Early MRI and dedicated breast PET biomarkers for hormone receptor-positive/HER2-negative early-stage breast cancer in the setting of neoadjuvant endocrine therapy in the I-SPY 2 TRIAL

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Purpose
To examine changes in functional tumor volume (FTV) on MRI and fluoro-2-deoxy-2-[18F]fluoro-2-deoxy-D-glucose (FES) uptake on dedicated breast PET (dPET) in patients with hormone receptor positive (HR+) HER2-negative (HER2-) breast cancer receiving neoadjuvant endocrine therapy (NET). To compare MRI change in NET in a similar cohort of patients receiving neoadjuvant chemotherapy (NAC).

Background
- Neoadjuvant endocrine therapy (NET) is increasingly utilized for HR+/HER2- breast cancer. In I-SPY 2, a sub cohort of HR+/HER2- patients receive NET in Endocrine optimization protocol (EOP).
- Biomarkers for NET are lacking. There is limited evidence that pathological response (such as pCR) or change in a biomarker (such as Ki67) after NET is predictive of survival outcome.1 Also, there is limited imaging research to assess response during NET.
- Dedicated breast PET (dPET) is an emerging PET technology specially designed for breast imaging. Using dPET combined with an estrogen receptor targeting tracer (18F-fluorodeoxyglucose, FES), functional interaction between estrogen and its receptor within breast cancer and parenchyma can be visualized.

Methods
Dedicated breast PET with 18F-fluoro-2-deoxy-D-glucose (FES-dPET)
- For patients in NET cohort at a single institution (UCSF)
- Maximum standardized uptake value (SUVMAX) over the tumor volume (or location) was measured to quantify FES uptake.
- *For example, where tumor uptake is indistinguishable from background

Dynamic contrast-enhanced breast MRI (DCE-MRI)
- Functional tumor volume (FTV) is derived as a quantitative measure of tumor burden from each MRI.

RESULTS
Longitudinal change in FTV on MRI (as of 09/2022)

<table>
<thead>
<tr>
<th>Period</th>
<th>NET cohort</th>
<th>NAC cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 weeks (T1)</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>12 weeks (T2)</td>
<td>60</td>
<td>63</td>
</tr>
<tr>
<td>6 months (T3)</td>
<td>46</td>
<td>44</td>
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</tbody>
</table>

No PET performed at this timepoint

Data from the I-SPY 2 Trial

Figure 1: Imaging time points before and during neoadjuvant treatment

Figure 2: Representative case in cohort MRI (upper row) and FES-dPET (lower row) maximum intensity projection (MIP) images. At T1 and T3, residual tumor is identified on MRI, but FES-dPET on dPET decreased and was indistinguishable from background. This illustrates that the ability of estrogen receptor of cancer cells to combine with estrogen decreased to background tissue level, although there is residual tumor on MRI.

CONCLUSIONS
These results suggest the potential for MRI and FES-dPET to be used in combination as biomarkers of early response to neoadjuvant endocrine treatment.