Abstract 10:7-1

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Angiogenesis and Imaging perfusion

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While aerobic vasculogenesis for cancers is well known, glycolytic vasculogenesis, ALPHA, has only recently been described. The major tenents of glycolytic vasculogenesis differ remarkably from aerobic metabolism, in that waste products and drainage vessels are more important than oxygenation by arteries. The glucose required for glycolysis does not depend upon local arteries because it diffuses well and is actively transported. Management of optimal lactate levels requires lymphatics and veins.

Low and moderate lactate levels are an energy source and a powerful pro-cancer modulator (building substrates, cellular motility, invasiveness, etc). Conversely, high lactate levels inhibits glycolysis by end product inhibition and low pH. When ATP and building substrates from glycolytic side reactions are reduced, cell growth, division, and proliferation are prevented causing Go cellular arrest.

For cancer to grow, lymphatics and veins must reduce lactate to more optimal levels. Lactate independent of oxygenation levels (normoxia, hypoxia, or hyperoxia) induces vasculogenesis via Hypoxia Induction Factor (HIF1a), vascular growth factors and attracts angioblastic stem cells. The ensuing development sequentially produces lymphatics first, then veins, and arteries. This sequence has been confirmed by numerous animal model studies (de novo cancer, transfected VEGF gene, corneal growth factor implants, tumor xenografts).

Relative to perfusion imaging, the ALPHA vasculogenesis concept better explains the molecular basis of CT and MRI perfusion measurements. Contrary to the traditional theory, increased arterial flow has not been useful for characterizing cancer. The most useful perfusion parameters (blood volume, contrast washout, kinetic curve analysis, Ktrans/Kep permeability) are related to veins rather than arteries. Blood volume and contrast washout depend on veins. Kinetic curve analysis depends on venous outflow. Permeability measured by K-trans and K-up occurs in the veins.

ALPHA glycolytic vasculogenesis complements traditional vasculogenesis and explains many clinical and imaging inconsistencies. With development, ALPHA may improve diagnosis and treatment of cancers.