Acute and Chronic Performance Evaluation of a Novel Epicardial Pacing Lead Placed by Percutaneous Subxiphoid Approach in a Canine Model

Roy M. John, MBBS, PhD; Kevin Morgan, AA; Lucas H. Brennecke, DVM; Michael E. Benser, PhD; Pierre Jais, MD

Background—Endovascularly implanted leads risk vascular injury and endocarditis, and can be difficult to locate in desired positions for LV pacing. We evaluated the acute and long-term stability, electric performance and histopathology of a percutaneously placed intrapericardial lead (IPL).

Methods and Results—Twelve adult mongrel dogs underwent defibrillator implants incorporating IPLs. Successful uncomplicated percutaneous implantation of an IPL was achieved in all. Early fluoroscopic shift noted with 3 of 6 of the initial version IPL-1 was not seen with the modified IPL-2. Mean±95% confidence interval bipolar capture threshold at 0.5-ms pulse width for the IPL increased from 0.69±0.14 V at implant to 1.50±0.34 V (P=0.003) at 12 weeks. The 12-week thresholds were higher for IPL compared with right ventricular endocardial leads (0.75±0.33 V; P=0.001) but not different compared with coronary sinus leads (1.33±0.58 V; P=0.994). IPL impedance increased from 742±46 Ω at implant to 1066±207 Ω at 12 weeks (P=0.007). R-wave amplitude at 12 weeks was 8.37±1.52 mV. There was no important phrenic nerve stimulation from IPL pacing. Histopathology in 8 animals showed adequate adhesion of the electrodes or mesh to the epicardium without damage to underlying vasculature. There was no evidence for late pericardial inflammation or effusion.

Conclusions—The IPL demonstrated adequate stability of position and acceptable electric parameters without chronic pericardial inflammation in this canine model and offers a potential alternative to endocardial pacing leads. (Circ Arrhythm Electrophysiol. 2015;8:659-666. DOI: 10.1161/CIRCEP.114.002076.)

Key Words: cardiac pacemaker, artificial ■ epicardial pacing ■ percutaneous epicardial pacing ■ pericardium
WHAT IS KNOWN
- Endovascularly placed pacing and defibrillating leads risk vascular injury, endocarditis and extracardiac stimulation, and maybe difficult to position in desired locations for left ventricular pacing.
- Access to the pericardium can be safely obtained percutaneously.

WHAT THE STUDY ADDS
- In a systematic evaluation of a novel percutaneously introduced intrapericardial lead, adequate pacing and sensing thresholds comparable with endocardially implanted coronary sinus leads were demonstrated in 12 canine experiments.
- Modifications to the original lead design improved stability within the pericardial space with adequate fixation to the epicardium. There was no evidence for chronic pericardial inflammation, effusion, or damage to the epicardial surface or underlying blood vessels.
- Intrapericardial lead has potential applications in cardiac pacing when transvenous access is not possible or desirable.

and 16 mm apart. These electrodes were insulated on their outer surface with a silicon-polyurethane copolymer; electrode contact with the myocardium was only possible on the internally facing surface. A polyester mesh to encourage tissue overgrowth and fixation surrounded the electrodes. The cable conductors were coated with copolymer insulation and coradially wound. These cables were wrapped around a central lumen that permits insertion of a stylet. Advancement of the stylet in the central lumen slenderized the distal end of the lead for introduction through a 13 Fr sheath introducer. Retraction of the stylet restores the original diamond loop of the lead and allow for deployment of the stabilizing wings in a suitable location of the epicardial surface within the pericardium. The lead was 92 cm in length. The diameter of the body of the lead was 6 Fr size. The proximal end has an IS-1 connector pin. This initial lead design (IPL-1) was implanted in 6 canines. Modifications were made to the initial design for implantation in the subsequent 6 experiments. The distal end of the main lead body was reduced to 5.5 Fr size to allow more flexibility. The distal nose tip was reduced in length, the humps on the wings were increased, the polyester mesh adjacent to the electrodes was enlarged and the polyester sock proximal to the diamond geometry was lengthened. This modified version is referred to as IPL-2 (Figure 1).

Implant Procedure
Twelve adult mongrel dogs weighing 20 to 26 kg were implanted with an implantable cardioverter defibrillator with cardiac resynchronization therapy under general anesthesia.

Using sterile technique with the animal in a supine position, a subxiphoid incision was made to the deep fascia and puncture of the pericardium was performed under fluoroscopy using a Tuohy needle, aided by injection of contrast and use of a guidewire to confirm entry to the space. A dedicated short steerable sheath (Agilis PF Introducer, St. Jude Medical) was used to deliver 1 IPL to the pericardial space and for positioning to overlie the lateral left ventricular epicardium, where satisfactory electric performance was confirmed and registered. During the procedure, care was taken to prevent air from entering the pericardial space. If necessary, air was removed using the side port available on the Agilis PF Introducer and a syringe. Using the introducer and syringe in this manner also allowed to check for bleeding within the pericardial space. In an attempt to prevent lead migration, suture sleeves with 3 ligatures were used to affix the lead to subcutaneous tissue at the subxiphoid location. The lead was then tunneled submuscularly to an incidence at the last rib space and then subcutaneously to a subcutaneous pocket for the pulse generator, which was fashioned with blunt dissection in the left dorsal side of the thorax area. The incision at the subxiphoid access site was closed and sutured.

A standard cut down of the left external jugular vein was performed. Under fluoroscopic guidance, one 7 Fr defibrillation lead with bipolar sensing tip electrodes (St. Jude Medical Models Riata 1580, 1581, or 7001) was placed in the right ventricle (RV) with the tip located in the RV apex for all 12 animals. Additional leads were placed for comparison with the IPL. For the first 6 animals, 1 active fixation sense/pace bipolar lead (St. Jude Medical Model 1688T) was placed in the right atrium. The remaining 6 animals received 1 bipolar lead (St. Jude Medical Model 1058T) implanted into a branch of the CS overlying the left ventricle. The RV, right atrium, and CS leads were tunneled subcutaneously to the previously formed pocket on the left side of the chest and secured with suture sleeves. The RV lead was plugged into the respective port in the implantable defibrillator with cardiac resynchronization therapy device. The IPL was plugged into the LV port and the right atrium or CS lead was plugged into the right atrium port of the device. The leads and device were implanted in the subcutaneous pocket and the pocket was closed using standard surgical procedures.

Figure 1. Ventral view (left) and a schematic representation of a cross-section at the electrode (right) of the intrapericardial lead version 2 (IPL-2). Right, 1=A layer of insulation overlying the outer surface of the electrode to prevent phrenic nerve capture. 2=Polyester mesh surrounding the electrode. 3=Active electrode to contact with the epicardial surface. Note the central bore in the electrode for steroid (not incorporated in the IPLs tested in this study). 4=Weld of the conductor coil to the ring of the electrode. 5=Central lumen of the lead.
Intraoperative Testing

Standard measurement of all lead parameters including cathodal pacing thresholds (measured at 0.5 ms pulse width), pacing impedances, and intrinsic amplitudes were made in the bipolar mode. For IPL-2, measurements were also made in the unipolar mode to the RV coil. Phrenic nerve stimulation (PNS) was assessed while pacing via the IPL in bipolar mode up to a maximal output of 7.5 V at 0.5 ms.

Fluoroscopic imaging in the anterior–posterior and lateral views, were stored to document the initial position of the IPL. With the animal in a lateral position, the stability of the IPL was challenged with the vigorous skeletal muscle contractions associated with 2 high energy R-wave synchronized shocks at 20 and 30 J delivered successively. After these shocks, repeat fluoroscopy images were obtained to record and any shift in position of the IPL.

Follow-Up

After the implantation procedure and testing, the animals were recovered and maintained in a standard animal housing facility. Electric parameters of all leads that included bipolar cathodal pacing thresholds (at 0.5-ms pulse duration), impedances, and intrinsic amplitudes were recorded at weekly intervals for 6 weeks, 2 weekly intervals to 12 weeks, at 4 weekly intervals to week 104, and thereafter, every 6 weeks to the latest time point or to the point of euthanization. At each pacing check, fluoroscopy images along the same 4 images recorded intraoperatively were collected for offline analysis. In addition, PNS was assessed at each pacing check through visual observation coupled with palpation of the diaphragm during testing. Finally, 2 synchronized programmer shocks as during the intraoperative testing, were delivered at week 4 and 12.

Explants and Pathological Examination

Out of the 12 canines, planned explant and pathological studies were performed in 5 animals at weeks 12, 12, 28, 40, and 104. Two animals were euthanized at weeks 152 and 176 for methicillin-resistant staphylococcal bacteremia. One animal was euthanized for failure to thrive at 188 weeks. Pathological evaluation was available in all 8 animals.

After euthanasia, the device was explanted. The leads were disconnected from the pulse generator and the IPL was dissected along the lead path to the entry site of the subxiphoid lead and photographed. A section of the rib cage was removed for clear view of the thoracic cavity and heart. The condition of the pericardial sac was also noted and photographed. The heart and leads were removed intact from the chest, rinsed and examined. After examination, the heart with leads attached was placed in formalin and prepared for histological evaluation.

Pathology

Gross examination of the pericardium, heart surface, and IPL was conducted on each heart. The pericardium was removed, where possible, to determine the degree of pericardial/epicardial adhesions and to expose the IPL. Gross photographs were taken to document the findings. The IPL including tissues adjacent to the 2 electrodes and the polyester mesh were dissected free of the remainder of the heart, and were processed, infiltrated, and embedded in methyl methacrylate. After methyl methacrylate polymerization, radiographs were made of the explanted heart and IPLs,

Statistical Analysis

Because of the uneven explant schedule of the animals, all analyses of lead parameters were analyzed only over the initial 12 weeks of implantation, the period over which all animals endured. To address non-normal data, a square root transformation was applied to all lead parameters. Changes in IPL-1 and IPL-2 parameters were taken together over these 12 weeks and were assessed using F tests from a repeated measures model assuming compound symmetry of the correlation matrix. To assess a few judiciously selected time points at which IPL parameters might have changed, paired t tests were used to compare IPL parameters at implant versus 1, 4, and 12 weeks post implant. Differences in lead parameters between the IPL-1 and IPL-2 leads were assessed using F tests associated with the lead main effect from the repeated measures model.

From the 6 animals implanted with IPL-2 leads, the IPL-2 pacing parameters were compared with those of the endocardial RV and endovascular CS leads. Paired t tests comparisons of the lead parameters of the IPL-2, endocardial RV, and epicardial CS leads were made at implant and 1, 4, and 12 weeks using a Tukey–Kramer adjustment for multiplicity. Statistical significance for all comparisons was taken as P<0.05. Continuous variables are expressed as mean±95% confidence interval when compared, mean±SD when purely descriptive, or median and interquartile range as appropriate.

Results

All 12 implants were achieved without complications with placement of the IPL in the desired location to overlie the left ventricular epicardial surface, 6 with the initial IPL-1 design and 6 subsequently with the IPL-2 design. Procedure time (from when the Agilis PF introducer was positioned within the intrapericardial space until the final positioning and electric testing) for placement of all IPLs was 14 (12–22) minutes. No acute complications occurred during lead placement. In particular, no animal had significant pericardial bleeding leading to cardiac tamponade or arrhythmias.

Stability of IPL

None of the IPL-1 nor IPL-2 leads were judged to have dislocated on delivery of the intraoperative defibrillation shocks. However, 3 of the 6 IPL-1 leads were identified having shifted implant position by fluoroscopic imaging comparison over the follow-up period; 2 were noted to have shifted at 1-week postimplant, and the other at 2 weeks postimplant but without significant changes in electric parameters. After this initial observation, all IPL-1 leads remained stable in subsequent follow up. All six IPL-2 leads remained stable, with no identifiable shift in lead position over the duration of the follow-up (Figure 2).

Electric Performance

The bipolar pacing impedances, capture thresholds, and R-wave amplitudes over the course of follow up of 158 weeks for all the IPLs are shown in Figure 3. The impedance and capture thresholds from the IPLs, taken together, exhibited significant increases over the 12-week maturation period (F test P<0.001 for the effect of implant duration on each of impedance and threshold). The IPLs sensing amplitudes did not exhibit a significant change over the 12-week maturation period (F test P=0.053). Bipolar capture threshold at 0.5 ms pulse width for all IPLs was 0.69±0.14 V at implant and 1.50±0.34 V at 12 weeks (t test P=0.003). Pacing lead impedance for all IPL leads was 74±24.6 Ω at implant and increased to 1066±207 Ω at 12 weeks (t test P=0.007). R-wave amplitude at implant was 12±4.3 mV and decreased to 8±4±1.5 mV (t test P=0.034). There was no difference in the electric performance of the IPL-1 versus the IPL-2 during 12 weeks in
capture threshold, R-wave amplitude and impedance (F tests
P=0.206, 0.778, and 0.493, respectively).

Comparisons of the IPL-2 pacing parameters to those of
the RV and CS LV leads at implant and 1, 4, and 12 weeks are
shown in Figure 4. Compared with the endocardial active fixa-
tion RV lead, IPL-2 had higher capture thresholds at 1, 4, and
12 weeks. However, there were no differences in the IPL-2
capture thresholds compared with those of the endovascular
CS lead at any of the time points. Pacing impedances for the
IPL-2 were higher than those of the RV lead at implant, 1,
4, and 12 weeks, but not different than those of the CS lead.
R-wave sensing for the IPL-2 was comparable to the RV lead
and significantly higher than that of the CS lead across the
observational period.

Pacing and sensing were tested in the unipolar mode for
both proximal and distal electrodes to the RV coil for IPL-2.

Figure 2. Anterior-posterior fluoroscopic views at
implant and at 116 weeks of an intrapericardial lead
version 2 (IPL-2) lead implant. The epicardial lead
overlies the posterior lateral left ventricle with no
discernible change in position during the period of
monitoring. CS indicates coronary sinus; and RV,
right ventricle.

Highest unipolar pacing threshold at 0.5 ms and lowest R
wave for either electrode was 1.0±0.6 V and 14.4±2.9 mV,
respectively at 12 weeks. Unipolar lead impedances for dis-
tal and proximal electrodes were 502±100 and 542±48 Ω,
respectively at 12 weeks.

None of the 12 animals exhibited PNS intraoperatively, at
the stimulus strength of 7.5 V at 0.5 ms. Over the course of
follow-up, 11 of the 12 animals did not exhibit any instances
of PNS. One animal, implanted with IPL-1, exhibited PNS at
pacing amplitudes between 6.0 and 7.5 V during 6 of its 40
follow-up evaluations.

Gross Pathology and Histology
Pathological data were available on all 8 euthanized animals at
time periods ranging between 12 and 188 weeks (Table I in the
Data Supplement). Figure 5 shows a gross appearance of the
posterior surface of an explant at 104 weeks. The entire lead including the wing and electrodes could be visualized in this specimen with minimal pericardial thickening or fibrosis. In gross examination, none of the animals developed a pericardial effusion.

There was variable degrees of adhesion and thickening of the pericardium with mild inflammatory changes seen in the early explants. However, there was no evidence of inflammation in the planned explants beyond 40 weeks. In all histological studies, there was good adhesion of the electrodes or mesh with the epicardium without damage to underlying blood vessels (Figure 6). No major epicardial vessels were directly beneath the pacing electrodes or mesh. In 1 IPL-1 explant, there was 3 mm of epicardial fat separating the proximal electrode from the epicardium (Figure 7). Despite this separation, there was adequate pacing threshold with this lead. The distal electrode in this explant was firmly opposed to the epicardium allowing for excellent pacing and sensing thresholds in the bipolar mode. Aside from this, 1 electrode overlying 3-mm epicardial fat, the thickness of fibrotic encapsulation around the electrodes separating them from the epicardium in the IPL-1 explants was 1 mm for 1 electrode, 0.4 to 0.5 mm for 3 electrodes, and <0.1 mm for the remaining electrodes. For the 2 IPL-2 explants, the encapsulation thicknesses around the 4 electrodes were all ≤0.1 mm.

In the explants after euthanization for methicillin-resistant Staphylococcus aureus infection, there was dense pericardial thickening and adhesions to the epicardium. However, there was no evidence for pericardial effusion.

Discussion
This report represents the first systematic evaluation of a passive fixation lead system designed for easy percutaneous delivery to the epicardial surface. The present series of experiments provide data on 2 versions of the epicardial
bipolar pacing lead. The main findings are as follows: (1) epicardial placement of the IPL can be safely achieved in canine models using a subxiphoid approach and dedicated tools to direct placement in areas where adequate pacing and sensing thresholds are obtained; (2) although IPL-1 lead design was associated with early dislodgement within the pericardial space, subsequent modifications in the IPL-2 design provided for lead stability, (3) IPL pacing thresholds and impedance were comparable to endovascular CS leads for LV pacing, but higher than the endocardial RV leads. Sensing for the IPL-2 was similar to that of the RV leads, (4) gross and histological examination of planned and unplanned explants showed early inflammatory changes but free of the development of effusion and adequate fixation of the electrodes to the epicardial surface without damage to myocardium or blood vessels.

Despite the greater ease of transvenous implants, incidence of cardiac implantable electronic device infections with endocarditis has risen over the years with higher rates for patient on dialysis.7,8 In addition, chronic upper extremity vascular occlusion and inadequate left ventricular branches to the CS for LV pacing necessitate the use of epicardial pacing wires. Surgical epicardial lead placement is associated with a higher upfront morbidity and mortality.9 Hence, an IPL that can be introduced percutaneously has appeal. Leads have been placed in pediatric patients by percutaneous subxiphoid pericardial access or via a small surgical subxiphoid incision to access the pericardial space.10,11 In the adult population, surgical access requires more extensive dissection. However, percutaneous pericardial access is now commonly used for epicardial ablation of arrhythmias and can be safely achieved in patients without previous cardiac surgery or pericardial disease.9 In this study using canine models, successful placement of a novel IPL in a desired location in the pericardial space to overlie the posterior lateral LV was successfully achieved in all 12 dogs.

Electric measurements in the IPL lead remained stable over several months after implantation despite the lack of steroid elution in these leads. Although the chronic thresholds in the IPL-2 leads were consistently higher than the endocardial RV active fixation lead, the maximum capture threshold registered was 2.5 V at 0.5 ms and still within the acceptable limits for an epicardial pacing lead. It was comparable to that of the LV leads placed via the CS. Histologically, varying degrees of fibrosis and epicardial fat were present beneath the electrodes. The bipolar design of the IPL leads would be expected to allow successful pacing capture and sensing from at least one of the electrodes.

The histological reaction to endocardial leads is well documented in animals and human studies.12–15 Typically, there is thrombus formation, localized inflammatory process with granulation tissue and gradual replacement with

![Figure 6](https://example.com/fig6.png)  
**Figure 6.** Histological appearance of the proximal electrode and its interface with the myocardium at 104 weeks in low power (left) and high power (right). Dense fibrous tissue lines the polyester mesh. No inflammatory cells were present. The base of the electrode was separated from the epicardial myocardium by 3 mm of fat, despite which there was adequate bipolar capture because of excellent apposition of the distal electrode. A small arteriole within the epicardial fat showed no abnormality from the overlying electrode.

![Figure 7](https://example.com/fig7.png)  
**Figure 7.** Histological appearance of the distal electrode and its interface with the myocardium in the same specimen as in Figure 6. Both the low (left) and high (right) power images show close apposition of the electrode to the myocardial surface with a thin fibrous layer separating the electrode and the myocardium. The polyester mesh is encased in fibrous tissue and separated from the myocardium by epicardial fat.
fibrous tissue. Defibrillation leads incite a greater fibrotic reaction compared with pacemaker leads. The findings relating to the passive fixation IPL leads followed a similar pattern but without the initial thrombosis. There was variable fibrotic reaction that resulted in adequate fixation of the electrodes and the surrounding mesh to the epicardial surface or pericardium. The fibrous tissue at the interface seems to be minimal and does not influence the electric measurements over the longer term. No epicardial vessels were entrapped beneath the lead in these experiments but second-order arterioles and venules beneath the electrodes were not affected.

Potential problems relating to an IPL lead include the issue of access to the pericardial space. In adults, access to the pericardial space for epicardial ablation for ventricular tachycardia was first described by Sosa et al and increasingly used for ablation. Nevertheless, a dry pericardial tap can be associated with complications that include intra-abdominal bleeding, laceration of the liver, injury to the coronary arteries, and cardiac perforation. RV puncture is the most common complication encountered in 4.5% of 215 consecutive cases in a series by Sosa et al. However, RV puncture rarely causes continued bleeding and often seals spontaneously. In the absence of previous pericardial inflammation or cardiac surgery, catheters and sheaths can be moved about freely within the pericardial space to deploy a lead in a desired area. In this series, we chose the posterior lateral LV for lead location because this is the area where activation commonly occurs latest during left bundle branch block and is thus, a good location for pacing for CRT. The issue of extracardiac stimulation, for example, phrenic nerve, is theoretically eliminated by the lead design that uses insulation over the outer surface of the electrodes. In this series, no late migration of the lead was seen. However, migration is possible in the presence of undetected pericardial effusion. Finally, in the event of infection that involves the pericardial space, removal will most likely entail surgical intervention. In the early stages, advancement of a sheath over the lead for retraction may be possible but we have no information about safety of this technique. In the present series, 2 animals developed staphylococcal infection, involving the pericardium in 1 and requiring euthanization at weeks 152 and 176. These were likely because of secondary seeding of the devices from an unidentified primary source.

Limitations
Complete data on the 12 animals is only available to 12 weeks and hence the demonstrated stability and performance of this lead is short term. Planned and unplanned sacrifices at various time points have, however, provided data on histopathology spanning 12 to 188 weeks. Four surviving animals have continued to demonstrate adequate lead performance. Finally, epicardial fat layers may be thicker in the human heart with possible interference with pacing capture although it is unusual to encounter significant adipose tissue over low posterior-lateral LV where IPL were positioned in the present series of experiments.

Conclusions
In this first systematic study of a novel percutaneously introduced IPL in the canine model, we have demonstrated adequate stability of the lead in the pericardial space without dislodgement, adequate pacing and sensing threshold and no damage to the epicardial surface or underlying small blood vessels. An IPL lead has potential applications in cardiac pacing when transvenous access is not possible or desirable.

Disclosures
Dr. John received modest honoraria for lectures from St. Jude Medical, Inc, Medtronic, Inc, and Boston Scientific, Inc. K. Morgan and Dr. Benser are employees of St. Jude Medical, Inc. Dr. Jais is a consultant to Biosense Webster, Inc, and St. Jude Medical, Inc. L.H. Brennecke reports no conflicts.

References


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SUPPLEMENTAL MATERIAL

Table: Time to explant for each experiment, gross and histological findings at pathological examination.
<table>
<thead>
<tr>
<th>Animal No. and type of lead</th>
<th>Explant time</th>
<th>Reason for Explant</th>
<th>General Gross Appearance</th>
<th>Pericardium Gross</th>
<th>Presence of fluid</th>
<th>Histology (presence of fibrosis and extent)</th>
<th>Inflammation yes/no</th>
<th>Underlying myocardium</th>
<th>Epicardial fat/Vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 IPL-1</td>
<td>12 wks</td>
<td>Planned</td>
<td>Mild epicardial bruising beneath distal electrode</td>
<td>Multifocal areas of fibrinous adhesion between epicardium and pericardium</td>
<td>no</td>
<td>Proximal electrode attached to epicardium by mild to moderate fibrous connective tissue and small areas of loose connective tissue.</td>
<td>Small numbers of lymphocytes and plasma cells. Mild to moderate granulomatous inflammation surrounding mesh on epicardial surface.</td>
<td>Normal</td>
<td>No fat or vessels</td>
</tr>
<tr>
<td>2 IPL-1</td>
<td>12 wks</td>
<td>Planned</td>
<td>Both electrodes firmly attached to epicardium and pericardium</td>
<td>Unremarkable</td>
<td>no</td>
<td>Electrodes firmly compressed against epicardium with thin fibrous capsule around the mesh</td>
<td>Mild inflammatory cell infiltration</td>
<td>Underlying myocardium normal</td>
<td>Epicardial fat present and small arteriole within fat unremarkable</td>
</tr>
<tr>
<td>3 IPL-2</td>
<td>28 wks</td>
<td>Planned</td>
<td>Grossly unremarkable</td>
<td>Minimal fibrosis all around lead body from site of entry into pericardium.</td>
<td>no</td>
<td>Fibrous tissue (&lt;100µm) between electrodes and epicardium, Both electrodes</td>
<td>Macrophages and giant cell infiltration beneath mesh that had separated</td>
<td>Normal</td>
<td>Small venule and arterioles beneath within epicardial fat between</td>
</tr>
<tr>
<td>No</td>
<td>IPL</td>
<td>Weeks</td>
<td>Status</td>
<td>Electrodes and Mesh</td>
<td>Epicardium</td>
<td>myocardium</td>
<td>Notes</td>
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<td>4</td>
<td>IPL-1</td>
<td>40 wks</td>
<td>Planned</td>
<td>Electrodes firmly adherent to epicardium and mesh encapsulated in fibrous tissue. from epicardium</td>
<td>Extensive fibrinous pericardial adhesion to epicardium all around the heart. No obvious fibrosis externally</td>
<td>Minimal fibrosis between electrodes and epicardium but electrodes and mesh encased in fibrous capsule. Mild chronic inflammatory infiltrate.</td>
<td>No blood vessels in vicinity of electrodes/mesh</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>IPL-1</td>
<td>104 wks</td>
<td>Planned</td>
<td>Translucent pericardium with no adhesions. No significant pericardial fibrosis of adhesions around the electrodes but some fibrosis around entry of lead to pericardial space.</td>
<td>No significant pericardial fibrosis of adhesions around the electrodes but some fibrosis around entry of lead to pericardial space.</td>
<td>No significant fibrotic reaction around electrodes but mesh attached to myocardium with mild fibrosis.</td>
<td>No inflammation</td>
<td>Normal myocardium</td>
<td>Proximal electrode separated from myocardium by 3 mm of fat. Small arteriole and vein unremarkable. Distal electrode in direct contact with myocardium with 50µm of fibrosis.</td>
</tr>
<tr>
<td>6</td>
<td>IPL-2</td>
<td>152 wks</td>
<td>Euthanized for MRSA Infection</td>
<td>Epicardium deep red and had extensive Mild multifocal pericardial fibrosis. Both</td>
<td>Minimal fibrosis under electrodes (&lt;</td>
<td>No inflammatory cell infiltrate.</td>
<td>Normal</td>
<td>No fat or vessels beneath</td>
<td></td>
</tr>
<tr>
<td>Litter</td>
<td>Weeks</td>
<td>Euthanized Reason</td>
<td>Findings</td>
<td>Electrode Attachments</td>
<td>Fibrosis</td>
<td>Inflammation</td>
<td>Myocardium Condition</td>
<td>Fat Thickness</td>
<td>Vessel Distance</td>
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<tr>
<td>7 IPL-1</td>
<td>176 wks</td>
<td>Euthanized for MRSA bacteremia</td>
<td>Minimal fibrotic reaction externally but pericardium firmly attached to epicardium over most of the heart</td>
<td>Both electrodes attached by fibrosis to epicardium and pericardium</td>
<td>no</td>
<td>Minimal fibrosis around polyester mesh attaching mesh to epicardial surface</td>
<td>No inflammation</td>
<td>Myocardium beneath electrodes and mesh was normal</td>
<td>0.8 mm of fat beneath electrode but no inflammatory infiltrate. Venule 0.5 mm from electrode in fat unremarkable.</td>
</tr>
<tr>
<td>8 IPL-1</td>
<td>188 wks</td>
<td>Euthanized for lymphoma</td>
<td>Extensive pericardial thickening and fibrosis</td>
<td>Pericardium adhered to epicardium. Electrodes encapsulated by fibrous tissue but poor attachment to epicardium</td>
<td>no</td>
<td>Mild fibrosis around proximal electrode but none around distal electrode</td>
<td>No</td>
<td>Normal myocardium</td>
<td>Electrodes separated from myocardium by 200 μm of fat and connective tissue. No blood vessels</td>
</tr>
</tbody>
</table>