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Abstract

POSTER SESSION ABSTRACTS | FEBRUARY 15 2018

Abstract P5-03-08: Development of a histology-based digital pathology image analysis algorithm for assessment of tumor infiltrating lymphocytes in HER2+ breast cancer FREE

M Barnes; A Sarkar; R Redman; C Bechert; C Srinivas

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Cancer Res (2018) 78 (4_Supplement): P5-03-08.

<https://doi.org/10.1158/1538-7445.SABCS17-P5-03-08>

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Introduction: Anthracycline-based chemotherapy regimens have been shown to increase risk of cardiac toxicity and other side effects especially in combination with HER2-targeting agents such as trastuzumab. Identification of biomarkers that can predict similar patient benefit in the context of targeted therapy between anthracycline and non-anthracycline-based regimens is attractive for personalized care. Histology-based assessment of tumor infiltrating lymphocytes (TILs) as a surrogate of the host immune response has been shown to be prognostic and potentially chemopredictive in triple-negative and HER2-positive breast cancers; however, the inter-play of TILs, tumor cells, other microenvironment mediators, their spatial relationships, quantity, and other image-based features have yet to be determined exhaustively and systemically. In anticipation of analyzing these aspects in the context of chemo and targeted therapy response in patient sample cohorts, we developed a digital pathology image analysis algorithm to identify tumor, stromal, and lymphocyte cells and acquire respective histology-based image features from hematoxylin and eosin (H&E) stained slides. **Materials and Methods:** An automated method involving cell detection, cell segmentation, feature extraction (capturing both local features and global context based features) and supervised machine learning (using a multi-class random forest based classifier, where a 3-class problem is represented using 3 1-vs-1 binary classifiers) were used to classify individual cells into the following 3 categories: tumor cells, stromal cells, and lymphocytes. Cell classification was compared against manually determined ground truth from three pathologists using simple confusion matrices. **Results:** From six H&E breast cancer cases, two pathologists manually and independently annotated the same tumor cells (6,458), lymphocytes (2,491), and stromal cells (744) in fourteen field-of-views (~ 0.3 mm² in size). Manual concordance of tumor cells (99.4%, 1434/1442), lymphocytes (80.0%, 680/849), and stromal cells (68.8%, 53/77) between two pathologists was moderate to high. Comparing only cells where two pathologists agreed (4,736) and an independent set of single cell annotations (547) from a third pathologist, image analysis classification showed high concordance for tumor cell (92.9%, 1107/1191), lymphocyte (90.4%, 572/636), and stromal cell (94.3%, 66/70) classification categories. Approximately 242 image features grouped into 22 unique data families were extracted from each cell analyzed. **Conclusion:** A H&E-derived TILs image analysis algorithm with associated feature extraction is feasible with preliminary findings of accurate cell classification. This tool will continue to be refined in anticipation of analysis in patient outcome cohorts.

Citation Format: Barnes M, Sarkar A, Redman R, Bechert C, Srinivas C. Development of a histology-based digital pathology image analysis algorithm for assessment of tumor infiltrating lymphocytes in HER2+ breast cancer [abstract]. In: Proceedings of the 2017 San Antonio Breast Cancer Symposium; 2017 Dec 5-9; San Antonio, TX. Philadelphia (PA): AACR; Cancer Res 2018;78(4 Suppl):Abstract nr P5-03-08.

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