Ovarian tumor attachment, invasion and vascularization reflect unique microenvironments in the peritoneum: Insights from *intravital* imaging and mathematical modeling

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We have established a xenograft model of human ovarian cancer relapse using SKOV3ip cells stably expressing GFP or RFP. Tumor cells are engrafted in nude mice by intraperitoneal injection, followed by intravital imaging of tumor attachment, growth and invasion after 1, 2 and 3 weeks. We report remarkably different tumor growth characteristics at distinct attachment sites, including spleen, omentum, and stomach/intestine, despite the similarities in the mesothelial lining on each surface. Once past the mesothelium, tumors attached to the spleen or omentum readily invade the "open" architecture of spleen and omentum. In contrast, tumors attached to the stomach or intestine are poorly invasive; rapid tumor expansion into the peritoneal space is supported by new blood vessels that extend from the outer lining of the stomach and intestine. Simulations of these complex processes are based upon the Cellular Potts computational framework. Modeling parameters, including the biomechanical constraints of tissue, relative adhesion between all cell types, chemotactic gradients and angiogenesis are derived from experiments. By combining experimental and simulation approaches, we gain important insights regarding the influence of the microenvironment on tumor growth, morphology and neo-vascularization.