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Education and Scanner Validation: Keys to Standardizing PET Imaging Research

by Adam Opanowski, CNMT, PET, NCT, RT(N)(ARRT) and Tina Kiss, CCRP

Standardization involves the consistent performance of PET imaging and adherence to protocols performed at each study site. Harmonization involves the identification and implementation of mechanisms to control for inconsistencies of data between the sites, particularly to ensure that images taken and data generated with different tomographic systems are comparable. When properly performed, the scanner images should be comparable and reproducible across sites for image noise and texture, quantitative accuracy and lesion detectability. Ideally, there should be no discernible difference between images acquired from the same patient at different locations or on different platforms. A major challenge for imaging researchers is producing reliable quantitative, semi-quantitative and qualitative data in multicenter clinical trials.

The Clinical Trials Network (CTN) has always believed that education is the vital link in promoting standardization, and that molecular imaging technologists play a critical role in the evolution of this field. To that end, the CTN offers a comprehensive list of courses developed by molecular imaging technologists and investigators experienced in performing multicenter clinical research protocols within the current regulatory framework. The goal must be to not only achieve high-quality imaging in clinical research but to also be compliant with international standards for Good Clinical Practice.

In addition to supporting excellence in training, the CTNs Scanner Validation Program works to ensure that PET/CT systems used in clinical research operate at optimal performance. The CTNs unique chest oncology phantom was designed as a clinical simulator containing a set of lesions that are challenging for the scanner and physician and tests their abilities in a number of areas. This exercise allows one to compare image quality and quantitative measurements at data densities and image noise that are similar to clinical imaging conditions and count rates. A valuable part of the program is identifying areas where a site may have problems with their scanner or dose calibrator and are unaware of them prior to this exercise. This is where both personnel training and equipment QC become equally important. Table 1 lists the key problem areas CTN identified on the initial attempt for 202 validations .

Table 1. *(from Paul E Christian)*

CTN Scanner Validation Site Problems	
Image quality	6%
Scanner calibration	5%
Failed to follow instructions	4%
Filled phantom incorrectly	3%
CT attenuation correction	2%
Dose calibrator	2%

To date, the CTN has validated over 230 scanners, many of which have been used in international CTN-pharma partner studies. The data on these scanners is, in itself, a valuable asset, providing essential information on scanner sustainability and identifies potential weaknesses in staff training. In addition to the CTNs Scanner Validation Program, other groups maintain phantoms for image standardization. One such effort, the National Cancer Institute's (NCI) CQIE (Centers for Quantitative Imaging Excellence), was set up to establish a resource of 'trial-ready'

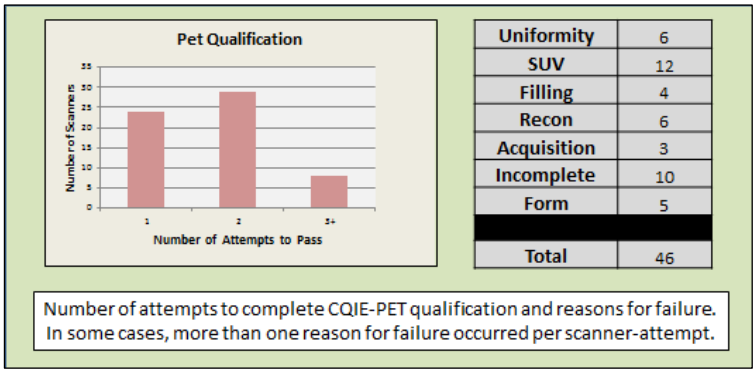
sites within the NCI Cancer Centers Program that are capable of conducting clinical trials in which there is an integral molecular and/or functional advanced imaging endpoint. The CQIE Program was developed with input from and collaboration with the broader scientific community including experts associated with ACRIN, AAPM, SNMMI and RSNA/QIBA, and is designed to qualify sites in the quantitative imaging methodologies described in Table 2:

Table 2.

BRAIN IMAGING	BODY IMAGING
Volumetric MR	Volumetric CT
DCE-MR	DCE-MR
Static and Dynamic PET-PET/CT	Static and Dynamic PET-PET/CT

Participating cancer centers undergo an initial qualification assessment and then annual requalification for an additional 3-year period. The qualification requirements include annual phantom scans, clinical test images (MR and PET), and a standardized set of routine QC activities. A total of 61 scanners at 58 NCI Cancer Centers were qualified; however, only 39% of scanners passed qualification specifications on the first round of imaging. As with the CTN validation program, reasons for failure included technical issues, like uniformity, SUV, reconstruction and operational failures such as incorrect phantom filling and improper image or form submission (see Fig 1). Continued observation and data tracking of site compliance with qualification procedures continues so as to judge the durability of CQIE training on sites' ability to maintain adequate data upkeep regarding scanners and technical personnel, as well as compliance with maintenance phantom scanning.

Figure 1.



Standardization and harmonization of imaging data in multisite clinical trials ultimately leads to improved efficiency and validity of using imaging biomarkers for therapeutic trials. In August 2011, the FDA published their draft "Guidance for Industry, Standards for Clinical Trial Imaging Endpoints" for public comments. Although the final rule has not yet been released, it is clear the need to improve standardization of PET imaging is essential; especially now, as industry includes more international sites in their multicenter trials. Scheduled, periodic scanner validations, along with routine quality control of the PET scanner and appropriate, ongoing training of imaging personnel, remain critical factors in achieving successful standardization. The importance of initiatives like the CTNs Scanner Validation Program and the NCIs CQIE, along with others in the US and around the world, loom large as we strive to bring better drug therapies to the patient in a more efficient and timely manner.