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Analysis of gene copy number variations using a method based on lab-on-a-chip technology

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ABSTRACT

Aims and background. Copy number variations (CNVs) contribute to genome variability and their pathogenic role is becoming evident in an increasing number of human disorders. Commercial assays for routine diagnosis of CNVs are available only for a fraction of known genomic rearrangements. Thus, it is important to develop flexible and cost-effective methods that can be adapted to the detection of CNVs of interest, both in research and clinical settings.

Methods. We describe a new multiplex PCR-based method for CNV analysis that exploits automated microfluidic capillary electrophoresis through lab-on-a-chip technology (LOC-CNV). We tested the reproducibility of the method and compared the results obtained by LOC-CNV with those obtained using previously validated semiquantitative assays such as multiplex ligation-dependent probe amplification (MLPA) and nonfluorescent multiplex PCR coupled to HPLC (NFMP-HPLC).

Results. The results obtained by LOC-CNV in control individuals and carriers of pathogenic *MLH1* or *BRCA1* genomic rearrangements (losses or gains) were concordant with those obtained by previously validated methods, indicating that LOC-CNV is a reliable method for the detection of genomic rearrangements.

Conclusion. Because of its advantages with respect to time, costs, easy adaptation of previously developed multiplex assays and flexibility in novel assay design, LOC-CNV may represent a practical option to evaluate relative copy number changes in genomic targets of interest, including those identified in genome-wide analyses.

Key words: semiquantitative analyses, gene dosage, genomic rearrangements, molecular diagnosis, genomic duplication.

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