Application of an Electrocardiographic Inverse Solution to Localize Ischemia during Coronary Angioplasty

Robert S. MacLeod* Martin Gardner‡ Robert M. Miller‡ B. Milan Horáček†

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Address for correspondence: Dr. Robert S. Macleod, Nora Eccles Harrison CVRTI, Building 500, University of Utah, Salt Lake City, Utah.
Telephone: (801)581-8183, FAX: (801)581-3128,
Email: macleod@cvrti.utah.edu.

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*Nora Eccles Harrison Cardiovascular Research and Training Institute, University of Utah, Salt Lake City, Utah
†Dept. of Physiology & Biophysics, Dalhousie University, Halifax, Nova Scotia, Canada
‡Dept. of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada

Abstract

This study demonstrates the utility of an electrocardiographic inverse solution, coupled with body surface potential mapping (BSPM), in localizing acute ischemia in patients undergoing percutaneous transluminal coronary angioplasty (PTCA). PTCA balloon inflations produce complete occlusion and acute transient ischemia, which can be detected electrocardiographically with BSPM. Comparisons between maps recorded both during and before the inflation of the PTCA balloon allow patient- and artery-specific characterizations of the resulting ischemia. Knowledge of the patient's coronary anatomy and the location of the occlusion site by coronary angiography permit an estimation based on cardiac hemodynamics of the region of myocardium most likely to suffer from PTCA-induced ischemia. Electrocardiographic inverse solutions provide a means of predicting cardiac potentials from body-surface maps. In this study, we describe an inverse solution we have developed to localize the transient ischemia produced by PTCA. To validate the procedure, we compared the locations of predicted ischemia in 7 patients with a qualitative estimate of the perfusion region based on fluoroscopic examination of each patient's coronary anatomy and PTCA balloon location. In each case, the region of ischemia predicted by the model included the perfusion zone determined fluoroscopically. These results suggest that electrical changes induced by acute ischemia can be localized with an electrocardiographic inverse solution.

Introduction

The primary goal of the electrocardiographic inverse problem is to relate quantitatively electrocardiographic signals on the body surface with underlying cardiac bioelectric sources. While the most general form of the inverse problem is phrased directly in terms of intracardiac sources, such a formulation is not unique, that is, one set of body surface potentials can yield multiple source configurations. If, on the other hand, we seek to calculate potentials on the epicardial surface, it is possible to obtain a unique solution for a given body surface potential distribution [1]. This paper describes such an epicardial inverse solution, and its application to localizing transient cardiac ischemia during coronary angioplasty.

The search for computationally tractable inverse solutions in terms of epicardial potentials has its origins in the 1970's [2] and has challenged investigators interest ever since (see *eg.,* [3,4] for recent reviews). The requirements of such an inverse solution include a set of equations which are the mathematical formulation of the biophysical relationships, a description of the irregular geometry of the thorax (including the source) in an efficient and computationally amenable form, and numerical and computational methods capable of producing accurate solutions given current computational resources. Once generated, solutions must be validated in order to establish realistic limits of accuracy so that the results may eventually be used in appropriate clinical applications.

Experimental validation of an inverse solution can take two forms, either *direct* validation, in which experimental conditions permit simultaneous measurements of both body-surface and epicardial potentials, or *indirect* validation, in which either the body or the epicardial potential distributions are not directly available but can be predicted from other measurements. Examples of the former approach include studies with instrumented animal preparations [5,6] and torso-shaped electrolytic tanks [7–9]. The use of animal preparations, especially those in which a perfused heart is submerged inside an electrolytic torso tanks, allows good control of measurement conditions and provides a geometrical and physical arrangement which can be well represented in a computer model [7]. The technical requirements of such systems, however, are considerable and available to only a few laboratories. The indirect approach has been employed in the calculation of epicardial and endocardial activation sequence maps in humans [10]. While this strategy offers much less control, it can provide valuable insight into both the actual and potential capabilities of such a procedure in clinical medicine. The primary difficulty lies in linking the quantity intrinsic to the model (*eg.,* epicardial potentials or isochrones) with another quantity that can be measured directly, ideally noninvasively.

We have developed a solution to the inverse problem in terms of epicardial potentials and in this paper we present results from an indirect validation study on human subjects. We measured body surface potentials in patients undergoing percutaneous transluminal coronary angioplasty (PTCA), a procedure which involves dilating a partially occluded coronary artery with a balloon-

tipped catheter for periods of from 10 to 120 s. PTCA has been referred to as a "controlled model of ischemia" in humans [11] because during the balloon inflation, distal blood flow is completely blocked, resulting in acute, transient ischemia. The results of this ischemia have been detected via numerous physiologic parameters, including cardiac function [12,13], hemodynamics of coronary perfusion [14] and body-surface electrocardiograms (ECGs). The latter studies have dealt with changes in ST segments and T waves [15], QRS complexes [16], and with body surface potential distributions [17–19].

The inverse solution itself is a discrete approximation of a system of integral equations which govern the relationship between electric potentials on the heart and body surfaces. The geometrical model which underlies this particular solution is a realistic model of the human thorax which was considered homogeneous in conductivity, that is, it contained only the heart and body surface and the region between the two (the volume conductor) had a constant, scalar conductivity. The numerical method used to formulate and solve the integral equations was the boundary element method, with linear variation over the triangular surface elements of the geometric model.

Body surface potential distributions recorded from each patient during angioplasty provided input data to the inverse solution, which in turn produced epicardial distributions estimating the corresponding epicardial potentials. The PTCA procedure facilitates detection and quantitative characterization of ischemic changes because the patient can be measured before, during, and after inflation; the patient provides the control for each inflation. Comparison of the estimated epicardial maps from before and during balloon inflation reveal local electrophysiological changes associated with the PTCA induced ischemia.

For the purpose of indirect validation of the inverse solution, we have linked the geometry of the coronary arteries of the patients and the location of the balloon at inflation with the predicted location of ischemia. Since the occlusion produced by the balloon is complete, we assumed that, barring extensive collateral circulation, there would be ischemia in the region normally perfused by the occluded artery and that this ischemia would produce electrocardiographic changes detectable through the inverse solution.

The aim of the study was then to evaluate our inverse solution using an indirect validation approach based on acute, local, PTCA induced ischemia. While validation of this sort can only be qualitative in nature, it nevertheless reveals important aspects of the accuracy and the clinical utility of the inverse solution.

Materials and Methods

The forward solution

To generate the inverse solution involved first solving the forward problem — calculating body-surface potentials in terms of epicardial potentials. For this, we made use of Green's theorem

and the boundary element method, as described in [2, 20, 21] and summarized in Appendix A. This formulation yields a matrix description of the forward problem, which can be stated as

$$\Phi_B = Z_{BH}\Phi_H, \tag{1}$$

where Φ_B is a set (vector) of body-surface potentials, Φ_H is a set of epicardial potentials, and Z_{BH} is the "forward transfer coefficient matrix". Z_{BH} contains all the geometric and conductivity information from the model geometry and is therefore unique to the particular geometry, but independent of the potentials on either epicardial or torso surface. To create Z_{BH} for anything but the simplest of geometries requires numerical computation and the details of this are described elsewhere [21]. Once Z_{BH} has been computed, converting epicardial potentials to body surface potentials and, thus, solving the forward problem, is a simple matter of matrix multiplication.

One of the key numerical issues in the forward problem is the trade-off between the spatial resolution of the geometrical model and the level of complexity with which each discrete element — in our case, triangle — of the model is treated. Higher spatial resolution increases the number of elements (and therefore equations), while more complexity adds to the computational overhead of the calculations and there is no simple relationship which can predict the net result on solution accuracy. The earliest solutions to the forward problem in electrocardiography, limited as they were by the existing computational resources, employed both relatively large (and hence few) elements, and assumed that the potential remained constant over each element [2]. Somewhat later studies increased the complexity by subdividing elements and assigning an interpolated potential to each sub-element [10, 22]. Not until the work of Messinger-Rapport and Rudy [20], based, in turn, on earlier work from mechanical engineering applications of the boundary element method by Cruse [23], were elements with truly linear variations in potential used. See Appendix B for a more detailed description of both forms of boundary elements. The model described here contains similar numbers of elements as those in [22], [3], and [10], but allows either subdivided or linear boundary elements to be used for computing.

The inverse solution

Once a satisfactory forward solution exists, we must somehow *invert* the process so that epicardial potentials can be predicted from body surface measurements. It is well established, however, that the inverse problem is *ill-posed* in the sense that small variations in any of the input values can produce unbounded oscillations in the output. The most successful means devised to compensate for the ill-posed nature of the inverse problem is to apply what is know as *regularization*, by methods first outlined by Tikhonov [24]. The theory and application of this method have been well described in the literature (*eg.*, [3]) so that for our purposes it is sufficient to write only the expression for the regularized inverse transfer coefficient matrix Z_{HB} as

$$Z_{HB} = \left(Z_{BH}^T Z_{BH} + tM\right)^{-1} Z_{BH}^T. \tag{2}$$

where Z_{BH}^T is the transpose of Z_{BH}. The matrix M is either the identity matrix I, or is derived from the gradient operator matrix G or the Laplacian operator matrix L. The scalar t is known as the *regularization parameter* and must be set beforehand based on either previous results or *a priori* knowledge of the problem. We can view regularization as a means of constraining or smoothing the solution, with the choice of the matrix M and the regularization parameter t determining the nature and extend of that smoothing. Hence the methods used to select M and t are critical to the problem.

Once regularized, the inverse solution is again a matrix of transfer coefficients, Z_{HB}, which relates epicardial (H) potentials to body surface (B) potentials as follows:

$$\Phi_H = Z_{HB} * \Phi_B, \tag{3}$$

One need only multiply each set of body-surface potentials by Z_{HB} to generate the corresponding set of predicted epicardial potentials.

To select the smoothing operator M and the regularization parameter t, we computed both epicardial and torso potentials directly using a single dipole source placed in the model torso geometry (see next section) [25]. We then generated inverse solutions which were regularized with each of the three variations on M, and optimized t for each set of results.

Calibration data

One way to test the validity of the forward and inverse solutions is to generate epicardial and body surface distributions from discrete sources. This is not a true validation, since discrete sources are only an approximation of the actual complex cardiac activation, but any general forward/inverse solution which does *not* agree with the discrete simulations must be viewed with skepticism.

For this study, we placed a single unit current dipole in a location corresponding to the mid-septum of the heart and oriented it along the three orthogonal axes of the torso geometry. We then computed both epicardial and body surface potentials with the same homogeneous, bounded torso volume conductor as we used in the full forward/inverse solution. The results, in the form of three sets of epicardial and body-surface potentials, became the reference, or *simulated* potentials against which all direct (*i.e.,* surface to surface) computations were compared. To test the accuracy of the forward solution, we took the simulated epicardial potentials, calculated torso potentials using the forward solution, and compared these with the simulated torso potentials. To test the inverse solution, we took simulated torso potentials, computed epicardial potentials, then compared these with simulated epicardial values.

Difference measures

The numerical measures of differences between potential distributions we used were:

Maximum Error: absolute maximum difference between the predicted and actual values.

Root-Mean-Square (rms) Error:

$$E_{rms} = \sqrt{\frac{\sum_{i=1}^{N}(\Phi_i^c - \Phi_i^a)^2}{N}}, \tag{4}$$

where Φ^c are the computed and Φ^a the actual potentials.

Relative Error: this is essentially the rms error normalized by the actual values according to

$$E_{rel} = \sqrt{\frac{\sum_{i=1}^{N}(\Phi_i^c - \Phi_i^a)^2}{\sum_{i=1}^{N}(\Phi_i^a)^2}}. \tag{5}$$

E_{rel} is zero for two identical sets of values Φ^a and Φ^c.

Correlation Coefficient: geometrically, we can picture this as the cosine of the angle between the vectors of potentials, which is computed by the expression

$$CC = \frac{\vec{\Phi^c} \cdot \vec{\Phi^a}}{|\vec{\Phi^c}||\vec{\Phi^a}|}. \tag{6}$$

The closer CC is to one, the more similar Φ^c and Φ^a are to each other, independent of any scaling factors that apply to all the potentials.

Model geometry

The numerical inverse solution used for this study was based on a realistic, homogeneous geometrical model of the human torso consisting of 352 nodes on the body surface and 92 nodes on the epicardial surface [26]. The basis of the geometry was a set of measurements made by Horacek [25] of a human torso, and those from a human heart by Macchi [27] and Ritsema van Eck [28]. One of the computational advantages of the boundary element method is that it requires a description of only the surfaces of the geometry *versus* the entire volume, as in finite element implementations. This reduces not only the size of the model itself, but also many steps in the calculations.

Our aims in constructing the model geometry were to maintain a manageably small number of elements in the model while retaining resolution where information content could be expected to be high, and to facilitate easy transfer of data from actual BSPM recordings to the model. To this end we included each of 117 measurement electrodes as nodes in the model, then placed additional nodes approximately at the midpoint between each electrode, for a total of 352 nodes. The mean spacing in the precordial region is approximately 2.5 cm, for the right anterior and posterior regions the spacing doubles to approximately 5 cm, yielding an overall mean spacing of 3.0 cm and a range of 1.7 to 5.1 cm. Manual triangulation yielded 700 triangles in the completely closed torso surface.

The basis of the epicardial surface description was a set of microtome slices of a *post mortem* human heart, which had been previously digitized [27,28]. At the same time, the location and orientation of this heart within the torso was determined from radiographic views of the same subject from whom the torso geometry was constructed. The node points of the epicardial surface lie on the outlines of 6 of the slices through the heart, made perpendicular to an axis running from the apex of the heart, through the root of the aorta. Digitization and manual triangulation of these slices produced 98 nodes and 192 triangles.

Data visualization

To generate hard-copy plots of the potential distributions, we projected the three-dimensional geometry to a plane, maintaining the same triangularization. The projections were based on a concept of an 'isometric' mapping, in which linear surface distances were maintained as much as possible. The torso geometry layout matches the BSPM standard of placing the anterior surface on the left, posterior on the right, so that the outside edges represent the right mid-axillary line. The method of projection for the epicardial surface also followed a convention in epicardial mapping by adopting the 'apical view'. The center of this display corresponds to the apex, with the epicardium splayed outwards in concentric rings. In our case, these rings were defined by the slices used to create the model, and were further distorted slightly so that linear distances between nodes in adjacent rings (slices) were preserved. To display potentials on both of these surfaces, we used triangularization and standard bilinear interpolation techniques [29] to produce contour lines with linear or logarithmic spacing between levels.

Mapping Studies

From a clinical study carried out at the Victoria General Hospital in Halifax, Canada, to examine the effects of PTCA on cardiac electrical activity, we selected sixteen patients in whom successful BSPM and PTCA were accomplished. Before the procedure, all subjects had significant ($\geq$ 60% diameter reduction) stenosis of the proximal sections of a single coronary artery, showed no clinical evidence of variant angina, and had resting ECGs which showed no diagnostic Q waves, or ST elevation or depression of more than 100 μV. Of this group, 8 patients had occlusions of the left anterior descending (LAD) artery, 4 of the right coronary (RC) artery, 3 of the left circumflex (LCx) artery, and one had both the LAD and RC arteries treated, but otherwise met all the inclusion criteria. This study was approved by the institutional review committee of the Victoria General Hospital and all patients provided signed, informed consent.

BSPM involved simultaneous recording of 120 ECG leads, relative to a Wilson's central terminal, continuously for up to 6-minute periods over the entire balloon inflation/deflation cycle. The details of the electrode configuration and mapping system have been presented elsewhere [30,31].

The recording protocol for this study included 15-s recordings before commencement of the PTCA procedure, and again between inflations to evaluate control conditions. To capture the electrocardiographic response to angioplasty, we recorded either the last 15 s of the balloon inflation, or the entire inflation/deflation cycle, beginning 30 s before balloon inflation and ending 2 min post deflation. For each patient, we carried out at least one of these long-duration recordings and every patient had at least 2 inflations recorded in some form.

BSPM processing consisted of selecting epochs of 10–30 s duration during which there was little change in ECG waveform, as determined from a selected precordial lead. In each of the resulting epochs a computer program clustered beats with similar waveform shape and then averaged the beats in the majority cluster for each lead. From the resulting average complex for a particular epoch, we constructed maps of isopotentials and isointegrals for areas under the QRS, ST, and QRST regions of the ECG. In order to emphasize the differences resulting from the angioplasty-induced ischemia, we also subtracted integral maps recorded just prior to inflation from those recorded during the inflation. These difference maps, which served as the focus of most of our analysis, are a unique feature of the PTCA model of ischemia since the patient provides a personalized control.

Radiologic Examination

For a 7-member subgroup of the 16 patients in the test group, (2 LAD; 2 RC, 2 LCx, 1 LAD/RC), we performed detailed radiographic examination for the purpose of inverse solution validation. For each case, a radiologist (R.M.M.) created a customized two-dimensional projection of the coronary tree of the patient, superimposed on the apical projection of the epicardium. These drawings included the major arteries and primary branches, and indicated clearly the relative dominance of left or right coronary arteries, as well as the location of the angioplasty balloon. The patients were selected only on the basis of the amplitude of PTCA-induced changes in the maps, not to match the size, shape, or gender of the model geometry.

Results

Forward/Inverse solution

Results from the forward calculations with discrete dipole sources provided both an independent measure of the accuracy of the forward solution, and a means of evaluating different smoothing operators and regularization parameters for the inverse solution.

Table 1 summarizes the results of the forward solution using two different methods for approximating the boundary-element integrals over the triangular surface elements. The first method used a triangle subdivision approach similar to that described in [22], the second the true linear element

approach [20]. With relative errors for the subdivision method ranging from 8.6% to 9.0%, and for the linear element method from 5.0% to 8.2%, the fit for both methods was very good with the linear method being marginally more accurate. Comparison of torso surface contour maps supported this result.

Please place Table 1 here

We then applied both zero-order and Laplacian smoothing operators M to the Tikhonov inverse procedure, and varied the regularization parameter t over several orders of magnitude. Each location in this parameter space was then evaluated by computing the maximum, rms and relative errors, and the correlation coefficients between epicardial potentials derived from the inverse solution, and those computed directly from the three orientations of the single dipole source. Input to the inverse solution was the set of torso surface potentials calculated directly from the same dipole source.

The optimal value for the regularization parameter t differed slightly for each difference measure, ranging, *eg.*,, from 0.5×10^{-4} to 1.0×10^{-4} for zero-order and from 5.0 to 90.0 for Laplacian smoothing operators. The best value for t also varied for the three dipole orientations, between, *eg.*, 0.7×10^{-4} and 1.5×10^{-4} in the case of zero-order and from 40 to 75 for Laplacian operators. Of importance in any practical application of the inverse solution is its performance when noise is present in the signal. In Figure 1 is shown a graph of the relative error and correlation coefficient with a single dipole source, for two different values of the Laplacian regularization parameter t, as progressively more noise was added to the torso potentials. Regularization at $t = 57$ was optimal for noiseless torso potentials ($E_{rel} = 0.188$, $CC = 0.982$), while at $t = 200$ the error was only slightly larger ($E_{rel} = 0.197$, $CC = 0.980$). With added noise, however, the errors increased much more rapidly for the 'optimal' case ($t = 75$) than for the slightly over-regularized case ($t = 200$). We compared the noise tolerance for other levels of regularization and selected 200 as the value which gave both relatively low error at low noise levels, and acceptable degradation at noise levels in the 10–30% range which we felt was realistic for the clinical mapping data.

Please place Figure 1 here

Comparison between methods used to estimate the variation in potential over the triangular surface elements of the model suggests a small advantage of the linear over the triangle-subdivision scheme. In our implementation, using true linear triangular elements was also faster to compute, by a factor of almost three, over subdivided elements. These findings led us to select the linear element method for application of the inverse solution to clinical mapping data. Comparison between different regularization functions M also indicated a clear and consistent advantage of the Laplacian over zero-order operators. Examination of the epicardial maps in Figure 2 supports this

result, since the maps generated by the zero-order inverse solution show local errors in all three dipole orientations.

Please place Figure 2 here

Inverse solution applied to PTCA data

All results of the inverse solution applied to BSPM data recorded during PTCA are shown as pairs of isocontour maps. One map of each pair represents the potential distribution over the torso surface, the other map, the corresponding distribution over the epicardial surface, as predicted by the inverse solution.

Figure 3 is a display of measured body-surface maps (outside columns) and the corresponding computed epicardial maps (inside columns), one pair for each of four sequential instants in time, from two different averaged beats. The first beat, whose maps are shown in the two left hand columns of Figure 3, represents the period just prior to inflation of the angioplasty balloon, with the catheter in place. The four pairs of maps form a sequence near the J-point, as indicated by the vertical lines in the V_3 lead shown at the top of each column of torso maps. The maps in the right hand columns represent the equivalent time instants from an averaged beat late in the occlusion phase, just before release of the PTCA balloon.

The projections used for the maps are described in the methods section, above. Superimposed on the apical view of the epicardium are shaded outlines of the main coronary arteries derived for each patient from angiograms recorded during the PTCA procedure. Using the clock dial as a reference, the LCx artery encircles the basal region of the heart from 11:00 to 3-6:00 in the polar view, while the RC artery also lies near the atrioventricular border running from 10:00 to 6–7:00. The arrows in the epicardial maps point to the location of the occlusion, relative to the coronary arteries of the patient. Contour lines in each plot are spaced according to a standard logarithmic scale covering one decade, relative to the extrema of each map, which are marked by the plus and minus signs, and labeled with values in microvolts (see figure legend for details).

Please place Figure 3 here

If we look first at measured data, the pairs of body-surface maps are very similar in the first two rows of Figure 3, but a clear difference develops by the third time instant, seen as an area of localized positive potential over the left anterior region of the right hand, peak-inflation body-surface map, which persists throughout the rest of the ST segment (not shown). This is reflected as ST-segment elevation in the V_3 lead shown above the right-hand column of maps in Figure 3. The location and topography of the maps identify this case as angioplasty of the LAD artery [18,19,21]. In the corresponding computed epicardial maps for the third and fourth time instants, there is also

an area of positive potential unique to the peak-inflation maps, which is located in the region under the LAD artery, distal to the site of occlusion marked in the display with an arrow. The location of this positive potential corresponds with the region which would suffer a lack of perfusion, and hence, presumably, acute ischemia, as a result of balloon inflation.

In order to enhance the changes between maps recorded before inflation of the angioplasty balloon, and those at peak inflation, we computed difference maps for all inflation epochs, relative to the pre-inflation recordings. To achieve some insensitivity to alignment, and also a large degree of data compression, we first integrated the signal from each map lead, generating "integral maps", and then subtracted these to form "integral difference maps". For the purposes of validating the inverse solution in this report, we show only integral difference maps derived from the "STT", the ST segment and T wave, as measures of the "net" effect of angioplasty-induced ischemia.

Figure 4 contains results from a single inflation in each of the cases in our selected group of seven patients, which contains two patients each who underwent PTCA of the LAD, RC, and LCx arteries, respectively, along with a single patient in whom both LAD and RC arteries were treated. The display consists of pairs of maps, one member of the pair for the measured body surface distribution (left-hand column) and one for the corresponding epicardial distribution (right-hand column), as predicted by the inverse solution. The body-surface maps are "peak" difference maps, produced by subtracting the maps recorded just before inflation of the angioplasty balloon from those measured during the peak phase of the inflation. The epicardial maps are thus also peak integral difference maps and do not represent potential distributions as they might be measured, but simply portray the distribution of the degree of difference or change in epicardial potentials brought about by inflation of the PTCA balloon. Studies of epicardial potentials in animals show that electrodes located directly over ischemic areas sense elevated potential in the ST segment [32] and hence in the STT integral maps. While the injury current that generated this localized ST elevation must also produce a complementary depression elsewhere on the epicardium, the return current path is more diffuse, and hence the resulting change in potential distribution is less suitable for localizing ischemia. Therefore, as we have subtracted pre-inflation maps from peak-inflation maps to create the difference maps, we view epicardial regions of positive difference as evidence of underlying regions of ischemia.

Please place Figure 4 here

For cases 3229 (LAD), 3230 (RC), 3235 (RC), 3223 (LCx), and 3200 (LAD and RC), the regions predicted as being ischemic by the inverse solution, indicated by positive contour lines, were also located distal to the site of balloon inflation in the predicted perfusion bed of the occluded artery. There were also regions of positive difference that *did not* overlie regions where ischemia would be expected on hemodynamic grounds, *eg.,* in patient 3229 there was a positive region near 3 o'clock on the epicardial map. Similarly, in patient 3211, the maximum lay over the left atrium and the

positive zone was not contiguous under the course of occluded LCx artery. In perhaps the biggest deviation from expectation, the difference map from patient 3196 showed a maximum over the upper left ventricle and left atrium while the apex, which, at least in its anterior aspects, should experience ischemia due to an LAD occlusion, displayed a reduction in ST integral value.

Discussion

The inverse solution described here includes only the epicardial and body surfaces and hence does not account for the inhomogeneous and anisotropic nature of the torso volume conductor. This level of simplicity offers the advantage of reduced geometrical and computational complexity, which, in this case, allowed us to generate complete forward and inverse solutions in the order of a minute on moderately powerful workstations. Moreover, some studies suggest that assuming homogeneity is a 'better' error that overestimating the deviation of conductivity values in inhomogeneous regions [33, 3].

In the studies described here, a single, realistic, human torso model was used for all calculations. From the recent reports, there is every reason to believe that the addition of *accurate, customized* geometrical information would improve the quality of our results. Without ready access to nuclear magnetic resonance equipment there is no acceptable means of gathering customized geometrical data on the patients for whom inverse solutions are computed. Despite the development of semi-automatic systems for acquiring and triangularizing 3D surface data [10, 34–36] the cost in terms of human effort and computing time of individualizing each inverse is still prohibitive. If such an individualized inverse solution were to be applied to the clinical setting, the time to generate a patient-specific forward matrix would, given present technology, limit its diagnostic capabilities. One possible solution might be to generate a set of inverse solutions based on a variety of basic body types and sizes.

The relative contribution of inhomogeneity and geometrical errors to inverse solutions is still on open matter. Values for errors induced by the omission of inhomogeneities as high as 300% have been reported in one inverse solution for epi/endocardial activation times [10]. Errors in geometry have also been found to induce errors in the same range [33]. These results have almost all been gleaned from modeling studies and hence suffer from the same lack of direct, experimental validation as the study reported here. To further confound the issue, there appears to be some interplay between factors. For example, the skeletal muscle may have a larger influence on torso potentials than epicardial potentials [33, 37] or fat which is on the epicardium could be a larger source of error than the fat located below the skin [38]). It has also been suggested that an inverse solutions based on one geometric model can be applied without significant additional error to other cases of approximately similar build due to the smoothing effect of regularization [33].

Another source of error for all inverse solutions that include Tikhonov regularization is the

setting of the regularization parameter. The essential difficulty is that while the value of this parameter affects the accuracy of the inverse, the only sure way to set its value is to know the solution beforehand. Moreover, there are data which suggest that the optimal value of regularization parameter is not constant over time, but varies throughout the cardiac cycle [39,40]. The two best known techniques for setting the regularization parameter when there is no *a priori* knowledge available are the CRESO [41] and the L-curve [42] methods. More recent investigations have focused on including the temporal continuity of the underlying electrophysiology in the regularization process, either as a separate operation [43], or in simultaneous combination with spatial regularization [44].

In most of the inverse solutions which have been applied to clinical data the approach has been more empirical, using what can best be described as "physiological constraints" to set regularization levels. We used another approach entirely, by letting epicardial and torso potentials calculated from a single dipole source determine the optimal regularization values. This methods offers the advantages of relative simplicity and the possibility of expansion to more complex discrete sources, which could even change in time to generate more realistic body surface potentials. However, this method also suffers from a potential bias since the same geometry is used for both the direct calculation of the dipole potentials for regularization and the resulting inverse solution. Another possible weakness of this approach is that the noiseless conditions of the model lead to unrealistic values of the regularization parameter. For this reason, we applied Gaussian noise at variable levels and found that by increasing regularization, we worsened the optimal (no noise) error, but gained considerable tolerance to a range of noise levels, effectively flattening the error *vs.* noise level curve. Hence, while the 'optimal' level for Laplacian regularization was 75, we chose a value of 200 for use with the BSPM data.

The use of integral maps as the input data for much of this study has advantages that go beyond the practical issues of data compression. Since PTCA offers the unique opportunity to compare the effects of ischemia against a control in the same patient, the situation begs to have those effects highlighted by difference maps. The computation of difference maps on an instant-by-instant basis, however, depends too sensitively on alignment of the signals to be useful [21]. Integral maps largely solve this problem, since errors in determining fiducial points have limited impact on the area under the ECG. A further justification for the use of integral maps in the context of inverse solutions was pointed out by Walker *et al.* [39]. Since the inverse solution is ill-posed, we must regularize it to restore continuity of the output. The regularization, however, applies a smoothing to the output so that fine detail and abrupt changes in the maps are not well resolved by the inverse solution. Integral maps, however, tend to be smoother in their topography, and hence may be more accurately predicted by an inverse solution. In addition — and this is the essential justification for using integral maps in any clinical context — the distribution of some integrals, especially of the QRST, has been shown to be highly suggestive of changes in repolarization [45–47]. For the purpose of this report, we presented ST-T integral maps, in large part because we found that **difference**

maps produced from ST, STT and QRST segments of the beat were virtually identical (except for a constant scaling factor) [21] and all included the ST segment most commonly used to detect ischemia.

Given all of the preceding discussion, it is perhaps little surprise that there are features in the inverse solutions we have computed that are not compatible with our knowledge of epicardial potential distributions. At this point, we can only surmise that these features arise, at least in part, due to the admittedly oversimplified view of the human torso as a homogeneous volume conductor. A further, perhaps even larger, source of error is the fact that the model geometry was *realistic* but not *anatomically correct* for the particular patients we measured, and that the same geometry was used throughout. The human thorax has a complex, irregular shape containing tissues with different conductivities, making assumptions of homogeneity and uniformity perhaps oversimplifications. A further potential source of error lies in the physiology of the PTCA-induced acute ischemia situation — our simple assumptions of coronary hemodynamics and lack of adequate information regarding the effects of collateral circulation in these patients. All of these factors probably contributed to the lack of model specificity, as seen in the spurious extrema of some of the epicardial difference maps — any further discussion of this issue would be purely speculative at this point.

From these caveats, it might appear tempting to suggest that the inverse solution, even though it leads to predictions of epicardial potential distributions, does not reveal anything that is not already present in the body surface maps. This is only partially true because the inverse contains information from the body surface potentials, but also takes into account geometrical relationships that have profound biophysical influence on electrocardiographic fields. The inverse-squared relation between potential and distance combined with the asymmetrical shape of the torso and the heart's location within combine to distort spatial relationships clearly visible on the epicardium when they are simply viewed as potentials at the torso surface. For example, discrete sites of epicardial activation merge into single features of body surface maps and the relative strength of posterior cardiac events is lost due simply to the relative distance to body surface electrodes. Despite the promise, the question that does remain is whether inverse solutions as they now exist can be trusted enough to replace, or supplement existing clinical methods. The results from our study cannot provide an unequivocal answer, but they do suggest that even under simplified assumptions, inverse solutions *include* something that looks to be correct. It remains to further refine the approach to extract that part of the inverse solutions that is most useful for diagnostics. Present efforts are therefore directed at both improving the spatial resolution and electrical fidelity of the geometrical model [34, 35, 38, 48], and completing experimental validation studies using a realistically shaped electrolytic tank and immersed, perfused canine hearts [49]. The immense potential that the inverse solution offers is what continues to motivate researchers to refine the mathematical methods required to predict accurately cardiac electrical activity from body surface measurements.

Appendix A: The forward solution

The forward problem can be formulated as a quasi-static Laplace's equation with known boundary conditions on the epicardial (Dirichlet) and body surfaces (Neumann). Applying Green's second identity to describe the scalar value of electric potential on the boundaries, leads to a pair of integral equations for the body and epicardial surfaces, respectively;

$$\phi_B^i - \frac{1}{2\pi}\int_{S_H} \phi_H \, d\Omega_{BH}^i + \frac{1}{2\pi}\int_{S_B} \phi_B \, d\Omega_{BB}^i + \frac{1}{2\pi}\int_{S_H} \frac{\nabla\phi_H}{r^i}\cdot d\vec{A} = 0 \tag{7}$$

and

$$\phi_H^i - \frac{1}{2\pi}\int_{S_H} \phi_H \, d\Omega_{HH}^i + \frac{1}{2\pi}\int_{S_B} \phi_B \, d\Omega_{HB}^i + \frac{1}{2\pi}\int_{S_H} \frac{\nabla\phi_H}{r^i}\cdot d\vec{A} = 0. \tag{8}$$

Here we have denoted ϕ_H and ϕ_B as the potential on heart and body surfaces, respectively; ∇ as the spatial gradient operator; r as the distance between the *observation point* and points on the *integration surface*; and the differential solid angle $d\Omega_{PQ}^i$ as the angle subtended by an elemental area of the integration surface Q at the i^{th} observation point on surface P. Likewise, ϕ_P^i is the potential at the i^{th} location on the surface P. Figure 5 shows the geometrical relationships in a schematic way.

Please place Figure 5 here

Equations 7 and 8 can only be solved in closed form for the simplest of geometries and so we must derive discrete equivalents for each term in the equations. We can then write a single discrete equation for each point on both surfaces and from this generate a system of linear equations (the collocation method) which can be solved numerically. The discrete versions of Equations 7 and 8 can be written as

$$p_{BB}^i\Phi_B + p_{BH}^i\Phi_H + g_{BH}^i\Gamma_H = 0 \tag{9}$$

and

$$p_{HB}^i\Phi_B + p_{HH}^i\Phi_H + g_{HH}^i\Gamma_H = 0, \tag{10}$$

where Φ is a column vector of electric potentials at all the discrete points on the surface indicated by the subscript (H = heart and B = body surface); Γ_H is the column vector of potential gradient on the heart surface; and the p's and g's are row vectors of coefficients derived from the integrals in the continuous equations, which express the geometrical contribution of each point on the surface of integration to the potential at the observation point i. The i refers to a specific observation point on either the heart (Equation 10) or the body (Equation 9) surface. Note that this form of equation requires that the geometrical coefficients (the p's and g's) can be separated from the potentials and potential gradients — a restriction which limits the possible numerical approaches. As discussed in some detail below, the manner in which this separation is achieved perhaps best characterizes the difference between numerical approaches to the forward solution [2,3,10,20].

If we now write Equation 9 for each point on the body surface and Equation 10 for each point on the heart surface, two sets of equations result, which in matrix notation can be written as:

$$P_{BB}\Phi_B + P_{BH}\Phi_H + G_{BH}\Gamma_H = 0 \tag{11}$$

and

$$P_{HB}\Phi_B + P_{HH}\Phi_H + G_{HH}\Gamma_H = 0. \tag{12}$$

The $P's$ and $G's$ are the matrices formed by collocating all the elements of the associated p^i and g^i row vectors — one row for each observation point. For the P_{HB} matrix, for example, each row contains N_B elements from one p^i_{HB} vector, and there are N_H rows, one for each value of i. Here again, the first subscript represents the surface containing the observation points, the second subscript the surface of integration. P_{HH} and G_{HH} are square matrices of size $N_H \times N_H$, P_{BH} and G_{BH} are sized $N_B \times N_H$, P_{BB} is another square matrix of size $N_B \times N_B$, and P_{HB} is sized $N_H \times N_B$.

By solving Equation 12 for Γ_H and substituting the result into Equation 11, we remove the need for explicit knowledge of the potential gradients. This leads, after sorting of variables, to

$$(P_{BB} - G_{BH}G^{-1}_{HH}P_{HB})\Phi_B = (G_{BH}G^{-1}_{HH}P_{HH} - P_{BH})\Phi_H, \tag{13}$$

which can be rewritten as

$$\Phi_B = Z_{BH}\Phi_H, \tag{14}$$

with Z_{BH} defined as

$$Z_{BH} = (P_{BB} - G_{BH}G^{-1}_{HH}P_{HB})^{-1}(G_{BH}G^{-1}_{HH}P_{HH} - P_{BH}). \tag{15}$$

Appendix B: Boundary element integration

The boundary element method requires that a scalar value (in this case electric potential) be integrated over surfaces that are described as the sum of discrete planar patches. The continuous integral is thereby replaced by a sum of terms, each of which represents an approximation of the local integral over a single patch. For the forward/inverse problem discussed here, each of the integrals in equations 7 and 8 must be replaced by a summation over all the triangular elements in a surface, *eg.,* from equation 7

$$\int_{S_H} \phi_H \, d\Omega^i_{BH} \approx \sum_{j=1}^{N_H} p^{ij}_{BH}\Phi^j_H, \tag{16}$$

where the integral over the continuous heart surface S_H has been replaced by a sum over N_H triangular elements of the term $p^{ij}_{BH}\,\Phi^j_H$, which includes an approximation of the integral over the triangle element.

Boundary element approaches differ in how they treat the integration over the planer elements. If the value of the scalar field is constant, or can be assumed so, then the integration is relatively simple and may even have a closed analytical solution. Barr *et al.* used this approach for their solution to the forward problem in electrocardiography[2]. The accuracy of the constant value assumption is a function of the rate of spatial change of the scalar value and the size of the discrete planar elements; if the elements are chosen small enough and the field varies slowly, then the assumption is valid. This condition leads to a second approach to boundary elements in which each original element is subdivided and a constant value is assigned to each of the resulting subelements. The specifics of this technique, which has been used by several investigators for electrocardiographic problems[10,22], depend on exactly how the triangle is subdivided, and how potentials are assigned to the resulting (constant) subelements. One important advantage of this method is that it permits adaptive solutions in which subdivision — if necessary, recursive subdivision — occurs only where and when required, resulting in increased computational efficiency.

A third approach to approximating the integrals in boundary elements is to allow the scalar value to vary over the surface element and then employ numerical surface integration (numerical quadrature) techniques for each element. In the model presented here, we used elements in which the potential was allowed to vary linearly with distance over each element, combined with numerical quadrature based on a method by Radon[50]. The formulation of the linear variation was first described for mechanical engineering problems by Cruse[23] and involves a bilinear interpolation technique using the potentials at each vertex of the triangle and the distances from each vertex to the desired point inside the triangle[21]. The numerical quadrature then becomes a weighted average of the potentials at the vertices.

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References

[1] Y. Yamashita. Theoretical studies on the inverse problem in electrocardiography and the uniqueness of the solution. *IEEE Trans Biomed Eng*, BME-29:719–725, 1982.

[2] R. C. Barr, M. Ramsey, and M. S. Spach. Relating epicardial to body surface potential distributions by means of transfer coefficients based on geometry measurements. *IEEE Trans Biomed Eng*, BME-24:1–11, 1977.

[3] Y. Rudy and B. J. Messinger-Rapport. The inverse solution in electrocardiography: Solutions in terms of epicardial potentials. *CRC Crit Rev Biomed Eng*, 16:215–268, 1988.

[4] R. M. Gulrajani, F. A. Roberge, and P. Savard. The inverse problem of electrocardiography. In P. W. Macfarlane and T. D. Veitch Lawrie, editors, *Comprehensive Electrocardiology*, pages 237–288. Pergamon Press, Oxford, England, 1989.

[5] R. C. Barr and M. S. Spach. Inverse calculation of QRS-T epicardial potentials from body surface potential distributions for normal and ectopic beats in the intact dog. *Circ Res*, 42:661–675, 1978.

[6] P. C. Stanley, T. C. Pilkington, and M. N. Morrow. The effects of thoracic inhomogeneities on the relationship between epicardial and torso potentials. *IEEE Trans Biomed Eng*, BME-33:273–284, 1986.

[7] P. Colli Franzone, G. Gassaniga, L. Guerri, B. Taccardi, and C. Viganotti. Accuracy evaluation in direct and inverse electrocardiology. In P. W. Macfarlane, editor, *Progress in Electrocardiography*, pages 83–87. Pitman Medical, 1979.

[8] B. J. Messinger-Raport and Y. Rudy. Noninvasive recovery of epicardial potentials in a realistic heart-torso geometry. *Circ Res*, 66, 4:1023–1039, 1990.

[9] B. Soucy, R. M. Gulrajani, and R. Cardinal. Inverse epicardial potential solutions with an isolated heart preparation. In *IEEE Engineering in Medicine and Biology Society 11th Annual International Conference*, pages 193–194. IEEE Press, 1989.

[10] G. J. Huiskamp and A. van Oosterom. The depolarization sequence of the human heart surface computed from measured body surface potentials. *IEEE Trans Biomed Eng*, BME-35:1047–1059, 1989.

[11] P. W. Serruys and G. T. Meester, editors. *Coronary Angioplasty: A Controlled Model for Ischemia.* Martinus Nijhoff Publishers, Dordrecht/Boston/Lancaster, 1986.

[12] P. W. Serruys, W. Wijns, F. Piscione, F. ten Kate, P. de Feyter, M. van den Brand, and P. G. Hugenholtz. Early changes in wall motion and wall thickness during percutaneous transluminal coronary angioplasty in man. *Can J Cardiol*, Suppl.:221A–232A, July 1986.

[13] A. M. Hauser, V. Gangadharan, R. G. Ramos, S. Gordon, and G. C. Timmins. Sequence of mechanical, electrocardiographic and clinical effects of repeated coronary artery occlusion in human beings: Echocardiographic observations during coronary angioplasty. *J Am Coll Cardiol*, 5:193–197, 1985.

[14] B. Meier, P. Luethy, L. Finci, G. D. Steffenino, and W. Rutishauser. Coronary wedge pressure in relation to spontaneously visible and recruitable collaterals. *Circulation*, 75:906–913, 1987.

[15] B. Griffin, A. D. Timmis, J. C. P. Crick, and E. Sowton. The evolution of myocardial ischemia during percutaneous translumincal coronary angioplasty. *Europ Heart J*, 8:347–353, 1987.

[16] G. S. Wagner, R. H. Selvester, N. B. Wagner, and M. W. Krucoff. QRS changes during acute ischemia induced by balloon occlusion of the LAD artery. *J Electrocardiol*, pages 18–19, 1988.

[17] T. J. Montague, R. M. Miller, M. A. Henderson, R. G. Macdonald, R. S. MacLeod, F. X. Witkowski, and B. M. Horáček. Persistent changes in the body surface electrocardiogram following successful coronary angioplasty. *J Electrocardiol*, 22 Supp. II:91–98, 1989.

[18] H. Spekhorst, A. SippensGroenewegen, G. K. David, M. J. Janse, and A. J. Dunning. Body surface mapping during percutaneous transluminal coronary angioplasty. *Circulation*, 81:840–849, 1990.

[19] M. Shenasa, D. Hamel, J. Nasmith, R. Nadeau, J.-L. Dutoy, and P. Savard. Body surface potential mapping of ST-segment shift in patients undergoing percutaneous transluminal coronary angioplasty. *J Electrocardiol*, 26(1):43–51, 1993.

[20] B. J. Messinger-Rapport and Y. Rudy. Regularization of the inverse problem in electrocardiography: A model study. *Math Biosci*, 89:79–118, 1988.

[21] R. S. MacLeod. *Percutaneous Transluminal Coronary Angioplasty as a Model of Cardiac Ischemia: Clinical and Modelling Studies.* PhD thesis, Dalhousie University, Halifax, N.S., Canada, 1990.

[22] T. C. Pilkington, M. N. Morrow, and P. C. Stanley. A comparison of finite element and integral equation formulations for the calculation of electrocardiographic potentials - II. *IEEE Trans Biomed Eng*, BME-34:258–260, 1987.

[23] T. Cruse. An improved boundary-integral equation method for three dimensional elastic stress analysis. *Computers & Structures*, 4:741–754, 1974.

[24] A. Tikhonov and V. Arsenin. *Solution of Ill-posed Problems.* Winston, Washington, DC, 1977.

[25] B. M. Horáček. Numerical model of an inhomogensous human torso. *Adv Cardiol*, 10:51–57, 1974.

[26] R. S. MacLeod, M. J. Gardner, R. G. MacDonald, M. A. Henderson, R. M. Miller, and B. M. Horáček. Validation of an electrocardiographic inverse solution using percutanteous transluminal coronary angioplasty. In *IEEE Engineering in Medicine and Biology Society 12th Annual International Conference*, pages 533–534. IEEE Press, 1990.

[27] E. Macchi. *Digital Computer Simulation of the Atrial Electrical Excitation Cycle in Man.* PhD thesis, Dalhousie University, Halifax, N.S., 1973.

[28] H. J. Ritsema van Eck. *Digital Computer Simulation of Cardiac Excitation and Repolarization in Man.* PhD thesis, Dalhousie University, Halifax, N.S., 1972.

[29] R. C. Barr, T. M. Gallie, and M. S. Spach. Automated production of contour maps for electrophysiology I. Problem definition, solution strategy, and specification of geometric model. *Comp & Biom Res*, 13:142–153, 1980.

[30] T. J. Montague, E. R. Smith, D. A. Cameron, P. M. Rautaharju, G. A. Klassen, C. S. Flemington, and B. M. Horáček. Isointegral analysis of body surface maps: Surface distribution and temporal variability in normal subjects. *Circulation*, 63:1167–1172, 1981.

[31] R. S. MacLeod, B. K. Hoyt, P. J. MacInnis, R. V. Potter, and B. M. Horáček. A body surface potential mapping unit for recording during coronary angioplasty. In *IEEE Engineering in Medicine and Biology Society 10th Annual International Conference*, pages 97–98. IEEE Press, 1988.

[32] R. P. Holland and H. Brooks. TQ-ST segment mapping: Critical review and analysis of current concepts. *Am J Cardiol*, 4:110–129, 1977.

[33] B. J. Messinger-Rapport and Y. Rudy. The inverse problem in electrocardiography: A model study of the effects of geometry and conductivity parameters on the reconstruction of epicardial potentials. *IEEE Trans Biomed Eng*, BME-33:667–676, 1986.

[34] C. R. Johnson, R. S. MacLeod, and P. R. Ershler. A computer model for the study of electrical current flow in the human thorax. *Computers in Biology and Medicine*, 22:305–323, 1992.

[35] C. R. Johnson, R. S. MacLeod, and M. A. Matheson. Computer simulations reveal complexity of electrical activity in the human thorax. *Computers in Physics*, 6(3):230–237, May/June 1992.

[36] A. van Oosterom. Triangulating the human torso. *Computer J*, 21:253–258, 1978.

[37] Y. Rudy and R. Plonsey. A comparison of volume conductor and source geometry effects on body surface and epicardial potentials. *Circ Res*, 46:283–291, 1980.

[38] C. R. Johnson, R. S. MacLeod, and A. Dutson. Effects of anistropy and inhomogeneity on electrocardiographic fields: a finite element study. In *IEEE Engineering in Medicine and Biology Society 14th Annual International Conference*, pages 2009–2010. IEEE Press, 1992.

[39] S. J. Walker and D. Kilpatrick. Forward and inverse electrocardiographic calculations using resistor network models of the human torso. *Circ Res*, 61:504–513, 1987.

[40] I. Iakovidis and R. M. Gulrajani. Regularization of the inverse epicardial solution using linearly constrained optimization. In *IEEE Engineering in Medicine and Biology Society 13th Annual International Conference*, pages 698–699. IEEE Press, 1991.

[41] P. Colli Franzone, L. Guerri, S. Tentonia, C. Viganotti, S. Spaggiari, and B. Taccardi. A numerical procedure for solving the inverse problem of electrocardiography. Analysis of the time-space accuracy from *in vitro* experimental data. *Math Biosci*, 77:353, 1985.

[42] P. C. Hansen. Analysis of discrete ill-posed problems by means of the L-curve. *SIAM Review*, 34(4):561–580, 1992.

[43] Y. Rudy and H. S. Oster. The electrocardiographic inverse solution. In T. C. Pilkington, Loftis B., J. F. Thompson, S. L. Woo, T. C Palmer, and T. F. Budinger, editors, *High-Performance Computing in Biomedical Research*, chapter 6, pages 135–155. CRC Press, 1993.

[44] D. H. Brooks, G. M. Maratos, G. Ahmad, and R. S. MacLeod. The augmented inverse problem of electrocardiography: combined time and space regularization. In *IEEE Engineering in Medicine and Biology Society 15th Annual International Conference*, pages 773–774. IEEE Press, 1993.

[45] F. N. Wilson, A. G. MacLeod, P. S. Barker, and F. D. Johnston. The determination and the significance of the areas of the ventricular deflections of the electrocardiogram. *Am Heart J*, 10:46, 1934.

[46] J. A. Abildskov, A. K. Evans, R. L. Lux, and M. J. Burgess. Ventricular recovery properties and QRST deflection area in cardiac electrograms. *Am J Physiol*, 239:H227–H231, 1980.

[47] S. S. Periyalwar, S. T. Nugent, and B. M. Horáček. Two-dimensional Fourier spectrum of QRST integral maps in classification of patients prone to ventricular arrhythmia. *IEEE Trans Biomed Eng*, BME-36:493–496, April 1989.

[48] C. R. Johnson, R. S. MacLeod, and M. A. Matheson. Computational medicine: Bioelectric field problems. *IEEE Computer*, 26(10):59–67, October 1993.

[49] R. S. MacLeod, R. L. Lux, and B. Taccardi. Translation of body surface maps between different electrode configurations using a three-dimensional interpolation scheme. In P. W. MacFarlane, editor, *Electrocardiology '93: Proceedings of the International Congress on Electrocardiology, XXth Annual Meeting*, pages 179–182. World Scientific, Singapore, 1993.

[50] J. Radon. Zur mechanischen Kubatur. *Monatsh. Math.*, 52:286–300, 1948.

Figure legends and tables

Figure 1 Relative error and correlation coefficient for the inverse solution from a single dipole source for two different values of the regularization parameter t with Gaussian noise added to the torso potentials before inverting. Noise level was computed as a percentage of the noiseless torso potential. Each value used for the graphs represents the mean of 20 runs with a random value of noise. Left-hand axis is scaled for relative error and right-hand axis for correlation coefficient.

Figure 2 Comparison of regularization operators on inverse solutions computed with linear triangular elements. Discrete dipole potentials (left-hand column) are compared with inversely calculated equivalents from Tikhonov zero-order (middle column) and Laplacian (right-hand column) regularization for all three dipole orientations.

Figure 3 Measured torso and computed epicardial potentials distributions for four sequential instants in time. The two outside columns contain body-surface equipotential maps displayed in a cylindrical projection with the anterior surface in the left half of each map and the posterior surface in the right half. The six shaded circles mark to locations of leads V_1toV_6. To the inside of each body-surface maps is the corresponding computed epicardial map, projected on an apical polar view of the heart. Superimposed on each epicardial map is a shaded outline of the patient's coronary arteries, with an arrow marking the site of the angioplasty balloon during inflation (proximal LAD in this case). The scalar ECG tracings at the top of the outside columns show a torso lead corresponding to V_3, with a vertical bar marking the four instants in time from which the maps were taken. Isopotential contour spacing in all plots is logarithmic over one decade, based on a fixed sequence of 1.0, 1.5, 2.2, 3.3, 4.7, 6.8, and 10.0, which is scaled by factors of 10 until the mantissa of the largest extremum falls below 10. For example, in the first body surface map of the figure, the largest extremum is -237.92, so that contours are fixed at $\pm$222., $\pm$150., 100, $\pm$68, $\pm$47, $\pm$33, and $\pm$22. Solid lines indicate positive values, broken lines, negative values. The left hand maps were recorded from the patient just prior to balloon inflation (Pre-inflation); the right hand set were recorded at the latter stages of the inflation, just prior to release of balloon pressure (Peak-inflation).

Figure 4 ST isointegral difference maps from seven different patients undergoing PTCA. In the left hand column are body surface distributions and in the right, the corresponding computed epicardial maps. Markings and scaling conventions are the same as in Figure 3, and the shaded

outline of the coronaries was customized for each patient. The coronary artery which was dilated during PTCA is indicated in the upper right hand corner of each map; the upper left corner contains the patient number. Maximum and minimum values are located at the plus and minus signs in each map and values shown are relative differences, each difference map being scaled by the rms value of its control map. In panel A, are maps from two cases of LAD artery inflation (patients 3196 and 3229) and from two cases of RC artery inflation (patients 3230 and 3235). Panel B contains maps from two patients with LCx artery angioplasty (patient 3211 and 3223) and maps from both LAD and RC artery inflations in the same patient 3200.

Figure 5 The geometry of the forward/inverse problem. In panel A, the observation point p is placed on the outer bounding body surface, S_B; in panel B, p lies on the inner bounding heart surface S_H. The Ω terms are the associated solid angles.

Table 1: Test of the forward solution for a single dipole source. Calculated torso potentials from both forward solutions were compared with simulated data. Units for the rms error and maximum error are μV, assuming unit values of torso conductivity and dipole moment. The axes of the torso geometry were oriented from right to left arm (x-axis), cranio-caudally (y-axis), and anterio-posterior (z-axis).

Test of Forward Solution Accuracy – Dipole Source

Model Type	Source	RMS Error	Max. Error	Rel. Error	Corr. Coeff.
Subdivision					
	X dipole	0.54	1.12	0.086	0.997
	Y dipole	0.68	1.53	0.089	0.998
	Z dipole	0.57	1.23	0.090	0.996
Linear					
	X dipole	0.32	0.95	0.050	0.999
	Y dipole	0.64	0.13	0.082	0.997
	Z dipole	0.45	0.16	0.070	0.998