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Effects of External Irradiation of the Heart on Cardiac Output, Venous Pressure and Arterial Pressure[1]

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During the past several years we have produced chronic heart failure by exposing either the right or left ventricle to approximately 20,000r of ^{60}Co gamma irradition (1). In characterizing this type of heart failure, we have been interested both in the changes of the pumping ability of the heart and in the direct effects of ionizing radiation on the heart. In these studies we have evaluated the pressure changes which occur in the venous and arterial pressure systems following unilateral exposure to 20,000r of ^{60}Co. The venous pressures were found to begin to rise about six days postirradiation and continue to increase until death. The arterial pressure was found to remain constant until just prior to death. Using these parameters in conjunction with microscopic examinations, we were able to obtain qualitative answers as to the degree of right or left heart failure.

In the present study we evaluated the resting cardiac output venous pressures, (both right and left atrial pressures) and arterial pressure changes following exposure of the right chest wall to 20,000r of ^{60}Co. Since the effects of the exposure must be related to the actual dose, dosimetry measurements were made on the ventricles of the heart and throughout the thoracic cavity.

The results thus found indicate that resting cardiac output is maintained until just prior to death following exposure to 20,000r of ^{60}Co. The dosimetry measurements indicate that with exposure doses of 20,000r only about 10,000r reaches the exposed ventricle.

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METHODS AND MATERIALS

Irradiation Technique

The technique used to irradiate the right ventricle has been previously described (1). Briefly, the animals were placed beneath a fluoroscope and the right heart (ventricle) shadow outlined on the lateral chest-wall. Then the animals were placed beneath a ^{60}Co therapy unit and the 4 x 4 cm ^{60}Co beam was centered directly over the shadow.

Instrumentation of the Dogs

Seven mongrel dogs were used in this portion of the study. In order to measure cardiac output, arterial pressure, right and left atrial pressure, the following technique was used in instrumenting the animals. This technique has also been described in previous publications (2). The general technique involves the implantation of an electromagnetic flow probe around the root of the aorta proximal to the brachiocephalic artery. During this same surgery, a polyvinyl catheter was inserted into the left atrium through the left atrial appendage. Another polyvinyl catheter was placed in the right atrium through the right jugular vein. The leads from the flow meter and the catheters were run under the skin and exteriorized from the back of the neck. The catheters were filled with heparin solution and closed.

Control measurements consisting of right atrial pressure, left atrial pressure, femoral arterial pressure, body weight, pulse rate and cardiac output were made in all dogs during the two week recovery. All pressure measurements were recorded on a Grass polygraph using Statham pressure transducers. Measurements of cardiac output made by using a Medicon electromagnetic flow meter (Model K-2000, 400 CPS) and heart rates were recorded on the Grass polygraph along with the pressure measurements.

About 2-3 weeks following surgery the animals were irradiated using the above procedure. Mean right and left atrial pressure, arterial pressure, heart rate and ventricular output were followed periodically until death.

Dosimetry

Preliminary dosimetry measurements were made by using silver activated phosphate glass (8). A calibration curve was determined from ^{60}Co irradiated glass needles. Victoreen ionization chambers which had been previously calibrated at the National Bureau of Standards were used to check the calibration curve. Both the calibrated needles and the needles used to measure the dose at various locations in the thoracic cavity were individually soaked and washed in reagent grade ethanol and acetone. After allowing them to air dry they were inspected for flaws. Prior to radiation exposures zero readings were established on each needle utilizing a G.K. Turner Model 11 Fluorometer. Four days post-irradiation the needles were again carried through the cleaning procedure and the fluorescence of the needles recorded.

Each needle prior to implantation was sealed in small lengths of polyvinyl tubing. These needles were then placed in the following positions in a dog which had been sacrificed.

1) In the exposure beam at 35 cm (2 dosimeters)
2) Directly beneath the external chest in the center of the beam (1 dosimeter)
3) Directly upon the exposed ventricle (5 dosimeters)
4) Directly upon the septum (2 dosimeters)
5) Directly upon the opposite ventricle (unexposed) (5 dosimeters)
6) Directly upon the diaphragm (1 dosimeter)
7) Directly upon the spine (1 dosimeter)

The needles were exposed at these positions when the extrapolated exposure dose of the ^{60}Co therapy unit was set at 5,000r to the right lateral chest wall, 1,000r to the right lateral chest wall, 5,000r to the left lateral chest wall and 1,000r to the left lateral chest wall.

RESULTS

Changes in Ventricular Output, Stroke Volume and Arterial Pressures

Figure 1 shows the resting values of ventricular output, stroke volume, and arterial pressure plotted against the time prior to and following irradiation of the right ventricle with 20,000r ^{60}Co. Heart rate, right and left atrial pressures were also measured, but they were found to be consistent with changes previously described (1).

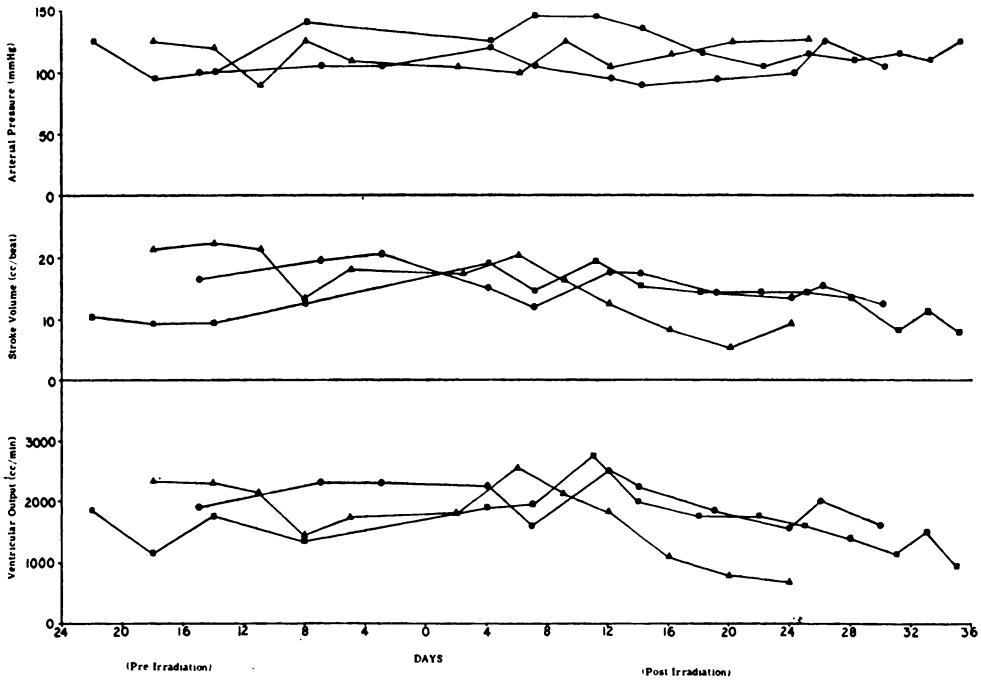

Fig. 1. Ventricular output, stroke volume and arterial pressure plotted against days before and after irradiation. The animals were irradiated on zero day.

The animals used in this study reclined quietly unrestrained during the measurement of ventricular output. However, it should be noticed in Fig. 1 that there was a variation in resting ventricular output prior to irradiation. This variation continues following irradiation. Generally, the resting ventricular output remained within the normal range until four to six days prior to death. The animal represented by the triangles in Fig. 1 had a reduction in resting ventricular output approximately 10 days prior to death. Most of the animals used in this study displayed a reduction in resting ventricular output four to six days prior to death and the variation in time could usually be related to the amount of muscle damage determined at autopsy.

The changes in resting stroke volume followed very closely the changes in resting ventricular output. This point can be seen by comparing the points of Fig. 1.

The arterial pressure was maintained essentially constant by all animals in this study as illustrated in the upper portion of Fig. 1. In a few cases a slight decline could be noted two or three days prior to death. However, it is usually well regulated.

Dosimetry

The doses measured by the silver activated glass phosphate dosimetry as related to the extropolated exposure dose (EED), *i.e.*, original calibrated dose time corrected for decay, are shown in Table I.

The column labeled MED relates to the total measured exposure dose and MDH is the actual dose measured on the ventricles of the heart. The measured exposure dose was found to be 19 percent less than the routinely used extrapolated exposure dose. The maximum dose received by the right ventricle when

TABLE I

DOSIMETRY RESULTS

Exposure Port	*EED**	*MED**	*MDH***	$\frac{MED}{EED}$	$\frac{MDH\text{***}}{EED}$	$\frac{MDH\text{**}}{MED}$
Right Lateral Chest						
Wall	5000r	4050		.81		
Right Ventricle			2400		.48	59.5
Left Ventricle			2050		.41	.507
Left Lateral Chest						
Wall	5000r	4050		.81		
Left Ventricle			2100		.42	.545
Right Ventricle			1800		.36	.445

*Extrapolated Exposure Dose Rate = 78 r/min

*Measured Exposure Dose Rate = 63.2 r/min

**Measured Absorbed Dose on the Ventricular Wall

***The Same Average Percentage was Found at EED of 1000r

the right lateral chest wall was exposed was 59.5 percent of the measured exposure dose (MED). Only 48 percent of the extrapolated exposure dose (EED) was measured on the right ventricle. The maximum dose received by the left ventricle using the same port of entry was 50.7 percent of the measured exposure dose (MED) and 41 percent of the extrapolated exposure dose. Note there is very little difference between the doses received by the right and left ventricles.

When the port of entry was the left lateral chest wall, the left ventricle received a maximum dose of 54.5 percent of the measured exposure dose (MED) and 44.5 percent of the extrapolated exposure dose (EED). The opposite ventricle received 44.5 percent of the measured exposure doses (MED) and 36 percent of the extrapolated exposure dose (EED).

In producing chronic congestive heart failure we have used an extrapolated exposure dose of 20,000r of ^{60}Co to either the right or left laterally chest wall. According to the dosimetry measurements shown in Table I, the actual dose received by the right and left ventricle when the port of entry was via the right lateral chest wall is 9,600r and 8,200 r, respectively. When the port of entry is via the left lateral chest wall, the dose is 7,200r and 8,400r, respectively, to the right and left ventricle.

The silver activated glass phosphate dosimeters which were placed on other organs in the thoracic cavity received amounts of radiation too small to measure.

Gross pathological findings at autopsy

The same general pathological conditions were found at autopsy in these animals as previously reported by others (1). The mass of tissue damaged in the right ventricle ranged from 70-90 percent of wet weight of the ventricle. The left ventricle appeared normal both from visual and microscopic observations. Free fluid was found in the thoracic cavity and abdomen of these animals. Liver congestion was visibly present and pitting edema was observed.

Discussion

In previous studies we have observed massive hemorrhagic infiltration of the right ventricle by the 14th day following irradiation. Coupled with these pathological observations, the atrial pressures begin to rise about six days post-irradiation which indicates qualitatively that the heart is failing (1). However, the animals in this study are able to maintain a normal resting ventricular output until 4-6 days prior to death. This emphasizes the ability of the heart to compensate for a decrease in functional cardiac mass. This ability to compensate was measured during resting conditions and would probably not be sufficient to maintain a normal circulatory function during severe work stresses. Since it is obvious that these animals are in heart failure many days prior to death, the measurement of resting ventricular output does not quantitate any reduction in functional cardiac muscle.

Although the dosimetry studies were preliminary, the doses obtained are extremely valuable. In all of our work thus far we have used the same ^{60}Co

therapy unit, and an extrapolated exposure dose of 20,000r. The measured exposure dose in this study was 19 percent of this extrapolated exposure dose, which is used routinely in the therapy center. Thus, in all of our work the actual exposure dose has been 16,200r. Using this exposure dose, the maximum dose to the right and left ventricle when the port of entry is the right lateral chest wall, is 9,600r and 8,200r, respectively. When using a left lateral port of entry, the dose is 8,400r and 7,200r, respectively, to the left and right lateral ventricle. Note with only a small difference in dose the latent period for microscopic damage for the exposed and unexposed ventricle is quite different. In fact, the latent period for the unexposed ventricle exceed the life of the animal in this preparation. However, we have exposed the right and left ventricle to extrapolated exposure doses somewhat less than 20,000r and have seen microscopic damage. Of course the survival time of these animals was increased. The results at these exposure doses agree with those reported by Phillips (7) and Michaelson (5).

Using an extrapolated dose of 10,000r or an actual dose to the exposed ventricle of 4,800r (using the data in the Table), we have seen limited myocardial fibrosis and complete atrial fibrosis.

SUMMARY

In summary, we would like to emphasize that doses of ionizing radiation in the therapeutic range may produce damage to the myocardium. The effect is probably an indirect effect resulting from increased permeability and fragility of the capillaries (9, 4, 3). The injury to the myocardium resulting from therapeutic doses may not be detected under normal resting conditions. Secondly, the latent period, time from exposure to microscopic changes in the cardiac muscle, is sensitive to small changes in dose.

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