



Percutaneous Mitral Therapies

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Transcatheter therapy in pts with MR REALLY?



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AHA
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Disclosure

- **Research Support/Grants:**
Edwards Lifesciences
- **Consulting / Employment:**
Medtronic
- **Stock Equity or Options:**
Direct Flow Medical
- **Other Relationships:**
Proctor for Edwards Lifesciences

COI

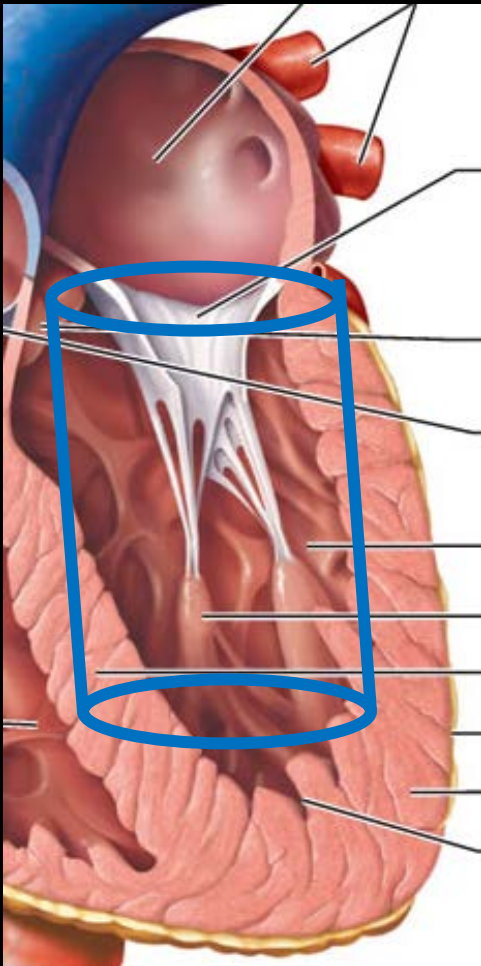
- **Medtronic: consultant**
- **DirectFlow Medical: consultant; equity**
- **QuantumCor; SAB**
- **Edwards Lifesciences; PARTNER site**



A rose is a rose, is a rose

But.....

**MR is not MR is not MR
(structural / ischemic /
cardiomyopathic)**



Structural MR (prolapse)
— a valvar problem



**Ischemic & Cardiomyopathic
MR — a ventricular problem**

Structural MR (Prolapse)



Mortality to 10 yrs



Surgery Sets a High Bar for Structural (prolapse) Disease Outcomes

Survival at 10 yrs --92%
Freedom from reoperation 93%.
Freedom from recurrent moderate or severe MR at 10 yrs 80%

... population.
... mitral reoperation -
... 7% had no or 1+ MR; 11% had 3+ or 4+

**BUT WHAT ABOUT ISCHEMIC
AND FUNCTIONAL MR?**

How Good is Surgery for Ischemic MR?

Operative mortality — ~7-15%

3 yr survival ~ 60-80%

Recurrent MR in at least 1/3 of pts.

**Recurrent MR and poor LVEF
predict poor outcome**

More answers coming soon:

Two current NIH surgical trials: both for ISCHEMIC MR

1. Moderate Ischemic MR Trial

CABG vs MV repair + CABG
end point 1 yr (F/U not done)

Does MVR with CABG make
a difference? (Prob not but pts feel better)

2: Severe Ischemic MR trial

MV repair +/- CABG vs MVR
enrollment complete (?AHA results)

Is MV repair with CABG better than MVR?
(prob no difference)



Micardia

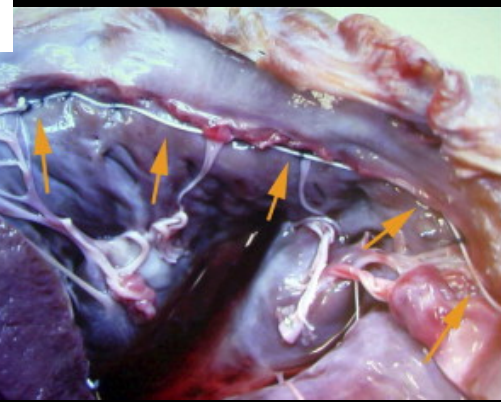
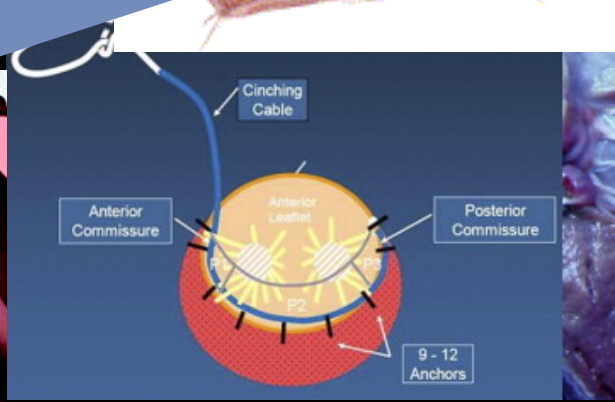


Valtech

Moving on to transcatheter possibilities

BACE

Accucinch



The somewhat mixed EVEREST II message

MitraClip is safer than surgery

MR reduction not as good

Long term outcomes

.....still unknown

So.....

Where does that leave the

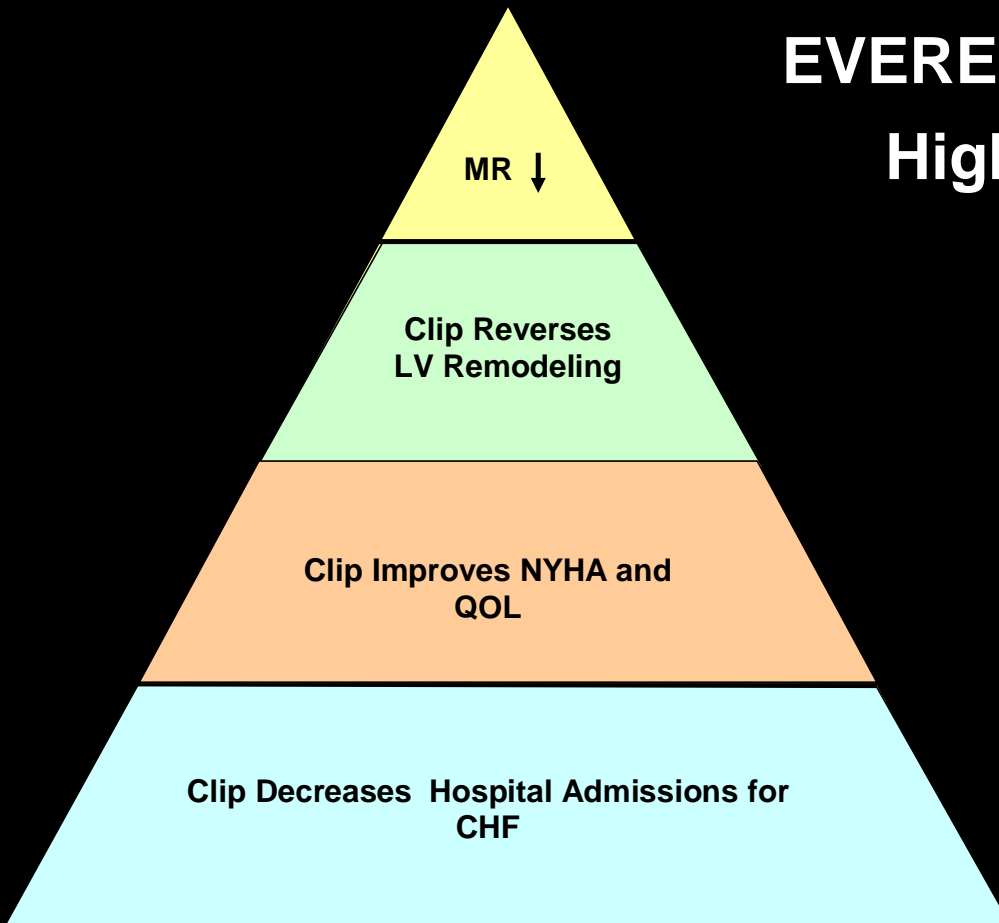
MitraClip?

**EVEREST was designed for
pts with mitral valve prolapse
but also included.....**

**Patients with pre-existing LV Dysfunction
and Functional Mitral Regurgitation (FMR)**

EVEREST Functional MR High Risk Registry

Summary



Maybe reduction of MR to 2+ or less is enough to improve outcomes in selected pts

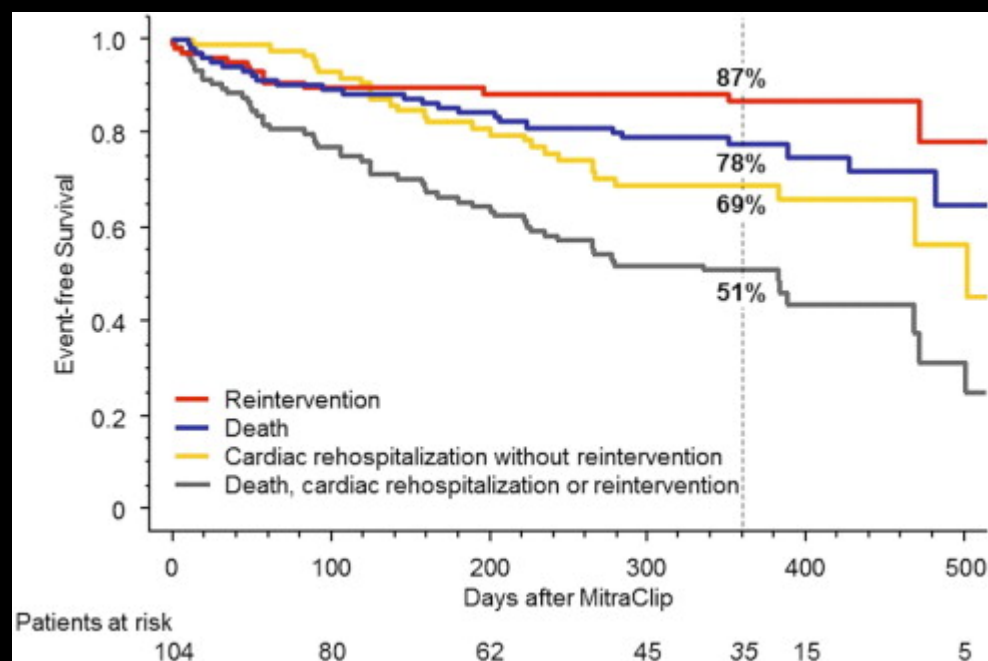
Based on this MitraClip gets FDA approval for high risk pts

Given the data available, & now with FDA approval ----- which patients are best treated with the MitraClip ?

The Real (European) World of Mitral Repair

Clinical outcomes of Mitraclip therapy in pts not amenable to surgery

Rudolph ; JACC 2011(German experience)



Take Home Message

For perc repair MR:

- Mitraclip helps selected pts with structural MR.....and some with functional MR
- LOTS of pts with functional MR might benefit with Clip treatment.....

We need a trial.

COAPT

North American trial

420 high risk CHF pts with FMR

Randomized to medical Rx

Primary endpoint – HF hospitalization rate

Who will be chosen????

Functional MR 3-4+(central A2-P2) in symptomatic pts at surgical risk STS>8, on OMT, EF>20, or high stroke/op risk

RESHAPE-HF European Trial

Commercial post market

80 FMR pts with severe CHF

Randomized to medical Rx

Primary endpoint = HF hospitalization
and death (composite)

Enrollment beginning

But wait.....
There's more!

Forecasting
what is & might
be hot (or cold)



CS approaches going ... going



Monarc: ~~59/69(86%) pts implanted~~

~~60% have reduced MR~~

Viacor: ~~21/26(84%) implanted~~

~~44% able to reduce MR~~

Carillon: 24/29 (83%) pts implanted

63% able to reduce MR

Summary: about 80% of pts chosen can be implanted:
of those about 1/2 get a 1-1.5+ reduction of MR

Innovation is alive and well in 2013



Leaflet Solutions

Evalve

Neochord

Cardiosolutions

Middle Peak

Annular Solutions

Mitralign

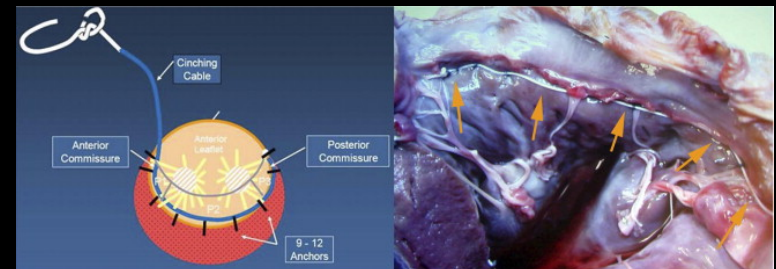
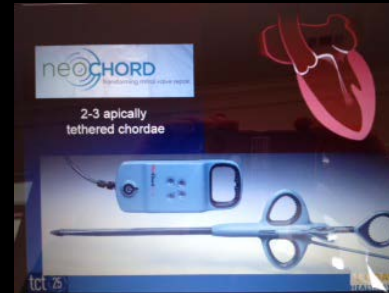
Guided Delivery Systems

QuantumCor

Valtech

Millipede

Accucinch



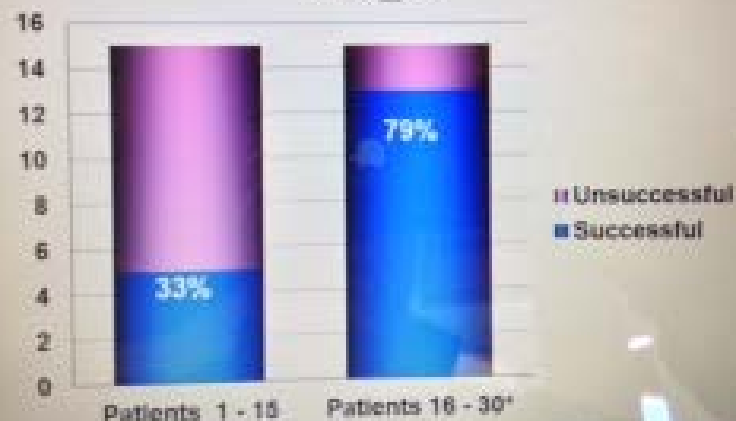
NeoChord successful live case performed at EACTS. Nov. 5, 2013

TACT Trial (Transapical Artificial Chordae Tendinae)

Success Rate by Neochords Deployed



TACT Trial: 12 Mo. Results MR \leq 2+



Summary: TACT Trial

(Transapical, off-pump artificial chordae)

Acute procedural success $47/52 = 90\%$

30 Day MR <2+ 74% of acute successes

MR @ 1 yr similar to 30 day results

Average procedure time ~ 2 hrs

Helping vets save pets

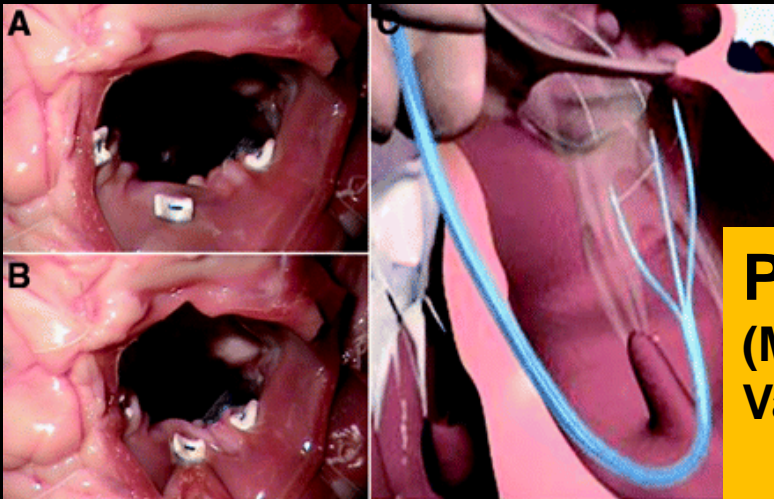
MitraSpacer:
collaborative effort
between Colorado State
Univ. and Avalon
Medical.

“Finishing
research
in experimental
animals...”

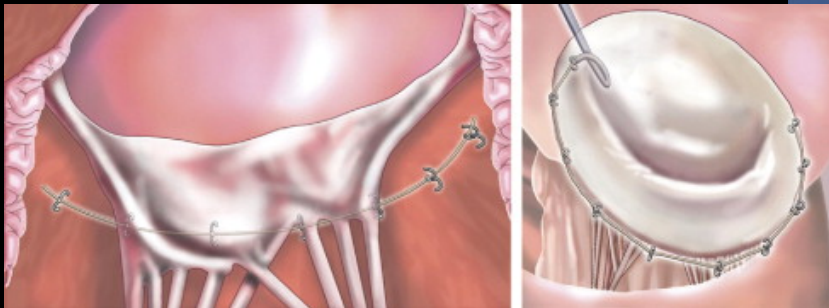
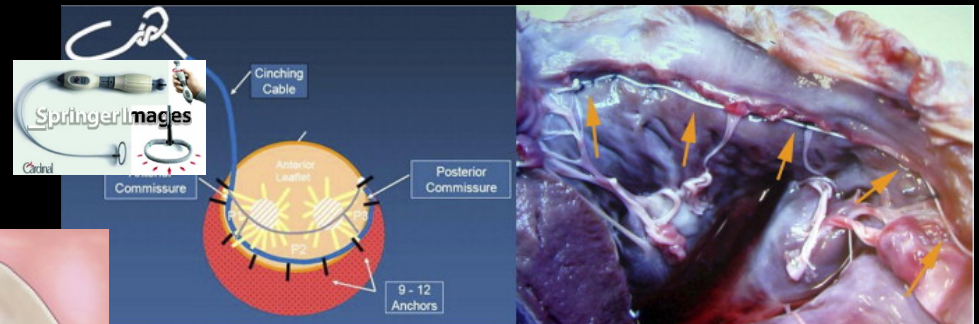


King Charles Spaniel





Posterior annuloplasty devices (Mitralign, Accucinch, Micardia Valtech, et al.)



**Will they succeed ? — surgical experience (-)
“Those who do not read history are bound...”**

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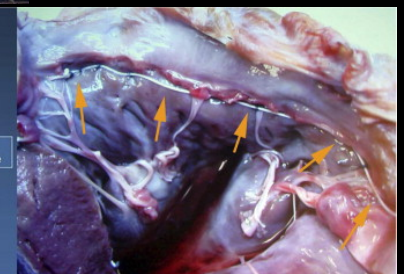
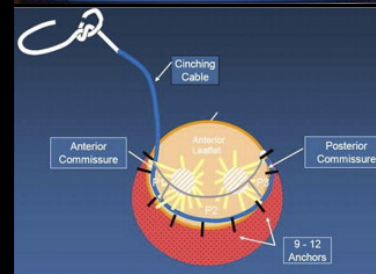
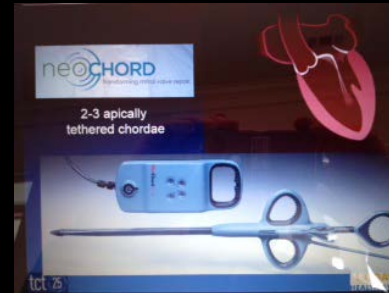
Guided Delivery Systems

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Valtech

Transseptal mitral cinching ring

Cases (~15) already underway in Europe

Promising results short term so far



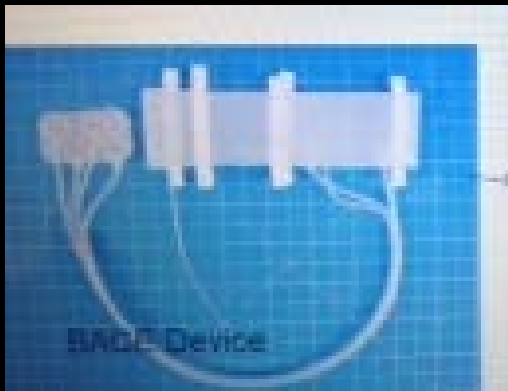
..& if it does not work long
term?

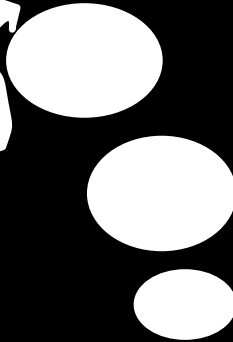
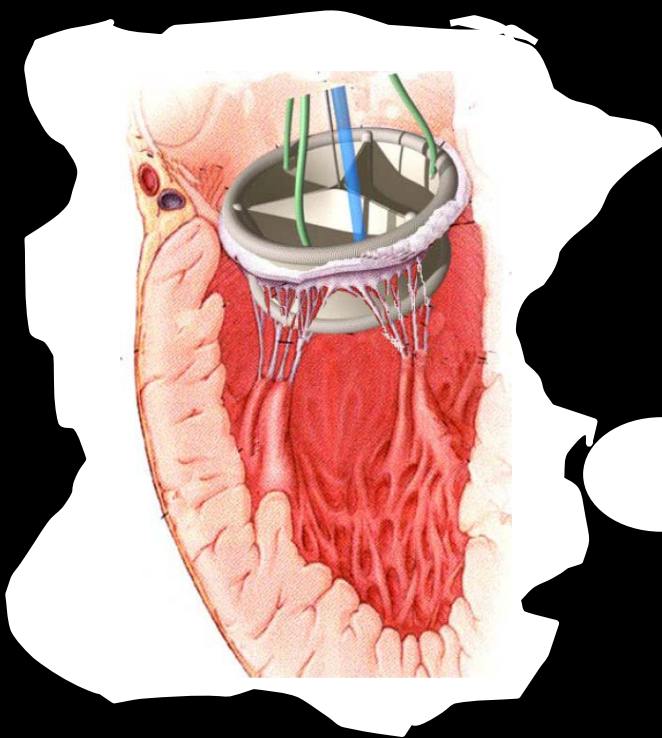
Tissue ingrowth = inflammation
= Ca^{++} =

a great landing zone for
TMVR

Adjustable Posterior ventricular support device (At CABG)

The “BACE” Concept





Promises....promises...

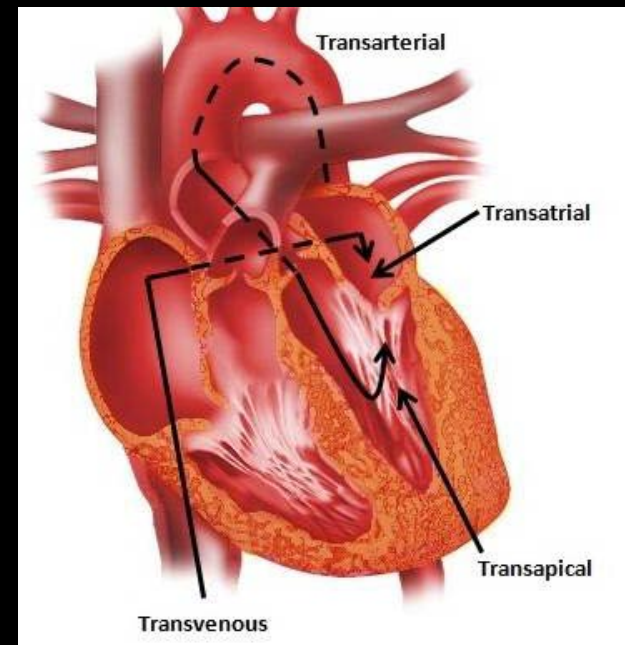
Why is TMVR so hard?

Mitral valve is larger .

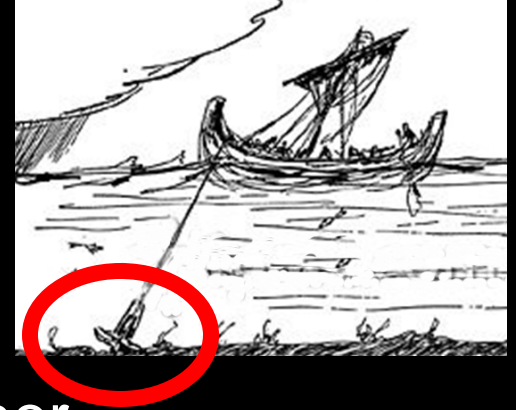
Ao diameter ~ 23-29mm: mitral ~ 40mm.

Implications for delivery (more material to compress, larger catheter sizes) and durability (larger valve means greater sheer stresses and higher pressure differentials).

Access more complicated (requiring either a venous/transseptal approach or a TA or transatrial approach)



But it boils down to anchoring



No Ca^{++} to secure the valve : need anchor

ALSO:

Aortic valve tends to be circular with an annular plane
mitral valve saddle-shaped annulus with an irregular,
D-shaped orifice.

PVL is not tolerated on the mitral side.

Must be low profile to prevent

- a) interaction with the aortic valve (AS or AR)
- b) damaging the subvalvar apparatus.

CardiAQ prosthesis (CardiAQ Valve Technologies, Winchester, MA). 1st in man June 2012

Device implanted “on pump”

Pt death: day 3 (?cirrhosis /multi-organ failure/ bowel infarct?)

No further implant to date: Gen 2 in place

Tendyne Valve



- Nitinol Stent Frame with porcine pericardium
- Left ventricular apical tether
- controlled deployment
- Requires no rapid pacing or CPB support

- Fully Retrievable and repositionable

Human Implant



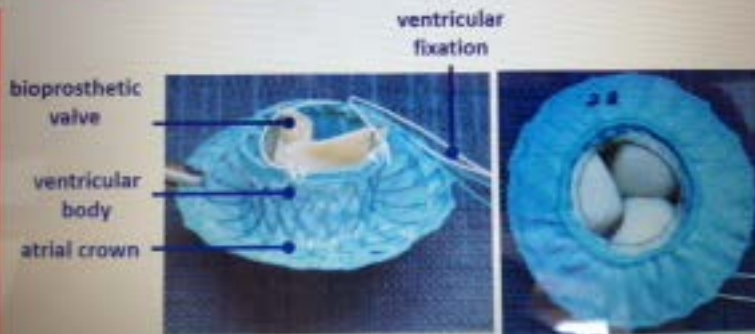
Ventriculogram Post Procedure



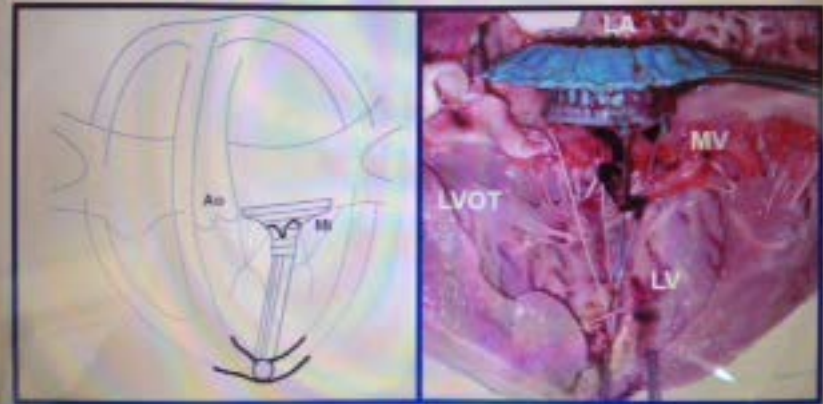
Baseline

Post Tendyne

→ Mitral Valved Stent

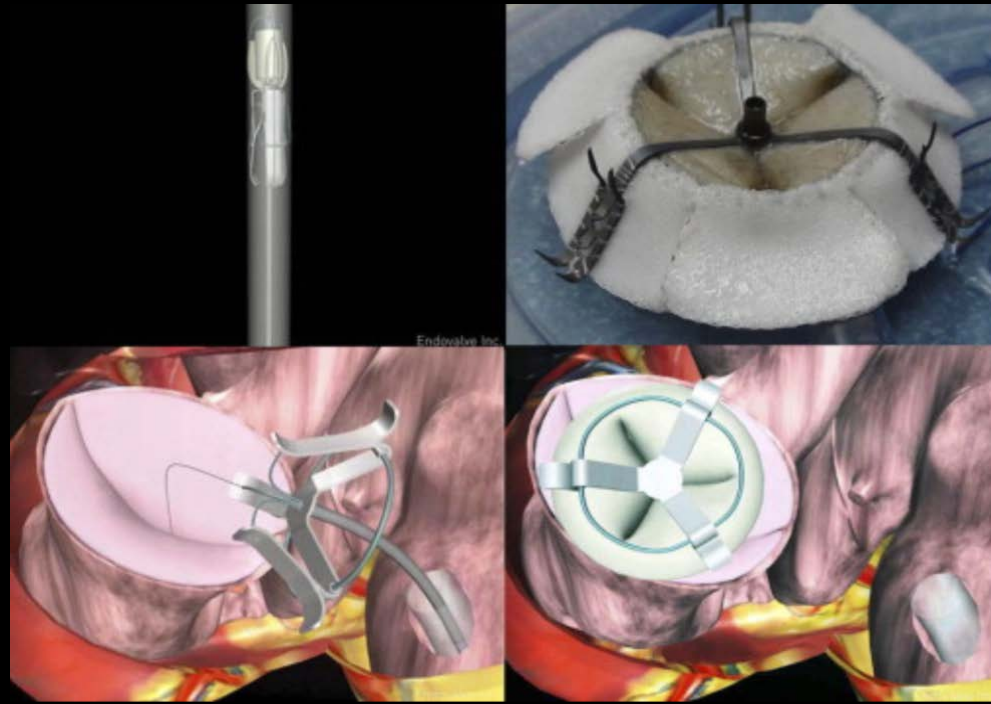


→ Transapical implantation: off-pump



Transseptal Endovalve

Currently “on hold”: animal studies to be cont’d as company prioritizes





Tiara Valve (TCT 2012)

British Columbia-based
Neovasc

81% of test animals successfully implanted.

Procedure times ranging from 17 to 26 min.

No obstruction of LV outflow tract,

No transvalvular gradients.

No significant paravalvular leak.

Echo at 3 mos after implant demonstrated continuing good function and integrity of the valve.

Chronic animal studies are ongoing.

Lutter valve

nitinol self-expandable valved stent

Lutter valve in swine : JTCVS2010



Trileaflet bioprosthesis contains atrial and ventricular fixation systems.

Eight pigs underwent TEE-guided transapical implantation through a mini-sternotomy.

Gradient across LVOT was not affected.

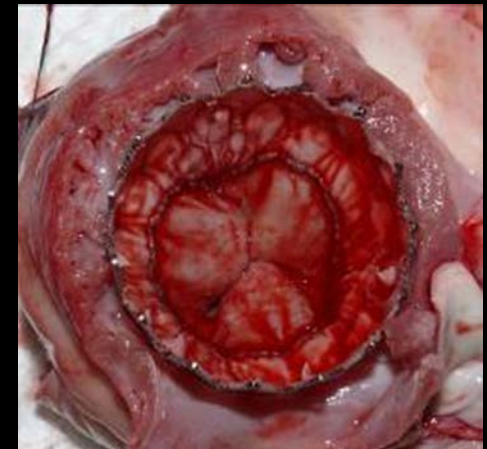
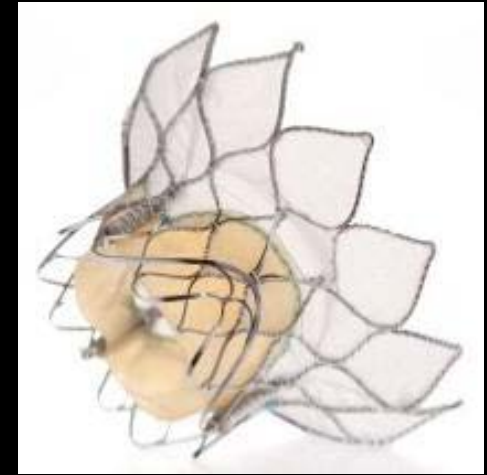
Average animal survival was 7.3 days (8 hours to 29 days).

Animals that died before 1 week ($n = 4$) had valved stent malpositioning. Animals that survived 1 week or more had accurate deployment and only trace post-deployment paravalvular leak. The causes of death in this latter group were endocarditis ($n = 1$), failure of atrial fixation ($n = 2$), and failure of ventricular fixation ($n = 1$). There was no valve embolization in any of the animals.

Medtronic Transcatheter Mitral Valve

• Design Priorities & Status: **Replacement**

- Preserve native mitral apparatus
- Self expanding Nitinol scaffold
- Bovine pericardium
- Valve with 3 cusps
- Large, flexible inlet conforms to anatomy
- Support arms capture and cover native leaflets, preventing LVOT obstruction
- Minimal extension into LV
- Acute animals complete. Chronic animals ongoing.



What TMVR must do:

- Deliver implant transseptally or transapically
- Deploy implant in proper position
- Securely anchor implant
- Ensure proper hemodynamics
- Avoid LVOT obstruction
- Avoid conduction system issues
- Preserve subvalvar apparatus
- Have no PVL/residual MR

4 keys: delivery, fixation, residual MR, SAM

The step by step path to Transcatheter Mitral Valve Replacement Here & Now..... or Here and Not Now?



1931 → 1937



TMVR

Not quite here.....

But stay tuned