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Benefits of Time-of-flight Positron Emission Tomography Computed Tomography with ^{13}N-ammonia

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Abstract

Noninvasive quantification of regional myocardial blood flow (MBF) and coronary flow reserve (CFR) by myocardial perfusion positron emission tomography/computed tomography (PET/CT) imaging is well-established and has additional diagnostic value over traditional visual analysis. A growing need for high sensitivity and high spatial resolution capable of assessing smaller targets with shorter acquisition time has led to technical advancements. These include whole-body imaging, 3-dimensional (3D) mode acquisition, application of new scintillator materials, and iterative reconstruction algorithms. Among these advancements, the combination of 3D mode acquisition and time-of-flight (TOF) technology has played an important role in clinical oncology PET/CT studies. In this review, I summarized studies that have focused on the use of TOF PET/CT with ^{13}N-ammonia (^{13}N-NH_3). Compared with conventional PET acquisition, the combination of 3D mode acquisition and the TOF imaging can improve noise and image quality in ^{13}N-NH_3 perfusion imaging. As a result, it yields high reproducibility and accurate measurement of CFR.
Keywords: ^{13}N-Ammonia, Coronary flow reserve, Myocardial blood flow, Time-of-flight
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The majority of cardiac positron emission tomography (PET) studies have been perfomed 2-dimensional (2D) mode systems. More recently, there has been growing interest in the use of 3-dimensional (3D) mode acquisition and time-of-flight (TOF) technology (1). TOF and 3D data acquisition is popular in clinical oncology PET studies. The TOF system recognizes the time difference in the arrival of a pair of coincident photons. Therefore, accuracy of determining the location of the annihilation event along the line-of-response (LOR) can be improved. Compared with conventional PET system, TOF-PET also improves the signal-to-noise ratio (SNR) in cardiac PET studies (2). The authors award winning work will describe the major advantages of TOF technology with ^{13}N-Ammonia (^{13}N-NH_3).

^{13}N-NH_3 PET

Non-invasive quantification of regional myocardial blood flow (MBF) and coronary flow reserve (CFR) is obtained by PET myocardial perfusion imaging (3). CFR is useful to evaluate multi vessel coronary artery disease or balanced ischemia. Detecting balanced ischemia is one of the limitations of semi quantitative visual analysis. Compared with single-photon emission computed tomography, PET yields better accuracy and sensitivity because of its higher spatial resolution, and more accurate attenuation correction (4). Several perfusion tracers such as ^{82}Rubidium (^{82}Rb), ^{13}N-NH_3, and ^{15}O-H_2O are available for the evaluation of myocardial perfusion. ^{13}N-NH_3, and ^{15}O-H_2O have higher extraction fractions (5-7). Therefore, these tracers are suitable for MBF quantification. Clearance of ^{13}N-NH_3 from the myocardium is slower than ^{15}O-H_2O, resulting in increased contrast between the myocardium and blood pool (8). ^{13}N-NH_3 PET showed good diagnostic accuracy diagnosis of coronary artery disease (9,10).

TOF PET system

The 2D mode system implemented slice-collimating septa. In contrast, the 3D mode system does not have septa.

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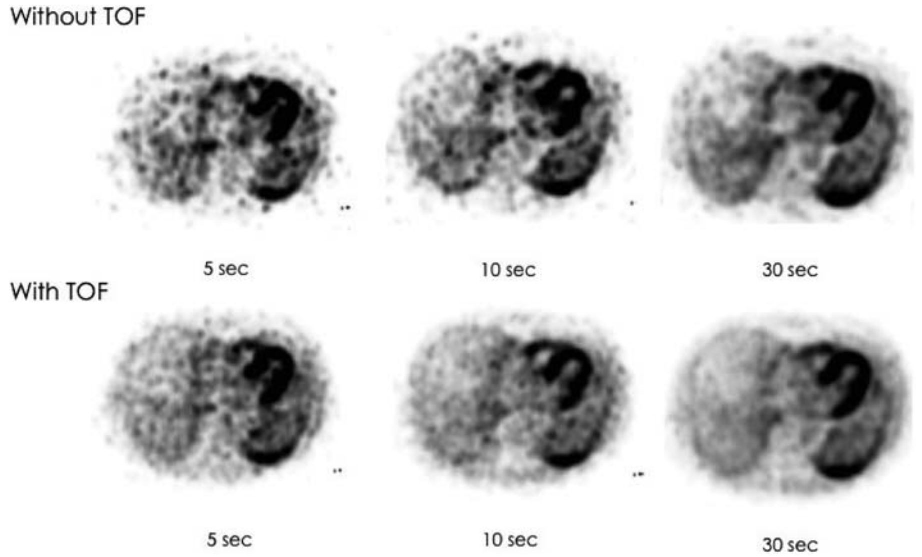

Fig. 1 (Dynamic images) Representative dynamic trans-axial images without TOF (top) and with TOF (bottom) under rest conditions.

Therefore 3D system detects the coincidences between two different detector rings in the PET scanner. As a result, the 3D system offers higher counting rates. On the other hand, 3D system has higher scatter fractions, random coincidences, and the count losses than that of the 2D mode system. These are limitations of the 3D system. However, those can be improved by new reconstruction algorithms for the 3D system (11,12). In conventional 3D PET, a valid event is recorded when the two coincident 511 keV annihilation photons are detected within the time window. The location of the annihilation point along the LOR is not precisely known. Thus, the reconstruction algorithm assumes a uniform probability for its location along the length of LOR lying within the object boundary. In contrast, TOF PET records the actual time difference in the arrival of the two annihilation photons at the detectors, which requires high time resolution. Conventional scintillators were not sufficient to provide any reasonable level of TOF information. The lutetium–yttrium oxyorthosilicate (LYSO) scintillator permits high timing resolution. In this regard, LYSO is used for PET/CT scanners using TOF.

We used a scanner with a timing resolution of 585 ps. The dimensions of the individual LYSO crystals are 4 mm × 4 mm × 22 mm in size, and the measured spatial resolution of the system is 4.8 mm. It has been shown in previous studies that the image contrast gain with TOF (1).

Improvement of signal-to-noise ratio

The time activity curves in the myocardium and blood are determined using dynamic image acquisition.

The higher SNR of TOF PET provides excellent image quality. Fig. 1 shows images with 5 sec, 10 sec, and 30 sec acquisitions, with and without TOF. TOF provided decreased noise compared with their respective counterparts. Image quality in TOF PET is excellent even with very short acquisition times such as 5 sec or 10 sec. Furthermore, the contrast between the myocardium and background is higher than without TOF PET, because TOF technology is effective in localizing the coincidence and reducing the propagation of noise along the LOR. These may contribute the improvement of image quality.

Improvement of partial volume effect

Radioactivity can be underestimated due to the partial volume effect (PVE). The tracer activity as observed by PET depends on myocardial wall thickness. This causes an underestimation of true tissue activity in segments with wall thinning or severe wall motion abnormalities (13). Fig. 2 shows the association of the recovery coefficient (RC) on the sphere diameter measured with 30 (upper panel) and 50 (lower panel) cm diameter sizes of phantoms with and without TOF reconstructions. The maximum value of measured radioactivity concentration decreased with decreasing sphere size. TOF reduced the partial volume effects.

Improvement of reproducibility

High reproducibility is required for MBF measurements. A variety of software have been developed for improvement of reproducibility (14). TOF may have impacts on the reproducibility of MBF measurements. Fig. 3 shows the CFR values for each segment with and without TOF. In our previous manuscript, a comparison of the difference of the MBF and CFR for each segment showed poor agreement in some cases. The poor agreement was found in particular in the apex (15). Apical wall thinning due to motion artifacts caused was the reason for the variability of apex. Moreover, the spillover from the RV blood pool into the myocardial wall was introduced as

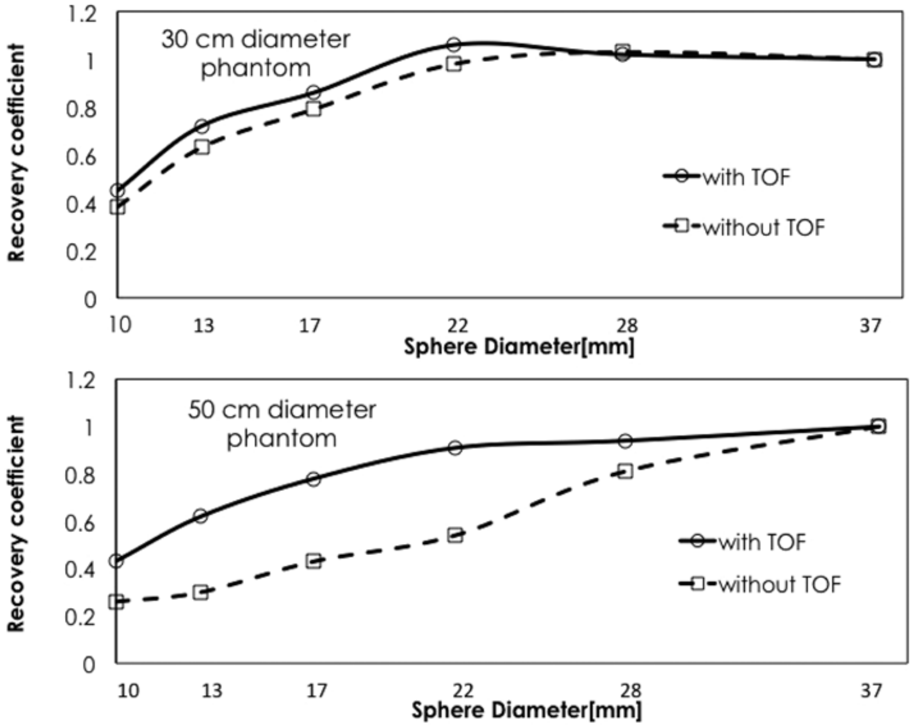

Fig. 2 (Recovery coefficients) Recovery coefficients for hot spheres of various diameters with TOF (solid line) and without TOF (broken line) obtained from noise-free scans in standard ϕ: 30 cm (top) and larger ϕ: 50 cm (bottom) phantoms. [From Ref (15) with permission by J Nucl Cardiol, Springer]

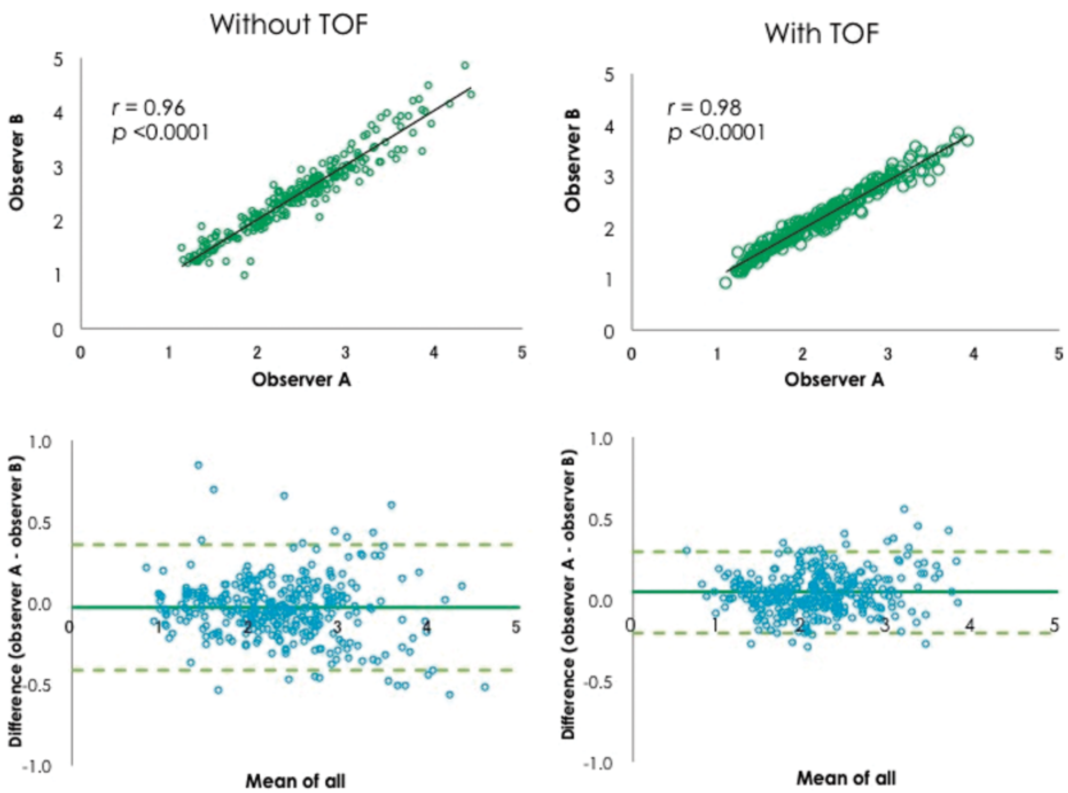

Fig. 3 (Correlations and agreements of quantitative values) Inter-observer Pearson's product moment correlation coefficient (top) and Bland-Altman plots (bottom) for segmental CFR without TOF (left) and with TOF (right). [From Ref (15) with permission by J Nucl Cardiol, Springer]

an extra parameter in the kinetic model analysis (16). Time-activity curves of the RV were used to correct for the spillover. In measurements of this nature, it is often difficult to place the voxels of interest (VOIs) accurately on the RV blood pool, resulting in variations of the measured values in segments adjacent to the RV. TOF-PET reduces the burden on an operator in placing the VOIs on the RV and LV blood pool, and the myocardium by providing better image quality.

Conclusions

PET technology has advanced remarkably over recent years. Among the various applications of this technology, the TOF-PET technique is becoming a mainstream approach. TOF-PET improved image quality and PVE in myocardial perfusion studies with ^{13}N-NH_3. In addition, TOF-PET offers high reproducibility and the accurate measurement of CFR.

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Conflicts of interest

None

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