Project: Implementation of Inverse Heart Map of Absolute QRST Integral

Critical Paper Review

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Electrophysiologic substrate and intraventricular left ventricular dyssynchrony in nonischemic heart failure patients undergoing cardiac resynchronization therapy

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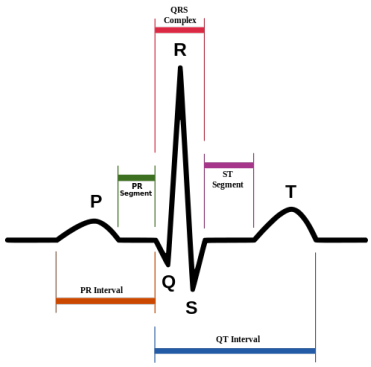
Background:

Every year, approximately 350,000 people in the United States die annually from sudden cardiac death [1]. Furthermore, half of these deaths from cardiac disease are from sudden cardiac death [1]. It is fairly well-known that ventricular arrhythmias are highly lethal and are often linked to sudden cardiac death. There are two kinds of ventricular arrhythmias: ventricular tachycardia is when there is a rapid, coordinated contraction of the ventricles, and ventricular fibrillation is when there is a rapid, uncoordinated contraction of the ventricles. Ventricular tachycardia can often degenerate into ventricular fibrillation, and therefore having a marker with which to predict patients who are at risk for ventricular arrhythmias will be invaluable.

ECGs are a very common and well-known way for doctors to diagnose patients with heart problems. They are, however, limited in the information they convey to the physician. They

do not provide very much specificity as to what the disease or arrhythmic substrate is, and do not provide good spatial resolution as to the possible location and therefore treatment of the ailment.

Below is a diagram of a typical ECG wave, outlining the P, Q, R, S, and T regions of the wave.



SAI (Sum Absolute Integral) of the QRST interval was shown by Tereschenko, et. al., [2] to be a good marker for ventricular arrhythmia susceptibility. SAI QRST has never been studied in conjunction with body surface potential maps and inverse epicardial maps, and was therefore a new area of exploration for our project. The main goal of our project was to see if SAI QRST and body surface mapping could be combined to provide a better marker for the risk arrhythmias, since epicardial inverse mapping would provide better specificity and spatial resolution.

One of our original goals was a potential application for Cardiac Resynchronization Therapy as a better marker for ICD implantation which is ineffective in approximately 60 - 70% of the population but is only refunded by Medicare/Medicaid if the QRS duration (QRSd) is greater than 120 ms [3].

Paper Choice:

The research was similar in concept in the sense that both our research and their research dealt with studying patients with left-bundle branch block, and using a new measure or marker of heart disease in conjunction with ECGi. However, their research dealt with non-ischemic (patients who did not have coronary artery disease as the underlying cause of their heart failure) patients whereas ours deals with ischemic (patients who had coronary

artery disease as the underlying cause of their heart failure) patients. Cardiac Resynchronization Therapy is applicable for both ischemic and non-ischemic patients. Nonetheless, it is a relevant paper that gave many insights into future directions of our project.

Introduction:

Cardiac Resynchronization Therapy (CRT) paces the ventricles through leads implanted through a vein in the right atrium and right ventricle and into the coronary sinus vein to pace the left ventricle. The idea of Cardiac Resynchronization Therapy is to restore synchrony of the heart and improve the mechanical performance. They procedure costs quite a bit of money, but is only effective in a proportion of the population. The PROSPECT[4] trials showed that echocardiographic methods are not good ways to predict success of CRT implants. It is, however, most widely accepted that QRS duration (QRSd) is the most relevant feature to predict CRT success. It is clear that very high QRSd indicates a high likelihood of dyssynchrony. However, it is not very clear what the effect of moderate QRSd levels are. There was seen to be improvement with CRT in people with moderate QRSd levels[5]. Therefore, this study set out to find out what tools could be used to better determine if CRT is suitable for a patient.

Summary of Methods:

The two main goals of the study were to find a common substrate that was causing dyssynchrony in patients who already had CRT devices implanted prior to the study. The second main goal of the study was to find a quantitative spatial index for dyssynchrony and see how it compared with QRS duration. ECGi was done under four different conditions: 1. Biventricular CRT pacing, 2. Left ventricular (LV) pacing, 3. Right ventricular (RV) pacing, 4. Nonpaced native rhythm (if applicable). Two of the patients had a nominal or “factory”-set ventricle to ventricle (V-V) delay that was deemed to be different from their optimally-set (V-V) delay. Isochronal lines on the epicardial surface were computed. Slow conduction is apparent as the crowding of isochrones. Activation-recovery intervals were also computed as the difference between recovery time (maximum positive value of the slope in the T-wave region), and activation time (steepest downward slope in the QRS segment of the ECG

waveform). As mentioned before, patients had a CRT device implanted at least 6 months prior to the study and were deemed to have non-ischemic cardiomyopathy through a recent angiography. Responders to CRT were shown by using echocardiography to determine a decrease in Left Ventricle (LV) Volume by 10%, and by improving their New York Heart Association class by decreasing the class to value greater than or equal to 1 (class I is the best, class IV is the worst).

The study was also seeking to find a quantitative index for LV electrical dyssynchrony and its relationship to QRSd. QRSd is an estimate of the duration of global ventricular activation as reflected on the body surface ECG. They measured LV electrical dyssynchrony through a measure they called “Electrical Dyssynchrony” or ED, which they defined to be the standard deviation of the activation times across the LV.

Important Figures in the Paper:

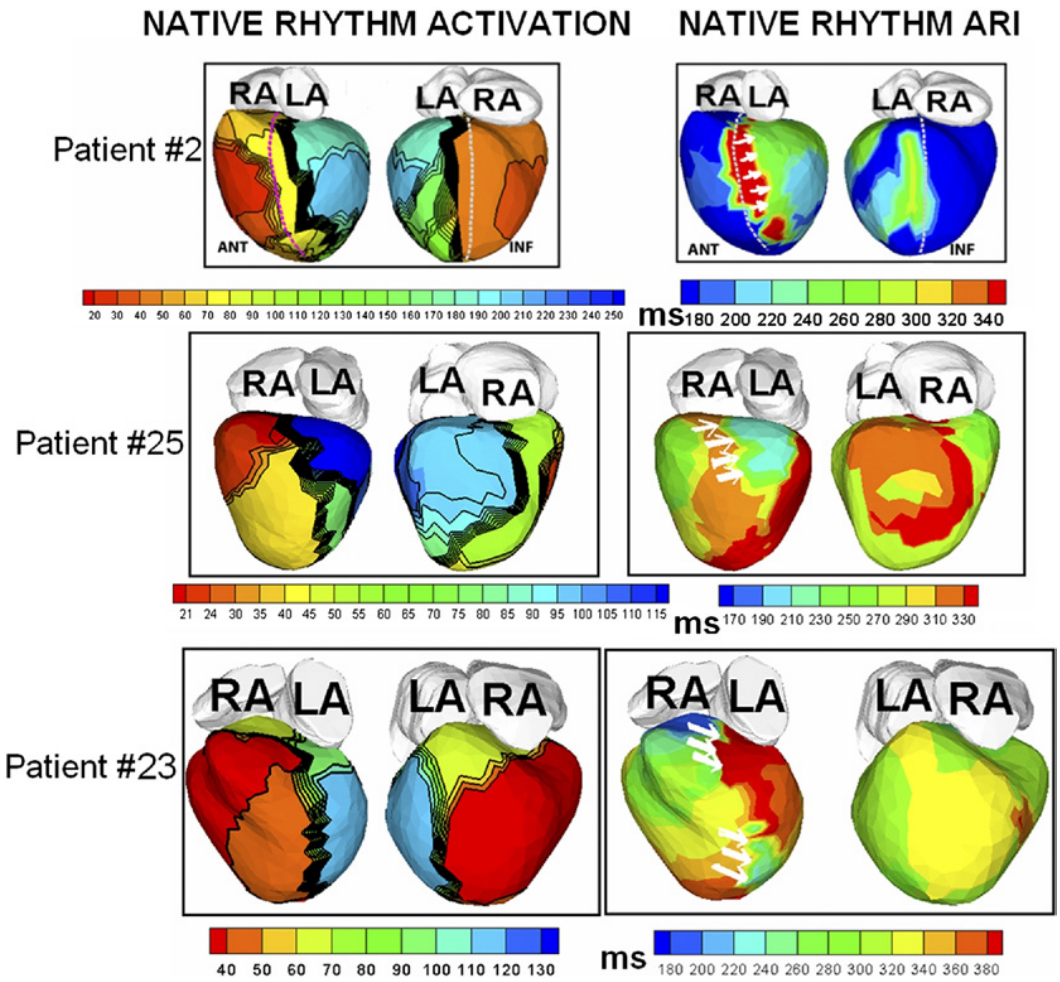


Figure 1 – showing the line of conduction block between the septum and the LV lateral wall in the native rhythm activation and in ARI, in responder patients 2, 25 and 23. All of these patients have a similar co-localization of the slowing down of currents in between the septum and the LV lateral wall.

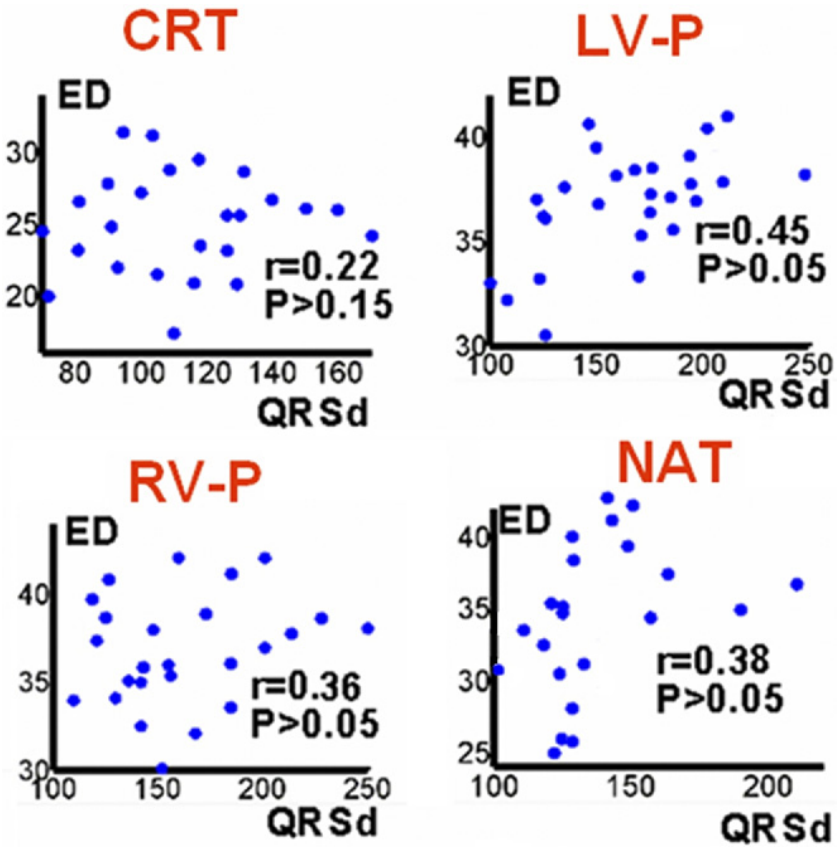


Figure 2- Scatter plots shown between Electrical Dyssynchrony and QRS duration in patients with Cardiac Resynchronization Therapy Rhythm, Left Ventricle paced (LV-P) rhythm, Right Ventricle paced (RV-P) rhythm, and Native Rhythm (NAT).

Results:

Finding a common substrate that caused dyssynchrony yielded that dyssynchrony in patients for whom CRT was successful was characterized by an inverse heart map with a line of conduction block between septum and the LV lateral wall (Figure 1). It was also seen that native rhythm activation and ARI can be used to co-localize areas of conduction block (Figure 1). These results corresponded to those maps taken invasively in the epicardium [6]. Even though there appeared to be not a very strong correlation between QRSd and ED, the author attributed that to "the two quantities not being synonymous", with QRSd being representative of global ventricular activation, and ED being a measure of LV activation dispersion. The authors claim that QRSd should not be used alone as strict cut-off for CRT

implantation, and imply that it should maybe used in conjunction with another measure such as ED, since QRSd alone seems inadequate to predict CRT responsiveness.

Critique:

I liked the fact that the paper went in depth into individual cases, illustrating in great detail what typical responders and non-responders epicardial maps looked like, and possible ways that re-entry of an electrical wave was occurring, thus causing a disturbance in the electrical circuit of the heart muscle. Furthermore, it was convincing to see that data from the epicardial projected data was consistent with invasive measurements taken from patients, as well as consistent with other animal models. I also liked how they used ECGi in more than one way to aid their study: 1.) A qualitative measure of the location of typical electrical conduction blocks in the heart as determined by ARI and activation times of the native signal. 2.) A quantitative way to measure the spatial dispersion of the activation times as a way to measure dyssynchrony of the heart.

However, the study seemed to have some conclusions that bothered me. Although they addressed this in the limitations section of their paper, I still think that it is a problem that they had only 22 patients where only 4 of them were non-responders, since we are also concerned with non-responders and it is not enough to study 4 patients and come up with a believable conclusion. Furthermore, I would have appreciated if they had given a more quantitative way to measure the location of the substrate that seemed to be characteristic of responders, rather than simply stating that the same approximate location of the substrate was seen in all patients. Lastly, they stated that a weak correlation existed between ED and QRSd (Figure 2), but at the same time, implied that QRSd should not be used alone as strict cut-off for CRT implantation, and should maybe be used in conjunction with another measure such as ED. Given the weak statistical correlation between ED and QRSd and the small sample size, I do not think that this is an entirely fair thing to state. I also do not like that they attributed the weak correlation between QRSd and ED, to “the two quantities not being synonymous”, because QRSd is a representative of global ventricular activation, and ED is a measure of LV activation dispersion. ED could have been just as easily re-calculated for the whole heart, but could have been called a different measure and

could have been compared with QRSd as a different parameter, so that they would measure close to the same thing, and could therefore be somewhat comparable.

Overall, however, I thought it was an insightful paper that showed multiple ways that ECGi would be useful for predicting CRT device success, and this has yielded new avenues for our research, such as seeing whether or not these same measures can be used in our own research to assess CRT success in ischemic rather than non-ischemic patients. If so, could these measures be used as a universal way to assess CRT success in patients.

References:

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2. Tereshchenko LG, Cheng A, Fetics BJ, et al. Ventricular arrhythmia is predicted by sum absolute QRST integral but not by QRS width. Journal of Electrocardiology 2010;43(6):548-552.

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