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Real-time imaging reveals the single steps of brain metastasis formation.

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Brain metastasis frequently occurs in individuals with cancer and is often fatal. We used multiphoton laser scanning microscopy to image the single steps of metastasis formation in real time. Thus, it was possible to track the fate of individual metastasizing cancer cells in vivo in relation to blood vessels deep in the mouse brain over minutes to months. The essential steps in this model were arrest at vascular branch points, early extravasation, persistent close contacts to microvessels and perivascular growth by vessel cooption (melanoma) or early angiogenesis (lung cancer). Inefficient steps differed between the tumor types. Long-term dormancy was only observed for single perivascular cancer cells, some of which moved continuously. Vascular endothelial growth factor-A (VEGF-A) inhibition induced long-term dormancy of lung cancer micrometastases by preventing angiogenic growth to macrometastases. The ability to image the establishment of brain metastases in vivo provides new insights into their evolution and response to therapies.

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