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## INTRODUCTION

For patients with locally advanced breast cancer, neoadjuvant chemotherapy (NAC) is a viable alternative to adjuvant chemotherapy in some patients and has been shown to increase the rates of breast-conserving surgery and decrease the need for complete axillary lymph node dissection.<sup>1-3</sup> Early prediction of response to NAC offers a potential opportunity to change the treatment approach if there is inadequate response.

Several studies using FDG-PET have shown a relationship between the maximum uptake values after 1 or 2 courses of chemotherapy and final pathological response.<sup>4,5</sup> Pathologic response to NAC can serve as an individual strong prognostic indicator for risk of recurrence.

The objective of this study was to evaluate the ability of high resolution breast PET imaging (BPI) with Fluorodeoxyglucose <sup>18</sup>F (<sup>18</sup>F-FDG) to predict response to neoadjuvant chemotherapy (NAC) prior to surgery. Our hypothesis was that metabolic imaging with BPI would demonstrate high sensitivity and specificity in predicting response to NAC when compared with final surgical pathology results.

## METHODS

Sixty one patients (62 at breast level) undergoing NAC for breast cancer were imaged with a high resolution BPI system before (baseline), and after completion (restaging) of NAC. Average age was 53.02 years (range 26-76). The median time delta between exams was 30 weeks (14-31). Tumor size and maximum uptake value (PUV max) measured from BPI images were compared with the extent of residual disease at surgery.

## RESULTS

Sixty one patients (62 at breast level, 1 bilateral case) completed imaging and proceeded to surgical resection after NAC. Using Breast PET to characterize tumor size in largest dimension and lesion maximum uptake value (PUV max) pre and post NAC. Tumor size post NAC was then correlated with final surgical pathology measurements. Breast PET imaging (BPI) results are presented in table 1.

- Pathology found residual tumor (pPR) in 67.7% (42/62); no residual tumor (pCR) in 32.2% (20/62)

- Breast PET correctly identified residual disease in 37/42 and correctly predicted a pCR in 19/20.

Table 1

N-62	
Sensitivity	(39/43) 90.69%
Specificity	(18/19) 94.73%
PPV	(39/40) 97.50%
NPV	(18/22) 81.81%
Accuracy	(57/62) 91.9%
BPI Mean Baseline PUVMax	6.16 (.96-15.2)
BPI Mean Restaging PUVMax	1.36 (0-15.5)
BPI Mean Baseline Tumor Size (largest dimension cm)	5.06 cm (1.3-8.0)
BPI Mean Restaging Tumor Size (largest dimension cm)	2.22 cm (0-4.3)
Mean Pathology Tumor Size (largest dimension cm)	2.47 cm (0-5.4)

## CASE IMAGES

### pCR

42 y/o female, multifocal IDC  
NAC: AC+Taxol  
Hormone/Biotherapy: N/A  
ER-, PR-, HER2 negative  
SLNB 0/1+

Baseline BPI



PUVMax 7.96  
Lesion size 4.5 cm

Restaging BPI

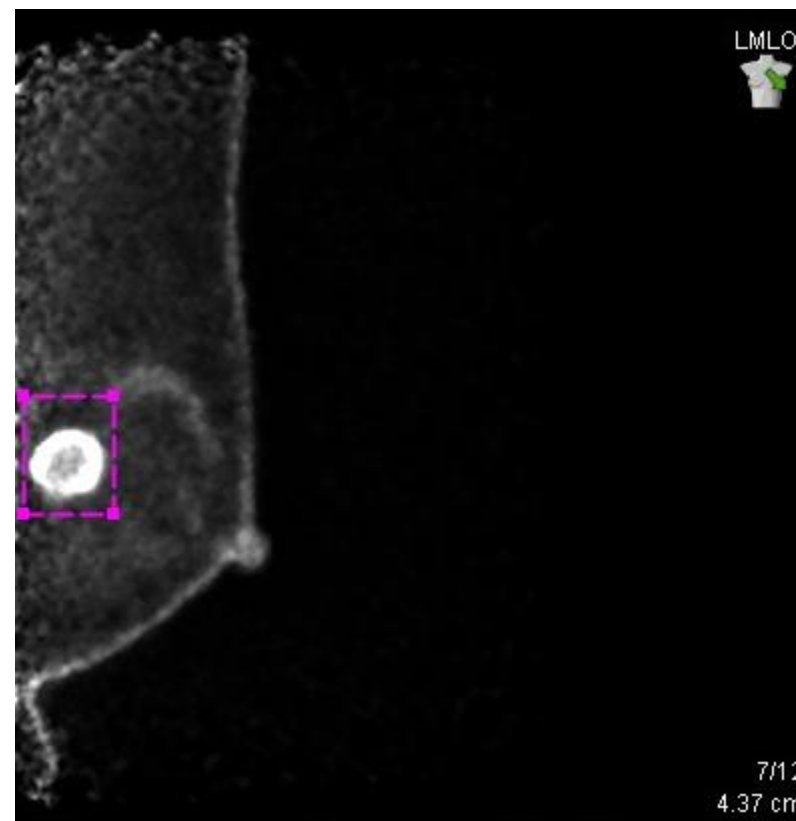


Delta: 203 days  
No residual FDG uptake

### pPR

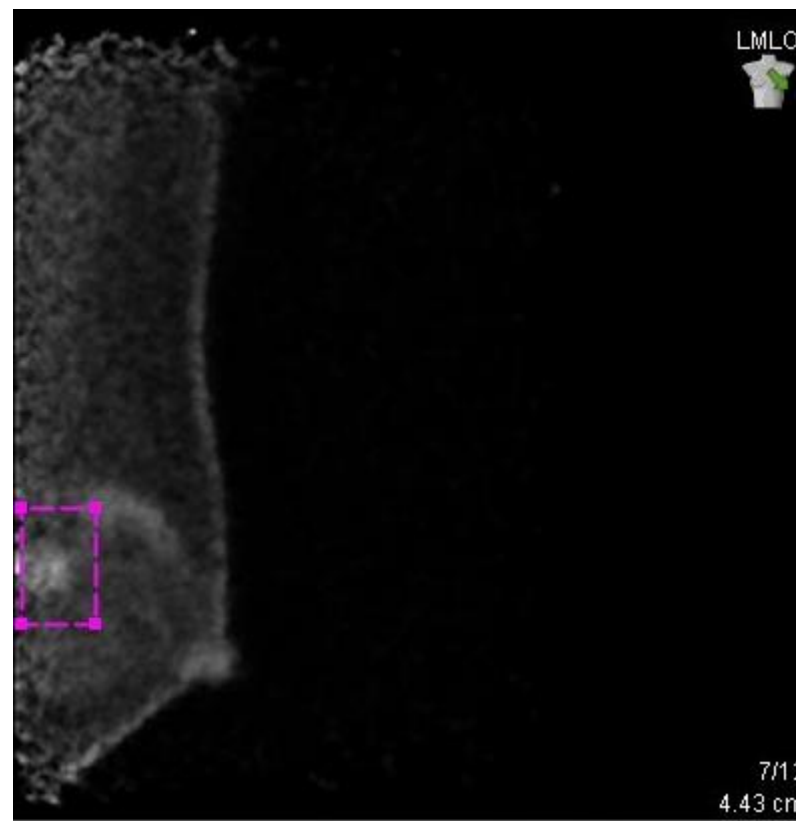
56 y/o female, unifocal IDC  
NAC: Carbo+Taxol+TAC  
Hormone/Biotherapy: N/A  
ER-,PR-,Ki-67-30%,HER2 negative  
SLNB 0/2+

Baseline BPI



PUVMax 6.0  
Lesion size 2.5 cm

Restaging BPI



Delta: 166 days  
PUVMax 1.6  
Lesion size 1.8 cm  
Pathology size 2.2 cm

## DISCUSSION

Over the last decade we have seen changes in neoadjuvant treatment guidelines which make it a standard option for primary operable disease for patients who are candidates for adjuvant systemic chemotherapy, irrespective of the size of the tumor. Neoadjuvant chemotherapy has shown similar long term survival benefit as adjuvant therapy. Neoadjuvant treatment of breast cancer is well established as a safe and effective therapeutic approach for primary and locally advanced breast cancer. The neoadjuvant approach offers the advantages of down-staging the disease, potentially reducing the extent of surgery and in an era of personalization of therapy, testing the efficacy of therapy administered to patients.

## CONCLUSIONS

This study demonstrates that high resolution breast PET Imaging (BPI) with Fluorodeoxyglucose <sup>18</sup>F (<sup>18</sup>F-FDG) has value in predicting response to NAC prior to definitive surgery. Changes in tumor size and tumor maximum uptake value (PUVmax) on BPI imaging performed at initiation of NAC and upon completion of NAC were highly accurate in predicting the presence or absence of residual disease when compared to final surgical pathology results. Estimation of tumor size post-NAC from BPI appears to correlate better with pathological tumor size than mammography, ultrasound, MRI or clinical assessment. These results demonstrate that the use of high resolution breast PET imaging (BPI) with Fluorodeoxyglucose <sup>18</sup>F (<sup>18</sup>F-FDG) is highly accurate in assessing tumor response to neoadjuvant chemotherapy in breast cancer patients. In the future our analysis can be expanded to assess differences in response based on tumor type, receptor and Her2 status.

## REFERENCES

- 1.) Fisher B, Brown A, Mamounas E, et al. Effect of preoperative chemotherapy on local- regional disease in women with operable breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-18. *J Clin Oncol.* 1997;15:2483-2493.
- 2.) Fisher B, Bryant J, Wolmark N, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. *J Clin Oncol.* 1998;16: 2672-2685.
- 3.) Hunt KK, Yi M, Mittendorf EA, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. *Ann Surg.* 2009;250:558-566.
- 4.) Duch J, Fuster D, Montserrat M, et al. <sup>18</sup>F-FDG PET/CT for early prediction of response to neoadjuvant chemotherapy in breast cancer. *Eur J Nucl Med Mol Imaging.* 2009;36:1551-1557.
- 5.) Koolen BB, Vrancken Peeters MJ, Wesseling J, et al. Association of primary tumour FDG uptake with clinical, histopathological and molecular characteristics in breast cancer patients scheduled for neoadjuvant chemotherapy. *Eur J Nucl Med Mol Imaging* 2012;39:1830-1838.