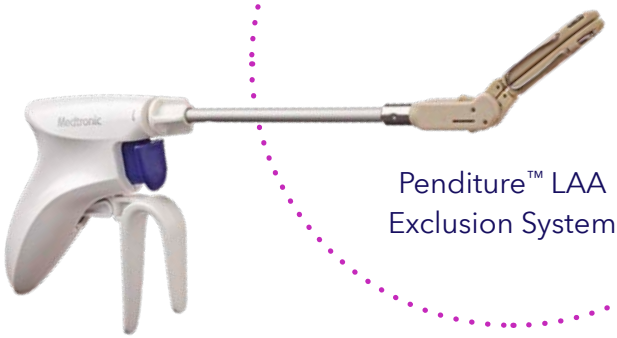
Medtronic

Left atrial appendage clipping in a canine model



Penditure™ LAA Exclusion System

Background

The left atrial appendage (LAA) is the main source of stroke in patients with atrial fibrillation, and atrial clipping is a treatment strategy to reduce the risk of blood clots in the LAA from entering the bloodstream and potentially causing a stroke in these patients.

Purpose and objectives

The objective of this study was to demonstrate substantial equivalence of the Penditure LAA exclusion system to the AtriClip®* Flex-V®* exclusion system when compared in a canine model 90 days after the procedure.

Study design

This Good Laboratory Practices (GLP) study was designed to evaluate the performance and safety of the study device (Penditure) in comparison to the control device (AtriClip Flex-V) in a canine model over 90 days. Twelve mongrel dogs (age range: 10.4–33.6 months) were enrolled in the study. A canine model was chosen because heart size, electrophysiological characteristics, and hemodynamics have been shown to be comparable to those of the human heart.

Six animals were assigned to the Penditure device, and six were assigned to the AtriClip Flex-V device for the 90–day study. A clinical user (interventionalist) performed the implantations.

For each animal, a thoracotomy was performed to expose the LAA. The study or control device was implanted on the LAA. One study or device was implanted per animal. Fluoroscopy was used for guidance. Transesophageal echocardiography (TEE) was performed post-implantation to evaluate device placement and to confirm LAA closure. Fluoroscopy was also performed for quantitative measurement of the distance between the straight metal segments of the clips to approximate tissue thickness in vivo.

At 7 days and 90 days (before euthanasia) post-implantation, TEE was performed again to evaluate device placement, confirm LAA closure, and document any abnormalities. Fluoroscopy was performed for quantitative measurement of the distance between the straight metal segments of the clips to approximate tissue thickness in vivo.

After the animals were euthanized, a pathological gross examination was performed, and the heart, implant, and major organs (brain, liver, kidney, spleen, lungs) were saved for histopathologic analysis by a veterinary pathologist. Inspection and photographic documentation of the LAA (both external and intra-atrial views) were performed. The clips and surrounding tissue underwent processing for histopathologic evaluation.

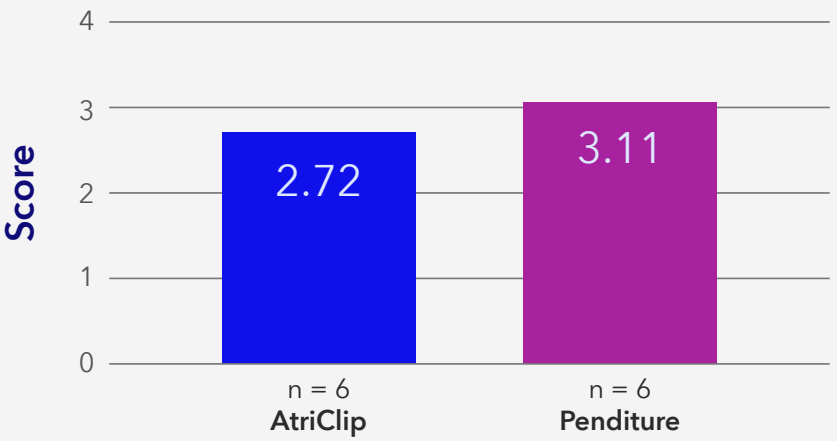
Results

Six mongrel dogs were successfully implanted with the Penditure device, and six mongrel dogs were successfully implanted with the AtriClip Flex-V device. No complications or procedural events occurred at implantation.

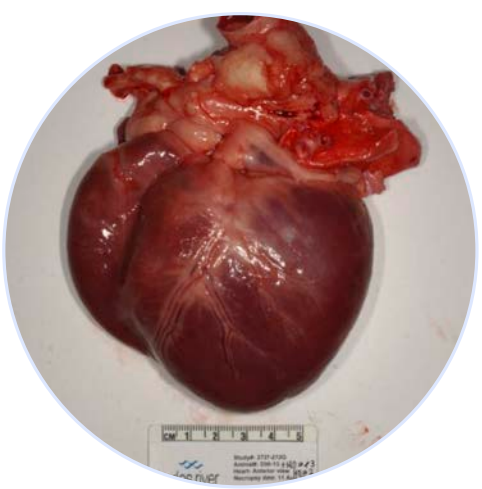
Tissue encapsulation (90 days)

- Evaluation of the LAA closure sites showed that the devices were often completely incorporated in remodeled tissue.
- **Mild to marked fibrous encapsulation was observed surrounding the Penditure device. Fibrous encapsulation is the end-stage healing response to biomaterials.**
- **The fibrous encapsulation scores were numerically higher in the Penditure group than the AtriClip Flex-V group (Figure 1).**

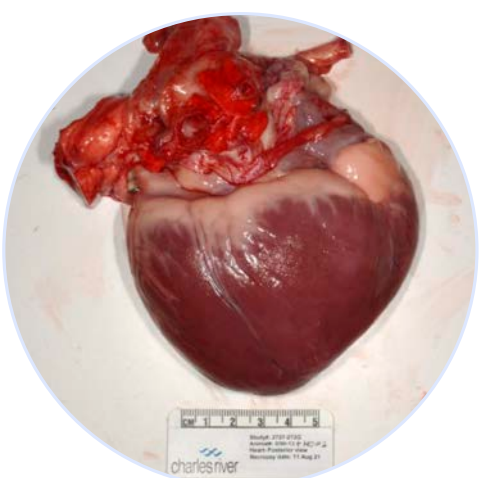
Figure 1 **Fibrous encapsulation** | 90 days



Penditure LAA exclusion system 90-day cohort



Heart, anterior view



Heart, posterior view

Histopathology data for inflammation and fibrosis

- The tissue reaction to Penditure was characterized by the presence of none or rare (1 to 5) neutrophils, none to mild (0 to 10) lymphocytes, and rare to mild (1 to 10) macrophages per high-power field with **overall inflammation graded as minimal or mild.**
- **Tissue ingrowth into the Penditure device was graded as minimal or mild** and was characterized by the presence of narrow to thick bands of fibrosis/fibrous connective tissue and few inflammatory cells between the PEEK bars and between the PEEK bars and the nitinol springs.
- **In summary, at 90 days, histopathological evaluation of the Penditure and AtriClip Flex-V devices showed that the overall inflammation (Figure 2), macrophages (Figure 3), multinucleated giant cells, fibrosis (Figure 4), and tissue ingrowth into the device (Figure 5) scores were lower in the Penditure group than the AtriClip Flex-V group.**

Figure 2 **Overall inflammation** | 90 days

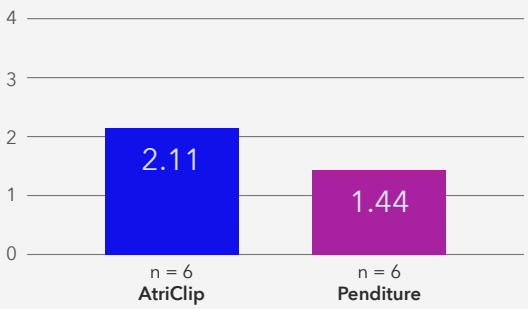


Figure 3 **Macrophages** | 90 days

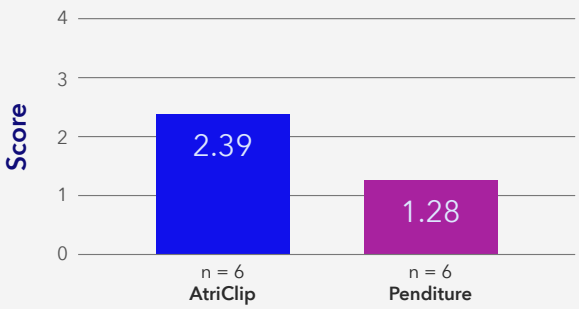


Figure 4 **Fibrosis** | 90 days

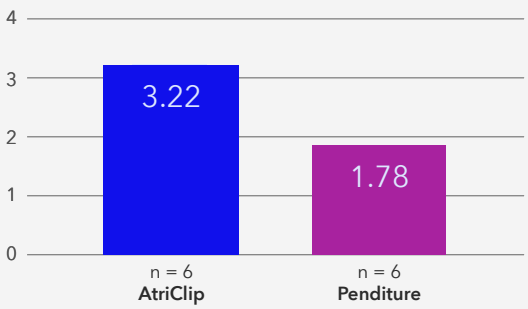
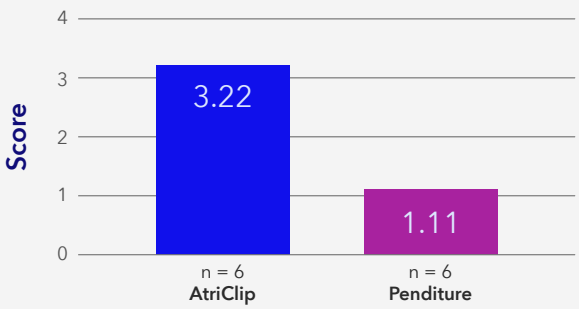


Figure 5 **Tissue ingrowth into the device** | 90 days



Atraumatic tissue closure

- Relative tissue trauma was given a score of 1 by the interventionalist for all of the Penditure and AtriClip devices. A score of 1 was defined as fully rebounded tissue with minimal to no evidence of contact.

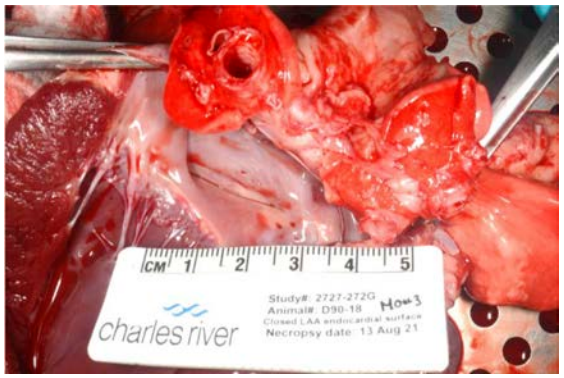
Device migration

- **At 7 days post-implantation and at the time of the final procedure, no migration, leakage, or abnormalities were observed for the Penditure or AtriClip Flex-V devices. All devices performed equally.**
- Gross necropsy, microCT, and histopathologic evaluation showed that the inflammation and healing, long-term (90–day) damage to the atrium or erosion into surrounding tissues after implantation, migration from time of implant, and non-target tissue evaluation acceptance criteria were met, demonstrating substantial equivalence of the Penditure LAA exclusion system to the AtriClip Flex-V LAA exclusion system.

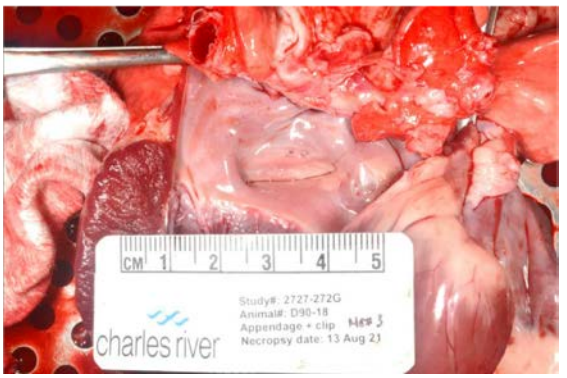
Successful LAA closure

- TEE assessments post-implantation, at 7 days or at the time of the final procedure, did not show any residual flow or abnormalities for any of the clips except for the AtriClip in one animal, where slight residual flow was observed at the tip of the clip at post-implantation and after closure.
- **At 7 days post-implantation and at the final procedure, no migration, leakage, or abnormalities were observed for the Penditure or the AtriClip Flex-V devices. All devices performed equally.**
- In all animals, the endocardial surface surrounding the closure site was smooth, and there was no visible opening between the left atrium and the LAA.

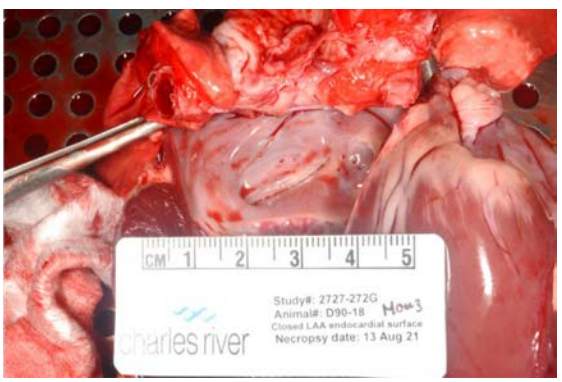
Penditure LAA exclusion system 90-day cohort



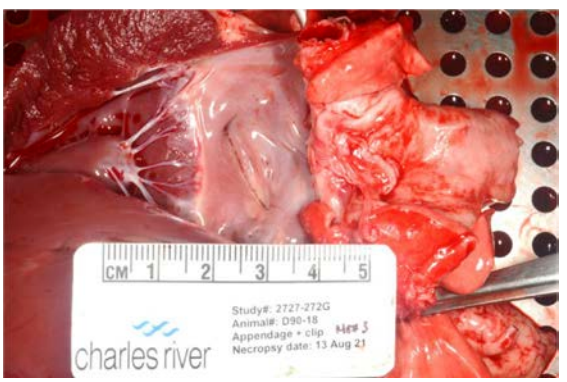
View 1 | Closed LAA endocardial surface



View 1 | Appendage with clip

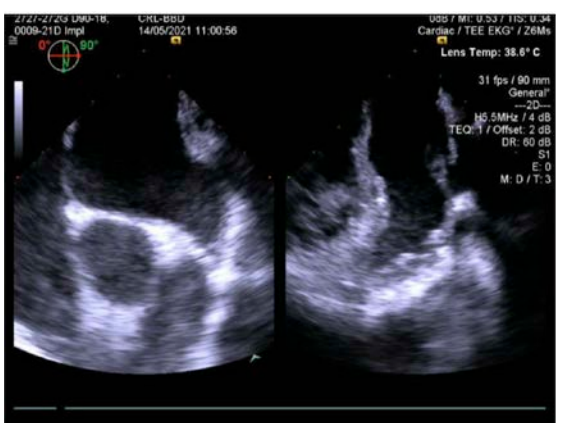


View 2 | Closed LAA endocardial surface

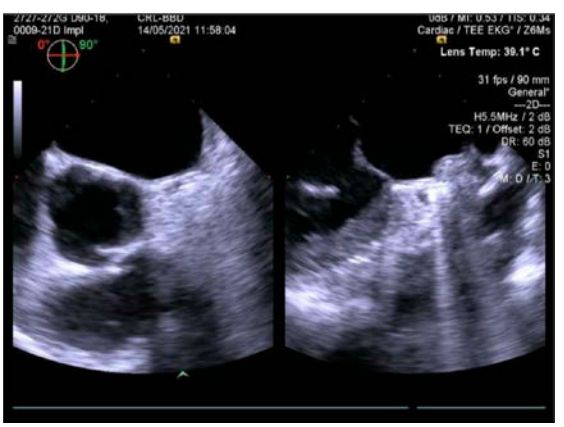


View 2 | Appendage with clip

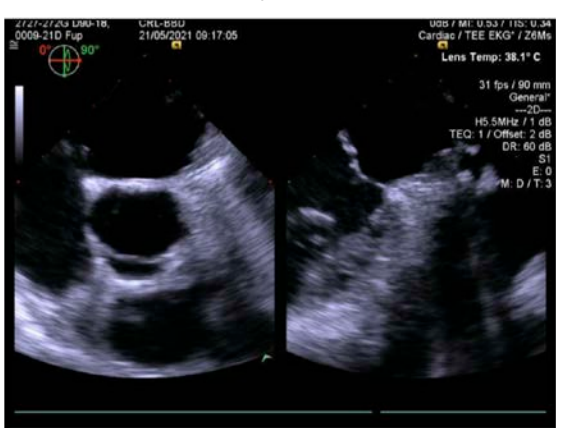
Penditure LAA exclusion system 90-day cohort



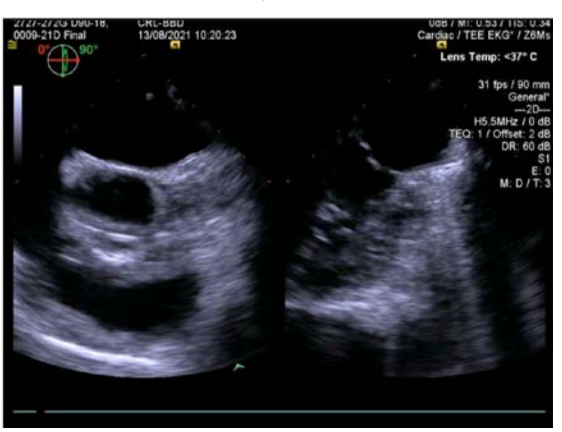
Pre-implantation



Post-implantation



7-day follow-up



Final

Conclusions

Overall, the Penditure LAA exclusion system showed a good safety profile without evidence of significant adverse effects. Gross necropsy evaluation showed a smooth endocardial surface and no visible opening between the left atrium and the left atrial appendage in all animals. The gross necropsy results appeared to be better in the Penditure device group, and the microCT results were relatively similar in both groups.

The histopathology results (overall inflammation, macrophages, multinucleated giant cells, fibrosis, and tissue ingrowth into the device) appeared to be better in the Penditure devices than in the AtriClip Flex-V devices. Gross necropsy, microCT, and histopathologic evaluation showed that the inflammation and healing, long-term (90-day) damage to the atrium or erosion into surrounding tissues after implantation, migration from time of implant, and nontarget tissue evaluation acceptance criteria were met, demonstrating substantial equivalence of the Penditure LAA exclusion system when compared to the AtriClip Flex-V LAA exclusion system.

Data on file. TPR-00003-X08
Testing facility study No. 2727-272G

Important Safety Information

Indications
The Penditure LAA Exclusion System is indicated for the exclusion of the left atrial appendage of the heart, performed under direct visualization and in conjunction with other cardiac surgical procedures. Direct visualization, in this context, requires that the physician can see the heart directly, with or without assistance from a camera, endoscope, and so forth, or any other appropriate viewing technologies.

Contraindications
- Do not use this device if the patient has a known allergy to nitinol (nickel titanium alloy).
- Do not use this device as a contraceptive tubal occlusion device.

Potential Adverse Effects
Possible complications related to the use of Penditure™ LAA exclusion system in combination with open heart surgery are: bleeding, tissue damage, thromboembolism, and pericardial effusion. For a complete listing of all indications, contraindications, precautions, and warnings, please refer to the Instructions for Use, which accompany each product.

Only physicians who are trained in standard cardiac surgical procedures can use this device.

For more information, contact your local Medtronic cardiac surgery representative.
U.S. Customer Service: 1-800-328-1357

Caution: Federal law (USA) restricts this device to sale by or on the order of a physician. For a listing of indications, contraindications, precautions, and warnings, please refer to the Instructions for Use.

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