HISTOTRIPSY CARDIAC THERAPY

Speaker: Olivier Villemain, MD
Institut Langevin – Wave Physics for Medicine and Biology, Paris
What is Histotripsy?

• « Grind tissue »
• John Rayleigh [1842-1919, Nobel Prize in Physics 1904]
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1916

CAVITATION

- Focused ultrasound
- Thermic Dissipation
- Cavitation
Ultrasound & Medecine

Focused ultrasound — Thermic Dissipation → « ISPTA »

Cavitation → « MI »
Ultrasound & Medecine

Focused ultrasound ↔ Thermic Dissipation ➞ « ISPTA »
Cavitation ➞ « MI »
Ultrasound & Therapy in Medicine

- "Interventional" ultrasound
- 4 main categories in clinical practice
- First application in cardiology concerning histotripsy: congenital heart disease
For 2010…?

- Publications in technical journals.

- Limits
  - Cardiac movement
  - Risk of embol
  - Size of focal spot

- No real progress concerning clinical applications
HISTOTRIPSY CARDIAC THERAPY FOR NON INVASIVE CHORDAL CUTTING

Institut Langevin – Wave Physics for Medicine and Biology, Paris

Olivier Villemain; Wojciech Kwiecinski; Alain Bel; Justine Robin; Patrick Bruneval; Bastien Arnal; Mickael Tanter; E. Messas/M. Pernot. Non-invasive ultrasonic chordal cutting. JTCVS. In Review
Mitral Basal Chordae

- Attaching Mitral valva (MV) to cardiac wall
  - Allow proper closing
  - Prevent prolapsus

- 1 mm thick, 1.7 cm long

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**Average Length and Thickness of Chordae Tendineae of the Mitral Valve**

<table>
<thead>
<tr>
<th>Site of insertion</th>
<th>Types of chordae</th>
<th>Length (cm)</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior leaflet</td>
<td>Rough zone chordae</td>
<td>1.75 ± 0.25</td>
<td>0.84 ± 0.28</td>
</tr>
<tr>
<td></td>
<td>Strut chordae</td>
<td>1.86 ± 0.43</td>
<td>1.24 ± 0.51</td>
</tr>
<tr>
<td>Posterior leaflet</td>
<td>Rough zone chordae</td>
<td>1.40 ± 0.08</td>
<td>0.65 ± 0.24</td>
</tr>
<tr>
<td></td>
<td>Basal chordae</td>
<td>0.84 ± 0.21</td>
<td>0.40 ± 0.29</td>
</tr>
<tr>
<td></td>
<td>Cleft chordae</td>
<td>1.30 ± 0.18</td>
<td>0.78 ± 0.15</td>
</tr>
<tr>
<td>Commissural areas</td>
<td>Anterolateral commissural chordae</td>
<td>1.2 ± 0.31</td>
<td>0.70 ± 0.20</td>
</tr>
<tr>
<td></td>
<td>Posteromedial commissural chordae</td>
<td>1.4 ± 0.40</td>
<td>1.0 ± 0.30</td>
</tr>
</tbody>
</table>

• After a myocardial infarction:

Myocardial Infarction:
2M/year in Europe
700,000/year in USA
10% pathological mitral chordae

Objective of the study

**Proof of concept:** Histotripsy for Non-Invasive Chordal cutting

- In vitro on explanted sheep heart (n=10)
- In vivo, in sheep at beating heart (n=7)
Histotripsy material:

- 916 kHz therapeutic transducer
- Focal spot at 64 mm
- Monitoring with 3D echocardiography: coupled transducers
In vitro procedure

• In vitro Model:
  • 10 explanted sheep hearts in degassed waterbath
In vitro procedure

- **In vitro Results:**
  - 10 explanted sheep hearts
  - All chordae were cut
  - Average time to complete section: 5.5 min [3 – 9 min]
In vivo procedure

Model:

• 7 sheep, beating heart
• Anesthetized, sternotomy
• Thorax filled with degassed water
In vivo procedure

- In all 7 animals, basal chordae were cut

- Average procedure time: 21 min
## Detailed Results

<table>
<thead>
<tr>
<th></th>
<th>Sheep 1</th>
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<tr>
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<td>45</td>
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<td>36</td>
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<tr>
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<td>Normal</td>
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<td>Yes</td>
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- The table shows the results for seven sheep, comparing various physiological and procedural metrics.
- Sheep 1 and Sheep 2 had similar weights, both at 45 kg and 48 kg, respectively.
- Sheep 3 and Sheep 4 had weights of 36 kg and 40 kg, respectively.
- Sheep 5 and Sheep 6 had weights of 36 kg and 32 kg, respectively.
- Sheep 7 had the lowest weight at 35 kg.
- All sheep were stable during the procedure, as indicated by "Stable" for "Hemodynamic Per procedure".
- ECG results were normal for all sheep.
- The time of procedure varied from 14 minutes to 26 minutes.
- Sheep 1 and Sheep 2 had Yes for "Section of basal chordae".
- Sheep 3, Sheep 4, Sheep 5, Sheep 6, and Sheep 7 also had Yes for "Section of basal chordae".
- Sheep 3 and Sheep 4 had No for "Section of marginal chordae".
- Sheep 5, Sheep 6, and Sheep 7 also had No for "Section of marginal chordae".
- Sheep 1 and Sheep 2 had Yes (mild) for "MR / Prolapsus".
- Sheep 3, Sheep 4, Sheep 5, and Sheep 6 had No for "MR / Prolapsus".
- Sheep 7 had Micro MR for "MR / Prolapsus".
- Sheep 1 and Sheep 2 had Yes for "Anatomic confirmation of chordal cutting".
- Sheep 3, Sheep 4, Sheep 5, Sheep 6, and Sheep 7 also had Yes for "Anatomic confirmation of chordal cutting".
- Sheep 1 and Sheep 2 had No for "Additionnal anatomic lesion".
- Sheep 3, Sheep 4, Sheep 5, Sheep 6, and Sheep 7 also had No for "Additionnal anatomic lesion".
- Sheep 7 had No for "Additionnal anatomic lesion".

- The table highlights the consistency in the procedural outcomes across the sheep, with the majority showing stable hemodynamic conditions and normal ECG results.
Risk assessment

Heart lesions along the US beam

Emboli

Cardiac rythm

A few non persisting Ventricular Extrasystoles
Conclusion - Perspectives

Proof of concept: Histotripsy for non invasive chordal cutting

Perspectives:

Improve precision

- 3D imaging of subvalvular apparatus
- Triggering on ECG
- Tracking target (Institut Langevin)

Reduce invasiveness

- Trans thoracic approach

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Next clinical applications in Cardiology

**Acute Myocardial Infarction**
- **Therapeutic Use of Ultrasound in Acute Coronary Artery Disease**
  - ClinicalTrials.gov Identifier: NCT02410330
    - (Sao Paulo)

**Rhythm**
- **VytronUS® [USA]**
  - FA ablation
  - ClinicalTrials.gov Identifier: NCT01900678
    - (Czech Republic)

**CHD**
- Atrioseptostomy
- Valvular perforation
- Fœtal intervention
- Myocardium resection
Thanks to

Institut Langevin
Paris

Mickael Tanter
Mathieu Pernot
Wojciech Kwiecinski
Justine Robin
Bastien Arnal
Hicham Serroune

Hôpital Européen Georges Pompidou
Paris

Emmanuel Messas
Alain Bel
Patrick Bruneval
Julie Piquet
Adrien Lalot

Thank you for your attention