EDITORIAL
Continuous Radionuclide Monitoring of Left Ventricular Function: Has the Time Come?

The ability to continuously monitor left ventricular ejection fraction would be of great value for the assessment of ventricular function in both the critically ill, as well as the ambulatory cardiac patient (*1*). While radionuclide studies of cardiac function can be performed with a variety of single- or multicrystal cameras, these are cumbersome for evaluating serial function and are not sensitive enough for the detection of rapidly changing physiologic events. As an alternative radionuclide approach, nonimaging detectors can provide a gated high temporal resolution time-activity curve that can be used to assess ejection fraction, relative ventricular volumes, and parameters of systolic and diastolic ventricular performance (*2,3*).

The major assumption of this nonimaging approach is that the left ventricular region can be isolated from other cardiac structures so that changes in radionuclide counts reflect changes in left ventricular ejection fraction and volumes. Recently, this technology has gained acceptance and has been used to address certain pathophysiologic questions which previously have been difficult to study (*4–6*). In this issue of the *Journal*, Broadhurst and colleagues report on the use of a new miniaturized nonimaging detector system (Cardioscint) for the continuous online monitoring of ejection fraction and ST segments. Their initial results raise the question of whether this new monitoring approach is practical for the continuous evaluation of ventricular function in the unstable cardiac patient.

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PRESENT NONIMAGING DETECTOR SYSTEMS

The concept of nonimaging detectors for evaluating left ventricular function came into clinical use in the middle 1970s with the development of the nuclear stethoscope by Wagner et al. (*7*). The basic idea of probe technology is to use the detector as a single large pixel to view the entire left ventricle. Spatial resolution which is required to produce the image that we see with the gamma camera is replaced by temporal resolution. The result is that a gated high temporal resolution time-activity curve can be obtained with nonimaging probes in as little as 10 sec. If data are acquired for 30 sec or more, the 10-msec resolution curve that is displayed can accurately measure ejection fraction, as well as parameters of diastolic function such as peak filling rate and time to peak filling.

The nuclear stethoscope (NIC II, Bios Inc., Valhalla, NY), which was the first commercial system available for use, consists of a NaI detector affixed to a single bore converging collimator. The probe has a 6-cm field of view and a maximal count rate of 140,000 cps. It is mounted on a moveable arm that allows two angular degrees of freedom. The entire device is easily portable and contains an onboard computer. Data can be stored or displayed in real time, in either a beat-to-beat mode or a gated-summed high temporal resolution format. A number of studies have compared the nuclear stethoscope against first-pass radionuclide angiography, equilibrium radionuclide angiography, and contrast angiography. These indicate a close correlation between ejection fraction measured by the probe and the established techniques (*1,8*).

The nuclear stethoscope has proven useful in a variety of clinical situations, including the evaluation of patients in the intensive care unit, the assessment of myocardial ischemia in the coronary care unit, during anesthesia induction, and in the postoperative evaluation of ventricular function in patients after coronary bypass surgery (*9,10*). Serial noninvasive monitoring with the nuclear stethoscope has proven useful in optimizing drug therapy and in assessing response to therapeutic agents in the coronary care unit. These studies suggest that noninvasive parameters obtained with the nuclear probe provide an accurate assessment of changes in cardiac output and correlate well with invasive hemodynamics. In studies by Breisblatt et al., response to agents such as i.v. nitroglycerin and i.v. nitroprusside could be inferred from the radionuclide nuclear probe data, without need for invasive measurements (*11,12*). Interestingly, following heart rate, blood pressure and pulmonary pressures in individual patients did not provide for optimal dosing, which was best obtained with serial radionuclide data.

The nuclear probe appears best suited for use in the critical care arena. A new nonimaging detector, the nuclear vest (Capintec, Inc., Ramsey, NJ), can provide an ambulatory evaluation of ventricular function during a patient's daily activities. Like the nuclear probe, the detector material is a thallium-activated NaI crystal with a parallel-hole high-sensitivity collimator housed within a molded plastic vest-

like garment that the patient wears. Both systems have approximately a 6-cm field of view with good resolution to a depth of 10 cm. Unlike the nuclear probe, which is positioned without the gamma camera using a series of positioning algorithms and following maximum stroke counts (as described by Broadhurst with the Cardioscint detector), the vest is positioned in front of the gamma camera using a target that allows the detector to cover only the left ventricular region of interest. The vest has a 2-channel electrocardiogram that can be used to correlate with changes in ejection fraction. The electrocardiographic and nuclear data are recorded on a tape recorder and played back for the analysis of data.

Data analysis is presently off-line with the vest as opposed to the real-time online assessment which can be obtained with the nuclear probe or the new Cardioscint system. The nuclear vest can be worn comfortably by a patient for up to 6 hr, but bedside use of this device for long-term monitoring is not practical. Similar to the nuclear stethoscope, validation studies have been performed with a cardiac phantom and equilibrium radionuclide angiography at rest and during exercise (*1,13*). Both of these devices rely on an estimated background, which varies between 70% and 75% of end-diastolic counts. Manual determination of background can be performed with the nuclear probe and Cardioscint systems, but the automated background approach used with all the nonimaging detectors correlates well with the gamma camera determination of ejection fraction.

The nuclear vest has provided physiologic information on changes in ventricular function during routine, as well as structured activities (such as exercise, mental stress, cold pressor testing) in normals, hypertensive patients, and patients with coronary artery disease. Particularly in the diagnosis of silent myocardial ischemia, it has become clear that transient decreases in left ventricular ejection fraction (lasting greater than 1 min) measured with the vest will proceed the development of chest pain or electrocardiographic changes by at least 30–90 sec (*14*). Additionally, in studies that have been performed to date, only 30% of the episodes where ejection fraction has been noted to fall are associated with electrocardiographic changes. In recent studies by Kayden et al., as well as our group, spontaneous decreases in ejection fraction in post-myocardial infarction patients were found to be predictive of patient outcome and recurrent cardiac events (*15*). These studies suggest that ejection fraction monitoring may be superior to the electrocardiogram for detecting and quantifying patients with myocardial ischemia (*16*). Changes in ejection fraction must be interpreted with caution, as changes in preload and afterload may effect the ejection fraction determination as well as events other than myocardial ischemia. The nuclear vest while now proven to have a role in the evaluation of the ambulatory cardiac patient will require further patient studies and some changes in design before it will be widely useful to the clinician.

A NEW MINIATURIZED DETECTOR

The present generation of nonimaging detectors have certain limitations for bedside monitoring. The vest is designed for the ambulatory patient and is not practical for long-term bedside monitoring. It is also limited by the requirement for gamma camera positioning. The nuclear stethoscope while useful at the bedside is cumbersome and requires significant operator interaction. The swinging mechanical arm, which must be held or placed on the patient's chest, makes it impractical for long monitoring periods. If continuous radionuclide monitoring is to be practical in the coronary care unit, then miniaturization of the nonimaging detector is essential. Previous attempts with cadmium/telluride and mercury/iodide as the detector material have met with technical problems and may have represented a concept ahead of its time (*17,18*).

The new miniaturized cesium/iodide optically-coupled photodiode detector developed by Broadhurst et al. in conjunction with Oakfield Instruments (Oxford, UK) and reported here, appears to confer advantages that previously have not been available with other bedside detector systems. It is lightweight, easily positioned, can be comfortably worn by the patient, and is capable of continuous monitoring of left ventricular function without significant operator interaction. It interfaces to a personal computer with user-friendly software so that data can be archived, trended, and continuously updated online. As a nonimaging detector its cost should be reasonable. The accuracy of this detector system over a wide range of left ventricular ejection fraction compares favorably with the gamma camera whether or not an automated background approach is used and even with the probe positioned blindly. While the initial results reported in this issue of the *Journal* are encouraging and warrant further assessment of this new detector system, there are a number of issues that still remain unresolved.

LIMITATION OF NONIMAGING DETECTOR SYSTEMS

What characteristics would be important for the ideal beside detector system (Table 1)? With any detector system it is essential that the left ventricular region of interest be isolated from other cardiac structures and that the detector remain over the left ventricle during the entire study. Movement of the detector could cause artificial increases or decreases in ejection fraction. All nonimaging detectors only evaluate global ventricular function and pro-

TABLE 1
Characteristics of the Ideal Detector System

- *Lightweight* and *portable*.
- *Easily positioned*, with user-friendly positioning algorithms.
- *Adequate field of view* to define the left ventricle (6 cm).
- *High counting* rates with linearity up to 50,000 cps.
- 10 msec *temporal* resolution.
- Ability to *continuously* monitor left ventricular ejection fraction and relative ventricular volumes.
- Ability to *store* and *archive* the left ventricular time-activity curve.
- Continuous monitoring of *background activity* and measurement of relative pulmonary blood volume.
- *Radionuclide stroke counts* must reflect *actual changes* in cardiac output and ventricular volumes.
- High resolution 2-channel *electrocardiogram* for ST analysis.
- *Generation of an image* to assess regional ventricular function.
- *Low cost* and *limited operator interactions* to allow for wide clinical use.

vide no information on regional wall motion. Despite this limitation, several studies including this one, show excellent ejection fraction correlation with the gamma camera even in patients with wall motion abnormalities (*19*).

During myocardial ischemia, however, regional dysfunction may occur without significant changes in global ejection fraction and could potentially be missed by the detector system. If the detector is placed over a well-contracting region in a patient with known asynergy, ejection fraction may be overestimated. The field of view of the detector system must be large enough to cover the left ventricle (6 cm), but not too large that other cardiac structures are included. A fixed region of interest is used with nonimaging detectors, compared to the variable region used with the gamma camera. This difference may overestimate end-systolic counts and cause an underestimation of ejection fraction. In patients with chronic obstructive pulmonary disease, obese patients, or women, the distance between the detector and source may increase and ejection fraction can be overestimated. While these potential problems have not been found in large patient series, this could be a concern in individual patients (*20*).

Another issue is the determination of background. While a fixed percentage of end-diastolic counts may be useful in stable physiologic states, this assumption may not be true in patients with ischemia or congestive heart failure where left ventricular end-diastolic pressure is changing and background radionuclide counts may increase. The nuclear vest system contains a second cadmium/telluride detector placed over the right lung to monitor background changes. Possibly a second background detector should be added to the new Cardioscint system, but further data are required before these changes should be considered. In long-term studies, it may be necessary to reevaluate background at frequent time intervals. Changes in radionuclide stroke counts should correlate well with changes in cardiac output by thermodilution or other methods. While this has been demonstrated with the nuclear stethoscope, and some preliminary data have been presented for the Cardioscint system, further studies are needed to verify that changes in radionuclide counts will be a reflection of actual changes in volumes.

FUTURE DIRECTIONS

The continuous online valuation of left ventricular function in the coronary care unit to diagnose and monitor patients with myocardial ischemia, as well as to guide patient treatment, has considerable potential. In the evaluation of the patient after thrombolytic therapy or coronary angioplasty, continuous monitoring may identify patients who develop coronary occlusion and recurrent ischemia. In the unstable cardiac patient following ejection fraction, relative ventricular volumes could replace invasive hemodynamics that are currently used to guide drug therapy with i.v. nitroglycerin or vasodilators. This new innovative detector system, however needs to be tested during long-term monitoring, and several important questions will need to be answered. How stable is the determination of ejection fraction over hours, and do significant changes in background occur that can not be accounted for with the routine decay of the radioisotope? For the assessment of ischemia, is the single lead electrocardiographic system sufficient? Ambulatory electrocardiographic systems utilize at least two leads and the ST analysis package of the Cardioscint system needs to be validated if it is to be used in the diagnosis of myocardial ischemia. Once the detector has been positioned, is the information reliable enough to make decisions concerning patient managenent? Can the system be used by a nurse or technologist or will it require continuous physician interaction? These questions will need to be answered before the value of this new detector system can be assessed.

While the ideal detector system is still not available to us, this new system provides many essential features. Has the time come to utilize continuous radionuclide monitoring of left ventricular function for the evaluation of the unstable car-

diac patient? This new system is possibly a start in the right direction.

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