DCE-MRI and Dynamic 15O-water PET/18F-FDG PET for Assessing Tumor Vascularity, Histology, and Response to Neoadjuvant Chemotherapy

S. C. Partridge[1], P. R. Eby[1], S. W. White[2], R. K. Doot[2], B. F. Kurland[3], E. K. Schubert[2], L. K. Dunnwald[2], C. D. Lehman[2], and D. A. Mankoff[2]

[1]Radiology, University of Washington, Seattle, WA, United States, [2]University of Washington, [3]Fred Hutchinson Cancer Center

Introduction Dynamic contrast-enhanced MRI (DCE-MRI) and positron emission tomography (PET) are two functionally different imaging modalities previously shown to be independently predictive of response to neoadjuvant therapy in breast cancer [1-3]. Preliminary studies using PET and MRI in combination to monitor and predict treatment response in breast tumors have shown promising results [4,5], however the extent of their agreement or discordance for tumor characterization is not well understood. A better understanding of the association between functional tumor measures by MRI and PET as to whether they provide complementary or redundant information would be valuable for improved clinical management of breast cancer. The purpose of this study was therefore to investigate the association between DCE-MRI enhancement kinetics, ^{15}O-water PET measures of blood flow, and ^{18}F-FDG PET metabolic measures of breast tumors and compare with tumor histology and pathologic response to neoadjuvant chemotherapy.

Methods We retrospectively evaluated exams for 19 patients with locally advanced breast cancer (LABC) who underwent both ^{15}O-water/^{18}F-FDG PET and DCE-MRI (14 patients were imaged prior to undergoing preoperative chemotherapy and 5 patients midway through treatment). Histologic tumor characteristics included tumor grade, ER, PR, HER2, and Ki67. Pathologic response was assessed following treatment. DCE-MRI was acquired on a GE Excite 1.5T magnet with a dedicated breast coil using a 3DFGRE sequence with fat-suppression, TR/TE = 6.7/4.2ms, 10° flip, 32cm axial FOV in 9 patients and 22cm sagittal FOV in 10 patients, 3 mm or less slice thickness, 1 mm or less in-plane resolution, and 90 sec scan time. Five time points were acquired; a pre-contrast scan followed by five sequential post-contrast scans centered at 1.5, 3, 4.5, 6, and 7.5 mins after contrast injection (0.1 mmol/kg body-weight Gd-DTPA). DCE-MRI measures included tumor volume, initial peak enhancement (PE) at 1.5 mins, and signal enhancement ratio (SER) characterizing the shape of the enhancement curve in the delayed phase[6,7], Figure 1. PET was performed on a GE Discovery STE PET/CT scanner with 7 min dynamic ^{15}O-water imaging over the chest and breast following a bolus injection of 25–40 mCi, and 60 min dynamic ^{18}F-FDG imaging following a 2 min infusion of 7–10 mCi, as described previously[1,8], Figure 2. PET measures included ^{15}O-water blood flow, ^{18}F-FDG transport rate constant from blood to tissue (K1), and FDG metabolic rate.

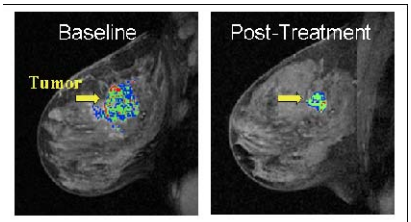


Figure 1. DCE-MRI in a 50 year-old female with LABC studied during neoadjuvant AC therapy. Sagittal MRI images depicting changes in the tumor enhancement profile with treatment (red=washout, green=plateau, blue=persistent enhancement). Reductions in tumor volume and enhancement characteristics including peak SER, and washout volume (red voxels) are predictive of response.

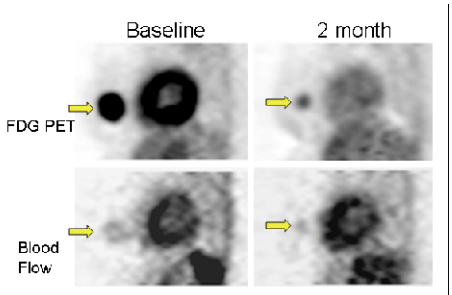
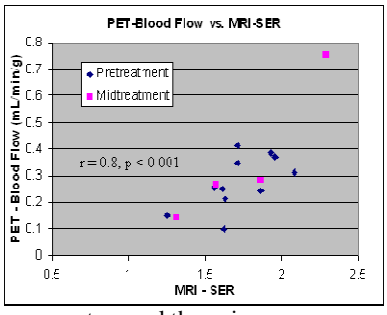
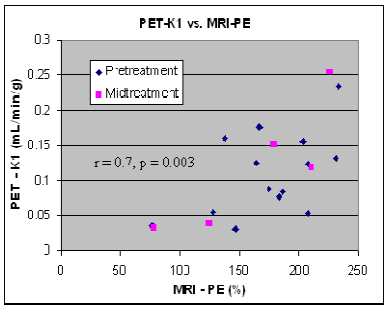


Figure 2. PET scans in a female with LABC studied before and during metronomic AC neoadjuvant therapy. Sagittal images reflect decreased tumor FDG uptake and blood flow with treatment. Tumor is indicated by arrows.

Results Blood flow measures by ^{15}O-water PET correlated significantly with DCE-MRI SER (r=0.8) and tumor volume (r=0.7). PET K1 measures correlated significantly with DCE-MRI peak PE (r=0. 7), SER (r=0.6) and tumor volume (r=0.6). By multivariate analysis, SER was the strongest independent MRI correlate of PET blood flow, Figure 3, and PE the strongest MRI correlate for K1, Figure 4. No significant correlations were observed between ^{18}F-FDG PET metabolic rate and the DCE-MRI kinetic parameters. Also, while PET blood flow and K1 were strongly correlated (r=0.9, p=0.0001), blood flow and metabolic rate were not (r=0.4, p=0.12). In comparison with histology, ER$^-$ and PR$^-$ tumors demonstrated significantly higher PE (p=.035), larger tumor volume (p=0.032), and higher FDG metabolic rate (p=0.046). Grade 3 tumors had significantly higher FDG metabolic rate (p=0.014) and larger tumor volumes (p=0.009) compared to lower grade tumors. Tumors exhibiting complete pathologic response following neoadjuvant chemotherapy demonstrated significantly lower DCE-MRI peak PE than other tumors (p=0.031).





Discussion The associations observed between PET and MRI measures may lead to a better understanding of angiogenesis, vascular permeability, and glucose transport in LABC. PET and DCE-MRI vascular measures were well correlated. A lack of correlation of metabolic rate with blood flow and DCE-MRI kinetics suggests that 18F-FDG PET provides complementary metabolic information independent of vascular factors. Several PET and MRI measures were independently associated with tumor histologic features and pathologic response to neoadjuvant treatment. The combination of MRI and PET may be helpful in understanding tumor pharmacodynamics in response to novel therapies.

References

1) Mankoff DA, Dunnwald LK, Gralow JR, et al. J Nucl Med, 2003. 44(11): p. 1806-14.
2) Partridge SC, Gibbs JE, Lu Y, et al. AJR Am J Roentgenol, 2005. 184(6): p. 1774-81.
3) Padhani AR, Hayes C, Assersohn L, et al. Radiology, 2006. 239(2): p. 361-74.
4) Semple SI, Staff RT, Heys SD, et al. Annals of Oncology, 2006. 17: p. 1393-98.
5) Chen X, Moore MO, Lehman CD, et al. Acad Radiol, 2004. 11(10): p. 1115-24.
6) Hylton NM. Magn Reson Imaging Clin N Am, 1999. 7: p. 411-20.
7) Esserman L, Hylton N, George T, Weidner N. Breast J, 1999. 5(1): p. 13-21.
8) Tseng J, Dunnwald LK, Schubert EK, et al. J Nucl Med, 2004. 45(11): p. 1829-37.