31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Visual 3Dx: Algorithms for quantitative 3-dimensional analysis of ECG signals

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Introduction: **The 12-lead ECG is useful for cardiac diagnosis but has limited sensitivity and specificity. To address this, we developed the Visual3Dx, a comprehensive method for describing cardiac electrical activity in time and space. The Visual3Dx transforms the ECG input into a time-variable heart vector, and normalizes each lead input to assure equal representation from all cardiac regions.**

Methods: **We compared the Visual3Dx to the standard 12-lead ECG for detection of acute myocardial ischemia (AMI) in 2 clinical models. Model 1 was AMI after 90 s of balloon coronary occlusion in 117 cases. Model 2 was 122 consecutive patients who: (1) presented to an urban emergency department with chest pain; (2) were admitted to coronary care and developed elevated cardiac troponin levels; and (3) had coronary arteriography within 6 hrs.**

Results: **In Model 1, the 12 lead ECG developed ST segment deviation diagnostic of AMI in 78/117 occlusions (67%), whereas using the same input ECG data, the Visual3Dx was diagnostic of AMI in 105/117 occlusions (90%; $p<0.001$). In Model 2, the first 12 lead ECG was diagnostic of AMI in 80/122 (66%), whereas the Visual3Dx was diagnostic in 103/122 (84%). In both Models, the largest sensitivity gains were seen in left circumflex and right coronary artery occlusions.**

Conclusions: **The Visual3Dx is a promising tool for 3D quantitative analysis of cardiac electrical activity that may improve diagnosis of AMI, especially in electrically remote regions of the heart. Additional studies will define diagnostic specificity and further improve 3D biomarkers of AMI.**

Keywords — **Cardiovascular diagnostic devices, user interface, clinical trials**

I. INTRODUCTION

The standard 12-lead electrocardiogram (ECG) is invaluable for initial diagnosis of suspected heart disease, but is limited by relatively low diagnostic sensitivity and specificity [1]. In part, these limitations can be attributed to the fact that the ECG provides a 2-dimensional (2D) representation of cardiac electrical activity, an inherently 3-dimensional (3D) event. In addition, inaccurate physician interpretation of ECGs remains a significant issue; studies have demonstrated errors of "major proportions" in 4% to 32% of routine ECG interpretations [2]. Such interpretive errors can lead to clinical mismanagement, such as failure to detect and appropriately treat patients with acute myocardial ischemia.

Over the years, various efforts have been made to address the diagnostic limitations of the ECG, including but not limited to vectorcardiography, body surface mapping, and magnetocardiography [3-5]. Vectorcardiography, one of the earliest such efforts, was developed and primarily used from about 1940 to the 1970s. A vectorcardiogram (VCG) is a spatial representation of cardiac electrical activity analyzed in three orthogonal planes. . Instead of presenting signal waveforms from the measurement points (waveforms), as it is the case with standard 12-lead ECGs, in VCG, the measurement points are positioned in such a way that three derived signals correspond to three orthogonal axes (X, Y, Z) defining the heart vector, and these signals are presented as projections of the vector hodograph onto three planes (frontal, sagittal, and horizontal).

In spite of its diagnostic promise, vectorcardiography declined considerably by the 1970s. The decline was fueled by the technique's limitations, including complexity, the need for special leads and equipment, and – because of the era's technological limitations - a relatively small yield of diagnostic information. However, even with limited technology, VCG proved at least as powerful as the ECG in diagnosing a number of important conditions, including myocardial infarction, chamber enlargement, conduction abnormalities, and preexcitation [3].

Remarkable gains in computational power create an opportunity to extract substantially more diagnostically valuable 3D information from the ECG signal, significantly enhance the ECG's diagnostic utility, and make it easier to use for the medical professional. We developed a set of algorithms and tools, named Visual3Dx, that provide a comprehensive method to describe cardiac electrical activity in time and 3D space. Visual3Dx extracts additional information from standard 12-lead ECG signals and uses it to generate a 3D representation of cardiac electrical activity as a function of time, in a manner that is novel and distinct from prior methods for generating synthesized lead systems. Visual3Dx also includes algorithms for real-time vectorial analysis and normalization tools to ensure accurate and balanced representation of all heart regions.

II. METHODS

The Visual3Dx approach comprises 2 main steps [6]:

1. Transform input from the standard 12 lead ECG into X,Y,Z components of the heart vector
2. Normalize the lead vectors to equalize electrical representation from all regions of the heart.

Transforming ECG input into X, Y, Z components of the heart vector. Several algorithms are available for

converting 12 lead ECG data to orthogonal components of the heart vector. One such algorithm is the inverse Dower matrix (ID):

$$ID = \begin{vmatrix} .156 & -.00893 & -.173 & -.0747 & .122 & .231 & .239 & .194 \\ -.223 & .875 & .056 & -.018 & -.104 & -.0209 & .0408 & .0476 \\ .0225 & .101 & -.229 & -.310 & -.246 & -.0626 & .0550 & .109 \end{vmatrix}$$

which is applied to 8 independent ECG signals (leads I, II and V_1-V_6) recorded from the standard positions of the leads.[i] The heart vector is calculated by matrix multiplication:

$$\vec{H} = ID \cdot \vec{V}$$

The X, Y, and Z components of the heart vector may be solved at any time point by applying the ECG data into the above equation.

Normalize the lead vectors. The Visual3Dx includes a suite of algorithms to correct the problem of regional variation in electrical attenuation. Individual lead attenuation factors (ρ_i) are calculated for each of the six precordial leads, the calculated individual r_is are used to derive a single attenuation factor ρ, and ρ is then used as the common attenuation factor for all precordial leads.

Precordial lead vector magnitudes are calculated as follows, where $V_i(t)$ is the recorded voltage over time from a lead and $Vd_i(t)$ is the derived voltage for each of the ECG leads. Derived lead voltages are calculated as a scalar product of the heart vector and a lead vector

$$Vd_i(t) = \vec{H}(t) \cdot \vec{L}_i \cdot \rho_i ,$$

where $\vec{H}$ denotes the heart vector and $\vec{L}_i$ is the unit lead vector defined by the direction of the position of the *i*-th electrode (e.g., precordial electrode 1 to 6), and ρ_i is the unknown lead vector magnitude for each electrode. Using least squares method, the unknown attenuation factor ρ_i for every lead can therefore be calculated as a minimum of the function:

$$F_i = \int_0^T \left[V_i(t) - \vec{H}(t) \cdot \vec{L}_i \cdot \rho_i \right]^2 dt$$

where *T* is the recording time. From this, we derive the relationship: as

$$\rho_i = \frac{\int_0^T V_i(t) \cdot [\vec{H}(t) \cdot \vec{L}_i] dt}{\int_0^T [\vec{H}(t) \cdot \vec{L}_i]^2 dt}$$

The normalized attenuation factor ρ is selected from the range of individual attenuation factors (ρ_i) for measured leads. Each individual attenuation factor is approximately equal to the ratio between a virtual cardiac signal derived from the heart vector for a given lead over some time period, and an actual cardiac signal recorded at the same lead for the same time period of time. In this manner, a normalized attenuation factor is chosen to minimize the difference between the derived signal and the signal as actually recorded.

Using the normalized attenuation factor, one can derive the time dependent voltage in any virtual lead at any time:

$$Vd(t) = \vec{H}(t) \cdot \vec{L}_i \cdot \rho$$

The normalization factor can be used to draw a virtual "sphere" of equal signal attenuation around the heart, and can be used to calculate a derived voltage at any point on the virtual sphere (Fig 1), whether or not that point corresponds to a measured lead.

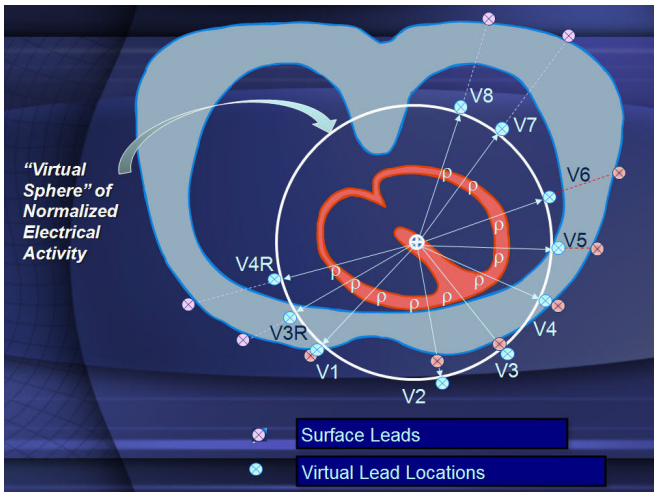

Fig. 1. Calculation of a "virtual sphere" of normalized cardiac electrical activity.

For example, as shown in Fig. 1, it is possible to calculate virtual leads corresponding to V_{3R}, V_{4R}, V_7 and V_8 even though there is no corresponding measured value. Importantly, normalization assures that the derived voltages may be directly compared to any other normalized voltages on the virtual sphere. Thus, for example, 1 mV of ST segment deviation in any of the derived leads is directly comparable to 1 mV of ST segment deviation in any of the normalized precordial leads.

In this manner, normalization allows direct comparison of cardiac voltage levels anywhere around the heart (Fig. 2). Thus, it is particularly helpful for ECG-based diagnostic markers that rely in part on the magnitude of recorded cardiac electrical signals (for example, ST segment shift in ischemia, R wave voltage in left ventricular hypertrophy, P wave voltage in atrial enlargement, and the like).

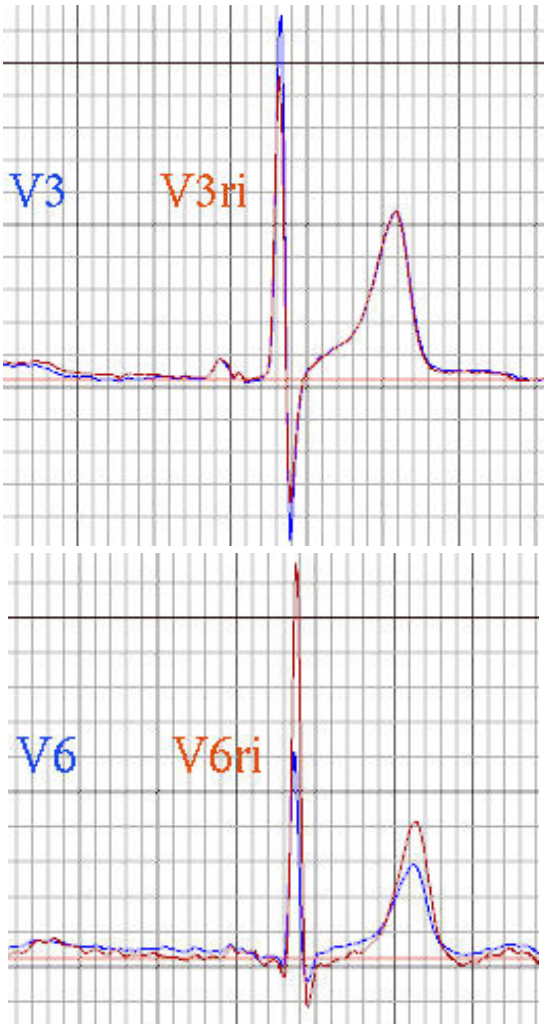

Fig. 2. Using a common attenuation factor to normalize lead voltages. In this figure, both the measured voltages in V_3 and V_6 (blue lines) and derived voltages (V_{3ri} and V_{6ri}, red lines) are shown superimposed. The derived voltages are calculated by use of the common attenuation factor as described. Note that in lead in V_3, the measured voltages generally larger than the derived voltage, whereas in lead V_6, the derived voltage is generally larger than the measured voltage. The derived voltages are calculated so that they would fall on the "virtual sphere" (Fig. 1).

III. RESULTS

Visual3Dx diagnostic sensitivity in ischemia induced by balloon coronary arterial occlusion.

The Visual3Dx was compared to the standard ECG for sensitivity in detecting myocardial ischemia in 51 patients undergoing balloon coronary artery occlusion during angioplasty. Both standard and Visual3Dxs were recorded during 117 balloon occlusions (46 occlusions in left anterior descending distribution (LAD), 34 in right coronary artery distribution (RCA), and 37 in left circumflex distribution (LCx). The criteria for ischemia on standard ECG were those set forth by the European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction. The criterion for ischemia on Visual3Dx is an ST magnitude >0.1 mv, measured 80 ms after the J point.

The Visual3Dx showed substantially better sensitivity than the standard ECG for detecting ischemia (90% versus 67%, respectively; Table 1). The sensitivity advantage was observed in each of the three coronary artery distributions. The sensitivity advantage of Visual3Dx over the standard ECG clearly was statistically significant ($p<0.001$), and was most apparent in the RCA and LCx ($p<0.001$ for both).

Site	Number	Visual3Dx			12 lead ECG			
		pos	neg	sens	pos	neg	sens	p
LAD	46	38	8	83%	32	14	70%	
RCA	34	33	1	97%	21	13	62%	<0.001
LCx	37	34	3	92%	25	12	68%	<0.001
Total	117	105	12	90%	78	39	67%	<0.001

Table 1. Comparison of sensitivity for Visual3Dx and 12-lead ECG during ischemia induced by coronary balloon occlusion. Occlusion sites: LAD = Left Anterior Descending distribution; RCA = Right Coronary Artery distribution; LCx = Left Circumflex distribution. Number = Number of occlusions at site; pos, neg = test positive or negative for ischemia, respectively; sens = test sensitivity; p = p value (chi-square or Fisher's exact test)

Beth Israel Deaconess Study of Visual3Dx in Acute MI

The study included 122 consecutive patients who: (1) presented to the Beth Israel Deaconess Medical Center (BIDMC, Boston, MA) Emergency Department with chest discomfort; (2) were admitted to BIDMC for suspected myocardial infarction; (3) developed elevated cardiac troponin I levels within 48 hrs of admission, and (4) underwent coronary arteriography within 6 hours of admission.

The primary endpoint was sensitivity of the first ECG for detection of acute myocardial ischemia, defined for the standard 12-lead as ST segment elevation or depression ≥0.1 mV 80 ms after the J point in two or more contiguous leads. In each instance, the same ECG data was processed by the Visual3Dx algorithm and a normalized vector magnitude lead ($V_M = [X^2+Y^2+Z^2]^{1/2}$) was generated. The Visual3Dx criterion for acute myocardial ischemia was ≥0.1 mV 80 ms after the J point in the V_M lead. The proportions of ECGs categorized as acute myocardial ischemia and non-diagnostic by both methods were compared using Fisher's exact test or χ square test.

The study showed that the standard ECG in these patients was diagnostic of acute ischemia in 80 of 122 patients

(65.5%), whereas the Visual3Dx was diagnostic in 103 of 122 patients (84.4%) (Table 2). This represents a 19% absolute percentage gain, and a relative 29% gain in diagnostic sensitivity for the Visual3Dx ($p<0.01$). Sensitivity results were also evaluated on an artery-by-artery basis. As was the case in the balloon coronary artery occlusion study (see Sec 3.1), the largest gains in sensitivity for the Visual3Dx relative to the standard 12-lead ECG was in the RCA and LCx distributions ($p<0.01$ and $p<0.001$, respectively).

Number of Positive Tests / Total Pts (%)				
	All	**LAD**	**RCA**	**LCx**
Standard 12-Lead	80/122 (66%)	30/43 (70%)	35/51 (69%)	15/28 (54%)
Visual3Dx	103/122 (84%)	35/43 (81%)	44/51 (86%)	24/28 (86%)
Relative gain in sensitivity	**+ 29%**	+ 16%	**+26%**	**+60%**
p value (vs. 12-Lead)	< 0.01	ns	< 0.01	< 0.001

Table 2. Comparison of sensitivity for standard 12-lead ECG vs. Visual3Dx on an artery-by-artery basis. Site of "culprit" coronary lesion identified at angiography: LAD = Left Anterior Descending distribution; RCA = Right Coronary Artery distribution; LCx = Left Circumflex distribution.

IV. CONCLUSIONS

In both clinical validation studies, the pattern of sensitivity gain for the Visual3Dx over the standard 12 lead was the same: in LAD occlusions, the sensitivity gain was relatively modest, but in RCA and LCx occlusions, the sensitivity gain was substantial. This pattern correlates well with theoretical expectations for the Visual3Dx process of converting the ECG signal into an X, Y, Z vectorial representation of heart electrical activity, and normalizing input for all leads. This enables accurate and full representation from electrically remote areas of the heart, such as the inferior, posterior and lateral walls (which are typically supplied by the RCA and/or LCx). Thus, data from two entirely distinct human models of myocardial ischemia indicate that the Visual3Dx's vectorial approach and normalization process hold great promise for improved diagnosis of ACS and other clinical manifestations of coronary artery disease.

The clinical studies presented here primarily address sensitivity and provide little information regarding diagnostic specificity. Additional studies in different patient groups are required to address the latter. One possible study group would be a large cross-section of patients presenting to an ED with chest pain and undergoing evaluation for possible ACS. Depending upon how the study group is defined and the distribution of patient profiles in the particular ED, one would reasonably expect it to have about 10-15% ACS and about 85-90% non-ACS. This heterogeneous group would provide substantial information on diagnostic specificity as well as additional information on specificity. Such studies are in progress.

These clinical studies rely primarily on ST segment analysis to diagnose acute myocardial ischemia. While ST segment deviation is a valuable diagnostic tool for this purpose, the Visual3Dx has a robust capability to evaluate a broad range of 3-dimensionally based biomarkers for acute ischemia. Such potential biomarkers include 3D angles between QRS and T loops and deformities in QRS and T vector loops. We are presently evaluating a suite of candidate 3D markers and believe they may be able to further improve sensitivity and specificity in diagnosis of ACS.

V. REFERENCES

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