Effects of Changes in Action Potential Duration on the Electrocardiogram in Type II Diabetes

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Background

Compared with Type 1 diabetes, Type 2 diabetes (T2DM) does not affect the production of inhibit organs to absorb the produced insulin. Based on studies on the relationship between cardiac diseases and T2DM, the fact that many myocardial diseases including elevated risk for myocardial infraction, heart failure, and sudden cardiac death are common in T2DM. Therefore, studies in T2DM can benefic clinical treatments in related myocardial diseases; on the other hand, symptoms of myocardial diseases can indicate whether the patients suffer T2DM as well.

According to clinical research and some related studies, T2DM can affect electric signals in heart, which means that the changes of electric signals in heart can indicate T2DM. In order to research the more accurate relationship between T2DM and electric signals, electrocardiogram (ECG) is used. Through ECG, changes of electric signals in three parts of a heart -- the right ventricle (idxRV), the subepicardium at the apex (EpiALV) and the subendocardium at the base (EndoBLV) can have different effects on action potential templates and body surface templates. Studying how sensitive to detect the changes in the three regions respectively can help the study in T2DM and myocardial diseases. By comparing spectrum magnitudes and principal component ratios by Matlab under different types of action potential templates, the different sensitivities in the three regions can be well represented.

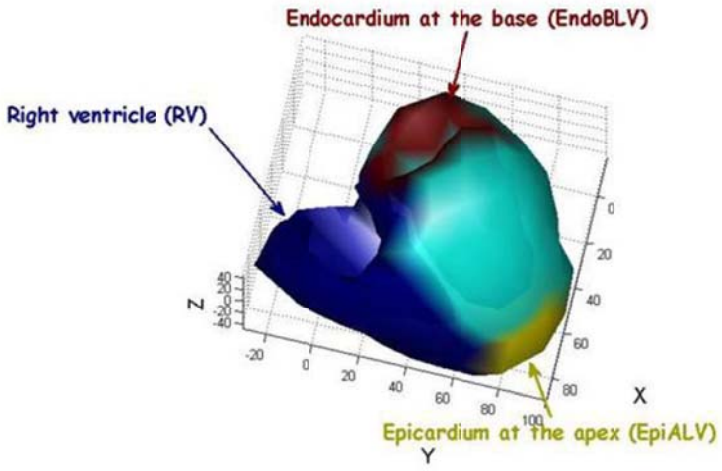


Figure 1: ECGSIM ventricle model, marked at three regions: the whole wall of the right ventricle (idxRV) (in blue), the subepicardium at the apex (EpiALV) (in yellow),

and the subendocarium at the base (EndoBLV) (in red). In these regions, unproportionate APD increase was found in a diabetic rat study [1].

Research Method

1. Building a model by Matlab to simulate the figures shown on ECGSIM

The most important step in the overall research is to find a good approximation to the action p otential templates in ECGSIM. One suggested research method was to create a dominantT(V) function that builds a repolarization transmembrane potential template waveform based on given body surface potentials V, and then generate the general repolarization transmembrane potential template Phi. Compared with ECGSIM figure shown in Figure 2 below, the dominantT(V) function could give a very closed approximation when the node number was large; however, when the node number was small, the QRS part was not as smooth as enough to approximate the ECGSIM (Figure 3). On the other hand, the algorithm to generate the dominantT(V) function was complicated. Therefore, we needed to come up with an easier and more accurate model. By analyzing the shape of the ECGSIM figure, we researched that a logistic cuidxRVe was a better mathematic model to simulate the ECGSIM figure.

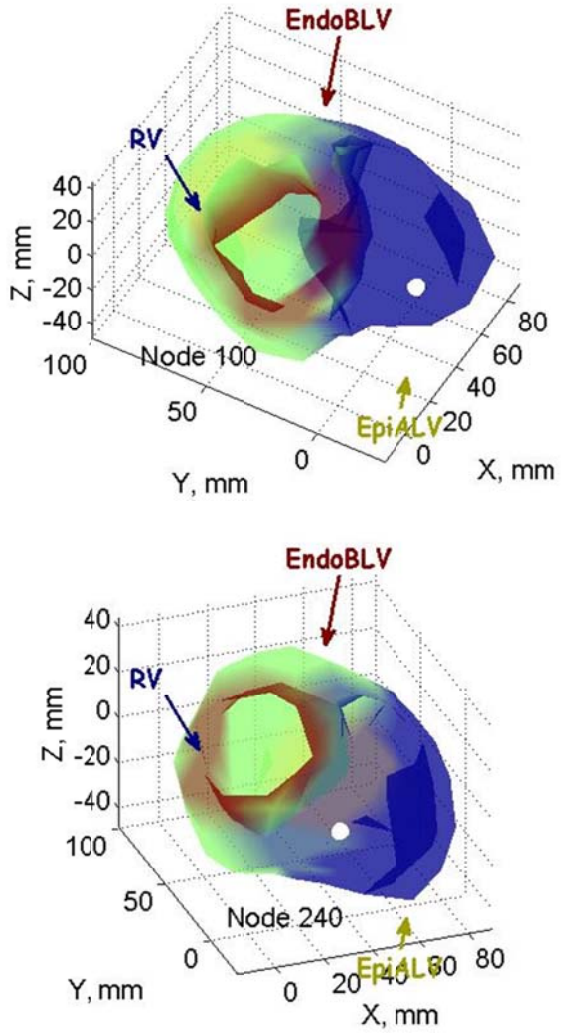


Figure 2: The marked white points show Node 100 and Node 240 on heart surface.

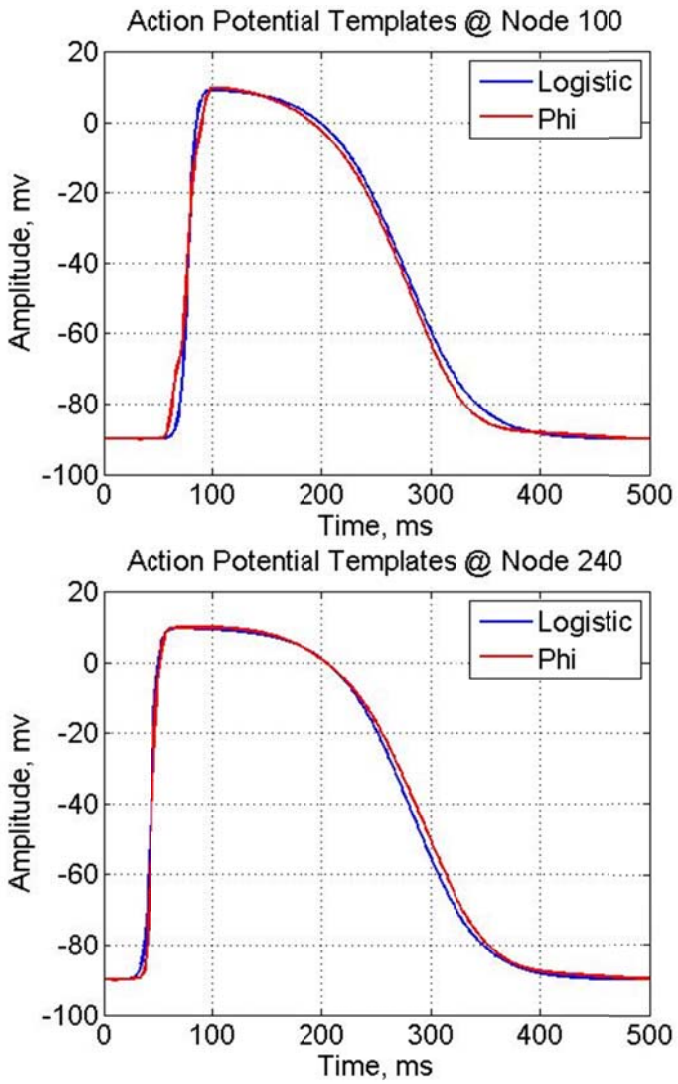


Figure 3: Comparisons of action potential templates generated by Logistic Curve and Phi through Matlab at Node 100 and Node 240 on body surface

2. Algorithm of Logistic Curve

The basic form for a logistic curve is:

$y=1/[1+\exp(-at)]$, where a is the parameter determining the shape of the logistic curve [2].

As in Wohlfart's formulation, a single logistic function was used for the depolarization phase:

$$\varphi_{dep}(t)=L_{a1}(t - T_{dep}),$$

where T_{dep} is the depolarization time and a_1 is associated with the upstroke velocity [2].

For the repolarization curve, the similar form is as follow:

$$\varphi_{rep}(t) = (1 - f)\,\varphi_{down}(t) + f\,\varphi_{spike}(t) - \varphi_{notch}(t)\ ,$$

where f is the fraction of the action potential amplitude corresponding to the height of the spike [2].

The function $\varphi_{down}(t)$ represents the downward slope of the TMP during the repolarization phase. The function $\varphi_{spike}(t)$ and $\varphi_{notch}(t)$ represent the spike and the notch respectively. In order to simplify $\varphi_{rep}(t)$, we set f = 0 as well as $\varphi_{notch}(t) = 0$, and then $\varphi_{rep}(t) = \varphi_{down}(t)$.

Accordingly, the term $\varphi_{down}(t)$ was derived as the integral of

$$T_{dom}(t) = L_{a2}\,(t\text{-}T_{rep})L_{\text{-}a3}(t - T_{rep}),$$

where a_2 and a_3 represent the maximal positive and negative slope of the dominant T wave, and T_{rep} is the repolarization time [2].

3. Determining parameters of the simplified logistic curve

Through Matlab simulation, we found proper a_1, a_2 and a_3 to approximate the logistic curve. As a matter of fact, the three parameters a_1, a_2 and a_3 are not independent to each other, but have the following relationship:

$$ari = mean\ (diff)\ /1.14$$

$$a_1 = 0.3$$

$$a_2 = 0.0897\text{-}2.91e\text{-}4*ari$$

$$a_3 = 25.46e\text{-}3+4.31e\text{-}5*ari$$

where diff is a 251*1 array recording the difference of repolarization time and depolarization t ime and the mean is to derive the mean value of the 251 difference.

Based on the solved the parameters a_1, a_2 and a_3, we could generate corresponding action potential template (AP) and body surface potential (BSP), which are shown below:

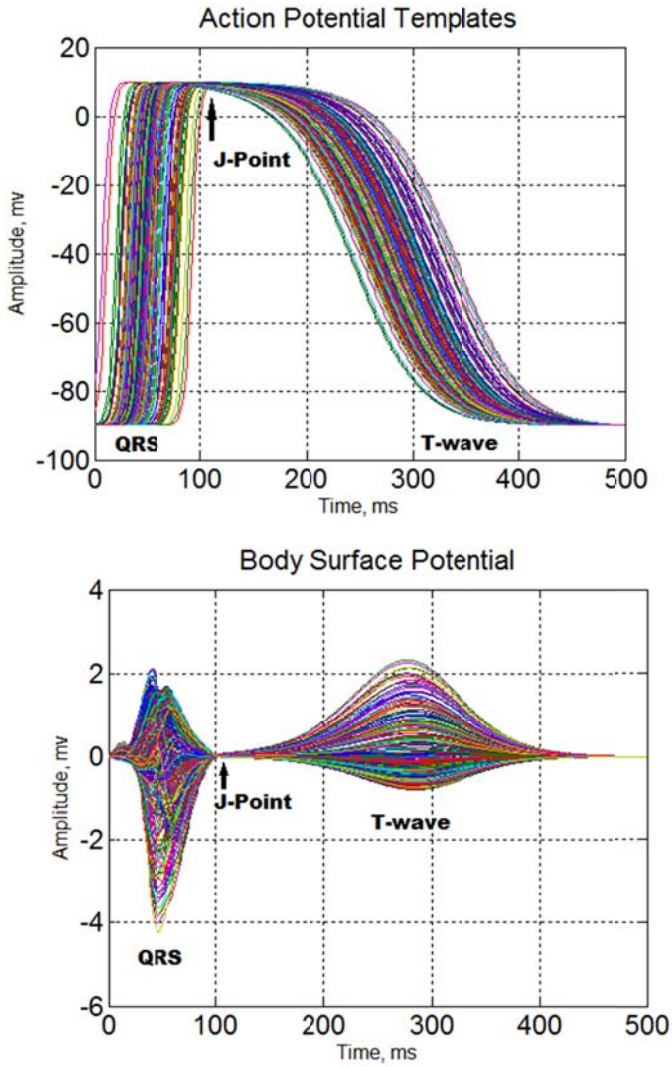


Figure 4: AP for 257 nodes (left) was generated based on the solved set of parameters a_1, a_2 and a_3.
BSP for 257 nodes
(right) was generated from the multiplication of AP (left) and electrical signals collected from a normal heart.
The J-Point is the separation point between the depolarization and repolarization part.

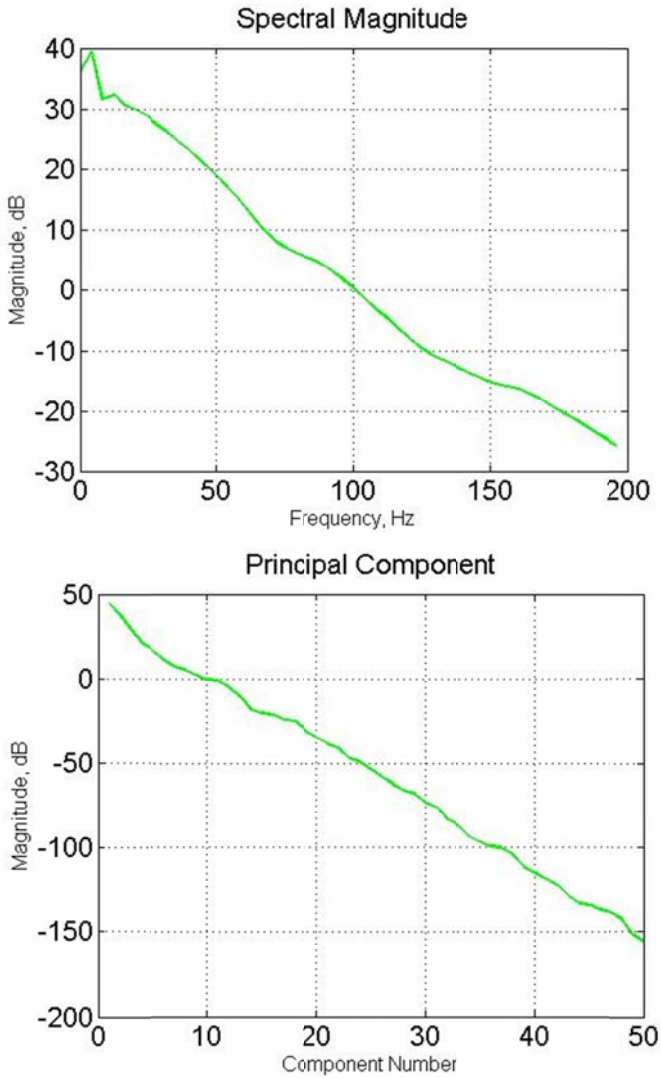


Figure 5: The Spectral Magnitude (left)
is the magnitude response of Fourier Transform of the generated BSP (Figure 4).
The Principal Component corresponding to the BSP (Figure 4) is derived by singular value decomposition algorithm in Matlab.

Research Steps

In order to research the sensitivities of the three regions of a heart -- the right right ventricle (idxRV), the subepicardium at the apex (EpiALV) and the subendocardium at the base (EndoBLV), we used the above discussed spectral magnitude and principal component methods to study this issue.

According to the studies on the diabetic rats with Type 1 diabetes, the action potential duration (APD) increase differed in three regions of the ventricle [1]. The APD measured after 90% of the

repolarization (APD_{90}) was found prolonged by 80%, 125% and 148% in the three regions -- idxRV, EpiALV and EndoBlV. To apply the findings in diabetic rats to a human study with T2DM, we multiplied the APD changes in the rat by 0.2, which was chosen relative to the normal pulse rates of human and rat [1]. The resulting 16%, 25% and 29% changes were used as APD prolongation percentages for the idxRV, EpiALV and EndoBLV areas of a human ventricle, respectively [1].

1) 16% APD prolongation for idxRV

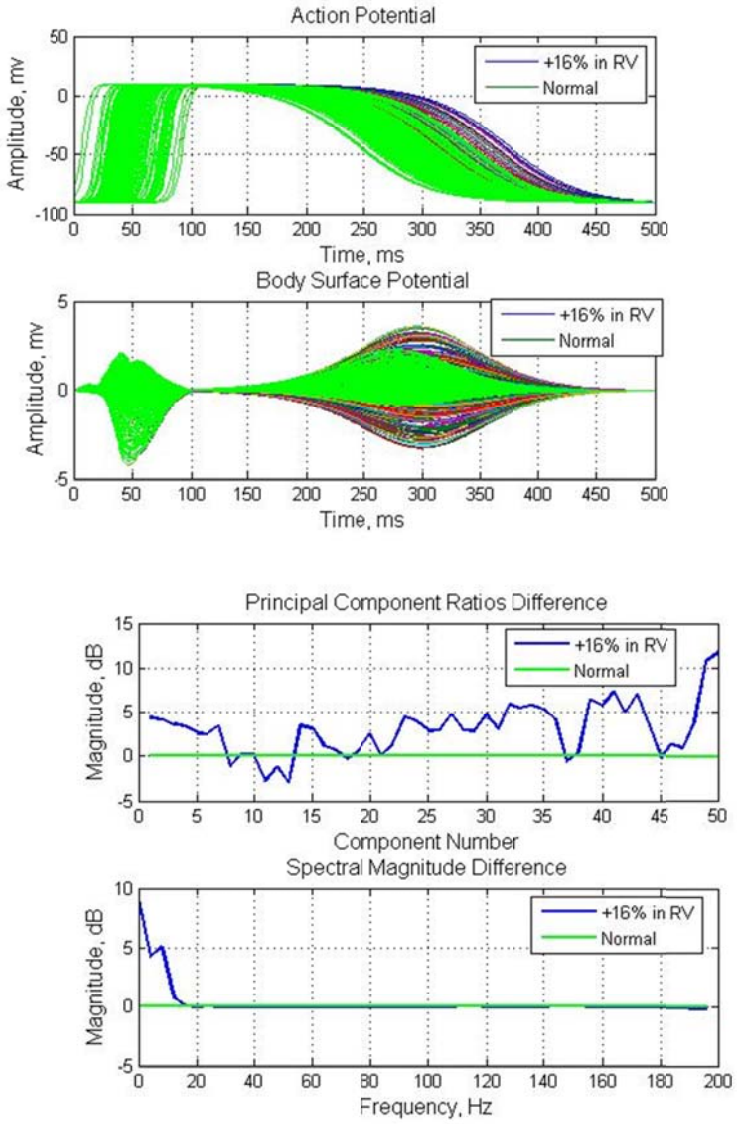


Figure 6: New AP and corresponding BSP based on 16% prolongation of APD_{90} for idxRV nodes. Figure 7: Comparisons of spectral magnitude and principal components for two different APD_{90}.

Figure 6 shows that when APD_{90} was prolonged by 16%, the time scale of T-wave region in the new AP increased compared with the one in normal AP. The peak value of T-wave region in the new BSP was delayed compared with the one in the normal BSP, and both the positive and negative peak values of T-wave region in the new BSP increased as well.

Figure 7 shows the difference of the Fourier Transform and the principal component of the normal BSP and the new BSP. We see that the increase in spectral magnitude happened on low frequency, and there were both increase and decrease in the principal component ratios difference.

2) 25% APD prolongation for EpiALV

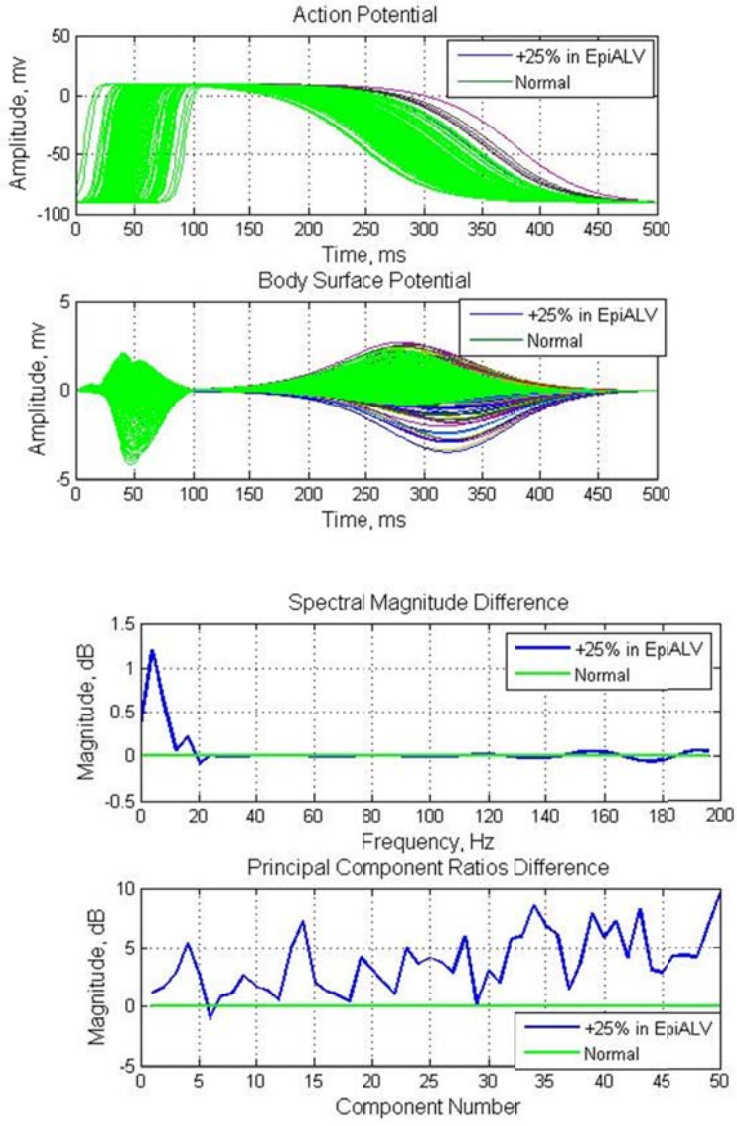


Figure 8: New AP and corresponding BSP based on 25% prolongation of APD_{90} for EpiALV nodes. Figure 9: Comparisons of spectral magnitude and principal components for two different APD_{90}.

Figure 8 shows that when APD_{90} was prolonged by 25%, the T-wave region of the new AP was not distributed as uniformly as the normal AP, and the time scale of T-wave region in the new AP increased compared with the one in normal AP. The positive part of the T-wave region in the new BSP was similar to the normal BSP; however, for the negative part, the peak value of T-wave region in the new BSP was delayed compared with the one in the normal BSP, and the negative peak value in the new BSP increased a lot as well.

Figure 9 shows the difference of the Fourier Transform and the principal component of the normal BSP and the new BSP. We see that the increase in spectral magnitude happened on low frequency, but there was also a little bit of increase on high frequency, which might be aroused by noise. There were both increase and decrease in the principal component ratios difference.

3) 29% APD prolongation for EndoBLV

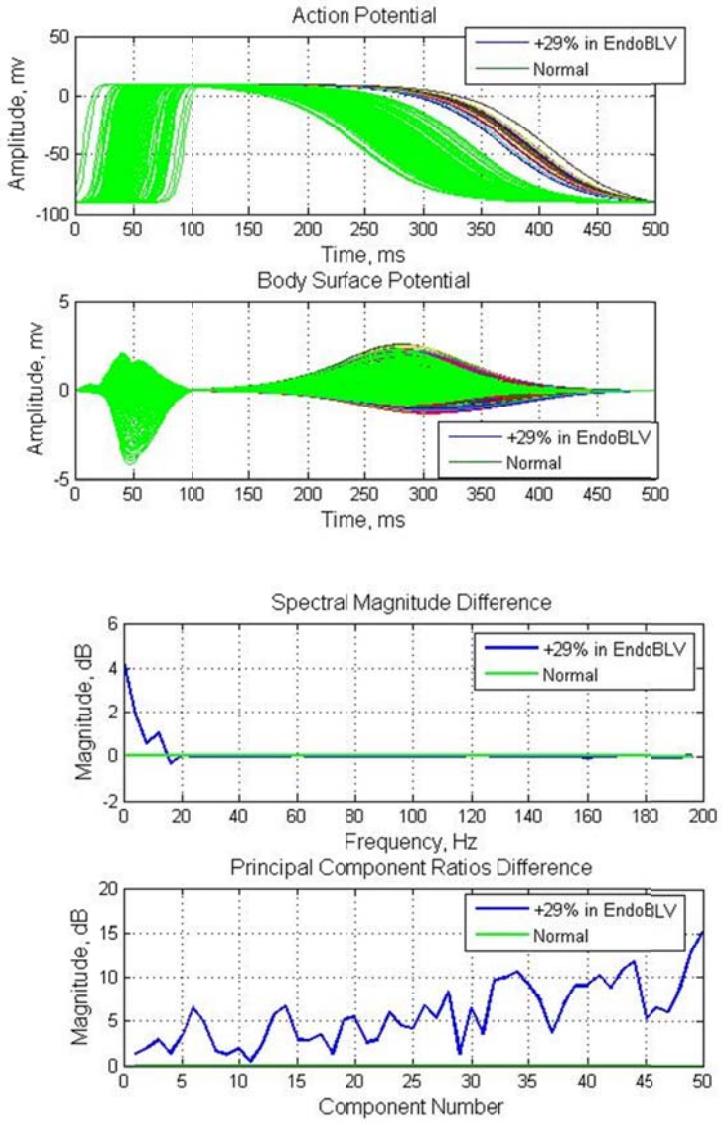


Figure 10: New AP and corresponding BSP based on 29% prolongation of APD_{90} for EndoBLV nodes. Figure 11: Comparisons of spectral magnitude and principal components for two different APD_{90}.

Figure 10 shows that when APD_{90} was prolonged by 29%, the T-wave region of the new AP was not distributed as uniformly as the normal AP, and the time scale of T-wave region in the new AP increased compared with the one in normal AP. As for the two BSPs, there was not a big difference expect for a little bit of increase in the new BSP.

Figure 11 shows the difference of the Fourier Transform and the principal component of the normal BSP and the new BSP. We see that the increase in spectral magnitude happened on low frequency, but there was only increase in the principal component ratios difference.

4) Combination of the three different regions -- idxRV, EpiALV and EndoBLV with different percentages of APD prolongation respectively

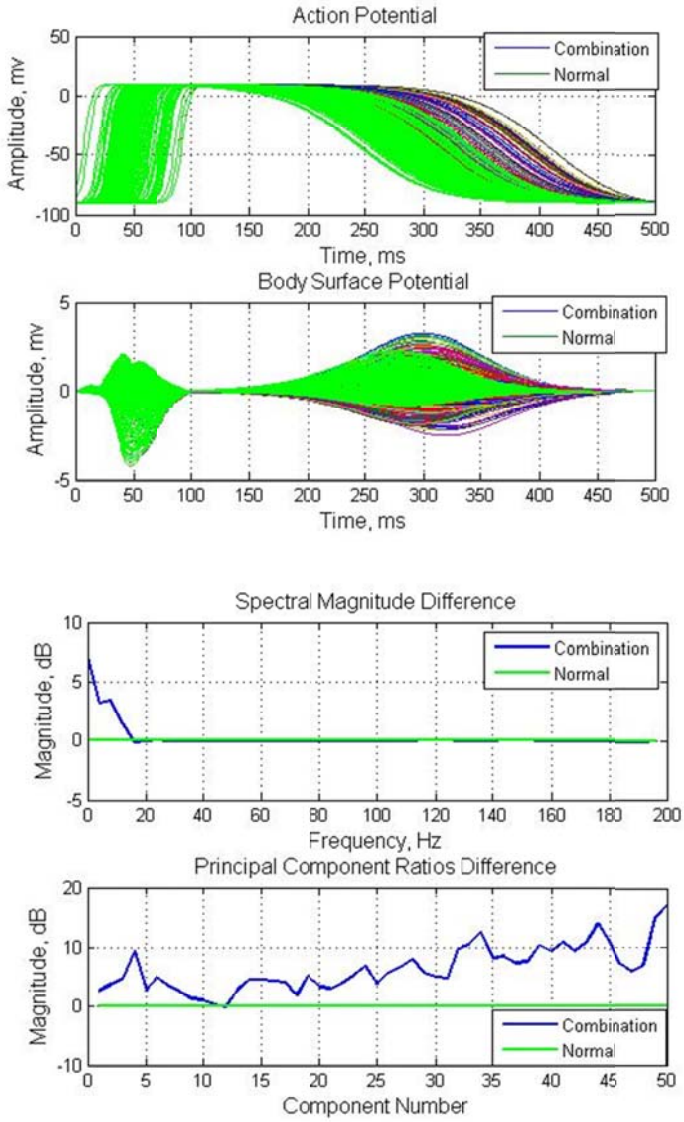


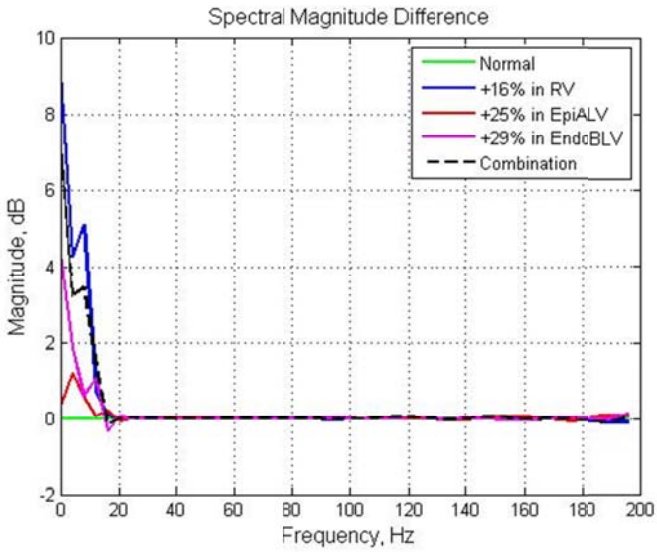
Figure 12: New AP and corresponding BSP based on the combination of the three regions

Figure 13: Comparisons of spectral magnitude and principal components corresponding to the with different percentages of prolongation of APD_{90}. normal and the new APs and BSPs.

Figure 12 shows that when the three regions with different percentages of prolongation of APD_{90} were combined, the time scale of T-wave region in the new AP increased compared with the one in normal AP. The peak value of T-wave region in the new BSP was delayed compared with the one in the normal BSP, and both the positive and negative peak values in the new BSP increased as well.

Figure 13 shows the difference of the Fourier Transform and the principal component of the normal BSP and the new BSP. We see that the increase in spectral magnitude happened on low frequency, and there was only increase in the principal component ratios difference.

5) Comparisons of spectral magnitude and principal component ratios difference in the three different regions



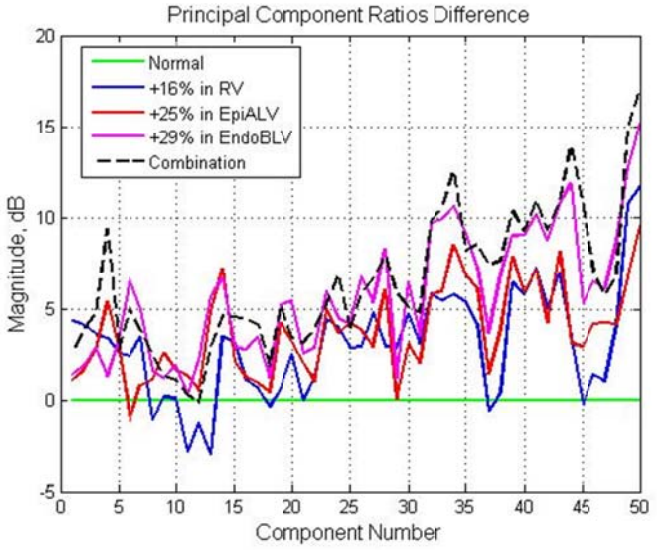


Figure 14: Comparisons of spectral magnitude in the three regions

Figure 15: Comparisons of principal component ratios difference in the three regions

with different increase percentages of APD_{90} prolongation. with different increase percentages of APD_{90} prolongation.

Result Conclusion

Figure 14 shows that the different increase percentages of APD_{90} prolongation could result in different spectral magnitude difference. Among those differences, the 16% increase of APD_{90} in idxRV caused the largest spectral magnitude difference, and the 25% increase of APD_{90} in EpiALV caused the smallest spectral magnitude difference. The differences in spectral magnitude in the three regions all occurred on low frequency, and they could cancel each other. Therefore, the combination of spectral magnitude difference was smaller than the one in idxRV.

Figure 15 shows the result of the principal component ratios differences in the three regions. From Figure 15, we see that the principal component ratios differences were almost positive, and the only negative difference occurred when the APD_{90} in idxRV was increased by 16%.

Based on the above figures and analysis, we see that different regions -- idxRV, EpiALV and EndoBLV in a heart have different sensitivities to the changes in the electric signals on the heart surface. Among the three regions, the idxRV region is the most sensitive because its spectral magnitude difference was the largest but its prolonged APD_{90} was the smallest (16%), and only the 16% increase in APD_{90} for the idxRV nodes showed negative principal component ratios difference. In addition, the combination of the three regions could lower the overall increase. The increase in spectral magnitude mainly occurred on the low frequency, so if some differences of spectral magnitude with small values could be regarded as noise. Since obesity may also arouse the changes in the electric signals on heart's surface, and the changes could be similar to the changes caused by T2DM. Therefore, there may be some relationship between obesity and T2DM as well, and by studying how sensitive the changes of electric signals could be changed in the three regions of a heart, more advanced clinical methods to treat T2DM may be put forward.

Further Discussion

Above analysis is based on the simulation on Matlab; however, the clinical measured data shows a big difference (shown below).

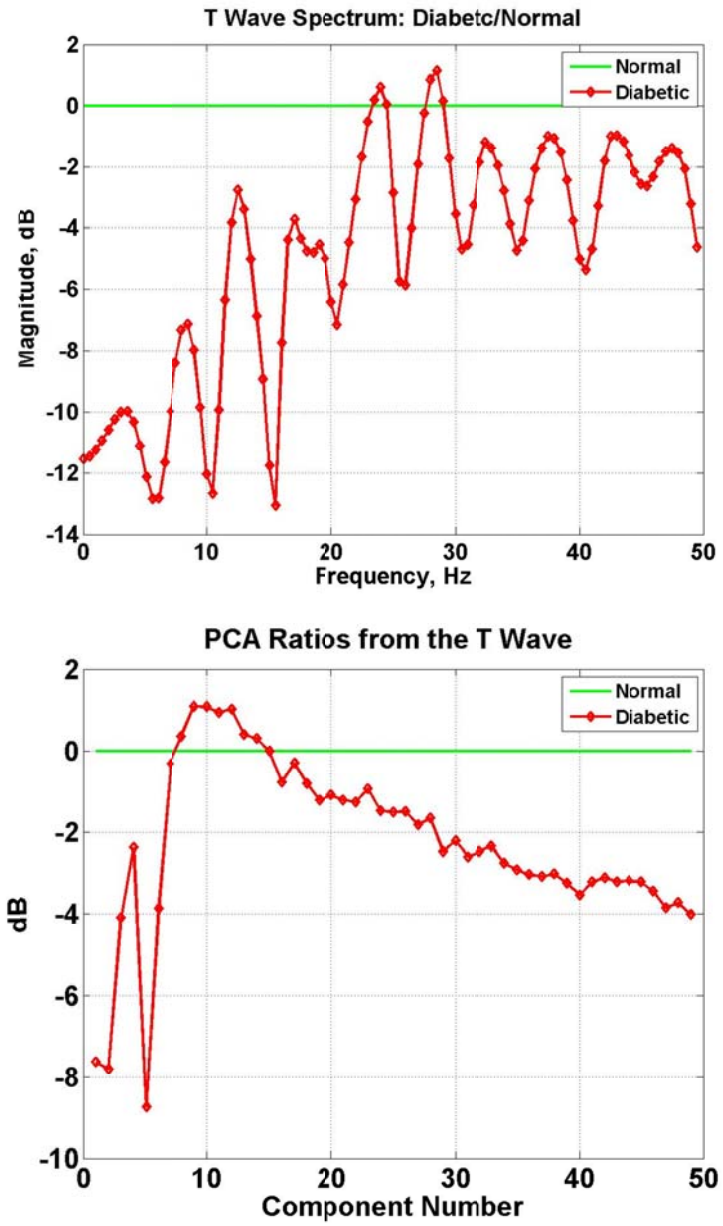


Figure 16: Clinical measured spectral magnitude difference and principal component ratios difference on the normal and diabetic subjects over T-wave.

From Figure 16, we see that the diabetic subjects decreased the spectral magnitude and principal component ratios; however, all differences in the spectral magnitude in simulation were increased, and almost all principal component ratios differences were increased as well. Therefore, we see a big difference between the simulation and clinical measurement. One possible reason causing this difference is that we always prolonged the APD_{90} in the three regions, so the results may be different if we shorten the APD_{90}.

However, when the APD_{90} were shortened in the three regions respectively, only the decrease in the EndoBLV could result in a negative spectral magnitude difference, and the largest decrease occurred when the APD_{90} was shortened by 25%. As for the principal component ratios difference, the decrease in the APD_{90} of the EndoBLV also mainly resulted in positive values.

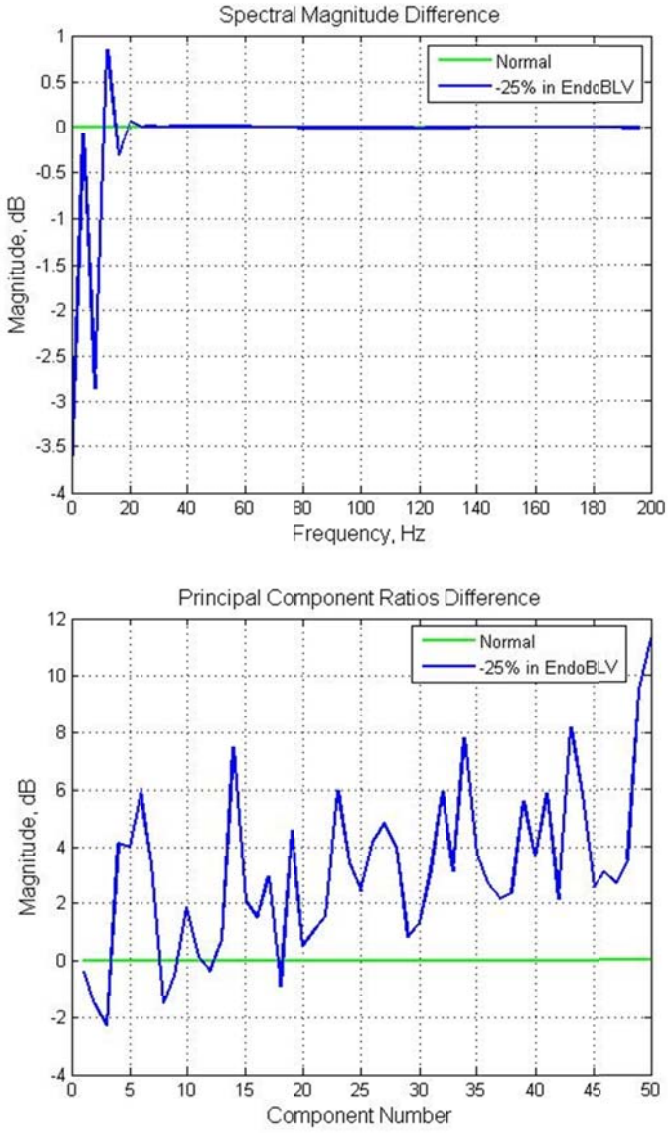


Figure 17: Comparisons of spectral magnitude and principal components on the normal and shortened APD_{90} in the EndoBLV.

In the spectral magnitude difference in Figure 17, we see that the largest decrease in spectral magnitude was around -3.6 dB; however, the increase in the RV could arouse the spectral magnitude difference to be increased by 9dB. Therefore, the combination of increases in the RV and EpiALV, and decrease in EndoBLV could also result in positive difference in spectral

magnitude. We may assume that there should be other reasons causing the negative values in the clinical measurement, like the effects of other organs. Hence, more related factors should be taken into account if this technology is planned to be used in clinical treatment in the future.

Reference

[1] S.Wang, “Electrocardiographic consequences of electrical and anatomical remodeling in diab etic and obese humans,” Ph.D. dissertation, Dept. Elect. Syst. Eng., Washington Univ., St. Louis, MO, 2009.

[2] A. van Oosterom[1] and V. Jacquemet[2], "A parameterized description of transmembrane potentials used in forward and inverse procedures," 1. Department of Cardiology, Center Hospitalier Universitaire Vaudois (CHUV), CH-1011 Lausanne, Switzerland. 2. Signal Processing Institute, Ecole Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland.