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# Non-Invasive Ultrasound Treatment of Calcific Aortic Stenosis First-in-Man

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I DO NOT have a financial interest/arrangement
or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.

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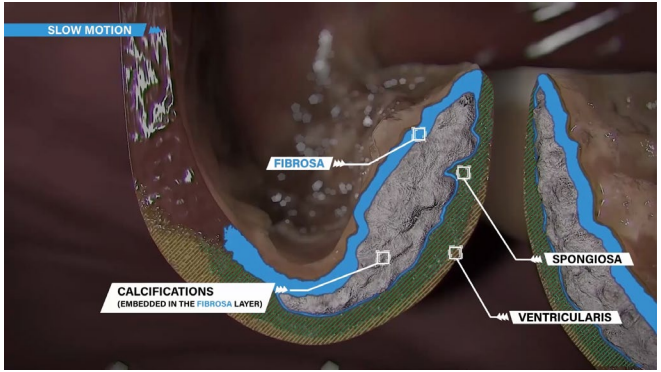
# Non-Invasive Ultrasound Therapy (NIUT)




**Focused, very high frequency and short ultrasound pulses create microscopic cavitation bubbles**

**When cavitation bubbles burst, they produce shockwaves**

**Shockwaves cause microfragmentation in valve calcium without tissue damage**

| Therapeutic ultrasounds | NIUT | Lithotripsy | HIFU* |
|---|---|---|---|
| Ability to penetrate deep in tissue | + | - | - |
| Preservation of tissue through which ultrasounds pass | + | + | - |
| Energy | Mechanical | Mechanical | Heat |
| Therapeutic effect | Hard tissue softening | Break-up of stone | Tissue ablation by coagulation necrosis |

** HIFU: High Intensity Focused Ultrasound*

# Bubble cavitation detection with Echo Imaging

# Study design

- **Design**: Prospective, multi-center clinical evaluation of the Valvosoft® NIUT (N=10) in severe symptomatic CAS patients not eligible for SAVR/TAVR (First-in-Man)
- **Objectives**: To evaluate the safety and feasibility of the Valvosoft® system in severe calcific aortic stenosis patients not eligible for valve replacement
  - Primary safety endpoint: procedure related mortality @ 30 days
  - Primary Performance endpoint: improvement in pressure gradients and aortic valve area post-procedure at one month measured by independent core lab
  - Secondary endpoints: safety and performance beyond one months
- **Centers**: Hospital Européen Georges-Pompidou, Paris, France and Amphia Hospital, Breda, The Netherlands

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**Prof. G. Laarman, NL & Prof. Tijssen, NL**

***Monitoring:*** **MD-Clinicals, Lonay, Switzerland**

***Core Lab:*** **Cardialysis, Rotterdam, The Netherlands**

# CARDIAWAVE

Non-invasive therapy to treat aortic stenosis

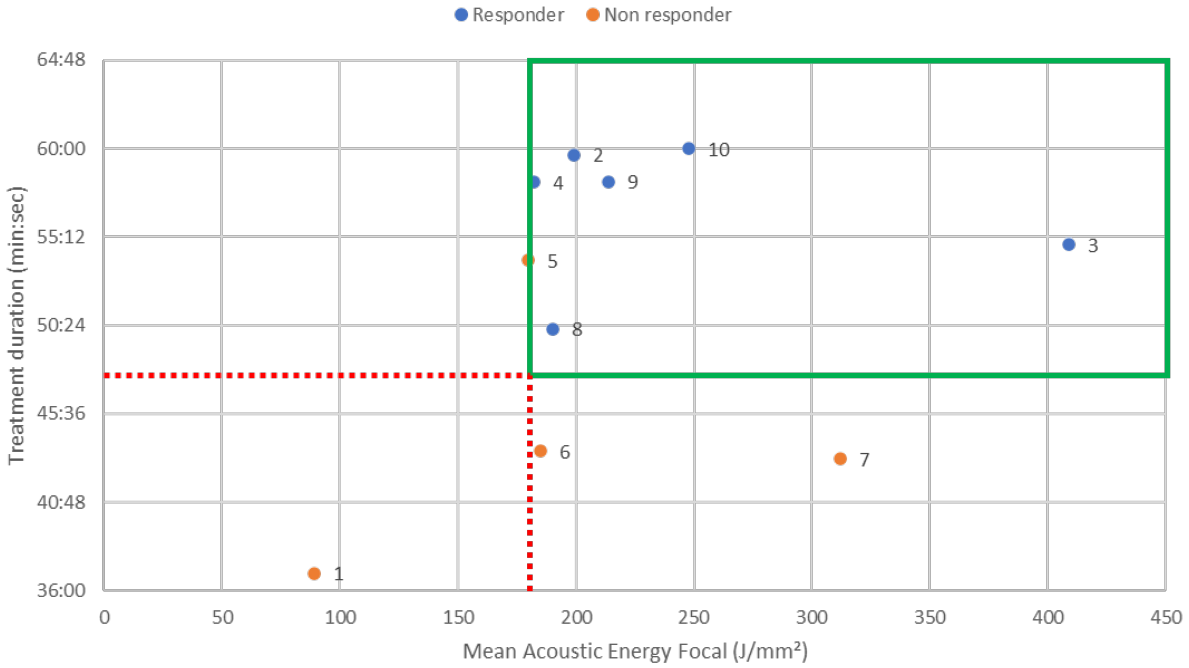
## Valvosoft® Procedure

# Results at one month

| Pt | Age | AVA (cm²) | | | Mean PG (mmHg) | | | Vmax (m/sec) | | | LVOT-CO (L/min) | | | NYHA | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Baseline | 1 month | Δ (%) | Baseline | 1 month | Δ (%) | Baseline | 1 month | Δ (%) | Baseline | 1 month | Δ (%) | Baseline | 1 month |
| 1 | 80 | 0.31 | 0.30 | -3 | 50.5 | 40.8 | -19 | 4.67 | 4.11 | -12 | 2.7 | 1.9 | - 30 | 4 | 4 |
| 2 | 77 | 0.50 | 0.84 | 68 | 25.8 | 20.4 | -21 | 3.25 | 2.94 | -10 | 2.5 | 4.0 | 61 | 4 | 3 |
| 3 | 79 | 0.61 | 0.93 | 52 | 32.3 | 27.3 | -16 | 3.71 | 3.58 | -4 | 3.9 | 5.1 | 32 | 4 | 3 |
| 4 | 79 | 0.74 | 0.84 | 14 | 52.3 | 35.9 | -31 | 4.72 | 3.83 | -19 | 5.2 | 4.9 | - 6 | 3 | 2 |
| 5 | 77 | 0.95 | 0.70 | -26 | 22.3 | 30.9 | 39 | 2.88 | 3.55 | 23 | 5.8 | 4.0 | - 31 | 4 | 3 |
| 6 | 91 | 0.54 | 0.63 | 17 | 38.4 | 51.3 | 34 | 4.00 | 4.64 | 16 | 3.6 | 4.6 | 26 | 4 | 2 |
| 7 | 86 | 0.57 | 0.69 | 11 | 30.5 | 31.2 | 2 | 3.66 | 3.72 | 2 | 3.2 | 3.9 | 21 | 4 | 3 |
| 8 | 93 | 0.72 | 0.80 | 11 | 48.0 | 25.5 | -47 | 4.49 | 3.21 | -29 | 4.8 | 3.7 | - 23 | 4 | 3 |
| 9 | 93 | 0.71 | 0.81 | 14 | 32.4 | 28.9 | -11 | 3.59 | 3.38 | -6 | 3.5 | 3.4 | - 2 | 3 | 3 |
| 10 | 86 | 0.48 | 0.51 | 6 | 42.9 | 36.1 | -16 | 4.11 | 3.82 | -7 | 2.9 | 3.0 | 1 | 2 | 2 |

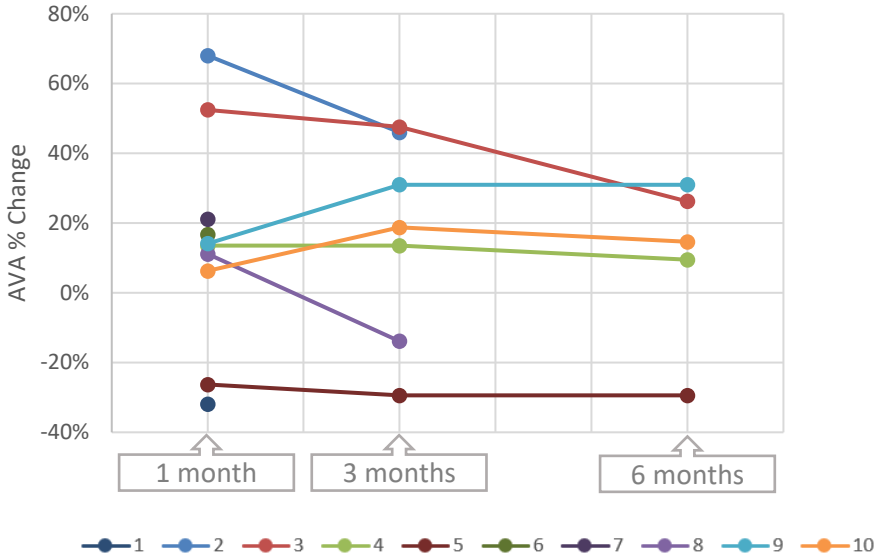
- Very old fragile patients with severe calcification and severe comorbidities
- No death, no CVA, no deterioration of cognitive function
- Some isolated extrasystoles during procedure that ceased when dose was lowered
- One hospitalization for right heart failure (resolved)
- 8 patients increased AVA, 7 decreased their mean PG and in 7 patients the NYHA class improved

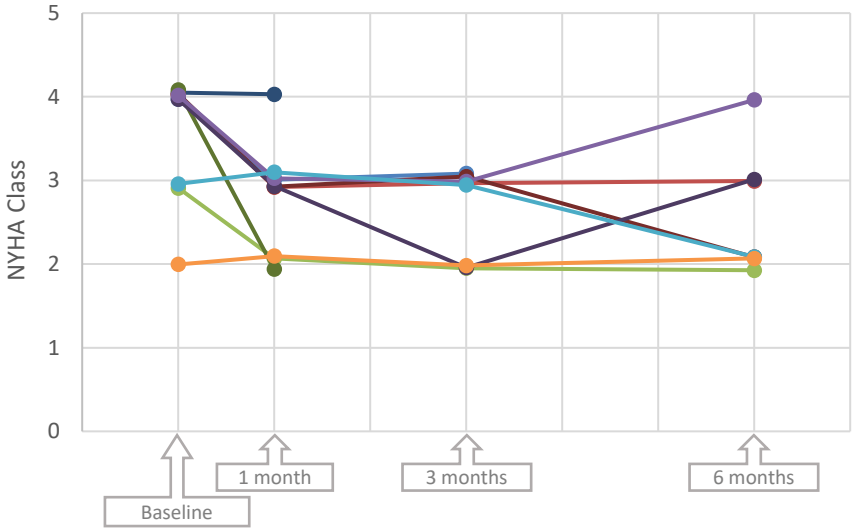
# What was different in patients who responded?




- **All six responders received >180J/mm² for at least 45 minutes**
- **Out of the 4 non-responders, 3 received less focal energy and/or for a duration shorter than 45 minutes**
- **A minimum of treatment duration and focal energy may be needed to obtain a clinically significant effect**

# Results at six months




- **2/4 non-responders died, 1/6 responders died due to progressive heart failure**
- **No stroke**
- **No Serious Adverse Events were adjudicated as procedure or device related**
- **Treatment effect maintained at 6 months for AVA and NYHA class**

# Next steps

## From Safety to Efficacy

- Higher energy dose to be applied
- Full 60 minutes duration of ultrasound application
- Repeated treatment sessions
- Improved device imaging guidance

## Expansion of indications

- Patients non-eligible for valve replacement
- Patients needing emergent non-cardiac surgery
- Bridge to TAVR
- Facilitate TAVR procedure
- Young patients to delay valve replacement
- Asymptomatic and moderately severe patients to delay disease progression

# Conclusions

- **Non-Invasive Ultrasound Therapy (NIUT) is a new way to treat Calcific Aortic Stenosis**
- **NIUT is feasible and safe in a FIM study involving 10 patients with severe symptomatic aortic stenosis not eligible for valve replacement**
  - No procedure or device related major adverse events at 6 months
  - Improvement of AVA, Pressure Gradient and NYHA in the majority of patients
  - Treatment result maintained at 6 months follow-up
- **Performance increases with longer treatment time and higher energy dose**
- **NIUT is complimentary to TAVR and can widen treatment possibilities for moderate and severe CAS patients**