has become an integral part our practice and is used in every SPECT/CT scan to both standardize the reviewing/reporting process and evaluate individual specific lesions. For everyday use this standardisation requires dedicated software at the reporting station able to set windows with SUV parameters and to directly quantify uptake. The SUW is a valuable tool based on xSPECT Quant that allows the user to replace a conventional viewing window based on a range from zero to the hottest pixel, with a quantitative window based on a standardised range using absolute uptake. Once the user is familiar with this technique it greatly enhances reporting confidence, clinical classification of lesions, and reproducibility. It is invaluable for serial oncology scans.
Our Android based database has proven a useful method of accumulating patient and scan data. Our interim analysis has found direct uptake values for degenerative pathology in the spine that are consistent with other studies, and we are developing a large bank of data that may prove useful in generating both normal and abnormal ranges for various pathologies. As criteria develop over time it may find more specific applications in improving the evaluation of degenerative pathology, fractures, sacroiliitis, and in assessing peri-prosthetic remodelling and complications.

Conclusions

xSPECT Quant has standardised our assessments both across patients and over time, and has proven invaluable in serial scans. In our practice it has further enhanced the benefits of xSPECT/CT Bone reconstruction [6], and provides an alternative method of windowing xSPECT/CT and SPECT/CT scans, based on absolute rather than relative tracer uptake. With wider adoption it may provide improved reporting standardisation and reliability.

Acknowledgements and Conflicts

Garran Medical Imaging has a collaboration agreement with Siemens Healthineers to assist in the evaluation xSPECT Quant.
Informed consent was obtained from all patients for the use of their deidentified data.