EDITORIAL

Nuclear Probes in Cardiology

Nuclear probes have been used in the measurement of circulation and cardiovascular function for over fifty years. However, it was not until a decade ago, with the advent of ^{99m}Tc radionuclide angiography and the development of scintillation devices that investigators turned their interest towards non-imaging nuclear probes. Wagner et al. (*1*) were the first to develop a clinically applicable instrument utilizing a sodium iodide-photomultiplier detector for beat-by-beat analysis of cardiac function using blood-pool angiographic techniques. The nuclear stethoscope (Bios Inc.) was then to become the basis of much of the development seen in probe technology today (*1*). Although most nuclear procedures are carried out using the gamma camera, there are situations where its high spatial resolution is not essential. Particularly in dynamic or long-term studies, it is difficult to maintain a constant spatial relationship between the patient and the camera head. The nuclear probes have the advantage of high temporal resolution and thus can be positioned over the heart to record change in cardiac radioactivity (volume), utilizing blood-pool ventriculography, thereby allowing both beat-by-beat and gated cardiac function studies.

In this issue of the *Journal*, Taki et al. (*2*) have described the application of a newly developed nuclear probe system based upon a miniature cadmium telluride detector. They have presented validation of their nuclear probe for the measurement of resting ejection fraction (EF) in comparison to that obtained by standard gamma camera methodology. The authors have also demonstrated a clinical application of this method for monitoring left ventricular function during dynamic supine exercise in patients undergoing coronary artery bypass surgery. They have shown that this system may be utilized to record ejection fraction values accurately, not only at rest, but also during exercise (*2*). In 54 patients undergoing coronary artery bypass grafting, Taki et al. have shown that the fall in EF observed prior to surgery was reversed when the patients were re-studied after recovery from surgery. Furthermore, they have also demonstrated the utility of continuous monitoring of EF during and after exercise.

Over the last decade, there has been a small, but dedicated group of enthusiasts, who have pursued the development of various miniaturized nuclear probes for continuous cardiac function monitoring (*3–5*). The disadvantage of the nuclear stethoscope detector was its considerable size and this did not allow the device to be fixed to the patient's chest wall. Thus, initial research has been directed towards solid state devices, such as, mercuric iodide (*3*) and cadmium telluride detectors (*4–6*). Although the mercuric iodide detector has a considerable higher energy resolution than cadmium telluride, it has the disadvantage of being somewhat brittle and the high-cost of production made it a commercially non-viable project. It appears that Taki et al. have overcome the reduced sensitivity of the cadmium telluride detectors and are able to perform gated studies using 20-sec acquisitions (*2*). More recently, we have developed a miniature cesium iodide detector that is optically coupled to a photodiode for continuous cardiac function monitoring, (Cardioscint, Oakfield Instruments Ltd.) which has been described in an earlier issue of this *Journal* (*7*). The CsI/photodiode detector is robust, low cost, has high count rate capabilities for ^{99m}Tc and is relatively lightweight. I feel that probe technology has now reached a stage where these new instruments are no longer in the developmental laboratory, but have unique clinical potential.

The last decade has seen a plethora of clinical studies, directed towards the study of coronary heart disease with a view to determining cardiac function and estimating risk. There is little doubt that the LVEF measured at rest or during exercise has independent prognostic value in coronary heart disease (*8–12*). In patients with significant obstructive coronary artery disease, it has been clearly demonstrated by radionuclide ventriculography that, exercise-induced myocardial ischemia is usually characterized by either failure to increase or a fall in ejection fraction in addition to development of regional left ventricular asynergy. The development of regional wall motion abnormality during exercise is thought to be a specific indicator of underlying myocardial ischemia (*10*), but there is no evidence that this finding has any value in assessing prognosis. Thus, nonimaging nuclear probes may be used instead of gamma cameras for the assessment of prognosis alone in patients with suspected coronary heart disease. The nuclear probes can be used to provide accurate estimates of resting and exercise EF, as demonstrated by Taki et al. and others (*2,13–16*). The added advantage of the Cardioscint (*7*) and VEST (*6,15*) is that, both these instruments incorporate electrocardiographic leads which are useful for monitoring ST-segment changes or arrhythmias in addition to left ventricular function.

With the advent of improved computer technology, it is possible to store the dynamic left ventricular volume data directly on floppy discs for rapid retrieval and analysis (*2,7,16*). The slight disadvantage of the VEST technique at present is that the radioactivity and ECG data are stored on cas-

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sette recorders which is subsequently analyzed and this may prove to be a time consuming and laborious process. However, this minor problem can be easily overcome by new-generation solid state memory for storage and online data processing. There are significant advantages of being able to monitor in real-time either in the beat by beat or "gated" modes during interventional cardiac studies (*2,7*).

In this era of interventional cardiology, the nuclear probes have an unique role to play, such as the demonstration of transient myocardial impairment during coronary angioplasty, as measured by the Cardioscint and VEST techniques (*17–19*). All three investigators have reported transient and rapid falls in EF associated with an increase in cardiac volume during inflation of the coronary angioplasty balloon, and these parameters were closely correlated with other standard criteria for myocardial ischemia (*17–19*). Hartmann et al. concluded that short periods of controlled myocardial ischemia during coronary angioplasty led to a decrease in systolic and diastolic left ventricular function during myocardial ischemia, as estimated by the Cardioscint (*18*). Whereas, Breisblatt et al. have used the Cardioscint for continuous monitoring of unstable patients in the postangioplasty period and they have used this technique to assess response to therapeutic interventions (*19*). Kayden et al. (*20*) have clearly demonstrated the utility of continuous ambulatory monitoring of left ventricular function with the VEST during recovery from acute myocardial infarction, in those who received thrombolytic therapy (*20*). Management of patients with unstable angina can also be aided by on-line cardiac function monitoring, particularly during interventions with potent vasodilators such as nitroglycerine (*21,22*). The probe methodology should also find wide usage in the field of clinical pharmacology. These techniques may be utilized in association with hemodynamic monitoring to assess therapeutic efficacy of new drugs in congestive heart failure (*23,24*). Broadhurst et al. have validated the Cardioscint changes against right heart pressure monitoring (Swan-Ganz technique) during stress atrial pacing in patients with stable angina, and demonstrated the relationships between the change in cardiac output, pulmonary artery wedge pressure and EF changes during pacing-induced myocardial ischemia (*3*). Even small changes in ambulatory pulmonary artery diastolic pressure correlated with simultaneous left ventricular volume changes, as measured by the VEST in a group of patients with coronary heart disease undergoing clinical evaluations (*25*). Thus, a wide range of methods have been used to validate the non-imaging nuclear probes.

Accurate measurement of diastolic left ventricular function can also be performed using the high resolution time-activity curves generated from the nuclear probes in rapid successive gated acquisitions lasting between 10–30 sec. Whereby, the peak filling rate can be displayed (as a trend) in relationship with other systolic parameters, cardiac volumes and ECG. Breisblatt et al. have validated the measurement of peak filling rate by the Cardioscint against a gamma camera (*19*). Hartmann et al. have made interesting observations in the postangioplasty period, and have shown that despite the normalization of EF and cardiac volumes to baseline after release of the angioplasty balloon, the diastolic function (as measured by peak filling rate) remains abnormal for a considerable period after the procedure. These techniques may provide a window for further in-depth study of patients with unstable coronary syndromes and help in their management.

The beat-by-beat LVEF mode may also find unique applications in the field of cardiac arthythmias. It may be possible to study the degree of impairment of cardiac function induced by different arrhythmia morphologies and aid in their subsequent management with drugs. Ambulatory (VEST) and stationary nuclear probes have important roles to play in the assessment of silent myocardial ischemia. Ambulatory electrocardiographic monitoring has been clearly defined in the evaluation of silent myocardial ischemia (*26*). However, in a large population of normal volunteers, ambulatory electrocardiographic measurements have shown false-positive ST-segment changes (*27*) thus, the addition of ambulatory left ventricular volume measurement may provide further diagnostic power. Using the VEST technique, many studies have clearly defined its role in the assessment of silent myocardial ischemia during recovery from myocardial infarction or after coronary artery bypass surgery (*28–31*).

The noninvasive nature of the nuclear probes also lend itself ideally to the measurement of physiological parameters. These methods have made a significant impact in the understanding of dynamic changes in left ventricular function during isometric hand-grip and cold pressor tests in normal subjects (*32*). More recently, the mental stress test has found an interesting application in patients with coronary heart disease (*33,34*)

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