Abstract
Noninvasive electrocardiographic imaging (ECGI) is a novel imaging technique that reconstructs epicardial (heart-surface) potentials from measured body-surface potentials and geometrical information on the torso and heart. In this thesis, a simplified model of the propagation and reconstruction of electrostatic potentials is used to investigate the mathematical foundation and medical implications of ECGI. We show that in principle it is possible to reconstruct heart-surface potentials. We furthermore conclude that error occurs when the heart size differs from the assumed heart size, and a higher error is present when the heart location differs. In addition, the validation of ECGI and its applications are mentioned. We end this thesis with the conclusion that ECGI carries the potential to become a valuable imaging tool for the electrical activity of the human heart.

1 Introduction
Heart diseases have an enormous impact on society and health care. They are the world’s leading cause of death. Unfortunately, diagnosing cardiac disorders and also imaging of normal structure or function of the heart is far from perfect, especially with regard to the imaging of electrical activity. In this area, the most important tool still is the 12-lead body-surface electrocardiogram (ECG). In the nineteenth century, the observation was made that the heart has electrical activity. The usefulness of the electrocardiogram was greatly accelerated by Nobel Prize winner Willem Einthoven about a century ago. His principles are the foundations of today’s practical use of the electrocardiogram. Although ECGs can be made fast, their connection to the heart’s physiology is not always apparent. We aimed at developing a more sophisticated imaging tool.

A novel imaging technique called “noninvasive electrocardiographic imaging” (ECGI) has been developed by using body-surface recordings of electrostatic potentials. This technique allows for detailed imaging of electrical activity of the heart. Thus, it is noninvasive and safe, and carries the potential to greatly enhance the field of cardiac medicine. This thesis aims to investigate both the mathematical foundations and the medical implications of ECGI.

1.1 ECGI background
The purpose of ECGI is to visualize and quantify the cardiac-electrostatic potentials from the body-surface potentials. These cardiac potentials spread throughout the body, also arriving at the body surface. The body-surface potentials can be measured with electrodes on the skin of the torso. For a standard ECG, 12 electrodes are used. ECGI uses a multitude of electrodes (typically two- to three hundred): the body-surface potentials are determined with a much higher resolution in ECGI than in an ECG. This supports ECGI in determining the electrical activity of the heart with more detail.

ECGI reconstructs the heart-surface (epicardial) potentials from body-surface potentials. The location and shape of the heart is determined by means of computed tomography (CT) and is used as anatomical reference for comparison with electrical maps of the heart. The physical dependence of the torso potentials on the heart potentials is determined by taking body geometry and composition into account. Then, using a vest consisting of a large number of electrodes, potentials on the body surface are measured. Using knowledge about the body’s geometry and composition, these body-surface potentials are reconstructed on the heart surface. This yields electrostatic potentials on the epicardium.

1.2 Thesis goal
In this thesis, ECGI is investigated in a simplified model, which consists of a heart and a torso as in Figure 1. Electrostatic potentials resulting from heart potentials map onto the body surface. Using these body-surface potentials, the electrostatic potentials on the heart can be reconstructed, and compared to the original, known potentials. The goal of this research is to investigate both the mathematical foundations and the medical implications and limits of ECGI.
It aims to visualize and quantify the electrical activity of the heart. Electrocardiography is the method of graphically determining the electrical properties of the heart [5]. The epicardial surface could be such a surface. The field on any other enclosing surface (such as the body surface) has, in principle, a one-to-one relation with the potential distribution on the inner (epicardial) surface. So, we have an inner heart surface and an outer body surface. The mathematical problem then is solving Laplace’s equation for the volume between those two surfaces, as explained by Lines [4] and others. Laplace’s equation can be written as:

$$\nabla^2 \Phi = 0 \text{ in volume } V$$  \hspace{1cm} (2)

in which V is the volume between the epicardial surface and the body surface, and with Φ being the electrostatic potential within the volume V. Then, the Dirichlet condition

$$\Phi = \Phi^o \text{ on heart surface } \mathcal{S}_H$$ \hspace{1cm} (3)

should hold, stating that the electrostatic potentials are the result of the epicardial potentials. Also the Neumann condition

$$\nabla \Phi \cdot \mathbf{n} = 0 \text{ on body surface } \mathcal{S}_B$$ \hspace{1cm} (4)

should hold, with n the outward surface normal. This condition is the result from the assumption that the air surrounding the body does not conduct currents [4].

By solving Laplace’s equation, we arrive at a set of equations that specify the relation between all nodes. Box 3 explains how the transfer matrix then is constructed in our method, which leads to equation 1.

$$\Phi_B = Z_{BH} \Phi_H$$  \hspace{1cm} (1)

We should note that Φ_H and Φ_B are actually functions of some spatial parameters related to the discretized heart and torso geometry. Z_{BH} is called the transfer matrix and transforms the heart-surface potentials to body-surface potentials. The mathematical formulation of the forward problem is explained in box 1. For now, assume that equation 1 is correct and that Z_{BH} depends on geometrical information only (i.e. on shape and location of the heart and torso). Then we are provided with a clear and easy method to calculate the relation between the heart- and body-surface potentials. This is a solution for the forward problem.

Inverse problem of electrocardiography

But why would we want to have a formulation for the forward problem, when we are only interested in the reversed, or inverse, problem? With the formalism de-
A torso that is homogeneous
Quasi-static propagation
Insignificant noncardiac electrical activity

According to the following equation:

$$\Phi_H = Z_{BH}^{-1} \Phi_B$$ (5)

Mathematically, the problem is not inverting $Z_{BH}$, but reducing the influence of noise. The inverse problem of electrocardiography is so called “ill-posed”. This means that little disturbances in measurement data will yield unconstrained errors in the solution, thereby making the solution useless. Since noise is always present in real world measurements, its influence should somehow be controlled or regularized. Equation 5 will therefore not be sufficient to get reliable heart potentials. Box 2 explains the mathematical foundations of this problem more in detail. For now, assume that equation 5 can be regularized and then yields correct heart potentials.

### 3 The model

In this section we will discuss the simplified model that was used to investigate the novel technique of non-invasive electrodography (ECGI) as developed by Rudy, Ramanathan and others [13].

The development of ECGI started decades ago with theoretical considerations about the forward and inverse problems. After years of experiments and overcoming mathematical problems, it developed to an application that is proving its medical usefulness. The model used in this thesis is far simpler, due to the complexity of ECGI. However, it is still able to provide a proof of concept and demonstrate the theoretical limitations of ECGI.

First, the approach that was taken by Ramanathan, Rudy and colleagues [13] is discussed. Then, our (simplified) model is explained.

#### 3.1 ECGI’s approach

The starting point in ECGI is the discretization of the heart and torso with the Boundary Element Method (BEM). This creates a mesh of each surface. Each node of the mesh can be assigned a potential and represents the electrical qualities of the heart from known body-surface potentials. The inverse problem of electrocardiography (i.e. determining the electrical qualities of the heart from known body-surface potentials) is closely related to the forward problem. In fact, if we somehow are able to inverse the transfer matrix $Z_{BH}$, we may be able to solve the inverse problem. After all, $Z_{BH}$ specifies the relation from heart- to body-surface potentials, so its inverse, denoted as $Z_{BH}^{-1}$, would give the relation from body to heart-surface potentials according to the following equation:

$$\Phi_H = Z_{BH}^{-1} \Phi_B$$ (5)

Ill-posed problems need to be regularized. Typically, this involves including additional assumptions, such as smoothness of solution. This assumption could also be used in the inverse problem of electrocardiography, since we would expect the solution to be reasonably smooth in both time and place: the potentials are not expected to change extremely from node to node or from moment to moment. In fact, the current application of ECGI uses spatial [12] and temporal [7] regularization. Another additional assumption that could be used for regularization is a bound on the norm of the solution: we know that the potentials on heart and torso will be in a certain range, thus we can express a preference for solutions that lie in this range. This, in fact, is done in Tikhonov regularization, which is used in our approach and more extensively explained in box 4.
3.2 Our approach
The same assumptions as described above hold for the model of this thesis. In our model, the heart and torso are initially represented by two eccentric spheres. Later on, a more realistic geometry is used, see Figure 1. Both heart and torso have a triangulated surface, hereby creating a surface with faces that have a minimal area and provide maximum detail.

Each node on the heart can be assigned a potential. By solving the forward problem, we can compute from this distribution of heart-surface potentials the body-surface potentials. If we then solve the inverse problem for these torso potentials (superimposed with noise for realism), we again get heart-surface potentials. By comparing these recalculated heart-surface potentials with the heart-surface potentials we started with, we can investigate the properties and limitations of ECGI.

The forward problem
The forward problem was implemented according to Barr [1]. He describes how the transfer matrix \( Z_{BH} \) for an arbitrarily-shaped heart surface within an arbitrarily-shaped torso surface can be computed. In Box 3, this method is summarized. In essence, the transfer matrix is constructed from submatrices that describe all possible relations between potentials on the heart surface and potentials on the torso surface. These relations only depend on geometrical information as shape and distance. This means that we only need to compute the transfer matrix once, even if we want to investigate different types of potential distributions. This advantage easily compensates for the amount of computational effort that is necessary to construct the transfer matrix.

With this forward solution, potentials at the torso nodes can be computed from potentials at the heart nodes. By colouring the surface triangles according to their surrounding node potentials, the potential distributions are visualized.

The inverse problem
By taking the mathematical inverse of transfer matrix \( Z_{BH} \), denoted as \( Z^{-1}_{BH} \), we can express the relation between the torso and heart potentials according to equation 5. As explained, equation 5 will not immediately result in a feasible solution: due to the ill-posedness, we need to regularize the solutions. Therefore, a Tikhonov regularization was used. In Tikhonov regularization, one tries to minimize the error with a preference for solutions with low (i.e. realistic) potential values [16]. Box 4 explains Tikhonov regularization as applied in this study.

Comparison
In summary, we apply a certain potential distribution to the heart surface, calculate the corresponding potentials on the body surface and subsequently solve the inverse problem to compute from these body-surface potentials the heart-surface potentials again. Thus, we end up with two sets of heart-surface potentials: the original ones, and the recovered ones. By comparing those two potential distributions, we can investigate the power and weaknesses of ECGI.

To compare the original and recovered heart potentials, we can express the relation between potentials on the heart surface and potentials on the torso surface. These relations only depend on epicardial and body surface potentials. We use the boundary element method to construct the transfer matrix \( Z_{BH} \) to relate the epicardial potentials \( \Phi_H \) to the body-surface potentials \( \Phi_B \) as described by equation 1. The following derivation is more extensively described in Barr [1] and MacLeod [6].

We start with Green’s second identity for two scalar, piecewise continuous position functions \( A \) and \( B \), which states that

\[
\int_S (A \nabla B - B \nabla A) \cdot \hat{n} dS = \int_V (A \nabla^2 B - B \nabla^2 A) \cdot dV
\]

where \( V \) is a volume inside the surface \( S \), and \( \hat{n} \) is the outward pointing vector of unit magnitude normal to the surface element \( dS \). Surface \( S \) can consist of several parts, and we will choose for two closed parts: an inner part (the heart surface \( S_H \)) and an outer part (the body surface \( S_B \)), with \( V \) being the volume in between.

We can use this equation to analyze voltages on the surface of a conducting volume, as long as no current sources exist between the inner and outer surface. Let’s define \( B \) as \( 1/r \), where \( r \) is the distance from observer point \( o \) (located in volume \( V \)), and \( A \) as the electrostatic potential \( \Phi \). We then arrive at the following equation:

\[
\int_S (\Phi \nabla^2 \frac{1}{r} - \frac{1}{r} \nabla \Phi) \cdot \hat{n} dS = \int_V (\Phi \nabla^2 \frac{1}{r} - \frac{1}{r} \nabla^2 \Phi) \cdot dV
\]

If there are no electrical sources within \( V \), as we assumed, then the potential \( \Phi \) satisfies the Laplace equation \( \nabla^2 \Phi = 0 \) (see Box 1), and the second term of the integral disappears. Furthermore, we can explicitly divide the surface into inner and outer portions, and use the fact that \( \nabla \Phi = 0 \) on the outer surface (since the air around the torso is assumed not to conduct current, see Box 1). This results in the following equation (see [1]):

\[
\Phi^o = -\frac{1}{4\pi} \int_{S_H} \Phi_H \frac{\hat{r} \cdot \hat{n}}{r^2} dS_H - \frac{1}{4\pi} \int_{S_H} \frac{\nabla \Phi_H \cdot \hat{n}}{r} dS_H
\]

\[
+ \frac{1}{4\pi} \int_{S_B} \Phi_B \frac{\hat{r} \cdot \hat{n}}{r^2} dS_B
\]

In this notation, \( \Phi^o \) stands for the electrostatic potential at the observer location \( \hat{r} \) for the unit vector in the direction of \( r \) and \( S_H \) and \( S_B \) for the heart and body surface respectively.

Equation 8 gives the potential at the observation point \( o \) in terms of the potential on the body surface and the potential and gradient on the heart surface. The observer can be stationed anywhere in the volume \( V \). By choosing a location very close to the inner or outer surface, \( \Phi^o \) is the same as \( \Phi_B \) or \( \Phi_H \) at the adjacent surface location. In this way, a set of simultaneous equations can be generated. Barr [1] describes this approach and constructs for each node on either surface such a discretized equation. All these equations subsequently built up the transfer matrix \( Z_{BH} \), arriving at a solution for the forward problem of electrocardiography in the form of equation 1.

Box 3: our approach to the forward problem
The forward problem of electrocardiography can be solved in terms of epicardial and body surface potentials. We use the boundary element method to construct the transfer matrix \( Z_{BH} \) to relate the epicardial potentials \( \Phi_H \) to the body-surface potentials \( \Phi_B \) as described by equation 1. The following derivation is more extensively described in Barr [1] and MacLeod [6].

We start with Green’s second identity for two scalar, piecewise continuous position functions \( A \) and \( B \), which states that

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\int_S (A \nabla B - B \nabla A) \cdot \hat{n} dS = \int_V (A \nabla^2 B - B \nabla^2 A) \cdot dV
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where \( V \) is a volume inside the surface \( S \), and \( \hat{n} \) is the outward pointing vector of unit magnitude normal to the surface element \( dS \). Surface \( S \) can consist of several parts, and we will choose for two closed parts: an inner part (the heart surface \( S_H \)) and an outer part (the body surface \( S_B \)), with \( V \) being the volume in between.

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\[
\int_S (\Phi \nabla^2 \frac{1}{r} - \frac{1}{r} \nabla \Phi) \cdot \hat{n} dS = \int_V (\Phi \nabla^2 \frac{1}{r} - \frac{1}{r} \nabla^2 \Phi) \cdot dV
\]

If there are no electrical sources within \( V \), as we assumed, then the potential \( \Phi \) satisfies the Laplace equation \( \nabla^2 \Phi = 0 \) (see Box 1), and the second term of the integral disappears. Furthermore, we can explicitly divide the surface into inner and outer portions, and use the fact that \( \nabla \Phi = 0 \) on the outer surface (since the air around the torso is assumed not to conduct current, see Box 1). This results in the following equation (see [1]):

\[
\Phi^o = -\frac{1}{4\pi} \int_{S_H} \Phi_H \frac{\hat{r} \cdot \hat{n}}{r^2} dS_H - \frac{1}{4\pi} \int_{S_H} \frac{\nabla \Phi_H \cdot \hat{n}}{r} dS_H
\]

\[
+ \frac{1}{4\pi} \int_{S_B} \Phi_B \frac{\hat{r} \cdot \hat{n}}{r^2} dS_B
\]

In this notation, \( \Phi^o \) stands for the electrostatic potential at the observer location \( \hat{r} \) for the unit vector in the direction of \( r \) and \( S_H \) and \( S_B \) for the heart and body surface respectively.

Equation 8 gives the potential at the observation point \( o \) in terms of the potential on the body surface and the potential and gradient on the heart surface. The observer can be stationed anywhere in the volume \( V \). By choosing a location very close to the inner or outer surface, \( \Phi^o \) is the same as \( \Phi_B \) or \( \Phi_H \) at the adjacent surface location. In this way, a set of simultaneous equations can be generated. Barr [1] describes this approach and constructs for each node on either surface such a discretized equation. All these equations subsequently built up the transfer matrix \( Z_{BH} \), arriving at a solution for the forward problem of electrocardiography in the form of equation 1.
Box 4: Tikhonov regularization

As explained in box 2, the ill-posed inverse problem needs regularization. In our approach, this is achieved with Tikhonov regularization. With this type of regularization, an ill-posed system of linear equations $Ax = b$ is replaced by the problem of seeking an $x$ to minimize

$$
\|Ax - b\|^2 + \alpha^2 \|x\|^2
$$

for some suitably chosen regularization parameter $\alpha > 0$. For the inverse equation 5, this would become (see [8]):

$$
\min_{\Phi_H} \left[ \|Z_{BH}^{-1}\Phi_H - \Phi_B\|^2 + \alpha^2 \|R\Phi_H\|^2 \right]
$$

In this formulation, $R$ is either:
- the unit matrix (Tikhonov zero-order)
- the surface gradient operator (Tikhonov first-order)
- the surface Laplacian operator (Tikhonov second-order)

Since research has demonstrated that the results are not significantly different in either choice, we choose for $R$ being the unit matrix.

The first term of equation 10 represents the least-square solution of the inverse problem as described by equation 5. The second term imposes bounds on the amplitude of the solution, and $\alpha$ controls the degree of the imposed constraint. When $\alpha$ is small, the first term dominates, giving the least-squares solution priority. A larger value of $\alpha$ makes the solution more constrained. The best choice for $\alpha$ balances accuracy and stability of the solution. In our study, $\alpha$ was fixed to a somehow arbitrarily chosen value.

There is a direct solution to problem 10, namely

$$
\Phi_H = \left( Z_{BH}^{-1} \right)^T Z_{BH}^{-1} \alpha R^T R^{-1} \left( Z_{BH}^{-1} \right)^T \Phi_B
$$

This equation yields a regularized solution of the inverse problem. Thus, when we want to calculate the electrostatic heart-surface potentials, we will solve equation 11 instead of equation 5.

When multiplied by 100, the relative RMSE can be interpreted as the error percentage relative to the highest original heart potential.

The root mean square differences do not take any physiologically important features into account. Unfortunately, there is no better metric available that objectively, quantitatively evaluates the difference among distributions, and also is physiologically justified [5]. Therefore, we have to use the root mean square error, rating low values as advantageous and high values as disadvantageous.

Data

The data used in this study was mainly extracted from ECGSIM, a simulation program to investigate ECG, created by Van Oosterom and Oostendorp [15]. Both geometrical data for heart and torso, and heart-surface potentials were extracted from their simulation. Also a more simple model was used, consisting of eccentric or concentric spheres. The heart-surface potentials for this model were determined by a dipole at the heart’s centre and carry little resemblance with physiological potentials.

4 Experiments

In this section, we will discuss the investigation of our model. Several experiments have been conducted, some with a focus on the model itself, others with special attention to medical implications. Each subsection starts with an explanation and motivation of the experiment, followed by its results and their discussion.

4.1 Validation of the model: analytical

Of course it is important to check whether the model output is as expected from theory. This provides us with a means to check for correct implementation of the algorithms. The model was validated in two different ways. At first, the heart and torso were modelled as two concentric spheres. Then a dipole was placed at the centre, resulting in a potential distribution at both the heart and body surface (Figure 2). The model computed the torso potentials from the heart potentials, which then were compared to the analytically known torso potentials as described by Barr [1].

The second validation was performed in a more realistic geometry and is discussed in the next section (see 4.2).

Results

The body-surface potentials from the method are unrealistic high (standard deviation $\sigma = 49.1$) compared to the analytically expected potentials ($\sigma = 1.23$). If, however, we divide both potential distribution by their corresponding standard deviations, we end up with exactly the same values ($E_{rms,rels} = 0.0038$). This means...
Figure 2: In validation the forward problem, a concentric spheres model is used. A dipole placed at the centre results in potentials at both heart and torso surface. The torso-surface potentials can either be calculated from the heart potentials as described by the forward problem, or directly from the dipole. This enables validation of the forward solution.

Discussion
As we can see from the analytic validation, the body-surface potentials are incorrectly valued but correctly distributed. This could be the result of an error in the implementation of the solution, resulting in a defect in the transfer matrix $Z_{BH}$. Fortunately, the distribution of potentials is more important than the exact values. Moreover, as we will see from further experiments, the reconstruction of heart potentials using these “faulty” body-surface potentials yields quite accurate results (see section 4.3). So, the error in the body-surface potentials that is introduced by the transfer matrix $Z_{BH}$, is probably cancelled when the heart-surface potentials are reconstructed with help of the inverse transfer matrix $Z_{BH}^{-1}$.

4.2 Validation of the model: ECGSIM
The second validation was performed in a more realistic geometry, see Figure 1. This geometry was taken from the ECGSIM package. This simulation program also provided realistic heart- and body-surface potentials. The heart-surface potentials were fed to our model, which computed the corresponding body-surface potentials. These were compared to the body-surface potentials that were generated by the ECGSIM package itself. This way, the cardiac electric activity of one whole heart beat was simulated and compared.

Results
Again, we see that the body-surface potentials resulting from our model are too high. However, there is no apparent linear relation between the two distributions, as there was with the analytical validation. Apparently, the more complex geometry introduces a more complex error in the transfer matrix.

We can divide both the computed and the known body-surface potentials by their corresponding standard deviations. This enables us to compare the distribution of potentials in more detail, thereby omitting the fact that the absolute values are too high. If we investigate the torso potentials for one whole heart beat, we see that the root mean square error remains fairly constant under this condition. Figure 3 shows the RMSE for one heart beat. The maximum absolute potential (of the known body-surface potentials) on a certain time is also shown. It can be seen that the RMSE is relatively small compared to the maximum potential in the first 100 ms, but quite high in certain other parts of the beat.

Discussion
The results indicate again that the calculated potentials on the body surface are too high. This time, the distributions themselves do not fit as well as in the analytical validation. Especially for low potentials, the root mean square error is relatively high. However, we can make only limited conclusions here. After all, the ECGSIM package, which provided the body-surface potentials to compare with, is a simulation package itself. It uses another source to compute the body-surface potentials than does our method. Therefore, we can merely conclude that although the computed and the ECGSIM body-surface potentials display differences, this does not have to mean that our model is invalid.

Considering both the analytical and ECGSIM validation, we can conclude that although the absolute values of the body-surface potentials are too high, their distribution fits reasonably well to perfectly well the expected potentials.

4.3 Reconstruction of heart potentials
The main goal of this research is to investigate whether reconstruction of heart-surface potentials from body-surface potentials is possible. In this section, we will reconstruct heart potentials in both the analytical concentric spheres case and the more realistic geometrical situation.

First, the body-surface potentials that result from the forward solution as described by the first experiments (see the two preceding sections) are perturbed with some noise. This is necessary to take the ill-posedness of the inverse problem into account (see section 2), as noise
Electrocardiographic imaging as a medical tool

Figure 3: This figure shows the absolute root mean square error (RMSE) of the computed and known body-surface potentials during one heart beat. It also shows the maximum body-surface potential of the known body-surface potentials. Both the known and computed body-surface potentials are divided by their standard deviations, to compensate for the fact that the computed potentials are too high.

Figure 4: The reconstructed heart potentials visualized. The color indicates the potential: red represents a high potential, blue stands for relatively low potentials. SNR abbreviates for “Signal to Noise Ratio”; it represents the level of noise being added to the body-surface potentials before reconstruction of the heart potentials. A lower value for SNR stands for a higher level of noise added.

is always present in real-world measurements. Then, these body-surface potentials with noise are used to compute the inverse solution, resulting in heart-surface potentials. These reconstructed heart-surface potentials are subsequently compared to the original heart-surface potentials.

Results
The reconstructed heart potentials in the concentric spheres situation are shown in Figure 4. For three different signal to noise ratios (SNRs), the heart potentials are reconstructed. The corresponding relative root mean square error is also stated in the figure.

Using the more realistic geometrical and potential data, we can investigate the reconstruction of heart potentials during one heartbeat. Figure 5 shows the absolute root mean square error (RMSE) during one heartbeat. To create a more realistic situation, 50 dB of noise was added to the body-surface potentials used to reconstruct the heart potentials.

On time $t = 50 ms$, the highest relative root mean square error (31%) occurs. For this situation, the original and reconstructed heart distributions were compared the same way as with the concentric sphere models. This is shown in Figure 6.

Discussion
The reconstruction of heart potentials in the concentric spheres model is accurate. Not only the distribution, but also the values of the potentials fit the original heart potentials reasonably well. Apparently, the error in the transfer matrix $Z_{BH}$, which results in too high body-surface potentials, is cancelled out by the inverse transfer matrix $Z_{BH}^{-1}$ used to reconstruct the heart-surface potentials.

In the more realistic case, the root mean square error is on certain moments relatively small compared to the maximum original heart potential. However, the highest
Figure 5: The reconstructed heart potentials in the realistic situation are compared to the original heart potentials by means of the root mean square error (RMSE) between the two distributions on a certain time step. It can be seen that the RMSE is relatively low compared to the maximum potential at that time step. Note that for this figure, no correction for too high values was necessary, as was the case with Figure 3.

Figure 6: The reconstruction of heart-surface potentials with realistic geometry and potential data on time \( t = 50ms \). The reconstruction is performed for different signal to noise ratios. The corresponding relative root mean square errors are relatively high.

relative root mean square error is 31%. Whether this high error is the result of the already faulty body-surface potentials, or the reconstruction method, is not clear.

Changing the Tikhonov regularization parameter, which was fixed until now, can lower the related root mean square error. However, this has the trade-off that the spread of the distribution becomes unrealistically high. Thus, changing the regularization parameter is no direct solution to this problem, although it could be of help.

Nevertheless, this gives a proof of concept: from only the body-surface potentials and a correct transfer matrix (based on geometrical information only), the heart-surface potentials can be reconstructed.

4.4 Sensitivity to heart size and location

The geometry of the torso and heart is determined at one certain moment. However, during a heartbeat, the heart expands and moves in the torso. So, the geometrical data will not be accurate during a certain part of the heartbeat. Therefore, the sensitivity of reconstruction to both heart size and location are investigated. In this investigation, the eccentric spheres model is used. In this model, heart and torso are both represented by a sphere, as in the concentric spheres model. However, this time, the centres of the spheres are not positioned at the same location. The eccentric spheres model is more realistic than the concentric spheres model, having the heart at a more realistic location. It is less complex than the more realistic model, which enables us to focus on influences of the location and site of the heart solely.

Firstly, the model’s sensitivity to heart size is investigated. The transfer matrix \( Z_{BH,m} \) is determined with the heart having a certain radius and certain potentials. This represents the heart and torso geometry at the moment of geometrical measurement. It would be assumed to be correct by the external observer. Then, we decrease the radius of the heart to 70% of its assumed size, as could be the case in heart contraction. Then we calculate the body-surface potentials, with a transfer matrix \( Z_{BH,r} \) based on this smaller heart. This transfer matrix is the “real” transfer matrix, reflecting the actual geometry and potential propagation. The “measured” transfer matrix \( Z_{BH,m} \) is the assumed matrix, which is used to reconstruct the heart potentials. Thus, two different transfer matrices are used for the forward and inverse solution, reflecting two different sizes of the heart: the assumed (measured) size, and the real size.

Secondly, a similar procedure is used to investigate the sensitivity of the model to a transposition of the heart that is not taken into account by the assumed transfer matrix.
Results
The results of the “wrong” heart size are shown in Figure 7 in the appendix. It shows that the heart potentials reconstructed by the assumed transfer matrix $Z_{BH,m}$ are too small. Also, the root mean square error is higher than when using the correct transfer matrix. If, however, we divide both reconstructed distributions by their standard deviation, we see that they are very similar (relative root mean square error of 3.4%).

The deviating heart location results are similar, as can be seen from Figure 8 in the appendix. Again, the reconstructed heart potentials are too low. However, this time the reconstructed heart potential distribution did not fit the correct distribution as well as in the deviating heart-size case. Dividing both reconstructed distributions by their standard deviation showed that they still had important differences, reflected by a relative root mean square error that still is 16.8%.

Discussion
The heart size is of influence on the reconstruction of the heart potentials: the reconstructed heart potentials are too low when it is assumed that the heart is bigger than it actually was. The distribution of potentials, however, is the same. This means that the reconstruction still yields accurate qualitative information.

This was not the case in the deviating location of the heart: the distribution of potentials was different from the correct reconstruction. Thus, transposition of the heart introduces more error in the reconstruction than heart size differences.

5 Theoretical considerations
The theoretical basis of the described model has implications for its use in medicine. In this section, we will shed light on this subject.

5.1 Reconstruction at depth
All this time we are considering heart-surface potentials. But is it also possible to reconstruct potentials beneath the heart surface, within in the heart wall (intramural)? This would provide even more important data than the surface potentials only.

From a theoretical basis, it is not possible to directly reconstruct intramural potentials. After all, we assumed (see Section 3.1) that the potential surface (of the heart) is a closed surface which contains all electrical sources of the heart. We cannot look at deeper levels of the heart, since some electrical sources of the epicardium would then lie outside the surface of integration.

However, knowledge about the heart’s physiology could be used to calculate the most probable electrical activity on a deeper level in the heart. After all, heart-surface potentials, in contrast to body-surface potentials, provide high-resolution reflection of underlying intramural activity [13]. In canine hearts, Oster et al. [10] showed that ECGI is able to estimate the intramural depth of pacing sites. They showed that epicardial potentials have a certain dependency on the intramural depth of the intramural pacing site in a human dog placed in a human torso tank. In general, epicardial potentials during intramural pacing are characterized by a central negative region and two flanking maxima. The center of the negative region indicates the underlying pacing location, and the orientation of the maxima to each other and to the minimum can be used to approximate the intramural depth of the pacing.

6 Discussion
In this section, several aspects of this research are discussed. First, the focus is on our model. The section thereafter pays attention to the relation between our model and ECGI.

6.1 Our model
As we saw in our experiments, the forward solution resulted in body-surface potentials that were much higher than expected. We concluded that this error was probably situated in the transfer matrix $Z_{BH}$. Reconstruction of heart-surface potentials resolved the problem of too high values, which supports the hypothesis that the error in the transfer matrix $Z_{BH}$ is cancelled out by its inverse $Z_{BH}^{-1}$.

The reconstruction of heart-surface potentials from body-surface potentials yields very accurate results in the simple spheres model. When using more realistic geometrical data, this reconstruction is not as good, but still the original and reconstructed heart-surface potential distributions display similarities. We can therefore conclude that this model provides a proof of concept: it is possible to reconstruct heart-surface potentials from geometrical information and body-surface potentials.

Other experiments showed that the reconstruction is quite sensitive to (unknown) heart translocation. For heart size differences, this was less the case. Both outcomes are important for medical practice, however: the heart is very dynamical in the torso. We can therefore not just assume that the heart will be in the same size and location during the whole heart beat as it was during the acquisition of the geometrical data (by means of CT scans).

On the subject of computational time, we can say that computing the transfer matrix takes a considerable amount of time, but when this matrix is computed, measured body-surface potentials can be used to reconstruct real time heart-surface potentials.
We furthermore saw that the root mean square error (RMSE) probably is not the best metric to specify the similarity between potential distributions: distributions that visually seem similar can have quite large errors when compared with RMSE. Moreover, this metric does not take the heart’s physiology into account. No better metric is known, however.

6.2 Relation with ECGI

But to what extent can we extrapolate the above discussion to ECGI? The approach of noninvasive electrocardiography as applied by Rudy and Ramanathan [13] is more complex than our very simple model. Nevertheless, the proof of concept still stands. Although torso inhomogeneities are not taken into account and make reconstruction more complex, research has shown that this does not impose problems: torso inhomogeneities have only limited influence on body-surface potentials [11]. Furthermore, it is possible to piecewise divide the torso in volumes with a certain conductivity and apply the described approach to each surface that surrounds such a volume [5], hereby modelling the influence of lungs, blood, bone, muscle etcetera.

ECGI is extended with other methods to regularize the ill-posedness of the inverse problem. For spatial regularization, not only Tikhonov regularization is used, but also the generalized minimal residual method [12]. Furthermore, temporal information is taken into account [7]. By using the fact that electrostatic potentials will not vary extremely fast in time, more accurate reconstructions are made.

As noted in the appendix, ECGI was validated in several studies and its applications are numerous. However, it is an upcoming technique and still is in development. Standards and guidelines should be developed and experience gathered to integrate ECGI in daily medical practice.

6.3 Conclusion

We can conclude that the model described in this thesis provides proof of concept: reconstruction of heart-surface potentials is possible from geometrical information and body-surface potentials. Although our model is simplified, it has shed light on the capabilities of ECGI. Noninvasive electrocardiographic imaging carries the potential to become a valuable imaging tool for electrical activity of the heart.

References


(v. July 10, 2007, p.10)
A  Results

Figure 7: Comparison of heart reconstructions for deviating heart sizes. The left heart shows the original heart potential distribution. The middle heart shows the correct reconstruction, using knowledge about the real heart size. The right reconstruction is the result of an faulty heart size assumption: it was assumed that the heart was bigger than it really was. It is clear, that this results in lower reconstructed heart potentials.

Figure 8: Comparison of heart reconstructions for deviating heart locations. The left heart shows the original heart potential distribution. The middle heart shows the correct reconstruction, using knowledge about the real heart location. The right reconstruction is the result of an faulty heart location assumption: it was assumed that the heart was more to the centre than it really was. It is clear, that this results in different reconstructed heart potentials.

B  Medical validation and application

All the previous discussion has focused on our model and on ECGI. This section aims to handle more real-world topics. As ECGI is now brought into application, we can check whether it achieves what it promises. Furthermore, the practical application of ECGI becomes more clear, shedding light on its medical usefulness.

It is important to note that ECGI can not only reconstruct heart surface potentials, but after some process- ing can also create electrograms and activation sequences (isochrones).

B.1 Validation

Many aspects of ECGI were validated experimentally in normal and abnormal canine hearts. Oster et al. [9], for example, induced local electrocardiac events by pacing a dog heart in a human torso-shaped tank. Electrodes measured both body-surface potentials and heart surface potentials. They saw that ECGI can detect a single minimum for single-site pacing (with an accuracy of 10 mm or less) and two minima for double-site pacing (with both pacing sites at least 17 mm apart). Furthermore, ECGI was able to reconstruct epicardial potentials, electrograms and isochrones over the entire epicardial surface, during the entire heart cycle.

In another research, Ghanem et al. [2] compared ECGI’s reconstructions of heart potentials to invasive direct epicardial potentials in open heart-surgery patients. Pacing sites were localized to approximately 1 cm, and epicardial end endocardial origins of activation could be distinguished. Reconstructed electograms correlated moderately with the invasive electrograms, probably hindered by the fact that recordings of body-surface potentials were not done simultaneously with recordings of the heart-surface potentials.

B.2 Applications

Several practical applications were investigated by Ramanathan and reported in a good technical report on ECGI’s abilities [13]. First of all, ECGI could be used for research of the heart’s normal electrophysiological activity. Epicardial breakthroughs (when the activation front reaches the surface, generating a local potential minimum) can be visualized for both normal and abnormal subjects. The timing and location of these breakthrough events gives important information about ventricular activation.

In patients, ECGI can image the focal origin of impulse formation or the exit sites of re-entry pathways during atrial and ventricular tachycardia. This technique is currently applied (still on an investigational basis) to guide clinical electrophysiologists to locate the sites of catheter ablation to disrupt the re-entrant circuit or eliminate abnormal foci, especially if they are located on the epicardium. Intini et al. [3] describe how ECGI can precisely locate the origin of focal left ventricular tachycardia in a young athlete in the first clinical application of ECGI. In this case, ECGI proved is use in guiding diagnosis and therapy of a clinical tachyarrhythmia.

ECGI can prove its value in screening people for risk of life-threatening arrhythmias (e.g. after a myocardial infarction), in order to take prophylactic measures. It
can also help to investigate arrhythmias to determine the most suitable intervention or choose the best cardiac location of treatment and evaluate that treatment.