ST. JUDE MEDICAL

Response Submitted to PACE Affirming Performance of Riata Leads

An article has been submitted to Pacing and Clinical Electrophysiology (PACE) journal responding to an editorial concerning Riata leads that is expected to be published by PACE on November 12, 2007.

A full copy of this article entitled "Lead Perforation: Incidence in Registries," written by Mark D. Carlson[*] MD, Roger A. Freedman[+] MD, and Paul A. Levine[*] MD, has been accepted and is expected to be published by PACE in December 2007.

A summary of the information in the article follows.

Pacemaker and implantable defibrillator lead perforation, although relatively uncommon, is a recognized potential complication of pacemaker or defibrillator lead implantation. Published event rates range from 0.1% to 0.8% for pacemaker leads and 0.6% to 5.2% for implantable defibrillator leads (1). Lead perforation is often attributed to one or a combination of factors including:

- patient characteristics (such as medical condition, structural heart disease, recent myocardial infarction, gender, low BMI, use of oral steroids or blood thinners, etc.)
- design characteristics of the lead
- implant techniques.

The performance of the Riata family of leads has been strong. Like other manufacturers of implantable pacemakers and defibrillators, St. Jude Medical encourages, logs and tracks all verbal and written reports with respect to any device or lead issue, including perforation. Among returned products and reported incidents involving 121,000 implanted Riata leads in the United States, a perforation incidence rate of 0.086% has been observed. This voluntary field reporting indicates an incidence of 0.057% for 86,000 Riata 8 French (8F) leads and 0.157% for 35,000 implanted 7F leads.

In addition to returned product analysis, St. Jude Medical has three large, prospective registries to actively monitor the performance of devices, both leads and pulse generators:

- The ACT Registry is designed to monitor clinical outcome, including device performance, of patients receiving ICD and CRT-D systems. It has enrolled 5,461 patients with systems implanted at 333 centers by over 400 physicians between November 2004 and March 2006. The ACT Registry follows 4,721 patients implanted with Riata leads, 4,704 of which are 8F leads and 17 of which are the newer 7F Riata ST leads. The median follow-up in the ACT Registry is two years and all patients have been followed for over one year. Details from this registry related to perforation are shown in the table below.

- The OPTIMUM Registry is designed to monitor the long-term performance of leads utilizing Optim™ insulation, a novel co-polymer that combines the best attributes of the standard lead insulating materials, silicon rubber and polyurethane, based on bench testing and in-vivo studies. The OPTIMUM Registry opened enrollment in August 2006 and as of October

2007, includes 2,877 patients at 128 centers with implants performed by 208 physicians. This registry currently follows 1,144 patients implanted with the 7F Riata lead, of which 220 have been followed for more than one year. Details from this registry related to perforation are shown in the table below.

- The third active registry, SCORE, started enrolling patients in June 2007. It will monitor indefinitely the performance of all implanted St. Jude Medical CRM products at 40 major US centers. Currently the number of Riata leads entered into the SCORE registry does not allow for meaningful analysis.

As recommended by the Heart Rhythm Society Task Force on Device Performance Policies and Guidelines (3), the lead data provided by these registries are updated, analyzed, and shared with the physician members of the St. Jude Medical Independent Leads Medical Advisory Board on a regular basis. This information is also provided as part of the Company's Product Performance Reports that are submitted to the FDA and available on St. Jude Medical's website.

As shown in Table 1 below, the incidence of Riata lead perforations in the ACT and OPTIMUM prospective registries is 0.33% to 0.34%. Like the data from voluntary returns and complaints analysis, these two prospective active registries indicate that both the 7F and 8F Riata lead have incidences of perforation below or at the low end of what has been reported in the medical literature for defibrillation leads (1,2). In addition, the rate of Riata perforation is comparable or below that observed for standard right ventricular pacing leads (0.50%) also being followed in the OPTIMUM registry. These rates affirm the strong performance and reliability of Riata.

As previously noted, factors contributing to lead perforation are patient characteristics, the design characteristics of the lead, and implant techniques. Khan and colleagues noted the importance of lead position in minimizing the risk of acute or delayed perforation, suggesting that attempts should be made first to place leads in the septal wall (1). Different leads have different handling characteristics and some physicians vary their implant techniques accordingly. The importance of "understanding anatomy and the nature of one's tools," cannot be over-emphasized (4). In particular, the practice of torquing the lead body after the helix has been fully extended is fairly common, but may contribute to the occurrence of perforations (5).

St. Jude Medical has implemented defibrillation lead design changes over time to enhance performance and reliability. The Riata lead included lead body and conductor enhancements designed to reduce the incidence of fractures, and has undergone several iterations including the introduction of the Optim™ insulation material designed to enhance handling, abrasion resistance, and long-term performance. Additional design modifications intended to improve ease of use and lead handling for some physicians are being implemented and will be contained within the next iteration of the device.

Physicians should continue to bring procedure complications and adverse events to the attention of the clinical community, the companies that manufacture the products involved, and the FDA. Prospective lead registries serve the important role of providing a more accurate estimate of the incidence of lead-related complications and provide perspective to case reports and returned product reports. Through these measures, physicians and device manufacturers may identify

implant techniques and device designs to further minimize the incidence of these events and continue to improve patient outcomes.

Table 1: ACT and OPTIMUM Registries: perforations

	ACT Registry€ (Incidence/Population)	**ACT€ Incidence (%)**	**OPTIMUM Registry (Incidence/Population)**	**OPTIMUM Incidence (%)**
Riata (7F & 8F)*	16/4721	0.34%	4/1207	0.33%
Riata 7F**	0/17	0%	4/1144	0.35%
Riata 8F†	16/4704	0.34%	0/63	0%
RV Pacemaker Leads	NA	NA	7/1383	0.50%

* 0.086% of 121,000 patients based on returns/complaints
** 0.160% of 35,000 patients based on returns/complaints
† 0.057% of 86,000 patients based on return/complaints
€ Includes migrations/dislodgments as the case report forms used in the ACT Registry did not explicitly call out perforations. Therefore, the data included here are conservative; the true incidence of perforations in the ACT Registry is probably lower.

Bibliography:

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* St. Jude Medical CRMD, Sylmar, CA
+ Director of Clinical Cardiology and Professor of Medicine, University of Utah Health Sciences Center, Salt Lake City, UT and member of the St. Jude Medical Independent Leads Medical Advisory Board