Cardiac Rhythm News
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MultiPoint™ pacing CRT technology shows promise in improving heart failure responder rates

A growing body of evidence, including the most recent randomised clinical trial results presented at HRS and CARDIOSTIM-EHRA EUROPACE, has shown that cardiac resynchronisation therapy (CRT) with MultiPoint™ pacing technology from St. Jude Medical shows promise in improving response rates in heart failure patients. *Cardiac Rhythm News* reviewed key data and also spoke to Dr. Andrew Flett (University Hospital Southampton, Southampton, UK) and Dr. Timothy Betts (Oxford University Hospitals NHS Foundation Trust, Oxford, UK) about their experience using MultiPoint™ pacing in their clinical practice.

Speaking on the need to improve response rates with CRT, Dr. Flett, who has implanted a number of patients with MultiPoint™ pacing technology and is also a participant on the ongoing MORE CRT MPP study says: "Defining CRT response is difficult, but allowing for that, there is a consistency in the trials showing that the benefits of CRT only reach around two out of three patients. We also know from the UK's national heart failure audit that despite the advances in optimal pacing and medical therapy, the prognosis for heart failure patients remains poor for a significant minority with one in three patients dead within a year of their index admission with heart failure. So there is clearly a need to improve response rates."

Dr. Betts, who has implanted over 80 patients with MultiPoint™ pacing, explains that this technology has a role in heart failure patients who are candidates for CRT. He says that patients who benefit from CRT are the ones with severely impaired left ventricular systolic function and ventricular dyssynchrony (as manifest by a QRS duration of >120ms and typically a broad left bundle branch block pattern). Agreeing with Dr. Flett, he says that "a significant challenge is that only 60–70% of CRT recipients will demonstrate a response. Therefore, MultiPoint™ pacing is a novel evolution in CRT that may improve response in certain CRT recipients."

The MultiPoint™ pacing technology utilises the St. Jude Medical™ Quartet™ quadripolar LV lead, which is uniquely designed with four electrodes capable of delivering pacing stimuli at multiple sites within the same vein. MultiPoint™ pacing is available in St. Jude Medical's latest CRT devices the Quadra Allure™ CRT-P and Quadra Assura™ CRT-D, both FDA approved (February 2016) and CE marked (December 2014).

Dr. Andrew Flett

Dr. Timothy Betts

Key clinical evidence – improved responder rates

A study of 110 patients by Zanon *et al* (*HeartRhythm* 2016;13(8):1644–1651) demonstrated that MultiPoint™ pacing combined with optimised lead placement—compared with conventional CRT and an optimised lead placement only strategy— elicits a greater acute haemodynamic improvement reversing the long-term progression of heart failure with response rates of around 90%.

Rinaldi *et al* (*Journal of Cardiac Failure* 2013;19(11):731–738) showed, in a multicentre study of 41 patients, that MultiPoint™ pacing provides mechanical benefits reducing mechanical dyssynchrony measured by tissue Doppler imaging relative to conventional biventricular pacing.

Additionally, Endrj *et al* (*HeartRhythm* 2015;12(8):1762–1769) demonstrated the electrical benefit with MultiPoint™ pacing in that the technology was able to recruit a greater portion of the left ventricle than conventional biventricular pacing, resulting in reduced activation times and QRS duration.

MutiPoint Pacing IDE study results

Results of the MultiPoint™ pacing (MPP) Investigational Device Exemption (IDE) study of over 500 patients, presented this year by Dr. Gery F Tomassoni (Lexington Cardiology at Central Baptist, Lexington, USA) at the 37th Heart Rhythm Society Scientific Sessions (HRS; 4–7 May, San Francisco, USA) and CARDIOSTIM-EHRA EUROPACE (8–11 June, Nice, France), have suggested that MultiPoint™ pacing is safe and effective and "can be used to improve responder rates".

Dr. Tomassoni highlighted the importance of MultiPoint™ pacing programming to determine the influence of this feature on CRT response. The results showed that at nine months, patients who were programmed with cathode spacing ≥30mm and 5ms left ventricular delay (n=52) had greatest response (92%) and all non-responders were converted to responders. In comparison, patients who were programmed with cathode spacing of <30mm (n=115) had a 63% response rate and 45% of non-responders were converted to responders. Another subgroup of patients who were programmed with cathode spacing ≥30mm and >5ms left ventricular delay (n=32) had a 69% response rate and 62% of non-responders were converted to responders.

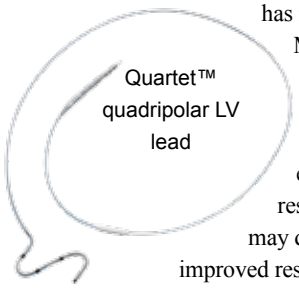
Additionally, Dr. Tomassoni noted that the trial showed that reverse remodelling tended to be greater in the MultiPoint™ pacing arm with 20% median reduction in left ventricular end-systolic volume (LVESV) (≥15% reduction) compared with 12.9% median reduction in LVESV in the biventricular arm (<15% reduction) in non-responders at nine months.

Real practice observations on response rates with MultiPoint™ pacing

Speaking on his experience using MultiPoint™ pacing in real practice, Dr. Betts says: "There are definitely some patients in whom MultiPoint™ pacing makes a difference. This could be seen at the time of implant, eg. through further narrowing of the QRS

or increase in blood pressure or dP/dt if undertaking acute haemodynamic evaluation. I have also seen non-responders at follow-up who have become responders once MultiPoint™ pacing is activated. In those patients in whom further improvement is seen at the time of implant, it is now our policy to activate MultiPoint™ pacing. Of course, there are a significant proportion of patients who will have a great response to CRT even with single-site stimulation and a small proportion who will not respond, at least symptomatically, no matter what we do. I believe, however, there is a group—probably those with significant myocardial scarring and slow ventricular conduction velocities—in whom MultiPoint™ pacing makes an appreciable difference. I think some of the most striking cases have been at the time of implant, when one can see a clear difference in ECG parameters (QRS width, axis, R wave magnitude in V1) or haemodynamic parameters when comparing single-site biventricular pacing to MultiPoint™ pacing. This difference is seen in an individual patient that illustrates the electrical effects of MultiPoint™ pacing, leading to better synchronisation. I have seen a number of patients where the QRS duration shortens by 10–20ms with the use of MultiPoint™ pacing."

Dr. Flett comments that patients in whom he has implanted MultiPoint™ pacing "seem to have done very well" and that he has seen examples of super responders. "They may do better because improved resynchronisation drives better haemodynamics allowing improved medical treatment and ultimately better positive remodelling," he notes. "One of the first cases I used MultiPoint™ pacing has done really well. He was a New York Heart Association (NYHA) class III patient who I upgraded from an implantable cardioverter defibrillator (ICD). He had to give up his hobby of sailing due to heart failure symptoms. I was able to demonstrate at the initial implant an improved blood pressure response with MultiPoint™ pacing on. At follow-up, I looked at a variety of echo parameters all of which implied he would be better off with MultiPoint™ pacing on than off. He is now NYHA class I and back on his boat."



Dr. Betts also highlights the positive effect of MultiPoint™ pacing in non-responder patients: "My own experience and that emerging from large studies shows that MultiPoint™ pacing improves response rates, certainly when using a binary outcome (responder vs. non-responder). The evidence tells us MultiPoint™ pacing can help people who are non-responders at six months. What we need to know now is who should have MultiPoint™ pacing at the time of implant. Why wait six months if the benefits could be gained immediately?

Device longevity with MultiPoint™ pacing

Regarding the impact of MultiPoint™ pacing on device longevity, Dr. Flett comments that before starting to use MultiPoint™ pacing he was "initially concerned about the potential for excessive battery drain as pacing from an extra location obviously has an effect on longevity."

He continues, "A conventional St. Jude Medical CRT device might be expected to last around seven years. It remains to be seen what the true effect on longevity for MultiPoint™ pacing devices is. With a low-capture threshold, the manufacturer predicts that the battery life might be reduced to around six years. This is comparable to the average longevity of similar conventional CRT devices."

When asked about whether longevity affects his decision-making in implanting MultiPoint™ pacing, Dr. Flett responded that longevity is "clearly important" and needs to be addressed in any decision about whether to use the MultiPoint™ pacing option. "One has to consider that more than half of heart failure patients will not survive to their first box change at six years. There are only a few that will make it to their second box change at 12 years. Even a marginal increase in exercise tolerance or reduced risk of heart failure decompensation would likely be worth it from the patients' perspective. I am, therefore, using it where the pacing parameters are favourable and the patient is symptomatic, particularly where I think there is a higher risk of CRT non-response or where the patient has a poor prognosis and the battery issue is likely a non-reality."

Advice for peers

As experienced implanters of CRT devices with MultiPoint™ pacing, Dr. Betts and Dr. Flett encourage and advise colleagues on how to use this novel technology.

Dr. Flett provides tips and tricks on when and how to activate MultiPoint™ pacing: "First, pay real attention to how you have conventional CRT set up. Ensure you have an optimal lead position and that you have optimised your inter-ventricular (VV) and atrio-ventricular (AV) delay, often Quickopt™ optimisation will do this quickly and easily. Work with your physiologists closely. Choose which pole you will use. I use the pole with the most latent activation using the QLV time."

He continues, "When you are happy that you have the best conventional CRT you can achieve, you can decide whether to activate MultiPoint™ pacing or not. First, ask yourself: Is there a favourable additional pole which is anatomically distinct with good parameters? Is there left ventricular scar seen on echo/cardiac magnetic resonance? Is the patient likely to see more benefit from a potential improved response than he/she is to suffer from an earlier box change?"

Dr. Betts comments: "I think MultiPoint™ pacing has a good theoretical benefit, which is now being demonstrated in practice. Its primary role is best for those who a good response to conventional CRT is hardest to achieve. I would encourage colleagues to use it from the outset as it has been shown to be safe, there is little to lose and potentially much to gain."

Indications and usage: St. Jude Medical™ ICDs and CRT-Ds are intended to provide ventricular antitachycardia pacing and ventricular defibrillation for automated treatment of life-threatening ventricular arrhythmias. AF Suppression™ pacing is indicated for suppression of paroxysmal or persistent atrial fibrillation in patients with the above ICD indication and sinus node dysfunction.

In patients indicated for an ICD, CRT-Ds are also intended to provide a reduction of the symptoms of moderate to severe heart failure (NYHA functional class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy (as defined in the clinical trials section included in the Merlin® PCS on-screen help) and have a left ventricular ejection fraction less than or equal to 35% and a prolonged QRS duration. They are also intended to maintain synchrony of the left and right ventricles in patients who have undergone an AV nodal ablation for chronic (permanent) atrial fibrillation and have NYHA class II or III heart failure.

Contraindications: Contraindications for use of the pulse generator system include ventricular tachyarrhythmias resulting from transient or correctable factors such as drug toxicity, electrolyte imbalance or acute myocardial infarction.

Adverse events: Implantation of the pulse generator system, like that of any other device, involves risks, some possibly life-threatening. These include but are not limited to the following: acute haemorrhage/bleeding, air emboli, arrhythmia acceleration, cardiac or venous perforation, cardiogenic shock, cyst formation, erosion, exacerbation of heart failure, extrusion, fibrotic tissue growth, fluid accumulation, haematoma formation, histotoxic reactions, infection, keloid formation, myocardial irritability, nerve damage, pneumothorax, thromboemboli, venous occlusion. Other possible adverse effects include mortality due to: component failure, device-programmer communication failure, lead abrasion, lead dislodgment or poor lead placement, lead fracture, inability to defibrillate, inhibited therapy for a ventricular tachycardia, interruption of function due to electrical or magnetic interference, shunting of energy from defibrillation paddles, system failure due to ionising radiation. Other possible adverse effects include mortality due to inappropriate delivery of therapy caused by: multiple counting of cardiac events including T waves, P waves, or supplemental pacemaker stimuli. Among the psychological effects of device implantation are imagined pulsing, dependency, fear of inappropriate pulsing and fear of losing pulse capability.