Title: The Effects of Cancer Stem Cell Seeding Location in an Agent Based Model of Tumor Growth.

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The cancer stem cell hypothesis, that cancers may be driven by a small population of cells with stem cell-like properties, such as increased proliferative potential, has been gaining support in recent years. Norton proposes that primary and metastatic tumors may be conglomerates of seeded cancer stem cells that have circulated through the vasculature and returned either to the primary or metastatic site. In this work, we seek to understand the role of cancer stem cell seeding in the development of a primary or metastatic tumor. We do this by developing an agent-based model of cancer stem cell seeding based on Enderling et al. stem cell model. The model considers seeding of cancer stem cells that can mitose indefinitely, either symmetrically into two cancer stem cells or asymmetrically into a cancer stem cell and a progenitor cell. Progenitor cells have a finite number of mitotic events after which they die and they can only divide symmetrically into two progenitor cells. The simulation takes place on a 3D spatial grid and mitosis is space limited such that when a cell has no space in one of its 26 adjacent neighbors, it becomes quiescent and no longer proliferates. The location of the seeding events are varied and the growth of the tumor is examined. We find that seeding becomes an important factor in the growth of the tumor when progenitor cells have a larger number of mitotic events before death. In conclusion, we find that the seeding rate and number of progenitor cell divisions contribute to tumor growth in nontrivial ways.