Percutaneous Mitral Valve Intervention: QuantumCor Device

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## Presenter Disclosure Information

Name: Richard R. Heuser  M.D.

Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization listed below.

<table>
<thead>
<tr>
<th>Company Name</th>
<th>Relationship</th>
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<tr>
<td>CSI</td>
<td>Minor Stock Holder</td>
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<tr>
<td>QuantumCor</td>
<td>Major Stock Holder/Medical Director</td>
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Ischemic Mitral Regurgitation

- Ischemic mitral regurgitation occurs in ~ 45% of patients after MI (7,800,000 MI’s annually)
- Chronic IMR is an independent predictor of mortality
- Reducing the distance between the anterior and posterior annulus (A – P diameter) reduces or eliminates IMR

Arch Intern Med. 2006;166:2362-2368
Background

Mitral regurgitation after a first non-ST-segment elevation acute coronary syndrome

- Mitral regurgitation occurs in 42%
- Age and EF were independent markers of development of MR
- Only MR has been found to be an independent predictor of long term outcome

European Heart Journal (2006) 27, 2655-2660
Background

Percutaneous Treatments for Mitral Regurgitation

Percutaneous Treatment for Ischemic Mitral Regurgitation is not new…

European Heart Journal (2006) 27, 2655-2660
Coronary Angioplasty for Acute Mitral Regurgitation Due to Myocardial Infarction

A Nonsurgical Treatment Preserving Mitral Valve Integrity

RICHARD R. HEUSER, M.D.; GERRY L. MADDUX, M.D.; JEROME E. GOSS, M.D.; BARRY W. RAMO, M.D.; GILBERT L. RAFF, M.D.; and NEAL SHAHOFF, M.D.; Albuquerque, New Mexico

Why Pursue Percutaneous Devices in FMR?

- Devices do work to some degree in some patients.
- Only a miniscule percentage of the 400,000 patients with HF and FMR are currently referred for surgery.
- These are still first generation devices.
- There is a whole lot of money and a lot of smart people working on this.
Background
Percutaneous Treatments for Mitral Regurgitation

- Leaflet Approaches
- Annular approaches
Percutaneous Mitral Valve Repair

- Obvious Strategy for PMVR is to combine direct valvular procedure with a percutaneous annuloplasty technique
- Mimics what is done surgically
Background
Background


A relatively small (1 cm, 20%) plication of the posterior annulus can normalize the S-L dimension and eliminate ischemic MR! Tibayan et al. *Circulation.* 2003;108:II-128-133
Background

• Ischemic mitral regurgitation (MR) is a common problem occurring in nearly 45% of all myocardial infarctions and results in harmful ventricular remodeling and increased morbidity and mortality.

• The QuantumCor™ device uses radiofrequency (RF) energy at sub-ablative temperatures to produce contraction of the mitral valve annulus and theoretically reduces mitral regurgitation.
Background

Mitral Annulus Slices

(Trichrome Stain)

Left, Posterior Leaflet Segment  Middle, Posterior Leaflet Segment  Right, Posterior Leaflet Segment
Safe Window of Collagen Heating is Possible

Shrinkage rate is dependent on temperature level

- Wide spectrum of temperatures feasible with RF
- Important to treat annulus within brief interval
- Tendon data show 20% shrinkage to be maximal, without loss of tensile strength*
- QuantumCor studies show >20% annular shrinkage is feasible
Method
Annulus Contraction in Sheep and Pig Hearts

- Annuluses treated circumferentially
- Temperatures set at 65°C
- Image analysis used to compute changes in dimensions

Area 11%
Perimeter 6%

Area 17%
Perimeter 10%

Area 21%
Perimeter 12%
**Results-Collagen Orthopedic Research**

**Issue:** Overdose of RF heat weakens collagen, leads to dilatation of annulus.

Method
Method

Boa-Surg

- 7 Electrodes/14 Thermocouples
- 3mm Length
- 2mm Spacing
- 40mm Loop Diameter
Acute Animal Procedure

- Intra-cardiac ultrasound (ICE) pre-procedure.
- Left thoracotomy-on pump.
- Access through the atrial appendage.
- Sutures in 4 regions of the annulus as markers (1-2cm).
Mitral Annulus Treatment Sites

Method

Anterior Leaflet

Posterior Leaflet

Site 1

Site 2

Site 3

Site 4
Method

Mitral Annulus Treatment Sites

- Anterior Leaflet
- Posterior Leaflet
- Site 1
- Site 2
- Site 3
- Site 4
- PA or Septal Lateral
Sixteen healthy sheep (six with naturally-occurring MR) had RF energy applied for a mean of 60 seconds at sub-ablative temperatures to replicate a surgical mitral annular ring. Four segments of the posterior mitral valve annulus were heated while on cardiopulmonary support via a left thoracotomy with access via the atrial appendage. Seven sheep were followed chronically. Two developed systemic infection after 30 day follow-up.
Method

Acute Animal Study

• Nine sheep received mitral annulus treatments with RF generated heat.
• All animals maintained on normothermic cardiopulmonary bypass and blood cardioplegic arrest.
• Heat treated annulus was from trigone to trigone. This included all of the posterior portion of the annulus.
• Intra-cardiac echo (ICE) measurements were performed pre- and post-treatment.
RESULTS

Mitral Annulus Treatment Sites

Site 1
2.6 ± 1.4 mm
P=.0016

Site 2
2.9 ± 1.3 mm
P=.0007

Site 3
3.1 ± 1.9 mm
P=.0024

Site 4
3.2 ± 1.5 mm
P=.0009

Anterior Leaflet

Posterior Leaflet
Mitral Annulus Treatment Sites

RESULTS

Anterior Leaflet

Posterior Leaflet

Site 4

PA or Septal Lateral

Reduced by 5.0 ± 2.1 mm (p < .001)
RESULTS

Acute Animal Study

A-P Dimension Pre and Post OP

Mean Reduction=21.0%       A-P Mean Reduction=5.7=+/−1.0 mm
RESULTS

June 27, 2006        Sheep # 10

Mitral Valve Pre-treatment
S-L Diameter 28.7 mm

Mitral Valve Post-treatment
S-L Diameter 20.3 mm
RESULTS

June 26, 2006        Sheep # 36 (acute 5)

Mitral Valve Pre-treatment

Mitral Valve Post-treatment

Color Flow - Trace to 1+ MR

Color Flow - No MR
BOA-SURG Probe
RESULTS

Animal Study Summary

16 Total Sheep Treated

- 7 Chronic
  - 2 Developed (4,6) Systemic Infection
    - 5 Currently Survived
- 9 Acute
RESULTS

Acute Success in All Animals

Acute and Chronic Pre-Post OP
N=16
Mean Reduction=23.82%    A-P Reduction=5.75+/-.86 mm
RESULTS
RESULTS

Chronic Animal Study

- Seven sheep in the treatment arm of the chronic study. Two dropped due to non-study related infection.
- Treatment protocol is the same as the acute study.
- Intra-cardiac echo performed @ pre- & post-treatment & 30, 60 & 90, 120 & 180 days.
- Seven data pts. @ 30 days; seven @ 60 days; four @ 90 days & one @ 120 days.
- Future plans-implement dosing & GLP Study.
- Increase follow-up durations to 180 days.
RESULTS

Mitral Annulus Treatment Sites
30 Day Data (N=7)

Percentage reduction at 30 days is 21.4%
Mean = 5.0 ± 0.6 mm
RESULTS

A-P Dimension Baseline VS 30 Days

Chronic Series

A-P Dimension (mm)

1 2 3 4 5 6 7

Baseline: 29.0, 26.0, 24.0, 24.0, 27.0, 26.0, 25.0
30 Days: 21.0, 22.0, 19.0, 19.0, 20.0, 21.0, 21.0
Mitral Annulus Treatment Sites

60 Day Data (N=7)

RESULTS

Anterior Leaflet

Posterior Leaflet

Site 1

Site 2

Site 3

Site 4

PA or Septal Lateral

Mean = 4.2 ± 0.7mm
RESULTS

A-P Dimension Baseline VS 60 Days

Chronic Series

A-P Dimension (mm)
Mitral Annulus Treatment Sites

90 Day Data (N=6)

Mean = 6.0 ± 2.5mm
RESULTS

A-P Dimension Baseline VS 90 Days

Chronic Series

<table>
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<tr>
<th>Chronic Series</th>
<th>Baseline</th>
<th>90 Days</th>
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<tbody>
<tr>
<td>1</td>
<td>28.0</td>
<td>24.0</td>
</tr>
<tr>
<td>2</td>
<td>26.0</td>
<td>24.5</td>
</tr>
<tr>
<td>3</td>
<td>24.0</td>
<td>21.0</td>
</tr>
<tr>
<td>4</td>
<td>24.0</td>
<td>21.4</td>
</tr>
<tr>
<td>5</td>
<td>27.0</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>26.0</td>
<td></td>
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Long Term Results

A-P Dimensional Stability in Long Term Ovine Study

Time Intervals

Pre | Post | 30D | 60D | 90D | 120D | 180D

A-P Dimension (mm)

29 | 23 | 24 | 24 | 19 | 20.4 | 19.4
RESULTS

Sham Results

A-P Dimensional Stability in Sham Ovine Study

<table>
<thead>
<tr>
<th>Time Intervals</th>
<th>Pre</th>
<th>Post</th>
<th>30D</th>
<th>60D</th>
<th>90D</th>
<th>120D</th>
<th>180D</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-P Dimension (mm)</td>
<td>27</td>
<td>28</td>
<td>27</td>
<td>26.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
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Pre: Pre-treatment
Post: Post-treatment
30D, 60D, 90D, 120D, 180D: Time Intervals (days)
Chronic Animal Series S-L Shrinkage Durability

S-L Dimension (mm)

Time

Pre Post 30D 60D 90D 120D 180D
Animal Study Summary

- Utilized the same power, temperature and time of application settings for both acute and chronic animals
- Acute Study-Reduced A/P diameter by average of 5.6 mm or 20.6 %.
- Chronic Study-Reduced A/P diameter by average of 5.9 mm or 22.7 %.
- 18 of 20 long term data pts. (90.0%) maintained A/P shrinkage over time, 30-120 days.
  - 2 animals re-dilated due to infections believed to be introduced during 30 day measurement procedure
- The procedure has not caused any MR
CONCLUSIONS

Surgical Ring Annuloplasty

106 Patients

- 33% has $\geq 2+$ MR at $\geq 6$ months
- Those with $< 2+$ MR has stable or increased EF
  67% vs. 40% of patients with $\geq 2+$ MR $P<.01$

Perhaps if the MR treatment could be repeated…this could be obviated

Recurrent Mitral Regurgitation Late After Annuloplasty
For Ischemic Mitral Regurgitation: An Echocardiographic Study
Shiota M, Gillinov M et al. JACC 2007
The Best Possible Application to the Less Invasive Approach for Mitral Regurgitation

- Functional MR
- Ischemic MR
- Extremely Reduced LV function
- Moderate MR
Percutaneous Treatments for Mitral Regurgitation

• Leaflet Approaches….limited with application.

• Annular Approaches….limited with possible obstruction of the circumflex coronary artery when approaching coronary sinus.
Percutaneous Treatments for Mitral Regurgitation

- Leaflet Approaches
- Annular Approaches

In all cases a foreign body is left in place and it can’t be repeated.
Percutaneous Treatment for Mitral Regurgitation

- With RF energy applied to the mitral annulus it may be possible to treat a larger population of patients with mitral regurgitation.
- If you don’t succeed you can repeat the procedure.
- Treat without affecting the coronary sinus.
- Use in conjunction with leaflet procedures.
Regulatory Pathway

**Too Early to Tell**

- Will it be easier because of no foreign body?
- Will it be easier because of the repeatable nature of the technique?
- Will it be easier because the power source has been in use for decades?
Percutaneous Mitral Valve Intervention: QuantumCor Device

The QuantumCor device may offer an option for some patients with mitral regurgitation.

- 1\textsuperscript{st} in the operating room.

- Eventually as a percutaneous treatment for mitral regurgitation that could be performed with standard EP RF consol in the catheterization laboratory.

Conclusion