CARMAT

Bioprosthetic Total Artificial Heart

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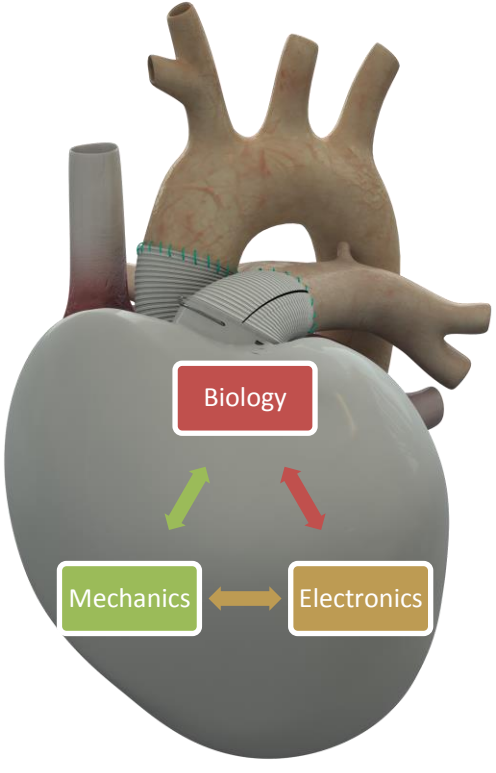
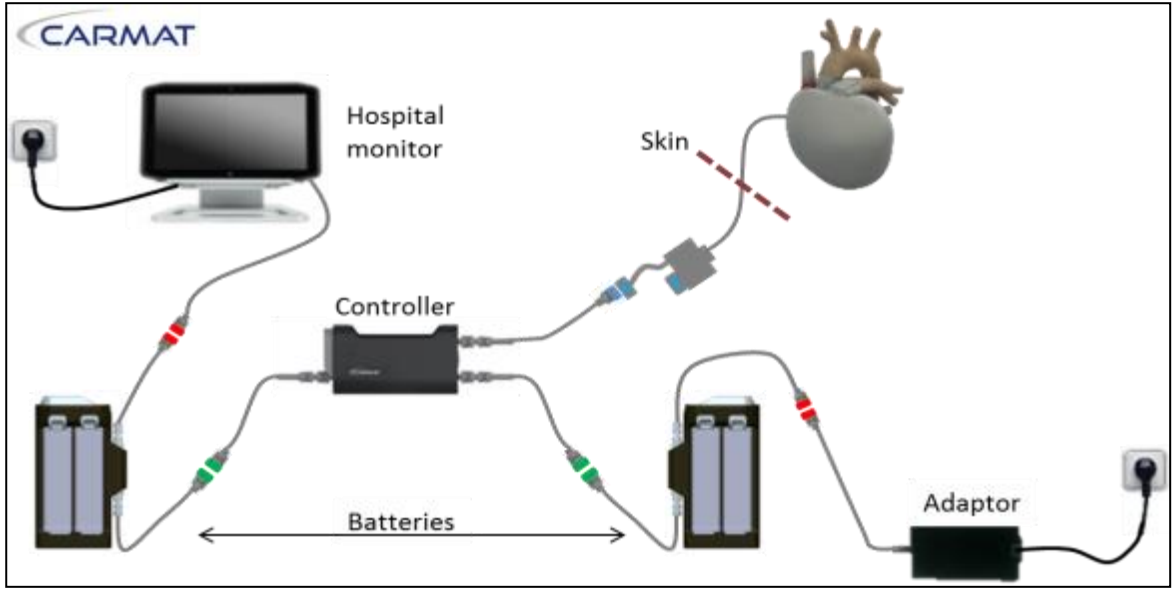
Carmat CMO
October, 2018

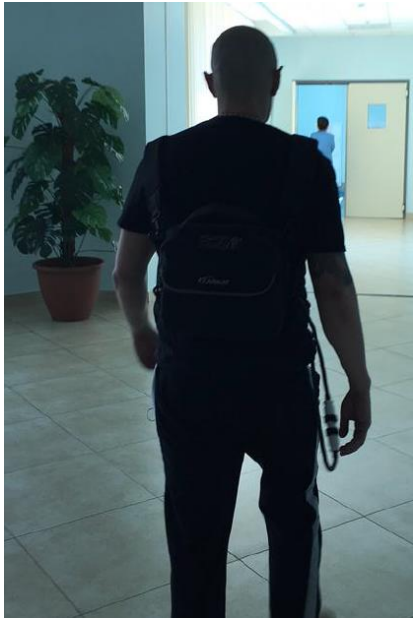
Distinguishing Features



- **Pulsatile biventricular** support
- Achieving good **hemocompatibility** is key objective
  - Bioprosthetic materials for blood contact
  - Avoiding shear stress
- Electrohydraulic actuation, **silent operation**
- **Closed loop**: auto-regulation
  - Embedded sensors, electronics, CPU

System Configuration



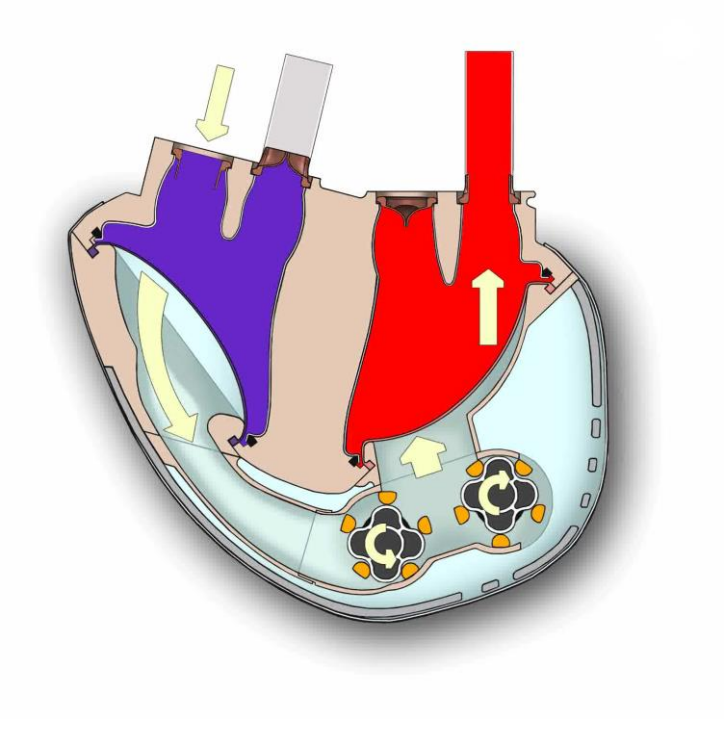


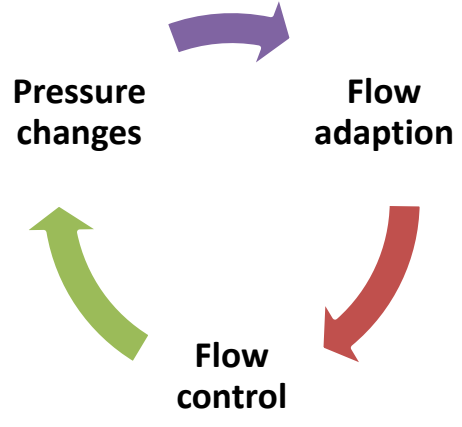
Wearable System

- Controller/monitor + 2x2 batteries
- Total weight 3 kg
- Autonomy at least 4 hours at 6 l/min

Electro-hydraulic actuation

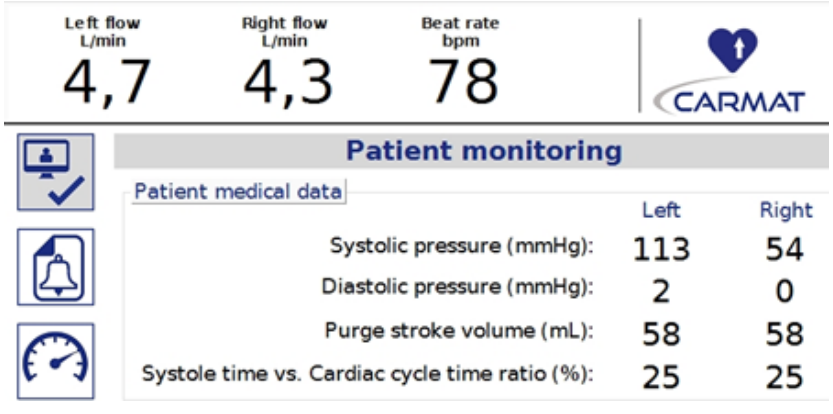
Two Pumps, Two Ventricles
One Heart

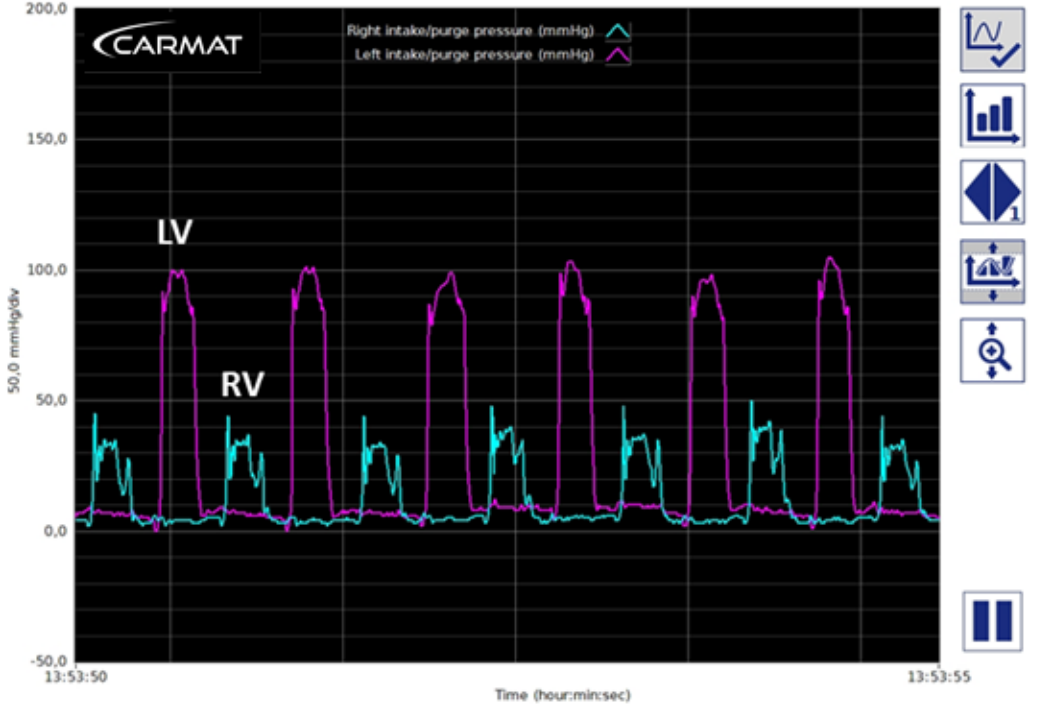




System detects changes in preload and responds with flow adaptation to obtain pre-set admission pressure

Carmat Screen: real-time Pressure and Flow information





CE-mark study

- Objective: obtain safety and performance data to support CE mark
- Patient cohorts
  - First cohort of 10 patients completed
    - France, Kazakhstan, Czech Republic
  - Second Cohort of 10 additional patients ongoing
    - Kazakhstan, Czech Republic, Denmark
- Primary endpoint: survival on device at 6 months or transplanted <6 months
- Secondary endpoints
  - Health status change (NYHA, 6MWT; EQ-5D-5L, SF36)
  - Frequency and incidence of adverse events (INTERMACS definition)
- Follow up until 2 years post-implant

CE-mark Study Population

- Based on ISHLT Guidelines for Mechanical Circulatory Support (J Heart Lung Transpl. 2013;32:21)

- Patients with end stage heart failure (DT&BTT), refractory to optimal medical management, requiring mechanical circulatory support but for whom LVAD is considered inefficient or contraindicated, such as*:
  - Biventricular failure necessitating RVAD support in addition to LVAD
  - Treatment-refractory recurrent ventricular tachycardia or fibrillation
  - Restrictive or constrictive physiology (hypertrophic cardiomyopathy, cardiac amyloidosis or other infiltrative heart disease)

Study Inclusion Criteria

1. Patient age: 18 to 75 years
2. Inotrope dependent or Cardiac Index < 2.2 L/min/m^2 while not on inotropes
3. On Optimal Medical Management as judged by the investigator based on current HF guidelines (ESC/AHA)
4. Eligible to biventricular MCS according to ISHLT guidelines for mechanical circulatory support
   a) Biventricular failure, with at least two of the following measurements implying RV failure
      1. RVEF ≤ 30%
      2. CVP ≥ 15mmHg
      3. CVP-to-PCWP ratio > 0.63
      4. TAPSE ≤ 14mm
      5. RVSWI ≤ 0.25 mmHg*L/m2
      6. RV-to-LV end-diastolic diameter ratio > 0.72
      7. Tricuspid insufficiency grade 4

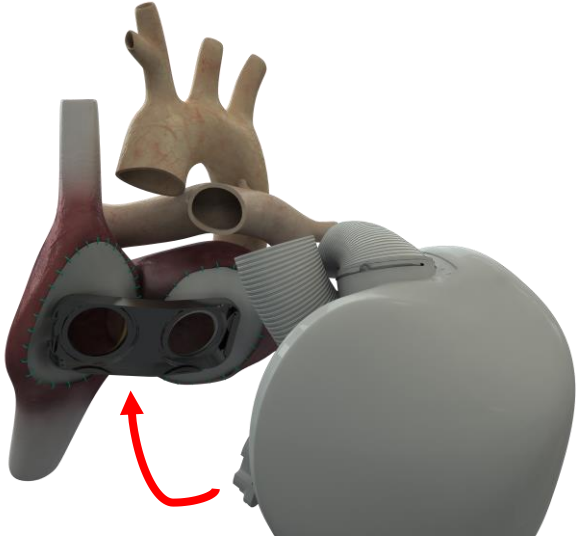
   b) Treatment-refractory recurrent and sustained ventricular tachycardia or ventricular fibrillation in the presence of untreatable arrhythmogenic pathologic substrate

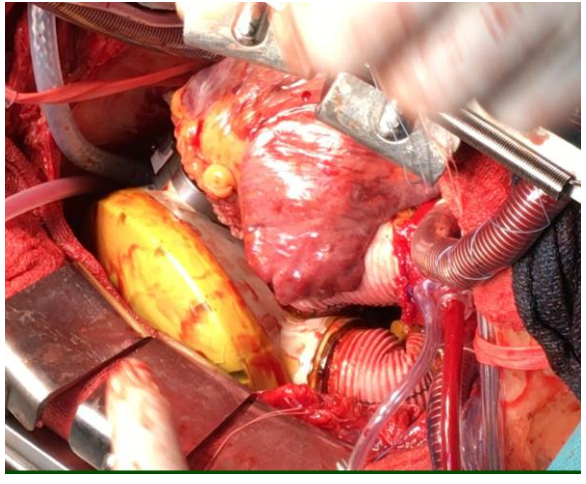
   c) Heart failure due to restrictive or constrictive physiology (e.g., hypertrophic cardiomyopathy, cardiac amyloidosis or other infiltrative heart disease)
5. Anatomic compatibility using 3D imaging (CT-scan)
6. Patient's affiliation to health care insurance, if local requirement
7. Signed informed consent obtained

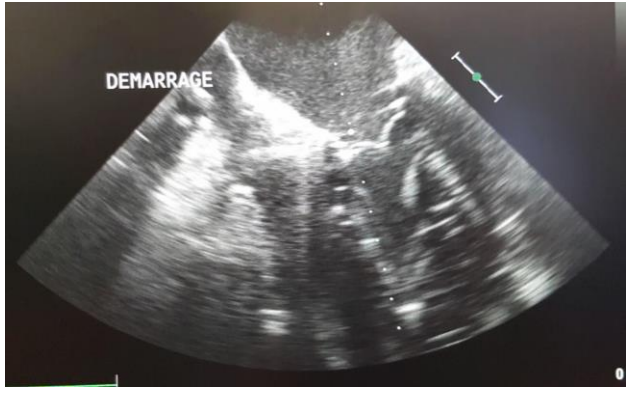
Exclusion Criteria

1. Body Mass Index (BMI) < 15 or > 47
2. Existence of any ongoing non-temporary mechanical circulatory support
3. Existence of any temporary mechanical circulatory support other than IABP
4. History of cardiac or other organ transplant
5. Patients who underwent cardiopulmonary resuscitation for > 30 min within 14 days
6. Known intolerance to anticoagulant or antiplatelet therapies
7. Coagulopathy defined by platelets < 100k/µl or INR ≥ 1.5 not due to anticoagulant therapy
8. Cerebro-vascular accident < 3 months or symptomatic or a > 80% carotid stenosis
9. Known abdominal or thoracic aortic aneurysm > 5 cm
10. End-organ dysfunction as per investigator judgment and following but not limited to these criteria:
    - Total bilirubin > 100µmol/L (4,8 mg/dL) or cirrhosis evidenced by ultrasound, CT-scan or positive biopsy
    - GFR < 30ml/min/1.73m2
11. History of severe Chronic Obstructive Pulmonary Disease or severe restrictive lung disease
12. Recent blood stream infection (<= 7 days)
13. Documented amyloid light-chain (AL amyloidosis)
14. Hemodynamically significant peripheral vascular disease with rest pain or extremity ulceration
15. Illness, other than heart disease, that would limit survival to less than 1 year
16. Irreversible cognitive dysfunction, psychosocial issues or psychiatric disease, likely to impair compliance
17. Participation in any other clinical investigation that is likely to confound study results or affect the study
18. Pregnancy or breast feeding (woman in age of childbearing will have to show negative pregnancy test)

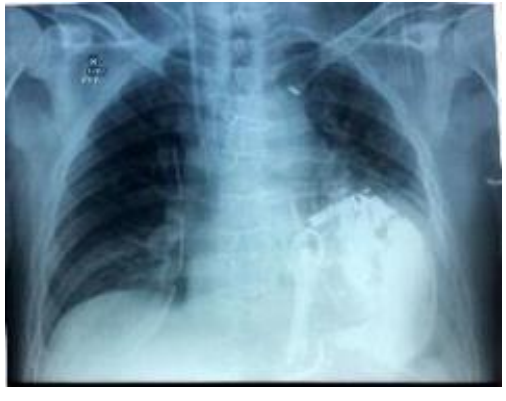
Implant Technique







TEE: de-airing/weaning



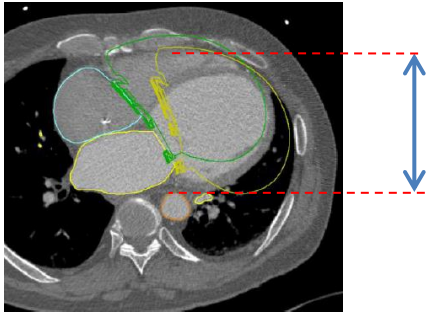
CE Study Update

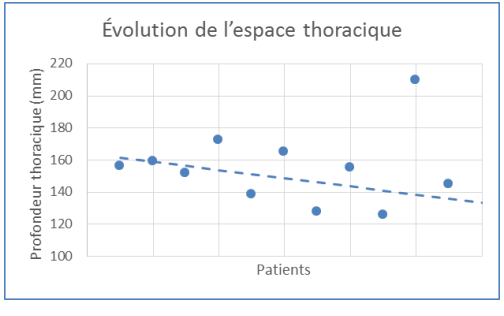
- 11 patients have been implanted with Carmat TAH
  - Nantes, Prague, Astana
  - BTC, BTT, DT
  - Patients have been discharged with the device
  - Patients have been transplanted successfully

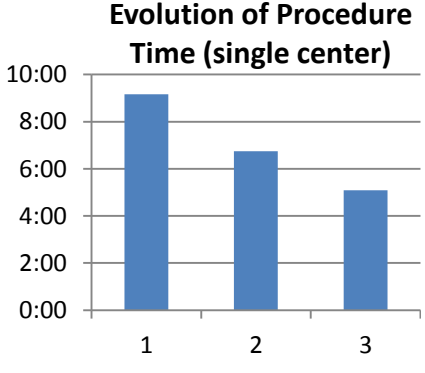
- Cumulative support duration >3.5 years

Screening and Implant Procedure – Learning Curve

- Avoid INTERMACS 1
- Less restrictive on anatomic fit
- Adaptive implant techniques
- Secondary sternal closure is standard
- 100% implant survival

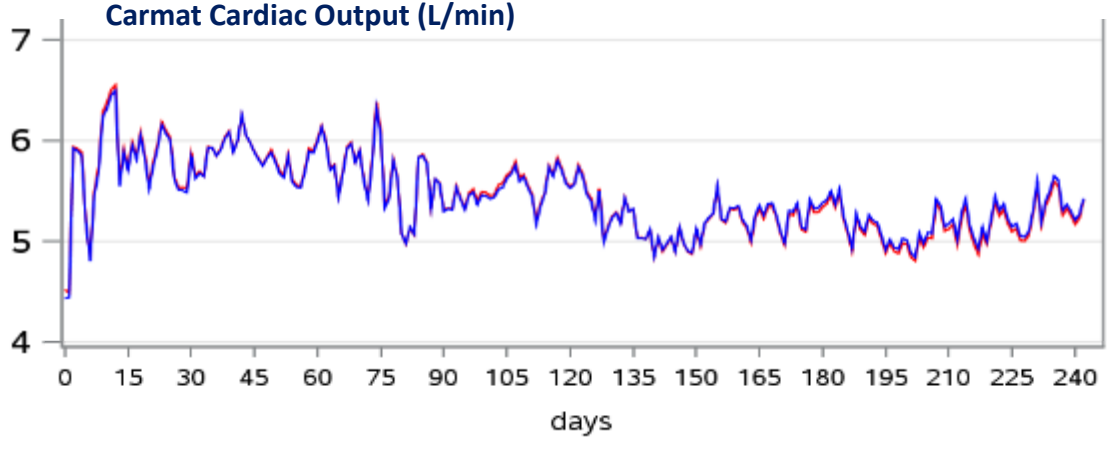


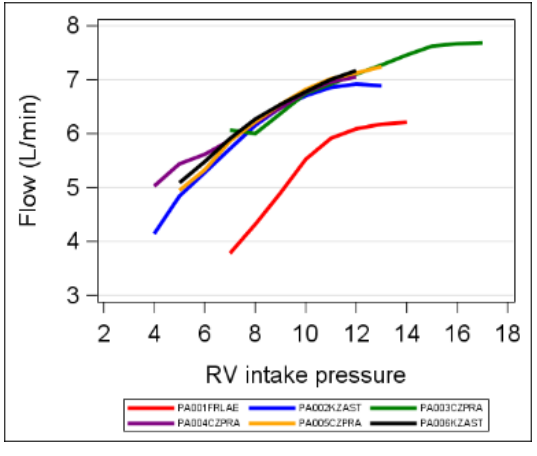




Observations on Device Performance

- Automatic mode is standard mode of functioning
- Device settings mostly unchanged after implant
- Variation in pump flow, as expected





ELSEVIER

RESEARCH CORRESPONDENCE

Effects of pre-load variations on hemodynamic parameters with a pulsatile autoregulated artificial heart during the early post-operative period

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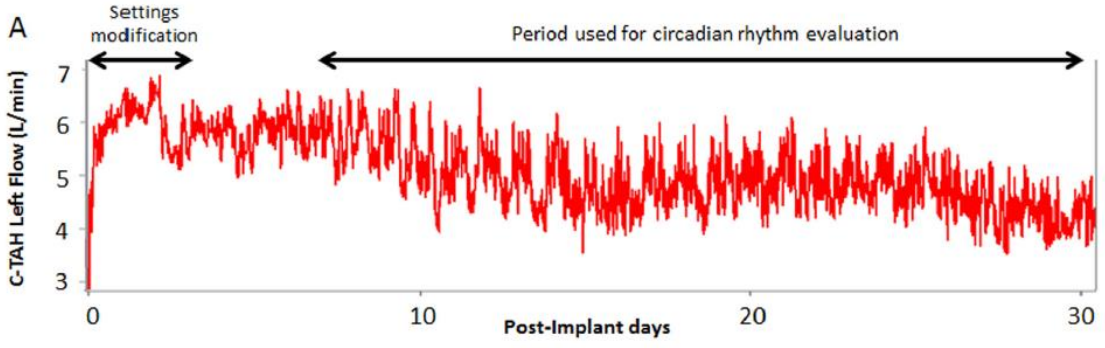
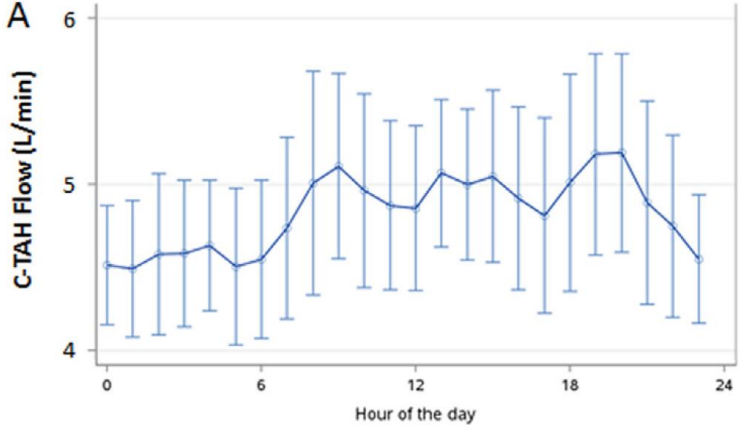
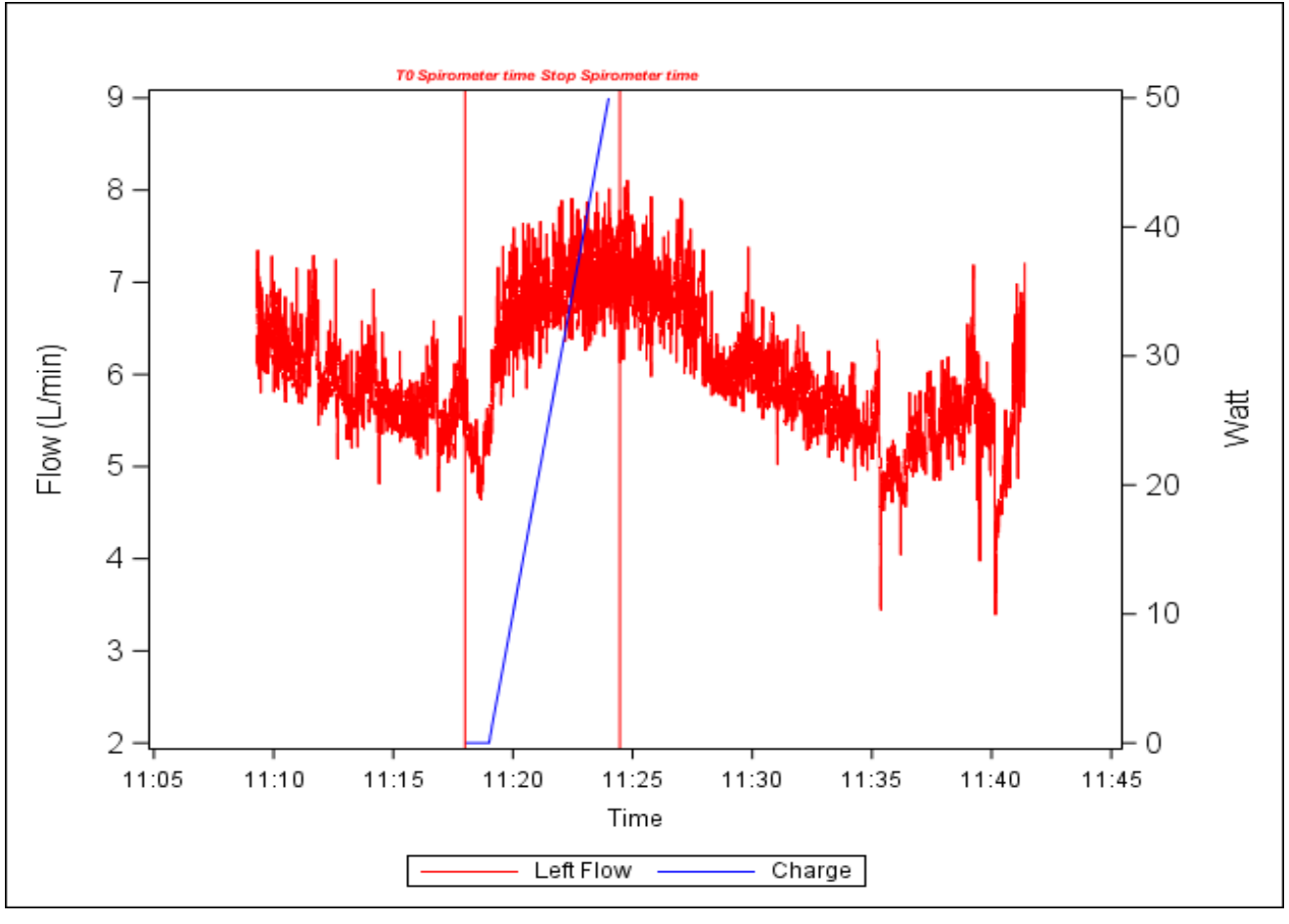


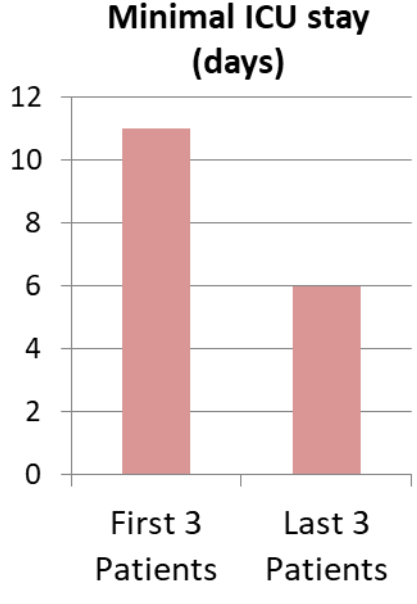


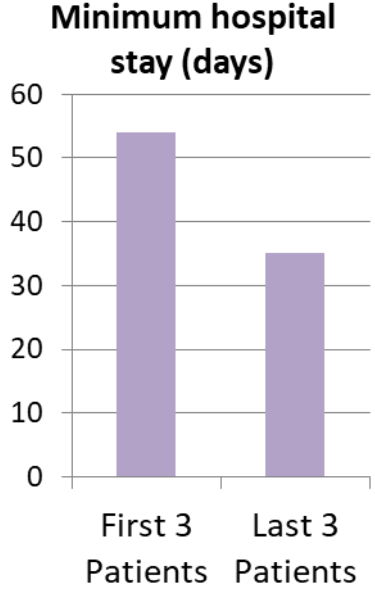
Exercise test @ 3 months



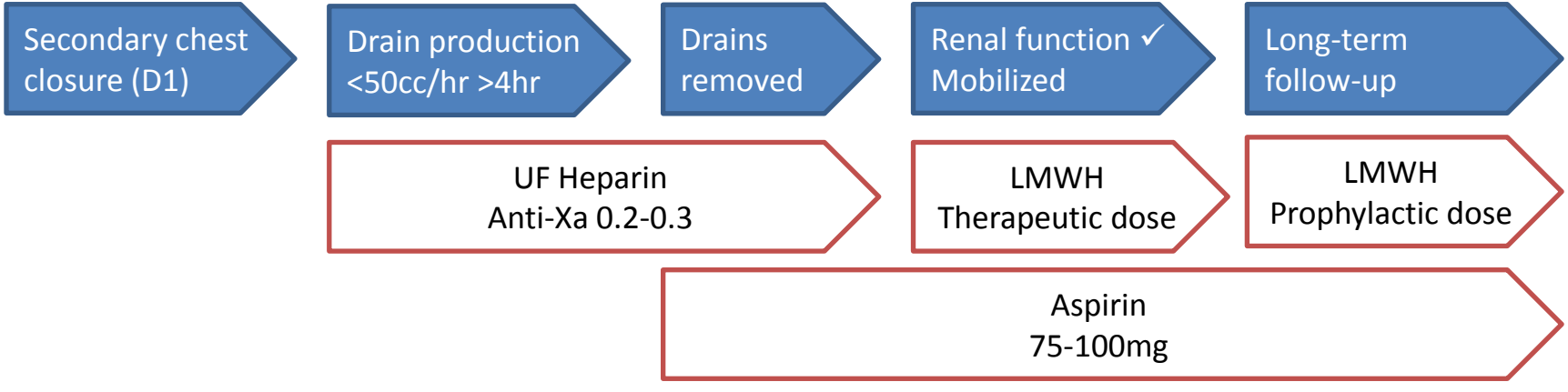
Patient Management – Learning curve

- Collaboration with ICU proctors
- Limit early post-op hyperperfusion
- Device hemodynamic data is utilized to guide patient management





Anti-coagulation guidelines



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Is the total artificial heart a step ahead in reducing VAD-related mortalities? #JACC

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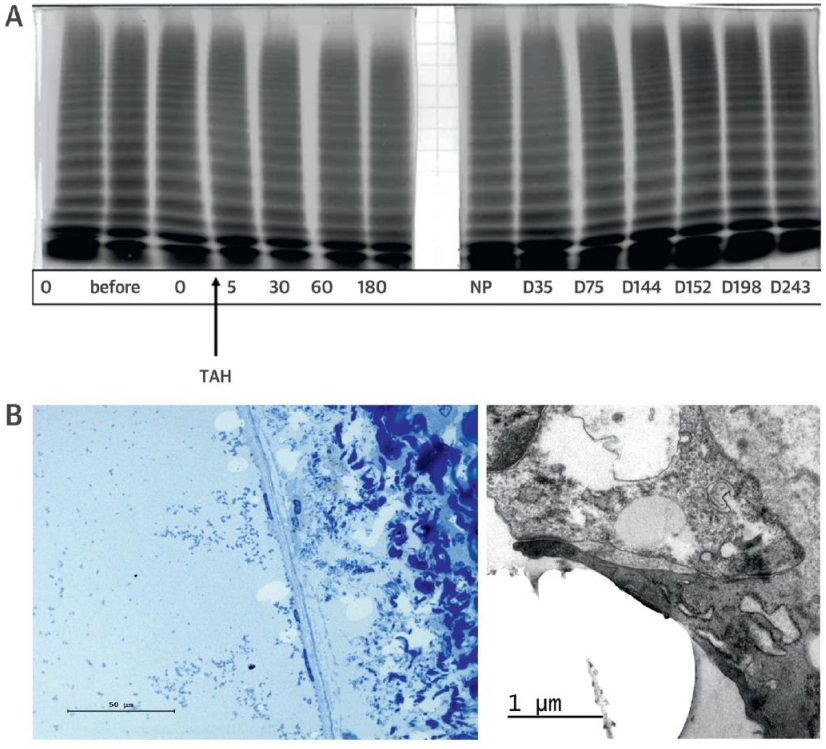
JULY 18, 2017:403–9

FIGURE 1 Biological and Histological Demonstration of Carmat TAH Hemocompatibility Profile



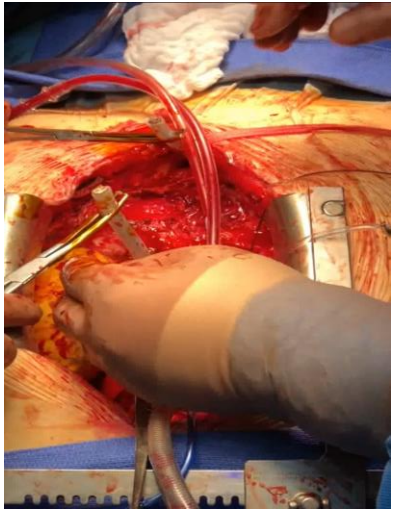
(A) Absence of acquired von Willebrand syndrome after Carmat total artificial heart (TAH) implantation. Representative time course of high-molecular-weight multimers after initiating the Carmat TAH. **(B)** Endothelial recovery of explanted glutaraldehyde-treated membranes. Semithin sections stained with **toluidine blue** showed a genuine endothelial covering on top of the fibrin cap **(left)**, and electron microscopy showed tight junctional structures **(right)**. D = day; NP = normal human pooled plasma.

Bioprosthetic Total Artificial Heart Induces a Profile of Acquired Hemocompatibility With Membranes Recellularization

- **Absence of hemolysis**
- **Absence of acquired von Willebrand syndrome**
- **Early neo-endothelialization on membranes**

Bridging to transplant is possible

- Transplant performed on multiple Carmat recipients
  - BTT and BTC (PHT)
- Longest Carmat support prior to transplant: 8 months
- No adhesions at explant around device body



Summary of ongoing Carmat CE Study

- Three sites activated (Astana, Prague, Copenhagen)
- >50% enrollment completed; building experience
- Satisfactory device performance profile
- Home discharge is possible
- Low anticoagulation regimen is well tolerated
- Explant/transplant is possible
- Obviously, we need more long-term data to assess safety and efficacy