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Listening to Molecules

Photoacoustic Medical Imaging and Sensing: High-power Compact VCSEL Subsystem as Game-changer

Meeting on Photonics Technologies for
Medical Diagnosis and Treatments at ICFO 4.12.2024

Dr. Patrick Leisching
CTO iThera Medical GmbH

Founded 2010 als IBMI Spin-off
Ca. 60 employees, 50 in Munich headquarter
2023: ca. 5 M€ revenue

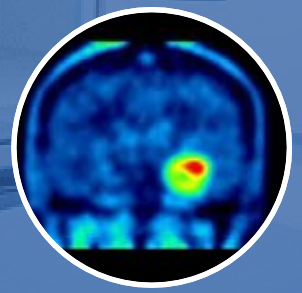
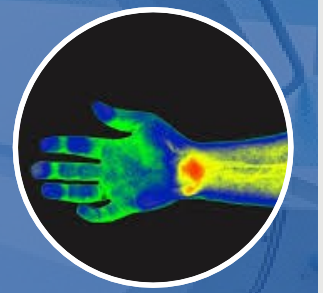
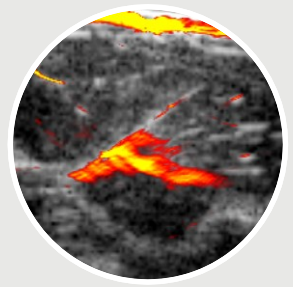
Agenda:

- **A short history of medical imaging technologies**
- **The basic parameters to understand photoacoustic medical imaging**
  - Crash course
  - What molecules & where is the sweet spot?
- **Hardware components of photoacoustic systems**
  - The technology gap between today and tomorrow
  - Subcomponents today & tomorrow
- **Does it work?**
- **Todays and future markets**
- **Conclusion and outlook**

OPTOACOUSTIC: A BREAKTHROUGH IMAGING TECHNOLOGY

1890s	1940s	1970s	1980s	1990s	2020s
X-Ray	Ultra-sound	CT	MRI	PET/ SPECT	Optical	OAI



What happens to light in tissue?

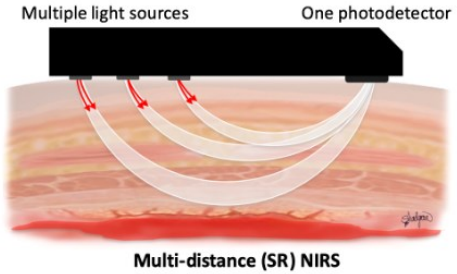


Fig. 1 A multi-distance SR NIRS sensor.

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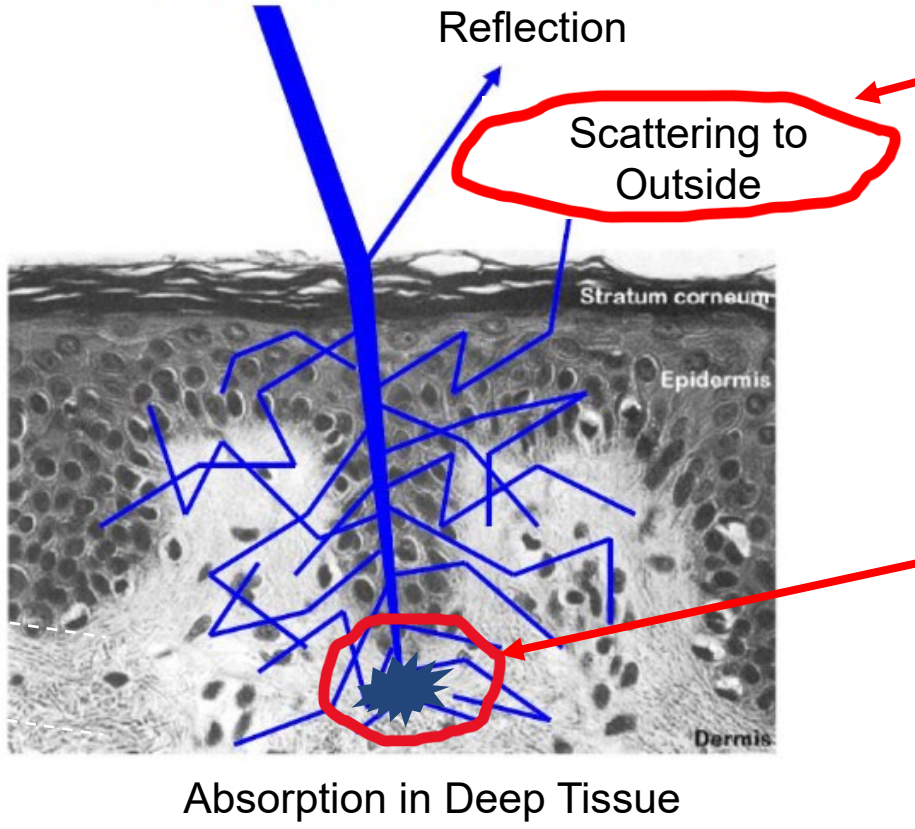

Near infrared spectroscopy:

diffusion length ca. 1mm, averaged scattered light

Optoacoustic effect:

ToF images up to 3-4cm, as ultrasound back-signal is less scattered & absorped

W. Bäumler, "Wechselwirkung von Licht und Gewebe", Lasertherapie der Dermatologie, Springer, 2006

OPTOACOUSTIC IMAGE FORMATION: ‘LIGHT IN, SOUND OUT’

MSOT = Multispectral Optoacoustic Tomography

MPE-limit@700nm: 20mJ/cm² & 200mW/cm²

Light absorption in tissue (standard concentration):

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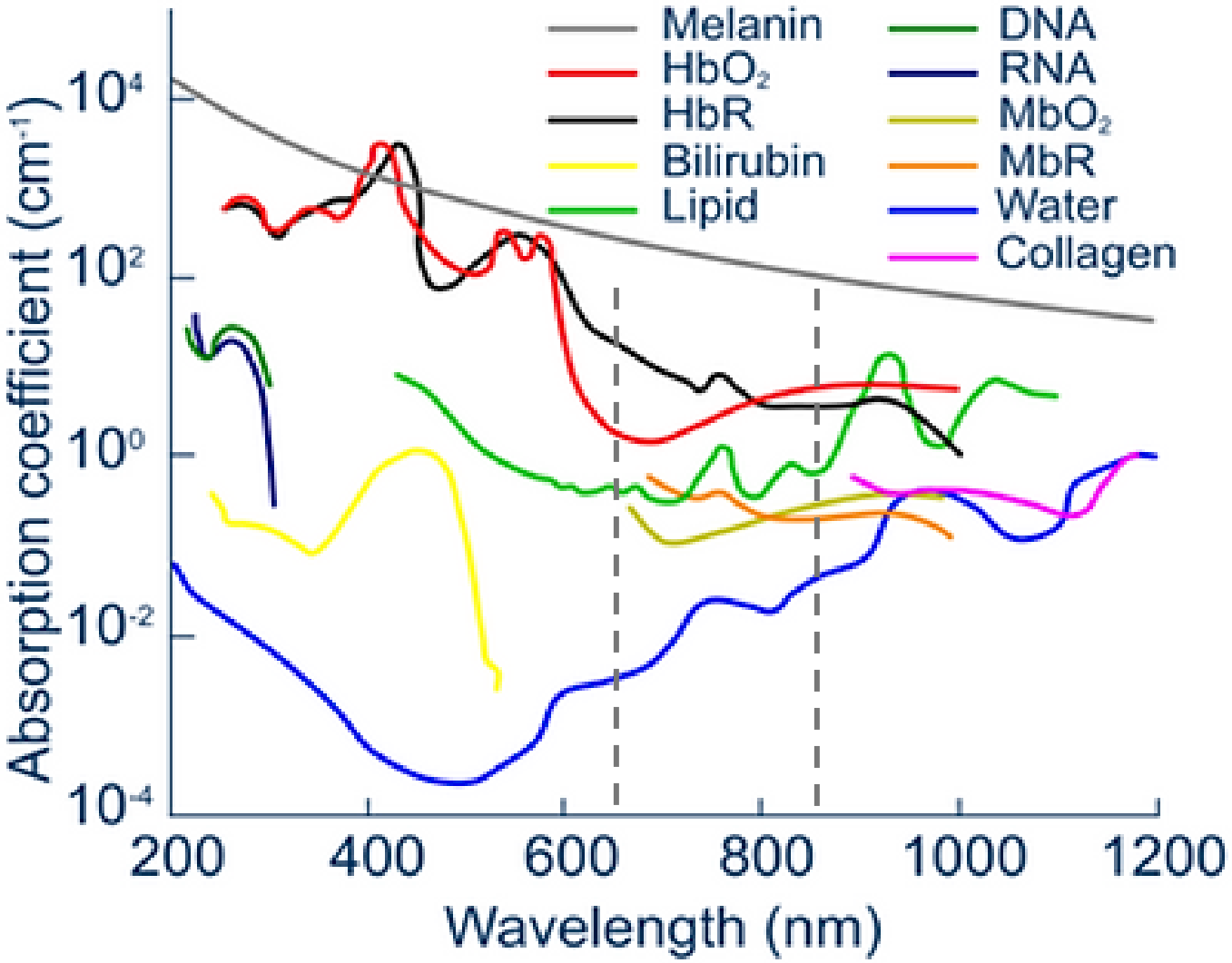
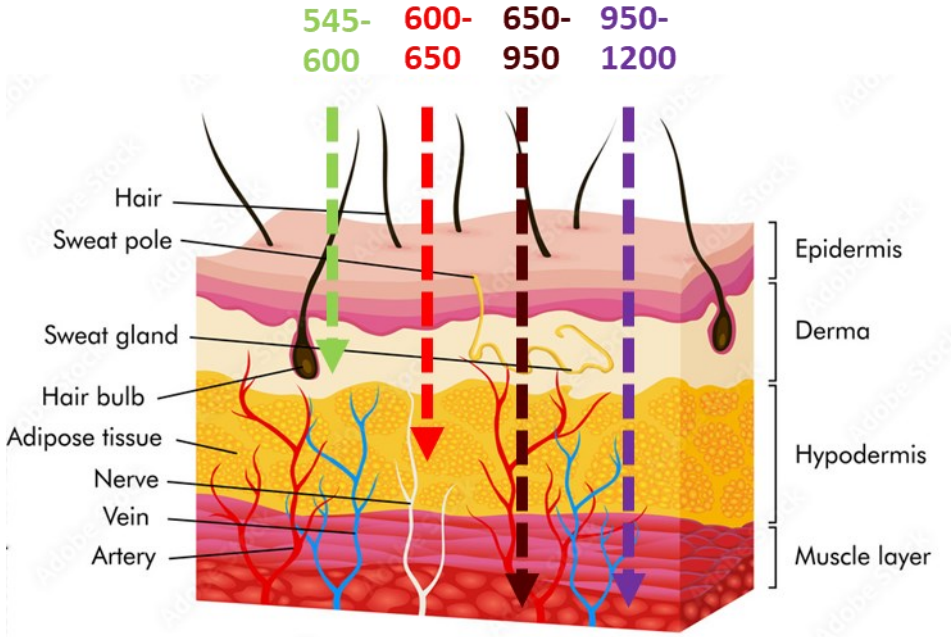
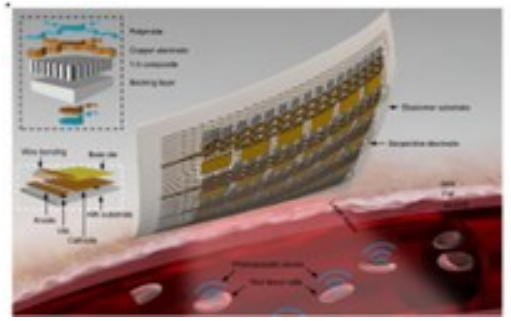




- High resolution surface vessels: 545-600nm
- Muscle oxy/deoxy: 650-980nm
- Muscle collagen: 900-1200nm


Off-label use
Leica

For wide-use there is a technology gap...



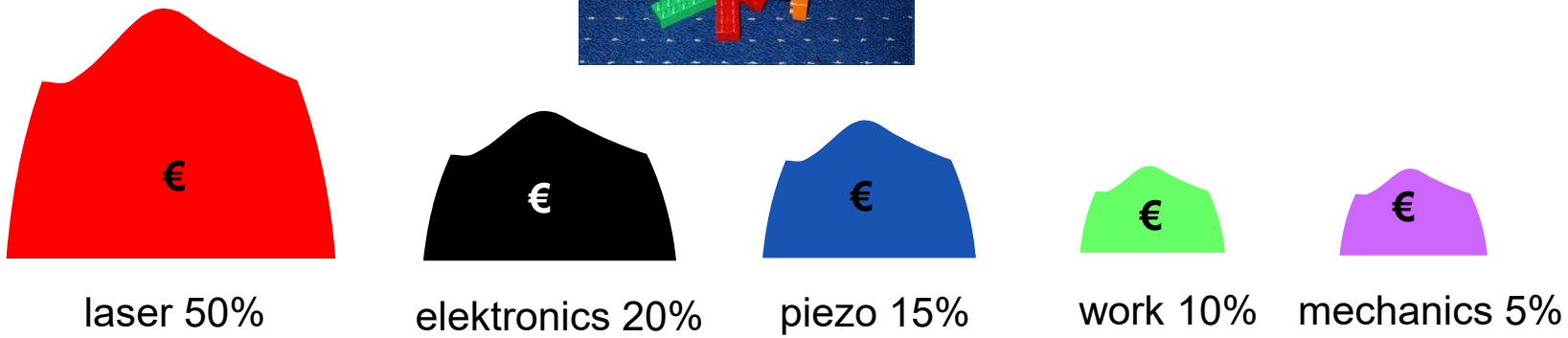
preclinical research (2012)

clinical research (2019, MDD)

clinical routine (2024, MDR/FDA)
BOM basis 500€/kg, total 200-400k€

specialist point-of-care endoscopie / laparoscopie sensors
BOM scales 100€-10k€; basis 10€/mm^2

Subcomponents of the photoacoustic devices

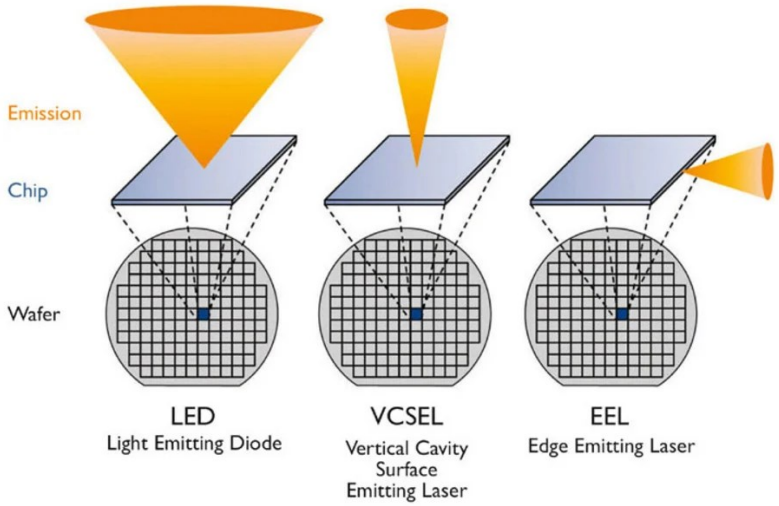


laser 50% elektronics 20% piezo 15% work 10% mechanics 5%

Overview photon sources for photoacoustic:

(VCSEL = vertical-cavity surface emitting laser)

	Wall-plug efficieny	CW power	Wavelength	Fiber-coupling	Pulse length 5-100ns	Arrays	3D integration w electronics	Speckle/ hot spots	Used by
YAG+OPO	<1%	1-10W (10ns/10mJ/25Hz)	680-1300nm (tunable)	yes	no	0D	no	yes	iThera 2024
LED	6.8%	100mW (10W 2D array)	350-1500nm (single lines)	no	no	2D class 1	no	no	Cyberdyne Acoustic X
Laser diode (edge)	50%	1W (100W 1D array)	405-1500nm (single lines)	yes	yes (GaN, discrete)	1D	yes, GaN	yes	Research
VCSEL diode (vertical)	50%	10mW (100W 2D array)	405-1500nm (single lines)	yes	yes (CMOS on chip)	2D class 1	yes, ToF CMOS	low	iThera 2025



- Only laser diodes & VCSEL enable high integration & wall-plug efficiency
- LED & VCSEL arrays: laser class 1
- Special applications with higher concentrated power: laser diodes
- Low-cost scalable mm^2 platform w integrated ToF electronics: VCSEL
- PICs: LD yes, VCSEL no

iThera strategic plan: replace YAG+OPO/Piezo by dual-wavel. VCSEL/ToF & PMUT/IC for perfusion/oxygenation

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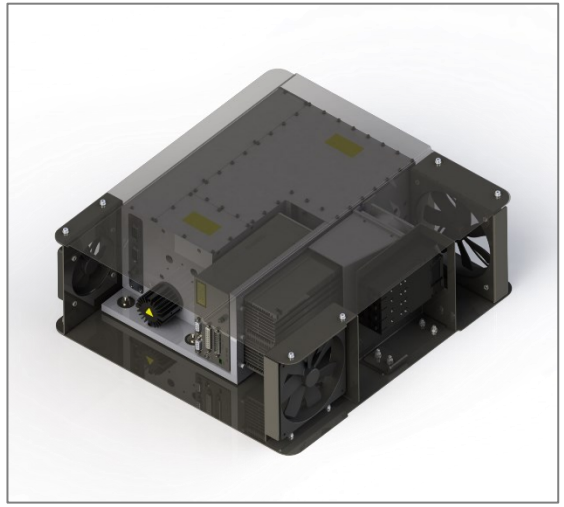
Control Panel

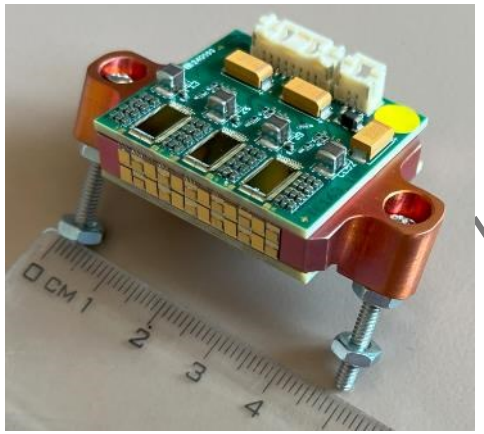
DAQ/NVIDIA

Handheld

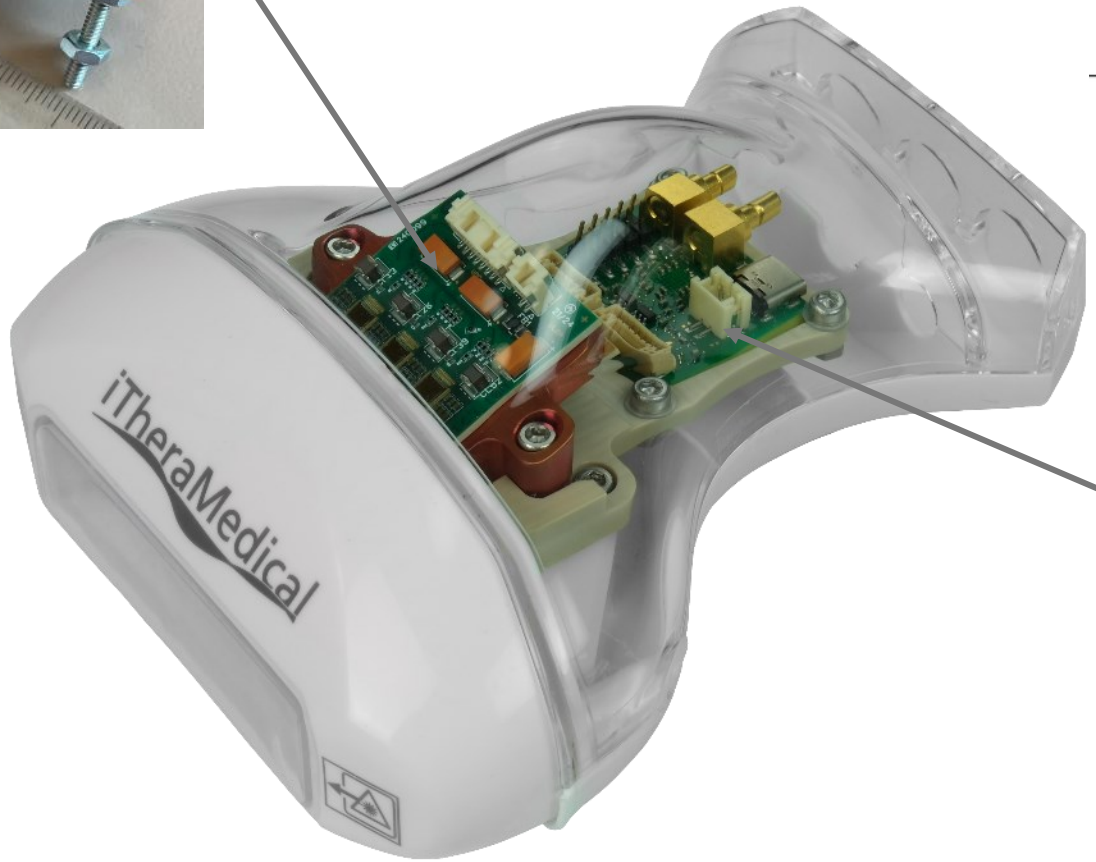
Laser

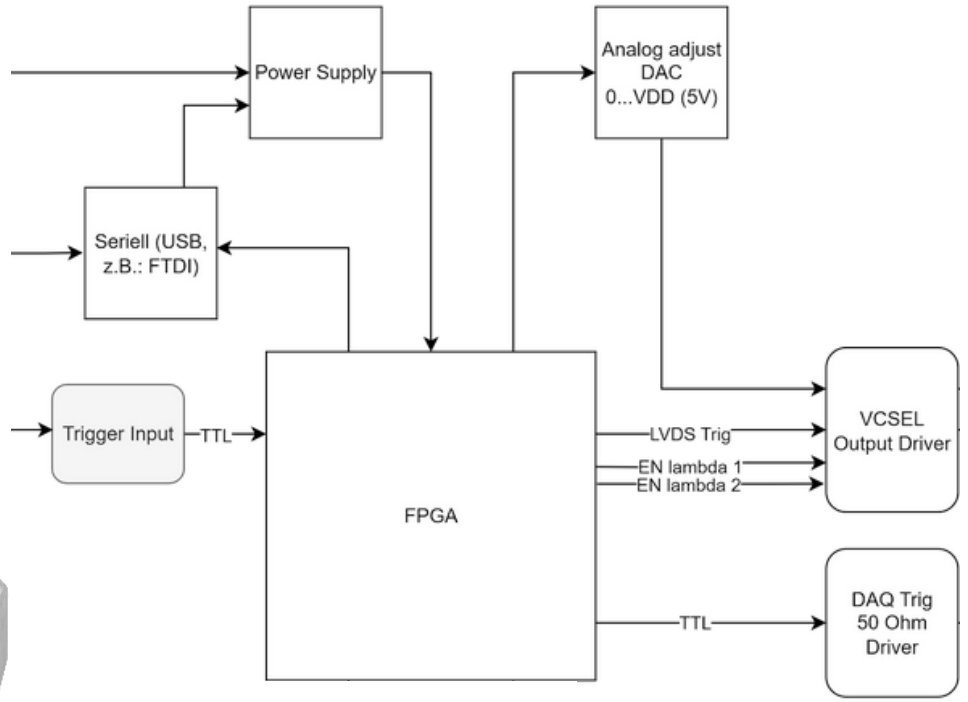


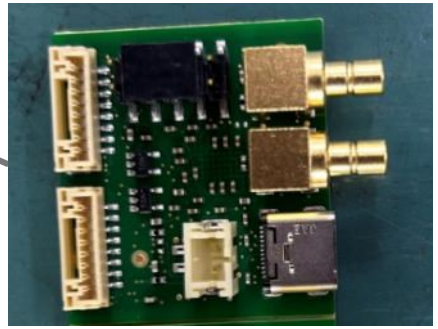
VCSEL subsystem in handheld:



Laser module







Control module

VCSEL Prototype: industrial manufacturing

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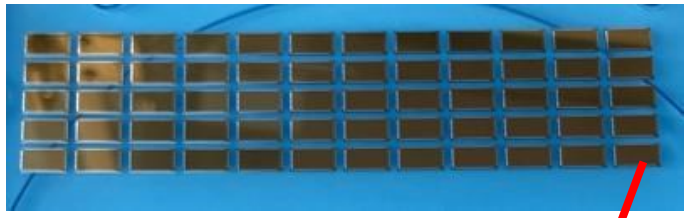
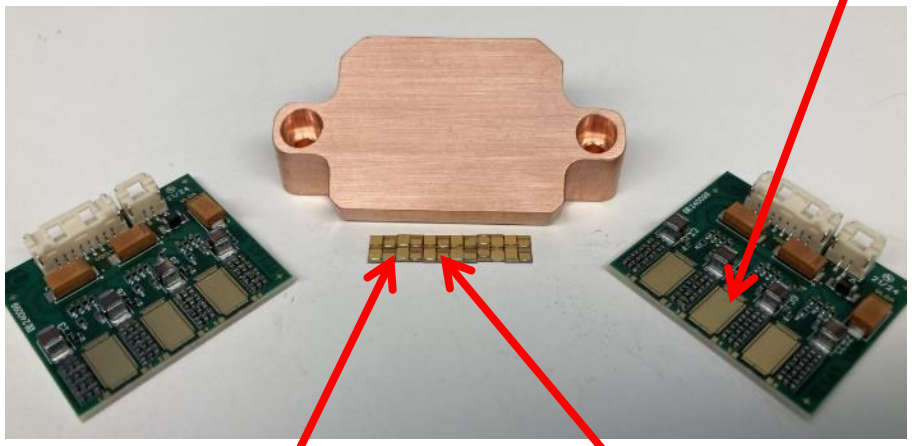
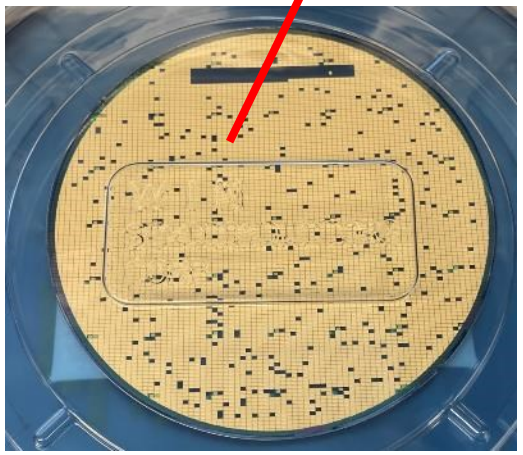
Driver ICs

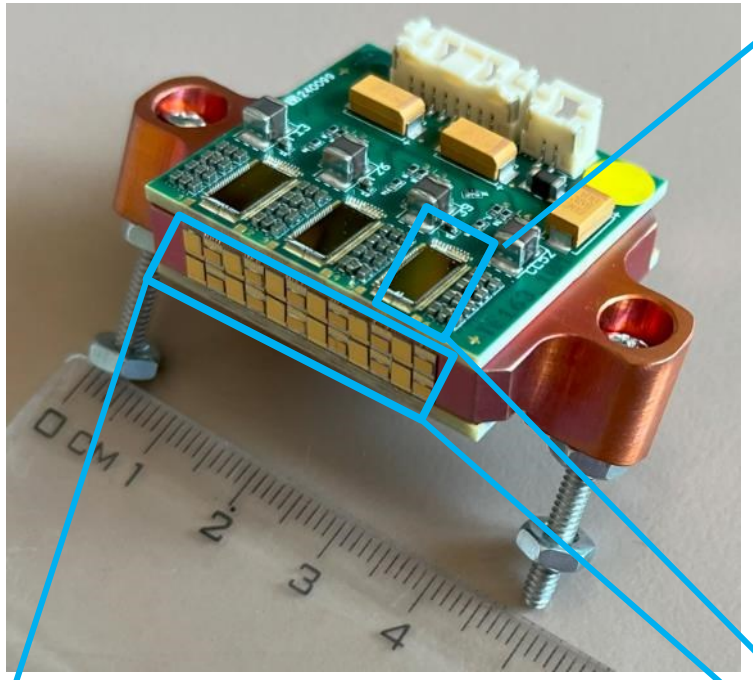


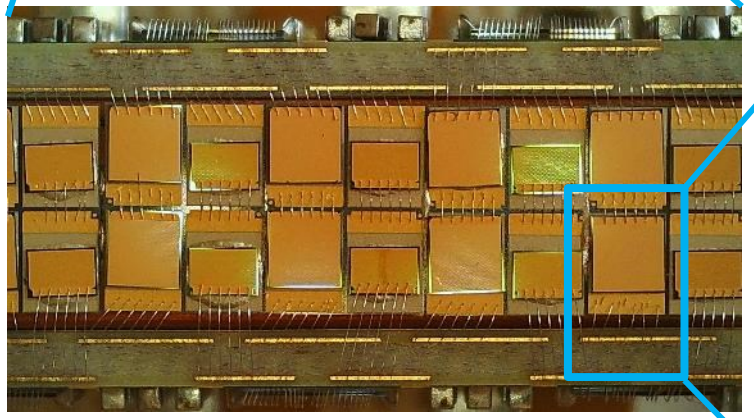


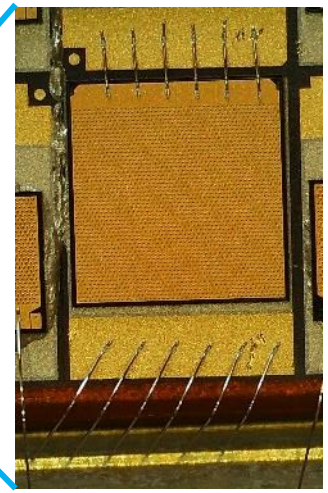


Wafer with VCSEL arrays

Submounts

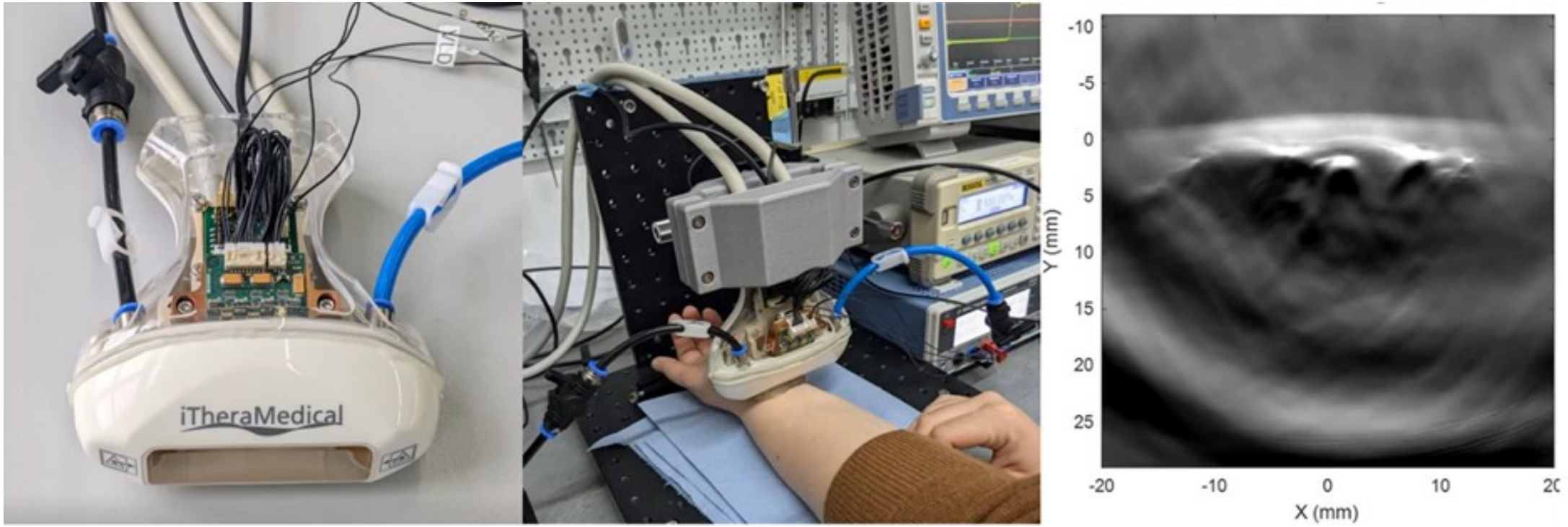






true industrial design

First optoacoustic image: vasculature in wrist of a healthy volunteer



First integrated prototypes show first images of vessels in wrist

Markets perfusion & oxygenation: How many units?

PAD stationary (u.a. Diabetis):

- **Top-down:** 500M diagnoses p.a., 500M treatment monitoring p.a.
  …20% with photoacoustic systems & code with 60€: >1Mrd p.a., ca. 500M€ for systems
- **Bottom-up:** 6000 PAD centers worldwide, ca. 500M€ for systems p.a.
- **Treatment cost:** >7Mrd€ 2030

PoC Ultrasound:

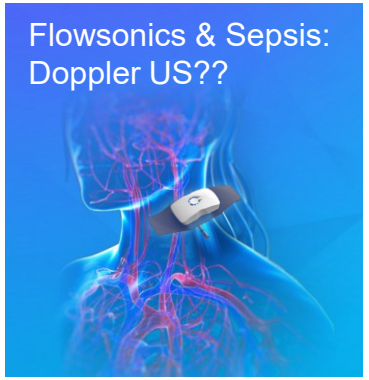
- Market for handheld ultrasound 2030: >1Mrd€ (….200.000 pcs x 5k€)
- https://www.exo.inc/article/exo-introduces-a-new-age-of-ultrasound-with-exo-iris

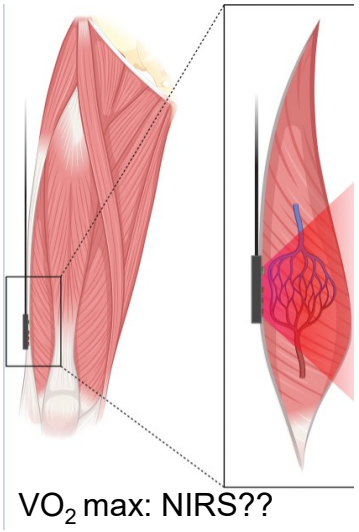
Patches Sepsis:

- Worldwide 50M cases p.a.
- Germany: ca. 300.000 cases with ca. 30.000€ cost p.a.: total 10Mrd€
  ….perfusion of muscle in 1-2cm tissue depth is key to improve & monitor treatment

HealthTech:

- 100M smartwatches p.a., VO_2 max sensor cost >10€
  …. “aerob/anaerob” zone estimated from pulse or “diffusion data”





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- Germany: ca. 300.00
  ….perfusion of muscle

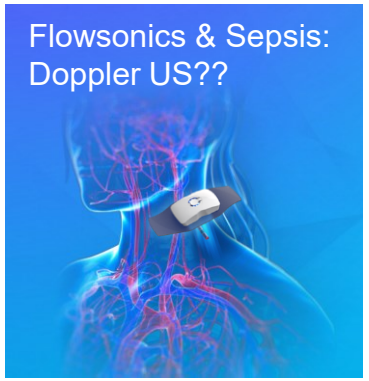
HealthTech:

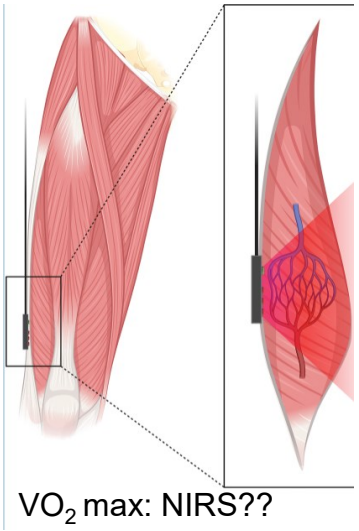
- 100M smartwatches p
  …. “aerob/anaerob” zc

Table 1. Comparison of the PAT hemodynamic measurements with NIRS and other optical methods reported in refs.5 and 28. The results are reported as mean ± SD.

Meth	Static SO_2 (%)	Blood flow(ml•100ml^{-1}•min^{-1})
NIRS	58.2 ± 4.38	1.41 ± 0.43
PA	54.9 ± 1.12	1.75 ± 0.42
Ref. [5,28]	57.8 ± 7.55	1.56 ± 0.54

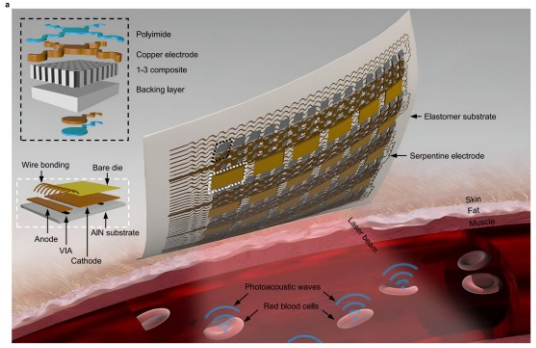
Cuff occlusion of the arm produced similar responses among volunteers using the two methods. PA signal showed higher standard deviation and lower maximum PA signal change at the end of the 2 minutes VO compared to NIRS. During the VO, the blood flow measured by PAT (1.75 ± 0.42) was close to that by NIRS (1.41 ± 0.43) and the other references (1.56 ± 0.54). The static SO_2 by PAT was 54.9 ± 1.12% compared to that by NIRS (58.2 ± 4.38%) and that by other optical methods (57.8 ± 7.55%).





Conclusion:

- The optoacoustic effect enables portable molecular imaging for medical applications
- Best for: Oxygenation & perfusion (Diabetis, Sepsis, VO_2max....€, €€, €€€)
- But: Today‘s photoacoustic systems are complex and expensive
  ...a factor of 100 in €, kg & W is missing: target 10€/mm² & 10µJ/mm²
- Solution: re-use LiDAR & ToF automotive/mobile technology
- Laser: VCSEL @680/760/800/850nm: >25% wall-plug, laser class 1
- Bulk piezos: to be replaced by xMUTs
- Electronics: automotive LIDAR & mobile ToF ICs are available



Welcome: Investors, customers, partners & employees