Radiofrequency Energy for PFO Closure

Successful Thermal Coaptation of Patent Foramen Ovale: First Experience and Temporal Histopathologic Healing in a Porcine Model

Hidehiko Hara MD[1], Elena Ladich MD[2], Renu Virmani MD[2], David Auth PhD[3], Joseph Eichinger[3], Robert S. Schwartz MD[4]

[1]*Toho University Medical Center Ohashi Hospital, Tokyo,*
[2]CV Path, International Registry of Pathology, Gaithersburg, MD,
[3]CoAptus Medical Corporation, Redmond, WA,
[4]Minneapolis Heart Institute and Foundation, Minneapolis, MN

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Disclosure statement

Hidehiko Hara MD	Consultant of Japan Lifeline
Elena Ladich MD	Nothing to disclose
Renu Virmani MD	Nothing to disclose
David Auth PhD	Consultant and Shareholder
Joseph Eichinger	Employee of CoAptus
Robert S. Schwartz MD	Consultant and Shareholder

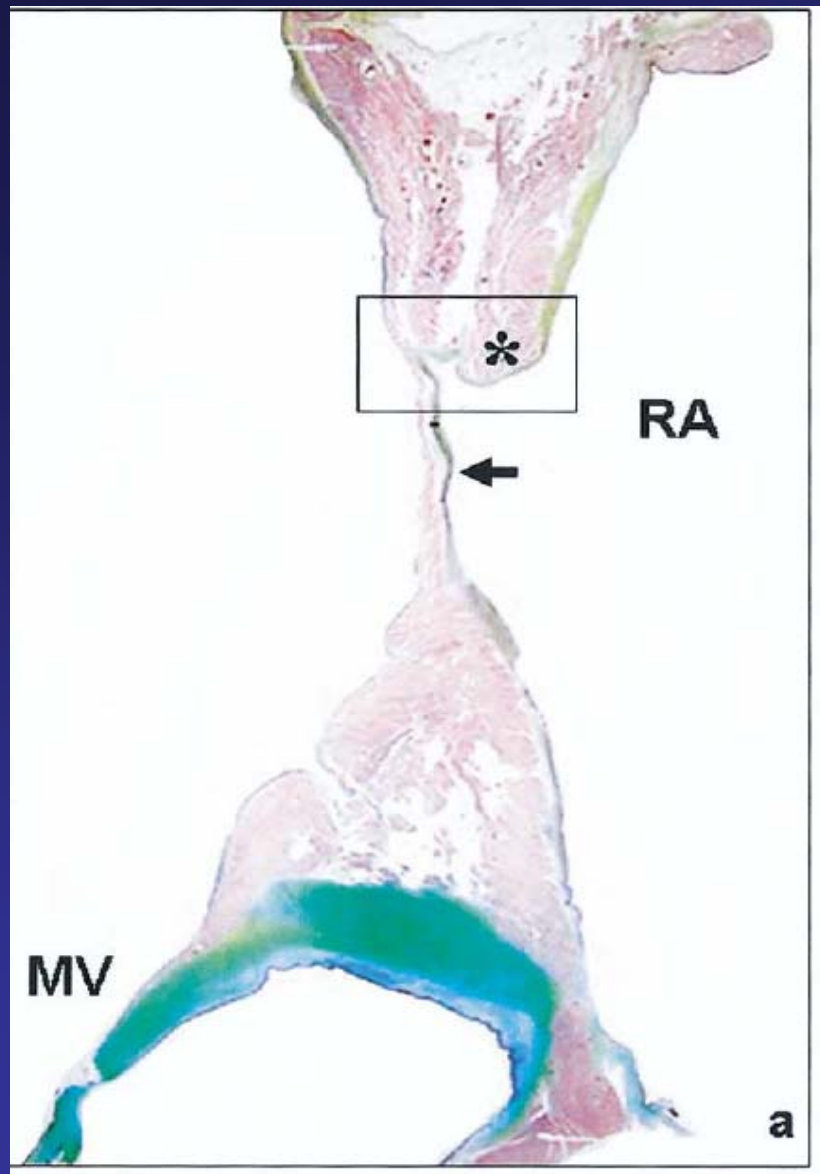
Background

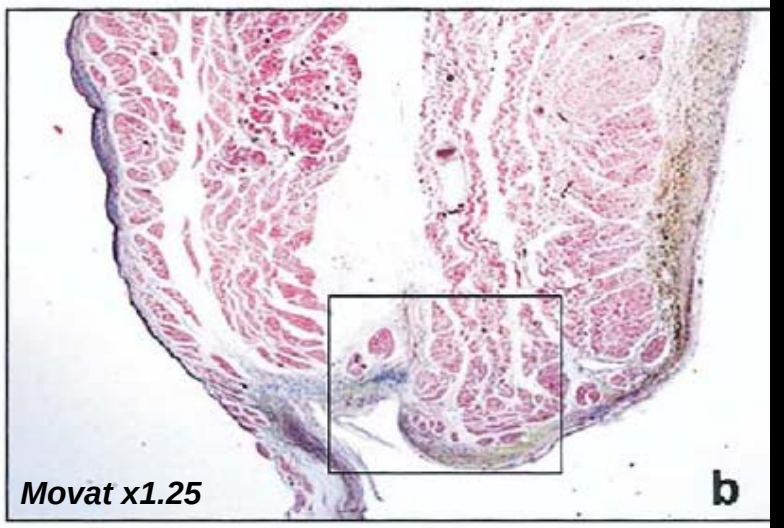
Percutaneous patent foramen ovale (PFO) closure with implantable devices is commonly used, and limits embolic complications.

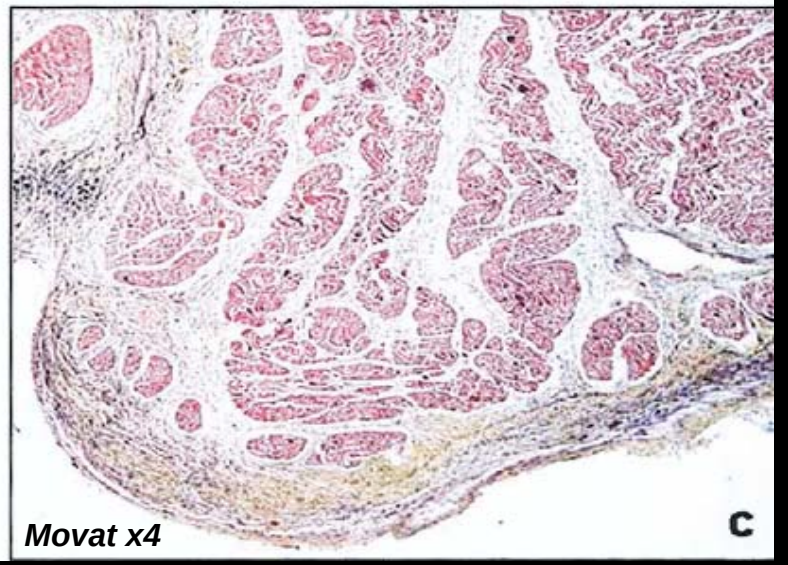
However, implantable closure devices placed across the atrial septum may exhibit thrombosis, device fracture or embolization.

A novel PFO closure strategy uses radiofrequency (RF)-based thermal energy to seal PFO without implanted devices.

Background



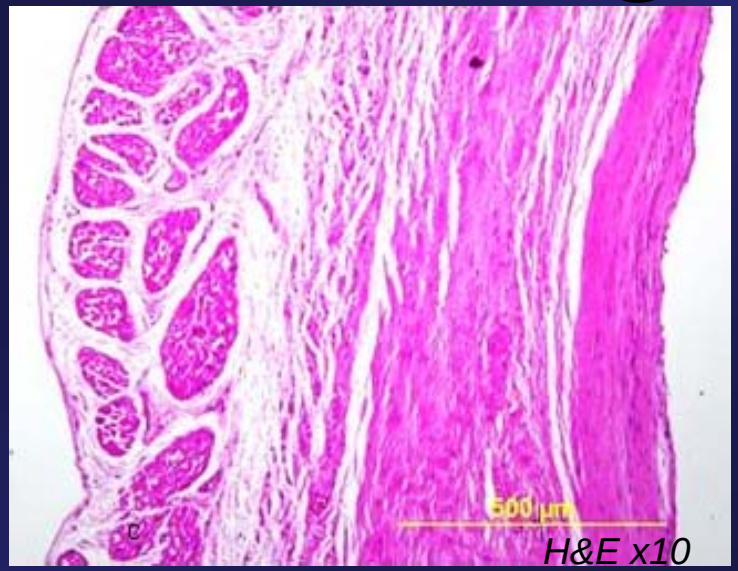




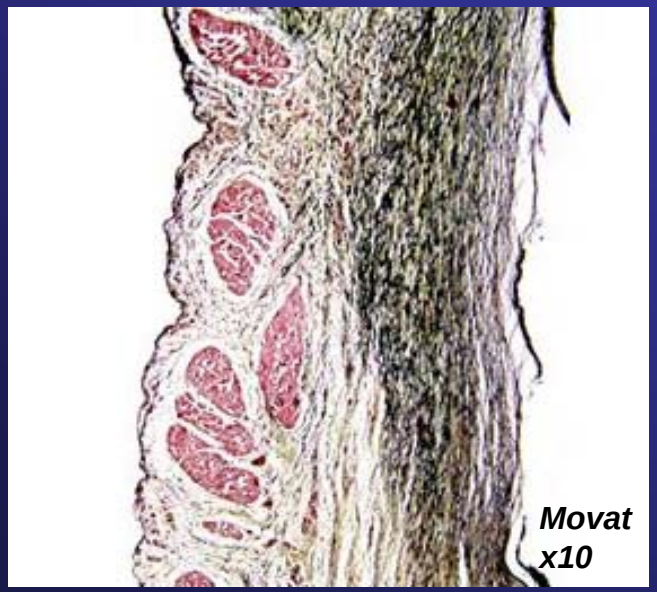
Hara H. et al. J Am Coll Cardiol 2005;46:1768 –76

Background

Human

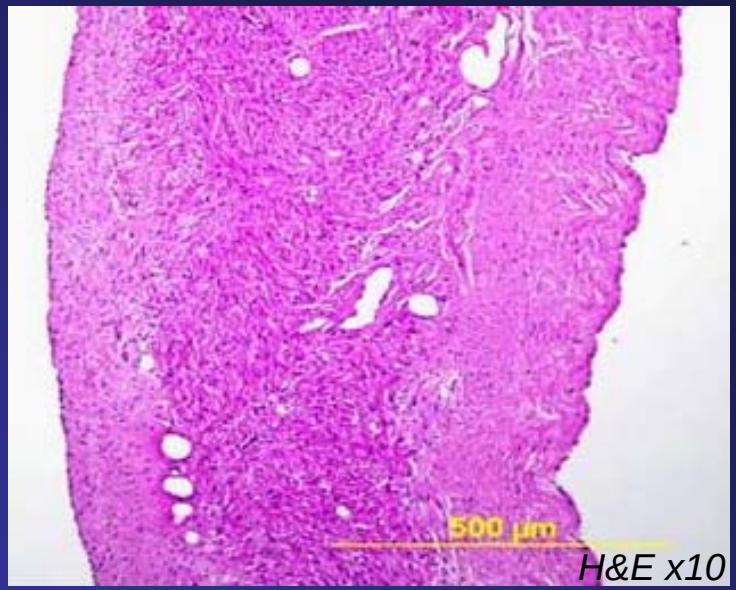


H&E x10



Movat x10

Swine



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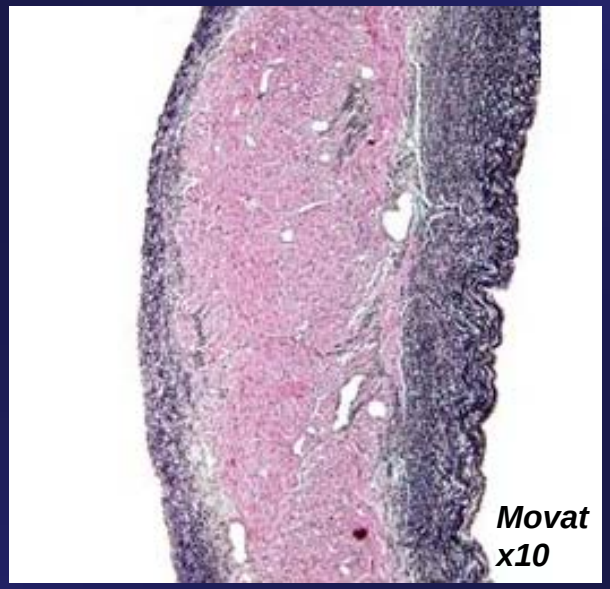
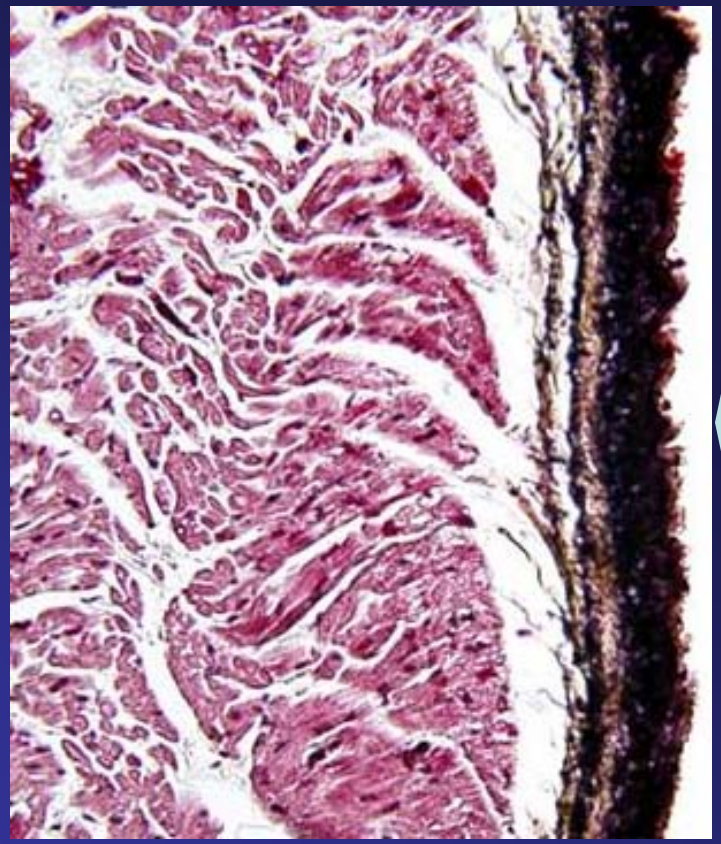


Movat x10

Hara H. et al. Catheter Cardiovasc Interv 2007 ;69:266-73.

Background

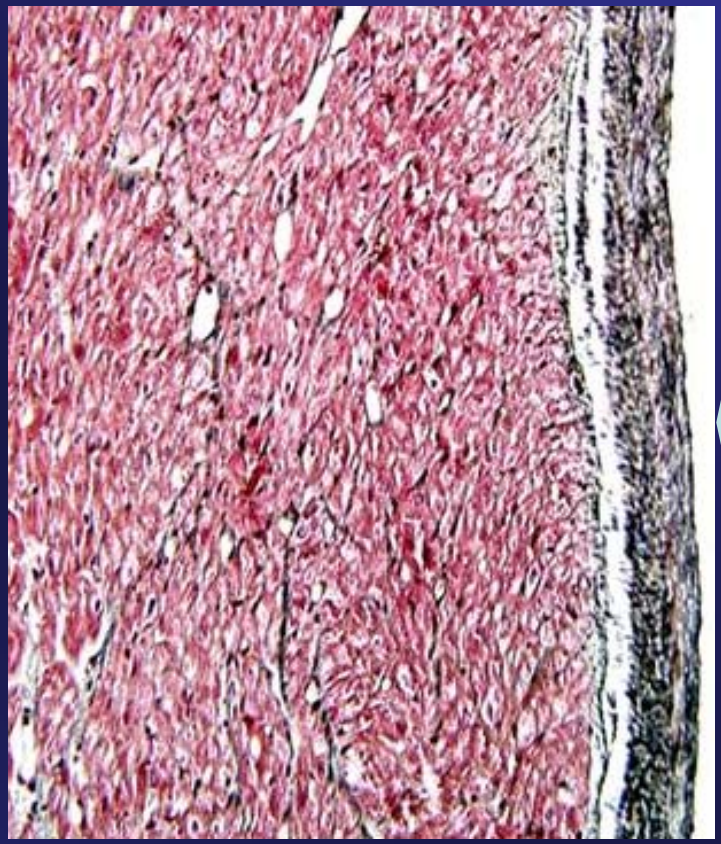
Swine



RA

Movat x20

Human



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Movat x20

Hara H. et al. Catheter Cardiovasc Interv 2007 ;69:266-73.

Methods

Thirteen (13) domestic swine were studied over time following thermal PFO closure. Three animals were euthanized within 1 hour, 5 after 7 days, and 5 at 28 days. Gross and histopathologic findings were examined.

Time post treatment Sacrifice		Number of swine treated
1 hour	→	3
7 days	→	5
28 days	→	5

Methods

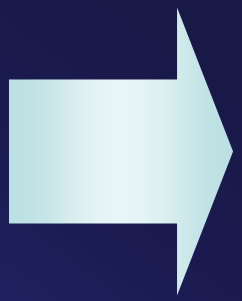
Gross Pathological examination 1

Major organs,

Major great vessels

were assessed

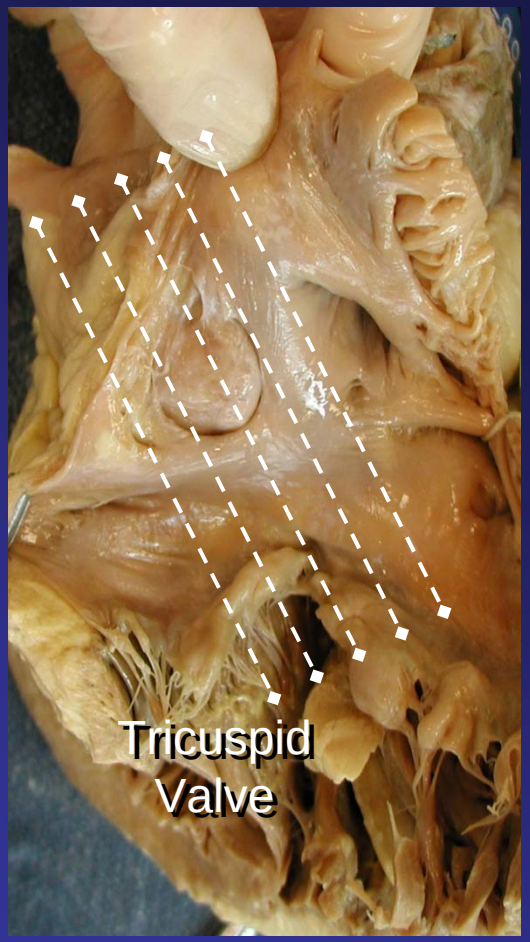
for embolization



Heart,
lungs,
liver,
spleen,
kidneys,
brain,
aorta,
pulmonary arteries

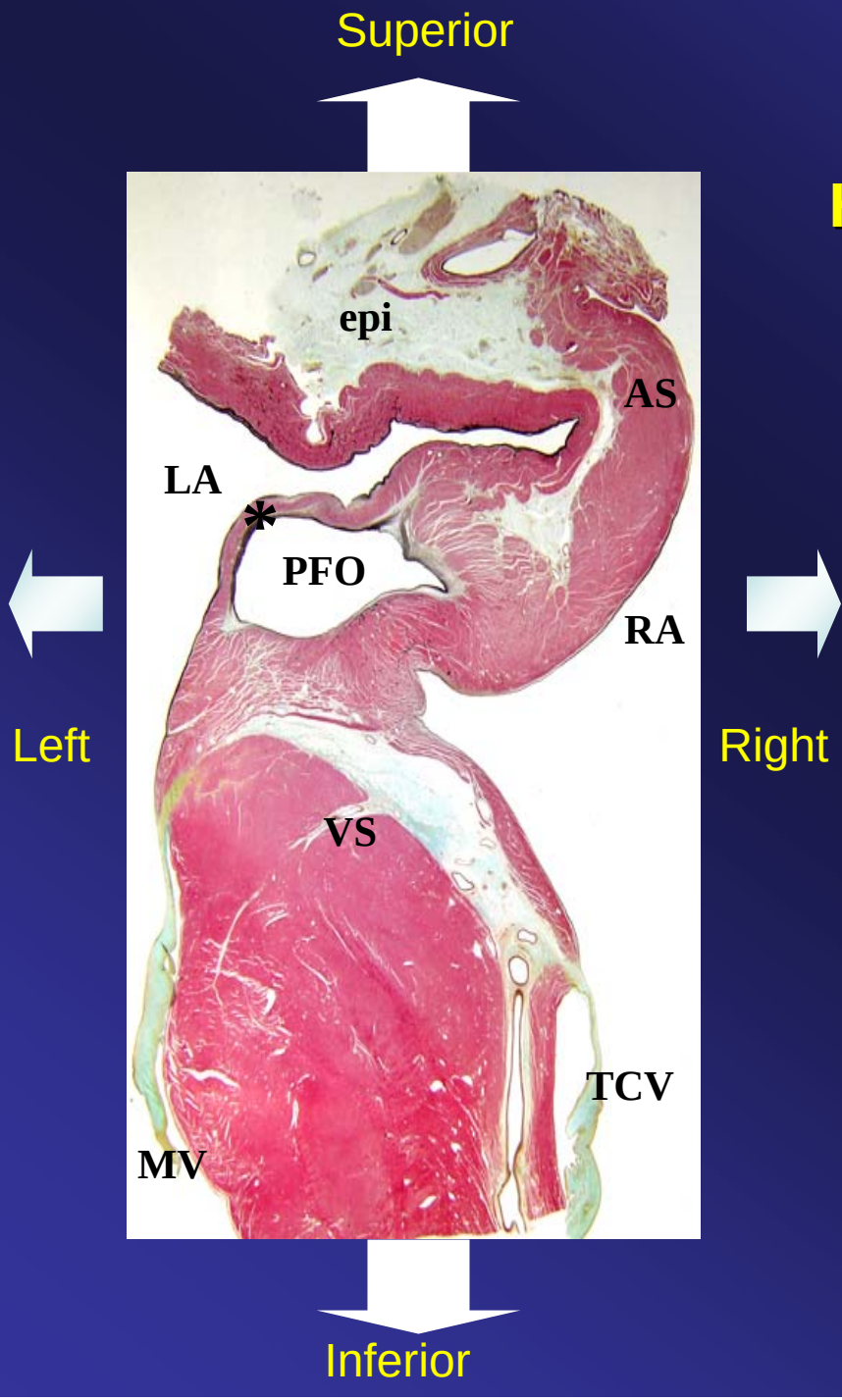
Methods

Histopathological Examination



Four to six tissue sections (4-5 mm thick) were obtained from the treated PFO area. The tissue sections were taken perpendicular to the interatrial septum and submitted from anterior to posterior, starting with the posterior aspect of the aorta (anterior margin) and included the atrial septum superior to the treated area as well as the ventricular septum with a portion of attached mitral and/or tricuspid valves for orientation.

Methods



Histological examination

All tissue sections were cut at 4-6 microns using a rotary microtome, mounted on a charged slide and stained with Hematoxylin & Eosin (H&E) and Movat pentachrome.

All sections were examined by light microscopy for thrombus, hemorrhage, foreign material, inflammation, necrosis, calcification and healing (*granulation tissue* and *fibrosis*).

Results

Gross Pathological examination 1

Heart,
lungs,
liver,
spleen,
kidneys,
brain,
aorta,
pulmonary arteries

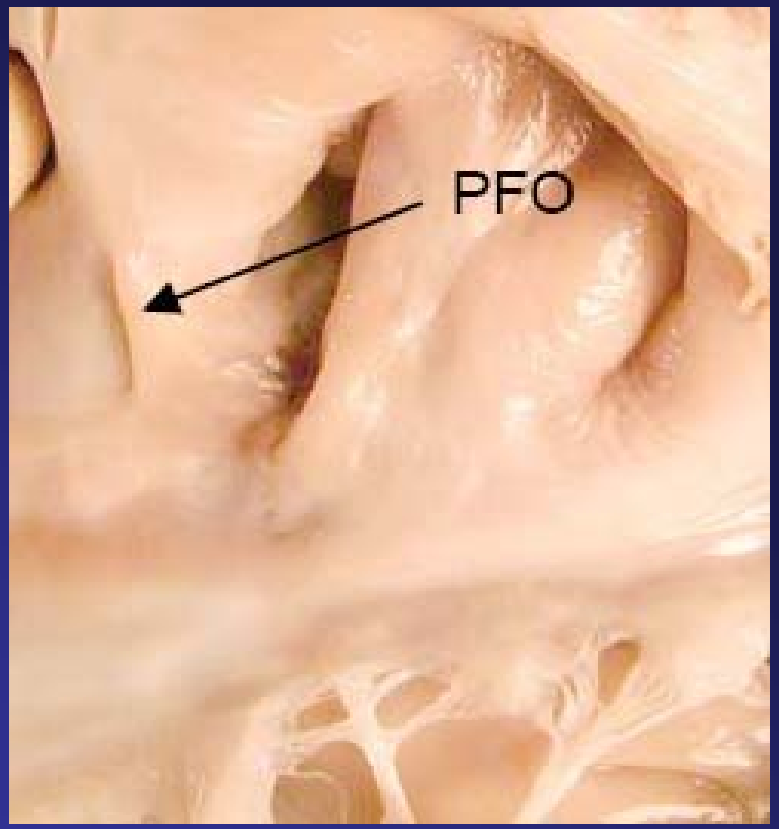
No evidence of myocardial infarction

No thromboembolic events

Results: Day Zero

Gross Pathological examination 2

LA



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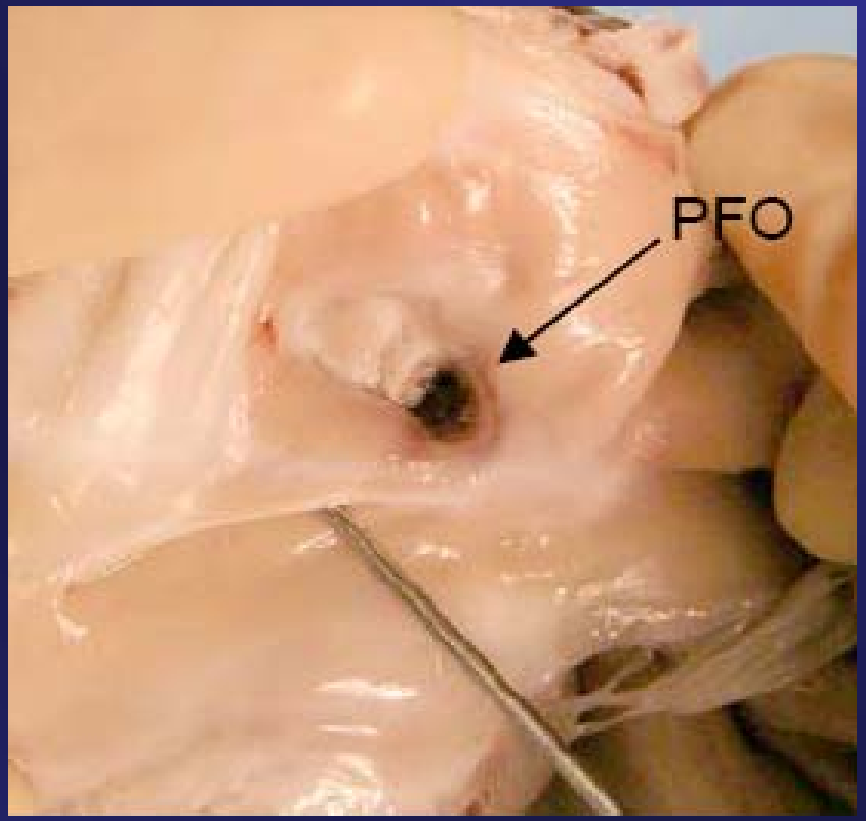
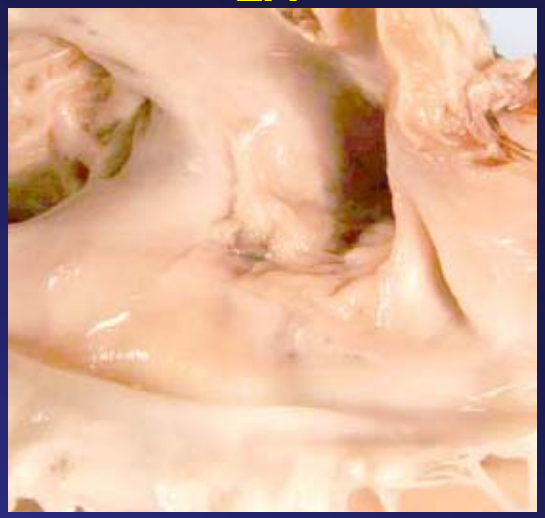


Foramen ovale typically showed focal, small hemorrhagic lesions on the right atrial side with brown friable material within tunnel; grossly, all fossa appeared sealed

Results: Day 7

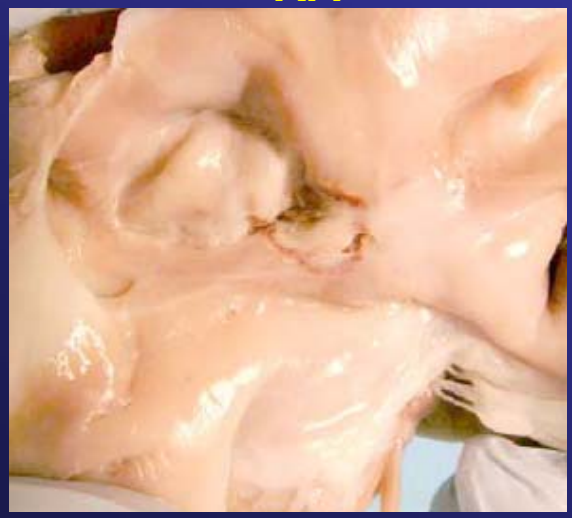
Gross Pathological examination 2

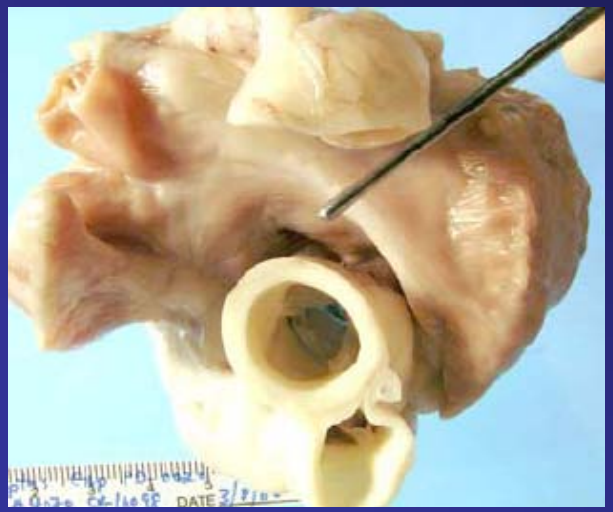
LA



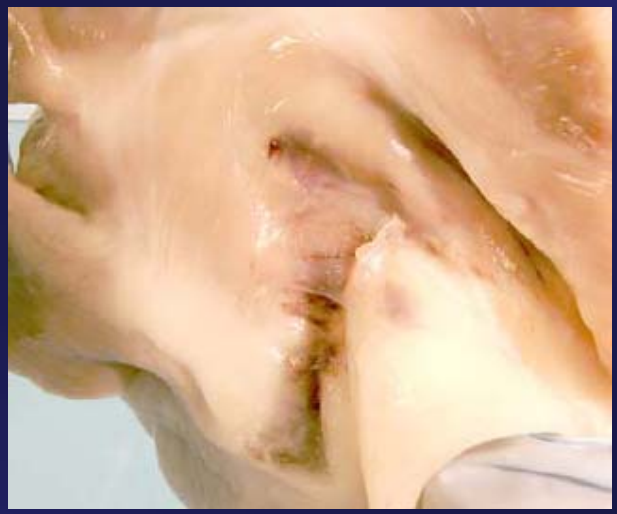
Treated areas of the foramen ovale showed tan white and slightly puckered lesions.

RA





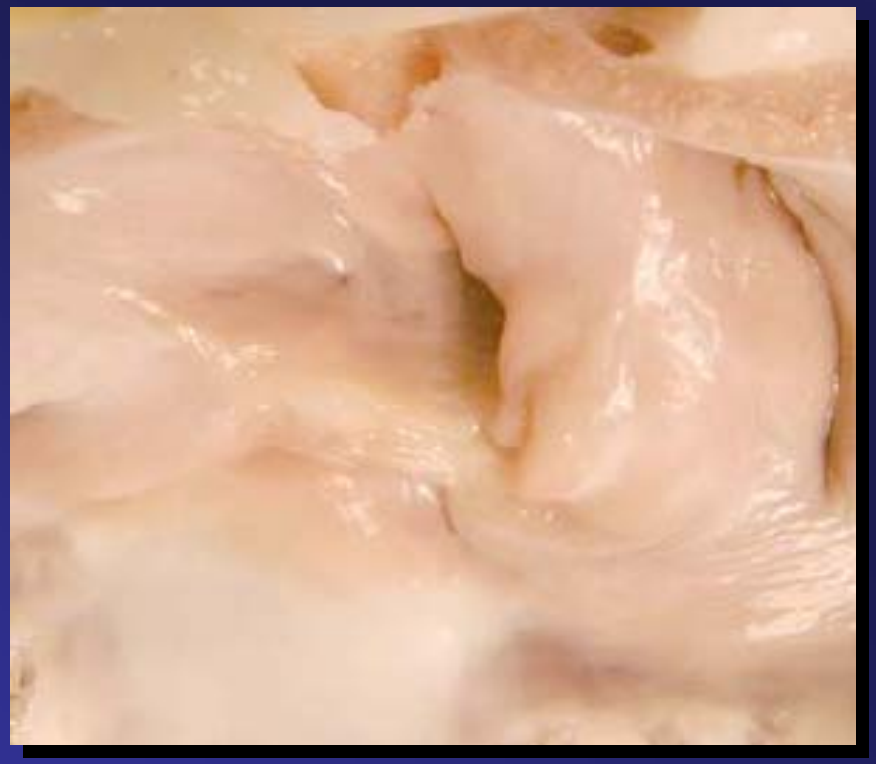
The left atrium showed irregular tan brown lesions opposite the treatment site
Grossly the fossa were sealed



Results: Day 28

Gross Pathological examination 2

LA



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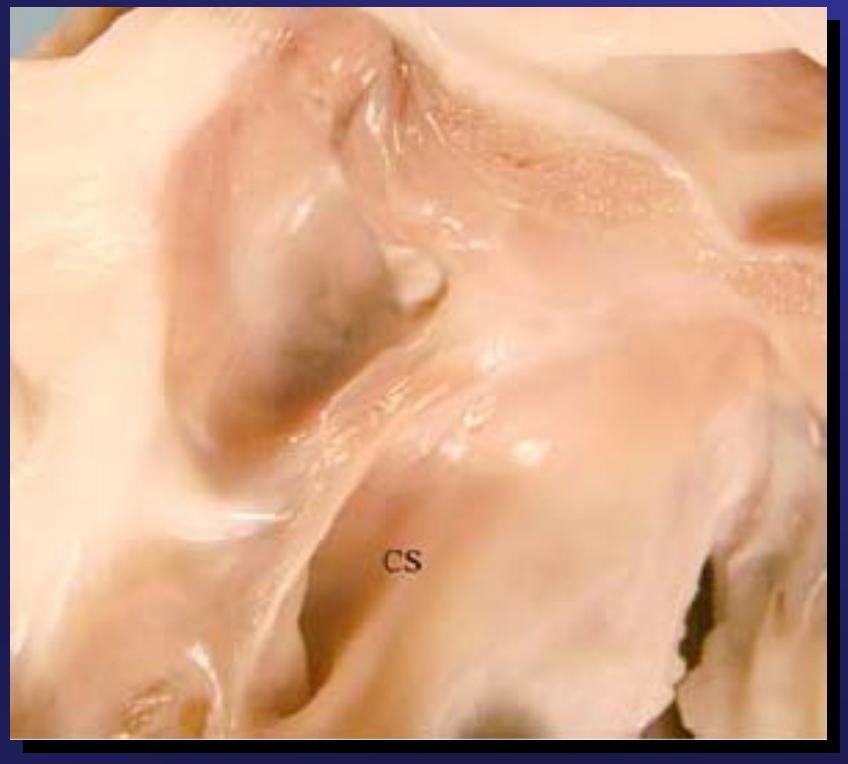
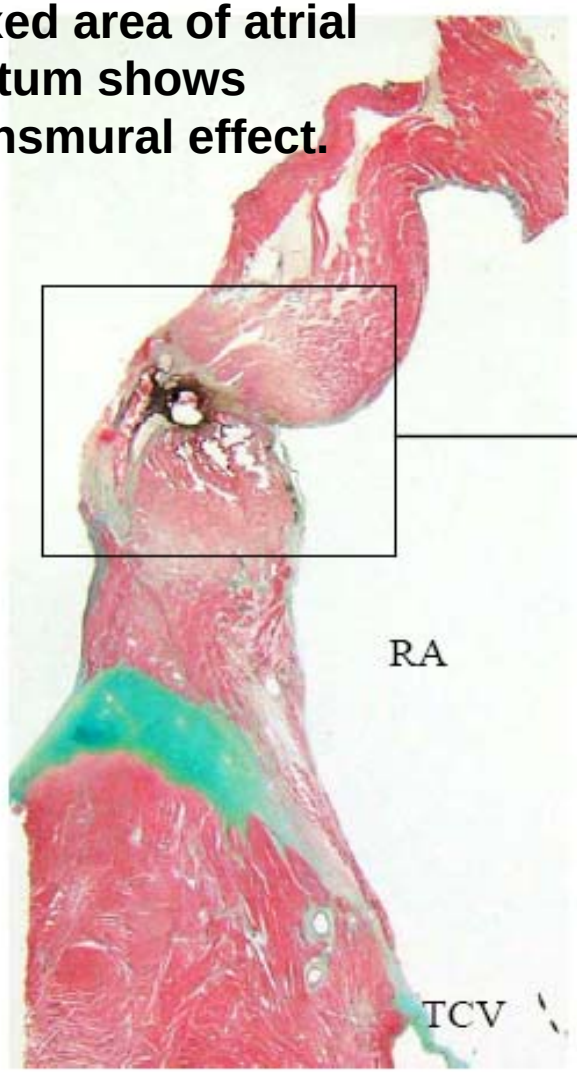


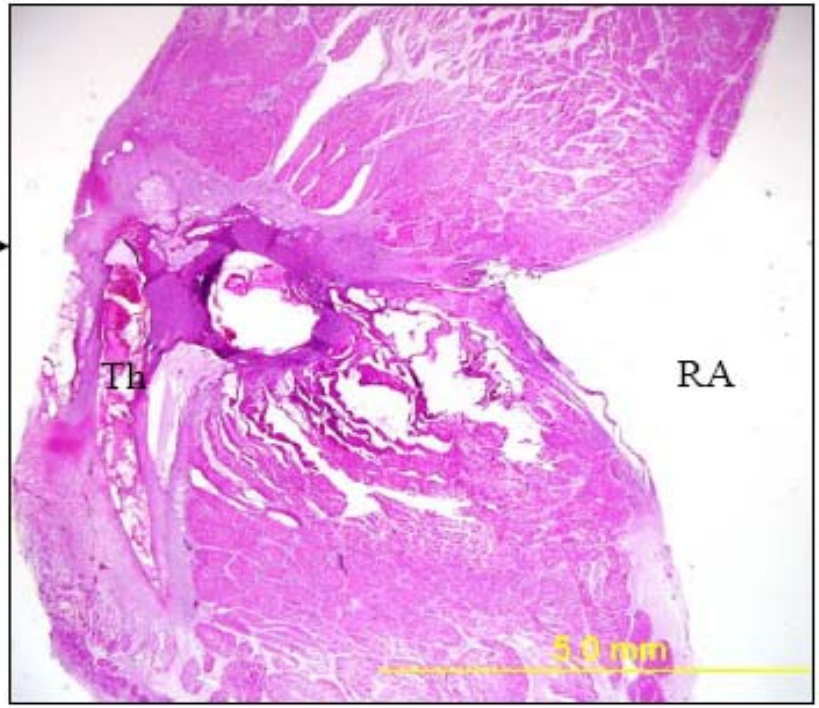
Foramen ovale typically showed small tan-white scars. The left atrium showed no gross lesions and the fossa were grossly sealed

Results: Day Zero

Histopathological examination

Boxed area of atrial septum shows Transmural effect.



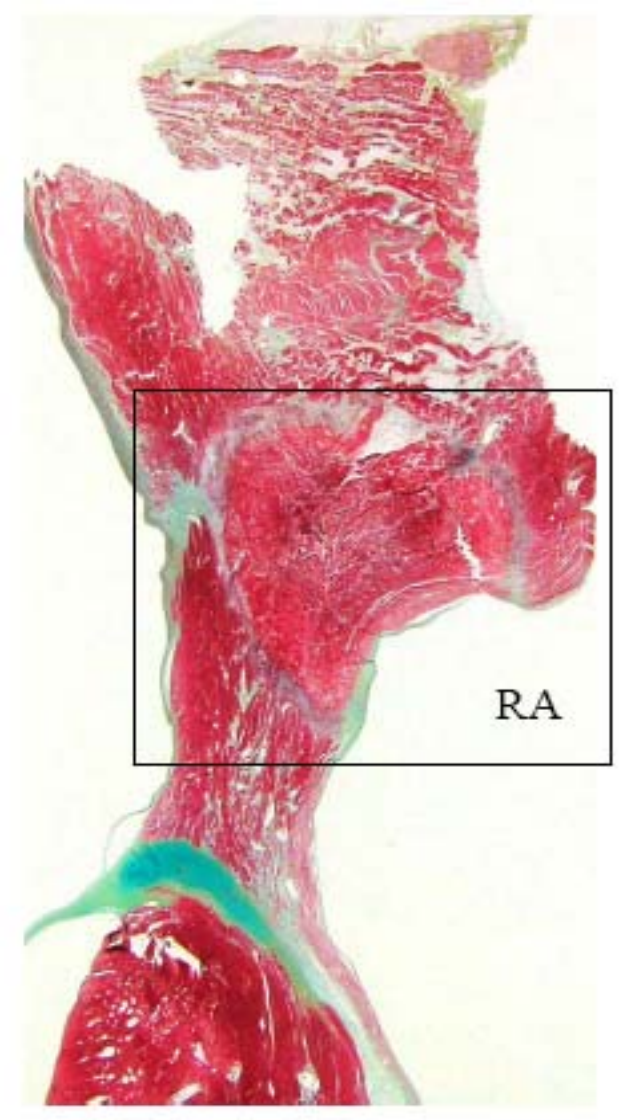


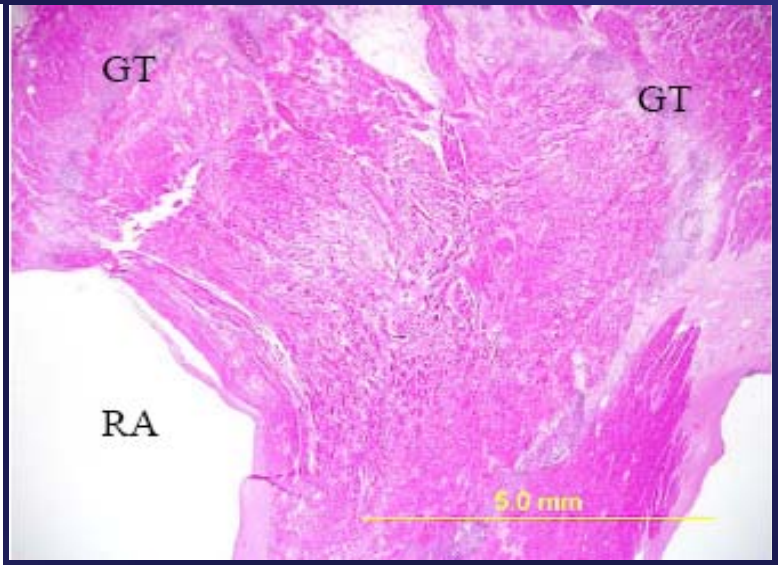
Higher magnification shows coagulative myocyte necrosis and marked tissue edema. Platelet thrombus is noted within the tunnel beneath the flap on the left atrial side.

Hara H. et al. Circulation . 2007 ;116:648-53.

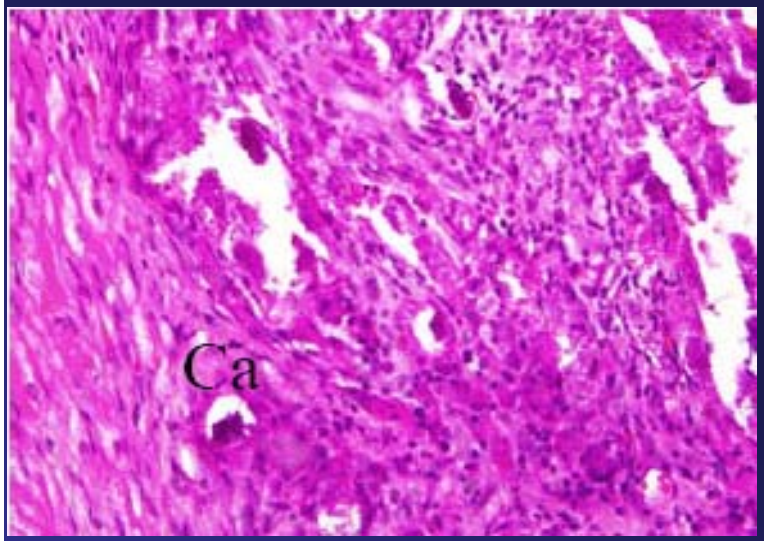
Results: Day 7

Histopathological examination





Whole mount Movat stained section shows rim of granulation tissue occupying >3/4 of the atrial septum.

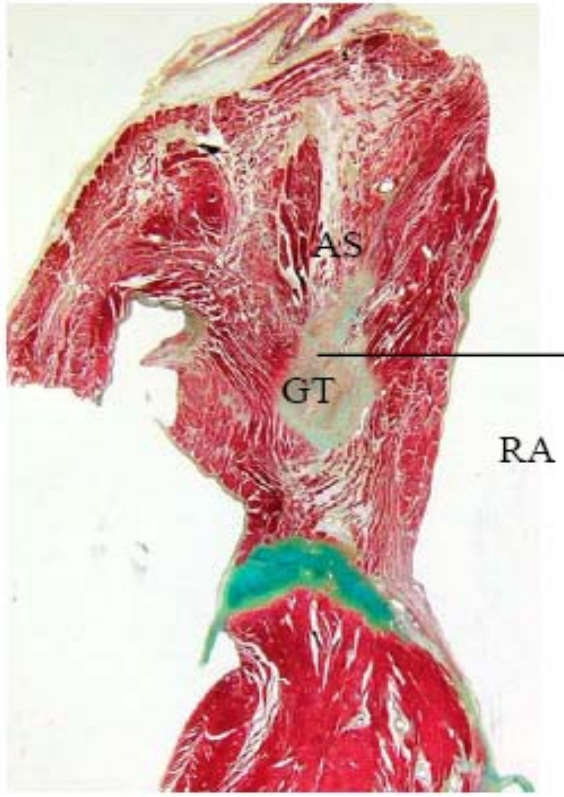


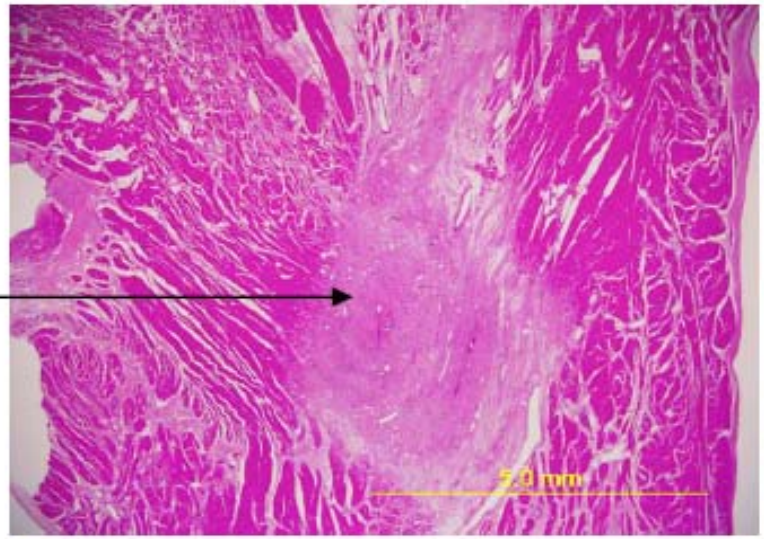
Higher magnification shows calcified myocytes (Ca) and chronic inflammation including giant cells adjacent to granulation tissue.

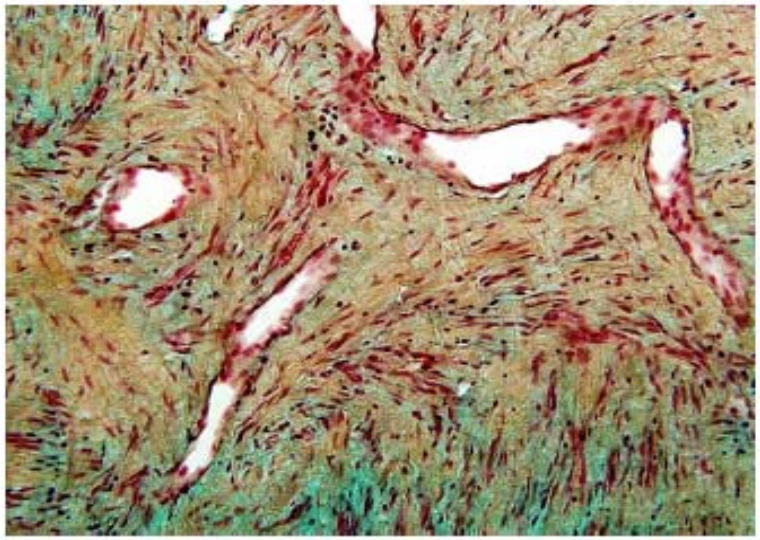
Hara H. et al. Circulation . 2007 ;116:648-53.

Results: Day 28

Histopathological examination







Higher magnification of granulation tissue consisting of fibroblasts, collagen, vascular channels (neovascularization)

Conclusions

RF based PFO closure is feasible, safe, and effective in swine.

Thermal healing, consisting of collagen formation, is nearly complete by 4 weeks.

This technique may allow substantial reduction in PFO closure risk over current device-based therapy.

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Patent Foramen Ovale Closure by Radiofrequency Thermal Coaptation

First Experience in the Porcine Model and Healing Mechanisms Over Time

Hidehiko Hara, MD; Thomas K. Jones, MD; Elena R. Ladich, MD; Renu Virmani, MD; David C. Auth, PhD; Joseph E. Eichinger, BS; Robert J. Sommer, MD; Robert A. Van Tassel, MD; Robert S. Schwartz, MD

Background—Percutaneous transcatheter patent foramen ovale (PFO) closure is now standard practice and may limit embolic complications for at least 10 years. Implantable PFO closure devices may be complicated by thrombosis, infection, device fracture, or embolization. A novel strategy uses radiofrequency-based thermal energy to seal PFO membranes, with no implanted device. We successfully used this method and examined histopathologic events in swine to characterize safety and efficacy.

Methods and Results—Thirteen domestic swine were examined over time after thermal PFO closure. Three animals were euthanized within 1 hour of treatment, 5 after 7 days, and 5 at 28 days. Gross and histopathologic findings were examined. Radiofrequency energy was delivered successfully in all cases, and PFOs were closed in 12 of 13 cases. One case was not suitable for histological examination because of laceration at euthanasia, and the other PFO was clinically closed, with no shunt at 7 days, but was histologically open. All of the other PFOs were confirmed closed histologically. Acute histological results showed edema, hemorrhage, and myocyte necrosis. Minimal thrombus formation occurred on the left atrial endocardial surface. At day 7, transmural thermal effects occurred through the atrial wall that extended to the epicardial surface. At day 28, thermal effects showed excellent scar formation. Collagen, matrix, and neovascularization were present in all cases. No animal experienced adverse events.

Conclusions—Thermal PFO closure is feasible, safe, and effective in swine. Thermal healing is nearly complete by 4 weeks and consists of collagen formation and tunnel closure. This technique may allow substantial reduction in PFO closure risk over current device-based therapy. (*Circulation.* **2007;116:648-653.**)

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Transcatheter Closure of Patent Foramen Ovale Without an Implant

Initial Clinical Experience

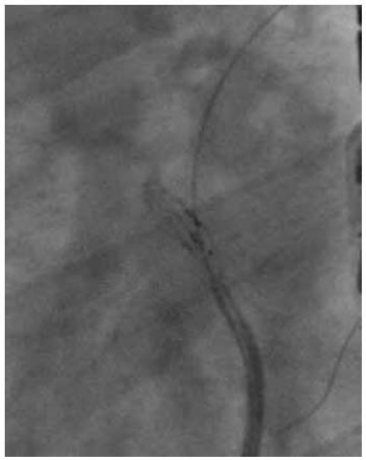
Horst Sievert, MD; Evelyn Fischer; Corinna Heinisch; Nico Majunke; Albrecht Roemer, MD; Nina Wunderlich, MD

Background—Currently available catheter techniques for closure of a patent foramen ovale (PFO) rely on the placement of an implantable closure device. The objective of the Paradigm I study was to evaluate the safety and feasibility of transcatheter closure of PFO using radiofrequency energy without an implanted device in patients with cryptogenic stroke or transient ischemic attack.

Methods and Results—Thirty patients were enrolled (15 females; mean age 48 years). Mean PFO size was 8.5±2.7 mm. Technical success (ie, successful application of radiofrequency energy) was achieved in 27 patients. The remaining 3 patients received an implantable closure device. All 30 patients were free from serious procedure-related adverse events. No recurrent strokes, deaths, or perforations occurred as a result of the procedure. The mean follow-up was 6 months, and 13 (43%) of the 30 patients experienced PFO closure after the first procedure. Nine of the patients whose PFOs remained patent after the first procedure elected to receive a second procedure using radiofrequency. The PFO was closed for 6 of those patients after the second procedure, which resulted in a secondary closure rate of 63%.

Conclusions—This study demonstrates that transcatheter closure of an intracardiac defect without a permanent implant is technically feasible. Achievement of improved primary closure rates through technique and device modifications will warrant randomized clinical comparison to permanently implanted devices. (*Circulation*. **2007;116:1701-1706.**)

The Cierra PFx™ System



- Permanent implant
- Arrythmias
- Thrombus risk
- Device erosion
- Device embolization

CoAptus™ PFO Closure System