Biophotonics research in Riga: recent projects and results

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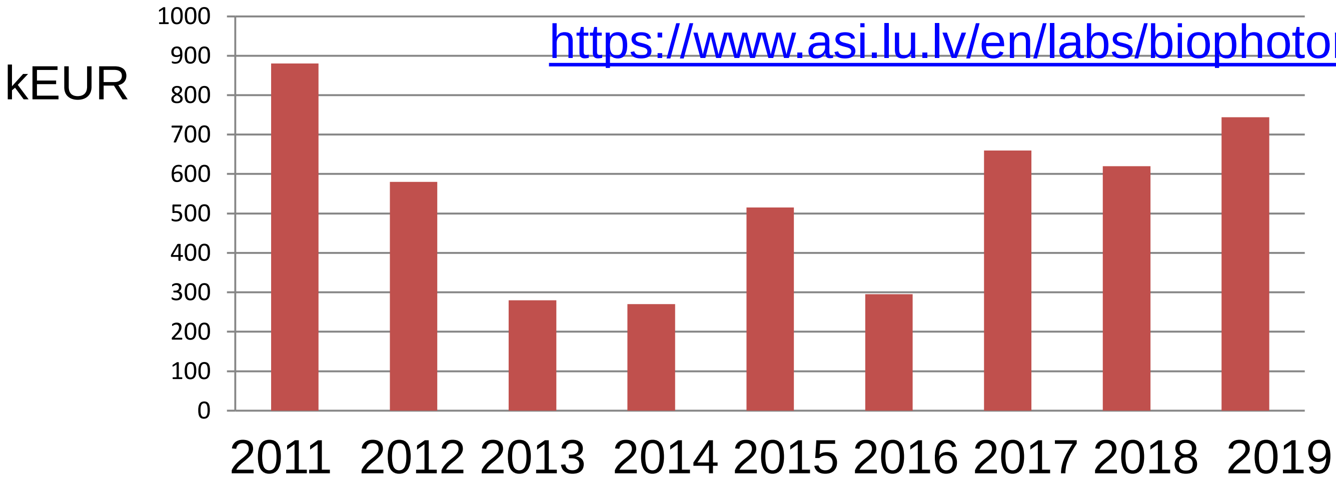
«Biophpotonics - Riga 2020», 24/08/2020

Biophotonics Laboratory at IAPS UL

- Established in 1997 as Bio-optics and fiberoptics group
- Main research direction: optical assessment of *in-vivo* skin
- ~25-30 staff members involved in projects, incl. 10 PhDs
- 2019: 12 research projects, incoming budget ~765 kEUR



https://www.asi.lu.lv/en/labs/biophotonics-laboratory/

Running and recently finished projects

- **European Community *Horizon-2020* projects***:*
  - *Laserlab-Europe*, # 871124 (**Alexey Lihachev/Vanesa Lukinsone**)
  - MSCA postdoc: *DogSpec*, # 745396 (**Blaž Cugmas**, finished 2020)
- **European Regional Development Fund (ERDF) projects:**
  - *Optical noninvasive hybrid method for early diagnostics of sepsis and therapy management* (**Andris Grabovskis,** finished 2019).
  - *Portable device for early non-contact diagnostics of skin cancer* (**Alexey Lihachev / Ilona Kuzmina**, finished 2019).
  - *Multimodal imaging technology for in-vivo diagnostics of skin malformations* (**Janis Spigulis**).
  - *Time-resolved autofluorescence methodology for non-invasive diagnostics of skin cancer* (**Alexey Lihachev**, postdoc).
  - *Development and clinical validation of a novel cost effective multi-modal methodology for early diagnostics of skin cancers* (**Ilze Lihacova**, postdoc).
  - *Development of prototype devices for nonivasive assessment of skin condition*, (**Edgars Kviesis-Kipge**, postdoc).

Projects (continued)

- **Latvian Council of Science (LCS) projects:**
  - *Photoplethysmography imaging for assessment of chronic pain* (**Andris Grabovskis**).
  - *Improving the early diagnosis of skin cancer with neural networks* (**Ilze Lihacova**).
  - *Fast detection of micro-organism activity by an optical non-contact method* (**Alexey Lihachev**).
  - *Advanced spectral imaging technology for skin diagnostics* (**Janis Spigulis**).
- + just started this year:
  - ERDF project (**Alexey Lihacev**)
  - ERDF - LV postdoc (**Blaž Cugmas**)
  - LCS project (**Mindaugas Tamošiūnas**)

FLPP
FUNDAMENTAL AND APPLIED RESEARCH PROJECTS

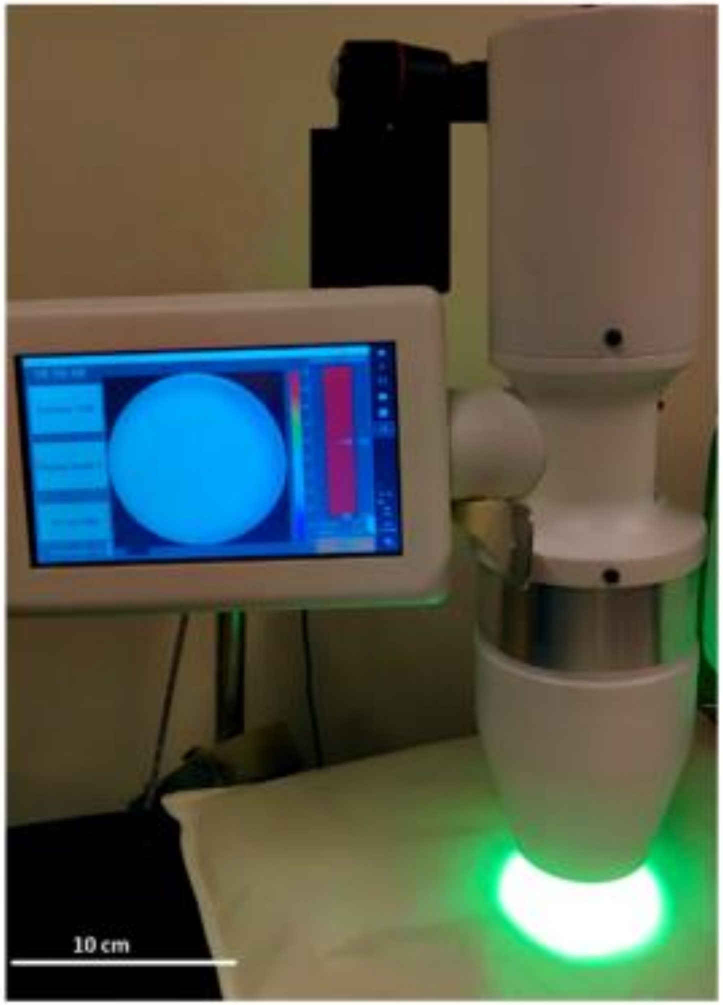
1. Early diagnostics of sepsis (A.Grabovskis & Co.)

Sepsis – 27M/yr cases worldwide, 8M with letal outcome. In Latvia ~ 900 deaths/yr. Very rapid progression – every hour between the shock (hypotension) and therapy decreases survival for 7%; only **2 out of 5 patients survive after 6 hours.**

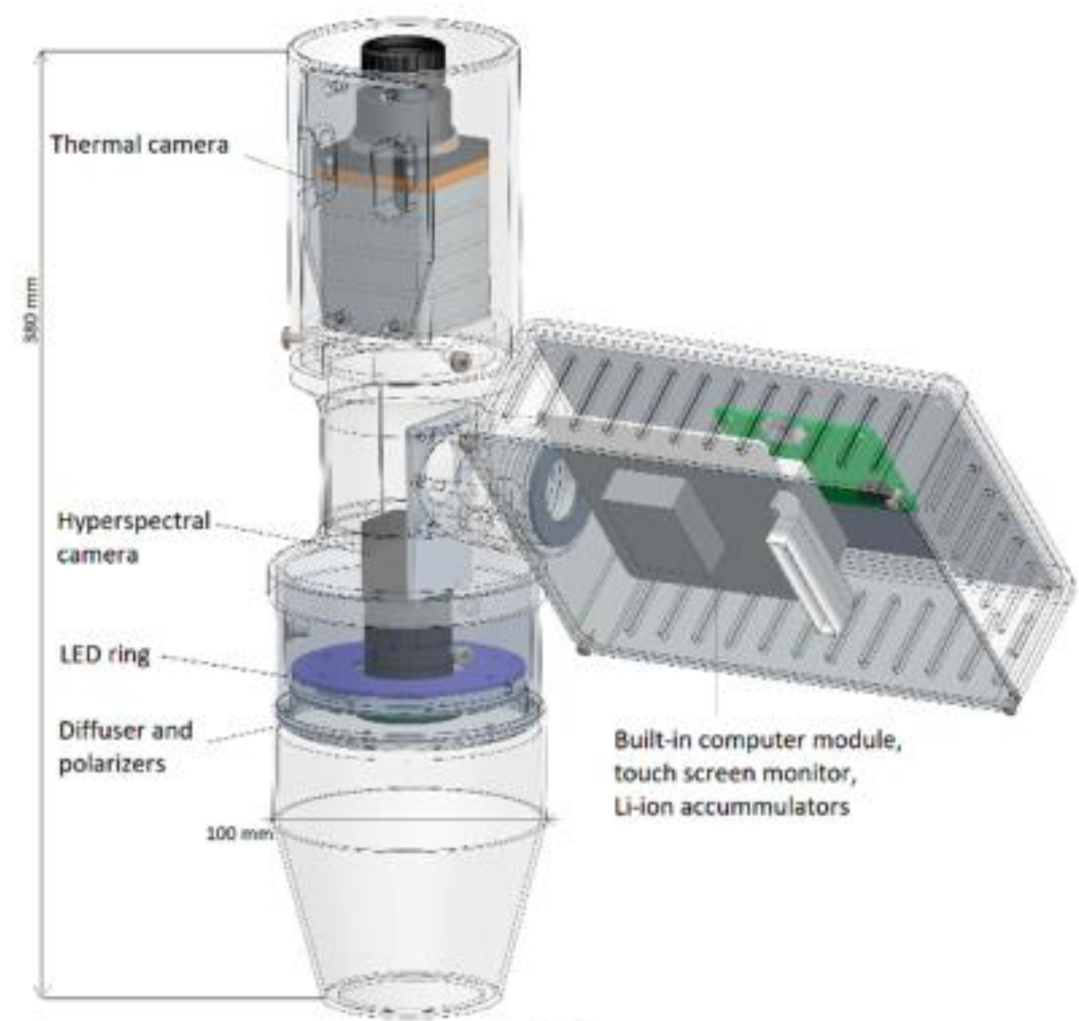
Still lack of reliable method/technology for early visualization and quantification of the shock signs. One of them – «marmorized» spots on the knees of patients.

Idea – **combined hyperspectral and thermal imaging of the knee spots** to follow the changes in blood oxygenation and microcirculation.

Prototype for hyperspectral/thermal imaging of skin (septic knees)



(a)

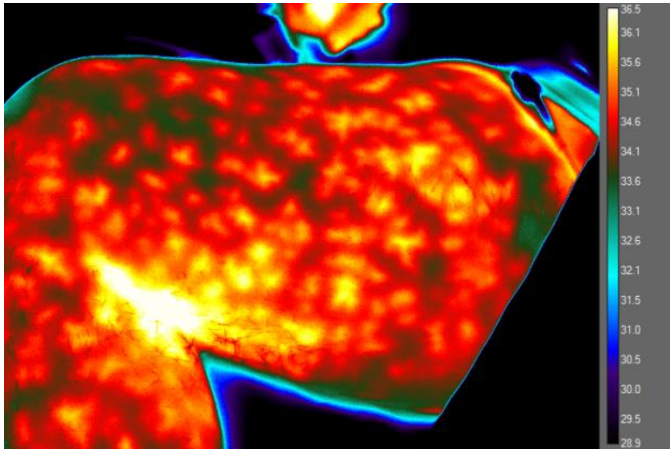


(b)

Model experiments and clinical studies

Immitation of sepsis spots on knees by leg occlusion (UL FB)

Knees of a sepsis patient at the Emergency Department of hospital (RAKUS)

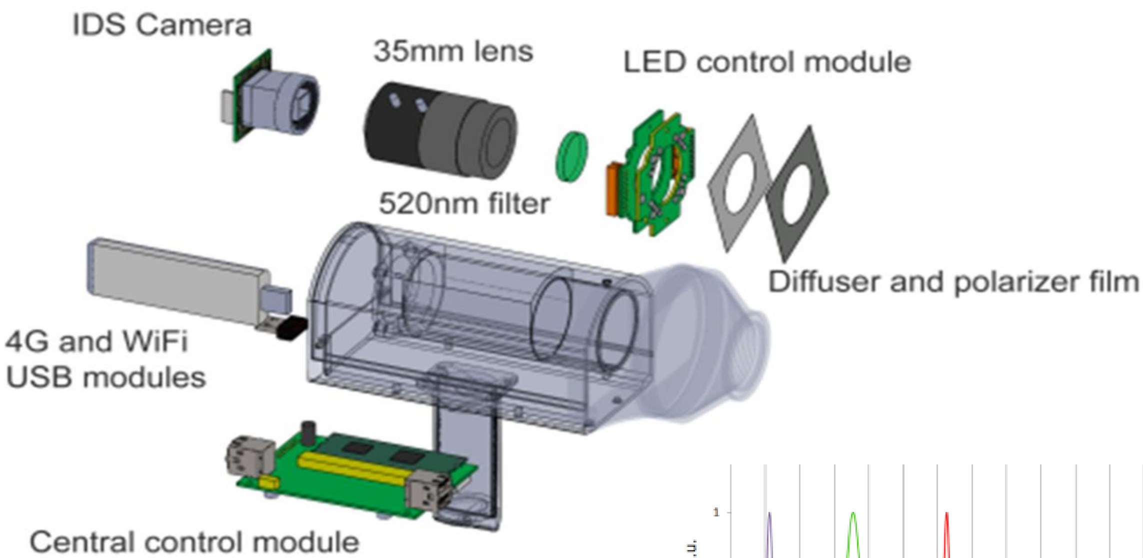


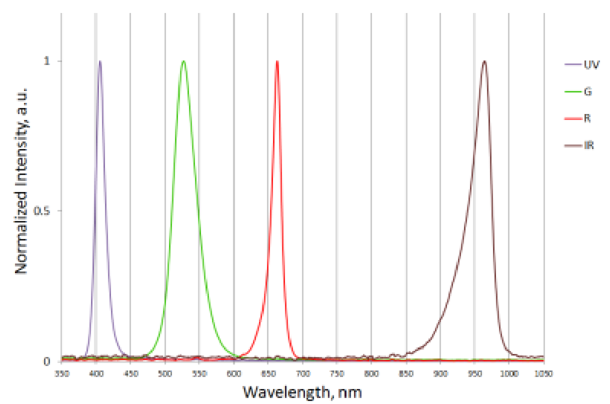
Thermal image: a knee of sepsis patient

Image processing → perfusion and SaO maps for monitoring of disease

U.Rubins et al., “Multimodal device for real-time monitoring of skin oxygen saturation and microcirculation function”, **Biosensors**, 9, 97 (2019).

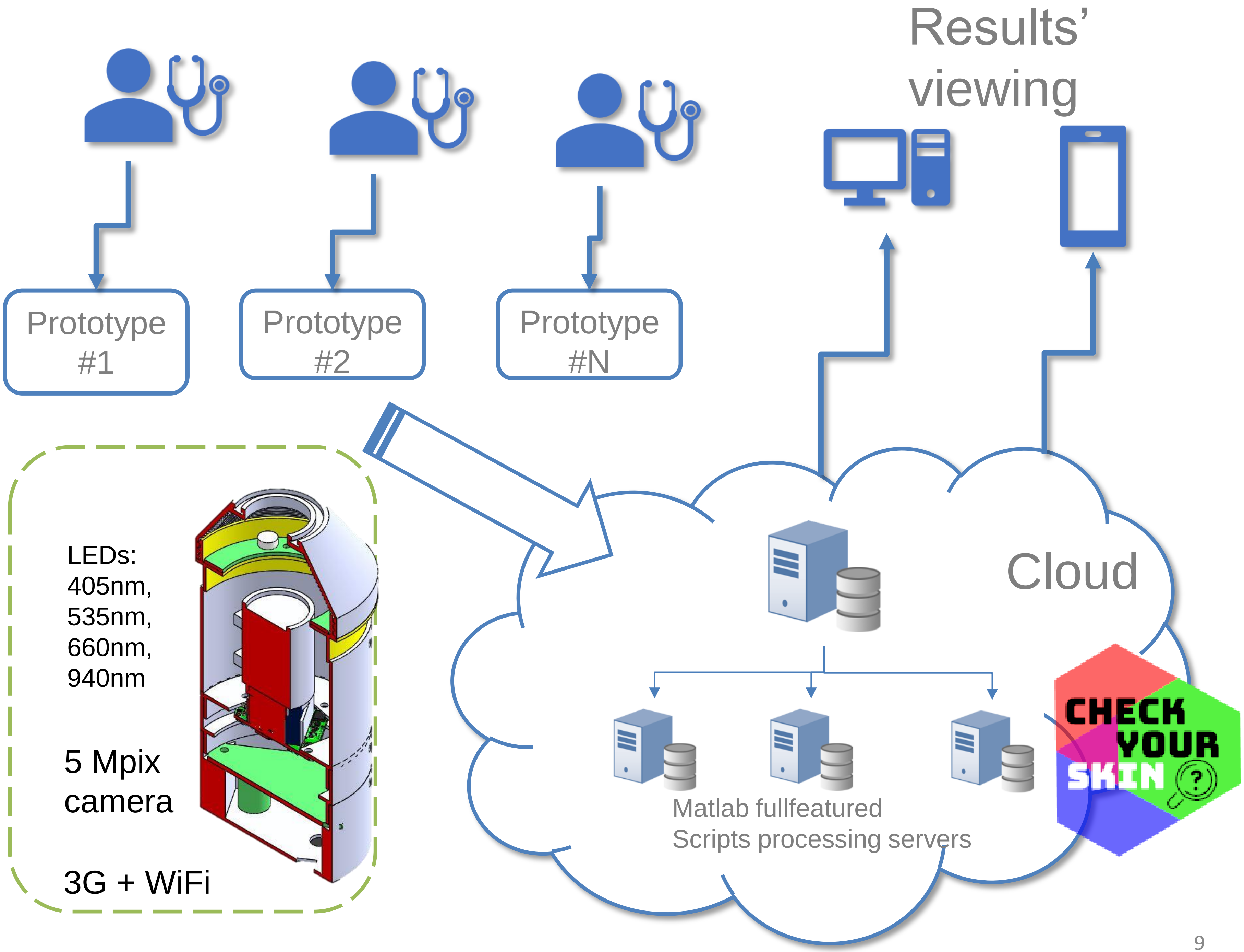
2. Skin melanoma checker (A.Lihachev/I.Kuzmina & Co)





4 prototypes, 1500+ clinical tests in LV, HU, BG; sensitivity ~85%, specificity ~95%

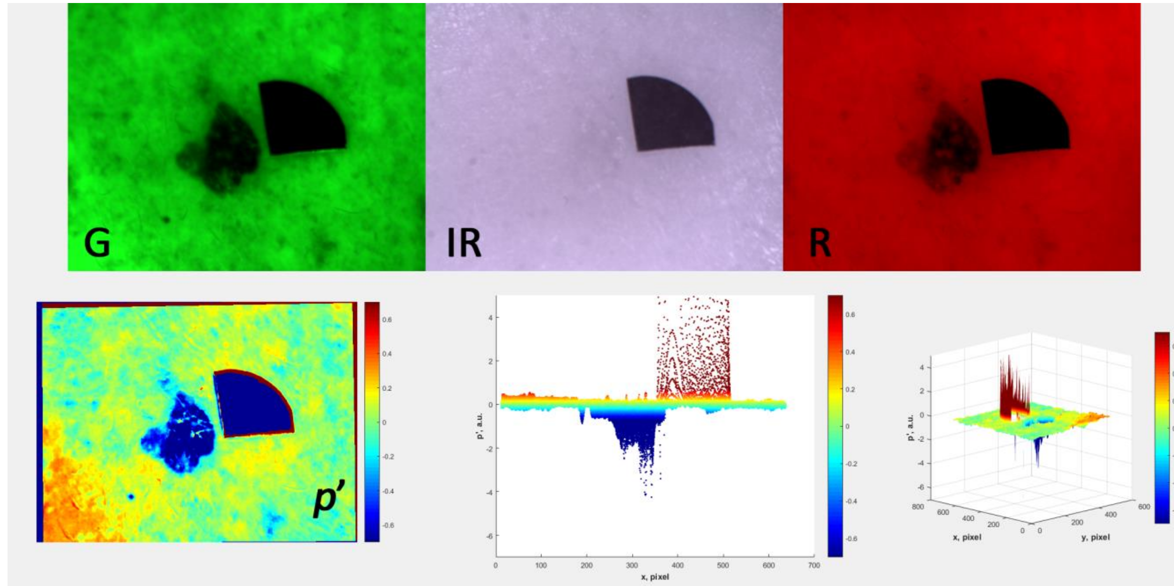
V.Lukinsone et al., “Multispectral and autofluorescence RGB imaging for skin cancer diagnostics”, *Proc.SPIE* **11065**, 110650A (2019).


Results' viewing
Prototype #1
Prototype #2
Prototype #N
LEDs: 405nm, 535nm, 660nm, 940nm
5 Mpix camera
3G + WiFi
Cloud
Matlab fullfeatured
Scripts processing servers
CHECK YOUR SKIN ?

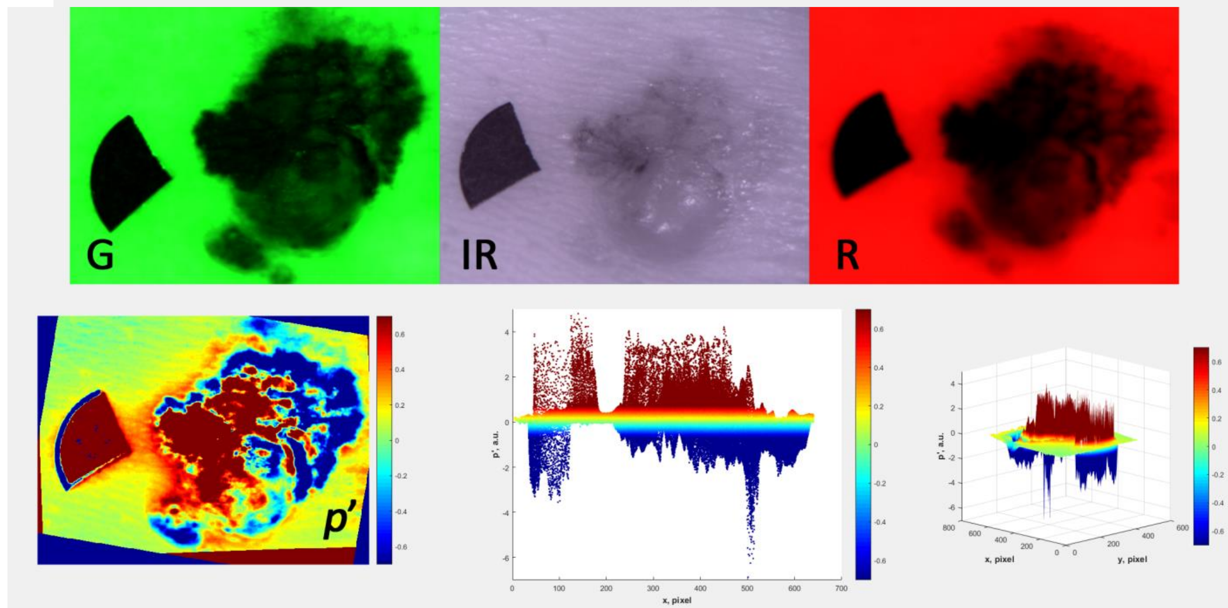
Images and histograms (criterion p’)

$$p' = lg\left(\frac{I(526)\cdot I_{skin}(663)\cdot I_{skin}(964)}{I_{skin}(526)\cdot I(663)\cdot I(964)}\right)$$

Melanocytic nevus



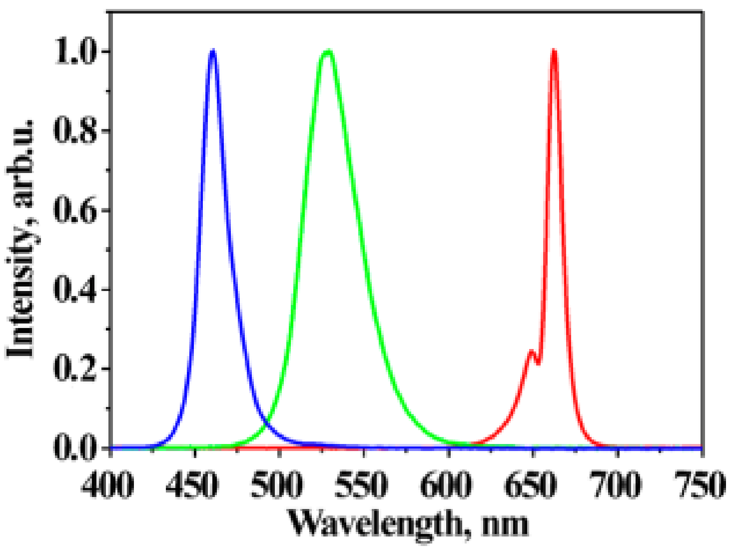
Melanoma



3. Multi-spectral-line imaging for skin chromophore mapping (J.Spigulis & Co.)

Conventional:

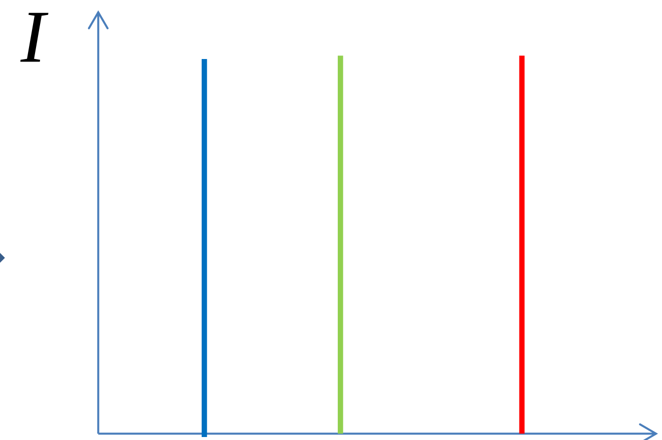
Spectral **band** images



Sequential (t>>0)

Novel:

Spectral **line** images

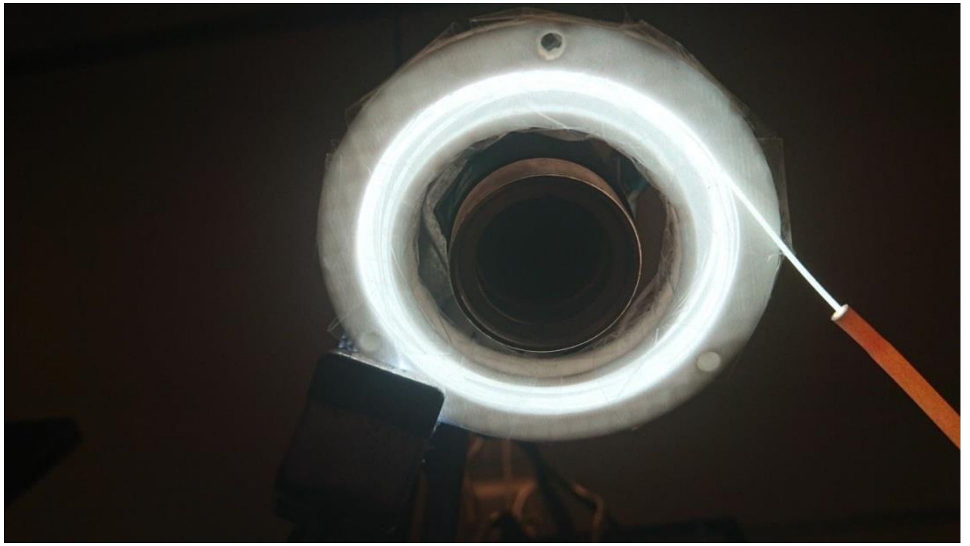


Single snapshot (t→0) λ

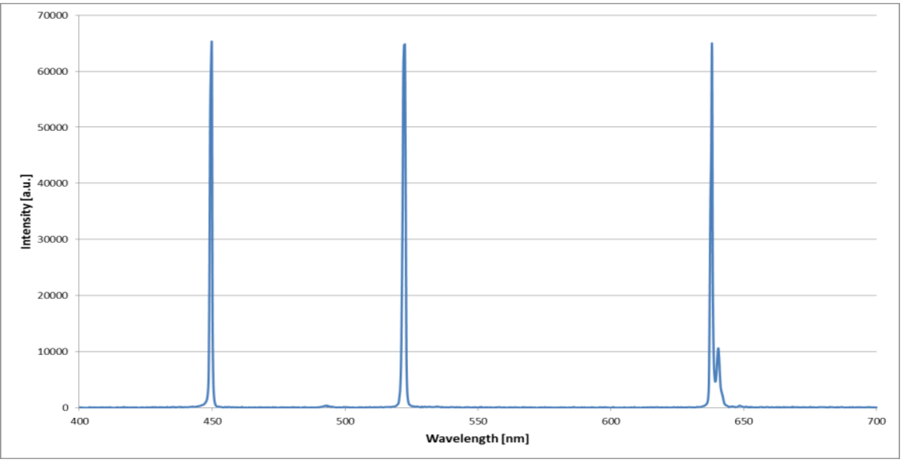
n =3 → n > 3

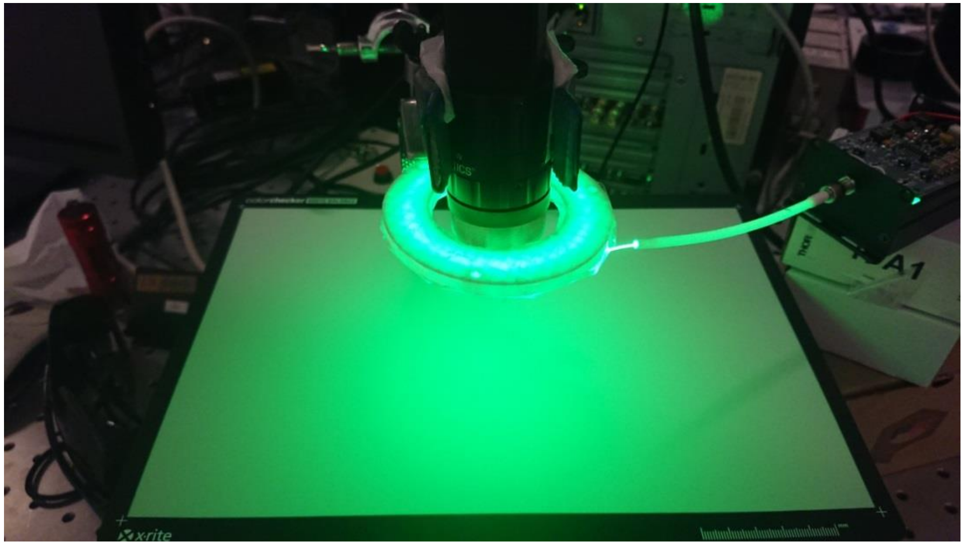
Benefits:
- Increased (ultimate) spectral selectivity, <0.01 nm
- Improved imaging quality (snapshot → avoided motion artefacts)
- Simpler/faster image processing (numbers instead of integrals over wavelength bands

Novelty: uniform four laser line illumination by a side-emitting optical fiber loop



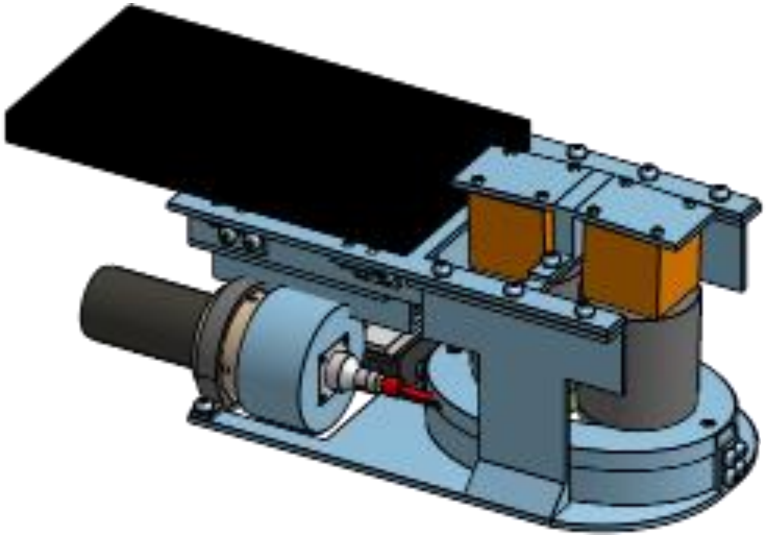
450/523/638 nm + 850 nm





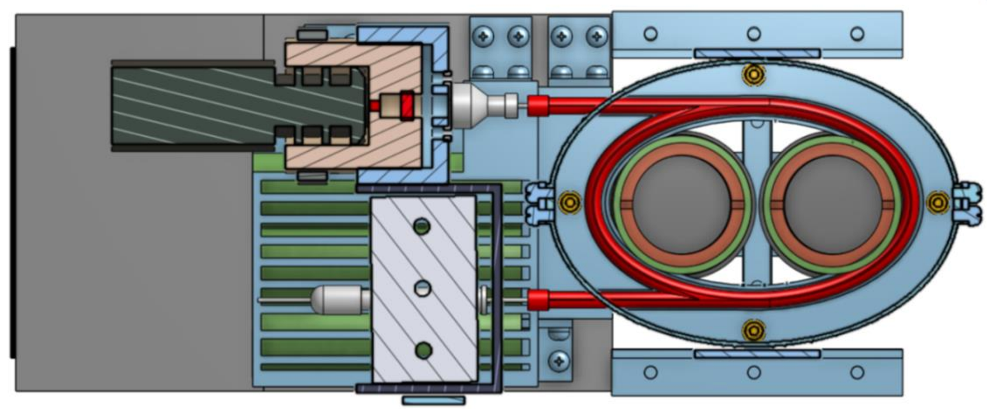
LV 11644 B, 1995. Side-emitting optical fiber (D. Pfafrods, M. Stafeckis, J. Spigulis, D. Boucher);
LV 15491 B, 2020 (J.Spigulis, I.Oshina, Z.Rupenheits, M.Matulenko)

The (4+1) wavelength prototype: design concept



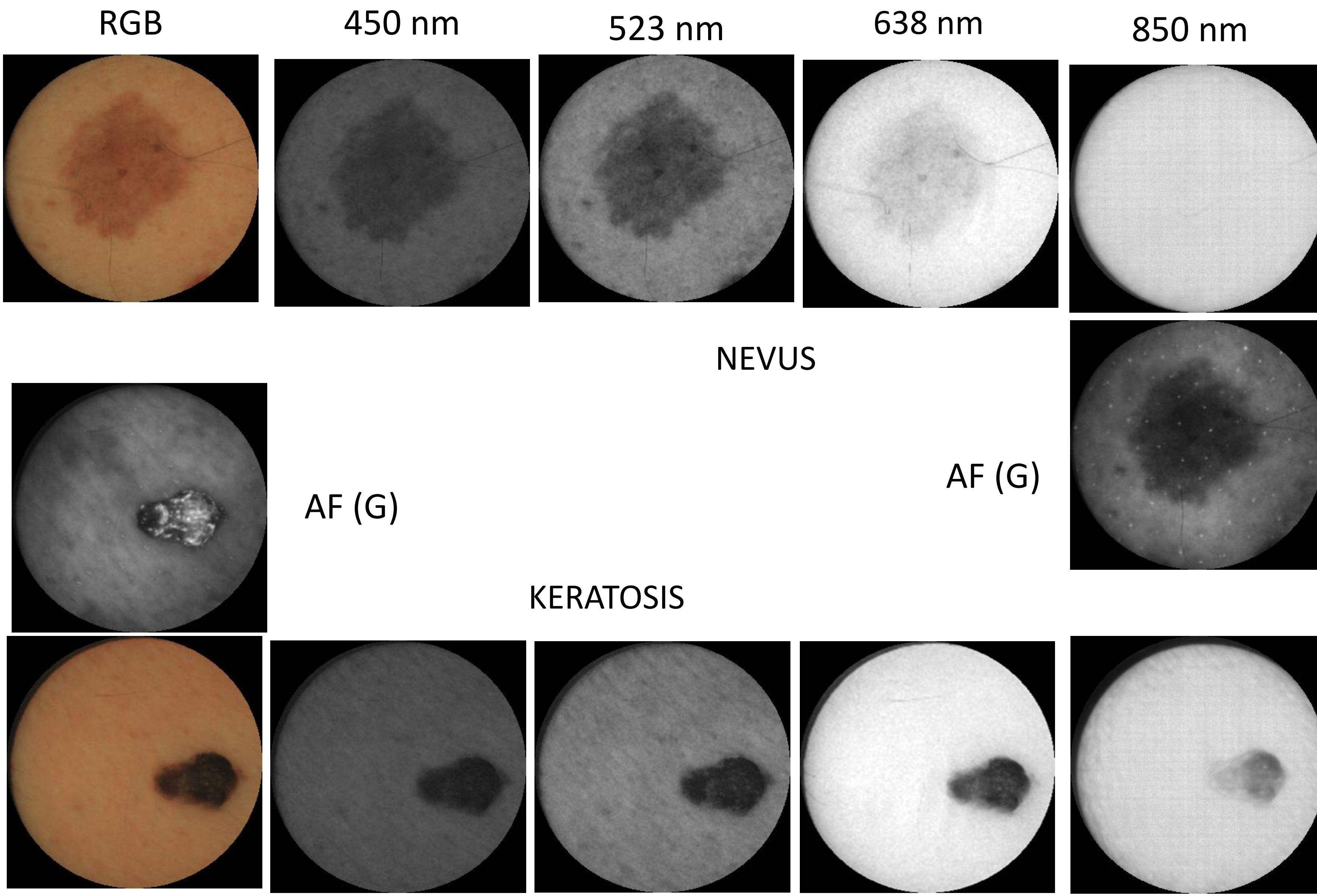
Step 1 - 450/523/638/850 nm illumination for snapshot mapping of 4 skin chromophores (HbO, Hb, Mel, Blr) and calculation of the MM criterion;

Step 2 – 405nm excitation for skin fluorescence imaging (MM – SK differentiation)



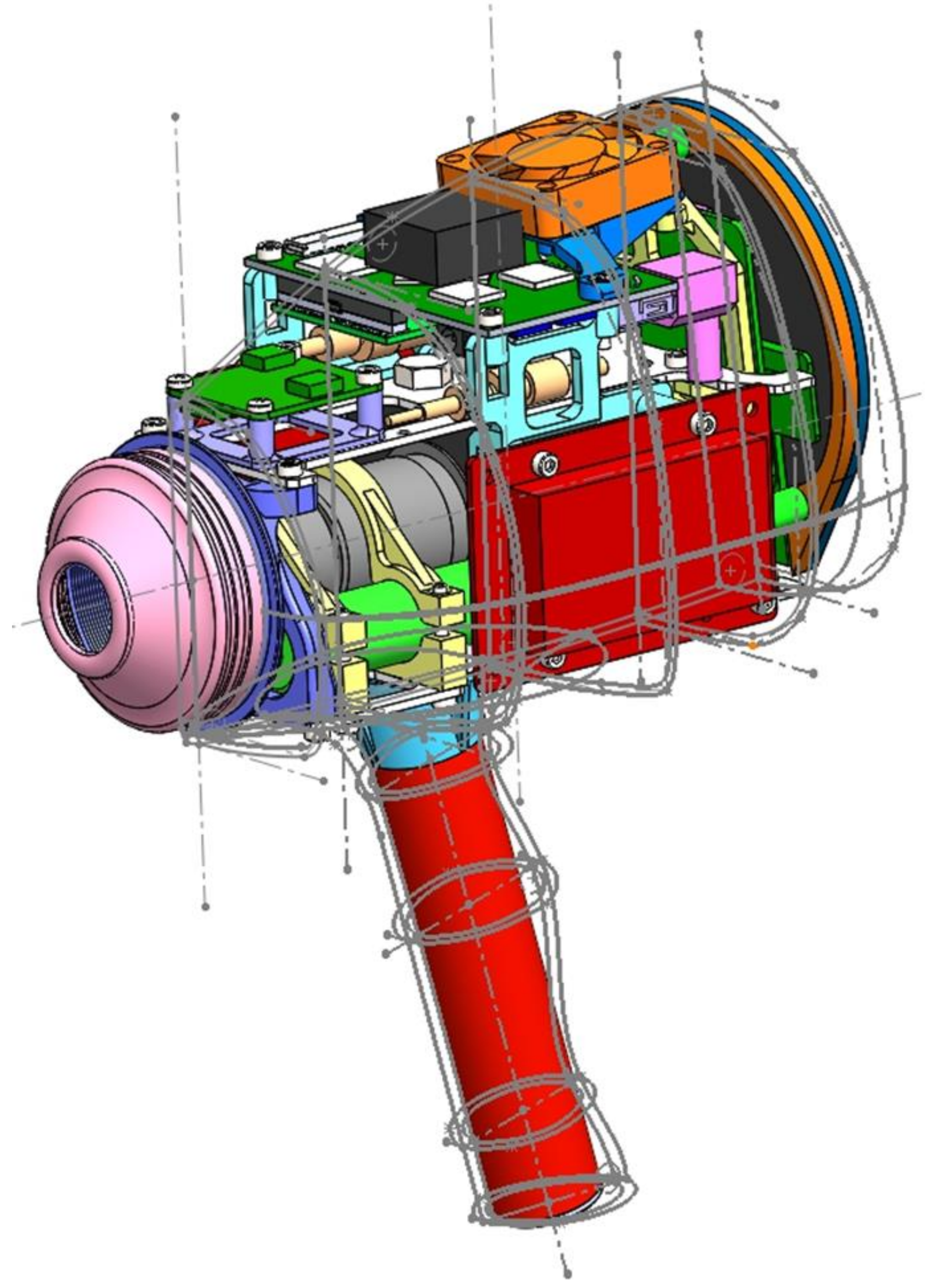
J.Spigulis et al., “A snapshot multi-wavelengths imaging device for in-vivo skin diagnostics”, Proc.SPIE 11232, 112320I-1 (2020).

Combined nevus *vs* seborrheic keratosis

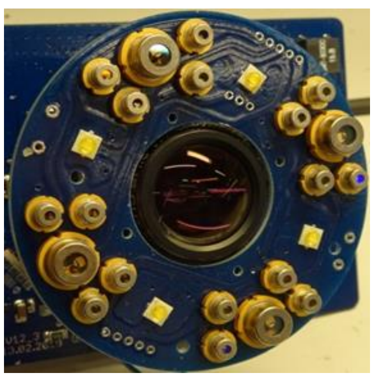


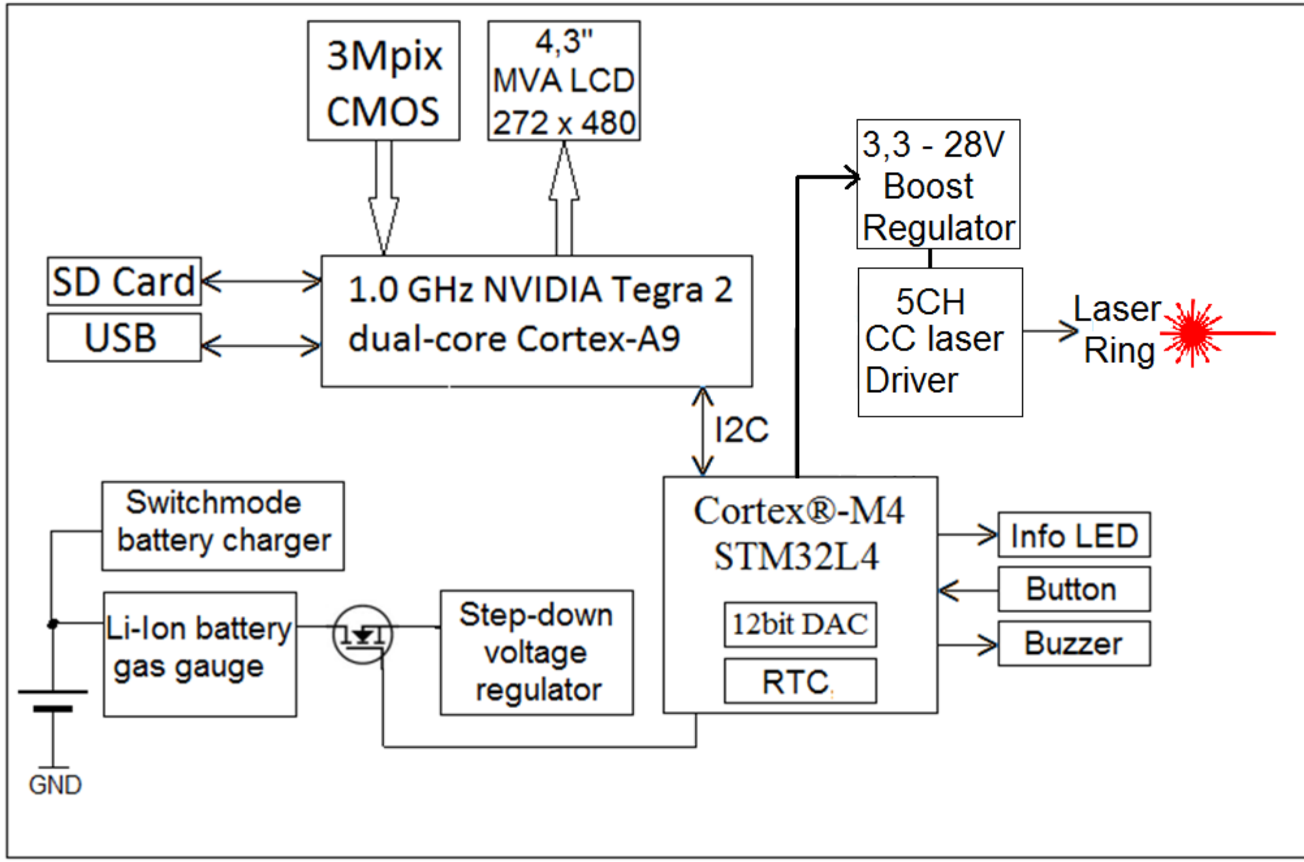
The four-band camera prototype

(405+450/523/638/850 nm, under development – demo during the coffee break)



Five laser line device with LD ring source (E.Kviesis-Kipge)

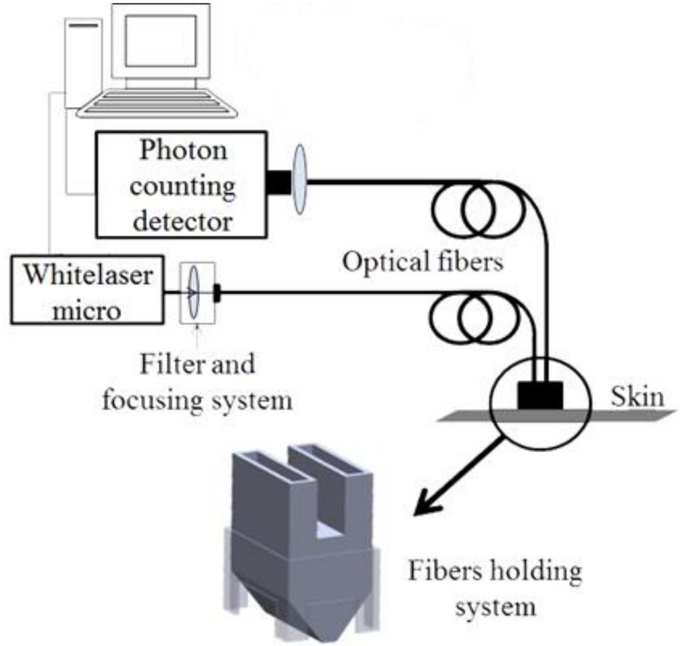


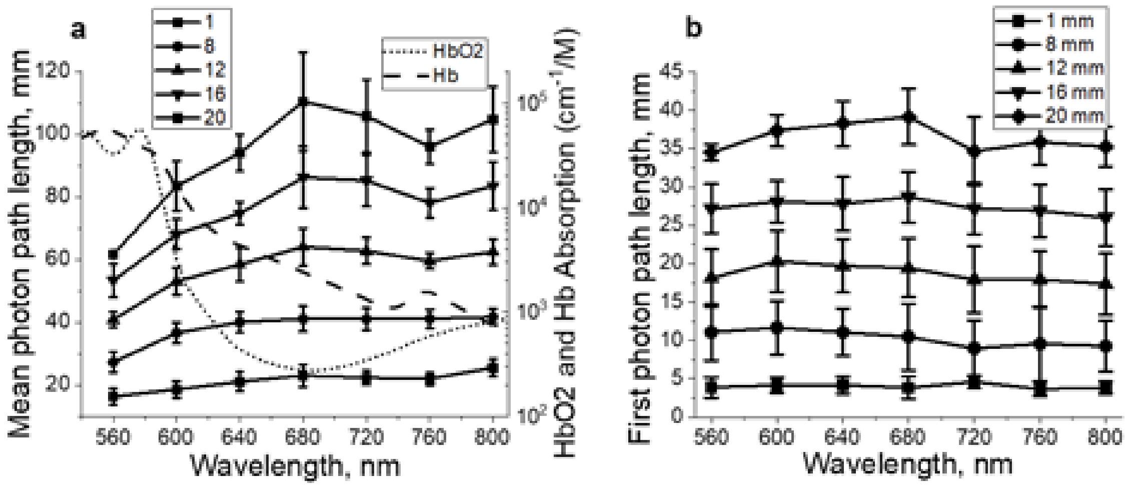


Laser diodes (x4): **405nm**-20mW, **450nm**-80mW, **525nm**-50mW, **655nm**-15mW, **845nm**-50mW

E. Kviesis-Kipge, "Development of skin chromophore mapping device using five spectral line illumination", OSA Technical Digest (2019), ITh4B.3 (2019).

4. Remitted photon path lengths in skin: time-resolved measurements (V.Lukinsone & Co.)



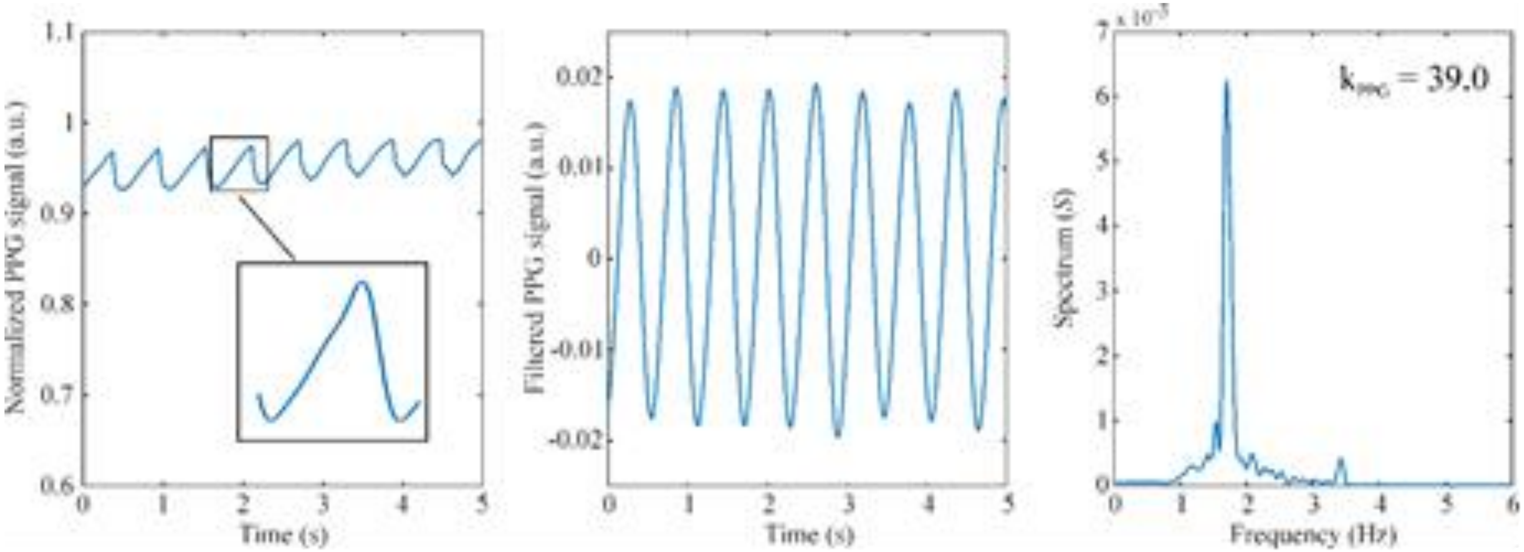


White laser FWHM 6 ps, 10 nm interference filters for 7 spectral bands 560-800 nm,
5 inter-fiber distances 1 ... 20 mm, 35 spectral-spatial combinations.
Results: MPL ~ 16 ... 105 mm, longer than modelled by MC; minimum at 760nm (Hb?)

Deconvolution: $b(t) = \int_0^t a(t-\tau) f(\tau) d\tau$

V.Lukinsone et al., “Remitted photon path lengths in human skin: in-vivo measurement data”, ***Biomed.Opt.Expr***. 11(5), 2866-2873 (2020).

5. Veterinary biophotonics: the first steps (B.Cugmas)



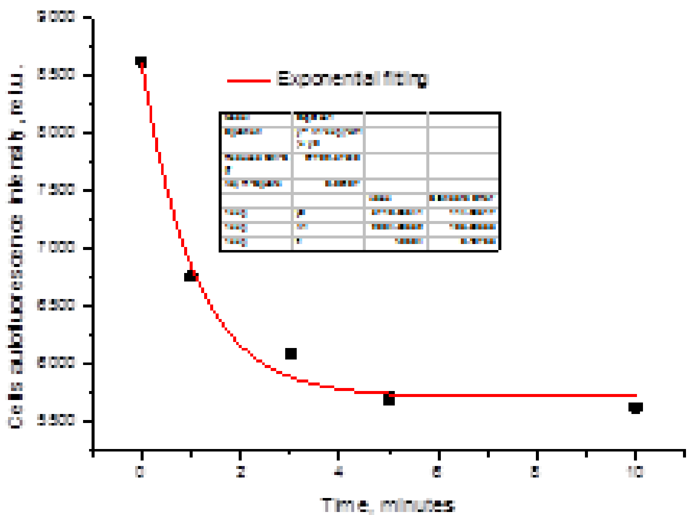
Canine photoplethysmography signals

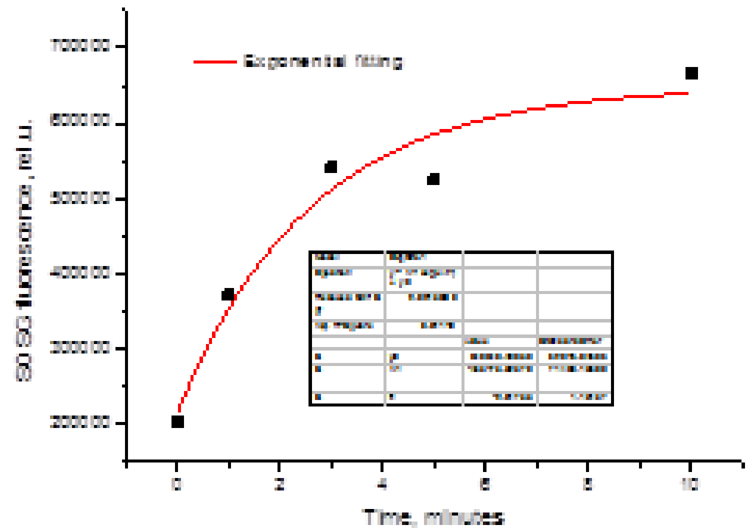
B.Cugmas, J.Spigulis, “Biophotonics in veterinary medicine: the first steps toward clinical translation”, *Proc.SPIE* **10885**, 108850I (2019). DOI: 10.1117/12.2507980.

B.Cugmas, E.Štruc, J.Spigulis, “Photoplethysmography in dogs and cats: a selection of alternative measurement sites for a pet monitor”, ***Physiol. Meas*.**, **40**, 01NT02 (2019). DOI: 10.1088/1361-6579/aaf433.

B.Cugmas et al., “Photoplethysmography for bovine heat detection: the preliminary results”, *Proc.SPIE* **11247**, 112470J (2020). DOI: 10.1117/12.2543858.

6. Photobleaching of cell autofluorescence: correlation with singlet oxygen production (A.Lihachev & Co.)



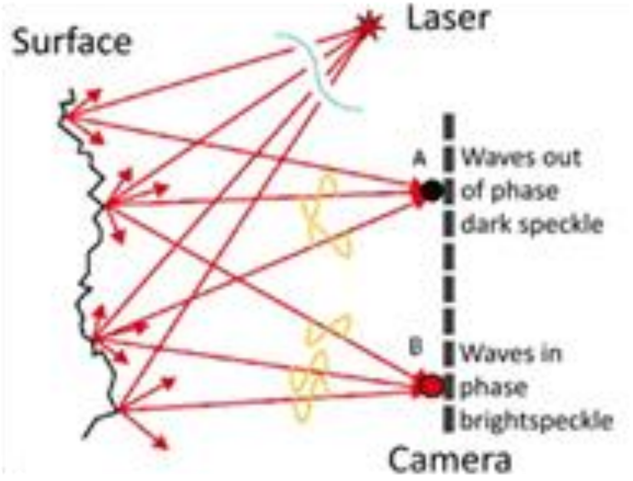


Left – melanoma cell autofluorescence intensity decrease during 10 minutes under 405nm continuous excitation measured at 480 nm band. $\tau_1 \sim$ 1.1 minute +/-18%.

Right – singlet oxygen fluorescence measured at 520 nm band under 473 nm excitation in the same experiment. $\tau_2 \sim$ 2.6 minutes +/-44%.

Conclusion: AF is quenched by singlet oxygen and other radicals emerged by irradiation.

7. Detecting of cell division (bacterial growth) by laser speckle contrast changes (A.Lihachev & Co.)



Fast growing *vibrio natriegens* bacteria

Due to mass produced electronics, the total price of the device is only ~50 EUR (12 EUR – Raspberry Zero W, 20 EUR – Raspberry Camera, 6 EUR – laser diode, 10 EUR – PCB) – affordable for any biology lab and/or teaching of students.

SUMMARY

- The 2018-2020 projects were mainly related to camera-based non-contact assessment of in-vivo skin malformations or cutaneous microcirculation changes
- Two new research directions initiated – on biophotonics applications in veterinary medicine and in cell biology
- A number of prototypes and technologies for improved clinical diagnostics and recovery monitoring developed
- The new prototypes have reached TRL of 4 or 5 → future focus on technology transfer to reach end-users
- We're open to all kinds of co-operation both in research and in implementation of results!

Acknowledgements for project support

- EC H2020: #871124 *LaserLab Europe* and #745396-DogSPEC-H2020-MSCA-IF-2016 *DogSpec*
- ERDF: #1.1.1.1/16/A/065, #1.1.1.1/16/A/197, #1.1.1.1/18/A/132, #1.1.1.2/VIAA/1/16/014, #1.1.1.2/VIAA/1/16/052, #1.1.1.2/VIAA/1/16/070
- LCS: # lzp-2018/2-0052, # lzp-2018/2-0051, # lzp-2018/2-0006

European Commission

Latvian Council of Science

THANK YOU !