Chaos in Cancer: Analyzing Network Morphology To Predict Tumor Angiogenesis Using Chaos Theory

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The unpredictable behavior of tumors is a problematic barrier to developing personalized therapeutic strategies for individuals with all forms of cancer. A leading cause of cancer's volatile evolution is attributed to tumor angiogenesis, the formation of blood vessels that fosters tumor survival, malignancy, and metastasis. Chaos theory examines the underlying set of deterministic laws of seemingly random dynamical systems not unlike anomalous vascular branching. The current investigation sought to determine if a computational network reconstruction of tumor vasculature applied to chaos theory could determine the extent of unpredictability in tumor angiogenesis. Using labeled mammograms extracted from the Breast Imaging Reporting and Data System, the magnitude of chaos in breast vasculature was uniquely determined using network analysis and feature importance to generate strange attractors. These equations were subsequently analyzed by bifurcation diagrams, fractal dimensions, and Lyapunov Exponents. Vascular networks with the greatest number of nodes, segments, and a smaller mean mesh size were the most chaotic. Angiogenic breast vasculature exhibited a higher Lyapunov exponent than non-tumorous vasculature. Further, a novel network-based drug discovery pipeline with r2 of 0.512 was tested with aromatase, and in vitro validation of the expected gain in entropy was confirmed using P. polycephalum. These newfound correlations between cancer and chaos indicate underlying chaotic angiogenic patterns that have not yet been explored. By bridging mathematical and biochemical concepts, the work proposed herein suggests a direct application of chaos theory to clinically relevant practice, including anti-angiogenic drug discovery and early diagnostics.

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