Mitral Loop Cerclage
for reducing functional mitral regurgitation

interim result of First-In-Man trial

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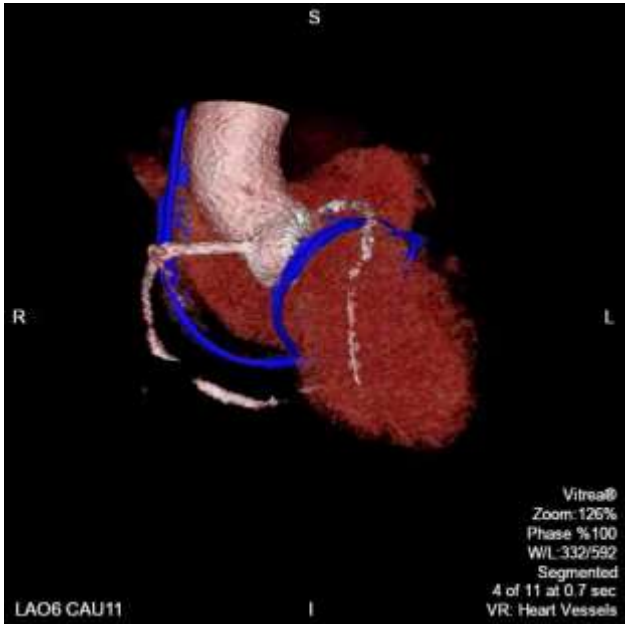


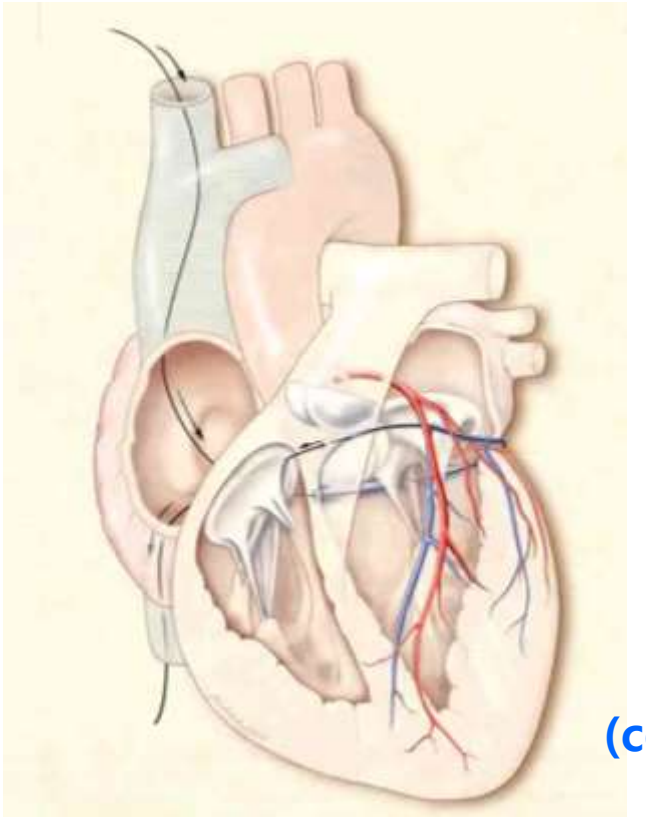
Disclosure of ‘Conflict of Interest’

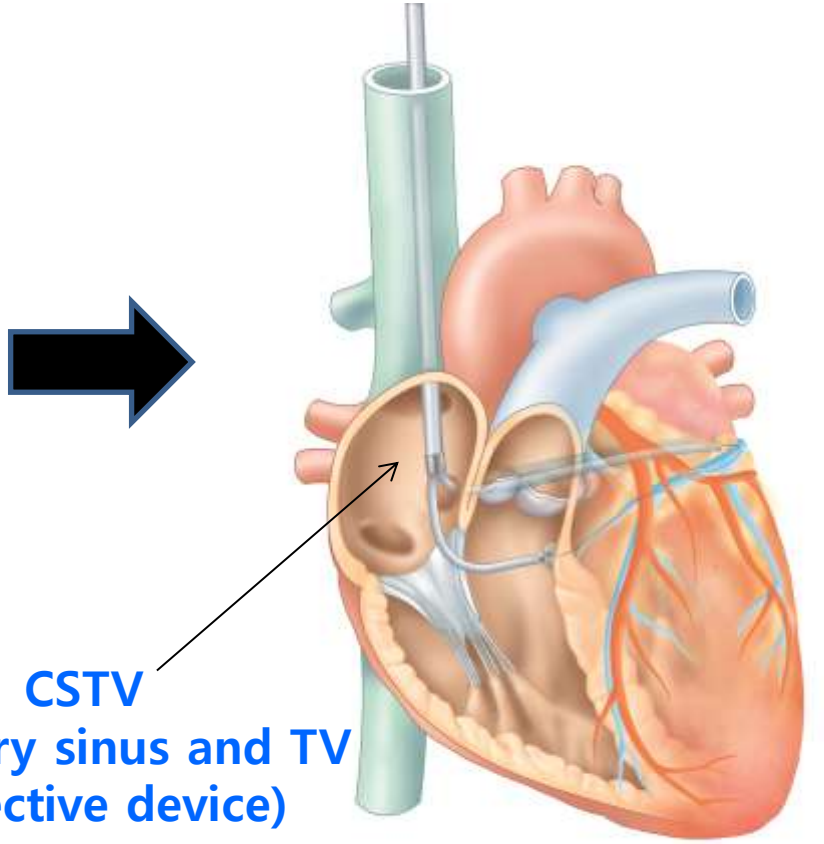
- Founder and stock holder : Tau-PNU Medical Co. of Pusan National University
- Intellectual Property of ‘Mitral Cerclage ’ and ‘Mitral Loop Cerclage’ that are assigned to NIH, or Tau-PNU or Pusan National University.
- Collaborator with NHLBI Division of Intramural Research (Z01-HL006040)

Mitral Loop Cerclage

- Circumferential tension around MV anuulus by LV basal squeezing

- Reinforce of safety issues
- improving technical feasibility





CSTV
(coronary sinus and TV protective device)

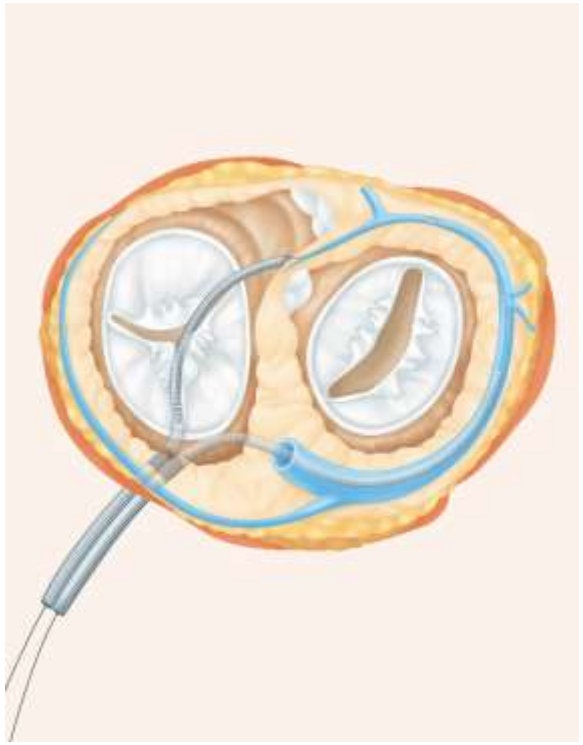
Mitral Cerclage + a bifid appliance = **Mitral Loop Cerclage**

Kim JH et al. JACC 2009; 54 :638-51

Kim JH et al. Eurointervention 2016; 8;11(14)

How to function?

(1) TV & conduction protection



Arch formation during tension

(2) Interactive tension adjustment

Septal lateral dimension

⬆

Tensioning through a tip of CSTV loop

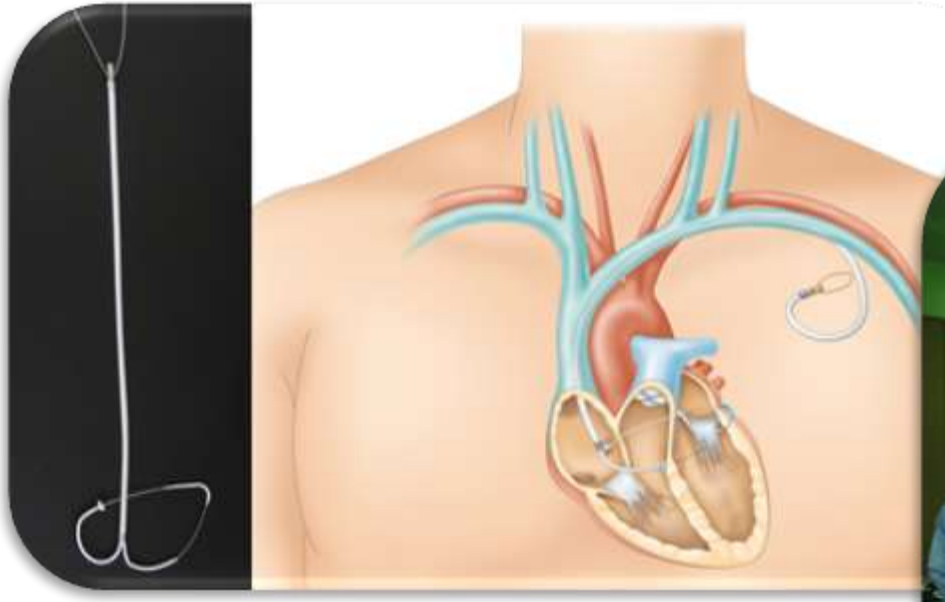
⬇

(3) Easy re-adjustment of tension when it is needed

Kim JH et al. Eurointervention 2016; 8;11(14)

The exploratory proof of concept study of Mitral Loop Cerclage (n=5)

The first case of Mitral Loop Cerclage FIM in PNUYH, Korea (July 10th 2015)

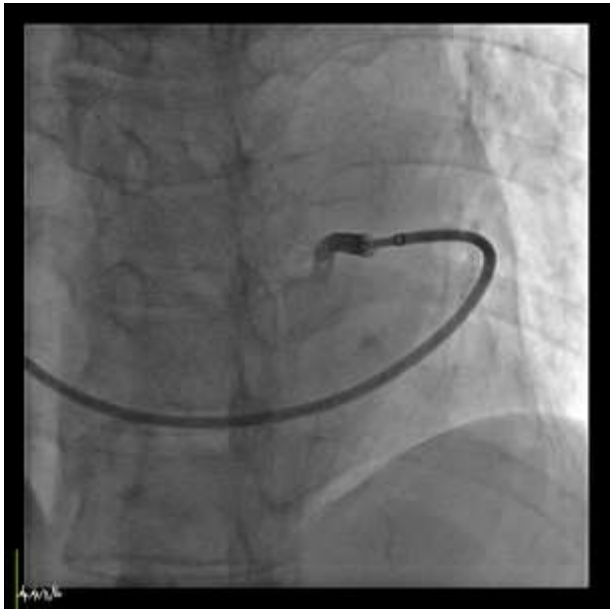


Inclusion : NYHA class III or IV dyspnea due to severe functional MR in spite of optimal medical TX at least for 3 months

Mean fluoroscopic time : 79 ± 20 min (n=4)

양산부산대학교병원
Pusan National University Yangsan Hospital

Procedure



Pressurized venogram

Delivery of CSTV

Interactive tension adjustment

The baseline characteristics of the enrolled cases (n=5)

Endpoints : Efficacy and safety endpoints at postprocedure, 1month and 6months

#	Proc date	Sex/ age	Mechanism of FMR	EF (%)	LVEDD (mm)	LVEDV (mL)	Imaging guidance	Procedural success
1	July 2015	F/76	Ischemic MR	65	72	190	AX+TTE (sedation)	Yes
2	Oct 2015	M/71	Annular dilation	61	63	229	AX+TTE (sedation)	No*
3	Oct 2015	F/74	Atrial fib. & annular dilation	58	65	218	AX+TEE (Gen Anesthesia)	Yes
4	Jan 2016	M/62	Non-ischemic cardiomypathy & leaflet tethering	34	74	260	AX+TEE (Gen Anesthesia	Yes
5	Feb 2016	M/68	Non-ischemic cardiomypathy & leaflet tethering	37	84	350	AX+TTE (sedation)	Yes

- Dimension and volumetric data were from cardiac CT measurement
- Procedure was aborted due to unsuitable anatomy of proximal septal vein. The patient was discharged next day without any complication.
- TEE was done under general anesthesia

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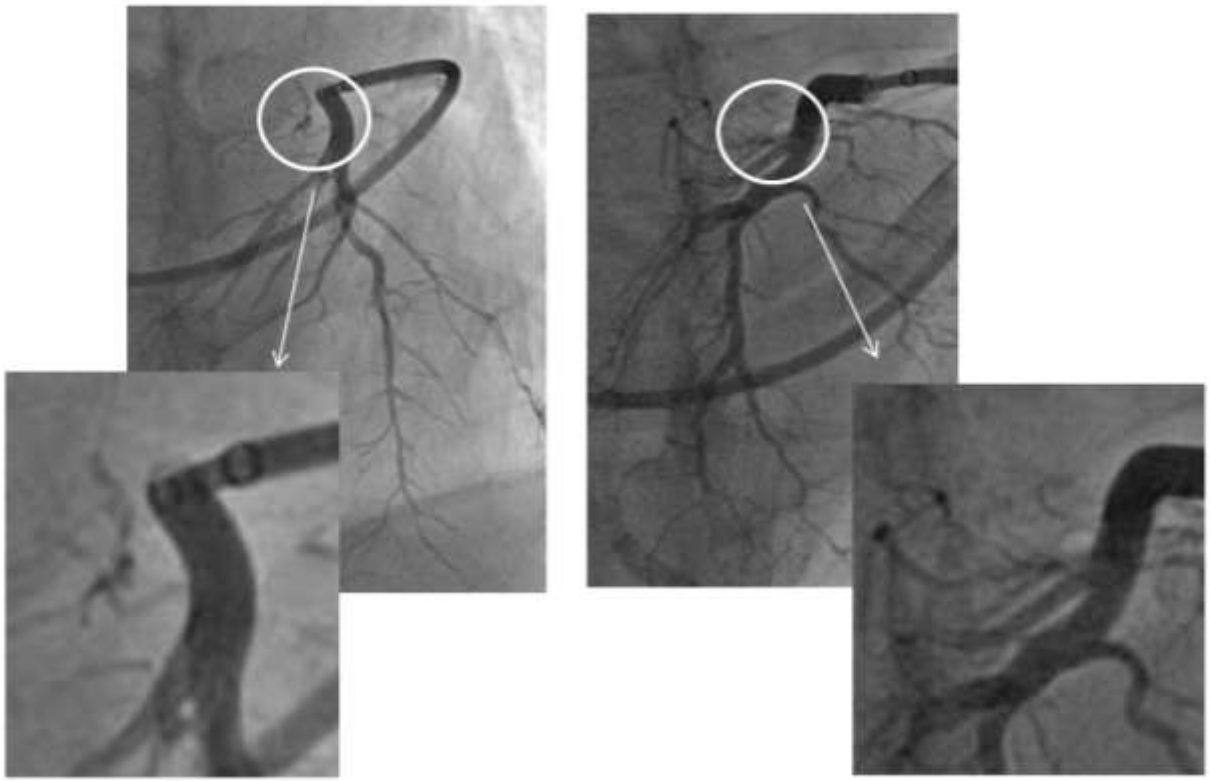
Endpoints : Efficacy and safety endpoints at postprocedure, 1month and 6months

#	Proc date	Procedural success
1	July 2015	Yes
2	Oct 2015	No*
3	Oct 2015	Yes
4	Jan 2016	Yes
5	Feb 2016	Yes

MLC#2. Poor proximal septal vein *vs* MLC#1. Good proximal septal vein



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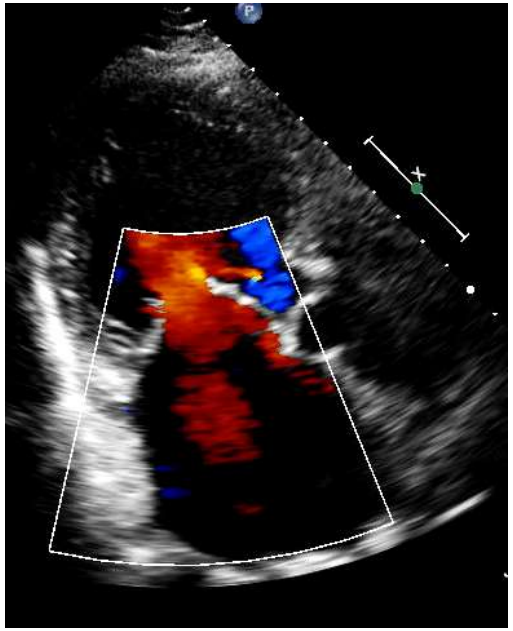
Case #1. 76/F, Progressive Dyspnea despite two years of OMT (NYHA class III-IV)

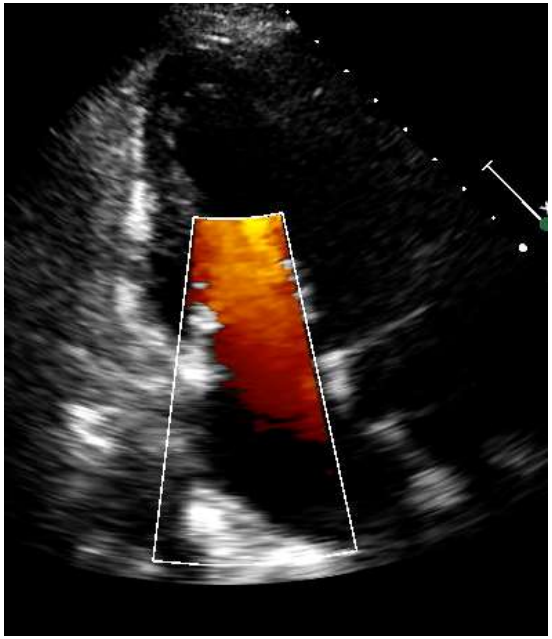
Asymmetric tethering due to akinesia of basal posterolateral wall

Baseline



- ERO 0.24 cm2
- RV 48 cc

Postprocedure



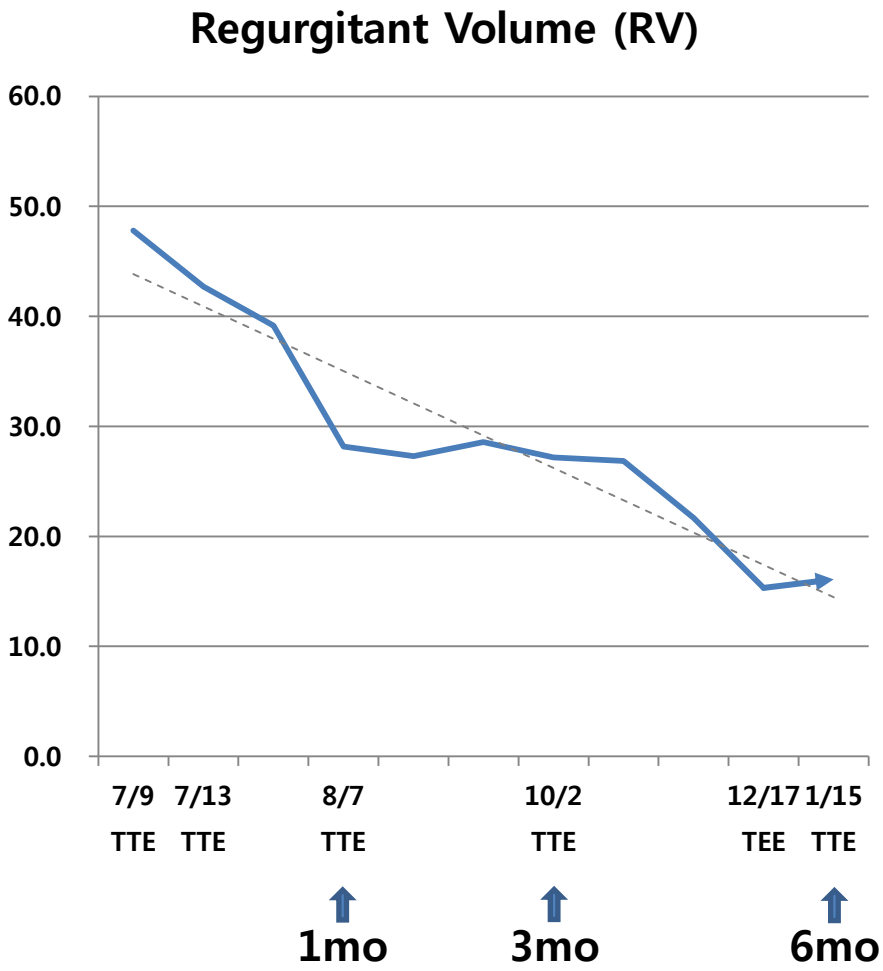
16% reduction of Septal to lateral dimension (SLD) (38mm -> 32mm)

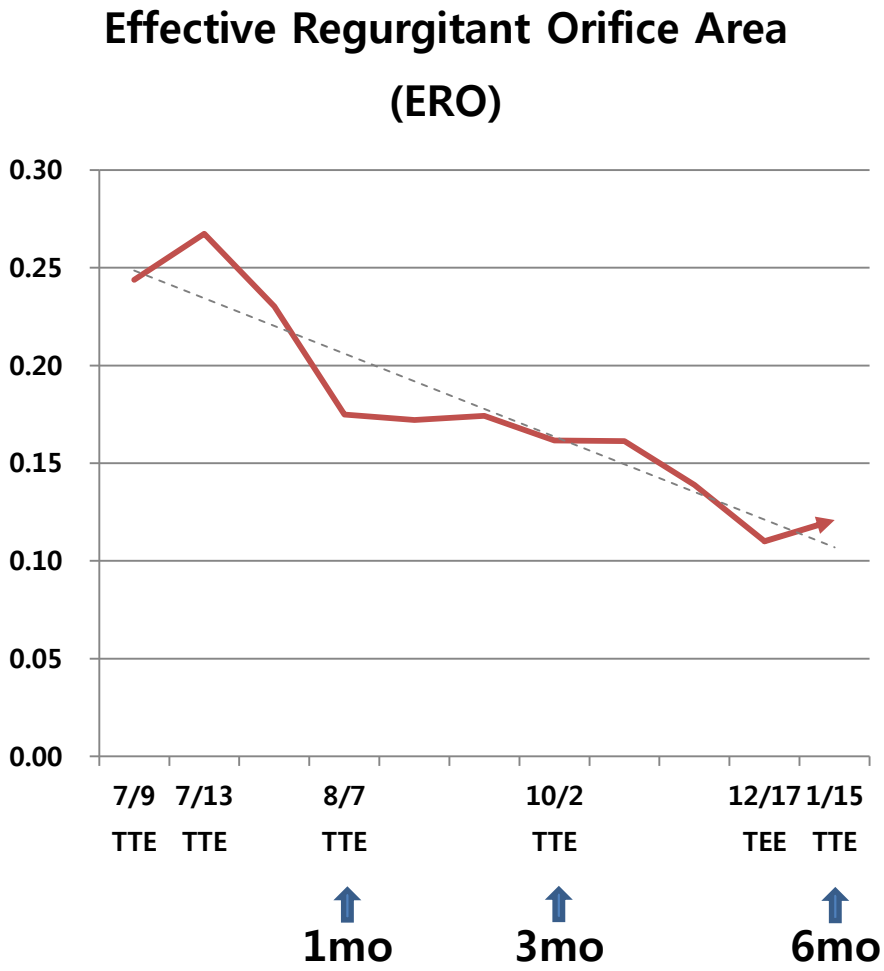
5 Months

- ERO 0.11 cm2
- RV 15 cc

Serial change of MR quantification of this case (asymmetric tethering)

NYHA class III/IV -> I

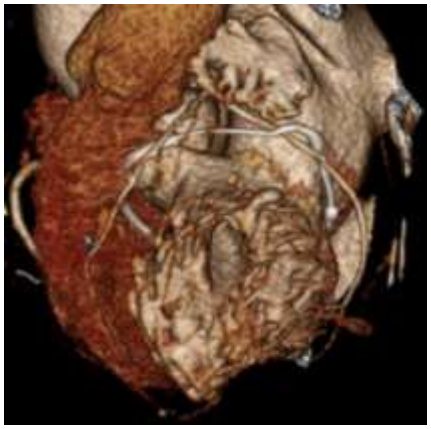




Reverse Remodeling & coronary artery protection

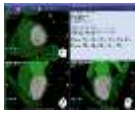
Preprocedure 6 months FU

6 weeks FU CT



6 month FU CT

LA volume



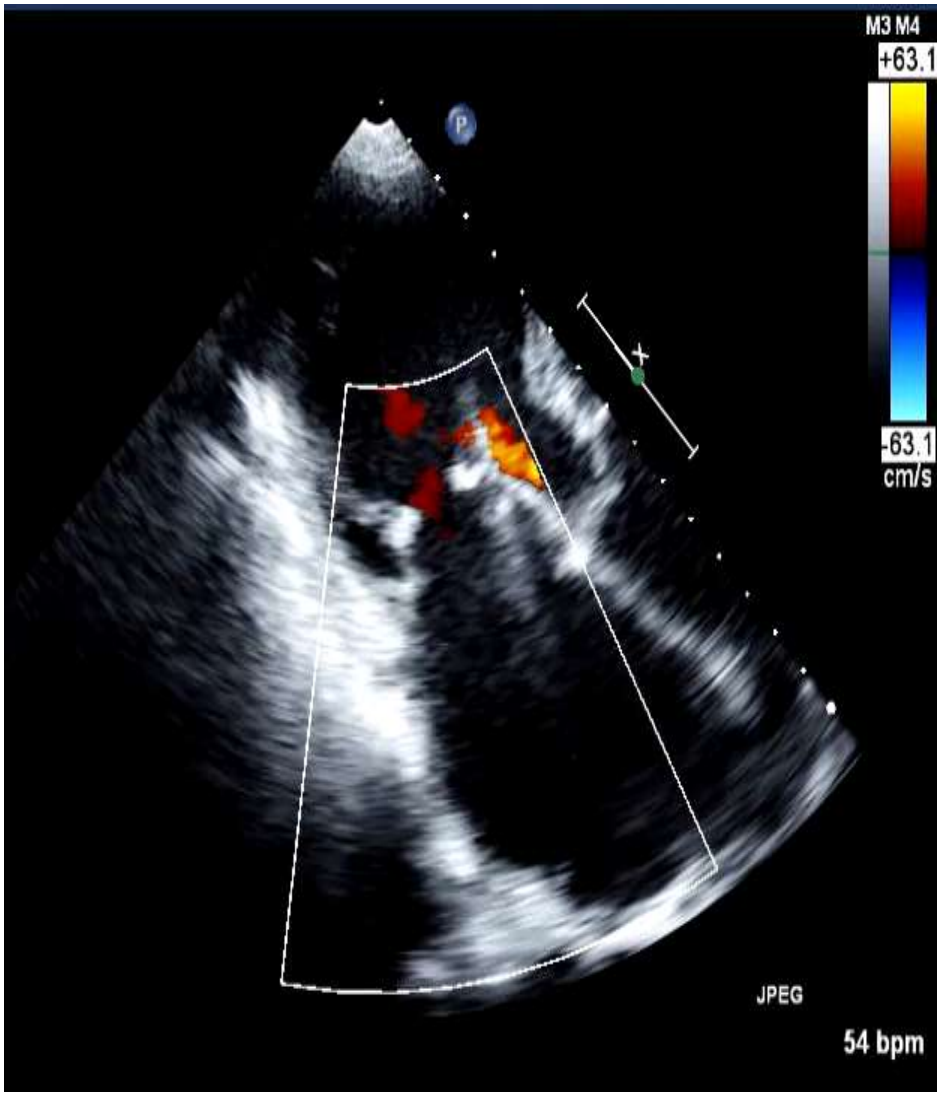
LV volume

	Baseline	6 weeks	6 months
LA volume (mL)	340	285 (16% ↓)	155 (54% ↓)
LVED vol (mL)	190	191	122 (36% ↓)

* CT volume data

Case #3. 74/F. Class IV Dyspnea despite aggressive medical Tx over 1year

Symmetric tethering due to persistent AF

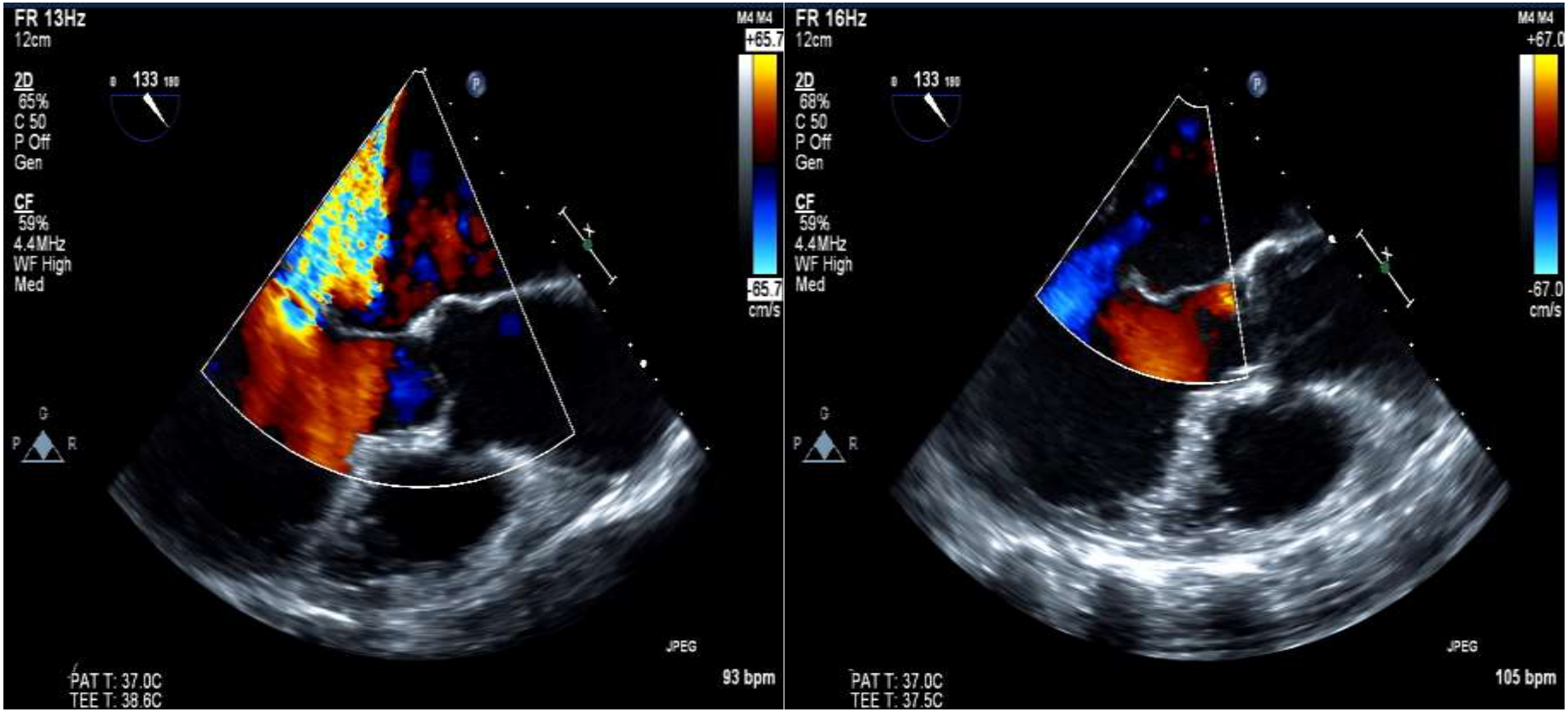


- ERO : 0.34 cm^2
- Regurgitant volume 63 ml
- EF 58%

BNP : 3269 pg/mL.

Interactive tension adjustment under imaging guidance

12% reduction of septal lateral annulus (45.2 →39.7 mm)

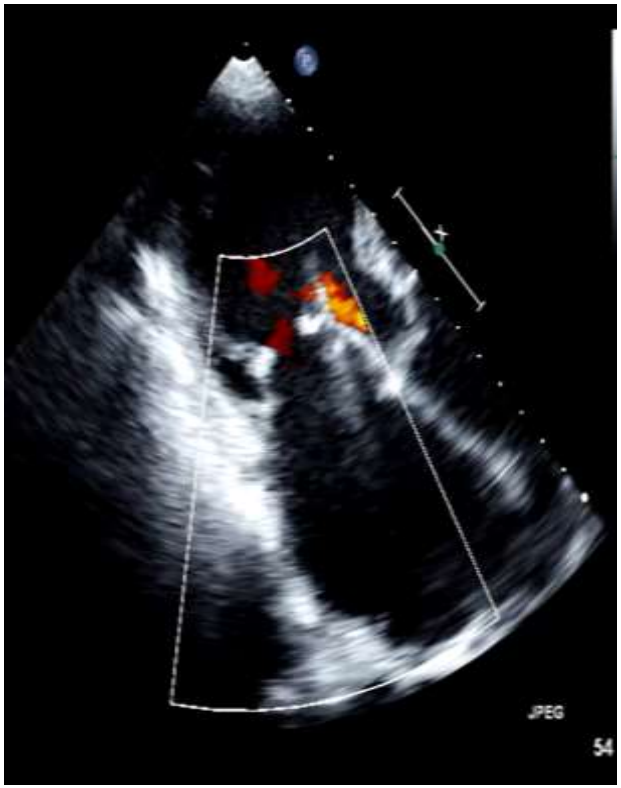


Before tension

After tension

Serial Echo FU data

Before

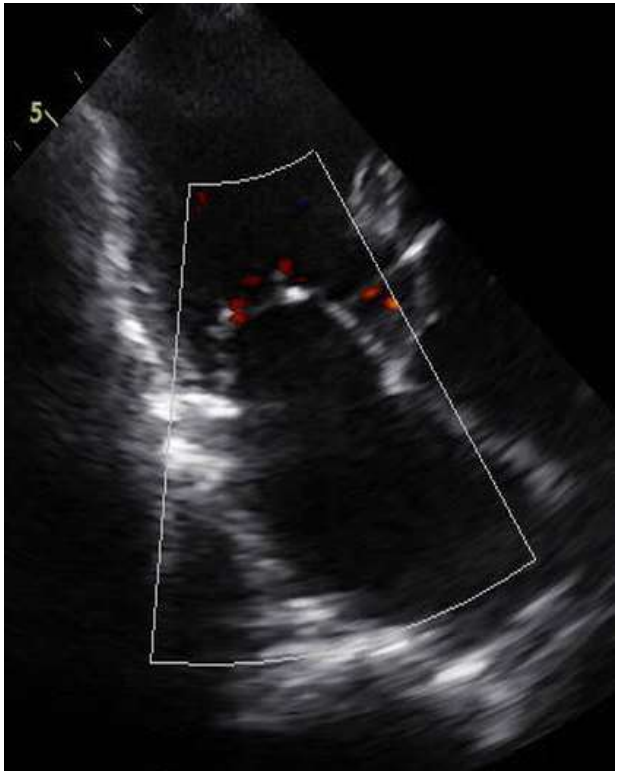


- ERO 0.34 cm^2
- RV 62.6 cc

1 month FU

- ERO 0.12 cm^2
- RV 20.2 cc

3 month FU



- ERO 0.14 cm^2
- RV 24.8 cc

Reverse remodeling & reversion of persistent AF to sinus rhythm

Reversion to sinus rhythm right after procedure and maintained during last FU (3 months FU)

	Baseline	4 weeks
LA volume (ml)	370	285 (23% ↓)
LVED volume (ml)	218	172 (19% ↓)

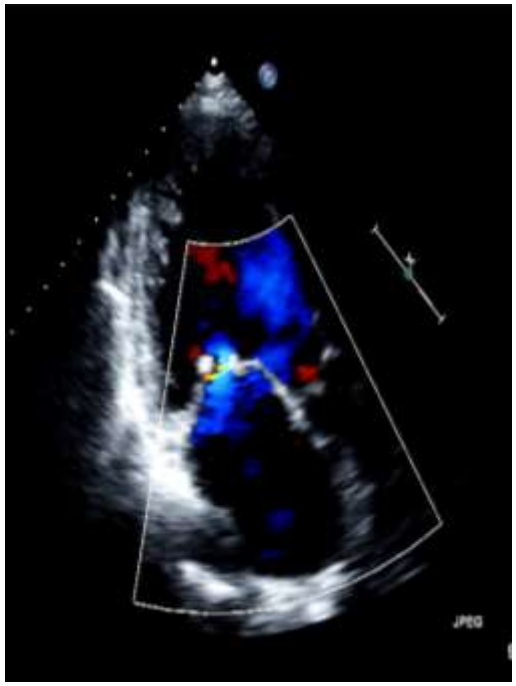
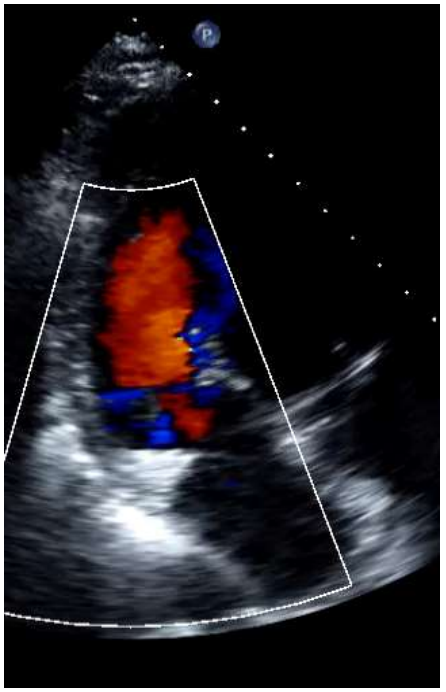
* CT volume data

BNP 3269 pg/mL

BNP 56 pg/mL

Case #4. 62/M, Dyspnea due to nonischemic dilated cardiomyopathy

(LVEDD 74mm, LVEDV 260mL, EF 34% NYHA class III-IV)

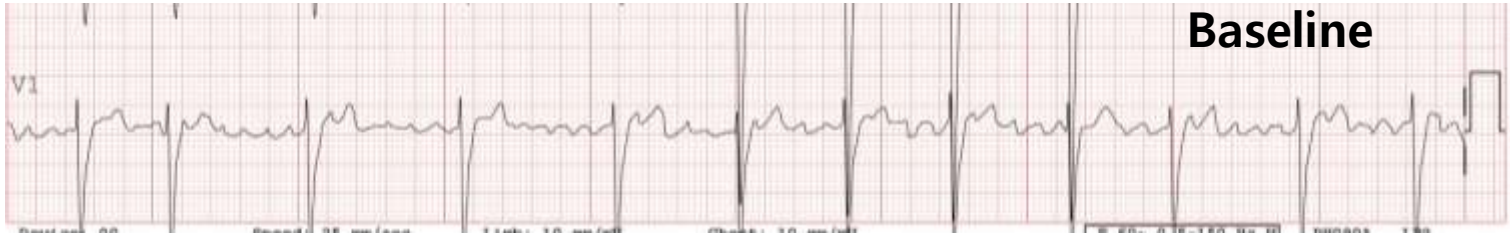
Before	Immediate postprocedure	1 month FU	3 month FU
			
• ERO 0.27 cm2 • RV 38.6 cc	• 18% reduction of SLD • (50.5 →41.3 mm)	• ERO 0.12 cm2 • RV 21.3 cc	• ERO 0.08 cm2 • RV 14.4 cc

Reverse remodeling & reversion of permanent AF to sinus rhythm

Reversion to sinus rhythm was found on last FU (3 month) ECG

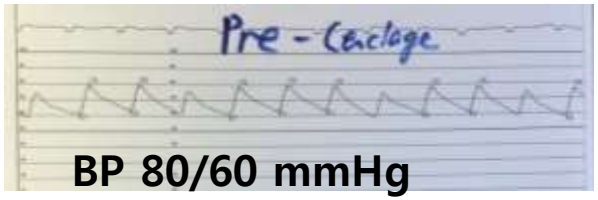
	Baseline	4 weeks
LA volume (ml)	274	209 (24% ↓)
LVED volume (ml)	260	215 (17% ↓)

* CT volume data

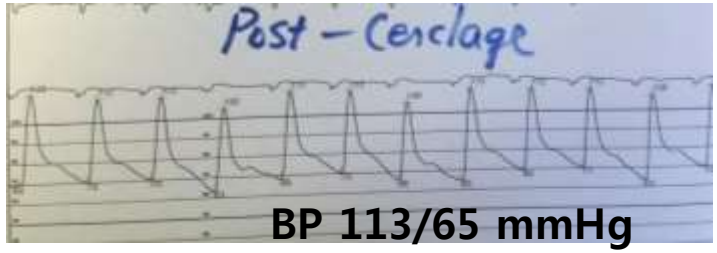


Case #5. 68/M, Cardiogenic shock due to end-stage of dilated CMP despite parenteral inotropic agents
(LVEDD 84mm, LVEDV 350 mL, EF 37%, NYHA class IV)

Urgent cerclage with IABP pump back-up !



BP 80/60 mmHg



BP 113/65 mmHg

baseline

Immediate postprocedure

- ERO 0.78 cm2
- RV 70.3 cc

- 11% reduction of SLD (43.2 → 38.6 mm)

Case #5. 68/M, Cardiogenic shock due to end-stage of dilated CMP despite parenteral inotropic agents
(LVEDD 84mm, LVEDV 350 mL, EF 37%, NYHA class IV)

- Improved Sx with significant reduction of MR but …
- Still severe residual MR without evident reverse remodeling at 1 month CT FU
- Tapering of inotrophic agent was not possible because any attempt led to aggravation of his vital sign

-> expired due to refractory HF at postprocedure 45 days

	Baseline	4 weeks
LA volume (ml)	281	281
LVED vol (ml)	350	340 (3% ↓)

* CT volume data

Baseline

- ERO 0.78 cm2
- RV 70.3 cc

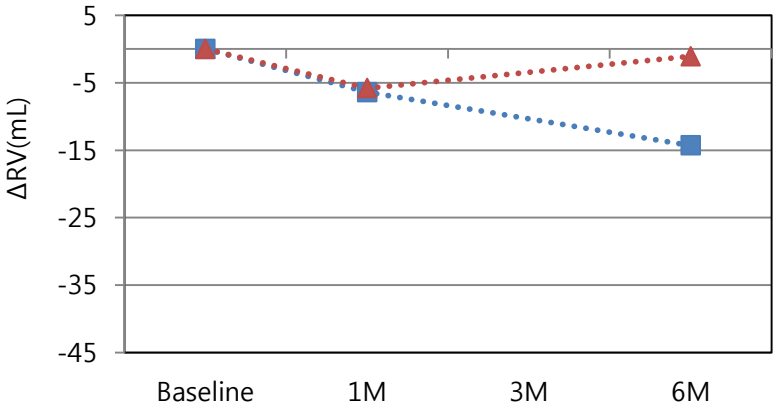
I month FU

- ERO 0.30 m2
- RV 43.1 cc

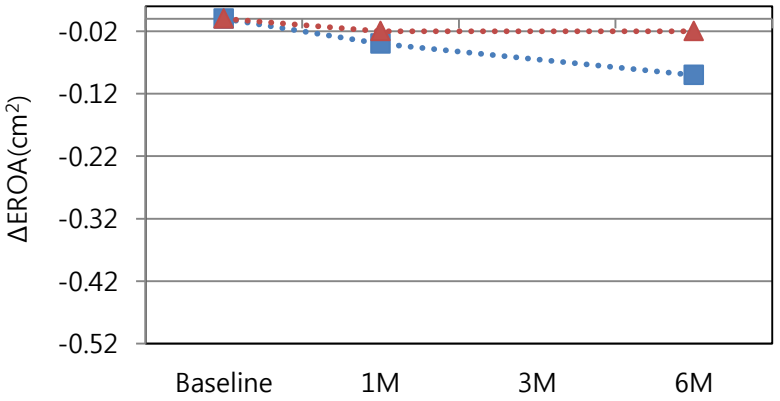
If this cerclage FIM data is put on the table of Carillon data (TITAN study*)…

Hemi-circumferential tension vs circumferential tension ?

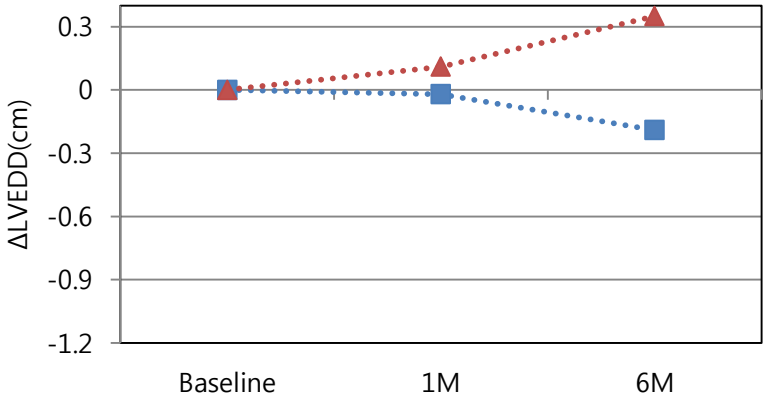
Regurgitant Volume



Effective Regurgitatnt Orifice Area



LV End Diastolic Diameter



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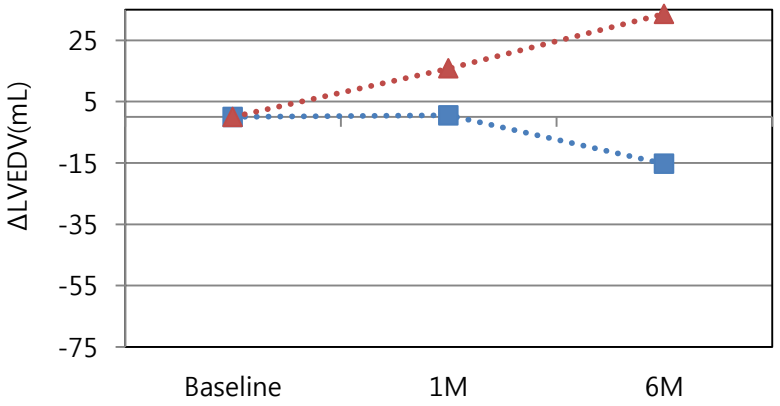

*European Journal of Heart Failure. 2012;**14(8)**:931-8.

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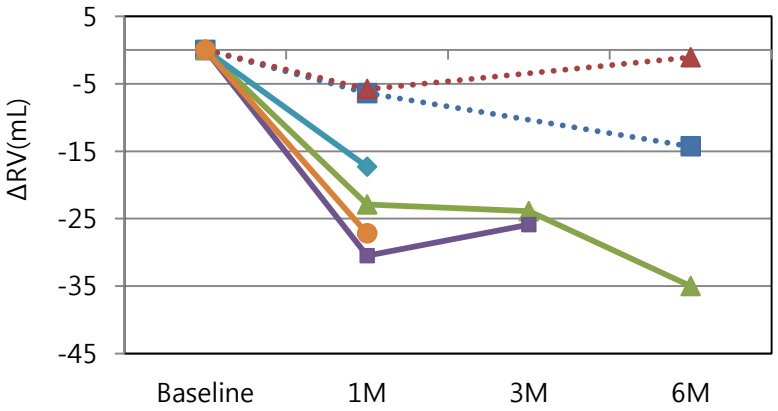
Regurgitant Volume



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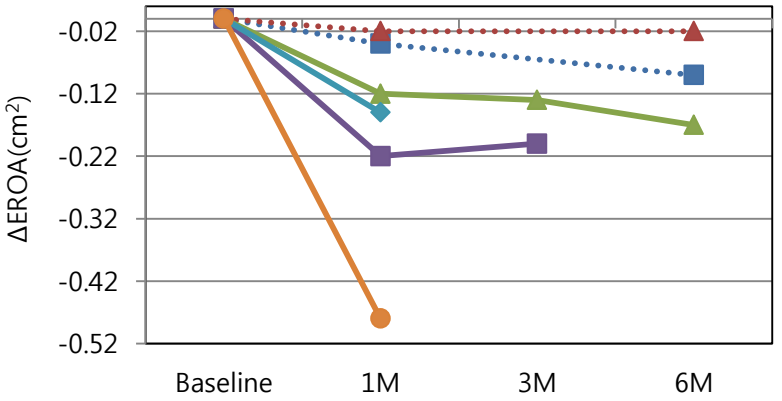
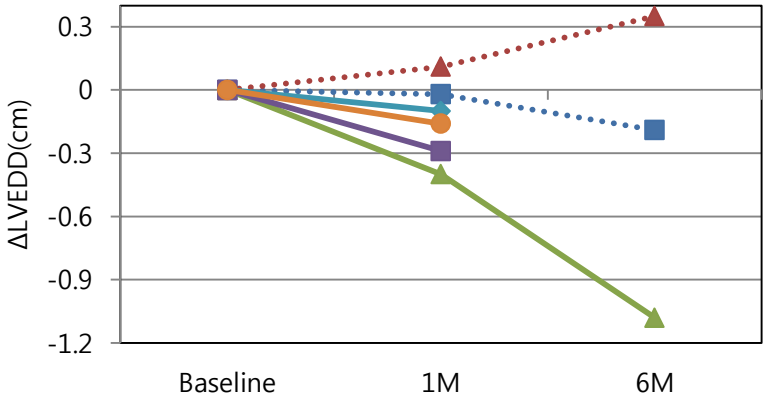
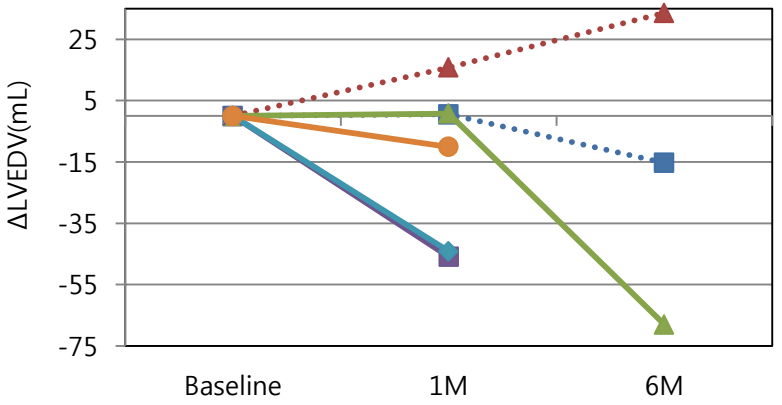


LV End Diastolic Diameter



LV End Diastolic Volume



*European Journal of Heart Failure. 2012;**14(8)**:931-8.

In summary

1. Mitral Loop Cerclage is a novel approach for treating functional MR as a catheter based approach via coronary sinus

2. Mitral Loop Cerclage in now under early phase of exploratory clinical trial in Korea as a 'proof of concept' study

3. Although long term data is not available yet, interim result of FIM showed that cerclage appears to have significant potential of reducing functional MR with remarkable reverse remodeling of dilated heart.

4. Atrial electrical remodeling shown as 'sinus rhythm recovery ' is also very interesting finding in this study

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Thank you for your attention