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Tissue microarray validation

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Keywords

Archive, breast cancer, tissue microarray

Context

For well over a century, pathologists have used formalin-fixed paraffin-embedded tissues for microscopic examination and subsequent diagnosis of human disease. This type of approach is usually limited to the analysis and/or detection of one or two specific features on a single slide from an individual section. The recent development of tissue microarrays (see Additional information) involves core needle 'biopsies' of multiple pre-existing paraffin-embedded tissue blocks and re-embedding them in the form of an arrayed master block. Thus, tissue from an entire cohort of specimens can be represented in a single block and processed under identical conditions. This study evaluated the potential of using tissue microarrays of archival formalin-fixed paraffin-embedded breast tumours to detect expression of three common antigens in breast cancer: estrogen receptor (ER), progesterone receptor (PR) and Her2/neu.

Significant findings

Most cases had at least six out of ten scorable cores. These were considered scorable if at least 10% of the core area contained tumour. Based on whole section staining, the percentage of ER, PR and Her2/neu positive sections was 68%, 56% and 24% respectively. Analysis of ER and PR by microarray showed agreement in 35 out of 36 cases (ER) and 34 out of 35 (PR). Her2/neu expression showed more variability but the average staining correlated with that of the whole section. Overall, analysis of two microarray cores was comparable to that of a whole tissue section showing 95% concordance. To ensure adequate representation of the tumour, a total of three cores from a cross section of the block should be taken. Archival material dating from 1932 was also suitable for this technique with, in general, no real changes in antigen expression over time for ER, PR, Her2/neu, Ki67 and cytokeratin.

Comments

Tissue microarray technology is a new technique which allows the simultaneous analysis of multiple tissue blocks in a single section. In this paper, the authors have assessed the feasibility of using this technology to study breast cancer. Their data suggest that only two cores per block of ten are needed to be representative of the original sample and that, in archival material, antigenicity is maintained for up to six decades. Tissue microarray technology has the potential not only to revolutionise the way in which tissues are analysed but also to accelerate high throughput screening of potential new diagnostic and prognostic tools. A previous concern of tissue microarray technology was that, because it reduced the amount of tissue available for analysis, the technique may not be representative of antigen expression patterns across a whole tumour. This study has allayed these initial concerns by demonstrating that this technology, with twofold redundancy, is a useful technique for analysing antigens in multiple breast tumour samples. As it reduces the amount of tissue required, it will be important when amounts of tissue available are limited. Furthermore, the results show that, in most cases, this technique is also suitable for use in archival material.

Methods

Archival material from 1932-1999 was selected from 38 cases of invasive breast cancer. Tissue areas corresponding to invasive carcinoma and normal epithelium were identified by hematoxylin and eosin staining and 10 core biopsies taken from each area (five from the periphery and five from the centre). Cores were transferred to a recipient masterblock. Sections were prepared from both the original block and the arrayed block and stained for ER, PR, Her2/neu, Ki67 and cytokeratin using standard immunohistochemical techniques. The results were analysed and compared.

Additional information

Kononen J, Bubendorf L, Kallioniemi A, Barlund M, Schraml P, Leighton S, Torhorst J, Mihatsch MJ, Sauter G, Kallioniemi OP: **Tissue microarrays for high throughput molecular profiling of tumour specimens.** *Nat Med* 1998, **4**:844-847 (PubMed%20abstract).

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