Development and analytical validation of a fully-automated platform for quantification of MetaSites to predict systemic metastasis.

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Abstract

Background: Tumor metastasis is responsible for the majority of death in breast-related death. Diagnosis of an early and accurate assessment of metastasis in breast cancer is a challenge. Tanabe et al. described a multiparametric method to predict metastasis for patients with BI-early stage invasive breast cancer. A MetaSite is a pivotal multicellular ensemble of adjacent stromal, stromal immune microenvironment, and other invasiveness tumor cell. To reduce pathologist working variability, an objective and reproducible automated laboratory process workflow to identify and quantify metastatic is a critical grading assay was developed. Methods: Digital pathology image coupled with image analysis tool was employed to develop a fully automated object method and validated for quantification of MetaSites in formalin-fixed paraffin-embedded tumor samples. By using this method, areas and quantification of MetaSites were automatically determined by integrating high resolution automated microscopy with multiple image analysis algorithms. A pathologist ensured overall diagnostic quality of the samples in addition to rejecting individual images for metaSite scoring. Results: In this analytical validation study, the platform was demonstrated to be more than 90% reproducible with a mean coefficient of variation of 5% to 20% for independent measurements of the same slide. Furthermore, MetaSite showed correlation coefficients (Pearson’s R) greater than 0.8 between measurements with no significant difference in absolute values by repeated measures analysis. Importantly, MetaSite scoring independently of tumor sections showed greater than 90% reproducibility in evaluating metastatic heterogeneity within the tumor, compared to MetaSite scoring by a single pathologist. Additionally, data of the same MetaSite showed correlation coefficients (Pearson’s R) greater than 0.8 between the scores with no significant differences in mean MetaSite scores. Conclusion: Taken together, this initial demonstration of the proof-of-concept test and analytical validation of a fully automated, highly reproducible MetaSite quantitation platform. With development and analytical validation of this test, it is now possible to provide physicians with information regarding the aggressiveness of the tumor and further prevention of cancer metastasis. This method is further validated in a large (n=121) case control study.

Introduction

Methods

Results

Results Continued

Conclusion

• The MetaSite™ Breast assay, utilizing automated digital pathology methods, demonstrates high reproducibility in accuracy and analytical precision review, thus enabling MetaSite™ Breast to be used in the clinical setting.

With precision and performance of the this as a way, specifically 1% CV ≤ 10%, the MetaSite™ Breast test meets or exceeds current industry standards for analytical performance of in situ tissue-based diagnostic tests.

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