

**Online supplement for Chawla et al. “Performance and healing of an expanded polytetrafluoroethylene multi chordal device at 6 months after repair of mitral leaflet flail in swine”**

**Materials and Methods:**

Animal acquisition, acclimation and care: Studies were performed at an AAALAC accredited laboratory, with approval from IACUC. Seven female Landrace cross-bred swine (3.7-4.7 months old, 54.3 – 60.6 kg) were purchased from Oak Hill Genetics. At arrival, animals were quarantined for 7 days in pens maintained at 61-81°F, and fed twice daily with a constant-nutrient diet (Harlan Teklad Mini Pig Diet, # 8753C). Water was provided *ad libitum*, and animal activity was recorded.

Surgical preparation: Swine were pre-medicated with Omeprazole (20-25mg PO on day -1 and 0), Aspirin (81mg PO for -3 days), Clopidogrel (75mg PO for -3 days), Nifedipine (30mg PO on -1 and 0), Florfenicol (15-20mg/kg IM on day -1), Ceftiofur Sodium (3-5mg/kg IM on day -1, 0 and +1), Cefotaxime sodium (1g IV, day 0), and Methylprednisolone (250mg IV on day 0). Prior to surgery, animals were sedated with Telezol (3-6mg/kg IM), Xylazine (2-3mg/kg IM), and a single dose of Buprenorphine (0.05mg/kg,IM) and Butorphanol(0.2-0.3mg/kg,IM) for analgesia. They were intubated and mechanically ventilated on isoflurane. Heart rate, respiratory rate, blood pressure, body temperature, tidal volume, EKG, SpO<sub>2</sub> and inhalant anesthesia were monitored. Dermal electrodes, auricular pulse oximetry and a rectal temperature probe were positioned. Surgical sites on the neck, left chest and groin were scrubbed and prepared for aseptic surgery. Blood was sampled every 30 minutes to measure blood gases, electrolytes and ACT levels.

Experimental MVP: A2 flail was induced by marginal chordal transection. In the first pilot animal, this was achieved via a transapical beating heart approach with echocardiography.

Though successful, the flail severity could not be controlled due to poor visibility. In the next six animals, chordae were transected while on pump. With the swine in right lateral recumbent position, a left thoracotomy was performed between the 4<sup>th</sup>- 5<sup>th</sup> intercostal space to access the heart. A transverse pericardiotomy was performed, the left internal thoracic artery (LITA) was mobilized and cannulated for arterial blood access and pressure monitoring. Heparin was administered prior to cannulation. Arterial cannulation was performed at the descending aorta at the level of the ligamentum, and venous cannulation through the right atrial appendage. A DLP catheter was inserted proximal to the arterial cannula, and cold crystalloid Plegisol(Hospira,Inc) was injected. The aorta was cross clamped and the heart was arrested. The mitral valve was accessed via the left atrium, the valve was inspected for clefts or other lesions, and the left ventricle was filled with saline to assess baseline coaptation. Marginal chordae inserting into the AL were identified and 1-3 chordae were cut to induce A2 flail and severe MR was confirmed.

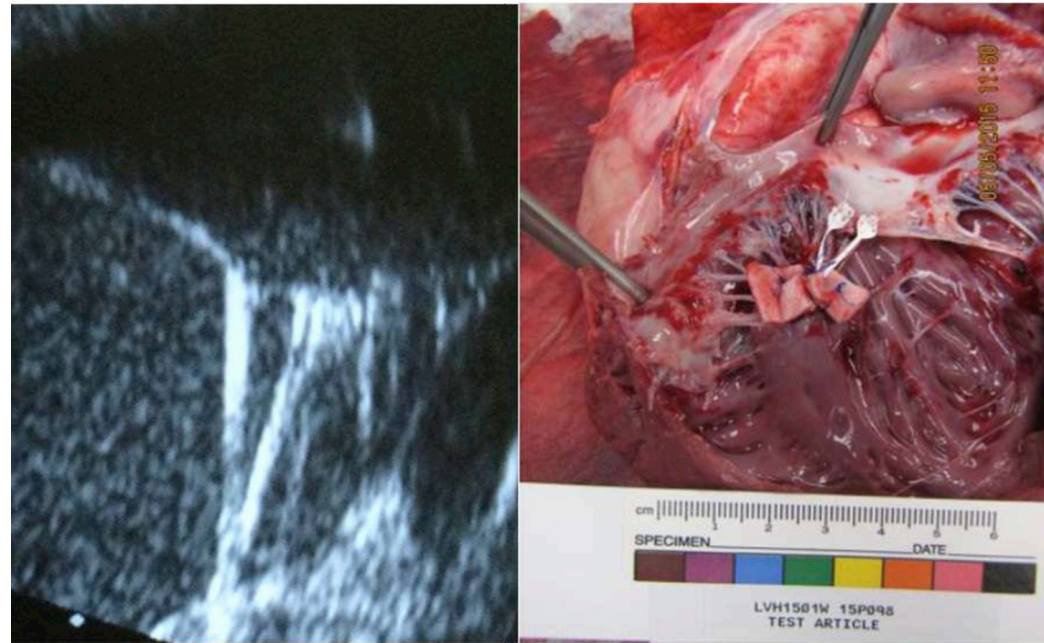
Mitral repair: Two 5“0” monofilament stay sutures were placed on either sides of the flail segment, to stretch it. The device was inserted into the MV, and the neo-PM was sutured to the native PM with two 5-0 ePTFE pledgeted sutures. The optimal neochordae length was determined by matching their lengths to the adjacent intact chordae. A pledgeted 6-0 ePTFE suture was used with a ventricular pledget (native pericardial pledget in 3 animals and ePTFE pledget in others). After matching the neochord length to the free edge, the neoleaflet section was sutured onto the atrial surface (*Figure 2*). We described the physiological basis for this measurement (14). Saline test was repeated and reduction in MR was recorded. The left atriotomy was closed, the heart was de aired, heart function was restored, and decannulated. A chest tube was used, and the thoracotomy was closed in layers with skin closure using subcuticular suture. Furosemide was administered for diuresis and additional analgesia.

Post-operative care: The pigs were returned to a cage for recovery while monitoring body temperature, pulse, respiration, until physiologically stable. Thereafter, the animals were monitored for 7 days. Buprenorphine (0.05mg/kg, IM) was administered 6-12 hours after the induction dose and PRN thereafter. Cefotiofur sodium (3-5mg/kg, IM) was administered once daily for seven days, and Florfenicol (15-20 mg/kg) was used as required. Daily doses of Aspirin (81 mg) and Clopidogrel (75 mg) were administered until termination, and Omeprazole (20-25 mg) was administered for eight days after surgery.

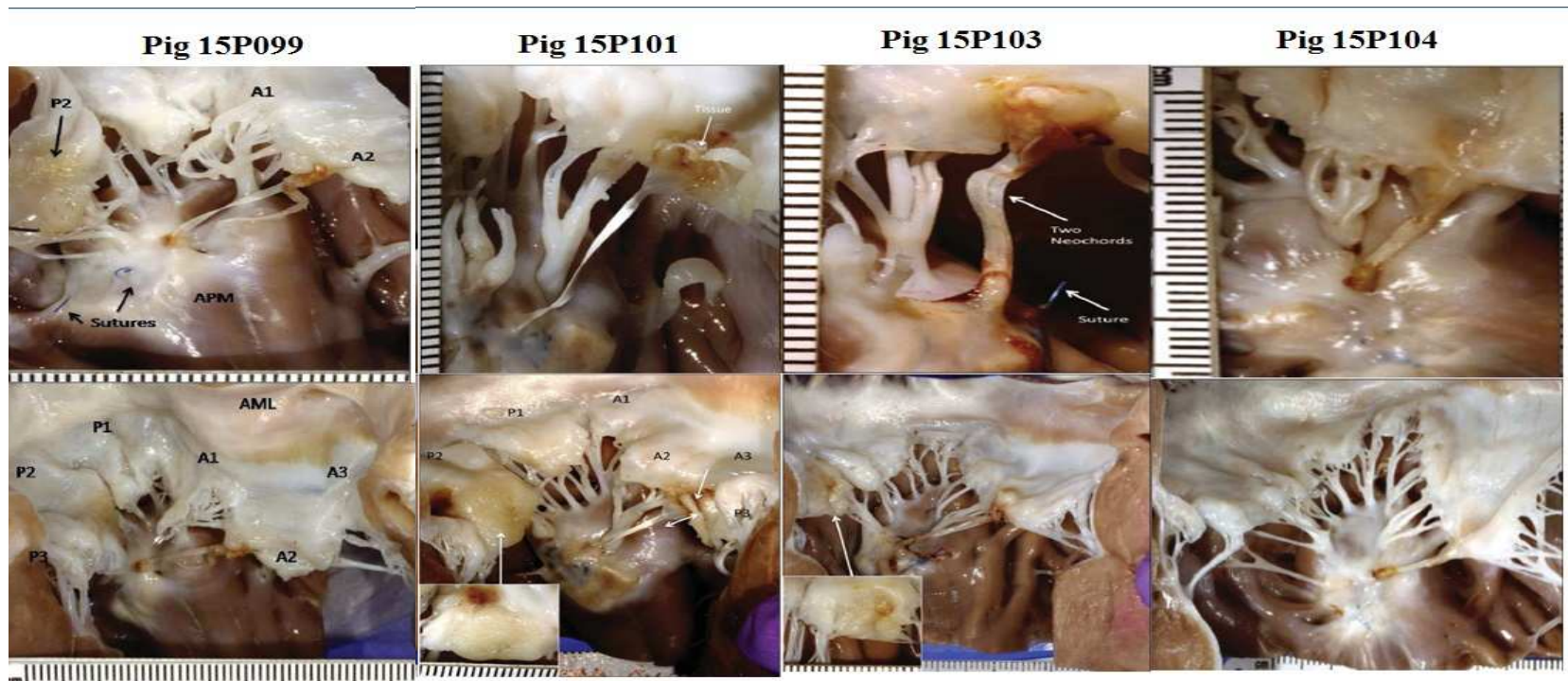
**Results:**

In life observations: Significant post-operative observations are presented. Inappetence after surgery was common, and was treated with extra nursing care. In animal 15P100, a small abscess draining at the caudal part of the thoracotomy incision was observed on day 26. The incision was cleaned for four days and antibiotics were administered. Animal 15P101 was febrile with slight tachycardia on day 5, which resolved with two doses of florfenicol and ketoprofen. On day 25, swelling of the thoracotomy was observed and treated with antibiotics. On day 39, a 2cm ruptured abscess in the dorsal incision was observed, which was cleaned and ultimately healed in few days. Animal 15P104 demonstrated swelling of the thoracotomy incision on day 26 and cleaning it for few days resolved the issue. No other significant in life observations were noted.

**Pig 15P098**



**Figure S2A:** (Left) Echocardiographic image of the device from a pig depicting the device; (Right) Explant photograph from the acutely terminated pig



**Figure S2B:** Explant photographs from each pig

**Table S2: Echocardiography Observations**

Animal Number	Observation Time Point	Cardiac Output (L/min)	Heart Rate (bpm)	Ejection Fraction (%)	Test Article Assessment		
					Integrity	Stability	Mineralization
<b>Acute Pilot Animal (Group 1)</b>							
15P098	Day 0 pre	NA	NA	NA	NA	NA	NA
	Day 0 post	NA	NA	NA	NA	NA	NA
<b>Excluded (Strut Chord Transected) Chronic 180 Day Survival Animal (Group 3)</b>							
15P050	Day 0 post	NA	NA	NA	NA	NA	NA
	Day 6	4.9	126	NA	Appears Intact	Appears Stable	No
	Day 28	5.6	100	NA	Appears Intact	Appears Stable	No
	Day 56	4.2	82	NA	Appears Intact	Appears Stable	No
	Day 93	3.8	71	58	NA	NA	NA
	Day 154	5.9	97	71	Appears Intact	Appears Stable	No
	Day 182	2.4	58	61	Does not appear intact	Does not appear stable	No
<b>Chronic 150 Day Survival (Group 2)</b>							
15P100	Day 4	3.8	102	NA	Appears Intact	Appears Stable	No
	Day 26	5.9	85	NA	Appears Intact	Appears Stable	No
	Day 54	4.0	69	NA	Appears Intact	Appears Stable	No
	Day 91	4.6	58	61	Appears Intact	Appears Stable	No
	Day 152	5.0	65	66	Appears Intact	Appears Stable	No
15P101	Day 3	5.7	147	NA	Appears Intact	Appears Stable	No
	Day 25	6.7	111	NA	Appears Intact	Appears Stable	No
	Day 53	4.3	85	NA	Appears Intact	Appears Stable	No
	Day 90	4.5	99	65	Appears Intact	Appears Stable	No
	Day 151	3.1	79	52	Appears Intact	Appears Stable	No
15P103	Day 5	6.7	114	NA	Appears Intact	Appears Stable	No
	Day 27	6.4	106	NA	Appears Intact	Appears Stable	No
	Day 55	4.7	92	NA	Appears Intact	Appears Stable	No
	Day 92	5.2	103	55	Appears Intact	Appears Stable	No
	Day 153	4.2	83	55	Appears Intact	Appears Stable	No
15P104	Day 4	6.4	125	NA	Appears Intact	Appears Stable	No
	Day 26	5.1	75	NA	Appears Intact	Appears Stable	No
	Day 54	2.4	59	NA	Appears Intact	Appears Stable	No
	Day 91	5.2	72	59	Appears Intact	Appears Stable	No
	Day 152	6.7	93	57	Appears Intact	Appears Stable	No
15P099	Day 5	11.1	145	NA	Appears Intact	Appears Stable	No
	Day 27	5.7	69	NA	Appears Intact	Appears Stable	No
	Day 55	5.6	66	NA	Appears Intact	Appears Stable	No
	Day 92	4.1	61	NA	Appears Intact	Appears Stable	No
	Day 153	2.6	56	54	Appears Intact	Appears Stable	No
	Day 181	4.8	99	58	Appears Intact	Appears Stable	No