

## Survey of QRS frequency at various left ventricular pacing sites for cardiac resynchronization.

### Background

Many heart failure patients with prolonged QRS complexes are candidates for cardiac resynchronization therapy (CRT). The accepted rationale for CRT is that the widened QRS slows left ventricular (LV) activation to such a degree that the contraction is dyssynchronous and the ejection of blood is significantly reduced. CRT is performed by the addition of a separate pacing lead within a branch of the coronary sinus (or surgically implanted on the LV surface) and pacing at that site simultaneously with right ventricular pacing. Clinical studies have shown that patients with certain widened QRS patterns, such as left bundle branch block (LBBB), are more likely to exhibit contractile as well as clinical improvement. However, not all patients exhibit improvement. Improving the patient selection criteria for CRT based on intrinsic QRS properties as well as LV site of pacing has been an active area of clinical study.

We have shown that frequency spectrum analysis of the intrinsic QRS complex using the Fourier transform algorithm can help identify patients who are likely to improve (AKA: responders)<sup>1</sup>. In addition, we have shown that the reduction of QRS low frequency power in certain ECG leads (in particular lead V3) shortly following implant also predicts CRT responders<sup>2</sup>. We hope to begin a prospective trial to select the optimal LV pacing site based on paced QRS frequency characteristics. However, the effect of various locations of LV pacing sites on the resultant QRS frequency characteristics is not precisely known within any given patient. This study will provide us with more complete, spatially distributed QRS data in order to determine the variability in frequency signals between known locations. In this way, we will be able to design the eventual prospective study by utilizing the variance of frequency results we determine in this study to determine the study size required and specific frequency goals.

### Research procedures:

Patients who are scheduled to undergo implantation of a left ventricular pacing lead via the coronary sinus branch veins will be approached for enrollment. This will include new CRT device implants (pacemaker or ICD) or upgrade of a currently implanted pacemaker or ICD. Patients will be approached during clinical outpatient clinic visits as well as preprocedural visits just prior to entering the laboratory for the scheduled implant. We will plan to enroll an equal (or near equal) number of male and females for a total of 20-30 subjects (depending on the encountered variability of results).

After cannulation of the coronary sinus, a clinically approved Biotronik Vision guidewire will be advanced into 3 coronary sinus branch veins receiving venous blood from the anterior, lateral and posterior regions of the left ventricle. This 0.014 in guidewire is electrically insulated except for a 15 mm section near the distal tip. When connected via the 30mm uninsulated section near the proximal end to a pacing circuit, it allows pacing impulses to be delivered to selected sites within the venous branch. In each branch vein, 3 pacing sites will be tested: apical, mid ventricular and basal. We will test the anterior and posterior veins first, and then test the usually targeted lateral vein. Then, after all 3 sites within the

lateral vein are tested, a standard LV pacing lead will be advanced over the guidewire, in the usual clinical manner, for final placement of that lead. The additional time required to position and pace the 3 sites (alone and in combination with a previously implanted RV pacing lead) should not exceed 5-10 minutes, with <2 minutes of fluoroscopy. In this manner, nine distributed sites around the LV will be assessed. The procedural and fluoroscopic time required to locate and test each site will be measured starting after placing the coronary sinus delivery sheath until the delivery of the LV lead over the guidewire.

The sensed and paced QRS complexes in the normal ECG limb leads and lead V3 will be saved digitally on our laboratory monitoring system (GE Prucka). These ECG signals will be then analyzed by our frequency algorithm, in which we will manually isolate the QRS complex for time frequency analysis in which the complex will be divided into 48 time segments. The algorithm will determine the average frequency of each segment and we will then average the first 16 segments together to represent the initial third of the QRS, the middle third will be derived from the next 16 segments and the final third from the remaining segments. We will then compare the frequency data from these QRS segments between the nine different ventricular locations to derive the positional variability. Once this is obtained, we should be able to determine the sample sizes required for a randomized comparison of frequency directed LV lead placement versus standard LV lead placement. Additionally, we will measure the time required to sense the signals paced at each LV site to the RV electrode and vice versa.

## References

1. Niebauer MJ, Rickard J, Polakof L, Tchou PJ, Varma N. QRS Frequency Characteristics Help Predict Response to Cardiac Resynchronization in Left Bundle Branch Block below 150 Milliseconds. *Heart Rhythm Journal* 2014; 11:2183-2189.
2. Niebauer MJ, Rickard J, Polakof L, Tchou PJ, Varma N. Early Changes in QRS Frequency Following Cardiac Resynchronization Predict Hemodynamic Response in Left Bundle Branch Block Patients. *J Cardiovasc Electrophysiol.* 2016; 27: 594-599.