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Metastasis Suppression by the Primary Tumor: A Natural Law

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We study metastatic cancer progression through an extremely general individual-patient mathematical model that is rooted in the contemporary understanding of the underlying biomedical processes yet is essentially free of specific biological assumptions of mechanistic nature. The model accounts for primary tumor growth and resection, shedding of metastases off the primary tumor and their selection, dormancy and growth in a given secondary site. However, functional parameters descriptive of these processes are assumed to be essentially arbitrary. In spite of such generality, the model allows for computing the distribution of site-specific sizes of detectable metastases in closed form. Under the assumption of exponential growth of metastases before and after primary tumor resection, we showed that, regardless of other model parameters and for every set of site-specific volumes of detected metastases, the model-based likelihood-maximizing scenario is always the same: complete suppression of metastatic growth before primary tumor resection followed by an abrupt growth acceleration after surgery. This scenario is commonly observed in clinical practice and is supported by a wealth of experimental and clinical studies conducted over the last 110 years. Furthermore, several biological mechanisms have been identified that could bring about suppression of metastasis by the primary tumor and accelerated vascularization and growth of metastases after primary tumor resection. To the best of our knowledge, the methodology for uncovering general biomedical principles developed in this work is new.