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Detection of the BRAF V600E Mutation in Primary and Metastatic Malignant Melanoma -- an Evaluation of the Immunohistochemical Approach

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The BRAF V600E mutation is found in over half of melanomas, making it an attractive therapeutic target; this led to the development of anti-BRAF drugs. Detection of this mutation is currently performed using pyrosequencing. A monoclonal antibody specific for the BRAF V600E mutant protein has been developed, thus immunohistochemistry (IHC) can be used for detection.

The primary aim is to evaluate IHC as a method of BRAF V600E detection compared to pyrosequencing. Secondary aims include analysing clinicopathological and survival data for primary melanoma cases with comparison to their BRAF V600E mutation status.{2LINBRK} After collecting the pyrosequencing data from patient records, 5 primary and 4 metastatic melanoma tissue microarrays were stained using the locked down protocol installed on the Roche Ventana Benchmark Ultra platform. The anti-BRAF V600E (VE1) mouse monoclonal antibody (Roche) was used. Informed consent from patients was obtained for their tissue to be used and stored under the Nottingham Health Science Biobank. Slides were scored using the H-scoring method and verified by a pathologist. SPSS v24.0 was used for statistical analysis.

Sensitivity and specificity of the antibody compared to pyrosequencing were deduced for the primary cohort (65.91% and 91.94% respectively) and the metastatic cohort (86.59% and 98.35% respectively). BRAF mutation status was significantly associated with age and site ($p<0.001$), ulceration ($p=0.027$), mitosis ($p=0.011$), tumour-infiltrating lymphocytes ($p=0.042$), and histological subtype ($p=0.013$). There were no significant associations between survival and BRAF V600E status.

The clinicopathological prognostic factors provide evidence for the BRAF V600E mutation as a positive prognostic indicator. IHC could be used to screen for BRAF V600E mutations, with negative cases being referred for molecular testing like pyrosequencing. This would ensure the detection of other BRAF mutations that could benefit from anti-BRAF drugs.