One of the most common disease that hits human teeth is undoubtedly the caries. This degradation mechanism of the tooth outmost layer is responsible for both loss of mechanical strength and reduction of volume due to erosion. This work investigates the in situ evolution of nano-scale morphology and the spatial distribution of HAp crystallites in human enamel during demineralisation in simulated caries. Multi-modal synchrotron techniques showed that the heterogeneous evolution of crystallites (size, preferred orientation and degree of alignment) could be attributed to a crystallographic-orientation-dependent anisotropic dissolution. In addition, ex-situ SEM/STEM imaging methods were employed for the nano-scale morphological analysis of the treated sample.