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Computer Modeling and Lead Field Theory in the Analysis and Development of Impedance Cardiography

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Abstract. Conventional impedance cardiography (ICG) methods estimate parameters related to the function of the heart from a single waveform, that reflects an integrated combination of complex sources. Several modified ICG measurement configurations have been suggested where for convenience or improved performance the standard band electrodes are replaced with electrocardiography (ECG) electrodes. However, measured data remain controversial, leading sometimes to errors and discouraging utilization of ICG. Development of ICG has been mainly empirical and its theoretical basis in terms of measurement sensitivity is incompletely understood. We have developed computerised methods and tools for calculating measurement sensitivity distributions of ICG electrode configurations. In this report, the methods were applied to investigate a) the sensitivity of the conventional and three modified ICG methods in detecting regional conductivity changes and b) the prospects of developing multiple aimed ICG recording configurations utilising the 12-lead ECG electrode locations. The methods were applied with three anatomically realistic volume conductor models: one based on Visible Human Man cryosection data and two on magnetic resonance (MR) images representing end diastolic and end systolic phases of the cardiac cycle. Preliminary clinical experimentation showed logical correspondence with the simulations. The first results indicate the applicability of the modelling approach in developing ICG measurement configurations. However, the level of clinical relevance and potential of the 12-lead method remains to be explored in studies employing more dynamic modelling and acquisition several simultaneous ICG channels along with invasive reference data.

Keywords: *Impedance, Cardiography, Lead Field Theory, Sensitivity Distribution, Computer Modeling, Visible Human Project, Electrode Configurations*

Introduction

An ideal method of assessing information on the cardiovascular system should be noninvasive, simple, atraumatic, inexpensive, reliable and also applicable in long-term surveillance outside the cardiac monitoring laboratory. Conventional ICG techniques provide

a single impedance tracing, from which parameters related to the pump function of the heart are estimated [1-4]. Most of the properties of ICG render it superior to other methods, the prominent exception being its limited reliability, which has hampered its acceptance as a clinical method. Most research on ICG has focused on comparison studies with reference CO methods, producing widely scattered results with impedance-derived CO. It has nonetheless been shown that in certain settings ICG can provide useful information on the circulatory system. What is lacking for its more widespread acceptance is thus that it be capable of producing quantitative and reliable measurement.

The original ICG developed in the 1960s by Patterson et al.[1] and Kubicek et al. [2] was based on a simple electrical analogy from the thorax, with the assumption that the recorded impedance variations measured on the surface of the thorax are essentially derived from blood flow-related changes in the pulmonary vascular bed and arteries resulting from the pumping action of the heart [5]. Although much work has been done to date, the development of ICG is still principally based on this same ideology introduced decades ago, relying strongly on an empirical approach. Several investigators have made modifications to the CO equation or the electrode montage, yet no method has as yet yielded reliable results. Continuing from the original development of ICG, use of over-simplified models has limited and confined improvement in the technique because of the gap between the model and the anatomy and physiology of the system investigated. The refinements frequently presented in the literature would not seem to constitute significant steps towards valid and stable ICG method.

Time varying changes in impedance (ΔZ) reflect the integrated combination of multiple sources, including tissue volume and movement, tissue resistivity, blood distribution and blood flow changes [6-8]. The contributions of these phenomena are reflected in ΔZ depending on the electrode configuration used for the measurement [6,7,9-11]. Computer models designed to calculate the current flow in the thorax have been used more recently in examining the ICG measurement configurations, producing supporting data for the anticipated conception of the complexity of the signal origin. Nevertheless no theoretical definition of ICG measurement sensitivity distribution has thus far been provided. With numerical computer models the anatomy can be accurately appraised, which should not only make for a better understanding of the properties of existing ICG methods, but facilitate the development of new ICG methods based more on theoretical grounds.

A theoretical foundation exists for analysis of the measurement sensitivity distribution of ICG based on the lead field theory introduced in 1953 for bio-electric (i.e. ECG) analysis [12-14] and later in the 1970s [15] for bio-impedance (BI) measurements. BI measurement sensitivity distribution reflects how conductivity changes throughout the volume affect the measured BI data. The application of lead field theory in ICG has not evolved to its potential; only initial studies with analytical models have hitherto been conducted to estimate the measurement sensitivity distribution in cylindrically shaped objects with uniform conductivity [16]. In this study, the lead field theory was utilized with computerized volume conductor models of the human thorax in analyzing conventional ICG configurations and in developing new ICG measurement configurations possessing more regional measurement, i.e. sensitivity, properties.

Methods

Impedance Cardiography Sensitivity Distribution

Lead Vector, Lead Field and Reciprocity. The lead vector concept explains the relationship between the electromotive source and the measured lead voltage. Suppose that a single dipole source vector of magnitude $\bar{p}$ is at a fixed location in a linear, resistive volume conductor of arbitrary shape and inhomogeneous conductivity. The measured unipolar lead potential, Φ_p, corresponding to $\bar{p}$, is affected by the proportionality coefficient vector,

having three orthogonal components. This transfer vector is dependent on the location of the measurement lead, the source dipole location, and the shape and the conductivity distribution of the volume conductor. Now, by reason of the linearity assumption, applying the superposition, the lead voltage can be expressed as the scalar product of the transfer vectors between the measurement locations forming the lead (e.g. locations a and b) and the dipole source as

$$V_{ab} = \Phi_a - \Phi_b = (\bar{c}_a - \bar{c}_b) \cdot \bar{p} = \bar{c}_{ab} \cdot \bar{p} \qquad (1)$$

where $\bar{c}_{ab}$ is the 3-D transfer coefficient describing the sensitivity of the bioelectric measurement at a specific location, the lead vector [17].

The lead field is a generalization of the lead vector; if the lead vectors are mapped as a function of the source position throughout the volume conductor, the single lead vectors will comprise a continuous vector field forming the sensitivity distribution, called the lead-vector field or simply the lead field.

If voltage measurement is made on the surface of an arbitrary volume conductor, the measured signal in the lead arises from all the sources in the conductor according to Eq. 1 at each location. The reciprocity theorem states that in linear systems, applying a unit reciprocal current I_r to the measurement lead gives rise to an electric field E in the volume conductor, and the associated current density field $\bar{J}$ has exactly the same form as the lead field. If individual current dipoles are characterized by current dipole moment per volume, $\bar{J}^i$, noting that $J = \sigma E$, the expression for the lead potential becomes

$$V_{LE} = \int_v \bar{c} \cdot \bar{p}\, dv = \int_v \frac{1}{\sigma} \bar{J}_{LE} \cdot \bar{J}^i\, dv \qquad (2)$$

where $\bar{J}_{LE}$ denotes the lead field [17,18].

As for the lead vectors, the lead field concept does not restrict the complexity of the volume conductor; this can be of an arbitrary shape and size with differing resistivities distributed in the volume.

Sensitivity Distribution of Bio-Impedance Measurement. The sensitivity distribution of a BI measurement can be obtained by means of the lead field theory. Now the source is not a current dipole within the volume conductor, but the (varying) conductivity distribution. The sensitivity distribution gives a relation between the impedance (and change in it) caused by a given conductivity distribution (and its change). It describes how effectively each region is contributing to the measured *Z*. If conductivity change is not involved, the measured impedance *Z* is obtained with

$$Z = \int_v \frac{1}{\sigma} \bar{J}_{LE} \cdot \bar{J}_{LI}\, dv \qquad (3)$$

where $\bar{J}_{LE}$ and $\bar{J}_{LI}$, obtained with reciprocal energization, are the current density fields (i.e. BI lead fields) associated with the current injection and voltage measurement leads [17, 19]. This equation gives the contributions from each region to the total impedance, and the dot product of the two fields expresses the sensitivity of the measurement to conductivity changes throughout the volume conductor. Effects of conductivity changes on measured impedance can be calculated by $\Delta Z = Z(t_1) - Z(t_1)$, where the time instants t_1 and t_2 refer to situations before and after a conductivity change, with the assumption that the changes in the lead fields are negligible due to the small conductivity change.

The impact of a certain conductivity variation in different regions depends on the sensitivity field. As the scalar field may possess positive and negative values depending on the orientation of the two lead fields, the measured impedance may either increase, decrease or be entirely unaffected in consequence of a conductivity change in a particular region.

Utilising Eq. 3 with finite difference method (FDM) computer modelling, information as to the respective capacity of different ICG measurements to detect conductivity and its changes in the thorax can be estimated [20]. In the FDM, the modelled volume is divided into a three-dimensional resistor network which reflects the thorax both geometrically and as a conductor. Methods to construct and solve accurate volume conductor computer models based on the FDM have been previously developed and validated [21].

The relative magnitude of the sensitivity field in a tissue type (or a group of tissues considered as one target volume) gives a measure of how conductivity variation in that tissue will affect the detected ΔZ. The overall sensitivity of a tissue type is obtained by integrating the sensitivity values of the tissue over the volume it occupies. This sensitivity value can then be compared with the absolute total sensitivity of the model as given by

$$\frac{\sum_{i=1}^{n_g} \rho_i S v_i}{\sum_{\substack{\text{all tissues} \\ \text{or groups}}} \left| \sum_{i=1}^{n_t} \rho_i S v_i \right|} * 100\% \qquad (4)$$

where n_g is the number of FDM elements in the target volume and n_t the number of tissue elements of a certain type. The denominator is the sum of the absolute partial contributions from all tissues (or tissue groups), and the numerator is the contribution of the target tissue.

Volume Conductor Models

To yield useful information, the FDM model must employ the anatomy of actual human structures. Three different anatomy models were employed in the study:

Visible Human Man model. A particularly accurate source of anatomical data, the U.S. National Library of Medicine?s Visible Human Man (VHM) [22-24] was employed as basis for detailed FDM modeling. The original cryosection images are 2048 by 1216 pixels in 24-bit colour, resulting in about 14 gigabytes of data in size. A total of 118 cryosection images from the top of the head to the pelvis were segmented using a modified IARD (image enhancement, amplitude segmentation, region growing, decision tree) volume segmentation method which directly provides volume elements of anatomy data for FDM mesh generation. Optional low-pass filtering, multiple amplitude segmentations, region growing and decision trees were applied for the semiautomatic segmentation procedure. Additional manual editing allowed classification of the smallest details. This resulted in approximately 4 000 000 voxels and 32 segmented and classified tissue types and organs. For data storage and image analysis the accuracy of the images was reduced to 250x250 pixels using an 8-bit gray scale colourmap. The resolution was from 0.044 to 5.7 cm^3 for the models utilised in the simulations.

Dynamic Model - Diastolic & Systolic models. The ECG triggered end-systolic and end-diastolic MR image data sets used by Wang and Patterson [8] were segmented. A two-phase thorax model (i.e. two models of the same person at different moments of the cardiac cycle) was constructed from these data producing end diastole model (EDM) and end systole model (ESM). The number of voxels was equal in both models, as the segmented outermost layer from the first data set was used as base for segmentation of the other set. Both models consisted of 70 slices and 30 tissue types. The resolution of FDM elements in the ECG-triggered models varied from 0.10 to 5.8 cm^3 resulting to 121431 elements.

Analysis of Conventional ICG

Contributions to the sensitivity distribution were assessed with the VHM thorax model for four ICG electrode configurations utilizing conventional band electrodes or modifications replacing the bands with spot electrodes:

a) Original configuration by Kubicek et al. using four band electrodes [2]

b) Configuration by Penney et al. using four spot electrodes [25]
c) Configuration by Bernstein using eight spot electrodes [3]
d) Configuration proposed by Woltjer et al. using nine spot electrodes [26].

Simulations were conducted to obtain the basal impedance, Z_0, lead fields in the thorax generated by the current and the measurement leads $\bar{J}_{LI}$ and $\bar{J}_{LE}$, and the resulting measurement sensitivity distribution *S*. Electrode configurations are shown in Fig. 1.

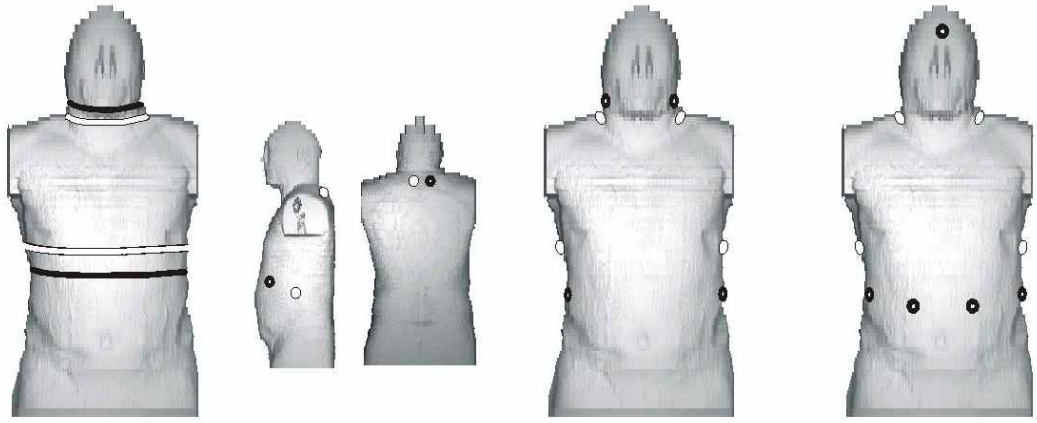

Figure 1. Placement of the electrodes on the VHM model for conventional band and three alternative spot ICG electrode configurations. Locations of the black spots are used for current injection and white spots for voltage detection in actual measurements.

Development of 12-Lead ICG

The prospects of recording multiple ICG waveforms with more selective sensitivity to particular regions of the thorax were investigated employing the 12-lead electrode system. The lead field concept can be applied even when several leads are combined. This facilitates synthesis of leads with desired properties, for example, more specific leads to detect sources induced by a heart disease.

The nine electrode locations of the 12-lead ECG electrode system were used separately to calculate a basic set of lead fields for each model, the VHM and two-phase models. A computer algorithm was developed to make possible combinations with the 12-lead electrode system using at maximum four electrodes at a time for either lead field in Eq. 3. Configurations, which utilise the same electrode location for current injection and voltage measurement, were omitted to reduce the skin-electrode impedance effect on ΔZ. Deriving ICG measurement combinations with the pre-calculated lead fields is a simple non-iterative calculation, since the system is assumed to be linear. E.g. a lead field between the chest leads V1 and V6 may be obtained by subtracting $V1_{LL}$ from $V6_{LL}$. On the other hand, the same result is obtained by subtracting $V1_{LA}$ from $V6_{LA}$. A total of 65476 impedance measurement configurations utilising the 12-lead electrode locations was thus derived.

A database was computed for each model and 65476 measurement configurations containing the information on the formation of Z_0 and proportional contributions according to Eq. 4. This was done for each classified tissue listed and for a number of different tissue groups reflecting functional structures of the cardiovascular system. Tissue groups were formed e.g. from the tissues forming the systemic and pulmonary circulation in addition to groups containing smaller number of tissues such as left atria together with left ventricle. Further, the same calculations were applied to the data produced by subtracting the sensitivity and Z_0 values simulated by the ECG-triggered models EDM and ESM.

Clinical Experiments

For the selected 12-lead-ICG measurements, first clinical experience was acquired by making recordings in volunteers and valve patients in supine position breathing

spontaneously. The study involved twelve healthy volunteers (age 30.5 ± 6.4 y mean ± SD, range 20 - 42 y; 11 male; 3 female, weight 79 ± 16 kg, 55 - 100 kg; height 179 ± 8.0 cm, 164 - 192 cm, BMI 24 ± 3.6 kg/m2, 17 - 30 kg/m2). The measurements were also taken preoperatively on a group of 9 patients with valvular heart disease (3 mitral, 6 aortic: age 58.4 ± 9.6, 35 - 72 y; all male; weight 76 ± 14 kg, 62 - 111 kg; height 171 ? 2.8 cm, 166 - 175 cm, BMI 26 ± 5.2 kg/m2, 20 - 39 kg/m2). Based on computer simulations with the VHM and two-phase models, 237 measurement configurations derived from the 12-lead system were selected as measurements to compare with the simulations.

The measurements were performed by CircMonä B202 (JR medical Ltd, Tallinn, Estonia), which includes an impedance channel delivering 0.7 mA at 30 kHz. A novel software-controlled switching device capable of electrically connecting the impedance measurement terminals to any number of applied electrodes was used in combination with the CircMon [27]. The electrode configuration used for impedance measurement could thus be altered rapidly by computer control without manual operation. A period of 10 s was measured with each configuration.

Results

Conventional ICGs

The conventional band electrode configuration and alternative configurations suggested to replace the bands were shown not to be specifically sensitive in measuring conductivity changes in regions generally considered important in measuring CO, namely the heart, lungs or aorta and other large vascular trees. More than half of the measurement sensitivity in each case studied was concentrated in the skeletal muscle. Furthermore, the results showed heterogeneous current field flow in the thorax, and modifying the electrode configuration resulted in different sensitivity distributions which must have an influence on the composition of measured signals. Sensitivity distributions are visualised in Figure 2.

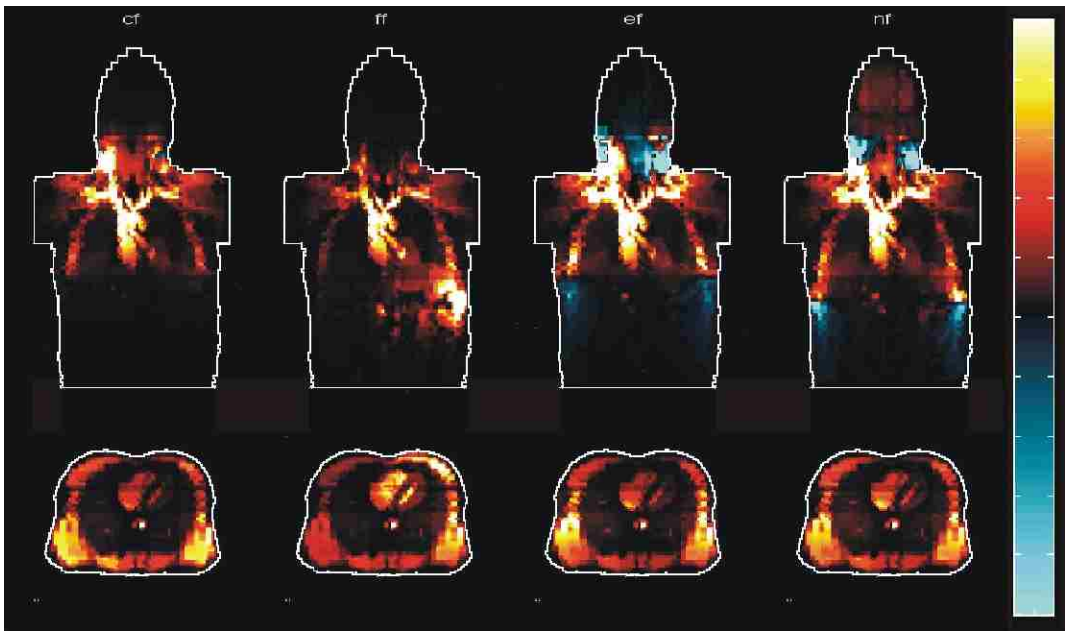

Figure 2. Mid-frontal and transversal views of sensitivity field distributions. a) conventional band, b) four-spot, c) eight-spot and d) nine-spot configurations. Zero sensitivity is indicated with black colour, positive sensitivities are visualized with hot colourmap and negative with cool colourmap. Average sensitivity values at viewing planes were used to scale the colourmap range for each case to obtain added brightness.

12-Lead ICG

Simulated electrode configurations indicated markedly different measurement sensitivity distributions between each other. As compared to the conventional ICG, clearly enhanced sensitivities were obtained in various tissues. However, no absolutely selective measurement configurations for particular structures of the cardiovascular system were obtained. As a consequence, no measurements applying any combination of the 12-lead electrodes will produce exclusive data from a particular region, although the partial contributions from various regions may be significantly increased.

Clinical Experiments

Clinical experiments with the ICG measurements derived from the 12-lead electrode system showed logical correspondence to the simulations, supporting the theoretically predicted differences between the configurations. Systolic ΔZ_{max} correlated significantly to the difference in basal impedances simulated with the two-phase model, but logically, no significant correlation was found to the VHM or either of the two-phase models when considered separately. The strongest correlations between sensitivity and measured waveform were noted for the right ventricle and the area under the systolic part of the impedance curve. Recorded 12-lead signals had characteristic waveforms and landmarks not coinciding with those of conventional ICG, indicating varied information content between the configurations. Furthermore, configurations were noted showing a suggestive resemblance to invasive data and morphological variations in disease. Fig. 3 shows example averaged waveforms recorded from both study populations.

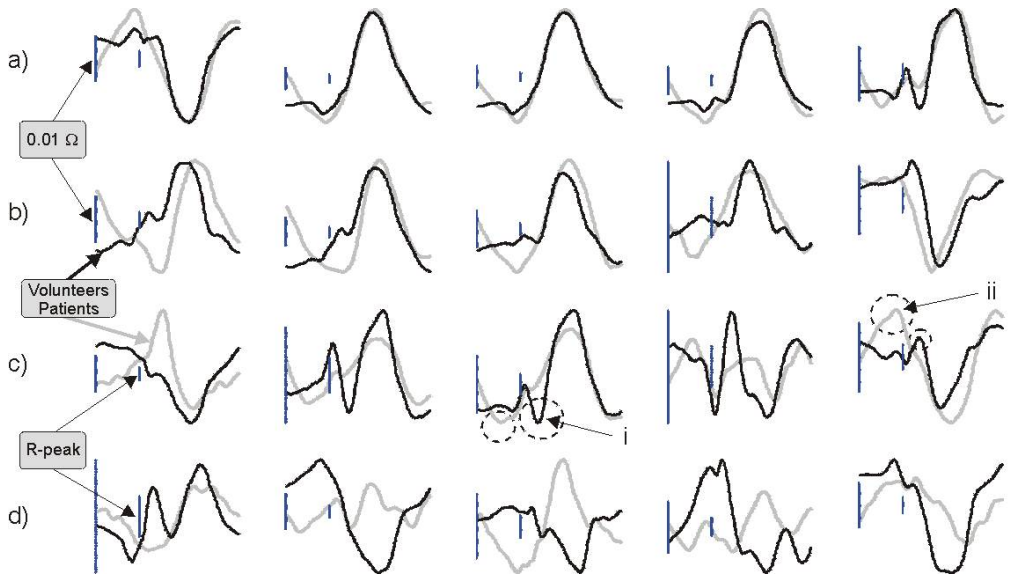

Figure 3. Examples of the 12-lead based ICG recordings shown as average signals from the study groups (volunteers and valvular patients). a) Tracings with small inter-group variation, b) changes between the groups in the time instant of the maximum impedance deflection, c) characteristic signals with notable peaks or deflections missing between the groups, d) large inter-group MAPEs. Tracings marked i and ii together identify the study populations.

Conclusions

Using ICG for measuring CO with conventional methods involves many assumptions and simplifications. The technique is by nature particularly indirect, reflecting complex simultaneous variations in the electrical, geometrical and physiological properties of tissues. To derive valid measures of cardiac-related parameters using BI measurements it is of primary importance that the signal contain the relevant information in a distinguishable manner. In this series of studies, the conventional ICG and a large number of measurement configurations derived from the 12-lead ECG electrode system were analyzed in respect of their measurement sensitivity distributions. The uniqueness of the methods used was that the sensitivity of the whole measurement setting was obtained in accurate models with a single simulation without approximations of quantitative conductivity changes occurring in the thorax. This was important in that an understanding of the ICG requires a conception of how the sensitivity of measurement is distributed, not only how large is the global impedance change due to a particular resistivity change in a specific organ.

Conventional ICGs

Simulation results emphasized the multiregional sampling sensitivity of the studied ICG configurations. For the conventional ICGs, only an approximately 5 % contribution from all blood masses and cardiac tissue was detected. This can be taken to imply that the valuable information, i.e. the information needed to determine the CO or other desired parameters, overlaps with a wide range of other information unretrievable from ΔZ. Although useful information has been obtained from the ICG waveform, it originates from a multiplicity of sources with unpredictably varying contributions depending on the characteristics and hemodynamic condition of the subject. Thus, particular caution is called for when applying ICG to clinical work. It is unlikely that a universally ideal electrode configuration providing accurate measurements exists for ICG. If the number of unpredictable factors contributing to or modifying the ICG waveform are many, at least as many specific measurements should be taken as there are contributing factors to establish the state of the system.

12-Lead ICG

Numerical modeling with the lead field theoretical approach made possible detailed analysis of a large number of configurations, in this study 65 476 derived from the 12-lead ECG electrode system. Increasing the contribution from a limited region may improve the physiological relevance of recorded data, which was achieved in theory with the regional multi-electrode measuring configurations. According to simulations with the VHM and the two-phase models, greatly increased sensitivities were obtained for each classified tissue with certain measurement configurations. For the tissues of the cardiovascular structures, a maximum of 75 % proportional sensitivity was attained. For the aortas and vena cavas the values were relatively small, since the electrode locations of the 12-lead system are not favorable for vertical measurements, especially when the right leg, often used in ECG acquisition, was ignored in the simulations. For this reason, the maximal sensitivity for the pulmonary circulation was twice that of the systemic circulation. Although highly elevated sensitivities were obtained, it was not possible to achieve fully selective measurements for any of the tissues. Moreover, even with these enhanced measuring configurations, everything still affects everything; nonetheless their relative contributions should be more favorable than in conventional methods to produce regional information.

Computer Models

The anatomical differences between the VHM and the two-phase models were considerable; for instance, the total volumes were 47 and 21 l for the VHM and the two-phase models, respectively. In spite of this, many of the most selective configurations for certain anatomical region or tissue were identical independent of the model applied. This result was unexpected, since to achieve high sensitivity in a certain region and low in others requires in principle a measuring configuration where lead fields of current and voltage electrodes are practically perpendicular to each other. Slight deviations in model geometry or electrode locations could

then markedly modify the partial sensitivity values. On the other hand, the derived configurations producing high sensitivities utilized more than four electrodes. Nonetheless these configurations with high sensitivity produced small basal impedances, which supports the conception that perpendicular electrode placement produces zero basal impedance. Also, as each tissue was considered as a whole in the analysis, the contribution from large tissues such as skeletal muscle could have been reduced by the fact that both positive and negative sensitivity values present can result in practically nil total sensitivity in that tissue. This, of course, does not imply that the tissue has no effect if its conductivity changes. On the other hand, however, the contribution from skeletal muscle has been noted to be almost nil when measured with conventional band electrodes placed on the abdomen [7, 28].

Clinical Experiments

Recorded 12-lead signals had characteristic landmarks not coincing with those of conventional ICG, indicating varied information content between the configurations. Furthermore, signals were noted showing a suggestive resemblance to invasive data and morphological variations in disease not present with conventional ICG. Valvular disease was detected when investigating at least two signals simultaneously, a single ICG signal cannot produce information for the identification of the existence of the disease. An important limitation in the clinical measurements is the instrumentation restricting the analysis of collected signals since only one channel can be recorded at a time. To collect a wide range of clinical data from patients during invasive measurements, the recording system should be implemented in a multi-channel form allowing parallel recording of several independent 12-lead ICG signals.

Conclusions

The findings demonstrated that the lead field approach is suitable in ICG, allowing transition from the empirical selection of a few parameters from empirically measured impedance waveforms to taking full advantage of the information embedded in a multiplicity of regional BI measurements. On the theoretical side, extending the two-phase to a multi-phase model one could simulate the ΔZ waveform and investigate geometrical and conductivity changes separately and not only assess the sensitivity distribution at one time instant. Comparisons with clinical data would facilitate the development of models and provide a guide in selecting valid tissue conductivities.

Ideally, it would be desirable to achieve measurement sensitivity only in the region of interest, producing selective information. Such measurement would require lead fields having null values anywhere else than in the target region, which is practically impossible for any surface electrode system. However, employing multiple measurements with different and known sensitivities to the relevant component in the system may convey useful information related to some specific event or region undetectable by conventional ICG methods. Presently, however, the lack of appropriate instrumentation restricts this approach.

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