

PI Name: LINDNER, JONATHAN R
Project Title: Contrast Ultrasound and Diabetic Microvascular Disease
Project Start: 30-SEP-2002
Project End: 31-AUG-2007
ICD: NATIONAL INSTITUTE OF DIABETES AND DIGESTIVE AND KIDNEY DISEASES

Abstract: *DESCRIPTION (provided by applicant): A diagnostic technique capable of accurately assessing pathologic changes of the peripheral microcirculation in patients with diabetes could be used to detect early microvascular complications, to assess response to new and established therapies, and possibly to detect large-vessel vascular disease. The overall purpose of this proposal is to apply the recently developed non-invasive perfusion imaging technique of contrast-enhanced ultrasound, which is able to assess skeletal muscle perfusion at the capillary level, for the evaluation of microvascular alterations associated with diabetes and insulin-resistance. The first aim of this proposal is to determine whether contrast ultrasound can be used to detect abnormalities in the skeletal muscle capillary responses to increased muscle oxygen demand (exercise) and to insulin in patients and animal models of insulin-resistance and diabetes. Any association between abnormal capillary responses and diabetic microvascular complications will be characterized. The second aim is to develop a method for detecting peripheral vascular disease and for assessing its physiologic significance on limb perfusion using contrast ultrasound in a canine model and in patients with peripheral vascular disease. Data from these studies will be clinically important since information will be provided on the total impact of combined large-vessel and microvascular disease on distal perfusion. The final aim will be to use contrast ultrasound with novel site-targeted ultrasound contrast agents that bind to activated leukocytes in regions of injury/inflammation to assess tissue inflammatory responses that occur in response to peripheral vascular disease and demand ischemia. Data from these studies will be used to determine whether inflammatory responses are enhanced in animal models of diabetes. Successful completion of these studies will represent the first step in developing a reliable, widely available, and inexpensive method for ultrasound detection and characterization of diabetic vascular disease and microvascular complications.*