A dedicated breast-PET/CT scanner: Evaluation of basic performance characteristics

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Purpose: Application of advanced imaging techniques, such as PET and x ray CT, can potentially improve detection of breast cancer. Unfortunately, both modalities have challenges in the detection of some lesions. The combination of the two techniques, however, could potentially lead to an overall improvement in diagnostic breast imaging. The purpose of this investigation is to test the basic performance of a new dedicated breast-PET/CT.

Methods: The PET component consists of a rotating pair of detectors. Its performance was evaluated using the NEMA NU4-2008 protocols. The CT component utilizes a pulsed x ray source and flat panel detector mounted on the same gantry as the PET scanner. Its performance was assessed using specialized phantoms. The radiation dose to a breast during CT imaging was explored by the measurement of free-in-air kerma and air kerma measured at the center of a 16 cm-diameter PMMA cylinder. Finally, the combined capabilities of the system were demonstrated by imaging of a micro-hot-rod phantom.

Results: Overall, performance of the PET component is comparable to many pre-clinical and other dedicated breast-PET scanners. Its spatial resolution is 2.2 mm, 5 mm from the center of the scanner using images created with the single-sliced-filtered-backprojection algorithm. Peak NECR is 24.6 kcps; peak sensitivity is 1.36%; the scatter fraction is 27%. Spatial resolution of the CT scanner is 1.1 lp/mm at 10% MTF. The free-in-air kerma is 2.33 mGy, while the PMMA-air kerma is 1.24 mGy. Finally, combined imaging of a micro-hot-rod phantom illustrated the potential utility of the dual-modality images produced by the system.

Conclusion: The basic performance characteristics of a new dedicated breast-PET/CT scanner are good, demonstrating that its performance is similar to current dedicated PET and CT scanners. The potential value of this system is the capability to produce combined duality-modality images that could improve detection of breast disease. The next stage in development of this system is testing with more advanced phantoms and human subjects. © 2018 American Association of Physicists in Medicine [<https://doi.org/10.1002/mp.12780>]

Key words: CT, dedicated breast imaging, PET

1. INTRODUCTION

The importance of early detection of breast cancer in women with dense breasts^{1–10} is an important motivating factor for the development of dedicated breast scanners. Many of these systems are based on the use of positron-emitting or single photon-emitting radiopharmaceuticals. The first positron-emitter-based system, known as positron emission mammography (PEM), was proposed in 1994 by Thompson et al.¹¹ It utilized a pair of stationary, planar detectors to produce maps of the distribution of ¹⁸F-Fluorodeoxyglucose (FDG) in the breast. Since this first scanner was introduced, systems utilizing rotating planar detectors and rings of detectors have been developed.^{12–22} In addition to positron-emitter based scanners, several based on the use of single-photon emitting radionuclides have been also constructed.^{23–28}

Dedicated breast imaging has extended beyond Nuclear Medicine methods to include the creation of x ray computed tomography (CT) systems. The first cone beam, breast-CT system was developed in 2001 by Boone, et al.²⁹ Subsequently, additional academic researchers have created similar devices,^{30–32} including one combined with a SPECT scanner,³³ the first commercially available, FDA-approved scanner³⁴ and phase-contrast-based systems.^{35,36} The potential benefit of these devices is the ability to improve soft tissue contrast, possibly enhancing detection of small lesions, detection of micro-calcifications and guidance of the biopsy of suspicious lesions.

The combination of breast-PET and CT scanners has the potential to produce a symbiotic relationship between the two modalities that promises to enhance detection and diagnoses of breast cancer. Specifically, CT images could add anatomical information regarding the size and shape of lesions identified with PET. PET images could aid in determining the metabolic activity, and possibility of malignancy, in lesions identified with CT. In addition, the information obtained from the CT images could be used to enhance corrections for physical processes degrading PET images (e.g., photon attenuation and Compton scattering), which is required if the images are to be used to quantitate radiotracer uptake. Furthermore, accurate quantitation of radiotracer uptake could be enabled by use of the CT images to calculate partial volume corrections for small structures identified in PET scans. It is likely that PET/CT imaging will not be used as a first line screening tool due to use of a systematic injection of radiopharmaceuticals. Instead, this procedure will be used to examine the breasts of women that have some pre-disposition for breast cancer (e.g., genetic or personal risk factors) with indeterminate mammograms due to high breast density or other factors. The first combined scanner was created at UC-Davis in 2009.^{37,38} In addition to this effort, the dedicated breast-PET system developed at West Virginia University^{39,40} has been modified to include a cone-beam x ray CT scanner. Specifically, one pair of its PET detectors was replaced with the components of a cone beam CT scanner (x ray source and panel detector). The purpose of this work is to evaluate the basic performance characteristics of both components of this new system.

2. MATERIALS AND METHODS

2.A. PET component

The PET component of the WVU breast-PET/CT scanner consists of a pair of detector heads, separated by 27.8 cm. Each detector head is comprised of a 96×72 array of $2 \text{ mm} \times 2 \text{ mm} \times 15 \text{ mm}$ LYSO scintillator elements, pitch = 2.1 mm, coupled to a 4×3 array of Hamamatsu model H8500 flat panel position-sensitive photomultipliers (PSPMTs).³⁹ Individual PSPMTs are readout by multiplexed electronics that reduces the output signals from sixty-four to four channels (2X and 2Y) (Vorg Electronics, Yorktown, VA, USA).⁴¹ These electronics also produce a single sum output signal whose amplitude is representative of the total amount of light detected by the PSPMTs. Thus, these pulses are equivalent to the amount of energy deposited by an annihilation photon in the scintillator. To maximize collection of scintillation light, including light produced by elements at the edges of the scintillator array, a new method for optically coupling the scintillator to the PSPMTs was employed. Specifically, each of the twelve PSPMTs is individually coupled to the LYSO array via a tapered, pixelated, 5.3 mm-thick light guide (Agile Engineering, Knoxville, TN, USA).⁴² Coupling of the light guides to the scintillation arrays and PSPMTs was performed with a silicone-based gel that provided good light transport and mechanical stability. While some scattered x rays are detected by the PET detectors, this effect is small because they are moved out of imaging position and, since we are not performing simultaneous scanning, detection of these events does not interfere with imaging. We also have found that with LYSO there is no afterglow from exposure to x rays. Thus, there is no necessity to include x ray shielding of the PET detectors.

To reduce the processing load on the hardware, the sum pulses from each PSPMT array were combined to create four columns of three PSPMTs. Thus, instead of combining 12 PSPMT sum signals to form a single channel, four summed outputs are produced, each containing information from three PSPMTs. This task was performed by a specially designed module created in collaboration with Vorg Electronics (Yorktown, VA, USA). The eight sum signals (four from each detector head) are processed by a discriminator/coincidence module developed in collaboration with Mesytec, GmBH (Putzbrunn, Germany). This device can accommodate a maximum of 16 input channels, each channel consists of a computer-controlled constant fraction discriminator and fast amplifier. The input from a given channel can be placed in coincidence with any combination of other inputs. For our application, signals from each column of one of the PSPMT arrays are in coincidence with the signals from the four columns of the opposing detector head. The width of the coincidence-timing window is selectable (our system uses an 8 ns-wide window).

When a coincidence event is identified, a TTL pulse is generated and used to initiate a conversion of the analog X and Y signals from the readout electronics to digital output by a specially designed 64-channel, FPGA-based analog-to-

digital converter (ADC) (AiT Instruments, Newport News, VA, USA). The center-of-mass of the light distribution is used, in conjunction with a previously calculated lookup table, to determine the position of photon interaction in the detector. Figure 1 shows a schematic of the data acquisition system. The energy of each event is calculated using a pre-measured table that converts the summed signal amplitude to energy. These values, as well as the position of each event, are stored in list mode format. To estimate the random coincidence rate, a second data acquisition system mirroring the first one is used, with the exception that analog to digital conversions are initiated by delayed triggers. Specifically, the trigger pulses from one of the detector heads are delayed by 14 ns and placed in coincidence with the prompt trigger signals from the other detector head. Separate coincidence units and computers are used to process the prompt and delayed triggers.

PET data are acquired by rotating the detectors in step-and-shoot mode. The dwell time at each position is user-selectable. On the basis of initial clinical tests of the first-generation system,⁴⁰ we estimate imaging time to be ~6 min per breast. The resulting list mode data are reconstructed using ordered set expectation maximization (OSEM),⁴³ except for NEMA NU4-2008-based measurements of spatial resolution, which utilized single-slice rebinned-filtered backprojection (SSRB-FBP).⁴⁴ Estimates of random coincidence and Compton scattered event rates, as well as the effect of photon attenuation are incorporated into the reconstruction algorithm (Eq. 1).

$$s_j^{n+1} = \frac{s_n^j}{\sum_i A_{ij}} \sum_i A_{ij} \frac{p_i \cdot C_i}{\sum_k A_{ik} s_k^n + r_i + sc_i}. \quad (1)$$

Here, s_j^n is the estimate of the activity in the j th source voxel for the n th iteration, p_i is the i th line-of-response (LOR) data, A_{ij} is the system matrix element giving the probability that an emission in source voxel p_i will result in a detected coincidence event in LOR j , r_i is the estimated number of random coincidences for LOR i and sc_i is the number of

scattered events for LOR i determined from a model-based estimator.⁴⁵ Photon absorption along each LOR is corrected by applying attenuation factors (C_i) calculated from segmented breast-CT images. The event energy acceptance window is 350 to 650 keV. The field-of-view (FOV) of the PET scanner is 20 cm (transaxial) $\times$ 15 cm (axial). Nominally, the reconstructed voxel size is 1 mm $\times$ 1 mm $\times$ 1 mm.

2.B. CT component

The CT component of the system consists of a Tungsten filament, pulsed x ray source (XRS-125-7K-P, Source-Ray, Inc., Ronkonkoma, NY, USA) (focal spot = 0.5 mm) and a 2520DX flat panel x ray detector (2 $\times$ 2 binning, 0.127 mm² detector pixel pitch) (Varian Medical Systems, Salt Lake City, UT, USA) operated in portrait orientation, minimizing the inactive region between imaging volume and patient chest wall. Indeed, selection of the 2520DX was mostly dictated by reduction in the inactive zone at the edge of the detector (5 mm) compared to common flat panel detector alternatives, such as the Varian 4030CB, which has a minimum inactive region of 34.3 mm. The upper edges of the x ray source, x ray detector and PET detector heads are co-planar. The distance between the top of edge of the x ray source housing and the exit port is 5.7 cm. An Aluminum bowtie filter (parabolic profile with thickness ranging from 2 cm at the edge to 2.6 mm in the center) is used to reduce radiation dose and scatter effects, in addition to reducing cupping caused by beam hardening.^{46,47} In addition to the bowtie filter, the x ray tube has 2.0 mm of Aluminum equivalent at 125 kVp fixed filtration. The source-to-detector distance (SD) is 68.5 cm, the source-to-rotation axis distance (SO) is 59 cm. This geometry is designed to maximize sampling of the chest wall region of the patient. While x ray beam energy is user selectable (70 kVp to 120 kVp), a typical scan utilizes an x ray energy of 80 kVp with a 6 mA beam current. Choice of x ray energy was based on work by Boone, et al.⁴⁸ The system is rotated at 9°/s for 40 s to complete a 360° clockwise rotation

Fig. 1. Schematic of the PET system's data acquisition system. [Color figure can be viewed at wileyonlinelibrary.com]

(300 total frames). The x ray beam is pulsed at 7.5 Hz (rise time is less than 5 ms). Data are reconstructed using the Feldkamp algorithm implemented on an array of graphics processing units (Hann filter, cutoff frequency = 2.0 mm^{-1}). Reconstructed voxel size is nominally $0.3 \text{ mm} \times 0.3 \text{ mm} \times 0.3 \text{ mm}$. The FOV of the CT component is 16 cm (transaxial) $\times$ 20 cm (axial).

2.C. Integrated PET/CT gantry

The PET and CT components are mounted on a computer controlled, rotating gantry (Fig. 2). The elements of the two scanners (two PET detector heads, x ray source and x ray detector) are mounted on linear slides so that their distances from the center of rotation can be changed to adjust scanner geometry for the desired mode of operation.³⁹ Most of the electronics needed to process PET signals (PSPMT readout electronics, trigger segmentation electronics and ADCs) are mounted on the detector heads. The PET trigger signals are routed to the coincidence-processing unit via a slip ring (Moog, Inc., Blacksburg, VA, USA). PET detector bias high voltages and USB2 connections from the data acquisition computers to the ADCs are routed through a circular cable carrier (Igus, Inc., East Providence, RI, USA), since the slip ring is not capable of carrying these types of signals. The cable carrier also contains the electronics control and power cables for the x ray tube, in addition to the data link and power for the x ray detector. The use of the slip ring and circular cable carrier permits motion of up to 370° . Rotation of the gantry is controlled by a Newport Corp. (Irvine, CA, USA) ESP300 controller. Finally, a computer controlled, three-axis rotating arm that can hold a Bard, Inc. (Tempe, AR, USA) biopsy gun is attached to the gantry.

The system has two modes of operation: PET and CT. In PET mode, the detectors are moved to their imaging separation (27.8 cm), while the x ray tube and detector are moved outward to their maximum limits so that they are out of the PET FOV. The parameters for the step-and-shoot motion (number of steps, step dwell time and rotation angle per step) are entered via the user interface. Typically, nine steps of 20° (in the counter-clockwise direction) are used to sample the 180° required for a PET acquisition. Twenty-degree angular sampling is sufficient to sample the field-of-view (FOV).⁴⁹ After the initial step, the system calculates a new dwell time for each subsequent step to account for radioactive decay of the radionuclide. At each position, data from the acquisition computers are transferred, via a local area network, to a twelve core-PET reconstruction computer (Dell Precision R5500).

Following a PET scan, the user has the option to reset the gantry to perform another PET scan or switch to CT mode. In CT mode, the PET detectors are moved to their maximum retraction position, out of the CT FOV. The x ray tube and detector are then moved inward to their imaging positions (SD = 68.5 cm; SO = 59 cm). The gantry is rotated counter-clockwise to the 365° start position. A clockwise rotation of 360° is required for the CT scan, the extra 5° of rotation allows the gantry to come up to speed at the start of the motion (no data is acquired during this time). During the scan, data are asynchronously transferred to the CT system computer for reconstruction. The CT images are registered with the PET images utilizing software written in the IDL software environment (Harris Geospatial Solutions, Inc., Broomfield, CO, USA). The software harmonizes image voxel sizes and utilizes a previously calculated rotation-translation matrix to align the images. CT images are also segmented for use with the attenuation and Compton scatter

FIG. 2. Picture showing the breast-PET/CT scanner in CT mode. [Color figure can be viewed at wileyonlinelibrary.com]

corrections utilized in the reconstruction of PET images [Eq. (1)].⁵⁰ The registered images are displayed using the AMIDE software package.⁵¹ Though not tested in this work, the system possesses an additional mode of operation where image-guided biopsy samples from suspicious regions observed in the PET-CT images can be obtained.

2.D. Performance testing

Since many of the performance characteristics of the PET component (spatial resolution, count rate performance, detection sensitivity, effectiveness of correction methods and recovery coefficients) are anticipated to be closer to that of a pre-clinical system than a clinical scanner, the NEMA NU 4-2008 protocol⁴⁴ was used to evaluate the system. Specifically, spatial resolution was assessed with data acquired from a point-like source (1850 kBq ²²Na bead in a 1 cm³ block of acrylic, Eckert & Ziegler Isotope Products, Valencia, CA, USA) at positions of 5 mm, 10 mm, 15 mm, 25 mm, 50 mm and 75 mm from the center-of-rotation at axial center of the scanner. Images of the point source at each position were produced using the SSRB-FBP algorithm. Full-width at half-maximum amplitude (FWHM) and full-width at tenth-maximum amplitude (FWTM) of the images of the point-like

TABLE I. Report for the NEMA spatial resolution measurements [FWHM/FWTM (mm)] as a function of transaxial position in the scanner’s FOV.

	5 mm	10 mm	15 mm	25 mm	50 mm	75 mm
Source at axial FOV center						
Radial	2.2/4.1	2.2/4.2	2.3/4.4	2.4/4.8	2.5/5.3	2.8/5.7
Tangential	2.2/3.8	2.2/4.0	2.2/3.9	2.3/4.1	2.4/4.0	2.4/4.4
Axial	2.2/4.3	2.2/4.2	2.2/4.4	2.2/4.6	2.3/4.8	2.3/5.0
Source translated ¼ axial FOV from center						
Radial	2.2/4.0	2.3/4.1	2.3/4.2	2.4/4.7	2.5/5.2	2.9/5.5
Tangential	2.2/3.9	2.2/3.7	2.2/4.0	2.3/4.2	2.4/4.3	2.5/4.6
Axial	2.1/4.3	2.2/4.3	2.2/4.4	2.2/4.7	2.2/5.0	2.3/5.1

source were measured and reported as spatial resolution in the radial, tangential and axial directions. These measurements were repeated in the transaxial plane shifted axially by ¼ of the axial FOV (3.75 cm). Count rate performance was evaluated by acquiring data from a 5 cm diameter, 15 cm long high density polyethylene cylinder that contains a 3.2 mm-diameter hole located 17.5 mm offset from its axis. The hole was filled with a solution initially containing 21 MBq of ¹⁸F (half-life = 110 min). This structure is known as the “rat-like phantom” in the NEMA NU4-2008

FIG. 3. Xoran custom CT-QC phantom. (a) Schematic drawing of the phantom (locations of some of the regions-of-interest used in the analysis of the images are shown), (b) picture of the phantom and (c) picture showing the phantom in the scanner. [Color figure can be viewed at wileyonlinelibrary.com]

FIG. 4. Count rate performance as a function of radioactivity in the rat-like phantom.

FIG. 5. Absolute sensitivity as a function of axial position.

protocol.⁴⁴ Data acquisition continued as the radionuclide decayed until the activity reached 0.52 MBq. The resulting data were sorted into sinograms from which estimates of total, true, random and scattered coincidence events rates, as well as the noise equivalent count rate (NECR) were calculated. Detection sensitivity was evaluated by stepping the ^{22}Na point-like source ± 7.5 cm along the central axis of the scanner in steps of 5 mm. At each position, coincidence

count rate was measured to calculate the detection sensitivity of the system as a function of position. Finally, the imaging performance of the system was assessed using the NEMA NU 4-2008 quality assurance phantom. This device is a 3.35 cm-diameter 5.6 cm-long cylinder that consists of three compartments: a 3.3 cm long hollow area (uniformity section), a 1.5 cm long insert containing two 8 mm-diameter cylinders (one filled with water, the other with air) that fits inside the uniformity section (accuracy of corrections section) and a 2 cm-long solid section that contains five fillable cylinders (diameters = 5 mm, 4 mm, 3 mm, 2 mm, and 1 mm) (the recovery coefficient section). The phantom was filled with 3.7 MBq of solution containing ^{18}F . PET and CT data were acquired and used to produce attenuation and Compton scatter corrected PET images using OSEM (3 subsets). These images were utilized to assess image uniformity, accuracy of attenuation and scatter corrections, and recovery coefficients (a gauge of reconstructed image resolution).

Performance of the CT component was evaluated using protocols developed by Xoran Technologies. First, a custom, 15 cm-diameter resolution/contrast quality control (QC) CT phantom was imaged, in combination with water equivalent phantoms, (Fig. 3) using the standard breast-CT imaging protocol described above. CT image noise and cupping were determined by measuring the standard deviations of data obtained from four 10 cm² regions-of-interest (ROI) placed around the perimeter of images of the water-equivalent phantom. Mean CT numbers measured for each of the reference materials (Teflon, LPDE, Acrylic and air) embedded within the QC phantom were compared to known values. Spatial resolution was assessed by measuring the modulation transfer function (MTF) from images of a 10 cm-diameter, 2.5 cm-thick acrylic disk containing a 50 μm -diameter tungsten wire. To demonstrate the imaging capabilities of the system, a micro-hot-rod phantom containing 1.5 MBq of FDG was scanned by the combined system. The PET scanning protocol used a 3 min dwell time per step (9 steps of 20°), the CT scan utilized the protocol described above.

Absorbed radiation dose to the breast is an important consideration for dedicated imaging systems, especially CT scanners. To gauge dose over the imaging area of the scanner, the air kerma was measured using a 10 cm-long ion chamber (Radcal model 20X6-3CT, Radcal, Inc., Monrovia, CA, USA) placed at the center of a 16 cm-diameter PMMA cylinder (Fluke Biomedical, Everett, WA, USA) during a standard CT imaging sequence (80 kVp, 6 mA), as described by AAPM guidelines.⁵² In addition, the free-in-air kerma was measured at scanner isocenter. The half value layer of the x ray beam was measured using an Unfors Xi Platinum base unit (Unfors-RaySafe AB, Billdal, Sweden) connected to an Unfors-RaySafe Xi R/F detector.

3. RESULTS

Table I shows results from the measurements of spatial resolution measurements at axial center and offset vertically by $\frac{1}{4}$ of the axial FOV. Figure 4 shows results from count rate

FIG. 6. Images of the NEMA NU4-2008 quality assurance phantom. (a) Accuracy of corrections section, (b) uniformity section (intensity profile through the center of the image is shown), (c) recovery coefficient section and (d) coronal view of the phantom. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE II. Report for the NEMA uniformity measurements from the uniform section of the phantom.

	Mean	Maximum	Minimum	%STD
$(\times 10^8)$ [Ratio with mean]				
Uniformity	3.95	4.5 [1.14]	3.5 [0.89]	5.8

performance testing. The peak true coincidence count rate is 39.5 kcps, measured at 15.7 MBq. Peak NECR is 24.6 kcps measured at 14.3 MBq; the NECR at 10 MBq is 22.2 kcps. The system scatter fraction and energy resolution is 27% and 17.5%, respectively. Figure 5 shows a plot of absolute sensitivity as a function of position in the scanner. The peak absolute sensitivity is 1.36%. Total system sensitivity is 218.9 kcps/MBq (24.1%). Images of the three sections (accuracy of corrections, uniform and recovery coefficient sections) of the NEMA NU 4-2008 quality assurance (QA) phantom are shown in Fig. 6. The images are from the tenth iteration of the OSEM reconstruction algorithm (3 subsets), with attenuation and Compton scatter corrections applied. Table II shows the results from the assessment of image uniformity. Table III shows results from measurement of the recovery coefficients from the five small diameter rods. Table IV shows the results from measurement of the accuracy of the attenuation and Compton scatter corrections.

An image of the CT QC phantom is shown in Fig. 7. Table V shows results from analysis of the images of the CT water-equivalent phantom that was scanned in conjunction with the QC phantom. Nominal target values based on the Xoran MiniCAT™ scanner (a currently-marketed CBCT system for paranasal sinus and temporal bone imaging) are also given. Figure 8 shows a plot of MTF at scanner isocenter. Analyses of images of the MTF phantom determined that the spatial resolution of the scanner is 1.1 lp/mm at 10% MTF amplitude. The images in Figure 9 demonstrate the combined

TABLE IV. Report for the NEMA accuracy of corrections (photon attenuation and Compton scattering) measurements from the cold cylinder section of the phantom.

Region	%SOR	%STD
Water-filled cylinder	1.6	3.3
Air-filled cylinder	1.2	3.8

FIG. 7. CT image of the QC phantom (inset shows a line profile across the bar region of the phantom). [Color figure can be viewed at wileyonlinelibrary.com]

scanning capabilities of the system. Specifically, it shows the PET, CT and registered PET-CT images of the micro-hot-rod phantom. The 1.6 mm-diameter rods are the smallest that can

TABLE III. Report for the NEMA recovery coefficient measurements from the hot-rod section of the phantom.

Diam.	1 mm	%STD	2 mm	%STD	3 mm	%STD	4 mm	%STD	5 mm	%STD
RC	0.12	10.5	0.33	11.8	0.69	10.1	0.80	8.7	0.89	4.1

TABLE V. Measurements of noise, cupping and CT number accuracy from images of the CT phantom (HU).

	Noise	Cupping	Water	Teflon	LDPE	Acrylic
Target	<50	<20	0	600	−100	50
Measured	33.7	5.6	−1.8	608	−98	54

FIG. 8. Plot of system MTF at isocenter as a function of spatial frequency. The dotted line denotes the 10% MTF level.

be delineated in the PET image, though some structure is visible in the 1.2 mm-diameter rod section. The good alignment of the two image sets illustrates the effectiveness of the registration process. The free-in-air kerma is 2.33 mGy, the air kerma measured at the center of a 16 cm-diameter PMMA cylinder is 1.24 mGy. The half-value-layer (HVL) of Aluminum for the x ray beam is 4.62 mm.

4. DISCUSSION

The complementary functional-anatomical information provided by PET and x ray CT applied to breast imaging promises to improve detection, diagnosis and treatment

assessment of breast cancer, especially in women with difficult to image breasts. For example, PET imaging could help detect breast lesions in dense breasts that may be challenging to visualize with x ray CT alone, while CT may aid in detecting lesions that possess limited radiotracer uptake. In addition, density maps of the breast provided by CT imaging could be used for corrections of photon absorption and Compton scattering effects in PET image data, which is important for accurate quantitation of radiotracer concentrations in lesions and normal tissue.^{53,54} Furthermore, breast-CT images could be used to correct for the partial volume in quantitative PET imaging. Use of anatomical images of the breast may also become particularly important for applications employing the next generation of more tumor-specific radiotracers, since it may not be possible to identify the outline of the breast (due to the low uptake of tracer in normal breast tissue) used to define the extent of the breast necessary for calculated photon attenuation correction methods.²¹ Furthermore, CT-derived density maps will likely be required for attenuation and scatter corrections of images of surgically enhanced or post-surgical breasts, because it will not be possible to assume uniform tissue density (an implicit assumption for the calculation of photon attenuation).

Exploration of the basic performance metrics of the PET scanner component of the combined system yielded good results. Specifically, its spatial resolution (Table I) is comparable to many pre-clinical PET scanners,⁵⁵ the breast-PET scanner developed by García Hernández, et al.,¹⁶ the scanner developed by the Kyoto University group,¹⁹ the MAMMI-PET system produced by Oncovision²¹ and the scanner constructed by the UC-Davis group.³⁷ Note the relatively small degradation of radial resolution as the source is moved toward the edge of the FOV. This phenomenon is due to the use of rotating planar PET detector heads, where the angle of incidence is lower at the periphery of the FOV (reducing depth-of-interaction effects) compared to the curved detector geometry present in ring scanners.⁴⁹ The modest peak NECR (Fig. 4), while comparable to the peak NECR reported for the MAMMI breast-PET scanner (25 kcps)²¹ and comparable to some pre-clinical scanners,⁵⁵ demonstrates a deficiency in the current design of the scanner's data acquisition scheme. Since, the outputs from the entire detector head are digitized for every coincidence event, there are unnecessarily high data processing loads on the electronics, reducing count rate performance. To address this weakness, work is under way to

FIG. 9. Images of the micro-hot-rod phantom. (a) PET image (diameters of rods, in mm, are shown), (b) CT image and (c) registered image.

localize the sub-sections of the detectors that are producing relevant signals so that only these signals are digitized, reducing the amount of processing per event.

The PET scanner's peak sensitivity (1.36%) (Fig. 5) is comparable to the MicroPET™ P4 scanner,⁵⁵ but slightly lower than the breast scanner created by García Hernández, et al. (2.0%),¹⁶ the MAMMI system (1.8%)²¹ and the system created by the Kyoto group (11.2%)¹⁹ due to our use of rotating planar detectors. We chose this geometry mainly because it simplifies integration of the CT scanner components and, importantly, because it facilitates access to the breast for image-guided biopsy. The results acquired from analyses of images of the NEMA NU4-2008-QA phantom, shown in Fig. 6 and Tables II–IV, characterize performance of the system when utilized with our implementation of OSEM [Eq. (1)]. The uniformity results (Table II) demonstrate the effectiveness of breast-CT-based photon attenuation and Compton scattering correction methods. The high spatial resolution of the scanner enhances recovery of counts from the rods in the phantom (Table III) (comparable to the capabilities of pre-clinical PET systems⁵⁵). The small spillover ratios calculated for the water- and air-filled cylinders (Table IV) reinforce the finding that the methods for corrections for random coincidences, photon attenuation and Compton scattering are effective.

Results from performance testing of the CT scanner (Fig. 7 and Table V) yielded promising results, demonstrating the ability of the system to accurately identify materials of different density and to visualize small, low contrast objects. This capability, along with good spatial resolution and relatively low image noise should enable detection of suspicious regions in the breast, as well as provide accurate density maps necessary for effective corrections of annihilation photon attenuation and scattering. The system's spatial resolution (1.1 lp/mm at 10% MTF) measured at isocenter (Fig. 8) compares relatively well with the resolution (1.4 lp/mm) of the first two generations of the UC Davis CT scanners (their Bodega and Cambria systems⁵⁶), but lower than the latest generation scanner (their Doheny system (3.6 lp/mm⁵⁶)), and the system that utilizes a photon counting x ray detector constructed by the Erlangen group operated in "standard mode" (2×2 detector binning) (1.4 lp/mm).³² The resolution is moderately lower than the FDA-approved scanner (1.6 lp/mm⁵⁷). Our system's resolution is much lower than the Erlangen group's scanner operated in " μ Ca mode", which utilizes 1×1 detector binning and a high-resolution reconstruction kernel (5.3 lp/mm³²) and the phase-contrast scanner developed by the University of Napoli group that utilizes synchrotron radiation (6.4 lp/mm).³¹ While the current spatial resolution is likely sufficient for detection of many breast lesions and calculation of photon attenuation, which is the initial goal of our system, we are planning to improve the spatial resolution of our CT scanner by changing detector binning to 1×1 and implementing an enhanced, iterative-based reconstruction algorithm. Improvements in resolution may permit the system to detect some microcalcifications and very small lesions. The combined imaging of the micro-hot-

rod phantom (Fig. 9) demonstrated the good spatial resolution of both systems, and the ability to combine the images from the two components of the system.

The free in-air kerma (2.33 mGy) and air kerma (1.24 mGy) are reasonable estimates of the magnitude of dose that could be expected during a breast-CT scan with our system. We did not calculate mean glandular dose (MGD) due to differences in the geometry of our kerma measurements compared to measurements on other scanners.⁴⁸ In addition, our measurements were performed for our reference x ray source settings (80 kVp and 6 mA), so the relationship between image quality (which is partially dependent on beam energy and current) and dose as a function of breast size was not explored. A more detailed study of this relationship is planned. The air kermas, are however, similar to that measured for other systems.⁴⁸

The final stage in development of the breast-PET/CT system will be to combine the gantry tested in this work with the patient bed currently under development (Figure 10). The bed includes tungsten-alloy panels to shield the PET detectors from annihilation photons produced by radiotracer uptake in organs of the patient. In addition to the bed, the final system will also include a breast holder to immobilize the breast during the scanning procedure using minimal force (no compression is necessary).

5. CONCLUSION

In this investigation, the basic performance characteristics of a dedicated breast-PET/CT system were assessed. NEMA NU4-2008 testing of the PET component of the system produced results that compare well to high-resolution small animal systems and other dedicated breast-PET scanners. The

Fig. 10. Schematic drawing of the complete breast-PET/CT scanner (gantry combined with the patient bed). Also shown is the immobilization apparatus that holds the breast during imaging. [Color figure can be viewed at wileyonlinelibrary.com]

CT component demonstrated good resolution (comparable to some existing systems) and contrast performance. The potential value of this system is its capability to produce combined dual-modality images that could improve detection of breast disease, especially in breasts challenging to examine with standard methods. The next steps in development of the WVU dedicated breast-PET/CT scanner are addition of Compton scatter reduction methods (anti-scatter grid or model correction), assessment of MGD as a function of breast size and exploration of the potential diagnostic imaging capabilities of dual-modality breast imaging using anthropomorphic phantoms and human subjects.

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CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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REFERENCES

- Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology*. 2002;225:165–175.
- Jackson VP, Hendrick RE, Feig SA, Kopans DB. Imaging of the radiographically dense breast. *Radiology*. 1993;188:297–301.
- Lehman CD, White E, Peacock S, Drucker MJ, Urban N. Effect of age and breast density on screening mammograms with false-positive findings. *AJR Am J Roentgenol*. 1999;173:1651–1655.
- Kerlikowske K, Grady D, Barclay J, Sickles EA, Ernster V. Effect of age, breast density, and family history on the sensitivity of first screening mammography. *JAMA*. 1996;276:33–38. PMID: 8667536.
- Buist DS, Porter PL, Lehman C, Taplin SH, White E. Factors contributing to mammography failure in women aged 40–49 years. *J Natl Cancer Inst*. 2004;96:1432–1440.
- Carney PA, Miglioretti DL, Yankaskas BC, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. *Ann Intern Med*. 2003;138:168–175.
- Pisano ED, Gatsonis C, Hendrick E, et al. Diagnostic performance of digital versus film mammography for breast-cancer screening. *N Engl J Med*. 2005;353:1773–1783.
- Yang WT. Emerging techniques and molecular imaging in breast cancer. *Semin Ultrasound CT MR*. 2011;32:288–299.
- Razzaghi H, Troester MA, Gierach GL, Olshan AF, Yankaskas BC, Millikan RC. Mammographic density and breast cancer risk in White and African American Women. *Breast Cancer Res Treat*. 2012;135:571–580.
- Pettersson A, Graff RE, Ursin G, et al. Mammographic density phenotypes and risk of breast cancer: a meta-analysis. *J Natl Cancer Inst*. 2014;106:dju078.
- Thompson CJ, Murthy K, Weinberg IN, Mako F. Feasibility study for positron emission mammography. *Med Phys*. 1994;21:529–538.
- Murthy K, Aznar M, Thompson CJ, Loutfi A, Lisbona R, Gagnon JH. Results of preliminary clinical trials of the positron emission mammography system PEM-I: a dedicated breast imaging system producing glucose metabolic images using FDG. *J Nucl Med*. 2000;41:1851–1858.
- Rosen EL, Turkington TG, Soo MS, Baker JA, Coleman RE. Detection of primary breast carcinoma with a dedicated, large-field-of-view FDG PET mammography device: initial experience. *Radiology*. 2005;234:527–534.
- Santos A, Almeida P, Martins M, et al. Design and evaluation of the clear-PEM detector for positron emission mammography. *IEEE Nucl Sci Sympos Conf Rec*. 2004;3:3805–3809.
- Weinberg I, Beylin D, Zavarzin V, et al. Positron emission mammography: high-resolution biochemical breast imaging. *Canc Res Treat*. 2005;4:55–60.
- García Hernández T, Vicedo González A, Ferrer Rebolledo J, et al. Performance evaluation of a high resolution dedicated breast PET scanner. *Med Phys*. 2016;43:2261.
- Nakamoto R, Nakamoto Y, Ishimori T, et al. Diagnostic performance of a novel dedicated breast PET scanner with C-shaped ring detectors. *Nucl Med Commun*. 2017;38:388–395.
- Nishimatsu K, Nakamoto Y, Miyake KK, et al. Higher breast cancer conspicuity on dbPET compared to WB-PET/CT. *Eur J Radiol*. 2017;90:138–145.
- Miyake KK, Matsumoto K, Inoue M, et al. Performance evaluation of a new dedicated breast PET scanner using NEMA NU4-2008 standards. *J Nucl Med*. 2014;55:1198–1203.
- MacDonald LR, Hunter WC, Kinahan PE, Miyaoka RS. Effects of detector thickness on geometric sensitivity and event positioning errors in the rectangular PET/X scanner. *IEEE Trans Nucl Sci*. 2013;60:3242–3252.
- Moliner L, Gonzalez AJ, Soriano A, et al. Design and evaluation of the MAMMI dedicated breast PET. *Med Phys*. 2012;39:5393–5404.
- Iima M, Nakamoto Y, Kanao S, et al. Clinical performance of 2 dedicated PET scanners for breast imaging: initial evaluation. *J Nucl Med*. 2012;53:1534–1542.
- Brem RF, Schoonjans JM, Kieper DA, Majewski S, Goodman S, Civelek C. High-resolution scintimammography: a pilot study. *J Nucl Med*. 2002;43:909–915.
- Steinbach D, Cherry S, Doshi N, et al. Small scintimammography detector based on a 5 inches PSPMT and a crystal scintillator array. *IEEE Nucl Sci Symp Conf Rec*. 1997;2:1255–1259.
- Pani R, De Vincentis G, Scopinaro F, et al. Dedicated gamma camera for single photon emission mammography (SPEM). *IEEE Nucl Sci Symp Conf Rec*. 1997;2:1615–1619.
- Brzymalkiewicz CN, Tornai MP, McKinley RL, Bowsher JE. Evaluation of fully 3-D emission mammatomography with a compact cadmium zinc telluride detector. *IEEE Trans Med Imaging*. 2005;24:868–877.
- Steinbach D, Majewski S, Williams M, Kross B, Weisenberger AG, Wojcik R. Development of a small field of view scintimammography camera based on a YAP crystal array and a position sensitive PMT. *IEEE Nucl Sci Symp Conf Rec*. 1996;2:1251–1256.
- Weigert JM, Bertrand ML, Lanzkowsky L, Stern LH, Kieper DA. Results of a multicenter patient registry to determine the clinical impact of breast-specific gamma imaging, a molecular breast imaging technique. *AJR Am J Roentgenol*. 2012;198:W69–W75.
- Boone JM, Nelson TR, Lindfors KK, Seibert JA. Dedicated breast CT: radiation dose and image quality evaluation. *Radiology*. 2001;221:657–667.
- Sarno A, Mettievier G, Russo P. Dedicated breast computed tomography: basic aspects. *Med Phys*. 2015;42:2786–2804.
- Sarno A, Mettievier G, Di Lillo F, Cesarelli M, Bifulco P, Russo P. Cone-beam micro computed tomography dedicated to the breast. *Med Eng Phys*. 2016;38:1449–1457.

32. Kalender WA, Kolditz D, Steiding C, et al. Technical feasibility proof for high-resolution low-dose photon-counting CT of the breast. *Eur Radiol.* 2017;27:1081–1086.
33. Shah JP, Mann SD, McKinley RL, Tornai MP. Three dimensional dose distribution comparison of simple and complex acquisition trajectories in dedicated breast CT. *Med Phys.* 2015;42:4497–4510.
34. Chen B, Ning R. Cone-beam volume CT breast imaging: feasibility study. *Med Phys.* 2002;29:755–770.
35. Sarno A, Mettievier G, Golosio B, et al. Imaging performance of phase-contrast breast computed tomography with synchrotron radiation and a CdTe photon-counting detector. *Phys Med.* 2016;32:681–690.
36. Willner M, Herzen J, Grandl S, et al. Quantitative breast tissue characterization using grating-based x-ray phase-contrast imaging. *Phys Med Biol.* 2014;59:1557–1571.
37. Wu Y, Bowen SL, Yang K, et al. PET characteristics of a dedicated breast PET/CT scanner prototype. *Phys Med Biol.* 2009;54:4273–4287.
38. Bowen SL, Wu Y, Chaudhari AJ, et al. Initial characterization of a dedicated breast PET/CT scanner during human imaging. *J Nucl Med.* 2009;50:1401–1408.
39. Raylman RR, Majewski S, Smith MJ, et al. The positron emission mammography/tomography breast imaging and biopsy system (PEM/PET): design, construction and phantom-based measurements. *Phys Med Biol.* 2008;53:637–653.
40. Raylman RR, Abraham J, Hazard H, et al. Initial clinical test of a breast-PET scanner. *J Med Imaging Radiat Oncol.* 2011;55:58–64.
41. Popov V, Majewski S, Weisenberger AG. Readout electronics for multi-anode photomultiplier tubes with pad matrix anode layout. *IEEE Nucl Sci Symp Conf Rec.* 2004;3:2156–2159.
42. Raylman RR, Vaigneur K, Stolin AV, Jaliparthi G. Arrays of segmented, tapered light guides for use with large, planar scintillation detectors. *IEEE Trans Nucl Sci.* 2015;62:694–698.
43. Smith MF, Majewski S, Raylman RR. Fully 3D iterative list-mode PEM-PET image reconstruction on a multiprocessor computer. Proceedings of the 9th International Meeting on Fully Three-Dimensional Image Reconstruction in Radiology and Nuclear Medicine. Lindau, Germany, July 9–13, 2007; pp. 64–67.
44. National Electrical Manufacturers Association. 2008. *NEMA Standard Publication NU 4-2008: Performance Measurements of Small Animal Positron Emission Tomographs*. Rosslyn, VA: National Electrical Manufacturers Association.
45. Ollinger JM. Model-based scatter correction for fully 3D PET. *Phys Med Biol.* 1996;41:153–176.
46. Zhang G, Marshall N, Jacobs R, Liu Q, Bosmans H. Bowtie filtration for dedicated cone beam CT of the head and neck: a simulation study. *Br J Radiol.* 2013;1028:20130002.
47. Kwan AL, Boone JM, Shah N. Evaluation of x-ray scatter properties in a dedicated cone-beam breast CT scanner. *Med Phys.* 2005;32:2967–2975.
48. Boone JM, Shah N, Nelson TR. A comprehensive analysis of DgN(CT) coefficients for pendant-geometry cone-beam breast computed tomography. *Med Phys.* 2004;31:226–235.
49. Smith MF, Raylman RR, Majewski S, Weisenberger AG. Positron emission mammography with tomographic acquisition using dual planar detectors: initial evaluations. *Phys Med Biol.* 2004;49:2437–2452.
50. Visvikis D, Costa DC, Croasdale I, et al. CT-based attenuation correction in the calculation of semi-quantitative indices of [¹⁸F]FDG uptake in PET. *Eur J Nucl Med Mol Imaging.* 2003;30:344–353.
51. Loening AM, Gambhir SS. AMIDE: a free software tool for multimodality medical image analysis. *Mol Imaging.* 2003;2:131–137.
52. AAPM Task Group 23. *Report No. 96: CT Dosimetry. The measurement, reporting and management of radiation dose in CT*; 2008.
53. Raylman RR, Smith MF, Kinahan PE, Majewski S. Quantification of radiotracer uptake with a dedicated breast PET imaging system. *Med Phys.* 2008;35:4989–4997.
54. Bowen SL, Ferrero A, Badawi RD. Quantification with a dedicated breast PET/CT scanner. *Med Phys.* 2012;39:2694–2707.
55. Goertzen AL, Bao Q, Bergeron M, et al. NEMA NU 4-2008 comparison of pre-clinical PET imaging systems. *J Nucl Med.* 2012;53:1300–1309.
56. Gazi PM, Yang K, Burkett GW Jr, Aminololama-Shakeri S, Seibert JA, Boone JM. Evolution of spatial resolution in breast CT at UC Davis. *Med Phys.* 2015;42:1973–1981.
57. O'Connell A, Conover DL, Zhang Y, et al. Cone-beam CT for breast imaging: radiation dose, breast coverage, and image quality. *AJR Am J Roentgenol.* 2010;195:496–509.