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Spatial organization and correlations of cell nuclei in brain tumors.

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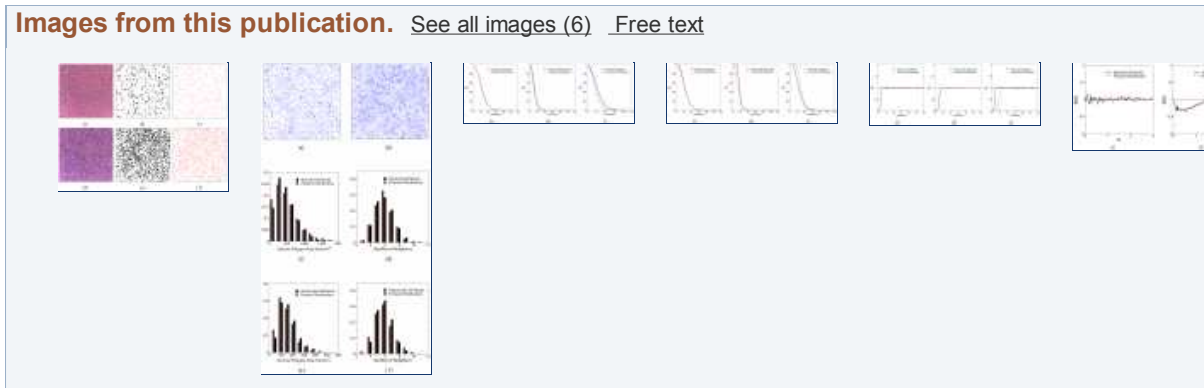
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Abstract

Accepting the hypothesis that cancers are self-organizing, opportunistic systems, it is crucial to understand the collective behavior of cancer cells in their tumorous heterogeneous environment. In the present paper, we ask the following basic question: Is this self-organization of tumor evolution reflected in the manner in which malignant cells are spatially distributed in their heterogeneous environment? We employ a variety of nontrivial statistical microstructural descriptors that arise in the theory of heterogeneous media to characterize the spatial distributions of the nuclei of both benign brain white matter cells and brain glioma cells as obtained from histological images. These descriptors, which include the pair correlation function, structure factor and various nearest neighbor functions, quantify how pairs of cell nuclei are correlated in space in various ways. We map the centroids of the cell nuclei into point distributions to show that while commonly used local spatial statistics (e.g., cell areas and number of neighboring cells) cannot clearly distinguish spatial correlations in distributions of normal and abnormal cell nuclei, their salient structural features are captured very well by the aforementioned microstructural descriptors. We show that the tumorous cells pack more densely than normal cells and exhibit stronger effective repulsions between any pair of cells. Moreover, we demonstrate that brain gliomas are organized in a collective way rather than randomly on intermediate and large length scales. The existence of nontrivial spatial correlations between the abnormal cells strongly supports the view that cancer is not an unorganized collection of malignant cells but rather a complex emergent integrated system.

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