《**Invited Special Lecture**》

Nuclear Cardiology
Providing Tools to Characterize Lesions in the Vasculature

H. William Strauss, MD
Division of Nuclear Medicine
Stanford University, Stanford, California

Nuclear cardiology can trace its roots to studies performed in 1917 to measure the circulation time in man. These pioneering studies used a new radiation detector—the Wilson Cloud chamber. In the 81 years since Blumgart performed those classic studies improvements in instrumentation and radiopharmaceuticals now permit the routine analysis of regional ventricular function, perfusion and metabolism. Table 1 lists many of the common studies performed with radiopharmaceuticals in patients with coronary disease.

Table 1. Measurements, radiopharmaceuticals, and common instrumentation used for the clinical evaluation of the heart

Measurement	Radiopharmaceutical	Instrumentation
Global and Regional Left Ventricular Function	^{99m}Tc red cells, ^{99m}Tc albumin, ^{99m}Tc perfusion agents (with gated SPECT)	Gamma Camera [Planar and SPECT], Probe, Vest
Perfusion	^{201}Tl, ^{99m}Tc Sestamibi, ^{99m}Tc Tetrofosmin, ^{99m}Tc Teboroxime, ^{92}Rb	Gamma Camera [Planar and SPECT], Positron Tomograph
Metabolism	^{18}FDG, ^{123}I fatty acids and modified fatty acids	Positron Tomograph, Gamma Camera [Planar, SPECT and coincidence]
Acute Necrosis	^{99m}Tc Pyrophosphate, ^{111}In-antimyosin FAB	Gamma Camera [Planar and SPECT]

Many of these procedures were developed over the decade between 1968 and 1978. In the following 20 years the technology for performing the procedures has been refined and extensive clinical application validated the use of these procedures in the clinical environment. The field is now poised for another round of growth. It is likely that the next few years will see the development of specific markers for atheroma, chronic ischemia, and myocardial apoptosis.

In unstable angina and acute infarction, for example, it is clear that not all atheromatous lesions are of equal prognostic importance. Quiescent lesions, which are primarily composed of fibrous tissue, perhaps with some calcification, are less likely to rupture. While some of these fixed stenoses may be associated with stress inducible ischemia, these are not the lesions which are

usually associated with sudden death. On the other hand, lesions with a high content of foam cells, lipids, and a thin endothelial cap are much more likely to rupture. Plaque rupture is associated with thrombus formation, vascular occlusion, and sudden death.

Two potential approaches to identify unstable plaque are: a. an agent that recognizes the increased concentration of selections found on endothelium in the vicinity of the lesion or b. localize on the activated monocytes or foam cells contained in the lesion. Like the endothelial cells in the region of the lesion, the activated cells have increased expression of monocyte chemoattractant peptide receptors.

Similarly, a series of growth factors involved in the production of new capillaries have been identified. The family includes fibroblast derived growth factor (FGF), vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF). Specific growth factors are associated with proliferation of endothelial cells, proliferation of vascular smooth muscle and formation of capillary tubular structures. Production of these growth factors is stimulated by hypoxia and by tissue injury. Upregulation of both production and receptors for these agents appears to occur in the immediate region of ischemia. These growth factors can be radiolabeled and the distribution of their receptors defined. Such imaging could serve as a marker of chronic ischemia.

Apoptosis is now known to play a role in transplant rejection. Apoptosis can be identified specifically using a ^{99m}Tc labeled form of a physiologic protein, annexin. Recent studies in rats with heterotopic heart transplants clearly identified apoptosis by marked tracer localization in the rejecting heart. When the animals were treated with cyclosporin, uptake of annexin promptly fell to control levels, in parallel with the histologic changes.

An interesting corollary to the development of these interesting radiopharmaceuticals is the recognition that visualization of these lesions may require a different approach to imaging. The small size of the lesion may make external detection of the sites difficult or impossible. As with intravascular ultrasound characterization of the extent of atheroma, an intravascular camera may be required to portray the sites of pathology. Mating such an instrument with either an optical imaging probe or ultrasound could permit multidimensional characterization of vascular abnormalities.

Advances in these areas will serve as the basis for the development of procedures to spur renewed growth of radionuclide cardiac imaging.