DEFORMATION IMAGING BY ULTRASOUND FOR THE ASSESSMENT OF REGIONAL MYOCARDIAL FUNCTION

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Abstract—Assessment of regional myocardial function, i.e. regional myocardial force development, remains an important goal in clinical cardiology as it gives important diagnostic and therapeutic information. Currently, a direct non-invasive measurement of regional force development is not feasible. However, regional function can be approximated by regional myocardial deformation as local force development and local deformation are closely linked.

Instantaneous tissue deformation is measured by ultrasound as the spatial gradient in local tissue motion between two acquisitions. Tissue motion can be estimated using several techniques such as the auto- and cross-correlation methodologies. Normalization of the instantaneous deformation to time gives a measure of the regional rate of deformation, i.e. strain rate. Integration of the strain rate curve over the cardiac cycle results in the total tissue strain.

In our laboratory, the application of ultrasonic strain and strain rate imaging in cardiology has been studied extensively. Different methodologies towards ultrasound based strain (rate) estimation have been developed and validated by prototyping on simulated ultrasound data sets and subsequently testing these methodologies in gel phantoms and animals using modified ultrasound scanners. Moreover, the clinical use of these techniques has been evaluated in a wide range of pathologies.

In this paper, an overview of this work will be given. Different methodologies towards cardiac strain (rate) estimation by ultrasound will be described. Clinical examples of the practical use of the current technique will be shown together with typical image artifacts and their potential solutions. Finally, it will be demonstrated that the combination of ultrasound cardiac deformation data with mechanical models of the left ventricle provides a way to actually estimate regional myocardial force development, i.e. true regional myocardial function.

INTRODUCTION

Ultrasound imaging is the clinical imaging modality of choice when diagnosing heart disease due to its bedside applicability, its real-time character and its excellent temporal resolution and this at a relatively low cost. In clinical practice, it can be used to visualize cardiac anatomy and blood flow which allows for a non-invasive diagnosis of pathologies such as ventricular hypertrophy, dilatation, cardiac tumors and valve disease. Additionally, echocardiography can be used to assess the performance of the heart in terms of ejecting blood, i.e. systolic function, and filling of the ventricles with blood after ejection, i.e. diastolic function. Hereto, several quantitative methodologies have been developed based on either gray scale or velocity imaging.

Gray scale imaging can be used to estimate systolic function by measuring for instance the relative change in diameter of the left ventricular cavity during ejection, i.e. the fractional shortening, or by calculating the relative amount of blood ejected during systole, i.e. the ejection fraction, based on a simple three-dimensional model of the left ventricular cavity and some measurements on the gray scale images [1]. Diastolic function on the other hand can for instance be assessed by measuring the displacement of the atrio-ventricular plane on gray scale images [2].

The introduction of velocity imaging (pulsed Doppler and color-flow) provided new tools to study myocardial function. The velocity profile of the blood as measured during ventricular filling at the mitral valve can for instance be used to characterize left ventricular diastolic function [1]. More recently, myocardial velocities measured at the mitral ring have also been used to this extent [3].

Although all of the above mentioned methods (and several others that are not discussed here) can easily be measured at bedside and are used in daily clinical practice for the quantitative assessment of myocardial function, none of them allows to measure regional differences in myocardial function as they only provide information on the perfor-
mance of the heart as a whole, i.e. on global cardiac function. However, many diseases such as coronary artery disease, result in regional abnormalities in myocardial performance. Such regional myocardial dysfunction is usually assessed qualitatively through visual appreciation of regional wall motion and deformation. Although some quantitative methods have been proposed to this extent, none of them has proven to be satisfactory. As the diagnosis of regional differences in myocardial function is important for patient therapy and prognosis, the quantitative assessment of regional myocardial function thus remains in important goal in clinical cardiology.

**Assessing Regional Myocardial Function**

The function of the heart is to pump oxygenated blood through the organs in the body supplying them with nutrients and to pump the de-oxygenated blood through the lungs, where new oxygen is taken up. The pumping function of the heart is obtained through its cyclic contraction caused by cyclic shortening and lengthening of individual heart cells. A cardiac (contractile) cell can shorten due to a redistribution of ions within the cell which results in a shape change, i.e. conformational change, of a large amount of myosin proteins each of which is associated with a force development of about 3-4 pN [4]. Regional function of the heart, i.e. regional myocardial function, can thus be defined as the regional ability to develop force as it is this local force development that will actively contribute to the pump function of the heart.

According to continuum mechanics, instantaneous three-dimensional strain $\varepsilon$ of an elastic body is directly related to all stresses $\sigma$ that act upon this body at a particular time instance $t$ through the elasticity $E$ of the object [5]:

$$\sigma_{ij}(t) = E_{ij}^{kl} \varepsilon_{kl}(t).$$

(1)

Unlike the situation typically encountered in mechanical engineering, myocardium can however not be modelled as a "passive" elastic body that is being deformed. It should rather be modelled as an "active" elastic body that is, in addition to the influence of external stresses, actively attempting to deform itself. This can be emphasized by replacing equation (1) with:

$$C_{ij}(t) + \sigma_{ij}(t) = E_{ij}^{kl} \varepsilon_{kl}(t),$$

(2)

where $C(t)$ represents the instantaneous active stress developed by the myocardium, i.e. regional contractility.

From the above reasoning it follows that regional myocardial function, i.e. regional myocardial stress development, and regional myocardial strain are intrinsically linked. As a direct (non-invasive) assessment of regional force development remains impractical, regional myocardial (contractile) function can thus in a first approximation be assessed by measuring regional myocardial deformation. In this approach, external stresses, i.e. $\sigma$ in equation (2), are thus assumed to be negligible.

**Ultrasonic Deformation Imaging of the Heart**

Since the early eighties, several methods have been proposed to estimate strain of tissues by means of ultrasound [6-9]. Further developments in ultrasound based strain estimation were induced in the early nineties by the introduction of elastography [10-12]. In this technique, tissue strain is linked to an externally applied (and thus known) force in order to assess the elastic properties of the tissue [13, 14].

The main difficulty in strain estimation of the heart is that most myocardial segments exhibit a combination of relatively large displacement and deformation during the cardiac cycle. Moreover, as clinical echocardiography is currently bi-dimensional, out-of-plane motion complicates accurate strain estimation. Nevertheless, several methods have been developed and have been shown to provide useful and accurate strain estimates of the heart.

**Principles of Ultrasonic Strain Rate Estimation**

Using the definitions in figure 1, strain can be written as:

$$\varepsilon = \frac{L_2 - L_1}{L_1} = \frac{(y_2 - y_1) - (y_1 - x_1)}{y_1 - x_1},$$

(3)

where $x_1, y_1$ and $x_2, y_2$ are the positions of a specific material point before and after deformation respectively. Dividing both sides of this equation by $\Delta t$, the time duration of the deformation process, gives:

$$\varepsilon = \frac{\Delta y}{\Delta x} = \frac{(y_2 - y_1)}{x_2 - x_1} \approx \frac{v_2 - v_1}{L_1}.$$

(4)

In other words, strain rate can be expressed as the spatial gradient in velocities.

![Figure 1: Measuring the position of particular material points of a bar with initial length $L_1$ at two time instances, $t_1$ and $t_2$, during the deformation, can be used to show that strain rate can be expressed as a velocity gradient.](image)

Strain rate estimation thus reduces to velocity estimation with subsequent application of a gradient operator. Ultrasound velocity estimators have been developed for many years and an excellent review was given by Jensen [15]. In general, the assumption is made that the reflected ultrasound signal is a scaled, delayed replica of the transmitted pulse.
By transmitting several pulses along each image line at a constant pulse repetition frequency (PRF), the motion of the reflected signal (and thus the scattering object) can be estimated. This motion directly determines the velocity of the object as the time interval between two position estimates is known (and equal to 1/PRF). Two important methods exist: in order to estimate the motion of the reflected signals. Both are briefly discussed below.

**Phase-shift estimators**

Phase-shift estimators make use of the fact that the phase of a sinusoidal signal is completely determined by two samples taken less than a quarter wavelength apart. Consequently, two such unique couples of samples are sufficient to completely determine the phase shift $\Delta \phi$ between two subsequent reflections. This phase shift can then be used to calculate the velocity $v$ since [15]:

$$ v = \frac{\Delta \phi \cdot c \cdot PRF}{4\pi f_T}, $$

with $f_T$ the frequency of the transmitted pulse and $c$ the velocity of sound in soft tissue.

Calculating the phase shift $\Delta \phi$ for all sampled points along the reflected signals can be done in a very computational efficient manner by use of the auto-correlation function [15]. Therefore, these estimators are often referred to as auto-correlation estimators.

Despite of the auto-correlation estimator being computationally favorable because of its real-time character, several disadvantages have been associated with it. The main ones are the limitation to small bandwidth signals, i.e. low axial resolution [11], aliasing [15], the increase in ambiguity of the estimation with decreasing center frequency [16] and attenuation effects [17]. Although in theory the estimator only requires two signals to estimate the phase shift $\Delta \phi$, in practice several signals are used in order to temporally average the estimates and thus reduce the estimators variance. For the same reason, the auto-correlation function is usually smoothed spatially by convolving it with a rectangular window.

**Time-shift estimators**

The phase shift $\Delta \phi$ in equation (5) can also be determined by estimating the motion of a signal pattern between two acquisitions. This is the time-shift estimate [15]. Several functions can be used to estimate the similarity between two signals as a function of their relative phase shift, i.e. to determine the motion of a particular signal pattern: the (normalized) cross-correlation, sum of absolute differences, sum of squared differences and others [18,19].

In general, these estimators overcome the limitations of low axial resolution and aliasing associated with phase-shift estimators [11,15,16]. However, they show to be more computative intensive and have thus not been made available in clinical systems that estimate velocity data sets within the two-dimensional image at high temporal resolution in real time. Moreover, in order to achieve subsample time-shift resolution without increasing the computational load significantly, the time-shift estimator function has to be interpolated. Several methodologies have been presented and compared in the literature [20].

**Spatial gradient estimation**

Myocardial velocity information can be obtained by either storing the velocity data sets as calculated by the scanner in a digital format (usually based on an auto-correlation approach) or by storing the raw data sets and calculating the velocities off-line. In both approaches, strain rate information is obtained by applying a gradient operator on the myocardial velocity estimates. As the calculation of numerical gradients is very noise sensitive, the velocity data are usually smoothed before applying the gradient operator. This can be done by applying a median or mean filter with a mask of typically 3x3mm. This however reduces the spatial resolution of the strain rate estimates.

Several approaches to calculate gradients numerically exist. Strain rate imaging has typically used linear regression through all velocity estimates within a well defined region (of typically 5-10mm depending on the echocardiographic view used). Moreover, in order to make the gradient estimation more accurate, a weighted velocity fit has been proposed [21,22]. A slightly different approach is used in "velocity gradient imaging" where the gradient is calculated by sub-dividing the myocardial wall in two regions and applying equation (4) directly, using the average velocity in each of these sub-regions as $v_1$ and $v_2$ respectively [23,24]. Other ways of assessing this gradient might be used but a direct comparison of different approaches has, to these authors knowledge, not been done.

**Implications of using phase shifts for velocity estimation**

Motion perpendicular to the image line does not result in a significant phase shift of the reflected signal. Using the phase shift $\Delta \phi$ as a basis for velocity estimation will thus only provide information on the axial component, i.e. the one along the image line, of the true three-dimensional motion. Since strain rate is calculated as the spatial gradient in myocardial velocities, this also implies that using this methodology, only one component of the three-dimensional deformation tensor can be estimated at a time.

**Acquisition rate**

Imaging of myocardial velocities was developed by adapting the filters of the more conventional blood velocity imaging, i.e. color flow imaging [25]. As a result, strain rate estimates...
Strain imaging

Strain images are obtained by temporally integrating the strain rate traces. Most often, integration is started at end-diastole (defined on a simultaneously recorded electrocardiogram (ECG)) and done over the whole cardiac cycle. Some examples are given in figure 4.

Several factors can cause the strain curve to drift, i.e. not to return to zero at the end of the cardiac cycle. This drifting is not possible from a physiologic point of view (as there is no net strain during a cardiac cycle) and can be compensated for automatically [33]. Whether this drift-compensation introduces an error in the strain estimates has not been studied in vivo validation of the method was obtained by comparing ultrasonic strain measurements with the values obtained by direct implantation of micro-crystals in animals [37]. Moreover, results in patients comparing strain values obtained by ultrasound with magnetic resonance imaging (MRI) tagging data were in good agreement [38]. Finally, not only the peak strain values but also the temporal behavior of the strain curves correlated well in a population of normals and patients between ultrasound and cine-MRI [39].

Normal strain (rate) profiles of the heart

The physiologic axes of the heart

In order to describe the three-dimensional deformation of the heart, a local heart coordinate system has been introduced [33]. It consists of three mutually perpendicular axes referred to as the radial (R), longitudinal (L) and circumferential (C) axis respectively. These are illustrated in figure 2. Normal strain components are referred to as RR, LL or CC strain, while CL, CR, LR, RL, RC and LC represent shear strains. RR, LL and CC strain represent respectively local wall thickening/thinning, longitudinal shortening/lengthening and circumferential shortening/lengthening of the ventricle.

As there are only a limited amount of acoustic windows through the thorax and as deformation can currently only be measured along the image line, not all normal strain components can be measured in all myocardial segments. As schematically illustrated in figure 3, ε_{LL} can be measured in all segments of the left ventricle and in the segments of the free wall of the right ventricle using the standard apical two- and four chamber echocardiographic views. However, ε_{RR} can only be measured in the inferolateral and anteroseptal walls while the assessment of ε_{CC} is limited to the anterolateral and inferoseptal walls in a parasternal short axis acquisition.

Normal findings

The different mechanical phases of the cardiac cycle are reflected in the normal cardiac strain rate profile. In the longitudinal direction, ejection of blood is associated with shortening of the ventricle resulting in negative systolic
strain rate values (see figure 4) while filling of the ventricle during diastole is associated with longitudinal shortening, i.e. positive strain rate values. Typically, two filling phases can be observed: early (or fast) filling, i.e. the "E-wave", when relaxation of the cardiac wall normally fills the ventricle for about 90% and atrial (or late) filling, i.e. the "A-wave", when the myocardial wall is deformed due to the raising pressure in the ventricular cavity as a result of atrial contraction. Both filling phases are separated by a period of no (or little) deformation, i.e. cardiac diastasis.

Normal values

Parameters that have typically been studied are: i) maximal systolic strain rate, ii) maximal early diastolic strain rate, iii) maximal late diastolic strain rate, iv) maximal systolic strain, and v) maximal strain after systole, i.e. postsystolic strain, and their timing with respect to the onset of the cardiac cycle. Accurate timing of the different mechanical phases of the cardiac cycle is thus required. The identification of end of ejection in particular has been shown to be essential [40,41]. Different methodologies have been developed for this purpose [42].

Longitudinal strain and strain rate values have been observed to be relatively homogeneous throughout the left ventricle. Normal peak longitudinal strain rate values are around -1.6, 2 and 1 s⁻¹ for systole, early and late diastole respectively. A normal peak systolic strain value in the longitudinal direction is about -20%. Normal values have been obtained in both children and adults [43,44]. During atrial filling, the longitudinal deformation of the wall begins at the basis of the ventricle and propagates towards the apex. The propagation velocity of this late diastolic deformation wave has been proposed as a parameter to detect pathologies [45,46]. In the normal heart, strain rate and strain values in the radial direction are approximately twice the longitudinal values. Finally, it has been shown that normal values in the right ventricle are higher and more heterogeneous [43,44].

Figure 3: Schematic illustration of the different strain and strain rate components that can be assessed with the current strain rate methodology using standard echocardiographic views.

STRAIN AND STRAIN RATE FOR THE ASSESSMENT OF REGIONAL MYOCARDIAL FUNCTION

As explained above, the rationale for strain rate imaging of the heart is summarized by equation (2) that shows that, as a first approximation, changes in myocardial deformation can be attributed to changes in local active stress development. This assumption has been validated in an animal study were regional active stress development was pharmacologically modulated through the infusion of "dobutamine", which has been shown to increase contractility, and "esmolol", that has been shown to have the opposite effect [47,48]. In this study, peak systolic strain rate was shown to change according to active stress development, i.e. lower values were measured during "esmolol" infusion while values increased linearly with the doses of "dobutamine" administered. More recently, this study was confirmed in an...
imals having regional abnormalities in myocardial active stress development due to ischemia [49]. Peak systolic strain rate has thus been identified as a useful index of regional myocardial function.

**POTENTIAL CLINICAL APPLICATIONS**

In order to illustrate the potentials of myocardial ultrasonic deformation imaging, many studies have been performed in both the animal and the clinical setting. One field of interest has been the development of an ultrasound technique that shows an increased sensitivity over the standard methodologies to detect sub-clinical disease, i.e. asymptomatic disease. In this context, studies have been conducted showing the increased sensitivity of strain rate parameters in patients with pathologies such as amyloidosis [50], aortic stenosis [51], ALCAPA [52] and others. Two other important potential clinical applications of the current technique will be discussed in the following sections.

**Quantitative stress echocardiography**

Patients with coronary artery disease make up an important group of the total cardiac patient population. Based on the stage in the evolution of the disease and the therapy used to treat the patient, the resultant functional characteristics of the myocardium can roughly be subdivided in the following groups: i) normal myocardium with normal perfusion, ii) ischemic myocardium, where an imbalance between oxygen consumption and oxygen supply (usually caused by hypo-perfusion) causes a change in muscle contraction, iii) stunned myocardium, where perfusion is (near) normal but where contractile function is abnormal (occurs after periods of ischemia), iv) hibernating myocardium, where chronic hypo-perfusion has resulted in an alteration of the myocardial microstructure and hence myocardial contractility is abnormal and v) infarcted myocardium which has become fibrotic due to an episode of total coronary occlusion. Infarcted myocardium has no chance of recovery. The extent of an infarction, i.e. whether it is transmural or not, can thus have important therapeutic consequences.

Although cardiac function can appear normal at rest, exercise can show potential underlying abnormalities in coronary blood flow as in this situation increased oxygen demand is not met by an adequate increase in supply due to the presence of a narrowing in this subtending coronary artery. In clinical practice, such induced changes in regional function can occur during either treadmill or bicycle exercise tests or may be induced pharmacologically by e.g. dobutamine. These exercise induced changes may be monitored by ultrasonic imaging in so-called stress-echocardiography which gives important diagnostic information. At present, stress echocardiography is performed in a qualitative manner by a visual assessment of regional wall motion and thickening. However, this approach has been shown to be both subjective and experience dependent [53]. An important application of ultrasound deformation imaging would thus be the quantification of stress echocardiography by quantitatively identifying regional differences in the response to exercise.

In order to better understand the regional deformation changes induced by exercise in the different ischemic substrates described above, a whole set of animal experiments were conducted in our laboratory. Normal myocardium is characterized by showing an increase in peak systolic strain rate during exercise while end-systolic strain initial increases and subsequently decreases. Any deformation occurring after the ejection phase, i.e. post-systolic strain, remains unaltered during stress. Although all of the ischemic substrates showed a reduced systolic strain rate, a reduced end-systolic strain and an increased post-systolic strain, stress testing could differentiate all of them. For instance, unlike normal myocardium, acutely ischemic myocardium responded to exercise by showing a reduction in peak systolic strain rate, a reduction in end-systolic strain and an increase in post-systolic strain while exactly the opposite response was observed for stunned myocardium [54]. Using the same three deformation parameters, non-transmurally infarcted myocardium could be differentiated from transmurally infarcted myocardium and from the other ischemic substrates [55].

Based on these observations in animal models, strain rate imaging during exercise should enable the differentiation of different ischemic substrates in a clinical setting and therefore be an important tool to set out therapy strategies. Initial clinical studies have already been performed not only showing the feasibility of this approach [56] but also its accuracy by comparing the results against nuclear techniques [57].

**Therapy follow-up, monitoring and guidance**

Strain rate imaging does not only provide useful information for diagnostic purposes but also for therapy optimization and follow-up. For instance, recent studies in patients with genetic metabolic diseases have shown that ultrasonic strain rate imaging could identify an improvement in cardiac function early after treatment while conventional methods required much longer follow-up periods to show benefit or could not identify changes at all [58,59].

Another potentially important application could be found in a patient population showing electrical conduction defects of the myocardium, which results in an asynchronous (and therefore less effective) contraction of the ventricles. If asynchronicity becomes too pronounced, these patients are currently treated using left ventricular pacing. Indeed, by introducing an electrode into a specific site of the ventricle during (minimally invasive) surgery, regional contrac-
tion can be induced by an external pacemaker. This kind of therapy is referred to as "cardiac resynchronization therapy" (CRT).

Recently, a study of our lab has shown that strain rate imaging was able to show functional improvement in resynchronized hearts [60]. This therapy monitoring might be further developed into therapy guidance by optimizing the delay between the spontaneous and artificially induced contraction based on intra-operative strain rate images.

**PITFALLS OF THE CURRENT METHODOLOGY AND POSSIBLE SOLUTIONS**

**Angle dependency**

One of the major limitations of the current implementation of velocity, strain rate and strain imaging is that only the axial component, i.e. the component along the image line, of the true three-dimensional velocity and deformation can be assessed. As a consequence, the strain (rate) values are angle dependent, i.e. dependent on the position of the cardiac wall within the ultrasound image [61]. The problem can be limited by making sure that ultrasound insonation is either perpendicular or parallel to the myocardial wall under investigation during acquisition of the velocity data [33]. Moreover, if some simple assumptions are made about the way the heart deforms, the strain rate error induced due to imaging the heart wall under an angle can be estimated and compensated for [21]. Based on theoretical modelling, it has recently been shown that, using the current methodology, the angle between the ultrasound beam and the myocardial wall under investigation should not be larger than about 15 degrees in order to keep the relative strain error below about 10% [62]. Although the effect of angle-dependency can thus be minimized in practice by appropriately acquiring the ultrasound data, it still implies that a significant amount of experience of the operator is required which automatically increases the inter-observer variability. Finding a solution to the angle-dependency problem could thus increase robustness and reproducibility of the current methodology significantly.

One possible solution to this problem is the combination of multiple one-dimensional measurements obtained from different transducer positions. Using techniques for image registration, the three-dimensional motion/deformation characteristics of the heart might then be reconstructed.

Another solution to this problem is given by estimating the velocity in multiple dimensions. Here, the time-shift estimator method as discussed above can be generalized in order not only to search for a specific signal pattern along the image line but also in neighboring image lines. This principle is illustrated in figure 5 and was initially proposed in the field of elastography [63]. More recently, a similar but slightly different approach was proposed by looking for the optimal match of a two-dimensional window in the subsequent image [64]. As in this way, both in-plane components of the velocity vector can be estimated, all in-plane strain and strain rate components can be obtained (both normal and shear). Recently, this approach has been shown to be feasible for two-dimensional strain rate imaging of the human heart in vivo [65]. This methodology has then been optimized based on simulations [19] and was recently validated in vitro against micro-crystal data [66]. Most likely, this approach will not only enable to measure several components of myocardial deformation from a single data acquisition but will also solve the angle-dependency problem of the current methodology.

Obviously, the same "tracking" principle can be used if three-dimensional data sets could be acquired at sufficient frame rate in order to obtain all components of the three-dimensional strain rate tensor. As three-dimensional echocardiography becomes feasible with the use of fastly rotating phased arrays or by using 1.75D or full 2D arrays, three-dimensional strain rate imaging could become possible in the relatively near future.

**Variance of the strain rate estimates**

A second important limitation of the current implementation of strain rate imaging is that strain rate estimates typically show a relatively large variance, i.e. strain rate curves are usually relatively noisy. Being the spatial derivative of the velocities, the strain rate is highly dependent on the quality of the velocity data. Therefore, velocity estimators with a small variance are favorable and velocity data will typically be regularized, e.g. filtered, in space and/or time prior to applying the gradient operator. This, however, reduces the spatial resolution of the technique.

A possible solution to this problem is to use a spatial gradient operator that is not that sensitive to input noise. Indeed, the relatively large variance of the strain rate estimates can to a large extent be attributed to the noise sensitivity of the numerical gradient operator, i.e. small changes or noise in the velocity estimates are significantly amplified by the gradient operator. One approach to obtain a more ro-
bust gradient operator has been based on fitting an analytical model to the velocity estimates and subsequently deriving the model analytically [67]. As, in general, there is no a priori information on the spatial distribution of the velocities, i.e. on the model to be fitted, the use of smoothing B-splines has been proposed [68]. Using this approach, estimates were shown to be less noisy while inhomogeneities in deformation characteristics were preserved.

**FUTURE PERSPECTIVES**

Notwithstanding the fact that the current strain rate methodology has been validated and has been shown to be clinically useful in the assessment of regional myocardial function, further developments of the technique will be required in order to find its access into daily clinical routine. Hereto, more robust, multi-dimensional strain rate estimators should (further) be developed. Better understanding the influence of cardiac mechanics and ultrasound data acquisition on the strain (rate) estimates will be important in this context. With this goal in mind, a virtual engineering environment was recently proposed by merging a kinematic model of the heart with a simulation environment for ultrasonic imaging [69]. This setup should allow to study the influence of cardiac mechanics, e.g. cardiac torsion, ultrasound data acquisition and data post-processing since (virtual) ultrasound strain and strain rate estimates can be compared to the true deformation characteristics given analytically by the model. Finally, in order to be clinically useful, post-processing time of the technique should be reduced by e.g. automatic tracking of the region of interest throughout the cardiac cycle. Promising results have already been obtained in this context through automated segmentation of the left ventricle [70].

Towards measuring active stress development

As discussed above, measuring regional myocardial deformation only represents a first approximation towards the assessment of regional myocardial function. Indeed in addition to regional myocardial active stress development, external stresses (i.e. \( \sigma(t) \) in equation (2)) can induce regional deformation. Although the validity of this approximation has already been tested experimentally in animal models [47, 49], it might turn out not to hold in any situation.

In order to attempt to estimate regional active stress development and thus to compensate for any deformation induced by external stresses, a spring-mass model of the left ventricle has recently been proposed [71]. It has been shown to predict active stress values in an animal model that are well within the range of active stress values measured in single muscle strips ex vivo. Moreover, during dobutamine infusion, i.e. pharmacological increase of cardiac contractility, significantly higher values for active stress development were found [72]. Mechanical models of the heart in combination with ultrasound deformation imaging might thus provide estimates on regional active force development.

**CONCLUSIONS**

Ultrasound strain (rate) imaging is a new imaging modality that can be used to quantify local myocardial deformation at high temporal resolution. The method offers new possibilities to study regional myocardial function which should give new insights into changes in local deformation over a wide range of cardiac pathologies and which could also provide a new quantitative tool to monitor the benefits of therapy. Although currently the technique remains angle dependent, new developments in multi-dimensional strain and strain rate estimation will most likely solve this problem. Moreover, more robust strain rate estimators will be developed together with tools to speed up data post-processing. These future developments will contribute to the acceptance of this technique in daily clinical routine.

**REMARK**

In order to improve and stimulate research in the field of ultrasonic deformation imaging of the heart, the following web site has been created: http://www.strainrateimaging.org.

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