Master Thesis

Systolic Time Intervals Measured by Electrical Impedance Tomography (EIT)

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Master’s Thesis
Masters in Biomedical Engineering

Systolic Time Intervals Measured by Electrical Impedance Tomography (EIT)

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Abstract

Electrical Impedance Tomography (EIT) is a non-invasive and low-cost functional imaging technique that measures thoracic impedance. Until now, it was primarily used to reveal respiration-related changes in the lungs. However, recent work has shown the feasibility of using this technology to monitor hemodynamic parameters. In particular, mean arterial blood pressure can be estimated via EIT, given that the timing of the aortic valve opening is available. This Master’s thesis aims at overcoming this limitation by investigating the possibility of measuring the aortic valve opening directly via EIT.

Cardiac EIT data were recorded on pigs and humans in apnea. In order to estimate the aortic valve opening, three different approaches were tested. Various questions that arose from the results obtained led to an extension of the scope of this thesis, in which the origin of cardiac EIT signals was investigated thoroughly. For this purpose, MRI and EIT data were recorded and analyzed in a comparative study.

Solely one of the three approaches suggested shows partly promising results for an estimate of the heart valve opening. The latter is based on the assumption that the ventricular impedance is proportional to blood volume so that its derivative gives an estimate for blood flow. For two subjects a good correlation ($r = 0.923$, $p < 0.001$) with the invasive reference measurements was obtained whereas the approach failed for the remaining four subjects. These mixed results can be explained by the weak contribution of perfusion to the whole cardiac signal in EIT. These findings are based on simulations and detailed analysis, which revealed that for both pigs and humans, cardiac EIT signals are dominated by heart-induced movement, which seems to be in contradiction to the literature.

The results presented suggest the possibility to estimate the heart valve opening via EIT. The main challenge encountered in this thesis resides in the controversial origin of cardiac-related signals, which seem to be mostly motion-induced. Understanding the genesis of these signals would require further experiments and simulations such as 1) dedicated EIT measurements with controlled protocol conditions and 2) more advanced 3D thoracic conductivity simulations. This will hopefully reveal an insight into the origin of cardiac EIT signals and clarify the potential of this technology for the monitoring of hemodynamic parameters.

Keywords  Electrical Impedance Tomography (EIT), Cardiac EIT, Pre-Ejection Period (PEP), Aortic Valve Opening, Ensemble Averaging, Perfusion, Pulsatility, Saline Bolus.
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I have very much enjoyed the opportunity to discuss challenging matters with other researchers in the field of EIT. It has confirmed me that certain phenomena in EIT are not yet well understood. Experience from others have helped a lot in solving certain problems or simply hypothesizing about possible solutions. Andy Adler and Bartłomiej Grychtol have helped expertly with mostly reconstruction-related issues. Whether for pig or human, Stephan H. Böhm has always been very keen in answering questions related to their anatomy and physiology.

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Chapter 1

Introduction

1.1 Motivation

According to the world health organization (WHO), cardiovascular diseases are the leading cause of death in the whole world [46]. About 30% of all deaths in 2008 were due to a malfunctioning cardiovascular system such as coronary heart disease or a stroke. To reduce the number of such deaths, besides following the guidelines of eating a healthy diet, regular physical activity and abandonment of tobacco [46], the early diagnosis of cardiovascular problems is necessary. This can be assisted by the availability of suitable devices not only for the clinical environment but also for long-term monitoring of hemodynamic parameters; and this non-invasively.

As it was shown recently [39], by simply applying a belt of electrodes around the thorax, the technology of electrical impedance tomography (EIT) offers the possibility to continuously and non-invasively monitor blood pressure. Assumed to be responsible for 16.5% of all global deaths yearly [46], high blood pressure is one of the main risk factors which has to be addressed when wanting to prevent a cardiovascular disease. Having the possibility via EIT to accurately estimate the opening of the heart valve (the moment when blood gets ejected into the aorta) would complete the method presented in [39], to be fully based on EIT (see also Figure 1.1). This would furthermore lead to a novel method for estimation of one of the systolic-time intervals (STI) - parameters important for classification of the heart’s health status.

![Diagram of blood pressure monitoring via EIT](image)

Figure 1.1: Blood pressure monitoring via EIT: block diagram of the principle highlighting the missing block (aortic valve opening estimation via EIT) by the dashed outline.
1.2 Focus of this Work

The main goal of this Master’s thesis was the retrospective exploration of available pig EIT data for an accurate estimate of the aortic valve opening - a parameter required to determine hemodynamic parameters such as blood pressure.

1.3 Heart Anatomy and Physiology

1.3.1 Introduction

This section gives an overview of the heart’s physiology by showing the heart cycle focused on the event when the aortic valve opens and the associated pre-ejection period (PEP). The reader is further introduced into the heart’s position by finally focusing on comparing the human with the porcine heart. For more detailed information one is referred to [27, 26], both giving a comprehensive introduction into the cardiovascular system.

As shown in Figure 1.2, the heart is a hollow organ consisting of specialized muscular tissue forming four chambers (two atria and two ventricles) and containing four valves (two inlet and two outlet valves) which enable an unidirectional blood flow. From an engineer’s perspective, the heart represents two serially connected and synchronized pumps, each with one atrium, one ventricle and two valves. The right part of the heart supplies the lungs with deoxygenated blood returning from the systemic circulation, whereas the left part collects oxygenated blood from the lungs and distributes it among the different organs in the systemic circulation.

Figure 1.2: Structure of the heart: pink/gray indicating oxygenated/deoxygenated blood, respectively. AoV/PuV stands for aortic/pulmonary valve (From Fig. 1.4 in [27], © 2010 JR Levick).
The contraction of the myocardium (cardiac muscle) is triggered by electrical stimulation of the natural pacemakers and can be recorded via Electrocardiography (ECG). In one heart cycle, happening approximately every second, about 50 ml of blood are pumped in each of the two arteries (aorta and pulmonary artery) by the heart. As also illustrated in Figure 1.3, the contraction of the heart proceeds as follows:

1. **Ventricular diastole**: The ventricles relax from the previous contraction (isovolumetric relaxation). As soon as their pressure falls below the atrial pressure the atrioventricular valves open and the ventricles start to passively fill with blood from the atria (ventricular filling).

2. **Atrial systole**: In the last third of the ventricular filling phase the atria contract (represented by the P wave in ECG) to actively push extra blood into the ventricles. (In normal activity this amount of blood is small. But this phase becomes important during exercise when a faster heart rate does not allow for passive ventricular filling).

3. **Ventricular systole**:
   
   (a) **Isovolumetric contraction**: Represented by the most significant feature in the ECG - the R peak of the QRS complex - the ventricles start to contract. Since the ventricular pressure is bigger than the atrial pressure but smaller than the pressure in the arteries, all four valves are closed and the contraction simply results in a pressure increase without a change in blood volume.

   (b) **Ejection**: As soon as the ventricular pressure overcomes the pressure in the aorta or the pulmonary artery, the aortic valve (AV or AoV) or the pulmonary valve (PV or PuV) respectively open. This opening leads to a rapid ejection of blood from the ventricles into the two main arteries (aorta and pulmonary artery) which is followed by a slower ejection phase during the second half of the ventricular systole. The moment when the valves open and ejection starts is exactly the event to be detected in this thesis. It simply cannot be measured by ECG but other measurement techniques can be used to assess this time non-invasively (see Section 1.4). In the ejection phase the atria have already relaxed from their previous contraction and start to fill with blood from the vena cava or pulmonary veins, respectively.
Figure 1.3: Tracings of pressure (aortic, atrial and left ventricular), flow (ventricle) and the corresponding ECG during one cardiac cycle (Adapted from Fig. 2.4 in [27], © 2010 JR Levick). The numbers in brackets at the top correspond to the items listed in the text describing the heart cycle. The delay between the ventricular contraction and the effective ejection of blood - the pre-ejection period (PEP) during the isovolumetric contraction - is highlighted in blue.
1.3.2 Pre-Ejection Period (PEP)

As illustrated in Figure 1.3 and mentioned above, there is a short delay between the start of ventricular contraction and the effective ejection of blood. This electromechanical delay is called the pre-ejection period (PEP) and is in the range of 30-40 ms in healthy people at rest [28].

The PEP is not influenced significantly by changes in the heart rate [28, 29]. It is rather the blood pressure, contractility or diseases of the left ventricle and aortic valve which implicate a change in PEP. It could be shown that the PEP is increased in hypertensive and decreased in hypotensive patients, respectively [10]. Furthermore, an increase in contractility - for example by the administration of adrenaline - decreases the PEP. Since the PEP depends on various factors it must be measured and cannot simply be estimated from another value such as for example blood pressure. More detailed influences on the PEP and other so-called systolic time intervals (STI) can be found in [28, 29]. The ratio between the PEP and the left ventricular ejection time (LVET) is a common left ventricular performance measure and can tell about myocardial failure [10].

Usually, the PEP is defined as the timing of the left ventricle. Authors in [23] investigated the PEP of both sides of the heart - denoted as LPEP/RPEP for left- and right-PEP, respectively - and could sometimes observe a significant difference in the timing of the two. The mean ratio of LPEP/RPEP was 1.25 with a range of 0.95-1.95. With assuming no delay in the start of contraction of the two ventricles this means that the two valves (aortic and pulmonary) simply open at different times. This implicates that when one wants to exactly detect the PEP, one must differentiate between LPEP and RPEP.

Different techniques to measure the PEP are discussed in Section 1.4.

1.3.3 Location and Movement of the Heart

The heart is located between the sternum and the vertebral column and is oriented as shown in Figure 1.4 (Middle). It is embedded in a fibrous sac, the pericardium which is connected to the diaphragm at its lower surface (see also Chapter 8 in [26]). This connection makes the heart rotate more vertically at every inspiration - due to a downward movement of the diaphragm (respiration-induced movement) [27].

The heart is mechanically stabilized via the big vessels connecting the heart at the valve plane. The apex, on the contrary, is not attached and therefore freely moving. During systole the valve plane moves towards the apex of the heart and helps atrial filling.

In conclusion, not only during respiration but also in apnea the heart structures are moving a lot especially during the ejection phase, which is nicely visualized in [15].

1.3.4 Difference in Anatomy Between Pig and Human

Most of the data available for this thesis was not recorded on humans beings but on domestic piglets. Even though the porcine heart anatomy is similar to the one of humans, there are some differences in their anatomy which are worth mentioning here.

Authors in [26] have devoted a separate chapter to the comparison of the heart from common animal models (among others also the pig) to the human one. In addition, [11] provide a very
detailed comparison of the hearts of the two species. According to them, the porcine heart is oriented as shown in Figure 1.4 (Middle). Its long axis lies basically in the transverse plane such that the heart is not tilted as in a human. When comparing human versus porcine MRI images in Figure 1.4 (Left and Right) one can see that the porcine heart is indeed less tilted but still not that much as suggested by literature - at least not for this particular case.

Another difference lies in the location of the lower heart boundary and the diaphragm. Usually the human heart adjoins the diaphragm on its caudal side whereas in pigs the diaphragm is located lower down such that the heart is fully surrounded by the lungs. This can also be clearly seen in the MRI images of Figure 1.4.

A more transversal orientation of the pig heart is favorable when performing cardiac EIT (using the usual transversal belt placement) since out-of-plane movements are reduced. This does then not require the special oblique belt positioning as proposed by [35] and further discussed in Section 1.5.3. On the other hand, when heart-lung movement artifacts are present in the recordings, they will be much more dominant in pigs due to the heart being fully surrounded by lung tissue.

Figure 1.4: Difference in Human and Porcine Heart Anatomy: (Left) MRI image of a human volunteer in sagittal view, (Middle) Heart orientation in pig and human (Adapted from [11], © 1998 Anatomical Society of Great Britain and Ireland), (Right) MRI image of a pig in sagittal view (with kind permission from Aarhus University). Both MRI scans were recorded during expiratory apnea.
1.4 State of the Art of PEP Monitoring

To determine the moment of the aortic valve opening and thus also the pre-ejection period (PEP) various non-invasive techniques exist. In the following three common techniques are presented. The interested reader is referred to [29, 9, 25] for further reading.

1.4.1 Ultrasound (Echocardiography)

In Echocardiography an ultrasound transceiver is placed on the thorax and measuring the reflections of previously emitted short ultrasonic pulses. This gives the possibility to see the position and movement of inside structures such as the heart valves. Even though considered as the gold standard for measuring STIs [9], this method is only applicable in a limited way in a clinical environment and not adequate for continuous long-term monitoring.

1.4.2 Phonocardiography (PCG)

This technique makes use of the heart sounds, which are audible sounds created by various effects: opening and closing of the heart valves, blood flow into the heart and vibrations of heart muscles. These sounds are exactly what a medical doctor is examining when applying a stethoscope to someone’s chest. However, the manual analysis requires a lot of experience and is not a plausible solution for long-term monitoring. Therefore, the heart sounds are recorded by placing a microphone on the chest and automatically processed afterwards.

Even though the exact genesis of the heart sounds is still debated, the origin of the two principle heart sounds (S1 and S2) can be briefly summarized as follows:

- S1: Is believed to be composed by four components among which one is caused by turbulence due to the ejected blood flowing through the aorta [5], thus enabling the estimation of the aortic valve opening as illustrated in Figure 1.5.
- S2: Coincides with the closing of both the aortic and the pulmonary valve.

![Figure 1.5: ECG vs. PCG tracing showing that the first heart sound (S1) coincides with the opening of the aortic valve (Adapted from [5]).](image)
Chapter 2 Background

The thoracic impedance measured is then differentiated in the temporal domain and usually inverted (multiplied by -1) to obtain the final ICG signal which is shown in Figure 1.6 (Left). The signal contains different characteristic points which can be used to estimate the opening and closure of the aortic valve, calculate the stroke volume (SV), etc. The opening of the aortic valve - the so-called B-point - is represented by a notch before a steep rising slope in the ICG tracing as illustrated in Figure 1.6 (Left).

Figure 1.6: (Left) Example of an ICG tracing (thick line) for one heartbeat with synchronously recorded ECG (thin line) (Adapted from [30]. Copyright © 2006, John Wiley and Sons). The B point in the ICG signal is represented by the small notch before the steep rising slope. It estimates the opening of the aortic valve. (Right) A possible ICG electrode placement (Adapted from [25]): two ring electrodes are placed around the neck and belly each, whereas one is used for current injection and the other for voltage measurement.

The origin of the ICG signal is complex and not clearly understood. Different signal contributors (aorta, pulmonary artery, ventricles, atria, etc.) are known but their proportional influence is unclear [12]. This is why ICG remains a controversial technique not fully accepted by the medical community. Nevertheless, ICG is one of the two main techniques used these days to non-invasively and continuously determine the aortic valve opening.

1.4.3 Impedance Cardiography (ICG)

In Impedance Cardiography (ICG) the electrical impedance of the thorax is measured. Usually four electrodes are used, of which two inject an alternating current of a few milliamperes (0.5-5 mA, 20-150 kHz) [12], whereas the other two measure the resulting voltage drop. Figure 1.6 (Right) shows such a possible electrode placement (for more possibilities see [25]).

The thoracic impedance measured is then differentiated in the temporal domain and usually inverted (multiplied by -1) to obtain the final ICG signal which is shown in Figure 1.6 (Left). The signal contains different characteristic points which can be used to estimate the opening and closure of the aortic valve, calculate the stroke volume (SV), etc. The opening of the aortic valve - the so-called B-point - is represented by a notch before a steep rising slope in the ICG tracing as illustrated in Figure 1.6 (Left).

An explanation of the other two heart sounds (S3 and S4) and further details about heart sounds and their signal processing techniques can be found in [11,5].

Compared to echocardiography, the PCG signals can be recorded and processed by a portable device. PCG is therefore one of two technologies presented here, which enable the continuous and non-invasive monitoring of the aortic valve opening not only in clinical environments.
1.5 Electrical Impedance Tomography (EIT)

After having presented the physiological event to be detected and different measurement techniques used to tackle this problem so far, this section describes electrical impedance tomography (EIT) - the technology used within this thesis, with the objective to detect the heart valve opening. As its name already states, EIT is based on measuring the electrical impedance of biological tissue. It was used in various studies to image the brain, breast, gastric activity, lungs and cardiac-related activity [7, 24].

This work fully focuses on thoracic EIT used to monitor pulmonary and cardiac activity. In a nutshell, thoracic EIT is applying a belt of electrodes around the thorax and measuring the impedance of all possible electrode configurations. These measurements are then fed into an advanced mathematical reconstruction algorithm, which results in an image sequence showing the thoracic impedance change. The observed change is due to the difference in impedance of the underlying tissues (change of air or blood volume, movement of organ, etc.). The lung impedance, for example, changes significantly between inspiration and expiration as also shown in detail by impedance values for most common thoracic tissue and structures in Appendix A.

Since the introduction of the first EIT device in 1978 by Henderson and Webster [22], a lot of research has been going on to investigate and further improve EIT. Nevertheless, EIT has not yet fully found its way into clinical practice. Various devices exist (see [18, 25] for a list) but are primarily used for research purposes. Two commercially available devices released recently (Dräger Medical in 2011, Swisstom in 2013) are a cause for hope that EIT will have its breakthrough into daily clinical practice in the near future.

Admittedly, the low spatial resolution of EIT images is a drawback compared to other imaging modalities such as computed tomography (CT) or magnetic resonance imaging (MRI). However, among others, portability, low costs and the use of non-ionizing radiation favor the use of EIT. Furthermore, being a functional imaging technique, EIT enables to acquire up to 50 images per second. This definitely makes EIT an interesting candidate not only for lung monitoring but also to monitor hemodynamic parameters non-invasively and continuously.

In the following two sections a description of the impedance acquisition and the subsequent image reconstruction is given. More information about EIT can be found in [24].

1.5.1 Impedance Measurements

In order to create a 2D image of the thoracic impedance change, the electrodes of the EIT belt have to be driven in a certain manner, which is described in this section. The value in impedance measured is influenced by the difference in bioimpedance of the thoracic organs and structures as listed in Appendix A.

When measuring bioimpedance a tradeoff between frequency, current and the complexity of the electronic design has to be made by keeping in mind the safety regulations (IEC 60601). Since with increasing frequency the maximal permitted current and the skin-electrode impedance increase or decrease respectively, using high frequencies is favorable. On the other hand, this augments the complexity of the analog circuitry such that a good compromise has to be found [25].
With \( n_E \) electrodes placed around the thorax, various ways of measuring the thoracic impedance exist. Generally speaking, a current is injected between two electrodes whereas at the other electrodes the resulting voltage is measured. These different patterns (adjacent, cross, opposite, trigonometric) are further addressed in [25, 24] and their choice depends on a tradeoff between complexity and performance. For the sake of simplicity this section only covers the pattern applied by EIT devices in this thesis, the "adjacent" current pattern with offset.

The impedance measurements are acquired in a time-multiplexed manner. In a first step a current is injected between two adjacent electrodes (1-2) and the voltage is measured between all other adjacent electrodes (3-4, 4-5, 6-7, ..., 15-16) as shown in Figure 1.7 (Left). This leads to \( n_E - 3 \) impedance measurements. As in Figure 1.7 (Right), the injecting electrodes are then changed to the next ones (2-3) and again, all the other electrodes adjacently measure voltage (4-5, 6-7, ..., 16-1). This is repeated until all adjacent electrodes have been stimulated (injecting current), resulting in a total of \( n_E(n_E - 3) \) impedance measurements.

Although they are easy to implement, adjacent stimulation patterns have bad performance and are thus even considered as "harmful" [3]. A way to improve this is by adding an offset; i.e. by inactivating a certain number of electrodes between the two injecting and measuring electrode pairs (for example stimulating electrode pairs 1-5, 2-6, etc. and not 1-2, 2-3, etc.). This is the way the devices used in this thesis are working. These are still not the optimal drive patterns [24, 3] but increase the performance by keeping the complexity of the device low.

1.5.2 Image Reconstruction

This section addresses the process to calculate the impedance images out of the voltage measurements discussed in the previous section.

In computed tomography (CT) collimated x-ray passes through the subject in straight beams.
Thus the beam gets only attenuated by tissue in a straight line between source and detector. Conversely, because in EIT the current of each impedance measurement diffusely propagates through the subject, EIT is a so-called soft field tomography modality [13]. A change in conductivity has - to a certain extent - influence on every single voltage measurement performed at the boundary. This is the reason why the reconstruction in EIT is a highly ill-conditioned problem [24].

Having a vector with voltage measurements ($v \in \mathbb{R}^{n_M}$) one wants to estimate the thorax’ inside conductivity ($\tilde{\sigma} \in \mathbb{R}^{n_N}$) by minimizing the least-squared error:

$$\tilde{\sigma} = \arg \min_{\sigma} ||v - f(\sigma)||^2, \text{ with: } f(\sigma) : D \subset \mathbb{R}^{n_N} \rightarrow \mathbb{R}^{n_M}$$  \hspace{1cm} (1.1)

where the function $f(\sigma)$ estimates boundary voltages measured at electrodes for a given conductivity distribution ($\sigma \in \mathbb{R}^{n_N}$). This function is known as the forward problem and described in the next paragraph. Figure 1.8 illustrates the whole reconstruction process by a block diagram.

**Forward Problem** The mapping of a given thoracic conductivity ($\sigma \in \mathbb{R}^{n_N}$) to the resulting voltage measurements ($v \in \mathbb{R}^{n_M}$) is obtained by using a finite element model. This is calculated with differential equations based on the Maxwell equations simplified by neglecting the magnetic field due to the low frequency applied [24, 25]. To further simplify the problem the function $f(\sigma)$ is linearized in its current operating point $\sigma_0$.

$$f(\sigma) \approx f(\sigma_0) + J(\sigma - \sigma_0), \text{ with } J_{ij} = \frac{\partial v_i}{\partial \sigma_j} \bigg|_{\sigma_0}$$  \hspace{1cm} (1.2)
where \( \mathbf{J}_{ij} \in \mathbb{R}^{NM \times NN} \) is the Jacobian or sensitivity matrix, mapping a small conductivity change to the resulting change in measurement voltages. Another simplification made is to use differential EIT, where only differences in voltage measurements are reconstructed, i.e. the difference voltage vector (\( \mathbf{v}_d = \mathbf{v} - \mathbf{v}_{\text{Ref}} \)) is now with respect to a reference voltage (\( \mathbf{v}_{\text{Ref}} \)), which is usually obtained by averaging the first hundreds of measurements. With this the problem stated in Equation (1.1) gets reduced as follows:

\[
\hat{\sigma}_d = \arg \min_{\sigma_d} \| \mathbf{v}_d - \mathbf{J} \sigma_d \|^2, \quad \text{with: } \sigma_d = \sigma - \sigma_0
\]  

(1.3)

Despite the simplifications (linearization, differential EIT) the problem remains ill-conditioned.

"Before we give up EIT altogether and take up market gardening, there is a partial answer to this problem [...]."

Lionheart et al. [24]

**Inverse Problem** If the solution is constrained by using some *a priori* information about the internal conductivity distribution, a reconstruction can be performed. This is done by the introduction of a Tikhonov regularization term controlled by the so-called hyperparameter \( \lambda \).

\[
\hat{\sigma}_d = \arg \min_{\sigma_d} \left\{ \| \mathbf{v}_d - \mathbf{J} \sigma_d \|^2_W + \lambda^2 \| \sigma_d \|^2_R \right\}
\]  

(1.4)

where:

- **W** is the *weighting matrix* used to attenuate voltage measurements which are classified as unreliable - too noisy.
- The *hyperparameter* \( \lambda \) controls the trade-off between regularization and noise. A high hyperparameter results in a smooth image with lots of noise attenuation whereas a small hyperparameter yields to a noisier image with better spatial resolution.
- **R** is the *regularization matrix* and can be chosen in various ways:
  a) When set equal to the identity matrix (\( \mathbf{R} = \mathbf{I} \)), zeroth-order Tikhonov regularization is used. This simply penalized for too high amplitudes of \( \sigma_d \).
  b) Setting \( \mathbf{R} \) based on edge-sensitive spatial filters (e.g. Laplacian) the reconstructed image is penalized for sharp edges and therefore forced to smoothness.
  c) Further possibilities can be found in [4, 13].

Equation (1.4) can furthermore be converted into Equation (1.5), from which follows that for the final EIT reconstruction only one matrix multiplication has to be performed as also illustrated in Figure 1.8. This is also known as the one-step Gauss-Newton (GN) reconstruction.

\[
\hat{\sigma}_d = (\mathbf{J}^T \mathbf{W} \mathbf{J} + \lambda^2 \mathbf{R})^{-1} \mathbf{J}^T \mathbf{W} \cdot \mathbf{v}_d
\]  

(1.5)

This is an example of the algorithm used in this thesis. Various other algorithms (non-linear, recursive, etc.) for EIT reconstruction exist, which would exceed the scope of this work. The interested reader is referred to [24].
1.5.3 Cardiovascular-Related EIT Work

As already mentioned, EIT was so far mostly used to monitor respiration. And yet there exist a few publications addressing the challenge of analyzing the cardiovascular system by means of EIT. In the following some of this work is discussed, which shows promising but partly also contradictory results for the use of EIT to analyze cardiovascular activity.

**Aortic Blood Pressure Monitoring**  Authors in [39] could give first evidence that it is possible with EIT to monitor aortic blood pressure non-invasively and continuously. The method is based on the principle that the arterial pressure pulse in the aorta is propagating with a certain velocity - the PWV (pulse wave velocity). This velocity is inversely proportional to the aortic blood pressure. The arrival of the pressure pulse dilates the aorta, which leads to an impedance change in the EIT image. Thus when measuring this arrival in the descending aorta and at the same time determining the start of the pulse propagation - by measuring the opening of the aortic valve - one can calculate the aortic pulse transit time (PTT). By using two calibration points, the PTT can then be related to the aortic blood pressure.

For the first experiments the PTT was calculated by measuring only the pulse arrival time in the descending aorta via EIT while the start of pulse propagation (aortic valve opening) was detected from an invasive catheter signal. Therefore this promising novel method of continuous blood pressure measurement was a big motivation to come up with a solution to also measure the aortic valve opening and thus the PTT directly and non-invasively via EIT.

**Cardiac (Output) Monitoring**  The heart’s long axis in humans does not lie exactly in the transverse plane where the EIT belt is usually placed (see also Figure 1.4). To take into account the inclination of the heart and reach a belt placement which is more aligned to the heart’s long axis [35] suggest an oblique belt placement. This should enable to separately visualize the atria and ventricles in EIT images. Authors in [35] compared the EIT images with dynamic MRI recordings and showed that the EIT’s impedance change in both regions is inversely proportional to the segmented area of blood in the corresponding heart chamber of the 2D MRI as depicted in Figure 1.9. It should be mentioned that the sampling rates used for the EIT and MRI were set to 25 Hz and 12.5 Hz, respectively.

In further studies this group used the oblique belt positioning to analyze the stroke volume [44] and the right ventricular diastolic function [36] by means of EIT. [31] used EIT to analyze variations in stroke volume in the descending aorta.

**Contradiction**  When analyzing heart-rate-filtered EIT recordings there seem to exist contradictory interpretations. In contrast to [35, 44], others [20, 31, 6] identify the heart as one single region with temporal signals all of similar phase. The other high impedance changes are assigned to the pulmonary perfusion (see also Figure 1.10).

The origin of ”perfusion” impedance changes is not well defined by the EIT research community. It has been shown that the signals’ pulsatile characteristics are related and synchronous with the heart activity [34]. It is therefore important to clearly point out, that EIT signals filtered at cardiac frequency should be referred to as pulsatility and not perfusion.
CHAPTER 1. INTRODUCTION

Figure 1.9: Comparison of the ventricles (Left) and atria (Right) by means of 2D MRI (Top) and EIT (Bottom) for one cardiac cycle: the cross sectional area of segmented blood (MRI) shown, seems to be inversely proportional to the impedance change in EIT (Adapted from [35], © 1996 IOP Publishing Ltd.).

Figure 1.10: Different interpretations of heart-rate-filtered EIT recordings: (Left) showing two peaks interpreted as ventricles (blue) and atria (red) with the corresponding MRI recording (Middle) (Both adapted from [35], © 1996 IOP Publishing Ltd.). (Right) However, other authors interpret the heart as one peak (red) and the rest as pulmonary perfusion (blue) (Adapted from [20], © 2011 Grant et al.).
impedance changes. In this way it is left open whether the pulsatile signals are generated by perfusion changes or (in addition) by other effects such as heart-lung movement, for example.

1.6 Contributions

In the course of this Master’s thesis, three different approaches to measure systolic time intervals in pig EIT have been developed and evaluated (Chapter 3). Among the three approaches one shows possibilities to be used in the future but still needs further research. This is partly due to the lack of knowledge - or also controversial opinions - of the EIT research community when it comes to the question of the genesis of cardiac EIT signals.

To gain a better understanding of the cardiac EIT signals, the available pig EIT data was thoroughly analyzed (Chapter 4). Some of the findings have been submitted in form of an abstract for the 26th Annual Congress of the European Society of Intensive Care Medicine (Appendix E). Furthermore, to model and understand cardiac EIT signals, a pilot study to measure the heart via EIT and MRI has been initiated and carried out during this thesis.

1.7 Organization of This Thesis

Besides the common methods and materials in Chapter 2, this thesis is divided into two main chapters. One describes the measurement of systolic time intervals in pig EIT (Chapter 3) and the other is dedicated to the origin of the cardiac signals in EIT (Chapter 4).
Chapter 2

Materials and Methods

This chapter starts with the description of the two EIT devices used to perform functional impedance measurements in Section 2.1 and the different experiments performed on piglets and humans in Section 2.2.

The two different methods used to reconstruct the impedance images are discussed in Section 2.3. It is followed by an introduction into ensemble averaging in Section 2.4 - a common technique to filter cardiac-related information in medical signal processing. Finally, the chapter concludes with a short explanation of the generation of the so-called power images in Section 2.5.

Unless otherwise stated, all the calculations and algorithms were implemented and run with Matlab (Version R2012b, 8.0.0.783, Win7 64-bit).

2.1 EIT Machines

The experiments available were performed with two different EIT machines which are shortly mentioned in the following paragraphs. The experiments on pigs were all performed with the Dixtal device whereas for experiments on humans, the Swisstom device was used.

A short comparison of the two machines is given in Table 2.1.

<table>
<thead>
<tr>
<th>Electrodes</th>
<th>FR [Hz]</th>
<th>f [kHz]</th>
<th>I [mA]</th>
<th>Skip</th>
<th>Additional Channels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dixtal</td>
<td>32 - passive</td>
<td>50.0</td>
<td>125</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Swisstom</td>
<td>32 - active</td>
<td>27.9</td>
<td>200</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 2.1: Comparison of the two EIT machines used and their key parameters. Imaging frame rate (FR), excitation frequency (f), injection current (I), number of electrodes skipped between two active ones (Skip) - sometimes also called offset.

2.1.1 Dixtal

The EIT device Enlight® (Timpel SA, Sao Paulo, Brazil), also known as Dixtal, uses 32 electrodes and produces 50 images per second. Sinusoidal currents of 10 mA at 125 kHz are in-
jected in a rotating sequence through two electrode pairs which are separated by three inactive electrodes. The resulting voltage is measured at non-injecting electrodes in the same rotating sequence as for the current injection. The exact stimulation pattern is explained in Appendix C.2.

Beside recording impedance measurement this device enables the synchronous recording of two analog channels at a sampling frequency of 250 Hz which can be used to acquire ECG or blood pressure signals.

There are a few dozen such devices in the whole world and they are primarily used for research purposes.

2.1.2 Swisstom

The EIT Pioneer Set (Swisstom AG, Landquart, Switzerland) is also working with 32 electrodes. Various other parameters such as frame rate, excitation frequency, electrode offset (number of non-measuring electrodes between two active ones) can be adjusted according to the user’s needs.

The main advantage of this EIT device lies in the fact that active electrodes are used \[19\], which are interconnected by a belt-bus. The introduction of a bus and thus the reduction of the number of cables is one advantage. But it is the presence of much shorter cable connections before the first active amplifier, which suggest a better noise performance compared to other device architectures.

The device is not yet available on the market. The one used for the experiments was one of the first prototypes available (An excitation frequency of 200 kHz with an image rate of 27.9 Hz was used. The number of inactive electrodes between two active ones was set to 4).

2.2 Experiment Setups

This section describes the experimental data, which this work is based on. The first two experiments were performed on pigs (Madrid in Section 2.2.1 and MIGET-SPECT in Section 2.2.2), whereas the third was done on humans (Heart EIT-MRI ETHZ in Section 2.2.3).

2.2.1 Madrid

Introduction In this study one single domestic piglet was anesthetized, mechanically ventilated and equipped with several measurement devices while it was lying on the back (supine position). These experiments were initially performed for a study to show the feasibility of measuring blood pressure with EIT as also discussed in Section 1.5.3 or \[39\]. This is why among the experiments the blood pressure was varied in a large range by administration of either nitroglycerine or noradrenaline while the heart rate remained more or less constant. Since a change in blood pressure also results in a change of the pre-ejection period (PEP) these experiments are well suited for this project. The hemodynamic parameters for all the 12 different experiments are listed in Table B.1 in Appendix B.1.

To monitor cardiovascular signals in each experiment better the mechanical ventilation was stopped for about 30 seconds so that the recordings are free from pulmonary signals.
2. MATERIALS AND METHODS

Measurement Devices  Besides recording the EIT data, various catheters were present, of which one was placed in the ascending aorta. This catheter gives exact timing information about the opening of the aortic valve and can also be used as a cardiogenic trigger, since no ECG is available. The pressure recordings were not performed with the EIT machine. However, there is the respiratory pressure signal available which was recorded with both the EIT machine and also the ‘Josephine’ pressure recorder as shown in Figure 2.1. This signal is used to synchronize the EIT signals with the pressure signal.

Belt Placement  The initial aim of the experiment was to measure the pulse transit time in the descending aorta. The EIT belt was therefore placed in the usual transversal configuration and so that the descending aorta was nicely detected. This makes us assume that - relative to the heart - the belt was placed low. There are no ground truth data such as CT or MRI, which would give information about the belt’s position or even the pig’s thorax shape.

Bolus Injections  Furthermore, hypertonic saline boluses were injected into three different anatomical locations: ascending aorta, right ventricle and pulmonary artery. Having about 4-fold better conductivity than blood, this bolus injections enable the localization of anatomical structures directly in the EIT images in a simple way.

2.2.2 MIGET-SPECT

Introduction  For this study 19 domestic piglets were anesthetized, mechanically ventilated and equipped with several measurement devices while lying on their back (supine position). This database contains recordings with two different protocols:

1. MIGET: The multiple inert gas elimination technique (MIGET) [45] was used to determine the distribution of pulmonary ventilation and perfusion and then compared with EIT.

2. SPECT: This protocol aimed at measuring lung perfusion by EIT and compare the results with single-photon-emission computerized tomography (SPECT) as in [6].

For the sake of simplicity this study is only referred to as MIGET in the following.
In both protocols lung injuries and collapses were intentionally induced to the pigs. Furthermore the positive end-expiratory pressure (PEEP) was changed among the experiments. Even though these interventions do not directly change the pre-ejection period (PEP) a change in pulmonary blood pressure can be expected and thus also an indirect change in (right) PEP.

As for the Madrid study, most of the MIGET experiments contain short sequences of apnea, which make it possible to analyze cardiovascular activity in EIT (see also Figure 2.3).

**Measurement Devices** For this experiment ECG and pulmonary aortic pressure recordings (PAP) were taken simultaneously with the EIT recordings. These two additional signals were directly recorded with the analog channels of the EIT device as depicted in Figure 2.2. With the ECG serving as cardiogenic trigger and the pulmonary pressure as reference for the pulmonary valve opening these experiments are very apt to be used in this thesis.

When recording pulmonary pressure the catheter must be inserted through the vena cava and therefore fed through the right heart which can cause big movement artifacts. This is why a lot of recordings had to be rejected from analysis.

**Belt Placement** With the aim to monitor ventilation and pulmonary perfusion, no special care has been taken of the positioning of the belt relative to the heart. The belt was placed in the usual transversal manner. There are no recordings available, which would give evidence of the positioning of the EIT belt or the animals’ thorax shape.

**Bolus Injections** As mentioned before, hypertonic saline bolus injections were used to determine pulmonary perfusion. Thus for every single experiment, a bolus was injected into the right atrium of the pig while the ventilation was halted. This bolus is then distributed further via the right ventricle into the pulmonary vessels and then via the left atrium into the left ventricle. Detecting the steep decrease in impedance due to the arriving bolus (see also Figure 2.3), gives the opportunity to detect the position of anatomical structures - such as atria and ventricles - directly in EIT recordings.

![Figure 2.2: Block diagram of the different measurements taken during the MIGET experiments.](image-url)
Figure 2.3: Impedance change for a MIGET recording clearly showing the pure apnea range (red shaded area) and the steep impedance decrease during bolus injection in a second apnea (green shaded area) in between the high oscillations due to ventilation.

2.2.3 Heart EIT-MRI ETHZ

**Introduction**  This is a pilot study carried out at the MRI User Lab at ETH Zürich, where EIT measurements and dynamic cardiac MRI scans were performed one after the other. The aim was to have EIT recordings and dynamic MRI scans in apnea, which allows comparing the pulsatility signals of EIT recordings with dynamic 3D conductivity simulations based on segmented MRI scans.

This experiment was initiated because observations in pigs (see Chapter 4) showed that cardiac-related signals cannot originate from changes in blood volume only as suggested by the literature [44, 35]. It was thought to be more likely that EIT pulsatility signals are dominated by heart-lung movement.

**Measurement Devices**  A prototype of the Swisstom EIT device (see Section 2.1.2) was used and an ECG was recorded in parallel using a BIOPAC MP150 (BIOPAC Systems, Inc., USA) recording device. Besides the synchronization signal of the EIT machine recorded with BIOPAC, a switch was used to either short-circuit the current source of the EIT device or bias a DC voltage onto the ECG electrodes, respectively. This produces artifacts which are visible in both the EIT and ECG recordings and thus allow a proper synchronization of EIT and ECG. The measurement setup is illustrated in Figure 2.4. Further details about the experimental protocol can be found in Appendix B.2.
**Belt Placement**  Both the usual transversal belt position, as well as the oblique belt position proposed in [35], were applied. To indicate the placement of the EIT belt, a water-filled silicone tube was used as belt phantom for the MRI recordings. Together with static MRI recordings of the thorax shape in apnea, a realistic model for EIT reconstructing can be created.

### 2.3 Image Reconstruction Software

The two software tools used to reconstruct EIT images out of the raw impedance measurements are explained in the following.

#### 2.3.1 Dixtal

The Dixtal EIT Analysis Tool (Version 0.0.7, Build Date: 11/5/2009) is the vendor-specific tool shipped with the Dixtal device described in Section 2.1.1.

As a model for reconstruction one cannot use a user-specific model but simply select among half a dozen models available. For reconstruction the model `P3_Pig1_heart` and the sharpest spatial filter (`Sharp-6`) were used. To the best of our knowledge a temporal smoothing filter is also applied during reconstruction.

This software is virtually a black box concerning the freedom of spatial and temporal filtering and the inability to adapt the reconstruction model (Figure 2.5 shows a comparison when applying three different spatial smoothing filters). The application is written in LabVIEW and still in beta stage, hence slow in execution and prone to spontaneous crashes. Nevertheless it incorporates a noise detection and measurement removal algorithm which efficiently removes single impedance measurements and thus nicely suppresses noise in recordings.

![Figure 2.5](image_url)

Figure 2.5: Comparison of three different spatial filters of the Dixtal reconstruction software: (Left) `soft-5`, (Middle) `intermediate` and (Right) `sharp-6`. The difference in spatial smoothing between the smoothest (Left) and the sharpest (Right) filter are clearly visible. These images are generated by pixel-wise calculation of the power at cardiac frequency (see Section 2.5).
2.3.2 EIDORS

The need for more flexibility and influence on the reconstruction procedure gave rise to a different reconstruction software. As a freely available open-source Matlab toolbox, which is developed and maintained by renowned EIT researchers, EIDORS (Electrical Impedance Tomography and Diffuse Optical Tomography Reconstruction Software) - also described in [4] - was an obvious choice.

The use of EIDORS opens a myriad of possibilities for EIT reconstruction: besides some predefined library models one can create an individual FEM model based on segmented MR/CT. Depending on the particular algorithm used for reconstruction various parameters such as spatial smoothing, noise suppression etc., can be adjusted (A comparison for difference in spatial smoothing is given by reconstruction with two different hyperparameters in Figure 2.6: Left and Middle.). This opens the opportunity to freely control all parameters to anyone’s liking but at the same time demands a thorough understanding of the full reconstruction process and the knowledge of the exact stimulation sequence of the EIT device.

In Appendix C one can find some information about the stimulation pattern specific to the Dixtal EIT device and also some hints on user-specific FEM modeling using Netgen [38].

GREIT This is a reconstruction algorithm initiated by a group of the world’s experts in EIT reconstruction at a conference in Graz, hence its name GREIT (Graz consensus Reconstruction algorithm for EIT). It is a linear reconstruction algorithm which is not simply based on the Jacobian and regularization matrix as described in Section 1.5.2 by the one-step Gauss-Newton (GN) algorithm. The GREIT algorithm calculates a reconstruction matrix with the aim to achieve a good spatial resolution with low position error, shape deformation and ringing. Furthermore, the electronic noise and electrode movement artifacts are minimized by feeding the algorithm with training data. More information about GREIT can be found in [2].

Compared to conventional inverse solvers - such as one-step Gauss-Newton (GN) solver with Laplacian regularization as used initially - this algorithm showed to be much less prone to noise and produces much nicer images at the boundaries without amplifying any errors close to certain electrodes. This is also shown in Figure 2.6 by comparing GREIT to two GN solutions.

Faulty Electrode Removal To treat faulty electrodes or simply remove too noisy impedance measurements the algorithm described in [21] was used if necessary. In a nutshell, this algorithm is based on the reciprocity of EIT measurements: in fact for each EIT frame an impedance measurement is always performed twice, simply with the stimulating (current injecting) and voltage measuring electrode pair exchanged. By assuming no temporal changes in between the two measurements, this reciprocity can then be used to compare the two measurements for equality and give rise to a certain quality factor for every single measurement.

Configuration Used The pig model used for reconstruction is similar to the library model pig_23kg_32el and is based on code adapted from [16]. For human EIT data the predefined library model adult_male_32el_lungs was used. Figure 2.7 shows the two FEM models together with the corresponding CT scans.
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Figure 2.6: Comparison of three different EIDORS reconstruction algorithms: (Left) one-step GN (Gauss-Newton) solver with hyperparameter \( \lambda = 1 \cdot 10^{-3} \), (Middle) the same with higher hyperparameter \( \lambda = 1 \cdot 10^{-2} \) and (Right) the result of the GREIT algorithm with noise figure \( \text{NF} = 0.5 \). The increased spatial smoothing by applying a higher hyperparameter is clearly visible for the two GN images. The GREIT algorithm gives similar results but with successfully suppressing errors at the boundaries. These images are generated by pixel-wise calculation of the power at cardiac frequency (see Section 2.5).

Figure 2.7: Plane view of the 3D FEM model used with EIDORS and the corresponding CT scans on which the models are based: (Left) for a pig and (Right) for a human thorax. The blue dots show the electrode positions except for electrode 1, which is marked red.

The reconstruction models and the corresponding matrices, unless otherwise stated, were made using the GREIT approach with a noise figure of 0.5 and assuming a homogenous background conductivity of one. The developer version of EIDORS (Version: 3.6+, 2012-07-13 04:24:45) in combination with Netgen FEM mesher (Version: 4.9.13, Win7 64-bit) were used in this thesis.

2.4 Ensemble Averaging

Introduction The ensemble averaging technique is applied to filter the EIT recordings to reveal cardiac-related changes only. This simple but yet powerful technique is a narrow comb filter, filtering at the cardiac frequency and its harmonics. Ensemble averaging (in the following also abbreviated as EA) is well suited to suppress unwanted noise and possibly also respiratory signals (when analyzing non-apnea sequences).
**Algorithm**  The key to perform EA is to have a so-called cardiogenic trigger available. This is necessary as an estimate for a periodically reoccurring event in the cardiac cycle. Usually the ECG’s R-wave peak is used as such a trigger.

The averaged signal $\text{EIT}_{\text{EA}}(t)$ is then calculated as follows:

$$
\text{EIT}_{\text{EA}}(t) = \frac{1}{N} \sum_{i=1}^{N} \text{EIT}_{\text{raw}}(t - T_i)w(t - T_i)
$$

where $\text{EIT}_{\text{raw}}(t)$ is the raw EIT input signal, $T$ a vector of length $N$ containing all the cardiogenic trigger times and $w(t)$ a time window centered around $t = 0$ with finite length (usually a rectangular window with length of about one heartbeat).

This means that every time a cardiogenic trigger arises, a segment of the EIT input signal shortly before and after the trigger event is captured and aligned symmetrically around $t = 0$. All these segments are then averaged to a single pulse as it is also depicted in Figure 2.8. The derivation for EA as a narrow comb filter in the frequency domain can be found in [25].

![Figure 2.8: A simple example of ensemble averaging: where the input (Left) consists of the raw EIT signal (blue) for some heartbeats together with the extracted R-wave peaks (red dots) of the ECG signal (green). The algorithm’s output (Right) is the filtered EIT signal (black) with the R-wave peak (red circle) which is the average of all EIT segments aligned at time zero (blue).](image)

**Stationarity**  The EA presented here is not like a simple comb filter and can therefore adapt to variations in the heart cycle (which are typically present in all mammals). Nevertheless it has to be kept in mind that the heart cycle variations should be minimal. In the present work the R-R intervals were plotted in a histogram and analyzed visually so as not to differ by more than a few percent for each of the experiments analyzed.

**Signal Quality Indicator**  To estimate the order of input signal at cardiac frequency compared to noise or unwanted signals in the input, a simple signal quality measure has been introduced. The signal quality indicator (SQI) measures the mean deviation of all single segments in the input signal compared to the final averaged output signal ($\sigma$ stands for the standard deviation):

$$
\text{SQI} = \frac{1}{N} \sum_{i=1}^{N} \frac{\sigma(\text{EIT}_{\text{EA}}(t)) - \sigma(\text{EIT}_{\text{raw}}(t - T_i)w(t - T_i))}{\sigma(\text{EIT}_{\text{EA}}(t))} \sum_{i=1}^{N} \frac{1}{\sigma(\text{EIT}_{\text{EA}}(t))}
$$
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Figure 2.9: Two methods of how EA is used in EIT reconstruction. Method 1 (Top) performs EA prior to reconstruction whereas for method 2 (Bottom) EA is applied after image reconstruction.

**EIT Reconstruction and EA** In this thesis EA is applied in two different ways, which are illustrated in Figure 2.9 and described in the following:

- **Method 1**: When performing EA on EIT data, it is advisable to average already the raw voltage measurements prior to the reconstruction. This accelerates the reconstruction procedure. However, this method is only applicable when using EIDORS for reconstruction.

- **Method 2**: For data where the Dixtal reconstruction software is used, the EA has to be performed after image reconstruction, which is more time and memory-consuming.

Since the EIT reconstruction used is a linear transform, both methods lead to the same result. The data used for cardiac signal analysis in this work was always filtered by EA prior to analysis. This means that for example an apnea segment consisting of 50 heartbeats is averaged to a single heartbeat which is then analyzed.

**Improved Ensemble Averaging** There were attempts made to include ensemble averaging in the EIT reconstruction as described in [37]. Due to a lack of time this could not be included in the current work but might be worth trying in the future if temporal filtering needs improvements.


2.5 Power Images

When analyzing thoracic EIT images it is desirable to know the positions of the lung and the heart. A way to reveal the potential positions of these two organs is to generate so-called power images. These images show for every single pixel in the image, the power present at a specific frequency.

Figure 2.10 shows an example of power images at cardiac (Middle) and ventilation frequency (Right), thus revealing the potential positions of heart (Middle) and lung (Right), respectively. Authors in [16] could show that when having a truthful reconstruction model (derived from the real CT scan), the positions in EIT sequences of regions with high energy at the corresponding frequency seem to coincide well with the corresponding organ’s position in the CT scan.

When having the EIT sequence already ensemble averaged, one can simply calculate the pixel-wise temporal standard deviation of the impedance signals to obtain something nearly identical to the cardiac power image described above. The only difference is that in the case with EA power in higher-order harmonics is also visualized. Since most of the power at cardiac frequency is present in the fundamental frequency, this does not alter the result noticeably.

In the following, when showing power images, the scale is omitted but is kept constant: red/blue equals high/low power. Furthermore, unless otherwise stated, the power image is always the one calculated at cardiac frequency. Please note that it is worth repeating here that what is revealed by filtering at cardiac frequency must be called a pulsatility image - and not perfusion image. As mentioned in Section 1.5.3, it is not clear how much of the signal is generated really by blood perfusion or simply by pulsatile effects (e.g. heart-lung motion).

Figure 2.10: The CT recording of a pig’s thorax (Left) and the corresponding power images at cardiac (Middle) and ventilation frequency (Right).
Chapter 3

Use of EIT for Systolic Time Interval Measurement in Pigs

3.1 Introduction

Motivation  So far EIT has been mainly used to monitor ventilation. As a non-invasive and low-cost functional imaging technology it would be well-suited to continuously monitor hemodynamic parameters. As it has been shown recently, it is possible to measure the mean arterial blood pressure non-invasively and continuously by means of EIT [39]. In the study cited, first experimental evidence was given but the timing of the aortic valve opening was still detected invasively. Having the means to detect the aortic valve opening via EIT would complete this method to a blood-pressure measuring device purely working non-invasively via EIT and ECG. In combination with ECG, the aortic valve opening would allow calculating the pre-ejection period (PEP), one of the so-called systolic time intervals (STI), which are of high interest for monitoring the heart’s health status.

Focus and Organization  This work was focused on the detection of the heart valve opening (aortic or pulmonary). In this chapter three different approaches, explored in this thesis, are presented. The possibility of measuring other systolic time intervals has not been explored.

3.2 Materials and Methods

In this section three approaches to measure the heart valve opening by EIT are presented.

- **Approach 1 (Ventricular Derivative)**: Uses the temporal derivative of the heart impedance changes to extract the ventricular blood flow. See Section 3.2.1.
- **Approach 2 (ICG-via-EIT)**: Tries to use EIT as an usual ICG. A well-known technique to detect the aortic valve opening. See Section 3.2.2.
- **Approach 3 (Pulse Arrival Time (PAT))**: Tries to locate the origin in impedance change inside the heart, which can then be further analyzed. See Section 3.2.3.
3.2.1 Approach 1: Ventricular Derivative

**Hypothesis**

Assuming that the impedance change in the heart region is generated by the ventricular blood volume changes $V_B(t)$ one can determine the blood flow $F_B(t)$ by differentiating the ventricular impedance change $I_V(t)$ in time, as it is shown in Equation (3.1).

$$V_B(t) \propto I_V(t) \implies F_B(t) = \frac{dV_B(t)}{dt} \propto \frac{dI_V(t)}{dt} \quad (3.1)$$

At the end of the atrial systole the ventricles are fully filled with blood. With the beginning of the ejection during ventricular systole the ventricles start to empty. This abrupt decrease in blood volume $V_B(t)$ leads to a decrease in conductivity and thus to an increase in impedance $I_V(t)$. Its temporal derivative $\frac{dI_V(t)}{dt}$ shows a steep rising slope due to the increased blood flow after the heart valve opening. Therefore, the time of the valve opening ($t_{Ejection}$) is located at the minimum of the temporal derivative $\frac{dI_V(t)}{dt}$ before its steep rising slope and after the ECG’s R-peak ($t = 0$).

$$t_{Ejection} = \arg \min_{t \in [0,t_{Max}]} F_B(t) = \arg \min_{t \in [0,t_{Max}]} \frac{dI_V(t)}{dt} \quad (3.2)$$

For the sake of simplicity the maximal search range $t_{Max}$ was fixed to 150 ms but should later be adapted to the rising slope as described above. The principle of this approach is also illustrated in Figure 3.1 and in Figure 3.2.

![Figure 3.1: Principle of approach 1: (Left) shows signals of interest averaged to about one heartbeat. (Right) the time axis is reduced to the moment of interest with the estimated ejection time ($t_{Ejection}$) indicated by a red circle. The black and red vertical lines in both plots correspond to the start of contraction (R-wave) and start of ejection (valve opening via PAP), respectively. A qualitative example for the minimum search range $[0, t_{Max}]$ is shown by the orange arrow.](image-url)
Algorithm - Heart ROI Segmentation  The impedance change $I_V(t)$ was calculated by summing up all impedance changes in a certain region of interest (ROI). To determine the pixels belonging to the heart region the watershed technique \cite{33} was applied to the power image at cardiac frequency (see Section 2.5). Among the segmented regions, the final ROI was chosen as the one having its maximum closest to where the heart location was expected (symmetrically centered on the right/left axis and more ventral ($X/Y = 16/8$), see Figure 3.3 (Middle)). Small regions consisting of less than a certain number of pixels - in our case 20 - were rejected from the choice.

In a last step the selected ROI was reduced by thresholding and including only the pixels with a power greater than half the mean peak power (mean over a 3x3 window centered at the pixel with maximal power within the initial ROI). Figure 3.3 shows an example of such a segmentation.

Figure 3.3: Heart ROI segmentation: (Left) shows the pulsatility power at cardiac frequency which is the input for the segmentation. (Middle) shows resulting regions of the watershed technique with the exclusion of too small regions. The selected region is shown in orange and the expected heart position is marked by a black circle. (Right) depicts the results by the full (dashed pink line) and reduced (solid pink line) heart ROI.
Algorithm - Valve Opening/PEP Detection  This paragraph describes how both PEP measurements (PEP_{EIT}: the estimate from EIT and PEP_{Ref}: the reference from PAP) were calculated. Please note that before the absolute times of the valve opening (t_{Ejection}) were discussed. Since the timings are relative to the ECG’s R-wave (contraction start at t = 0), the absolute ejection time is equal to the PEP (PEP_{EIT}= t_{Ejection}). In the following, the measurement of the valve opening time is expressed directly as PEP.

- **Measuring the PEP reference: PEP_{Ref}**
  First the ensemble averaged pulmonary pressure signal was filtered with a 4th-order Butterworth low-pass filter at 100 Hz. The steep rising slope was detected by the maximum in the first temporal derivative. The valve opening - and thus also the PEP_{Ref} - was then determined by finding the maximum in the second temporal derivative before the rising slope just mentioned. So it is positioned at the moment where the pressure signal has the highest, so to speak, velocity in pressure change. An example is shown in Figure 3.1 by the red vertical line.

- **Measuring the PEP estimate: PEP_{EIT}**
  The ventricular impedance signal \(I_V(t)\) was calculated by summing up the pixels in the heart ROI as described in the paragraph about segmentation. To further smoothen the signal it was filtered with a fourth-order Butterworth low-pass filter at 25-fold the cardiac frequency (determined via the median of the ECG’s R-R-intervals). The estimated valve opening - and thus also PEP_{EIT} - was determined by finding the minimum of the filtered \(dI_V(t)/dt\) in a given interval \((t_{Range} = [0, 150] \text{ ms})\), as also shown in Equation (3.2).

All the discrete derivatives were calculated with a smoothened symmetrical kernel [17]:

\[
y[t] = \frac{x[t + 3]}{60} - \frac{3 \cdot x[t + 2]}{20} + \frac{3 \cdot x[t + 1]}{4} - \frac{3 \cdot x[t - 1]}{4} + \frac{3 \cdot x[t - 2]}{20} - \frac{x[t - 3]}{60} \approx \frac{dx(t)}{dt} \tag{3.3}
\]

Materials and Data Preparation  This algorithm was verified using the data from the MIGET experiment (see Section 2.2.2). Pigs with too few recordings, missing ECG/PAP or too noisy EIT were immediately discarded from the analysis. In a second step, all the experiments from the pigs of interest showing too big artifacts in the PAP recordings had been removed prior to the analysis. This reduced the number of available pigs from an initial nineteen to six.

The EIT voltage measurements were 5-fold upsampled to 250 Hz to match the frequency of ECG and PAP. All the signals (EIT, ECG, PAP) were then ensemble averaged using the ECG’s R-wave as cardiogenic trigger and a window size of 250 samples. The image reconstruction was performed on the averaged voltage measurements using EIDORS and the GREIT algorithm.

The results of the ventricular derivative approach are shown in Section 3.3.1.
3.2.2 Approach 2: ICG-via-EIT

**Hypothesis** By Impedance Cardiography (ICG) - a common but controversial technique discussed in Section 1.4.3 - the valve opening can be detected by extracting the timing of the so-called B-point. Even though the electrodes in EIT are placed differently than for ICG, it might be possible to extract ICG-like signals out of a few of the raw EIT impedance measurements.

As previously discussed, the exact genesis of the ICG signal is unclear [12]. Nevertheless, it seems obvious that an impedance measurement containing information about the valve opening must contain a big contribution from an event related to the rapid ejection of blood generated by: either the decrease in ventricular blood volume, the distension of the ascending aorta or another (movement) artifact related to it. This gives rise to the assumption that raw EIT impedance measurements with high sensitivity in the heart region might have ICG-like characteristics.

*Please note that what has so far been named the raw EIT impedance measurements can further be referred to as voltage measurements. Since the EIT devices measure the voltage by injecting a constant current, these measures are proportional and can be regarded as equal if one is not interested in their absolute values.*

**Algorithm** Using an EIT device with 32 electrodes leads to 1024 voltage measurements (per frame) of which a bit more than 800 are useful for further processing. The challenge for this approach consists in selecting a few voltage measurements, which contain proper ICG-like signals, out of the available set.

As shown by the block diagram in Figure 3.4, the algorithm makes use of both, the reconstructed EIT images but also the voltage measurements as follows:

1. First the power image at cardiac frequency was used to segment the heart region of interest (ROI) as described in Section 3.2.1.

2. The knowledge about the heart’s location helps to find measurements which are most sensitive in this heart ROI. Using the Jacobian matrix $J$ (calculated during the reconstruction process from the forward FEM model) the ensemble averaged EIT voltage measurements were arranged according to their sensitivity in the ROI.

   For all the FEM nodes in the heart ROI (HeartMembers) the Jacobian matrix (linearized sensitivity of voltage measurements to a conductivity change, introduced in Section 1.5.2) was summed up, which results in a vector (Sens) giving a sensitivity measure in the heart region for every single voltage measurement.

   $\text{Sens} = \left| \sum_{j \in \text{HeartMembers}} J_{ij} \right|$ \hspace{1cm} (3.4)

3. Furthermore, several criteria were applied to quantify the reliability of the measurements:

   *Please note that those criteria were based on a first idea and could not be fully tested as discussed in Section 3.3.2. Some of them might therefore be an inadequate choice.*
Measurements with a high signal quality indicator (SQI, see Section 2.4) were classified as more reliable.

Any measurement with injecting and measuring electrodes too close (at least three inactive electrodes in between were required) was rejected. Those measurements are usually very sensitive in the superficial layers of the thorax (skin, etc.) and therefore not of interest.

Not implemented: The faulty electrode detection algorithm (see Section 2.3.2) could further be used to eliminate unusable measurements.

---

**Figure 3.4: Block diagram of the ICG-via-EIT approach.**

**Descending Aorta Pulse Arrival Time (PAT)** The idea of using the raw impedance signals brought up the question whether this method could be used to detect the pulse arrival time (PAT) in the descending aorta - similar to how it is done in [39], but without performing a reconstruction to the EIT data prior to analysis.

Since this task was out of scope for this thesis, the algorithm has not been implemented. The aim was therefore just to show whether it might be possible to calculate the PAT via this method with manual analysis and without giving a solution to how to choose the appropriate measurement. Nevertheless, the basic algorithm would be similar to the one for the heart described above, simply with the ROI representing the aorta’s position.

The aorta position was derived from bolus injections and manually set (X/Y=19/22) - this is also shown in Section 3.3.2. The first two dozen measurements of interest were browsed for potential candidates and two measurements were further analyzed by fitting a tanh model (described in Section 3.2.3 and [40]) to the voltage measurements.

**Materials** The results of this approach applied to the Madrid experiments are shown in Section 3.3.2. All the images were reconstructed using EIDORS (one-step Gauss-Newton algorithm with Laplacian regularization).
3.2.3 Approach 3: Pulse Arrival Time (PAT)

**Hypothesis**  This approach is based on the assumption that the heart region in EIT images is represented by one single region as suggested in [20, 31, 6] and that the impedance signals in this region are mostly dominated by blood change in the ventricles. The moment when the heart valves open and the heart starts emptying, a steep increase in impedance is expected. This impedance change starts at a specific location, which could be close to the apex of the heart or close to the heart valves.

The aim of this approach is to localize where the impedance change happens first. If it is possible to identify the same (group of) pixel(s) as the starting point among different experiments on the same subject, these pixels can then further be analyzed in the temporal domain for a feature revealing the moment of heart valve opening.

**Algorithm**  Figure 3.5 shows a block diagram of the PAT approach, which consists of the following steps. Each of these steps is then described in more detail in the following paragraphs.

1. **PAT Calculation**: pixel-wise estimation of the time when an impedance change takes place.
2. **ROI Localization**: the heart ROI was segmented in the PAT image and the origin of impedance change was localized.
3. **Temporal Feature Extraction**: the temporal impedance signals of the pixels localized were further analyzed by extracting a feature about the valve opening.

**Algorithm - Pulse Arrival Time (PAT) Calculation**  To quantify the timing of the impedance changes of the pixels their so-called pulse arrival time (PAT) was calculated. This was done by the pixel-wise detection of a certain feature in the ensemble averaged impedance signals, which results in a single image with each pixel corresponding to the time of occurrence of this feature. An example of such a PAT image can be seen in Figure 3.6 (Middle). The PAT approach is further described in [39].

The detected feature used to generate the PAT images can be freely chosen. In our case, a feature tracking the timing of the steep increase in impedance is suitable. The simplest might be to detect the minimum before the steep rising slope. But this method is prone to noise which is still abundant in EIT sequences despite ensemble averaging. A more sophisticated approach
Chapter 3. Use of EIT for Systolic Time Interval Measurement in Pigs

consists of fitting a parametric model onto the impedance signal. Besides the better robustness to noise, this also gives the possibility to estimate timings more accurately without being limited in temporal resolution to the sampling period of the EIT system.

An appropriate method already used in other work [39, 31], is to fit a parametric tanh model $m_{\Omega}(t)$ (see Equation (3.5)) and extract the timing of its inflection point as PAT value.

$$m_{\Omega}(t) = A \tanh\left(\frac{t - \mu}{\sigma}\right) + C \quad \text{(from [40])}$$ (3.5)

where the set $\Omega = \{A, \mu, \sigma\}$ consists of the parameters (amplitude $A$, PAT $\mu$ and slope $\sigma$). The fit was performed by minimizing the quadratic error between the impedance signal and the parametrized model $m_{\Omega}(t)$. The pulse arrival time (PAT) then corresponds to the inflection point of the fitted tanh model. This method is further described in [40].

Besides this model, others such as a parabola (fitted on the lower inflection point of impedance change) were tested but showed to be more influenced by noise and were thus rejected.

Algorithm - ROI Localization  First the heart region of interest (ROI) was segmented by a seeded region growing algorithm applied to the averaged impedance signals. The initial seed was placed where the maximum in the pulsatility power image (see Figure 3.6 (Left)) is localized. Each of the neighboring pixels was incorporated in the ROI if its corresponding impedance signal a) correlated well ($R > 0.8$) with its neighbor already in the ROI and also b) with the impedance signal of the initial seed location ($R > 0$). In this way it is ensured that all the necessary neighbors are included in the ROI but for example lung pixels with opposite phase to the heart (seed location) are avoided. The results of such a segmentation is shown in Figure 3.6 (Middle) by the pink line.
In a second step the PAT image was reduced to the heart ROI determined as described before. This spatially reduced PAT - shown in Figure 3.6 (Right) - was similar in shape in all the different experiments on a single piglet. The origin of impedance change (marked by a yellow bullet) must then be exactly localized in all the experiments. As shown in detail by the results in Section 3.3.3, it was neither possible to perform such an exact localization nor to find a feature about the valve opening in the temporal signals of the pixels in these regions. This is why this approach has not been developed further. For the exact reasoning about this, the reader is referred to the results in Section 3.3.3.

**Materials** The results shown in Section 3.3.3 are based on the Madrid experiments reconstructed using Dixtal’s reconstruction software, thus with ensemble averaging after the image reconstruction.
3.3 Results

3.3.1 Approach 1 - Ventricular Derivative

From the seven pigs analyzed, the ventricular derivative approach showed good results for two pigs (Arthur and Marco), which were further analyzed in more detail. The remaining four pigs (Paco, Roy, Rudolph, Sancho) did not show satisfactory results.

Detailed waveforms for four experiments are shown in Figure 3.8. For the ‘good’ pigs in the upper two rows the impedance signal $I_V(t)$ in the heart ROI shows an inflection point close to the effective valve opening (red dotted line). This point is clearly extracted by taking the first derivative $\frac{dI_V(t)}{dt}$ and detecting its minimum. Two ‘bad’ pigs in the lower two rows on the other hand have much lower cardiac power in the heart ROI and do not show such a clear inflection point in the impedance signal $I_V(t)$. More detailed results for all the experiments can be found in Appendix D where all the figures of the ‘good’ pigs as well as two experiments for each ‘bad’ pig are available.

The experiments from the two pigs with promising results were further analyzed by correlation shown in Figure 3.7 (Left) and a Bland Altman plot in Figure 3.7 (Right). The estimated PEP via EIT (PEP$_{EIT}$) shows a high correlation ($r=0.923$ with $p<0.001$) and thus a linear relationship with the PEP measured via the pressure catheter (PEP$_{Ref}$). As visualized in the Bland Altman plot, the PEP via EIT shows a bias of about -10 ms, thus a constant underestimation.

![Correlation Plot for PEP Estimate vs. Reference](image1.png)
![Bland Altman Plot of EIT and Reference PEP Measurement](image2.png)

Figure 3.7: (Left) Correlation plot between the non-invasively measured PEP estimate via EIT (PEP$_{EIT}$) and the invasive reference via pulmonary artery pressure (PEP$_{Ref}$). (Right) Shows the agreement of the two measurement modalities using a Bland Altman plot. The nine data points are based on four experiments from Arthur (circle) and five from Marco (cross), respectively.
'Good' Pigs

'Bad' Pigs

Figure 3.8: Results of the ventricular derivative approach for four different pigs: Arthur, Marco, Roy, Sancho (in descending order) showing the ensemble averaged temporal signals in the left and the heart ROI (delineated in black) segmented power images in the right column. The red dotted line and red circle in the left column correspond to the invasive reference measurement $\text{PEP}_{\text{Ref}}$ and the non-invasive estimate $\text{PEP}_{\text{EIT}}$, respectively.
3.3.2 Approach 2 - ICG-via-EIT

The ICG-via-EIT approach presented in Section 3.2.1 used to estimate the aortic valve opening did not show any successful results which would be worth presenting here. By semi-manual inspection of the voltage measurements at the very beginning some promising results were found (ICG-like signals from EIT voltage measurement which seemed to have a B-point detectable with an accuracy of about ±10 ms.). It was mistakenly thought that these signals would originate from the heart region which lead to the development of this approach. It later turned out that in the heart region no ICG-like signals could be found.

On the other hand, the approach of analyzing raw voltage measurements might be of interest for the detection of the pulse arrival time (PAT) in the descending aorta. For two manually selected measurements (indices 749 and 751: voltageEit(idx,:)) with high sensitivity in the descending aorta (as illustrated in Figure 3.9), the PAT measured directly via the voltage signal shows a strong correlation with the mean arterial blood pressure as depicted in Figure 3.10. This enables continuous and non-invasive measurement of blood pressure as introduced in Section 1.5.3 and [39].

Figure 3.9: (Left) the descending aorta was localized at pixel (X/Y=19/22, encircled in black) by analyzing a bolus injected into the left atrium traveling down the aorta. (Middle) and (Right) show the sensitivity of both voltage measurements (index 749 and 751, respectively). Blue, yellow show a high and white shows a low sensitivity (to conductivity changes) for the specific measurement. These two voltage measurements clearly have a high sensitivity on conductivity changes happening in the descending aorta (black circle).
3.3.3 Approach 3 - Pulse Arrival Time (PAT)

The PAT approach proved inappropriate for cardiac EIT signals. Whether a constant location for the start of impedance change nor a temporal feature for the heart valve opening could be found, so that no overall performance analysis can be presented here.

Figure 3.11 shows the partial result of the PAT approach for three different hemodynamic conditions of the same pig from the Madrid experiment. The cardiac pulsatility power images are very similar for all the experiments. Also the PAT images do not change significantly. What can be seen further in the 3D PAT plots is that their shapes show similarities. The lowest PAT (origin of impedance change) depicted by the yellow bullet marker is always located more to the left (anatomical orientation, thus right in the image) and the impedance change then 'propagates' more to the center until it reaches a certain plateau always situated around where the power image has its maximal values (center of the heart). This was consistent for all the twelve experiments analyzed.

Among other things, there was an attempt to localize the origin of impedance propagation by taking the lowest PAT value inside the heart ROI which is close to the center of the heart. The location of this point varied by up to three pixels among the experiments. Hence, it was impossible to locate this point as a single pixel. Furthermore, manual analysis was performed by visual inspection of the averaged impedance signals at and around the origin of impedance propagation for every single experiment. No feature was found which would give rise to the opening of the heart valves.
Figure 3.11: Partial results for the PAT approach applied to three experiments from the Madrid pig: (Left) Baseline (11), (Middle) Hypertension (15) and (Right) Hypertension (19). For each of the experiments three different plots are shown: (Top) cardiac pulsatility power with the heart ROI delineated in pink, (Middle) PAT image with the heart ROI (dashed pink line) and (Bottom) PAT as 3D plot zoomed to the heart ROI. The yellow bullet marks the approximate location of the lowest PAT (origin of impedance change) in the heart ROI.
3.4 Discussion

3.4.1 Approach 1: Ventricular Derivative

As shown in Figure 3.8 and in more detail in Appendix D, the ventricular derivative approach showed useful results for two out of six pigs only. With the limited number of nine experiments on these two pigs, it could be shown that the PEP estimate via EIT correlates well with the invasive pulmonary aortic catheter reference (see Figure 3.7). However, the PEP via EIT is constantly underestimated by about 10 ms on average. This might be worth investigating further at a later stage but for the moment there are many other issues to be resolved first.

The temporal impedance signal in the heart region $I_V(t)$ is clearly dominated by a phenomenon not related to the ventricular blood volume (as thoroughly discussed in Chapter 4). On the contrary, is the contribution of the blood volume fairly small so that the ventricular emptying results in a barely visible inflection point in the overall signal. Thanks to the high-pass characteristics of the derivative applied to extract the blood flow $F_B(t)$, the dominating but more low-frequency signal is being suppressed and the small blood volume signal appears to be amplified. This can be seen as a very simple source separation, which seems to work in a few cases. In other cases where the dominating signal contributor has high-frequency components close to the valve opening or the contribution of the blood volume is simply too small, the algorithm fails. It remains unclear what generates and influences this dominating signal. Several factors such as differences in anatomy, belt positioning (longitudinal axis or oblique tilting), lung volume changes, changes in hemodynamics (blood pressure, pulse), can be thought of as influencing factors. Admittedly, it would be naive to think of this approach as the final solution to the problem. But it appears to be a difficult task to solve without any knowledge of the exact genesis of the dominating cardiac EIT signals.

Furthermore, applying the derivative requires caution. It has to be clearly stated that the MIGET experiments used for analysis were - compared to others - of good quality and quite clean (little noise only). One can imagine that in an everyday clinical environment more noise is abundant which then even gets amplified by the derivative. Therefore one might think of more robust solutions to extract the inflection point in the signal.

3.4.2 Approach 2: ICG-via-EIT

With the ICG-via-EIT approach no positive results were obtained when trying to estimate the aortic valve opening of voltage measurements in the heart region. Nevertheless, the approach was successful when analyzing raw voltage signals sensitive in the descending aorta: the aortic pulse arrival time (PAT) detected correlates well with the mean arterial pressure.

As mentioned before, the signals initially analyzed showed ICG-like behavior and were mistakenly thought to originate from the heart region (having high sensitivity of impedance measurement in the heart). It finally turned out that the measurements in question have high sensitivity in the left lungs. This brought up the hypothesis that what had been measured was an impedance change in the pulmonary artery, which would explain the possibility to detect a feature related to the heart valve opening. But on the other hand, it could easily have been a movement artifact and thus detected just by chance and nonexistent in other subjects.
the exact origin of the ICG signals are unclear and the acceptance of the technique itself is controversial, it was decided to focus on other solutions to solve the problem of detecting the heart valve opening.

Although out of scope of this thesis, it could be shown that by the ICG-via-EIT approach the pulse arrival time (PAT) in the descending aorta can be estimated. Using one single raw impedance measurement the pulse transit time (PTT) of the arterial pressure pulse can be estimated. Twelve experiments on the same pig with large variations in blood pressure showed a strong correlation ($r = -0.943$, $p < 1E - 5$) between aortic PTT and the mean arterial blood pressure (MAP) as depicted in Figure 3.10. The correlation is not as strong as when measuring the PTT in the reconstructed EIT images (done in [39]) but it might still have its potentials. One could think of applications where time or computation consumptions play an important role. Thanks to this approach continuous image reconstruction can be avoided (an initial reconstruction to detect the descending aorta would still be necessary). In addition, one might think of placing a drastically reduced number of electrodes at specific places only and thus sensing the descending aorta with a reduced hardware setup.

The particular impedance measurements for PTT detection in the aorta have, however, been manually selected. Therefore, if one wants to pursue this approach, an appropriate algorithm for selecting the ‘good’ impedance measurement(s) is still necessary.

3.4.3 Approach 3: Pulse Arrival Time (PAT)

The PAT approach, applied to both the Madrid but also the MIGET experiments, did not lead to any positive results. The initial hypothesis that impedance signals are dominated by changes in blood volume could be disproved.

As the results for the Madrid experiments in Section 3.3.3 show, the PAT in the heart region shows a similar shape when plotted in 3D for all the experiments of the same subject. But when trying to track down the origin of the impedance change in the heart, it cannot be localized at a static position by a (group of) pixel(s). Moreover, the position of the suspected origin of impedance change is located much to the left and away from the pixels which show high pulsatility power. Even though EIT is not a morphological imaging modality this position is most probably located out of the anatomical area of the heart. Among other reasons this raises serious doubts that what was detected as the origin of impedance change could contain some information about the heart valve opening.

If the impedance changes in the heart region were only due to changes in blood volume, this might be an interesting approach.


3.5 Conclusion

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Table 3.1: Comparison of the three approaches presented. With i) initial step of the algorithm and c) continuous estimation of the feature of interest.

In this chapter three different approaches for estimating the heart valve opening by EIT have been presented, two of which do not show a positive result. An overview of these approaches is shown in Table 3.1.

Firstly, the method of analyzing the ventricular derivative being proportional to blood flow, is the approach which suggests positive results. An analysis of two pigs limited to nine experiments showed a good correlation ($r = 0.923$, $p < 0.001$) between the non-invasively estimated PEP by EIT and the invasive reference. The PEP varying by 32 ms over all the nine experiments was estimated with an average error of $−9.8 \pm 5.7$ ms. Nevertheless, it remains unclear why this approach does not work (at all) for experiments performed on other pigs. Changes in ventilation parameters could change the heart’s position relative to the EIT belt and might make a detection of valve opening impossible in different experiments on the same pig.

Secondly, the ICG-via-EIT approach did not show the possibility to extract ICG-like signals from impedance measurements through the heart. This may be due to the difference in electrode placement compared to real ICG or the fact that the real ICG signal is more likely generated by the big arteries and not the heart itself.

Thirdly, the PAT approach is not applicable with the cardiac pulsatility signals not dominated by changes in blood volume.

The current results clearly lead to the conclusion that even though the ventricular derivative approach might be a possibility to extract the heart valve opening by EIT, further investigations are necessary to answer various open questions such as the influence of belt positioning, influence of difference in left and right PEP, exact genesis of cardiac EIT signals, etc.

It is strongly recommend to further investigate and gain understanding about the main contributors of the cardiac EIT signals before continuing to approach the task of measuring hemodynamic parameters by EIT. Furthermore, it is warmly suggested recording the thorax shape and belt position via CT or MRI in addition to future EIT recordings. This could exclude potential error sources by the use of an exact reconstruction model and might give the possibility to find anatomical explanations for different phenomena observed. As long as there are still many open
questions about cardiac EIT signals, reducing the number of possible error sources might facilitate future work and make it more target-oriented.

Even though it is beyond the scope of this thesis, it could be shown that the estimation of the aortic pulse arrival time (PAT) is possible via raw EIT voltage signals. If this way of estimating the PAT in the descending aorta might be of advantage compared to the method using the reconstructed EIT images, the approach has to be extended by developing an algorithm which automatically selects the appropriate impedance measurement(s) for analysis.
Chapter 4

Interpretation of Cardiac EIT Signals

4.1 Introduction

As presented in Chapter 1 (Section 1.5.3), there are contradictory opinions about the origin of cardiac EIT signals. After discussions with long-standing experts in the EIT community and also stated in [34], the origin of cardiac-related impedance change is not completely understood. It could be shown in the previous chapter, that the cardiac EIT signals in pigs cannot originate from blood volume changes (only), as usually suggested by the literature for human EIT [35]. Thus, the question remains open which physiological effects are contributing to the pulsatility - and not perfusion - signals in EIT, as also illustrated in Figure 4.1.

However, to extract hemodynamic parameters out of cardiac EIT recordings, it is of utmost importance to first understand the genesis of cardiac-related signals. Therefore, this chapter is fully dedicated to the interpretation of cardiac EIT in pigs and humans.

Figure 4.1: The different contributors of the cardiac EIT signal are unclear and to be investigated.
4.2 Organization of This Chapter

To investigate the origin of cardiac EIT signals different hypotheses have been explored during this Master’s thesis. Dedicated experimental and modeling investigations have been performed on pigs and on human data. Each of these methods has a dedicated section which are organized as follows:

- Section 4.4 (Temporal Signals in Pigs) covers a detailed analysis of cardiac EIT signals in pigs. The aim was to show that the temporal signals cannot originate from changes in blood volume only.
- Section 4.5 (Bolus-Pulsatility-Paradox in Pigs) shows the difference in localization of the heart in EIT via two different methods: hypertonic saline bolus injections - the gold standard technique - versus pulsatility power images. The goal was to reveal the heart position in the EIT image by the two methods and compare them.
- Section 4.6 (Simulation of a 3D Pig Heart) describes the conductivity simulation performed in order to show the strong influence of heart-induced lung movement on the EIT images.
- Section 4.7 (Temporal Signals in Humans) covers a detailed analysis of cardiac EIT signals in humans. Influences of different belt positions and the timing of the temporal signals were investigated and compared to pig EIT. The aim was to reveal whether the findings from pigs in Section 4.4 also apply in humans.
- Section 4.8 (Dynamic Cardiac MRI in Humans) briefly discusses the results of dynamic cardiac MRI scans performed with the aim to reveal heart-induced movement in humans.

Before concluding the chapter in Section 4.10 the results of these five methods are summarized in Section 4.9.

4.3 Materials

All the EIT recordings presented in the following were reconstructed with EIDORS using the GREIT algorithm with a noise figure of NF=0.5 and the library models as discussed in Section 2.3.2. Prior to the reconstruction the signals were ensemble averaged as shown by Method 1 in Figure 2.9 in Section 2.4. All the data was taken from expiratory apnea sequences only.
4.4 Temporal Signals in Pigs

4.4.1 Introduction

The pig data analyzed for the heart valve opening in the previous chapter were examined more thoroughly in the temporal domain. The aim was to show that impedance changes in cardiac EIT cannot be dominated by changes in blood volume.

4.4.2 Methods

The pulsatility power images of pig EIT recordings shown in the previous two chapters usually have two regions with high cardiac activity (see Figure 4.2 for an example). In a first step all the pixels in these two regions were analyzed in the temporal domain. Therefore, the two regions were first segmented by the watershed technique [33] with an algorithm adapted from the one presented in Section 3.2.1. Then, the temporal signals of the two regions of interest (ROI) were normalized (subtract the mean value and divide by the standard deviation) and plotted for visual inspection. In this way a potential coincidence in time between the impedance signals and the heart valve opening is visible. Furthermore, the ECG’s P- and R-wave were plotted, which allow the analysis of EIT signals with respect to the onset of atrial or ventricular contraction.

The analysis mentioned above was performed on one experiment of three different pigs (Arthur, Roy and Sancho) of the MIGET experiment and also on the pig of the Madrid experiment at three different hemodynamic conditions (baseline, hyper- and hypotension).

4.4.3 Results and Discussion

Figure 4.2 (Left) shows the pulsatility image for three pigs of the MIGET experiment. All of the three show two strong peaks in the power image: one more ventral and centered (black outline, anterior peak) and one more to the back and left of the pig (red outline, posterior peak). (Right) In the temporal plots, the dispersion of the single pixel signals (dotted lines) compared to the averaged signal (solid line) is very small. The minimum/maximum of the black/red impedance signal, respectively, is once located after and twice before the pulmonary valve opening. Neither do the black nor the red signal show a clear feature synchronized with two ECG points (P- or R-wave) or the pulmonary valve opening. However, some of the black signals show a slight inflection point around the moment of pulmonary valve opening. Figure 4.3 shows comparable results for a single pig in three different hemodynamic states. Neither the black nor the red signals show a synchronization with the aortic valve opening. Here too, the dispersion between averaged signal and single pixel signals is low. Furthermore, the extrema of both signals clearly vary with changes in blood pressure. The minimum of the black signal is once located at/before/after the aortic valve opening in baseline/hypertension/hypotension, respectively.

For all four pigs it can be concluded that the main contributors of the impedance signals in the two most active regions are clearly not synchronized with the heart valve opening. According to their sign one could assume that the anterior peak (black outline in Figures 4.2 and 4.3) is influenced by ventricular activity (movement, blood volume, etc.) whereas the posterior peak (red outline in Figures 4.2 and 4.3) by atrial activity; i.e. at the moment of heart valve
Figure 4.2: Pulsatility power images (Left) and corresponding time signals (Right) from pixels with high pulsatility power in heart region for three different pigs of the MIGET experiment (Arthur: Top, Roy: Middle, Sancho: Bottom). The fine dotted lines in the temporal plots show the normalized impedance signal of every single pixel in the selected region (marked in the power image with the same color). The thick solid lines then depict the average impedance change in the whole region. The blue, black and red vertical lines in the temporal plots correspond to the occurrence of the ECG-P-wave, ECG-R-wave and pulmonary valve opening, respectively.
Figure 4.3: Pulsatility power images (Left) and corresponding time signals (Right) from pixels with high pulsatility power in heart region for the same pig of the Madrid experiment at three different blood pressures (Baseline 132/100 mmHg: Top, Hypertension 160/124 mmHg: Middle, Hypotension 88/55 mmHg: Bottom). The fine dotted lines in the temporal plots show the normalized impedance signal of every single pixel in the selected region (marked in the power image with the same color). The thick solid lines then depict the average impedance change in the whole region. The red vertical line in the temporal plots corresponds to the aortic valve opening.
opening the ventricles/atria contain a lot/little blood and thus are the black/red impedance signal lowest/highest, respectively. But if the signals of the anterior peak were purely due to changes in ventricular blood volume, it would need to have its minimum exactly at the moment of the heart valve opening, which is definitely not the case. The time of the minimum varies over the experiments on different pigs (Figure 4.2), but also on the same pig with changing blood pressure (Figure 4.3). This leads to the conclusion that in pigs cardiac EIT signals are not dominated by changes in blood volume; certainly not with the usual transversal belt configuration used in those experiments. However, with the more transversal orientation of the pig heart as discussed in Section 1.3.4, even the use of an oblique belt placement [35] is not expected to lead to significant changes.

Nevertheless, in some pigs one can observe an inflection point of the ventricular impedance signals at the moment of the valve opening, which is assumed to be due to changes in ventricular blood volume. This was used to determine the valve opening by “Approach 1: Ventricular Derivative” in Section 3.2.1. However, it is not understood what exactly generates this signal and how the belt position influences the strength of this contributor in the final signal. It is therefore highly recommended to further investigate the origin of both the dominating signal but also the anatomical reason for this blood-volume-like contributor. The following points are suggested for future experiments on pigs:

- The EIT belt must be placed in the usual transversal position so that the middle of the heart lies at the same height as the belt. The placement is verified and adjusted with the aid of an imaging technique, preferably CT.
- Two more belts are then placed, one above and one below the initial belt. This allows determining the influence of different belt placements on the EIT signals.
- To change hemodynamic conditions such as blood pressure or also the PEP, noradrenaline or nitroglycerine should be administered [39].
- If possible all the different experiments should be recorded with either partly dynamic or at least static CT to track a possible movement or displacement of the heart.
- Furthermore, it is of advantage to perform more experiments on differently aged and sized pigs. Also consider that a higher abundance of fatty tissue surrounding the heart might change the result significantly.

4.5 Bolus-Pulsatility-Paradox in Pigs

4.5.1 Introduction

The use of hypertonic saline bolus injections as contrast agents in EIT has been a well-known technique for a long time [8]. Having a fourfold higher conductivity than blood, the arrival of the bolus results in a sharp decrease in impedance, which is clearly visible in the EIT image sequence. Besides, for example, determining the regional lung perfusion [6] it can be used to localize different anatomical structures such as the descending aorta [39].

The question to be answered by this experiment was how good the position of the heart localized via bolus injection matches with the peaks observed in the pulsatility power images.
4.5.2 Methods

In the MIGET experiments a hypertonic saline bolus was injected into the right atrium. From there the bolus travels through the right ventricle and the pulmonary arteries into the lungs and then returns through the left atrium into the left ventricle. When the bolus is present in the left or right atria and ventricles it reveals the location of the heart in the EIT images.

To extract the bolus-related impedance change, the non-averaged image sequences were filtered with a bandpass filter (cutoff frequencies of 0.01 and 0.5 Hz) in the temporal domain. The filtered impedance change was then shown at different moments in time, which reveal the position of different structures such as the left and right heart. The location of the heart determined by the bolus injection was then compared to the position of high cardiac activity in the pulsatility power images described in the previous section. If this high cardiac activity was purely due to changes in blood volume, their position is not expected to differ much from the heart localized via bolus injections.

4.5.3 Results and Discussion

The comparison of heart localization via bolus injections compared to pulsatility power images is shown in Figure 4.4 by the example of two pigs. The figure clearly shows the bolus (yellowish pixels) at its different positions when traveling from the right heart through the pulmonary circulation to the left heart. The heart localized by bolus injections in (c) and (g) does clearly not correspond to the assumed heart position from the pulsatility power image in (a). These results were found consistently in twelve pigs analyzed as shown in Appendix E. Furthermore, to avoid potential errors due to reconstruction, the impedance changes were also reconstructed using the Dixtal software and led to the same results (not shown here).

Because of this clear mismatch in localization it is thought that the peaks in the pulsatility images are due to heart-induced movement artifacts and thus located where the heart interacts with surrounding structures (lungs, fat, etc.). Together with the temporal signals discussed in the previous section, this supports the hypothesis that cardiac EIT signals in pigs are not due to changes in cardiac blood volume but dominated by heart-induced movement artifacts. These findings were submitted to a conference in form of an abstract as shown in Appendix E.

However, it has to be kept in mind that EIT is an imaging technique where the spatial localization of a certain anatomical structure is not as accurate as for instance in CT or MRI. It is therefore questionable whether the mismatch between peaks in bolus and pulsatility images is not simply an effect of the reconstruction algorithm. During bolus injection the atria and ventricles change their impedance in the same direction which is reconstructed in the image as one single dot located in the center of the heart. On the other hand, a change in blood volume happens with opposite phase in the atria and ventricles. Due to this asynchrony the reconstruction algorithm tends to separate the two signals and thus pushes the two peaks in the pulsatility image away from the center along the heart’s long axis. Even if this were the case, the conclusions stated before remain valid: Heart signals in pig EIT is dominated by heart-induced movement artifacts and not by changes in blood volume. However, if the mismatch in localization is due to the reconstruction, this could be an argument against the use of bolus injections for localizing the heart structures in EIT images.
Figure 4.4: Two pigs of the MIGET experiment (Top: Arthur, Bottom: Sancho): pulsatility power (a), in comparison with seven states of the conductivity change due to bolus injection: bolus injected into the right atrium (b), travels through the right ventricle (c), into the lungs (e), and back to the left atrium (f), and ventricle (g). The segmented black/red regions in the power image (a) correspond to the same as the black/green in the bolus images (c) and (g). RA/RV and LA/LV stands for right/left atrium/ventricle, respectively.
4.6 Simulation of a 3D Pig Heart

4.6.1 Introduction

As it was shown in the two previous sections, the impedance changes in the heart region do not correspond to blood volume changes. It was therefore hypothesized that the impedance changes are mostly due to heart-lung movement. To support this hypothesis it was evaluated how much of the impedance change can be attributed to heart-lung movement artifacts in comparison with changes in blood volume. This was done by means of a very simple numerical model simulating two representative moments of the cardiac cycle.

4.6.2 Methods

Figure 4.5 shows the model used to perform these simulations. The lungs (blue) are represented by two 2D ellipses extruded to 3D. The heart consists of the atria (red) and ventricles (brown), each half a 3D ellipse. When the length of atria or ventricles is reduced, the volume previously occupied by the heart is replaced by lungs, thus imitating heart-lung movement. The conductivity values attributed to the different structures were calculated using the values in Appendix A and set as follows: \( \sigma_{\text{Heart}} = 2.0 \), \( \sigma_{\text{Lungs}} = 0.2 \) and \( \sigma_{\text{Background}} = 1.0 \). For simulating different stages in the heart cycle both, the length and conductivity of atria and ventricles were modulated as follows:

- **State 1, Pre-Ejection**: The ventricles are fully filled with blood and the atrial blood volume is lowest:
  \[ \sigma_{\text{Ventricles}} = 1.3 \cdot \sigma_{\text{Heart}}, \sigma_{\text{Atria}} = \sigma_{\text{Heart}} \quad \text{and} \quad \text{Length}_{\text{Ventricles}} = 100\%, \text{Length}_{\text{Atria}} = 90\% \]

- **State 2, Post-Ejection**: The ventricular blood volume is lowest and the atria are fully filled with blood:
  \[ \sigma_{\text{Ventricles}} = \sigma_{\text{Heart}}, \sigma_{\text{Atria}} = 1.3 \cdot \sigma_{\text{Heart}} \quad \text{and} \quad \text{Length}_{\text{Ventricles}} = 90\%, \text{Length}_{\text{Atria}} = 100\% \]

The simulation was performed three times by modulating: 1) both movement and conductivity change, 2) only movement or 3) only conductivity change. For each simulation one image was obtained. It was reconstructed from the difference in simulated electrode voltages obtained from the transition of conductivity distribution of State 1 to State 2 (pre-ejection to post-ejection), thus simulating the most relevant transition in the heart cycle.

4.6.3 Results and Discussion

Figure 4.6 shows the resulting conductivity change for the three cases simulated as described before. For all three simulations two peaks are observable. A black one (decrease in conductivity) in the ventricular and a yellowish one (increase in conductivity) in the atrial region. For both effects (movement and conductivity change) simulated independently, the change in ventricular conductivity is of the same magnitude. In the atrial region the movement-induced conductivity change is even twice as big as the one due to a change in atrial conductivity only. Thus, both phenomena simulated, the change in blood volume and heart-lung movement, create changes in impedance at the same location in the image and with the same sign.
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Figure 4.5: 3D heart model in a circular shaped thorax with the atria and ventricles represented by two half ellipses in red and brown, respectively. The heart’s long axis is rotated to the left by 30° and tilted downwards by 25° to mimic its true anatomical position in pigs. The blue ellipses extruded in 3D are the lungs. For clarity of presentation, the lungs are not fully shown in both images. In reality, the heart is fully surrounded by the lungs. (Left) shows a 2D top view and (Right) a 3D view with the 32 electrodes as green circles. The heart’s short axis diameter is 28% of the whole thorax diameter while the ventricles and atria are a length of 23% and 13%.

According to this simplistic simulation and with the current modulation parameters it can be concluded that already a small movement of the heart against lung tissue can create an impedance change of the same magnitude as the one due to a change in atrial or ventricular blood volume. The simulated images resemble the pulsatility images obtained from real measurements. Even though the simulation used is very simplistic, this would speak for the hypothesis that the signals observed in pigs could be generated by both, the dominating heart-induced movement artifacts but also a little contribution of changes in cardiac blood volume.

Figure 4.6: Conductivity changes from the simulated 3D pig heart model in a circular thorax: (Left) conductivity change and movement at the same time, (Middle) movement only and (Right) conductivity change only. Orange corresponds to no change in conductivity whereas black and yellow illustrate a decrease or increase in conductivity, respectively.

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4.7 Temporal Signals in Humans

4.7.1 Introduction

The results of pig EIT shown in the previous sections support the hypothesis that EIT pulsatility signals are dominated by heart-lung movement rather than by changes in cardiac blood volume. To verify this hypothesis in humans, a pilot study was performed as part of this Master’s thesis.

4.7.2 Methods

In the pilot study, besides cardiac EIT in expiratory apnea, 4D cardiac MRI (Magnetic Resonance Imaging) recordings were performed. This provides the basis to perform a 3D conductivity simulation of the heart’s activity to validate the simulation results with the real EIT recordings. To reveal differences in EIT belt positioning the usual transversal and the oblique placement were applied (see Section 1.5.3 or [35]). This experiment named “Heart EIT-MRI ETHZ” is further described in Section 2.2.3.

The human EIT data was treated identically to the pig EIT data as described in Section 4.4.2. The aim was to analyze the temporal signals but also the influence on the difference in belt placement.

4.7.3 Results

The pulsatility images in Figure 4.7 show two highly active regions for both volunteers. As previously observed in pigs, there is the anterior peak (black outline) and the posterior peak (blue outline) which is now located to the right side of the subject. For the oblique belt position a third peak (red outline) appears on the left side. It is less strong than the other two. The temporal signals of the two posterior peaks (blue and red) have the same phase and are similar in shape. The impedance signals for the anterior peak (black) show a rise in impedance after the start in ventricular contraction (R-wave). For the first volunteer there is a slight decrease in impedance observable after the start of ventricular contraction, which is much less abundant in the recordings of the second volunteer. On the other hand, the black signal for the second volunteer shows a very long plateau where the signal remains nearly constant from -400 to 0 ms.

The temporal signals and the pulsatility images for humans show similarities with the ones shown before for pigs, the pulsatility images simply seem to be flipped at the sagittal axis (left/right swapped).

4.7.4 Discussion

Before discussing the signals in human EIT, it is worth mentioning the difference of the heart’s orientation in the two species. As one could observe in the power images, both in pigs (Figures 4.2 and 4.3) and humans (Figure 4.7) two strong peaks are observable, but the images from human recordings seem to be mirrored at the sagittal axis (flipped right/left). This can be explained by the difference in orientation of the heart as shown in Figure 4.8. The heart’s long axis in pigs is oriented from left dorsal towards right ventral whereas for humans it is flipped at the sagittal axis and thus from right dorsal towards left ventral. Since most of the heart movement
CHAPTER 4. INTERPRETATION OF CARDIAC EIT SIGNALS

Oblique Belt Configuration - Volunteer 1

Transversal Belt Configuration - Volunteer 1

Oblique Belt Configuration - Volunteer 2

Figure 4.7: Pulsatility power images (Left) and corresponding time signals (Right) from pixels with high pulsatility power in the heart region for two human volunteers of the ETHZ experiment at two different belt positions (oblique: Top and Bottom, transversal: Middle). Due to too noisy recordings the transversal belt configuration for volunteer 2 is not shown. The fine dotted lines in the temporal plots show the normalized impedance signal of every single pixel in the selected region (marked in the power image with the same color). The thick solid lines then depict the average impedance change in the whole region. The black vertical line in the temporal plots corresponds to the ECG-R-wave.
Figure 4.8: Comparison of the heart orientation in pigs and humans. An estimate of the heart’s long axis is shown by the red arrow with the arrowhead pointing towards the apex. All scans were taken in expiratory apnea. (Left) CT scan of a pig showing the looping catheter in the ventricles by the white shiny line. (Middle) MRI scan of a pig tilted to the left revealing atria and ventricles (with kind permission from Aarhus University). (Right) MRI of a human with long axis orientation different than in pigs.

is expected along its long axis a rotation of the axis naturally results in a reorientation of the anterior and posterior peaks in the pulsatility power image. This has been verified by changing the heart’s orientation in the 3D heart model simulation according to the long axis orientation in Figure 4.8 which showed a reorientation of the anterior and posterior peaks as observed in the real recordings (results not shown here).

Also the temporal signals of the anterior and posterior peak seem to be similar for both species. It is therefore assumed that what is observed in pigs by the anterior and posterior peaks can be related to the observations in humans simply with the posterior peak located more to the right and not to the left of the subject. This spatial difference is attributed to the different orientation of the heart’s long axis.

Having explained the reason for the difference in location of the anterior and posterior peaks in human pulsatility images compared to pigs, the temporal impedance changes in humans are now being addressed.

According to [35] the anterior/posterior peak must correspond to the ventricular/atrial blood volume change when using the oblique belt position (see also Section 1.5.3). As shown in Figure 4.7 for the first volunteer, the supposed ventricular signal (black) shows a decrease in impedance after the ECG’s R-wave. This would mean that the ventricular blood volume increases even after the ventricular contraction has started. Usually, after the start of contraction, the ventricular volume remains constant until the blood is ejected into the large arteries, which leads to a decrease in ventricular blood volume and thus one would expect an increase in impedance. What is more, the long plateau (black signal: low impedance before the R-wave) observed for the second volunteer would mean that for about 400 ms before ventricular contraction the ventricular blood volume does not change significantly. At least due to the atrial contraction (P-wave) a slight decrease in impedance would be expected, which does not seem to be present. That this has happened 400 ms before the R-wave is very unlikely since a P-R-interval of more
than 200 ms would indicate a pathology called heart block \[27\].

These two reasons and what was observed in pigs, raise enormous doubts about the fact that in humans the cardiac EIT signals are solely due to changes in blood volume as stated in \[35\]. According to the observations in this thesis blood volume changes might contribute a small part to the cardiac EIT signals, which are most probably dominated by movement artifacts.

The difference between oblique and transversal belt clearly changes the arrangement of the peaks in the pulsatility images. As expected, the peaks are better separated for the oblique placement. This belt placement also reveals a third peak (a second posterior one located to the left of the subject) the origins of which are unclear. However, the difference in temporal signals of the supposed ventricular signal (black) for volunteer 1 does not show enormous changes between transversal and oblique placement.

Admittedly, these conclusions are based on a very limited number of observations in humans and must be verified on other subjects before drawing a definite conclusion. Unfortunately, for logistical reasons, the heart valve opening could not be measured during the experiments carried out. This further restricts the credibility of the analysis. It is therefore warmly recommended to perform more measurements on different subjects while simultaneously measuring the heart valve opening with PCG or a similar technique.

### 4.8 Dynamic Cardiac MRI in Humans

#### 4.8.1 Introduction

In the previous sections it was hypothesized that heart-lung movement mostly dominates the cardiac EIT signals. As described in Section 4.7.2 dynamic cardiac MRI scans were performed on humans. They are analyzed in this section in order to reveal the location and magnitude of heart-induced movement in apnea.

#### 4.8.2 Methods

For both volunteers the MRI scans were performed in expiratory apnea. In one heart cycle 30 images were acquired for each of the 40 slices. Both short and long axis scans were performed. Currently, only the results of one volunteer were analyzed visually by four representative slices, two of each axis orientation (short, long). By a manual segmentation of the myocardium and heart-lung interface the heart-movement can be observed during a whole cardiac cycle.

#### 4.8.3 Results and Discussion

Figure [4.9] shows the results of one volunteer by two representative slices of both axis orientations at four different instants in time. To observe the biggest difference one should observe the first (t=1/30) and the third (t=11/30) columns which represent the moments right before and after ventricular ejection. As delineated by the red dashed line, the heart-lung interface barely shows any visible movement between the two instants. In the short axis scans one can observe a little movement between the heart and the structures located lower down ventrally. This is not lung tissue but these are organs located below the diaphragm. On the other hand, it can clearly be
Figure 4.9: Dynamic cardiac scan on a human volunteer for two slices at two different planes each (the two top rows: two slices in long axis view, the two bottom rows: two slices in short axis view) at four different instants in time of the cardiac cycle. So that one row corresponds to one slice taken at four different moments. The red and green outlines show the manual segmentation of the heart outline and myocardium, respectively. The segmentation was performed for the first instant in time only (leftmost column, t=01/30) and plotted in the subsequent images for comparison purposes. In the image in the upper right corner the different tissue and structures are labeled: lungs (L), blood (B), myocardium (M), aorta (A), pericardium (P) and fatty tissue (F).
seen - especially in the short axis scans - that the blood volume decreases and the myocardium takes up more place (green dashed line). The biggest movement of the myocardium against surrounding structures can be observed ventrally of the apex. There the fatty tissue which includes the pericardium occupies the place freed by the vanishing myocardium of the apex.

Contrary to expectations, dynamic cardiac MRI shows that in humans, lung tissue is hardly affected by the heart's pulsatile movements. However, it is the fatty tissue ventrally of the apex which is in motion due to the heart.

These findings contradict the assumptions of heart-lung movement made for the simulation presented in Section 4.6. Even though the heart does not significantly move lung tissue, the apex exerts movement to the fatty tissue located ventrally. Since fat has an even higher impedance than the lungs (see Appendix A), the influence of this fat-heart interface movement would be comparable or even stronger than the movement simulated for the heart-lung interface. Thus, if one wants to apply the observations from humans to this pig heart model, the simulation can be declared as acceptable from this perspective.

Obviously, the simulation remains simple and could still be expanded in different ways. A question raised from the MRI scans is the influence of the compression of the myocardium on its impedance. The short axis scans show a difference in myocardial thickness of up to factor two in the left ventricle. It remains unclear how much this might change the myocardial impedance and whether this has to be considered in the simulation. Another point of investigation was raised by the big difference in impedance for transversal and longitudinal muscle fiber orientation [43, 14, 41]. But the fact that the orientation changes only slightly during the cardiac cycle [42] leads to the conclusion that this effect does not have to be considered for simulation.

The MRI recordings should be segmented and used to perform dynamic 3D conductivity simulations, which can be compared to the real EIT recordings.
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4.9 Summary

In the following, the results of each of the experiments presented in the previous sections are briefly summarized.

- Section 4.4 (Temporal Signals in Pigs) shows that cardiac EIT signals in pigs can clearly not be dominated by changes in blood volume. For some experiments there is a faint contributor of blood volume, which is not well understood and must be investigated by further experiments on pigs.

- Section 4.5 (Bolus-Pulsatility-Paradox in Pigs) shows a clear mismatch between the localization of the heart via bolus injection and via pulsatility power image. This is most likely because the heart activity in the pulsatility image is movement-dominated and therefore located at the heart’s boundary. Another possibility for this spatial displacement could also be the reconstruction algorithm pushing antiphased changes away from each other.

- Section 4.6 (Simulation of a 3D Pig Heart) concludes that heart-induced lung movement can be a big contributor to the overall cardiac EIT signal, which supports the heart-movement hypothesis.

- Section 4.7 (Temporal Signals in Humans) reveals power images which are, compared to pigs, flipped at the sagittal axis (swapped left/right). This is due to different long axis orientations of the two species’ hearts. The temporal signals raise enormous doubts that human cardiac EIT should be dominated by changes in blood volume. The data is too limited to draw a final conclusion and further experiments have to be carried out.

- Section 4.8 (Dynamic Cardiac MRI in Humans) shows hardly any movement of the heart-lung interface, which would lead to impedance changes. But around the apex there is movement of the heart against fatty tissue which has an even higher impedance than lungs. Thus the prior hypothesis of heart-induced movement artifacts remains unchanged.
4.10 Conclusion

In this chapter ensemble averaged cardiac EIT signals from expiratory apnea sequences of pigs and humans were analyzed.

Pixels with the highest activity at cardiac frequency were determined by locating the peaks in the pulsatility power images. Usually two peaks were observed. The anterior one is located in the ventricular region and the posterior one more in the atrial region. The temporal impedance signals of these two highly active regions in pig EIT are clearly not dominated by changes in blood volume. Moreover, it is thought that cardiac-related movement artifacts contribute the most to cardiac EIT signals in pigs. Nevertheless, for some of the experiments the anterior peaks’ signals show a small contributor of the ventricular blood volume change. The influence of belt positioning or other factors on its abundance are not understood and must be investigated further by an experimental protocol recommended for validation.

Hypertonic saline bolus injections, the gold standard method used for organ localization in EIT, reveals the heart in pigs at a different position than where it is localized by pulsatility images. This also suggests that cardiac pig EIT signals originate from movements of the heart interface to surrounding tissue. However, this mismatch in localization could also be due to the reconstruction algorithm, which tends to push apart structures having antiphased signals even if they are located very close to each other. This would imply that the method of localizing structures like the heart in EIT via bolus injections has to be scrutinized.

Also in the two human subjects analyzed two highly active regions were observed in the pulsatility power images. Compared to the pig EIT recordings their orientation is flipped at the sagittal axis, which is simply explainable by the different anatomical orientation of the two species’ hearts. Despite the very limited number of experiments and the lack of a reference for the heart valve opening, there are grave doubts that in humans the cardiac EIT signals are dominated by changes in blood volume as suggested in the literature. To support this conclusion one should perform further experiments on different human subjects together with a reference measurement for the heart valve opening.

By means of a simulation of a very simple 3D pig heart model it could be shown that a heart-lung interface movement would lead to a big impedance change in the heart region. Even though dynamic cardiac MRI on humans shows barely any heart-lung movement, a displacement of the fatty tissue around the apex could be determined. This is similar to the expected and simulated heart-lung movement. However, the simulation performed is very limited. Due to a lack of time the 3D segmentation of the dynamic cardiac MRI scans and the following simulations could not be performed anymore as part of this thesis. It is warmly recommended to perform dynamic conductivity simulations based on these real data and compare them to the EIT recordings performed on the same subject. In doing so, a better understanding of the different contributors generating human cardiac EIT signals can be gained.
Chapter 5

Overall Conclusion

The main goal of this Master’s thesis was to find an accurate estimate of the aortic valve opening from cardiac EIT recordings in pigs.

Three approaches were applied to measure the heart valve opening via EIT, two of which (PAT and ICG-via-EIT) did not show any satisfactory results. The positive results of the third approach (Ventricular Derivative) are limited to two among the six pigs analyzed. The non-invasively estimated PEP from nine experiments in these two pigs showed a good correlation ($r = 0.923$, $p < 0.001$) with the invasive reference PEP measurement. One reason for the failure of the approach for the remaining four pigs and of the other two approaches lies in the fact that the origin of cardiac EIT signals is controversial in the literature and generally not well understood. This led to a thorough analysis of cardiac EIT in pigs and humans. They have shown that impedance signals in the heart region in pigs and most probably also in humans are not dominated by blood volume changes as stated in the literature for human EIT. Moreover, it is thought that heart-induced movement dominates the pulsatile cardiac EIT signals.

This would mean that EIT does not offer the possibility to determine absolute hemodynamic parameters such as the stroke volume and thus the cardiac output. However, when having gained a deep enough understanding of the genesis of the cardiac EIT signals, one could continue to extract timing values such as the heart valve opening. It may either be a small signal of changes in ventricular blood volume or the apex movement which is present in the cardiac EIT signal. No matter which it is, either should have an abrupt change at the moment of ventricular ejection, which must be detectable somehow.

Before continuing to further analyze cardiac EIT signals for such features, it is strongly recommended to perform more experiments and simulations concerning their origin. For this an experiment on pigs is suggested which should help to reveal the source of the faint signal contributor exploited by the ventricular derivative approach to estimate the PEP. Within this thesis the foundation to perform 3D conductivity simulations for human EIT has been built by the recording of dynamic cardiac MRI and EIT on the same subject. The MRI data should be segmented so that the simulation can be performed and their results can be compared to the real EIT recordings. Furthermore, the number of data of human EIT recordings is limited to draw a final conclusion. It is therefore suggested to carry out more experiments with the simultaneous measurement of the heart valve opening.
In short, it can be concluded that cardiac EIT is not measuring perfusion but pulsatility. This might limit its application and make it less promising than what the literature proposes. Nevertheless, once the origin of cardiac signals in EIT is better understood, the extraction of features such as the heart valve opening will hopefully be possible.
Appendix A

Thoracic Tissue Bioimpedance Values

<table>
<thead>
<tr>
<th>Biological tissue</th>
<th>Measured resistivity</th>
<th>From [A]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistivities in [Ω.cm]</td>
<td>F=50 kHz</td>
<td>F=100 kHz</td>
</tr>
<tr>
<td>Collapsed lung</td>
<td>3179</td>
<td>2742</td>
</tr>
<tr>
<td>Inflated lung</td>
<td>6210</td>
<td>5732</td>
</tr>
<tr>
<td>Bone</td>
<td>950</td>
<td>921</td>
</tr>
<tr>
<td>Chest wall muscle</td>
<td>672</td>
<td>537</td>
</tr>
<tr>
<td>Full chest wall</td>
<td>1373</td>
<td>1258</td>
</tr>
<tr>
<td>Rib, with muscular interstice</td>
<td>855</td>
<td>689</td>
</tr>
<tr>
<td>Heart (filled with blood)</td>
<td>532</td>
<td>448</td>
</tr>
<tr>
<td>Heart wall</td>
<td>551</td>
<td>454</td>
</tr>
<tr>
<td>Skin (without fat)</td>
<td>3194</td>
<td>3075</td>
</tr>
<tr>
<td>Skin (with 4mm fat)</td>
<td>2407</td>
<td>2369</td>
</tr>
<tr>
<td>Fat</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Blood</td>
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</tbody>
</table>

Table A.1: Resistivity measurements for structures and organs present in a pig’s thorax. The values were measured at 50 and 100 kHz and compared with a meta-analysis study (Adapted from [25], [A] corresponds to [14]).
## Appendix A. Thoracic Tissue Bioimpedance Values

Table 9.1: Typical values of resistivity for biological tissues present within the thoracic cavity of a pig, measured at 50 kHz and 100 kHz. Comparison to values from a meta-analysis study is provided as well.

<table>
<thead>
<tr>
<th>Biological tissue</th>
<th>Measured resistivity F=50 kHz</th>
<th>F=100 kHz</th>
<th>From [1]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collapsed lung</td>
<td>3179</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Inflated lung</td>
<td>6210</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>950</td>
<td>5.10 × 10^7</td>
<td></td>
</tr>
<tr>
<td>Chest wall muscle</td>
<td>672</td>
<td>200</td>
<td></td>
</tr>
<tr>
<td>Full chest wall</td>
<td>1373</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Rib, with muscular interstice</td>
<td>855</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Heart (filled with blood)</td>
<td>532</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Heart wall</td>
<td>551</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Skin (without fat)</td>
<td>3194</td>
<td>500</td>
<td>- 10^5</td>
</tr>
<tr>
<td>Skin (with 4mm fat)</td>
<td>2407</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>7000</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>&lt; 200</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

Inflated lung: ~ 6000 Ω cm
Bone: ~ 1000 Ω cm
Fat: ~ 7000 Ω cm
Skin: ~ 3000 Ω cm
Heart wall: ~ 500 Ω cm
Blood: < 200 Ω cm
Air: ~ inf Ω cm

Figure A.1: Thoracical impedance distribution in a human. Impedance values are according to Table A.1 and [14] (Adapted from [25], the thoracic image was adapted from [32]).
Appendix B

Experiment Appendices

B.1 Madrid Experiment

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Arterial BP [mmHg]</th>
<th>Mean Arterial BP [mmHg]</th>
<th>Mean Pulse [bpm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-4</td>
<td>Bolus injections into ascending aorta</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5-7</td>
<td>Bolus injections into right ventricle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-10</td>
<td>Bolus injections into pulmonary artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11 - Baseline</td>
<td>132/100</td>
<td>117</td>
<td>116</td>
</tr>
<tr>
<td>12</td>
<td>123/88</td>
<td>106</td>
<td>98</td>
</tr>
<tr>
<td>13 - Hypertension</td>
<td>121/90</td>
<td>107</td>
<td>113</td>
</tr>
<tr>
<td>14</td>
<td>150/120</td>
<td>135</td>
<td>128</td>
</tr>
<tr>
<td>15</td>
<td>157/123</td>
<td>139</td>
<td>121</td>
</tr>
<tr>
<td>16</td>
<td>160/124</td>
<td>142</td>
<td>125</td>
</tr>
<tr>
<td>17</td>
<td>134/91</td>
<td>115</td>
<td>126</td>
</tr>
<tr>
<td>18</td>
<td>99/56</td>
<td>83</td>
<td>121</td>
</tr>
<tr>
<td>19 - Hypotension</td>
<td>88/55</td>
<td>74</td>
<td>127</td>
</tr>
<tr>
<td>20</td>
<td>90/58</td>
<td>76</td>
<td>122</td>
</tr>
<tr>
<td>21</td>
<td>77/46</td>
<td>63</td>
<td>116</td>
</tr>
<tr>
<td>22</td>
<td>81/53</td>
<td>68</td>
<td>110</td>
</tr>
</tbody>
</table>

Table B.1: Overview of the Madrid experiments describing the most important hemodynamic parameters for the experiments of interest.

B.2 Heart EIT-MRI Experiment

The following four pages contain a blank study protocol of the ETHZ EIT-MRI experiment to show what exactly has been measured.
Study protocol for the study of heart-related EIT signals with 4D MRI validation

Status: 08.03.2013, created by Fabian Braun and updated by SHB / fbn

**Biometric parameters:**

Date of birth [dd.mm.yyyy]:

Gender:

Weight: [cm]:

Height: [cm]:

Circumference above breast line formed by the two nipples [cm]:

Circumference below breast line formed by the two nipples: [cm]:

Arm span (to measure arm span volunteer should stand with the heels against a wall, arms stretched out to a maximum reaching with the middle finger of one hand into the corner of the room, measurement is from wall to middle finger of free hand) [cm]:

**1st EIT measurements:**

Same position as in the MRI with volunteer lying on the back, arms relaxed and stretched out along body.

**Belt positions:**

1. Oblique belt position as defined by Swisstom’s belt the middle of which running dorsally 20 cm below C7 and ventrally on the “under breast line” (line defining the “under bust girth” of a bra)

2. Transverse belt at level of Th 10. Dorsally this plane runs between processi spinosi of Th 9 and 10 which should be located ventrally about 6.7 cm below the nipple line through the ventral space between rips 5 and 6 (more towards rib 6) at MCL and the tip of the processus xiphoideus.

3. *(optional, if enough time available, only in 2nd measurement)* Displace the transverse belt +/- 3cm in longitudinal direction and perform only expiratory apnea to reveal difference in heart signals due to too high/low placed belts.

Take the following EIT measurements and record each one of them in a separate file:

At the beginning of every single recording the ECG and EIT recording must be synchronized (sync. button AND hit on chest).

I. **OBLIQUE BELT**
1. Respiration (necessary at all???)
   a) Quiet breathing for at least 1 minute
   b) Deep breathing for at least 1 minute
2. Short period of quiet breathing followed by the longest possible apnea at relaxed expiration (must reveal cardiogenic oscillations)
   - This is repeated until at least a total of 200 heartbeats during apnea are recorded
   \[ \text{Total required apnea time of } 200 \text{s at heart rate of } 60 \text{bpm} \Rightarrow \sim 7 \text{ apnea of 30 seconds} \]
3. Short period of quiet breathing followed by the longest possible apnea at relaxed inspiration (must reveal cardiogenic oscillations)
   - This is repeated until at least a total of 200 heartbeats during apnea are recorded
   \[ \text{Total required apnea time of } 200 \text{s at heart rate of } 60 \text{bpm} \Rightarrow \sim 7 \text{ apnea of 30 seconds} \]

Repeat the exact protocol of above with a

II. STRAIGHT BELT

Documentation of belt position:
- Document belt position by photo
- Mark belt position on body surface with marker pen.
- Take photo showing the marks
- Remove EIT belt
- Apply belt phantom (silicon tube filled with water or oil) to middle line of EIT belt’s position for visualization in MR scan

EIT Device Settings (please complete):
- Device Type (SW and HW Versions) = ???
- NUMBER_ELECTRODES = ???
- EXCITATION_FREQUENCY = ???
- SWITCH_SETTLING_TIME = ???
- INJECTION_PATTERN = (skip) ???
- IMAGE_RATE = ???
- INJECTION_CURRENT = ???
MRI analysis:

- The volunteer enters the MR suite wearing the phantom belt in oblique EIT belt position.
- Lying on the back, arms’ position is relaxed and stretched out along the body.
- All the experiments are first performed in expiratory apnea (if not otherwise stated): Short period of quiet breathing followed by the longest possible apnea at relaxed expiration.

I. **Survey scan (belt phantom in oblique plane):**

1. Quiet breathing, deep expiration and full thoracic MRI scan at expiration hold
2. Quiet breathing, deep inspiration and full thoracic MRI scan at inspiration hold

**Aim:** These images will be used create a 3D model of thorax, heart and lungs for reconstruction.

- Static scan in apnea showing full thorax at height of EIT belt
- Acquire sufficient 2D slices of transversal plane such that +/- 10cm above and below of belt phantom are covered.
- Lungs, heart, full thorax outline and also belt phantom must be visible and distinguishable.

II. **4D Cardiac scan:**

1. Short period of quiet breathing followed by the longest possible apnea at relaxed expiration
2. These procedure is repeated until enough slices are recorded

**Aim:** These images will be used to create a dynamic 3D model of the beating heart and its surroundings moving at cardiac frequency. The model is used for simulating the genesis of heart-related EIT signals.

- The heart is scanned dynamically in apnea along its longitudinal axis (oblique plane).
- Sufficient 2D slices of about 6mm thickness are acquired such that the whole heart is covered. (Multiple apnea segments will be necessary to cover all the slices.)
- The scans are acquired dynamically such that for every slice around 20 images at different times in the cardiac cycle are available (these images contain information about sampling time relative to last R-peak and R-R interval information).
- The FOV, spatial resolution, contrast is as discussed based on an example image.

III. **Respiratory heart-movement scans:**

1. Slow and quiet breathing

**Aim:** Show heart movement due to respiration and understand respiration induced heart movement.

- Dynamic scan along the longitudinal axis of the heart (oblique plane) is taken during respiration.
- One single 2D slice in the middle of the heart is acquired over time of some breaths.
- The scan is then repeated with switching to transversal plane.
IV. **Survey scan (belt phantom in transversal plane):**

- The belt phantom is displaced from oblique to transversal position and the survey scan - as described above – is repeated with this belt configuration.

**MRI Device Settings**

- Device Type =
- ECG Type =
- Sequence Settings Survey Scan =
- Sequence Settings 4D Cardiac Scan =
- Sequence Settings Respiratory Movement Scan =

If the results are sufficient and there remains enough time one can perform further experiments with trying imaging the cardiac scans in different planes or the whole images at inspiratory apnea.
Appendix C

Hints for Using EIDORS

C.1 Netgen FEM Mesher

When one wants to create a new FEM model based on CT data using the Netgen mesher it can turn out to be quite a tedious task. Netgen crashes or simply hangs while trying to generate a FEM model. Below you find some hints which could help with the creation of a model.

1. First, read the Netgen EIDORS FAQ on:
   [http://eidors3d.sourceforge.net/faq.shtml#netgen](http://eidors3d.sourceforge.net/faq.shtml#netgen)

2. Start building the minimal model with no electrodes and only the outline shape:

   ```
fmdl = ng_mk_extruded_model({2,trunk,[4,50],.1},...
   [0,0],[0.1 0 0.05]);
   ```

3. If this worked fine try adding the inside shapes one-by-one:

   ```
fmdl = ng_mk_extruded_model({2,{trunk, lung1},[4,50],.1}, ...
   [0,0],[0.1 0 0.05]);
   ```

   - Try smoothing the shapes using `fourier_fit(trunk)` as described in the FAQ.
   - Reducing the number of points in the shape, changing the sense of rotation (`lung1 = flipud(lung1)`) or the starting point (`lung2 = circshift(lung2, 4)`) might help.

4. If this worked fine add the electrodes:

   ```
fmdl = ng_mk_extruded_model({2,{trunk, lung1, lung2},[4,50],.1},...
   [electh,1+0*electh],[0.1 0 0.05]);
   ```

   - Here you can try to discretize the angle (see the FAQ) to avoid failure due to electrodes which are located exactly opposite of each other.
C.2 Dixtal Stimulation Patterns

This appendix quickly explains the exact impedance measurement and stimulation sequence in Dixtal devices.

The 1024 samples in one frame of the resulting voltage vector: \( v_{\text{Eit}}[1024][\text{nFrames}] \) consists of the following measurements and is also explained by the pseudo-code further below:

- The first 32 measurements are performed with electrodes 1 and 5 injecting a current.
  - Measurement 1 is the voltage measurement between electrodes 1 and 5
  - Measurement 2 is the voltage measurement between electrodes 2 and 6
  - Measurement 3 is the voltage measurement between electrodes 3 and 7
  - etc.
  - Measurement 32 is the voltage measurement between electrodes 32 and 4
- Measurement 33-64 are performed with electrodes 2 and 6 injecting a current.
- etc.
- Measurement 993-1024 are performed with electrodes 32 and 4 injecting a current.

\[
\text{elOffset} = 4; \\
\text{injectingElectrode1} = \text{zeros}(1,32 \times 32); \\
\text{injectingElectrode2} = \text{zeros}(1,32 \times 32); \\
\text{measuringElectrode1} = \text{zeros}(1,32 \times 32); \\
\text{measuringElectrode2} = \text{zeros}(1,32 \times 32);
\]

\[
\text{for } i\text{Injecting} = 1 \text{ to } 32 \\
\quad \text{for } i\text{Measuring} = 1 \text{ to } 32 \\
\quad \quad \text{injectingElectrode1}[(i\text{Injecting}-1)\times32 + i\text{Measuring}] = i\text{Injecting}; \\
\quad \quad \text{injectingElectrode2}[(i\text{Injecting}-1)\times32 + i\text{Measuring}] = \text{modulo}(i\text{Injecting} + \text{elOffset} - 1, 32) + 1; \\
\quad \quad \text{measuringElectrode1}[(i\text{Injecting}-1)\times32 + i\text{Measuring}] = i\text{Measuring}; \\
\quad \quad \text{measuringElectrode2}[(i\text{Injecting}-1)\times32 + i\text{Measuring}] = \text{modulo}(i\text{Measuring} + \text{elOffset} - 1, 32) + 1;
\]

The number of unused electrodes (offset) can sometimes vary but was constant at 4 for our experiments. This can be verified by plotting the so-called U-shapes and extracting the difference in location of the extrema which give rise to when the injecting and measuring electrodes were the same: \( \text{plot}(\text{squeeze} (\text{sum}(v_{\text{Eit}}))) \);

The Dixtal-specific simulation sequence (including standard interleaving: 1, and offset of 4) for EIDORS can be generated with the newly created function:
\[
[\text{stim, meas_select}] = \text{generateDixtalStimulationPattern}(1, 4);
\]
Appendix D

Detailed Results for Ventricular Derivative Approach

This appendix contains the detailed result of the ventricular derivative approach analysis. For each experiment analyzed, the ensemble averaged temporal signals (green: ECG, blue: PA pressure, black: heart ROI impedance $I_V(t)$ and its derivative $\frac{dI_V(t)}{dt}$ in red, red dotted line and red circle correspond to PEP$_{Ref}$ and PEP$_{EFF}$, respectively) are shown in the left column with the corresponding power image at cardiac frequency (the heart ROI is delineated in black) in the right column.

For the two pigs (Arthur and Marco), which showed good results all the experiments are shown in Appendix D.1 whereas for the pigs (Paco, Roy, Rudolph, Sancho) showing unsatisfactory results, two experiments per pig are presented in Appendix D.2.

Please note that with the main focus on the shape and temporal evolution all the signals have been normalized for visualization in one single plot.

D.1 'Good' Pigs
APPENDIX D. DETAILED RESULTS FOR VENTRICULAR DERIVATIVE APPROACH

EA Signals: _arthur_10_24_2006−07_47_54PM_sr1_conv.vol

\[ \text{PEP}_{\text{Est}} = 31.9 \text{ms}, \text{PEP}_{\text{Ref}} = 47.9 \text{ms}, \text{Abs.Error} = 16.0 \text{ms} \]

EA Signals: _arthur_10_24_2006−09_34_36PM_sr2_conv.vol

\[ \text{PEP}_{\text{Est}} = 35.9 \text{ms}, \text{PEP}_{\text{Ref}} = 47.9 \text{ms}, \text{Abs.Error} = 12.0 \text{ms} \]

EA Signals: _marco_10_23_2006−02_40_27PM_mp4−pre_conv.vol

\[ \text{PEP}_{\text{Est}} = 55.9 \text{ms}, \text{PEP}_{\text{Ref}} = 55.9 \text{ms}, \text{Abs.Error} = 0.0 \text{ms} \]
APPENDIX D. DETAILED RESULTS FOR VENTRICULAR DERIVATIVE APPROACH

D.2 ‘Bad’ Pigs

- EA Signals: _paco_10_16_2006−02_44_48_mp4+pos_conv.vol
  - PEP\textsubscript{Est}=47.9ms, PEP\textsubscript{Ref}=87.9ms, Abs.Error=39.9ms

- EA Signals: _paco_10_16_2006−03_36_42_mp4menospr_conv.vol
  - PEP\textsubscript{Est}=35.9ms, PEP\textsubscript{Ref}=127.8ms, Abs.Error=91.9ms

- EA Signals: _roy_10_26_2006−03_53_19PM_seletiva_conv.vol
  - PEP\textsubscript{Est}=63.9ms, PEP\textsubscript{Ref}=55.9ms, Abs.Error=8.0ms

- EA Signals: _roy_10_26_2006−07_44_29PM_hc1_conv.vol
  - PEP\textsubscript{Est}=147.8ms, PEP\textsubscript{Ref}=127.8ms, Abs.Error=20.0ms
APPENDIX D. DETAILED RESULTS FOR VENTRICULAR DERIVATIVE APPROACH

EA Signals: _rudolph_02_12_2007−02_05_02PM_mbv_conv.vol

PEP_{Est}=51.9ms, PEP_{Ref}=71.9ms, Abs.Error=20.0ms

Power Image with Heart ROI

EA Signals: _rudolph_02_12_2007−04_45_40PM_mp4menospo_conv.vol

PEP_{Est}=51.9ms, PEP_{Ref}=59.9ms, Abs.Error=8.0ms

Power Image with Heart ROI

EA Signals: _sancho_10_20_2006−01_22_28_mbv_conv.vol

PEP_{Est}=16.0ms, PEP_{Ref}=107.8ms, Abs.Error=91.9ms

Power Image with Heart ROI

EA Signals: _sancho_10_20_2006−02_38_20_mp4−pre_conv.vol

PEP_{Est}=28.0ms, PEP_{Ref}=39.9ms, Abs.Error=12.0ms

Power Image with Heart ROI
Appendix E

ESICM Abstract

Abstract Preview - Step 3/4
- print version -

Topic: 10. Imaging in intensive care
Title: INVESTIGATION ON THE ORIGIN OF CARDIOGENIC ACTIVITY IN ELECTRICAL IMPEDANCE TOMOGRAPHY (EIT)

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Text:

Introduction. Electrical Impedance Tomography (EIT) is a functional imaging technique successfully used to monitor ventilation. Being non-invasive and low cost, EIT is an appealing candidate for a new generation of hemodynamic monitors. Recent works describe the use of EIT to measure hemodynamic parameters such as blood pressure [1] or stroke volume [2].

Objectives. This study aimed at testing the hypothesis that cardiogenic EIT activity in pigs is dominated by heart movement phenomena rather than changes in blood volume.

Methods. Twelve piglets were anesthetized and mechanically ventilated in the supine position. EIT data were recorded using the Enlight® device (Timpel SA, Brazil) with 32 equidistantly placed electrodes. ECG and pulmonary artery pressure (PAP) were recorded synchronously. Image reconstruction was performed with EIDORS [3] using the GREIT approach and a 3D pig shaped thorax model. Two independent maneuvers were performed for each pig.

Pulsatility maneuver: ventilation was interrupted for 30 seconds while cardiogenic-induced impedance changes were recorded using ECG-gated ensemble averaging [1]. Cardiac pulsatility power images were generated by calculating the pixel-wise temporal standard-deviation of the averaged impedance tracings, localizing the position of maximum heart-related impedance change.

Bolus injection maneuver: ventilation was interrupted for 30 seconds while a hypertonic saline bolus was injected into the right ventricle. Bolus-induced impedance changes were retrieved by band-pass filtering the recorded sequence of EIT images, localizing the position of maximum blood flow within the heart chambers.

Results. Figure 1a illustrates the location of maximal pulsatility power as outlined by the two black lines does not match with the position of the heart chambers identified during bolus injection (yellow pixels) in Figure 1b and 1d. The two cardiogenic centers of activity depicted by pulsatility images appear in the region where the heart interacts with the surrounding tissue. These results were found consistently in all pigs.
Conclusion. There is a clear mismatch between the heart region localized by 1) cardiogenic pulsatility images and 2) hypertonic bolus injections. We therefore hypothesize that, in pigs, cardiogenic EIT activity might be dominated by heart movement phenomena rather than changes in blood volume.

Reference(s).
Bibliography


