# Deep learning model for predicting hormonal therapy response using FES-PET in ER+ HER2- metastatic breast cancer

M. S. Abdelhalim[1], A. M. Saad[2], A. K. Morsi[2], A. H. Algendy[2], K. A. Belal[1], A. S. Hussein[2], A. M. ElDrieny[3], S. W. Fouad[2], Y. A. Elsaid[4], O. Awad[5], A. A. Ismail[2], H. M. Hegazy[1], B. El Sabaa[6], S. H. Gamie[2], A. A. Elsaid[2]

## Objective

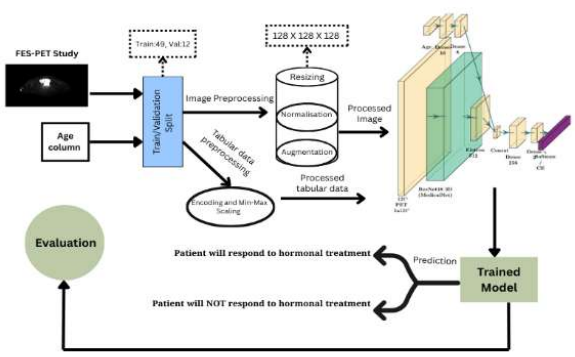
Endocrine therapy is the cornerstone of treatment for estrogen receptor–positive (ER+), human epidermal growth factor receptor 2–negative (HER2-) metastatic breast cancer, yet intrinsic and acquired resistance limit benefit. Reliable biomarkers are needed to identify likely responders. Conventional clinical factors (age, prior therapy, disease burden) offer modest predictive value. Molecular imaging with 16α-[18F] fluoroestradiol positron emission tomography (FES-PET) enables non-invasive, whole-body assessment of estrogen receptor availability and correlates with endocrine sensitivity. With advances in artificial intelligence, deep learning can integrate subtle imaging features with clinical variables for outcome prediction. This study evaluated whether FES-PET combined with simple clinical factors could predict endocrine therapy response using a deep learning framework.

## Materials and Methods

We retrospectively analyzed 60 patients treated at a private cancer center in Alexandria, Egypt, who underwent baseline FES-PET (18F-FES, Cerianna) prior to initiation of endocrine therapy. Imaging volumes were resampled to 128 by 128 by 128 voxels to standardize input. Clinical features included patient age, number of prior endocrine therapy lines, number of chemotherapy lines, and history of breast surgery (mastectomy versus breast-conserving surgery). All variables were normalized and concatenated with image-derived features. A three-dimensional ResNet-18 architecture, pre-initialized with weights from MedicalNet, was fine-tuned for classification. To mitigate class imbalance, focal loss was employed. The dataset was stratified into a training set (n = 48) and a test set (n = 12). Performance was evaluated after each epoch using accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC).

## Conclusion

This pilot study provides proof-of-concept that a deep learning framework integrating FES-PET imaging with simple clinical variables may predict endocrine therapy response with high accuracy in patients with ER+/HER2- metastatic breast cancer. The observation that robust performance was achieved after minimal fine-tuning suggests that transfer learning may be particularly advantageous in small, heterogeneous clinical datasets where conventional training would be limited by overfitting. Nevertheless, the modest sample size and limited independent test cohort necessitate cautious interpretation, and external validation in larger, prospective, multi-institutional datasets will be critical. If confirmed, such models could be incorporated into clinical workflows to support treatment planning, sparing non-responders from ineffective therapy while enabling more personalised and precise care pathways




## Results

The model converged rapidly, achieving optimal performance after only two epochs. At this point, it correctly classified 11 of 12 test cases, corresponding to a sensitivity of 100 percent for identifying responders and a specificity of 67 percent for non-responders. Overall classification accuracy reached 91.7 percent, with an estimated AUC of 0.83, reflecting strong discriminatory ability. Continued training beyond three epochs did not yield improvements, suggesting that transfer learning afforded efficient adaptation to this small clinical dataset. Performance analysis demonstrated that integration of clinical features with FES-PET imaging contributed to balanced classification, highlighting the added value of combining routinely available patient variables with advanced image-derived features.

