Breast cancer accounts for the majority of new cancers diagnosed and cancer deaths for women worldwide (1). Breast cancer was recently estimated to account for 24% (2,088,849 of 8,622,539) of new cancers diagnosed and 15% (626,679 of 4,169,387) of cancer deaths in women across 185 countries (1). In the United States, 30% (276,480 of 912,930) of new cancers diagnosed and 15% (42,170 of 285,360) of cancer deaths in women are estimated to be caused by breast cancer in 2020 (2).

Molecular imaging provides a noninvasive method for detecting and providing functional characterization of breast cancer. The most commonly used molecular imaging agent for oncology is fluorine 18 fluorodeoxyglucose (18F-FDG) that accumulates within tissues with high glucose metabolism. 18F-FDG PET/CT whole-body imaging can be used for identifying distant metastases in patients with newly diagnosed locally advanced and inflammatory breast cancer (3,4), for restaging patients with suspected recurrence (5), and for monitoring treatment response for patients with locally advanced and metastatic breast cancer (6,7).

Contrast-enhanced MRI of the breasts produces high-spatial-resolution images to anatomically characterize tumor morphology and functionally assess lesion perfusion, characterized by the time-dependent uptake and washout of gadolinium-based contrast agents (8,9). Breast MRI is the most sensitive method for breast cancer detection and is used clinically as a supplemental screening tool for women at increased lifetime risk of breast cancer development, preoperative staging for women with newly diagnosed breast cancer, and assessment of response to neoadjuvant therapy (10).

There is increasing interest in combining high-spatial-resolution anatomic and perfusion information obtained...
Glucose Uptake in Primary Invasive Breast Cancer

Abbreviations

ER = estrogen receptor, \(^{18}\)F-FDG = fluorine 18 fluordeoxyglucose, LoA = limits of agreement, normSUV\(_{max}\) = tumor SUV\(_{max}\) normalized to normal breast SUV\(_{max}\), normSUV\(_{mean}\) = tumor SUV\(_{mean}\) normalized to normal breast SUV\(_{mean}\), SUV\(_{max}\) = maximum standardized uptake value, SUV\(_{mean}\) = mean standardized uptake value

Summary
Measurement agreement of the glucose uptake in primary invasive breast cancer was demonstrated between PET/CT, the current reference standard, and simultaneous time-of-flight breast fluorine 18 fluordeoxyglucose PET/MRI.

Key Points
- Correlation between fluorine 18 fluordeoxyglucose tumor uptake values measured with breast PET/MRI and PET/CT was strong (\(r = 0.95\)–0.98).
- No difference existed between breast PET/MRI and PET/CT for tumor maximum standardized uptake value (SUV\(_{max}\)) normalized to normal breast tissue SUV\(_{max}\) (normSUV\(_{max}\): 6.3 ± 1.0 vs 6.3 ± 1.1, respectively; \(P = .58\)).
- The least amount of measurement bias between breast PET/MRI and PET/CT was observed with normSUV\(_{max}\) (+3.86%; 95% limits of agreement: −28.92, +36.64).
- Comparable results between 10-minute and 30-minute image acquisition times indicate that simultaneous breast PET/abbreviated MRI is also feasible.

using MRI with functional metabolic information obtained from PET for a more comprehensive analysis of breast lesions. Historically, this has been performed by coregistration of images acquired separately from a dynamic contrast-enhanced breast MRI and a PET/CT performed in the prone position (11–15). With the advent of combined PET/MRI scanners, breast PET/MRI can now be performed in a single imaging session (16–20). Depending on the scanner design, the acquisition of PET and MRI data occurs either sequentially or simultaneously. Multichannel radiofrequency coils have been designed specifically for breast PET/MRI to limit attenuation, which is important for accurate quantification of radiopharmaceutical uptake (21–23).

The clinical utility of breast PET/MRI for diagnosis and local-regional staging of breast cancer has been studied using subjective, visual assessment of \(^{18}\)F-FDG uptake (19,24–26). Results from recent small studies suggest that multiparametric breast PET/MRI with \(^{18}\)F-FDG may have an advantage for predicting therapy response compared with either modality alone (27–30). Therapy response assessment is an established clinical application of PET/CT, and substantial efforts have been invested to standardize its use to measure quantitative imaging biomarkers for oncologic treatment response through national initiatives such as the Quantitative Imaging Biomarkers Alliance (31). Given the fundamentally different attenuation methods between PET/CT and PET/MRI (32), it is important to verify semiquantitative radiopharmaceutical uptake parameters between these two modalities if intended to be used to assess therapy response. Previous studies were performed with patients positioned supine without a dedicated breast radiofrequency coil using an avalanche photodiode-based PET/MRI scanner without time-of-flight capability, which are major quantitative limitations (33–38). A newer simultaneous PET/MRI scanner is now clinically available which uses silicon photomultipliers with time-of-flight capability, which offers increased PET sensitivity as well as the potential for dose reduction of \(^{18}\)F-FDG (18,39).

The future success of breast PET/MRI implementation for therapy response assessment hinges on establishing its quantitative accuracy for measuring radiopharmaceutical uptake.

The overall goal of this research was to develop and test a simultaneous, time-of-flight PET/MRI acquisition protocol specific for breast imaging and quantitative evaluation of primary breast cancer. We hypothesized that semiquantitative assessment of tumor glycolytic activity using simultaneous breast PET/MRI would be feasible and comparable to that of prone PET/CT using harmonized PET reconstruction parameters. The purpose of this method comparison study was to compare tumor uptake of \(^{18}\)F-FDG measured with simultaneous, time-of-flight breast PET/MRI with uptake obtained with prone time-of-flight PET/CT in participants with newly diagnosed primary invasive breast cancer.

Materials and Methods

Study Design
This Health Insurance Portability and Accountability Act–compliant, institutional review board–approved (#2015–0563) single-institution, prospective study was performed from January 2016 to August 2018 via convenience sampling. Women 18 years of age or older with biopsy-proven invasive breast cancer undergoing preoperative breast MRI were eligible. There are no established guidelines for patient selection criteria for use of preoperative breast MRI; however, surgeons at our institution are more likely to order breast MRI for women younger than 50 years of age at diagnosis, with invasive lobular carcinoma, with mammographically dense breasts, and with mammographically occult breast cancer. Participants who were pregnant, lactating, had breast implants, underwent surgical excision or neoadjuvant therapy for the current breast cancer, had a body habitus that exceeded the bore of the PET/MRI scanner (body mass index greater than 36 kg/m\(^2\)), or had contraindications to MRI were not eligible. Eligible participants identified through screening were approached for study enrollment. There were 44 eligible women contacted who declined participation. A total of 23 eligible women provided written informed consent and were included in the study. None of the eligible participants who consented to the study were excluded from analysis. Participant demographics, tumor histologic and pathologic subtype, and clinical information were obtained from the electronic medical record. As indicated by the fifth edition of the American College of Radiology Breast Imaging Reporting and Data System Atlas (40), scheduling preoperative breast MRI for patients with newly diagnosed breast cancer does not require menstrual cycle timing, and thus, menstrual cycle information was not obtained.

Imaging Protocol
The single-injection, dual-imaging protocol is illustrated in Figure 1. For all participants, the sequence of imaging was
standardized with PET/CT performed first followed by PET/MRI. The Discovery PET/CT 710 (GE Healthcare) and Signa PET/MR (GE Healthcare) scanners were used for this study. The Discovery 710 system is composed of a PET component with lutetium-based scintillator crystals and conventional photomultiplier tubes with time-of-flight capability and a 64-section CT (41). The Signa PET/MRI system is composed of lutetium-based scintillator crystals and solid-state silicon pho-

tomultipliers with time-of-flight capability integrated within a wide-bore 3.0-T MRI scanner (18).

After fasting for at least 6 hours, women underwent PET/CT of the breasts without intravenous contrast material 55 minutes ± 4.9 (standard deviation) (range, 46–66 minutes) after injection of an average of 381.1 MBq (range, 321.9–425.5 MBq; 10.3 mCi, range, 8.7–11.5 mCi) of 18F-FDG (SOFIE). Blood glucose levels were 90 mg/dL ± 10.4 (range, 75–109 mg/dL). Average body mass index was 28.8 kg/m² (range, 21.9–35.8 kg/m²). Women were scanned prone at one bed position centered at the level of the breasts for 10 minutes using a modified breast MRI coil housing with metal components removed to replicate positioning between the PET/CT and PET/MRI scanners (Figure E1 [supplement]). A low-dose CT scan was obtained for attenuation

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**Table 1: Participant and Lesion Characteristics**

| Participant No. | Age (y) | Lesion Size (cm) | Histologic Subtype | Grade | ER | PR | HER2 |
|-----------------|---------|------------------|--------------------|-------|----|----|------|
| 1               | 51      | 3.6              | Invasive mucinous carcinoma | 1     | Positive | Positive | Negative |
| 2               | 45      | 8.6              | IDC                | 2     | Negative | Negative | Negative |
| 3               | 48      | 4                | ILC                | 1     | Positive | Positive | Negative |
| 4               | 62      | 2.4              | IDC                | 2     | Positive | Positive | Negative |
| 5               | 59      | 2.8              | IDC                | 2     | Positive | Positive | Negative |
|                 |         | 1.7              | IDC                | 2     | Positive | Positive | Negative |
| 6               | 50      | 8.8              | IDC                | 3     | Negative | Negative | Positive |
| 7               | 36      | 3.5              | IDC                | 3     | Positive | Positive | Positive |
| 8               | 38      | 4.4              | IDC                | 3     | Positive | Positive | Negative |
| 9               | 59      | 2.9              | IDC                | 3     | Positive | Positive | Negative |
| 10              | 68      | 2.6              | IDC                | 2     | Positive | Positive | Negative |
| 11              | 65      | 1.1              | IDC                | 1     | Positive | Positive | Negative |
| 12              | 52      | 3.4              | IMC w/lobular      | 1     | Positive | Positive | Negative |
| 13              | 38      | 6.8              | ILC                | 1     | Positive | Positive | Negative |
| 14              | 33      | 6.9              | IDC                | 3     | Positive | Positive | Positive |
| 15              | 49      | 1.8              | ILC                | 2     | Positive | Positive | Negative |
| 16              | 47      | 4.8              | IDC                | 2     | Positive | Positive | Negative |
| 17              | 43      | 2.8              | IDC                | 2     | Positive | Positive | Negative |
| 18              | 43      | 1.6              | IDC                | 2     | Negative | Negative | Positive |
| 19              | 60      | 1.8              | IDC                | 1     | Positive | Positive | Negative |
| 20              | 41      | 2                | IDC                | 3     | Positive | Positive | Negative |
| 21              | 49      | 4.5              | ILC                | 2     | Positive | Positive | Negative |
| 22              | 70      | 1.7              | ILC                | 2     | Positive | Positive | Negative |
| 23              | 35      | 7                | ILC                | 2     | Positive | Positive | Negative |

Note.—Lesion size is the longest dimension measured by using MRI. ER = estrogen receptor, HER2 = human epidermal growth factor receptor 2, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, IMC = invasive mammary carcinoma, PR = progesterone receptor.
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**PET/CT**

PET/CT images of a patient with high-grade invasive ductal carcinoma (IDC) showing axial images from the same patient as in Figure 2. Axial images from participant 9 (Table 1) who was a 59-year-old woman with grade 3 IDC (estrogen receptor–positive, progesterone receptor–positive, and human epidermal growth factor receptor 2–negative) measuring 2.9 cm in the right breast (arrow). The PET/CT tumor maximum standardized uptake value (SUV max) was 6.73, tumor mean standardized uptake value (SUV mean) was 4.11, and normal breast SUV mean was 0.88. The PET/CT tumor SUV max was 6.11, tumor SUV mean was 3.04, and normal breast SUV mean was 0.70. The sequence shown for MRI is the early-phase postcontrast T1-weighted fat-suppressed fast spoiled gradient-echo images.

**PET/MRI**

PET/MRI images of the same patient as in Figure 2, showing axial images from the same participant as in PET/CT. Axial images from participant 9 (Table 1) who was a 59-year-old woman with grade 3 IDC (estrogen receptor–positive, progesterone receptor–positive, and human epidermal growth factor receptor 2–negative) measuring 2.9 cm in the right breast (arrow). The PET/MRI tumor maximum standardized uptake value (SUV max) was 6.73, tumor mean standardized uptake value (SUV mean) was 4.11, and normal breast SUV mean was 0.88. The PET/CT tumor SUV max was 6.11, tumor SUV mean was 3.04, and normal breast SUV mean was 0.70. The sequence shown for MRI is the early-phase postcontrast T1-weighted fat-suppressed fast spoiled gradient-echo images.

**PET**

PET images of the same patient as in Figure 2, showing axial images from the same participant as in PET/CT. Axial images from participant 9 (Table 1) who was a 59-year-old woman with grade 3 IDC (estrogen receptor–positive, progesterone receptor–positive, and human epidermal growth factor receptor 2–negative) measuring 2.9 cm in the right breast (arrow). The PET/MRI tumor maximum standardized uptake value (SUV max) was 6.73, tumor mean standardized uptake value (SUV mean) was 4.11, and normal breast SUV mean was 0.88. The PET/CT tumor SUV max was 6.11, tumor SUV mean was 3.04, and normal breast SUV mean was 0.70. The sequence shown for MRI is the early-phase postcontrast T1-weighted fat-suppressed fast spoiled gradient-echo images.

**Fused**

Fused PET/MRI images of the same patient as in Figure 2, showing axial images from the same participant as in PET/CT. Axial images from participant 9 (Table 1) who was a 59-year-old woman with grade 3 IDC (estrogen receptor–positive, progesterone receptor–positive, and human epidermal growth factor receptor 2–negative) measuring 2.9 cm in the right breast (arrow). The PET/MRI tumor maximum standardized uptake value (SUV max) was 6.73, tumor mean standardized uptake value (SUV mean) was 4.11, and normal breast SUV mean was 0.88. The PET/CT tumor SUV max was 6.11, tumor SUV mean was 3.04, and normal breast SUV mean was 0.70. The sequence shown for MRI is the early-phase postcontrast T1-weighted fat-suppressed fast spoiled gradient-echo images.

Women subsequently underwent breast PET/MRI using an eight-channel breast coil (GE Healthcare) 83 minutes ± 8 (range, 75–113 minutes) after injection of 18F-FDG. A standard prone clinical breast MRI examination was performed, including axial precontrast three-plane localizer, two-dimensional T2-weighted fat-suppressed fast spin-echo, and diffusion-weighted imaging. Axial T1-weighted fat-suppressed fast spoiled gradient-echo images prior to and three times after the administration of intravenous gadolinium-based contrast agent (gadobenate dimeglumine; 0.1 mmol/kg; MultiHance; Bracco Diagnostics) power injected at 2 mL/min were obtained. MRI sequences were performed simultaneously with PET data acquisition for 30 minutes. Precontrast Dixon-based fat and water images were obtained for MR attenuation correction using the following: 5° flip angle, echo times of 1.1 and 2.2 msec, repetition time of 4.0 msec, and a bandwidth of ±167 kHz. Data were acquired over a 50 × 50 × 33 cm³ field of view with a 256 × 128 × 64 matrix size. All MR attenuation correction data were reviewed by an experienced medical
Image Assessment

For all women, the biopsy-proven malignancy contained a marker clip to confirm tumor location. For tumor SUV measurements, volumes of interest were drawn with an isocontour using a threshold of 30% of the lesion’s SUV$_{\text{max}}$ (Mirada Medical XD3 v3.6). For normal breast tissue SUV, a 1-cm$^3$ spherical volume of interest was applied in the normal fibroglandular tissue of the contralateral breast. A board-certified radiologist (A.M.F.) with 7 years of experience in breast imaging and molecular imaging performed the measurements on the images from the PET/CT and the 0–30-minute reconstructed PET/MRI. Volumes of interest were propagated automatically from the 0–30-minute reconstructed PET/MRI data set to the 0–10-minute reconstructed PET/MRI data set.
Table 2: Comparison of 18F-FDG Uptake Parameters with Tumor Characteristics

| Parameter       | PET/MRI | PET/CT | PET/MRI | PET/CT |
|-----------------|---------|--------|---------|--------|
|                 | SUV\textsubscript{max} | SUV\textsubscript{mean} | SUV\textsubscript{max} | SUV\textsubscript{mean} | normSUV\textsubscript{max} | normSUV\textsubscript{mean} | normSUV\textsubscript{max} | normSUV\textsubscript{mean} |
| ER Positive     | 7.9 ± 1.4 | 4.5 ± 0.8 | 6.9 ± 1.1 | 3.5 ± 0.6 | 6.1 ± 1.1 | 3.5 ± 0.6 | 6.1 ± 1.3 | 3.1 ± 0.7 |
| P value         | .27     | .23    | .20     | .27    | .17    | .40    | .20    | .35    |
| Subtype         |         |        |         |        |        |        |        |        |
| IDC             | 10.2 ± 1.8 | 5.8 ± 1.0 | 8.6 ± 1.4 | 4.4 ± 0.7 | 7.3 ± 1.3 | 4.2 ± 0.8 | 7.3 ± 1.5 | 3.8 ± 0.8 |
| ILC             | 5.9 ± 1.5 | 3.1 ± 0.9 | 5.0 ± 1.4 | 3.5 ± 1.3 | 4.8 ± 1.6 | 2.6 ± 1.0 | 4.9 ± 2.1 | 2.4 ± 1.1 |
| P value         | .26     | .18    | .18     | .34    | .20    | .18    | .23    | .18    |
| Grade           |         |        |         |        |        |        |        |        |
| 1 and 2         | 6.5 ± 1.2 | 3.7 ± 0.7 | 5.6 ± 0.9 | 3.1 ± 0.6 | 4.7 ± 0.8 | 2.7 ± 0.5 | 4.7 ± 0.9 | 2.3 ± 0.5 |
| 3               | 14.5 ± 3.0 | 8.1 ± 1.7 | 12.5 ± 2.3 | 6.5 ± 1.3 | 11.1 ± 2.5 | 6.2 ± 1.4 | 10.9 ± 3.1 | 5.7 ± 1.8 |
| P value         | .007    | .01    | .003    | .02    | .004   | .004   | .009   | .01    |

Note.—Unless otherwise indicated, data are means ± standard error. Mann-Whitney unpaired t tests were performed to determine statistical differences. PET/MRI data were based on 0–10-minute reconstructions. ER = estrogen receptor, 18F-FDG = fluorine 18 fluorodeoxyglucose, IDC = invasive ductal carcinoma, ILC = invasive lobular carcinoma, normSUV\textsubscript{max} = tumor SUV\textsubscript{max} normalized to normal breast SUV\textsubscript{mean}, normSUV\textsubscript{mean} = tumor SUV\textsubscript{mean} normalized to normal breast SUV\textsubscript{mean}, SUV\textsubscript{max} = maximum standardized uptake value, SUV\textsubscript{mean} = mean standardized uptake value.

Table 3: Comparison of 18F-FDG Uptake Measured Using 0–10 Minute Versus 0–30 Minute Reconstructed PET/MRI Data

| Parameter       | 0–10 Minute Data | 0–30 Minute Data | P Value |
|-----------------|------------------|------------------|--------|
| Tumor           |                  |                  |        |
| SUV\textsubscript{max} | 8.5 ± 1.3 | 8.6 ± 1.3 | .19    |
| SUV\textsubscript{mean} | 4.8 ± 0.8 | 4.9 ± 0.8 | .09    |
| Normal breast   |                  |                  |        |
| SUV\textsubscript{mean} | 1.4 ± 0.09 | 1.4 ± 0.09 | .10    |
| Normalized      |                  |                  |        |
| normSUV\textsubscript{max} | 6.3 ± 1.0 | 6.4 ± 1.0 | .10    |
| normSUV\textsubscript{mean} | 3.6 ± 0.6 | 3.7 ± 0.6 | .03    |

Note.—Unless otherwise indicated, data are means ± standard error. Wilcoxon signed rank test was performed to determine statistical differences. 18F-FDG = fluorine 18 fluorodeoxyglucose, normSUV\textsubscript{max} = tumor SUV\textsubscript{max} normalized to normal breast SUV\textsubscript{mean}, normSUV\textsubscript{mean} = tumor SUV\textsubscript{mean} normalized to normal breast SUV\textsubscript{mean}, SUV\textsubscript{max} = maximum standardized uptake value, SUV\textsubscript{mean} = mean standardized uptake value.

Statistical Analysis
A sample size of 23 was chosen a priori based on the expectation that the lower limit for a one-sided 95% CI for the Pearson correlation coefficient will exceed 0.80 when the correlation estimate is 0.90 (42). Sample size calculations were performed using PASS 13 (NCSS, Kaysville, Utah). Continuous measurements are represented as mean ± standard error. Corresponding median and range values are included in Table E1 (supplement) and Table E2 (supplement). Bland-Altman analysis was performed to determine measurement bias and 95% limits of agreement (LoA) (43,44). Comparisons between PET/MRI and PET/CT 18F-FDG uptake values were analyzed using Spearman rank correlation and Wilcoxon signed rank test. The Mann-Whitney test was used to analyze the association of 18F-FDG uptake parameters with tumor characteristics including histologic subtype (invasive ductal carcinoma vs invasive lobular carcinoma), grade (1 and 2 vs 3), and estrogen receptor (ER) status (positive vs negative). P values less than .05 were considered significant. Statistical analyses were performed using Prism 6.04 (GraphPad Software, San Diego, Calif) and SPSS Statistics version 25 (IBM, Armonk, NY).

Results

Study Population Characteristics
Twenty-three women (mean age, 50 years; range, 33–70 years) with 24 separate biopsy-proven sites of invasive breast carcinoma participated in the study and all completed both the PET/CT and PET/MRI examinations, meeting the pre-designated sample size. Pathologic findings included 16 invasive ductal carcinomas, six invasive lobular carcinomas, one invasive mammary carcinoma with lobular features, and one invasive mucinous carcinoma (Table 1). Most tumors were histologic grades 1 or 2 (18 of 24; 75%) and were ER positive, progesterone receptor positive, and human epidermal growth factor receptor 2 negative (19 of 24, 79%). The average lesion size was 3.8 cm (range, 1.1–8.8 cm) measured with MRI.
Imaging Examination Quality

All examinations were performed once without the need for any technical repeat examinations. No substantial imaging artifacts were observed. Representative examples demonstrating the imaging examination quality and reproducibility in participant positioning between PET/CT and PET/MRI examinations are included in Figures 2 and 3. Visual 18F-FDG uptake was identified for all biopsy-proven malignant lesions, including a small (1.1-cm), grade 1, ER-positive, progesterone receptor–positive, and human epidermal growth factor receptor 2–negative invasive ductal carcinoma (Fig 3).

Association of ER Status, Histologic Subtype, and Tumor Grade with 18F-FDG Uptake

18F-FDG uptake parameters were higher in grade 3 tumors compared with grade 1 and 2 tumors for both modalities (Table 2). Higher 18F-FDG uptake in ER-negative tumors compared with ER-positive tumors as well as higher 18F-FDG uptake in invasive ductal carcinoma compared with invasive lobular carcinoma in both modalities were observed; however, the differences were not statistically significant (Table 2).

Figure 4: Comparison of tumor fluorine 18 fluorodeoxyglucose (18F-FDG) uptake using breast PET/MRI versus prone PET/CT. Scatterplots for PET/MRI versus PET/CT and line of identity for, A, tumor maximum standardized uptake value [SUV$_{\text{max}}$]; B, tumor mean standardized uptake value [SUV$_{\text{mean}}$]; C, tumor SUV$_{\text{max}}$ normalized to normal breast SUV$_{\text{mean}}$ (normSUV$_{\text{max}}$); and, D, tumor SUV$_{\text{mean}}$ normalized to normal breast SUV$_{\text{mean}}$ (normSUV$_{\text{mean}}$). Spearman rank correlation ($r_s$) with 95% CIs; P < .001 for all.
Glucose Uptake in Primary Invasive Breast Cancer

Measurement Agreement of Tumor ^18^F-FDG Uptake between PET/ MRI and PET/ CT

As defined by Bland-Altman analysis, measurement bias for PET/MRI versus PET/CT was +1.12 (95% LoA: −1.98, +4.22) for tumor SUV max, +1.14 (95% LoA: −1.28, +3.56) for tumor SUV mean, +0.04 (95% LoA: −3.37, +3.44) for the normSUV max, and +0.37 (95% LoA: −1.51, +2.25) for tumor SUV mean normalized to normal breast SUV mean (normSUV mean) (Fig 5). Measurement bias as a percentage for PET/MRI versus PET/CT was +11.13% (95% LoA: −16.96%, +39.23%) for tumor SUV max, +24.75% (95% LoA: −6.96%, +56.47%) for tumor SUV mean, +3.86% (95% LoA: −28.92%, +36.64%) for normSUV max, and +15.69% (95% LoA: −17.33%, +48.70%) for normSUV mean (Fig 5). Thus, normSUV max was the uptake parameter with the least amount of measurement bias.

Discussion

The purpose of this study was to develop and test a simultaneous, time-of-flight PET/MRI acquisition protocol specific for breast imaging by comparing tumor ^18^F-FDG uptake parameters measured with prone breast PET/MRI to prone PET/CT in participants with newly diagnosed primary invasive breast cancer. Strong correlation was demonstrated between tumor uptake values measured with PET/MRI and PET/CT (r = 0.95–0.98). We observed slightly higher tumor SUV max, SUV mean, and normSUV mean ^18^F-FDG uptake measured by PET/ MRI compared with PET/CT. There was no significant difference between modalities for normSUV max. The best agreement between PET/MRI and PET/CT measurements was observed with normSUV max ^18^F-FDG uptake.

Studies comparing the diagnostic performance of conventional supine, whole-body PET/MRI with PET/CT for staging and restaging have shown that PET/MRI performs as well as PET/CT for most malignancies, including breast cancer (45). Additional research focused on semiquantitative analyses of tumor glucose uptake has generally found good correlation between the two modalities; however, several publications have reported statistically significant quantitative differences. Our results with breast PET/MRI were similar to the study published by Al-Nabhani et al which showed that tumor SUV mean was 10% higher with whole-body PET/MRI compared with PET/CT (P < .01) (34). In contrast, other studies have reported higher tumor uptake values measured with PET/CT compared with whole-body PET/MRI. The study published by Drzega et al included 32 patients, three with breast cancer, and reported higher lesion SUV mean values with PET/CT compared with whole-body PET/MRI (P < .01) (33). Results published by Wiesmüller et al showed that ^18^F-FDG SUV max and SUV mean of 94 lesions were 22% and 10% lower, respectively, at whole-body PET/MRI compared with PET/CT (P < .01) in their study of 46 patients, three with breast cancer (35). No significant differences in SUV max, SUV mean, or metabolic tumor volume between whole-body PET/MRI and PET/CT were found in the 25 primary breast cancers analyzed by Pace et al (36). Similarly, no significant difference in SUV max (P = .15) or SUV mean (P = .07) between whole-body PET/MRI and PET/CT were found in 31 breast cancer metastases in a study by Pujara et al (37). A study published by Groshar et al, which included 33 patients, 12 with breast cancer, found +7%, +13.9%, and +8.3% mean difference in SUV max, SUV peak, and SUV mean, respectively, when comparing PET/CT with whole-body PET/MRI values using Bland-Altman analysis (38).

With the exception of Groshar et al, who randomized the imaging examination order, all of the prior studies were designed with the PET/CT acquisition first followed by PET/MRI. This scan order would be expected to result in increased uptake values measured with PET/MRI because of the longer time for ^18^F-FDG accumulation in malignancies (46–49). However, this result was not consistently observed in these prior publications.

| Parameter | PET/MRI | PET/CT | P Value |
|-----------|---------|--------|---------|
| Tumor     |         |        |         |
| SUV max   | 8.5 ± 1.3 | 7.3 ± 1.1 | <.001  |
| SUV mean  | 4.8 ± 0.8 | 3.7 ± 0.6 | <.001  |
| Normal breast |       |        |         |
| SUV max   | 1.4 ± 0.09 | 1.3 ± 0.09 | .02    |
| Normalized |        |        |         |
| normSUV max | 6.3 ± 1.0 | 6.3 ± 1.1 | .58    |
| normSUV mean | 3.6 ± 0.6 | 3.2 ± 0.6 | .005   |

Note.—Unless otherwise indicated, data are means ± standard error. PET/MRI data were based on 0–10-minute reconstructions. Wilcoxon signed rank test was performed to determine statistical differences. ^18^F-FDG = fluorine 18 fluorodeoxyglucose, normSUV max = tumor SUV max normalized to normal breast SUV max, normSUV mean = tumor SUV mean normalized to normal breast SUV mean. SUV max max = maximum standardized uptake value, SUV mean = mean standardized uptake value.
implying that contributing factors beyond scan order and/or uptake time exist. Furthermore, these previous studies used first-generation avalanche photodiode PET detectors without time-of-flight capability and did not use a dedicated breast radiofrequency coil which may contribute to the differences observed with our study.

We found that the $^{18}$F-FDG uptake parameter with the least amount of measurement bias (+3.86%) between the two modalities was norm-SUV$_{\text{max}}$. Furthermore, the 95% LoA values were $-28.92\%$ and $+36.64\%$, which were the closest to clinically acceptable limits of $\pm 30\%$ based on the PET Response Criteria in Solid Tumors definition for partial response and progressive disease (50). Thus, breast PET/MRI seems to provide an acceptable approximation of tumor glucose uptake as that of PET/CT, the current reference standard. This result raises the possibility that simultaneous breast PET/MRI could be used interchangeably with prone PET/CT for tumor uptake quantification when using norm-SUV$_{\text{max}}$ and harmonized PET image reconstruction parameters.

With the exception of norm-SUV$_{\text{mean}}$, our results showed no significant difference in tumor $^{18}$F-FDG uptake parameters using data from the first 10 minutes of the breast PET/MRI examination compared with data from the full 30-minute examination. In addition to facilitating a more direct comparison of the PET/MRI data with the 10-minute PET/CT examination, this finding has two important practical implications. First, this implies that the injected dose of $^{18}$F-FDG could be reduced which would decrease the overall radiation exposure to the patient. In a study of 26 women with breast cancer who underwent a breast PET/MRI examination using the Signa scanner also used in this study, Sah et al found that a simulated dose reduction of up to 90% resulted in clinically acceptable subjective PET image quality (39). They estimated that a 90% administered dose reduction would result in approximately 0.45-mSv effective dose equivalent radiation exposure for an average patient weighing 75 kg, which is comparable to the 0.44-mSv average effective dose of a digital mammographic examination (51). Second, there is increasing interest in shortening the length of clinical breast MRI examinations. Our data suggest that a 10-minute PET acquisition could be feasibly combined with an abbreviated breast MRI protocol.

The study had some limitations. There was potential selection bias because not all patients with newly diagnosed breast cancer undergo preoperative breast MRI at our institution. Also, participants with large body mass index were not eligible for the study because of limitations in the scanner bore diameter (60 cm). With clinical scheduling constraints beyond our control, the scan order was not randomized which resulted in slightly different $^{18}$F-FDG uptake times (approximately 15 minutes). This effect was minimized by...
directly comparing the first 10-minute acquisition time of the breast PET/MRI with the 10-minute PET/CT examination. To avoid partial volume effects on SUV quantification, participants with tumors smaller than 1 cm were not eligible, which resulted in relatively large tumor sizes in the study cohort.

The results of this work demonstrate that semiquantitative assessment of $^{18}$F-FDG uptake of primary invasive breast carcinoma using simultaneous breast PET/MRI provides an acceptable approximation of tumor glucose uptake as does PET/CT, the current reference standard. Measurement differences were minimized between tumor $^{18}$F-FDG uptake using breast PET/MRI and prone PET/CT when normalized to normal breast tissue uptake. Establishing the measurement agreement between PET/CT and simultaneous breast PET/MRI for tumor $^{18}$F-FDG uptake is an important first step for potentially implementing this new hybrid imaging method for quantitatively assessing the glycolytic activity of primary breast cancer. Furthermore, the MRI component of breast PET/MRI has an added clinical advantage over PET/CT for evaluation of the size and extent of primary tumor enhancement. Further research is warranted to assess the feasibility of using breast PET/MRI to monitor neoadjuvant therapy response.

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