Cancer is the leading cause of death worldwide, accounting for 12.7 million cases\(^1\) and 7.6 million deaths\(^2\) in 2008. That number is expected to rise to 21 million cancer cases\(^3\) and 13.1 million deaths\(^2\) by 2030. Treatments that prolong survival by a few weeks and cause tumor shrinkage in only 10-15% of patients are in widespread use.\(^3\)

Also, chemotherapy drugs can be costly—it is not uncommon for the cost of these drugs alone to reach up to $100,000 per year.\(^3,6\) It’s therefore important for clinicians to make an early determination of the effect of the treatment and change course, as needed, to positively impact the outcome.

PET/CT may help core teams match the right therapy to the right patient. Metabolic changes in a tumor occur more rapidly than anatomical/structural changes in tissues. PET/CT can help physicians determine how well a treatment is working after as few as one to two cycles of chemotherapy; with CT alone, it may often take six cycles of chemotherapy to determine if the treatment is effective.\(^3,4,5,6,7\)

“One of the advantages of PET, when compared to other modalities, is its relative ease to precisely measure the concentration of a material,” says Paul E. Kinahan, PhD, Department of Radiology, University of Washington. “PET is also a very sensitive
method—it can detect nanomolar concentrations of radio-labeled tracers. No other modality can touch that level of sensitivity.”

By far the most commonly used radio-labeled tracer is FDG (18F-flourodeoxyglucose), which is a glucose analogue that is avidly taken up by many cancers. The primary measurement used in clinical PET is the Standardized Uptake Value, or SUV. The SUV is the measured concentration of FDG divided by the patient size and amount of injected FDG. In this way, comparing SUVs reduces two of the largest sources of variability in FDG-PET imaging.

While accurate SUV measurement wasn’t the focus in the early clinical use of PET, it is gaining momentum as a common practice today. The reason, explains Dr. Kinahan, is due to the potential to quickly assess a patient’s response to therapy, thus optimizing treatment choices or to follow potential disease progression or response over longer time periods.

“Measurement accuracy is important when something changes,” he adds. “If we are comparing patient images over a period of time, then both knowing and reducing the variability is critical to success.” He also notes that while it is widely recognized that SUVs aren’t required for diagnosis, the trend has changed to report SUVs upon diagnosis. Today, oncologists want this information to obtain an overall picture for prognosis and to decide what to do next for treatment.

Yet, in clinical practice, SUV variances remain. “There is good data published in several papers that demonstrate if you scan and carefully repeat the scan again, the best-case measurement has roughly 10% to 12% of variance,” Dr. Kinahan says. However, he also cites a recent paper that shows if imaging centers are not careful the variance can be as high as 50%. “If we are basing clinical decisions on the measurement values (SUVs), and the variance is this high, there is a problem.”

To help address the variance in SUVs, Dr. Kinahan believes the industry needs to address a basic issue regarding measurement accuracies. “An SUV number by itself doesn’t mean as much as an SUV number that has an assigned plus or minus for accuracy. What we need in the report is the degree of known variability.” For example, an SUV should be assigned a plus or minus (±) with a percent, such as ±12%.

Dr. Kinahan believes imaging centers and hospitals can reduce the variance in SUVs by paying close attention to four key aspects in PET scanning. First, is an underlying biologic variability: if a patient did not fast as instructed, their elevated blood glucose levels compete with FDG uptake. Educating patients on the importance of following pre-PET scan instructions will help minimize the impact of this variable.
Secondly, differences in scanning protocols can impact SUV variability, specifically differences in the time between the injection of FDG and start of the PET scan. “Uptake increases over time, and therefore it is important to consistently image patients at the same time post-injection,” he says. In fact, a published article co-authored by Dr. Kinahan demonstrated that the largest effect on SUV variance was inconsistent uptake periods.9,10

The third effect is due to operator error when recording data into the scanner. “Even though PET imaging is relatively straightforward, today’s systems require the operator to record data and then manually enter it. A mistake in any one field will lead to an error in the SUV,” he says. “(Workflow and system) automation can help reduce operator error, and the PET imaging field should address this as a collaborative effort.”

The last main factor, is that every PET system has a different method for calibration to control how it scales data, and this calibration is typically left to the imaging center with minimal checks (if any) on the calibration process itself. Thus there is additional room for an error that persists until the next calibration.11

“As a field, we should be able to scan patients and consistently obtain the same SUV values regardless of the type of scanner or where the patient is scanned” Dr. Kinahan says. Situations where one imaging center is equipped by different vendors and obtains different SUVs despite scanning the same way are not uncommon.

Yet, there are several movements across the industry that may help drive standardization across imaging platforms and encourage the adoption of quantitative PET imaging. The Radiological Society of North America (RSNA) formed the Quantitative Imaging Biomarkers Alliance (QIBA), an initiative to advance quantitative imaging and the use of imaging biomarkers in clinical trials and clinical practice by engaging researchers, healthcare professionals and industry. QIBA has developed a ‘Profile’—similar to the iHE profiles for integrating/connecting imaging and information systems—that is currently available for public comment (see link). Additionally, there is a multi-society, multi-vendor, ‘Harmonization’ project headed-up jointly by Dr. Kinahan at the University of Washington, Dr. John Sunderland at the University of Iowa, and Dr. Joel Karp at the University of Pennsylvania. The Harmony Project is also a joint collaboration.

---

Figure 1. Typical PET/CT calibration procedure showing the dependency on time calibration for decay correction and measurement of net injected dose. There are several potential sources of error in this process.
between SNM-CTN, QIBA, ACRin, and EANM as well. Under a contract award from the National Cancer Institute, this project aims at developing and implementing guidelines for the consistent performance of quantitative imaging procedures for PET and PET/CT. Further, Dr. Kinahan believes the current focus on pay for performance may also further drive the need for quantitative imaging, as reimbursement may potentially be tied to how well centers can demonstrate consistent, reliable imaging study results.

One thing is certain to Dr. Kinahan: the era of quantitative PET/CT imaging has arrived. As oncologists continue to request SUVs, radiologists and technologists have to provide them. “It is in the patient’s and really, everyone’s best interest, to generate reliable data that provides quantitatively accurate SUVs and changes in SUVs over time, particularly when that change may impact the choice of therapy in cancer treatment. This is a necessary tool in our development of patient-specific therapies.”

References


Paul Kinahan, PhD, is a Professor of Radiology, Adjunct Professor of Bioengineering, Physics, and Electrical Engineering and Head of the Imaging Research Laboratory at the University of Washington. Paul Kinahan received BASc and MASc degrees in Engineering Physics from the University of British Columbia, and his PhD in Bioengineering from the University of Pennsylvania. He is currently a member of the Science Council of the AAPM, co-chair of the RSNA Quantitative Imaging Biomarkers Alliance (QIBA) Nuclear Medicine Modality group, and co-Director of the ACRin PET/CT core laboratory.