

Nanoscale Mapping of the Mechanical Modifications Occurring in the Brain Tumour Microenvironment by Atomic Force Microscopy: The Case of the Highly Aggressive Glioblastoma and the Slowly Growing Meningioma

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Abstract : Glioblastoma multiforme (GBM) is an extremely aggressive brain tumor, characterized by a diffuse infiltration of neoplastic cells into the brain parenchyma. Although rarely considered, mechanical cues play a key role in the infiltration process that is extensively mediated by the tumor microenvironment stiffness and, more in general, by the occurrence of aberrant interactions between neoplastic cells and the extracellular matrix (ECM). Here we provide a nano-mechanical characterization of the viscoelastic response of human GBM tissues by indentation-type atomic force microscopy. High-resolution elasticity maps show a large difference between the biomechanics of GBM tissues and the healthy peritumoral regions, opening possibilities to optimize the tumor resection area. Moreover, we unveil the nanomechanical signature of necrotic regions and anomalous vasculature, that are two major hallmarks useful for glioma staging. Actually, the morphological grading of GBM relies mainly on histopathological findings that make extensive use of qualitative parameters. Our findings have the potential to positively impact on the development of novel quantitative methods to assess the tumor grade, which can be used in combination with conventional histopathological examinations. In order to provide a more in-depth description of the role of mechanical cues in tumor progression, we compared the nano-mechanical fingerprint of GBM tissues with that of grade-I (WHO) meningioma, a benign lesion characterized by a completely different growth pathway with the respect to GBM, that, in turn hints at a completely different role of the biomechanical interactions.

Keywords : AFM, nano-mechanics, nanomedicine, brain tumors, glioblastoma

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