Evolving Role of Ki67 as a Predictive and Prognostic Marker in Breast Cancer

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Proliferation and autonomous growth are key hallmarks of malignancy and breast cancer is no exception to this [1]. Recently a lot of emphasis has been laid on proliferation in breast cancer with many emerging molecular techniques like Oncotype Dx utilizing proliferation genes as predictive tools to direct patient therapy [2]. However, given the high costs associated with these molecular tests there is constant effort to find suitable surrogate immunohistochemical markers. Ki67 (anti-MIB1) has emerged as a rapid and inexpensive method to detect proliferation in breast tumours. It has been an integral part of the biomarker profile along with estrogen receptor (ER), progesterone receptor (PR) and human epidermal receptor 2 (HER2), used as surrogates to assign breast carcinomas to various molecular subtypes [3]. There is robust data to show that Ki67 is an excellent prognostic and predictive marker.

As early as the 1980's high proliferation rates, as determined by high Ki67 index, were reported to be associated with poor outcome and early recurrences in breast cancer. A recent meta-analysis [4] concluded that high ki67 levels were associated with shorter overall survival. Another meta-analysis [5] showed a significantly worse disease free as well as overall survival for patients with positive Ki67 expression in node positive as well as node negative breast cancers. In amǑM ꞁ3ÄM iŚgh op. ᵐkʈ da® p. b4i ᵟǑ

One study showed that Ki67 indexes determined by automated technique may be more reliable and more accurately classify patients to their molecular subtype [11]. However, breast is a heterogeneous tissue and selection of appropriate areas of tumour by a trained pathologist is essential. With the appropriate optimization of programs, digital image analysis can be used to validate Ki67 values.

In summary, there is good evidence in the literature that Ki67 can be a good predictive and prognostic factor. However, consensus over staining techniques, estimation of Ki67 and standardized cut-off values is lacking. Recommendations, as proposed by the Breast Cancer Working Group, are a good initial step towards harmonization. Automation techniques may be helpful in providing more objective solution but need further validation through future studies. Thus, Ki67 as a reliable factor for prognostication and prediction, though promising, is still not ready for use in routine practice.

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