● 特別演題

The Reliability of Modern Pacing Leads

Michael J. Ebert　K. B. Stokes　R. McVenes
Medtronic, Inc. 7000 Central Ave. NE, Minneapolis, MN 55432 USA

SUMMARY

Pacing lead designs are differentiated by ease of implant, electrical characteristics, reliability and removability. There is no lead that is easy to implant in any location in all patients. As a result there is a range in lead styles to provide options. Good lead, fixation and electrode design facilitate generator programming that reduces current drain and provides optimal therapy while assuring safety. New electrode technology has achieved low, stable thresholds with excellent sensing and high impedance.

Lead reliability has improved with increasing knowledge of the environment in the body and performance data provided by clinical actuarial studies. To be reliable a lead must be biocompatible, biostable and provide a stable electrode position. A lack of biocompatibility could result in compromised performance of the lead evidenced by poor electrical parameters, sustained inflammation and other complications. The development of standardized material biocompatibility testing has minimized any issues regarding the effect of materials on the body. We are still learning about the effects the body has on the lead. The body attacks foreign objects chemically as well as physically. The result of this attack can be evidenced in the lead insulation as ESC, MIO, compression failure, wear and mineralization. Clinically, regardless of the mechanism, a hole in the outer lead insulation could result in muscle stimulation, muscle inhibition, increased current drain and possibly sensing problems in unipolar leads. A breach of the insulation between the conductors in a bipolar lead can result in pacing and/or sensing problems. Patient symptoms, EKG's, Holter monitor and pulse generator diagnostics can be used to identify system issues, which includes lead failure. In the future, pulse generator algorithms will detect impending lead failure before symptoms appear.

Lead encapsulation occurs due to endothelial damage and blood flow perturbations caused by the lead. A thrombus forms on the lead that, if it does not resolve, can organize into a fibrotic sheath. The process of removing a lead requires disengaging the sheath by countertraction or laser catheter. The lead must be isodiametric and strong enough to withstand the pulling. Strong lead body junctions prevent the lead from coming apart. The future may include new biologically active surfaces to facilitate safe, easy chronic lead removal.

In conclusion, a better understanding of the human body, improved lead designs, improved materials and clinically based postmarket surveillance have resulted in more reliable, easier to use leads.

The failure mechanisms that effect lead insulation differ depending upon the insulation material. Polyurethane lead insulation is susceptible to environmental stress cracking (ESC) and metal ion oxidation (MIO). Silicone lead insulation is susceptible to compressive creep, cut-through, wear and mineralization.

ESC by definition is the formation of internal or external cracks in a plastic caused by tensile stresses less than that of its short-term mechanical strength, when such strength has been reduced by aging or exposure to some environmental condition[1]. ESC in implanted polyurethane leads is deep crazed or torn cracks in the bulk polymer from the outer (tissue contacting) surface inward. ESC is not a failure mechanism if the cracks do not penetrate completely through the insulation. **Fig. 1** shows an oxidized surface next to a ligature site. **Fig. 2** shows a magnified view of **Fig. 1** revealing the surface cracking. **Fig. 3** and **4** show a breach in the insulation resulting from ESC[2].

The sequence of events following injury is acute inflammation, chronic inflammation, granulation tissue, foreign body reaction and fibrosis[3]. Macrophages arrive at the injury during the chronic inflammation phase and part of their role is to ingest small particles (bacteria). However, with a device the macrophage becomes frustrated because it cannot ingest the device. **Fig. 5** shows the sequel of events that occur when a macrophage encounters a device. The

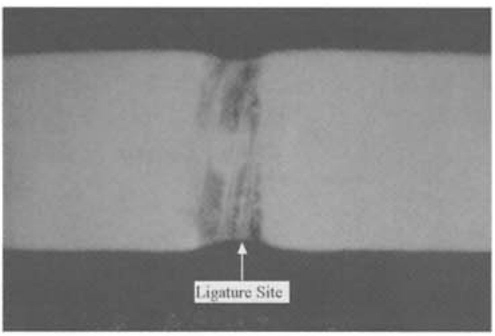

Fig. 1 Oxidized surface adjacent to ligature

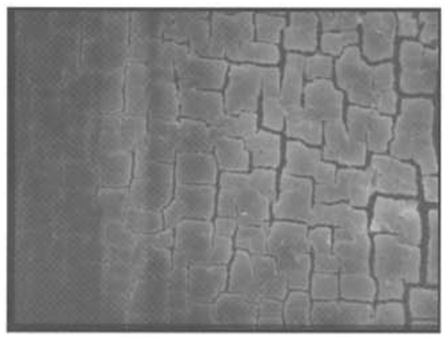

Fig. 2 Adjacent to ligature 500X magnification

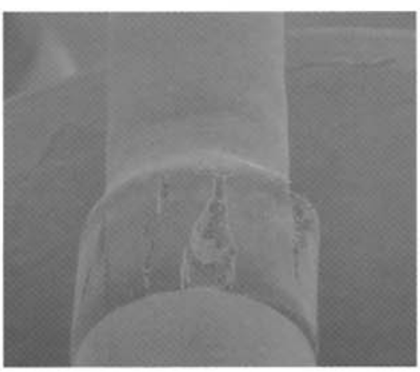

Fig. 3 ESC breach at anode

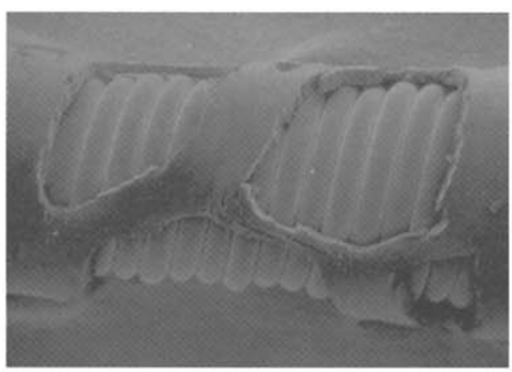

Fig. 4 Extreme example of ESC

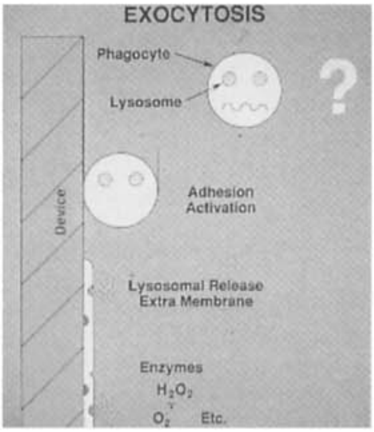

Fig. 5 Macrophages attacking a device surface

Fig. 6 Craze

Fig. 7 Crack formed from a craze

macrophage adheres to the surface and combines with other macrophages to form foreign body giant cells. Lysosomal release of strong oxidants and enzymes are intended to destroy the foreign body.

ESC occurs when the oxidants combine with a protein catalyst (like α_2-macroglobulin or ceruloplasmin) and stress in the polymer to break the ether linkage in the polyurethane. **Fig. 6** shows the polyurethane chains and the formation of a craze. The craze is the result of the residual stress and the protein absorption initiated by surface oxidation. The polymer chains break because of the presence of the protein, the residual stress and the oxidants to form the crack (**Fig. 7**).

ESC is prevented in Pellethane® polyurethane leads by using thicker polymer sections, annealing the insulation to relieve residual stress or by using a polyurethane with less ether (55D). ESC can also be prevented using silicone rubber or some new different polymers as the insulation material.

Metal ion oxidation (MIO) is a bulk oxidation of the polyurethane by metal ions or catalyzed by metal ions. **Fig. 8** shows MIO cracks on the inside surface of the polyurethane lead insulation. MIO cracks start where the coil contacts the polyurethane. In order for MIO to occur there must be a source of metal ions. Cobalt ions are present as a corrosion by-product of MP35N or Elgiloy coils. There also needs to be a source of oxygen, at least initially. MIO can be accelerated by moisture ingress into the lead, stress in the conductor (accelerates conductor corrosion), electrolytes in the lead and possibly by proteins inside the lead. Electric current from the pacemaker is not a requirement for MIO. MIO can be prevented in pacing leads by using barrier coatings or using a new metal for the conductor that would not release cobalt ions during corrosion. Thicker insulation has been effective in reducing MIO. However, thicker insulation results in bigger, stiffer leads. New polymers could be found that are not susceptible to MIO, but they may be susceptible to another degradation mechanism. Silicone rubber can be used for insulation as it is not susceptible to MIO. However, silicone rubber insulation is susceptible to mechanical damage in the body.

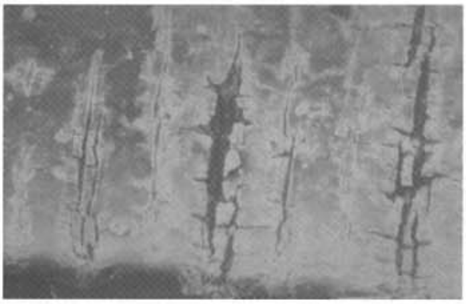

Fig. 8 MIO inside lead insulation

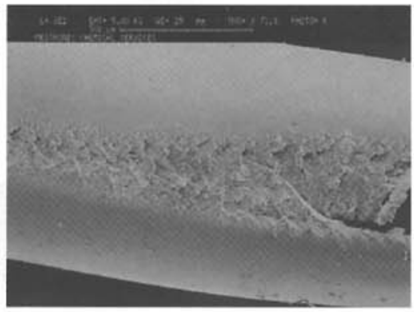

Fig. 9 Wear on a silicone rubber lead

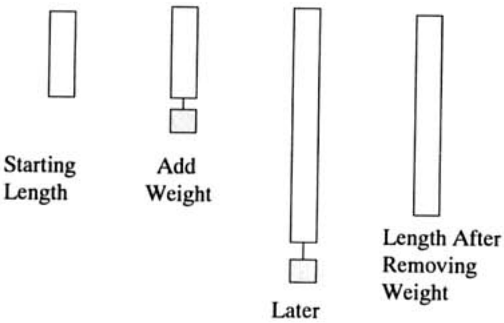

Fig. 10 Example of tensile creep

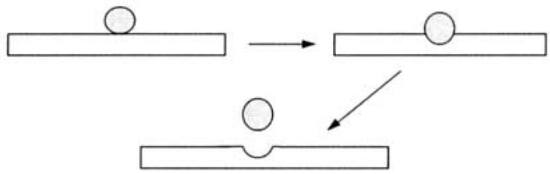

Fig. 11 Example of compressive creep

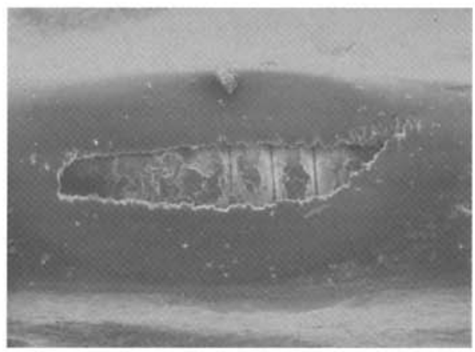

Fig. 12 Creep failure of a silicone rubber lead

Insulation materials are exposed to mechanical forces *in-vivo*. Polyurethanes are stronger mechanically than silicones and less susceptible to mechanical damage. Silicone insulation can fail due to wear (**Fig. 9**), compressive creep (**Fig. 12**) or crush. Wear results when another object rubs back and forth over the lead. **Fig. 9** shows the wear that occurred in the first rib and clavicle region on a failed lead.

Creep is the permanent deformation of a plastic resulting from prolonged application of a stress below the elastic limit. For example, if you hang a weight on a piece of plastic and leave it for some amount of time, the sample gets longer. When the weight is removed, if the material does not return to the original length, the change in length is due to creep (**Fig. 10**). Creep can occur under compression as well as tension. Under compression the plastic flows away from the load (pressure) and takes a new shape. Compressive creep can result in a breach of the silicone outer insulation (**Fig. 11**). Creep has not been a failure mechanism for polyurethane leads. In a pacing system the sustained load (stress) is applied by the pulse generator, other leads, sutures

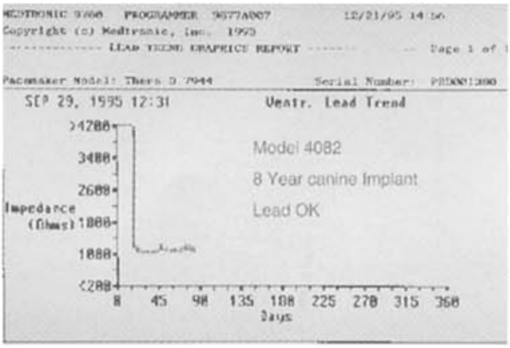

Fig. 13 Thera® lead trend on a good lead

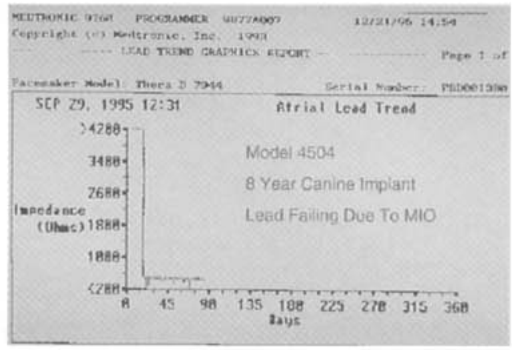

Fig. 14 Thera® lead monitor on a failed lead

Table 1 Comparison of the lead performance based upon Medtronic Returned Product Analysis data and CLS data

Model number	Number sold in US	Years implanted	Returned product survivability*(%)	CLS survivability*(%)
4012	96791	13	99.2	66±4.3
4512	11562	11	99.4	85±5.8
4004	74485	8	99.2	58±5.2
4504	16637	7	99.3	73±7.6
6971	56261	15	99.5	82±5.1

*Based on data in the September, 1998 Medtronic Product Performance Report

tied on the lead body or bones/ligaments such as those in the first rib/clavicle region. Creep failures can be prevented with thicker silicone insulation or a better silicone rubber. Creep has not been a significant failure mechanism for present Medtronic leads but has been for some competitors with too thin insulation.

Insulation failures will have different clinical manifestations depending upon the lead polarity and which insulation fails in a bipolar lead (outer or inner). An insulation failure in a unipolar lead would decrease the impedance and possibly change the threshold. If the unipolar lead insulation breach were in the skeletal muscle there could be muscle inhibition or stimulation. If the outer insulation in a bipolar fails there would be no effect unless the breach was in the skeletal muscle. An inner insulation failure in a bipolar lead can result in intermittent oversensing/undersensing, intermittent pacing, loss of sensing and eventually a complete short (inner and outer coils touching) resulting in complete loss of capture. One method of determining lead failure has been a significant decrease in pacing impedance. Analysis of canine data with failing leads has shown intermittent impedance drops prior to lead failure.

Detecting lead problems before symptoms appear is difficult. One tool that has been helpful has been the Thera® Lead Impedance Trend Monitor. **Fig. 13** shows a Thera® lead trend monitor data for a Model 4082 lead that had been implanted 8 years in a canine and was verified to be okay at explant. **Fig. 14** shows the Thera® lead data for a Model 4504 lead that had been implanted for 8 years in a canine and was failing due to MIO. Note the transient decreases that

Table 2 Performance of currently manufactured polyurethane and silicone insulated leads

Model number	Years implanted	CLS survivability*(%)
4024 (polyurethane)	6.0	99.9±0.2
4524 (polyurethane)	5.3	99.6±0.5
5024M (silicone)	7.0	99.4±0.3
5524M (silicone)	5.7	99.6±0.3
4058 Ventricle (polyurethane)	7.5	93.7±4.3
4058 Atrium (polyurethane)	7.7	96.1±3.4

*Based on data in the September, 1998 Medtronic Product Performance Report

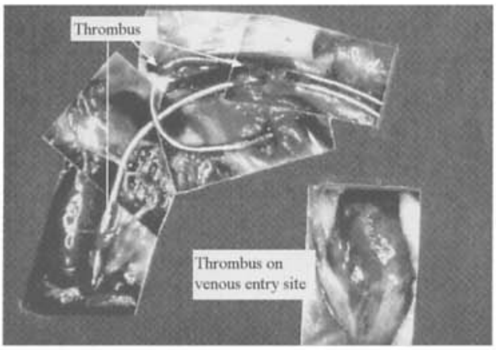

Fig. 15 Thrombus formation after 10 days in canine

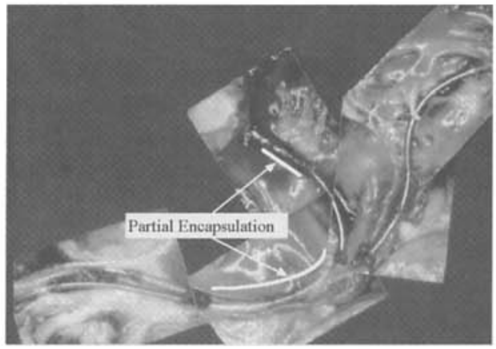

Fig. 16 Partial lead encapsulation in canine

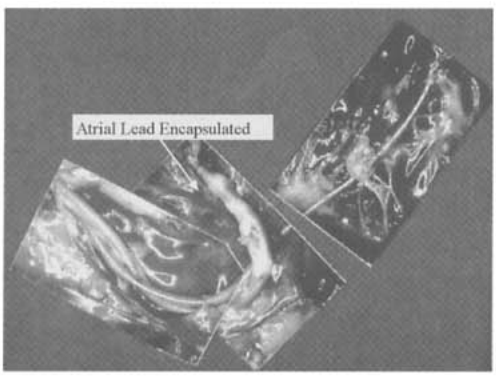

Fig. 17 Complete lead encapsulation

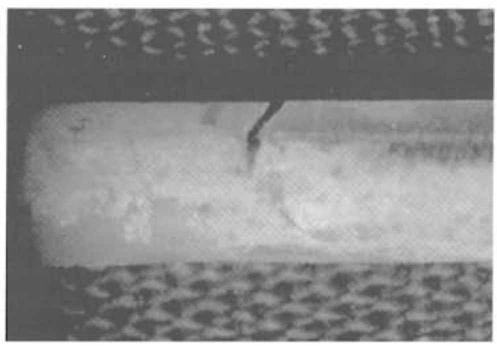

Fig. 18 Mineralized lead

are greater than 50 % of the baseline impedance. Large transient decreases in impedance are indicative of inner insulation problems (like MIO) and large transient impedance increases would be indicative of conductor fracture.

Lead performance has been measured by using returned product or by an ongoing clinical study. Because only a small percentage of leads are explanted, analysis of returned products does not reflect the actual clinical lead performance. The Medtronic Chronic Lead Study (CLS) is clinical based. **Table 1** shows a comparison of the lead performance based upon Medtronic Returned Product Analysis data and CLS data. Note the large difference in lead survivability based upon the reporting method.

Table 2 shows the performance of currently manufactured polyurethane and silicone insulated leads. Although the current polyurethane lead performance data is very good the inner polyurethane insulation is still susceptible to MIO, although at a substaintially reduced rate compared to past leads. The next Medtronic polyurethane lead family (Novus) should perform even better than the Model 4024 since the inner insulation is silicone and is not susceptible to MIO. In addition, the silicone insulation used in the Novus lead family is improved (NuSil 4719). It has been designed especially for leads to reduce compressive creep.

Leads are difficult to extract chronically due to the fibrous tissue encapsulation[4]. After a lead is implanted, thrombus occurs due to endothelial injury as a result of the lead hitting against the vein wall. **Fig. 15** shows thrombosis 10 days after implant in a canine. The thrombosis can undergo lysis or it can organize to form the start of the fibrous encapsulation. Chronically, thrombosis can form due to stasis from the lead being in the veins and heart. The thrombus organizes and the tissue encapsulation grows over the lead. **Fig. 16** shows partial encapsulation of two leads, atrial and ventricular. Ultimately, the lead can become completely encapsulated (**Fig. 17**). The fibrous capsule can differentiate into cartilage and bone making lead extraction difficult. The lead and tissue can also become mineralized by the body as shown in **Fig. 18.** New tools, like eximer lasers, are making lead extraction easier and safer.

Medtronic's goal is 100% lead survival for all patients. Until this goal is achieved we will strive to provide the highest reliability devices and develop lead early replacement indicators. Also, we will keep physicians informed about our lead performance through our clinically based Chronic Lead Study, and work toward easy chronic lead removability. Leads can fail by many mechanisms. Some of the most common failure mechanisms are: ESC, MIO, compressive creep and crush. Present Medtronic leads have excellent reliability, but future leads will be even more reliable.

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