Recent work in our lab has shown that dysplastic Barrett’s Oesophagus (BO) tissue contains multiple genetically distinct clones (Leedham et al., Gut 2008). In order to better characterise this genetic heterogeneity, and determine how the heterogeneity contributes to tumour progression, we have constructed maps of the mutations present within every crypt from a number of Barrett’s EMR specimens. At least 30 crypts were laser capture microdissected from each EMR and individually genotyped. In each EMR, a founding point mutation (in p53 or p16) was detected in the dysplastic crypts. Microsatellite loss of heterozygosity (LOH) analysis of chromosomes 17p, 17q, 18q, 5q, 9p and 3p revealed multiple clones with diverse patterns of LOH that had arisen after the initial point mutation. The maps show diverse patterns of mutation and clonal expansion within microscopic regions of Barrett’s tissue, suggesting that clonal evolution in BO can occur within small areas of tissue. We believe that competition between these clones is the driving force for the development of oesophageal adenocarcinoma.