

**S010** Diagnostic validation of conformation sensitive capillary electrophoresis

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Conformation Sensitive Capillary Electrophoresis (CSCE) is a rapid and sensitive method for mutation scanning based on differential mobility of homoduplex and heteroduplex DNA under electrophoresis. We performed a blinded and randomised investigation of >400 different *BRCA1* and *BRCA2* variations in three laboratories to determine the analytical accuracy of CSCE for diagnostic investigations. Sensitivity >99% (95% CI) was achieved using both manual analysis by visual inspection of traces in Genemapper (Applied Biosystems) and automated analysis in Bionumerics (Applied Maths). However, specificity by manual analysis (93.1-95.6% 95% CI) was significantly better than that achieved using automated analysis (88.7-91.8 95% CI). Therefore a two phase approach comprising automated primary analysis followed by visual inspection of the most subtle shifts would provide the most effective analysis. We conclude that CSCE using the protocols established by this validation is a valuable alternative to sequencing for diagnostic mutation scanning as it provides commensurate analytical accuracy but with significantly reduced processing time and cost.