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MAXIMUM LV DP/DT$_{MAX}$ ACHIEVED WITH MULTIPOINT™ PACING AS MEASURED BY NON-INVASIVE MEANS IN A TERMINAL HEART FAILURE PATIENT

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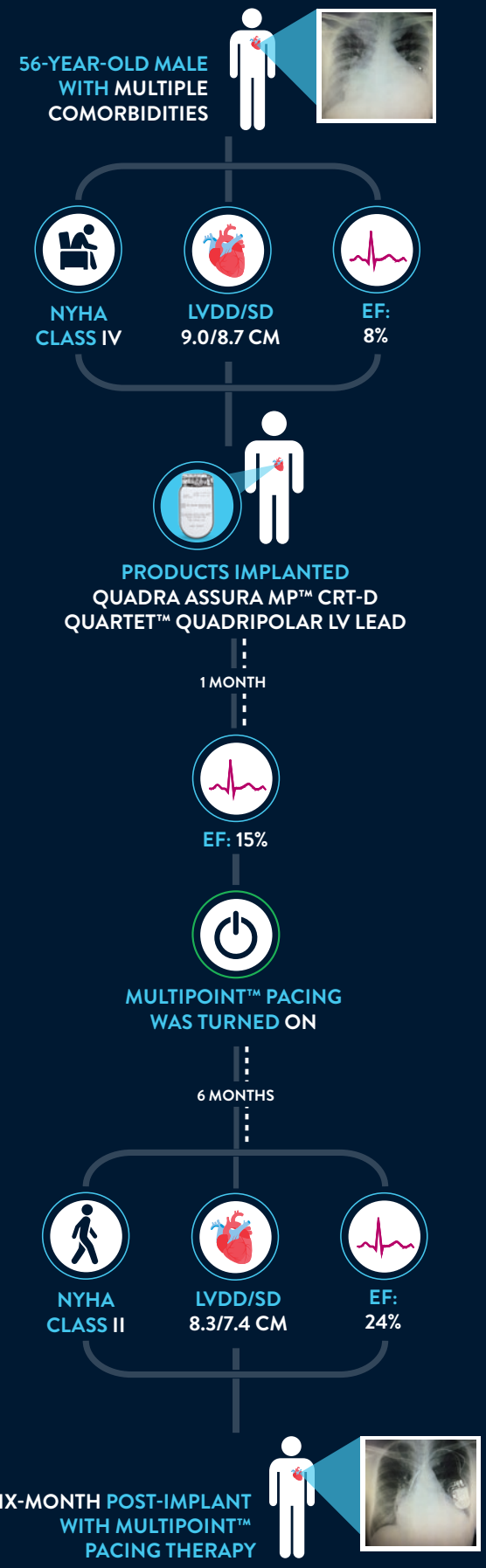
MULTIPOINT™ PACING CASE STUDY

HEMODYNAMIC CHANGES IN A PATIENT UNDERGOING CARDIAC RESYNCHRONIZATION THERAPY



PATIENT HISTORY

A 56-year-old man with advanced heart failure was initially referred for consideration of heart transplantation. He presented with repeated heart failure hospitalization since the beginning of 2014 and continued to deteriorate despite best-tolerated optimal medical therapy (NYHA Class IV ambulatory).

The patient's detailed medical history revealed multiple co-morbidities, including a history of Crohn's disease and Behcet syndrome with severe aortitis. He has a medical history of Crohn's disease and Behçet syndrome with severe aortitis. He underwent prosthetic aortic valve replacement (AVR) and mitral valvuloplasty in 2006 for severe aortic and mitral regurgitation. Due to recurrent infective endocarditis, he required lifelong clindamycin treatment. Other significant co-morbidities included renal cell carcinoma with left nephrectomy performed in 2005. MRI of the brain showed multiple old infarcts.

Taking into account the above medical history, he was considered neither a suitable candidate for heart transplant nor an implantable left ventricular assist device (LVAD) recipient. After much detailed discussions, cardiac resynchronization therapy (CRT) was offered as a last resort for him and a special effort was made to ensure the best possible CRT programming and optimization for this desperate patient.

PROCEDURE

The patient's baseline characteristics included the following:

1. ECG: Sinus rhythm with LBBB pattern (QRS duration 225 ms)
2. Echocardiography: Markedly dilated left ventricle (LV) with globally impaired contraction (LVdd/sd was 9.0/8.7 cm, ejection fraction 8%), moderate mitral regurgitation, AV prosthesis functioning with no paravalvular leakage seen

The patient underwent successful CRT-D implantation (Quadra Assura MP™ CRT-D, Abbott) with LV quadripolar lead (Quartet™ Quadripolar LV Lead 1458Q/86, Abbott) positioned in coronary sinus lateral branch in January 2015 (Figures 1a and 1b).

Acute direct invasive hemodynamic measurements of LV dP/dt_{max} could not be performed during the procedure due to the presence of mechanical aortic valve prosthesis. Instead, both acute data during implantation and subsequent chronic hemodynamic data were collected by using Nexfin™ hemodynamic monitoring system (Edwards Lifesciences) (Figure 2). The result of the dP/dt_{max} by Nexfin system measured during implantation is shown in Table 1.

Figure 1a. Retrograde coronary sinus venogram (LAO view) delineating CS branches. The metallic aortic valve prosthesis and mitral valvuloplasty ring could be clearly visualized.

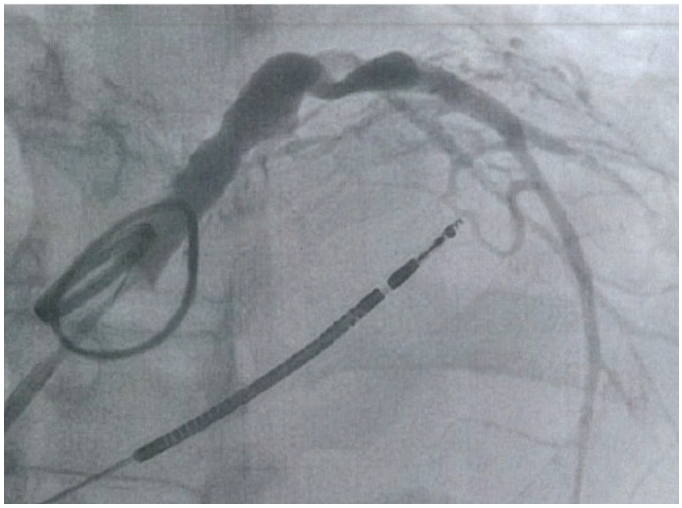
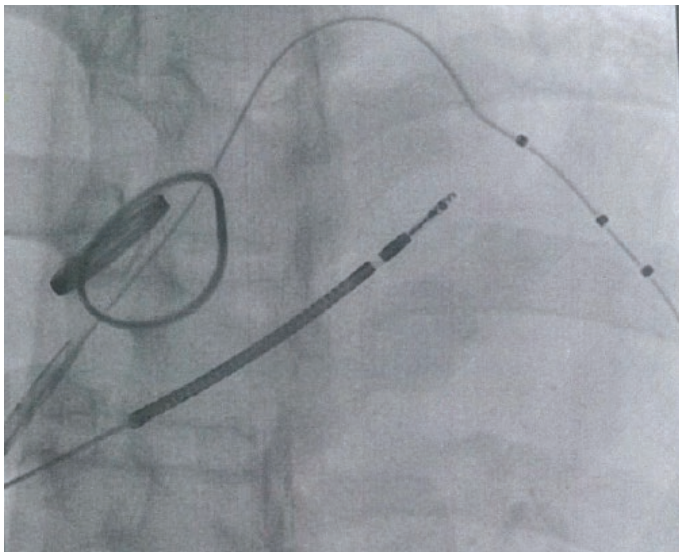


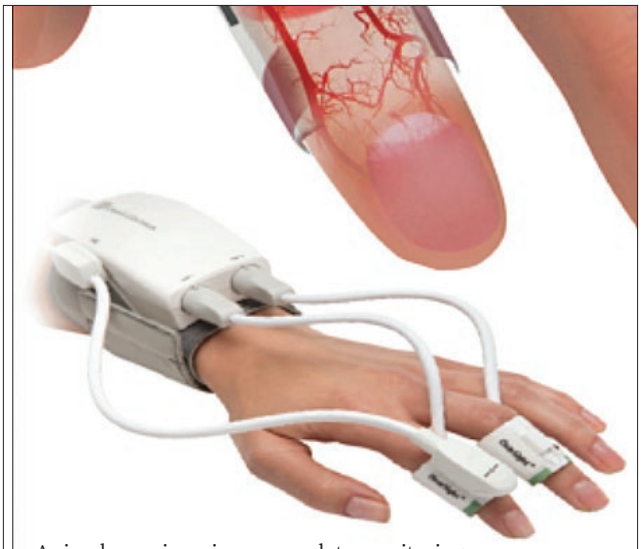
Figure 1b. Position of LV Quadripolar lead in CS posterolateral branch



Other additional features utilized for further optimization of device programming (all from Abbott) are shown in Figure 3:

1. QuickOpt™ timing cycle optimization
2. VectSelect™ programmable LV pulse configuration
3. RV-LV conduction time measurement
4. DeFT Response™ technology

In view of markedly dilated LV, MultiPoint™ Pacing (Abbott) was not turned on until one month follow-up when the final position of the LV lead was fixed and stabilized. We repeated the echocardiogram at one month post-conventional biventricular pacing, three and six months after MultiPoint™ Pacing was programmed at best selected configurations as guided by dP/dt_{max}.



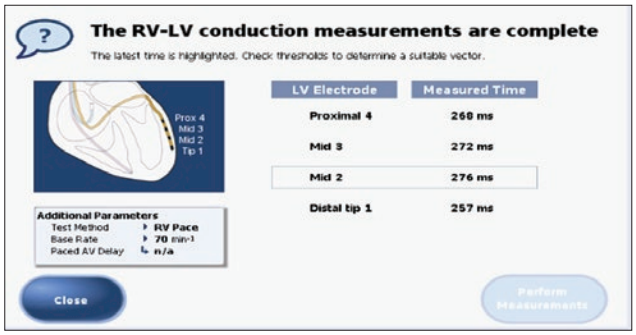
A simple, noninvasive approach to monitoring key hemodynamic parameters.

- Stroke Volume (SV)
- Stroke Volume Variation (SVV)
- Cardiac Output (CO)
- Systemic Vascular Resistance (SVR)
- Continuous Blood Pressure (cBP)

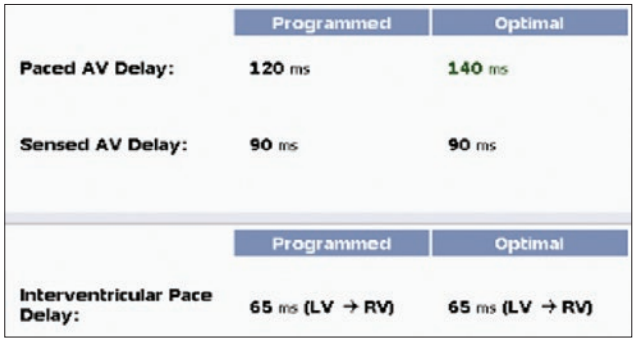
Cross-section of cuff application.

To accurately mirror arterial line output, real-time finger pressure measurement is performed 1000 times per second utilizing the volume clamp method.

Figure 3. Measurement of RV-LV conduction and QuickOpt™ optimization for recommendations of MultiPoint™ Pacing setting



Measurement of RV-LV conduction delay try to find out the longest conduction time and shortest conduction time.



QuickOpt™ optimization measurement

Table 1. Results of LV dP/dt_{max} measurement by Nexfin™ system during implant

Types of measurement	Mode of Pacing	dP/dt_{max} Measurement
Baseline	ApVs	856
RV pacing only	ApRVp	891
LV pacing only LV pacing D1 to M2	ApLVp	1107
Bi-V pacing with nominal setting LV: D1 to M2 PAV: 140 ms/SAV: 90 ms/Simultaneously	ApBiVp	1133
Bi-V pacing with QuickOpt™ optimization LV: D1 to M2 PAV 140 ms/SAV 90 ms/ LV first 65 ms	ApBiVp	1126

Table 2. Measurement of dP/dt_{max} by Nexfin™ system one-month follow-up

Mode of pacing			dP/dt measurement (mmHg)
MultiPoint™ Pacing	LV1: M2-P4 LV2: M3-M2	LV1 - LV2 Delay: 5 ms LV2 - RV Delay: 30 ms	1120
		LV1 - LV2 Delay: 10 ms LV2 - RV Delay: 25 ms	1124
		LV1 - LV2 Delay: 15 ms LV2 - RV Delay: 20 ms	1161
		LV1 - LV2 Delay: 20 ms LV2 - RV Delay: 15 ms	1209
		LV1 - LV2 Delay: 25 ms LV2 - RV Delay: 10 ms	1262
		LV1 - LV2 Delay: 30 ms LV2 - RV Delay: 5 ms	1273

RESULTS

The patient was discharged home with CRT pacing under conventional biventricular pacing configuration, namely PAV 140 ms/SAV 90 ms with LV first 65 ms by QuickOpt™ optimization, and quadripolar LV lead vector of D1-P4 since this configuration had the lowest capture threshold without phrenic nerve stimulation. His ECGs at baseline and post CRT implantation were showed in Figures 4a and 4b.

Figure 4a. ECG at baseline with LBBB pattern (QRS duration: 225 ms)

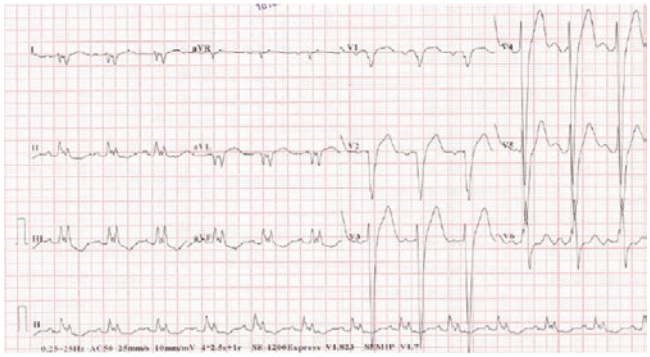
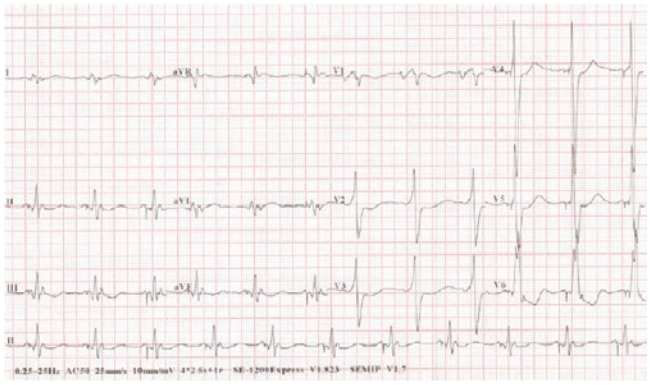


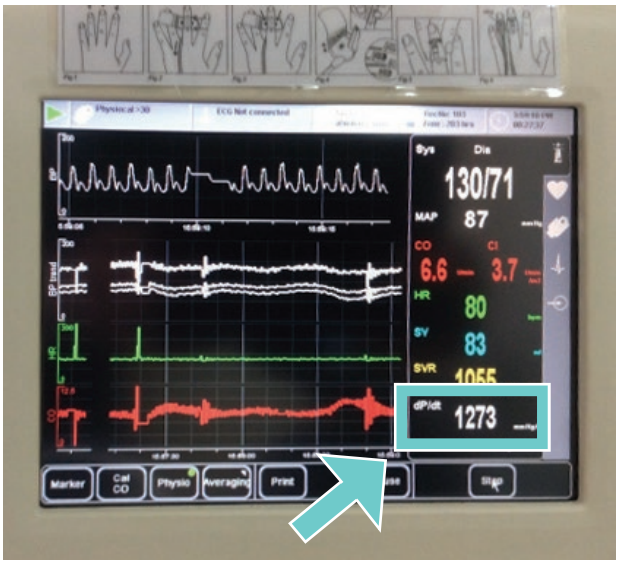
Figure 4b. ECG at post-CRT-D implantation



The patient returned at one month post-implantation and was reassessed with an echocardiogram (LVdd/Sd 9.3/8.6cm, EF 15%) and underwent repeat cardiac resynchronization therapy optimization using Nexfin™ continuous hemodynamic monitoring system as guidance (Figures 5a and 5b). Due to non-invasiveness of Nexfin™ system, we devised a more detailed study by testing various combinations of MultiPoint™ Pacing programming in order to identify the best cardiac output with maximum dP/dt_{max}. In this case, the best MultiPoint™ Pacing configuration was LV1(M2-P4) to LV2(M3-M2): 30 ms and LV2(M3-M2) to RV 5 ms as shown in Table 2. His latest echocardiogram performed six months post-implant showed significant remodeling effects (LVdd/sd 8.3/7.4 cm, EF 24%). A comparison of his chest X-rays before CRT-D implantation and at six months was shown in Figures 6a and 6b showing evidence of significant reduction in cardiomegaly. Clinically, the patient has significant improvement in exercise tolerance (NYHA Class II) during subsequent follow-ups.

Figure 5a. Patient undergoing detailed study with various MultiPoint™ Pacing programming combinations.

Figure 5b. Best dP/dt_{max} 1273 mmHg (arrow) indicated with best optimal MultiPoint™ Pacing setting



DISCUSSION

Cardiac resynchronization therapy has been shown to improve exercise capacity and quality of life and to reduce heart failure hospitalizations and mortality in patients with NYHA Class III and IV heart failure.[1,2] In randomized studies, the number of NYHA Class IV heart failure patients enrolled has been very low. Many NYHA Class IV patients are still considered unsuitable for survival studies and have been systematically excluded from clinical trials because of the expectation of a much shortened lifespan. The COMPANION trial's sub-analysis of NYHA Class IV patients demonstrated that CRT-P and CRT-D improve only the combined endpoint of time to all-cause mortality and hospitalizations in ambulatory NYHA Class IV patients but could not show a benefit on survival.[3-5]

In reality, the line between NYHA classes is not distinct and determination of disease severity in heart failure requires a wide range of clinical, biochemical and functional parameters. As a result, universally accepted and definable measures are still lacking. Furthermore, many of these patients are ambulatory but require repeated hospitalizations with resource-consuming treatments, and neither heart transplant nor implantation of assist devices are appropriate treatment for them. The patient reported here illustrated the actual reality case in which carefully titrated MultiPoint™ Pacing therapy allowed significant reverse remodeling in an otherwise desperate patient with end-stage heart failure, which we encountered other than those patients included and reported in large randomized clinical survival studies.

Invasive acute hemodynamic response by measuring dP/dt_{max} to guide LV lead implantation predicts chronic remodeling in patients undergoing CRT.[6] This was contraindicated in this patient with mechanical aortic valve prosthesis and thus we resorted to use an alternative non-invasive hemodynamic monitor Nexfin™ system as a guide to clinical decisions for guiding MultiPoint Pacing therapy for this patient. In fact, due to its non-invasive nature, future refinement of MultiPoint Pacing programming during short- and long-term follow-ups becomes an added bonus.

The measurement of cardiac output (CO) has been traditionally limited to critically ill patients in the intensive care unit. However, with an increasing number of heart failure patients undergoing device therapy such as CRT, goal-directed therapy of maximizing CO and dP/dt_{max} values in acute setting and long-term management guided by non-invasive manner is desirable. The recently introduced Nexfin™ monitoring system is a completely non-invasive system requiring only the use of pneumatic finger cuff, without the insertion of any intravascular lines. It consists of a model-based method that provides beat-to-beat measurement of CO by analysis of the non-invasive finger arterial blood pressure trace, which is measured continuously by the use of an inflatable finger cuff. Stroke volume is determined by dividing the pulsatile systolic area of each beat by impedance, which is estimated by the device based on patient characteristics.

Numerous studies have been published validating this technique for monitoring blood pressures when compared to invasive monitoring.[7,8] Although this was associated with some conflicting results as to its potential usefulness with recent studies, it showed promising results in regards to its ability to trend when compared to pulmonary artery catheter values,[7,9] transthoracic echocardiography and esophageal Doppler.[10] Furthermore, we propose that CO and dP/dt_{max} data obtained by a less invasive technique, even if slightly less accurate, may be preferable if it can be obtained more rapidly and conveniently, and allows tracking and titrating the short-term and long-term effects of MultiPoint™ Pacing in patients with advanced heart failure implanted with CRT.

CONCLUSION

In addition to a novel and innovative approach at the optimization of therapy using the Nexfin system, this case study reflects a significant clinical improvement with MultiPoint Pacing in the conversion of a hemodynamically unstable NYHA class IV heart failure with multiple comorbidities, who was previously rejected for advanced heart failure treatments.

Figure 6a. X-ray pre-implant

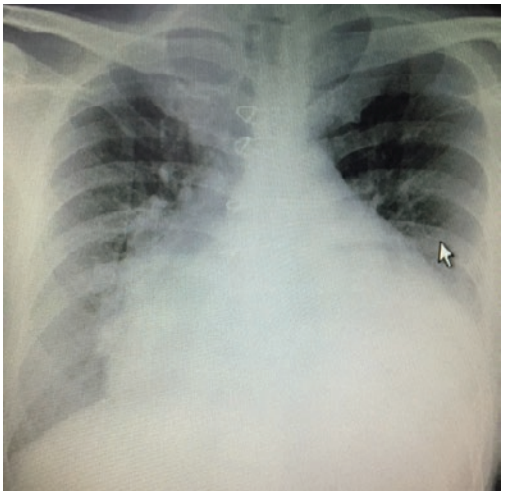
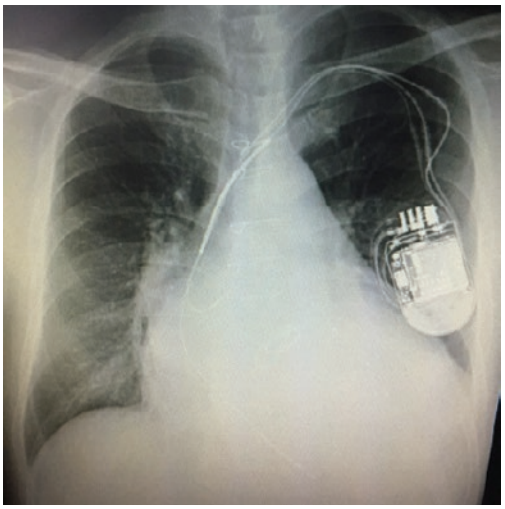


Figure 6b. Six-month post-implant with MultiPoint™ Pacing therapy



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Brief Summary: Please review the Instructions for Use prior to using these devices for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

Quartet™ LV lead
Indications and Usage: The Quartet lead has application as part of an Abbott Biventricular system.
Contraindications: The use of the Quartet lead is contraindicated in patients who:
• Are expected to be hypersensitive to a single dose of 1.0 mg of dexamethasone sodium phosphate.
• Are unable to undergo an emergency thoracotomy procedure.
• Have coronary venous vasculature that is inadequate for lead placement, as indicated by venogram.

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Indications: Abbott 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 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 hemorrhage/bleeding, air emboli, arrhythmia acceleration, cardiac or venous perforation, cardiogenic shock, cyst formation, erosion, exacerbation of heart failure, extrusion, fibrotic tissue growth, fluid accumulation, hematoma 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.

Refer to the User's Manual for detailed indications, contraindications, warnings, precautions and potential adverse events.

28623-EM-MLP-0515-0014(5) | Item approved for U.S. and OUS.

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