Technical Considerations for Nuclear Medicine Studies of Cardiac Transplant Patients

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Heart transplantation has become an important means of treating end stage cardiac disease. There is a need to monitor function and possible rejection of cardiac transplants. Several methods have been used and proposed for this purpose. In this article, several technical aspects of the proper imaging and interpretation of thallium and gated studies of heart transplant patients will be discussed.

Nuclear medicine studies are important in the evaluation of cardiac transplants. They are non-invasive and relatively inexpensive examinations that can be done repeatedly, and they give valuable information to the clinician. However, certain technical problems are encountered while performing these studies, and these problems have not been previously addressed in the nuclear medicine literature.

There are basically three different surgical procedures used for heart transplantation. In the orthotopic transplant, the native heart is removed and replaced by a donor heart. In the heart-lung transplant, which is necessitated by chronic pulmonary disease, both native heart and lung(s) are removed and replaced with a donor heart and lung(s). In the heterotopic transplant, a small donor heart, known as the "piggy back" heart, is transplanted on the right side and attached to the native heart.

Endomyocardial biopsy, currently the standard method for documenting the rejection of a cardiac transplant, is not an ideal method. The biopsied area may be scarred by a prior biopsy (*1*) and, therefore, not represent the heart as a whole. Angiography has also been used to diagnose rejection (*2*). Both procedures are invasive, unpleasant, expensive, and entail the risk of complications (*3*). Alternative non-invasive methods for diagnosing rejection have been tried using indium-111 (^{111}In) labeled lymphocytes (*4*), ^{111}In-labeled antimyosin (*5,6*), magnetic resonance imaging (MRI) studies (*5, 7,8*), gated blood pool studies (*9–11*), thallium myocardial imaging (*12*), and echocardiology (*13*). Echocardiology is not suitable for some patients due to their body habitus, i.e., they have a limited echo window due to transplant position. Clinical signs of congestive heart failure will occur much later than do signs of ventricular dysfunction detected through endomyocardial biopsy or nuclear medicine.

As of October 1990, Baptist Medical Center of Oklahoma (Oklahoma City, Oklahoma) has performed 100 heart transplants of both heterotopic and orthotopic types, as well as 4 heart-lung transplants. For 43 of these cases, we have evaluated the ejection fraction and ventricular volume information from gated studies (*9,10*), along with results of thallium myocardial imaging (*11*); we compared these results with the clinical and biopsy data to predict which patients would experience rejection. Some of the technical factors that we assessed while conducting this research deserve special attention and are discussed below.

GATED BLOOD POOL IMAGING

The procedure followed for gated blood pool studies involves a modified in vivo/in vitro tagging of red blood cells (*14*). The injection of cells is made in the left arm so that the volume sample can be drawn from the right arm during the LAO acquisition. Care must be taken when administering the intravenous injection of technetium-tagged red blood cells since infiltration of the radionuclide will result in inaccurate ventricular volumes.

The Orthotopic Heart

The ECG setup for the orthotopic transplant is the standard 3-lead ECG used in most non-transplant patients. R-wave intervals, however, are much more consistent due to the denervated heart.

Images are obtained in the LAO projection about midway between the sagittal and coronal planes, which demonstrates maximum separation of left and right ventricles. This angle is recorded and used on all subsequent studies. These angles could be quite severe as a result of surgical placement of the transplanted heart. Thirty-two frames in a 64 × 64 × 8 matrix are acquired for six min or for maximum pixel saturation. Fifteen ml of blood is drawn from a site other than the injection site and stored in an anti-coagulated tube. Later, it is pipetted and used to determine the activity present per ml. A marker is placed over the middle of the ventricle at the LAO angle. The camera is then moved to an anterior position

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and a 128 × 128 × 16 static image is taken for 30 sec. This marker image is acquired only during the initial study to determine chest wall thickness. This procedure has been described in detail in the literature (*15*).

Anterior and left lateral gated equilibrium images are also obtained.

Processing

To better standardize areas of interest, an automated area-determination program is used. Thirty-two areas are drawn and a volume curve is generated from these data. Diastole, systole, peak filling rate, peak emptying rate, and ejection fraction are determined from this curve. Consistency in the placement of background areas and accurate record keeping of factors used is extremely important for reproducibility of serial studies.

Ventricular volumes are determined using a commericially available Geometric Volumes Program (*15*). In brief, the depth from chest wall to middle of the left ventricle is ascertained by a trigonometric function using the camera angle and a known length. This depth is then used for all subsequent studies on the patient including soft-issue attenuation calculations.

The Heterotopic Heart

Anatomy of the heterotopic heart differs drastically from that of the orthotopic transplant. This can cause inaccurate R-R intervals, resulting in a poor quality exam. Radiologically translucent electrodes should be placed on the right side of the chest wall. Placement of these electrodes will depend upon the anatomical positioning of the donor heart. Electrodes must be placed in such a manner as to maximize the R-R interval obtained from the donor heart.

Images are obtained in both anterior and RAO projections. This RAO angle is usually very slight. Due to the overlying ventricular anatomy, separation of the left and right donor ventricles is difficult to obtain. A slight caudal tilt of about 15° from the coronal plane can be helpful with separation of atria from ventricles or ventricles from each other.

The anatomical location of the donor heterotopic heart is in the lower right midsection of the chest, directly superior to the right diaphragm. The LV is inferior to the RV and is most often connected to the native heart at the right atrium (Figs. 1 and 2). Processing is similar to the orthotopic transplant. Close attention should be paid to the placement of the background area of interest. The diaphragm should be avoided; placement is more adequate in the right lung field.

THALLIUM IMAGING

Stress thallium imaging has been performed using oral dipyridamole, treadmill, and intravenous (IV) adenosine. The preferred method for stress is the exercise treadmill. For patients who cannot exercise, IV adenosine (*16*) has shown excellent results. Our patients have experienced unpleasant side effects with the oral administration of dipyridamole (*17*). The exercise response of the transplanted heart differs from that of the normal heart. Due to its denervated state, the heart rate of the transplanted heart does not increase as rapidly with exercise, only with the increase of catecholamines within the blood. The consequence of this is a slower increase in heart rate and a slower recovery from exercise. The chances of achieving maximum exercise are decreased due to this phenomenon.

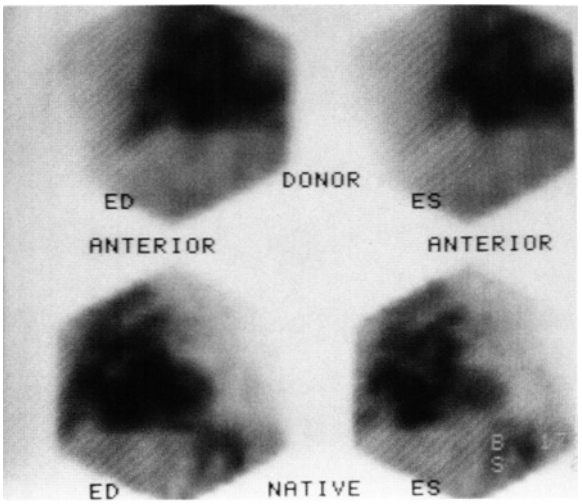

FIG. 1. Gated ED and ES frames of a heterotopic transplant. The top two images are the donor heart; the bottom two images are the native heart.

Four mCi of thallium-201 (^{201}Tl) are administered at peak exercise. The patient is monitored until the heart rate decreases, then a 5 min anterior image is obtained. In patients who cannot tolerate the stress treadmill, the following IV adenosine procedure is used. The adenosine is infused using an IVAC pump for 6 min at a rate of 140 μg/kg/min. Thallium is injected three min after commencement of the adenosine infusion, using a second IV line. Imaging is done according to the treadmill protocol. Single-photon emission computed tomography (SPECT) images are then obtained at 40 sec per stop for 32 frames with a 64 × 64 × 16 matrix, over a 180° arc. This tomogram is followed by a 45° LAO

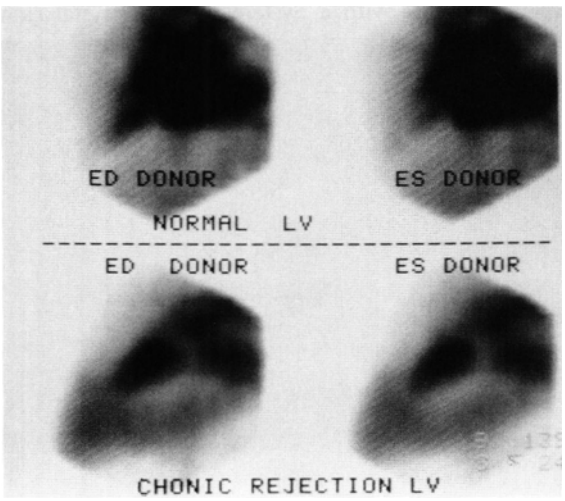

FIG. 2. Top set of images illustrates normal LV function of two heterotopic hearts. The bottom images demonstrate the effect of chronic rejection.

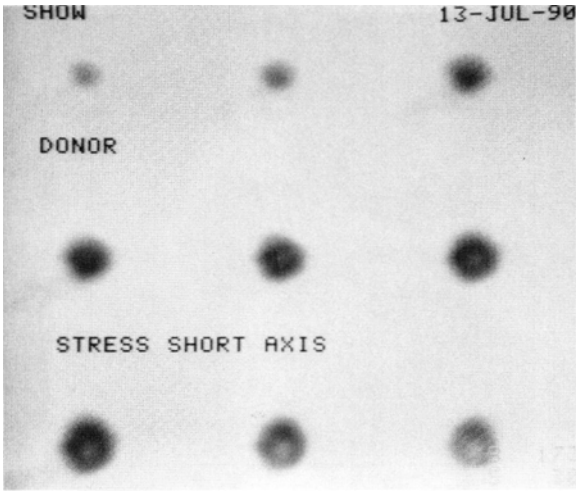

FIG. 3. Stress short axis images of donor heart, apex to base.

static view. The patient is brought back four hr later for delayed imaging.

Images are reconstructed using a 0.78 Hamming filter with a simple back projection method of reconstruction (Figs. 3 and 4). A bullseye plot is generated from the data obtained by the SPECT reconstruction (*18*).

The Heterotopic Transplant

Electrodes are placed in a mirrored arrangement of the normal 12-lead SPECT setup. Stress is achieved using the standard Bruce protocol, oral dipyridamole, or IV adenosine.

A 4-mCi dose of ^{201}Tl is administered upon achieving the target heart rate. An immediate anterior static image is obtained, which includes both the native and donor hearts. A 360°, 64 stop tomographic study is acquired at 30 sec per stop. This method makes reconstruction possible for both the native and donor hearts.

RESULTS AND DISCUSSION

At Baptist Medical Center, we initially attempted to image transplanted hearts with a System 77 multicrystal camera (Baird Corp., Boston, MA). This proved inadequate due to the reoriented, elaborate anatomy encountered. The volume program is based on the RAO projection, while the transplanted heart may be reoriented.

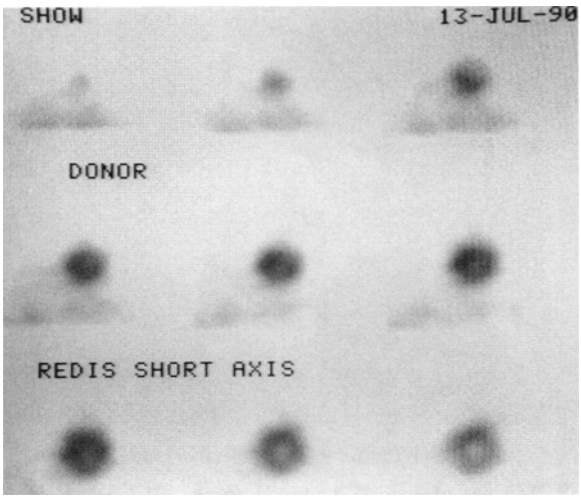

FIG. 4. Redistribution short axis images of donor heart, apex to base.

Another major problem experienced with the first-pass method was the split bolus encountered with the heterotopic heart. It was due largely to this set of circumstances that gated ventriculography was chosen over other methods to evaluate this select group of patients. After evaluating several methods, the program provided by the ADAC Nuclear 3300 computer (ADAC Corp., Milpitas, CA) was chosen. It must be stressed that one does not look for absolute values, but rather a change in ventricular volumes from the baseline studies. To reduce errors, the same operator and equipment should be used to run all the volume program studies.

Thallium imaging has been a successful means of evaluating cardiac grafts. However, certain problems should be addressed in imaging the cardiac transplant. Serial studies should be completed utilizing the same equipment. Bullseye data should be reviewed carefully as the program database is based on a normal non-transplant population. A lung/heart ratio should be calculated on the immediate anterior view. The orthotopic transplant proved to be by far the easiest type of transplant to acquire and process. Reorientation of the heterotopic transplant on some computer systems proved to be a problem due to the angles needed. This problem was solved by reorientating data into a mirror image projection using an ADAC computer so that the area of interest formerly on the left side of the screen appeared on the right side of the screen. The heart was then in a normal position for processing.

Original SPECT acquisitions of the heterotopic transplant were done with 180° acquisition from RPO to LAO. Later, a 360° acquisition was found to be a more desirable method. The orientation of the resulting short axis views differed from the normal by a 20°–30° clockwise tilt. This makes comparing the transplanted heart to any group of normals a possible source of error.

Due to suboptimal stress and side effects such as nausea, which are associated with the use of oral dipyridamole, we used the stress treadmill or IV adenosine for transplant patients (*16*).

CONCLUSION

Nuclear medicine studies are important in the evaluation of cardiac transplants. However, there are certain special problems encountered during nuclear medicine imaging of these patients. In the orthotopic heart, post surgical changes often cause a shift in the usual position of the septum. For the heterotopic heart, there are complex anatomic changes. This article describes the post surgical changes and details the methodology necessary for optimal study of these patients using nuclear medicine techniques.

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