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The reasons for the failures of conventional anticancer therapies are varied and multiple. It is however, becoming increasingly clear that physiological conditions in tumors, arising primarily from inadequate and non-uniform vascular networks, can play significant roles in the lack of therapeutic responsiveness of neoplasms. However, the impact of the tumor microenvironment far exceeds its direct effects on therapeutic treatment modalities. For example, tumor hypoxia can contribute to processes that directly favor malignant progression and increased metastasis. New treatment strategies aimed at improving tumor response through targeting cells existing in these microenvironments or the aberrant tumor vasculature itself, therefore are of high interest. Non-invasive imaging strategies may aid not only in identifying tumors that would be effectively treated with such strategies but also in providing effective means of monitoring treatment effectiveness and therapeutic outcomes.