

## **Selective sentinel Lymph node after neoadjuvant systemic therapy according to alteration of <sup>18</sup>F-FDG PET/CT uptake in axilla and molecular subtype in node positive breast cancer: a pilot study**

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**BACKGROUND:** There is an increasing proportion of node-positive breast cancer patients who will attain axillary lymph nodes pathologic complete response (Ax-pCR) after neoadjuvant chemotherapy (NAC). However, there exists no universally recognized imaging method or surgical procedure to predict axillary LNs response to NAC.

**HYPOTHESIS:** Using PET/CT in combination with sentinel lymph node biopsy (SLNB), we aimed to investigate whether this could be the optimal procedure to omit axillary lymph node dissection (ALND) after NAC in patients promising to obtain Ax-pCR.

**METHODS:** This pilot study enrolled clinical stage T0-4, N1-2, M0, primary invasive breast cancer patients at presentation documented confirmed by fine-needle aspiration biopsy or core needle biopsy who were planning to undergo neoadjuvant systemic treatment. All enrolled patients planned to undergo four or six cycles of NAC. Baseline [<sup>18</sup>F]-fluorodeoxyglucose (FDG) PET/CT scanned (result recorded as SUV<sub>max-1</sub>) before the first cycle and a comparative scan (SUV<sub>max-2</sub>) after two cycles treatment respectively. After NAC, patients who accepted SLNB and ALND were eventually included in the whole cohort to verify the accuracy of SLNB. We removed the marked lymph node with the guidance of a hook wire punctured before surgery and sent as SLN. Receiver operating characteristic (ROC) curve of absolute decreasing rate between the SUV<sub>max-2</sub> and SUV<sub>max-1</sub> ( $\Delta\text{SUV}_{\text{max}} = |(\text{SUV}_{\text{max-2}} - \text{SUV}_{\text{max-1}}) / \text{SUV}_{\text{max-1}}|$ ) was performed to access the predictive value of PET/CT in the cohort and different subgroups. The strategy of combined FDG PET/CT and SLN biopsy was employed to categorize patients who might best benefit from this clinical procedure

**RESULTS:** Of 80 cases recruited in this pilot study, 65 were included in the final analysis. The overall Ax-pCR rate has obtained 57.4% after NAC, and it was as high as 75% in ER-negative HER2-positive patients. In our study, we redefined the subgroup in terms of immunohistochemistry (IHC) staining and Ax-pCR rate as low Ax-pCR level group (ER+ HER2- patients, Group A), moderate Ax-pCR level group (containing ER+ HER2+ and ER- HER2- patients, Group B) and high Ax-pCR level group (ER- HER2+ patients, Group C). Calculating the area under the curve (AUC) of these subgroups, we observed the optimized predictive value of FDG PET/CT in Group B (AUC= 0.96), while not in Group A (AUC=0.55) and Group C (AUC=0.50). Filtering potential Ax-pCR cases through ROC in combination with SLNB resulted in a calculated accuracy rate of 100% in Group B which indicated a clinical procedure including FDG PET/CT. ALND should be considered for ER-positive and HER2-poor patients (Group A) given to the poor Ax-pCR rate of 26.7% and insensitive to FDG PET/CT. And for ER-negative HER2 positive patients, the accuracy rate of SLNB can access to 91.7% with 92.3% detection rate regardless of undergoing FDG PET/CT. PET/CT was a potent tool in predicting axillary LNs pCR in TNBC and ER-pos HER2-pos breast cancer but not in HER2 positive cases, and subsequently, the recommendation was that additional refinements in patient selection are needed to guide the use of SLN surgery in this setting.