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Does Tensile Rupture of Tumor Basement Membrane Mark the Onset of Cancer Metastasis?[1] SAI PRAKASH, Chemical and Biomolecular Engineering, Johns Hopkins University — Recognizing a conceptual analogy from polymer physics and reasoning via induction, we infer the plausibility that a malignant tumor (carcinoma) grows in size until a threshold determined by its mechanochemical state in relation to its microenvironment whence, peripheral cells undergo epithelial-to-mesenchymal transitions (EMT) facilitating metastasis. This state is equated to the tensile yielding/rupture of the proteolytically-weakened basement membrane (BM) that encapsulates the growing neoplasm. BMs are typically constituted of tri-continuous hydrogel networks of collagen-IV, laminin, and interstitial fluid, with connector proteins such as nidogens, and perlecans. We test this postulate by formulating a theoretical model based on continuum fluid-solid mechanics, diffusion, and biochemical kinetics of energy metabolism. Herein, a prototypical, viscous tumor spheroid grows radially, consuming metabolic nutrients while being constrained by an elastic BM *ca.* 0.5-2 microns-thick, and cell adhesion molecules (CAMs), chiefly cadherins and integrins. The model is computationally analyzed via Comsol®. Results validate the *a priori* conjecture, and predict subsequent crack-tip stresses shifting strains on the CAMs from compressive to tensile, that might also indicate mechanotransduced switches in their conformations, such as from non-invasive, adhesive E-cadherins to invasive, non-adhesive N-cadherin phenotypes.

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