

e13057

Publication Only

**PERCIST-like response assessment with FDG PET based on automatic segmentation of all lesions in metastatic breast cancer.**

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**Background:** In metastatic breast cancer (MBC), treatment response is often assessed with FDG PET per PERCIST which evaluates changes in  $SUL_{peak}$  of the single hottest tumor lesion identified on the baseline and follow-up images. PERCIST therefore does not consider tumor heterogeneity. This work aims to compare responses determined with the automatic segmentation of all lesions to response determined manually per PERCIST. **Methods:** 10 MBC patients ( $61 \pm 14$  y/o) undergoing either chemo- or hormonotherapy were randomly selected from the prospective EPICURE study (NCT03958136). A baseline and two follow-up FDG PET were acquired at pre-, early- (1 month) and mid-treatment times for each patient. All metastatic lesions on all images were manually segmented by experts. Using the Advanced Normalization Tools (ANTs) image registration method, we wrapped baseline lesion segmentations to automatically obtain the follow-up ones. These registered segmentations were compared to the ones done manually using standard biomarkers:  $SUL_{peak}$ , lesion size and Total Lesion Glycolysis (TLG). Differences between baseline and follow-up images were visually represented by coloring the follow-up segmentations: in green for responsive lesions (decreasing  $SUL_{peak}$ ) and in red for progressive ones (increasing  $SUL_{peak}$ ). Two expert physicians were then asked to evaluate treatment response while seeing these colored segmentations. They assessed the FDG PET images in pairs, evaluating for each patient the baseline and one of the corresponding follow-ups in a blinded manner: either the early- or the mid-treatment follow-up. Evaluations were then compared: i) early- vs mid-treatment response and ii) follow-up response vs patient's clinical outcome. **Results:** Biomarkers extracted from the registered segmentations were similar to the ones extracted from the manual segmentations, with a Lin correlation coefficient of 0.92, 0.87 and 0.95 for the  $SUL_{peak}$ , lesion size and TLG respectively. These findings were obtained within ~10min, whereas the manual segmentation of the three PET images for any given patient took ~1h. With the use of colored segmentations, early follow-up evaluations were predictive of mid-treatment response in 65% of the cases. The blinded physicians agreed with the clinical outcomes 85% and 95% of the time for the early- and mid-treatment images respectively. **Conclusions:** With segmentations automatically derived from ANTs registration, we managed to extract biomarkers that are comparable to the ones obtained with manual segmentations; both segmentations carried similar information. ANTs fast registration and biomarkers computation can make it a useful tool in clinical routine. In addition, lesion coloring helped evaluate treatment response and early-treatment follow-up images were shown to be predictive of mid-treatment response. Clinical trial information: NCT03958136. Research Sponsor: FEDER-FSE.