Cardiac Function, Fiber Shortening, and Dynamic Geometry

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Many models for the study of the pump function of the heart emphasize the importance of cardiac geometry and detailed dimensional data. Because of the lack of accurate measuring techniques, approximate geometries such as shells of revolution have been applied. In this study, methods are presented that measure the dynamic geometry of the working, isolated canine heart by means of ultrasound-velocity tomography techniques. In addition, cardiac dimensions, intramural deformations, and fiber shortening have been measured dynamically in the in situ canine heart throughout the cardiac cycle with implanted radiopaque markers and biplane roentgen techniques. Results of regional contraction and relaxation patterns are presented. Epicardial fiber shortening between apex and base were computed and found to be dependent on the duration of the preceding RR interval.

To meet the demands of the body, the heart propels the blood by cyclic contraction and relaxation of its individual muscle fibers. Contraction of the total myocardium reflects the summated and integrated function of its individual contractile elements. Ultrastructural alterations in the myocardium (for instance, from coronary insufficiency) may lead to impairment of regional myocardial contractile behavior. Because of compensatory mechanisms of the still healthy muscle fibers, this regional dysfunction will be reflected only in a late stage in overall parameters such as pressure and flow. Further erosion of the cardiac reserve occurs if the limits of compensatory mechanisms are reached.

Although the contractile properties of individual (for example, papillary) muscle fibers have been analyzed extensively and described well by their length-tension-velocity curves, cardiac function cannot yet be understood and explained from these fundamental studies. This may in part be ascribed to the complex anatomic arrangement of the fibers in the myocardium, their not yet clarified interaction and contraction sequence, and the complex changes in geometry during the cardiac cycle.

During contraction, the individual fibers generate forces, introducing stresses in the myocardium and finally leading to pressure generation in the ventricular cavities, with ejection of blood into the systemic and pulmonary circulation. Currently, no direct measurements are available to obtain length-tension-velocity relationships in the intact heart or the important related myocardial parameters such as regional stresses and strains. To gain insight into these parameters, we have undertaken two different approaches in our laboratory. First, a model of the heart was developed[1-3] on the basis of the sliding-filament theory. The heart was considered a thick-walled cylinder or ellipsoid of revolution, consisting of up to 10 shells of revolution in which fibers were supposed to be oriented according to data found in the literature.[4] The mechanical behavior of the fibers was derived from published data of the sliding-filament theory.[5,6]

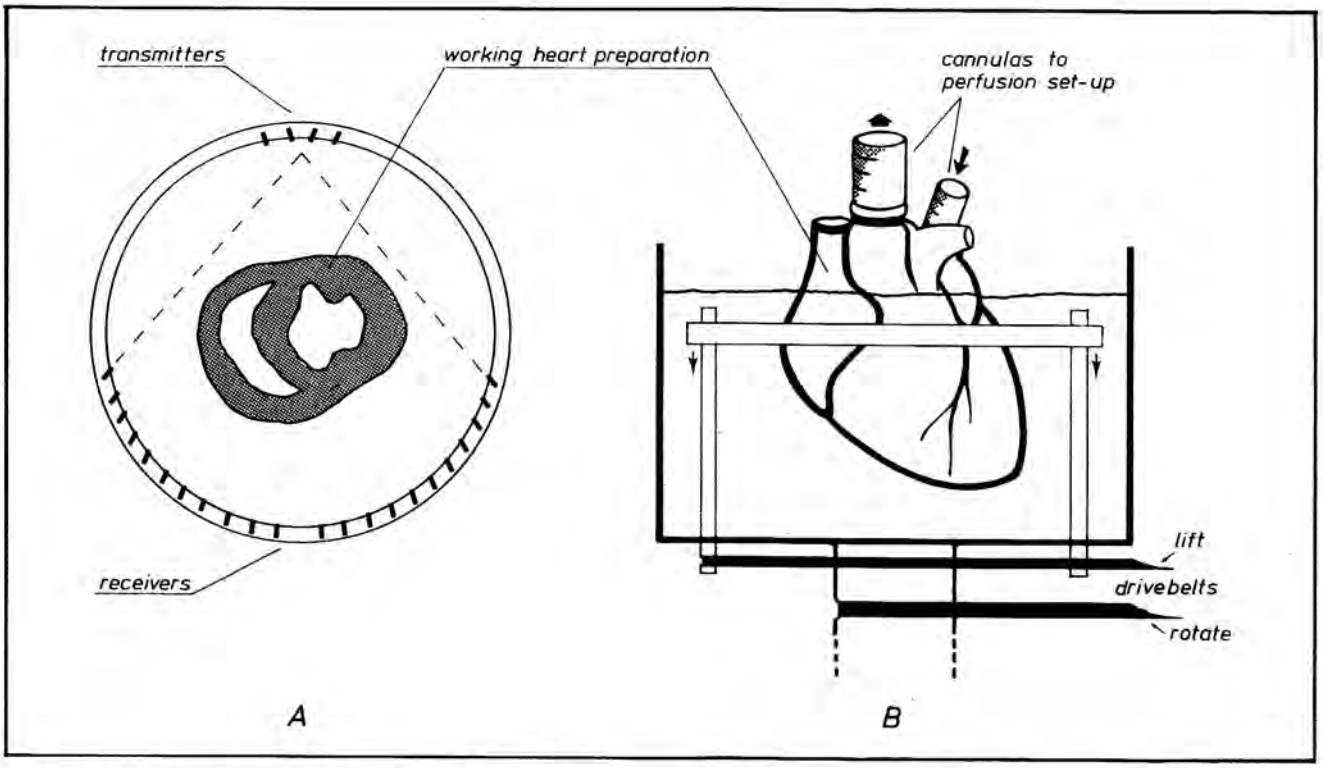

Fig. 1. Schematic representation of the ultrasound tomograph, showing the heart submerged in fluid *(B)* and surrounded by a ring containing ultrasound transmitters and receivers *(A)*.

In the second approach, originated at the Mayo Clinic, we computed myocardial stresses and strains with the help of the finite-element technique.[7,8] This technique was applied to the true geometry of the isolated canine heart, obtained by multiplanar x-ray reconstruction methods. The myocardium was considered to be homogeneous, isotropic, and linearly elastic. Both studies emphasized the importance of accurate knowledge of cardiac geometry and intramural deformations for the computation of regional wall stresses and intraventricular pressures. Continuation of these studies required the availability of dimensional data of the heart and its three-dimensional geometry during the cardiac cycle. In this study, methods are presented to measure these parameters.

METHODS

The Isolated, Working Canine Heart.—Experiments to measure the dynamic three-dimensional geometry were carried out on isolated dog hearts. Beagles weighing about 10 kg were anesthetized with sodium pentobarbital (30 mg/kg intravenously) and intubated. Anesthesia was maintained by a sodium pentobarbital infusion of 3 mg/kg per hour. Artificial ventilation was started with a 1:1 mixture of N_2O and O_2. Ventilation parameters were adjusted according to the end-tidal CO_2 concentration and to regular arterial blood gas determinations. Sodium bicarbonate solution was administered to maintain plasma pH at 7.4. The electrocardiogram and central arterial pressure were monitored continuously.

After induction of muscle relaxation with 1 mg of pancuronium bromide intravenously, the thorax was opened in the right fifth intercostal space. The dog was heparinized until activated clotting time was between 300 and 400 s and the pericardium was opened. Large-bore cannulas were inserted into the cranial and caudal caval venes and into a femoral artery. These cannulas were connected to a standard extracorporeal pump circuit with oxygenator and heat exchanger. The extracorporeal circuit was primed with 1,000 ml of citrate-phosphate-dextrose blood, 500 ml of Ringer's lactate solution, and 500 ml of Rheomacrodex. To the priming volume were added 2 g of calcium gluconate and 2,000 IU of heparin.

After slow exchange of the intracorporeal and extracorporeal volumes, the dog was cooled to 27°C (esophageal temperature). In approximately 1 minute the heart was removed and the coronary arteries were flushed with modified Tyrode's solution at 4°C. The ascending aorta and the pulmonary trunk were cannulated with the heart

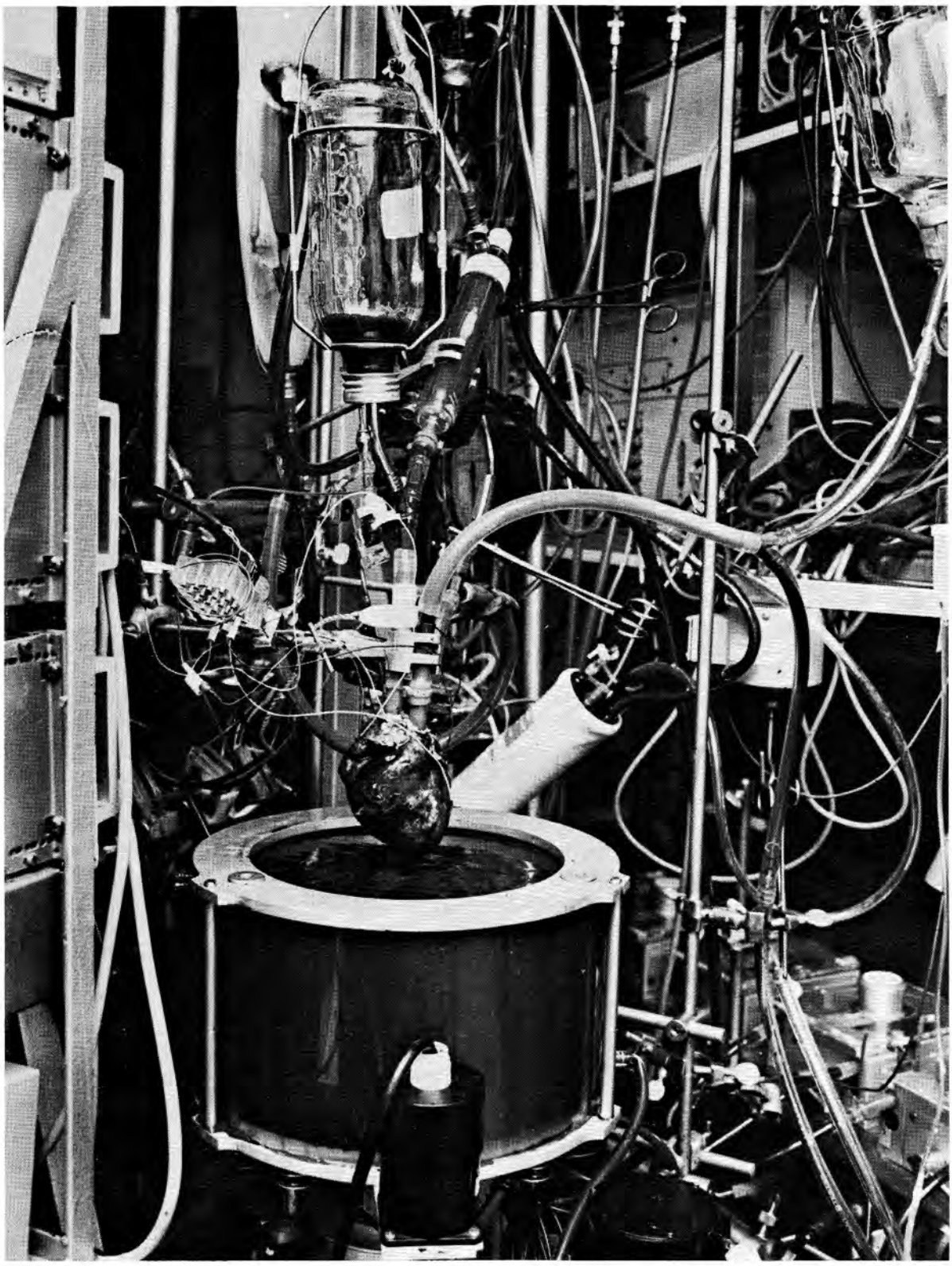

Fig. 2. Photograph of the experimental set-up showing the working heart before it is submerged in the tomograph. Starling resistance, compliance (air-filled bottle), aortic pressure, and flow transducers can be seen.

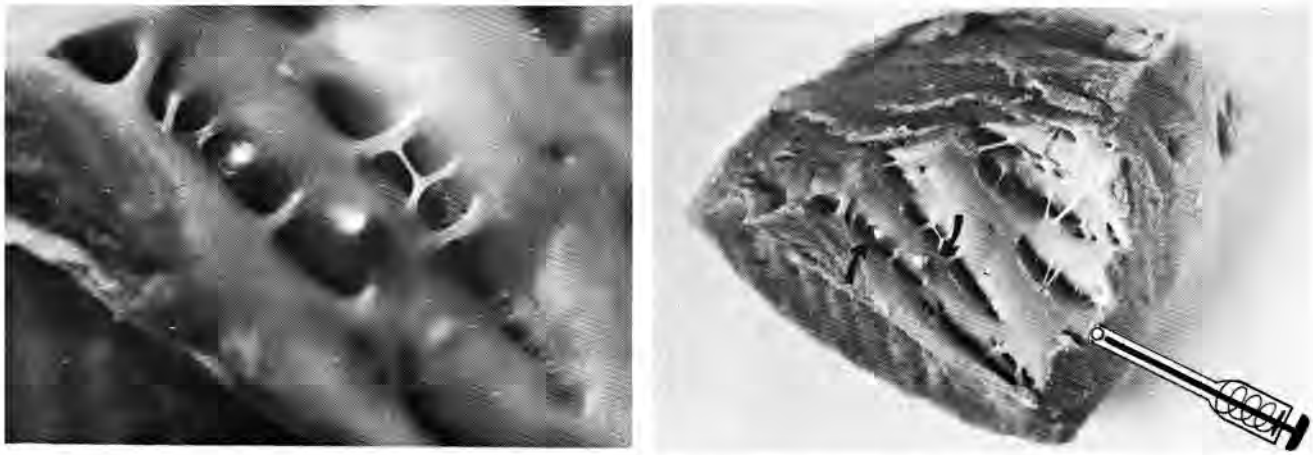

Fig. 3. Excised myocardial tissue, showing two implanted markers *(arrows)* and, schematically, the needle designed for marker implantations, containing a marker at its tip and a stylet to release the marker. The *left panel* shows an enlarged section of the *right panel.*

submerged in the cold solution, and right ventricular and left ventricular drains were installed through the atrial appendages. The caval venes were closed with sutures, as were the lung openings in the left atrium. A large-bore cannula was installed in the left atrium. Arrest of coronary artery flow during these procedures lasted approximately 30 minutes. Retrograde aortic perfusion by the method of Langendorff rewarmed the heart to 36°C. Simultaneously, blood was supplied to the left atrium and removed through the left ventricular drain. If spontaneous rhythm did not return, defibrillation was initiated at 15 watts per second, and when the ventricular drains were clamped, calcium gluconate usually had to be supplied. When the left ventricle generated adequate pressure, the ventricular drains were removed and retrograde aortic perfusion was stopped.

The left atrium was supplied with oxygenated blood at 36°C and at a fixed pressure. The left ventricular afterload consisted of a compliance and a Starling resistance. Flow rate and pressure were measured in the ascending aorta.

The outputs of the left and right ventricles were collected, oxygenated, heated, filtered, and returned to the left atrium. Blood gases and pH were carefully controlled. The volume of the circulating blood was approximately 2.5 liters, with a hematocrit of 20 to 30%.

The heart was paced with epicardial electrodes sutured to the right atrium. An electrocardiogram was recorded from two epicardial electrodes sutured to the left ventricle. Under standard conditions of left atrial pressure (7 mm Hg), aortic pressure (70 mm Hg), and heart rate (140/min), a left ventricular stroke volume of about 11 ml was maintained for about 2 hours.

Ultrasound-Velocity Tomography.—To measure the three-dimensional geometry of the isolated working heart, we developed an ultrasound tomograph[9,10] consisting of a cylinder filled with fluid in which the beating heart was submerged. Around the heart a ring was mounted, containing 4 ultrasound transmitters on one side and 22 receivers facing the transmitters on the other side (Fig. 1). The cylinder can be rotated around the heart by means of a stepping motor in steps of 1.8 degrees; this allows ultrasound transmission time measurements from 200 different angles of view. The transducer ring can be raised or lowered with the help of a stepping motor to obtain transmission data from different cross sections of the heart from base to apex. Figure 2 shows the part of the experimental set-up containing the heart.

The cardiac cycle was subdivided in periods of 20 ms, in each of which a complete set of 44 transmission times is measured. Just before the next heart beat the cylinder is rotated over 1.8 degrees, and measurements are performed from a different angle of view. In total, 200 heart beats are required to provide the data needed for a reconstruction of one cross section of the heart. Data of the corresponding phases in the successive heart beats are selected and used for reconstruction. Stationarity (that is, beat-to-beat reproducibility of geometry) of the 200 heart beats is approached by electrical stimulation of the heart. Stimulation, selection of transmitter and receiver combinations, detection of transmission times, data handling and storage, rotation of the cylinder, and vertical displacements of the transducer ring are all controlled by minicomputer.

Cardiac geometry is obtained by reconstruction of the spatial distribution of the ultrasound velocity in the plane of measurement. This velocity is characteristic for the medium through which the ultrasound waves are propagated and is different for blood, myocardial tissue, and

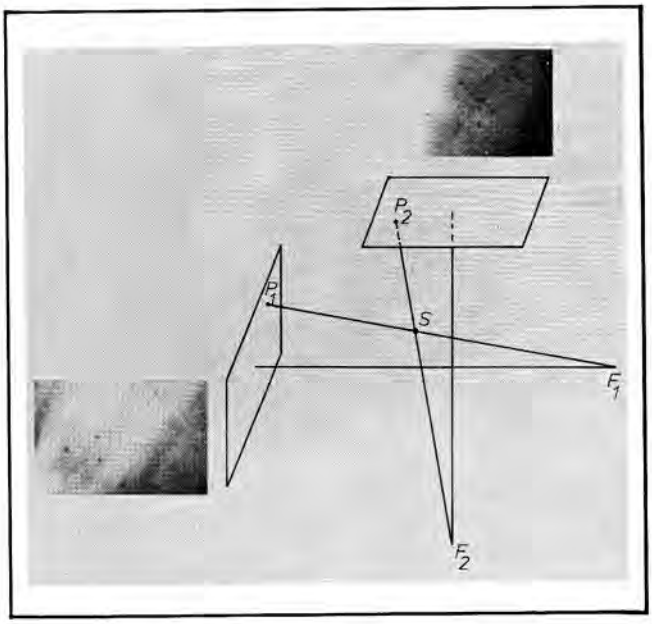

Fig. 4. Schematic representation of the reconstruction of the spatial position (S) of a marker from its two orthogonal projections, P_1 and P_2, and two corresponding x-ray pictures. F_1 and F_2 represent the x-ray foci.

the fluid surrounding the heart. Transmission times (T) from transmitter to receiver in our set-up can be written as ("straight path approximation"):

$$T = \int_A^B (v(x,y))^{-1} ds$$

where v(x,y) represents the spatial distribution of the ultrasound velocity in a particular cross section, A and B are the coordinates of the transmitter and receiver in the plane of measurement, and s is the straight line between A and B. The solution of v(x,y) from a large set of transmission times is a problem well known in mathematics. The Austrian Radon proved already in 1917 that the value of an integrand in a specified point can be obtained from an infinite set of straight-line integrals through that point.[11] Nowadays, different techniques have been developed to solve these sets of equations in practical situations, complicated by noise and other factors. Some of them are used with computed tomography scanning techniques, in which similar problems arise, to reconstruct attenuation from x-ray projections. Our solution uses orthogonal function expansion techniques.[12,13]

Implantation of Radiopaque Markers in the In Situ Dog Heart.—For the measurement of ventricular dimensions, intramural deformations, and fiber shortening and orientation, radiopaque markers were implanted at various locations in the myocardium of a dog heart. Our implantation procedure, published previously,[14,15] will be summarized below. Beagles (10 to 15 kg) were anesthetized with methadone and inapsine administered by continuous drip infusion. Ventilation was maintained with a positive-pressure respirator at a rate of 20 per minute; pH, P_{CO2}, and P_{O2} were controlled. The heart was exposed by a left thoracotomy through the left intercostal space.

Subepicardial markers were stitched into the left ventricular wall after being inserted in the lumen of braided suture material.

Subendocardial markers were implanted with the help of a hollow, blunt needle (Fig. 3) (outer diameter 1.4 mm, inner diameter 1.0 mm) in which a platinum marker fitted tightly. The needle with a marker at its tip was inserted into the ventricular myocardium and pushed forward gently until the endocardial membrane was sensed. Then the marker was ejected by a stylet and the needle was withdrawn. By approaching the heart from different di-

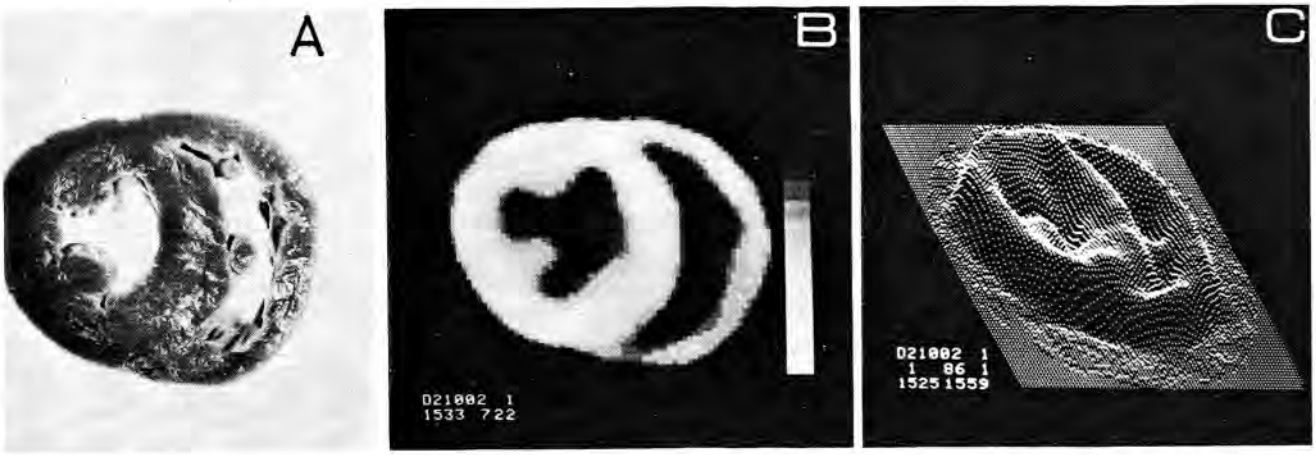

Fig. 5. *A*, Cross section of a postmortem heart. *B*, Cross section reconstructed with ultrasound-velocity tomography in the plane of *A*. *C*, Plot of ultrasound velocities (plotted vertically) in the plane of measurement.

rections, one could place markers anywhere in the myocardium, even in the septum.

Intramural markers were implanted by means of the same needle. For this purpose, the needle was provided with a metal collar, of which the distance to the tip of the needle could be adjusted easily to the depth desired for implantation of the marker. The needle with a marker at its tip was pushed forward into the myocardium until the collar prevented further penetration of the needle. Then the marker was released by pressing the stylet.

After implantation of 10 to 20 markers, stimulation electrodes were sutured on the right atrium. After the thorax was closed, the heart was paced and the marker motion was recorded on film with the help of rotational x-ray equipment at 84 frames per second. An electrocardiogram, left ventricular and aortic pressures, and cine pulses were recorded.

Determination of Ventricular Dimensions, Wall Thickness, and Fiber Shortening.—The x-ray films were analyzed with the help of a digital videodensitometer interfaced to a computer. Marker projections within a film frame were pinpointed by light pen, and their coordinates were computed as the centroid of intensity of a grid around the marker selected. Spatial marker coordinates were found by selecting the corresponding projections of a particular marker from its two orthogonally projected film frames with the use of the reconstruction procedure described by Elshuraydeh and associates[14,15] (Fig. 4). Test phantoms containing platinum markers at precisely known distances showed an accuracy of the reconstruction method of 0.2 mm. From the spatial marker coordinates, ventricular dimensions, wall thickness, torsion, and rotation of the heart can be derived. Dynamic fiber orientation and fiber shortening can be computed as well. Epicardial fiber orientation is found by placing three markers in a triangular composition (side length 5 to 10 mm) at the epicardium. The spatial trajectories of the vertices of the triangle (markers) are computed throughout the cardiac cycle. By comparing end-systolic and end-diastolic configurations of the triangles, one can compute the direction of maximal shortening within the triangle. This direction is assumed to be the fiber direction, and the computed shortening is considered to be fiber shortening.

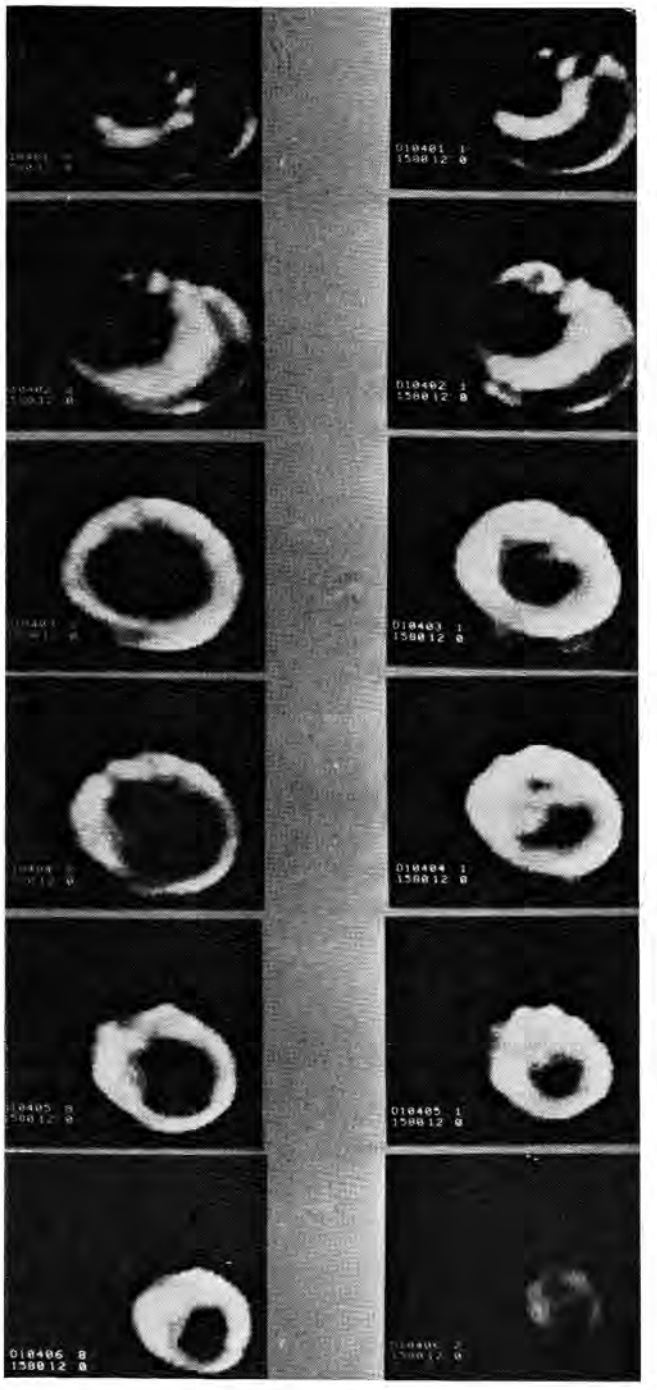

Fig. 6. Reconstructed cross sections from base to apex (top to bottom) of a beating heart for two phases in the cardiac cycle—*left panels*, at end diastole; *right panels*, at end systole.

RESULTS

Ultrasound Velocity Tomography.—Experiments have been performed to record the three-dimensional geometry of the working isolated canine heart under various experimental conditions. The effect of changes in heart rate, preload, and afterload on the dynamic geometry will be published separately. Figure 5 presents a reconstructed cross section of a postmortem heart *(B)* and a photograph of the slice of the corresponding cross section of the heart *(A)* after the experiment was performed. Figure 5 *C* is a three-dimensional plot of the reconstructed ultrasound velocity distribution (plotted verti-

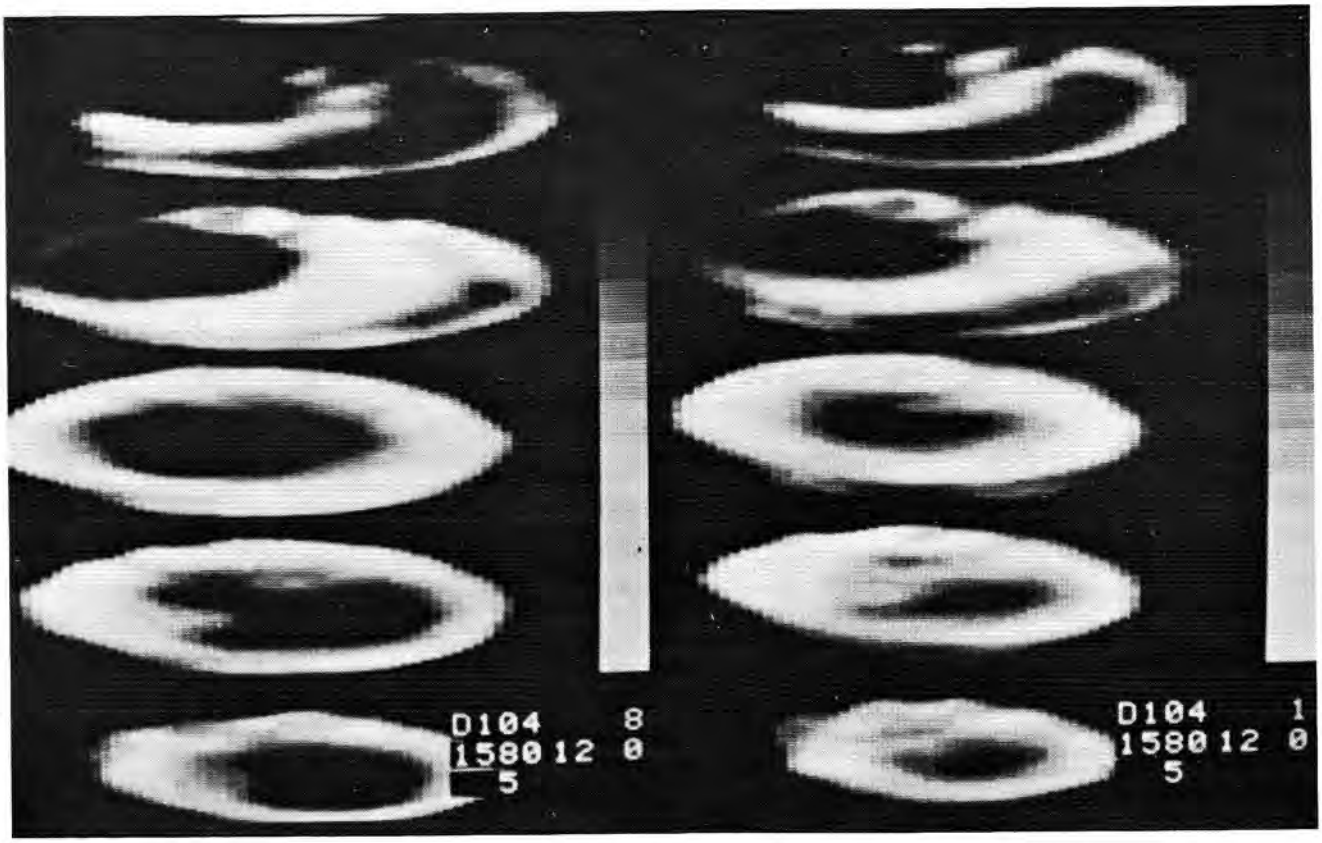

Fig. 7. Reconstructed cross sections from base to apex of a beating heart for two phases in the cardiac cycle *(left panel,* end diastole; *right panel,* end systole), showing a quasi three-dimensional display.

cally) as a function of coordinates in the plane of reconstruction. In Figure 6, reconstructed cross sections from base to apex of a beating heart are shown for two phases in the cardiac cycle. Distinct changes in geometry during the cardiac cycle can be observed, along with the motion of the papillary muscles. Since the filling of the right ventricle is not controlled actively, its free wall will occasionally coincide with the ventricular septum. To prevent this complication in our next experiments, we will also take care of right ventricular filling.

In Figure 7, a different way of displaying the reconstructed cross sections is chosen. Apart from visual inspection of these pictures or, even better, of a movie of reconstructions of cross sections for subsequent phases in the cardiac cycle, quantitation of the observed phenomena is needed for a deeper insight into cardiac contraction. As a first step in this direction, the area enclosed by the left ventricular contour is plotted (Fig. 8). Although this parameter reflects the integral effects of contraction and relaxation of muscle fibers at that particular level, regional differences in cardiac contraction can be seen. During the isovolumic contraction phase, distinct geometric changes of the heart occur. During ejection, the contraction seems to start somewhere at mid ventricle and propagates with different speeds to base and apex. Also, during the isovolumic relaxation phase, pronounced changes in geometry occur, whereas in the filling period different relaxation velocities of myocardial tissue can be noticed.

The method developed allows measurement of cardiac geometries for various phases in the cardiac cycle. As mentioned, the present tomograph makes reconstructions at intervals of 20 ms. Because of a lack of clear (intramural) landmarks (except the roots of the papillary muscles), it is difficult to pinpoint spatial trajectories of particular points in the heart during the cardiac cycle. Therefore, our second method was developed. This method, however, does not lend itself to accurate measurements of geometry. Therefore, the combination of the methods can be seen as a powerful tool in the study of cardiac mechanics.

Radiopaque Ventricular Markers.—By implanting markers at various locations in the heart, one can obtain dimensional data such as (1) inner and outer long and

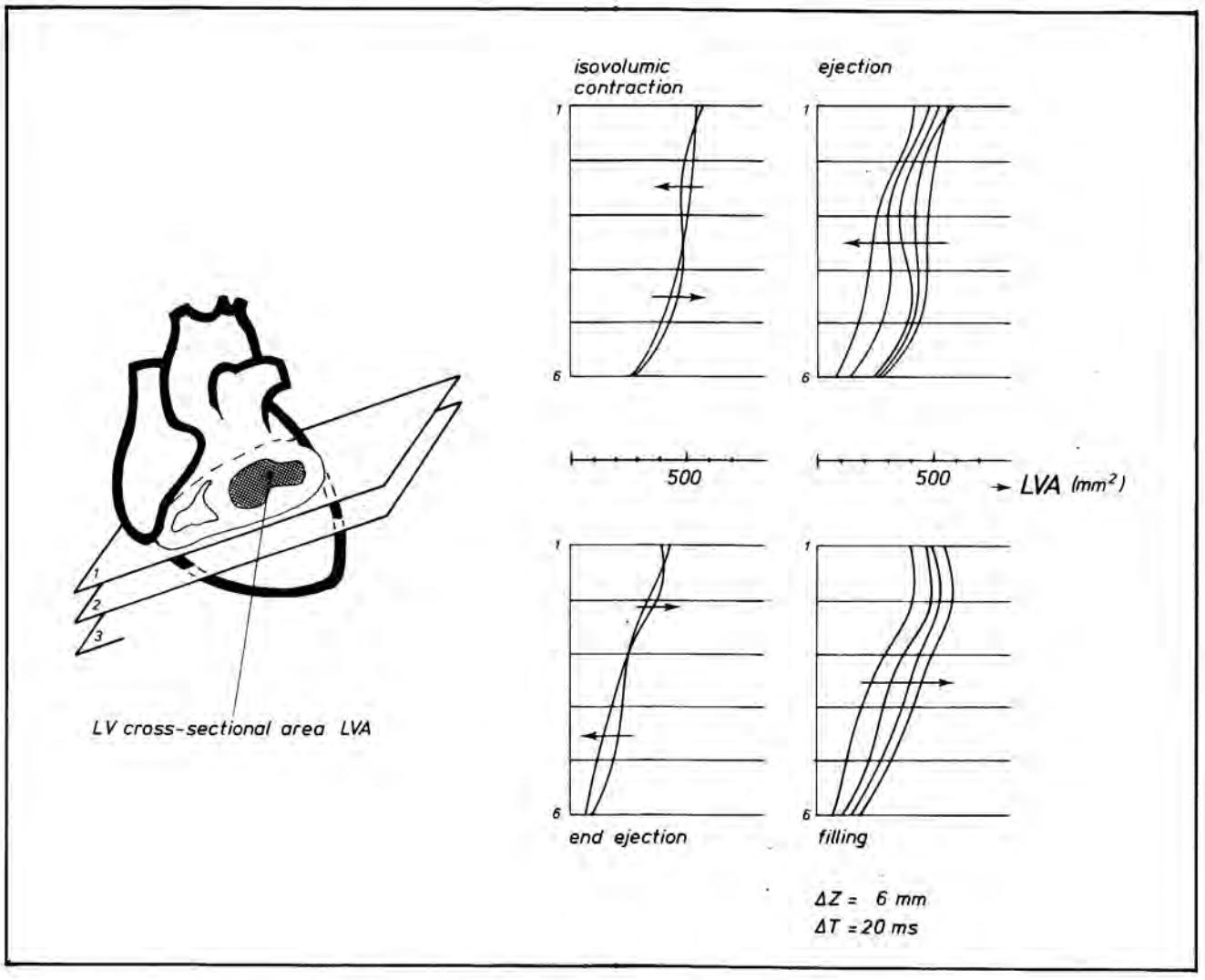

Fig. 8. Plots of left ventricular cross-sectional area (LVA) for different cross sections from base (1) to apex (6). The time interval between successive lines is 20 ms. Vertical distance between cross sections is 6 mm.

short axes, (2) regional wall thickness, (3) regional contraction and relaxation patterns, (4) ventricular torsion and rotation, and (5) fiber orientation and fiber shortening during the cardiac cycle.

Results of experiments analyzing these parameters in detail will be published elsewhere. As an example of such measurements, fiber shortening is presented for four successive heart beats (Fig. 9), in which an extrasystolic beat is induced by electrical stimulation of the heart. The stimulus interval after the extrasystole is compensated for changes in atrioventricular nodal conduction so that the RR interval of the postextrasystolic beat equals the basic RR interval (controlled postextrasystolic potentiation). As can be seen, changes in fiber shortening occur in the extrasystolic and postextrasystolic heart beats relative to the basic beat.

DISCUSSION

Assessment of myocardial muscle function, apart from the performance of the ventricle as a pump, is of continuing concern to the clinical cardiologist. This is of importance when surgical interventions are considered in order to correct abnormal hemodynamic loads imposed by ventricular lesions, aneurysms, or abnormal shunts. Because of various compensatory mechanisms, severe loss of myocardial function may not become manifest in ventricular pump function until late in the course of the disease. Various indices derived from hemodynamic measurements have been used to assess quantitatively ventricular overall performance. How-

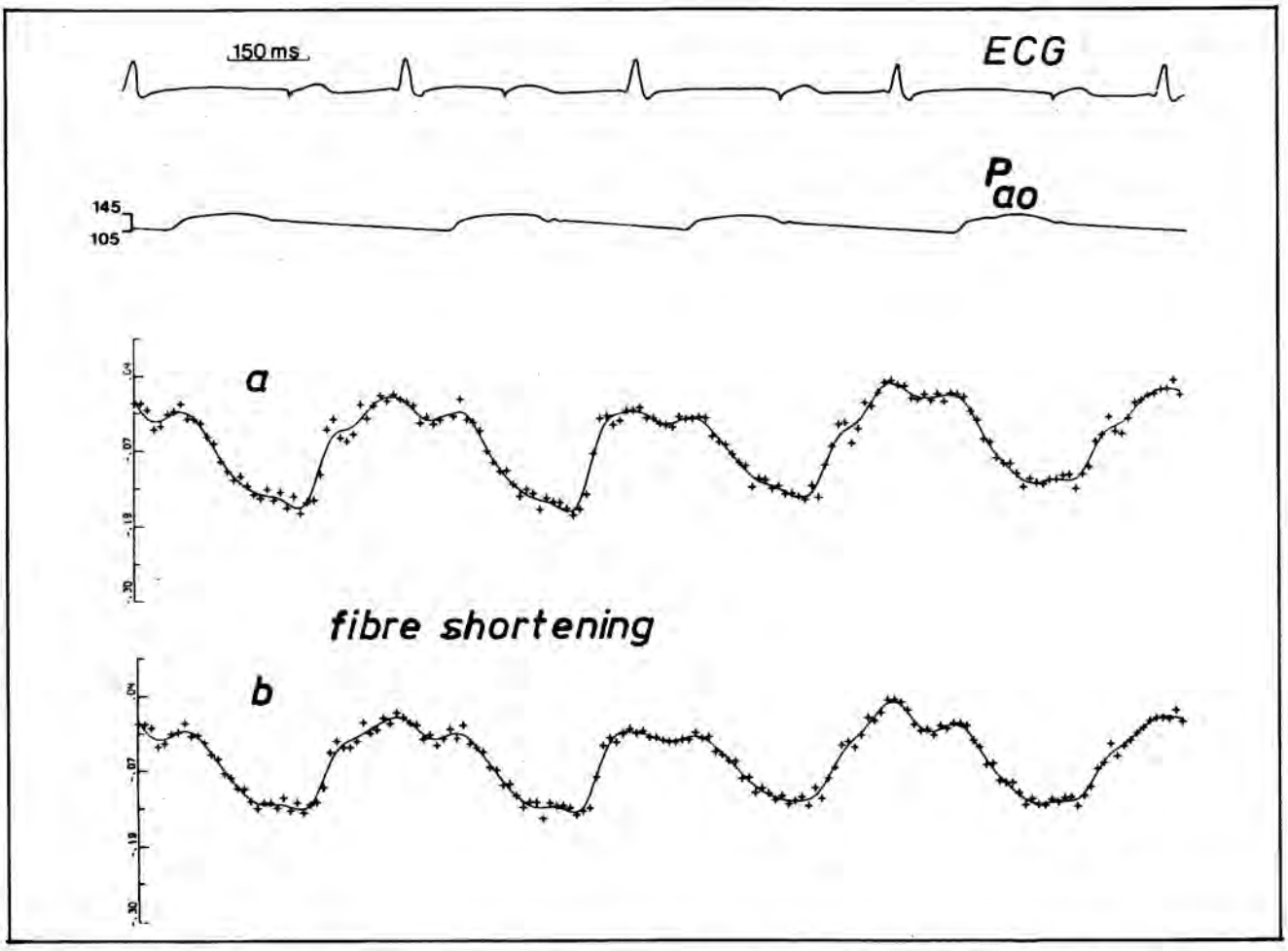

Fig. 9. Plots of epicardial fiber shortening in four successive beats between base and mid ventricle *(a)* and between apex and mid ventricle *(b)*. Fiber shortening is normalized to end-diastolic length. Aortic pressure, P_{ao}, is in mm Hg.

ever, these indices do not reflect the intrinsic regional contractile state of the myocardium.

Stresses generated in the walls of the ventricle caused by contraction and relaxation of the individual muscle fibers may play an important role in the assessment of regional cardiac function, and knowledge of stress values may reveal mechanisms of cardiac behavior in the normal and the diseased heart. For instance, because of chronic volume and pressure overload on the left ventricle, wall stress would increase; however, hypertrophy is a compensatory mechanism that increases wall thickness and therefore tends to maintain wall stresses within normal limits. In addition, wall stress is one of the determinants of myocardial oxygen consumption and plays an important role in the behavior of the coronary circulation. Because wall stresses are not directly accessible to measurement, different investigators have tried to compute stresses with the help of model studies of the heart and theories of elastic media. Frequently, approximate geometric forms such as spheroids or ellipsoids are taken for the ventricular shapes. Already in 1892, Woods[16] applied the law of Laplace for the evaluation of wall stresses in the heart. In a later stage, Burch and associates[17] and Burton[18] demonstrated the importance of size and shape of the ventricle in relation to its performance. Since then, many authors have calculated wall stresses under different assumptions of geometry, homogeneity, linear elasticity, and isotropy of cardiac muscle.[7,8,19-22] No completely satisfactory theory has yet been developed.

Our intention is to work on these problems for the coming years by developing new models based on the current ones. The true geometry of the heart, measured with help of the ultrasound tomograph, will be implemented. Data on intramural, endocardial, or epicardial motion of selected parts of the ventricle can also be

determined with the marker method and implemented in the models. Our implantation method, which has been used for some years, is rapid and causes no severe damage to the heart. No opening of the heart is required, as has been proposed in other, derived procedures.[23] With the use of new versions of the finite-element technique, which will allow incorporation of regional anisotropy and inhomogeneity, we expect that new facts will be revealed and that insight in ventricular function will be deepened.

It is Dr. Earl H. Wood[24] who deserves the credit for having added so many new ideas, techniques, and impulses in this particular field. Especially with the development of the DSR, horizons have been widened and possibilities opened for the application of many of the ideas originated in the experimental laboratory to the intact human heart noninvasively. Looking back on his distinguished career, one can say that Dr. Wood, during his part of the continuous scientific relay race, has changed the little wooden stick into a real scepter.

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