Q.SUV™
Quantitative SUV you and your patients can trust
What if SUVs were accurate and consistent?
Introduction

Medical oncologists order Positron Emission Tomography (PET) scans to investigate their patient’s disease state and progression. If the PET report is clear and conclusive, it will help them make important treatment decisions.

Can more accurate and consistent PET quantitation contribute to improved clarity and conclusiveness?

According to our recent survey, 92% of medical oncologists agreed that if the Standard Uptake Value (SUV) could be more accurately measured and understood, it would likely improve clarity and conclusiveness of the PET scan\(^1\).

Why is PET quantitation becoming more important?

With a remarkable ability to help clinicians “find” disease, PET's largest clinical application is cancer staging. Treatment response assessment is a growing application, which relies on PET's ability to help clinicians “follow” disease. In this role, quantitation accuracy and consistency becomes critical.

Unfortunately, iterative reconstruction technologies designed to improve PET image quality are a key limiting factor of quantitation accuracy. In other words, the ability to “find” limits the ability to “follow”.

GE Healthcare’s Q.Clear technology offers up to 2x improvement in both image quality and quantitation accuracy. Q.Clear eliminates the compromise between image quality and quantitation consistency with significant gains on both counts.

SUVs derived from conventional technology are under converged, and measurement deviations do not follow a simple pattern.

SUVs delivered by Q.Clear are fully converged, hence more accurate and more consistent. This must be noted upfront to imaging physicians and referring physicians that will review the PET scan.

To distinguish SUVs provided by Q.Clear vs. conventional reconstruction, we introduce Q.SUV, defined as the Standard Uptake Value obtained from Q.Clear reconstruction.

We believe the adoption of Q.SUV measurements is an important step to deliver more clarity and conclusiveness to referring physicians. Based on feedback received to date, the oncology community welcomes Q.SUVs and will expect to see them in PET reports.

Q.SUV is part of our journey to make PET a great tool to help clinicians “find” and “follow” disease with a strong synergy between the two.
Value of More Accurate Quantitation for Referring Physicians

“Absolutely, this would change my practice. PET is still very subjective in terms of the radiologist.” - Medical Oncologist interviewed by Consulting Company Sg2 for GE Healthcare

Quantitation is a feature that helped establish PET as a research tool in the 1980s. PET quantitation is a core element in thousands of scientific publications related to neurology, cardiology and oncology dating back over 30 years. In 1984, Dr. Steven Bergmann proposed that PET could be used to estimate myocardial blood flow in dogs [1]. In 1989, Bohm et al. designed a brain atlas adjustable to a patient's anatomy to improve the quantification and evaluation of PET data. This improvement made it possible to compare results from individuals or groups of individuals [2]. Studies of PET quantitation of brain receptors abound in scientific literature.

As PET became more widely used as a clinical tool, physicians in the vanguard of nuclear medicine proposed malignancy thresholds for different types of tumors. In 1998, Dr. Val Lowe studied 89 solitary pulmonary nodule patients and proposed a standardized uptake value (SUV) threshold of 2.5 [3]. That same year, Dr. Johan Vansteenkiste suggested that the optimum SUV threshold for identifying malignant lymph nodes in non-small cell lung cancer was 4.4 [4]. And in 1999, Dr. Dominique Delbeke proposed an SUV threshold of 3.0 for pancreatic carcinoma [5].

However, due to a high incidence of errors, SUV has not become an unequivocal indicator of malignancy. Physiological bias accounts for some of the inaccuracies. Even more are caused by instrumentation.

In a 2010 report titled “A Systematic Review of the Factors Affecting Accuracy of SUV Measurements,” Dr. Michael C. Adams states, “Quantitative measurements such as SUV for interpreting FDG PET scans are limited because of the considerable overlap between SUV measurements in malignant and benign lesions. Most clinical PET interpretations are based on visual assessment of the FDG accumulation as well as the pattern of disease.” [6]

Imprecise SUV numbers have generated wide-ranging opinions about the relevance of SUV during the reading process. The controversy often blurs the line between scientific rigor and personal preference, but there is no dispute that today SUV is not the driver for reading physicians, although it does have an ancillary role.

While visual interpretation is paramount in the initial interpretation of PET, images don’t always tell us how complex neoplastic processes in the body are reacting to therapeutic interventions. So, quantitative tools become an important way to document the intensity of metabolic activity in tumors and to track how these tumors are (or are not) reacting to treatment.

The most commonly used tools are based on SUV calculations, but quantitative tools suffer from inherent variability. These are dependent on the physiologic milieu of the patient at that particular time, such as basal glucose serum levels or particular dietary contents consumed within the last few days prior to the test. They also depend on the acquisition and image reconstruction parameters used by the imaging device, among others. We know that these values cannot be utilized in the strictest sense. Methods to decrease quantitative variability with increased precision are necessary for appropriate oncologic treatment assessment and planning.
In our practice, we combine our visual evaluation of the images, supported by \( \text{SUV}_{\text{max}} \) data, for tumor response assessment and overall treatment strategy evaluation.

Jaime Montilla-Soler, MD
Director of Molecular Imaging
H. Lee Moffitt Cancer Center and Research Institute,
Tampa, Florida, USA

We find SUVs to be extremely valuable in planning strategies for biopsies. We can target certain areas of a tumor, based on the highest SUV, in hopes of sampling the most aggressive component of a tumor. This strategy proves especially valuable when we have tumors with regions of necrosis or sparse cellular tissue, which if biopsied, can result in a non-diagnostic pathology result. As clinicians are starting to rely more and more on SUV readings, we need to be confident that they are accurate and reproducible.

As we continue to learn more about the utility of PET imaging, we are realizing the importance of providing our referring clinicians the SUV in our reports. This is particularly important with lymphoma. The SUV assessment may alter the chemotherapy regimen similar to the grading of a tumor in a pathology report. Knowing this, we are starting to work more closely with our oncologists so we can provide them the most accurate assessment of the various cancers they may treat.

Aaron Binstock, MD
President, Suburban Radiologic Consultants
Coon Rapids, Minnesota, USA

Referring oncologists ask for SUVs

Both imaging physicians and referring oncologists look at scientific evidence in understanding the benefits of PET SUVs in different tumor types. But while imaging physicians seem to regard them as indicators, referring physicians find informational value in SUVs, and they are responsible for translating information into treatments for patients.
A survey of 100 US medical oncologists conducted by ITG Market Research found that 82% review SUV numerical data 80% or more of the time. 95% also strongly agree/somewhat agree that SUV numbers help them better understand the PET scan findings, impressions, disease state or disease progression.

How often do you review SUV numerical data provided in PET the report?

- 80% to 100% of the time: 82
- 60% to 80% of the time: 8
- 40% to 60% of the time: 5
- 20% to 40% of the time: 1
- 0% to 20% of the time: 2
- I do not receive SUV in the PET reports: 2

Graph 1: Survey of 100 US medical oncologists conducted by ITG Market Research for GE Healthcare

The results of the survey are intriguing, and they raise an important question: Since SUVs carry such large error bars, why do referring oncologists use them to make sense of PET reports?

A simple question, perhaps, without a simple answer.

First, numbers are generally welcomed by referring physicians. In nuclear cardiology, for example, the demand for quantitative measurements, like ejection fraction, is driven by cardiologists more than by nuclear medicine physicians.

Oncologists deal with lab tests and other measurements that carry large error bars. They reach conclusions using several imperfect numbers and data points at the same time. Each individual measurement does not lead to a final conclusion, but each one contributes to it. So why not look at a surrogate measurement of tumor activity?

I believe the vast majority of oncologists understand a good deal about the vagaries of the SUV determination. However, that doesn’t keep them from desiring that information, because it’s often the single most important and most clinically predictive piece of information they obtain, despite its flaws. They should always filter that information through the lens of all the remaining clinical information they have on their patients to come to a final conclusion. They understand that, in many instances, it is appropriate to assume that the SUV is not sufficiently accurate, or may be artifactually too high or too low — but they can still use it as a starting point. The best analogy I can think of is, if I was a carpenter, and knew that my tape measure was not completely accurate and might register either too high or too low, I still would not abandon it if it were still the best measurement tool to which I had access. I would know that, in some cases, I should err on one side or the other when making my initial cuts, and then use the bigger picture of how the cut piece of wood fit into the project I was building, before making
final adjustments afterwards. I believe that is how most oncologists are currently using the SUV.

However, this is clearly not sufficient. If we are going to help blaze the trail into so-called “precision medicine,” then our measurements must be both more precise and more accurate. While we know that other measurements, such as total lesion glycolysis, etcetera, may well take the place of a simple SUV determination for many applications, all the imprecision of our measurements affects all our current measurable parameters. We simply must do a better job of refining the data we provide to the oncologists, as they try to refine their therapeutic options for patients.

Dr. Landis Griffeth
Director
Nuclear Medicine
Baylor University Medical Center
Medical Director for Functional Imaging,
The US Oncology Network

Recently, GE Healthcare engaged the consulting company Sg2 to get the perspective of medical oncologists about the use of PET studies and SUV measurements. We also wanted to better understand how clinicians integrate PET studies into their clinical decision-making. Sg2 compiled 14 extensive phone interviews with medical oncologists that are solely referrers (not trained PET readers). Below are the most relevant findings of the study:

If you received a PET report without SUV information, would you contact the radiologist?

78% (11 of 14) responded yes. While including the SUV was the sign of a quality report to most of the medical oncologists, it appeared that if it was missing, the assumption was that the radiologist did not feel it was useful to the interpretation:

“I would think it was strange if the report did not mention metabolic uptake.”

“Yes, this would concern me only since we are used to having the SUV value.”

When is SUV useful?

Most frequent responses were: longitudinal studies for lymphoma; determination of prognosis based upon the change over the time of treatment; identification of active versus inactive disease; for patients with multiple abnormalities to help determine where to direct biopsy; assessment of response in lymphoma and solid tumors.

What are the typical limitations of SUV?

Some frequent responses: SUV is not useful when changes over time are small; lack of clinical studies to identify clinical conditions that are represented by SUV value; lack of standardization.

Do you look at the PET image or rely on both the image and the radiologist’s report?

Most said they look at the images if there were findings in the report that surprised them — or would look at the images together with the radiologist in a setting such as tumor board. None suggested that they would interpret the images themselves (whereas several suggested that they had more confidence in their ability to “read” CT images).

“I look at the images myself and review at tumor board. The report is useful because it clarifies what I may or may not be seeing.”

“The image is important but not enough. The report is necessary for conclusion and treatment.”

“We look at images, but reports are more important.”

Are you satisfied with language, clarity, conclusiveness and overall guidance provided by PET reports?

Several mentioned that studies coming from other imaging centers were not of the quality they received from their “home” center. Several mentioned the importance of being able to compare PET with previous imaging studies, or have it put in context with the
results from other CT or MR studies. Several commented that radiologists are sometimes too cautious and that it can be difficult to determine the conclusion of the interpretation as there are too many “possible this” or “that.” A personal relationship with the radiologist and the ability to talk with them about a particular patient was very important to their level of confidence in the study.

What improvements would you like to see in PET reports?

Among the responses: standardization among imaging facilities and radiology groups; comments and conclusions about how different tumors are staged (especially for longitudinal studies); more precision in the report conclusion; comparisons not only with prior PET scans but also prior CT and MR, and prior SUV values should be included in the report.

“Radiologists must be more clear and sharp about the findings in the report.”

“Results should include a clear statement about patient and the staging of tumor.”

If SUVs were to become more accurate and consistent, would that impact the way you use PET as a decision-making tool?

All oncologists interviewed suggested that more accurate SUVs would be useful — particularly important was consistency of measurements. Most saw value in removing some of the subjective nature of the interpretation of PET images. Few had any real understanding of the physiological factors introducing errors into SUV numbers today — but they did recognize the inconsistency of values across different scanners and
locations. Several commented that understanding SUV in the context of evidence-based clinical pathways would be helpful and would make SUV more important to them in managing patients.

“If there were more strict criteria using numbers that are reproducible in multiple institutions that would be more useful than subjective description in radiology report.”

“Absolutely, this would change my practice. PET is still very subjective in terms of the radiologist.”

“Certainly, consistency is better. It almost feels like some radiologists influence the report based on SUV. I do think some radiologists don’t understand what SUV is showing us.”

What types of improvements would make SUVs more valuable for your clinical needs?

Specific points included: more precise definition of the “positive PET scan” describing the metabolic uptake; more precision and reproducibility; well-established and published criteria that is reliable and reproducible, for example: clinically, what is meant when SUV drops from 7 to 2 but tumor size stays 3cm? How does this impact treatment decision?
Improving Clarity and Consistency

“The accuracy of image interpretation and the quality of the diagnostic report are critical to the continued success of PET/CT in the medical community.” - Ryan Niederkohr, MD

In 2013, the Journal of Nuclear Medicine published an article titled Reporting Guidance for Oncologic ¹⁸F-FDG PET/CT Imaging. In it, Ryan D. Niederkohr et al. commented “The accuracy of image interpretation and the quality of the diagnostic report are critical to the continued success of PET/CT in the medical community. When referring physicians receive a high-quality, clinically relevant report their confidence in (and subsequent use of) this imaging modality may increase. Unfortunately, the converse is also true: when referring physicians receive reports that are confusing or contribute little to patient care, the value of PET/CT is diminished and the test could potentially be considered unnecessary. Therefore, it is imperative that reports be of high quality, both for optimal patient outcome and for the long-term success and viability of PET/CT as an imaging modality.” [7]

Referring oncologists use PET reports for important clinical decisions. The clarity and conclusiveness of the PET reports are major contributors to good decision-making.

Many factors contribute to the clarity of the PET study. The article from Dr. Niederkohr goes through an extensive list of requirements to create a high-quality PET/CT report. Within the scope of what PET technology can do to support this cause is better PET quantitation.
Conventional iterative reconstructions using ML-EM or OSEM suffer from high noise when run to its full convergence. To avoid this result, the algorithm is typically stopped after 2-4 iterations. This is an effective method to reduce noise in the PET images, but the noise reduction comes at a cost of reduced quantitative accuracy and the potential introduction of distortions in small objects. [8]

This effect is demonstrated with a simple simulation as shown in Figure 1. Two small active objects of the same size and activity level are simulated, with one of the small objects placed between the two large elliptical objects of uniform activity distribution. Reconstructed images are shown using OSEM with 2 iterations and 25 iterations. While the fully converged 25-iteration image shows much improved contrast and a significant reduction in spatial distortions, excessive noise is introduced in the low count but fully-converged image.

If SUVs could be more accurately measured and understood, how likely would you say this would improve clarity and conclusiveness of the PET scan?

<table>
<thead>
<tr>
<th>Likelihood</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Very likely</td>
<td>55</td>
</tr>
<tr>
<td>Somewhat likely</td>
<td>37</td>
</tr>
<tr>
<td>Neutral</td>
<td>6</td>
</tr>
<tr>
<td>Not very likely</td>
<td>2</td>
</tr>
<tr>
<td>Not at all likely</td>
<td>0</td>
</tr>
</tbody>
</table>

Graph 3: Survey of 100 US medical oncologists conducted by ITG Market Research for GE Healthcare

Both of our surveys conclude that for referring physicians, SUV plays an important role—a role that could be expanded with improved accuracy. This fact provides great motivation to improve PET quantitation.

Q.Clear, a breakthrough technology from GE Healthcare, is a significant step in this direction.

Q.Clear is an iterative image reconstruction technique that accurately models the inherent PET physics to deliver up to up to 2x improvement in PET quantitation accuracy (SUV\_{\text{mean}}), and up to 2x improvement in image quality (signal-to-noise ratio).
A clinical example of this effect is shown in Figure 2. Excessive noise is introduced into the high iteration images. To avoid this, an under-converged image, like the two-iteration image shown, is typically used in clinical practice.

GE Healthcare’s Q.Clear is a Bayesian penalized likelihood (PL) reconstruction algorithm, which incorporates an additional term in the objective function. This term increases as image noise increases, reducing the objective function, which has the effect of steering the optimization algorithm away from noisier images. This allows the algorithm to achieve full convergence without the detrimental effects of excessive noise found in today’s reconstruction technologies.

With conventional OSEM, the accuracy of quantitative imaging in PET is compromised by the necessary under-convergence required to control image noise. Q.Clear provides a fully-convergent PET image reconstruction technique, enabled by controlling image noise through regularized reconstruction.

Figure 3 shows a real clinical dataset with a hot sphere of known activity, which was added to the raw dataset and re-reconstructed using Vip Replay technique. Since the activity of the sphere is known, the expected SUV is also known. In this case, the SUV reading is expected to be 14 g/ml. With 2 iterations, the SUV measured by OSEM is 8.2, 42% lower than expected. At 25 iterations, the SUV is much closer to the real value, but the signal-to-noise ratio has deteriorated to a level that is not acceptable for a clinical read of the scan. On the right side, Q.Clear was run to full convergence yielding the expected SUV 14.0. The image quality has not deteriorated; on the contrary, the signal-to-noise ratio is two times better than OSEM at 2 iterations in this experiment.

![Figure 2: Clinical data reconstructed with a range of OSEM iterations. Excessive noise is introduced as the image reaches convergence.](image)
The Q.Clear algorithm is designed so that edges are preserved while background image noise is kept low, thus providing superior image quality. Because Q.Clear is always run to convergence, iterations and subsets are no longer inputs provided to the user as is commonly done in OSEM. In addition, since the image noise is controlled inside the iterative reconstruction as part of regularization, post filters are not necessary [8]. Figure 4 shows a simplified scheme of how Q.Clear reconstruction works.

Figure 3: Clinical experiment to demonstrate Q.Clear reconstruction. A real clinical dataset is blended with a hot sphere of known activity. Patient BMI: 52.5, ROI: 15 mm, OSEM: 6.4 mm, TOF, PSF.

Figure 4: Conventional iterative reconstruction does not control noise within the iterative loop. Q.Clear has noise modelling and control built into the reconstruction engine. Noise modelling and control is applied to every voxel at every step of the iterative loop.
A Refined Metric System: **Q.SUV**

Conventional iterative reconstruction delivers SUVs that are not fully converged. As a result, imaging and referring physicians do not have full confidence in conventional numerical measurements. Q.Clear delivers fully-converged SUVs. The difference between conventional and Q.Clear SUVs depends on lesion size and location, and the deviation does not follow a simple pattern.

As we phase Q.Clear into clinical practice, it's important to distinguish SUV values provided by Q.Clear vs. the ones provided by under-convergent methods. To make a clear distinction, we define **Q.SUV** as the Standard Uptake Value generated by Q.Clear technology - the quantitative SUV you and your patients can trust.

**Q.SUV** is not a new definition of Standard Uptake Value. The concept and calculation process are exactly the same. The Q label informs imaging physicians and referring physicians that the iterative reconstruction was run to full convergence, hence the quantitation data is more accurate and consistent than conventional methods.

It will be very useful for referring oncologists to know that a PET scan was read based on **Q.SUV** measurements. For one, they will expect the values to be slightly different. Also, they will be more confident in measurements that are more accurate and consistent.

We believe the adoption of **Q.SUV** measurements is an important step to deliver more clarity and conclusiveness to referring physicians.

Our surveys have clearly indicated that referring oncologists look at SUV measurements, and the majority say they would benefit from a more accurate measurement. Based on feedback received to date, the oncology community will welcome **Q.SUVs** and expect them in PET reports.

Quantitation helped establish PET as a research tool in the 1980s. There may be a lot more it can do to improve clinical PET scans in the near future.
Clinical Results

Figure 5: Discovery PET/CT 710 F18-FDG scan – Quantitation: SUVmax (g/ml)
Lesion size measured on CT: 2.5 cm

Figure 6: Discovery PET/CT 710 F18-FDG scan – Quantitation: SUVmax (g/ml)
Better Visualization and Quantitation of Lesions Close to Each Other
Improved Quantitation of Small Lesions

- OSEM
  - SUV: 3.9
- OSEM w/TOF & PSF
  - SUV: 6.1
- Q.Clear
  - Q.SUV: 10.1

Figure 7: Discovery PET/CT 710 - F18-FDG scan – Quantitation: SUVmax (g/ml)

CT Measurements: 2D Diam 5 mm / Vol 80 mm³

Improved Visualization and Quantitation of Small Lesions

- OSEM
  - SUV: 3.9
- OSEM w/TOF & PSF
  - SUV: 6.5
- Q.Clear
  - Q.SUV: 11.4

Figure 8: Discovery PET/CT 710 – 68 DOTATOC scan – Quantitation: SUVmax (g/ml)
Figure 9: Discovery PET/CT 610 F-18 FDG scan – Quantitation: SUVmax (g/ml)

Improved Visualization and Quantitation of Lymph Nodes

OSEM

SUV 3.8

Q.Clear

SUV 11.1

Figure 10 - Discovery PET/CT 710 – 68 DOTATOC scan – Quantitation: SUVmax (g/ml)

Improved Visualization and Quantitation of Small Lesions

OSEM

SUV – 10.6

Q.Clear

Q.SUV – 24.3

OSEM w/TOF & PSF

SUV – 15.0

SUV – 6.2

Q.SUV – 18.3

Figure 10 - Discovery PET/CT 710 – 68 DOTATOC scan – Quantitation: SUVmax (g/ml)
CLINICAL CASE:

Characterization of Small Pulmonary Nodules, by Prof. Fergus Gleeson. Images and case study courtesy of: Churchill Hospital, Oxford, United Kingdom

Patient History:

A patient in their mid-thirties had an FDG PET/CT scan following the finding of subcentimetre right upper lobe pulmonary nodules on end-of-chemotherapy CT following sigmoid carcinoma resection.

Initial Report Findings:

FDG PET/CT demonstrated two faint FDG-avid nodules in the right upper lobe (first row: 8 mm SUVmax = 1.8, second row: 7 mm SUVmax = 2.2) with no evidence of other metastatic disease. The nodules were histologically proven to be metastases following surgical resection.

Q.Clear Image Analysis (retrospective):

Original patient RAW data was reconstructed at GE Healthcare utilizing GE’s latest PET/CT reconstruction technology, Q.Clear. After reconstruction, images were sent back to Professor Fergus Gleeson for review: “Reconstruction with Q.Clear led to an increase in SUVmax of the nodules (first row: 8 mm SUVmax = 4.4, second row: 7 mm SUVmax = 4.3) with a negligible change in background liver SUV mean (0.1).”

Q.Clear Potential Clinical Implications:

“The Q.Clear images provide superior quantitation of SUVmax with enhanced definition of small FDG-avid abnormalities. In my opinion, this advantage would give us greater diagnostic confidence in the assessment of small FDG-avid pulmonary nodules.”

Prof. Fergus Gleeson
A Consultant Radiologist with specialist interests in PET/CT and thoracic radiology, and Professor of Clinical Radiology, University of Oxford, United Kingdom.

The reconstructed Q.Clear images were not used for diagnosis or treatment in this case, but for retrospective analysis only and may not be indicative of results in actual practice. This case study is based on Prof. Gleeson’s review of the reconstructed images only and not on the use of Q.Clear in his clinical practice.
References:


[8] Q.Clear White Paper by Steve Ross, PhD, Principal Engineer IQ and Physics, GE Healthcare
About GE Healthcare

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imagination at work

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1) Double-blinded survey with 100 medical oncologists conducted by ITG Market Research for GE Healthcare.

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