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MASTER

A CdTe AMBULATORY VENTRICULAR FUNCTION MONITOR

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Introduction

Studies with radionuclides have been developed which permit the evaluation of cardiac pump function, regional wall motion, regional metabolism and regional blood flow. Such measurements with radionuclides have been made in the clinic or at the hospital bedside. Usually, one, or in some cases serial studies can be carried out over several hours. The ability to perform continuous measurements while individuals go about their routine activities would open new areas of patient evaluation. Given this capacity, information concerning both normal and abnormal cardiac function and the effects of new pharmaceutical agents on cardiac function could be evaluated.

This applies not only to the measurement of normal cardiac function in asymptomatic individuals, but, as well to patients with symptoms and particularly in the evaluation of new pharmaceutical agents for such people.

It is possible to measure the ejection fraction and indeed the volume curve without the use of a gamma camera. A gated probe method has been developed and is presently marketed which uses a single scintillation probe which is interfaced to a multiscaling counter in the form of a computer.^{3,4} The multiscaler is triggered to recycle by the patient's R-wave in much the same fashion as the gated imaging technique. Multiple cardiac cycles are recorded in phase to produce a high-quality time-activity curve for the left ventricle. The background is then determined by counting over a suitable zone of lung for the same sampling time and subtracting the lung counts, on a point-by-point basis, from the precordial activity. The reliability of this method for calculating ejection fraction has been validated recently by Waxler, et al.,⁵ both at rest and at the time of peak exercise. Although the equilibrium probe method lends itself to the repetitive measurement of ventricular function, the present device is totally unsuitable for ambulatory measurements.

Several requirements may be identified for a system intended for the ambulatory measurement of cardiac ejection fraction. The entire system including the detector, any electronics, and the power source must be lightweight. It must have only modest current requirements in order that a power source which will not be excessively heavy can permit use of the system over several hours at least. It must also be rugged to withstand the stresses of daily activities without being damaged or posing a hazard to the patient. Finally, it must be compact and self-contained offering no significant restriction to the normal activities of the wearer.

These requirements place some restrictions upon the choice of detector. Thallium activated sodium iodide is excessively sensitive to temperature. In fact, any detector requiring a photomultiplier tube is likely to be too delicate, and, due to the presence of the evacuated glass envelope and high voltages, would present too great a potential danger. Gas detectors, particularly the GM tube, can be made quite rugged, however, the GM tube is far too slow and too inefficient to record sufficient events for the activities involved. A simple, pressurized proportional chamber could work adequately, however, the necessary pressures of xenon combined with the high-voltage requirements make such a detector unfavorable. The remaining possibilities are scintillators (other than NaI(Tl)) combined with light sensitive diodes (avalanche silicon, e.g.) or room-temperature solid-state detectors. The former is not yet a proven technology, and there are few solid-state detectors capable of operation at room temperatures. Silicon

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One radionuclide method which is presently used to obtain both regional and global cardiac function data is multiple gated imaging of the cardiac blood pool.¹ This requires a scintillation camera, an R-wave trigger and a computer capable of image manipulation. After injection of approximately 20mCi of a ^{99m}Tc-labeled blood-pool agent, time is allowed to permit equilibration of the radiopharmaceutical. During imaging with the camera, the data is accumulated as n images (where n is usually between 16 and 64, depending upon manufacturer) which are defined by dividing the cardiac cycle into n time bins. The R-wave of the electrocardiogram (ECG) waveform is used as the fiducial mark to define the start of the cycle. The result is a set of images, each averaged over several hundred heart beats, which represent the shape and volume of the contents of the chambers of the heart. These images may be used to study myocardial wall motion, and also to compute several parameters of cardiac pump function. Given the assumption that the radioisotope is fully equilibrated, and that the difference in photon attenuation from the front to the back of the heart is negligible, it is possible to obtain a quantity proportional to the volume of the chambers of the heart at any point in the cycle (yielding a ventricular volume curve) and, taking the derivative, to obtain the rate of inflow and outflow of blood. It is also possible to define a parameter called the ejection fraction, which is the fraction of blood present (when the ventricle is most full-end diastole) which is pumped by that ventricle in a single cycle. Abnormal ejection fractions have been shown to be powerful indicators of both the current state of the heart and of its future status given the state of a patient's disease.² Although multiple gated blood-pool imaging can be, and often is performed, under conditions of physiological stress, (such as pedalling a bicycle-like device against a variable load) such conditions are likely to be artificial for two reasons. They cannot duplicate the conditions of emotional stress which are entirely different than anything which can be elicited in the clinic, and which may be far more severe than that of simple exercise. Also, for more sedentary patients, the evoking of abnormal responses during exercise probably has little bearing upon the effect of disease on a patient's life. Thus, there is a clear need for a means of measuring these parameters during the ordinary course of everyday life.

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can be made to operate in this mode, however, its mass absorption at 140 keV is relatively low. The remaining alternative is cadmium telluride. This detector material has a high density and a mass absorption yielding a linear attenuation coefficient of approximately 2cm^{-1} for 140 keV photons. In addition, a detector based upon CdTe requires only low bias voltages at extremely low currents (less than 50 volts at less than 5 μA , depending upon the detector size). Although it has some drawbacks, notably in the present limitation of detector active areas, cadmium telluride appears to be the most practical detector for this application.

We have designed and constructed a prototype system for ambulatory monitoring of cardiac volume curves and ejection fractions over extended periods based around a collimated CdTe array. The performance of the first version is undergoing preliminary testing in phantoms and patients.

System Description

The portable portion of the system is pictured in figure 1 and consists of several separate modules mounted in a canvas vest. An onboard MC6800-based microprocessor with associated firmware performs a beat-by-beat average of each channel of data in a fashion analogous to the acquisition of multiple gated blood-pool images. Counts from single cardiac cycles are sorted into time bins of 13 ms. each for both channels of nuclear data. A similar procedure is performed for the digitized ECG waveform, using sample sizes of 13 ms. The processor sorts the incoming data and records it as an audio frequency-modulated signal on a subminiature tape recorder. The data output consists of a series of records, each containing an averaged volume curve, averaged background curve and averaged ECG waveform for a two-minute period. Data from cycles in which the R-to-R interval is either abnormally short or abnormally long are buffered separately. For every eight records of normal data, there is then one record of curves from the short and one record from the long beats. These have been averaged over the whole 16-minute period. Following completion of the data gathering, the audio tape is read out into an Ohio Nuclear VIP 450 computer. Figure 2 is a block diagram of the system detailing the various separate modules.

Detector

In their present form the two detectors consist of arrays of 2mm-thick cadmium crystals. The precordial detector consists of nine 16mm-diameter crystals connected in parallel in a single small enclosure. The background detector is an array of 5 10mm diameter crystals in a similar enclosure. Figure 3 details the mounting configuration of the crystals. They are positioned by a polystyrene foam insert and electrical contact is made to each crystal via a small block of soft conductive foam. The enclosure is assembled under a slight compression. Electrically, the detectors are connected in parallel before amplification. Despite the larger noise arising from so many detectors connected to a single preamplifier, a very usable signal results. The sensitivity is quite high, but the spectral resolution is degraded excessively for scatter rejection. A new front end, consisting of an emitter follower line driver for each detector in the detector case is now being developed while initial phantom and clinical experiments are carried out with the existing array.

Collimator

In order to define the observed field and to create an acceptable object-to-background count rate, a collimator over the heart is necessary. Previous devices of this sort have employed single tube "cannon" collimators. Indeed, our preliminary results, prior to the construction of the prototype system, were obtained with such a collimator and a single cadmium telluride detector. For ambulatory use, however, a more compact detector-collimator combination was required. In order to achieve a length:width ratio of only 2:1, it was necessary to use a lead tube 3.2 cm long. Also, a detector array which has an area more nearly comparable with that of the heart combined with a multichannel parallel-hole collimator should significantly increase the signal-to-background count rate. The dimensions of the collimator were determined partly by the restrictions of available sections of parallel-hole collimator, and partly by the desired sensitivity and resolving requirements. Thus, a section of parallel-hole collimator with triangular holes 2 mm on a side, constructed of lead foil 0.1 mm thick and originally 2.5 cm high was filled with a hard plastic foam (Emerson and Cuming FPH-FR). Thus supported, the collimator could easily be sawed into thin section, increasing the sensitivity and degrading the resolution to values comparable to that of the single bore collimator. It was initially thought that improved spatial resolution would result in an improved signal to noise ratio in the count rate. This, however, proved to reduce the overall sensitivity excessively and most recently thinner sections of collimator are being used. The current collimator height is 3.5 mm.

Detector Preamplifier and Discriminator

Two channels of low-noise charge-sensitive preamplifiers and shaping amplifiers are used to minimize the amplifier noise contribution. These are constructed using two parallel JFETs and a single bipolar transistor in cascade configuration driving an emitter follower stage. The amplified output is then shaped, the baseline restored, and it is then discriminated by a single level comparator and the TTL output fed directly to the microprocessor.

ECG and R-Wave Detector

The ECG input is differential between the right and left arm with the left leg serving as ground. The signal is filtered (high pass) and then divided, with one portion of the signal going to a bandpass filter, absolute value amplifier and an R-wave detector. This is then digitized with a one-shot and applied to the CPU. The other portion of the filtered ECG signal goes to a low-pass filter and analogue-to-digital converter and then to the CPU.

Processor and Software

All software for the CPU resides in read-only memory. It is configured in such a fashion that no initiation beyond a reset is required to begin operation of the system.

Data Output and Readout

Processed data from the CPU in the form of repeating groups of eight records from normal length beats (plus one each from the short and long beats) is converted to an FM audio tone which is recorded on a commercial microcassette dictating recorder. The cassette recorder is capable of storing several hours worth of data. This is then played back via a serial

interface into the image memory of an Ohio Nuclear model VIP 450 computer. Data is either analyzed locally or put on 9-track magnetic tape for analysis elsewhere.

Physical Considerations and Power

At present, the full ambulatory use of the system is hampered by the large power demand of the CPU. This requires a 6 amp-hour gelled electrolyte battery for the +5 volt power supply. Other supplies are furnished by small rechargeable (or mercury) batteries, including the detector bias of 22V. Future versions of the system will use a CMOS CPU and other logic components to reduce the power consumption.

Clinical Procedure

Current evaluation of the system is being performed with patients already injected with 2° mCi of ^{99m}Tc red blood cells for cardiac function studies. Thus, testing creates no additional radiation burden and is performed upon patients whose cardiac function is already well known. The scintillation camera is used to locate the left ventricle from the left anterior oblique position. With the discriminator output connected to a multichannel analyzer in multi-scaling channel scaling mode, the detector position and angle are adjusted to yield the maximum signal-to-background ratio. The positioning is quite critical and the previous over-collimation enhanced this effect.

Results

Several studies have been performed on patients and on phantoms. The volume curves generally exhibit the expected shape and to the extent that quantitation is possible, the data agrees with the programmed data (for the phantom) and with the results of tests in the clinic.

Figure 4 is the result of a test done using a simple moving source phantom. A small ^{57}Co source ($E=122$ keV) was placed on a reciprocating piston and a switch arranged to trigger the ECG input of the system. The photograph of figure 4 is the computer output depicting the first eight count rate curves for the main (precordial) array. In figure 5, these eight curves are superimposed, and it may be seen that, within the limits of random error, they are identical.

In this instance, the source of ^{99m}Tc was relatively far from the detector (5 cm) and 1.2 cm in diameter so that the array response is not uniform, but is, rather sharply varying. This is due primarily to collimator edge effects. Figure 6 is the result of a similar test performed with a point source of ^{99m}Tc and the detector much closer (1.5 cm) to the source. Here, the detector had been placed on a laboratory stand and its height with respect to the source varied after each two-minute record. The result is a 2-dimensional map of the sensitivity of the detector array at the specified distance. The "hole" in the center of the array appears here because this was an earlier version of the detector array which was missing the center crystal (see figure 2).

Figure 7 is the output resulting from a single run of data from a test using a small beating heart phantom. This phantom consisted of a 1 cm diameter elastic rubber bulb connected via tubing to a lcc syringe. The syringe was squeezed and withdrawn by a reciprocating piston, and a switch used to trigger the beginning of each cycle. The syringe and bulb system were filled with a solution containing 0.9mCi of ^{99m}Tc and the bulb was immersed in a water bath, to simulate

a scattering medium. This is a worst case, since the density of water is significantly greater than that of lung tissue. There was no radioactivity in the scatterer. For this run, the phantom was adjusted to yield an ejection fraction of 100%. In other words, all of the fluid in the bulb was expelled with each stroke. It may be seen that the "precordial" rate (squares) decreases to a minimum value while the background (diamond symbols) remains essentially constant. The measured ejection fraction, without subtracting the background, was 92%. If it is assumed that the flat portion of the precordial curve represents the background (and noise) rate, then the ejection fraction is approximately 100%. The background cannot be determined precisely from this data because the background curve was not normalized.

The data from one patient is shown in figure 8. This patient had an ejection fraction of 51% as measured by multiple gate blood-pool imaging. Difficulties with the ground connections on the precordial detector resulted in an unnecessarily high background, which was actually electrical noise. Thus the ejection fraction cannot be reliably determined from these data. The shape of the curve, however, is correct and agrees with that obtained in the clinic.

Discussion

We have constructed a prototype of a highly compact, wearable system for measuring the ventricular volume curve and cardiac pump function during the course of a patient's normal activities. The need for a device of this type, with its ability to measure cardiac function during periods of stress not present in the clinic and to measure the actual impact of disease upon the individual patient, is clear. Moreover, the device offers an opportunity to observe cardiac function in normal individuals under conditions which previously were wholly inaccessible, and to assess the effect of therapeutic agents in individuals with diagnosed disease.

Present plans call for modification of the detector array by the addition of a source follower JFETS for each crystal within the detector case. This will effectively reduce the capacitance across each crystal thereby increasing the voltage at the preamplifier output and reducing the noise. This will also permit individual adjustment of the detector bias and/or output to reduce the degradative effect of unequal pulse heights (for the same photon energy) on the total pulse-height spectrum. Should it be determined that better energy resolution is necessary, we will investigate the possibility of reducing the number of crystals per charge-sensitive preamplifier, and of adding biased amplifiers for each preamplifier before scanning the signal. A biased amplifier would be set to eliminate the low-level noise and prevent its addition among the channels.

Summary

A prototype device consisting of two arrays of CdTe detectors, ECG amplifiers and gate, microprocessor and tape recorder was devised to record simultaneous ECG and radio-nuclide blood pool data from the left ventricle for extended periods during normal activity. The device is intended to record information concerning both normal and abnormal physiology of the heart and to permit the evaluation of new pharmaceuticals under everyday conditions. Preliminary results indicate that the device is capable of recording and reading out data from both phantoms and patients.

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Fig.1 The ambulatory ventricular function monitor

Fig.2 Ambulatory system block diagram

Fig.3 Detector array mounting configuration

Fig.4 Data output from moving source simulation

Fig.5 Data of figure 4 directly superimposed

Fig.6. Data output from moving point source close to collimator creating a detector field map.

Fig.7 Data output from beating heart phantom

Fig.8 Patient data output