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# CLINICAL APPLICATIONS OF A PRESSURIZED XENON WIRE CHAMBER GAMMA CAMERA UTILIZING THE SHORT LIVED AGENT $^{178}$Ta

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A pressurized xenon wire chamber camera has been developed for applications in nuclear medicine. The device employs a high speed delay-line readout and digital processing system providing a peak count rate of 850000 cps, spatial resolution of 2.5 mm and highly uniform imaging characteristics. A short-lived generator produced radionuclide, $^{178}$Ta, having an emission energy of 55–65 keV has also been developed. It provides greatly reduced radiation dosimetry compared with any commercial isotope in current use and is imaged very effectively with the wire chamber camera. Performance of this camera and isotope for first-pass radionuclide assessment of cardiac function compares favorably with the accepted standard of this technique, the multicrystal gamma camera and $^{99m}$Tc. Currently ongoing studies in exercise cardiac assessment, bedside imaging in myocardial infarction patients and pediatric cardiac imaging, point the way to unique applications of this technology in cardiology.

## 1. Introduction

Conventional gamma cameras utilized in nuclear medicine are all based on NaI crystal technology and have many recognized limitations. These include poor spatial resolution imposed by the encumbrance of phototube light collection, poor intrinsic uniformity, and low speed performance as a result of the lengthy light emission duration. The devices are also quite heavy, bulky, expensive and difficult to maintain. This work describes a gamma camera employing a pressurized xenon wire chamber detector with many advantages over the NaI camera technology [1]. Clinical cardiology studies performed with it utilizing the new radiopharmaceutical $^{178}$Ta are described. This agent has an ideal emission energy for use with the xenon wire chamber and has a short half-life (9.3 min) providing the benefit of greatly lowered patient radiation dose compared with standard agents.

## 2. Camera design

The basic wire chamber detector has been previously reported [1]. The general design features are as follows. The sensitive area is 25 cm diameter circular. The entrance window consists of a spherically formed aluminum shell of thickness 0.75 mm. This structure performs elastically to a pressure of 9 atm. The wire grid electrodes consist of two orthogonally oriented cathodes separated by 6 mm from the central anode grid. All three grids have 2 mm wire spacing. The anode and cathode wire diameters are 20 $\mu$m and 100 $\mu$m respectively. Symmetrical drift spaces are provided on either side of the cathodes so that the total thickness of xenon is 5 cm. The gas mixture is 90% xenon–10% methane at 3 atm absolute pressure.

A high speed delay line readout is employed utilizing directly coupled delay lines of 10 ns/cm delay. The delays to each end of each delay line are digitized by 600 mHz scalers. High speed digital circuitry then checks each coordinate for pile-up by summing the two delays for that coordinate. Events passing this sum test are placed in a frame buffer within 400 ns of the initiating anode signal.

Energy discrimination is performed by window selection on the anode signal. For the work reported, a 30% window was utilized.

Imaging is performed in the fluorescence escape mode, meaning that only photoconversions are accepted in which the xenon fluorescence photon either escapes from the detector or is separated in time sufficiently to prevent interference with readout of the primary conversion.

The detector provides a spatial resolution of 2.5 mm FWHM over the energy range of 28–81 keV. A high degree of image uniformity is achieved with the delay line readout. No uniformity corrections have been required in any of our clinical work. As a result of the digital nature of the readout technique, a very high degree of stability is exhibited as well.

The beneficial characteristics of the camera for use in clinical work are summarized in table 1. The peak count rate with 30% energy window and ambiguity rejection is 850000 cps. This is many times that of single crystal NaI cameras which peak at about 150000 cps. The spatial resolution and image uniformity are substantially superior to any nuclear medicine imaging

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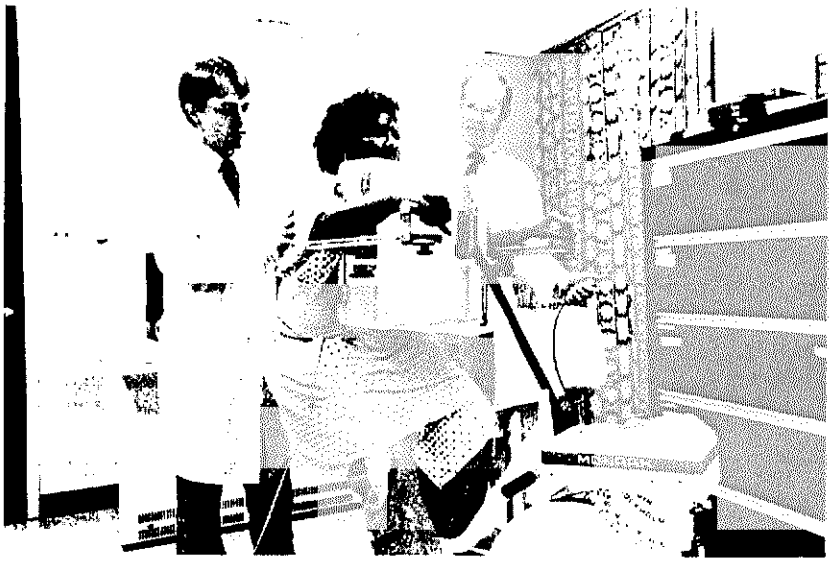


Fig. 1. Wire chamber camera as utilized in the nuclear cardiology laboratory.

Table 1
Wire chamber camera benefits

| | |
|---|---|
| Peak count rate | 850000 cps |
| Spatial resolution | 2.5 mm |
| Intrinsic image uniformity | 5% |
| Weight | 23 kg |
| Cost | Substantially less than standard NaI cameras |

device available. The total weight of the camera head, including shielding and collimator is 23 kg. This is, of course, many times lower than any NaI crystal camera. Commercialization of the device is under way in the form of a highly compact, portable, fully computerized camera. The projected cost of this product is substantially below that of any NaI camera.

In fig. 1 the wire chamber camera is shown as it is used in the nuclear cardiology laboratory for study of ambulatory patients. Studies can be easily performed at rest and during bicycle exercise.

## 3. $^{178}$Ta radiopharmaceutical

The radionuclide $^{178}$Ta is an ideal agent for use with the wire chamber camera. Its characteristics are listed in table 2. The emission energy of 55–65 keV is low enough to provide good detection efficiency and high enough to provide good transmission from the patient [1]. The half-life of 9.3 min provides a very low patient absorbed radiation dose of $\frac{1}{20}$ that of technetium (as $^{99m}TcO_4^-$) or about $\frac{1}{2}$ mrem per injected mCi.

Table 2
$^{178}$Ta characteristics

| | |
|---|---|
| Emission energy | 55, 65 keV |
| Half-life | 9.3 min |
| Whole body dose | $\frac{1}{20}$ $^{99m}$Tc |
| Generator produced | 22 day parent $^{178}$W |

The $^{178}$Ta agent is supplied by a generator system based on the 22-d parent isotope $^{178}$W. This system, originally reported by Neirinckx et al. [2], has been refined in our laboratory for clinical use [3]. This generator is shown in fig. 2. A single unit provides more than


Fig. 2. $^{178}$W/$^{178}$Ta clinical generator.

200 patient studies and can be utilized for a period of 30 days [4].

## 4. Clinical studies

Several clinical cardiology studies utilizing this technology are completed or in progress at the Baylor College of Medicine. In all of these studies, the first pass radionuclide angiography technique with $^{178}$Ta is employed. This is a powerful yet simple cardiac diagnostic modality in which a blood labeling agent is rapidly injected as an intravenous bolus. Rapid sequential images are then acquired during the first transit through the cardiopulmonary system. Individual assessment of left and right heart chambers is provided by this technique without the cross contamination difficulties inherent to the more commonly employed multiple-gated technique in which radioisotope is in all cardiac chambers throughout the procedure. In addition, due to the brief duration of data acquisition, assessment is easily performed at the very peak of exercise. This technique is significantly limited at present by the relatively slow sodium iodide imaging devices. Even when the speed of these devices is increased at the sacrifice of cost and complexity, as is the case with multicrystal gamma cameras, the injectable dose limits of $^{99m}$Tc become a problem. The high speed wire chamber camera using the short-lived $^{178}$Ta provides a technology with the promise of fundamental improvement in this very important technique.

In the first study to be described, we have compared first-pass radionuclide angiography with the multicrystal camera and $^{99m}$Tc with that utilizing the wire chamber camera and $^{178}$Ta. This study has been previously published and will only be briefly summarized here [3]. Thirty-eight patients were studied. Each had the wire chamber camera study followed within 1 h by the multicrystal camera study. The standard clinical dose of $^{99m}$Tc (20 mCi) was used. A wide range of $^{178}$Ta activity ranging from 14 to 53 mCi was administered to allow evaluation of the effect of dose on study quality. The multicrystal camera studies were analyzed with the standard commercial software while the wire chamber camera studies were analyzed using specially developed software for the DEC LSI-11/23 computer which also provided wire chamber camera data acquisition. In both cases, left ventricular ejection fraction was determined and regional wall motion images were produced for cinematic evaluation.

The image acquisition parameters for the two techniques are shown in table 3. The most important difference is that the wire chamber camera utilized a much higher resolution collimator having half the acceptance solid angle compared with the standard 1 in. multicrystal camera collimator.

Table 3
Imaging parameters

| | Wire chamber | Multicrystal |
|---|---|---|
| Collimator | 31 msr | 63 msr |
| Matrix | 32 × 32 | 14 × 21 |
| Pixel size | 0.75 cm | 1.1 cm |
| Area | 24 × 24 cm$^2$ | 15 × 23 cm$^2$ |
| Frame interval | 25 ms | 25 ms |

Fig. 3 (colour plate) displays sequential end-diastolic images through 16 heart beats following bolus injection of $^{178}$Ta. Serial images with high statistical quality of all cardiopulmonary structures are provided on a beat by beat basis.

High quality left ventricular wall motion images were obtained in every patient in the study. Fig. 4 (colour plate) displays several examples of such images. Fig. 4A is a study in a 79 kg male subject with normal ventricular function. Fig. 4B is a study in a 77 kg male subject showing abnormal inferior basal wall motion resulting from a prior inferior myocardial infarction. Fig. 4C is a study in an 83 kg male subject showing abnormal apical wall motion resulting from prior occlusion of the LAD coronary artery. Fig. 4D is a study in a 69 kg female subject exhibiting severe global dysfunction resulting from triple vessel coronary disease.

Segmental wall motion assessment by the two techniques was compared for the following three left ventricular segments – lateral, apical, and infero-basal walls. Using a wall motion scoring system with −1 corresponding to dyskinesis, 0 corresponding to akinesis and 3 corresponding to normal motion, identical values were obtained with the two techniques for the group's mean aggregate score. Likewise individual comparisons of patients with abnormal segments yielded nearly indistinguishable results [3].

Comparison of the ejection fractions obtained with the wire chamber study and the multicrystal camera study showed an excellent correlation with an $R$ value of 0.94. The linear regression line was very close to unity having a slope of 0.94 and intercept of 0.02 [3].

The primary limitation of the conventional first-pass technique is the low-image statistics which can be obtained, as a result of the low count rate capability of the NaI cameras, combined with the limited dose levels permissible with $^{99m}$Tc. Table 4 compares the count statistics achieved with the two techniques. Although only slightly higher activity levels of $^{178}$Ta were utilized (a mean of 26 mCi versus 19 mCi of $^{99m}$Tc), a much higher mean count rate was seen with the wire chamber camera: 310 000 counts/s versus 149 000 counts/s. This occurred despite using a much higher resolution collimator with the wire chamber camera and is a result of the much more efficient collimation possible with the

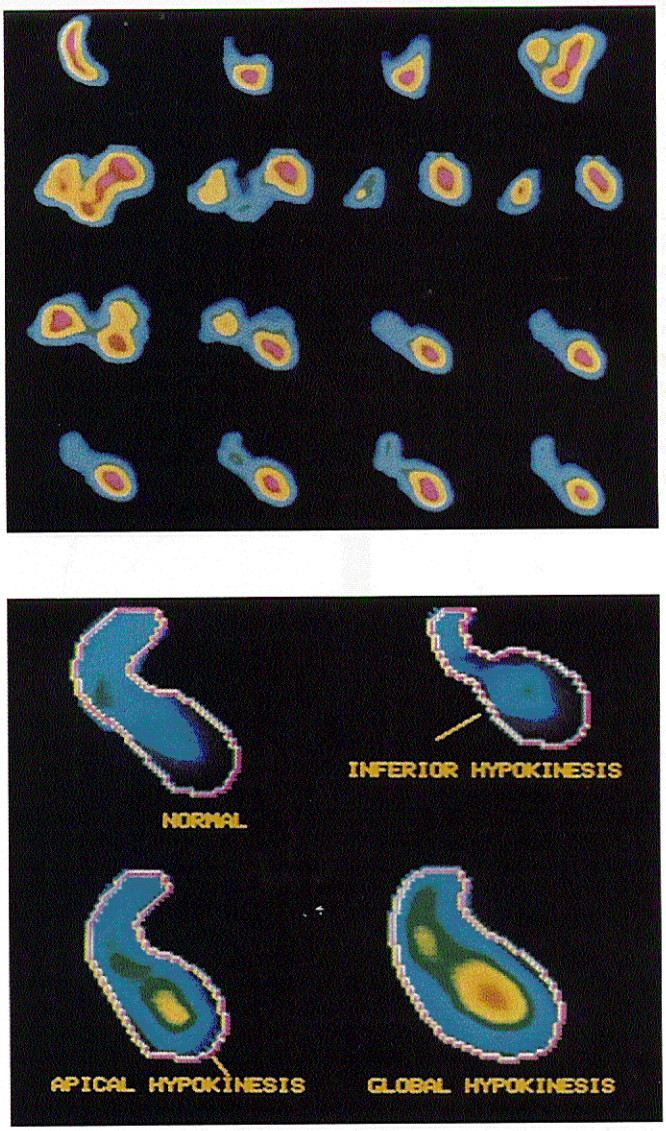



Fig. 3. First transit end-diastolic images following bolus injection of 20 mCi $^{178}$Ta.

Fig. 4. Left ventricular wall motion images obtained by first pass study utilizing the wire chamber camera and bolus injection of 20–50 mCi $^{178}$Ta. Normal subject (upper left), abnormal inferior wall motion (upper right), abnormal apical wall motion (lower left), severe global dysfunction (lower right).

Table 4
Count statistics comparison

| | Injected dose (mCi) | Count rate (cps) | LV count sensitivity (EDC/(mCi × s × msr)) |
|---|---|---|---|
| MWGC/$^{178}$Ta | 26 ± 10 | 310 600 ± 125 000 | 176 ± 132 |
| MCC/$^{99m}$Tc | 19 ± 2 | 147 500 ± 18 000 | 108 ± 49 |

low energy $^{178}$Ta. The last column compares the absolute sensitivity of the cameras for left ventricular imaging defined as the number of counts obtained in the left ventricular region of interest of the representative cycle per second per millisteradian of collimator opening angle. From these values it is seen that the intrinsic sensitivity of the wire chamber camera was 1.6 times higher than the multicrystal camera.

No indication of saturation occurred up to the highest injected activity of 53 mCi. At this activity level, count rates approaching 600 000 cps were reached. Thus the optimal injected dose from the point of view of image statistical quality probably lies in the 50–100 mCi range [3]. Such a dose level would result in substantial improvement in statistics over that obtained in this study and an even more substantial improvement over standard multicrystal studies.

We conclude that the wire chamber camera and $^{178}$Ta provides first-pass studies with excellent quantitative agreement with the accepted standard of first-pass technique, the multicrystal camera and $^{99m}$Tc. Images of improved spatial resolution and statistical quality were obtained with similar activity levels of $^{178}$Ta relative to $^{99m}$Tc. With higher activity levels of $^{178}$Ta, substantial, further improvement should be possible while still maintaining much lower patient dosimetry compared to $^{99m}$Tc.

One of the most frequently utilized diagnostic procedures in nuclear medicine is that of rest/stress assessment of cardiac performance. Many patients presenting with chest pain have completely normal coronary arteries. Exercise assessment provides a non-invasive means of screening such patients to avoid the need to perform invasive and far more expensive procedures such as coronary angiography. This area of application of the wire chamber camera is being evaluated in a

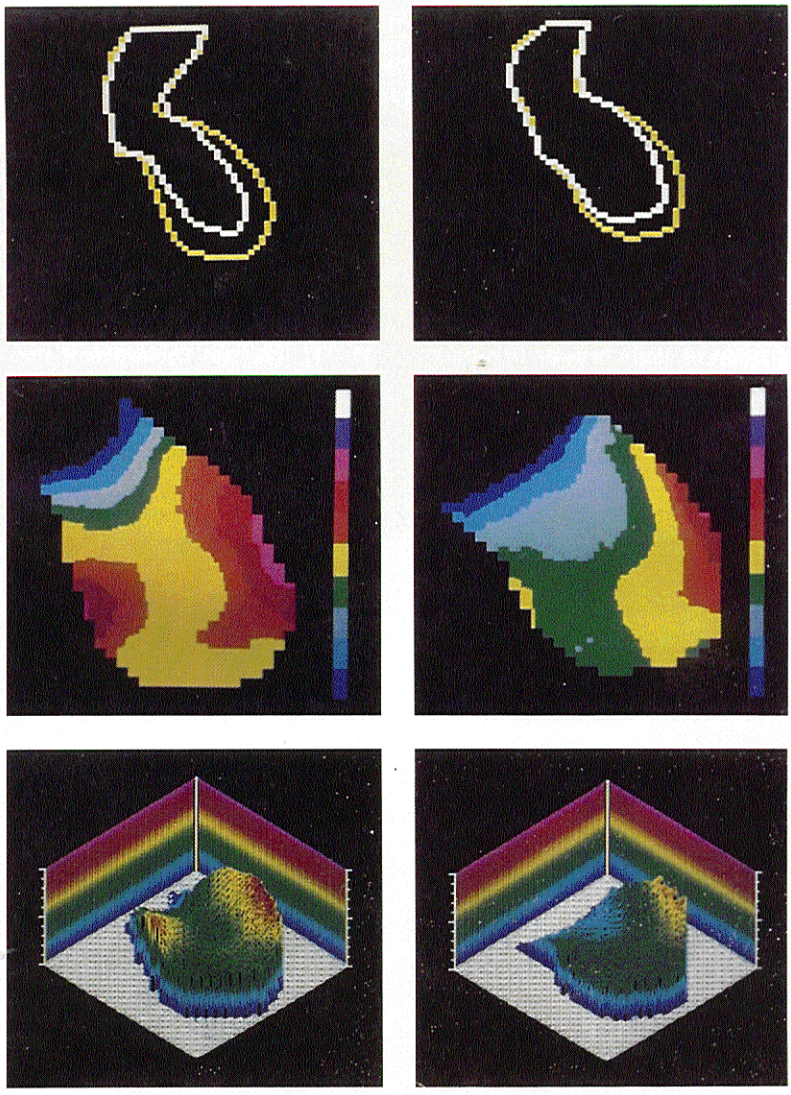


Fig. 5. Rest (left) and stress (right) wall motion images (top) and regional ejection fraction images (middle and bottom) obtained by first pass study utilizing the wire chamber and bolus isotope injection.

study comparing wire chamber first pass radionuclide angiography with stress $^{201}$Tl tomography and coronary angiography. In this study, abnormalities in wall motion induced by exercise stress can be correlated with both perfusion defects seen with thallium tomography and coronary anatomy determined by angiography.

An example from this study is shown in fig. 5. Resting images are shown on the left and corresponding images obtained at peak exercise on the right. At the top are wall motion images showing motion of the ventricular border from end diastole to end systole. The bottom four panels are corresponding regional ejection fraction images displayed in two dimensional and three dimensional format, respectively, in the middle and at the bottom. In these images, the ejection fraction calculated at each point within the ventricular border is displayed according to the indicated color scale. In this patient, resting apical function is abnormal as indicated by low ejection fraction values and degraded wall motion in this region. At peak exercise, significantly degraded function is seen along the inferior wall indicating compromised right coronary artery flow. Catheterization results correlated well with these findings showing a total occlusion of the left anterior descending coronary artery which supplied the apical wall and a tight stenosis of the right coronary artery, which supplied the inferior wall. The wire chamber regional function results correlated well with $^{201}$Tl tomography.

In another ongoing protocol, daily bedside first-pass studies are performed in patients during their stay in the coronary care unit following myocardial infarction. For this study, the camera is mounted on a portable stand and connected to the computer via a 30 m cable. A view of such a study done in the coronary care unit is shown in fig. 6. Fig. 7 is an example of a series of studies done over five successive days in a patient following left anterior descending occlusion and reperfusion using tissue plasminogen activator (TPA). Note the substantially improved ventricular function on days two through five following restoration of coronary flow on day one.

Images from the smallest patient studied to date, a 27 kg pediatric patient, are shown in fig. 8. The images at the top are end-diastolic and end-systolic left ventricular images at rest. At the bottom are corresponding images obtained at peak exercise.

Despite the very high heart rate of about 200 beats per minute during exercise and the very small patient size, excellent detail can be seen in the images and very accurate quantitative parameters were obtained.

## 5. Conclusions

The xenon wire chamber detector operated at moderate pressurization provides a sensitive nuclear medicine imaging detector suitable for use with low energy radiopharmaceuticals ranging in energy from 40 to about 80 keV. The device described here distinguishes itself from others reported in several significant respects [5–11]. The gas containment pressure vessel is highly compact and light weight and at the same time provides a very sizable safety margin for operation at 3–5 atm. The high speed delay line readout combined with digital

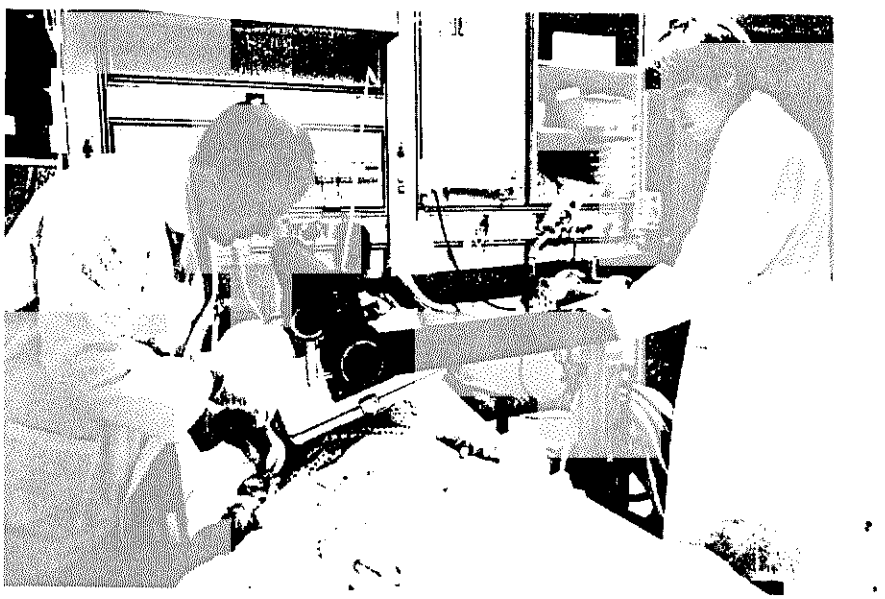
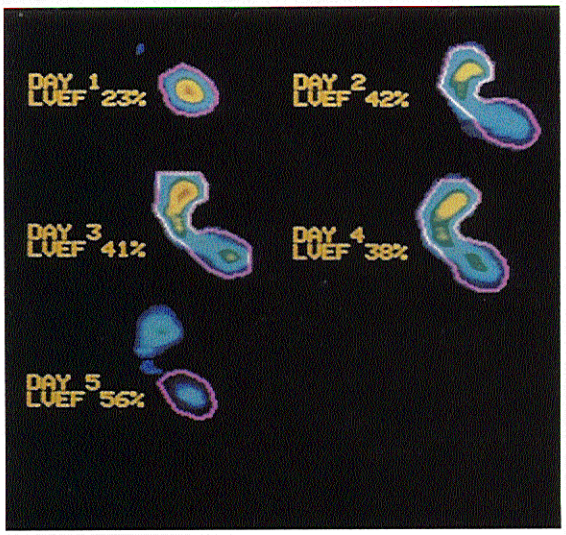


Fig. 6. Portable wire chamber camera utilized in coronary care unit.



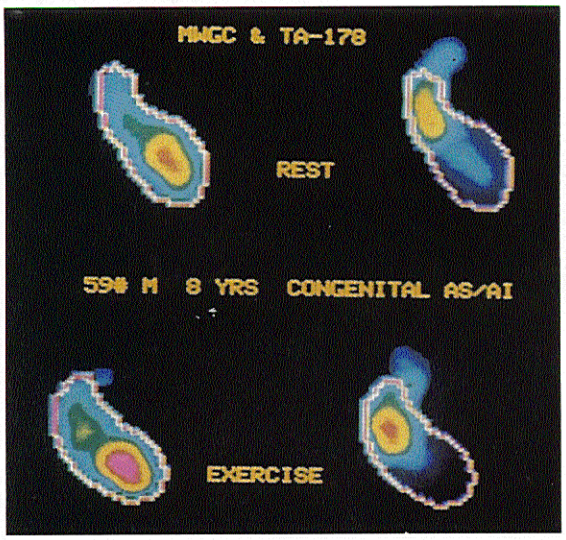




Fig. 7. Five sequential CCU studies on successive days following myocardial infarction. Intravenous thrombolytic therapy (tissue plasminogen activator (TPA)) was administered on day 1. The first study was obtained immediately following therapy.

Fig. 8. Pediatric rest (top) and stress (bottom) studies in 27 kg patient with aortic stenosis/aortic insufficiency.

ambiguity rejection circuitry provides a system which takes advantage of the intrinsic high speed character of the detector while maintaining simplicity and low cost.

The overall system utilized with $^{178}$Ta provides unique advantages particularly in first-pass cardiac imaging which depends heavily on a high speed detector and the ability to inject large activity levels. For this technique, the wire chamber and $^{178}$Ta provides images which are superior by allowing higher resolution collimation, while at the same time providing higher image statistical quality by allowing higher injected doses. Owing to the vast reduction in patient radiation dose per injected mCi, patient dosimetry is reduced even when substantially larger injected doses are employed. Validity of the quantitative measurements of left ventricular ejection fraction and regional wall motion has been established in a sizable clinical comparative study.

The wire chamber camera is beginning to be utilized in a number of clinical areas in which high quality low dose first pass technique is advantageous. Improved detection and quantification of exercise induced ischemia is perhaps the most important of these, and preliminary studies in a limited number of patients look

promising. The high degree of portability which can be provided as a result of the vastly lowered size and weight of the device should prove to be of great benefit in bedside applications. Such studies currently are provided only by motor driven cameras weighing thousands of pounds and occupying substantial bedside floor space. Even with the relatively crude prototype wire chamber device currently in use, significantly improved convenience has been exhibited for intensive care studies. Finally the feasibility of low dose assessment of cardiac function in pediatric patients is beginning to be evaluated. High quality images have been obtained in patients down to 27 kg with more than an order of magnitude reduction in radiation dose relative to $^{99m}$Tc.

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