InSiDe: A Cardiovascular Screening Device Based on Silicon Photonics

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SPIE Photonics Europe.

6 April 2022

This project has received funding from the European Union's H2020 Programme for research, technological development and demonstration under grant agreement No 871547

The InSiDe project

InSiDe: **In**tegrated **Si**licon photonics for Cardiovascular **Di**s**e**ase monitoring

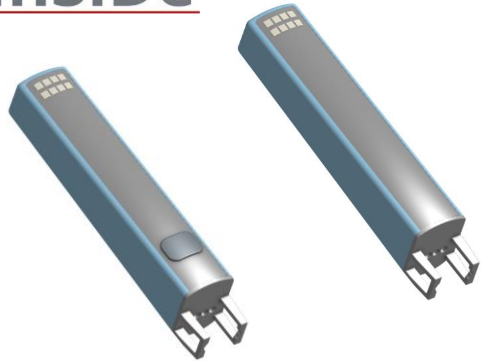
- Horizon 2020 - Innovation Action - Application driven Photonics components
- Follow up of CARDIS-project, start 1 Jan 2020, duration 48 months

Objective

- Develop handheld wireless clinical investigational CVD screening device
- Demonstrate in clinical feasibility studies efficacy and usefulness to GPs and cardiologists

CardiS

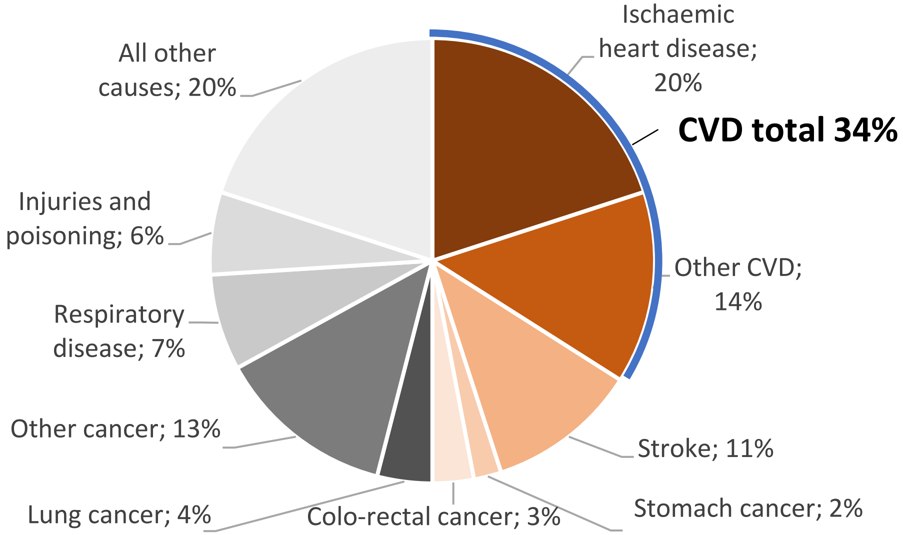
InSiDe



imec Medtronic GHENT UNIVERSITY POLITECNICO DI TORINO Tyndall National Institute ARGOTECH MICROCHIP Maastricht University Inserm La science pour la santé From science to health Fundi€o

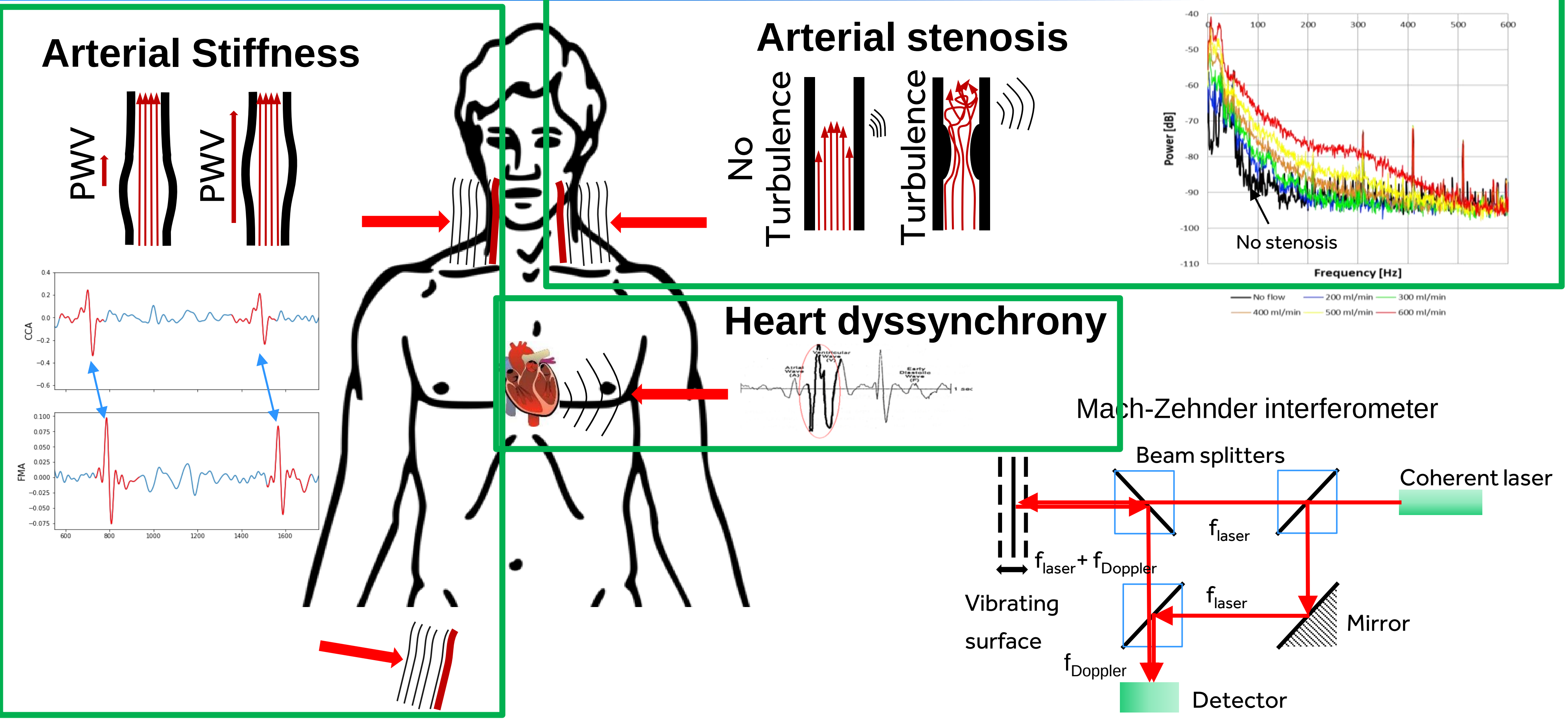
Rationale

- Cardiovascular diseases are the main contributors to global morbidity and mortality responsible for 34% of global deaths
- Need for CVD screening device for preventative therapy (at GP)
- Three important CVD risk factors are
  1. Arterial stiffness
  2. Arterial stenosis
  3. Abnormal cardiac contraction patterns
- Measure via LDV instead of arterial tonometry (gold standard)

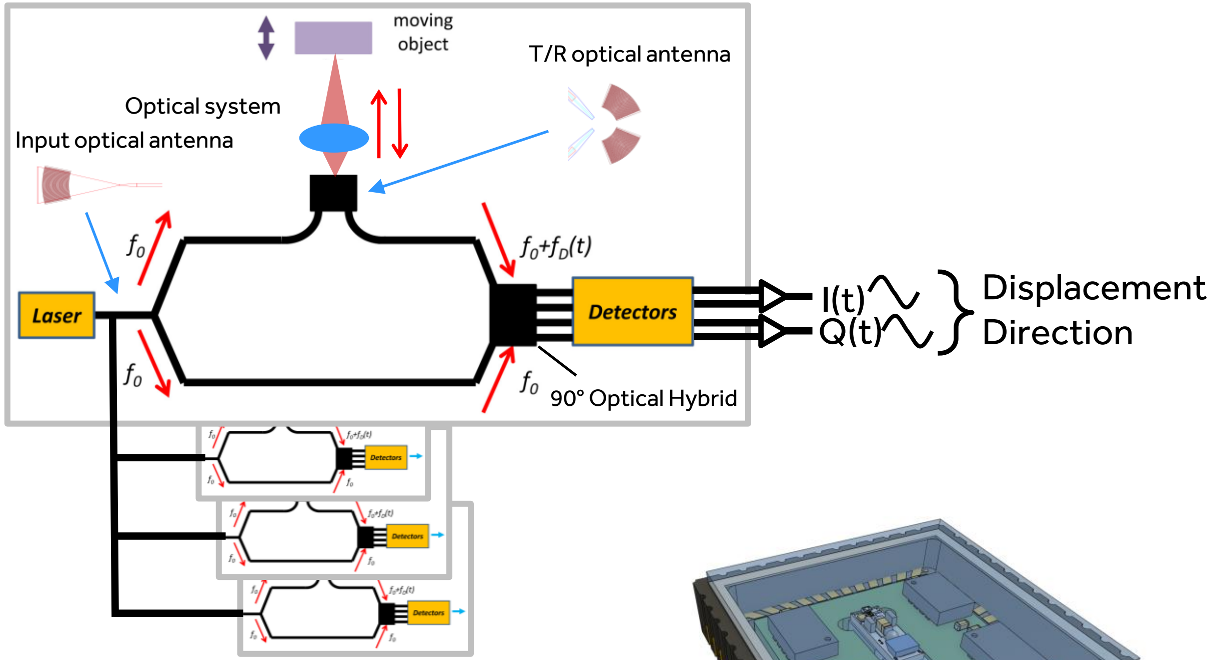


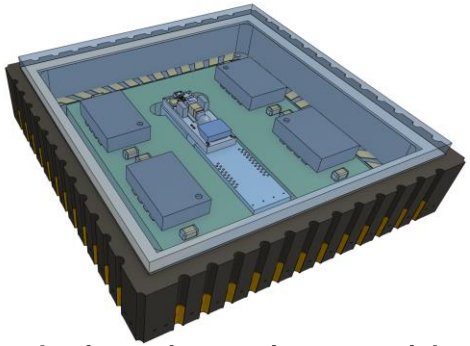
CVD Statistics 2017

Working principle - LDV



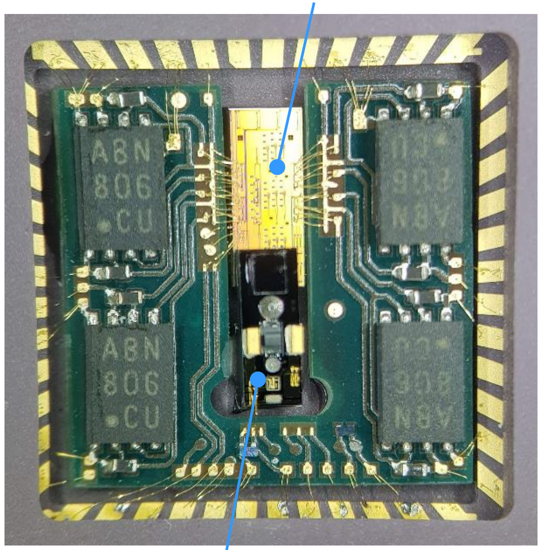
Four beam interferometer





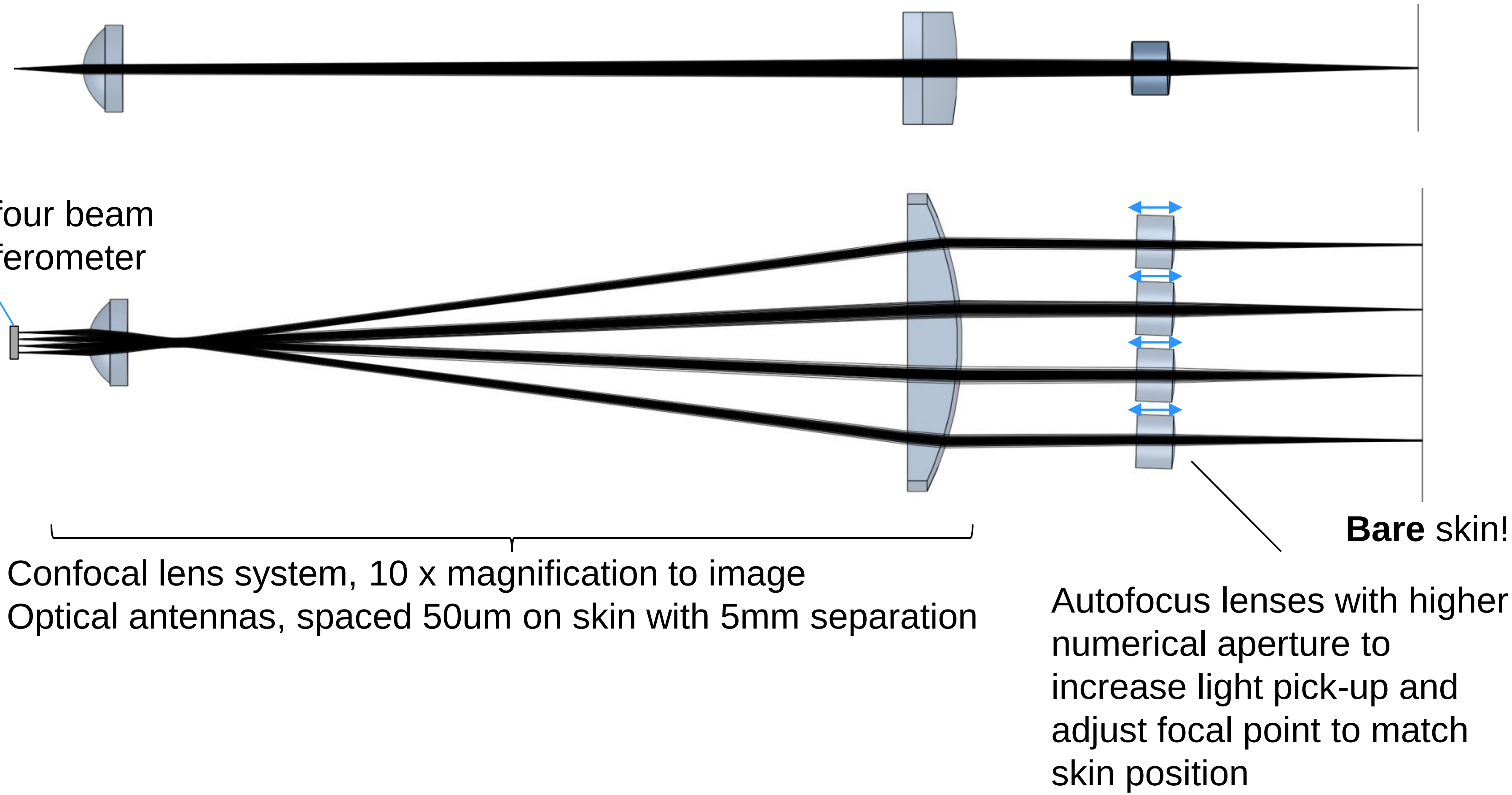
Sealed packaged assembly
with integrated amplifiers

Homodyne CMOS wafer scale M-Z
interferometer with Ge PDs



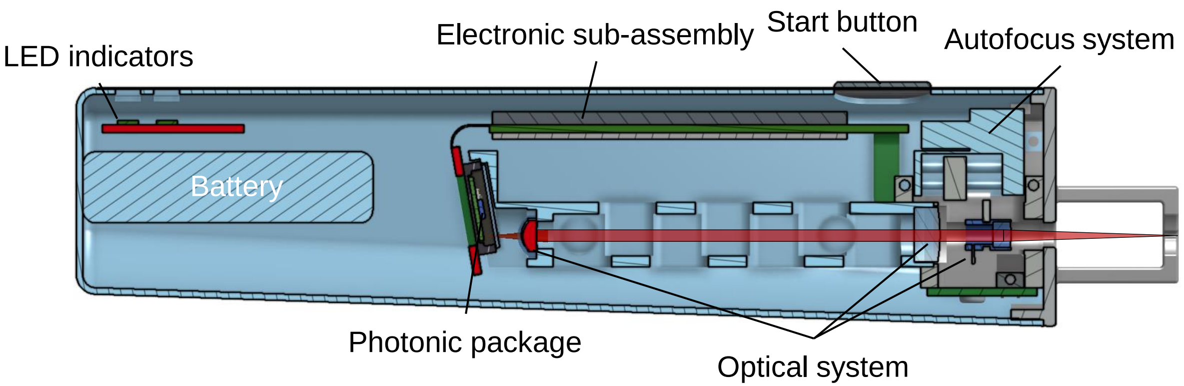
1310nm top mounted
laser assembly

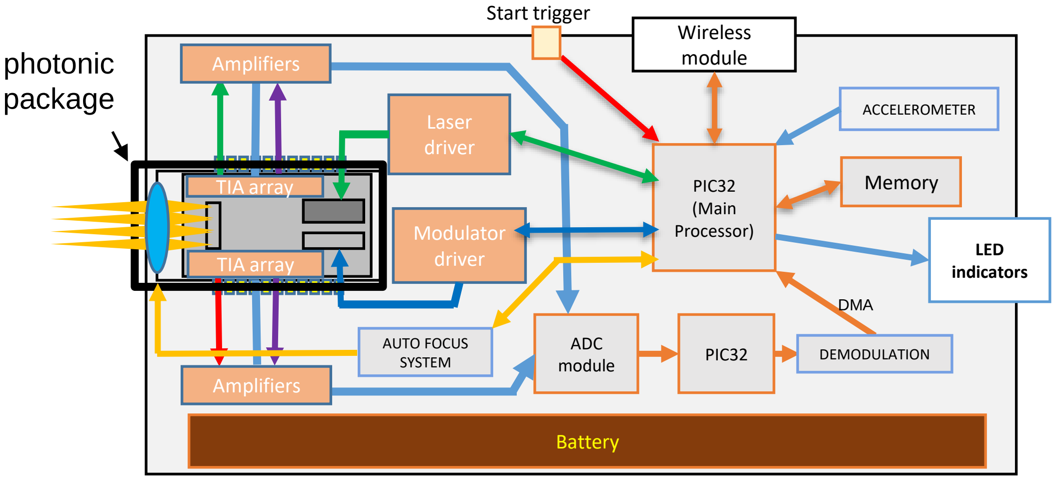
Optical system – measure vibrating bare skin



System diagram

- Handheld self contained, battery operated device
- Interferometer control
- Data acquisition
- Real-time demodulation and transmission of demodulated displacement time series data
- WiFi

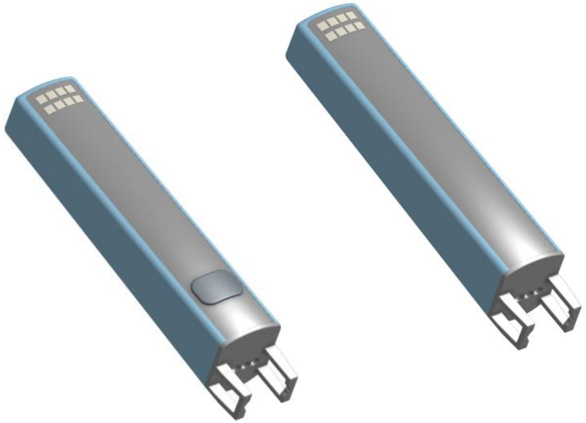




Overall concept

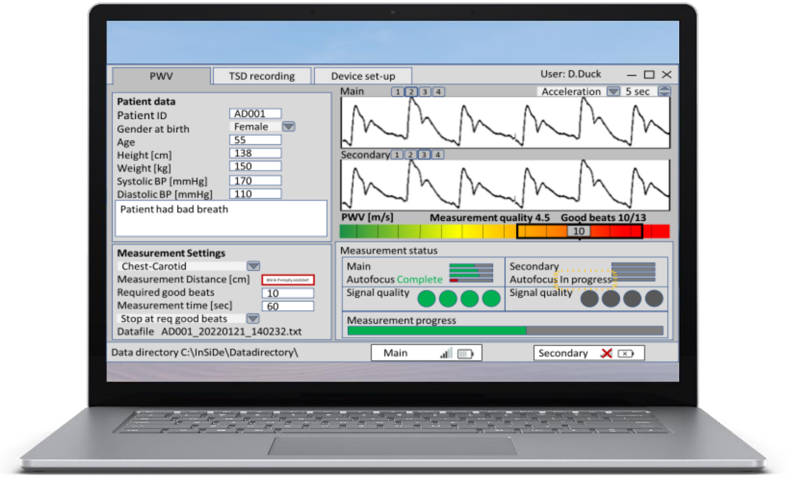
Main and secondary handpiece

- 4 beam laser interferometers
- Main/secondary synchronized measurements for PTT
- Local demodulation of raw signals to displacement data
- Wifi transfer of displacement data to external computer



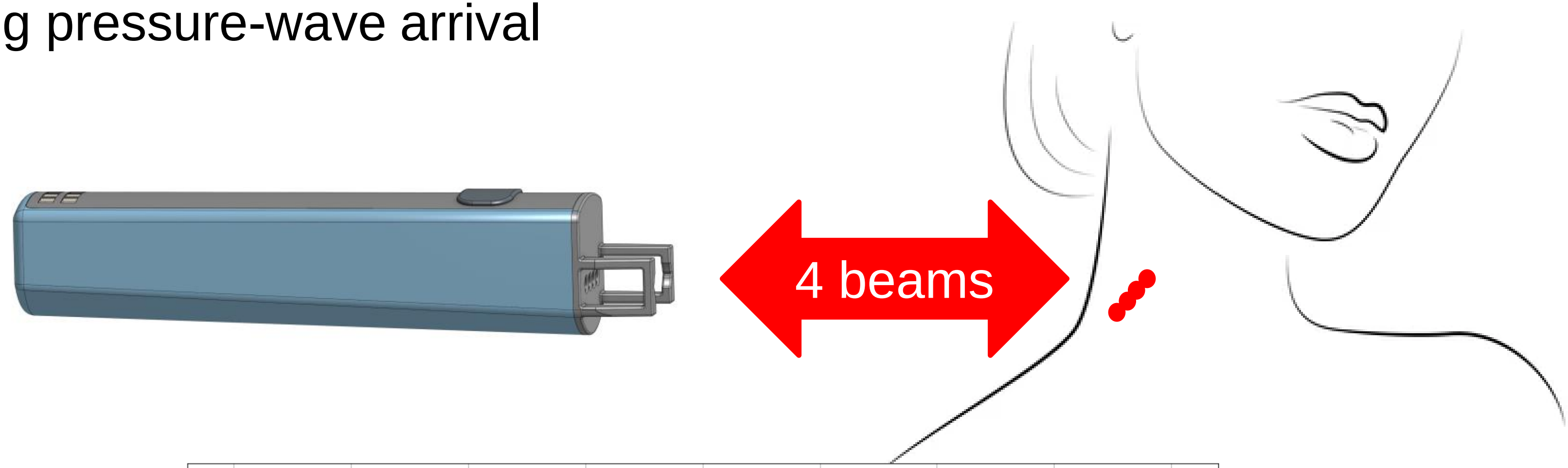
Laptop

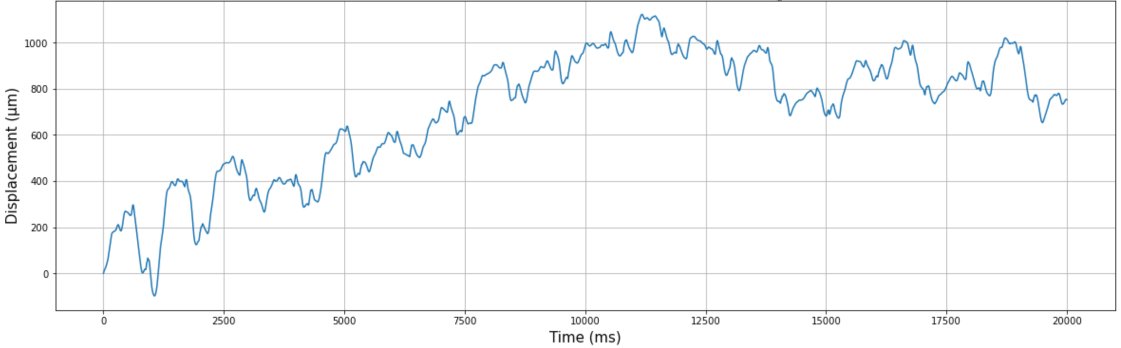
- Data processing
- Algorithms to get biomarker metrics
- Graphical user interface for data presentation



LDV Data

- Get displacement of skin in time following pressure-wave arrival

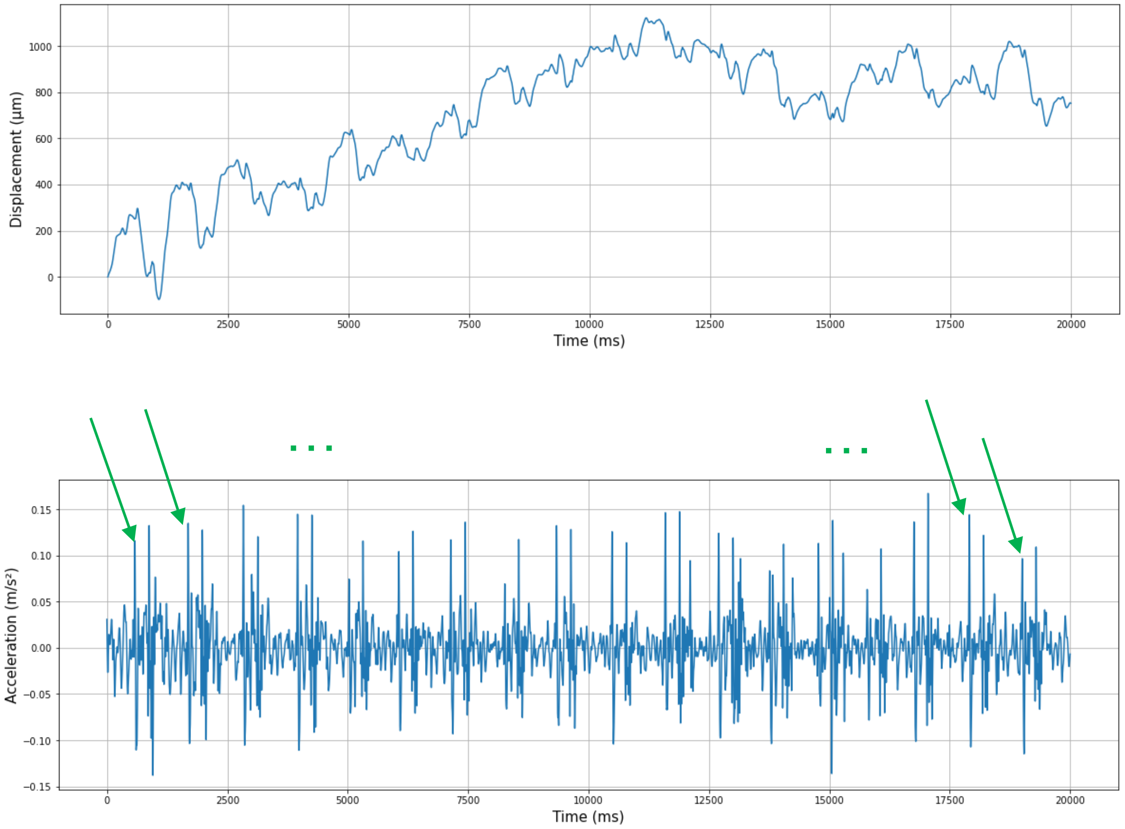




LDV Data

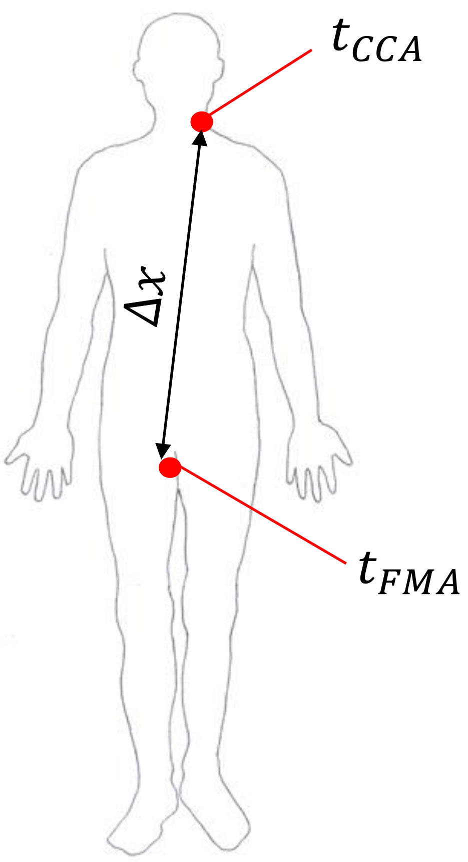
- Timepoint of interest for PWV?
    - Foot-of-the wave
    - Point of maximum acceleration

$$\frac{d^2x}{dt^2}$$



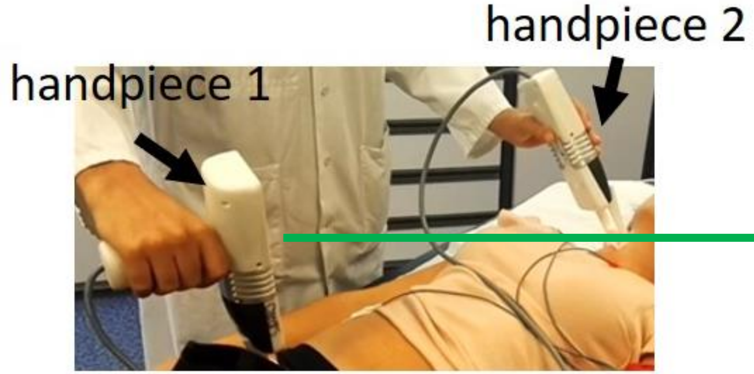
LDV Data

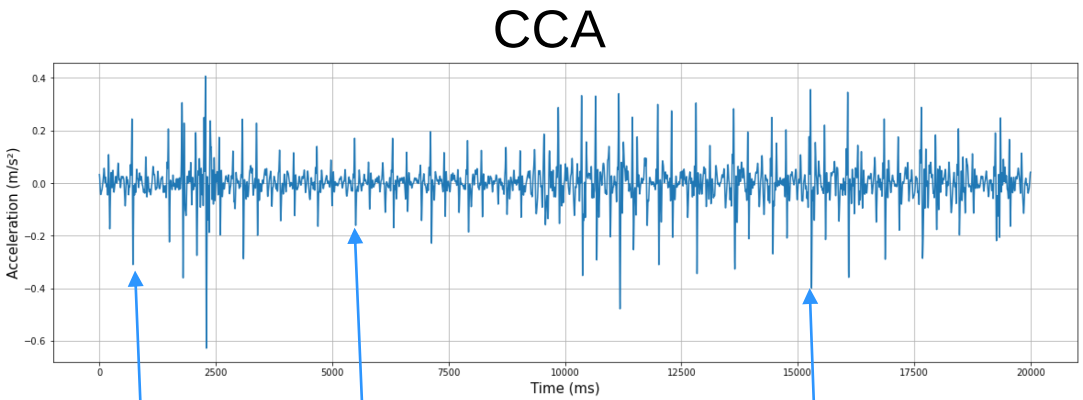
- carotid-femoral PWV as measure for arterial stiffness
  - Structure arterial wall allows elasticity
  - Pressure wave travels from heart to:
    - Carotid artery (CCA)
    - Femoral artery (FMA)
  - Measured time delay between arrival at both sites & distance → $\text{PWV} = \frac{\Delta x}{\Delta t} = \frac{\Delta x}{t_{FMA} - t_{CCA}} = \frac{\Delta x}{PTT}$
  - PWV increases as arteries stiffen

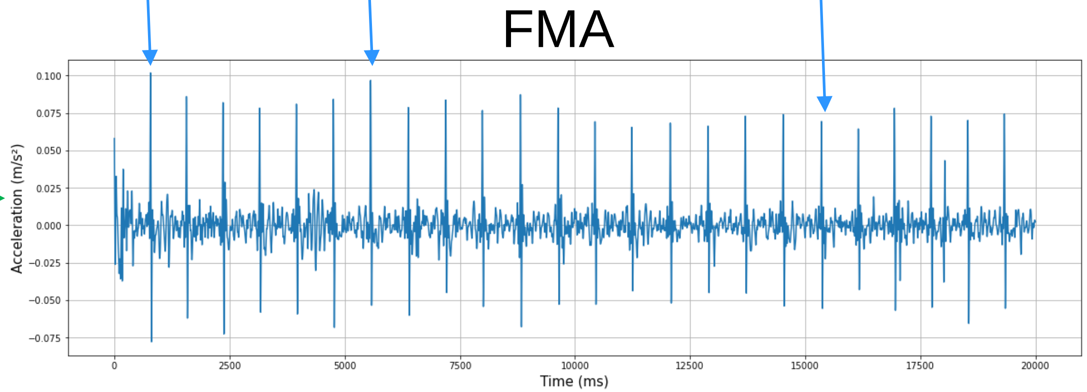


LDV Data

- PWV: Measure two sites simultaneously
- Get acceleration
- Identify correct peaks
- Estimate pulse transit times (PTT)



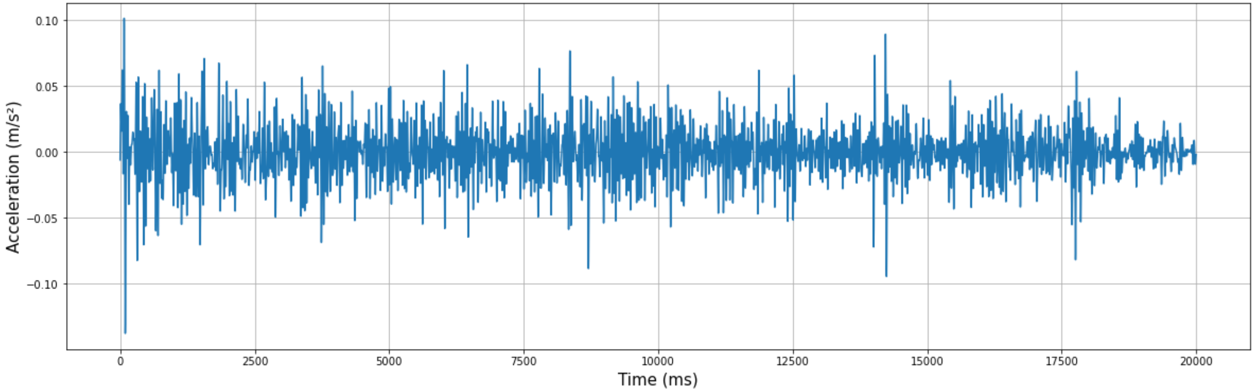




Signal quality assessment

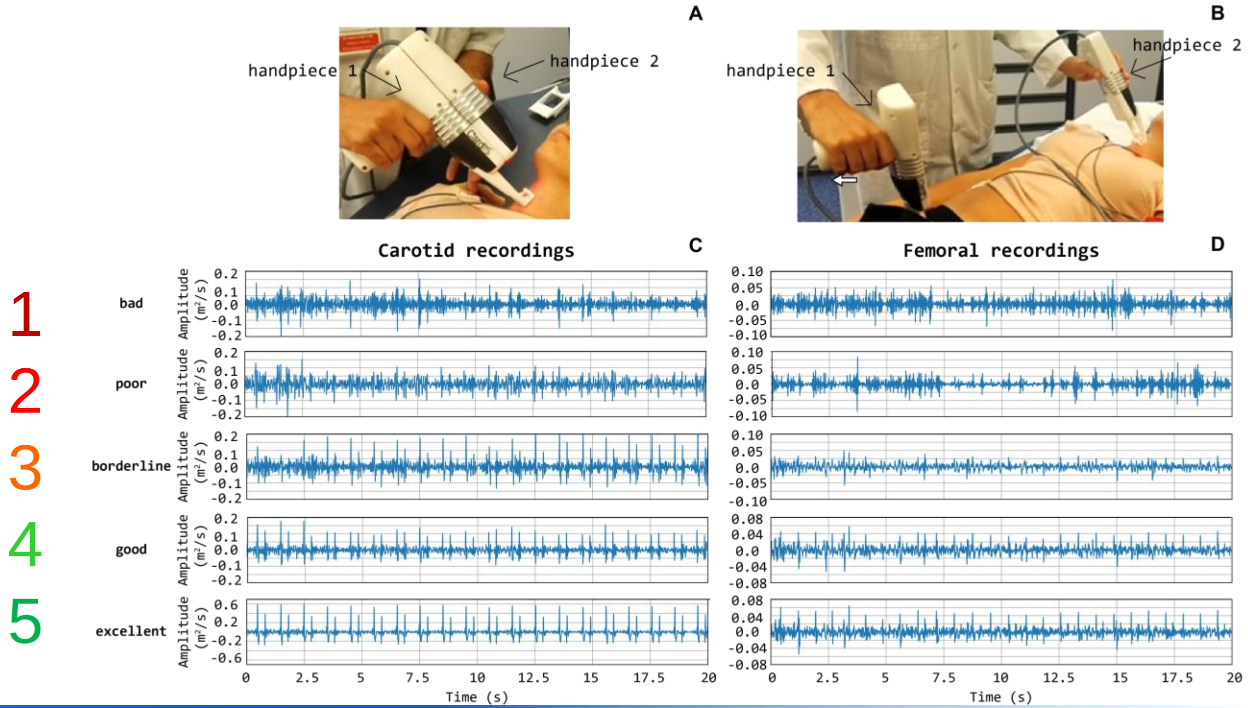
Need for quality metric:

1. Guide user to quality measurements
   - 4 beams to decrease positioning demands
   - Still difficult to find e.g. Femoral artery (FMA)
   - Need to know when poor quality signals → readjust positioning
2. Assess credibility of measurement
   - Only process qualitative signals for PWV, …



Quality assessment

- Ground truth: Visual scoring (Q_{vis}) done by prof. Patrick Segers
  - Manual score of every signal in our databases
  - Scale 1 – 5 (1 = very poor & 5 = excellent quality)

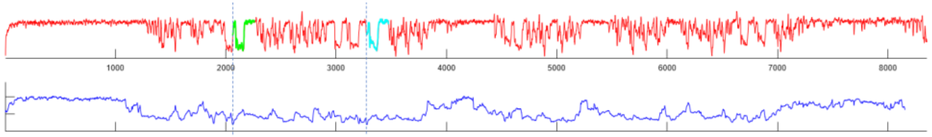


Quality assessment

Q_{vis}

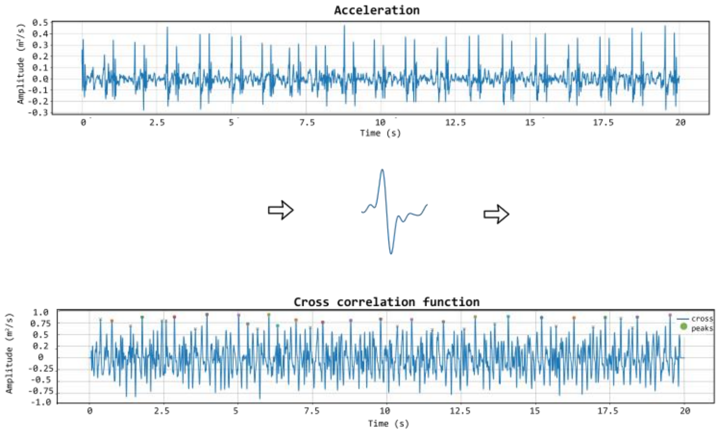
Q_{MP}

- Metric based on ‘the matrix profile’ (MP)



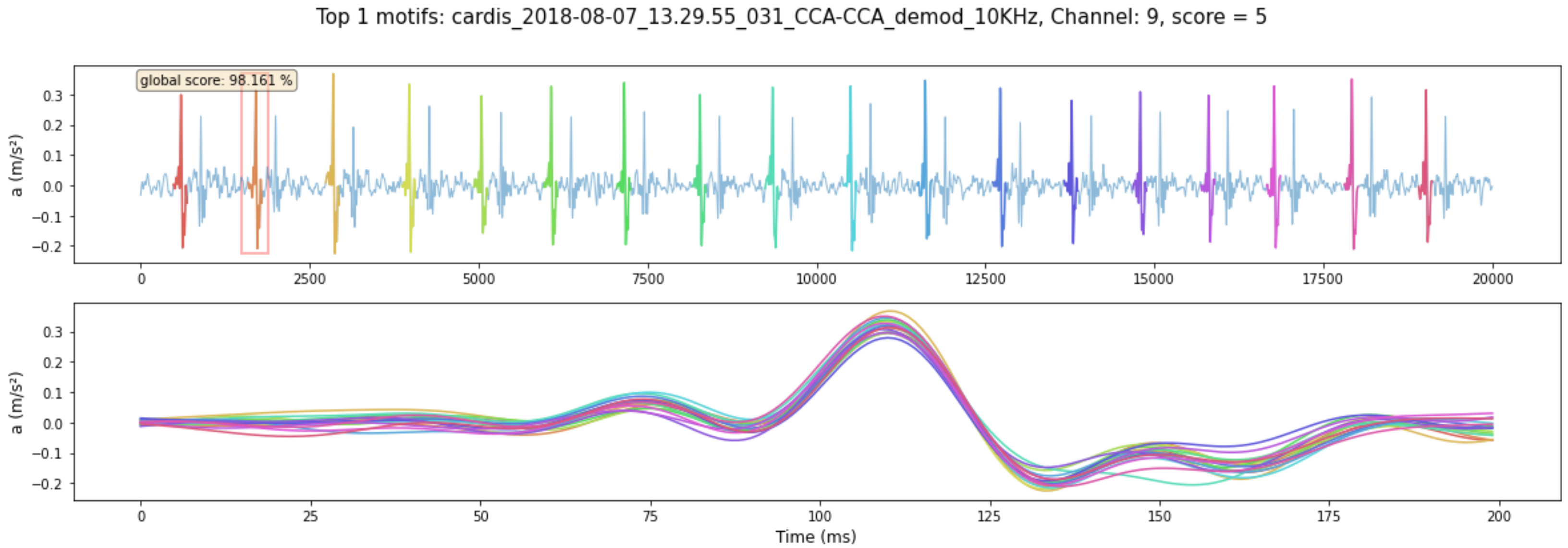
Q_{TM}

- Metric based on ‘Template matching’ (TM)



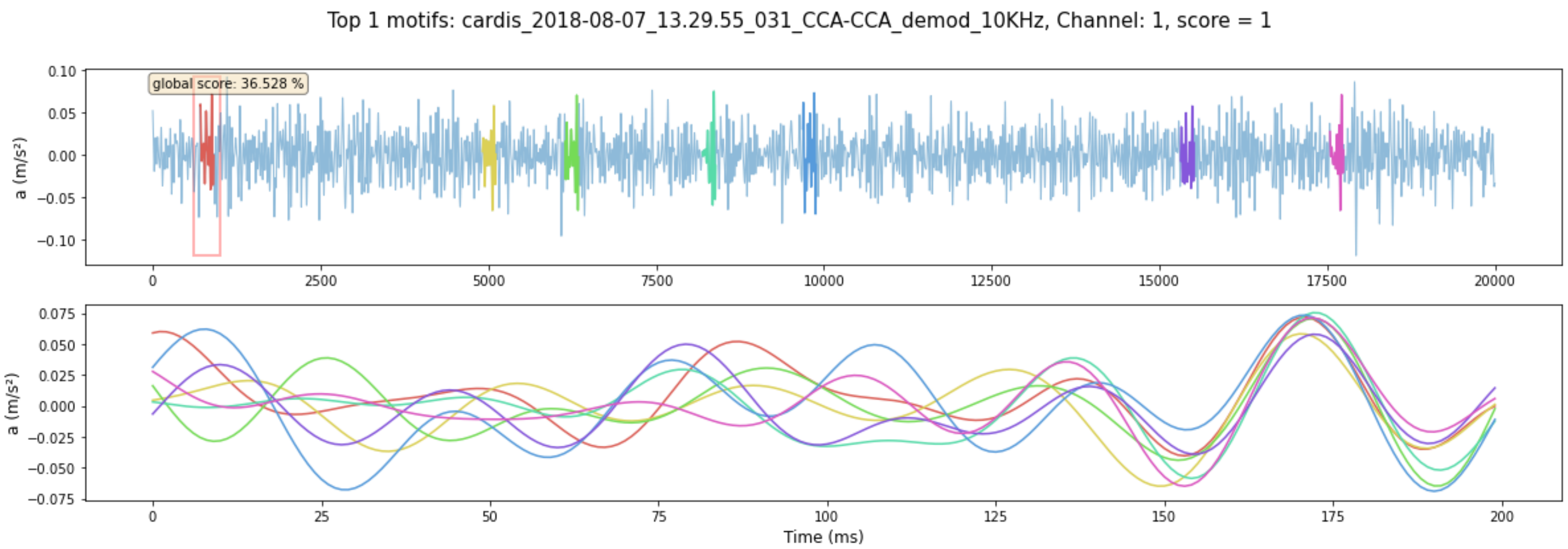
Quality assessment

- Example very good quality signal:
  1. All subsequences of similar amplitude
  2. Time - instants of peaks nearly identical
  3. All beats represented in motif (= recurring pattern in time)
- Automated score correlates with Q_{vis}



Quality assessment

- Example poor quality signal:
  - Noisy subsequences remain in motif
  - Again, automated score correlates with Q_{vis}



InSiDe

Template Matching and Matrix Profile for Signal Quality Assessment of Carotid and Femoral Laser Doppler Vibrometer Signals

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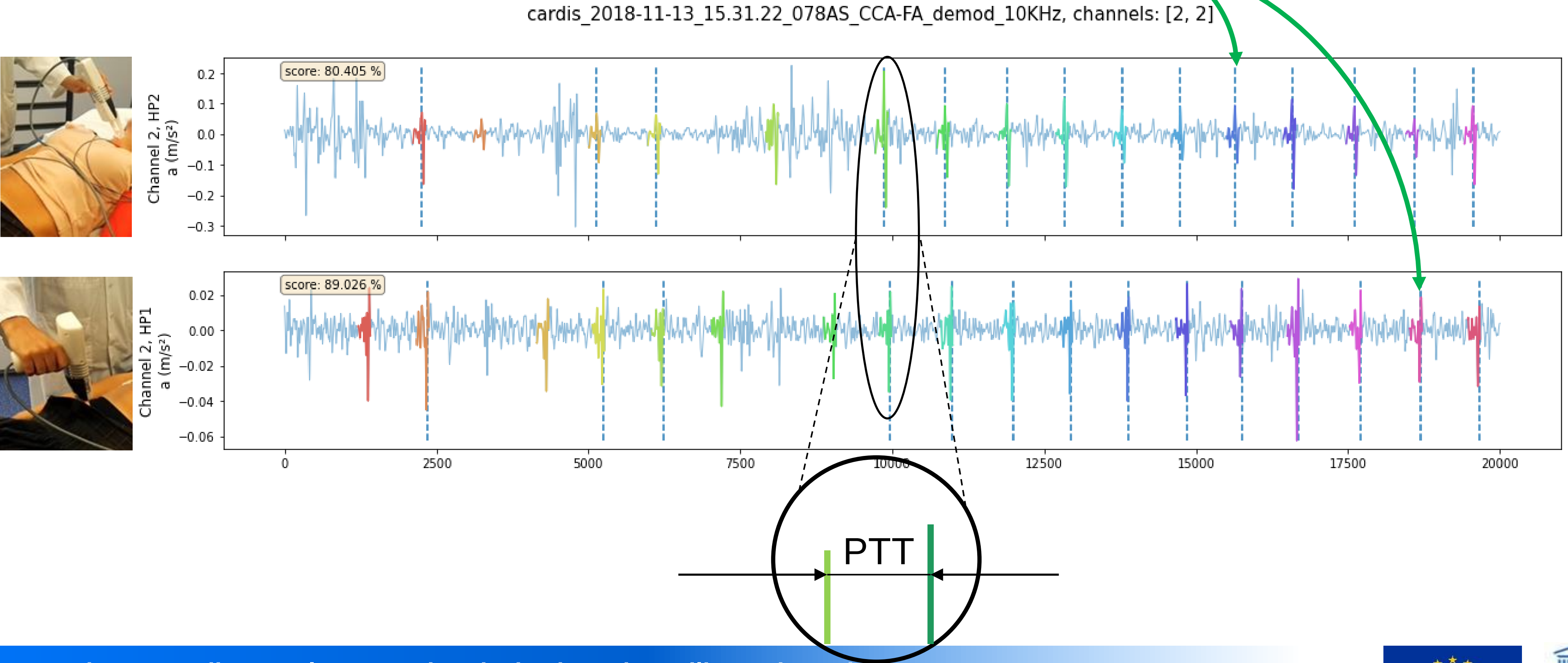
PWV strategy

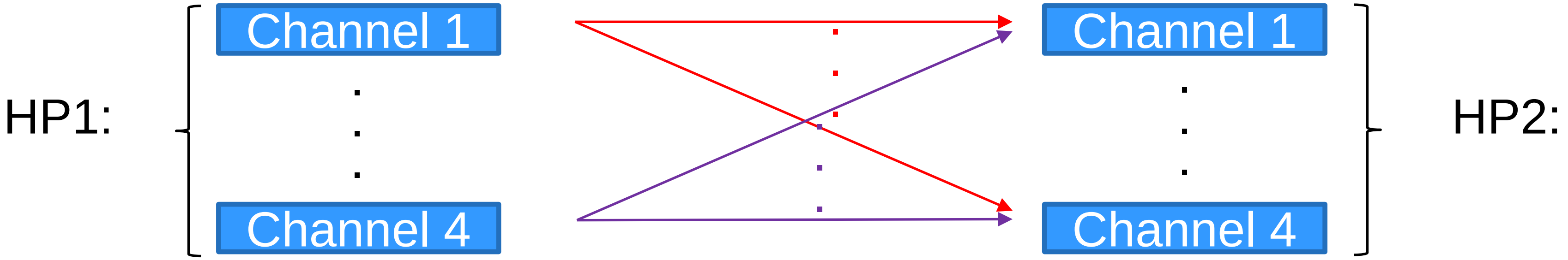
- Interested in finding pulse transit times (PTT)
- Motifs derived by MP or TM possible, currently TM



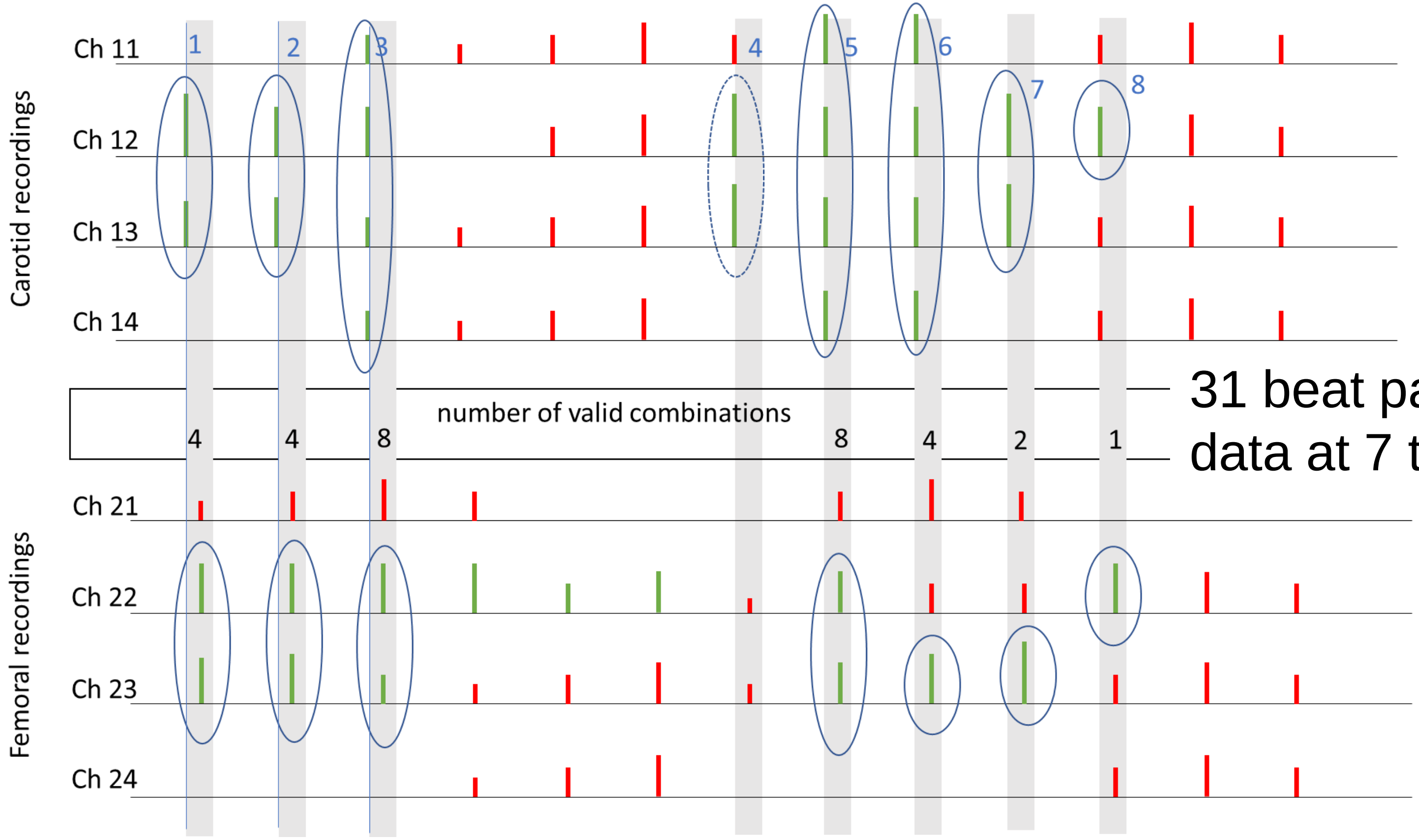
PWV strategy

- Current strategy:
  - Consider all channel pairs of 1 dataset: HP1 – HP2
  - Get PTT’s
  - in our case: 16 combinations = 16 arrays of PTT values
- Ideally, use only high quality signals

DATASET: cardis_2018-11-13_15.31.22_078AS_CCA-FA_demod_10KHz



PWV strategy

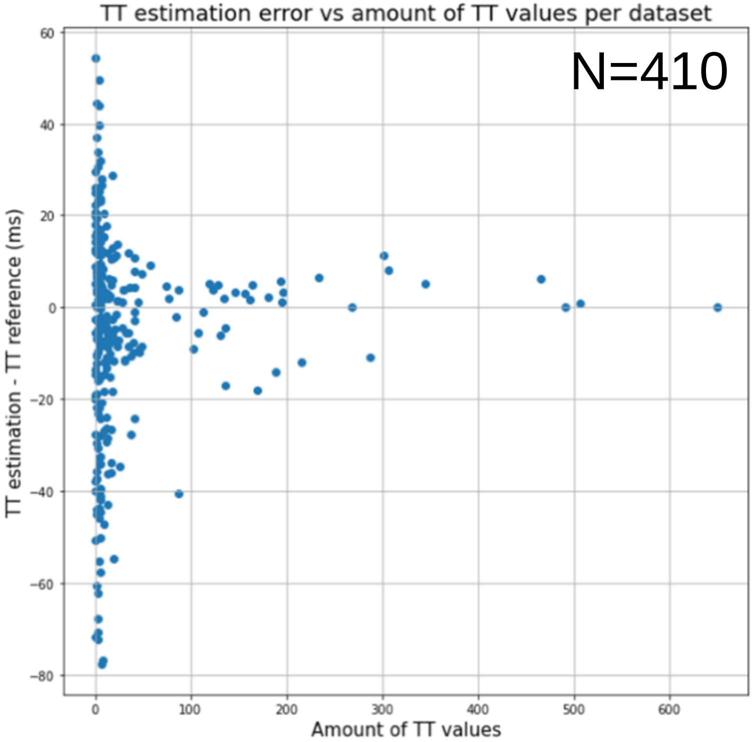


31 beat pair combinations
data at 7 time points

→Take median PTT as final estimate of recording

PWV strategy

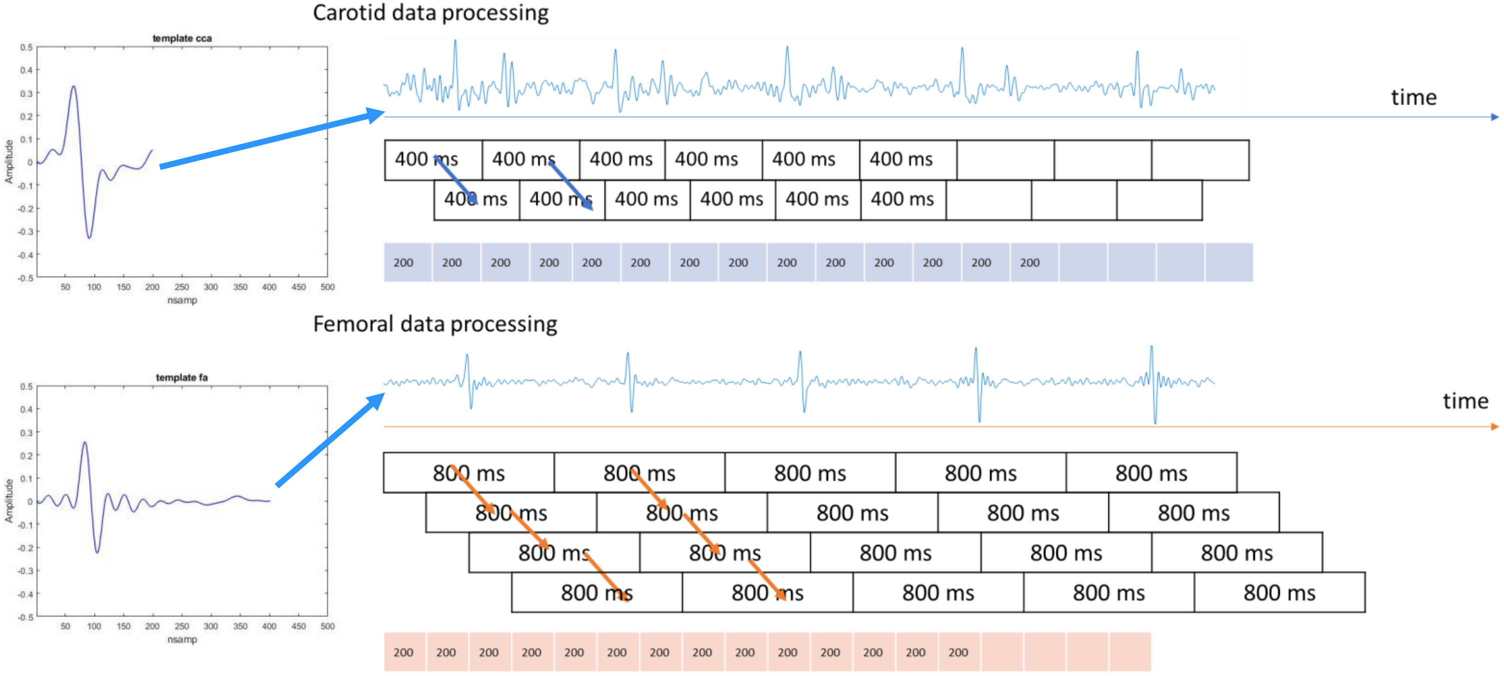
- Compare with PTT values from reference (CARDIS)
- Factors having an impact:
  - Total number of PTT estimations (BP) in 1 dataset
  - Number of timepoints at which transit time estimations are made (TP)
- Conclusion: Need enough BP & TP!

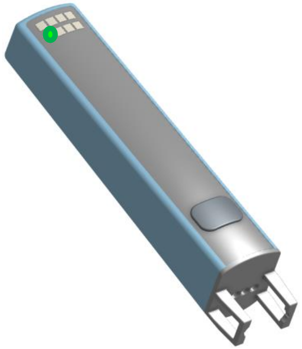


The higher the number of TT estimates for a given dataset, the higher the agreement with the reference

Real-time implementation

- Real time quality measure: xcorr with template ≥ treshold → LED
- (near) real time PWV estimation
- Measure until BP ≥ 75 & TP ≥ 5 → compute PTT & PWV





Next steps

- Release of clinical investigational device (in development)
- Algorithms for stenosis detection & assessment of cardiac contraction patterns
- Beamforming – combining qualitative beams to reduce stochastic noise → increase SNR

Funded by the European Union's Horizon 2020 Programme under Grant Agreement No. 871547

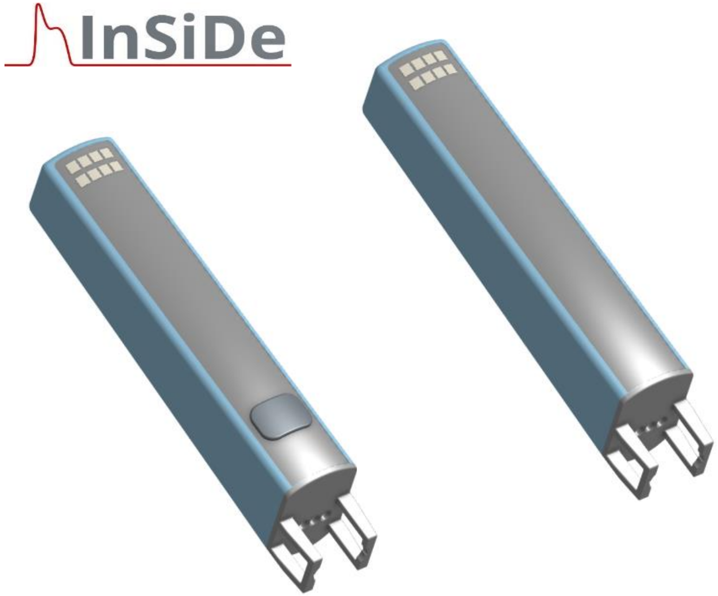
Questions?

http://www.inside-h2020.eu

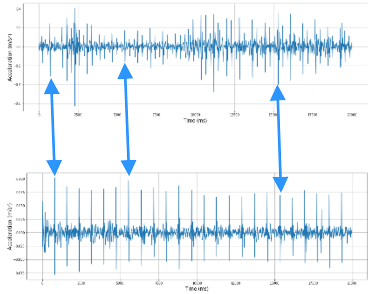
Quick Summary

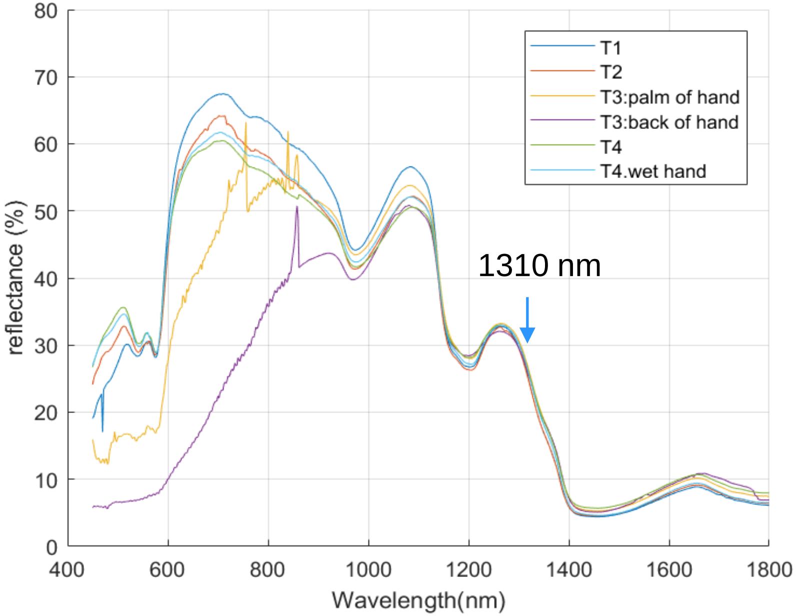
InSiDe Objective:

- handheld wireless clinical investigational CVD **screening** device
- Clinical feasibility studies → prove efficacy and usefulness to **GPs** and cardiologists

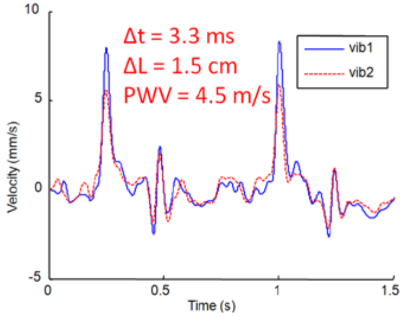


Backup slides

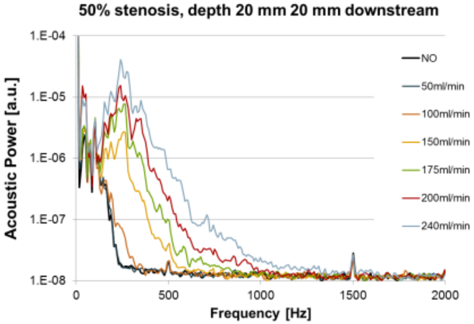




reflectance (%)
Wavelength(nm)
T1
T2
T3:palm of hand
T3:back of hand
T4
T4.wet hand
1310 nm
0
10
20
30
40
50
60
70
80
400
600
800
1000
1200
1400
1600
1800



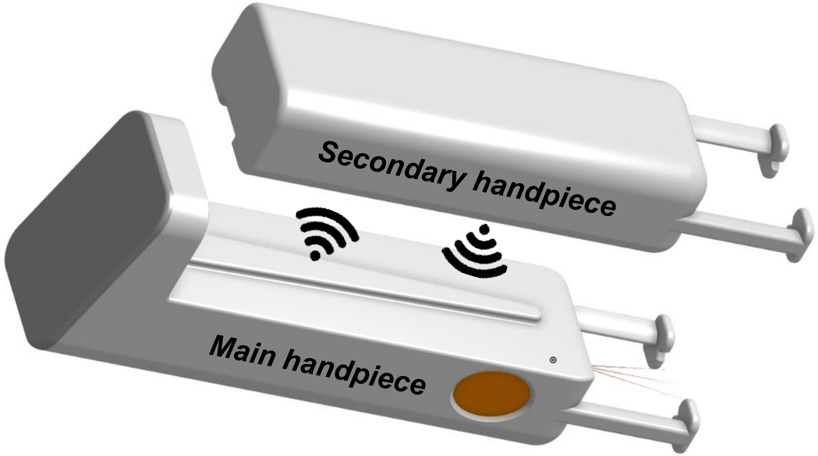
Δt = 3.3 ms
ΔL = 1.5 cm
PWV = 4.5 m/s
vib1
vib2
Velocity (mm/s)
Time (s)
10
5
0
-5
0
0.5
1
1.5

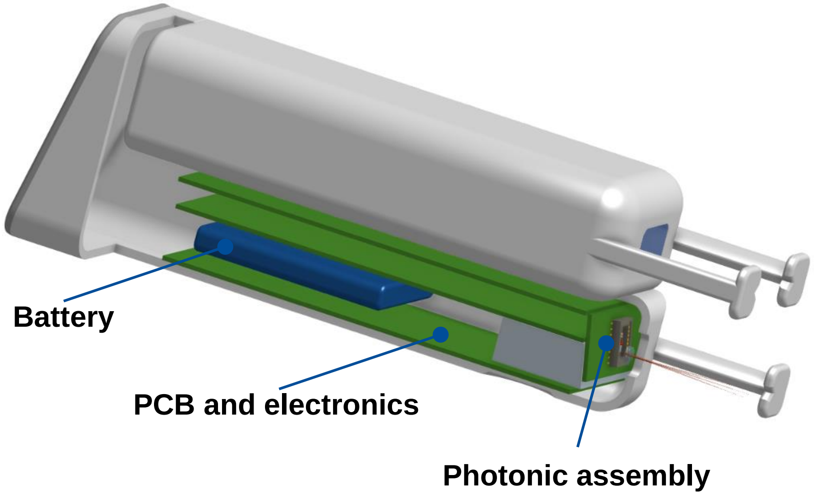


50% stenosis, depth 20 mm 20 mm downstream
Acoustic Power [a.u.]
Frequency [Hz]
NO
50ml/min
100ml/min
150ml/min
175ml/min
200ml/min
240ml/min
1.E-04
1.E-05
1.E-06
1.E-07
1.E-08
0
500
1000
1500
2000

Overall concept

A handheld, battery-operated split device, which can be operated as one unit as well as two separate units and can conduct timed recordings in order to measure pulse wave velocity, arterial stenosis and cardiac contraction patterns.

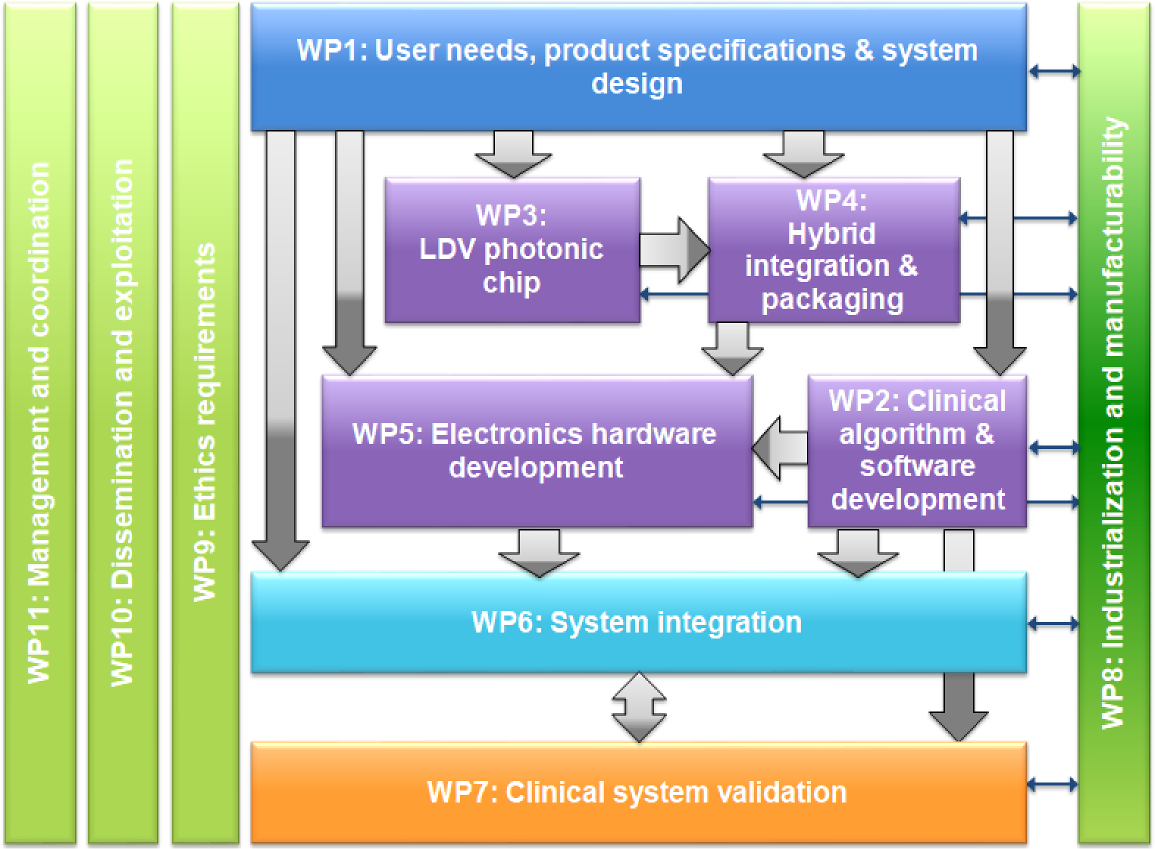




Overall concept

- Device based on a 4-beam laser Doppler interferometer in each demonstrator half part.
- 1300nm operation to assist direct measurement on skin
- Silicon-on-Insulator photonics technology used to manufacture the 4-beam LDV chip.
- Integrated spacer for robust measurement of the targeted cardiovascular feature (superficial artery, chest cage for heart contraction patterns).
- Wireless connection between devices and to external computer/smart phone
- Interferometer control and demodulation integrated in the handheld device
- Simple user interface to guide operator during measurement
- Further signal processing algorithm and advanced user interface on external computer

Project structure



WP1 - User needs, product specs, system design

- Define the user requirements and translate to system specifications.
- Conduct overall system design.
- Steer the S&T activities to be consistent with end-user requirements.
- Detail regulatory pathway for a first product.

WP2 – Clinical algorithm and software development

- Update the CARDIS data-acquisition software with real-time visual feedback on acceleration signals and beat detection.
- Demonstrating the feasibility and validation of LDV-measured heart-carotid pulse wave velocity as a biomarker of ascending aorta stiffness.
- Demonstrating the feasibility and validation of LDV-measured chest motion as biomarker of cardiac contraction and abnormalities in heart valves.
- Demonstrating the feasibility and validation of LDV measurements to assess carotid artery stenosis.
- Real-time assessment of carotid-femoral Pulse Wave Velocity, heart-carotid Pulse Wave Velocity, cardiac contraction and valve abnormalities using Laser-Doppler vibrometry.

WP3 – LDV photonic chip development

- Design, fabricate and characterize an LDV PIC for 1.3 µm light and with designs for speckle mitigation.
- Design and fabricate a working optical system.
- PIC design to ensure that light signals with a total power of at least 20 mW can be sent into the PIC without a strong insertion optical loss (<3dB) in the waveguide sections of the LDV PIC.
- The performance of the LDV PIC should be robust against normal chip fabrication deviations.

WP4 – Hybrid integration and packaging

- Design of an integrated laser assembly (MOB) that is compatible with a scalable fabrication and integration approach.
- Development of a scalable and volume compatible MOB assembly and integration process.
- Develop a prototype photonic sub-system for use in early electronic system and clinical tests.
- Develop a final photonic sub-system that is scalable and compatible with volume production.

WP5 – Electronics hardware system development

- Design of a two-part electronic system for data collection, processing and synchronization of results.
- Develop an analogue preconditioning circuit to convert signals from the photonic device into digital format
- Develop a circuit to process and store data
- Develop a circuit to synchronize the two hand pieces of the InSiDe demonstrators
- Develop a circuit to charge the internal batteries of the InSiDe demonstrators.

WP6 – System integration

- Deliver two additional samples of the CARDIS Demonstrator device.
- System integration of two generations of InSiDe clinical investigational device (InSiDe-α and InSiDe-β)
- System verification and release of the InSiDe-α and InSiDe-β clinical investigational devices.

WP7 – Clinical system validation

- Proof-of-principle validation of LDV measurements in patients for assessing 1) carotid artery stiffness, 2) carotid artery stenosis, 3) cardiac contraction and 4) cardiac valve dysfunction.
- Clinical validation will be conducted using the CARDIS system from M1 to M28, with the InSiDe-α prototype system from M28 to 42 and with InSiDe-β optimized version from M43 to M48
- Generation of a research & evidence roadmap for further internal and external clinical validation for multiple indication.

WP8 – Industrialization and manufacturability

- Evaluation of design for volume manufacture.
- Supply chain, cost analysis and market value assessments.
- Environmental and life cycle assessment.

Consortium partners

imec	Imec is a world-leading independent research center for nano electronics and nano technology. Imec's research bridges the gap between fundamental research at universities and technology development in industry.
Medtronic	Medtronic is the world's largest medical technology company, offering a wide range of innovative therapies within the fields of cardiac and vascular diseases, diabetes, neurological and musculoskeletal conditions.
GHENT UNIVERSITY	Universiteit Gent (UGent) is the 2nd largest university in Belgium. Participating labs are the Photonics Research Group (optics and chip technology), IBiTech-bioMMeda (arterial mechanics and physiology) and IDLab (signal processing expertise).
Tyndall National Institute Institiúid Náisiúnta	Tyndall has a long and successful track record in participating in and coordinating EU projects. A key focus within these projects is the development of silicon photonic-based technologies, where Tyndall is a principal packaging partner.
POLITECNICO DI TORINO	For 160 years, Politecnico di Torino has been educating engineers, architects, designers and urban planners with integrity, a rigorous approach and according to high quality standards. These professionals have been playing an important role in the growth of our city, our industry and our country.

Consortium partners

InSiDe

MICROCHIP	Microchip Technology Caldicot Ltd is a leading provider of smart, connected and secure embedded control solutions. The company's solutions serve more than 120.000 customers across the industrial, automotive, consumer, aerospace and defense, communications and computing markets.
ARGOTECH	Mission of Argotech is to provide worldwide customers manufacturing services, customized product design and process development, engineering services and consulting in the field of optics, electronics and mechanics.
Inserm La science pour la santé From science to health	INSERM is a French public scientific and technological institute dedicated to biomedical research and human health. Among the most prestigious research institutions in the world, it is involved in the entire range of activities from the laboratory to the patient's bedside. One of these teams is dedicated to clinical research concerning large arteries. INSERM is associated with Université de Paris, which has a strong dominance in biology, medicine and biotechnology.
Maastricht University	Universiteit Maastricht has 5 faculties, including Health, Medicine and Life Sciences (FHML). This latter faculty is linked to the Maastricht Universitty Medical Center (MUMC). FHML and MUMC are dedicated to cardiovascular diseases.
Fundi€o	Fundico is a consultancy company with the objective to assist industrial companies and research organisations with the submission of financing R&D proposals and the management and coordination of these R&D projects in case of financing.