Digital Analysis of Tumour Microarchitecture as an Independent Prognostic Tool in Breast Cancer

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Background:
Pathological assessment remains the gold standard for treatment decision making in breast cancer. As only a portion of the histological information is accessible by eye, recognition and quantification of complex patterns and relationships among constituents of the tumour microenvironment is feasible only with digital image analysis. This approach has the potential to exploit previously unquantifiable features as prognostic parameters. This paper builds on a previous small-scale study, and expands preliminary findings to a large cohort of patients with detailed histological and outcome data.

Design:
Digitised keratin-stained tissue microarrays from 857 patients with invasive ductal carcinomas of no special type were analysed. Virtual slides were saved as ndpi files, captured as jpeg fi les and processed with a public domain image analysis software. Our aim was to assess the prognostic potential of tumour cell arrangement in variably sized groups (nests). The underlying working hypothesis was based on the the concept that tumour nest microarchitecture affects tumour-stroma interaction, and impacts tumour progression.

Results:
We separately evaluated cases from the 4 major molecular subtypes. ER+ HER2- grade 2 tumours showed significant correlations between microarchitectural features (high nest number, low mean area and perimeter) and axillary lymph node (LN) involvement (p=0.004, 0.01, 0.001). These features were not correlated with tumour size. For other grades of this molecular subtype and all grades of other molecular subtypes, these features were not associated with LN status. Furthermore, from cases that presented with positive LNs, those with later distant metastasis (DM) had a lower mean nest area than those without subsequent distant metastasis. The difference was significant in grade 1 ER+ HER2- tumours and grade 3 ER- HER2+ tumours. Triple negative grade 3 tumours with initial LN involvement and subsequent DM showed a significantly higher number of nests than corresponding cases without DM.

Conclusions:
Image analysis can tackle the difficulty of objective description and quantification of histological features, and promises to open up new horizons in histomorphometry. In this study, we showed that tumour microarchitectural features can be employed as prognostic markers for identifying breast cancer patients with increased metastatic potential. Our methodology has the potential to develop into a valuable clinical test.