Self-learning intracardiac blood pressure estimation models for CHF, ACS, AS

(Non-Invasive Cardiac Chambers Blood Pressure Monitoring Using Ultrasound)

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Goal:

to Prevent **Decompensated Heart Failure**,
Improve Life Quality
and Expectancy

Reduce Cost Of Therapy

Background

- LVEDP and RVEDP are major CHF markers
- Intra-cardiac pressure changes (ICPC) preside symptomatic events development, hence ICPC real-time monitoring is critical.
- Currently filling ventricular pressures may be assessed either through catheterization procedure or locally via implantable devices.

The Clinical Burden: 67 Million People Worldwide

600,000 new CHF patients are diagnosed every year

and added to more than 5,700,000 CHF patients in USA only

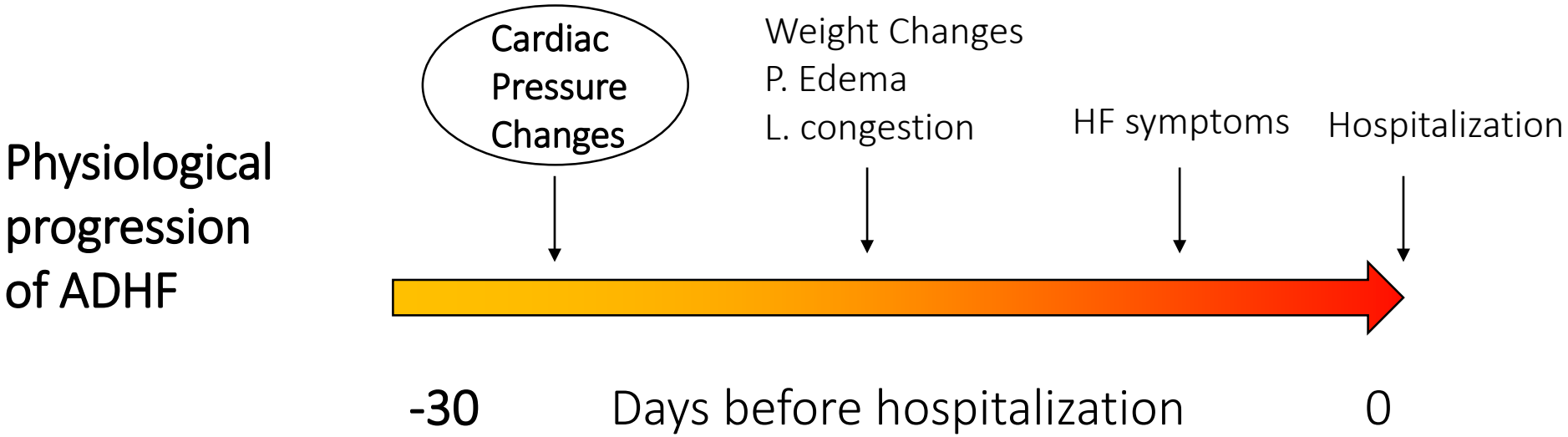
The yearly burden of CHF therapy in the US rose from 10 B USD to 30.7 B USD

Heart Failure Remote Monitoring: A Review and Implementation How-To
Elizabeth A. Kobe, Marat Fudim, J. Clin. Med. Published 26.09.2023

Our game changing non-invasive technology is adequate for

all NYHA stages of CHF patients

Hemodynamic Information is critical: Cardiac pressure changes occur long before other HF symptoms become visible



Invasive Solutions Currently Available

CardioMEMS HF System, Abbott (PA implant), RFID

- 44% reduction in heart failure hospitalizations
- Patients showed significant reduction in mean PA pressures at 12 months
- $13,190 reduction in heart failure hospitalization costs per patient-year
- 30% reduction in mortality
- Preventing the first HFH through hemodynamic-guided management may lead to a lower risk for subsequent HFH, and better outcomes
- Cost of CardioMEMS per device – **$17,750**
- Implantation procedure per person – **$ 1,280**
- Complications (such as bleeding, infection and thrombosis) each **$5,770**

Invasive Solutions Currently Available

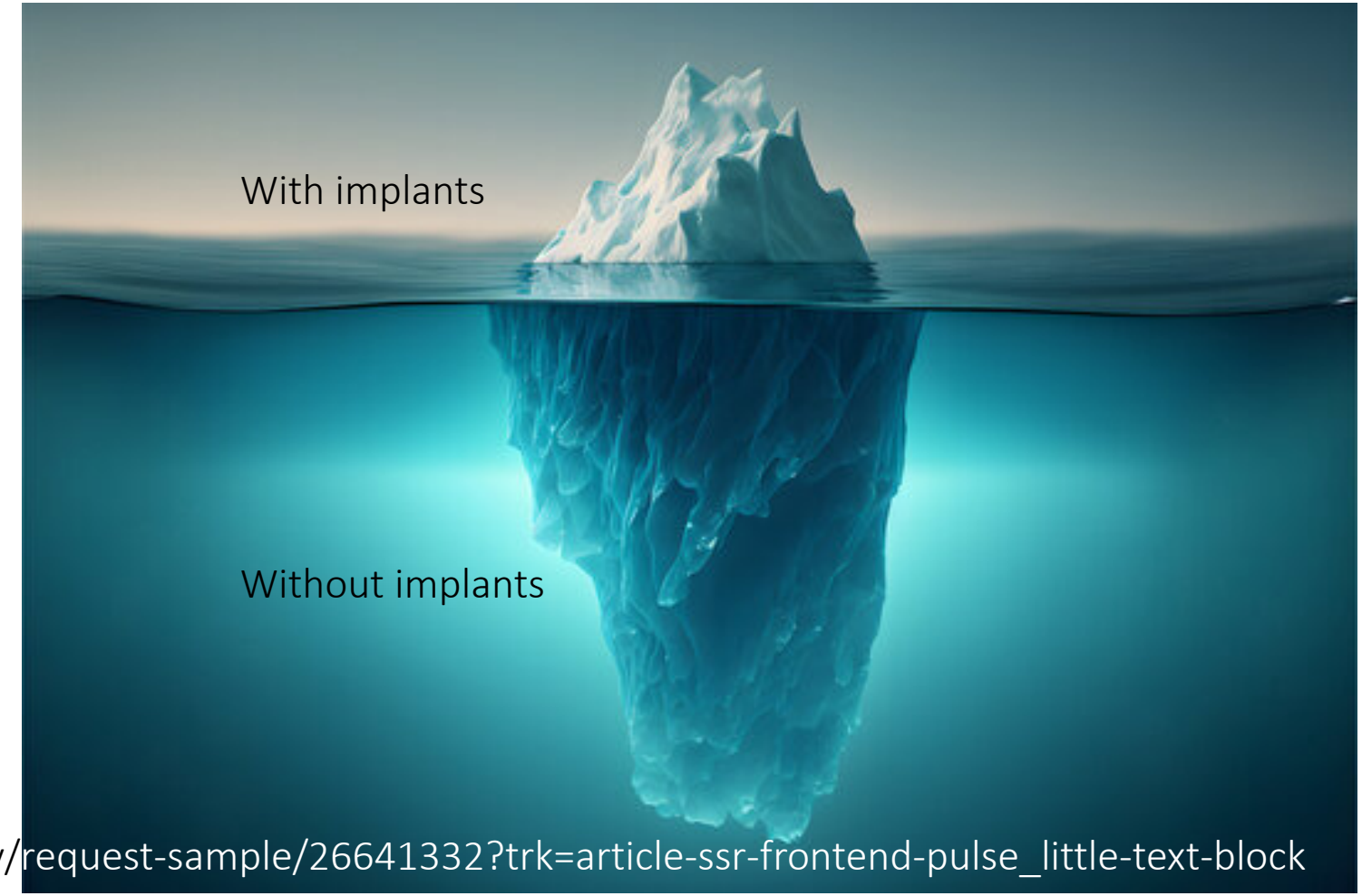
V-LAP Victorious Medical (IAS implant), RFID

- After 6 months, NYHA class improved in 40% of the patients
- Using the PSM (Patient Self-Management) approach, a significant decrease in the annualized rate of HF-related hospitalizations was observed compared to a similar period prior to PSM utilization (0 admissions per patient under PSM versus 0.69 admissions per patient prior to PSM, P=0.004).
- Vectorious Medical Technologies received FDA Breakthrough Device designation, while
- Clinical trials towards FDA are yet under way (till 2027) https://classic.clinicaltrials.gov/ct2/show/NCT05712824

Illustration of the vast population of CHF patients that may benefit of ICPM

The **global Cardiac Monitoring market** was valued at **US$ 17,320M** (millions) in 2023

and would reach **US$ 21,580M** by 2030, witnessing a CAGR of 3.2% during the forecast period of 2024-2030



https://www.marketreportsworld.com/enquiry/request-sample/26641332?trk=article-ssr-frontend-pulse_little-text-block

ICPM technology and optimization of Heart Failure therapy

A standard wireless ultrasound device is used, and the innovation is in a mathematical analysis of the acquired data.

- Offering for complex patients valuable real time non-invasive data of filling pressures of left(right) chambers both instant and mean LVEDP/LAP (RVEDP/ RAP).
- These parameters may improve the strategy for the management of systemic congestion and fine-tune (guide) the (combined) diuretic and after-load reduction therapy for NYHA stage III & IV of Heart Failure patients such as

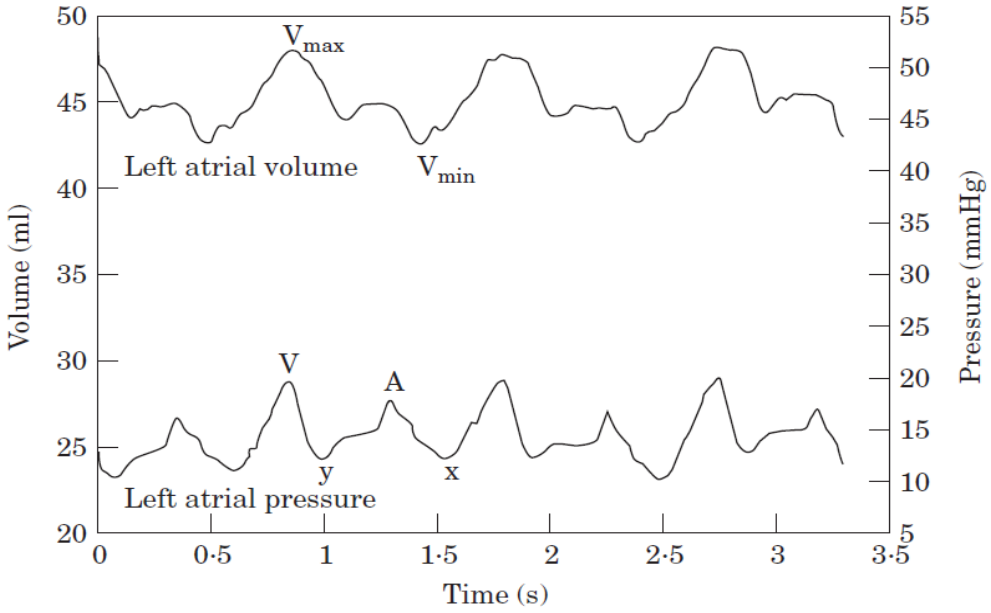
1) patients with acute coronary syndrome (ACS) elected for percutaneous coronary intervention (PCI)

2) patients with Aortic Stenosis (AS) elected for transcatheter aortic valve implantation (TAVI)

3) patients catheterized for CHF

ICPM – Method Background

According to the basic state-of-the-art research (Stefanidis et al. 2001), the waveforms of left atrial volume and simultaneous left atrial pressure are similar.



$$\boldsymbol{P}(t) = F(\boldsymbol{V}(t))$$

In our previous research (reported to CSI in 2019, 2021, 2022) the possibility to perform an accurate calculation/estimation of cardiac chambers' blood pressure noninvasively with perfect fit to the sensor-measured pressures during heart catheterization was demonstrated.

The cross- calibration has shown the stability of the method when using calibration results of the Ultrasound data to measured pressure both before (to after) and after (to before) stent insertion.

Similar results were obtained for sheep models (https://biomedres.us/pdfs/BJSTR.MS.ID.001466.pdf) where we have obtained a broad statistic.

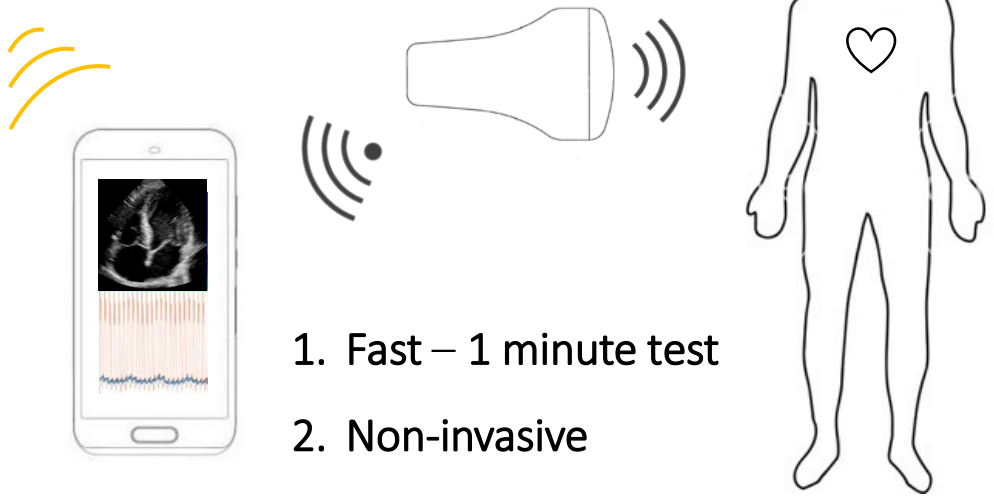
ICPM – Innovative Non-Invasive Real-Time Intra-Cardiac Pressure Monitoring System

ICPM usage simplicity:

- Portable Ultrasound Device
- Cell Phone or any mobile device

Connectivity to Cloud, API to healthcare providers

Data processing algorithm



1. Fast – 1 minute test
2. Non-invasive
3. Operated at home as a follow-up tool
4. Cloud based service
5. Patient, GP, HF Nurse & Cardiologist are informed

The system has been successfully

calibrated and tested on 36 patients

in ZIV medical center Israel,

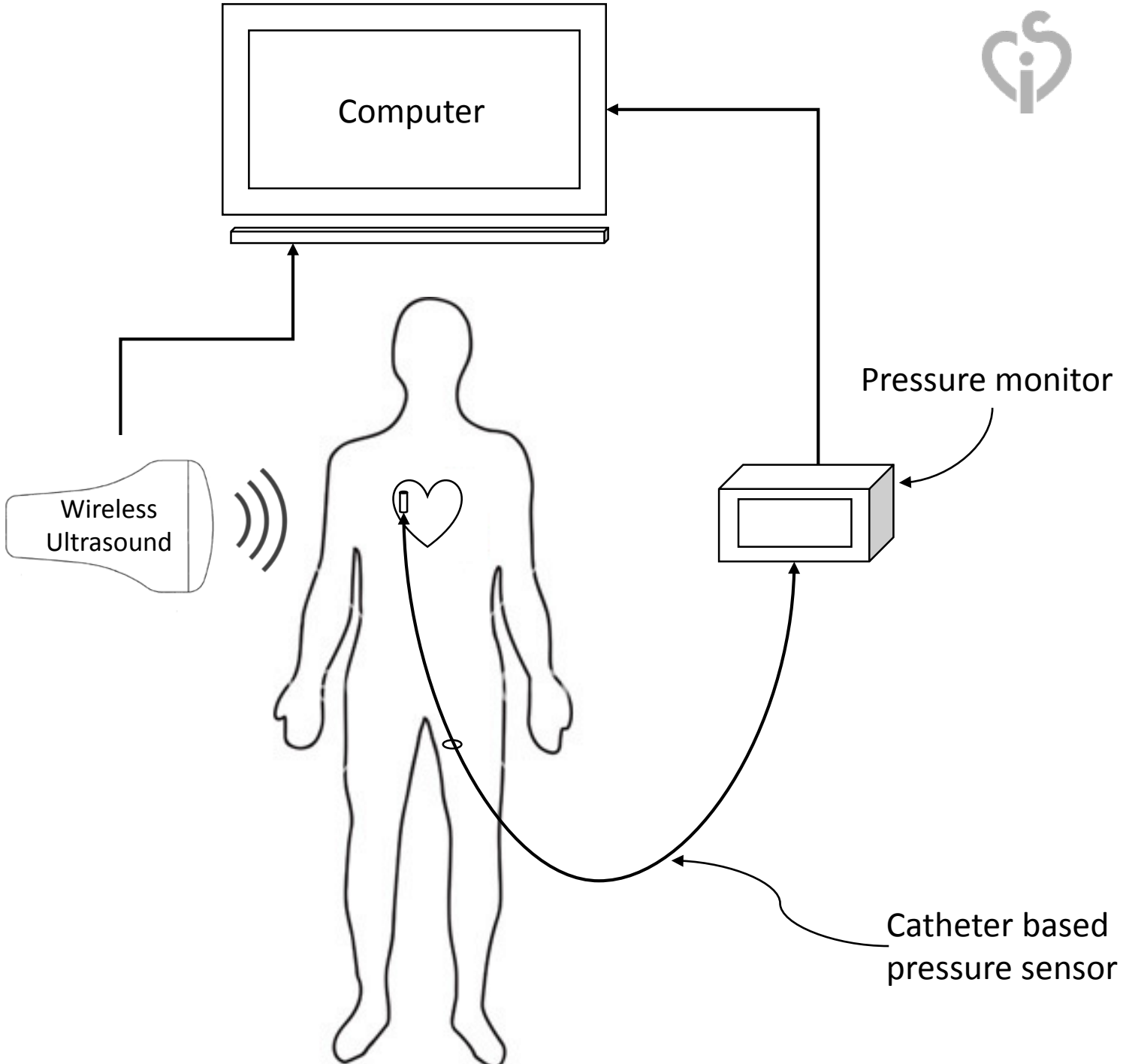
and has been reported to CSI 2019, 2021, 2022.

Calibration Process

Comparison of

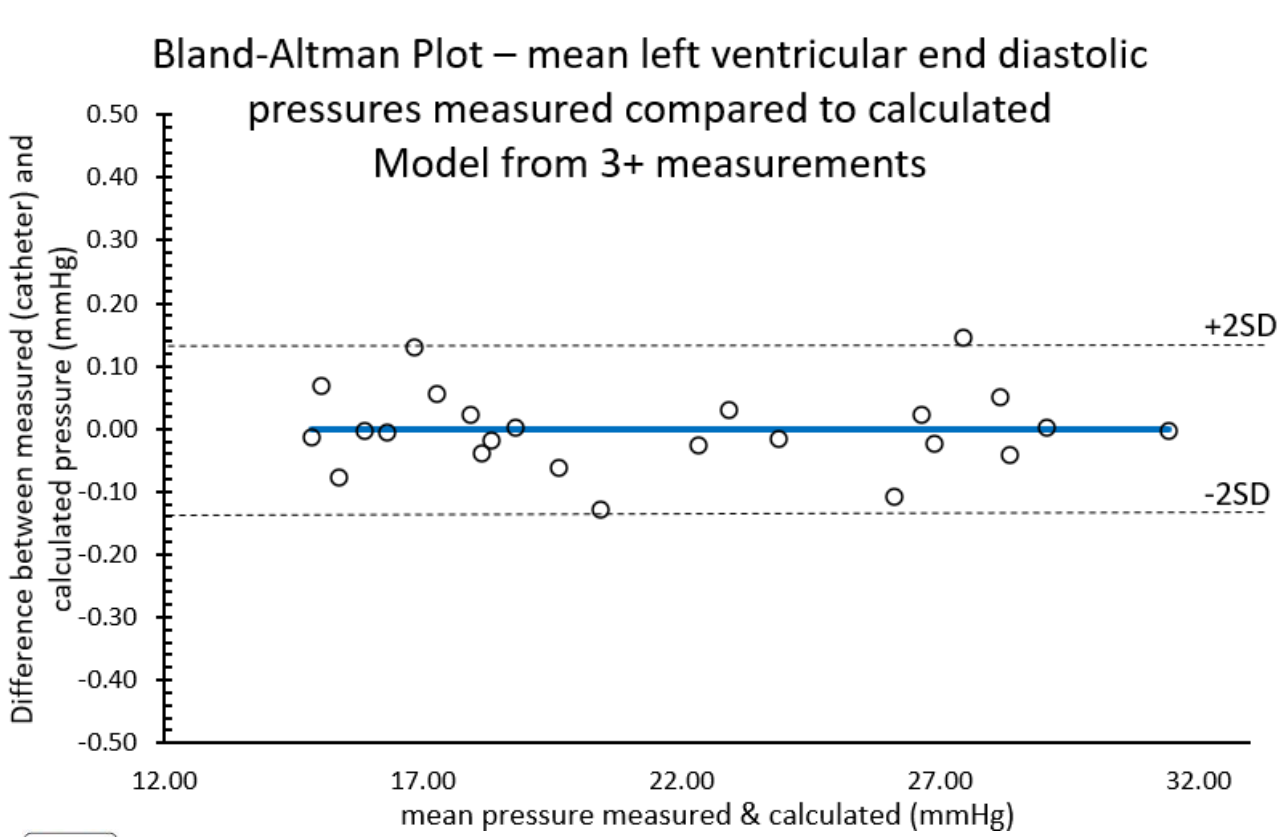
- Intracardiac blood pressures calculated from ultrasound imaging

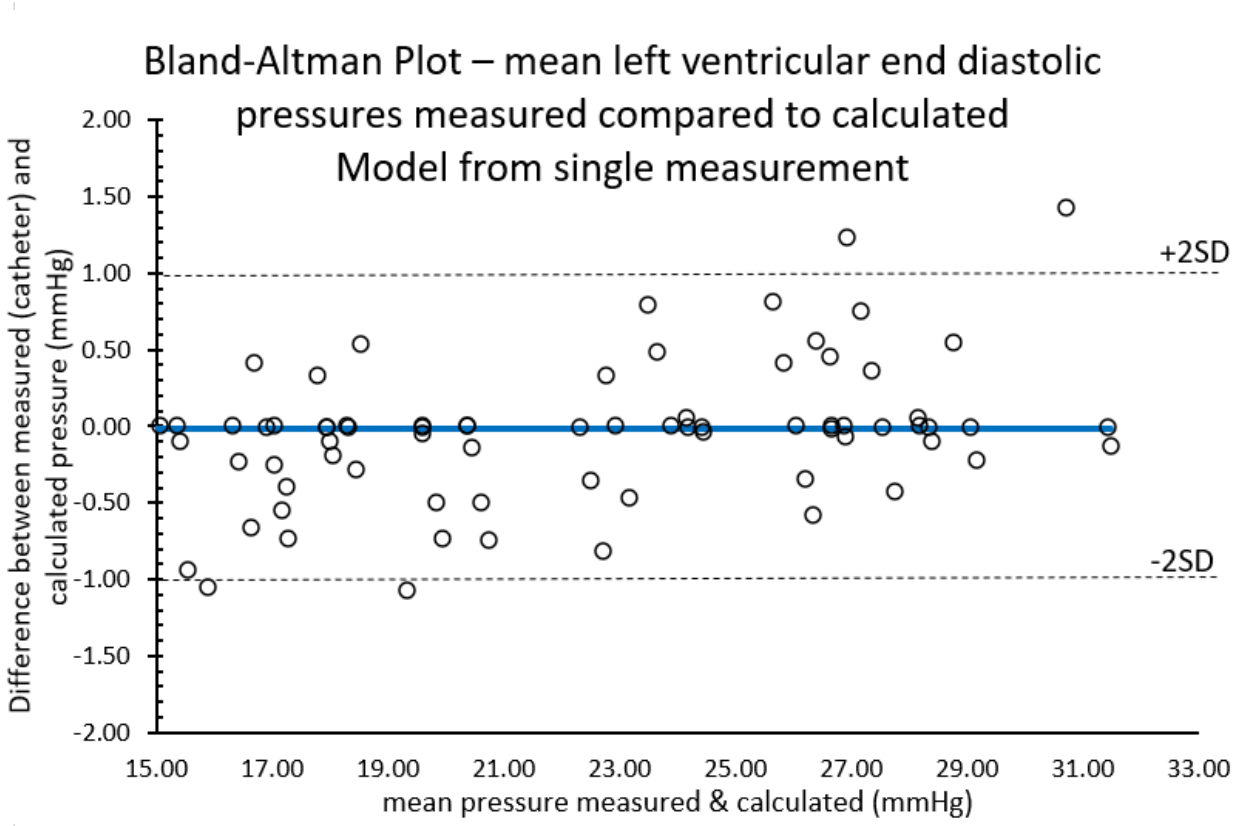
- To blood pressures obtained during hemodynamic catheterization for patient.



ICPM in Action: LVEDP model

Bland – Altman diagrams for different calibration models





Study Objectives

We propose a wide multi-Center study with the following objectives

Primary objective is to acquire sufficient data to build self-learning intracardiac blood pressure estimation models for CHF, ACS, AS patients permitting the system to work in fully non-invasive form without hemodynamic catheterization currently needed for individual system calibration.

Secondary objective is to establish the effectiveness of ultrasound-based pressure monitoring on patient hospitalizations and outcomes comparing calibrated patients and a control group.

Study Groups

- **CHF Swan-Ganz** monitored patients recorded on admission and before discharge
- Non-STEMI patients and patients with acute coronary syndrome (ACS) elected for percutaneous coronary intervention (**PCI**)
- Patients with Aortic Stenosis (AS) elected for transcatheter aortic valve implantation (**TAVI**)
- Aim: **300 patients** data acquisition (of 3 study groups)
- Easy recruitment for informed consent: Non-Invasive and does not prolong the procedure (IRB).

Study Methods

During routine catheterization procedure the intracardiac pressures of a patient will be measured in the heart chambers as accepted.

Simultaneously, the transthoracic ultrasound examination with recording of the heart movement will be performed and the data will be stored.

The patients will be then monitored non-invasively using ultrasound for pressure changes, and this data will be made available to their cardiologist.

A control group will be comprised of age-matched and diagnosis-matched patients with similar BMI and heart size who will not have left atrial pressure monitored and available to the cardiologist.

Outcomes will be compared and include mortality or major morbidity (cardiac hospitalization, resuscitation, heart transplantation).

Study Flow

- Simultaneous recording of
    - ECG
    - Catheter based LVEDP/RVEDP/LAP/RAR/PCWP
    - Ultrasound (non-filtered) 4 Chamber Apical View
- Preferably with repeated calibrations sampling for 50 seconds each before and after procedure.
- Ultrasound-only recordings as follow-up
- Required hardware will be provided by Pi-Harvest

Follow Up

Cardiology clinic follow up

- repeated ultrasound evaluation during hospital stay and outpatient visits
- comparison of outcomes between
  - patients with pressure monitoring
  - control group without pressure monitoring.

Pre-specified outcomes

The outcome is defined successful if the calculated pressures do not deviate above 3 mmHg from the directly measured pressures.

Confirmation of the study hypothesis may allow introduction of non-invasive monitoring of intracardiac pressures as LVEDP /RVEDP to timely manage CHF, ACS, AS patients.

Ethical and Safety

The examinations that will be performed are non-invasive and will be done during planned catheterization for indications that are guided by the patient's medical status and not by the needs or requirements of the study.

We will specifically ensure that the ultrasound examination will not compromise the patient's safety; for example – that the duration of the procedure, which may be longer due to ultrasound measurements, will not affect the patient's health.

Simultaneous Catheter based ECG, LVEDP and Apical 4 Chambers View data acquisition with online automated LVEDP estimation from Ultrasound data