

Biomedical Engineering Seminar

Imaging of Myocardial Angiogenesis

Albert J. Sinusas, M.D.

Associate Professor of Medicine and Diagnostic Radiology

Yale University School of Medicine

Thursday, February 20, 2003

2-3 pm

United Technologies Building, Room 150, Storrs

Abstract:

Non-invasive imaging strategies will be critical for defining the temporal characteristics of angiogenesis, and assessing efficacy of angiogenic therapies. The presentation will review non-invasive imaging strategies for identifying the hypoxic stimulus for angiogenesis, as well as the physiological consequences of angiogenesis, and the use of targeted imaging to non-invasively track the angiogenic process over time. Myocardial hypoxia is known to stimulate angiogenesis in the heart, thereby providing a potential marker for the initiation of angiogenesis. Myocardial hypoxia can be identified non-invasively with ^{99m}Tc -nitroimidazole single photon emission computed tomography (SPECT) imaging, and thereby identify myocardial regions in which angiogenesis would be stimulated. Effective angiogenesis should result in an improvement in resting myocardial perfusion and a reduction in regional myocardial hypoxia. Thallium-201 SPECT perfusion imaging is an established approach for evaluation of changes in regional myocardial perfusion, which can be performed simultaneously with the ^{99m}Tc -labeled hypoxia agent.

However, hypoxia is not the sole force driving angiogenesis. The angiogenic response is also modulated by the composition of the extracellular matrix and intercellular adhesions, including integrins. Integrins are family of heterodimeric cell surface receptors capable of mediating an array of cellular processes, including cell adhesion, migration, proliferation, differentiation, and survival. The specific $\alpha v \beta 3$ integrin has been identified as a critical modulator of angiogenesis. Therefore, the angiogenic process can be directly tracked non-invasively by SPECT imaging of radiolabeled ligands targeted to modulators of angiogenesis, like the $\alpha v \beta 3$ integrin. To evaluate the ability of SPECT imaging to directly track the angiogenic process in vivo, we have compared SPECT imaging strategies employing an ^{111}In -labeled $\alpha v \beta 3$ antagonist and ^{99m}Tc -labeled nitroimidazole, with conventional radiolabeled microsphere measures of regional myocardial flow, ^{201}Tl perfusion, and immunohistological analysis of angiogenesis, using chronic rodent and canine models of ischemia induced angiogenesis. We have found that, an ^{111}In -labeled $\alpha v \beta 3$ antagonist (RP748) provides excellent in vivo images and may be a non-invasive targeted marker of angiogenesis in models of coronary occlusion and reperfusion. Future approaches for imaging myocardial angiogenesis will include; more conventional quantitative imaging of myocardial perfusion, function and metabolism; imaging of hypoxia or regional alterations in permeability, as well as targeted imaging of endothelial cell or non-endothelial cell markers and the extracellular matrix.

Dr. Albert Sinusas is an Assoc. Professor of Medicine & Diagnostic Radiology and Director of Cardiovascular Nuclear Imaging & Stress Lab of Yale Univ. School of Medicine. Dr. Sinusas graduated from Univ. of Vermont College of Medicine in 1983 and completed residency and fellowship from Univ. of Oklahoma Health Sci Ctr and Univ. of Virginia Health Sci Ctr in 1986 and 1988, respectively. Dr. Sinusas received numerous awards from Society of Nuclear Medicine and also in Best Doctors in America.