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Albinsson, John

DOI:
10.1016/j.ultrasmedbio.2014.05.010
10.1007/s11517-016-1593-7
10.1007/978-3-319-12967-9_4
2017

Document Version:
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Albinsson, J. (2017). Advancements of 2D speckle tracking of arterial wall movements (First ed.) Lund university: Department of Biomedical Engineering, Lund university DOI: 10.1016/j.ultrasmedbio.2014.05.010, 10.1007/s11517-016-1593-7, 10.1007/978-3-319-12967-9_4

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Advancements of 2D speckle tracking of arterial wall movements

John Albinsson

LUND UNIVERSITY

DOCTORAL DISSERTATION
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To be defended in Segerfalksalen, BMC, Lund, on May 12 at 09:15.

Faculty opponent
Professor Hevré Liebgott
CREATIS, University of Lyon
Cover illustration

Figure shows the principals of motion estimation using the block-matching method presented in Paper I. The three ultrasound images depict a skeletal muscle (extensor digitorum communis) of a volunteer. The nine crosses in each image indicates the position of the center of one kernel.

ISBN: 978-91-7753-220-0 (printed version)
ISBN: 978-91-7753-221-7 (electronic version)
Report nr: 2/17
ISRN: LUTEDX/TEEM—1108—SE
Printed in April 2017 by Tryckeriet i E-huset, Lund, Sweden

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Title: Advancements of 2D speckle tracking on arterial wall movements

Abstract:
Cardiovascular diseases are the leading cause of death worldwide. In order to improve the diagnostics and facilitate early interventions of cardiovascular diseases, knowledge about the physiology of the vascular system in both healthy subjects and in subjects with vascular disease is needed. In order to learn more about the physiology of the vascular system and possibly predict cardiovascular diseases, accurate motion estimations of the arterial wall is needed. It has been the aim of this thesis to develop more robust motion estimation methods for use on cine loops to investigate the entire thickness of the arterial wall.

In this thesis, the concept of 2D speckle block matching was expanded with the use of an extra kernel for improved robustness and tracking accuracy. It was shown that the use of an extra kernel reduced the motion estimation errors when using a constant kernel size (in silico and on phantoms), or reduced the needed size of the kernel while maintaining the level of motion estimation errors (in vivo). Further, a sub-sample estimation method has been developed which combines two previously presented methods: parabolic and grid slope sub-sample interpolation. It was found that by combining the two methods with a threshold determining which method to use, the proposed method reduced the absolute sub-sample estimation errors in simulated and phantom cine loops. A limited in vivo evaluation of estimations of the longitudinal movement of the common carotid artery using parabolic and grid slope sub-sample interpolation and the proposed method were conducted showing that the method worked well in vivo.

The two methods were combined to estimate the longitudinal wall movement of the right common carotid artery on 135 healthy volunteers for improved understanding of the wall movements. The results show that the pronounced variation in patterns of longitudinal movement of the common carotid artery previously shown in young healthy subjects is also present in middle-aged and older healthy subjects. However, the patterns of movement seen in middle-aged and older subjects are different from those commonly seen in young subjects, including the appearance of two additional distinct phases of movement, and thus new complex patterns of movement.

The use of ultrasound sampled at a high frame rate has the potential to visualize previously unknown information of the longitudinal movement. An iterative scheme for Lagrangian motion estimations in cine loops collected at high frame rates was developed. A phantom evaluation using ultrasound cine loops showed a reduction by an average 54% in the estimated velocity errors compared to a standard method. It also showed a reduction by an average 73 % in the estimated displacement errors. A feasibility test of tracking in vivo indicated good agreement with motion estimations using a low frame rate cine loop.

This thesis thus present and evaluate refined methods to measure vascular function through the estimation of longitudinal movement.

Keywords: Ultrasound, block-matching, tissue motion, longitudinal movement

Classification system and/or index terms:

Supplementary bibliographical information:
ISRN: LUTEDX/TEEM—1108—SE
Report-nr: 2/17

ISSN and key title:
ISBN:
978-91-7753-220-0 (Print)
978-91-7753-221-7 (Electronic)

Recipient’s notes:
Number of pages: 144
Price: No

Security classification:

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Signature: John Albinsson
Date: 2017-04-10
Public defence
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Advisors
Associate Professor Magnus Cinthio
Department of Biomedical Engineering, Lund University

Associate Professor Tomas Jansson
Clinical Sciences Lund, Biomedical Engineering, Lund University, Lund, Sweden
Medical Services, Skåne University Hospital, Lund, Sweden

Associate Professor Åsa Rydén Ahlgren
Department of Medical Imaging and Physiology, Skåne University Hospital, Malmö, Sweden
Department of Translational Medicine, Lund University, Malmö, Sweden

Faculty Opponent
Professor Hevré Liebgott
CREATIS, University of Lyon

Board of Examination
Professor Johan Carlson
Department of Computer Science, Electrical and Space Engineering at Luleå University of Technology, Luleå

Professor emeritus Tomas Gustavsson
Department of Signals and Systems, Chalmers, Göteborg

Associate Professor Kerstin Jensen-Urstad
Karolinska Institutet, Solna

Deputy member:
Associate Professor Sven Månsson
Medical Radiation Physics, Malmö, Lund University

Chairman
Associate Professor Johan Nilsson
Department of Biomedical Engineering, Lund University
Dedication

To my loved ones
Present and absent

You can’t change the world
But you can change the facts
And when you change the facts
You change points of view
If you change points of view
You may change a vote
And when you change a vote
You may change the world

—Depeche Mode
Abstract

Cardiovascular diseases are the leading cause of death worldwide. In order to improve prevention and treatment of cardiovascular diseases, knowledge about the physiology of the vascular system in both healthy subjects and in subjects with vascular disease is needed. The study of the movement of the arterial wall can increase that knowledge. Studies of the radial component of the movement of the arterial wall have already done that for centuries. However, our knowledge of the longitudinal component is scarce. Although the knowledge concerning the longitudinal movement of the wall of the common carotid artery has increased significantly since it was first reported a decade ago, the function of and the mechanisms underlying this movement are still not fully understood, and further research is needed. Our experience is that only images of the highest quality are likely to give accurate and reliable longitudinal motion estimations of the arterial wall using block-matching. As capturing that level of quality is demanding also for very skilled sonographers, the numbers of collected cine loops, i.e. sequences of ultrasound images, to be useful for longitudinal motion estimations can be somewhat limited. It is thus of interest to develop more robust motion estimation methods for use on cine loops of lower image quality to investigate the entire thickness of the arterial wall. In order to not limit the use of our methods, the aim while developing the presented methods were a generic in vivo use on all tissue with a reasonable stable speckle pattern.

In this thesis, the concept of 2D speckle block matching was expanded with the use of an extra kernel for improved robustness and tracking accuracy. Tests were performed both on how the motion estimation errors change using a constant kernel size, and conversely, what kernel size is required to maintain a constant motion estimation error. It was shown that the use of an extra kernel reduced the motion estimation errors (mean = 48 % [in silico]; mean = 43 % [phantom]) with a constant kernel size, or reduced the size of the kernel (mean = 19 % [in vivo]) while maintaining the level of motion estimation errors.

Further, a sub-sample estimation method has been developed which combines two previously presented interpolation methods: parabolic and grid slope. It was found that by combining the two methods with a threshold determining which method to use, the proposed method reduced the absolute sub-sample estimation errors in silico and phantom cine loops compared to sub-sample interpolation of the image (14 %), parabolic sub-sample interpolation (8 %), and grid slope sub-sample interpolation (24 %). A limited in vivo evaluation of estimations of the longitudinal movement of the common carotid artery using parabolic and grid slope sub-sample interpolation and the proposed method were conducted. The magnitudes of the movement in two cine loops from the same volunteer were used to calculate the coefficients of variation of the three sub-sample methods which
were found to be 6.9, 7.5, and 6.8 %, respectively. Moreover, the proposed method is computationally efficient and has low bias and variance.

The two methods were combined to estimate the longitudinal wall movement of the right common carotid artery on 135 healthy volunteers for improved understanding of the wall movements. The results show that the pronounced variation in patterns of longitudinal movement of the common carotid artery previously shown in young healthy subjects is also present in middle-aged and older healthy subjects. However, the patterns of movement seen in middle-aged and older subjects are different from those commonly seen in young subjects, including the appearance of two additional distinct phases of movement, and thus new complex patterns of movement. Three of the five phases showed a significantly correlation with age. Also, indications of changes in the prevalence of different patterns of the longitudinal wall movement with age were seen.

The use of ultrasound sampled at a high frame rate has the potential to visualize previously unknown movement patterns. However, the displacement of the studied object will mostly be very small between two consecutive images which will result in large relative estimation errors if using block-matching. Thus, an iterative scheme for Lagrangian motion estimations in cine loops collected at high frame rates was developed. A phantom evaluation using ultrasound cine loops sampled at 1300 frames per second showed a reduction by an average 54 % in the estimated velocity errors (set velocities 1.1 and 2.2 mm/s). It also showed a reduction by an average 73 % in the estimated displacement errors (set displacements 0.6 and 1.1 mm). A feasibility test of tracking in vivo indicated that the estimations agreed well with estimations using a low frame rate.

In conclusion, in this thesis three methods are presented for robust and fast motion estimation using 2D speckle block matching. The methods have been tested using cine loops collected in silico, on phantoms, and (most importantly) in vivo, and they have shown robust tracking performance. The methods could be important tools for estimating motions in vivo and thus for furthering our knowledge about the physiology, e.g. of the vascular system, in both healthy and diseased individuals.
Populärvetenskaplig sammanfattning


I denna avhandling presenteras tre snabba och robusta metoder för mätning av rörelser i sekvenser av ultraljudsbilder. Metoderna har vid tester på rörelser i simulerade ultraljudsbilder, ultraljudsbilder av objekt som efterliknar mänsklig vävnad, och (slutmålet) ultraljudsbilder från människor, producerat mätningar vars noggrannhet är signifikant bättre (i flera fall 50 %) än jämförbara metoder.


Denna avhandling består av fem vetenskapliga studier. I dessa studier har vi undersökt de tre stegen som används vid blockmatchning och utvecklat metoder för en förbättrad bestämning av rörelser. Vi har infört användandet av två mallar i stället för en och dessutom använder vi en sökmetod som minskar beräkningstiden jämfört med
konventionella metoder. Efter en undersökning av hur andra steget påverkar det tredje steget, kunde vi utveckla en ny metod för sub-pixel bestämning. En möjlighet att skaffa mer kunskap om rörelser är att använda ultraljudsbilder som har samlats in med en hög bildhastighet. Problemet för en blockmatchningsmetod är då att rörelserna per bild blir väldigt små, vilket leder till att den ofrånkomliga mätosäkerheten i rörelsebestämningen ger stora sammanslagna fel. Genom upprepade rörelsebestämningar mellan bilder på olika tidsavstånd har vi kunnat förbättra noggrannheten i bestämningen av både den lokala och totala rörelsen. Vi har även i ultraljudsbilder insamlade vid normal bildhastighet (ca 50 bilder per sekund) uppskattat den längsgående rörelsen i halspulsådern på mer än 100 friska frivilliga forskningspersoner. Fem distinkta faser i rörelsen kunde definieras (varav två hittills okända) och individerna kunde delas in i fem olika grupper. Alla grupper innehöll inte alla faser och de hade olika förhållanden mellan storleken på faseri i sina rörelsemönster. Även om detta har utökat vår kunskapsbas om kärlväggen fysiologi och det normala åldrandet av kärlväggen, så behövs det mer forskning för att använda denna nya kunskap inom sjukvården.
Acknowledgements

Nine years ago, I stepped into Elmät looking for a Master thesis project. The project turned into a manuscript and after some detours it suddenly transformed into a Doctoral thesis. Now when it is time to summarize this work, there are a number of individuals that have been very important and helpful along the way to whom I would like to show my gratitude.

Thank you Magnus! Without your support and enthusiastic response to my work this goal would never have been reached. People has commented my struggle to get my papers published, but I think that your struggle to battle my opinion on the results and to get me going in the right direction have been greater. Naturally, this project hadn’t existed at all if not Sofia Brorsson had asked you to do it, but it was you Magnus who pushed the whole distance. Please take care.

But we were not without help. From the early manuscripts to the final version of this thesis, the proofreading of Tomas has been fundamental for the quality of the text. Åsa, you entered a little later and still claim that you do not understand the technical stuff in my manuscripts. However, your questions and skillful reviewing have several times forced me to take a step back and to re-write my texts for them to be understandable. A great thank you to both of you.

A special thanks goes to Maria and Tobias, to whom I said “Hello” in the master-thesis-room and with whom I still share a room. The comments about our crammed room have been plenty but I have never had reason for complaints. Your presence and friendship have been a great help during this time.

During my time as a PhD-student, I have had the privilege to spend some of my time abroad. With the support given both in Florence and in Sendai, the experience of my visits were amazing and I will have great memories for the rest of my life. Thank you for your support.

I would also thank all the customers of the Cookie Empire and everyone else that made all my coffee breaks, or rather cookie breaks, a pleasant pause from work. A special thanks goes to the leader of the pack, Johan, whose support has been crucial during my time as a PhD-student.

I would like to greatly acknowledge the sponsoring organizations. Without the financial support from the Swedish Foundation for International Cooperation in Research and Higher Education, the Knut and Alice Wallenberg Foundation, the Medical Faculty,
Lund University, the Skåne County Council’s Research and Development Foundation, and from the Swedish Research Council this work would not have been possible. Thank you!

Last, but perhaps greatest, I would like to thank my family which has been a solid support through this time even if they do not know what I have been doing.
List of publications

I. Improved Tracking Performance of Lagrangian Block-Matching Methodologies Using Block Expansion in the Time Domain In Silico Phantom and In Vivo Evaluations

John Albinsson, Sofia Brorsson, Åsa Rydén Ahlgren, and Magnus Cinthio


Author’s contribution: Method development; planning of in silico set-up and ultrasound measurements; motion estimations in all cine loops and analyze of data; main author of manuscript.

II. Tracking Performance of Several Combinations of Common Evaluation Metrics and Sub-pixel Methods

John Albinsson, Tomas Jansson, and Magnus Cinthio

_16th Nordic-Baltic Conference on Biomedical Engineering, IFMBE Proceedings 48, DOI: 10.1007/978-3-319-12967_4, 2015_

Author’s contribution: Planning of project; simulating cine loops; motion estimations and analyze of data; main author of manuscript.

III. A combination of parabolic and grid slope interpolation for 2D tissue displacement estimations

John Albinsson, Åsa Rydén Ahlgren, Tomas Jansson, and Magnus Cinthio

_Medical & Biological Engineering & Computing, DOI: 10.1007/s11517-016-1593-7, 2016_

Author’s contribution: Method development; planning of in silico set-up, ultrasound measurements, motion estimations, and analyze of data; main author of manuscript.
IV. Phases and resulting patterns of the longitudinal movement of the common carotid artery wall in healthy humans – influence of age and gender

Magnus Cinthio, John Albinsson, Tobias Erlöv, Niclas Bjarnegård, Toste Länne, Åsa Rydén Ahlgren

Manuscript

Author’s contribution: Developing the methods used for motion estimation; participated in the classification of the movement patterns and the planned statistics, co-author the manuscript

V. Iterative 2D speckle tracking in cine loops from high frame rate ultrasound

John Albinsson, Hideyuki Hasegawa, Hiroki Takahashi, Åsa Rydén Ahlgren, and Magnus Cinthio

Manuscript – submitted 20170307

Author’s contribution: Method development; motion estimations and analyze of data; main author of manuscript.
Abbreviations

2D – two dimensional
3D – three dimensional
CC – Cross-Correlation
FS – Full Search
GS15PI – sub-sample method developed in paper II
IQ – In-phase Quadrature
NCC – Normalized Cross-Correlation
RF – Radio Frequency
SAD – Sum of Absolute Difference
SSD – Sum of Squared Difference
1. Introduction

Clinical investigations and research using ultrasound is an important clinical image modality and is very likely to continue to be. Among several benefits, the high temporal resolution in an ultrasound acquisition makes it very suitable for investigating dynamic processes in vivo in real time. In many cases, an important step towards the sought after information is estimating the observed motions in the ultrasound cine loops.

This thesis has investigated motion estimations in ultrasound cine loops using block-matching in general, and has applied the accumulated knowledge to estimate the longitudinal movement of the intima-media complex of the common carotid artery in vivo in healthy volunteers. The investigations were conducted using both frame rates used in clinical investigations, and plane wave imaging for high frame rate sampling.

1.1 Outline of the thesis

The outline of this thesis is as follows: Chapter 2 introduces ultrasound and presents the fundamentals of how it works, how the image data are presented, and how the types of image data are related. Chapter 3 presents information about motion estimation methods in consecutive images in general, and some methods specifically developed for use with ultrasound. Chapter 4 describes block-matching which is the base method used in the papers presented in this thesis. Important parts of a block-matching method are defined and some basic knowledge is presented. The sources of ultrasound images and their pros and cons are presented in Chapter 5. Chapter 6 gives a description of the longitudinal movement of the arterial wall. A short description of the papers included in the thesis is given in Chapter 7 followed in Chapter 8 by a discussion relating to both the papers with some general reflections on conducting research before a summary in Chapter 9 of the primary knowledge gained during this work. The thesis is concluded in Chapter 10 with some prospects.
2. Ultrasound

The content in this chapter can be found in a variety of textbooks, e.g. [1, 2], unless otherwise specifically referenced.

2.1 Fundamentals

Sound is oscillating pressure variations travelling through a medium. Three groups of sound has been defined based on their oscillation frequency: infrasound (below 20 Hz), acoustic sound (20 Hz – 20 kHz), and ultrasound (above 20 kHz). In clinically used ultrasound, the commonly used frequencies range from 1 to 20 MHz which is a compromise between spatial resolution and the depth that is visible in the images.

The so called “pulse-echo method”, i.e. a short pulse of ultrasound is transmitted into a patient and the resulting echoes received, is used to form an image of the interior of the patient (Figure 1). The echoes are a natural result of ultrasound

![Stylistic representation of the pulse-echo method. On short ultrasound pulse is transmitted from the probe and reflected to varying degrees from encountered volumes with acoustic impedance differing from the surrounding tissue. A possible sampled signal (an A-line) is show at the bottom.](image-url)
passing from an area with one level of acoustic impedance into an area with a different level of acoustic impedance.

\[ Z = \rho * v \]  

(1)

Here \( Z \) is the acoustic impedance, \( \rho \) is the density of the media, and \( v \) is the speed of sound in the media. The fraction of sound that is reflected is given by the reflection coefficient:

\[ R_A = \frac{Z_2 - Z_1}{Z_2 + Z_1} \]  

(2)

Here \( R_A \) is the coefficient of reflection for amplitude, \( Z_1 \) is the acoustic impedance in the current media, and \( Z_2 \) is the acoustic impedance in the next media. The difference in acoustic impedance of different types of soft tissue in the human body is usually rather low. The benefit is that while some of the ultrasound energy will be reflected when the ultrasound encounter a new acoustic impedance (typically a new type of tissue) and provide data for the image formation, most of the energy will continue deeper inside the body to potentially be reflected there. Normally, an ultrasound image is built one line (or column) at a time by transmitting a pulsed beam of ultrasound which is focused at a certain user defined depth in the patient. The beam will have a certain elevational thickness and its minimal width at the point of focus. The beam is produced by a number of piezoelectric elements in a probe. As the acoustic impedance both varies within each type of tissue and the reflecting surfaces are often not smooth, the reflected ultrasound reaching the probe will be a superimposed wave of reflections. Adding the sampled ultrasound data by timing the data from the various probe elements so the direct echoes will have been reflected at the same depth along the line to be produced will have the effect that the reflections from this point will get a constructive interference while reflections from other points will interfere destructively. This process is called beamforming. If the reflections were produced by a large structure in the body, several neighboring pixels will contain similar information and together they will form a visible structure. In many cases the reflections will be from objects that are small, unevenly shaped and/or have a small difference in the acoustic impedance towards the surrounding tissue. The reflections will be weak and depending on the angle of the ultrasound and the resulting ultrasound image will have a pattern that resembles noise. This pattern, so called speckle, is quite different from noise as it is stable over time and reproducible by repositioning the probe and the reflecting tissue in the same geometrical position. However, as the speckle pattern is created by superimposing several weak reflections, the pattern will change as the probe is
moved compared to the reflecting tissue. This is a fairly slow process often requiring a movement within the image plane in excess of 10 mm before being clearly visible. Typically, ultrasound data are collected one line per transmitted ultrasound pulse with consecutive lines translated sideways to build a two-dimensional (2D) image. The process is then repeated to sample image data over time to study how movement of objects. Equipped with a special transducer, some modern ultrasound scanners can sample data in three spatial dimensions (3D). The data are then sampled as a stack of 2D data, where each set of 2D data is collected in an image plane parallel to the first but with a perpendicular offset. One drawback of creating an image line by line is the time needed for the collection of data which can lead to motion artifacts within an image. This is an increasing problem when sampling 3D cine loops. One solution is plane wave imaging in which an unfocused plane wave is transmitted using all elements in a transducer and all elements are used in receive (see Chapter 2.3).

Ultrasound has a number of benefits compared to other imaging modalities:

- Safety; there are no known long term risks of using ultrasound in vivo.
- Portability; an ultrasound machine is highly portable and is easy to move to the bed of a patient.
- Price; an ultrasound machine has the lowest price tag of the image modalities except for superficial optical systems.
- Timing; an ultrasound investigation is conducted in real time with a temporal resolution high enough to study most of the physiological events in the body. The use of plane wave imaging can further improve this resolution.
- Resolution; the spatial resolution of a state-of-the-art ultrasound machine is better than PET and SPECT, and is on par with MRI and x-ray/CT.

This makes ultrasound superior in many and diverse imaging situations. However, there are also limitations. Among the considerations of the use of ultrasound are:

- Risks; Two short term risks are heating of and implosions in the tissue, but these risks are well known and can easily be avoided.
- Gases; when used in vivo ultrasound cannot penetrate gas filled cavities due to the very low acoustic impedance of most gasses which excludes investigations of healthy lungs and can cause problem when investigating the intestines.
- Bones; ultrasound cannot normally enter bones in vivo due to the very high acoustic impedance of bones.
• Scatter and absorption; soft tissue is made up of a rather inhomogeneous material when looking on a cellular level. This causes quite an amount of signal loss as the sound waves are reflected away from the transducer. This loss is an increasing problem in severely obese patients. As both the axial resolution and loss of signal increases with the frequency of the ultrasound the operator has to optimize the used frequency.

Ultrasound is commonly used in vivo to investigate blood flow and soft tissue, e.g. [3-11]. The use is very diverse and has several application areas. The blood flow investigations range from functionality tests of the heart valves by estimations of the blood flows in the heart, through the blood flow in arteries, to the perfusion in the kidneys. Soft tissue investigations range from inspection of the heart muscle and the eyes to prenatal ultrasound investigations.

2.2 Ultrasound data for motion estimation

The most basic ultrasound signal is the amplified voltage measured from a piezoelectric probe. Displaying the received echoes after a transmitted ultrasound pulse on an oscilloscope gives what is called an A-mode line. By repeatedly transmitting and sampling the A-mode line at a reasonable pace without displacement of the transducer, an M-mode image is produced by displaying the A-mode lines side-by-side (Figure 2). The M-mode image facilitates the possibility to see how the studied reflectors move by a comparison of the lines. If the A-mode lines are sampled at slightly different horizontal positions or with slightly different angle towards the surface, the combined lines will form an image over the spatial distribution of the reflectors. It is also possible to create 3D images by further shifting the probe perpendicular to the previous scan plane. However, even if an image can be acquired by translating a single probe, the spatial resolution will be poor and today the ultrasound probe contains an array of piezoelectric elements to improve image quality.

The ultrasound data sampled from a number of piezoelectric elements are beamformed into a line of data similar to an A-mode line but with an improved image quality and is mostly called RF (radiofrequency) data when an image is to be sampled. The beamformed data (RF data) is converted by filtering, IQ-demodulation, and resampling into In-phase Quadrature (IQ) data [12]. This converts the sampled real valued pressure data into a complex number with an amplitude and a phase starting at zero for the first sampled RF data. The number of data points are also normally reduced and, if performed correctly, the RF data can be reformed from the IQ data. The magnitude of the IQ data have much larger
dynamic range than any screen, and thus the logarithm with base 10 of the data are calculated before presenting it on a screen as a brightness (B-) mode image with the value of the data shown as different levels of pixel intensity (Figure 2).

Many types of motion estimation using ultrasound data involves the 2D (or lately 3D) data. Earlier it was most common to use RF data as the calculated motion estimations were more accurate. Today the benefit of using RF data is still the higher axial data density. The main drawback is the limited access of the RF data especially...
when using clinical ultrasound machines. A lesser limitation is the large amount of data involved using RF data. The benefits of IQ data are the possibility to convert the data into both RF data and B-mode data, the access to the phase data, and usually a smaller amount of data compared to RF data. Again, the main drawback is the limited access of the IQ data especially when using clinical ultrasound scanners. The main benefits of using B-mode data are the ease of accessing the data. The DICOM data available on most ultrasound scanners, i.e. the B-mode data presented in an international standard, are of the highest quality. A drawback is the reduced axial resolution. A comparison of motion estimation accuracy using B-mode and RF data were made in Paper III and further discussed in chapter 7.3.

2.3 Plane Wave Imaging

The concept of ultrafast ultrasound imaging, i.e. more than 1000 frames per second, was introduced in 1977 by Bruneel et al [13] but the technology at the time was not mature for an implementation. It would demand hundreds of parallel data handling systems of a more modern fabrication before a realization using pulsed ultrasound would be presented in 1999 [14]. In order to reach this high frame rate, the number of ultrasound transmissions had to be reduced. This is achieved by using one broad plane, or unfocused, ultrasound wave to insonify the entire volume of interest. Several or all available transducer elements are then used to sample the ultrasound echoes from the volume.

Early implementation of plane wave imaging had problems with a reduction of contrast levels and to some extent spatial resolution [15]. In order to increase the image quality in various applications, compounding based on incoherent averaging [16] and coherent summation has been proposed [17]. Another important part of the improvement of plane wave imaging was the concept of synthetic aperture imaging [18, 19].

The major benefit of plane wave imaging is its very high temporal resolution and has thus made it possible to further study transient phenomena in vivo, e.g. shear wave elastography [20], pulse wave velocity [21, 22], Doppler imaging [23], vector flow imaging [24], and functional ultrasound [25].
Motion estimation can be conducted in a number of ways. This chapter starts with a description of the two viewpoints of motion, i.e. Eularian and Lagrangian. It continues with an overview of motion estimation using sequences of images in video, excluding a large group of methods using block-matching (which is treated in Chapter 4). This chapter ends with a description of methods for estimating motion using ultrasound.

### 3.1 Eularian vs Lagrangian

The concepts of Eularian and Lagrangian viewpoint on movement [26] is mostly used in fluid mechanics and within research areas using movement of particles. With a Eularian viewpoint (Figure 3) the starting position is the same in each frame and thus a different particle or parcel of particles is tracked in each frame. With a Lagrangian viewpoint the same particle or parcel of particles is tracked from one image to the next throughout a sequence of images. Transforming motion estimations obtained with a Eularian viewpoint into a Lagrangian viewpoint, or vice versa, is possible. However, the accuracy of the transformation is highly dependent on the density of the motion estimations, the complexity of the investigated field of motion, and the accuracy of the motion estimations.

Figure 3. Eularian and Lagrangian viewpoints on motion estimations. The gray square in each viewpoint shows the same kernel. The entire images are moved with the same velocity and thus the arrows are identical in both viewpoints.
The optimal viewpoint of a motion depends on the desired density of the motion estimations. The benefit of a Euclidian viewpoint is the lack of accumulated errors as each motion estimation starts anew in each image. It is also possible to discard motion estimations which are obviously erroneous if holes in the field of estimations are acceptable and/or making a better estimation using spatial filters. However, if the number of motion estimations are low and/or the motion estimations have a large variance, the use of a Lagrangian view could be beneficial. The Lagrangian viewpoint demands that the position of the object/s of interest can be accurately estimated throughout the sequence of images. If the number of objects of interest is low this will highly reduce the number of calculations needed for a complete motion estimation. However, the accuracy of the motion estimations is highly dependent on the accumulated tracking error for each object.

One benefit with a Lagrangian viewpoint is that plotting the estimated position in the cine loop is an easy way to judge the correctness of the motion estimations by visual inspection. This can be performed whether the true movement is known or not. If the position of a kernel remains close to the chosen structure or speckle, the user can be assured that the motion estimation correctly tracks the motion. This possibility is severely limited when using a Euclidian viewpoint.

Overall: A Lagrangian viewpoint is recommended when a sparse density of motion estimations is needed, and a Euclidian view is recommended when a dense density of motion estimations is needed.

### 3.2 Motion estimation in video images

Motion estimation in TV/video is frequently used in compression of the image signals. The most commonly used group of methods is block-matching (see Chapter 4). Other methods do exist though many of them are more common outside video compression. A comparison of estimating motions in video and in ultrasound cine loops is mostly relevant when using ultrasound B-mode data as IQ and RF data incorporates more usable data, i.e. phase data. There exist two major differences between video and B-mode data: 1) video has much more clearly defined objects, e.g. houses, cars, and humans; 2) the difference in velocity in a small region of an image is likely much higher in video, e.g. two meeting cars, while ultrasound images normally have a smoother velocity field.

The presence of distinct objects give access to tools when estimating motion in video that are rather useless in B-mode data, e.g. segmentation of an image and individual tracking of the segments. Structures and textures in an image also promote the use of optical flow estimations, which constitutes a large group of methods. A dense
optical flow estimation tries to match every pixel in an image with a pixel in another image. Although several assumptions exist, the most common is that the intensity of a pixel should be constant between images [27] which is not always true. Another source of ambiguity is the need of a clear structure, preferably a point or corner, to adequately estimate the motion of a pixel. This can be solved by defining additional information, e.g. texture and structure, of the pixels surrounding the pixel of interest. If the intensities of a number of other pixels are used we come close to classifying the method as a block-matching method instead.

Phase-correlation schemes use fast Fourier transforms and works with the phase correlation matrix or normalized cross power spectrum \( Q(u, v) \) for motion estimation [28].

\[
Q(u, v) = \frac{B(u,v)A(u,v)^*}{|A(u,v)A(u,v)^*|} = e^{-i(ux_0+vy_0)}
\]  

where \((u, v)\) are the Fourier domain coordinates, \(A\) and \(B\) are the discrete Fourier transforms of two matrices with image data, * indicates the complex conjugate, and \((x_0, y_0)\) are the displacement between matrices \(A\) and \(B\). The values of \((x_0, y_0)\) can then be determined as a plane [29] or as lines in a plane [30]. It is also common to work with the phase correlation surface after calculating the inverse discrete Fourier transform of the phase correlation matrix. For a high accuracy of the displacements \((x_0, y_0)\), sub-sample estimation of \((u, v)\) is needed. Phase-correlation schemes have also shown good results in estimating large rotations, scalings, and translations [31].

### 3.3 Motion estimation using ultrasound

Several groups of methods exist for motion estimation in ultrasound images with Doppler being the most commonly used, but speckle tracking (see chapter 4), ultrasound reflectors, and ultrasound phase data are also used.

#### 3.3.1 Doppler

The Doppler shift in ultrasound is a change in the frequency between the transmitted and received frequencies caused by a relative motion of a reflecting object between the transmitter and receiver.

\[
f_D = \frac{2f_tv\cos\theta}{c}
\]  

Here \(f_D\) is the Doppler shift, \(f_t\) is the transmitted frequency, \(v\) is the speed of the moving object, \(c\) is the speed of sound in the medium, and \(\theta\) is the angle between the direction of the relative velocity and the direction of the transmitted sound. The main drawbacks of using the Doppler shift for motion estimation is well known:
the angle dependency of the Doppler shift; also, for low velocities the shift will be very small and prone to be noisy. Estimating the Doppler shift uses two methods for transmitting: continuous and pulsed ultrasound. Continuous ultrasound has one transmitter and one receiver with the investigated volume being in the area where the ultrasound beam of the transmitter and field of view of the receiver overlaps. The estimation of the Doppler shift in this area is continuous and no spatial information is gained. The pulsed Doppler uses the same transducer for transmit and receive of the ultrasound. A time gate on the received ultrasound set by the user defines the investigated volume. For the continuous Doppler, the Doppler shift is estimated as a direct difference between the transmitted and received frequencies. The pulsed Doppler cannot do that due to absorption in the media between the transducer and the investigated volume which should cause a downshift in the center frequency. Estimation of the Doppler shift is instead estimated as a phase shift detected between successively transmitted ultrasound pulses. The direction of the detected movement is determined through use of quadrature sampling. However, the repetition frequency of the transmitted pulse has to be sufficiently high compared to the investigated velocity in order to avoid aliasing. For both continuous and pulsed Doppler the velocity estimation is normally made in one volume though special versions exist were multiple estimations are made along a line [32].

For motion estimations in an area of an ultrasound image, power or color Doppler can be used. They are both utilizing pulsed Doppler as transmission mode but the results are presented somewhat differently. Color Doppler presents both direction (from or towards transducer) and mean magnitude of motion in a small area. Power Doppler uses the energy of the Doppler shift to estimate the mean magnitude of motion in an area (no direction). However, both methods lack angle correction, the estimated values are less accurate, and each estimation usually covers larger volumes than both continuous and pulsed wave Doppler. Also, as the methods samples the Doppler shift by repeated pulses, a too low pulse repetition frequency will lead to aliasing of the estimations.

Estimation of Doppler shift is primarily used for investigations of blood flow as the estimated velocities are more trustworthy and stable compared to estimating the Doppler shift for tissue motion due to the higher velocities to estimate. However, the accuracy of the estimation of the Doppler shift decreases with increased spatial gradient of a velocity within the sampled area. Another benefit of estimating the Doppler shift is the possibility to listen to the shift by sending the signal to a loudspeaker as the Doppler shift of the blood flow in many of major vessels is in the audible range. The chosen size of the investigated volume when estimating the
Doppler shift follows the same rule as most motion estimation methods; using a large area/volume will mostly give a better motion estimation, but the estimate will be of the average movement in the investigated area/volume.

### 3.3.2 Other techniques using ultrasound

If the estimated motion is very small, i.e. smaller than half the wavelength of the ultrasound (about 0.1 mm @ 7.5 MHz) it is possible to estimate motion using the phase of RF or IQ data. Such small motions have been investigated in e.g. heart wall vibrations [33], artery-wall strain [8], and magneto-motive ultrasound [34].

One problem when estimating motion in plane wave images is the often minimal movement between two consecutive images due to the high frame rate. One solution is to use the phase of the complex cross-correlation between the kernel and the blocks. This has been shown axially by Pesavento et al. [35] and laterally by Chen et al. [36]. A recurring problem using ultrasound images is the problem of estimating lateral motions as the spatial resolution normally is lower in the lateral direction. By use of a two-peaked apodization, i.e. transverse oscillation [37], it is possible to introduce a controlled lateral phase pattern when beamforming the ultrasound data with an increase of the lateral motion estimation accuracy [38]. The drawback of these implementations is the need for it to be part of the beamforming of the image data which is not always possible. However, it was discovered that it indeed was possible, with only minor degradations of tracking accuracy, to introduce transverse oscillations in both beamformed RF data and in B-mode data using either convolution or filtering [39]. As when using the phase of RF data in the axial direction, the maximal length of movement to be estimated is half a wavelength of the oscillations.
4. Tracking using block-matching

Block-matching, or speckle tracking, is a commonly used method for motion estimation. There exist a number of different implementations for 1-D, 2-D, and 3-D data using both RF and B-mode data, e.g. [4, 40-45]. But every block-matching method have some common characteristics.

4.1 Parts of a speckle tracking method

Using speckle tracking, the user selects an area within an image for which motion should be estimated with the help of another image depicting the same objects. However, it is sampled at a later time instance at which time some or all objects might have moved. The selected area in the first image (a kernel) has a size set by the user. A speckle tracking method searches in the second image for an area (a block) with the highest similarity to the kernel. In order to succeed, the speckle tracking method needs: a method for determining similarity by calculating evaluation metric values which gives a numerical value to the similarity between the kernel and each block with which it is compared; it needs a search methodology to know which blocks to compare to the kernel; and, for increased tracking accuracy, a sub-sample estimation method is needed. A speckle tracking method can use additions to the mentioned parts, but the kernel, evaluation metric method, and the search methodology are required.

4.2 Kernels

A kernel is an area of an image often containing an object of interest which the user wants to find in another image. For practical reasons, the kernel shape is most commonly chosen as a rectangle. In general, increasing the size of the kernel results in more accurate motion estimations. If there are velocity variations within the kernel the most prominent feature is likely to dominate the motion estimation. Increasing the velocity inhomogeneity within a kernel is likely to decrease the accuracy of the motion estimations. This can give a situation were increasing the area of the kernel will result in a decreased tracking accuracy.

Sampling of the kernel in an image is simple when using a Eularian viewpoint. The position of the kernel is a given in each image, so direct use of the sampled values in the image within the perimeter of the kernel solves the problem. However, when using a Lagrangian viewpoint the intention is to track the same particle or parcel of particles throughout a number of images. Given that most of the movements in a
series of images are decimal, the center position of the kernel will be in-between sample values in most of the images. Thus, sampling of the kernel directly from the image data is not advisable. A number of solutions exist:

a) Keep using the old kernel. If the changes of the interesting parts of the images are limited, using the old kernel makes sure that we track the interesting object but the larger the changes in the image the more likely the risk for incorrect tracking.

b) Resample the kernel using the sampled values closest to the estimated position in the image. The method is quick and easy but the risk is very high that the difference between the position of used data and the object to track will increase over a number of images and we will track something else.

c) Correction value for the position. The kernel is renewed by using the sampled values in the image closest to the estimated position in the image (as in b) AND a correction value, i.e. the distance between the estimated position and position of the used samples. The correction value is added to the estimated position in the next image and becomes the estimated position for the kernel in this image. This corrects for the difference between the position of the used kernel and the position of the tracked target. The method is quick and easy with a low risk for drift of the kernel from the original target.

d) Interpolation of image data. The most common method for resampling the kernel is to interpolate the sampled values [46] in the image and using the interpolated values closest to the estimated decimal position. The method is somewhat time consuming but very reliable.

e) Prediction of the kernel. Using the sampled values in previously used kernels, the data in the new kernel is predicted, e.g. using Kalman filters [47].

4.3 Evaluation metric values

The concept of speckle tracking is to find the block most similar to the kernel. This can be achieved by calculating an evaluation metric value between the kernel and a block in order to estimate the similarity between them. In order to find the best matching block in the next image, a search methodology is used to determine the number of comparisons to calculate. The most commonly used methods are (in alphabetic order):
Cross-Correlation (CC)

\[ \alpha = \sum_{i=1}^{l} \sum_{j=1}^{k} (X_{i,j} - \bar{X})(Y_{i+m,j+n} - \bar{Y}) \]  

(5)

Normalized Cross-Correlation (NCC)

\[ \alpha = \frac{\sum_{i=1}^{l} \sum_{j=1}^{k} (X_{i,j} - \bar{X})(Y_{i+m,j+n} - \bar{Y})}{\sqrt{\sum_{i=1}^{l} \sum_{j=1}^{k} (X_{i,j} - \bar{X})^2 \sum_{i=1}^{l} \sum_{j=1}^{k} (Y_{i+m,j+n} - \bar{Y})^2}} \]  

(6)

Sum of Absolute Difference (SAD)

\[ \alpha = \sum_{i=1}^{l} \sum_{j=1}^{k} |X_{i,j} - Y_{i+m,j+n}| \]  

(7)

Sum of Squared Difference (SSD)

\[ \alpha = \sum_{i=1}^{l} \sum_{j=1}^{k} (X_{i,j} - Y_{i+m,j+n})^2 \]  

(8)

Here \( \alpha \) denotes the evaluation metric value; \( m \) and \( n \) denotes the displacement between the kernel and the block; \( l \) and \( k \) denotes the size of the blocks; \( X_{(i,j)} \) and \( Y_{(i,j)} \) denotes the pixel values at position \((i, j)\) in the kernel and the compared block, respectively, while \( \bar{X} \) and \( \bar{Y} \) denotes the average pixel values of the kernel and the block.

A major difference between the four methods is that when using CC and NCC the user searches for the maximum likeness while when using SAD and SSD the user searches for the minimum difference.

One benefit of using NCC is its normalization which reduces the influence of the average intensity in the images. Fluctuations in the average intensity can reduce the tracking accuracy of the other methods. NCC is mostly considered to have the highest stability and give the best tracking accuracy but it uses more computational power.

### 4.4 Search methodologies

The basic search method to find the block most similar to the kernel is to compare the kernel to all possible blocks in the image, i.e. a full search (FS). Comparing the kernel to all blocks in an image is rather inefficient and in most cases unnecessary as the expected motion of the kernel is limited to a fraction of the size of the image. Thus using a priori information about the likely length of the motions to estimate, a region of interest is chosen in which a comparison between kernel and all possible blocks is conducted. As the region of interest must be larger than the maximal motion for a possible correct estimate, the size of the region of interest is a balance...
between the time needed for calculating the evaluation metric values for all blocks and the risk of having a motion with a size larger than the region of interest.

Plotting the evaluation metric values for a FS will show a sampled surface depicting a bowl (Figure 4) or top depending on the used method for calculating the evaluation metric values. Study of the surface shows that it can in most cases be considered smooth in an area close to its extreme point. This gives the possibility to use so called sparse search methods that only calculates the evaluation metric values for a selected number of blocks. This reduction in blocks comes from clever picking of blocks in conjunction with iterative searching. The surface of the evaluation metric values is thus estimated and the block closest to an extreme point is chosen as center for the next iteration.

The sparse search methods can further be divided in two groups: one group with a finite number of iterations, e.g. three step search [48], four step search [49], and orthogonal search algorithm [50]. The finite number of iterations results in a restriction that the method cannot investigate every possible block in an image and in principle the method will have a set region of interest. The second group of sparse search methods, e.g. hexagon search [51] and Adaptive Rood Pattern Search [45],

![Figure 4. Similarity calculated between a kernel and all possible blocks in the next image in a region of interest using Sum of Absolute Difference (SAD).](image)
differs in that the iterations do not stop until an extreme point has been found. The used blocks are carefully selected in a pattern determined by the method with the goal to iteratively search for the extreme point on the surface. The iterative search removes the need of a region of interest and thus removes the risk of having a motion with a size larger than the region of interest. As the methods only investigates a limited number of blocks, the number of calculations is reduced. However, as the iterations can converge on any extreme point, there is a risk that the point of convergence is a local extreme point and not the searched for global extreme point.

In most cases the kernel size is fixed during the search. A variation of the FS is to do an iterative FS starting with a large kernel size and using the estimated motion of the kernel as a criterion when reiterating the motion estimation with a smaller kernel size [52, 53]. The starting large kernel size will then give a high accuracy of the “global” motion in the image while the later smaller kernels will zoom in on the local motion. The smaller kernels will have a higher accuracy than expected by their size as they have a priori information of the motion from the large kernels used as a restricted search region.

A problem for all methods is repeated structural patterns in the image. The patterns have the possibility of creating a number of extreme points in the surface of evaluation metric values with a risk of choosing the incorrect point depending on the similarity of the values in the various extreme points. This problem is typically higher using RF data (primarily in the axial direction) than using B-mode data. The risk of finding a false extreme point is higher when using sparse tracking methods than using FS.

### 4.5 Sub-sample estimation methods

The sub-sample estimation methods are needed to decrease the motion estimation errors from the minimal average error of one fourth sample achieved without use of any sub-sample estimation method. This minimum estimation error assumes motions that are evenly distributed on the decimal level in space and time. Most sub-sample estimation methods can be divided into one of three groups depending on how the sub-sample estimation is performed: interpolation of the image data, interpolation of the evaluation metric values, and mathematical estimation using evaluation metric values.

a) Interpolation, or up-sampling, of the image data is a reliable method for sub-sample estimation of motion. Several methods can be used for interpolation but methods resulting in a continuous derivate over pixel borders, e.g. cubic [46] or bicubic interpolation, are recommended (see
Paper II). The improvement of the resolution depends on the interpolation factor. The drawback of this group of sub-sample estimation methods is the need for computational power. Though interpolation of the image data is fairly fast today, a new motion estimation using the interpolated image data is required with a calculation time correlated to the square of the interpolation factor. Also using a large interpolation factor (100+) will produce large amount of interpolated data which increase the computation times due to the handling of the data.

b) Interpolation, or up-sampling, of the evaluation metric values uses the fact that the surface of the evaluation metric values can be considered to be smooth close to the searched-for extreme point (Figure 4). However, the up-sampling of the evaluation metric values should not only result in a higher density of values but also be able to give both a new position and a new magnitude for the extreme point if a sub-sample position is correct. One solution is to use a filter [54] for the interpolation. The result of the method improves with the number of evaluation metric values meaning that problems can arise close to edges of the image data.

c) Mathematical sub-sample estimation using evaluation metric values also uses the smoothness of the surface of the evaluation metric values. Fitting a function, e.g. cosine or parabola, to three or more of the evaluation metric values (the extreme value and one situated on each side of it). By analytical solving of the function for its local extreme point, the sub-sample position can be found. However, it has been shown that fitting a function to a set of data is likely to produce incorrect results as the fitted function will not match the true curve of the fitted data possibly causing bias in the estimations [54]. Direct calculation of the sub-sample position can be achieved by e.g. grid slope interpolation [55] which were used in Papers II and III.
The cine loops used for evaluating motion estimation methods can originate from three sources (Figure 5): *in silico* – simulated in a computer, *phantom* – physical object with a likeness of tissue scanned with an ultrasound machine, and *in vivo* – ultrasound scans of living volunteers.

![Figure 5. Examples of ultrasound images from the three sources: a) in silico, b) phantom, and c) in vivo. Each part of the image shows an area 20 x 15 mm. Parts of figure can be found in Paper III.](image)

### 5.1 In silico

The first step of testing a new motion estimation method is in many cases to apply the method to image data simulated in a computer. A number of packages can be found on the internet, e.g. Field II [56, 57] and k-Wave [58, 59], and many more exist in various research labs around the world. The computers of today allow simulations to be calculated in a reasonable amount of time with increasingly accurate ultrasound models both concerning the physics and depicted physiology. Although the resulting cine loops will differ somewhat from those downloaded from an ultrasound machine, the benefits far outweigh the drawback in the initial test phase. As the user controls every step from the position of the scatterers of the simulated object, through the sampling of the data in the elements, to the beamforming, the image data can be fully controlled. As the motion of the scatterers in the simulated model is set by the user, the difference between the motion
estimations and the ground truth is more accurately known than when using phantom or in vivo data.

5.2 Phantoms
The use of phantoms as objects in an ultrasound investigation bridges in silico and in vivo data. Ex vivo investigations of tissue has in this thesis been classified as phantom studies. A number of substances with characteristics resembling human tissue, e.g. acoustic impedance, speed of sound, and absorption, are available. It is also possible to mold several of the substances, e.g. agar/gelatin and polyvinyl alcohol (PVA), for a desired form of the phantom. Having the phantom in a known situation gives a good control of its position at the time of the sampling of the ultrasound images. Also, the ultrasound machine used when sampling the phantom ultrasound data, are in most cases planned to be used when sampling in vivo data. Thus the resulting image data can resemble an in vivo measurement more than in silico data. Although the use of mechanical and robotic set-ups gives good control of the position of the phantom, the true position of the different parts of a phantom is not known as accurately as in the in silico data. It can also be very hard to manufacture phantoms in which complicated motions occur.

5.3 In vivo
The goal of developing a new ultrasound application is often research in vivo. Ultrasound cine loops with in vivo movements is, however, a rather difficult media in which to make motion estimations given the amount of absorption, noise, scattering, and multiple reflection which all decreases the image quality and disturbs the motion estimations.

A common problem during in vivo ultrasound investigations is out-of-plane movement. All image modalities have a field-of-view in which an object can be viewed. A 2D ultrasound investigation samples the image data with a certain elevation thickness with disrespect to the direction of an observed 3D-motion. Thus, great care has to be taken in order to capture a motion along a line fully within the image-plane. An angle between the image-plane and the motion will result in a velocity component perpendicular to the image-plane which will be unknown and, many times, not readily apparent. In some instances, the structure of the investigated tissue can be an indicator of out-of-plane movement, e.g. when investigating the arterial wall of the common carotid artery in a view parallel to the surface of the transducer, where the intima-media complex should be visible along the entire artery. Conducting motion estimations in the presence of an out-of-plane movement will result in an underestimation of the real physiological movement.
Also, if tracking with a Lagrangian viewpoint, it is possible that the interesting volume of tissue will move out of the ultrasound image-plane, and, thus, cannot be tracked. When investigating non-linear movements it might not be possible to avoid out-of-plane movement when sampling 2D cine loops. A modern solution is to sample 3D cine loops to better capture the movement.

The wish to have the best possible image quality can be a problem when estimating motion using \textit{in vivo} cine loops. Although the use of persistence gives improved image quality when sampling ultrasound cine loops, it is also likely to blur the information needed for motion estimation, and will likely obstruct any attempts of motion estimation using block-matching. Also the use of multiple points of focus can cause problems by reducing the sampled frame rate to a degree where motion estimation becomes problematic.

The main difficulty of using \textit{in vivo} data when testing a motion estimation method is, however, a reduced knowledge of the true motion in a cine loop. The “true” motion might be obtained using another image modality, e.g. magnetic resonance imaging, or by motion estimation in the same cine loop using an existing motion estimation method, or using (echogenic) beads surgically positioned \textit{in vivo} [60, 61]. Ethical considerations will of course arise and the inserted object can both reduce the quality of the ultrasound images and disturb the tissue motion.
Cardiovascular diseases are the leading causes of death worldwide [62]. A wish to better understand and predict diseases in the cardiovascular system has been a driving force for research of the cardiovascular system. The arterial wall consists of the tunica intima (the innermost layer), the tunica media (the middle layer), and the tunica adventitia (the outer wall). The intima is a sheet of flat endothelial cells resting on a thin layer of connective tissue. The endothelial layer is the main barrier to plasma proteins; further, it secretes many vasoactive products. Finally, it is mechanically weak. The tunica media supplies mechanical strength and contractile power. It consists of spindle-shaped, smooth muscle cells embedded in a matrix of elastin and collagen fibres. Sheets of elastin mark each boundary of the tunica media. The tunica adventitia is a connective tissue sheath with no distinct outer border. It serves to tether the vessel loosely in place. The adventitia consists of longitudinally oriented collagen and elastic fibres. The adventitia of the larger arteries contains small blood vessels, the *vasa vasorum* (literally “vessels of vessels”), and in the largest arteries these penetrate into the outer tunica media as well. Their task is to nourish the thick tunica media of the large vessels [63]. An established way to characterize the arterial wall using ultrasound is to measure the thickness of the two inner layers – the intima-media thickness [64]. The typical double-line pattern in ultrasonic images arising from the lumen-intima and media-adventitia boundaries can be used to measure the intima-media thickness either manually using calipers or automatically [65-69]. The knowledge that the arterial wall has a radial movement connected to the pulsation of the blood has been known for a long time and the radial motion, i.e. the diameter change of the artery, has been investigated since the 1970th using ultrasound. The diameter change has been measure in 1D and 2D RF-data [70-73], and using B-mode [68, 74-76]. Another widely used measure is pulse wave velocity [22, 77-79] as it gives an indication of the stiffness of the vessel wall [80]. The finding of a longitudinal movement of the arterial wall of the same magnitude as the diameter change was first presented by our group [81] in 2002. Since the discovery of the longitudinal movement of the arterial wall, several papers have been published elaborating on and confirming not only the presence of a longitudinal vessel wall movement in large arteries, but also a longitudinal shearing within the vessel wall; the intima-media complex (the vessel wall layers closest to the lumen) of the carotid artery showing a larger movement than the adventitial layer (the outer vessel wall layer) [82, 83]. Other studies have indicated a possible relation between the maximal amplitude of the longitudinal movement of the common carotid artery wall and risk factors for vascular disease [84]. It is, however, of interest,
to not only study the maximal amplitude of longitudinal movement, but also the complex bidirectional multiphasic pattern of the longitudinal movement. It is possible that also the pattern of the longitudinal movement can be of predictable value (Paper IV).

The largest longitudinal movements of the common carotid artery have been observed in the intima-media complex. Thus, it is likely in these layers that a potential change of the magnitude and/or pattern of the longitudinal movement in a patient can be detected first. Considering that the intima-media complex is thin, has a marked radial curvature, and has a 3-dimensional motion pattern in Cartesian coordinates (radial plus longitudinal movement in cylindrical coordinates), acquiring cine loops of sufficient image quality is problematic. A precise positioning of the transducer is necessary in order to minimize the out of plane movement of the arterial wall. Even with a precise positioning of the transducer it can be difficult to visualize the near vessel wall (closest to the transducer) due to the clutter produced by the tissue.

In earlier investigations [83, 85], three distinct bi-directional phases of the longitudinal movement pattern were identified (Figure 6). The figure shows that an antegrade movement (along the direction of blood flow) can be observed in early systole, followed by a large distinct retrograde movement (opposite the direction of blood-flow) during late systole, and a second antegrade movement in diastole followed by a gradual return to the initial position. The pattern of the radial movement of the arterial wall, the distension, is caused by pressure waves [86]. The mechanisms underlying the different phases of the longitudinal movement is, however, mainly unknown, and it is likely to involve several factors. One hypothesis is that blood flow shear stress, acting along arteries, is one of the forces underlying the longitudinal movement. However, 1) this force is too small compared to the longitudinal elasticity of the arterial wall [87] and 2) in studies on the porcine artery it has been shown that a marked increase in the longitudinal movement can take place independently of wall shear stress from the blood flow [88]. It has been suggested that the retrograde phase of the longitudinal movement is caused by the motion of the heart. It is well known that the heart moves towards the apex in systole [89, 90]. If that suggestion is correct, then a gender specific difference of the longitudinal movement pattern could exist in elderly cohorts due to possible differences in the stretching of the ascending aorta [91]. It has also been shown that significant longitudinal movement can be estimated in a non-straight phantom with pulsating flow [92] suggesting that the blood pressure can influence the longitudinal movement. If the direct pulse wave during systole affects the longitudinal movement, surely reflected waves in the arterial system can do so too.
Figure 6. Longitudinal movement (solid) of the intima-media complex of the far wall of the common carotid artery and the corresponding diameter change (dashed) of a 28-year-old woman. The small circles mark the onset of an antegrade movement (along the direction of the blood flow) in early systole (Phase A). It is followed by a large distinct retrograde movement (against the direction of the blood flow) during late systole (Phase B) and a second antegrade movement in diastole (Phase C), followed by a gradual return to the initial position. Figure originally from Paper IV.
7. Included papers

7.1 Paper I

This paper investigated the effect of adding one extra kernel when estimating motion (Figure 7). Investigation of the motion estimations made using a sparse block-matching method showed that the length of most of the errors were one sample or less. Averaging the positions of the motion estimations using the sparse block-matching method and a FS method with a 3x3 sample search region was believed to improve the tracking accuracy with only a minor increase in calculation time.

In silico and phantom cine loops were used to evaluate the performance of an extra kernel. The results showed that tracking accuracy improved (mean = 48%, p < 0.005 [in silico]; mean = 43%, p < 0.01 [phantom]) compared to not using the extra kernel. As mentioned in 4.1.1, larger kernel size results in a general increase of tracking accuracy. Thus an increased tracking accuracy when using an extra kernel could be used to “buy” the use of a smaller kernel size without reduction in the tracking accuracy compared to not using an extra kernel. Using in vivo cine loops of the common carotid artery where the longitudinal movement of the arterial wall was estimated, an optimization for tracking accuracy were made using the sparse...
block-matching method both with and without use of an extra kernel. With
maintained tracking accuracy, a reduction (mean = 19%, \( p < 0.01 \)) in kernel size
were achieved.

It was shown that either an increased tracking accuracy or a decreased kernel size
could be achieved with the use of an extra kernel which prove the contradiction
between kernel size and tracking accuracy. Though the use of an extra kernel added
to a basic motion estimation method clearly improve the tracking accuracy, the use
of a biased sub-sample estimation method can concern the reader. But it is believed
that the improved tracking accuracy comes from both the use of an extra kernel and
the averaging of the two estimated positions. In worst case the averaging of the two
estimated positions will result in the largest bias being kept and in best case the
biases will be removed.
7.2 Paper II

This paper investigated the motion estimation performance of eight sub-sample methods when used in combination with three different evaluation metric methods. When the performance of a sub-sample estimation method is presented, it is normally investigated using only one evaluation metric method. However, as the shape of a theoretical surface (Figure 4) of evaluation metric values will differ between methods, the estimation errors of a sub-sample method were hypothesized to be affected. The aim of this paper was to investigate the performance of sub-sample estimation methods of the three groups presented in 4.5 using three different evaluation metric methods.

The investigation used simulated cine loops depicting a block moving in the lateral direction with a constant velocity. The results showed that the used evaluation metric method affected the motion estimation performance of the sub-sample estimation methods (Figure 8). The effect on the motion estimation performance varied with the sub-sample estimation method and one or several performance values of were affected: mean estimation error, standard deviation of estimation error, and calculation time. This indicates that a reported tracking performance for a sub-pixel estimation method can be significantly different when combined with another evaluation metric.

Though the main purpose of the evaluation metric method is to find the block most similar to the kernel, the shape of the evaluation metric values for all blocks in a region will influence both the used search methodology and the sub-sample estimation method. It should be clear that some sub-sample estimation methods are more specifically developed for use with one evaluation metric method than others. A test is thus required if only a part of a published method is used, i.e. it should always be tested as the images in which motion estimations are conducted affects the performance of a motion estimation method (author’s opinion).
Figure 8. Tracking error per image of the motion estimation performed on the in silico cine loops against the set movement per image of the cine loops. The boxes indicate the lower and upper quartiles and the median. The bar line indicate 99% of the values. Outliers are indicated as points. Each box is based on 4,900 estimations explaining the seemingly large numbers of outliers. No error larger than 0.25 pixels is shown but they were part of all the statistics. Figure originally from Paper II.
7.3 Paper III

This paper investigated the effect of combining two published sub-sample estimation methods (Figure 9). Parabolic sub-sample interpolation for 2D block-matching motion estimation is computationally efficient. However, it is well known that the parabolic interpolation in the range of \( y - 0.5 \) to \( y + 0.5 \) samples gives a biased motion estimate with a maximum bias for displacements of \( y \pm 0.25 \) samples (\( y = 0, 1, \ldots \) ) (Figure 9). Grid slope sub-sample interpolation is less biased, but it shows large variability for displacements close to \( y.0 \). The proposed solution is to combine these sub-sample methods using a threshold to determine when to use which method. The threshold were determined to \( \pm 0.15 \) samples using motion estimations in phantom cine loops. Hence the new method GS15PI.

The new method was compared to three sub-sample interpolation methods: sub-sample interpolation of the image, parabolic sub-sample interpolation, and grid slope sub-sample interpolation. The evaluation used methods sampled \textit{in silico}, on phantoms, and \textit{in vivo}. In order to compare the sub-sample methods in an as objective manner as possible, the \textit{in vivo} evaluation was limited to the longitudinal movement of the arterial vessel wall of the common carotid artery of 21 healthy volunteers. Only the retrograde motion, against the blood flow, was used in the comparison as it is the most distinct and regular phase of the motion pattern at the measured site. Evaluated on simulated and phantom cine loop, GS15PI reduced on average the absolute sub-sample estimation errors by 14, 8, and 24%, respectively. The drawbacks of the parabolic and modified grid slope sub-sample estimation methods were reduced in GS15PI as predicted (Figure 10). When evaluated \textit{in vivo}, the motion estimations using parabolic and grid slope sub-sample interpolation and GS15PI resulted in coefficient of variation values of 6.9, 7.5, and 6.8%, respectively.

It was expected that the total motion estimations should be smaller when using RF data compared to using B-mode data. However, the results in this paper were not conclusive and the results indicate that both RF data and B-mode data can be
preferable. As the trends found indicate similar behavior for all sub-sample methods, it can be suspected that the sources of the used data are the cause of this inconsistency.

Figure 10. Comparison of the bias of three sub-sample estimations methods. In this figure, y is a natural number. Figure originally from Paper III.
7.4 Paper IV

This paper investigated the longitudinal movement patterns of the intima-media complex of the wall of the right common carotid artery in 135 healthy volunteers. Although the knowledge and understanding of the longitudinal movement pattern of the arterial wall have increased in the last decade, the physiology behind the pattern is not yet understood. Further, putative changes in the longitudinal movements with aging have not been defined. Our group has previously shown that the movement pattern of the common carotid artery for an individual is stable over a four-month period [93] and that the pattern of movement in young healthy subjects can markedly differ, also between subjects of the same age and gender. Three major phases of movement have previously been identified [93]. The large cohort of healthy volunteers in this study included subjects of a wide range of age and gave the possibility to define changes in the longitudinal movement in the normal aging process of the arterial system.

In this study we defined two phases of longitudinal movement of the common carotid artery that have not previously been described. The first additional phase was rapid, retrograde and started just before end-diastole, and ended approximately at the time of the start of systole (Figure 11a). This phase was most prominent in volunteers 50-65 years of age. The second additional phase was antegrade and occurred during, or directly after the dicrotic notch was observed in the diameter curve (Figure 11b). This phase was not distinct in all individuals; especially not in the young. The size of the phase ranged from only a change in velocity of the retrograde phase to a distinct antegrade motion in older individuals. The healthy individuals could also be divided into five different groups based on the resulting pattern of the longitudinal movement. The results in this paper suggest a relationship between the movement pattern and aging of an individual, or perhaps rather the aging of the cardiovascular system. All individuals were without known health problem, and the results can be useful both for comparison in studies of individuals with a known disease, and serve as a base for further studies of the physiology of the vascular system in healthy individuals.
Figure 11. Longitudinal movement (solid) of the intima-media complex of the far wall of the common carotid artery, and corresponding diameter change (dashed). The small circles mark the onset of an antegrade movement in early systole. a) Shows a 53-year-old male with a distinct large retrograde movement (marked by a large oval) just before end-diastole. b) Shows a 60-year-old female with a distinct antegrade movement (marked by a large oval) at the time when the dicrotic notch is observed in the diameter change curve. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow.
7.5 Paper V

This paper investigated a new motion tracking scheme for improved motion estimations with a Lagrangian viewpoint in high frame rate cine loops. Cine loops sampled at high frame rate are increasingly used and interest of estimating motion in them is high. One reoccurring problem using in vivo measurements is the short movement between consecutive images due to the high frame rate and relative slow movements, e.g. a frame rate of 1300 s⁻¹, motion velocity of 2 mm/s, and a sample density in the direction of movement of 10 mm⁻¹ results in a displacement per frame of 0.015 samples. For such short motion, it is very likely that the relative motion estimation errors will be high if using a block-matching method. If a Lagrangian viewpoint is used for the motion estimations, the accuracy of the estimated positions will most likely decrease with the number of consecutive images as the errors of the estimated positions will accumulate from previous estimations. We propose to perform the motion estimations iteratively and in the first iteration take rather large steps between the used images. The positions in the images between the first iteration will then be estimated using the previous iterations (Figure 12). The estimations will have three benefits: in the early iterations, the motion between used images will be larger and the relative error small, the motion estimations will be based on two independent kernels in all images, and the accumulated errors for the estimated position will be smaller due to less number of estimations needed before reaching the image of interest.

Figure 12. The iterative tracking scheme is shown for an initial length of iteration of 4 images. Figure originally from Paper V.
The new tracking scheme was tested on phantom cine loops sampled at 1302 frames per second and beamformed using three different methods: delay-and-sum, phase correlation imaging, and transverse oscillation. The phantom were scanned with two transducers with 100 and 200 µm pitch, i.e. the distance between the center of the elements in the transducer. Comparisons were made both for estimations of the velocity and the total displacement of the phantom. Motion estimations in cine loops sampled at a low frame rate were conducted for comparison.

The iterative motion estimation scheme works well with the used block-matching method (Figure 13). Longer initial iteration length resulted in smaller standard deviation in the estimates than the shortest initial iteration lengths. It also resulted in mean estimation errors closer to zero than using the medium initial iteration lengths. Neither the pitch of the transducer or beamforming method had a major influence on the estimation errors. The size of the pitch of the transducer had much larger influence when using a low frame rate sampling.

Figure 13. Estimated lateral positions using the proposed iterative tracking scheme shown in black. The same motion estimation method were used for the cyan line but without the iterations. Figure originally from Paper V.
The results in Paper V showed that our hypothesis, that block-matching methods prefer longer movements, is true. It is also clear from the figures that the method still could estimate small movements (Figure 13). Please note, that the small oscillations observed in Figure 13a, when the phantom had reached full displacement, have been confirmed to be true. The results also indicate that the size of the pitch only gave a limited effect on the motion estimation errors when using high frame rate images. This could be compared to the reduction of the motion estimation errors when using a smaller pitch and the low frame rate images. This indicates that the use of a focus during transmit is the underlying effect on the motion estimation errors when using different sizes of pitch. Although the beamforming methods clearly affects the images visually, an evaluation metric method will act as a strong filter and remove most of the effect of the beamforming method. Thus the accuracy of motion estimation using block-matching is more affected by the shape of the surface of evaluation metric values than the samples in the image. This is clearly shown by the minor differences in tracking accuracy for the beamforming methods.
8. Discussion

The research in this thesis include three innovative methods presented in Papers I, III, and V. One common characteristic is that they use two sources of information to improve the performance of motion estimations: in Paper I two motion estimations are performed using two different kernels from sequential images; in Paper III the sub-sample estimation of one method is used with a threshold to determine whether a second sub-sample estimation method should be used instead; and in Paper V two motion estimations are performed using two different kernels from the anteroposterior images which have opposite relative velocities. Using two, or more, different sources of information during motion estimation may be used in other situations; e.g. can the use of RF data and B-mode data for the same kernel be beneficial? Preferably the used methods should be as independent as possible. However, all methods will be using the ultrasound images as their source of data which implies that total independence can never be achieved. The use of two estimation methods can easily be confused with use of a priori information and depending on the use of the a priori information they can be the same. The idea when using multiple estimation methods, is that the strengths of the methods should be used to remove any weakness.

The change from using data sampled in two dimensions to the use of data sampled in three dimensions cause only minor changes in many methods of motion estimation. The major influence of using 3D image data is the time needed to sample the data in each image as a relatively slow sampling time can result in shearing of the data as the depicted objects will move during sampling. If sufficiently high sampling rate can be achieved, the use of 3D images will very likely increase our understanding of the studied objects.

That the image quality affects the motion estimations performed is clear. The quality will be affected by both the used ultrasound equipment and the settings used during acquisition. This introduces problems when comparing methods for motion estimation. Implementing another researchers motion estimation methods can be problematic as researchers often optimizes their methods without reporting the exact procedure, and that optimization is often depending on the used cine loops. Trying the alternative, to reproduce the cine loops of other researchers, will also be difficult. In silico cine loops can be rather well recreated when simulated by someone else though randomness entered in scatter location and strength as well as any added noise can have a small effect. The main problem using in silico cine loops are that many authors are rather lax in detailing the settings when simulating their cine
loops. Phantom measurements will be influenced by both the setting on the ultrasound machine and the phantom. Though the used equipment is rather well described, descriptions of the used settings on ultrasound machine are mostly rather sparse except on the used frame rate. Sometimes, facts about the used phantom are also missing. Significant differences can be observed between the in vivo cine loops used by different research groups. Not only are the settings mostly unknown but, most important, each individual is different. Thus motion estimations conducted in two individuals are likely to result in slightly varying results. When developing a new motion estimation method the available cine loops are used; both for developing and testing the method. It is then possible to develop a method that works very well with the cine loops in the testing but when testing the method on other cine loops the motion estimation errors can differ drastically. A solution to this problem, and a way for easier comparison of different motions estimation methods, would be an open database or competitions [94] with cine loops depicting different object of varying complexity. This could result in better and more objective comparisons with agreed upon evaluation metrics.

One aim of Paper II was to evaluate the effect on the motion estimation errors for a given sub-sample estimation method when the evaluation metric method was changed. The reason for changes in the motion estimation errors is different for the three types of sub-sample estimation methods:

a. Interpolation of the data points; most if not all effects of the evaluation metric method arise during search for the extreme point. The different evaluation metric methods give slightly different tracking accuracy with the same search method (Figure 8).

b. Interpolation of evaluation metric values; any effects depends on the sub-sample estimation method. As the theoretical curve or surface of the evaluation metric values differs between the evaluation metric methods, the sub-sample estimation methods ability to accurately mimic the theoretical curve or surface of the current evaluation metric method will determine the accuracy of the interpolations and the accuracy can thus differ between evaluation metric methods. However, the fit of the function in amplitude is not as important as the spatial fit, i.e. the extreme point should be at the correct position.

c. Analytically solving the min/max problem for the evaluation metric values; again the fit between the theoretical curve and the used function determines the estimation accuracy. However, the fit of the function in amplitude is not as important as the spatial fit, i.e. the extreme point should be at the correct position.
Out of plane movement is an insidious problem with ultrasound when measuring motion and care has to be taken to position the ultrasound probe so the investigated motion is taking place in the image plane. The problem is that unless the investigated object contains a surface or line that is known to be parallel with the investigated motion it is very hard to detect a slow out of plane motion and if a lot of speckle decorrelation exists, even a fast out-of-plane motion can be hard to detect. It has been suggested to use the correlation of the speckle before and after movement [95] but that is mainly valid if no in-plane motion exists as the changes in the correlation values due to the in-plane values are in the same order or larger than the changes caused by the out of plane motion (Figure 14). Another problem when measuring \textit{in vivo} is the existence of non-linear motions, especially if the motion is not limited to a plane. In this case, the best solution for the user is to find the position for the transducer that minimize the out of plane movement. In worst case the entire motion can only be piecewise estimated with reasonable out of plane movements. In the future, the use of 3D ultrasound image is likely to solve this problem entirely.

![Figure 14](image.png)

Figure 14. The evaluation metric values using normalized cross correlation for 80 kernels when moving a phantom in the lateral direction without out of plane motion. Please note that the motion estimations for all movements were correct at pixel level.
9. Summary

This thesis has presented new block-matching motion estimation methods developed for generic in vivo use. The methods have been evaluated and compared to existing methods in silico, on phantoms, and in vivo. Our findings include:

- The use of an extra kernel from an earlier frame – which was shown to reduce the estimation errors while maintaining the kernel size, or to decrease the kernel size while maintaining the level of the estimation errors. Also, a possible increase of usability has been observed in vivo, although not quantified, compared to our previous methods.

- A combined sub-sample motion estimation method – which combines two sub-sample estimation methods and reduces the negative attributes of the two combined sub-sample estimation methods while retaining their positive attributes.

- An iterative motion estimation scheme for use in high frame rate cine loops – the tracking scheme was shown to give accurate estimations with a Lagrangian viewpoint over 1024 images in Paper V but longer (~6000 images) cine loops have successfully been used (unpublished data).

- The first two methods have been used to extend our knowledge of the longitudinal movement of the arterial wall in vivo. The combined methods performed well; motion estimations were acquired in all valid subjects. Three previously movement phases and two additional movement phases were investigated. The results suggest a relationship between the longitudinal movement pattern and aging of an individual. Cine loops at a low (~50 Hz) frame rate were used but we now have the tools to investigate the longitudinal movement at a high (~1500 Hz) frame rate.

This thesis thus present and evaluate refined methods to measure vascular function through the estimation of longitudinal movement.
10. Future considerations

There are two major paths leading from this thesis: one path leads towards improved methods for motion estimation using ultrasound data; and the other path leads towards a better understanding of the human physiology. In most of the work, SAD has been used for estimating similarity. The benefits of SAD include low calculation times and high accuracy of motion estimations using B-mode data. The drawback is that SAD, in my experience, gives a rather low accuracy when estimating motions using RF data. An equally fast method but with a higher accuracy could be beneficial. Although GS15PI reduced the bias of the two used sub-sample methods, the break point of 0.15 was tested on one series of cine loops and might not be optimal. Also, replacing one of the sub-sample estimation methods with another method could further improve the results. On the physiological path, one step has already been taken in Paper IV. A much larger material of motion estimations from both healthy individuals and from individuals with cardiovascular diseases and cardiovascular risk factors, are needed to determine if the magnitude of the longitudinal movement and/or the movement pattern can be used as a biomarker for cardiovascular disease. However, the methods presented should not only be limited to studies of the cardiovascular system as they are universal tools for motion estimations in B-mode or pixelated image data.

When it comes to investigating the longitudinal vessel wall movement of the common carotid artery, the next step could be 3D volumes of the artery at a frame rate of at least 50 Hz. That would require a 2D-array ultrasound transducer, center frequency 7-12 MHz, with a field of view large enough to see the full movement of the artery during a full heart cycle, e.g. a cube with sides at least 2 mm long. In order to avoid shearing of the ultrasound images, plane wave imaging is probably needed but then the image quality also needs to be improved. With this set-up, the intima-media complex should be visible in every ultrasound investigation and it would be much easier to collect image data with sufficient image quality for accurate motion estimations.

It is 15 years since the first measurements were presented on longitudinal movement. Considering that most of the measurements have been conducted on healthy volunteers the meaning of the different phases of the longitudinal movement in a health perspective is still difficult to see today. With the tools investigated in this thesis, it is now time to approach the clinical world and collect data from patients to try to see if these phases can be used as indicators and hopefully early indicator of diseases. Such work has already been started, e.g. in a European
project denoted SUMMIT ("Surrogate markers for micro- and macro-vascular hard endpoints for innovative diabetes tools"). However, the need for high quality in vivo cine loops of both healthy and diseased individuals are large and the motion estimation methods of today are still not capable of estimating motion in all collected cine loops. Although the research in this thesis show an increased robustness in the motion estimations and will be valuable tools in present research, it is believed that further improvements will be needed in the future. Thus, research should be made to both increase the performance of the motion estimation methods and to increase the usability of the cine loops by signal processing of the image data.

Although we in Paper V found that the beamforming method had a minor influence on the motion estimation errors when using our iterative block-matching tracking scheme, it is believed that the beamforming method has an important role to fill: to visualize the echoes in the ultrasound images. The image quality of cine loops from a commercial ultrasound machine and the high frame rate cine loops used in Paper V differs a lot and the reduced image quality impedes accurate motion estimations in the high frame rate images. Improving the image quality is thus necessary in order to get good motion estimations in vivo high frame rate images.
11. References


IMPROVED TRACKING PERFORMANCE OF LAGRANGIAN BLOCK-MATCHING METHODOLOGIES USING BLOCK EXPANSION IN THE TIME DOMAIN: IN SILICO, PHANTOM AND IN VIVO EVALUATIONS

JOHN ALBINSSON,* SOFIA BJORSSON,†† ASA RYDÉN AHLGREN,§ and MAGNUS CINTHIO*

*Department of Biomedical Engineering, Lund University, Lund, Sweden; †School of Business and Engineering, PRODEA Research Group, Halmstad University, Halmstad, Sweden; ‡Health and Welfare, Dala Sports Academy, Dalarna University, Falun, Sweden; and §Clinical Physiology and Nuclear Medicine Unit, Department of Clinical Sciences, Lund University, Malmo, Sweden

(Received 16 September 2013; revised 6 May 2014; in final form 14 May 2014)

Abstract—The aim of this study was to evaluate tracking performance when an extra reference block is added to a basic block-matching method, where the two reference blocks originate from two consecutive ultrasound frames. The use of an extra reference block was evaluated for two putative benefits: (i) an increase in tracking performance while maintaining the size of the reference blocks, evaluated using in silico and phantom cine loops; (ii) a reduction in the size of the reference blocks while maintaining the tracking performance, evaluated using in vivo cine loops of the common carotid artery where the longitudinal movement of the wall was estimated. The results indicated that tracking accuracy improved (mean 5 48%, p < 0.005 [in silico]; mean 5 43%, p < 0.01 [phantom]), and there was a reduction in size of the reference blocks while maintaining tracking performance (mean 5 19%, p < 0.01 [in vivo]). This novel method will facilitate further exploration of the longitudinal movement of the arterial wall. (E-mail: john.albinsson@bme.lth.se) © 2014 World Federation for Ultrasound in Medicine & Biology.

Key Words: Ultrasound, Motion estimation, Longitudinal movement, Speckle tracking, Arterial wall movement.

INTRODUCTION

Ultrasound has been used extensively to study the movement of blood and tissue (Baker 1970; Bohs and Trahey 1991; Bonnefous and Pesqué 1986; Cinthio et al. 2005a; de Jong et al. 1990; Farron et al. 2009; Kanai et al. 2003; McDicken et al. 1992; Tortoli et al. 2006; Wells 1969). Tissue motion measurements provide functional information on the tissue of interest and have attracted attention for various applications such as evaluation of cardiac (Amundsen et al. 2006; Byram et al. 2010; D’hooge et al. 2002; Mailloux et al. 1989; McDicken et al. 1992), vascular (Arndt et al. 1968; Cinthio et al. 2006; Eriksson et al. 2002; Hansen et al. 2009; Hasegawa et al. 1998; Maurice et al. 2008) and skeletal muscle (Björsson et al. 2008; Kubo et al. 2003; Macaluso et al. 2002) function. It has been found that tissue motion measurements not only can provide new information on the tissue-of-interest (Arndt et al. 1968; Cinthio et al. 2006; Kanai et al. 2003), but can also provide prognostic information for patients suspected of having cardiovascular disease, with both cardiac (Madler et al. 2003; Marwick et al. 2004) and vascular (Blacher et al. 1999) applications.

Until recently, measurements of arterial wall movements have focused on changes in diameter (Nichols and O’Rourke 2005). However, we succeeded in measuring and describing a distinct reproducible bidirectional multiphasic longitudinal movement, that is, movement parallel to the blood flow, of the arterial wall of the same magnitude as the diameter change in the common carotid artery (Cinthio et al. 2005a, 2006; Persson et al. 2002, 2003). Significant longitudinal movement of the same magnitude as the diameter change has been seen in the aorta as well as in the brachial and the popliteal arteries (Cinthio et al. 2006). We also found that the outer part of the arterial wall, the adventitial region, in these arteries exhibit the same basic pattern of longitudinal movement, but the magnitude of movement is smaller than that of the intima–media complex, thereby indicating the presence of previously unknown substantial shear strain and, thus, shear stress intramurally (Cinthio et al. 2006). In
addition, we found that the major circulating hormones that play a role in vascular tone, adrenaline and noradrenaline, can dramatically increase longitudinal movement (Ahlgren et al. 2009), suggesting that the longitudinal movement can be a missing link between mental stress and cardiovascular disease (Ahlgren et al. 2012b). It has been hypothesized that the pattern and/or magnitude of longitudinal arterial wall movement can be used as a biomarker for cardiovascular disease (Ahlgren et al. 2009), suggesting that the longitudinal movement (both longitudinal and radial components) of the arterial wall also in cine loops, where the intensity of the specific echo structures is unstable. By implementation of a block-matching method with a Lagrangian flow description, that is, the reference block follows the same structure throughout a cine loop, reference blocks from several previous frames can be used during motion estimation. In this way, the effective area for block matching is increased, while the spatial resolution of the motion estimation is maintained. Thus, we proposed a block-matching method using two reference blocks of equal size (Albinsson et al. 2010), one from the latest frame (search frame −1) and the other from the preceding frame (search frame −2), to search for the same relevant block in the search frame. With a frame rate high compared with the rate of tissue and speckle deformation in the images, only minor differences between the two reference blocks will be observed. Furthermore, because the addition of an extra reference block does not change the actual size of the block, the spatial resolution of motion estimations remains unchanged. We thus believe that the use of an extra reference block will lead to increased performance in the motion estimation without changing the spatial resolution of the motion estimations. We also believe that the effect of an extra reference block can be used for the alternative benefit: the size of the reference block can be decreased to increase the spatial resolution of the motion estimations while maintaining motion estimation performance.

The aim of the study described here was to evaluate the tracking performance of a basic block-matching method using an extra reference block. In the evaluation, we used three different types of ultrasound cine loops: (i) simulations in Field II (Jensen 1996; Jensen and Svendsen 1992), (ii) phantom measurements, (iii) in vivo examinations of 20 healthy volunteers in which the longitudinal movements of the intima–media complex of the common carotid artery wall were estimated. In the simulations and in the phantom measurements, the motion estimation was compared with set displacements. In the in vivo cine loops, the motion estimation was compared with both a basic method and our reference method (Cinthio et al. 2005a, 2005b) for measurement of the longitudinal movement of the arterial wall.

**METHODS**

In this article, the terms **axial** and **lateral** are used frequently. These terms refer to the orientation of the
image and ultrasound transmission, with axial and lateral movement describing vertical and horizontal movement in the image. This should not be confused with radial and longitudinal movement of the arterial wall in the \textit{in vivo} measurements.

\textbf{Block matching}

In block matching, a reference block is compared with several blocks in the search frame to determine which block is most similar to the reference block. In this study, we used the sum of absolute difference (SAD) (Bohs and Trahey 1991) as the matching criterion to determine the most similar blocks in the search frame. As an example using ultrasound images of an artery, a matrix of SAD values was calculated between a reference block from search frame –1 and all possible blocks in an area of the search frame, that is, a full search. Setting the position of the block with the lowest SAD value to (0, 0), the SAD values of all blocks along the row and the column of the matrix with the lowest SAD value are illustrated in Figure 1. The slope of the lines, down to the minimal SAD value for the block with the best match, is determined by the uniqueness of the reference block and how much it has changed in the next frame. This holds true both if the reference block is taken from search frame –1 and if the reference block is taken from search frame –2 (Fig. 1). Because of speckle deformation and out-of-plane movement, a reference block obtained from search frame –2 has undergone changes compared with the block from search frame –1. However, as indicated in Figure 1, it is feasible to use two reference blocks from two different previous frames if the frame rate is high compared with the rate of tissue or speckle deformation in the images.

\textbf{Basic block-matching method}

The basic block-matching method incorporated two algorithms: a sparse iterative search algorithm, and a sub-pixel estimation method. The size of the reference blocks used was optimized separately for each of the three types of cine loops (\textit{in silico}, phantom and \textit{in vivo}).

The sparse iterative search algorithm was a modified version of adaptive rood pattern search (Nie and Ma 2002), used for estimating the motion of the block from search frame –1 to the search frame at pixel resolution. Adaptive rood pattern searches estimate motion in two steps and searches for the smallest SAD value in an unlimited search region. In step 1 (large squares in Fig. 2), our modified version calculated the SAD values for six blocks, each centered on one search position: the center position, the four surrounding adaptive positions and the adaptive movement position. The center position was provided either by the user or by previous block matching. The four adaptive positions were above, below, to the left and to the right of the center position, with a distance set to the largest component (axial or lateral) of the movement vector (minimum = 1 pixel). The location of the movement position was calculated by adding the movement vector, obtained as the vector between the position of the reference block in search frame –2 and its position in search frame –1, to the center position. The movement vector was recalculated in each new frame to adapt to changes in velocity. In the starting frame, four movement vectors (instead of one vector) with axial and lateral components 3 pixels long were used, marking corners in a box around the center position. In step 2 (large circles in Fig. 2), which was iterative, the center position was positioned at the search position with the minimum value of SAD calculated in step 1 or in the previous iteration. The distance to the four adaptive positions, where SAD values were calculated, was set to half the distance used in step 1 or in the last iteration (only natural numbers were used). The iterations continued with a minimum distance of one until a block with minimum value of SAD was reached, a position designated \((x_{\text{min}}, y_{\text{min}})\).

To estimate the lateral and axial sub-pixel positions, the calculated SAD values of five adjoining blocks were used. An example is given in Figure 2, where the blocks...
are positioned at S1 through S5, with S3 at (x_{\text{min}}, y_{\text{min}})_{1}, with S3 at (x_{\text{min}}, y_{\text{min}})_{1}$. The choice of parabolic interpolation (Cespedes et al. 1995) for the in vivo measurements used a full-search block-matching approach with very small search regions (<1 mm$^2$) and blocks (approximately 0.01 mm$^2$). Cross-correlation was used as matching criterion. To minimize the block size in the radial direction and to be able to track the longitudinal movement in the carotid artery of volunteers with a large radial movement, a priori contour tracking of the intima echo in the radial direction was used. Sub-pixel resolution was achieved by interpolating the pixel values of the frames. This method was chosen as our reference method as it, as far as we know, still is the best to measure the three distinct reproducible bi-directional phases of the longitudinal movement of the common carotid artery wall: the first antegrade movement, that is, a movement in the direction of the blood flow; a retrograde movement, that is, a movement in the direction opposite blood flow; and the second antegrade movement (Ahlgren et al. 2012a; Cinthio and Ahlgren 2010; Cinthio et al. 2006).

Use of an extra reference block from the previous frame

The reference block was expanded in the time domain using the reference block obtained in search frame –2. The extra reference block was matched in the search frame with nine blocks each centered on the whole-pixel position (x_{\text{min}}, y_{\text{min}})_{1} and its eight neighboring positions. The position of the block with the minimum SAD value was denoted (x_{\text{min}}, y_{\text{min}})_{2}. The sub-pixel position determined by the extra reference block was estimated by eqn (1) with the block centered on (x_{\text{min}}, y_{\text{min}})_{2} as S3 (Fig. 2). The final optimal position for the block was calculated as the average of the sub-pixel position for the basic method and the sub-pixel position for the extra reference block. The reference block obtained in search frame –1 was used as the extra block for block matching in search frame +1. In the first frame of tracking, no reference block existed in search frame –2, and thus, the use of an extra reference block was not applicable. Figure 3 illustrates the workflow for movement estimation using an extra reference block.

Reference method

The chosen reference method (Cinthio et al. 2005a, 2005b) for the in vivo measurements used a full-search block-matching approach with very small search regions (<1 mm$^2$) and blocks (approximately 0.01 mm$^2$). Cross-correlation was used as matching criterion. To minimize the block size in the radial direction and to be able to track the longitudinal movement in the carotid artery of volunteers with a large radial movement, a priori contour tracking of the intima echo in the radial direction was used. Sub-pixel resolution was achieved by interpolating the pixel values of the frames. This method was chosen as our reference method as it, as far as we know, still is the best to measure the three distinct reproducible bi-directional phases of the longitudinal movement of the common carotid artery wall: the first antegrade movement, that is, a movement in the direction of the blood flow; a retrograde movement, that is, a movement in the direction opposite blood flow; and the second antegrade movement (Ahlgren et al. 2012a; Cinthio and Ahlgren 2010; Cinthio et al. 2006).
The effect of the use of an extra reference block was investigated using three types of ultrasound images: cine loops created in silico, cine loops obtained from measurements on a phantom, and cine loops obtained from in vivo examinations of the common carotid artery wall. The three types of cine loops were chosen to test the effect of the use of an extra reference block on progressively more realistic data: (i) realistic speckle, (ii) speckle and echo structures with noise, and (iii) a clinical setup in which out-of-plane movement can be a factor.

In silico cine loops. Twenty cine loops of B-mode data, each containing 50 frames, were simulated using Field II (Jensen 1996; Jensen and Svendsen 1992). The simulated model consisted of a laterally moving body of a uniformly random distribution of scatterers, each scatterer having random scattering strength. The lateral movement was set to be constant in each cine loop. The movement in the different cine loops was in the range 0.1–2.0 pixels per frame in steps of 0.1 (24–488 μm/frame). The settings used in the simulations are presented in Table 1. The settings used allowed a pixel density of 8.1 pixels/mm axially and 4.1 pixels/mm laterally. The size of the block was set to 1.11 mm axially and 2.20 mm laterally (9×9 pixels) for tracking in all cine loops. No noise was added to the cine loops.

Phantom measurements. Twenty-eight cine loops of B-mode data, each containing 80 frames, were collected on lateral and diagonal phantom movements. The ultrasound machine used was a Vevo 2100 imaging system (VisualSonics, Toronto, ON, Canada) equipped with a linear array transducer (center frequency = 30 MHz). The frame rate was 100 Hz, and the pixel density was 45.8 pixels/mm axially and 39.4 pixels/mm laterally. The size of the block was set to 0.72 mm axially and 0.84 mm laterally (33×33 pixels) for tracking in all phantom cine loops. One transmit focus was used, and the persistence function was turned off to avoid averaging between frames.

The phantom was made of 1.0 g agar (Agar-Agar, Merck KGaA, Darmstadt, Germany) dissolved in 50 g water (Burlew et al. 1980), with 25 mg graphite powder (Graphite 25 μm, Merck, Darmstadt, Germany) and 2.5 g glass beads (type A2429 glass, mean diameter 93 μm, Potters Industries, Valley Forge, PA, USA). To our experience, this design gives a mix of speckle and distinct echoes comparable to the tracked area of the clinical cine loops investigated.

Table 1. Settings for the in silico cine loops simulated in Field II

<table>
<thead>
<tr>
<th>Setting</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width of element</td>
<td>0.215 mm</td>
</tr>
<tr>
<td>Height of element</td>
<td>6 mm</td>
</tr>
<tr>
<td>Distance between elements</td>
<td>0.030 mm</td>
</tr>
<tr>
<td>Number of elements in transmit/receive</td>
<td>64</td>
</tr>
<tr>
<td>Focus in transmission (fixed focal point)</td>
<td>40 mm</td>
</tr>
<tr>
<td>Focus in receiving</td>
<td>Dynamic focusing</td>
</tr>
<tr>
<td>Center frequency</td>
<td>6 MHz</td>
</tr>
<tr>
<td>Speed of sound</td>
<td>1540 m/s</td>
</tr>
<tr>
<td>Sampling rate</td>
<td>100 MHz</td>
</tr>
<tr>
<td>Number of scan lines</td>
<td>128</td>
</tr>
<tr>
<td>Size of phantom (width × height × depth)</td>
<td>40 × 50 × 10 mm³</td>
</tr>
</tbody>
</table>
The phantom measurements were obtained using a system including a water tank and stepping motors (Vexta PH26-15, Oriental Motors, Tokyo, Japan) connected to a graphical user interface. The movements were measured with two different phantom transducer angles, 88° and 52°, against the line of movement. The angles were measured with a protractor and had an estimated error of ±1°. The angles were also confirmed by measurements in the cine loops. The phantom was not at any time subjected to compression or deformation, which is a reasonable approximation of the arterial wall movement of the intima–media where the estimations were performed. The movement of the phantom was adjusted to be in the image plane of the transducer, and the velocities were set in the range of 2–15 mm/s in steps of 1 mm/s (0.5–5.9 pixels/frame). The velocity of the phantom was confirmed as an average over several seconds using a triangulation laser (M5L/2, MEL Mikrolektronik GMBH, Eching, Germany) and an oscilloscope (Tektronix TDS 360, Tektronix, Beaverton, OR, USA) by measuring the rotational speed of the threaded bar that moved the phantom sled. The estimated error of the measured velocity compared with the set velocity was ±1%. To correct for any measurement errors in the ultrasonic method caused by the temperature dependence of the speed of sound in water, the water temperature was measured with a thermometer before and after the experiments. This temperature was used to establish the true speed of sound (Lubbers and Graaf 1998), which in turn was used to correct the axial measurements. The lateral measurements were unaffected by this temperature dependence.

In vivo measurements. Two independent recordings were made on each of 20 healthy volunteers (10 males aged 27–57 y, 10 females aged 25–49 y). The common carotid artery on the right side of the volunteers was scanned such that the longitudinal direction is the horizontal orientation of the image. A distinct echo of an inhomogeneity or an irregularity of the arterial wall had to be visible in all the images during several cardiac cycles. In addition, to ensure that the recordings were performed properly, the longitudinal movement had to be visible along the visualized vessel wall segment. An electrocardiogram was recorded during all the examinations. The collection of the in vivo data has been extensively described by Cinthio and Ahlgren (2010). The volunteers gave their informed consent according to the Helsinki Declaration, and the study was approved by the ethics committee of Lund University, Lund, Sweden.

All investigations were performed with an ultrasound system (HDI5000, Philips Medical Systems, Bothell, WA, USA) equipped with a linear array transducer (Model L12-5). One transmit focus was used, and the persistence function was turned off to avoid averaging between frames. No image processing was applied. To our experience, images subjected to filtering, persistence, multiple focuses and/or spatial compounding contain less unique features and, thus, are less optimized for motion estimation. The settings used allowed a frame rate of 55 Hz and a pixel density of 19.2 pixels/mm in each direction. To achieve the smallest usable block, its size was optimized individually and independently for each tracking method and cine loop. The optimization was made by visually comparing the estimated position of the block with the movement of the echoes and speckle in the cine loop. With similar levels of optimization, the tracking performance should be similar for all methods tested, with a difference only in the size of the block used. The sizes of the blocks were in the ranges 0.26–0.47 mm axially and 0.57–1.61 mm laterally (5–9 × 11–31 pixels) for the basic method and in the ranges 0.26–0.47 mm axially and 0.36–1.09 mm laterally (5–9 × 7–21 pixels) for the basic method with the use of an extra reference block. The first reference block was positioned at the same coordinates in the image (maximum of ±1-pixel deviation) as in the investigation conducted by Cinthio and Ahlgren (2010).

Statistical analysis

The possible benefits of using an extra reference block were evaluated in two different ways: (i) by calculating the absolute tracking error of the motion estimation in cine loops made in Field II and on phantom measurements, and (ii) by using the method of Bland and Altman (1986). The absolute tracking error per frame could be calculated for the in silico data as all movements were known. In the phantom measurements, the average movement per frame was calculated by finding the starting and ending positions of each block and dividing by the number of frames – 1. This was done because of the low sampling rate when confirming the set velocity of the phantom, which gave rise to an unknown level of stability of the velocity. The absolute values of all errors were used to prevent two erroneous estimates to accidentally give one accurate estimate of the movement over two frames. In vivo, the analyses were made both between the results from use of the two tracking methods (the basic method and the basic method with the use of an extra reference block) and using the results obtained by our reference method (Cinthio et al. 2005a, 2005b). According to the method of Bland and Altman (1986), the difference between the two repeated measurements was plotted against their mean. The systematic difference, the random difference and the coefficient of variation (CV) were also calculated. The systematic difference is defined as
systematic difference \( = \frac{1}{2n} \sum_{i=1}^{n} d_i \) (2)

where \( d_i \) is the difference between the measurements of each subject, and \( n \) is the number of patients. The random difference was defined as

random difference \( = \sqrt{\frac{1}{2n} \sum_{i=1}^{n} d_i^2} \) (3)

The CV was calculated and defined as

\[
CV = \frac{\text{random difference}}{\text{overall mean}} = \sqrt{\frac{1}{2n} \sum_{i=1}^{n} d_i^2} = \sqrt{\frac{1}{2n} \sum_{i=1}^{n} m_i}
\] (4)

where \( d_i \) is the difference between the measurements of each subject, \( n \) is the number of patients and \( m_i \) is the measurement.

A paired Student t-test was used to evaluate the putative significance of differences in improvements in tracking accuracy between in silico and phantom measurements, as well as to evaluate the putative significance of the decrease in area of the reference block used in vivo.

**RESULTS**

In silico and phantom measurements

Figure 4 (a, b) illustrates the distribution of the absolute tracking error per frame of the motion estimations performed on the in silico cine loops. Compared with the basic method, the use of an extra reference block significantly decreased absolute tracking errors by 48% on average (\( p, 0.005 \)). Comparing (a) and (b) in Figure 4, the improvement in tracking with use of an extra reference block is obvious; note the difference in the positions of the center of mass.

Figure 5 (a, b) illustrates the distribution of the absolute mean tracking error per frame of the motion estimations performed on the cine loops obtained from phantom measurements. Compared with the basic method, the use of an extra reference block significantly decreased absolute tracking errors by 43% on average (\( p < 0.01 \)). Also here, an improvement in both the precision and accuracy of tracking using an extra reference block can be seen.

Table 2 summarizes the errors of the motion estimations in the in silico cine loops and phantom measurements, respectively.

Previous research has indicated that the use of parabolic interpolation in motion estimation is liable to provide a biased estimation (Geiman et al. 2000). This effect is clearly seen in the distribution of the errors from the motion estimation when plotted against the velocity set in the in silico cine loops (Fig. 6) in which movements of 1 and 2 pixels exhibit small average errors, whereas movements close to 0.25, 0.75, 1.25 and 1.75 pixels exhibit, as expected, large average errors. This bias can also be seen in Figure 4 as a broadening of the base in the distribution of the absolute tracking errors. The use of an extra reference block largely reduced the bias caused by use of parabolic interpolation (Fig. 6b), and we believe that the averaging of the positions estimated from the basic method and the extra reference block were the reason for this reduction. It can be suspected that bias exists also when estimating the movements in the phantom cine loops. However, even if a similar broadening of the errors can be seen in Figure 5, no clear evidence of any bias can be seen when the errors are plotted against the set velocity. It can be suspected that the noise in these cine loops, or an unknown variability of the velocity of the phantom, diminishes the effects of the bias.

In vivo measurements

Figure 7 illustrates the estimation of the longitudinal movement of the intima–media complex of the common
carotid artery wall of a 30-y-old male. For the 40 in vivo measurements, the antegrade movement (LMov 1), that is, displacement in the direction of blood flow, was a mean of 312 μm (SD = 222). The subsequent second antegrade movement (LMov3) was a mean of 577 μm (SD = 218). Figures for the systematic and random differences for the basic method and the basic method with the use of an extra reference block are given in Table 3. The intra-observer variation (CV) for the different phases of movement for all volunteers were 22%, 18% and 22%, respectively, using the basic method, and 21%, 13% and 17%, respectively, using the basic method with the use of an extra reference block. Though the mean area of the block was decreased when the extra reference block was used compared with when the basic method was used, the intra-observer variation was maintained. The differences in CV values between the methods indicate that either there is a difference in optimization level or the basic method cannot possibly track as well as the basic method with the use of an extra reference block.

With the basic method, the mean area of the block was 0.31 mm² (SD = 0.13) in the range 0.15–0.76 mm², whereas with the basic method with the use of an extra reference block, the mean area of the block was 0.25 mm² (SD = 0.09) in the range 0.09–0.51 mm². This equals a decrease in the area of the block of 19% (p < 0.01). Figure 8 illustrates the difference against the mean values between the basic method using an extra reference block and the reference method used (Cinthio et al. 2005a, 2005b) (see also Table 3). Six cine loops were excluded in the CV calculated for the reference method as they contained no specific echo structure with enough stability, and thus, the reference method was not able to track the movement.

Though not seen in the data, it can be suspected that bias resulting from parabolic interpolation exists also when estimating the movements in the in vivo cine loops. As the block will move different distances between frames, the bias (which can have positive or negative

<table>
<thead>
<tr>
<th>Type of cine loop</th>
<th>Tracking method</th>
<th>Lateral motion estimation error (pixels)</th>
<th>Axial motion estimation error (pixels)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean of absolute error per frame</td>
<td>Standard deviation</td>
</tr>
<tr>
<td>In silico</td>
<td>BM</td>
<td>0.073</td>
<td>0.040</td>
</tr>
<tr>
<td></td>
<td>EB</td>
<td>0.035</td>
<td>0.026</td>
</tr>
<tr>
<td>Phantom lateral movement</td>
<td>BM</td>
<td>0.035</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>EB</td>
<td>0.021</td>
<td>0.014</td>
</tr>
<tr>
<td>Phantom diagonal movement</td>
<td>BM</td>
<td>0.053</td>
<td>0.038</td>
</tr>
<tr>
<td></td>
<td>EB</td>
<td>0.035</td>
<td>0.025</td>
</tr>
</tbody>
</table>

BM = basic method; EB = basic method using an extra reference block.
* Errors are presented as the mean of the absolute error per frame and the corresponding standard deviation. The error is calculated as the difference between estimated and set movement. The basic method and the basic method with the use of an extra reference block were used. The improvements in tracking errors were significant for both the in silico cine loops (p < 0.005) and the phantom measurements (p < 0.01).
DISCUSSION

It was hypothesized that the incorporation of an extra reference block would increase the tracking performance of a block-matching based method without changing the spatial resolution of the motion estimations. In this work, this effect was illustrated in the estimation of movements in both in silico and phantom cine loops. The in vivo measurements indicated the expected alternative benefit of using an extra reference block: the spatial resolution of motion estimations could be significantly increased by reducing the size of the block while the tracking performance still conformed to the basic method. The results from the in vivo measurements also indicated that the basic method with the use of an extra reference block had a tracking performance with only slightly higher variability than the reference method.

The reference method used for the in vivo measurements is specialized for estimating the longitudinal movements of the arterial wall and employ a priori information. CV values on the three distinct reproducible phases of the longitudinal movement of the arterial wall—first antegrade, retrograde and second antegrade—using this method were reported to be 14%, 13% and 16%, respectively (Cinthio and Ahlgren 2010). Figure 8 and the CV values indicate that the basic method with the use of an extra reference block has a tracking accuracy of the same magnitude as the reference method without any observable bias. The reference method gave CV values better than those obtained with the basic method with the use of an extra reference block, but the reference method requires echo structures with higher stability in the cine loops. In 6 of the 40 in vivo cine loops, the stability of the echo structures was too low for the reference method to successfully estimate the movements. Please note that the basic method with the use of an extra reference block successfully estimated the movements in these cine loops and, importantly, they are included in the CV value estimation of the proposed method. The reference method gave CV values better than those obtained with the basic method with the use of an extra reference block, but the reference method requires echo structures with higher stability in the cine loops. In 6 of the 40 in vivo cine loops, the stability of the echo structures was too low for the reference method to successfully estimate the movements. Please note that the basic method with the use of an extra reference block successfully estimated the movements in these cine loops and, importantly, they are included in the CV value estimation of the proposed method. The successful tracking with the basic method with the use of an extra reference block in every in vivo cine loop is probably explained by the fact that it relies more on speckle tracking than on echo tracking, indicating that the demands on the stability of the echo structures can be reduced. The fact that the basic method with the use of an extra reference block can track the different phases of longitudinal movement of the arterial wall using smaller blocks in cine loops with less stable echoes will facilitate future exploration of the pattern and the magnitude of longitudinal movement, as well as intramural shear strain. Exploration of the longitudinal displacement and resulting intramural shear strain of the arterial wall can provide completely new information on vascular mechanics and the function of the circulatory system.

One drawback with the use of an extra reference block is that the maximum velocity that can be tracked is reduced by 50% because the target area has to be within the field of view for three consecutive frames compared with two consecutive frames for the basic method. The tracked target has then moved from one side of the frame to the other. With the settings used in vivo in this study, the basic method can track a maximum velocity of 1 m/s, whereas the basic method with the use of an extra reference block will probably have an average value close to zero in a cine loop.

Fig. 6. Absolute tracking error per frame of the motion estimation performed on the in silico cine loops against the set movement per frame of the cine loops, using (a) the basic method and (b) the basic method with the use of an extra reference block. The boxes indicate the lower and upper quartiles and the median. The bar line indicates 99% of the values. Outliers are indicated as points. The figure is based on 98,000 estimations explaining the seemingly large numbers of outliers. Note the variation in the mean errors for different movements when using the basic method (a). This is due to the biased estimations given by the parabolic interpolation. Also note the decreased bias when using an extra reference block originating in the proceeding frame (b).
A reference block can track a maximum velocity of 0.5 m/s. In the cine loops used in this study, the tissue velocities were at no time greater than 0.05 m/s; most of the velocities were in the range 0–0.015 m/s.

An ongoing discussion is whether to use radiofrequency or B-mode data when estimating movement in cine loops. The spatial resolution of motion estimations and tracking accuracy is the main focus, but we want to raise one more issue in this discussion: accessibility to the data. In this study, we had access to both the B-mode and radiofrequency data on in silico and phantom measurements, but for the in vivo cine loops, only B-mode data were available, as is normally the case in clinical environments where physicians and clinical researchers can save B-mode data only as DICOM or .avi files. Initial tests with the proposed method on DICOM files from a clinical ultrasound machine indicate the feasibility of estimating longitudinal movement of the arterial wall in saved DICOM files (unpublished data). The work by Yli-Ollila et al. (2013) confirms the possibility of using DICOM data for motion estimations. This can lead to easier access to clinical data in the development of methods and subsequent clinical research.

Though we have not seen any article that describes the use of one extra reference block in a block-matching algorithm, the use of pixel information from prior blocks has been investigated, using Kalman-based methods, with promising results (Golemati et al. 2012; Zahnd et al. 2013). The main difference between their methods and that described here is the reference block used for tracking. With a Kalman-based method, the pixel values of the reference block are predicted in the next frame, whereas our method uses the actual pixel values from the previous frame. Kalman methods can be expected to be more time consuming, but as they also use another method to calculate the positions to sub-pixel resolution, no comparison can be made. These methods use a memory factor as a tool to use more data from the previous block for better predictions; in future studies, we should investigate the effect of using more than one extra reference block when tracking. As the only prerequisites for implementing an extra reference block are a Lagrangian flow description of the tracking method and a frame rate higher compared with the rate of tissue or speckle deformation in the images, it is the authors’ belief that the use of an extra reference block can be beneficial in many different tracking methods.

Even though no bias could be proven to disturb the in vivo movement estimations, and even if the use of an

**Table 3.** Comparison between the reference method (Cintio et al. 2005a, 2005b) and either the basic method or the basic method with the use of an extra reference block on 34 measurements in vivo*

<table>
<thead>
<tr>
<th>Tracking method</th>
<th>Cine loop used</th>
<th>Number of measurements</th>
<th>Systematic/random difference</th>
<th>LMov 1</th>
<th>LMov 2</th>
<th>LMov 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM – MC</td>
<td>Same</td>
<td>34</td>
<td>Systematic</td>
<td>–12</td>
<td>42</td>
<td>–29</td>
</tr>
<tr>
<td></td>
<td>Same</td>
<td>34</td>
<td>Random</td>
<td>47</td>
<td>82</td>
<td>74</td>
</tr>
<tr>
<td>EB – MC</td>
<td>Same</td>
<td>34</td>
<td>Systematic</td>
<td>0.1</td>
<td>23</td>
<td>–25</td>
</tr>
<tr>
<td></td>
<td>Same</td>
<td>34</td>
<td>Random</td>
<td>47</td>
<td>58</td>
<td>62</td>
</tr>
<tr>
<td>BM – BM</td>
<td>Two different, same subject</td>
<td>40</td>
<td>Systematic</td>
<td>13</td>
<td>–17</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Two different, same subject</td>
<td>40</td>
<td>Random</td>
<td>74</td>
<td>111</td>
<td>114</td>
</tr>
<tr>
<td>EB – EB</td>
<td>Two different, same subject</td>
<td>40</td>
<td>Systematic</td>
<td>6</td>
<td>–28</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>Two different, same subject</td>
<td>40</td>
<td>Random</td>
<td>76</td>
<td>86</td>
<td>90</td>
</tr>
</tbody>
</table>

MC = reference method; BM = basic method; EB = basic method using an extra reference block; LMov 1 = first antegrade displacement; LMov 2 = retrograde displacement; LMov 3 = second antegrade displacement.

* Intra-observer variability of BM and EB using 40 in vivo measurements are also included. An antegrade displacement is a displacement in the direction of the blood flow. A retrograde displacement is a displacement in the direction opposite the blood flow.
extra reference block likely reduced the bias from the sub-pixel determination, tests with an unbiased sub-pixel interpolation method should be performed to further investigate whether bias from use of parabolic interpolation is an issue when tracking in vivo also when using an extra reference block.

In this work, we differentiate between lateral movement, that is, horizontally in the frame; axial movement, that is, vertically in the frame; longitudinal movement, that is, movement along an arterial vessel; and radial movement, that is, diameter changes in the arterial vessel. We investigated purely lateral movement (in silico and phantom), purely diagonal movement (phantom) and mixed movement (in vivo). The effect on tracking performance with the use of an extra reference block when the investigated movements are purely axial, or a combination of out-of-plane movement and either an axial or a lateral movement, can thus only be hypothesized. The tracking performance in the axial direction will very likely be improved to the same extent as in the lateral direction, but for out-of-plane movement, the situation is more difficult to predict. An out-of-plane movement with an axial or lateral movement will increase the rate of decorrelation of the speckle and, thus, decrease the overall tracking performance of the method. Such decorrelation will probably reduce the positive effect of the use of an extra reference block until the effect disappears. However, in that situation we also question whether the basic method will work. This will be the subject of future work.

CONCLUSIONS

In a Lagrangian flow description, a basic block-matching method with the use of one extra reference block, originating in the preceding frame, has been found to reduce errors in the motion estimation of in silico and phantom cine loops without reducing the spatial resolution of the motion estimations. It has also been found, in in vivo estimations of the longitudinal movement of the arterial wall, that the use of an extra reference block can significantly reduce the size of the reference block, thus improving the spatial resolution of the motion estimations, without any reduction in tracking performance. Furthermore, in comparison with our reference method, the basic method with the use of an extra reference block could in several cases successfully track the longitudinal movement in vivo when the stability of the echo structure was reduced. This will facilitate future exploration of the longitudinal movement and the intramural shear strain of the arterial wall and its physiologic, pathophysiologic and clinical implications.

Acknowledgments—We thank Mrs Ann-Kristin Jonsson for skillful technical assistance. This study was supported by grants from the Swedish Research Council (grant number 2012-3552), the Knut and Alice Wallenberg Foundation (grant number KAW 20060170) and the Medical Faculty, Lund University.

REFERENCES


Abstract— Motion estimation in a series of consecutive images is used in a variety of areas, e.g. video compression and investigation of tissue characteristics and organ function in medical images. Several methods exist both for estimating motions on a pixel level, e.g. block-matching in which two blocks in consecutive images are compared by an evaluation metric, and on a sub-pixel level. In this paper, we have evaluated the tracking performance of all combinations between three evaluation metrics and eight sub-pixel estimation methods. The tracking performance of a sub-pixel method varies depending on the evaluation metric used. This indicates that a reported tracking performance for a sub-pixel estimation method can be significantly different when combined with another evaluation metric. Also there is a large variation in the time needed for the motion estimations depending primarily on the sub-pixel method used but also on the evaluation metric.

Keywords— Sub-pixel estimation, block-matching, motion estimation, ultrasound

I. INTRODUCTION

Motion estimation in a series of consecutive images is used in a variety of areas, e.g. video compression and investigating tissue characteristics and organ function in medical images. For example in ultrasound where tissue motion measurements results in functional information on the tissue-of-interest, and have attracted attention for various applications such as evaluation of cardiac [1], vascular [2], and skeletal muscle [3] function. It has been shown that tissue motion measurements can not only provide new information about the tissue-of-interest [2], but can also provide prognostic information for patients having suspected cardiovascular disease, both with cardiac [4] and vascular applications [5].

Several methods for estimating motion in a series of digital images exist, e.g. optical flow and phase correlation. In this work, we have used a basic block-matching method implemented with a small search region. In order to estimate the motion in an area, a block representing the area is chosen and compared to every block in the search region with the block most similar with the original block assumed to depict the same object. To determine the similarity between two blocks, an evaluation metric, e.g. sum of absolute difference (SAD), sum of squared difference (SSD), or two dimensional normalized cross correlation (NCC), can be used.

However, most of the time, the length of the motion of an object between two successive images is not an exact number of pixels. Therefore, an estimation of the motion on a level of pixels is not enough as the relative error between estimated movement and true movement will, at least for short distances, be larger than acceptable. Several methods exist to determine the motion on a sub-pixel level. The methods can roughly be divided into three sub-groups: 1) analytically solved using the evaluation metric values as input, 2) interpolation of evaluation metric values, and 3) image interpolation. Both the first and second group uses the evaluation metric values in order to determine the sub-pixel position; values that differ depending on the evaluation metric used.

In motion estimations, two performance criterions are vital: estimation time and tracking error. Naturally the error should be kept as small as possible in order to give a correct estimation; but for real-time applications also the estimation time is critical. Often, the size of the estimation error is negatively correlated to the estimation time.

We have found no previous study that evaluates the impact on the performance of a sub-pixel method when used together with different evaluation metrics. The aim of this work was to evaluate the performance of eight sub-pixel position methods when combined with three different evaluation metrics in silico.

II. MATERIAL AND METHODS

A. Image sequences

The investigations in this paper have been made on simulated ultrasound images. In ultrasound images, horizontal direction is commonly denoted lateral while vertical direction is denoted axial; a convention that has been adopted in this paper.

The cineloops (50 images each, pixel density: 8.1x4.1 pixel/mm) were simulated using Field II [6]. The lateral velocities included 0.3, 0.6, 0.9, 1.4, 2.2, and 2.8 pixels/image whereas the axial velocity was 0 pixels/image. Motion estimation was performed on 100 blocks (15x7
pixels each) in each image using a full-search scheme (11x11 pixels) centered on the pixel position of the searched-for block. The searched-for blocks were evenly distributed above and below the focus depth.

B. Evaluation metrics

The performance for motion estimation was evaluated for three evaluation metrics:

- **SAD**
  \[ \alpha = \sum_{i=1}^{n} \sum_{j=1}^{k} |X_{i,j} - Y_{i+m,j+n}| \]  
  (1)

- **SSD**
  \[ \beta = \sum_{i=1}^{n} \sum_{j=1}^{k} (X_{i,j} - Y_{i+m,j+n})^2 \]  
  (2)

- **NCC**
  \[ \gamma = \frac{\sum_{i=1}^{n} \sum_{j=1}^{k} (X_{i,j} - \bar{X})(Y_{i+m,j+n} - \bar{Y})}{\sqrt{\sum_{i=1}^{n} \sum_{j=1}^{k} (X_{i,j} - \bar{X})^2} \sqrt{\sum_{i=1}^{n} \sum_{j=1}^{k} (Y_{i+m,j+n} - \bar{Y})^2} } \]  
  (3)

Here, \( \alpha, \beta, \) and \( \gamma \) denotes the calculated evaluation metric value; \( m \) and \( n \) denotes the displacement between the two blocks; \( l \) and \( k \) denotes the size of the blocks; \( X_{i,j} \) and \( Y_{i,j} \) denotes the pixel values at position \( (i,j) \) in the tracked block and the compared block, respectively, while \( X \) and \( Y \) denotes the average pixel values of the respective blocks.

C. Sub-pixel estimation methods

A total of eight sub-pixel position methods were evaluated. Three of the methods were analytically solved: 1. 1D parabolic interpolation (1D PI), 2. grid slope interpolation (GS) [7], and 3. 2D parabolic interpolation (2D PI). Three of the methods interpolated the calculated evaluation metric values to a factor 128:1: 4. 1D PI, 5. 2D PI, and 6. 2D cubic interpolation (2D Cubic). Two methods interpolated the image data to a factor 128:1: 7. 2D PI and 8. 2D Cubic.

1. **1D PI** fits a one dimensional second-degree polynomial (4), to three evaluation metric values with the center value corresponding to the block with the best similarity to the searched-for block.

\[ y = ax^2 + bx + c \]  
(4)

The polynomial was fitted separately laterally and axially in order to get a sub-pixel estimation in both directions. Fitting + (4) gave, when analytically solved, the sub-pixel estimation:

\[ \Delta x = \frac{\alpha_1 - \alpha_3}{2(\alpha_1 + \alpha_3 - 2\alpha_2)} \]  
(5)

Here, \( \alpha_1 \), \( \alpha_2 \) (center), and \( \alpha_3 \) were evaluation metric values and \( \Delta x \) was the sub-pixel part of the movement with a value less than \( \pm 0.5 \) pixels.

2. **GS** estimates the sub-pixel position separately laterally and axially by use of two evaluation metric values from the current image: the center value corresponding to the block with the best similarity to the searched-for block and the value closest to zero of the two values next to the center value (left or right for lateral or up or down for axial estimation). GS also uses an evaluation metric value calculated between the searched-for block and a block in the same image as the searched-for block at the position of the evaluation metric value used in the current image:

\[ \Delta x = 0.5 \left(1 - \frac{\alpha_2 - \alpha_4}{\alpha_{2,0} - \alpha_{4,0}} \right) \]  
(7)

Here \( \alpha_2 \) (center) and \( \alpha_4 \) were evaluation metric values in the current image and \( \alpha_{2,0} \) and \( \alpha_{4,0} \) were evaluation metric values in the previous image. It should be noted that one of \( \alpha_{2,0} \) and \( \alpha_{4,0} \) were zero [7].

3. In **2D PI** the second-degree polynomial was two dimensional.

\[ z = a + bx + cy + dx^2 + exy + fy^2 \]  
(6)

The polynomial was fitted to nine evaluation metric values with the value in the center corresponding to the block with the best similarity to the searched-for block. The polynomial was then solved analytically by finding the extreme point close to the center position.

4. The polynomial (4) was used for interpolating evaluation metric values in 127 evenly distributed points between each pixel position before finding the position with the best evaluation metric value. This was done separately axially and laterally.

5. The polynomial (6) was used for interpolating evaluation metric values in 127 evenly distributed points between each pixel position both axially and laterally before finding the position with the best evaluation metric value.

6. **2D Cubic** used cubic spline interpolation [7] in order to interpolate nine evaluation metric values to 128:1 both axially and laterally. The optimal position was given directly by the best evaluation metric value.

7. The polynomial (6) were fitted to nine pixel values and were used to interpolate a square, \( \pm 0.5 \) pixels both laterally and axially, around the center pixel to 128x128 samples for a total of 15x7 original pixels before performing a full-search with the chosen evaluation metric.

8. **2D Cubic** used cubic spline interpolation [7] in order to interpolate 15x7 pixel values to 128:1 both axially and laterally original pixels before performing a full-search with the chosen evaluation metric.

D. Evaluation of tracking performance

The tracking performance of each combination of evaluation metric and sub-pixel estimation method was evaluated...
by measuring the estimation time and by calculating the difference between the set movement and the estimated movement. The axial and lateral estimation errors were treated separately. The errors of the motion estimation (pixel/image) for each combination of evaluation metric, sub-pixel position method, and velocity are presented as boxplots in Figure 1. Values outside ±0.25 pixel are part of the statistics but not shown in the figure. The average estimation time in seconds needed for each image (100 blocks) is presented between the lateral and axial errors.

III. RESULTS AND DISCUSSION

Figure 1 shows average estimation time between the lateral and axial estimation errors. For every combination of evaluation metric and sub-pixel estimation method, the estimation errors have been combined in a boxplot. The results show an expected trade-off between estimation time and size of estimation errors. The smallest estimation error is in general obtained when the image was interpolated whereas the analytically solved methods are up to 150 times faster.

Reading the description of GS, we find nothing indicating that the method was tested or even intended to be used for determining sub-pixel positions axially. It could be hypothesized that the method are sensitive for noise when the distances between samples are short. This should explain the difference in the variance of estimation errors axially and laterally as the axially distance is a factor 2 shorter.

The large difference in tracking performance using 2D PI for image interpolation can be explained by discontinuities in the interpolated image, i.e. the interpolation will produce edges halfway between two original pixels where two polynomials meet. The edges will also cause a fluctuation of energy in the image. A great strength of NCC can be seen in Figure 1 as its tracking performance is significantly better for this sub-pixel method than the other evaluation metrics.

A tendency that can be observed in the results of several sub-pixel methods is the presence of bias in the tracking errors, i.e. the error is dependent on the size of the movement in the images.

However, several combinations give satisfying results both in terms of estimation error magnitude and estimation time. The figure also indicates, for the first time, possible combinations of methods for improved performance, e.g. using SAD and analytically solved 1D PI (axial)/GS(lateral).

Though the investigations in this paper have been made on ultrasound images, we are confident that similar results would be seen in clinical images obtained with other modalities such as MRI or CT.

IV. CONCLUSIONS

It is well known that the choice of evaluation metric can have a significant impact on both estimation time and the magnitude of the estimation error when using block-matching for motion estimation. Here, we show that a combination of evaluation metric and sub-pixel estimation method have an effect on the size of the estimation error. Thus, even if two evaluation metrics have the same tracking performance on a pixel level, the total tracking performance can differ depending on what sub-pixel estimation method is applied.

ACKNOWLEDGMENT

This study was supported by grants from the Swedish Research Council

REFERENCES


Corresponding author:
Author: John Albinsson
Institute: Biomedical Engineering
Street: Ole Römers väg 3
City: Lund
Country: Sweden
Email: john.albinsson@bme.lth.se
Fig. 1 Tracking error per image of the motion estimation performed on the in silico cineloops against the set movement per image of the cineloops. The boxes indicate the lower and upper quartiles and the median. The bar line indicates 99% of the values. Each box is based on 4,900 estimations explaining the seemingly large numbers of outliers. No error larger than 0.25 pixels is shown but they were part of all the statistics.
A combination of parabolic and grid slope interpolation for 2D tissue displacement estimations

John Albinsson1 · Åsa Rydé Ahlgren2 · Tomas Jansson3,4 · Magnus Cinthio1

Received: 18 April 2016 / Accepted: 26 October 2016
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Abstract Parabolic sub-sample interpolation for 2D block-matching motion estimation is computationally efficient. However, it is well known that the parabolic interpolation gives a biased motion estimate for displacements greater than |y2| samples (y = 0, 1, …). Grid slope sub-sample interpolation is less biased, but it shows large variability for displacements close to y.0. We therefore propose to combine these sub-sample methods into one method (GS15PI) using a threshold to determine when to use which method. The proposed method was evaluated on simulated, phantom, and in vivo ultrasound cine loops and was compared to three sub-sample interpolation methods. On average, GS15PI reduced the absolute sub-sample estimation errors in the simulated and phantom cine loops by 14, 8, and 24% compared to sub-sample interpolation of the image, parabolic sub-sample interpolation, and grid slope sub-sample interpolation, respectively. The proposed method is computationally efficient and has low bias and variance. The method is another step toward a fast and reliable method for clinical investigations of longitudinal movement of the arterial wall.

Keywords Ultrasound · Sub-sample estimation · Block matching · Speckle tracking · In silico · In vivo

1 Introduction

Tissue motion measurements using ultrasound can provide functional information about the tissue of interest and have attracted attention for various applications such as the evaluation of cardiac [14, 21, 22, 27, 32], vascular [4, 5, 19, 28], and skeletal muscle [9, 18, 30] function.

One vascular application of interest is the measurement of the longitudinal movement of the arterial wall, i.e., the motion along the arteries [12, 17, 35, 36]. In large arteries, the displacement is greatest in the layers closest to the lumen—the intima–media complex—and is of the same magnitude as the diameter change [13] (Fig. 1). The outer layer—the adventitia—shows the same basic pattern of movement, but the displacement is smaller, thereby demonstrating the presence of previously unknown substantial shear strain and thus shear stress, intramurally [13, 23, 33, 46]. Recent studies have reported that the amplitude of the longitudinal displacement of the arterial wall is reduced in patients with carotid plaques, suspected coronary artery disease, type 2 diabetes [38–40, 42, 45], and periodontal disease [47], suggesting that the longitudinal movement of the arterial wall might prove to be a valuable marker for future risk of cardiovascular disease. Furthermore, in a study on the porcine carotid artery, we recently reported that longitudinal movement and intramural shear strain undergo profound changes in response to the important endogenous hormones adrenalin and noradrenalin [2].
These findings might have important implications for vascular disease both in the short- and long term and might constitute a link between mental stress and cardiovascular disease [2].

In order to calculate high-resolution motion estimates using block matching, three components are needed. (1) A search method is needed to determine which blocks the kernel should be compared to in order to find the most similar block [24]. (2) A method is needed to determine similarity [20] by calculating evaluation metric values between the kernel and the compared blocks. The value can be either the maximum likeness, e.g., the normalized cross-correlation [37], or the minimum difference, e.g., the sum of the absolute difference [7]. (3) A sub-sample estimation method is needed to determine movements at sub-sample accuracy. The sub-sample estimation method can be one of the following three subgroups: (a) interpolation of the data points [31], (b) interpolation of evaluation metric values [10], or (c) analytically solving the min/max problem for the evaluation metric values [10]. The number of calculations needed for the three subgroups show that for the average method of each group the computational load is highest with (a) and lowest with (c). The motion estimations can be conducted with the ultrasound data in any of several forms, e.g., B-mode, radio-frequency, or after a Fourier transformation.

During the last decade, several tracking methods based on block matching have been developed to measure longitudinal movement of the arterial wall in ultrasound cine loops [3, 12, 13, 15, 34, 41, 44, 45]. The most common method to obtain sub-sample estimations is the use of image interpolation. Interpolation of the image gives good sub-sample estimations but is very time-consuming. Albinsson et al. [3] fitted three evaluation metric values with a parabolic function, which is a computationally efficient method to determine sub-sample displacements. However, it is well known that the parabolic function gives a biased estimation for displacements greater than 0.2l samples (l = 0, 1, …) [8]. Another sub-sample method, grid slope interpolation [16], gives fast unbiased motion estimates, but it has a large variability of the motion estimates for displacements close to 0 samples (see also below). Considering that the drawbacks of the two sub-sample methods occur at different sub-sample displacements, a possible solution is to combine the two sub-sample methods. We therefore propose a new method, from now on denoted GS15PI, in which the sub-sample displacement is first estimated with a parabolic function. If the absolute sub-sample estimation is greater than a threshold (chosen to be 0.15), the sub-sample estimate is recalculated by grid slope interpolation.

The aim of this work was to evaluate the new sub-sample estimation method and to compare its performance to three sub-sample estimation methods: sub-sample interpolation of the image, parabolic sub-sample interpolation, and grid slope sub-sample interpolation. The evaluations were conducted on simulated and phantom ultrasound cine loops consisting of both B-mode data and radio-frequency data using different settings for the signal-to-noise ratio, velocity, and kernel size. Also, data from an in vivo study of the longitudinal displacement of the common carotid artery in healthy humans were used to evaluate the methods.

2 Materials and methods

Ultrasound is a modality based on reflected acoustical waves. The detected oscillating signals are beamformed and saved as radio-frequency (RF) data. A brightness mode (B-mode) image is created from the RF data by envelope detection and scan conversion. In the conversion into B-mode data, the RF data are normally down-sampled in the axial direction and displayed on a logarithmic scale. Thus, the two data types will typically have the same lateral sample distance, whereas the RF data will have shorter axial sample distance. The data points in RF signals are typically called “samples” because they are sampled from the acoustical waves, and the B-mode data points are called “pixels” because they represent the intensity data in an image.

Throughout this text, the word “sample” should be read as “sample and/or pixel” because the effects described are the same for both RF and B-mode data.
2.1 Ultrasound cine loops

Ultrasound cine loops of three types of objects were used: a simulated object, a phantom object, and the far wall of the common carotid artery in vivo.

Ultrasound simulations were created using Field II [25, 26] running under MATLAB R2013a (The MathWorks, Inc., Natick, MA, USA). The settings used in the simulations are presented in Table 1. The in silico model consisted of a body of scatterers with random distribution and scatter power that was displaced a set distance between two images. The cine loops were divided into three groups according to the direction of the displacement: horizontal, vertical, or diagonal (45°). The movement of the scatterers was (0.1; 0.3; 0.5; 0.7; 0.9; 1.2; 1.6; 2.0; 2.4; 2.8) pixels per image in all three groups. From each simulation, three cine loops were created with different levels of signal-to-noise ratio (SNR) by adding white noise to the RF data: no noise, SNR 21 dB, and SNR 16 dB. The RF data were down-sampled by a factor of 16 in the vertical direction during the scan conversion into B-mode data. The settings allowed a pixel density in the B-mode images of 8.1 pixel/mm axially and 4.1 pixel/mm laterally. Motion estimations were conducted using both the RF data and the B-mode data.

Phantom data were collected using both a research ultrasound machine, an Ultrasound Advanced Open Platform (ULAOP) [43] (University of Florence, Italy) equipped with a 4- to 13-MHz linear transducer (LA523, Esaote SpA, Florence, Italy), and a commercial ultrasound machine, a Philips EPIQ 7 equipped with a 3- to 12-MHz linear transducer (Philips Medical Systems, Bothell, WA, USA). Both B-mode data and RF data (down-sampled by a factor of 8 during the scan conversion) were available from ULAOP. The pixel density in the B-mode images was 8.1 pixels/mm axially and 4.1 pixels/mm laterally (the same as the in silico data). Only B-mode data in the DICOM format were available from the Philips EPIQ 7. The pixel density was 21.5 pixels/mm both axially and laterally. Settings were chosen to obtain a frame rate close to 50 Hz using the highest line density, and persistence was turned off in order to avoid averaging between images. The phantom (a sponge) was moved in a water bath at velocities in the range of 2–15 mm/s in steps of 1 mm/s both purely laterally and diagonally within the scan-plane. B-mode data from in silico and phantom measurements are shown in Fig. 2.

Table 1 Settings in Field II for the in silico cine loops

<table>
<thead>
<tr>
<th>Setting</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width of element</td>
<td>0.215 mm</td>
</tr>
<tr>
<td>Height of element</td>
<td>6 mm</td>
</tr>
<tr>
<td>Distance between elements</td>
<td>0.030 mm</td>
</tr>
<tr>
<td>Number of elements in transmit/receive</td>
<td>64</td>
</tr>
<tr>
<td>Focus on transmission (fixed focal point)</td>
<td>40 mm</td>
</tr>
<tr>
<td>Focus on receiving</td>
<td>Dynamic focusing</td>
</tr>
<tr>
<td>Elevational focus (acoustic lens)</td>
<td>18 mm</td>
</tr>
<tr>
<td>Center frequency</td>
<td>6 MHz</td>
</tr>
<tr>
<td>Simulated transducer</td>
<td>LA523 (Esaote SpA, Florence, Italy)</td>
</tr>
<tr>
<td>Speed of sound</td>
<td>1540 m/s</td>
</tr>
<tr>
<td>Sampling rate</td>
<td>100 MHz</td>
</tr>
<tr>
<td>Number of scan lines</td>
<td>128</td>
</tr>
<tr>
<td>Size of phantom (width \times height \times depth)</td>
<td>40 \times 50 \times 10 mm³</td>
</tr>
<tr>
<td>Number of scatterers</td>
<td>20,000</td>
</tr>
</tbody>
</table>

Fig. 2 B-mode images from the three ultrasound sources: a in silico, b ULAOP, and c Philips EPIQ 7. The images each depict an area of 20 $\times$ 15 mm².
The right common carotid artery of 40 healthy volunteers (aged 20–69 years) was examined after at least 10 min of rest in a supine position using a Philips IU 22 equipped with a 5- to 12-MHz linear array transducer (Philips Medical Systems, Bothell, WA, USA). All volunteers gave informed consent according to the Helsinki Declaration, and the study was approved by the Ethics Committee of Lund University. Two cine loops were acquired for each volunteer. Settings were chosen to obtain a frame rate close to 50 Hz using the highest line density, and persistence was turned off in order to avoid averaging between images. DICOM data were exported for off-line motion estimations of the far wall of the common carotid artery. The pixel density was 21.5 pixels/mm both axially and laterally.

2.2 Methods for motion estimation

A tracking scheme for 2D motion estimation was implemented using a full-search method and the sum of the absolute difference as the evaluation metric. The sub-sample positions were determined using four different methods: (1) interpolation of the image data values using cubical splines (CUBIC), (2) parabolic interpolation (PI), (3) modified grid slope interpolation (GSmod), and (4) the proposed method (GS15PI).

2.2.1 Search method

The full-search method searched for the best matching block among all possible blocks within a region of interest using the sum of the absolute difference [7] as the evaluation metric. In the B-mode, the size of the region of interest was the size of the kernel + 10 samples both axially and laterally. In the RF data, the size of the region of interest was the size of the kernel + 10 samples laterally, while it was (the size of the kernel + 10) × 16 samples axially. The kernel sizes used in silico and in the phantom measurements were $0.9 \times 0.7$ mm$^2$, $1.8 \times 1.7$ mm$^2$, and $2.8 \times 2.7$ mm$^2$ (Table 2). The kernel sizes for the in vivo motion estimations were visually optimized for each volunteer. The chosen size was used in the two cine loops and for all sub-sample methods.

2.2.2 Sub-sample estimation methods

CUBIC was used to interpolate the ultrasound data 128 times both axially and laterally using cubical splines [29]. Only the data in the square of the current image centered on the position of the center of the block with the best similarity to the kernel were interpolated. The size of the square was two samples larger than the kernel both axially and laterally. The kernel was not interpolated but was compared to an equal number of interpolated samples obtained at every 128th sample of the interpolated segment. A full search was conducted in the entire interpolated square in order to find the best match at sub-sample resolution.

PI was used to estimate the sub-sample position by fitting a one-dimensional second-degree polynomial to three adjacent evaluation metric values [10] where the center value corresponded to the center position of the block with the best similarity to the kernel. The polynomial was fitted separately laterally and axially. The analytical solution of the polynomial gave the sub-sample estimation as:

$$\Delta x = \frac{\alpha_1 - \alpha_3}{2(\alpha_1 + \alpha_3 - 2\alpha_2)} \quad (1)$$

where $\alpha_2$ (center), $\alpha_1$, and $\alpha_3$ (on each side of center) denote evaluation metric values and $\Delta x$ denotes the sub-sample part of the movement.

Grid slope interpolation [16] was used to estimate the sub-sample position by using four evaluation metric values that were calculated between the kernel and four blocks. Two blocks were from the current image—the block with the best similarity to the kernel and the one with the second best similarity. The other two blocks originated in the previous image at the position of the blocks used for the evaluation metric value in the current image. The sub-sample estimation was calculated by:

<table>
<thead>
<tr>
<th>Table 2 Parameters investigated and their different settings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Image data type</td>
</tr>
<tr>
<td>Size of kernel: (B-mode in silico and ULAOP) [pixels]</td>
</tr>
<tr>
<td>(B-mode Philips EPIQ 7) [pixels]</td>
</tr>
<tr>
<td>(RF in silico) [samples]</td>
</tr>
<tr>
<td>(RF ULAOP) [samples]</td>
</tr>
<tr>
<td>Size of kernel: all cine loops (mm)</td>
</tr>
<tr>
<td>Noise—SNR</td>
</tr>
<tr>
<td>Velocity—direction</td>
</tr>
<tr>
<td>Velocity—in silico (pixels/frame)</td>
</tr>
<tr>
<td>Velocity—phantom (mm/s)</td>
</tr>
</tbody>
</table>
where $\alpha_2$ (center) and $\alpha_i$ denote evaluation metric values in the current image, and $\Delta \alpha_{2,0}$ and $\Delta \alpha_{i,0}$ denote the evaluation metric values in the previous image. This method was, in the original work, evaluated on B-mode data using the sum of the absolute difference on horizontal motion only [16].

To expand the utility of the grid slope interpolation methodology, we modified it by setting the variable $\alpha_{2,0}$ to zero and setting the variable $\alpha_{i,0}$ to the evaluation metric value calculated between the best and second best matching blocks in the current image. This resulted in a method denoted GSmod. The sub-sample distance was estimated separately laterally and axially.

Our proposed method, GS15PI, was developed to take advantage of the best characteristics of PI and GSmod. GS15PI first estimates a sub-sample displacement using PI. If the estimated absolute sub-sample displacement is larger than 0.15 samples, the sub-sample estimation is recalculated using GSmod and accepted without further testing. The threshold of 0.15 samples was chosen after an empirical study on phantom movements (unpublished data).

### 2.3 Evaluation of the motion estimations

The settings that were investigated (summarized in Table 2) covered four sub-sample interpolation methods and five parameters—image data type, kernel size, noise (only for simulated data), direction of movement, and velocity of the object. In this work, two types of results were collected for 100 kernels for each combination of settings—the estimated displacements and the total estimation time used for the sub-sample estimations. Using in silico data, the different combinations noise levels, motion directions, and velocities resulted in 90 cine loops. Using three kernel sizes on each cine loop resulted in a total of 270 parameter settings to be evaluated for each combination of sub-sample method and image type. Using phantom data, there were 84 parameter settings.

A motion estimation error (per image) was defined as the geometrical difference between the set displacement and the estimated displacement, except in Table 4 where the lateral and axial components of the estimation errors were calculated separately. The mean value and standard deviation (SD) were estimated for each setting. The calculation time for a sub-sample motion estimation was measured separately from the search method. The time measurement was taken for 100 sub-sample motion estimations and averaged to give the mean time used for one sub-sample estimation.

The longitudinal movement of the common carotid artery in healthy humans at rest can show dramatically different multi-phasic patterns, even in subjects of similar age and gender [1, 13, 44]. An antegrade longitudinal movement in early systole is followed by a retrograde movement in systole (Fig. 1). The retrograde movement is the most distinct phase, present in all subjects, and is often the largest movement [1, 13, 44]. Therefore, we have chosen to use the magnitude of the retrograde movement in systole when comparing the PI, GSmod, and GS15PI sub-sample estimation methods in vivo. However, in some subjects, the antegrade movement in early systole is absent or very small, which makes the onset of the retrograde movement indistinct. In the present study, these subjects were excluded because the focus of this study was to evaluate the performance of the sub-sample estimation methods and not to evaluate the measurement of the phenomenon itself. Because the magnitude of the longitudinal displacement of the common carotid artery wall seems to decrease with distance from the heart [48], care was taken to perform the measurement at the same position in the two cine loops. The magnitude of the retrograde movement in systole was estimated over the course of 3–5 cardiac cycles per cine loop using a semiautomated method applied to the longitudinal movement curve (Fig. 1). The semiautomated method was initiated by a click on the position of the onset of the antegrade movement in systole. The evaluation of the sub-sample methods was performed by calculating the coefficient of variation (CV) [6] between the mean estimations of the magnitude of the retrograde movement in systole from two cine loops from the same volunteer.

### 3 Results

Using the combined in silico and phantom data, the mean estimation errors were smaller using GS15PI as compared to the other sub-sample methods. GS15PI on average reduced the estimation errors by 14% compared to CUBIC, by 8% compared to PI, and by 24% compared to GSmod. GS15PI also reduced the standard deviations by 12% compared to CUBIC, by 28% compared to PI, and by 2% compared to GSmod. However, there was a large variation in the results depending on the image source and data type in which the motion estimations were conducted (Table 3). In Table 3, the motion estimation errors were calculated using all kernel sizes, motion directions, speeds, and noise levels (where applicable).

The drawbacks of PI (bias in the motion estimations greater than $\gamma_{0.2}$) and GSmod (variation in the motion estimations close to $\gamma_{0.0}$) were clearly decreased for GS15PI. Figure 3 shows an example of the lateral component of the estimation errors using the following settings: in silico B-mode data, horizontal movement, SNR 21 dB, and a kernel size of $1.8 \times 1.7$ mm$^2$. The bias of PI is visible as a...
deviation of the median error of each velocity from zero (Fig. 3a). The variation of GSmod is seen as the height of the box for y=0 (Fig. 3b). It can also be seen that GSmod had a small linear bias, which is consistent with the result presented by Geiman et al. [16] for the level of SNR in the image data. In Fig. 3c, the improvements in GS15PI can be seen as smaller variation at y=0 and median errors closer to zero. However, there are outliers at y=2, y=3, y=7, and y=8 (Fig. 3c).

The motion estimation errors were analyzed according to axial and lateral estimation errors (Table 4), motion direction (vertical, horizontal, and diagonal) (Table 5), kernel size (Table 6), and noise level (Table 7). As expected, axial errors were smaller than lateral errors, smaller errors were obtained using vertical motion direction than horizontal or diagonal motion directions, and better motion estimations were obtained by larger kernels and less noise. Also as expected, motion estimation using RF data gave smaller errors than using B-mode data, although there were exceptions for the small and medium-sized kernels using data from ULAOP (Table 6). The best results for all sub-sample methods over all image types were obtained using DICOM data from the commercial state-of-the-art Philips EPIQ 7 machine. One exception to the expected results was the larger motion estimation errors using CUBIC on RF data compared to the estimation errors using GS15PI (Tables 3, 4, 5, 6, 7). There was no dependence between the motion estimation errors and the magnitude of the movement. Figure 4 shows an example of estimated accumulated displacements using the four sub-sample interpolation methods in a phantom at three different velocities and diagonal motion direction using the Philips EPIQ 7.

When using in silico data, the mean estimation time was longest for CUBIC followed by GSmod, GS15PI, and PI (Fig. 5). That CUBIC had a more than 27 times longer estimation time than the other methods was expected. When CUBIC was excluded, the sub-sample estimation time was about 1.1 times longer using RF data compared to using B-mode data.

The CV values and kernel sizes in vivo were calculated for 21 volunteers (aged 22–67 years) who had a distinct onset of retrograde movement in systole (Fig. 1). The used kernel sizes were in the range of 7 × 13 pixels to 11 × 29 pixels (which is equivalent to 0.29 × 0.55 mm² to 0.46 × 1.22 mm²) with a mean kernel size of 7.1 × 25 pixels (0.30 × 1.05 mm²). The CV values for the in vivo motion estimations of the retrograde movement in systole using PI, GSmod, and GS15PI were 6.9, 7.5, and 6.8%, respectively. Figure 6 shows in vivo estimations of the longitudinal movement of the common carotid artery wall in one volunteer using the three sub-sample methods.

4 Discussion

We have presented a new ultrasound sub-sample motion estimation method, GS15PI, in which the best characteristics of two published methods, parabolic interpolation and grid slope interpolation, are combined to reduce their respective drawbacks of biased and noisy motion estimations (Fig. 3). The performance of GS15PI was evaluated on in silico, phantom, and in vivo cine loops. The new

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**Table 3 Mean estimation errors and corresponding standard deviation (SD) in µm for sub-sample estimation using in silico and phantom cine loops**

<table>
<thead>
<tr>
<th>Image source</th>
<th>Data type</th>
<th>Sub-sample method</th>
<th>CUBIC</th>
<th>PI</th>
<th>GSmod</th>
<th>GS15PI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philips EPIQ 7</td>
<td>B-mode</td>
<td>11 (8.9)</td>
<td>13 (20)</td>
<td>13 (8.1)</td>
<td>11 (8.5)</td>
<td></td>
</tr>
<tr>
<td>ULAOP</td>
<td>B-mode</td>
<td>85 (200)</td>
<td>95 (200)</td>
<td>90 (200)</td>
<td>92 (200)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RF</td>
<td>78 (190)</td>
<td>77 (200)</td>
<td>67 (200)</td>
<td>72 (200)</td>
<td></td>
</tr>
<tr>
<td>In silico</td>
<td>B-mode</td>
<td>41 (140)</td>
<td>49 (140)</td>
<td>69 (140)</td>
<td>48 (140)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>RF</td>
<td>32 (32)</td>
<td>20 (21)</td>
<td>28 (24)</td>
<td>18 (21)</td>
<td></td>
</tr>
</tbody>
</table>

The mean values were calculated over all settings for each data type and sub-sample method. The results are presented according to image data type (B-mode or RF data) and sub-sample estimation method (CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method).
method performed well on both B-mode data and RF data, and the results were at the same level or better for both the magnitude of the motion estimation errors and the estimation time compared to image interpolation and parabolic and grid slope interpolation.

In general, our proposed method showed good stability in its motion estimations. Although the method did not always have the lowest motion estimation errors, the consistently low motion estimation errors resulted in an overall improvement compared to the motion estimation errors of the other sub-sample methods using in silico and phantom cine loops. A decrease in the standard deviation was also noted. This reliability in the motion estimations was also shown in the in vivo study. However, the outliers of the motion estimation errors at y.2, y.3, y.7, and y.8 shown in Fig. 3c indicate that the tuning of the method might not be optimal. GS15PI uses a threshold level of 0.15 samples to determine whether to use parabolic interpolation or grid slope interpolation, and a somewhat lower threshold level might have decreased the motion estimation error and variance at y.2, y.3, y.7, and y.8. Considering that the threshold was determined using phantom cine loops different from those used in this study (unpublished data), it is possible that the optimal threshold is dependent on some parameter in the cine loops. The implemented threshold was an on/off fixed-value version, and an adaptive version should also be considered in future work.

The mean values were calculated over all settings. The results are presented according to image data type (B-mode or RF) and sub-sample estimation method (CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method).

### Table 4

<table>
<thead>
<tr>
<th>Image source</th>
<th>Data type</th>
<th>Error component</th>
<th>Sub-sample method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CUBIC</td>
</tr>
<tr>
<td>Philips EPIQ 7</td>
<td>B-mode</td>
<td>Axial</td>
<td>−0.20 (6.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lateral</td>
<td>3.5 (12)</td>
</tr>
<tr>
<td>ULAOP</td>
<td>B-mode</td>
<td>Axial</td>
<td>4.3 (99)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lateral</td>
<td>0.56 (200)</td>
</tr>
<tr>
<td>RF</td>
<td>Axial</td>
<td></td>
<td>3.0 (95)</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td></td>
<td>−9.4 (180)</td>
</tr>
<tr>
<td>In silico</td>
<td>B-mode</td>
<td>Axial</td>
<td>15 (62)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lateral</td>
<td>35 (130)</td>
</tr>
<tr>
<td>RF</td>
<td>Axial</td>
<td></td>
<td>2.1 (1.8)</td>
</tr>
<tr>
<td></td>
<td>Lateral</td>
<td></td>
<td>32 (33)</td>
</tr>
</tbody>
</table>

The results are presented according to image data type (B-mode or RF) and sub-sample estimation method (CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method). The kernel size was 1.8 × 1.7 mm², and for the in silico data, the SNR was 21 dB. Motion direction: V—vertical, D—diagonal, and H—horizontal

### Table 5

<table>
<thead>
<tr>
<th>Image source</th>
<th>Data type</th>
<th>Motion direction</th>
<th>Sub-sample method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CUBIC</td>
</tr>
<tr>
<td>Philips EPIQ 7</td>
<td>B-mode</td>
<td>H</td>
<td>4.9 (2.2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D</td>
<td>5.6 (3.0)</td>
</tr>
<tr>
<td>ULAOP</td>
<td>B-mode</td>
<td>H</td>
<td>13 (8.3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D</td>
<td>25 (23)</td>
</tr>
<tr>
<td>RF</td>
<td>H</td>
<td></td>
<td>18 (12)</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td></td>
<td>36 (60)</td>
</tr>
<tr>
<td>In silico</td>
<td>B-mode</td>
<td>H</td>
<td>2.8 (2.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V</td>
<td>4.5 (3.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D</td>
<td>6.2 (4.1)</td>
</tr>
<tr>
<td>RF</td>
<td>H</td>
<td></td>
<td>12 (9.0)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>V</td>
<td>5.9 (7.6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>D</td>
<td>11 (8.4)</td>
</tr>
</tbody>
</table>
The results were mostly as expected when analyzing the effects of the different parameters (Tables 4, 5, 6, 7). In line with other studies, the motion estimation errors decreased when the information in the kernel increased with kernel size. It is also known that less noise results in smaller motion estimation errors due to decreased rates of change in the speckle pattern. Different rates of change in the speckle pattern are also the likely cause for the differences in motion estimation errors between the three motion directions. A dependency between the actual distance between the sampled data and the size of the motion estimation errors was observed, i.e., a longer distance between samples resulted in larger motion estimation errors. No dependency between the velocity and the motion estimation errors was seen. This might be due to the limited change in the speckle pattern because we had relatively short movements per frame, and our intention was to have in-plane movements.

The motion estimation errors using CUBIC on RF data were larger than expected when compared to the other sub-sample methods (Tables 3, 4, 5, 6, 7). Because CUBIC performed well using B-mode data, the possibility of an implementation error was unlikely. In order to reduce the computation time during sub-sample estimation, we did not interpolate the kernel. This could be a possible explanation for the increase in these motion estimation errors, and further studies are needed to determine whether this is the case.

A limitation in this study was the absence of tests concerning strain and shearing in the simulations and in the phantom cine loops. Thus, how these motions affect the motion estimation errors of GS15PI compared to the other methods can only be speculated. However, the motion estimation errors using the in vivo cine loops, which incorporate a low level of strain in the investigated area, indicate that GS15PI has some robustness to strain. Further studies are needed to evaluate the influence of higher levels of strain and shearing when using GS15PI. Another limitation in our in vivo evaluation was the exclusion of CUBIC in the motion estimations.

### Table 6 Mean estimation errors and corresponding standard deviation (SD) values in µm separated according to kernel size using in silico and phantom cine loops

<table>
<thead>
<tr>
<th>Image source</th>
<th>Data type</th>
<th>Kernel size (mm²)</th>
<th>Sub-sample method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philips EPIQ 7</td>
<td>B-mode</td>
<td>0.9 × 0.8</td>
<td>CUBIC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 × 1.7</td>
<td>PI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 × 2.7</td>
<td>GSmod</td>
</tr>
<tr>
<td>ULAOP</td>
<td>B-mode</td>
<td>0.9 × 0.8</td>
<td>GS15PI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 × 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 × 2.7</td>
<td></td>
</tr>
<tr>
<td>RF</td>
<td></td>
<td>0.9 × 0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 × 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 × 2.7</td>
<td></td>
</tr>
<tr>
<td>In silico</td>
<td>B-mode</td>
<td>0.9 × 0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 × 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 × 2.7</td>
<td></td>
</tr>
<tr>
<td>RF</td>
<td></td>
<td>0.9 × 0.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 × 1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.8 × 2.7</td>
<td></td>
</tr>
</tbody>
</table>

### Table 7 Mean errors and corresponding standard deviation (SD) values in µm separated according to noise level using in silico cine loops

<table>
<thead>
<tr>
<th>Image source</th>
<th>Data type</th>
<th>Noise level</th>
<th>Sub-sample method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Philips EPIQ 7</td>
<td>B-mode</td>
<td>SNR 16 dB</td>
<td>CUBIC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SNR 21 dB</td>
<td>PI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No noise</td>
<td>GSmod</td>
</tr>
<tr>
<td>ULAOP</td>
<td>B-mode</td>
<td>SNR 16 dB</td>
<td>GS15PI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SNR 21 dB</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No noise</td>
<td></td>
</tr>
<tr>
<td>RF</td>
<td></td>
<td>SNR 16 dB</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>SNR 21 dB</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No noise</td>
<td></td>
</tr>
</tbody>
</table>

The results are presented according to image data type (B-mode or RF) and sub-sample estimation method (CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method). The motion direction was diagonal, and for the in silico data, the SNR was 21 dB.
As expected, the computation time for CUBIC was much longer than the other sub-sample methods (approximately 27 times longer) because CUBIC involves many more calculations. This large difference has to be considered when the differences in the motion estimations are small. Please note that the difference in the computation time between the GS15PI and PI or GSmod methods was on the order of 1/10 of a millisecond.

The purpose of the in vivo study in this work was to compare GS15PI to parabolic and grid slope interpolation of in vivo data. Therefore, we wanted a dataset in which the effect of the sub-sample method was dominant and thus we wanted to minimize other sources of error such as the time for the onset of the movement. Therefore, we restricted the comparison to volunteers with a distinct retrograde movement. The in vivo results in this study show promising results with CV values of 7%; however, comparisons with other studies should be made with care. The selection of the volunteers in the present study improves our results.

Fig. 4 Example of motion estimations in a phantom. The black lines indicate the set accumulated displacement for the diagonal motions at 3, 8, and 13 mm/s. The panels in the two rows show the accumulated axial and lateral motion estimations of nine kernels using CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method.

Fig. 5 Mean time to perform one estimation using the evaluated sub-sample methods on in silico cine loops for B-mode and RF data. The estimation times are presented according to image data type (B-mode and RF) and sub-sample estimation method (CUBIC—image interpolation, PI—parabolic interpolation, GSmod—modified grid slope interpolation, and GS15PI—our proposed method).

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compared to other studies, and the improved image quality of modern ultrasound machines likely has an influence on the motion estimations. Previously presented CV values of measurements of the retrograde longitudinal movement of the common carotid artery are 12.5% [11], 16% [44], and 13% [3]. Zahnd et al. [45] reported a CV value of 20% for the total longitudinal movement during a cardiac cycle.

The proposed sub-sample interpolation method, GS15PI, has only been evaluated on the longitudinal wall movement of the common carotid artery in vivo. However, the proposed method has potential to be used in all applications where block matching is used. Further studies are needed to evaluate this.

5 Conclusion

The proposed sub-sample method GS15PI, in which the best aspects of parabolic interpolation and grid slope interpolation are combined, was found to have promising performance when compared to three other sub-sample methods with in silico and phantom cine loops of both ultrasound B-mode data and RF data. Compared to parabolic and grid slope interpolation, the proposed method also performed well when estimating the longitudinal movement in the common carotid artery in vivo. The proposed method is computationally efficient compared to image interpolation and has low bias compared to parabolic interpolation and low variance at y.0 compared to grid slope interpolation. The method is another step toward fast and reliable clinical investigations of longitudinal movement of the arterial wall.

Acknowledgements This study was supported by grants from the Swedish Research Council (Grant No. 2012-3552), the Swedish Foundation for International Cooperation in Research and Higher Education (STINT) (Grant No. IG2011-2056), the Medical Faculty of Lund University, and the Skåne County Council’s Research and Development Foundation.

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60. Swedlund S, Gan L-M (2011) Longitudinal common carotid artery wall motion is associated with plaque burden in man...

John Albinsson is a Ph.D. student at the Department of Biomedical Engineering, Lund University. His thesis is about tissue motion estimations in ultrasound images.

Åsa Rydén Ahlgren M.D., received her Ph.D. degree in 1998 from Lund University, Sweden. Her current research includes vascular mechanics and the longitudinal displacement of the arterial wall.

Tomas Jansson received his Ph.D. degree in 1999 from Lund University, Sweden. His current research includes magnetomotive ultrasound imaging and auditory perception of Doppler signals.

Magnus Cinthio received his Ph.D. degree in 2004 from Lund University, Sweden. His research interests include characterization of the arterial wall using ultrasound and magnetomotive ultrasound imaging.
Paper IV
Phases and resulting patterns of the longitudinal movement of the common carotid artery wall in healthy humans – influence of age and gender

Magnus Cinthio\textsuperscript{1}, John Albinsson\textsuperscript{1}, Tobias Erlöv\textsuperscript{1}, Niclas Bjarneård\textsuperscript{2}, Toste Länne\textsuperscript{2}, Åsa Rydén Ahlgren\textsuperscript{3,4}

\textsuperscript{1}Department of Biomedical Engineering, Faculty of Engineering, Lund University, Lund, Sweden
\textsuperscript{2}Department of Medical and Health Sciences, University of Linköping, Linköping, Sweden
\textsuperscript{3}Department of Translational Medicine, Lund University, Sweden
\textsuperscript{4}Lund University, Skåne University Hospital, Department of Medical Imaging and Physiology, Malmö, Sweden
Abstract – Despite indications that there is a link between the longitudinal displacement of the common carotid wall and cardiovascular health, the changes in longitudinal displacement of the arterial wall in the normal aging process of the arterial wall are largely unknown. The aim of the present study was therefore to explore the phases, and resulting patterns, of the longitudinal displacement of the intima media complex of the human common carotid artery wall in relation to age and gender. For this purpose, the right common carotid artery of healthy, non-smoking men and women of different ages was investigated, using an in-house developed non-invasive ultrasound method. The results show that the pronounced variation in the patterns of longitudinal movement of the common carotid artery, previously shown in young healthy subjects, is also present in middle-aged and older healthy subjects. However, the patterns of movement seen in middle-aged and older subjects are different from those commonly seen in young subjects, including the appearance of two additional distinct phases of movement, and thus new complex patterns of movement. Our findings show that the longitudinal movement of the common carotid wall can not only give new information on the aging process of the arterial tree, but also give new insights to the coupling of the left ventricle with the systemic circulation.

Keywords – Longitudinal displacement, Axial displacement, Arterial wall, Ultrasound, Block-matching
Introduction

Hemodynamic forces acting on the arterial wall are considered important modulators of vascular tone and remodelling, and are increasingly implicated in the development of atherosclerosis. Blood flow wall shear stress (WSS) and the diameter change of arteries due to the pulsatile blood pressure during the cardiac cycle have been subject of extensive research. WSS is an important determinant of endothelial cell function, which is among the factors that influence the production of vasoactive substances such as nitric oxide, prostacyclin, and endothelin (Nichols and O’Rourke 2005). Measurement of radial movements of arteries is an established tool in cardiovascular research (Ahlgren et al. 1995; Brands et al. 1997; Laurent et al. 2001; Eriksson et al. 2002; Stehouwer et al. 2008), forming the basis for estimation of arterial wall stiffness. Increased stiffness of large central arteries has been shown to be an independent risk factor for cardiovascular mortality (Blacher et al. 1999).

While the diameter change of arteries has been the subject of intensive research, the longitudinal displacement of the arterial wall, i.e. the movement of the wall along the arteries, parallel to blood flow, has not until recently attracted attention, and studies on the longitudinal movement are still sparse. Using in-house developed ultrasonic methods we have shown that in both large predominantly elastic arteries and in large muscular arteries there is a distinct bi-directional displacement of the intima-media complex during the cardiac cycle (Cinthio et al. 2006). Further, we have shown that the intima-media complex of these arteries exhibits a longitudinal displacement that is larger than that of the adventitial region (Cinthio et al. 2006; Nilsson et al. 2010). Thus, there is shear strain and shear stress within the arterial wall, later confirmed by others in studies on the common carotid artery (CCA) (Zahnd et al. 2011b; Idzenga et al. 2012). Furthermore, in a study on the porcine carotid artery, we recently reported that longitudinal movement and intramural shear strain undergo profound changes in response to the important circulatory hormones adrenalin and noradrenalin (Ahlgren et al. 2012c). These findings indicate that the longitudinal movements and resulting intramural shear strain can constitute an important overlooked mechanism in the cardiovascular system.

Recent studies have indicated that the maximal amplitude of the longitudinal displacement of the CCA is reduced in subjects with suspected and manifest atherosclerotic disease (Svedlund et al. 2011; Svedlund and Gan 2011; Zahnd et al. 2011a; Zahnd et al. 2012; Soleimani et al. 2015). This suggests that the maximal longitudinal displacement of the arterial wall during a cardiac cycle might prove to be a valuable marker for future risk of cardiovascular disease. We have previously shown that in young healthy humans the pattern of the longitudinal movement of the CCA at rest is distinct multi-phasic and stable over a four-month period (Ahlgren et al. 2012a). However, the pattern of movement can differ dramatically between subjects of similar age and gender. We hypothesize that not only the total amplitude of movement, but also the pattern of longitudinal movement can provide important information on cardiovascular function.
Despite indications that there is a link between the longitudinal movement of the CCA and cardiovascular health, the changes in longitudinal movement in the normal aging process of the arterial wall are largely unknown. Further, the determinants of the phases of longitudinal movement remain largely unexplored. Characterisation of the complex bidirectional multi-phasic pattern of movement of the CCA during aging can provide important new information both on the aging process of the arterial wall, and possibly, on the coupling of the left ventricle with the systemic circulation, as well as serve as a base for studies on risk factors and vascular disease. Further, characterization of the pattern and amplitude of longitudinal movement in the aging process of the arterial wall might also give new insights to the mechanisms underlying the longitudinal movements.

The aim of the present study was to explore the phases, and resulting patterns, of the longitudinal movement of the intima-media complex of the human CCA wall in relation to age and gender. For this purpose, the CCA of healthy, non-smoking men and women of different ages was investigated, using an in-house developed non-invasive ultrasound method.
Material and Methods

Subjects
We recruited 150 healthy subjects: 65 men (20–76 years of age) and 85 women (22–73 years of age). None of the subjects reported previous cardiopulmonary disease, hypertension, diabetes, or smoking, and none were taking any medication. All subjects gave informed consent according to the Helsinki Declaration, and the study was approved by the Ethics Committee, Lund University.

Ultrasonic measurements of the arterial wall
B-mode ultrasound was used to measure longitudinal movement, lumen diameter at diastole, distension (i.e., diameter change) and intima-media thickness over a preselected segment of the common carotid artery wall. Before the ultrasonic recordings were performed, the carotid arteries were scanned to evaluate the possible presence of atherosclerotic plaques. The investigations were performed using one of two commercial ultrasound systems (model HDI 5000 and IU22, Philips Medical Systems, Bothell, WA, USA), each equipped with a 38 mm 5–12 MHz linear-array transducer. A frame rate close to 60 Hz was used. All measurements were performed in a quiet room with the subject in the supine position after ≥10 min of rest. The examinations were carried out by two experienced ultrasound technicians. Care was taken to minimize the pressure of the transducer and to avoid introduction of false movements by the operator. During the measurements, the artery was scanned in the longitudinal direction, oriented horizontally in the image. The measurements were performed 2–3 cm proximal to the bifurcation. Blood pressure was measured non-invasively immediately after the ultrasound recordings were performed.

Off-line analysis of the arterial wall characteristics
The image data were transferred to a personal computer for post processing and offline cine-loop analysis in Matlab® (The MathWorks Inc., Natick, MA, USA), where the algorithms for measurement of the longitudinal movement in reference to the transducer (Albinsson et al. 2014; Albinsson et al. 2016), lumen diameter, diameter change and intima-media thickness (Nilsson et al. 2014) were implemented. The recording with the best quality from each subject was chosen and longitudinal movement, lumen diameter, diameter change, and intima-media thickness of the artery were measured.

To suppress measurement noise and to enhance real longitudinal movement of the arterial wall, an average cardiac cycle was estimated from three to six cardiac cycles using a modified version of Woody average (Sörnmo and Laguna 2005). In short, the longitudinal movement curve was interpolated 1000 times using spline interpolation, each cardiac cycle was extracted and standard averaged. Then, each cardiac cycle was cross-correlated to the average cardiac cycle to find the lag, and adjusted in time to obtain best agreement. This procedure was repeated until optimal alignment was achieved. In the correlation between the averaged cardiac cycle and each of the three to six cardiac cycles, only a part of the signal, the period around systole, was used, as the characteristics of longitudinal movement of the arterial wall is most distinct around this period of the cardiac cycle (Cinthio et al. 2006).
Both qualitative and quantitative analyses of the longitudinal movement were performed.

First all curves of the longitudinal movement (both the original three–six cardiac cycles and the average cardiac cycle movement curves) were qualitatively analysed regarding phases of movement and pattern of movement by visual inspection. Minimum lumen diameter was used as a reference to identify end-diastole at the measurement site occurring approximately 100 ms after R-wave in an ECG-recording. The results from the qualitative analysis are presented in the subsections Phases of movement and Patterns of movement.

The size of the different phases of the longitudinal movement were measured on the averaged movement curve, as it was easier to identify all the phases of movement in the averaged curve at the occasions when the original curve was somewhat noisy. However, in most of the subjects all the phases of movement were clearly visible in the original curve. Lumen diameter, diameter change, arterial strain, and intima-media thickness were automatically estimated in the original three–six cardiac cycles diameter and intima-media thickness curves. In all instances, the semiautomatic estimation of the turning points in the curve of the longitudinal movement and the automatic estimation in the diameter and intima-media thickness curve were visually inspected. If something incorrect was detected it was manually corrected.

**Statistics**

Linear regression was used to evaluate possible relations between measures of the arterial wall and age. First, the order of the linear model was tested. Then the best model was found, the correlation coefficient ($r$) and p-value were calculated to obtain a measure how well the model explain the data. P < 0.05 was taken as significant. Data are presented as means (SD), unless otherwise stated.
Results

Fifteen subjects were excluded because high blood pressure (> 140 mmHg systolic pressure and/or > 90 mmHg diastolic pressure, n = 5) and/or an atherosclerotic plaque (n = 12) were found at the examination.

As expected the CCA strain (based on the diameter change) decreased significantly with age in both men and women (r = 0.67, p < 0.0001, k = -0.14 %/year, range 6.1–21.3 % and r = 0.62, p < 0.0001, k = -0.14 %/year, range 4.6–18.9 %, respectively). Further, as expected the intima-media thickness of the CCA increased significantly with age in both men and women (r = 0.77, p < 0.0001, k = 6.7 µm/year, range 450–1127 µm and r = 0.61, p < 0.0001, k = 4.6 µm/year, range 445–904 µm, respectively). Furthermore, the end-diastolic diameter increased significantly in men (r = 0.42, p < 0.05, k = 14.4 µm/year, range 5.0–7.4 mm), but not in women (r = 0.16, p = 0.16, k = 5.5 µm/year, range 4.2–7.2 mm). Data for different age groups and gender are given in Table I.

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<thead>
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<th>Age group</th>
<th>Men</th>
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<th>45-54</th>
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<th>65-</th>
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<tbody>
<tr>
<td>Number of subjects</td>
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<td>18</td>
<td>7</td>
<td>4</td>
<td>8</td>
<td>13</td>
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<tr>
<td>Diameter min (µm)</td>
<td>5659 SD(473)</td>
<td>5816 SD(314)</td>
<td>5765 SD(550)</td>
<td>5916 SD(596)</td>
<td>6001 SD(482)</td>
<td>6491 SD(738)</td>
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<tr>
<td>Distension (µm)</td>
<td>778 SD(142)</td>
<td>841 SD(168)</td>
<td>639 SD(88)</td>
<td>591 SD(122)</td>
<td>483 SD(170)</td>
<td>585 SD(143)</td>
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<tr>
<td>Arterial strain (%)</td>
<td>13.8 SD(2.9)</td>
<td>14.7 SD(3.6)</td>
<td>11.2 SD(1.8)</td>
<td>10.0 SD(1.6)</td>
<td>8.0 SD(2.4)</td>
<td>9.0 SD(1.9)</td>
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<tr>
<td>IMT (µm)</td>
<td>497 SD(44)</td>
<td>550 SD(69)</td>
<td>592 SD(68)</td>
<td>682 SD(87)</td>
<td>789 SD(163)</td>
<td>805 SD(147)</td>
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<th>Age group</th>
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<th>35-44</th>
<th>45-54</th>
<th>55-64</th>
<th>65-</th>
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<td>9</td>
<td>14</td>
<td>21</td>
<td>3</td>
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<tr>
<td>Diameter min (µm)</td>
<td>5417 SD(215)</td>
<td>5456 SD(483)</td>
<td>5421 SD(453)</td>
<td>5471 SD(447)</td>
<td>5527 SD(599)</td>
<td>6152 SD(584)</td>
</tr>
<tr>
<td>Distension (µm)</td>
<td>812 SD(128)</td>
<td>741 SD(140)</td>
<td>588 SD(97)</td>
<td>560 SD(171)</td>
<td>525 SD(130)</td>
<td>522 SD(260)</td>
</tr>
<tr>
<td>Arterial strain (%)</td>
<td>15.0 SD(2.2)</td>
<td>13.7 SD(2.7)</td>
<td>10.9 SD(2.1)</td>
<td>10.2 SD(3.0)</td>
<td>9.6 SD(2.4)</td>
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<tr>
<td>IMT (µm)</td>
<td>502 SD(32)</td>
<td>588 SD(89)</td>
<td>633 SD(74)</td>
<td>676 SD(95)</td>
<td>703 SD(92)</td>
<td>832 SD(67)</td>
</tr>
</tbody>
</table>

Table I: Summary of the basic measurement of the common carotid artery for different age groups and gender. All data are presented as mean (SD).
Phases of movement

During the cardiac cycle, a distinct multiphasic bidirectional longitudinal movement of the intima-media complex was observed in all subjects. The phases of the longitudinal movement were defined in relation to the diameter curve, minimum lumen diameter representing the end-diastole at the measurements site.

In younger subjects (<50 years), the patterns of the longitudinal movement of the carotid artery wall were similar to what has previously been reported by us (Cinthio et al. 2006; Cinthio and Ahlgren 2010; Ahlgren et al. 2012b) and Yli-Ollila et al. (Yli-Ollila et al. 2013); consisting of three distinct bidirectional phases, followed by a gradual return to the initial position (Fig. 1).

The first phase, which we in this study denote Phase A, is a distinct antegrade movement, i.e. a movement in the direction of the blood flow shortly after, or at, end-diastole. The end of the antegrade Phase A occurs when the next distinct phase (Phase B) starts. The antegrade Phase A was observed in most subjects but was sometimes very small.

Phase B is a distinct retrograde movement, i.e., a movement in the direction opposite to blood flow, starting in conjunction with, or shortly before, peak systole is seen in the diameter curve. The end of the retrograde Phase B occurs in diastole in conjunction with, or just after, the dicrotic notch is seen in the diameter curve. This is the most retrograde position of the wall during diastole.

Phase B is followed by an antegrade movement in diastole, which we in this study denote Phase C. Its start is distinct and occurs directly after the retrograde Phase B. The end is sometimes distinct, but it may also stop gradually. To automatically identify the end of the Phase C; it was defined as the first position when the antegrade velocity was ≤ 0 mm/s.

In the older age group (>50 years), two phases that have not previously been reported become visible. A phase, which we in this study denote Phase W, is a distinct, rapid retrograde movement starting just before end-diastole at the measurement site, i.e. preceding the start of the antegrade Phase A. The retrograde Phase W was first noted in male subjects 50–65 years of age, in whom this phase is prominent. However, after noting this, the retrograde phase W could be noted in most subjects although it was smaller in younger subjects and in the oldest ones. Figure 2 shows examples of a distinct large retrograde Phase W in three subjects 53–57 years of age. The end of the retrograde Phase W is the start of the antegrade Phase A. To automatically find the start of Phase W in the averaged cardiac cycles, either the last turning point before the antegrade Phase A, or the first position when the velocity of the longitudinal movement was < -1 – -3 mm/s (depending of the magnitude of the displacement) was found.

Another phase, which we in this study denote Phase X, also became obvious when subjects >50 years of age were studied. Phase X is an antegrade movement occurring during, or directly after, the retrograde Phase B in the period around, or just before, the dicrotic notch is seen in the diameter change curve (Fig. 3). This phase was not distinct in all subjects; especially not in younger subjects, in whom only a hardly detectable velocity change (Fig. 3a) or a minimal antegrade movement
during retrograde Phase B could be seen. In most subjects >50 years of age, it was a distinct antegrade movement, interrupting the retrograde Phase B (Fig. 3b). In the few cases when the most retrograde position during diastole occurred at the same time as the start of Phase X (Fig. 3c), the end of the retrograde Phase B was defined as the starting position of Phase X. The start of the antegrade Phase C was in those cases defined to be the time when the retrograde movement after Phase X turned into an antegrade movement (Fig. 3c). An antegrade Phase X was seen in 93% of the subjects >50 years of age, while it was only seen in 38% of the subjects <50 years of age. However, in the subjects <50 years of age the displacement of Phase X was very small. Further, Phase X seems to become an obvious antegrade phase of movement at younger age in men than in women. This was especially notable when the velocity of the movement was analysed (Fig. 4). The median value of the velocity was positive, i.e., indicating the presence of Phase X, at earlier age in men (age group 35-44) than in women (age group 45-54) (Fig. 4). At older ages, the velocity, and the displacement (see below), seems to increase faster in women than in men.

The basic characteristics of the different phases of movement are summarized in Table II.
Figure 2. Longitudinal movement of the intima-media complex (solid) of the CCA with a distinct large retrograde Phase W (marked by dashed grey as well as a large oval in the centre cardiac cycle) and corresponding diameter change (dashed) in a) 53-year-old male, b) 55-year-old male and c) 57-year-old male. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow, i.e., an antegrade movement. The small circles mark the onset of an antegrade movement in early systole (the antegrade Phase A). Phase W is a retrograde movement that precedes the antegrade Phase A. The retrograde Phase W begins just before end-diastole at the measurement site.
Figure 3. Longitudinal movement (solid) of the intima-media complex of the far wall in the CCA and the corresponding diameter change (dashed) of a) a 27-year-old female, b) a 60-year-old female, and c) a 63-year-old female. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow, i.e., an antegrade movement. The small circles mark the onset of an antegrade movement in early systole (the antegrade phase A). The large ovals mark the position of Phase X in the centre cardiac cycle. Note that Phase X occurs during, or directly after, Phase B in the period around, or just before, the dicrotic notch is seen in the diameter change curve.
Phase of movement | Characteristics
--- | ---
Antegrade Phase A | Antegrade movement in early systole starting at, or just after, end-diastole at the measurement site.
Retrograde Phase B | Retrograde movement starting after Phase A in systole, before the diameter change curve has reached its maximum. It ends around, or just after, the dicrotic notch is seen in the diameter change curve.
Antegrade Phase C | Antegrade movement in diastole starting after Phase B or Phase X.
Retrograde Phase W | Retrograde movement starting just before end-diastole at the measurements site, i.e. just before the arterial diameter has reached its minimum.
Phase X | Antegrade movement or retrograde velocity change occurring during, or directly after, Phase B in the period around, or just before, the dicrotic notch is seen in the diameter change curve.
Patterns of movement

In younger subjects (<50 years of age), the patterns of the longitudinal movement of the arterial wall were similar to what has previously been reported by us, and others (Cinthio et al. 2006; Cinthio and Ahlgren 2010; Ahlgren et al. 2012b; Yli-Ollila et al. 2013), and can be divided into three different types. Yli-Ollila et al. (2013) recently denoted these patterns of movement backward-oriented, bi-directional and forward-oriented, respectively, whereas we in this study also has chosen to denote them backward-oriented Type I, Type II and forward-oriented Type III, respectively. Figure 5 show examples of these patterns of movement.

The backward-oriented Type I pattern is shown in figure 5a, d, and g. The backward-oriented Type I pattern is characterized by a small antegrade movement in early systole (the antegrade Phase A), which is much smaller than the retrograde movement in systole (the retrograde phase B). The backward-oriented Type I pattern is defined by a ratio between the antegrade Phases A and the retrograde Phase B that is smaller than 0.3.

The Type II pattern is shown in figure 5b, e, and h. The Type II pattern is characterized by a somewhat larger antegrade Phase A in relation to the retrograde Phase B (compared to their relation in the backward-oriented Type I pattern). Type II is defined by a ratio between the antegrade Phase A and the retrograde Phase B that is between 0.3 and 1.

The forward-oriented Type III pattern is shown in figure 5c, f, and i. The forward-oriented Type III pattern is characterized by a larger antegrade Phase A than the retrograde Phase B, and is defined by a ratio between the antegrade Phase A and the retrograde Phase B that is larger than 1.

In the older age groups (>50 years of age) two other distinct types of patterns of movement become apparent. Figure 6 shows six examples of a pattern, from now on denoted backward-oriented Type IV. The backward-oriented Type IV pattern is characterized by absence of an antegrade movement in early systole, i.e. absence of an antegrade Phase A. A retrograde movement starts before end-diastole at the measurement site, i.e. long before the normal start of the retrograde Phase B. It is followed by an antegrade movement in diastole (Phase C). Phase X is sometimes visible. Our interpretation is that the two retrograde Phases W and B have fused. To separate the retrograde Phase W and retrograde Phase B in the backward-oriented Type IV pattern cases, the acceleration of the movement was analysed. The velocity and the acceleration of the longitudinal movement are altered at the time when the antegrade Phase A usually occurs in the Type I, II and III patterns of movement. The backward-oriented Type IV pattern shows similarities with the backward-oriented Type I pattern, and some subjects were hard to classify. Figure 7 shows six examples of patterns of movement which are hard to classify as backward-oriented Type I or backward-oriented Type IV. In this study, we denote these patterns backward-oriented Type I/IV.

Figure 8 shows another type of pattern, which we in this study denote forward-oriented Type V. The forward-oriented Type V pattern is characterized by a large antegrade movement in early systole, i.e. a large antegrade Phase A, and no, or a small and indistinct, retrograde movement in systole (retrograde Phase B). The antegrade Phase A is the dominating phase in a forward-oriented
Type V pattern. The other phases of movement can sometimes be difficult to identify. This pattern of longitudinal movement was a common pattern in subjects >65 years of age, present in 5 of 15 the subjects in this age-group, but only seen in 3 of 90 subjects below 55 years of age (Table III).

The basic characteristics of different patterns of movement are summarized in Table IV.

Table III show the prevalence of the different patterns of longitudinal movement for different age groups and gender. In subjects <35 years of age the most common patterns of movement were backward-oriented Type I, Type II and forward-oriented Type III. Also in subjects 35-54 years of age the most common patterns of movement were backward-oriented Type I, Type II and forward-oriented Type III, but some backward-oriented Type I/IV and forward-oriented Type V could be seen. In subjects >54 years of age the most common patterns of movement were backward-oriented Type IV, backward-oriented Type I/IV and forward-oriented Type V, but some Type II could be seen. The forward-oriented Type V was not present in any of the 56 subjects below age of 35 and in only three cases below age of 55. The backward-oriented Type I, Type II and forward-oriented Type III seems more prevalence in women than in men in the age-group 45–54.
Figure 5. Longitudinal movement (solid) and corresponding diameter change (dashed) of the intima-media complex of the CCA in nine subjects of different ages illustrating different patterns of longitudinal movements. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow, i.e., an antegrade movement. The small circles mark the onset of an antegrade movement in early systole (the antegrade phase A). Phase A is followed by a retrograde movement (Phase B) later in systole and a second antegrade movement (Phase C) in diastole. The backward-oriented Type I pattern of movement is characterized by a small Phase A, followed by a large Phase B. The ratio between Phase A and Phase B is less than 0.3. The Type II pattern is characterized by a ratio between the antegrade Phase A and the retrograde Phase B between 0.3 and 1. The forward-oriented Type III pattern is characterized by a larger antegrade Phase A than the retrograde Phase B, and, thus, a ratio >1. a) 29-year-old male. b) 29-year-old female. c) 20-year-old male. d) 30-year-old female. e) 36 year-old female. f) 39 year-old female. g) 45 year-old male. h) 44-year-old male. i) 47-year-old female.
Figure 6. Six examples of backward-oriented Type IV pattern of longitudinal movement of the intima-media complex of the CCA (solid) and corresponding diameter change (dashed). For longitudinal movement, a positive deflection denotes movement in the direction of blood flow. The backward-oriented Type IV pattern is characterized by absence of an antegrade movement in early systole, and a large retrograde movement that starts before end-diastole at the measurement site, i.e. long before Phase B, the retrograde movement in late systole seen in subjects with the type I-III pattern. Phase X is clearly visible in all subjects above. a) 49 year-old male. b) 55 year-old female. c) 67 year-old-male. d) 60 year-old female. e) 54-year-old female. f) 69 year-old-male.

Figure 7. Three examples of backward-oriented Type I/IV patterns of longitudinal movement of the intima-media complex of the CCA (solid) and corresponding diameter change (dashed). The small circles mark the onset of an antegrade movement in early systole (the antegrade phase A). A backward-oriented Type I/IV pattern is characterized by a distinct antegrade movement in early systole (Phase A) and a distinct retrograde movement both before (a large Phase W) and after (a large Phase B) Phase A. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow. a) 57 year-old female. b) 60-year-old male. c) 67 year-old-male.
Figure 8. Three examples of Type V pattern of longitudinal movement of the intima-media complex of the CCA (solid) and corresponding diameter change (dashed). The small circles mark the onset of an antegrade movement in early systole (the antegrade phase A). The Type V pattern is forward-oriented and characterized by a large antegrade movement in early systole (a large Phase A), and that Phase B, the retrograde movement in systole, is indistinct and/or small. For longitudinal movement, a positive deflection denotes movement in the direction of blood flow. a) 62 year-old female. b) 66 year-old male. c) 67 year-old male.

Table III: Summary of the prevalence of the different patterns of longitudinal movement for different age groups and gender.
<table>
<thead>
<tr>
<th>Movement pattern</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Backward-oriented Type I</td>
<td>A small antegrade movement in early systole (antegrade Phase A), which is much smaller than the retrograde movement in systole (retrograde phase B). Ratio Phase A/Phase B &lt; 0.3.</td>
</tr>
<tr>
<td>Type II</td>
<td>A somewhat larger antegrade Phase A in relation to the retrograde Phase B, compared to the backward-oriented Type I pattern. Ratio Phase A/Phase B between 0.3 and 1.</td>
</tr>
<tr>
<td>Forward-oriented Type III</td>
<td>A larger antegrade Phase A than retrograde Phase B. Ratio Phase A/Phase B &gt; 1.</td>
</tr>
<tr>
<td>Backward-oriented Type IV</td>
<td>Characterised by absence of an antegrad movement in early systole (antegrade Phase A). The retrograde movement starts before end-diastole at the measurement site, always long before the “normal” start of the retrograde Phase B, and it is followed by an antegrade movement in diastole (Phase C).</td>
</tr>
<tr>
<td>Backward-oriented Type I/IV</td>
<td>Similar as Backward-oriented Type IV but a distinct antegrade Phase A is visible.</td>
</tr>
<tr>
<td>Forward-oriented Type V</td>
<td>Characterised by a large antegrade movement in early systole (i.e. a large antegrade Phase A), and a small or indistinct, retrograde movement in systole (i.e. a small or indistinct retrograde Phase B). The other phases of movement can sometimes be difficult to identify.</td>
</tr>
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</table>

Table IV: Summary of the characteristics of the different pattern of longitudinal movement.
Size of the phases of movement

The displacement and velocity of each phase for each age group and gender are summarised in Table V. In addition, the maximum longitudinal displacement, i.e. the difference between the most antegrade position and the most retrograde position, independently of phase, during a cardiac cycle, are presented.

The displacement and the velocity of Phase A decreased significantly with age in men ($r = 0.26$, $p < 0.05$, $k = -3 \mu m/year$, range $0–871 \mu m$) but not in women ($r = 0.02$, $p = 0.86$, $k = 0 \mu m/year$, range $0–1344 \mu m$).

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<td>Nbr of Subjects</td>
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<td>LMovMax (µm)</td>
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<td>Phase A (µm)</td>
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<td>Phase B (µm)</td>
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</tr>
<tr>
<td>Phase C (µm)</td>
<td>470 SD(226)</td>
<td>460 SD(256)</td>
</tr>
<tr>
<td>Phase W (µm)</td>
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<td>-76 SD(76)</td>
</tr>
<tr>
<td>Phase X (µm)</td>
<td>11 SD(18)</td>
<td>1 SD(4)</td>
</tr>
<tr>
<td>Vel. Phase A (mm/s)</td>
<td>5.8 SD(3.7)</td>
<td>6.1 SD(3.9)</td>
</tr>
<tr>
<td>Vel. Phase B (mm/s)</td>
<td>-4.8 SD(1.4)</td>
<td>-5.6 SD(2.9)</td>
</tr>
<tr>
<td>Vel. Phase C (mm/s)</td>
<td>6.2 SD(3.2)</td>
<td>5.7 SD(3.1)</td>
</tr>
<tr>
<td>Vel. Phase W (mm/s)</td>
<td>-101 SD(61)</td>
<td>-89 SD(84)</td>
</tr>
<tr>
<td>Vel. Phase X (mm/s)</td>
<td>0.6 SD(1.5)</td>
<td>-0.9 SD(1.7)</td>
</tr>
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</table>

Table V. Summary of the measurement for each age group and gender. All data are presented as mean (SD)
The displacement but not the velocity of Phase B decreased significantly with age both in men and women ($r = 0.26$, $p < 0.05$, $k = -4$ µm/year, range 56–1326 µm, and $r = 0.37$, $p < 0.001$, $k = -7$ µm/year, range 97–1333 µm, respectively).

The displacement and the velocity of Phase C decreased significantly with age both in men and women ($r = 0.31$, $p < 0.05$, $k = -5$ µm/year, range 14–1373 µm, and $r = 0.52$, $p < 0.0001$, $k = -10$ µm/year, range 0–1402 µm, respectively).

The displacement and the velocity of Phase W increased significantly with age in men ($r = 0.35$, $p < 0.05$, $k = 2$ µm/year, range 0–514 µm). The velocity of Phase W but not the displacement increased significantly with age in women ($r = 0.16$, $p = 0.16$, $k = 1$ µm/year, range 1–603 µm).

The displacement and the maximum velocity of Phase X increased quadratically with age both in men and women ($r = 0.75$, $p < 0.0001$, range 0–206 µm, and $r = 0.45$, $p < 0.001$, range 0–546 µm, respectively, Fig 9). Further, Phase X seems to increase at younger age in men than in women. This was especially notable when the regression curve of the maximum velocity of the Phase X was analysed (Fig. 9). The regression curve passed zero mm/s earlier in men (at age 37 years) than in women (at age 43 years) (Fig. 9). At older ages, the variability of both the displacement and the maximum velocity of Phase X was larger in women than in men (Fig. 9).

The maximum longitudinal displacement during a cardiac cycle, independently of phase of longitudinal movement, did not significantly decrease with age in either men or women ($r = 0.16$, $p = 0.22$, $k = -2$ µm/year, range 220–1374 µm, and $r = 0.13$, $p = 0.25$, $k = -3$ µm/year, range 137–1402 µm, respectively).
Figure 9. Scatter plot of the displacement of Phase X in a) men and b) women, and the maximum velocity of Phase X in c) men and d) women. Both displacement and the maximum velocity of Phase X increased quadratically with age, both in men and in women. Correlation coefficients (r) and p-values are given.
Discussion

We have, to the best of our knowledge, for the first time described the different phases and the resulting multiphasic pattern of the longitudinal movement of the intima-media complex of CCA for a wide range of ages in healthy subjects of both genders. The pronounced variation in the patterns of longitudinal movement of the CCA that have been shown in young healthy subjects (Cinthio et al. 2006; Ahlgren et al. 2012b) is also seen in middle-aged and older healthy subjects. However, the patterns of movement seen in middle-aged and older subjects are different from those commonly seen in young subjects, including the appearance of two new distinct phases of movement, and thus new complex patterns of movement. One of these phases, Phase X, increase quadratically with age. Further, a gender difference might be present, with an earlier increase of the size and velocity of Phase X in men than in women. As discussed below, our finding show that the longitudinal movement of the common carotid wall can not only give new information of the aging process of the arterial tree, but also give new insights to the coupling of the left ventricle with the systemic circulation, i.e. the ventricular-vascular interaction.

In young subjects (<35 years of age) three dominating patterns of longitudinal displacement of the intima-media complex of the CCA wall was seen, in this study denoted backward-oriented Type I, Type II and forward-oriented Type III. The Type I and Type II patterns show many similarities, especially when the ratio between Phase A and B are close to 0.3, and it can be discussed if these should be looked upon separately or if the discriminating ratio is the optimal. However, when initially only studying young subjects it seemed reasonable to separate them.

The most common variants in subjects >55 years of age were the backward-oriented Type IV, the backward-oriented Type I/IV, and the forward-oriented Type V, although the Type I-III patterns, commonly seen in young, also was seen in some subjects. Interestingly, these “young” patterns seem to be more prevalent in women than in men in this age group (Table III). Notable, the Type IV, Type I/IV, and Type V patterns of movement were also seen in a few subjects <45 years of age, and it can be speculated if this indicate early vascular aging in these subjects.

Another striking finding with increasing age was the appearance of an increasingly prominent antegrade phase, Phase X, which is seen at the time, or close to, when the dicrotic notch is seen in the diameter change curve (Fig. 3). The dicrotic notch is considered to reflect the closure of the aortic valve (Nichols and O’Rourke 2005). The increase of Phase X with age seems to be quadratic with a possible gender-difference.

Another finding with aging was the appearance of the distinct, rapid retrograde movement, Phase W, occurring just before the first antegrade movement starts, i.e. preceding Phase A, when the diameter of the artery has nearly reached its minimum.

The underlying factors for the markedly different patterns of movement are at present unknown, and this study, being observational, cannot explain the underlying mechanisms. Thus, no definite conclusion regarding the mechanisms underlying the longitudinal can be drawn. However,
characterization of the movement in healthy subjects, and their changes with aging, is one step towards a deeper understanding of the underlying factors.

Arteries in the body are naturally under a condition of longitudinal tension (Nichols and O’Rourke 2005). In predominantly elastic arteries, such as the human aorta and CCA, the circumferential elastic modulus has been shown to be age and sex dependent (Kawasaki et al. 1987; Hansen et al. 1995). Studies on the longitudinal elastic modulus of arteries are sparse, and the results from earlier in vitro studies are not clear-cut (Nichols and O’Rourke 2005). The complex bidirectional multi-phasic pattern of longitudinal movement of the human CCA wall implies that opposing forces are involved, and that the size and the timing of the individual forces can vary. Underlying forces that have been suggested include shear stress from blood flow, left ventricular contraction, pulse pressure and smooth muscles cell activation in the arterial wall (Cinthio et al. 2006; Zahnd et al. 2011a; Ahlgren et al. 2012a; Ahlgren et al. 2012c; Idzenga et al. 2012; Yli-Ollila et al. 2013). Specific phases of the longitudinal movement might also be associated with the diameter change and elastic recoil (Cinthio et al. 2006). Further, the intramural shear strain may be important for the resulting movement (Sjöstrand et al. 2017).

The multi-phasic pattern of longitudinal movement of the human CCA is more complicated than the bi-phasic pattern that seems to be present in the human abdominal aorta, brachial and popliteal arteries (Cinthio et al. 2006) and the porcine CCA (Ahlgren et al. 2009). The latter arteries are not as well investigated as the human CCA, but the pattern of longitudinal movement of the wall of these arteries seems to be in large characterized by a distinct antegrade movement and a somewhat less distinct retrograde movement of the same size. This is thus in contrast to the complex pattern seen in the CCA. One difference between the carotid artery and the other arteries mentioned is the distance to the heart. It is well known that the base of the heart moves substantially toward the ventricular apex in systole, and that this atrioventricular valve plane displacement decrease with increasing age (Höglund et al. 1988; Simonson and Schiller 1989). Further, it has been shown that the left ventricle rotate along its long-axis and a twisting motion, and that this is affected by aging (Kaku et al. 2014). Both the displacement of the heart in the longitudinal direction and the rotation of the heart might have impact on the aortic arch and its branches. Thus, it would not be surprising if one, or both, of these movements influence the longitudinal displacement of the CCA. The other arteries mentioned are located at quite a distance from the heart and thus, are likely to be less influenced by the displacement of the heart. The likely influence of the heart is supported by recent work by Zahnd et al. (Zahnd et al. 2015) who has demonstrated regional differences in the longitudinal displacement of the carotid artery wall along the length of the CCA, quantifying attenuation of the longitudinal movement with increasing distance to the heart. With a clear loss of longitudinal motion along the CCA, it seems reasonable that a cardiac factor may affect the magnitude of the longitudinal displacement of the carotid artery wall.

The primary hemodynamic forces that act on the arterial vessel wall consist of pressure acting perpendicular to the vessel wall, resulting in cyclic diameter change and a circumferential or radial strain, and pulsatile blood flow acting as a shear force in the direction parallel to the vessel wall. In
pharmacological experiments, creating a wide range of pulse pressures, we have found strong correlations between the maximal antegrade longitudinal displacement of the porcine carotid artery and pulse pressure (Ahlgren et al. 2012c). During their travel in the arterial tree, the pulse waves are reflected when they meet a transition from one vascular impedance to another (Nichols and O’Rourke 2005). In an early study on the longitudinal movement of the CCA, we noted that the timing of the different phases of the longitudinal movement in relation to the distension of the artery, i.e., the diameter change, shows good agreement with the expected arrival of the pulse wave, reflected pulse wave, and re-reflected pulse wave, respectively (Cinthio et al. 2006), thus suggesting that a longitudinal shear force from the pulse wave might be present. However, as stated above, the pulsatile blood pressure is considered to act only perpendicular to the vessel wall, i.e. not along the vessel.

In this study we found that with aging a distinct antegrade displacement (Phase X) is seen at the time when the dicrotic notch, considered to reflect closure of the aortic wall and accompanying changes in blood pressure, is seen in the diameter change curve. Thus, our finding of the Phase X constitutes an additional indication that the pressure wave might have impact on vascular mechanics not only in the radial direction (“creating” diameter change), but also in the longitudinal direction, i.e. along the arteries, in contrast to current conjecture.

A seemingly plausible hypothesis is that the shear force from the blood flow is an important factor underlying the longitudinal arterial wall movements. However, in pharmacological experiments on porcine, creating different hemodynamic conditions using adrenaline and noradrenaline and the β1-selective beta-blocker metoprolol, we have shown that a pronounced increase in longitudinal movement of the carotid artery (several hundred percent compared to baseline in some instances) can take place independently of blood flow WSS. These results, in combination with the fact that the shear force from the blood flow is very small (of the same size as the force a soft feather express when it is drawn over a plain surface) compared to the stiffness of the artery (Nichols and O’Rourke 2005), strongly indicate that the WSS is not an important force underlying the longitudinal movement of the arterial wall in healthy subjects.

The different phases and patterns of the longitudinal movement of the carotid artery wall are not easily explained. It seems especially challenging to explain the dramatically different pattern of movement seen on older healthy subjects - in some subjects the pattern of movement was markedly forward-oriented (Type V pattern), while in others the pattern was about the opposite with a dominating retrograde movement (Type IV and Type I/IV patterns). In this context, it should be emphasized that great care has been taken to have the transducer oriented in the same direction in all subjects.

The tension in the arterial wall is lowest in end-diastole just before the blood pressure increases in early systole, and starts distending the artery. At the same time, in early systole, a distinct antegrade longitudinal movement, i.e., in the direction of blood flow, (Phase A) can be observed in most subjects. In most of the young subjects, Phase A starts without any preceding distinct retrograde
movement. Therefore, some antegrade force must actuate this movement. As the shear force from the flowing blood is most likely not responsible (see above), smooth muscles cells within the arterial wall, pulse-wave propagation and/or ventricular motion are the main candidates. Due to the fact that the heart displace in the longitudinal direction towards apex during systole, we, however, find it less likely that the atrioventricular valve plane displacement of the heart is underlying Phase A in young subjects. Later in systole, phase A is followed by a retrograde movement, i.e., in the direction opposite blood flow, in all young subjects. Phase B was larger than Phase A in many subjects; therefore it seems likely that a retrograde force actuate this movement. As just mentioned, during systole the heart is displaced towards the apex. Our hypothesis is therefore that ventricular contraction create a retrograde force that is distributed along the arterial wall, and is therefore a strong candidate underlying Phase B. This is supported by the fact that the size of the Phase B seems to decrease with aging, and that the atrioventricular valve plane displacement is known to decrease with aging. However, smooth muscle cell activation within the media cannot be excluded to impact both Phase A and B, although smooth muscle cells are considered to be sparse in the human CCA. In diastole, around the time of the dicrotic notch, the retrograde Phase B is followed by an antegrade movement (Phase C). The size of Phase C is often approximately the same as of phase B, and often starts distinctly; thereafter its velocity gradually decrease. During this period, the heart displace upwards, decreasing the retrograde force and allowing the tension in the arterial wall to decrease. This arterial wall relaxation might allow an elastic recoil, causing the antegrade Phase C. However, in some older subjects Phase C seems “active”, since Phase C seemed to be larger than Phase B. In these subjects, it was, however, sometimes difficult to separate Phase B, C and X, thus this should be interpreted with caution. Phase W is a retrograde movement that take place just before Phase A in diastole at a time when the lumen diameter not yet have reached its minimum. Due to period in the cardiac cycle, our main hypothesis is that the mechanism behind phase W might be due to the mechanism described by Fukui et al. (Fukui et al. 2007). As the diameter increases, the tissue stretches in the circumferential direction. If the tissue is not elastic enough, in relation to the distending blood pressure, it needs to recruit tissue from a more distal position, which is not yet distended, and therefore a retrograde movement starts. Clearly, further studies are needed to clarify the mechanisms underlying the different phases of longitudinal movement.

As stated above, the antegrade Phase X, becoming prominent with aging, takes place at a time when the dicrotic notch is observed in the diameter change curve. The dicrotic notch is a secondary upstroke in the descending part of the blood pressure curve, reflected in the diameter change curve, and regarded to correspond to closure of the aortic valve (Nichols and O’Rourke 2005). The accompanying pressure changes may create an antegrade force that causes Phase X. Arterial stiffness is probably influencing all phases of the longitudinal movements. However, in this study a quadratic increase of Phase X is observed. Our findings also indicate that Phase X may increase earlier in men than in women. This corresponds well with findings of measurements of local stiffness (such as Ep and β) with an earlier increase in men than in women (Hansen et al. 1995).
Our group (Cinthio et al. 2006; Nilsson et al. 2010) as well as others (Zahnd et al. 2011b; Idzenga et al. 2012) have previously shown that in large arteries the intima-media complex shows a larger longitudinal displacement than the adventitial region during the cardiac cycle, thus, there is shear strain intramurally. In this study we have focused on the phases and resulting patterns of longitudinal displacement of the intima-media complex, and intramural shear strain has not been analysed. At present, it is not known if the intramural shear strain, (i.e. the relation between the longitudinal displacement of the intima-media complex and the longitudinal displacement of the adventitial region), change with aging, or how putative changes in intramural shear strain may influence the longitudinal movement of the intima-media complex. These issues are being addressed in on-going studies.

The phases and the pattern of the longitudinal movement might have the potential to be used as an early marker of vascular disease. Tat et al. 2016 (Tat et al. 2016) recently reported that subjects with a pattern of movement similar to Type V is common in subjects with atherosclerotic plaques, whereas healthy subjects had a pattern similar to type IV. However, the investigated subjects were few and the patients with plaque and the healthy subjects were of different ages. This study shows that both types of patterns are present in middle-aged and older healthy subjects without plaques in the investigated carotid artery. Further studies are needed to define the influence of specific risk factors on changes in the pattern of longitudinal displacement of the arterial wall, as well as to define the changes in longitudinal displacement in patients with manifest vascular / atherosclerotic disease. Further, it is also of interest to study the pattern of the longitudinal motion in relation to parameters of local arterial stiffness based on measurements of the diameter change.

**Conclusion**

This study shows previously unknown changes in vascular mechanics of the CCA with aging. Further, our findings show that the longitudinal movement of the common carotid wall can not only give new information of the aging process of the arterial tree, but also give new insights on the ventricular-vascular interaction. Further studies are needed to clarify these issues.
References


Iterative 2D tracking in high frame rate ultrasound imaging

John Albinsson¹, Hideyuki Hasegawa, Hiroki Takahashi, Åsa Rydén Ahlgren, and Magnus Cinthio,

Abstract— In order to study longitudinal movement and intramural shearing of the arterial wall with a Lagrangian viewpoint using high frame rate imaging, a new tracking scheme is required. We propose the use of an iterative tracking scheme in which the cumulative number of estimations needed for each frame is reduced and each estimated position is improved by the use of two kernels and unbiased sub-sample estimation. The tracking scheme was evaluated on phantom B-mode cine loops and considered both velocity and displacement for a range of initial frame intervals (1–128) at the start of the iterations. The cine loops had a frame rate of 1302 fps and were beamformed 1) using delay-and-sum, 2) using phase coherence imaging, or 3) using transverse oscillation. Both the mean estimation errors and the standard deviations decreased with increasing initial iteration length. An increased velocity or larger pitch increased the motion estimation errors and the standard deviation. The mean estimation errors were not significantly different for any of the beamforming methods used. Overall, the tracking scheme reduced the accumulated errors in the phantom measurements and showed minute high-frequency displacements both in the phantom measurements and when tested in vivo.

Index Terms—Motion estimation, high framerate, Longitudinal arterial movement, longitudinal movement, axial movement

I. INTRODUCTION

Fast and ultrafast ultrasound imaging have been used as the basis for the development of a number of methods intended for diagnosing and exploring different phenomena in vivo, e.g. shear wave elastography [1-4], acoustic radiation force impulse imaging [5], skeletal muscle contraction [6], functional ultrasound of the brain [7], cardiac motion [8, 9], and vector flow imaging [10-12]. The arterial walls have been investigated by estimating the radial strain in the common carotid artery [13] and the radial pulse wave velocity [14, 15]. Our group has previously presented several papers [16-18] where we used cine loops sampled at a low frame rate to explore the longitudinal movement of the common carotid artery wall. Although our group and other groups [19, 20] have increased our knowledge about the movements of the arterial wall, the physiology behind the observed longitudinal vessel wall movement pattern is largely unknown. It is our belief that the use of plane-wave imaging in combination with 2D motion estimation can increase our understanding of this phenomenon.

Plane-wave imaging results in ultrasound frames sampled at a high frame rate, but the high sampling rate comes at a price; because each frame produced with plane-wave imaging is constructed using only one transmission, the reduced transmitted power results in a lower signal-to-noise ratio. Also, the low-resolution frames created from one ultrasound transmission generally have degraded spatial resolution [21] compared to low frame rate ultrasound frames. Different beamforming techniques such as transverse oscillation (TO) [22] and phase coherence imaging (PCI) [23, 24] have been developed in order to improve the usability of the cine loops. However, when using block matching for estimating lateral tissue motion in high frame rate cine loops, there is still a problem. Due to the high frame rate, the depicted objects move only a very short distance between consecutive frames in vivo, and the motion to be estimated will often be small compared to the expected estimation error. This is especially true for lateral movement because ultrasound frames normally have lower spatial resolution in the lateral direction and thus a larger expected estimation error. Consequently, Lagrangian tracking in every frame is very likely to give a large accumulated error even with an unbiased motion estimator. The motion estimations can be improved by averaging motion estimations over multiple frames, but this will decrease the effective frame rate and will function as a low-pass filter on the motion estimations in the time domain. This can potentially hide vital information in the motion estimations.

In this paper we propose to estimate 2D motions with a Lagrangian viewpoint in high frame rate ultrasound cine loops using an iterative motion estimation tracking scheme in which the initial length between the used frames is larger than one. Contrary to phase-sensitive motion estimation methods (e.g. [14, 25]) where the motion must be small to avoid aliasing, our experience shows that the relative motion estimation error
decreases for block-matching methods when the length of the motion increases [26]. Because the motion between two frames in high frame rate ultrasound cine loops is often very small and the speckle decorrelation is limited, the risk for the speckle decorrelation over several, e.g., 128, frames is small but the total motion over this number of frames will be larger and easier to accurately estimate by using existing block-matching methods. The position of the kernel in the in-between frames can thereafter be iteratively estimated based on the already performed estimations in the anteroposterior frames by motion estimations originating from these known positions. The tracking scheme is hypothesized to reduce the size of the cumulative errors both by using two separate motion estimations for each estimated position, thus reducing each estimation error, and by using much fewer estimations from the start of the tracking before reaching the investigated frame.

Our objective was to evaluate the proposed 2D tissue motion estimation tracking scheme in high frame rate ultrasound cine loops. The ultrasound data from a moving phantom were collected using two transducers with a 100 µm and 200 µm pitch, respectively. The used cine loops were beamformed using delay-and-sum (DS), PCI, or TO. The proposed tracking scheme was evaluated for a range of initial frame intervals at the start of the iterations considering both velocity and displacement. The motion estimation errors of the proposed tracking scheme were also compared to the motion estimation errors using low frame rate cine loops.

II. MATERIAL AND METHODS

The proposed iterative motion estimation tracking scheme was evaluated on cine loops depicting a phantom moving in a set pattern (Fig. 1). The tracking scheme was tested for the effect of the initial length of the iterations, the pitch between elements in the transducer, the velocity of the phantom, and the method of beamforming. A feasibility test of the tracking scheme in vivo was also conducted.

A. Motion estimations

The proposed motion estimation tracking scheme consists of two parts if \( k > 1 \), where \( k \) denotes the frame interval in block matching, otherwise only part 1 is used (Fig. 2 shows \( k = 4 \)).

1. Movement was estimated with a Lagrangian viewpoint between every \( k \)th frame (solid lines in Fig. 2a) where \( k = (1, 2, 4, 8, 16, 32, 64, \text{ or } 128) \). The new position of the kernel was estimated twice. The first estimation used a sparse block matching method as described below, and the second estimation used an extra kernel from the previous frame and performed a full search in a 3-by-3 pixel region using sum-of-absolute-difference (SAD). The resulting second position was sub-sample estimated (see the sparse block-matching method) before the final estimated position of the kernel was calculated as the average of the two estimated sub-sample positions [27].

2. Iteratively: the position of the kernel at the middle of the frame interval in the previous iteration (\( k \) frames interval in the first iteration, \( k/2 \) frames in the second iteration, etc.) was determined by estimating the movements between the middle frame and the anteroposterior frames (dashed lines in Fig. 2b). The estimated positions calculated from those two movements were averaged to determine the kernel position in the middle frame. The movements were estimated using the sparse block-matching method with the sub-sample estimation method described below. The iterations continued until the position of the kernel was estimated in every frame (dashed lines in Fig. 2c).

The sparse block-matching method searched iteratively with five search positions in a diamond shape (the fifth position was in the center) using SAD [28]. In the first iteration, a sixth search position was used, and this was located at a position predicted from earlier estimations. The size of the diamond was initially determined by the predicted position and then halved in each consecutive iteration until the search positions were adjacent to each other. In each iteration, the center position was placed at the position with the lowest SAD value from the previous iteration. The iterations continued until a minimum SAD value had been found. Sub-sample estimation was first performed by parabolic interpolation; if the estimate was \( y \pm 0.15 \) pixels, where \( y \) was any natural number, the estimate was used, otherwise a modified grid slope sub-sample estimator was used to recalculate the estimate [26].

The size of a kernel was 1 mm axially and laterally. The used axial kernel size was 41 pixels, and the lateral kernel size was 11 pixels using the 100 µm pitch transducer and 5 pixels using the 200 µm pitch transducer.
B. Cine loops

The phantom cine loops were collected at 1302 fps by an ultrasound scanner (RSYS0002, Microsonic, Tokyo, Japan) equipped with two linear array ultrasonic probes. The two probes had a center frequency of 7.5 MHz and a pitch of 100 µm and 200 µm, respectively. The pixel densities in the cine loops were 40.6 mm\(^{-1}\) axially and either 10.0 mm\(^{-1}\) or 5.0 mm\(^{-1}\) laterally depending on the pitch of the transducer. Each probe was moved repeatedly back and forth at constant velocity with short stops at each turning point (Fig. 1). Two different velocities were used: 2.0 mm/s laterally and 1.0 mm/s axially with displacements of 1.0 mm laterally and 0.5 mm axially; and 1.0 mm/s laterally and 0.5 mm/s axially with displacements of 0.5 mm laterally and 0.25 mm axially.

The collected radio frequency data were beamformed using three different methodologies: DS [13], TO [22], and PCI [23]. In the present study, one frame was obtained from four plane wave transmissions. By creating 24 receiving beams per transmission, one frame was composed of 96 scan lines. In receive, a Hanning apodization was used for DS and PCI, and an apodization consisting of two Hanning functions was used for TO. The total receiving aperture was divided into 6 sub-apertures to obtain the phase coherence factor [23].

Cine loops were also collected at a lower frame rate (41 fps) with a normal focused transmit–receive scheme. These cine loops used the same transducers, probe movements, and kernel size, and motion estimations were conducted in every frame \( k = 1 \), see above.

The \textit{in vivo} cine loop depicted the vessel wall of the common carotid artery in a 42-year-old male. The cine loops were collected at 1302 fps using the probe with 200 µm pitch. The frames were beamformed using DS. The volunteer gave his informed consent according to the Helsinki Declaration.

C. Evaluation of motion estimations

Two evaluation values were calculated using 81 kernels for each setting. The first was a comparison of the set displacement to the estimated displacement for each kernel. The displacements were calculated as the distance moved by each kernel between the start and end positions of the displacement (Fig. 1). These positions were estimated for each kernel from the average position in 4 frames (low FR) or 51 frames (high FR). The second was a comparison of the set velocity to the estimated velocity of each kernel. The velocities were estimated as the slope of a line fitted to the positions of the kernels in 8 consecutive frames (low FR) or in 101 frames (high FR).

The statistical significance of changes in the mean estimation errors and standard deviations were tested for two cases. In the first case, the estimation errors using an initial length of iteration \( k = 1 \) were used as the reference for the estimation errors using other initial lengths of iteration and cine loops sampled at a low frame rate. The cine loops were beamformed using DS. In the second case, motion estimations using an initial length of iteration of 128 frames for the three methods of beamforming and cine loops sampled at low frame rate were compared. Significance testing was conducted with \( p < 0.05 \) as the significance level utilizing ANOVA for changes in mean values and the two-sample F-test for changes in standard deviations. Because the ANOVA was balanced and the changes in the standard deviations were limited, the unequal standard deviations were deemed to have negligible influence on the tests.
III. RESULTS

Fig. 3 shows that the proposed iterative method (k = 64) can visualize small high-frequency oscillations when the phantom stops and can accurately visualize the full deflection (velocity = 2.0 mm/s laterally and 1.0 mm/s axially). The normal frame-to-frame tracking (k = 1), on the other hand, drifts away, and it is difficult to judge the validity of the small oscillations. In the evaluation of the proposed tracking scheme, a lower acceleration was used to minimize the oscillations.

Fig. 4 and 5 show the lateral and axial estimation errors when estimating velocity using DS beamformed cine loops. The mean estimation errors and the standard deviations decreased with increased length of iteration, and increased velocity of the phantom increased the standard deviations. A smaller pitch decreased both the mean value and the standard deviation of the lateral estimation errors, while the axial estimation errors were for the most part unaffected. Using a smaller pitch was more important when using low frame rate imaging than when using high frame rate imaging.

Fig. 6 and 7 show the lateral and axial estimation errors when estimating the displacement using DS beamformed cine loops. The mean estimation errors and the standard deviations decreased with increased initial length of iteration. A small pitch gave decreased mean estimation errors when increasing the velocity, while a large pitch gave increased mean estimation errors when increasing the velocity. Increasing the velocity generally increased the standard deviation.

Tables I through IV present the estimation errors both when estimating velocity and when estimating the displacement for the three different beamforming methods using an initial iteration length of 128 frames. In most cases, the use of cine loops sampled at a low frame rate gave mean motion estimations errors significantly larger than the mean motion estimation errors when using high frame rate cine loops (p < 0.05). The mean estimation errors for the three beamforming methods were for the most part not significantly differentiated.

Fig. 8 shows the estimated longitudinal movement of the intima-media complex of the common carotid arterial wall of a 42-year-old healthy male. The estimations clearly show a bi-directional longitudinal movement pattern of an anticipated magnitude. The estimated movement curve, showing approximately 1.2 heartbeats, also indicates repeatability of the movement pattern. Though no ground-truth exists, the major movement patterns correspond well with low frame rate motion estimates, indicating that the proposed tracking scheme could enable the study of longitudinal movement in high frame rate imaging of the intima-media complex.

IV. DISCUSSION

We have for the first time presented a tracking scheme for iteratively estimating 2D motions with a Lagrangian viewpoint in cine loops with high or ultrahigh frame rates. The proposed motion estimation scheme performed well in the phantom study when estimating both velocity and displacement. The results showed increased tracking accuracy using longer initial length of iterations, while the used beamforming method was of minor importance. The tracking scheme presented here is
easy to implement and can be used with most block-matching motion estimation methods.

It was hypothesized in the Introduction that it would be easier to accurately estimate a large motion than a small motion. This is clearly shown in Fig. 3 as the accumulated motion estimation errors decreased with a larger initial length of iteration. Fig. 4–7 show the following:

1. Using a small initial length of iteration gave rather small mean estimation errors but gave large standard deviations. Each of the motion estimations in the first iteration gave a very small error, but they accumulated to rather large errors and did so along different paths.

2. Using a medium initial length of iteration gave larger mean estimation errors but smaller standard deviations. All estimations were roughly equal, but the initial motion estimations underestimated the motions. The later iterations gave accurate estimations for the in-between frames, but their starting points from the first iteration were incorrect.

3. Using a large initial length of iteration gave small mean estimation errors and small standard deviations. The distance moved between each frame in the first iteration was large enough for the motion estimations to be accurate and for the later iterations to give accurate estimations for the in-between frames.

The benefit of the implemented iterative method came not only from the use of two kernels for each estimation but also from the length of the movement between the frames in the first iteration. Considering that the initial length of iteration should be “long enough” for the best tracking accuracy and

<table>
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<tr>
<th>Pitch</th>
<th>100 µm</th>
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<tbody>
<tr>
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<td>1000 µm/s</td>
<td>2000 µm/s</td>
<td>2000 µm/s</td>
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<tr>
<td>Significance</td>
<td>a, b</td>
<td>a</td>
<td>a</td>
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</tr>
<tr>
<td>Low FR</td>
<td>−150 ± 120</td>
<td>−800 ± 130</td>
<td>−60 ± 220</td>
<td>−1300 ± 260</td>
</tr>
<tr>
<td>High FR</td>
<td>−96 ± 280</td>
<td>−310 ± 420</td>
<td>210 ± 220</td>
<td>−180 ± 880</td>
</tr>
<tr>
<td>PCI</td>
<td>−19 ± 150</td>
<td>−230 ± 610</td>
<td>130 ± 180</td>
<td>26 ± 1200</td>
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</table>

All values are given in µm/s. Motion estimations were made using $k = 128$ for the high frame rate cine loops. Significance was calculated as $p < 0.05$ in each column where a = Low frame rate (FR) different from High FR, and b = Beamforming methods differentiated from each other. Here DS = delay-and-sum, TO = transverse oscillation, and PCI = phase coherence imaging.

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<tr>
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<tbody>
<tr>
<td>Velocity</td>
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<td>500 µm/s</td>
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<td>Significance</td>
<td>a, b</td>
<td>a</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Low FR</td>
<td>48 ± 140</td>
<td>−31 ± 160</td>
<td>49 ± 150</td>
<td>−12 ± 270</td>
</tr>
<tr>
<td>High FR</td>
<td>DS 61 ± 88</td>
<td>−4.6 ± 200</td>
<td>−110 ± 170</td>
<td>180 ± 240</td>
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<tr>
<td>PCI</td>
<td>14 ± 94</td>
<td>−81 ± 230</td>
<td>−81 ± 200</td>
<td>72 ± 300</td>
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</table>

All values are given in µm/s. Motion estimations were made using $k = 128$ for the high frame rate cine loops. Significance was calculated as $p < 0.05$ in each column where a = Low frame rate (FR) different from High FR, and b = Beamforming methods differentiated from each other. Here DS = delay-and-sum, TO = transverse oscillation, and PCI = phase coherence imaging.
that the velocities vary drastically in \textit{in vivo} measurements, it is likely that the tracking performance of the proposed tracking scheme can be optimized \textit{in vivo} by using an initial length of iteration that adapts to the tissue velocity aiming to achieve the longest possible movement without significant speckle decorrelation. Potentially the best results could be achieved by using transducers with different pitch, e.g., using a smaller pitch gives more accurate motion estimations. However, this effect was much smaller for the high frame rate cine loops than for the low frame rate cine loops. It is our belief that the focusing in the transmit phase is causing much of the benefits of using a small pitch as seen for the high frame rate cine loops. The main features of the \textit{in vivo} curve estimated using a high frame rate cine loop agree well with our low frame rate \textit{in vivo} measurements. A circle marks the onset of a heart cycle at the end of diastole. The initial length of iteration was set to 64 frames.


despite the potential limitation is the chosen velocities of the phantom. With a unknown uncertainty in the reference displacements and velocities that are used when calculating the estimation errors. Looking at the results for motion estimation in the low frame rate cine loops in Fig. 4 and 5, the effect of using transducers with different pitch was anticipated in effect if not in amplitude, e.g., using a smaller pitch gives more accurate motion estimations. However, this effect was much smaller for the high frame rate cine loops than for the low frame rate cine loops. It is our belief that the focusing in the transmit phase is causing much of the benefits of using a small pitch as seen for motion estimations conducted in low frame rate cine loops.

Sparse block-matching uses the hypothetical surface created if all blocks in a region are compared to the kernel with an evaluation metric method, i.e., a full search. The exact form is not very important as long as the extreme point of the surface is situated at the correct position for the motion of the kernel and that the surface is smooth, although a very flat surface close to the extreme point is likely to affect the motion estimation. Thus it is not surprising that the differences in motion estimation errors between beamforming methods are rather small because even if the methods used for beamforming will have a large visual effect on the resulting B-mode frames, the evaluation metric method will act as a filter and remove most of these effects.

There are two limitations in the phantom study. The first limitation is the chosen velocities of the phantom. With a

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### TABLE III

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<tr>
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<td></td>
<td>200 μm</td>
<td>a</td>
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<td></td>
<td>200 μm</td>
<td>a</td>
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</table>

All values are given in μm. Motion estimations were made using \( k = 128 \) for the high frame rate cine loops. Significance was calculated as \( p < 0.05 \) in each column where \( a = \) Low frame rate (FR) different from High FR, and \( b = \) Beamforming methods differentiated from each other. Here DS – delay-and-sum, TO – transverse oscillation, and PCI – phase coherence imaging.

### TABLE IV

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<tr>
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<td>a</td>
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<td></td>
<td>200μm</td>
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All values are given in μm. Motion estimations were made using \( k = 128 \) for the high frame rate cine loops. Significance was calculated as \( p < 0.05 \) in each column where \( a = \) Low frame rate (FR) different from High FR, and \( b = \) Beamforming methods differentiated from each other. Here DS – delay-and-sum, TO – transverse oscillation, and PCI – phase coherence imaging.
maximal velocity of 2 mm/s we are well below fast tissue motions in vivo. However, the results from the in vivo measurement (Fig. 8) indicate that the proposed tracking scheme works well with higher velocities. The second limitation is that the largest initial length of iterations was k = 128 because it is believed that larger values of k might influence the tracking performance. Larger values of k were not possible to test due to the combination of using a Lagrangian viewpoint, the search-region of the used block-matching method, the velocity of the phantom, and the size of the ultrasound frames.

V. CONCLUSION

High frame rate imaging provides excellent time resolution of motion and enables visualization of fast processes such as the pulse wave propagation of the arterial wall. The radial pulse wave propagation has been visualized using high frame rate imaging [14, 15], but it has been more challenging to visualize the longitudinal movement and hence the propagation of the longitudinal movement of the arterial wall. A robust method for estimating 2D motions in high frame rate cine loops is needed for estimation of the longitudinal movement, and here we have presented a tracking scheme that might fill that role. It is clear that our tracking scheme reduced the accumulated errors while still showing minute high-frequency displacements in the phantom measurements. In addition, Fig. 8 shows motion estimations of the longitudinal movement of the intima-media complex of the common carotid artery wall in vivo. This indicates that the proposed tracking scheme might be a powerful tool in the continued research on the longitudinal movement of the arterial wall.

REFERENCES