Measurement of myocardial tissue deformation by correlation interpolation of pulsed ultrasonic echo signals

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**Measurement of Myocardial Tissue Deformation
by Correlation Interpolation of
Pulsed Ultrasonic Echo Signals**

**Measurement of Myocardial Tissue Deformation
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Pulsed Ultrasonic Echo Signals**

Proefschrift

ter verkrijging van de graad van doctor
aan de Rijksuniversiteit Limburg te Maastricht,
op gezag van de Rector Magnificus, Prof. mr. M.J. Cohen,
volgens het besluit van het College van Dekanen,
in het openbaar te verdedigen
op donderdag, 30 mei 1991 om 16.00 uur

door

Petrus Godefridus Maria de Jong

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Promotores : Prof.dr. R.S. Reneman
Prof.dr.ir. A. Hasman
Co-promotores : Dr.ir. T. Arts
Dr.ir. A.P.G. Hoeks
Beoordelingscommissie : Prof.dr. H.J. van den Herik, voorzitter
Prof.dr.ir. N. Bom (EU Rotterdam)
Prof.dr.ir. D.H. van Campen (TU Eindhoven)
Dr.ir. J.M. Thijssen (KU Nijmegen)
Prof.dr. H.J.J. Wellens

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Al ken ik alle geheimen en alle wetenschap,
als ik de liefde niet heb, ben ik niets.

1 Kor. 13,2

*Voor Annemiek
Voor mijn ouders*

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Chapter 1

General Introduction

1.1 The heart and its dynamic behaviour

The heart is a hollow, thick-walled muscle, pumping blood through the vascular system. A long-axis cross-section of the heart is shown schematically in figure 1.1a. The heart consists of four cavities, the *right* (1) and *left* (2) *atrium* and the *right* (3) and *left* (4) *ventricle*. The atrial and ventricular cavities are separated by the atrial and the ventricular *septum* (5), respectively. The blood returning from the *systemic circulation* is collected in the right atrium. Blood from the *pulmonary circulation* is collected in the left atrium. The left atrium is separated from the left ventricle by

Figure 1.1: A schematic long-axis view of a cross-section of the heart (panel a) and a short-axis cross-section of the heart at a level between the base and the apex (panel b). 1=right atrium, 2=left atrium, 3=right ventricle, 4=left ventricle, 5=septum, 6=mitral valve, 7=tricuspid valve, 8=aortic valve, 9=aorta, 10=pulmonary valve, 11=pulmonary artery.

the *mitral valve* (6), and the right atrium from the right ventricle by the *tricuspid valve* (7). During the *systolic phase* the blood in the left ventricle is ejected through the *aortic valve* (8) into the *aorta* (9). Similarly, the right ventricle empties via the *pulmonary valve* (10) into the *pulmonary artery* (11). All four aforementioned valves are located in the *basal plane* of the heart. The *apex* is located opposite to the base across the ventricles. At the apex, the ventricular walls are relatively thin. In figure 1.1b a schematic short-axis cross-sectional view of the heart is shown at a level approximately one quarter of the base to apex distance below the base. The free wall of the right ventricle is significantly thinner than that of the left

ventricle. The inner and outer surfaces of both ventricles are the *endocardium* and the *epicardium*, respectively. The endocardial structure is irregular, and contains many *trabeculations*. The tissue of the cardiac wall between the endocardium and the epicardium is referred to as the *myocardium*, and consists mainly of striated muscle.

The different phases of the cardiac cycle occur practically synchronously on the right and left side of the heart. So, for simplicity the phases are described with respect to the left half of the heart only. In the *diastolic phase* the left ventricle is passively filled with blood from the left atrium. Filling is completed by the atrial contraction, which is initiated by depolarization of the *sinus node*. The depolarization wave travels from the atrium through the *atrio-ventricular node* to the fast conducting bundle of His and the Purkinje network. This causes the left ventricle to contract and marks the beginning of the *systolic phase*. The pressure increase in the left ventricle causes the closure of the mitral valve. As long as the ventricular pressure is lower than the aortic pressure, the aortic valve remains closed. Because then both ventricular valves are closed, left ventricular volume remains constant. During this *isovolumic contraction phase*, left ventricular pressure increases rapidly. When left ventricular pressure exceeds aortic pressure, the aortic valve opens and the *ejection phase* begins. At the beginning of the ejection phase, aortic flow increases rapidly to a maximum. Thereafter, the aortic flow decreases approximately linearly. During this phase, the aortic leaflets are moving inward the flow channel [78]. At the end of the ejection phase a slight backflow completes the closure of the aortic valve. In the *isovolumic relaxation phase* left ventricular pressure decreases rapidly. When the ventricular pressure drops below the left atrial pressure, the mitral valve opens and the *rapid filling* of the left ventricle starts. The blood in the mitral valve tract is accelerated. When the atrial and ventricular pressure are approximately equal, mitral deceleration begins.

1.2 Pulsed ultrasonic echocardiography

Ultrasound techniques are widely used in the clinic [24,97]. In cardiology, *two-dimensional echocardiography* (2DE) is a method commonly used to obtain real time images of the heart non-invasively. Ultrasound is considered not to cause biological harm to living tissue [98,100]. In the present study, echocardiographic equipment has been used to determine cardiac tissue deformation qualitatively. Before dealing with the problem of measuring deformation, an introduction will be given to echocardiography and the different modes used for ultrasonic imaging.

1.2.1 Principles of pulsed echocardiography

In echocardiography, high frequency sound waves, with a center frequency in the range from 2 to 10 MHz, are used to visualize the heart [24,97,99]. With a *piezo-electric crystal* [97], an electric signal is converted to an ultrasonic pulse. The pulse consists of one or a few cycles of the center frequency, and is generated at a *pulse repetition frequency* (PRF) of a few kilohertz. The sound propagates into the cardiac tissue and is partially reflected by the cardiac boundaries and by fiber structures within the myocardial tissue [24,97]. After reflection, the piezo-electric crystal is used to receive the *high frequency echo signals* (*RF signals*). Assuming a constant speed of propagation in the intervening tissues, the time delay between the transmission of the sound pulse and the reception of the echo from a specific tissue area is linearly related to the distance between the reflecting structures and the transducer. Using this property, regional displacement of cardiac tissue is associated with a shift in time delay of two successively received echo signals.

In practice, the sound waves are attenuated due to absorption by the cardiac tissue. The absorption is proportional to the square of the transmission frequency used. Consequently, echo signals from a reflecting structure at a large distance from the transducer are more attenuated than signals from nearby located reflectors. As a result, the maximum depth of investigation is limited. Furthermore, a next ultrasonic pulse should only be transmitted if the echos due to the previous pulse are attenuated sufficiently. Otherwise the far echos, initiated by the previous pulse, may be mixed up with the echos from nearby regions, initiated by the next pulse. Consequently, the PRF of the ultrasonic pulses has to be chosen in accordance to the attenuation of the sound waves by the tissue and the maximum depth of investigation.

1.2.2 Different modes of ultrasonic imaging

The ultrasonic echo signals returning from the cardiac tissue are converted to a signal representing the position of reflecting structures. Various methods are used to present the ultrasonic echo information [24]. The most basic method to represent an echo signal is the *Amplitude-mode* or *A-mode* (Fig. 1.2a). In this mode, the envelope of the received RF signal is plotted directly on the screen as a function of echo depth. The A-mode is transformed to the *Brightness-mode* or *B-mode* by converting the amplitude to screen luminosity (Fig. 1.2b). In *Motion-mode* or *M-mode* (Fig. 1.2c), the successive received B-mode lines are plotted side by side on the screen. Using M-mode, motion of structures can clearly be shown.

With the A, B and M-mode, the heart is represented as a function of time in one dimension. A two-dimensional view can be obtained by scanning of the region of interest with the ultrasonic beam. With the *linear scanning* technique, the beam is moved parallelly over the area of investigation. This motion can be performed me-

Figure 1.2: Modes to represent single echo lines. Panel a: A-mode; panel b: B-mode; panel c: M-mode.

chanically or electronically [13]. In echocardiology, the *sector-scan* technique is commonly used. With this technique, the beam is rotating around a sector point, which causes the echo signals to be received from a sector shaped area. With a *mechanical sector scan transducer* (Fig. 1.3a), an ultrasonic crystal is rotating around an axis while transmitting the sound pulses and receiving the echos. An electrical version of the mechanical sector scan transducer is the *phased-array transducer* (Fig. 1.3b). In this transducer type many small rectangular ultrasonic crystals are positioned in line. If all crystals transmit a short ultrasonic pulse synchronously, an ultrasonic beam results along the axis of the transducer. However, if the elements are activated successively and mutually delayed, the resulting beam is transmitted under an angle with the axis. Consequently, the beam can be transmitted in an arbitrary direction in the sector-shaped area by modifying the activation delay between the crystals. The activation pattern is created by special electronic instrumentation.

With ultrasonic B-mode or M-mode imaging, a reflecting structure is displayed on the screen using envelope detection of the RF signal thereby discarding the phase information. Then, principally the spatial resolution of the image is limited by the length of the ultrasonic pulse. This length is determined by the bandwidth of the transmitted pulse and the frequency transmission of the medium.

The construction of the 2DE image requires some time because the area of investigation has to be scanned line by line. In general, 2DE images are obtained at a rate of approximately 25 images per second. Consequently, a structure might be displayed somewhat deformed when it is rapidly moving through the sector area. Secondly, the axial and lateral dimensions of the ultrasonic beam are different in most ultrasonic imaging systems. This causes small point-shaped reflectors not to be imaged as points anymore.

Figure 1.3: Sector scanning: panel a: mechanical sector scan transducer; panel b: phased array transducer.

1.3 Determination of myocardial deformation

The geometry of the heart changes during the cardiac cycle. These changes are generally referred to as *cardiac deformation*. Known modes of global deformation of the heart are the *diameter decrease* of the cavities during contraction [30,44,92], *thickening* of the wall during the ejection phase [5,26] and *torsion* of the heart around its long axis [2,10,14,42]. The diameter decrease of the cardiac cavities is associated to the global pump function of the heart. Thickening of the cardiac wall during the ejection phase is related to the contraction of the myocardial fibers [30,31], while the amount of torsion yields information about the distribution of fiber shortening across the cardiac wall [2,14]. The global modes of cardiac deformation are related to the distribution of regional deformation of the myocardial tissue. Regional tissue deformation can be quantified by measuring gradients in regional tissue velocity or displacement. Both global and regional deformation of the myocardial tissue have been found to be affected considerably if regional cardiac performance is poor, for example, due to coronary artery disease [32,37,54]. Consequently, measurement of several parameters of regional cardiac deformation may yield information about cardiac tissue performance in the region of interest. In the next two sections, a short overview is given of the current techniques to measure tissue deformation.

1.3.1 Invasive measurement of tissue deformation

Many techniques to measure myocardial deformation require thoracotomy. One dimensional deformation of cardiac tissue has been determined by using *strain gauges* [25,62] or by using a pair of ultrasonic crystals. The latter method relies on the principle that when an ultrasonic pulse is transmitted, the measured transit-time of the pulse is proportional to the distance between the crystals. Both crystals can be positioned at or just underneath the epicardium to measure tissue deformation along the surface [83]. To measure wall thickness the crystals can be positioned at the epicardial and endocardial surface [85]. Using the latter technique, thickening of the left ventricular wall in the dog was found to vary from 10 to 30% [32,83,85]. Hartley *et al.* [37] measured radial strain, which is associated with cardiac wall thickening, with the use of a single epicardial crystal. Regional tissue velocity was determined by using a pulsed Doppler technique. Radial strain in the canine cardiac wall was found to range from 5 to 30%. Two dimensional deformation of the epicardial surface has been measured by means of a *triangulation technique* using ultrasonic crystals [68], strain gauges [51], *inductive coils* [4,6,73] or *optical markers* [72,74]. Three dimensional cardiac deformation has been measured by following *radiopaque markers*, which were implanted in the myocardial tissue. The markers can be visualized by using a *biplane cineradiographic* technique [27,93].

1.3.2 Non-invasive measurement of tissue deformation

Besides the invasive techniques, several techniques have been developed to measure myocardial deformation transcutaneously, such as *magnetic resonance imaging* (MRI) [18,59,86,101] and tissue velocity estimators using echocardiography. In the present study tissue deformation will be determined using transcutaneous ultrasound. Therefore, only the current ultrasound techniques to measure tissue displacement non-invasively will be discussed in the present section.

The displacement and deformation of myocardial tissue has been measured by determining the position of the myocardial borderlines in the M-mode image [35,41, 89,90,92] or the 2DE image [26,58,84,88,91] of the heart as a function of time. Wall thickness can be estimated as the distance between the epicardial and endocardial boundary in the image. Using this technique, Troy *et al.* [90] and Feneley *et al.* [26] found mean cardiac wall thickening to range from 48 to 67% during systole. The 2DE image of the heart can also be processed by *optical flow computing* [56,57,63] to calculate a velocity vector field in the area of interest. From this velocity field the displacement of various structures within the image can be reconstructed. Finally, the displacement of a structure within the 2DE image of the heart may also be determined by shifting two successive images relatively to each other until a best fit is found [49,71,84]. The resulting shift between the images is related to the actual displacement of the cardiac tissue in the associated time interval.

In a second group of techniques, RF signals are processed directly to calculate cardiac tissue velocity. Subsequently, tissue deformation is determined by measuring differences in velocity between distinct regions within the cardiac wall. Firstly, tissue velocity can be measured with *ultrasound Doppler* methods, regularly used for the determination of blood velocity [7,8,17,48,52,61,70,77]. If a structure is moving, the frequency of the ultrasonic echo signal differs from the frequency of the transmitted ultrasonic pulse. This difference, the *Doppler frequency shift*, is linearly related to the velocity of the moving structure along the line of observation [29,38,77,97]. Secondly, *correlation* techniques can be applied to successive echo signals to determine cardiac tissue velocity [12,22,23,28,43,50,96]. With these methods the crosscorrelation function between two echo signals is calculated. The position of the top of the function indicates the mutual shift between the signals [69]. Assuming a constant velocity of sound within the tissue, the echo shift is proportional to the actual displacement of the cardiac tissue along the line of observation as occurring between two pulse transmissions. This displacement is proportional to tissue velocity along the same line.

1.4 Aim of the study

In several investigations, regional deformation of cardiac tissue has been measured. The available techniques can be divided into the invasive and the transcutaneous methods. In general, the invasive techniques are quite accurate in determining tissue deformation, because measurements can be performed directly on the myocardium. Using inductive coils or optical markers, strain has been determined with an accuracy better than ± 0.01 [4,74]. The major disadvantage of the methods is the need for thoracotomy, which makes it unsuitable for clinical investigations. Besides, the myocardial tissue may be damaged by positioning the ultrasonic crystals or markers [102].

The transcutaneous techniques are generally based on ultrasonic echocardiography. Unfortunately, the 2DE and M-mode image have a low spatial resolution. As a result, tissue deformation, as assessed by processing of these images, will have a low spatial resolution too. The spatial resolution may be improved by processing the RF signals directly. Firstly, Doppler techniques have been used to measure tissue velocity. These techniques may yield an estimation of tissue displacement with a resolution of less than $1\text{ }\mu\text{m}$, but in general the temporal resolution of the estimation is quite low [52]. Secondly, correlation techniques have been used to measure the displacement of the cardiac tissue. The spatial resolution of the technique is limited by the depth sampling frequency, while the resolution in time is directly related to the PRF, which may be quite high. Unfortunately, the correlation methods generally need a high computational effort.

In this thesis a new technique is described to measure cardiac tissue velocity transcutaneously by processing pulsed ultrasonic echo signals directly. It is based on calculating the crosscorrelation function between successive echo signals. By modeling the shape of the top of the function its position can be determined more accurately and faster than with current correlation techniques. The position of the top is directly related to displacement of the tissue, and thus to tissue velocity. From the obtained estimates of regional tissue velocity, the deformation of the tissue is determined by calculating gradients in velocity as the ratio of the difference in measured velocity in separate regions and the distance between the centers of these regions.

The performance of the new technique is determined through several evaluations. Firstly, *artificial echo signals* are used in a computer simulation to study the linearity of the estimation and the influence of additional noise (chapter 3). Secondly, *real echo signals* are obtained by the use of a 2DE imaging system. In this evaluation, a rotating phantom is used to simulate uniformly moving cardiac tissue (chapter 4). By varying the velocity of rotation of the phantom, different tissue velocities are simulated. The angular velocity of the disk is measured by estimating simultaneously the velocity of two distinct regions located oppositely with respect to the center of rotation. Finally, a study in seven closed-chest dogs (chapter 5 and 6) and a single pilot study in a human (chapter 7) are presented. In these studies, parameters as *strain* in the left ventricular wall, *cavity diameter change* and *cardiac rotation* are measured as a function of time in order to evaluate the correlation interpolation technique in vivo.

Chapter 2

Principles of Correlation Interpolation

The contents of this chapter have partly been published in the article: *Determination of tissue motion velocity by correlation interpolation of pulsed ultrasonic echo signals*, by P.G.M. de Jong, T. Arts, A.P.G. Hoeks and R.S. Reneman, *Ultrasonic Imaging*: 84-98 (1990).

2.1 Introduction

In section 1.3.2 several existing techniques have been described to measure the displacement of moving myocardial tissue transcutaneously by processing a sequence of ultrasonic echo signals. For this purpose, ultrasonic pulses are transmitted into the cardiac tissue. The echo signals are sampled along the echo depth, while sampling in time occurs with the PRF. With one group of techniques tissue displacement is measured on the basis of the crosscorrelation function between successive echo signals. To this end, several samples of the crosscorrelation function are calculated. Subsequently, the largest calculated correlation value is searched for. The position of this top indicates the shift between the echo signals. Assuming a constant velocity of propagation of the ultrasound through the tissue, this shift is linearly related to the actual displacement of the tissue along the line of observation. However, in the most basic approach the position of the top is determined with an accuracy of ± 0.5 times the distance between two sample points in depth.

In the present chapter, the correlation technique to estimate signal shift is modified to the *correlation interpolation technique*. With this new technique the cross-correlation function between successive echo signals is modeled in the vicinity of the top. Subsequently, the position of the top is estimated by an interpolation based on only five samples of the correlation function. As a result, signal shift is measured with subsampling accuracy using a considerably lower computational effort than other correlation techniques. In the next sections, the new technique will be described in more detail.

2.2 General theory

The correlation interpolation technique is a new method to determine the relative shift between successive echo signals by analyzing a number of successive signals simultaneously. While periodically transmitting an ultrasonic pulse into a tissue, the echo signal received represents the reflection intensity of the tissue as a function of depth. When a reflecting structure moves with velocity v_0 under an angle α with the ultrasonic beam, the successive echo signals shift gradually in echo depth (Fig. 2.1). The received echo signal $y(x, t)$ depends on two variables being depth x and time t :

$$y(x, t) = s(x - vt) + n(x, t) \quad (2.1)$$

with:

$$v = 2v_0 \cos(\alpha)$$

The function $s(x - vt)$ represents the reflectivity as a function of depth, which is moving with velocity v . The term $n(x, t)$ represents noise which is uncorrelated with the function $s(x - vt)$. A *two-dimensional autocorrelation function* of the signal $y(x, t)$ is defined by:

Figure 2.1: Schematic representation of received echo signals. PRF denotes the pulse repetition frequency and f_x the depth sampling frequency. Displacement of signals due to tissue motion is indicated by the broken line.

$$R_{yy}(X, T) = E_{x,t}\{y(x, t)y(x + X, t + T)\} \quad (2.2)$$

The operator $E_{x,t}$ indicates expected value by random selection of x and t in the xt -area of interest. The parameters X and T denote shift in depth and time, respectively. Assuming absence of correlation between the functions $s(x - vt)$ and $n(x, t)$, combination of Eq.(2.1) and Eq.(2.2) results in:

$$R_{yy}(X, T) = R_{ss}(X, T) + R_{nn}(X, T) \quad (2.3)$$

with:

$$\begin{aligned} R_{ss}(X, T) &= E_{x,t}\{s(x - vt)s(x - vt + X - vT)\} \\ R_{nn}(X, T) &= E_{x,t}\{n(x, t)n(x + X, t + T)\} \end{aligned}$$

Under the condition of *ergodicity* of the signal $s(x - vt)$, the expectation on the basis of random selection of two variables x and t may be replaced by the random selection of one variable $u = x - vt$. A signal is defined to be ergodic if the statistical properties of the signal do not change with the variable at the abscissa [69]. The values of the function $y(x, t)$ in Eq.(2.2) are only available in a grid of sampling

points with sampling intervals Δx and Δt for depth and time, respectively. Thus, the autocorrelation function $R_{yy}(X, T)$ can be estimated numerically for discrete values of X and T , to be defined by integers I and J , respectively:

$$\hat{R}_{yy}(X, T) = \frac{1}{i_{max}j_{max}} \sum_{j=1}^{j_{max}} \sum_{i=1}^{i_{max}} y(x, t)y(x + X, t + T) \quad (2.4)$$

with:

$$x = i\Delta x, X = I\Delta x$$

$$t = j\Delta t, T = J\Delta t$$

where i, j, I, J are integers.

The numbers i_{max} and j_{max} define the number of samples used for averaging in depth and time, respectively. The total number of samples used equals the product of i_{max} and j_{max} . Eq.(2.4) is used to estimate the autocorrelation function. The larger the total number of samples used, the better the estimate will be.

In the correlation interpolation method, the function $R_{yy}(X, T)$ is approximated by a model in the vicinity of the correlation maximum. This model is based on Eq.(2.3) and contains only a few parameters. By calculating the estimate of $R_{yy}(X, T)$ for a few points, the parameter values are solved and an estimate of the parameter v is obtained.

2.3 The model

By use of the *Wiener-Khinchin relations* [69], the autocorrelation function $R_{yy}(X, T)$ of a signal $y(x, t)$ is related to its *power density spectrum* $Y(\omega, T)$ as:

$$R_{yy}(X, T) = \mathcal{F}^{-1}\{Y(\omega, T)\} \quad (2.5)$$

where the operator $\mathcal{F}^{-1}$ indicates inverse *Fourier-transformation* [15], and ω denotes the angular frequency in echo depth. Assume the power density spectrum $S(\omega)$ of $s(u)$ is bandlimited and rectangular with center frequency ω_c , bandwidth ω_b and power density amplitude S_0 , as shown in figure 2.2. With these assumptions, the autocorrelation function of $s(u)$ can be expressed as the real part of Eq.(2.5) as:

$$\begin{aligned} R_{ss}(X, T) &= R_{ss}(U) = \operatorname{Re} \left\{ \mathcal{F}^{-1}\{S(\omega)\} \right\} \\ &= \operatorname{Re} \left(\frac{1}{2\pi} \int_{-\infty}^{\infty} S(\omega) e^{j\omega U} d\omega \right) = \operatorname{Re} \left(\frac{1}{\pi} \int_{\omega_c - \omega_b/2}^{\omega_c + \omega_b/2} S_0 e^{j\omega U} d\omega \right) \\ &= \frac{\omega_b}{\pi} S_0 \cos(\omega_c U) \frac{\sin(\omega_b U/2)}{\omega_b U/2} \end{aligned} \quad (2.6)$$

with $U = X - vT$. Furthermore, it is assumed that the power density spectrum of

Figure 2.2: Rectangular signal power spectrum, with central frequency ω_c , bandwidth ω_b and power density S_0 .

the noise term $n(x, t)$ at a fixed value of t has the same shape as the power density spectrum of the signal $s(x - vt)$. This similarity in shape is likely to be introduced by the bandpass characteristics of the ultrasound transducer used, which filters both signal and noise. As a result of the similarity of the signal and noise spectrum, the noise term in Eq.(2.3) may be written as:

$$R_{nn}(X, T) = \begin{cases} \frac{N_0}{S_0} R_{ss}(X, T) & \text{for } T = 0 \\ 0 & \text{for } T \neq 0 \end{cases} \quad (2.7)$$

where N_0 denotes the power density amplitude of the noise component. For $T \neq 0$ the autocorrelation function of $n(x, t)$ equals zero, because at different values of t the signals are bandpass filtered separately, implying absence of mutual correlation in the noise components of these signals. Using Eq.(2.3), Eq.(2.6) and Eq.(2.7), the autocorrelation function $R_{vv}(X, T)$ in Eq.(2.3) is found to be:

$$R_{vv}(X, T) = \begin{cases} (1 + \frac{N_0}{S_0}) R_{ss}(X, T) & \text{for } T = 0 \\ R_{ss}(X, T) & \text{for } T \neq 0 \end{cases} \quad (2.8)$$

with $R_{ss}(X, T)$ being defined according to Eq.(2.6). This model description of the autocorrelation function requires five parameter values: $S_0, N_0, \omega_c, \omega_b$ and v . The latter values may be obtained by calculating $R_{vv}(X, T)$ in five separate points using Eq.(2.4) and solving the resulting set of equations. Note that $\hat{R}_{vv}(X, T)$ as obtained in Eq.(2.4) is an estimation of $R_{vv}(X, T)$ by using only a limited number of samples for calculation.

2.4 Solution for narrow-band signals

If the signal $s(x - vt)$ has a narrow frequency band ($\omega_b \ll \omega_c$), Eq.(2.6) can be simplified to:

$$R_{ss}(X, T) = \frac{\omega_b}{\pi} S_0 \cos(\omega_c U) \quad (2.9)$$

with $U = X - vT$. Using Eq.(2.4), the autocorrelation function $R_{vv}(X, T)$ is estimated in 5 points with (X, T) coordinates $(0, 0)$, $(\Delta x, 0)$, $(0, \Delta t)$ and $(\pm \Delta x, \Delta t)$. According to Eq.(2.8) and Eq.(2.9), $R_{vv}(X, T)$ is written in terms of the parameters $\omega_b, \omega_c, S_0, N_0$ and v . It holds:

$$\begin{cases} R_{vv}(0, 0) &= \frac{\omega_b}{\pi} (S_0 + N_0) & (a) \\ R_{vv}(\Delta x, 0) &= \frac{\omega_b}{\pi} (S_0 + N_0) \cos(\omega_c \Delta x) & (b) \\ R_{vv}(0, \Delta t) &= \frac{\omega_b}{\pi} S_0 \cos(-\omega_c v \Delta t) & (c) \\ R_{vv}(\Delta x, \Delta t) &= \frac{\omega_b}{\pi} S_0 \cos(\omega_c \Delta x - \omega_c v \Delta t) & (d) \\ R_{vv}(-\Delta x, \Delta t) &= \frac{\omega_b}{\pi} S_0 \cos(-\omega_c \Delta x - \omega_c v \Delta t) & (e) \end{cases} \quad (2.10)$$

This set of five equations contains four solvable unknowns. In order to solve the parameter v , we have used the following calculation scheme. Using Eq.(2.10a) and Eq.(2.10b), it follows:

$$\omega_c \Delta x = \arccos \left(\frac{R_{vv}(\Delta x, 0)}{R_{vv}(0, 0)} \right) \quad (2.11)$$

Subtracting Eq.(2.10e) from Eq.(2.10d) results in:

$$\frac{R_{vv}(\Delta x, \Delta t) - R_{vv}(-\Delta x, \Delta t)}{2} = \frac{\omega_b}{\pi} S_0 \sin(\omega_c v \Delta t) \sin(\omega_c \Delta x) \quad (2.12)$$

The factor $\sin(\omega_c \Delta x)$ is calculated using the result of Eq.(2.11). Using Eq.(2.12) and Eq.(2.10c), it is found:

$$\omega_c v \Delta t = \arctan 2 \left(R'_{vv}, \sin(\omega_c \Delta x) R_{vv}(0, \Delta t) \right) \quad (2.13)$$

with:

$$R'_{vv} = \frac{R_{vv}(\Delta x, \Delta t) - R_{vv}(-\Delta x, \Delta t)}{2}$$

The function $\arctan 2(y, x)$ delivers the polar angular coordinate, associated with the cartesian x and y coordinates. Finally, the parameter v is solved by division of

the result of Eq.(2.13) by that of Eq.(2.11) and multiplication by $\Delta x/\Delta t$:

$$\begin{aligned}
 v &= \frac{(\omega_c v \Delta t) \Delta x}{(\omega_c \Delta x) \Delta t} \\
 &= \frac{\arctan 2 \left(R'_{vv}, \sin \left(\arccos \left(\frac{R_{vv}(\Delta x, 0)}{R_{vv}(0, 0)} \right) \right) R_{vv}(0, \Delta t) \right) \Delta x}{\arccos \left(\frac{R_{vv}(\Delta x, 0)}{R_{vv}(0, 0)} \right) \Delta t} \quad (2.14)
 \end{aligned}$$

This calculation procedure is quite safe with regard to division by zero and invalid function arguments. The term $R_{vv}(0, 0)$ denotes a sum of squares and is always positive as long as a signal is present. The argument of the arccos function in Eq.(2.11) is always between -1 and 1. The sampling interval Δx should be chosen so that $\sin(\omega_c \Delta x)$ is in a range well beyond zero. The latter term is maximal if the center frequency is sampled approximately 4 times per period along the x -direction. To avoid aliasing in the arctan2 operation in Eq.(2.13), the angle $(\omega_c v \Delta t)$ should be within the range of $-\pi$ to π radians. Finally, according to the definition of v in Eq.(2.1), the velocity component in the direction of the transducer is found by halving the value of v . The implementation of the correlation interpolation technique into a computer algorithm is described in detail in appendix A.

In the final solution of the echo velocity v according to Eq.(2.14) the parameter ω_c is not present. This implies that the center frequency of the echo signals has not to be substituted in order to estimate the echo velocity. Consequently, the estimation of tissue velocity will not be influenced by changes of the center frequency of the echo signals, for example, induced by frequency dependent absorption of the ultrasound by the tissue.

2.5 Solution for wide-band signals

In case of a larger bandwidth of the signal $s(x - vt)$, the solution for v given by Eq.(2.14) is not exact anymore because the limited validity of Eq.(2.9). Nevertheless, the calculations can still be performed as if the signal had a narrow bandwidth. In figure 2.3, for signals with a flat and bandlimited frequency band, the relation between the exact solution on the basis of Eq.(2.8) and the estimate on the basis of the calculation scheme, as described by Eq.(2.9) through Eq.(2.14), is shown for a ratio of absolute bandwidth to center frequency of 0, 1 and 2, respectively. Since the central frequency is assumed to contain 4 samples per period, the highest frequency is sampled properly in all examples. From figure 2.3, it may be concluded that even for a relatively large bandwidth, being equal to the center frequency, the velocity estimator performs quite well. Because real echo signals may have quite a large bandwidth, it is preferable to preprocess the signals with a bandpass filter with a

Figure 2.3: Theoretical analysis of the performance of the algorithm when processing rectangular bandlimited signals with a ratio of absolute bandwidth to center frequency (Relative BandWidth) of 0, 1 and 2, respectively. Real and calculated displacement between signals is denoted by x_{sp} and $\hat{x}_{sp}$, respectively. The larger the bandwidth, the greater the discrepancy between calculated and real displacement will be.

bandwidth less than or equal to the center frequency. By doing so, errors in the estimation of the velocity due to nonlinear characteristics are small as shown in figure 2.3.

2.6 Estimation of signal parameters

With the present technique, echo velocity is calculated by solving Eq.(2.10). The latter set contains five equations with four solvable variables. In section 2.4 the echo velocity v has been solved in order to estimate tissue velocity. However, also the center frequency ω_c and the signal to noise power ratio S_0/N_0 of the echo signals may be solved. In the present section the formulas to estimate the specific parameters are derived.

The center frequency ω_c of the echo signal can be calculated directly from Eq.(2.11). It holds:

$$\omega_c = \frac{1}{\Delta x} \arccos \left(\frac{R_{vv}(\Delta x, 0)}{R_{vv}(0, 0)} \right) \quad (2.15)$$

The ratio of signal power S_0 and noise power N_0 of the echo signals can be calculated using the following scheme. First, Eq.(2.10c) is reformulated as:

$$\frac{R_{vv}(0, \Delta t)}{\cos(-\omega_c v \Delta t)} = \frac{\omega_b}{\pi} S_0 \quad (2.16)$$

Note that the term $\cos(-\omega_c v \Delta t)$ in the left hand side of Eq.(2.16) can be calculated using Eq.(2.13), and therefore can be considered to be known. Subtracting Eq.(2.16) from Eq.(2.10a) yields:

$$R_{vv}(0, 0) - \frac{R_{vv}(0, \Delta t)}{\cos(-\omega_c v \Delta t)} = \frac{\omega_b}{\pi} (S_0 + N_0) - \frac{\omega_b}{\pi} S_0 = \frac{\omega_b}{\pi} N_0 \quad (2.17)$$

Division of Eq.(2.16) and Eq.(2.17) finally yields the signal to noise power ratio S_0/N_0 . It holds:

$$\frac{R_{vv}(0, \Delta t) / \cos(-\omega_c v \Delta t)}{R_{vv}(0, 0) - R_{vv}(0, \Delta t) / \cos(-\omega_c v \Delta t)} = \frac{S_0}{N_0} \quad (2.18)$$

The parameters ω_c and S_0/N_0 may be used in the characterization of biological tissue using ultrasound [9,53,64,79,81,80,87,94,95]. However, it should be noted that in the present study only the parameter v is considered. Characterization of cardiac tissue is beyond the scope of the present study.

2.7 Conclusions

In the present chapter the newly developed correlation interpolation technique is described to measure the shift between successive echo signals, which are sampled in depth. With the technique the shape of the top of the crosscorrelation function between two signals is modeled by a cosine function. The position of the top is directly related to the shift between successive signals. The signal shift is determined with subsampling accuracy by interpolation of only five samples of the correlation function. Consequently, the computational effort of the method is relatively low. In principle, the technique has been developed for narrow-band echo signals. However, processing signals with a bandwidth equal to the center frequency was found to introduce minor errors in the estimation of echo shift. Applying the correlation interpolation technique, the center frequency and the signal to noise power ratio of the received echo signals can also be determined. The latter parameters may be used to characterize the myocardial tissue.

Chapter 3

Simulations

The contents of this chapter have partly been published in the article: *Determination of tissue motion velocity by correlation interpolation of pulsed ultrasonic echo signals*, by P.G.M. de Jong, T. Arts, A.P.G. Hoeks and R.S. Reneman, *Ultrasonic Imaging*: 84-98 (1990).

3.1 Introduction

In chapter 2 the correlation interpolation technique to measure the displacement in depth between successive echo signals has been described. With the method, signal shift is calculated on the basis of 5 samples of the crosscorrelation function between two signals. The technique estimates signal shift with subsampling accuracy using a low computational effort.

In the present chapter, the performance of the method is evaluated in a computer simulation. For that purpose, an artificial echo signal with a bandwidth to center frequency ratio of approximately 1 is generated. Successive signals are obtained from this single signal by shifting it linearly along the depth direction. Subsequently, the generated echo shift is estimated by applying the correlation interpolation technique. From the results, the accuracy and linearity of the technique are evaluated. To evaluate the noise sensitivity of the method, Gaussian noise is added to the generated signals in several signal to noise power ratios. Again the signals are processed with the correlation interpolation technique and the results are evaluated. Two Doppler algorithms, regularly used for the determination of blood velocity, are implemented to compare the performance of the correlation interpolation technique with existing techniques to measure velocity.

When applying the correlation interpolation technique, the narrow-band approximation as derived in section 2.4 is used, although the artificial signals have a wide frequency band. As demonstrated in section 2.5 signals with a bandwidth equal to or less than the center frequency may be processed by the correlation interpolation technique without a significant decrease of the accuracy of the estimation of signal shift.

3.2 Setup of simulations

3.2.1 Generation of test signals

Echo signals as obtained by ultrasonic echographic equipment were simulated by bandlimited noise. For this purpose, noise $h_0(x)$ with a Gaussian amplitude distribution was generated with a random number generator and bandpass filtered with a 6 point convolution bandpass filter (1,1,-2,-2,1,1). This filter has a center frequency of 0.22 times the sample frequency, yielding signals with approximately 4.5 samples per period, and a bandwidth to center frequency ratio of 1. In figure 3.1 the amplitude response of this filter, and the power density spectrum of a generated test signal are shown as a function of normalized frequency. For testing purposes, successive signals $h_j(x)$ were created by shifting a calculated noise signal $h_0(x)$ linearly in time. This shifting was obtained by a combination of an integer shift and interpolation of $h_0(x)$, all before the bandpass filtering was performed. The number

Figure 3.1: Amplitude response $|B|$ of the bandpass filter (panel a) and resulting signal power spectrum H (panel b, arbitrary units) of an arbitrary test signal as a function of normalized frequency.

x_{jp} represents the shift between successive signals expressed in number of sampling intervals. Then the j -th signal was calculated by:

$$h_j(x) = \cos\left(\frac{r\pi}{2}\right) h_0(x + p\Delta x) + \sin\left(\frac{r\pi}{2}\right) h_0(x + (p+1)\Delta x) \quad (3.1)$$

with $p = \text{int}(jx_{jp})$ and $r = jx_{jp} - p$. Here Δx denotes the sampling interval in depth, as defined in Eq.(2.4). By this interpolation method, the power of the signal is independent of the shift.

Signals generated on the basis of different random number sequences are not correlated. Using this property, noise signals were obtained in the same way as the signal itself. Noise signals of this kind were added to the artificial echo signals with signal to noise power ratios of 10 and 1, respectively. So, in the simulation different scanning signals contain different noise components, while the signal components are a shifted version of the same basic signal.

3.2.2 Comparison with Doppler techniques

To compare the correlation interpolation method with other methods used for velocity measurement, two Doppler techniques were implemented. These techniques determine the frequency shift of the ultrasonic signal, due to displacement of the tissue, with respect to a stable reference frequency [29,38,97]. When the tissue is moving with velocity v_0 , under an angle α with the ultrasonic beam, the transmitted signal is received with a Doppler frequency shift f_d :

$$f_d = 2 \frac{v_0}{c} f_c \cos(\alpha) \quad (3.2)$$

where f_c denotes the frequency of the transmitted signal, and c the velocity of sound in the tissue. The phase shift between successive signals at a certain depth can be determined by *demodulating* the signals using $i_{\max}$ samples in depth. *Quadrature demodulation* of the j -th received echo signal yields the *in-phase* $x_d(j)$ and *quadrature* $y_d(j)$ signal components. These two components describe the demodulated input signal in its complex representation $z(j)$:

$$z(j) = A(j)e^{j\phi(j)} = x_d(j) + jy_d(j) \quad (3.3)$$

where $A(j)$ denotes the amplitude of the signal (see figure 3.2). In principle, the

Figure 3.2: Complex representation of the demodulated input signal.

estimation of the Doppler frequency shift $\hat{f}_d(j)$ can be determined by calculation of the time derivative of the phase $\phi(j)$ of the signal $z(j)$:

$$\hat{f}_d(j) = \frac{1}{2\pi} \frac{d\phi(j)}{dt} \quad (3.4)$$

From Eq.(3.3) and figure 3.2, it is clear that the phase $\phi(j)$ can be expressed as:

$$\phi(j) = \arctan\left(\frac{y_d(j)}{x_d(j)}\right) \quad (3.5)$$

Several estimators have been described to estimate the Doppler frequency shift from $x_d(j)$ and $y_d(j)$. Two of those estimators will be discussed in the next two paragraphs. Note that according to Eq.(3.2) the velocity of the moving tissue depends on the center frequency of the RF signal. Consequently, the latter frequency has to be known in order to estimate tissue velocity.

The instantaneous frequency detector

Using Eqs.(3.4) and (3.5), and substituting a first order difference equation for the differentiation, the Doppler frequency shift can be approximated by:

$$\begin{aligned}\hat{f}_d(j) &= \frac{1}{2\pi}[\phi(j) - \phi(j-1)] \\ &= \frac{1}{2\pi} \left[\arctan \left(\frac{y_d(j)}{x_d(j)} \right) - \arctan \left(\frac{y_d(j-1)}{x_d(j-1)} \right) \right]\end{aligned}\quad (3.6)$$

Due to the sample time of unity used, $\hat{f}_d$ is expressed as a fraction of the PRF. Using the *arctan* operation, the aliasing-free interval is between $\pm \pi/2$ radians. When the *arctan* operation is implemented with the *arctan2* function, as defined in Eq.(2.13), the aliasing-free interval is doubled to $\pm \pi$ radians. Averaging over j_{max} signals in time can be performed by calculating Eq.(3.6) for j_{max} successive signals and averaging the corresponding values of $\hat{f}_d(j)$.

The probability density function of $\hat{f}_d(j)$ is wider than the frequency distribution of the Doppler signal [38,39,52]. As a result, even with correctly sampled signals instantaneous frequencies can be found outside the frequency range of the signal. This phenomenon may even lead to frequency aliasing. After averaging over a number of successive signals, the incorrect interpreted frequency samples introduce biasing of the average to lower frequencies. As a result, tissue velocity is underestimated, especially for center frequencies close to the boundaries of the interval.

The complex autocorrelation detector

Another algorithm to estimate the Doppler frequency shift is based on approximation of the *complex autocorrelation function*. When we consider:

$$\Delta\phi(j) = \phi(j) - \phi(j-1) \quad (3.7)$$

as used before in Eq.(3.6), it holds:

$$\begin{aligned}\tan(\Delta\phi(j)) &= \tan \left[\arctan \left(\frac{y_d(j)}{x_d(j)} \right) - \arctan \left(\frac{y_d(j-1)}{x_d(j-1)} \right) \right] \\ &= \frac{x_d(j-1)y_d(j) - x_d(j)y_d(j-1)}{x_d(j)x_d(j-1) + y_d(j)y_d(j-1)}\end{aligned}\quad (3.8)$$

Using Eq.(3.6) and performing an *arctan* operation on Eq.(3.8) yields:

$$2\pi\hat{f}_d(j) = \arctan \left(\frac{x_d(j-1)y_d(j) - x_d(j)y_d(j-1)}{x_d(j)x_d(j-1) + y_d(j)y_d(j-1)} \right) \quad (3.9)$$

The discrete estimate $\hat{C}_{xx}(m)$ of the *complex autocorrelation function* $C_{xx}(m)$ of a function $z(j)$ is defined as:

$$\hat{C}_{zz}(m) = \frac{1}{j_{max}} \sum_{j=1}^{j_{max}} z(j)z^*(j-m) \quad (3.10)$$

where * denotes complex conjugate. Regarding Eq.(3.9), it is found that the numerator and denominator in the expression are equal to the imaginary and real part of $\hat{C}_{zz}(m)$, with $m = 1$ and $j_{max} = 1$. When calculating $\hat{C}_{zz}$ on the basis of only two successive signals, the complex autocorrelation detector is equal to the instantaneous frequency detector. To improve the estimation of the correlation function, often a larger value for j_{max} is applied. For the estimation of the Doppler frequency shift it is found:

$$\hat{f}_d(j) = \frac{1}{2\pi} \arctan \left(\frac{Im\{\hat{C}_{zz}(1)\}}{Re\{\hat{C}_{zz}(1)\}} \right) \quad (3.11)$$

The relationship between autocorrelation and spectral density shows an important feature of the algorithm [52]. Consider an arbitrary wide band Doppler spectrum, which is partially aliased (Fig. 3.3). Calculating $C_{zz}(m)$ out of the power

Figure 3.3: Power density function of an arbitrary aliased Doppler signal as a function of frequency. The aliasing frequency of the Doppler spectrum is equal to $\pi \text{ rad}\cdot\text{s}^{-1}$.

density function $Z(\omega)$ of the signal $z(j)$ by use of the Wiener-Khinchin relations [69] yields:

$$\begin{aligned} C_{zz}(m) &= \mathcal{F}^{-1}\{Z(\omega)\} = \frac{1}{2\pi} \int_{-\infty}^{\infty} Z(\omega) e^{j\omega m} d\omega \\ &= \frac{1}{2\pi} \int_{-\pi}^{\pi} Z(\omega) e^{j\omega m} d\omega \end{aligned} \quad (3.12)$$

For $m = 1$, as used in the complex autocorrelation detector, this yields:

$$\begin{aligned} C_{zz}(1) &= \frac{1}{2\pi} \left[\int_{-\pi}^c Z(\omega) e^{j\omega} d\omega + \int_a^{\pi} Z(\omega) e^{j\omega} d\omega \right] \\ &= \frac{1}{2\pi} \int_a^b Z(\omega) e^{j\omega} d\omega \end{aligned} \quad (3.13)$$

So Eq.(3.13) shows that partial aliasing of continuous Doppler spectra is accounted for correctly. Moreover, $C_{xx}(m)$ is not biased by adding white noise, because the estimated contribution to $C_{xx}(m)$ equals zero [52]. Of course, noise will affect the variance of the estimate.

3.2.3 Simulations

The three methods are applied to the same set of test signals. In order to investigate the sensitivity to noise, the shift between successive signals is determined at signal to noise power ratios of 10 and 1, respectively. In order to evaluate the behaviour of the different methods with respect to the shape of the sampling area, the number of sampling points has been fixed to 64 and the following sizes have been used: 2×32 , 4×16 , 8×8 , 16×4 and 32×2 samples in depth and time, respectively. In the current setup, the complex autocorrelation detector and the instantaneous frequency detector cannot use less than 4 samples in depth per signal, because demodulation has to be performed over at least one signal period of the reference signal. This limitation does not hold for the correlation interpolation technique.

In order to evaluate the sensitivity to noise when changing the number of sampling points in depth and time, the error introduced is assessed for the Doppler methods as well as for the correlation interpolation method. For this evaluation the sampling areas used are the 9 combinations of 4, 8 and 16 samples in depth with 2, 8 and 32 samples in time.

Generally, the Doppler methods are applied to RF signals with a relatively narrow bandwidth. The center frequency in depth is locked to the demodulation frequency and is generally a quarter of the sampling frequency. Thus, the calculated displacement between successive echo signals is the product of Doppler frequency shift and sampling frequency, divided by the center frequency of the signal. The correlation interpolation technique delivers the depth shift between successive echo signals directly. The echo signal may have a large bandwidth and the center frequency does not need to be locked to the sampling frequency.

3.3 Results

In figure 3.4, for signals with a bandwidth equal to the center frequency, the displacement as calculated with the correlation interpolation algorithm is shown as a function of the real displacement. In the absence of noise, the relation is quite linear up to the displacement where aliasing occurs. This aliasing occurs around half the periodicity of the center frequency of the signal. For displacements close to the aliasing point, the method seems less precise. The effect of the large bandwidth on the linearity is little, especially for small displacements. When noise is added, the location of the aliasing points, the slope and the linearity appear to be unchanged.

Figure 3.4: Calculated displacement $\hat{x}_{sp}$ versus real displacement x_{sp} of bandlimited signals, as processed with the correlation interpolation method. Displacement is expressed in sampling interval size. An averaging sequence of 32 samples in depth over 2 successive signals was used. Panel a: no additional noise; panel b and c: additional noise with signal to noise power ratios of 10 and 1, respectively.

Under the extreme condition that noise power equals signal power (Fig. 3.4, panel c), scattering of the measurements becomes large, but the method still works reasonably well. For several averaging ranges in depth and time, the standard deviation of the estimate is shown in table 3.1. The performance improves by increasing the number of samples in depth used for averaging, the number of signals used in time, or both. The standard deviation does not vary significantly differently from the reciprocal of the square root of the total number of samples used.

The results obtained by the instantaneous frequency detector and the complex autocorrelation detector are shown in figure 3.5. Two different levels of added noise were used. The number of depth samples used for demodulation was equal to 32, while the frequency shift was calculated over 2 successive signals in time. Linearity and aliasing properties of both methods are similar to those of the correlation interpolation method, although the correlation interpolation technique appears to be less sensitive to noise. In this respect, the complex autocorrelation detector performs better than the instantaneous frequency detector. The standard deviation of the estimation is presented in table 3.1 for several depth and time averaging ranges. When increasing the number of signals in time used per measurement, both methods show a similar improvement in performance.

Figure 3.5: Calculated Doppler frequency $\hat{f}_d$ versus real displacement x_{sp} using demodulation: instantaneous frequency detector (above) and complex autocorrelation detector (below) at signal to noise power ratios of 10 (panel a) and 1 (panel b), respectively. Averaging was performed over 32 samples in depth over 2 successive signals in time.

In figure 3.6 and table 3.2, the three methods are compared with respect to variation of the shape of the sampling area, while the number of samples used remains constant at 64. The results are obtained for depth-time averaging ranges of 4×16 , 8×8 , 16×4 and 32×2 samples in depth and time, respectively. The signal to noise power ratio used was equal to 10. If depth is limited, the complex autocorrelation detector and the correlation interpolation algorithm perform similarly. The aliasing area of the instantaneous frequency detector is smoothened due to averaging many signals, while the slope of the linear part is somewhat smaller than unity. While the total number of sampling points remains the same at greater depth and shorter time intervals, performance of the correlation interpolation method appears to be nearly unchanged. Under these conditions, the performance of the complex

Figure 3.6: Results of processing bandlimited signals with the instantaneous frequency detector (above), the complex autocorrelation detector (middle) and the correlation interpolation method (below) versus real displacement x_{sp} . Areas of 4×16 (panel a), 8×8 (panel b), 16×4 (panel c) and 32×2 (panel d) samples in depth and time were used.

autocorrelation detector deteriorates considerably. However, the instantaneous frequency detector improves with respect to unity slope and aliasing effect, and finally performs similarly as the complex autocorrelation detector. In this respect, the correlation interpolation method is superior in motion detection when averaging over many samples in depth.

Table 3.1: Standard deviation of the estimation of displacement, expressed in sampling interval size, when processing bandlimited signals with three different methods at various signal to noise ratios (SNR). Displacement was calculated using 9 different combinations of the number of samples in depth and signals in time. The standard deviation is calculated within the interval of -1.4 to 1.4 sample intervals, because this interval appears to be free of aliasing in all cases investigated.

xt area	Instantaneous Frequency Detector		Complex Autocorrelation Detector		Correlation Interpolation Algorithm	
	SNR=10	SNR=1	SNR=10	SNR=1	SNR=10	SNR=1
4×2	0.33	0.77	0.35	0.63	0.23	0.73
4×8	0.25	0.37	0.20	0.37	0.11	0.37
4×32	0.18	0.49	0.07	0.31	0.05	0.19
8×2	0.51	0.84	0.50	0.90	0.19	0.62
8×8	0.20	0.42	0.17	0.67	0.08	0.26
8×32	0.15	0.54	0.09	0.26	0.04	0.13
16×2	0.34	0.86	0.39	0.83	0.15	0.47
16×8	0.20	0.49	0.18	0.50	0.05	0.17
16×32	0.15	0.51	0.13	0.24	0.04	0.12

3.4 Discussion

In order to determine the velocity of a depth signal moving in time, the correlation interpolation method is evaluated using test signals obtained by band limitation of noise. The method needs 5 correlation sums to be calculated over the region of interest. The shape of the correlation function in depth and time is estimated. Maximum correlation is determined on the basis of this estimate. Comparing the performance with existing methods based on Doppler frequency shift analysis [52], the correlation interpolation method appears to be less sensitive to noise in the signal. Added noise does not cause a systematic error in the estimate.

Although the algorithm is based on sinusoidal signals, displacement between successive signals can be determined accurately when processing bandlimited signals with a bandwidth up to the central frequency (Fig. 3.4). The calculated displacement is linear with the real displacement, implying that nonlinearities, induced by a large bandwidth, are small, as is also shown by theoretical analysis (Fig. 2.3). If the bandwidth of a signal in depth is larger than the mean frequency, the bandwidth should be reduced by appropriate bandpass filtering before further analysis. How-

Table 3.2: Standard deviation of the estimation of displacement, expressed in sampling interval size, when using three different methods and exchanging depth and time resolution.

	Instantaneous Frequency Detector	Complex Autocorrelation Detector	Correlation Interpolation Algorithm
xt area	SNR=10	SNR=10	SNR=10
4×16	0.24	0.13	0.06
8×8	0.20	0.17	0.08
16×4	0.21	0.21	0.06
32×2	0.25	0.27	0.09

ever, this is not likely to occur because most echo systems have a relative bandwidth between 0.5 and 1 due to the filtering effect of the transducer used [39,97]. For many applications, such a band limitation is not a severe disadvantage. Because the frequency band is quite wide with respect to the mean frequency, the band limitation may be performed by convolution with a relatively short impulse response consisting of 5 or 6 points. Due to the limitation in bandwidth, the signal has a periodic appearance, causing aliasing. By this phenomenon, a second correlation maximum occurs at a distance of the order of the periodic length corresponding with the center frequency of the bandpass filter. Thus, the area in which the correct correlation maximum is found is limited to the range from -0.5 to 0.5 times the periodic length. This is clearly demonstrated with the correlation interpolation technique (Fig. 3.4) as well as with the demodulation techniques (Fig. 3.5).

Linearity and aliasing properties of the instantaneous frequency detector and the complex autocorrelation detector are similar to those of the correlation interpolation method. However, when using a short depth range over many successive signals, the slope of the instantaneous frequency detector tends to decrease (Fig. 3.6). This underestimation has been reported before [38,39,52], and is due to erroneous contributions of instantaneous frequencies to the result, especially for wide band Doppler signals (section 3.2.2). Smoothing of the estimation at the aliasing points is due to averaging successive estimations of the instantaneous frequency (Eq.(3.6)). The latter two disadvantages are not present in the performance of the complex autocorrelation detector. Both detectors are sensitive to a change of the shape of the area used in depth and time (Fig. 3.6 and table 3.2). When a short depth interval is used over many successive signals, the performance of the complex autocorrelation detector is similar to that of the correlation interpolation method. However, when using a large depth range, the performance deteriorates, because the required good correlation with the demodulation frequency deteriorates with increasing sig-

nal length. After all, wide band signals have short coherence lengths, and when the depth interval used for summation exceeds this length, the quality of correlation diminishes. This implies that for a given frequency characteristic of the signals only the corresponding summation length may be used. In practice, pulsed Doppler techniques are used over approximately 16 samples in depth, which is only possible when the bandwidth of the RF signal is small. With the correlation interpolation method the depth interval is not limited by such a correlation length (Fig. 3.6 and table 3.2).

The correlation interpolation method is based on estimating expected values of correlation products. According to the theory, the selection of the area in depth and time, where the individual products are obtained, is irrelevant as long as the signals may be considered ergodic (section 2.2). This irrelevancy is confirmed by the finding that changing the shape of the area of summation in depth and time hardly influences the performance of the correlation interpolation method (Fig. 3.6). So spatial resolution and time resolution can be exchanged freely.

The test signals used in the present study are obtained by bandfiltering of Gaussian noise. Mutual shift between successive signals is created by interpolation of the noise samples by use of Eq.(3.1) before filtering is performed. With this specific interpolation scheme the total power of the interpolated signal is independent of the applied signal shift. This in contrast to linear interpolation, for which it can be shown that the power of an interpolated signal is minimal at a signal shift of half the distance between two samples. Because in the latter case the properties of the test signal directly depend on the applied signal shift, linear interpolated signals are less suitable for the evaluation of the performance of the correlation interpolation technique.

In the present simulation a constant velocity of the reflecting tissue is assumed. Consequently, the Doppler signal produced by demodulation contains a single frequency component. In practice not all reflectors within the depth range of investigation will move at the same velocity. This will increase the standard deviation of the estimate of signal displacement.

Using the instantaneous frequency detector, analysis of N sampling events requires $0.25N$ moderately accurate arctangent operations. These operations can be performed quickly, even enabling real time processing of the echo signals received [38]. The complex autocorrelation detector is more complex. The number of multiplications is N , and therefore the method needs more computational effort. The correlation interpolation method is even more complex and requires $5N$ multiplications. Nevertheless, computational effort is still linear with the number of samples used, and unlike techniques based on finding the maximum correlation, iteration techniques are not needed. Calculation of the whole correlation function can be performed most efficiently using fast Fourier transformation, which requires many more computational operations.

3.5 Conclusions

The correlation interpolation method estimates the displacement between two or more bandlimited signals in succession. The method is quite insensitive to noise in the signal. The number of mathematical operations needed is linear with the number of sample points used for analysis. The width of the interval free of aliasing is one period of the mean frequency. Within this interval the method appears to be linear and accurate. The method can simultaneously average the signal contributions in depth and time. Increase of the depth averaging interval and decrease of the time averaging interval, while the number of points used remains constant, does not significantly influence the performance of the algorithm. The correlation interpolation method performs better than the instantaneous frequency detector and the complex autocorrelation detector, especially when the number of depth samples used is large and noise is significant.

Chapter 4

Experimental Evaluation of the Correlation Interpolation Technique

The contents of this chapter will be published in the article: *Experimental evaluation of the correlation interpolation technique to measure regional tissue velocity* by P.G.M. de Jong, T. Arts, A.P.G. Hoeks and R.S. Reneman, *Ultrasonic Imaging* (in press 1991).

4.1 Introduction

In the present chapter the correlation interpolation technique is evaluated experimentally by simulating moving cardiac tissue. For this purpose a disk, containing uniformly distributed scattering particles, is rotating around an axis. Echo signals along a single line of observation within the disk are obtained by a phased array 2DE imaging system. Different values of tissue velocity are simulated by varying the velocity of rotation of the disk. Principally, only the component of velocity along the line of observation can be measured (section 2.2). In the setup used, no gradient in this component of velocity is present along the line of observation.

Firstly, the performance of the estimation of tissue velocity is evaluated by processing the received high frequency echo signals (RF signals). The number of samples in depth and the number of RF signals in time used for calculation of velocity are varied independently. In this analysis the accuracy and linearity of the velocity estimation are evaluated. Secondly, the angular velocity of the disk is estimated by measuring the difference in velocity along two separate lines of observation within the disk. In all calculations, the velocity of ultrasound within the disk is assumed to be constant and equal to $1540 \text{ m}\cdot\text{s}^{-1}$.

In the present evaluation real echo signals obtained using an ultrasound imaging system are used for analysis. Note that the properties of these signals are different from those of the theoretical signals used in chapter 2 and the artificial echo signals used in chapter 3. Firstly, the frequency spectrum of the RF signals is not rectangular. The center frequency and bandwidth of the spectrum depend on the depth of investigation due to the frequency dependent absorption of ultrasound. Secondly, the ultrasonic beam has finite dimensions. Consequently, echo signals will be received from a sample volume with a certain width and length. Within this sample volume scatterers with different velocities may be present. So the resulting echo signal is a mixture of echos from particles with different velocity. This may cause an increase of the error in the velocity estimate.

4.2 Methods

4.2.1 Experimental setup

The RF signals were recorded with a 3.5 MHz phased array ultrasound imaging system (HP 77020) in an experimental setup as shown in figure 4.1. The ultrasonic beam of the system was approximately 2 mm wide. The duration of the ultrasonic pulse was $0.55 \mu\text{s}$ (appendix B). When using ultrasonic pulses with a center frequency of 3.5 MHz, this is associated with approximately 1.5 signal periods. In M-mode, maximally two M-lines could be positioned independently within the sector scan. Single lines were obtained at a rate of 930 signals per second. This rate

Figure 4.1: Block diagram of the experimental setup.

decreased to 465 signals per second when two lines are visualised simultaneously. The ultrasound machine was modified to obtain the RF signal along the M-line. The received RF signal was filtered analogously with a 4th order Butterworth lowpass filter (section B.1.3). Subsequently, the signal was fed into an interface containing static RAM memory which can store 0.5 MByte of 8-bit RF data on-line at a sampling rate of 11.4 MHz which is approximately 4 times the emission frequency. The number of samples in depth along an M-line could be chosen in powers of 2 ranging from 64 up to 8192, which is equivalent to a depth interval ranging from 4.4 mm to more than the length of an M-line. The number of successive echo signals to be stored is limited by total memory size divided by the depth range. For example, when the depth range is set at 1024 samples (equivalent to 69.2 mm of tissue), 512 successive echo signals can be stored. Using a signal rate of 930 Hz, recording time is 0.55 s. The stored data were transferred to a Torch TripleX computer system, which was used for off-line processing of the echo signals. The images produced by the imaging system could be plotted by use of a video printing device.

The phantom that scatters ultrasound is a cylindrical Agar disk. The disk was made by mixing 7.5 g Agar and 1.5 ml Sephadex G-200 powder (particle size 50 μm) in 150 ml hot water. After cooling, a soft disk of gel remained, 4 cm high and 6.5 cm in diameter. The disk was placed in water, and mounted to an axis, which was driven by a motor. Different tissue velocities were simulated by varying either the velocity of axial rotation or the distance between the M-line and the axis, or both. The number of disk rotations per second was measured by a counter circuit using a disk

Figure 4.2: Schematic representation of the cylindrical phantom and the positioning of the M-lines. R denotes the distance from transducer to the center of the disk, and r the distance from center to the region of interest. Angular velocity of the disk is denoted by ω . In experiments using two M-lines simultaneously, ϕ denotes the angle between the lines.

containing 16 holes, which was attached to the axis. The probe of the ultrasound scanner was also placed in water, scanning the disk perpendicular to the axis in the plane of the disk (Fig. 4.2). In appendix B the components of the experimental setup are described in more detail.

4.2.2 Experiments

In a first series, the line of observation was positioned at a perpendicular distance r from the center of the disk of 0, 10, 20 and 30 mm, respectively (line 1 in Fig. 4.2) at angular velocities of the disk of -4π through $+\pi$ in steps of $\pi \text{ rad}\cdot\text{s}^{-1}$ which is equivalent to -2.0 through 0.5 in steps of $0.5 \text{ revolutions}\cdot\text{s}^{-1}$. Next, rotation of the disk was measured by the use of two separate lines located on opposite sides of the center of the disk (lines 1 and 2 in Fig. 4.2) at several angular velocities (-1.0 , -2.0 and $-4.0 \text{ rad}\cdot\text{s}^{-1}$). Three different angles between the lines were used (0.13 , 0.26 and 0.52 rad). Asymmetrical line configurations around the center of the disk were used with angles of asymmetry of 0.05 , 0.11 and 0.21 rad . The angle of asymmetry is

defined as the angle between the bisectrix between both lines of observation and the line through the axis of rotation. In all experiments, the distance R between the transducer and the center of the disk (Fig. 4.2) was equal to 56 mm.

4.2.3 Data analysis

Before analysis the sampled signal has been bandpass filtered digitally with a 7-point template (1,0,-3,0,3,0,-1). This results in a filter with a center frequency of approximately 3 MHz and a bandwidth to center frequency ratio of approximately 1.

The correlation interpolation method provides an estimation $\hat{x}_{sp}$ of the displacement between two successive echo signals, expressed in units of depth sampling distance. In our setup, one depth sampling distance displacement between successive echo signals equals $67.5 \mu\text{m}$, being half the distance of propagation of ultrasound during a depth sampling interval ($0.5 \times 1540 \text{ m} \cdot \text{s}^{-1} / 11.4 \text{ MHz} = 67.5 \mu\text{m}$). For the current mean signal frequency (3.5 MHz) and depth sampling frequency (11.4 MHz), the borders of the aliasing-free range lie at approximately ± 1.6 sampling distances displacement, equivalent to $\pm 108 \mu\text{m}$. The estimated displacement between successive signals is directly related to velocity, because the time interval between two successive echo signals is known. The velocity component v along each line is calculated from the estimated displacement $\hat{x}_{sp}$ using:

$$v = \hat{x}_{sp} \frac{c \text{ PRF}}{2 f_s} \quad (4.1)$$

where f_s denotes the sampling frequency used along the depth axis and c the speed of sound. Using 2 symmetrically located echo lines simultaneously, the angular velocity $\hat{\omega}$ of the disk is estimated by:

$$\hat{\omega} = \frac{(v_1 - v_2)/2}{R \sin(\phi/2)} \quad (4.2)$$

where v_1 and v_2 denote the velocity components towards the transducer along M-line 1 and M-line 2, respectively. The parameter ϕ denotes the angle between the two lines of observation, and R denotes the distance between the transducer and the center of the disk.

4.3 Results

In figure 4.3 measured displacement between successive echo signals is plotted as a function of time for standstill and two different velocities of rotations of -1.0 and -2.0 revolutions $\cdot\text{s}^{-1}$ (-2π and $-4\pi \text{ rad} \cdot \text{s}^{-1}$). In this example, the distance between the echo line and the center of the disk was 20 mm. The region of interest was located at the minimum distance from latter center, and was chosen to be 2.2 mm in depth, which

Figure 4.3: Calculated displacement $\hat{x}_{sp}$ between successive signals versus time for 3 different angular velocities of the disk. The region of interest was located at 20 mm from the center of the disk. Averaging was performed over 32 samples in depth (2.2 mm) and 2 signals in time (1.1 ms). A displacement of 1 sampling distance between successive signals corresponds to a velocity of the phantom of $63 \text{ mm}\cdot\text{s}^{-1}$ (PRF=930 Hz).

is associated with 32 samples of the high frequency echo signal. When increasing the velocity of rotation, the measured displacement increased linearly, while the level of random fluctuations increased slightly.

In figure 4.4, for different lines of observation (located at 0, 10, 20 and 30 mm from the center of the disk), the calculated velocity is plotted as a function of the velocity of rotation, using the same size of the region of interest as in figure 4.3. For each line, linearity was better than ± 0.03 sampling distances per echo interval, which is associated with a standard deviation of $\pm 2 \mu\text{m}$ in displacement. The standard deviation of the noise, as shown in figure 4.4, appeared to be quite independent of the velocity of rotation or position of the line of observation, and was approximately equal to ± 0.09 sampling distances.

In figure 4.5a the estimated displacement between 2 successive echo signals is shown for the echo line located 20 mm from the center of the disk, at a velocity of rotation of $-3\pi \text{ rad}\cdot\text{s}^{-1}$. The depth range used for averaging was set at 8, 16 and 32 sampling intervals, equivalent to 0.55, 1.1 and 2.2 mm, respectively. An increase of the depth averaging range reduced the standard deviation of the estimated displacement. The latter standard deviation appeared to be reciprocal to $\sqrt{N}$, with N the number of samples used for analysis. A similar reduction can also be obtained by increasing the number of successive signals used for averaging (Fig. 4.5b). In table 4.1, mean values and standard deviations of the estimation of displacement are

Figure 4.4: Calculated displacement $\hat{x}_{sp}$ between successive echo signals versus angular velocity ω of the disk for several positions of the line of observation. Again averaging was performed over 32 samples in depth and 2 signals in time. A displacement of 1 sampling distance between successive signals corresponds to a velocity of the phantom of $63 \text{ mm}\cdot\text{s}^{-1}$ (PRF=930 Hz).

summarized for the different line positions and velocities of rotation. In table 4.2, mean values and standard deviations are shown for different averaging ranges in depth and time.

When performing the dual-line experiment, the velocity of rotation was calculated from the estimations of velocity along both lines by means of Eq.(4.2). In figure 4.6, mean values and the standard deviations of the calculated angular velocity are shown as a function of the angle between the lines, for several velocities of rotation. In this case, the lines were positioned symmetrically around the center of the disk. Calculated rotational velocity was not significantly dependent on the angle between the lines (Fig. 4.6). The standard deviation was found to decrease at larger angles. In a separate experiment at a velocity of rotation of $-1 \text{ rad}\cdot\text{s}^{-1}$, asymmetry was introduced to the M-line configuration. Mean and standard deviation were found to be relatively insensitive to the asymmetry introduced. In table 4.3, mean values and standard deviations of the estimated velocity of rotation are summarized for the dual-line experiments.

Figure 4.5: Calculated displacement $\hat{x}_{sp}$ between successive echo signals versus time for 3 different averaging ranges in depth over 2 successive signals (panel a) and for 3 different averaging ranges in time over 32 samples in depth (panel b). A displacement of 1 sampling distance between successive signals corresponds to a velocity of the phantom of $63 \text{ mm}\cdot\text{s}^{-1}$ (PRF=930 Hz).

4.4 Discussion

In the present study, the correlation interpolation method was evaluated using realistic echo signals obtained from an ultrasound imaging system. The echo signals were received from a rotating phantom containing ultrasound scattering particles.

Applying the algorithm to 32 samples in echo depth over 2 successive echo signals in time, the standard deviation of the estimate of echo displacement between successive signals was found to be approximately ± 0.09 sampling intervals (Fig. 4.3; tables 4.1 and 4.2), which is associated with a standard deviation in actual tissue displacement of $\pm 6.1 \mu\text{m}$. This is far more accurate than the method of Troy [90], where position and wall thickness were determined by analysis of Polaroid pictures taken from the M-mode image. 2DE image processing methods [49,56,57,84,88] have an accuracy in displacement in the order of $\pm 2 \text{ mm}$. The accuracy found with the correlation interpolation technique in this experimental study is of the same order as obtained by applying the technique to artificial test data at a signal to noise power ratio of 10 (chapter 3).

A good spatial resolution may be obtained by processing the RF signals directly, using a pulsed Doppler method [8,15,16,34,48,52,60,61,67] or a correlation technique [20,22,23,28,96]. Pulsed Doppler techniques are often applied to estimate blood flow velocity in vessels. Velocity is obtained by analysis of the RF signals over

Figure 4.6: Mean and standard deviation of the calculated angular velocity $\hat{\omega}$ versus the angle ϕ between the lines for 3 different angular velocities of the disk.

a few wavelengths in depth, and over several echo pulses in time. The accuracy of the Doppler frequency measurement can be improved by increasing the number of echo signals in time to be used for signal analysis, while in regular pulsed Doppler techniques averaging in depth is predefined by the bandwidth of the emitted ultrasonic pulse [70]. When using correlation techniques, generally two successive RF signals are analyzed. In principle, the depth range used for analysis is not limited. Thus, in general, correlation techniques have a high resolution in time, whereas the resolution in depth is relatively low. In many analysis systems based on correlation, the accuracy of the position in depth is limited by the discretization of the RF signal in depth, caused by sampling. Accurate determination of shift is associated with a high sampling frequency. However, an increase in sampling frequency requires more data storage capacity and an increased computational effort. Both the spatial resolution and the computational effort can be improved by modeling the top of the correlation function [23,28].

In the present study, we have used the correlation interpolation technique to calculate the shift between successive echo signals. Theoretically, in this method, several advantages of other methods are combined. The top of the correlation function is modeled by a cosine function. The number of samples used for analysis is quite low due to bandpass filtering along the depth coordinate before analysis. The noise suppressing capability is determined by the number of samples used for analysis, irrespective of the ratio of the number of samples used in depth to the number of echo signals used in time. In practice, however, enlarging the interval in depth and in time has to be done with care. Enlargement in depth is limited by gradients

Table 4.1: Mean and standard deviation of measured displacement, expressed in sampling interval size. Results are shown for 4 different distances r from the area of interest to the center of the disk. An averaging range of 32 samples in depth over 2 successive signals in time was used.

32×2 Rad·s ⁻¹	$r \approx 0$ mm		$r \approx 10$ mm		$r \approx 20$ mm		$r \approx 30$ mm	
	mean	SD	mean	SD	mean	SD	mean	SD
π	0.033	0.066	0.535	0.101	1.118	0.105	1.558	0.086
0	0.000	0.054	0.000	0.067	0.001	0.059	0.000	0.065
$-\pi$	-0.034	0.071	-0.543	0.100	-1.080	0.122	-1.620	0.090
-2π	-0.063	0.069	-1.183	0.110	-2.075	0.073	-3.123	0.107
-3π	-0.092	0.085	-1.746	0.091	-3.152	0.110	-4.616	0.114
-4π	-0.123	0.088	-2.251	0.091	-4.181	0.084	-6.169	0.104

in velocity within the sample volume. Similarly, the length of the time interval to be used for analysis is limited by the change of velocity in time. When using a small averaging range in depth, the accuracy of the correlation interpolation method is equal to that of the Doppler methods (chapter 3) [45,52]. However, for larger averaging ranges in depth, the performance of the Doppler methods deteriorates considerably, while the performance of the correlation interpolation method remains unchanged.

With the correlation interpolation technique displacement is estimated by determining the phase shift between successive signals. Due to noise, the estimation of shift may deteriorate. The standard deviation of phase per sample point approximates the ratio of noise and signal amplitude. For example, using a signal to noise power ratio of 10, this deviation is approximately 0.3 rad. By using 32 samples in depth, the standard error of the mean decreases by a factor of $\sqrt{32}$ to 0.05 rad. In the present setup, this phase shift is equivalent to 0.03 times the distance between successive samples in depth, or a displacement of 2 μm . The precision as obtained in the present study is in this range.

The cardiac wall is about 10 mm thick and it thickens by approximately 20% during the systolic phase (duration about 150 ms) [25,32,37,85]. This implies that the distance between two areas within the cardiac tissue, initially 4.4 mm apart (equivalent to 64 depth sampling intervals), will increase by approximately 0.88 mm due to the thickening. When 5 successive echo signals are used for analysis, the time averaging range is equal to 4.4 ms. In this time interval, the two areas will deviate from each other by approximately 26 μm . Due to the fact that the accuracy of the estimation of displacement improves with the square root of the number of samples used (Fig. 4.5, table 4.2), the standard deviation of the estimation will be approximately $\pm 3 \mu\text{m}$. With this accuracy, cardiac deformation can be measured

Table 4.2: Mean and standard deviation of measured displacement, expressed in sampling interval size. Results are shown for 4 different averaging ranges in depth and time, being 8×2 , 16×2 , 32×5 and 32×17 depth samples by successive signals. The distance from area of interest to center of the disk was 20 mm.

$r \approx 20$ mm	8×2		16×2		32×5		32×17	
Rad·s ⁻¹	mean	SD	mean	SD	mean	SD	mean	SD
π	1.124	0.166	1.120	0.133	1.119	0.043	1.120	0.027
0	0.000	0.035	0.001	0.061	0.000	0.016	0.000	0.004
$-\pi$	-1.083	0.199	-1.084	0.142	-1.082	0.046	-1.081	0.020
-2π	-2.074	0.085	-2.072	0.077	-2.073	0.029	-2.073	0.019
-3π	-3.155	0.200	-3.152	0.137	-3.152	0.054	-3.147	0.031
-4π	-4.181	0.133	-4.181	0.097	-4.179	0.053	-4.175	0.034

sufficiently accurate by means of the correlation interpolation method. The influence of motion perpendicular to the direction of the beam has not been investigated. According to the theoretical model, the influence should be minor if the size of the sampling volume in width and depth is large as compared to the fraction of the volume that is refreshed between two pulses due to motion. Generally, in the current setup this fraction is less than 10% when motion occurs with $100 \text{ mm} \cdot \text{s}^{-1}$, which is an upper limit of cardiac tissue velocity under most circumstances.

Generally, when using correlation techniques to follow echos in the 2DE or M-mode image [71,88,89], the phenomenon of speckle may interfere [65]. When mixing two (or more) signals each having a relatively narrow bandwidth around slightly different center frequencies, interference maxima and minima in amplitude are found to move along the line of observation. After envelope detection the maxima are seen as speckle. The correlation interpolation technique is quite insensitive to this phenomenon of interference because it determines the phase shift between RF signals directly. The maximum of interference may move considerable, while the phase shift remains practically unaffected. Despite the presence of considerable speckle in the image of the disk, the accuracy of the determination of velocity behaved according to the theoretical analysis.

In our setup, using echo signals with a center frequency of 3.5 MHz and a depth sampling frequency of 11.4 MHz, the measurement of displacement is theoretically free of aliasing in an interval of ± 1.6 sampling distances. In the experiments, aliasing was found to occur at ± 1.8 sampling distances, which is close to the theoretical prediction. The latter aliasing range is associated with a velocity of $114 \text{ mm} \cdot \text{s}^{-1}$ at a PRF of 930 Hz, or $57 \text{ mm} \cdot \text{s}^{-1}$ at a PRF of 465 Hz. Because in the real heart the maximum tissue velocity is in the order of $100 \text{ mm} \cdot \text{s}^{-1}$ [25,32,37], a tracking algorithm should be applied to avoid aliasing of the velocity estimation. With

Table 4.3: Mean and standard deviation of measured angular velocity $\hat{\omega}$ of the disk, expressed in $\text{rad}\cdot\text{s}^{-1}$. Three different velocities of rotation were used at 3 different angles ϕ between the two M-lines. At an angular velocity of $-1 \text{ rad}\cdot\text{s}^{-1}$, several angles of asymmetry $\Delta\phi$ were added to the angle between the lines. An averaging range of 32 samples in depth over 2 successive signals in time was used.

32×2		$\omega = -1 \text{ rad}\cdot\text{s}^{-1}$		$\omega = -2 \text{ rad}\cdot\text{s}^{-1}$		$\omega = -4 \text{ rad}\cdot\text{s}^{-1}$	
$\phi \text{ (rad)}$	$\Delta\phi \text{ (rad)}$	$\hat{\omega}$	SD	$\hat{\omega}$	SD	$\hat{\omega}$	SD
0.13	-	-1.01	0.57	-1.98	0.60	-4.15	0.74
	0.05	-0.94	0.61				
0.26	-	-0.96	0.32	-2.03	0.36	-4.29	0.42
	0.05	-0.91	0.28				
	0.11	-1.04	0.39				
0.52	-	-0.93	0.18	-2.12	0.28	-4.22	0.20
	0.05	-0.96	0.24				
	0.11	-0.96	0.29				
	0.21	-1.03	0.18				

such algorithm, two successive echo signals are mutually shifted in depth over a distance based on the previous estimation of velocity. As a result of this preshift, the displacement between the two signals is most probably within the aliasing-free range. After the shift between the signals has been calculated, the preshift used is added to the estimation in order to obtain the real displacement of the signals. The tracking algorithm used in the present study is discussed in detail in appendix A.

The relation between calculated and real displacement is linear for all M-line positions investigated (Fig. 4.4). This linearity was also found in the theoretical analysis (chapter 3) and proved to be independent of the averaging ranges used in depth or in time. Because tracking was performed in all calculations, linearity exceeds the boundaries of the aliasing interval. Without tracking, clipping induced by aliasing would appear at a calculated displacement of ± 1.8 sampling distances.

In the second series of experiments, the velocity of rotation of the disk was estimated from two simultaneous velocity measurements on opposite sides of the center of rotation. The estimation of angular velocity appeared to be quite insensitive to the angle between the two lines of observation. The standard deviation decreased with increasing angle (Fig. 4.6, table 4.3). The standard deviation of the calculated angular velocity is larger at small angles because then the subtraction of velocity components in the nominator of Eq.(4.2) becomes inaccurate. The estimation of angular velocity was found not to be significantly affected when the two lines were positioned asymmetrically around the center of the disk. As a result, knowledge

of the exact position of the center of rotation is not necessarily needed. In future investigations this determination of angular velocity may be used to estimate the rotation or torsion of the heart. In the experiments, the angular velocity of the disk was approximately $-1 \text{ rad}\cdot\text{s}^{-1}$, which is in the physiological range for the rotation of the various cross-sections of the heart [2,36].

In the present study, real RF signals from a finite sample volume along the ultrasonic beam are processed to measure velocity. As mentioned in section 4.1, the properties of such a real echo signal are different from those of the artificial signals used in chapter 3. Firstly, the center frequency and bandwidth of the echo signals are a function of depth due to the frequency dependent absorption of the ultrasound by the tissue. Secondly, echo signals are received from a sample volume in depth containing regions with different velocities. The related echo signals will be shifted by different distances, causing a deterioration of the correlation. Furthermore, a gradient of tissue velocity may be present within the volume. Due to these factors the signals may not be ergodic, as assumed in the correlation interpolation technique (section 2.2). Consequently, the deviation of the velocity estimate may exceed the levels found in the theoretical analysis of the technique as described in chapter 3. Note that the influence of latter phenomena highly depends on the actual size of the sample volume, the absorption of the ultrasound and the velocity distribution of the reflecting particles. In the present study, echo signals are received from a small tissue region, located at a fixed distance from the transducer. Along the line of observation, no gradient of velocity is present. Consequently, the latter factors are probably of minor importance when calculating the velocity of the rotating disk.

4.5 Conclusions

A rotating Agar disk with ultrasound scattering particles was used as a phantom of moving tissue. Echo signals along a line through the disk were recorded by means of a phased-array ultrasound imaging system. When applying the correlation interpolation algorithm to 32 data samples in echo depth, the displacement between successive echo signals could be determined with a standard deviation of ± 0.09 sampling intervals. The standard deviation decreased with increasing number of data points used for analysis. Extension of the number of data points can be performed in depth, in time or both. The measurement of the displacement was linear within ± 0.03 sampling interval. The accuracy of displacement estimation was found to be sufficient to determine wall thickening in the heart. The velocity of rotation of the disk was determined by measuring simultaneously the difference in velocity in two regions on separate lines. The exact position of both regions with respect to the center of rotation was found to be irrelevant.

Chapter 5

Myocardial Wall Thickening and Left Ventricular Cavity Diameter in the Dog

The contents of this chapter will be published in the article: *Measurement of myocardial wall thickening and diameter changes in the dog using correlation interpolation of ultrasonic echo signals* by P.G.M. de Jong, T. Arts, E.C. Cheriex and R.S. Reneman (in preparation 1991).

5.1 Introduction

The volume of the left ventricular cavity decreases during the ejection phase of the heart. Because the volume of the left ventricular wall remains virtually constant, the wall thickens during this phase of the cardiac cycle. In several studies wall thickening was found to be decreased considerably in regions of poor contracting myocardium, for instance, due to ischemia [32,37]. Consequently, quantitative information about regional myocardial function may be obtained by assessing wall thickening in the region of interest. For this purpose, several invasive as well as non-invasive techniques have been developed to measure deformation of the cardiac wall.

Feigl and Fry [25] designed a mechanical force transducer with strain gauges, which was positioned directly on the left ventricular free wall. Due to changes in wall thickness, the transducer was deformed, causing the strain gauges to be lengthened or shortened. Consequently, changes in the electrical impedance of the gauges were related to thickening of the cardiac wall. Using this technique, wall thickening during the systolic phase was found to be approximately 20%.

Wall thickening has also been determined with the use of two ultrasonic crystals, positioned oppositely at the endocardial and epicardial surface of the wall [32,33, 68,75,83,85]. This method relies on the principle that when an ultrasonic pulse is transmitted, the measured transit-time of the pulse is proportional to the distance between the crystals. Hartley *et al.* [37] developed a technique to measure the radial strain associated with cardiac wall thickening. Using a single crystal at the epicardial surface, the velocity of the myocardial tissue at a selected depth was measured by means of a pulsed Doppler technique. By integrating tissue velocity over time an estimation of tissue displacement through the depth range of investigation could be obtained. Hartley showed that this estimation of displacement is related to the amount of cardiac wall thickening. With these techniques using ultrasonic crystals, myocardial thickening was found to range from 5 to 30%.

In the open chest preparation, Myers *et al.* [66] imaged the cardiac wall using M-mode echocardiography (section 1.2.2). Within the image, the epicardial and endocardial borderlines of the left ventricular wall were detected. The thickness of the wall was estimated by measuring the distance between both borderlines. By analyzing a sequence of images, recorded during the cardiac cycle, thickening of the wall was determined as a function of time. Lieberman *et al.* [54] applied two-dimensional echocardiography (2DE, section 1.2.2) directly on the epicardium of the left ventricle. In the 2DE images of the heart, the endocardial and epicardial contours were detected, and wall thickening was determined over a sequence of images as the distance between both boundaries. In both studies thickening of the cardiac wall was found to be approximately 30%.

With the techniques described above, thoracotomy is required to assess myocardial deformation. Several techniques have been developed to measure cardiac tissue deformation by means of transcutaneous echocardiography. Troy *et al.* [90] determined wall thickness in the human heart by measuring the distance between the epicardial and endocardial boundary in a Polaroid recording of an M-mode image of the cardiac wall. Feneley *et al.* [26] determined left ventricular wall thickening transcutaneously from 2DE images as well as from M-mode images of the human heart. For this purpose, the myocardial boundaries within the image were detected and the distance between both boundaries was measured. In these studies wall thickening was found to range from 40 to 67%.

In general, in echocardiographic imaging the spatial resolution is limited. The 2DE as well as the M-mode images are formed by rectifying the received high frequency echo signal (RF signal) and presenting its envelope on the screen by brightness coding. Inherently, envelope detection discards phase information of the echo signal, causing a low resolution of the echo image. This resolution is in the order of a few wavelengths of the transmitted ultrasound signal, which is equivalent to approximately 1 mm in depth. Consequently, the determination of cardiac tissue deformation on the basis of such images will have a maximal accuracy in the same order.

The spatial resolution of the estimation of tissue deformation can be improved by processing the high frequency echo signals directly. Successive RF signals are received at discrete moments in time, associated with the transmission of successive ultrasonic pulses. When the tissue under investigation is displaced between two pulse transmissions, successively received echo signals are shifted in depth. The shift between two echos is directly related to the displacement of the tissue, and can be calculated by determining the position of the top of the crosscorrelation function of successive signals [20,50,96]. In the simplest approach, the crosscorrelation function is calculated by performing a convolution on two echo signals. Then the function is obtained at discrete points, separated by intervals determined by the depth sampling frequency. The maximum of the function is likely to fall between two samples, causing the accuracy of the location of the top of the function to be limited to the sampling interval. A relatively long part of the echo signal, received from a tissue region of several millimeters, has to be used to obtain an accurate estimation of the samples of the correlation function [69]. For long signals, the crosscorrelation function may be calculated more efficiently by fast Fourier transformation of the signals, followed by multiplication of the spectra in the frequency domain and inverse Fourier transformation. Using this technique, the shift between the signals can be estimated at subsampling accuracy. Eventhough the method is more efficient and accurate than a simple convolution, the computational effort is quite high due to the Fourier transformations used.

In this thesis the correlation interpolation technique has been described. With this technique the top of the crosscorrelation function of successive echo signals is determined by interpolation of only five samples of the latter function. In a theoretical and experimental evaluation the method was found to determine velocity rather accurately (chapters 3 and 4) [45,47]. In the present chapter, the results are described of some experiments to investigate whether the correlation interpolation method can also be applied successfully in the beating canine heart to measure regional cardiac tissue velocity. For this purpose, in 7 experiments a cross-section of the left ventricle was imaged transcutaneously with the use of a 2DE imaging system. Ultrasonic echo signals were obtained along a single line of observation within the image. The component of regional tissue velocity along the line of observation was estimated by processing the echo signals with the correlation interpolation algorithm. Strain in the anterior and posterior wall as well as ventricular cavity diameter were estimated from the obtained estimates of regional tissue velocity. The relation between cavity diameter and strain was determined during the systolic phase. To evaluate the sensitivity of the technique with respect to changes in cardiac deformation, the experimental protocol was repeated after myocardial performance was depressed by an intravenous administration of imipramine [55,76].

5.2 Methods

5.2.1 Experimental setup

Experiments were performed on 7 mongrel dogs with a mean weight of 27 kg. The animals were premedicated with a solution containing 10 mg oxycodone HCl, 1 mg acepromazine and 0.5 mg atropinesulphate per ml ($0.2 \text{ mg}\cdot\text{kg}^{-1}$ intramuscularly). Anesthesia was induced by intravenous administration of sodium pentobarbital (Narcovet, $10 \text{ mg}\cdot\text{kg}^{-1}$). Following endotracheal intubation, anesthesia was maintained with oxygen/nitrous oxide and 0.5% fluothane. The lungs were ventilated with a positive pressure respirator (Pulmomat). The ECG was derived from limb leads.

The canine heart was imaged with a 3.5 MHz phased array ultrasound imaging system (HP 77020) in a setup as shown in figure 5.1. The animal was placed on its left side. A right parasternal approach of the heart was used, yielding a classical short-axis view of the left ventricle. Ultrasonic pulses were transmitted along a single line of observation within the 2DE image at a PRF of 930 or 465 Hz. The RF signal, received along this line, was filtered, sampled and stored in a digital memory (appendix B). The data collection protocol was started at the rising slope of the R-wave of the electrocardiogram (ECG). After data storage in the digital memory was completed, its contents were transferred to a Torch TripleX computer system and stored on disk. Using the described protocol, several measurements

Figure 5.1: Block diagram of the experimental setup.

were recorded and echo data were stored. After completion of the experiment, the stored data were processed off-line. During the experiment, the ECG signal was continuously recorded on a physiological recorder, while hard copies of the 2DE or M-mode images were made on a video printer.

5.2.2 Experiments

A short-axis cross-section at the mid-papillary level of the left ventricle was imaged using the 2DE imaging system. Within the image of the heart, a single line of observation was positioned through the left ventricular cavity. Along this line, echo signals from both the anterior and posterior wall were received. Two different types of recordings were made. Firstly, the echo signals from the anterior and posterior cardiac wall were recorded separately. For this purpose, a depth range of 34.6 mm (512 samples) was stored using a PRF of 930 Hz. Secondly, the echo signals of both the anterior and the posterior wall were recorded simultaneously. In this case, echo signals from a depth range of 69.2 mm (1024 samples) were recorded using a PRF of 465 Hz. Both settings yielded a total recording time of 1.1 s.

After the first series of measurements in the control situation, imipramine was administered intravenously ($7.5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$) [55,76]. Infusion of imipramine results in a reproducible model of a reversible heart failure in the dog [55]. After a stabilization period of 15 minutes, the above mentioned measuring protocol was repeated.

5.2.3 Data analysis

During off-line analysis, the stored RF signals were processed with the correlation interpolation algorithm. First, correlation products were calculated in successive areas containing 16 samples in depth (1.1 mm) over 3 successive signals in time. Subsequently, the resulting products of two adjacent areas in depth were added for each calculation of tissue velocity. So, tissue velocity was obtained in areas of 2.2 mm in depth, having an overlap in depth of 50% with adjacent areas on both sides. To avoid aliasing in the estimation of tissue velocity, a tracking algorithm was used in addition to the correlation interpolation technique (appendix A).

Using the analysis as described, tissue velocity is calculated as a function of time in successive depth gates, which are located at fixed positions along the line of observation. In time, samples of the velocity estimation in each depth gate are obtained at intervals of twice the time interval between two pulse transmissions. However, during cardiac contraction the tissue is moving. As a result, a specific part of the tissue may move through several successive gates in depth. The position of a specific point within the moving tissue may be followed in depth on the basis of the estimated value of tissue velocity. Assume the point to be followed to be initially located within the i -th depth gate. Then its estimated position $\tilde{x}_i$ with respect to the transducer can be calculated as a function of discrete time t using:

$$\tilde{x}_i(t) = x_i(0) + \sum_{k=0}^{t-1} v(\tilde{x}_i(kT), kT) \times T \quad (5.1)$$

Here $x_i(0)$ denotes the initial position of the point of interest, $v(\tilde{x}_i(t), t)$ the estimation of tissue velocity at time t and position $\tilde{x}_i(t)$ and T the sampling interval in time. When performing the summation in Eq.(5.1), each new estimated position $\tilde{x}_i(kT)$ is likely to fall between two successive positions in depth for which tissue velocity has been estimated. In this case, the velocity of the tissue in between both depth positions is estimated by interpolation of the corresponding estimations of tissue velocity. The position as calculated by Eq.(5.1) is reset at the beginning of each cardiac cycle. For this purpose, the cardiac cycle time is estimated from the physiological recordings of the ECG signal.

Natural strain ϵ_r in both walls is estimated as a function of time by calculating the distance between two separate points within each wall using:

$$\epsilon_r(t) = \ln\left(\frac{\tilde{x}_i(t) - \tilde{x}_j(t)}{x_i(0) - x_j(0)}\right) \quad (5.2)$$

Here $\tilde{x}_i(t)$ and $\tilde{x}_j(t)$ denote the estimated position of two points within the same wall, initially located in depth gate i and j , respectively, at time t . The initial position of both points is denoted by $x_i(0)$ and $x_j(0)$. The diameter D_{mw} of the left ventricular cavity is estimated as a function of time by calculating the distance

between two points in the midwall region of both the anterior and the posterior wall of the left ventricle using:

$$D_{mw}(t) = \tilde{x}_{pmw}(t) - \tilde{x}_{amw}(t) \quad (5.3)$$

where $\tilde{x}_{amw}(t)$ and $\tilde{x}_{pmw}(t)$ denote the estimated position of two points, located in the midwall region of the anterior and posterior wall, respectively, at time t . The moment that the cavity diameter starts to decrease due to the ejection of blood is defined as the beginning of the ejection phase. According to Arts *et al.* [2], this moment occurs approximately 70 ms after the occurrence of the R-wave in the ECG. Physically, the moment that the outflow of blood from the cavity stops denotes the end of the ejection phase. Therefore, in the present study the moment that the cavity diameter does not decrease anymore is defined as the end of the ejection phase.

A mathematical model of the dynamic geometry of the intact left ventricle has been described by Dumesnil *et al.* [21]. In this model the relation between cavity diameter D_{mw} between midwall positions in opposite walls and the thickness WT of the wall is expressed as:

$$WT = C D_{mw}^{-b} \quad (5.4)$$

where C is constant. In this model, a value of b equal to 1 denotes a cylindrically symmetric deformation with only radial tissue displacement [21]. In a spherical geometry the value of b becomes equal to 2. If changes in cardiac diameter are relatively small, as compared to the mean diameter, the expression in Eq.(5.4) may be approximated by a linear relationship in the vicinity of the mean value [85,92]. In the present study, strain is estimated instead of absolute thickness of the cardiac wall. Strain is associated with regional wall thickening. Therefore, in the present study the relationship between relative cavity diameter and strain is determined. The parameter b of the relation was calculated over the time interval associated with the ejection phase.

5.3 Results

An example of the calculated cardiac tissue velocity as a function of time in the dog is shown in figure 5.2. Tissue velocity is plotted for 63 successive regions in depth in a total tissue range of 69.2 mm. A positive tissue velocity denotes tissue movement towards the transducer. In the figure, the estimated position of the anterior and posterior wall as well as of the left ventricular cavity are indicated. Within both walls, the velocity curves are clearly distinguishable and neighbouring curves are quite similar as far as their shape is concerned. In contrast, no clear pattern can be recognized in the curves obtained by velocity calculation within the left ventricular

Figure 5.2: Calculated tissue velocity as a function of time for several positions in echo depth along a line of observation through the left ventricle. The estimated location of the anterior and posterior wall and the ventricular cavity is indicated. In this example, the heart rate of the dog was 114 min^{-1} .

cavity. The velocity curves of tissue regions within both walls appear to be periodic with the cardiac cycle. In this single measurement, cardiac tissue velocity was found to range from -180 to $+60 \text{ mm}\cdot\text{s}^{-1}$.

With the use of Eq.(5.1), the position of several points within the cardiac wall was followed in time. In figure 5.3 the distance to the transducer of several successive points within the anterior wall (panel a) and the posterior wall (panel b) is plotted as a function of time. The points were initially located in the center of successive depth gates, 1.1 mm apart. The solid vertical lines in the figure denote the beginning of a new cardiac cycle as marked by the R-wave of the ECG. At these time instants the calculated position was reset. The estimated moments of the beginning (BE) and the end of the ejection phase (EE) are marked by broken vertical lines.

The estimation of strain as a function of time for the anterior and posterior wall is shown in figure 5.4. The outmost curves in figure 5.3a and 5.3b were used for calculation. Strain appears to increase considerably during the ejection phase, reaching its maximum close to the moment of the end of this phase.

The upper curve in figure 5.5a denotes the left ventricular cavity diameter D_{mw} , relative to its initial value $D_{mw}(0)$ at the beginning of each cardiac cycle. The mid-wall regions in the anterior and posterior wall, which were used for calculation of the cavity diameter, are marked with an asterix (*) in figure 5.3a and 5.3b, respectively. The lower curve in the panel denotes the rate of decrease of the relative cavity diameter, as shown in the upper curve. During the ejection phase (between the broken

Figure 5.3: Calculated distance $\bar{x}_i$ to the transducer of several points within the anterior wall (panel a) and the posterior wall (panel b) as a function of time. The solid vertical lines denote the moment of occurrence of the R-wave of the ECG, at which the estimations were reset. The broken vertical lines denote the estimated moments of the beginning and the end of the ejection phase (BE and EE, respectively).

vertical lines), the rate of diameter decrease rapidly increases to a maximum value. Subsequently, the rate decreases slowly to zero. Consequently, during this phase the shape of the lower curve is similar to an aortic flow curve, as generally reported in physiological experiments [3,6]. In figure 5.5b the strain in the anterior and the posterior wall during the systolic phase is shown as a function of the estimated left ventricular cavity diameter. For this figure, the data from figure 5.4 and 5.5a were used for calculation. The relation is plotted for two successive heart beats.

In a second series of measurements, the performance of the heart was depressed by intravenous administration of imipramine. In figure 5.6 strain in the anterior and posterior wall is shown as a function of time. The measurements were performed in the same animal, of which the results in the control situation are shown in the figures 5.2 to 5.5. The increase of strain during the ejection phase (between the broken vertical lines) appears to be decreased with respect to the measurement under control conditions (Fig. 5.4). In figure 5.7a the relative cavity diameter and the rate of diameter decrease are shown as a function of time during infusion of imipramine. Cavity diameter change appears to be decreased with respect to the control situation. In figure 5.7b the corresponding relation between strain and cavity diameter during the ejection phase is plotted.

Figure 5.4: Strain ϵ_r in the anterior (panel a) and posterior left ventricular wall (panel b) under control conditions. Strain was calculated using the outer position curves in figure 5.3. The solid vertical lines denote the beginning of a new cardiac cycle. The broken vertical lines denote the estimated moments of the beginning (BE) and the end (EE) of the ejection phase.

In table 5.1 the results on strain and ventricular diameter, as obtained in all experiments, are summarized. The values are expressed as mean values $\pm$ standard deviations. The parameter n denotes the number of measurements used for statistical analysis.

5.4 Discussion

In the present study, the correlation interpolation technique has been used to measure regional cardiac tissue velocity in the canine heart. Parameters of cardiac deformation, as strain and cavity diameter change, were estimated during the ejection phase from the estimated velocities. Measurements were performed under control conditions and during the administration of imipramine, which depresses the performance of the heart.

In the present study, strain is defined as the relative thickening in time of a tissue region, located within the cardiac wall. For this purpose, the distance between two separate points within the tissue was calculated. The mean increase of strain during the ejection phase was found to range from 0.14 to 0.20, which is in good agreement with the results obtained in studies using ultrasonic crystals on the myocardial surfaces [32,33,37,75,85]. In several other investigations, cardiac wall thickness was determined by measuring the distance between epicardial and endocardial border-

Figure 5.5: Panel a: Measured relative cavity diameter $D_{mw}/D_{mw}(0)$ (upper curve) and its derivative (lower curve, arbitrary units) as a function of time. The solid vertical lines denote the moment of occurrence of the R-wave of the ECG, at which the estimation was reset. BE and EE denote the estimated moments of the beginning and the end of the ejection phase, respectively. Panel b: Strain versus relative cavity diameter for the anterior wall (●) and the posterior wall (▲) during the systolic phase of two successive cardiac cycles (— denotes the first beat, - - - the second beat).

lines within the 2DE or M-mode image of the heart [26,54,66,90]. In these studies, strain in the wall is reported to range from 0.41 to 0.59, which is significantly more than the values obtained by means of crystals on the myocardium or those obtained in the present study. Feneley *et al.* [26] explained this overestimation by the following fact. At the endocardium a subendocardial layer of trabeculae is present. This layer consists of several thin layers of tissue and is hardly visible in a 2DE image. At the end of the systolic phase the diameter of the ventricle is decreased. As a result, the subendocardial tissue layer is compressed and becomes a solid layer at the endocardial surface. Now this layer may become clearly visible in the echo image and may erroneously be recognized as a boundary of the massive layers of myocardial tissue. Consequently, cardiac wall thickness, as determined with myocardial borderline detection, may yield an overestimation of the end-systolic wall thickening. Because in the present study the distance between two points within the wall is determined as a function of time, no overestimation of strain due to borderline detection will occur. The mean value of cavity diameter decrease during the ejection phase was found to be approximately 12%, which is in accordance with the results of other investigations [75,85,92].

Figure 5.6: Strain ϵ_r in the anterior (panel a) and posterior left ventricular wall (panel b) during administration of imipramine. The solid vertical lines denote the beginning of a new cardiac cycle. The broken vertical lines denote the estimated moments of the beginning (BE) and the end (EE) of the ejection phase.

Intravenous administration of imipramine was used to depress the performance of the myocardial tissue [76]. Infusion results in a reversible failing heart [55]. Due to the low cardiac performance, strain and cavity diameter change during the ejection phase of the heart are expected to be decreased. In the example shown, the increase of strain during the ejection phase decreased from approximately 0.18 and 0.19 to approximately 0.16 and 0.07 for the anterior and posterior wall, respectively. Summarized for all measurements performed, mean strain and cavity diameter decrease were both found to decrease during administration of the drug. Consequently, the correlation interpolation technique appears to be accurate enough to detect changes in myocardial performance.

Sasayama *et al.* [85] and Vignon *et al.* [92] reported a linear relationship between the left ventricular cavity diameter and cardiac wall thickness during the ejection phase. In the present study, a similar relation between cavity diameter and strain was found. In this evaluation, a mathematical model of the geometry of the left ventricle, as described by Dumesnil *et al.* [21] was used. In this model, the ventricle is represented by a thick-walled ellipsoid. Dumesnil showed that the thickness of the cardiac wall is proportional to the cavity diameter D_{mw} , raised to the power $-b$. In the present study, under control conditions the mean value of the parameter b was found to be 1.63 for the anterior and 1.71 for the posterior wall. During the

Figure 5.7: Results during infusion of imipramine. Panel a: Measured relative cavity diameter $D_{mw}/D_{mw}(0)$ (upper curve) and its derivative (lower curve, arbitrary units) as a function of time. The solid vertical lines denote the moment of occurrence of the R-wave of the ECG, at which the estimation was reset. BE and EE denote the estimated moments of the beginning and the end of the ejection phase, respectively. Panel b: Strain versus relative cavity diameter for the anterior wall ($\bullet$) and the posterior wall ($\blacktriangle$) during the systolic phase of two successive cardiac cycles (— denotes the first beat, - - - the second beat).

administration of imipramine, the parameter b was found to be slightly increased, especially for the posterior wall (table 5.1). In the present setup the estimation of b yields no clear indication for the actual performance of the myocardial tissue.

With the correlation interpolation technique tissue velocity is estimated in several gates, located at fixed distances from the transducer. However, during the cardiac cycle the myocardial tissue is moving with respect to the transducer. To follow a specific point within the tissue in time, its position has been calculated by means of Eq.(5.1). The accuracy of this estimate is related to the accuracy of the estimation of tissue velocity. According to signal analysis, the variance of a sum of stochastic independent variables equals the sum of variances of each variable [69]. Consequently, the standard deviation of the position estimate equals $\sqrt{N}$ times the standard deviation of the tissue displacement estimate, where N denotes the number of summations performed. Using correlation interpolation, tissue velocity is estimated with a standard deviation of approximately $\pm 5 \text{ mm}\cdot\text{s}^{-1}$ (chapter 3) [45]. As a result, in an interval of 2.2 ms, tissue displacement is determined with an accuracy of approximately $11 \mu\text{m}$. Using approximately 256 summations per cardiac cycle, this yields a standard deviation of the position estimate of approximately

Table 5.1: Mean values and standard deviations of measurements in seven dogs under control situations and during administration of imipramine. $\Delta\epsilon_r$ denotes the increase of strain during the ejection phase. The parameter n denotes the number of estimations used for statistical calculation.

	Control			Imipramine		
	mean	SD	n	mean	SD	n
$\Delta\epsilon_r$ Anterior Wall	0.15	0.08	36	0.14	0.08	33
$\Delta\epsilon_r$ Posterior Wall	0.20	0.08	25	0.14	0.06	25
Strain Ratio Ant/Post	0.9	0.4	10	1.2	0.5	13
Cavity Diameter Decrease [%]	13.5	3.5	18	10.9	3.6	15
b value Anterior Wall	1.63	0.44	8	1.76	0.49	12
b value Posterior Wall	1.46	0.33	8	1.99	0.55	11
Heart rate [min^{-1}]	146.8	32.6	24	128.4	23.0	24

$\pm 176 \mu\text{m}$. With respect to the amount of tissue displacement measured within the myocardial tissue of 2 to 5 mm (Fig.5.3), the relative accuracy is better than 9%.

During the ejection phase, the decrease of the cavity diameter of the ventricle (Fig. 5.5a, lower curve) was found to be similar to the shape of a normal aortic flow curve. This phenomenon may be explained as follows. During the ejection phase blood is pumped out of the ventricle. The volume of expelled blood is equal to the volume decrease of the left ventricular cavity. The latter cavity volume is closely related to the diameter of the cavity. As a result, changes in ventricular cavity diameter are directly related to changes in cavity volume, and thus to aortic blood flow. Note that this similarity only exists during the ejection phase of the heart. In the diastolic phase, the ventricular cavity is filled with blood from the left atrium. In this phase, cavity diameter changes are associated with the volume increase due to filling, and not to aortic flow. In the isovolumic contraction phase, which precedes the ejection phase, the geometry of the left ventricle changes without a change of cavity volume. As a result, cavity diameter may change, although the cavity volume remains constant.

The size of the digital memory, as used for the instantaneous storage of echo signals, is limited. Consequently, the setting for the depth range directly limits the total number of successive echo signals to be stored. In the present study, echo signals were stored over a depth range of 34.6 or 69.2 mm of tissue. In both cases, total recording time was 1.1 s, which was achieved by choosing a PRF of 930 or 465 Hz, respectively. In the experiments, mean cardiac cycle time of the canine heart was approximately 550 ms. So echo signals could be stored over approximately two complete cardiac cycles. In the human heart the dimensions of the ventricle are larger and the cardiac cycle time is longer as compared to the canine heart.

Consequently, the size of the memory may turn out to be insufficient to store echo signals from a specific region of interest in the human heart over a complete cardiac cycle.

When determining the mutual shift between two sinusoidal signals, a shift of more than half the length of the signal period can not be detected unambiguously. Using ultrasonic pulses with a center frequency of 3.5 MHz, this maximal signal shift is associated with a tissue displacement of 110 μm . Erroneous estimation of tissue displacement yields aliasing of the estimation of tissue velocity. The value of tissue velocity above which aliasing occurs depends on the center frequency of the ultrasonic pulses and on the time interval between successive echo signals, which is related to the PRF used. Using a PRF of 930 Hz in the present setup, the maximum detectable tissue velocity is equal to 102.3 $\text{mm}\cdot\text{s}^{-1}$. This value is reduced to 51.1 $\text{mm}\cdot\text{s}^{-1}$ when the PRF is decreased to 465 Hz. In the real myocardium the maximum instantaneous tissue velocity may be in the order of 100 $\text{mm}\cdot\text{s}^{-1}$ [25,32,37]. To avoid aliasing of the estimation of cardiac tissue velocity, a tracking algorithm was used in addition to the correlation interpolation technique (appendix A). With the tracking algorithm, successive echo signals are preshifted in depth with respect to each other before processing. By shifting the signals the mutual shift is maintained as small as possible. The applied preshift is based on the previous estimation of signal shift. By the use of tracking, the chance of erroneous determination of signal shift is minimized.

It should be noted that using the correlation interpolation technique on ultrasonic echo signals, only the component of tissue velocity along the line of observation is measured. Motion of the tissue perpendicular to the ultrasonic beam can principally not be detected with echography. Consequently, cardiac tissue displacement, as determined on the basis of the velocity estimation, only reflects the component of displacement along the echo line. Furthermore, in the present study real RF signals from a finite sample volume along the ultrasonic beam are processed to measure cardiac tissue velocity. The properties of these real echo signals are different from those of the artificial signals as used in the theoretical analysis of the technique (chapter 3). Firstly, the center frequency and bandwidth of the echo signals are a function of depth due to the frequency dependent absorption of the ultrasound by the tissue. Secondly, echo signals are received from a sample volume in depth containing several scattering particles in different regions. When separate particles within the sample volume move with different velocities, echo signals with different amounts of echo shift may be mixed up. Finally, a component of tissue velocity, perpendicular to the ultrasonic beam, may be present, which causes the tissue to move through the beam. This makes it principally impossible to follow a specific point within the tissue in depth during a complete cardiac cycle. As a result of these three factors, the

signals may not be ergodic, as assumed in the correlation interpolation technique (section 2.2). Consequently, the deviation of the estimate of cardiac tissue velocity, as obtained in the present study, may exceed the levels found in the theoretical analysis of the technique.

5.5 Conclusions

In the present study, the correlation interpolation technique has been used to estimate cardiac tissue velocity in separate regions within the canine myocardium. Strain in the left ventricular wall and cavity diameter changes during the cardiac cycle could be estimated without the need to follow myocardial borderlines or anatomical structures within the myocardial tissue. Both estimations were found to be in a range frequently reported in investigations using ultrasonic crystals on the myocardial surface. Depressing cardiac performance by the administration of imipramine yielded a decrease of mean strain and cavity diameter change during the ejection phase. From the present study it is concluded that the correlation interpolation technique can be applied to estimate several parameters of myocardial deformation in the real heart using transcutaneous echocardiography.

Chapter 6

Measurement of Cardiac Rotation in the Dog

6.1 Introduction

During the cardiac cycle the geometry of the heart changes [1,5,10,14,42]. This cardiac deformation is related to the pump function of the heart. The ejection of blood is established by a volume decrease of the cardiac cavities during the contraction phase. The decrease in cavity diameter causes the thickness of the cardiac wall to increase due to the incompressibility of the myocardial tissue. When cardiac contraction is performed without a simultaneous torsional motion of the heart, the fibers in the inner layers of the myocardial wall would shorten more than the fibers in the outer layers. In the real situation, a homogeneous distribution of fiber shortening across the cardiac wall is maintained by torsional motion of the heart [2,5,14]. In model studies as well as in experiments, it was found that this cardiac torsion is affected considerably when the performance is poor in part of the myocardium [6,11,36,93]. Consequently, the torsion of the heart may indicate whether a poor performing area is present in the myocardial tissue.

In literature two different definitions are used for ventricular torsion. According to one definition, torsion is an axial gradient of rotation of the heart, expressed in $\text{rad}\cdot\text{m}^{-1}$. This gradient may be determined by measuring the difference in angular rotation of the myocardial tissue at two separate levels between base and apex, and dividing this by the distance between the levels. In a second definition, the shear angle of the outer surface of the ventricle is determined, which is directly related to ventricular torsion [5]. The amount of shear is expressed in rad. In many investigations cardiac rotation at a particular level between base and apex is measured instead of ventricular torsion. This angle of rotation, expressed in rad, is determined with respect to the initial position of the tissue under investigation, or with respect to a specific point of reference within the heart, such as the base. From the latter measurement no distinction can be made between rigid body rotation and torsional deformation.

Several techniques have been used to measure cardiac rotation and torsion. Using cardiac surgery, markers were implanted in the myocardial tissue in the dog [93] and in man [36,44]. The rotation of the myocardial tissue was measured by following the markers during the cardiac cycle with a biplane cineradiography technique. In these studies, the rotation of the apex with respect to the base was found to range from 0.31 to 0.52 rad. Epicardial shear of the left ventricle has been measured in the dog with the use of magnetic coils [4,6] or optical markers [74], which were positioned on the epicardial surface. The shear angle at the surface was calculated from changes in mutual distance between the coils or markers. In these studies epicardial shear was found to range from 0.10 to 0.15 rad.

Transcutaneously, rotation and torsion of the heart have been measured by means of magnetic resonance imaging (MRI) [18,101]. With MRI tagging of the myocardial tissue is achieved by selective radio-frequency saturation of thin planes intersecting

the myocardium. In the tagged regions, tissue protons are in a different magnetization state than those in nontagged regions. This difference persists for only 400 to 500 ms when using a magnetic field of 0.3 to 0.6 T. During this time, the difference in magnetization can be detected by MRI, and the selected myocardial tissue can be displayed on a screen. Using this technique, Buchalter *et al.* [18] found the mean rotation of the apex in the human left ventricle with respect to the base to be 0.20 rad at the epicardium and 0.33 rad at the endocardium.

Using two-dimensional echocardiography (2DE, section 1.2.2), Arts *et al.* [2] recorded images of the long-axis projection of the left ventricle and of the transverse projections at the mitral valve, mid-papillary and low-papillary level. The latter images were recorded during different cardiac cycles, but at the same time delay after peak-ECG. Combination of the latter images yielded a three dimensional representation of the ventricle at a few moments during the ejection phase. Based on these measurements the gradient in rotation along the long axis was found to be related with a mean shear angle of 0.13 rad at the outer surface of the left ventricle. Unfortunately, the images as obtained with MRI or 2DE imaging have a low spatial resolution of approximately 1 to 2 mm [86]. Consequently, the accuracy of the estimation of cardiac rotation and torsion is limited.

In the present chapter, the results are described of a study in which the rotation of the canine left ventricle is determined using the principle as described in section 4.2.3. For this purpose, cardiac tissue velocity is estimated in two regions within the myocardium by using the correlation interpolation technique. Both regions of interest are located oppositely with respect to the ventricular cavity, and in a plane perpendicular to the base to apex axis. It should be noted that the present study is not intended to be an accurate evaluation of cardiac rotation in the dog. The experiments were performed to investigate the possibility to measure rotation of the heart transcutaneously by using pulsed echography.

6.2 Methods

6.2.1 Experiments

The experiments were performed on seven mongrel dogs. The experimental setup as well as the protocol used for medication of the animals has been described in detail in section 5.2.1. A short-axis cross-section at the mid-papillary level of the left ventricle was recorded by use of a 2DE imaging system. Two separate lines of observation were positioned at a fixed position within the sector scan image. One echo line was located through the left ventricular free wall, while the other line was located laterally through the septum (Fig. 6.1). The distance R from the transducer to the center of the left ventricular cavity and the angle ϕ between both echo lines were estimated from the 2DE image on the scanner or from the video

Figure 6.1: Schematic representation of the left ventricle and the positioning of the two echo lines. The angular velocity of the ventricle is denoted by ω . R denotes the distance from the transducer to the center of rotation, while the angle between the two echo lines is denoted by ϕ . A and B denote the areas of investigation along each line. The numbering of the lines of observation is in accordance with figure 4.2.

printer recording of the image. Echo signals were received alternately along both echo lines. The protocol for the transmission of the ultrasonic pulses associated with both lines is described in appendix B.

Along both lines of observation, a region of interest of 2.2 mm in depth was indicated within the myocardial tissue. In figure 6.1 these regions are indicated by A and B along echo line 1 and 2, respectively. In these specific regions, the line connecting the center of the cavity with the region is approximately perpendicular to the related echo line. The lines were positioned carefully in order to keep the indicated regions within the wall during the entire cardiac cycle. The acquisition of ultrasonic echo signals along both lines of observation was started at the rising slope of the R-wave of the ECG signal (appendix B). Echo signals from a tissue range of 34.6 mm along each echo line, including the regions of interest, were sampled and stored in a digital memory over a recording time of 1.1 s. Subsequently, the stored data were transferred to the computer system and stored on disk.

A second measurement was performed during intravenous administration of imipramine. This drug depresses cardiac performance [55,76]. The related experimental protocol is described in detail in section 5.2.2.

6.2.2 Data analysis

The echo signals received from the regions of interest A and B (Fig. 6.1) were processed with the correlation interpolation technique to estimate the component of cardiac tissue velocity along the line of observation. For each calculation of tissue velocity, 32 samples in depth (2.2 mm) were used over 3 successive echo signals in time (4.4 ms). The angular velocity of the heart was estimated from the difference in calculated tissue velocity between region A and B using Eq.(4.2). The angle of rotation $\hat{\phi}$ of the ventricle was calculated by time integration of the estimated angular velocity $\hat{\omega}$ using:

$$\hat{\phi} = \int_0^{T_R} \hat{\omega} dt \quad (6.1)$$

where T_R denotes the duration of the recording. The estimated rotation angle $\hat{\phi}$ was reset at the beginning of each cardiac cycle, as defined by the occurrence of the R-wave of the ECG.

6.3 Results

In the present study, the angular velocity of the canine heart has been estimated in 7 measurements under control conditions and in 7 measurements during administration of imipramine. Consequently, in total 28 estimations of tissue velocity were carried out. Only in 10 measurements the component of tissue velocity along the line of observation was determined successfully. In the other cases, the velocity estimation was deteriorated by aliasing or by a low correlation between successive echo signals. Cardiac tissue velocity was successfully estimated simultaneously along both echo lines in only two measurements, the results of which are presented. The first measurement was recorded under control conditions, while the second one was recorded during the administration of imipramine. Both measurements were performed within the same animal.

In figure 6.2 the component of cardiac tissue velocity in the region of interest along both lines of observation is plotted versus time for the measurement under control conditions. A positive value of tissue velocity denotes tissue movement towards the transducer. In figure 6.3 the calculated angular velocity of the heart (panel a) and the estimated angle of rotation (panel b) are plotted versus time for both successful measurements. A negative angular velocity denotes a clockwise rotation of the myocardial tissue. In both experiments, the distance R between the transducer and the center of the ventricular cavity was approximately 60 mm. The angle ϕ between the lines of observation was equal to 0.77 rad in the first measurement, and 1.04 rad in the second one.

Figure 6.2: Calculated cardiac tissue velocity in the regions of interest along echo line 1 (panel a) and echo line 2 (panel b) as a function of time. The solid vertical lines denote the beginning of each cardiac cycle as defined by the occurrence of the R-wave in the ECG.

6.4 Discussion

In the present study the angular velocity of the heart has been measured by calculating the difference in tissue velocity between two regions within the cardiac tissue. Using the present setup, only 35% of all measurements on cardiac tissue velocity were successful. To calculate the angular velocity, the estimation of tissue velocity has to be determined simultaneously in both regions of interest. Consequently, only in 14% of all experiments cardiac rotation could be estimated. The low rate of success may be caused by two factors. Firstly, the two lines of observation within the sector image are stored alternately, causing a decrease of the PRF to 465 Hz per echo line. As a result, in the present setup tissue velocity can theoretically be calculated without aliasing upto a velocity of only $51.1 \text{ mm}\cdot\text{s}^{-1}$. To avoid aliasing of the velocity estimate, a tracking algorithm was used in addition to the correlation interpolation technique (appendix A). The instantaneous increase of tissue velocity, however, may still be so large that tracking fails. Secondly, a large component of tissue velocity is present perpendicular to the lines of observation. During the systolic phase the left ventricle contracts, while the position of the echo lines is fixed. As a result, cardiac tissue is moving perpendicularly through the ultrasonic beam. If this motion is small, successively received echo signals may still have a high mutual correlation. However, if this motion is large, the correlation between successive signals may decrease. After all, in the latter situation successive echo signals are received from different tissue regions within the wall. Another cause of failure of the

measurement may be the fact that structures from outside the myocardium with a high reflectivity enter the region of interest. Such structures cause echo signals with a much higher amplitude than the amplitude of the echo signals from the surround-

Figure 6.3: Calculated angular velocity $\dot{\omega}$ (panel a) and total angle of rotation $\hat{\phi}$ (panel b) of the left ventricle at the mid-ventricular level versus time. The upper panels show the results as obtained under control conditions, the lower panels as obtained during administration of imipramine. The solid vertical lines denote the beginning of each cardiac cycle.

ing tissue. Consequently, the estimation of tissue velocity may be affected. The related problems may be solved by using a higher PRF for the echo lines or by using more than two lines of observation within the image. Unfortunately, the ultrasound imaging system used in the present investigations was limited to the use of maximal two echo lines at a fixed PRF of 465 Hz per line.

The angular velocity of a cross-section of the myocardium has been calculated using Eq.(4.2). In the latter equation, angular velocity is expressed in terms of regional tissue velocity v , the distance R from the transducer to the center of rotation and the angle ϕ between the lines of observation. In chapter 4, the influence of ϕ has been investigated with respect to the accuracy of the estimation. From the latter evaluation the standard deviation of the estimate was found to decrease with an increasing value of ϕ (Fig. 4.6). Using an angle between both echo lines of 0.52 rad, the standard deviation was found to be approximately $\pm 0.2 \text{ rad}\cdot\text{s}^{-1}$. In the present measurements, the value of ϕ was in the range of 0.75 to 1.0 rad. Regarding the results presented in chapter 4, the value of ϕ used may be assumed to be of minor influence on the deviation of the estimate.

In the current experiment, the rotation of the heart was assessed in one plane, perpendicular to the longitudinal axis and close to the mid-ventricular level. The maximal angle of rotation in the particular plane was found to be approximately 0.07 rad. Regarding the results obtained in other investigations, the latter value of the rotation angle is in a physiological range [18,36,44]. In the present experiments, no estimation can be obtained of the torsion of the ventricle, because for that purpose the difference in rotation at two separate levels between base and apex has to be calculated.

6.5 Conclusions

In the present study, the angular velocity of the ventricle has been estimated from the difference in tissue velocity between two separate tissue regions. Both regions were located inside the myocardial tissue, oppositely with respect to the ventricular cavity. Using the latter setup, determination of cardiac tissue velocity in both regions appeared to be difficult. In only 2 out of 14 experiments cardiac rotation could be estimated. The problems encountered in the measurement were probably caused by a low repetition frequency of the ultrasonic pulses, associated with the echo lines of observation. In the two measurements in which tissue velocity could be determined simultaneously along both echo lines, the angular velocity of the heart and the angle of cardiac rotation were found to be in a physiological range. Angular velocity of the heart can be estimated by measuring cardiac tissue velocity in two separate areas within the ventricular wall. However, the present setup should be improved to obtain a higher rate of success.

Chapter 7

Tissue Velocity and Deformation in the Human Heart: a Case Report

7.1 Introduction

Several investigations have been performed to measure myocardial tissue deformation in the human heart. A few of these investigations were performed using cardiac surgery. In these studies, markers were positioned in the myocardial tissue [36,44]. After recovery of the patient, the markers were visualized using a biplane cineradiographic technique. On the basis of the obtained images, the position of each marker was determined as a function of time. Subsequently, cardiac deformation was estimated from changes in mutual distance between the markers.

However, most investigations on the deformation of the human heart have been performed transcatheterally. Firstly, an image of a cross-section of the heart can be obtained by using magnetic resonance imaging (MRI) [18,59,86,101]. Using this technique, thickening of the cardiac wall has been estimated by measuring the distance between the myocardial borderlines within the image [59,86]. Rotation of the ventricle has been measured following magnetically marked regions of tissue over a sequence of images during the cardiac cycle [18,101]. Secondly, deformation of the myocardium has been measured by using echocardiography. By measuring the distance between the endocardial and epicardial borderlines in a sequence of 2DE or M-mode images of the heart, thickening of the cardiac wall has been estimated. Using this technique, myocardial thickening was found to range from 48 to 67% [26,90,92]. The estimation of myocardial tissue deformation obtained by using MRI, 2DE or M-mode imaging has a relatively low accuracy due to the low spatial resolution of the images.

In this thesis a new technique has been described to measure regional cardiac tissue velocity along a line of observation through the heart using echocardiography. In the canine heart the technique was found to determine cardiac tissue velocity and tissue deformation in the region of interest rather accurately (chapter 5). However, it should be investigated whether the technique can also be used to measure deformation of the myocardial tissue in man. For this purpose, a case study on one healthy human volunteer is described in the present chapter. If cardiac deformation indeed can be determined successfully in the human heart, the technique may be applied in the clinical situation.

7.2 Methods

7.2.1 Experiments

A single experiment was performed in one human subject using the same instrumental setup as described in section 5.2.1, although triggering on the ECG signal was not performed. A short-axis cross-section at the mid-ventricular level of the left ventricle of the subject was recorded using a 2DE imaging system. Within the 2DE

image, a single line of observation was positioned centrally through the left ventricular cavity. The ultrasonic pulses associated with this echo line were transmitted at a PRF of 930 Hz, and the echo signals received along the line were recorded.

Data acquisition was started manually at an unknown moment during the cardiac cycle. Echo signals from a depth region of 34.6 mm, containing the anterior wall of the left ventricle, were sampled and stored in a digital memory, as described in appendix B. The echo signals were stored over a total recording time of 1.1 s. After data acquisition was completed, the echo signals were transferred to the computer system and stored on disk for off-line analysis.

7.2.2 Data analysis

Cardiac tissue velocity along the line of observation was calculated in successive regions in depth by processing the received echo signals with the correlation interpolation technique. For this purpose, 32 samples in depth (2.2 mm) over 3 successive echo signals in time (2.2 ms) were used for analysis. Estimations of tissue velocity were obtained at separate positions within the tissue, located 1.1 mm apart (section 5.2.3). The position $\tilde{x}_i$ with respect to the transducer of several points within the cardiac wall was calculated as a function of time from the estimation of tissue velocity. For this purpose, several points within the myocardial tissue were followed in depth using Eq.(5.1). Strain ϵ_r of the cardiac tissue was determined as a function of time using Eq.(5.2).

7.3 Results

In figure 7.1 an example of the calculated tissue velocity in a region within the anterior wall is shown as a function of time. The region is located at a fixed distance from the transducer. A positive value of velocity denotes a displacement of the tissue towards the transducer. In figure 7.2a for the anterior left ventricular wall the distance $\tilde{x}_i$ to the transducer is plotted versus time for six points within the tissue. For this purpose, the points were followed in depth using Eq.(5.1). In the first 400 ms of the recording the cardiac tissue is moving away from the transducer, and thus towards the center of the left ventricular cavity. The pattern of tissue displacement repeats itself in time with a cycle length of approximately 1000 ms, which is associated with a heart rate of 60 min⁻¹. In figure 7.2b strain ϵ_r in the anterior wall is plotted versus time. Strain was calculated over a depth range of 5.5 mm. In this single measurement, the increase of strain occurs during a time interval of approximately 260 ms, and reaches a maximal value of approximately 0.37. After strain has decreased to zero again, it stays at this level until the next cycle.

Figure 7.1: Calculated cardiac tissue velocity in a region within the anterior cardiac wall of a human heart. For calculation of velocity, echo signals from a tissue region of 2.2 mm in depth were used over 2.2 ms in time.

7.4 Discussion

Anatomically and physiologically the human and the canine heart are similar. In general, the human heart is somewhat larger and its cardiac cycle is longer. In the present study, cardiac tissue velocity could be determined analogously to tissue velocity in the canine heart. Maximum tissue velocity in the human myocardium was found to be in the order of $50 \text{ mm}\cdot\text{s}^{-1}$ (Fig. 7.1), which is lower than measured in the canine heart (section 5.3). This may be related to the low heart rate in the human subject, which was twice or three times lower than that in the dog experiments (table 5.1). Because of the low tissue velocity, aliasing of the velocity estimation did not occur as often. In general, processing of the echo signals received from the human myocardium was not found to be essentially different from processing of the echo signals received from the canine heart.

The large dimensions and the long cardiac cycle of the human heart, as compared with the canine heart, did cause a problem concerning the storage of echo data. In the human heart, the minimum depth range required to simultaneously store echo signals from the anterior and posterior wall is approximately 100 mm. When storing the signals over a complete cardiac cycle of approximately 1 s, in the current setup 1.4×10^6 samples should be obtained. Consequently, for human applications a digital memory of 1.5 MByte is required. Since the capacity of the digital memory in the

Figure 7.2: Distance $\tilde{x}_i$ to the transducer of successive areas within the anterior left ventricular wall of a human subject (panel a) and radial strain ϵ_r in this wall (panel b) versus time. Successive curves denote the results for several points initially located 1.1 mm apart. Radial strain was estimated over a depth range of 5.5 mm.

buffer-interface circuit is limited to 0.5 MByte of echo samples, concessions had to be made. Either the recording time had to be reduced to 0.55 s or even 0.28 s, or the depth range had to be limited to 69.2 mm or less.

The duration of the time intervals in which thickening and thinning of the cardiac wall occurs is in the physiological range [2,19,82]. The amount of strain, as measured in this single experiment, is approximately 0.37. In several echocardiographic studies, strain in the human myocardial tissue was found to be higher, in the range from 0.41 to 0.59 [26,90,92]. In these investigations strain may be overestimated due to erroneous detection of myocardial borderlines in the echo image, as discussed in section 5.4. After a complete cardiac cycle, strain has decreased to zero again, which indicates that the thickness of the wall is back to its initial value. Consequently, the error made in the integration of tissue velocity to follow successive points within the tissue in depth is probably small.

In the present experiment, the ECG signal of the human subject was not recorded, which caused data collection to be started manually. In the single measurement described, the recording appeared to be started close to the beginning of the systolic phase. It should be noted that data acquisition is started at an arbitrary moment during the cardiac cycle when manual starting of data storage is used. Consequently, the time interval, in which cardiac deformation occurs, may be completely missed when echo data are stored during a recording time shorter than the cardiac cycle length.

7.5 Conclusions

In the present case study, no essential problems were encountered in measuring cardiac tissue velocity in the human heart. Cardiac tissue velocity, regional tissue displacement and strain were found to be in a physiological range. A practical problem was the limited size of the digital memory, causing signals to be stored over only a small part of the cardiac cycle or over a limited depth range. Therefore, the size of the memory should be increased to at least 1.5 MByte to be able to record the parameters on cardiac deformation in humans adequately. Considering the results of the present study it is concluded that the method is likely to be suitable to assess cardiac deformation in the human heart.

Chapter 8

Summary and Conclusions

8.1 Summary of the present study

In the present study, the correlation interpolation technique is introduced as a new method to measure cardiac tissue velocity using transcutaneous echocardiography. With this technique, short ultrasonic pulses are transmitted at a certain pulse repetition frequency (PRF). The high frequency echo signals from the tissue under investigation are received, sampled and stored. When the tissue is displaced between the transmission of two successive pulses, the related echo signals are mutually shifted in depth. The shift between the signals is proportional to the displacement of the tissue, and is calculated by means of the crosscorrelation function between successive echo signals. The mutual signal shift is indicated by the position of the top of the latter function. The shape of the top has been modeled by a cosine curve. On the basis of this model only five samples of the crosscorrelation function are used to determine the position of the top by interpolation. The signal shift was calculated accurately and faster than with current techniques based on correlation.

The correlation interpolation technique has been evaluated in several ways. Firstly, the technique was compared with two Doppler velocity estimators using numerically simulated echo signals (chapter 3). These signals were obtained by filtering Gaussian noise, and had a bandlimited power spectrum with a bandwidth to center frequency ratio of approximately 1. Successive signals were obtained by uniformly shifting a signal in depth. Mutual signal shift was varied to investigate the accuracy and linearity of the estimation of signal shift. Sensitivity to noise was investigated by adding noise to the signals at various levels of the signal to noise power ratio. Using 32 samples in depth and two successive signals in time for analysis at a signal to noise power ratio of 10, signal shift could be determined with a standard deviation of ± 0.09 times the distance between two samples in depth. This deviation increased to ± 0.26 sampling distances when adding noise at a signal to noise power ratio of 1. The standard deviation of the estimation of signal shift appeared to be proportional to the reciprocal of the square root of the total number of samples used for calculation, independent of the ratio of the number of samples in depth and time used. Using a small depth interval for analysis over several signals in time, the performance of the correlation interpolation method is comparable to the Doppler techniques. When a large depth interval is used over a short interval in time, the correlation interpolation technique performs better, especially when additional noise is significant.

Secondly, the method was evaluated in an experimental setup, in which moving cardiac tissue was simulated by an Agar disk containing scattering particles (chapter 4). The disk was mounted on a rotating axis, and was imaged with a 2DE imaging system. Ultrasonic pulses with a center frequency of 3.5 MHz were transmitted along a single line of observation through the disk at a PRF of 930 Hz. The echo signals were sampled at a frequency of 11.4 MHz. When analyzing echo signals

from a depth region of 2.2 mm (32 samples) within the disk over a time interval of 2.2 ms (3 signals), the shift between successive echo signals could be determined with a standard deviation of approximately ± 0.09 sampling distances. In the setup used, this accuracy is associated with an accuracy of the velocity estimation of the disk of approximately $\pm 6 \text{ mm}\cdot\text{s}^{-1}$. The standard deviation decreased when the number of data points used for analysis was increased. The estimate of signal shift was found to be linear within ± 0.03 sampling distances. Based on a theoretical evaluation of tissue displacement in the real heart, the latter accuracies were found to be sufficient to estimate cardiac tissue deformation. The angular velocity of the disk could be measured by calculating the difference in velocity along two separate lines of observation through the disk. Angular velocity was determined with a standard deviation of approximately $\pm 0.2 \text{ rad}\cdot\text{s}^{-1}$ in case the angle between both lines was equal to 0.52 rad. By increasing the angle between the lines, the accuracy of the estimation increased considerably.

Finally, the correlation interpolation technique was used to measure cardiac tissue velocity in the beating heart in seven closed-chest dogs and in one adult human. In the dog (chapter 5), tissue velocity was measured in several regions within the anterior and posterior left ventricular wall. Strain in the wall was calculated on the basis of tissue velocity in two separate regions within the cardiac wall. Changes in the diameter of the ventricular cavity were estimated by determining the change in distance between two points, located in the midwall regions of the anterior and posterior wall. During the ejection phase, strain in the cardiac wall and the cavity diameter decrease of the left ventricle could be determined successfully. The rotation of the canine left ventricle could not be measured accurately due to failures in estimating signal shift (chapter 6). In a second series of measurements, the performance of the cardiac tissue was depressed by intravenous administration of imipramine. As a result, strain and cavity diameter decrease during the ejection phase of the cardiac cycle were found to be slightly decreased.

In one single case study wall thickening and changes in ventricular diameter were estimated in a human volunteer (chapter 7). In this study it was investigated whether there were limitations to apply the technique in man. For this purpose, echo signals received from the anterior left ventricular wall were processed. Cardiac tissue velocity and strain within the cardiac wall could be determined successfully. No essential problems were encountered in measuring cardiac tissue velocity in the human heart. The size of the digital memory appeared to be too small to store echo signals from an appropriate depth range over a complete cardiac cycle.

8.2 Conclusions and recommendations

In the present study, the correlation interpolation technique was developed to estimate the shift between two or more successive echo signals. The performance of the technique was evaluated through two simulations and two experimental studies in the beating heart. From these evaluations, the following can be concluded.

8.2.1 Conclusions from the theoretical simulations

- Using a small depth range for calculation, the performance of the correlation interpolation method is equal to that of the instantaneous frequency detector and the complex autocorrelation detector. When the number of depth samples used is large and noise is significant, the correlation interpolation technique performs better.
- The standard deviation of the estimation of signal shift is proportional to the reciprocal of the square root of the total number of samples used for calculation. The estimate was not affected by the applied ratio of the number of samples in depth and time used for calculation.
- Signal shift could be determined without aliasing within an interval ranging from -0.5 to 0.5 times the period length associated with the mean frequency of the signals. Within this interval, the estimation of signal shift was found to be linear and not biased by additional noise.
- The number of mathematical operations needed for calculation of signal shift is linear with the number of sample points used for analysis. Because only five samples of the crosscorrelation function are calculated, computational effort is less than with current correlation techniques.

8.2.2 Conclusions from the experimental evaluation

- The shift between successive echo signals could be determined with a standard deviation of ± 0.09 times the distance between two samples when using 32 samples in depth for calculation over two successive echo signals in time. In the setup used, this accuracy is associated with a standard deviation of the velocity estimation of $\pm 6 \text{ mm}\cdot\text{s}^{-1}$.
- The accuracy of the estimation of signal shift was confirmed to be proportional to the reciprocal of the square root of the total number of samples used.

- The angular velocity of the disk could be measured by calculating the difference in tissue velocity in two separate areas. The accuracy increased substantially when increasing the angle between both lines of observation, and was independent of the position of the lines with respect to the center of rotation.

8.2.3 Conclusions from the study in the canine heart

- Strain in the anterior and posterior wall of the left ventricle and the diameter decrease of the left ventricular cavity during the ejection phase of the heart could be measured successfully.
- Depressing the cardiac performance by administration of imipramine caused a decrease of strain in the anterior and posterior wall and a decrease of cavity diameter change during the ejection phase.
- The rotation of the left ventricle could be determined successfully in only 14% of the measurements.
- Maximum regional tissue velocity in the canine heart was found to be in the order of $180 \text{ mm} \cdot \text{s}^{-1}$, which exceeds the maximum velocity that can be determined without aliasing, using the current setup. Aliasing could be minimized by applying a tracking algorithm in addition to the correlation interpolation technique.

8.2.4 Conclusions from the case study in the human heart

- Tissue velocity and strain in the anterior wall of the left ventricle could be measured successfully.
- The size of the digital memory was found to be too small to store echo signals from an appropriate depth range over a complete cardiac cycle.

8.2.5 Technical recommendations

For further investigations on cardiac deformation by means of the correlation interpolation technique, the following improvements in the experimental setup are recommended.

- In the current experimental setup a 0.5 MByte digital memory is available to store the received echo signals instantaneously. Because of the relatively large dimensions and low heart rate of the human heart, echo signals could not be recorded over an appropriate depth range during a complete cardiac cycle. Therefore, it is recommended to expand the capacity of the memory to at least 1.5 MByte when using a PRF of 930 Hz.

- The PRF of the pulses, associated with the lines of observation, might be increased. This yields a higher maximum value of tissue velocity, which can still be measured without aliasing. Moreover, a component of tissue velocity perpendicular to the ultrasonic beam may be of less influence on the velocity estimate when using a high PRF. However, one should keep in mind that the PRF has to be properly selected in relation to the depth of interest and the attenuation of the ultrasound by the tissue. In this way depth unambiguity of the echo signals can be maintained. An disadvantage of an increase of the PRF is that more echo signals are received in time, which requires a larger digital memory.
- In the current setup, data storage was started at the rising slope of the R-wave in the ECG signal. The moment of occurrence of the next R-wave was estimated from paper recordings of the ECG, which may introduce some errors. It is more appropriate to sample the recorded ECG signal and store it in the digital memory simultaneously with the ultrasonic echo signals. In this way a more exact relation between the stored data and the recorded ECG is obtained.
- The software of the correlation interpolation algorithm may be optimized to reduce the current computation time. In the future, the algorithm may be implemented in hardware to obtain a much faster, perhaps even real time, analyzing system.

Appendix A

Software Implementation of the Correlation Interpolation Technique

A.1 The correlation interpolation algorithm

In chapter 2 the correlation interpolation technique is introduced as a method to measure cardiac tissue velocity by processing ultrasonic echo signals received from the heart. For this purpose, five samples of the crosscorrelation function between successive echo signals are calculated. In practice, this calculation is carried out by time-domain processing of the signals. However, the algorithm used in the present study is different from algorithms generally used for the calculation of the crosscorrelation function.

In figure A.1 two arbitrary signals are shown. The signals are sampled in depth with the sample frequency f_x while successive signals in time are obtained at the pulse repetition frequency (PRF). If the echo signals are received from a moving tissue, successive signals are shifted relative to each other by an amount proportional to the velocity of the tissue.

Figure A.1: Two arbitrary sampled signals which are shifted relative to each other due to tissue motion. The square of broken lines denotes a basic cell for calculation, containing two samples of each echo signal.

A *basic cell for calculation* is defined as a square, containing four adjacent samples of two successive signals (Fig. A.1). The correlation interpolation algorithm is used to calculate five samples of the crosscorrelation function of the two signals. For this purpose, five parameters are calculated from the four samples within the basic cell using the following scheme:

$$\begin{cases}
 S_1 = 2f_{11}f_{22} - 2f_{12}f_{21} & (a) \\
 S_2 = 2f_{11}f_{22} + 2f_{12}f_{21} & (b) \\
 S_3 = 2f_{11}f_{12} + 2f_{21}f_{22} & (c) \\
 S_4 = 2f_{11}f_{21} + 2f_{12}f_{22} & (d) \\
 S_5 = f_{11}^2 + f_{12}^2 + f_{21}^2 + f_{22}^2 & (e)
 \end{cases} \quad (A.1)$$

According to the definition of the crosscorrelation function $R_{vv}(X, T)$ in Eq. (2.4), the parameters S_1 to S_5 can be expressed in terms of R_{vv} . It holds:

$$\begin{cases}
 S_1 = 2(R_{vv}(\Delta x, \Delta t) - R_{vv}(-\Delta x, \Delta t)) & (a) \\
 S_2 = 2(R_{vv}(\Delta x, \Delta t) + R_{vv}(-\Delta x, \Delta t)) & (b) \\
 S_3 = 4R_{vv}(\Delta x, 0) & (c) \\
 S_4 = 4R_{vv}(0, \Delta t) & (d) \\
 S_5 = 4R_{vv}(0, 0) & (e)
 \end{cases} \quad (A.2)$$

The correlation sums $R_{vv}(X, T)$ in Eq.(2.14) are obtained by averaging the contributions of a finite number of adjacent basic cells, as expressed by Eq.(A.1), and subsequently solving Eq.(A.2). The major advantage of the use of a basic cell to calculate the correlation function is its inherent symmetry. All contributions to the correlation sums are obtained from data ordered symmetrically around the center of each basic cell.

A.2 The tracking algorithm

Echo signals are received at discrete moments in time, in association with the PRF. In the time interval between two successive signals, the tissue under investigation may move. As a result, successive echo signals are shifted with respect to each other. However, when the shift between two sinusoidal signals is more than half the signal period, the mutual shift cannot be determined unambiguously. A clear example of this problem is the case in which two signals are mutually shifted over exact one signal period. Then basically any shift detection algorithm detects a signal shift of zero instead of one period. This erroneous detection of signal shift causes aliasing in the estimation of tissue velocity.

The value of tissue velocity associated with a signal shift of half a signal period is proportional to the PRF. As a result, aliasing is avoided by selecting a high PRF in accordance with the maximal tissue velocity to be expected. The PRF of the ultrasound imaging system used in the present study is fixed at 930 Hz in the single M-line mode and 465 Hz in the dual-line mode. Consequently, the PRF cannot be adjusted to the specific situation of investigation. Therefore, a tracking algorithm is used to follow a moving signal segment in time during data analysis.

In the present study, the following tracking algorithm is used in combination with the correlation interpolation algorithm. First, two additional basic cells are defined, as shown in figure A.2. The positioning of these cells causes the second

Figure A.2: Positioning of the two extra basic cells when using the tracking algorithm. Cell 0 is basically used with the correlation interpolation algorithm, cell 1 and 2 are used when tracking is performed.

echo signal to be processed as if it is shifted with respect to the first signal over +1 or -1 sampling interval. Subsequently, for each of the three basic cell configurations the velocity of the tissue is estimated using the correlation interpolation algorithm. The basic cell configuration, in which the estimated value of echo velocity is found to be closest to zero, is determined. Apparently, latter configuration cancels the shift between the signals most optimal. Symmetrical around this configuration, three new basic cells are chosen for the next calculation. Using this strategy, the signals to be processed are preshifted in order to maintain the mutual shift as small as possible. Consequently, the chance of an erroneous measurement of signal shift is minimized. However, in case the amount of signal shift increases between successive calculations by more than half a signal period, the tracking algorithm will fail. Such rapid increase of shift between echo signals may be caused by acceleration of the tissue under investigation.

Appendix B

Collection of Ultrasonic Echo Signals

B.1 The experimental setup

A block diagram of the experimental setup used in the present study to obtain high frequency echo signals is shown in figure 4.1. The setup consists of an ultrasound imaging system and an interface circuit for transfer of the echo data from the imaging system to the computer. In the next sections, the equipment used will be discussed in detail.

B.1.1 The ultrasound imaging system

In the experiments a Hewlett-Packard HP77020 ultrasound imaging system, equipped with a 3.5 MHz phased array transducer, is used. The echo information received can be displayed in sector scan B-mode as well as in M-mode. The scanner is equipped with *Time Gain Compensation* (TGC) to correct for the attenuation of the echo signals by the tissue as a function of distance to the transducer. In M-mode, two M-lines can be positioned independently within the sector scan image. The echo signals received along these M-line(s) are obtained by a modification of the machine. The protocol for the transmission of ultrasonic pulses by the transducer is shown in figure B.1. In single M-line mode, the ultrasonic pulses, associated with the M-line, are transmitted at a pulse repetition frequency (PRF) of 930 Hz. Between succes-

Figure B.1: M-line protocol of the ultrasound imaging system. Above the M-line sequence is shown for single M-line mode, where M₁ denotes the moment of transmission of the ultrasonic pulse associated with the M-line. Below, the situation is shown for the dual-line mode, where M₁ denotes the moment of transmission associated with the first M-line, and M₂ with the second line. At the moments marked with 'scan', regular pulses are transmitted to maintain the sector scan image on the screen.

sive M-lines, two additional pulses (denoted by 'scan') are transmitted, which are used by the imaging system to maintain the sector scan image on the screen. The echo signals induced by these pulses are not important for our investigations and are therefore not stored. In dual M-line mode, the ultrasonic pulses for the two separate M-lines are transmitted at short time intervals at a PRF of only 465 Hz per M-line. After the second M-line, again regular pulses are transmitted. For each M-line a trigger signal is available, which is used to synchronize data collection.

B.1.2 Dimensions of the ultrasonic beam

The ultrasound imaging system is equipped with a phased array transducer which emits short ultrasonic bursts with a center frequency of 3.5 MHz. To obtain infor-

Figure B.2: Panel a: Beam scan of the phased-array transducer used at a distance of 50 mm from the transducer. Panel b: 3D-representation of the beam scan as shown in panel a.

mation about the two-dimensional intensity distribution of the ultrasonic beam in a cross-sectional plane at a given distance from the transducer, a *beam scan* technique has been used [40]. With this technique, a microphone is placed at a certain distance from the transducer. By moving the transducer in two orthogonal directions, the cross-section of the intensity pattern of the beam is scanned. In figure B.2, a typical beam scan of the transducer used is shown at a distance of 50 mm. In the middle of the picture in figure B.2a, the maximum intensity is plotted as a white circular area. Each black-to-white transition indicates a decrease of 3.2 dB of sound intensity. The -6 dB contour in the beam scan is commonly used to define the width of the ultrasonic beam. From the figure it is derived that at a distance of 50 mm

the beam is approximately 2 mm wide. The minimum beamwidth was found at a distance of approximately 80 mm, being the *focal point* of the transducer.

In axial direction, the length of the sample volume depends on the duration of the emitted ultrasonic burst and the frequency characteristics of the transducer and signal processing circuit. The length of the pulse, received at the microphone, was evaluated by displaying the signal on an oscilloscope. The pulse length appeared to be approximately $0.55\ \mu\text{s}$, associated with a depth range of 0.42 mm.

B.1.3 Sampling and buffer-interface

The high frequency echo signals received along the selected M-line(s) are sampled and stored in a fast memory by use of the buffer-interface circuit. The block diagram

Figure B.3: Block diagram of the buffer-interface circuit.

of the interface circuit is shown in figure B.3. After *amplification*, the analog echo signals are filtered by use of a 4th order *Butherworth lowpass filter* (LPF). The cut-off frequency of the filter is approximately 4.5 MHz. Amplitude response and circuit layout of the filter are shown in figure B.4. After passing a *logarithmic amplifier* the signals are converted to an 8-bit digital signal by use of an *analog to digital converter* (ADC). In the computer analysis of the signals, the logarithmic compression is accounted for. The sampling frequency for the ADC as generated by the *clock unit* is 11.4 MHz. The clock unit synchronizes the internal clock signals to the M-line trigger signals. After sampling, the echo signals are fed into the *memory read/write controller*. The controller coordinates the instantaneous storage of the sampled signals into the 0.5 MByte *Static Random Access Memory* (SRAM). The M-line trigger signals are used for the synchronization of the storage. After the

Figure B.4: Amplitude response $|H_{lp}(f)|$ and circuit layout of the 4th order Butterworth lowpass filter section. $R = 500 \, \Omega$, $L_1 = 15 \, \mu\text{H}$, $L_2 = 39 \, \mu\text{H}$, $C_1 = 150 \, \text{pF}$ and $C_2 = 56 \, \text{pF}$.

memory is filled, the controller also handles the data transfer from memory to the computer system using a handshake protocol. The data collection protocol is started manually, by computer or by ECG trigger via the *start module*. In the latter case, the R-wave in the ECG is detected by comparing the amplitude of the signal to a threshold level.

Two parameters of the buffer-interface are to be set during operation. The first parameter, *linelength*, determines the number of samples per echo signal to be stored in depth. Due to the finite size of the memory, the value of *linelength* directly determines the number of successive echo signals to be stored. For example, choosing a *linelength* of 512 samples in depth, which is equal to a depth range of 34.6 mm when using a sampling frequency of 11.4 MHz, yields a total number of 1024 signals to be stored in the memory. In single M-line mode ($\text{PRF} = 930 \, \text{Hz}$), this is equivalent to a recording time of 1.1 s. The second parameter, *delay*, determines the delay time between the occurrence of the M-line trigger and the moment the sampling is actually started. The delay is used to position the depth range to be sampled and stored along the line of observation. The delay can be set at 0, 52 or $90 \, \mu\text{s}$, equivalent to a skip of 0, 40 or 69 mm in depth. The delay is generated by a *delay unit* which is triggered by the M-line trigger signals. Finer tuning of the position of the M-line in depth can be performed by the control of the scanner in steps of 5 mm over a maximum range of 40 mm.

B.1.4 The computer system

The computer system used for off-line data analysis is a *Torch TripleX* mini computer system. It is equipped with a 68020 μ -processor accelerator board, a 68881 floating point co-processor and a 40 Mb harddisk. The computer has the *UNIX System V* operating system. Data input is handled by a *parallel input/output* (PIO) interface board connected to the systems internal data bus. Through this PIO board the handshake protocol with the buffer-interface circuit is performed. The software for data transfer and analysis is written in the programming language C.

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Samenvatting

Het meten van de vervorming
van hartspierweefsel door
correlatie interpolatie
van ultrasone echosignalen

Inleiding

Het hart is een holle, dikwandige spier, die als pomp fungeert in de bloedsomloop van het lichaam. Het hart is opgebouwd uit 4 holle delen, de linker en de rechter *boezem* en de linker en de rechter *kamer* (zie figuur 1). Een hartcyclus kan globaal worden verdeeld in twee fasen. In de eerste fase (de *diastole*) bevindt het hart zich in een toestand van rust. Gedurende deze tijd wordt het hart vanuit de bloedsomloop gevuld met bloed. De tweede fase is een actieve fase (de *systole*) waarin door samentrekking van de spierlagen van het hart de druk in het hart wordt vergroot en het bloed wordt uitgedrukt. De periode van uitpompen wordt de *ejectiefase* genoemd. Het bloed uit de rechter kamer wordt daarbij naar de longen geleid via de *longslagader*, terwijl het bloed uit de linker kamer via de *aorta* naar de rest van het lichaam wordt getransporteerd. Een viertal *hartkleppen* zorgt ervoor dat het bloedtransport in de juiste richting verloopt.

Uit Arts [1]

Figuur 1: Schematisch lange-as aangezicht van een doorsnede van het hart. 1=rechter boezem, 2=linker boezem, 3=rechter kamer, 4=linker kamer, 5=septum, 6=mitraal klep, 7=tricuspidale klep, 8=aorta klep, 9=aorta, 10=pulmonale klep, 11=longslagader.

Als gevolg van het samentrekken verandert de vorm van het hart gedurende een hartcyclus. Ten gevolge van het uitpompen van bloed gedurende de ejectiefase neemt het kamervolume af, en dus ook de diameter van de kamers. Daarnaast treedt er tijdens het samentrekken van het hart een *verdikking* van de hartwand op. Deze verdikking is afhankelijk van de mate waarin de afzonderlijke spiervezels samentrekken. Tenslotte voert het hart tijdens het uitpompen van het bloed een wringende beweging uit, die *torsie* wordt genoemd. De grootte van deze torsie hangt samen met de mate van verkorting en de oriëntatie van de spiervezels in de hartwand.

Uit onderzoek is gebleken dat de vervorming van het hartspierweefsel verandert wanneer een gedeelte van het weefsel slecht functioneert. Een voorbeeld hiervan is de aanwezigheid van een plaatselijk infarctgebied in het hartspierweefsel. Als gevolg van een (gedeeltelijke) verstopping van één of meerdere kransslagaders is de bloeddoorstroming in zo'n gebied sterk afgenomen of zelfs helemaal verdwenen. Hierdoor heerst er lokaal in het weefsel een tekort aan zuurstof, en ontstaat er een opeenhoping van afvalstoffen. Beide factoren leiden tot een verslechterde mechanische functie van de hartspier, en kunnen zelfs het afsterven van het betrokken stukje spierweefsel veroorzaken. De slechte mechanische functie veroorzaakt een verstoring van het vervormingspatroon van het hartspierweefsel, zoals bijvoorbeeld een afname van de lokale wandverdikking. Door de vervorming te meten kan dus een schatting worden gemaakt van de actuele conditie van het hartspierweefsel.

Doel van de studie

Om de vervorming van de hartspier te meten zijn reeds vele technieken ontwikkeld, die globaal in twee groepen kunnen worden verdeeld. De eerste groep bevat methoden die een open-hart operatie vereisen om direkt aan het hartspierweefsel te kunnen meten. Hoewel met deze technieken in het algemeen de vervorming van het hart vrij nauwkeurig kan worden bepaald, zijn ze ongeschikt voor klinische toepassingen wegens de noodzaak tot operatie. De tweede groep bevat technieken die door de intacte huid heen een afbeelding van het hart kunnen maken (zgn. *transcutaan* = door de huid heen). Deze technieken maken in het algemeen gebruik van *ultrageluid*, *röntgenstraling* of *magnetische velden*. Op basis van een reeks afbeeldingen van het hart, gemaakt op opeenvolgende tijdstippen gedurende een hartcyclus, kan een schatting worden gemaakt van de vervorming van de hartspier gedurende zo'n cyclus. Helaas is in het algemeen de kwaliteit van de verkregen beelden slecht, zodat de vervorming van het weefsel niet nauwkeurig kan worden bepaald.

Om toch de vervorming van de hartspier nauwkeurig én transcutaan te kunnen meten is in de huidige studie een nieuwe techniek ontwikkeld waarmee de lokale weefselsnelheid in de hartspier gemeten kan worden. Op basis van snelheidsverschillen binnen het spierweefsel kan vervolgens de vervorming van het weefsel berekend worden. De methode maakt gebruik van ultrageluid, dat door de huid heen gestraald wordt. In de gebruikte dosis is ultrageluid onschadelijk voor levend weefsel, en daarmee voor de patiënt.

De ontwikkelde techniek

Met behulp van een *transducer* (zender en ontvanger voor ultrageluid), die op de huid wordt geplaatst, worden korte ultrageluidspulsen met een centrale frequentie van 3.5 MHz uitgezonden naar het hart. Deze pulsen worden met tussenpozen van 1.1 ms opgewekt, en worden langs een rechte lijn (de *ultrageluidsbundel*) uitgezonden. Elke puls zal reflecties (echosignalen) veroorzaken op structuren in het hartspierweefsel, zoals spiervezels. Deze echosignalen worden weer ontvangen door de transducer. Als het weefsel tussen twee opeenvolgend uitgezonden pulsen is verschoven langs de ultrageluidsbundel, zullen de bijbehorende echosignalen ook ten opzichte van elkaar verschoven zijn. Uit deze verschuiving van de echosignalen kunnen de verplaatsing en de lokale snelheid van het weefsel worden berekend.

Om de verschuiving van de echosignalen nauwkeurig te bepalen is er een nieuwe methode ontwikkeld, de *correlatie interpolatie techniek*. In deze methode wordt de *kruiscorrelatiefunctie* tussen twee echosignalen berekend. Zo'n correlatiefunctie geeft de mate van overeenkomst aan tussen twee signalen. Door de kruiscorrelatie te berekenen voor een aantal onderlinge verschuivingen van de signalen, kan de verschuiving bepaald worden die de beste overeenkomst oplevert. Deze verschuiving, die dus overeenkomt met de positie van de top van de kruiscorrelatiefunctie, is in het algemeen een goede benadering van de werkelijke onderlinge verplaatsing van de echosignalen. In de meeste correlatietechnieken worden eerst vele waarden van de kruiscorrelatiefunctie berekend, om daarna de positie van de top te kunnen bepalen. De correlatie interpolatie techniek maakt echter gebruik van slechts vijf waarden van de functie. De positie van de top wordt door middel van interpolatie van deze vijf waarden zeer nauwkeurig bepaald. Door het beperkte aantal functiewaarden dat wordt gebruikt kan de berekening veel sneller worden uitgevoerd dan met de conventionele correlatietechnieken. Uit de aldus verkregen schatting van de verschuiving van de signalen kan direct de verplaatsing van het hartspierweefsel langs de ultrageluidsbundel berekend worden, en daarmee ook de lokale weefsel-snelheid. Uit snelheidsverschillen binnen het hartspierweefsel kan tenslotte de vervorming van het weefsel worden berekend.

Opzet van het onderzoek

De correlatie interpolatie techniek werd in 4 verschillende situaties getest. Ten eerste werd de techniek toegepast op kunstmatige echosignalen, gegenereerd door de computer. De eigenschappen van deze testsignalen waren zoveel mogelijk in overeenstemming gekozen met de eigenschappen van echosignalen, zoals die te verwachten zijn in een echte meting aan bewegend hartspierweefsel. Door de verschuiving van de testsignalen te berekenen met de correlatie interpolatie techniek werden enkele basiseigenschappen van de methode, zoals de nauwkeurigheid, lineariteit en ruisgevoeligheid bepaald.

Ten tweede werd de techniek toegepast op reële echosignalen van een testobject. Voor dit doel werd een schijf gemaakt van een doorzichtig gel, homogeen gevuld met kleine deeltjes (grootte ongeveer $50\text{ }\mu\text{m}$) waartegen de ultrageluidsgolven reflecteren. De schijf werd gemonteerd aan een as, die met diverse snelheden kon draaien. Vervolgens werd het ultrageluid de schijf ingestraald, en werden de echosignalen langs een bepaalde observatielijns door de schijf ontvangen. Hiervoor werd een Hewlett-Packard HP77020 ultrageluids echosysteem gebruikt. Uit de ontvangen echosignalen werd met de correlatie interpolatie techniek zowel de snelheid van de schijf als zijn rotatiesnelheid berekend.

Ten derde werden echosignalen ontvangen van het kloppend hart van de hond en geanalyseerd met de techniek. Bij 7 honden werden met het echosysteem afbeeldingen gemaakt van de hartspier. De hoogfrequente echosignalen langs één of twee observatielijnen in het echobeeld werden opgeslagen en bewerkt. In een controle toestand werden de verdikking van de voor- en achterwand alsmede de verandering in de diameter van de linker kamer bepaald. Daarnaast werd getracht de rotatie van het hart te bepalen. Nadat deze metingen in de controle toestand waren verricht, werd aan het proefdier *imipramine* toegediend. Deze stof veroorzaakt een tijdelijke verslechtering van de conditie van de hartspier. In deze toestand werden weer de wandverdikking en de diameterverandering gemeten om te onderzoeken of een afname van de spierfunctie met de nieuwe techniek ook daadwerkelijk meetbaar was als een verandering in vervorming.

Ten slotte werd naast het dierexperimenteel onderzoek één meting verricht bij een proefpersoon. In deze studie werd nagegaan of de meettechniek ook toegepast kan worden bij de mens.

Resultaten

Uit de evaluatie met testsignalen en de metingen in de experimentele opstelling bleek dat de nauwkeurigheid van de methode ruim voldoende was om de vervorming van het hart te kunnen meten. Zo kon de snelheid in een weefselgebiedje van 2.2 mm lengte met een nauwkeurigheid van ongeveer $6\text{ mm}\cdot\text{s}^{-1}$ worden bepaald. De snelheidsschatting was lineair en werd nauwelijks beïnvloed door ruis in het signaal. Tevens bleek in de testopstelling dat de rotatiesnelheid van de schijf met succes bepaald kon worden uit het snelheidsverschil tussen twee gebieden in de schijf.

De experimenten bij de hond en de proefpersoon gaven resultaten voor de verdikking van het hartspierweefsel en voor de afname van de diameter van de linker kamer tijdens de ejectiefase die in overeenstemming zijn met de resultaten van diverse studies in de literatuur. Zo zien we in figuur 2a een voorbeeld van de verdikking van het hartspierweefsel in de voorwand van de linker kamer van de hond. De opname beslaat juist twee volledige hartcycli. Duidelijk is te zien dat er een verdikking van de wand optreedt gedurende de ejectiefase, die is aangegeven met de verticale stippellijnen. In figuur 2b is van hetzelfde hart de relatieve diameter weergegeven als

Figuur 2: Verdikking $\Delta d/d_0$ van de voorwand van de linker kamer (a) en de relatieve diameter D/D_0 van de linker kamer (b) als functie van de tijd. De doorgetrokken verticale lijnen geven het begin aan van elke nieuwe hartcyclus. De verticale stippellijnen geven het begin (BE) en het einde (EE) aan van de ejectiefase.

functie van de tijd. Zoals verwacht neemt de diameter af gedurende de ejectiefase. In tegenstelling tot wandverdikking en diameterverandering bleek de rotatie van het hart niet goed meetbaar.

Toediening van imipramine aan de hond veroorzaakte een tijdelijke verslechtering van de mechanische functie van het hartspierweefsel. Als gevolg van deze verslechtering werd tijdens de ejectiefase een kleinere verdikking van het spierweefsel gemeten dan normaal. Daarnaast was ook de diameterafname van de linker hartkamer gedurende de ejectiefase verminderd. Uit de experimenten bleek dus dat met de nieuwe techniek een afname van mechanische functie inderdaad meetbaar was als een verandering in de vervorming van het hartspierweefsel.

Tot slot

Samenvattend kan geconcludeerd worden dat met de correlatie interpolatie techniek een nieuwe methode is ontwikkeld om snel en nauwkeurig de lokale weefselsnelheid in de hartspier te kunnen meten. Uit de snelheidsinformatie kunnen vervolgens parameters met betrekking tot de vervorming van het hartspierweefsel berekend worden. Daarnaast bleek de techniek voldoende gevoelig te zijn om een afname van spierfunctie te kunnen detecteren als een verandering in weefselvervorming. Na verdere ontwikkeling van de methode is het dan ook te verwachten dat de correlatie interpolatie techniek in de toekomst gebruikt zal kunnen worden voor de transcutane bepaling van de lokale hartspiervervorming bij de patiënt.

Nawoord

Wanneer je aan het einde van je promotietijd terugkijkt op ruim 4 jaar onderzoek, dan bemerk je weer eens dat je al die tijd niet alleen bezig bent geweest. De onderzoeksresultaten die in dit proefschrift staan beschreven zijn dan ook mede tot stand gekomen door de inzet van vele collega's. Hoewel het natuurlijk onmogelijk is om op deze plaats iedereen persoonlijk te bedanken, wil ik toch graag enkele personen speciaal noemen.

In eerste instantie gaat natuurlijk veel dank uit naar mijn directe begeleiders, Theo Arts en Arnold Hoeks. Zij zijn een onmisbare steun geweest op het gebied van hartspiermechanica en ultrageluidstechnieken. De grondigheid waarmee Theo de voorlopige versies van dit proefschrift en diverse artikelen doorlas dwingt bewondering af, evenals de hoeveelheid parate kennis van Arnold op het gebied van ultrageluid. In het laatste stadium van het onderzoek werd de begeleiding geïntensiveerd met twee promotores, Rob Reneman en Arie Hasman. Ook zij hebben steeds weer tijd vrij weten te maken voor het doorlezen van de voorlopige versies van het proefschrift. De besprekingen met hen over de voorgestelde correcties zijn altijd zeer plezierig verlopen.

Naast een theoretische ondersteuning hebben diverse mensen bijgedragen aan de praktische uitvoering van het onderzoek. Ik denk daarbij met name aan de leden van het Ultrageluidslaboratorium voor hun hulp bij de technische realisatie van de experimentele opstelling, en aan het personeel van de operatiekamers voor het verzorgen van de dierexperimenten. Daarnaast wil ik Miel Cheriex en Caroline Lucas bedanken voor de diverse malen dat zij tijd hebben vrijgemaakt voor het uitvoeren van mijn experimenten. Graag bedank ik ook Rosy Hanssen voor haar secretariële ondersteuning, die vooral de volledige verwerking van twee omvangrijke artikelen omvatte.

Behalve de inhoudsdeskundige bijdragen aan het onderzoek zijn zeker ook de sociale contacten binnen je werkomgeving van groot belang. Ik ben daarom blij dat ik in de afgelopen 4 jaar veel mensen heb leren kennen met wie ik ook naast het werk goed kon opschieten. Daarom bedank ik graag iedereen die heeft bijgedragen aan een aangenaam verblijf binnen het Biomedisch Centrum en de vakgroep Biofysica. In het bijzonder wil ik mijn paranimfen, Jacqueline Bosman en Peter Bovendeerd, bedanken voor hun bijdrage aan de voorbereidingen van de promotie. In de laatste maanden voor de promotiedatum hebben zij gezorgd voor een prettige samenwerking, en hebben zo hier en daar voor mij wat werk uit handen genomen.

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Curriculum Vitae

Peter de Jong

- 14 mei 1964 : Geboren te Roosendaal.
- 1976-1982 : Gymnasium-B, Norbertus College te Roosendaal
- 1982-1986 : Studie Elektrotechniek, Technische Universiteit Eindhoven
Hoofdrichting Regel- en Systeemtechniek
Afstudeerrichting Medische Elektrotechniek
- 1987-1991 : Promotieonderzoek, Rijksuniversiteit Limburg te Maastricht
Vakgroep Biofysica, deelproject Hartspiermechanica
- 1990 : Young Persons Award (Euroson '90, Jeruzalem):
Aanmoedigingsprijs van de European Federation of Societies
for Ultrasound in Medicine and Biology