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**Objectives:** Most supervised learning approaches currently applied in radiomics consist in classifying patients in groups (eg, responder versus non-responder, short overall survival versus long overall survival). With these methods, individual information from each patient is used only to assign a patient to a group. To preserve detailed information of each patient, we are developing an alternative approach that consists in identifying a “twin patient” based on radiomic features and clinical parameters in a patient database, i.e. another patient with feature values similar to the ones observed in the tested patient. Here, we studied whether this approach could predict the response to neoadjuvant chemotherapy in breast cancer patients.

**Methods:** 117 patients with a triple-negative breast cancer were included in this study. All patients underwent a baseline 18F-FDG PET/CT using Gemini GXL 16 (Philips, 41 patients) or Discovery 710 Elite (GE, 76 patients) with a standard imaging protocol, before a neo-adjuvant chemotherapy associating anthracycline and taxane. The pathological response was assessed on the surgical specimen after chemotherapy according to the Residual Cancer Burden (RCB score). Based on PET images, the primary lesion of each patient was segmented using a threshold set to 40% of SUVmax, and a 6 mm thick ring around the tumor region was also used to measure the peri-tumoral metabolic activity. In each resulting volume of interest, we computed 48 radiomic features using LIFEx software (intensity resampling: 128 gray-levels between 0 and 40 SUV; spatial resampling: 2x2x2 mm) [1]. Radiomic features were harmonized between the two PET devices using ComBat [2]. The profile of each patient included 96 radiomic features and 3 clinical variables (age, Ki-67 expression, body mass index), each expressed as z-score. Using a leave-one-out approach, we computed the Euclidian distance between the profile of the tested patient and the profiles of all patients of the database. The smallest distance was used to identify the twin of the tested patient. This procedure was repeated by defining profiles including only 2, 4 and 6 features using a systematic feature selection process. The performance was evaluated using the Youden Index (YI=Sensitity+Specificity-1) to predict the response to neoadjuvant chemotherapy.

**Results:** In our cohort, 68 patients were identified as responders to therapy and 49 patients as non-responders. Without feature selection, YI was 0.13 (Se=45% ; Sp=68%). When using 2 features only, the best performance was obtained for the combination of Entropy_Tumor and LZE_Ring with YI=0.36 (Se=59% ; Sp=76%). With 4 features, the best YI (=0.50) was obtained by adding Energy_Ring and SRE_Ring to Entropy_Tumor and LZE_Ring (Se=73% ; Sp=76%). With 6 features, the best combination was obtained by adding LZE_Tumor and LZHGE_Ring, yielding a YI of 0.56 (Se=80% ; Sp=76%). When we selected features, clinical variables were never included in the best combination, and radiomic features extracted from the peri-tumoral regions (ring) improved the identification of relevant twins.

**Conclusion:** We demonstrated that the so called “twin patients” defined as sharing a number of similar radiomic features were likely to present similar response to neo-adjuvant chemotherapy. Feature selection improved the performance by including only features relevant to the prediction task into the profile. Unlike the conventional group-based patient management, the twin approach uses the detailed individual information of each patient previously treated. Further studies involving an independent cohort and more features in the combination are underway to further explore the potential of this concept. The identification of patient similarities also acts as a discovery approach to formulate new biological hypotheses, for instance, highlighting here the association between peri-tumoral heterogeneity and response to therapy.