ADVANCED MULTISPECTRAL AND MULTIMODAL IMAGING FOR SKIN DIAGNOSTICS

Janis Spigulis

Biophotonics Laboratory

Institute of Atomic Physics and Spectroscopy (ASI)

University of Latvia, Riga

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University of Latvia, www.lu.lv

- Established in 1919
- 13 faculties
- > 15 000 students
- ~ 150 study programs
- 17 research institutes
- > 50 research fields
- Main building since 1862 (Riga Polytechnicum) → 1919 UL
- New academic center →future university campus

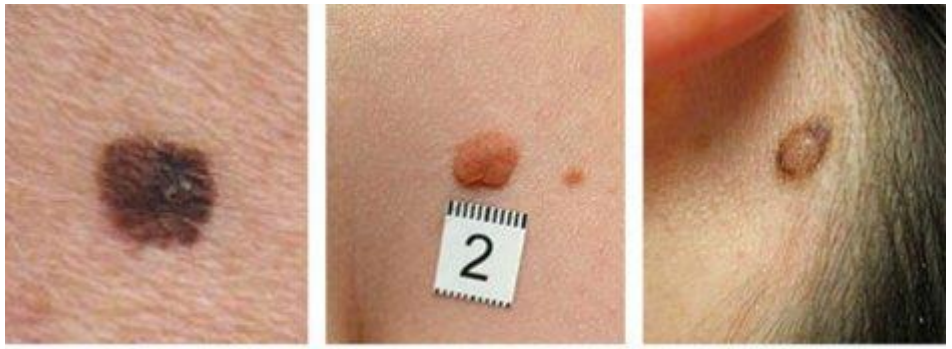
Biophotonics lab in Riga: our profile

Aim – to develop **affordable for end-users** non-invasive methods, devices and technologies for clinical diagnostics and monitoring, by exploiting optical features of *in-vivo* skin:

- **Skin autofluorescence** (AF):
  - photo-bleaching (AFPB) effects, skin "photo-memory"
  - parametric AFPB rate imaging → diagnostic potential studies
  - ps-range kinetics
- **Skin diffuse reflectance spectroscopy** (DRS**)**:
  - fibre-optic contact probe DRS,
  - multi-spectral imaging → skin chromophore mapping → potential for distant skin assessment
- **Skin blood pulsations** (photoplethysmography, PPG)
  - bilateral, multi-site and multi-spectral PPG
  - distant (wireless and non-contact) PPG → clinical applications

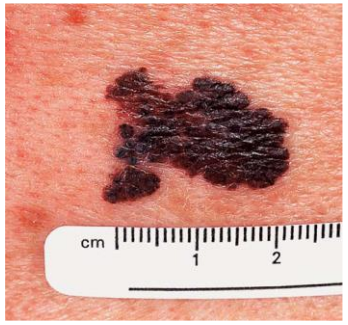
Skin malformations: bening and malignant

Nevi



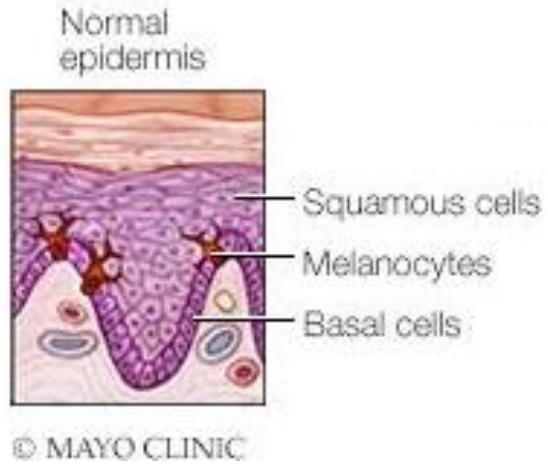
Dysplastic nevus

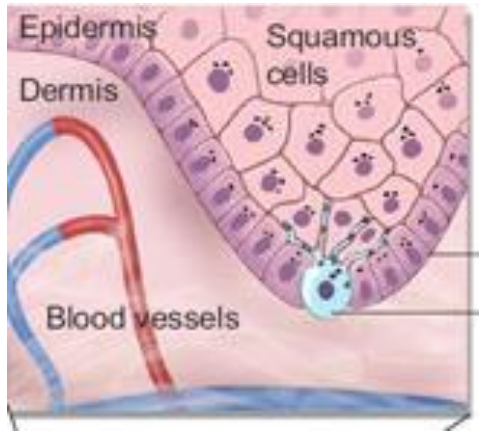
Melanoma

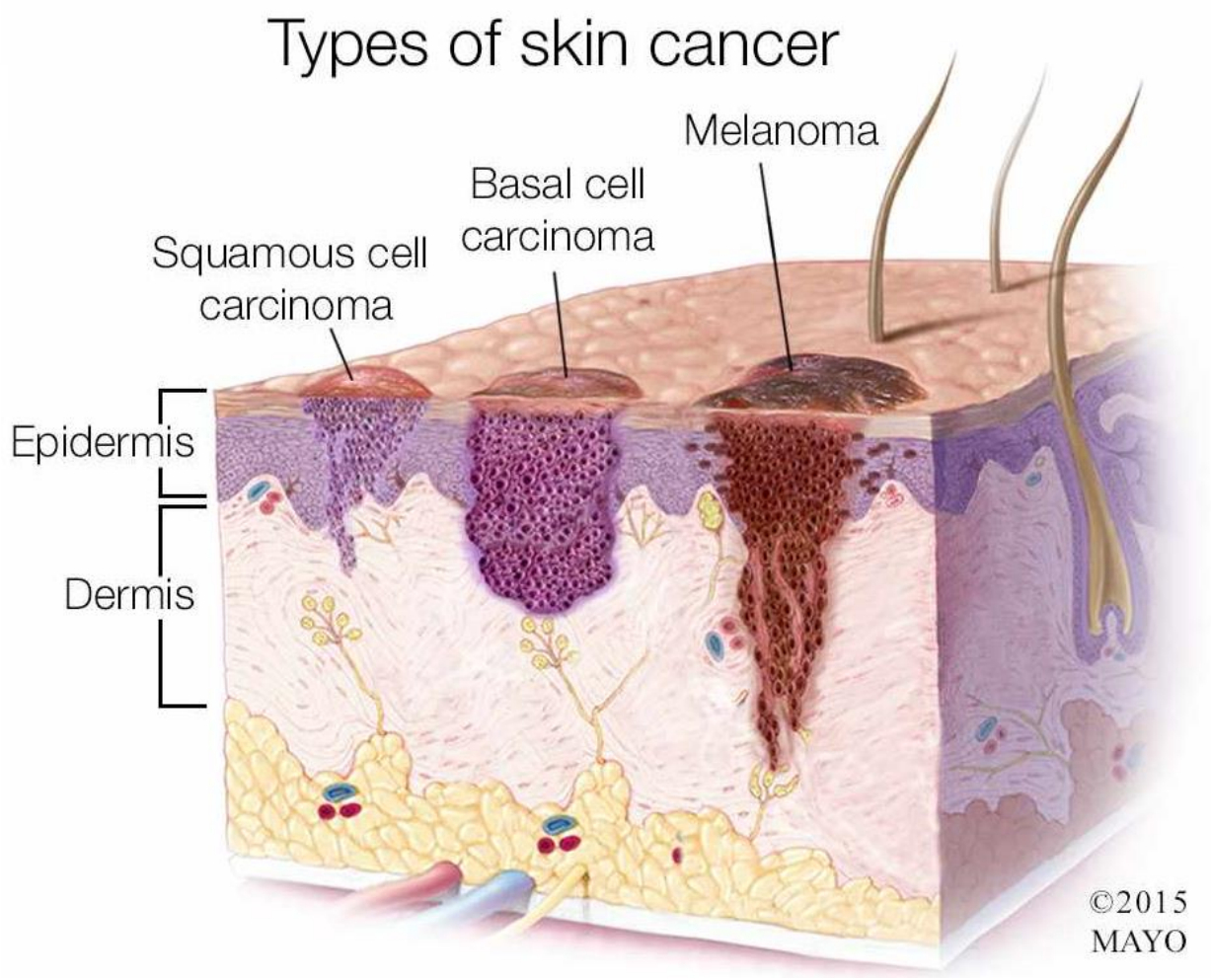


Basal cell carcinoma

Benign lesions - AiM at melanoma: http://www.aimatmelanoma.org/aim-for-answers/about-melanoma/moles-and-other-lesions/benign-lesions-lesions-that-are-not-cancerous.html
D. S. Rigel et al *Cancer of the Skin*. Elsevier Inc., 2005.







https://www.mayoclinic.org/diseases-conditions/basal-cell-carcinoma/symptoms-causes/syc-20354187
http://clermontoncology.com/cancer-education/melanoma/

Dermatoscopy: visual diagnostics

https://www.medgadget.com/2011/01/handyscope_turns_iphone_into_professional_dermatoscope.html

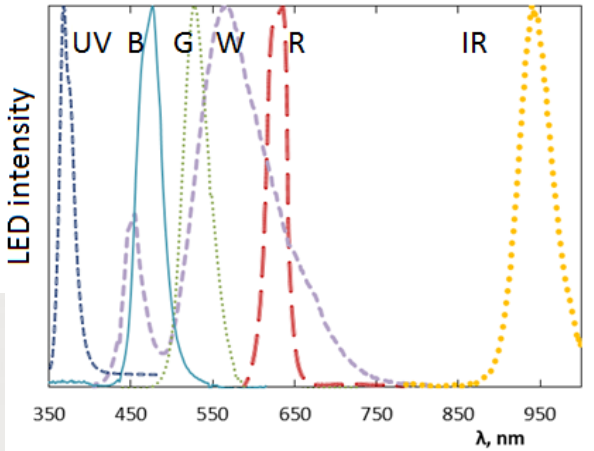
https://www.ebay.com/p/3gen-DermLite-II-Hybrid-M-Polarized-Dermascope/1108164329

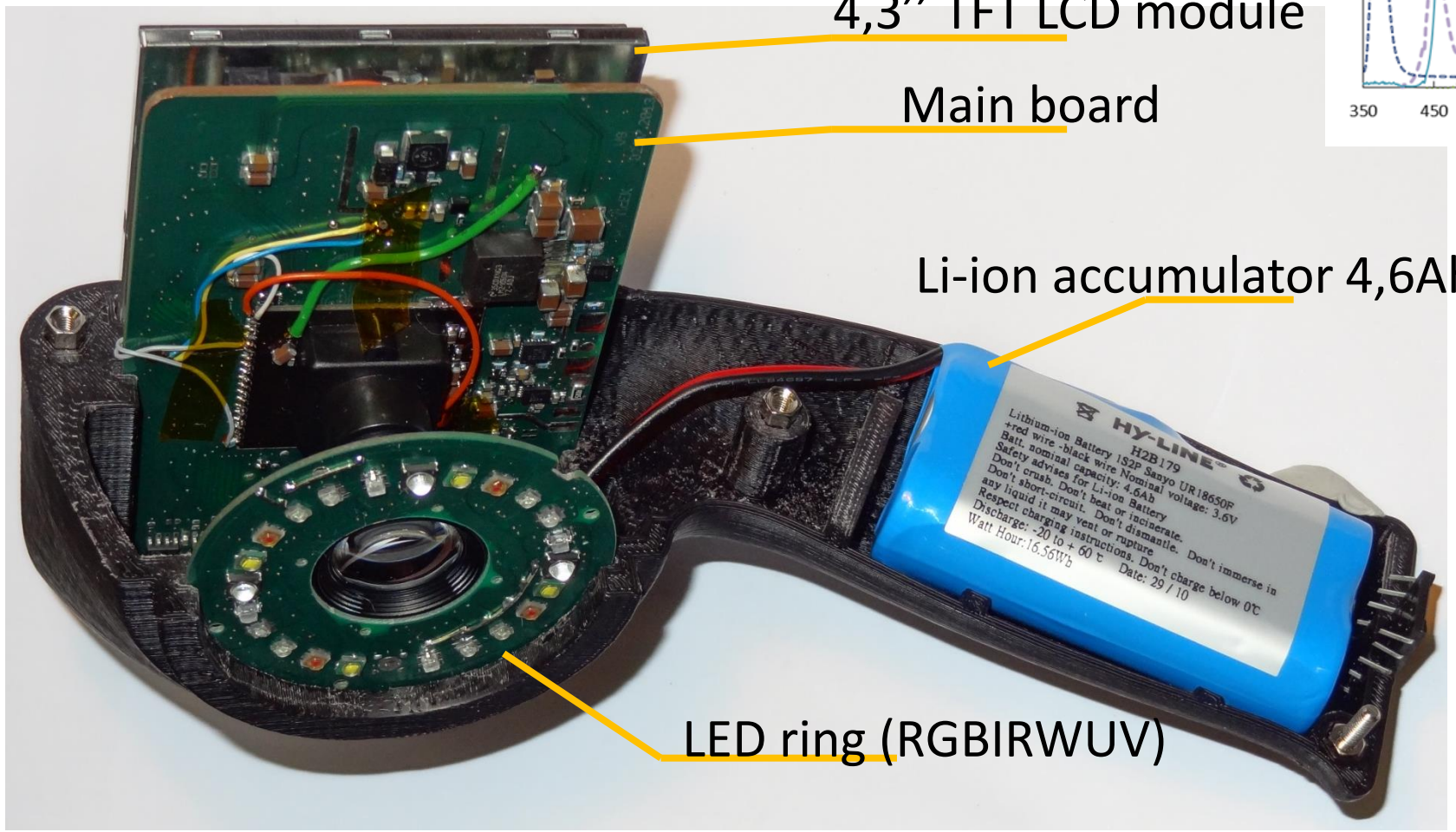
SkImager: a proof-of-concept device (2014)

- Performs complex multimodal skin imaging by camera-recording:
  - RGB reflectance image at white polarized illumination → revealing subcutaneous structures
  - 4 spectral images at narrowband LED illumination (450, 540, 660, 940nm) → distribution maps of melanin, haemoglobin, bilirubin, erythema index, melanoma/nevus index, skin oxigenation
  - Photoplethysmography video-image at green illumination → PPG amplitude distribution → skin blood perfusion map
  - Autofluorescence video-image at UV-excitation → map of photo-bleaching rates → skin fluorophore map

J.Spigulis, U.Rubins, E.Kviesis-Kipge, O.Rubenis. SkImager: a concept device for *in-vivo* skin assessment by multimodal imaging. *Proc.Est.Acad.Sci*., 63(3), 213-220 (2014).

SkImager: what's in



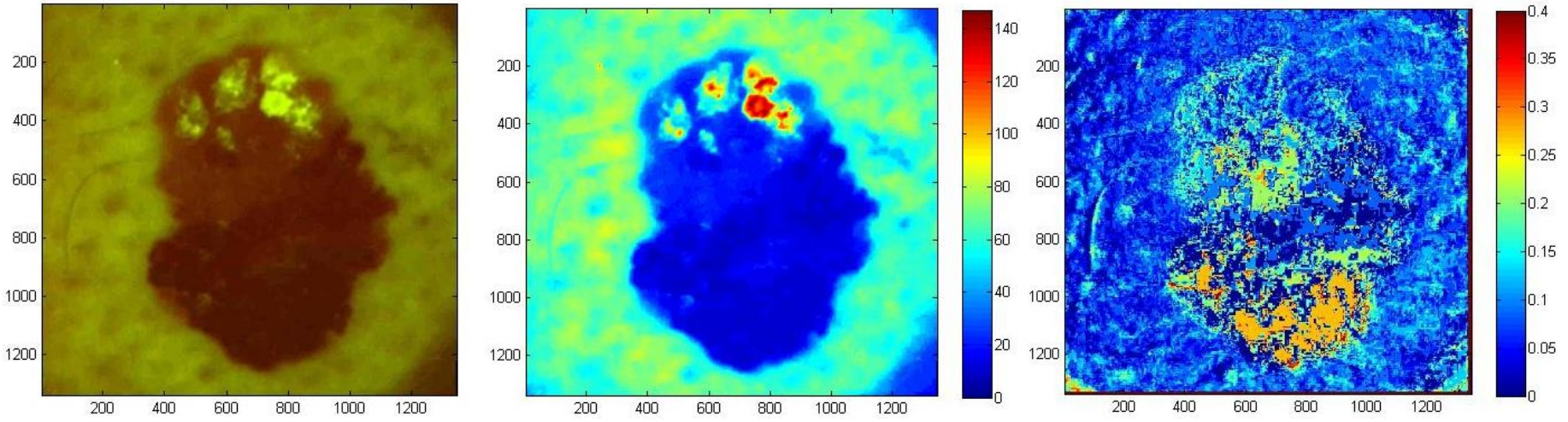


Fluorescent skin imaging by a smartphone camera (2015)

- **cw 405 nm LED ring**
- **~20 mW/cm²**
- **LP camera filter >515 nm**
- **20 seconds video**
- **framerate 0.5 fr/s → skin autofluorescence photobleaching parameters → fluorophore distribution maps**

Atypical skin nevus

Smartphone RGB photo at 405nm LED irradiation, AF image and photobleaching rate map



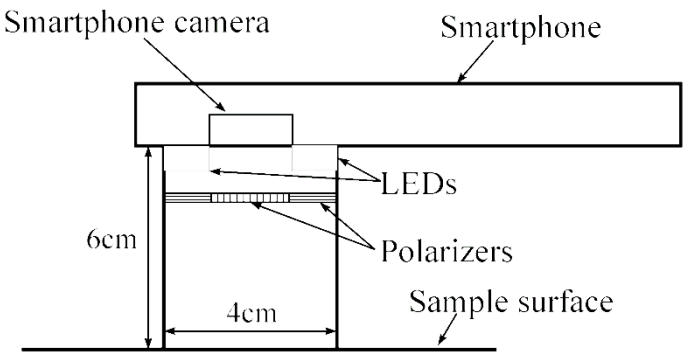
a b c

Filtered color image (a), AF intensity G-band image (b) and photobleaching rate map (c).

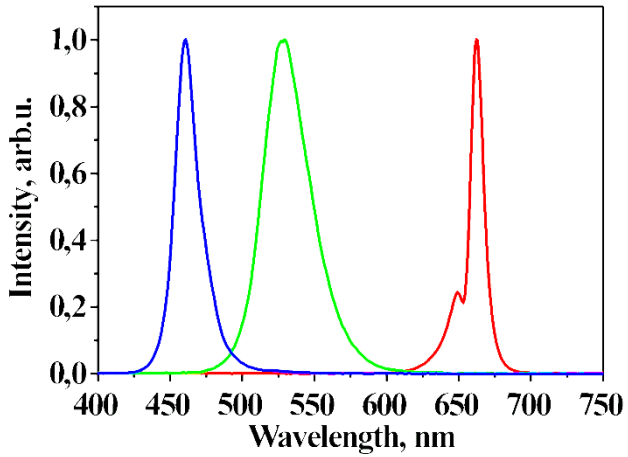
*Histological analysis of the removed tissue samples confirmed **three different types of tissue cells** within the lesion area: the upper part mostly prevailed by intradermal nevus, the middle part by dysplastic nevus, and the lower part by junctional nevus.*

A.Lihachev, et al. Autofluorescence imaging of Basal Cell Carcinoma by smartphone RGB camera. *J.Biomed.Opt*., 20(12), 120502 (2015).

RGB-LED smartphone system for multispectral imaging (2015)



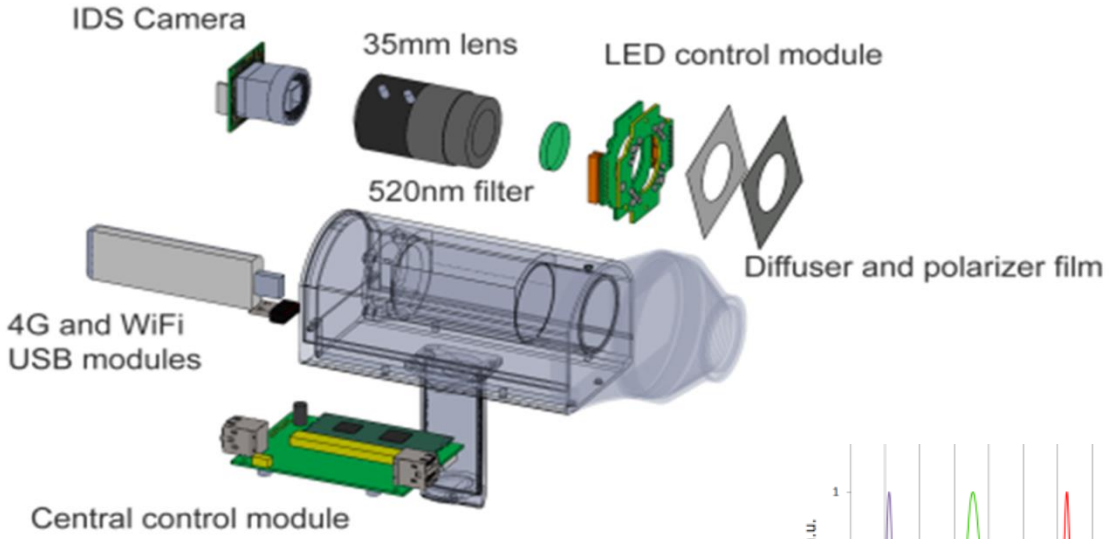
(a)

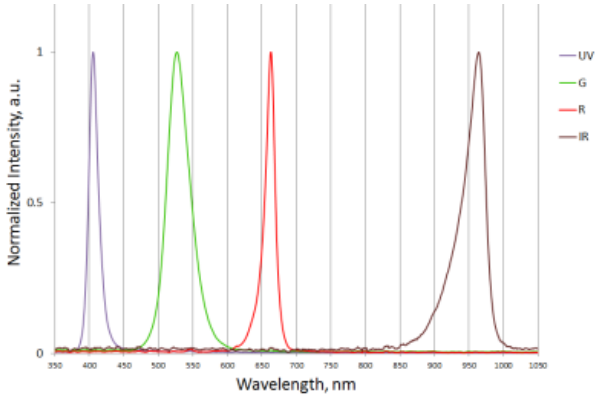


(b)

Kuzmina I., et al. Study of smartphone suitability for mapping of skin chromophores. *J.Biomed.Opt.*, **2015**, 20(9): 090503

Skin melanoma checker (2018-2019)





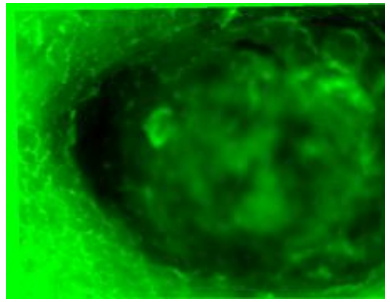
$$p' = lg\left(\frac{I(526)\cdot I_{skin}(663)\cdot I_{skin}(964)}{I_{skin}(526)\cdot I(663)\cdot I(964)}\right)$$

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

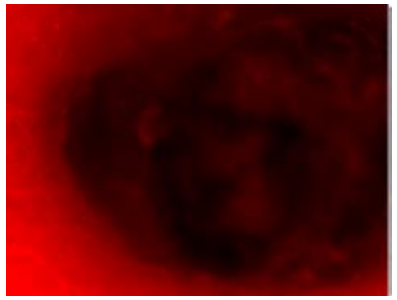
V.Lukinsone et al., "Multispectral and autofluorescence RGB imaging for skin cancer diagnostics", *Proc.SPIE* **11065**, 110650A (2019).

p’ parametric map for melanoma

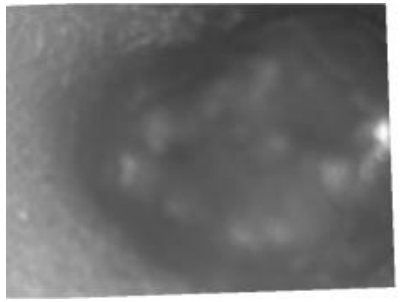
λ=526nm



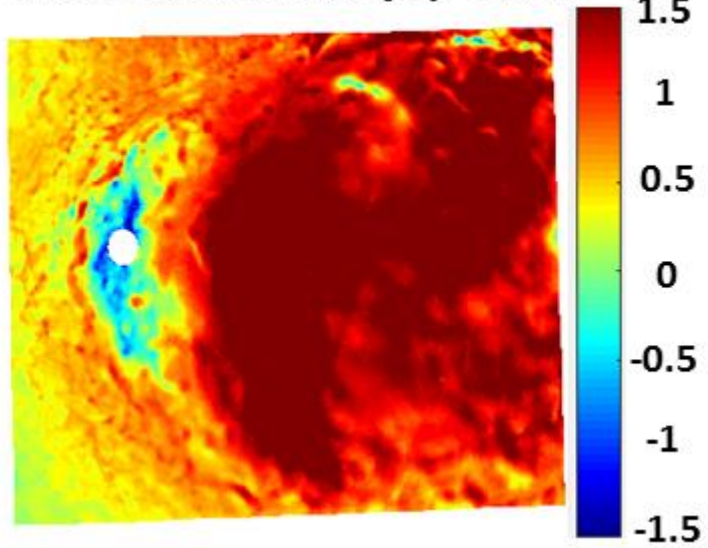
λ=663nm



λ=964nm



Melanomas kritērija p’ karte

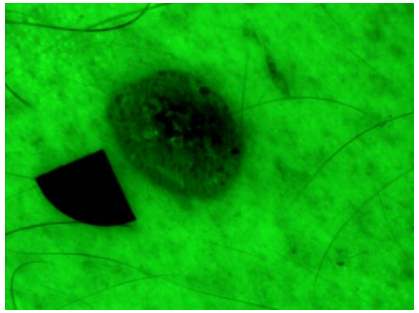


Melanoma: $p' > 1$

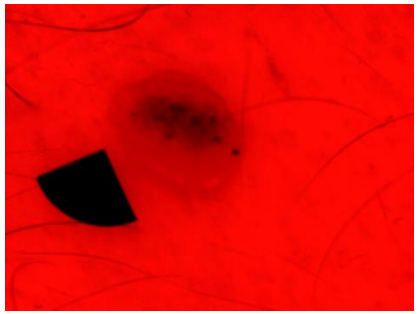
$$p' = lg\left(\frac{I(526)\cdot I_{\bar{a}da}(663)\cdot I_{\bar{a}da}(964)}{I(663)\cdot I(964)\cdot I_{\bar{a}da}(526)}\right)$$

Non-melanoma example

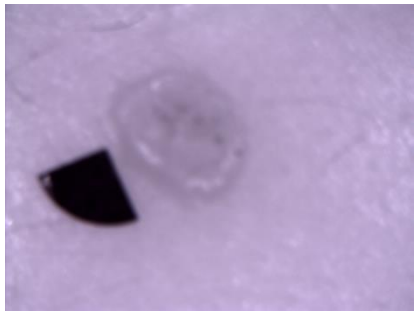
λ=526nm



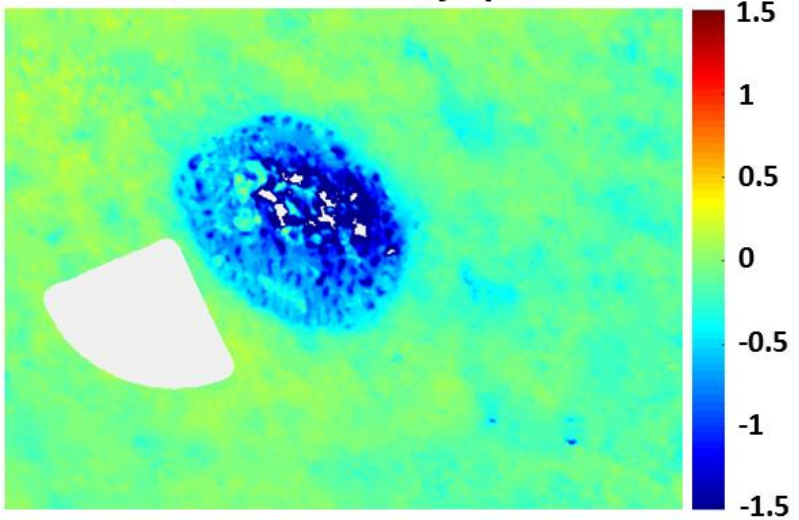
λ=663nm



λ=964nm



Melanomas kritērija p’ karte



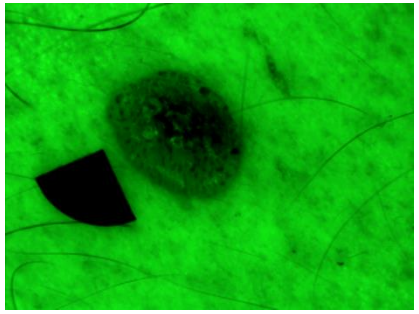
$$p' = lg\left(\frac{I(526)\cdot I_{\bar{a}da}(663)\cdot I_{\bar{a}da}(964)}{I(663)\cdot I(964)\cdot I_{\bar{a}da}(526)}\right)$$

Melanomai p’ > 1

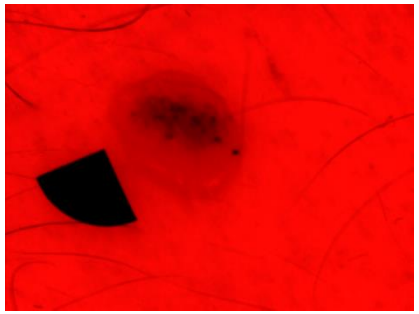
Working images: *seborrheic keratosis*

RGB image at white illumination

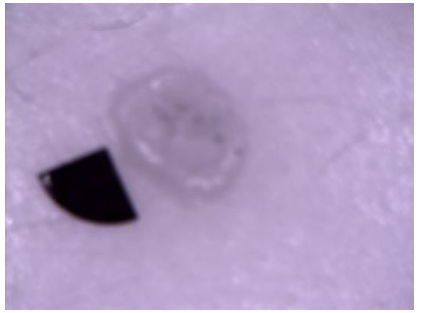
λ=526nm



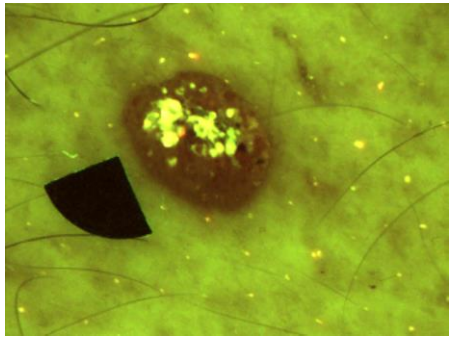
λ=663nm

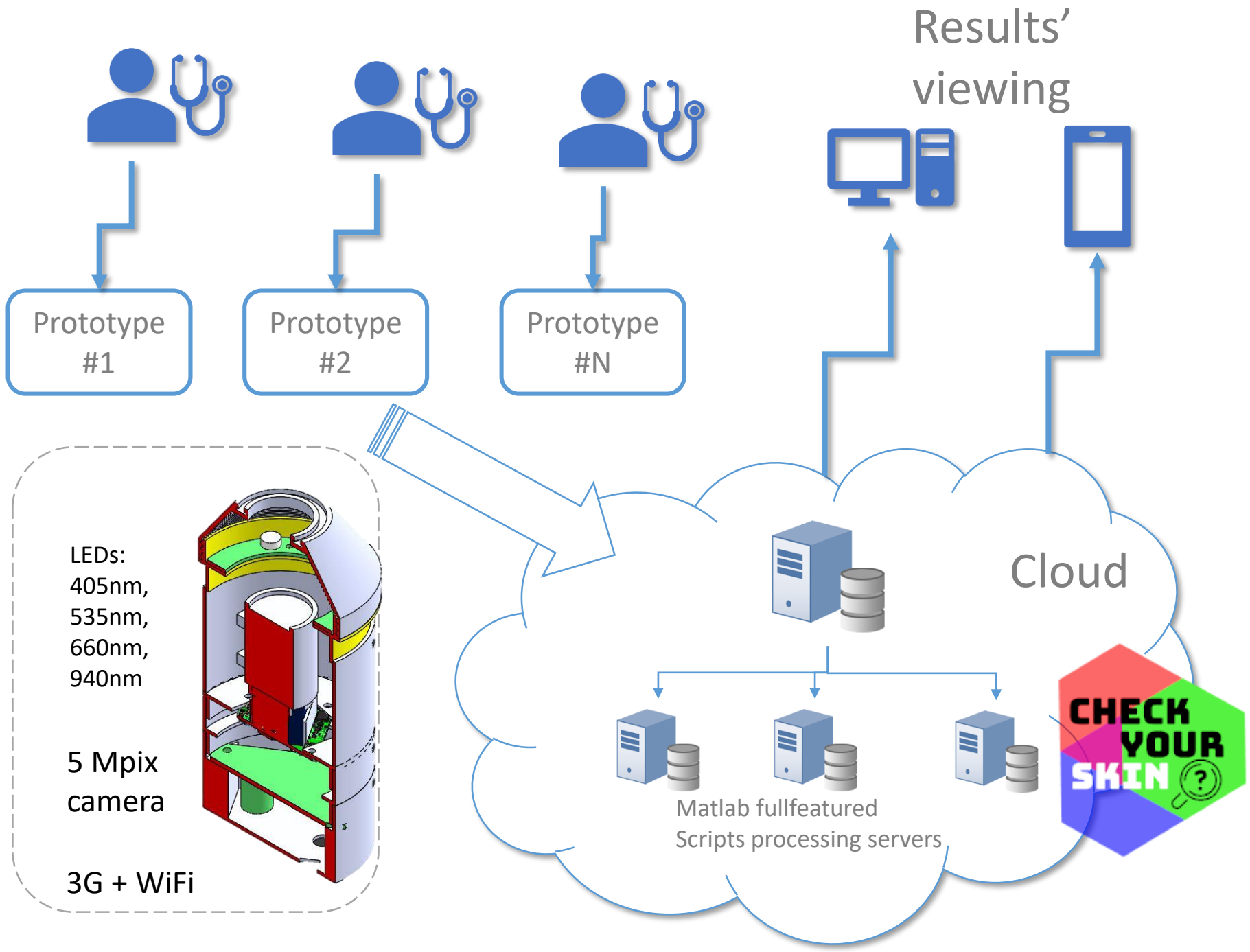


λ=964nm



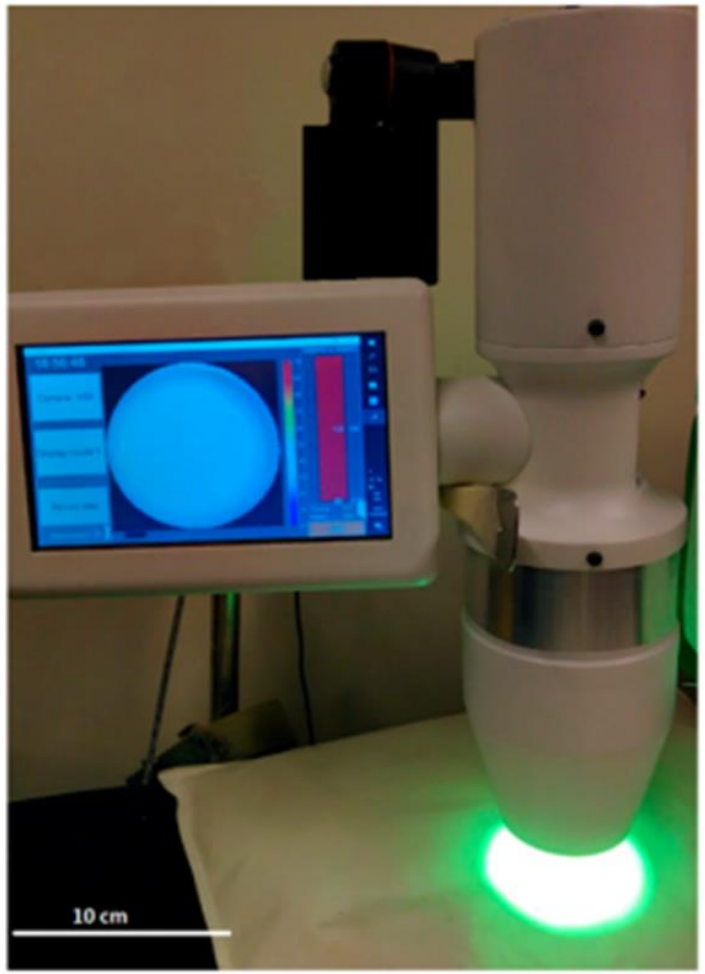
Autofluorescence image at 405nm excitation

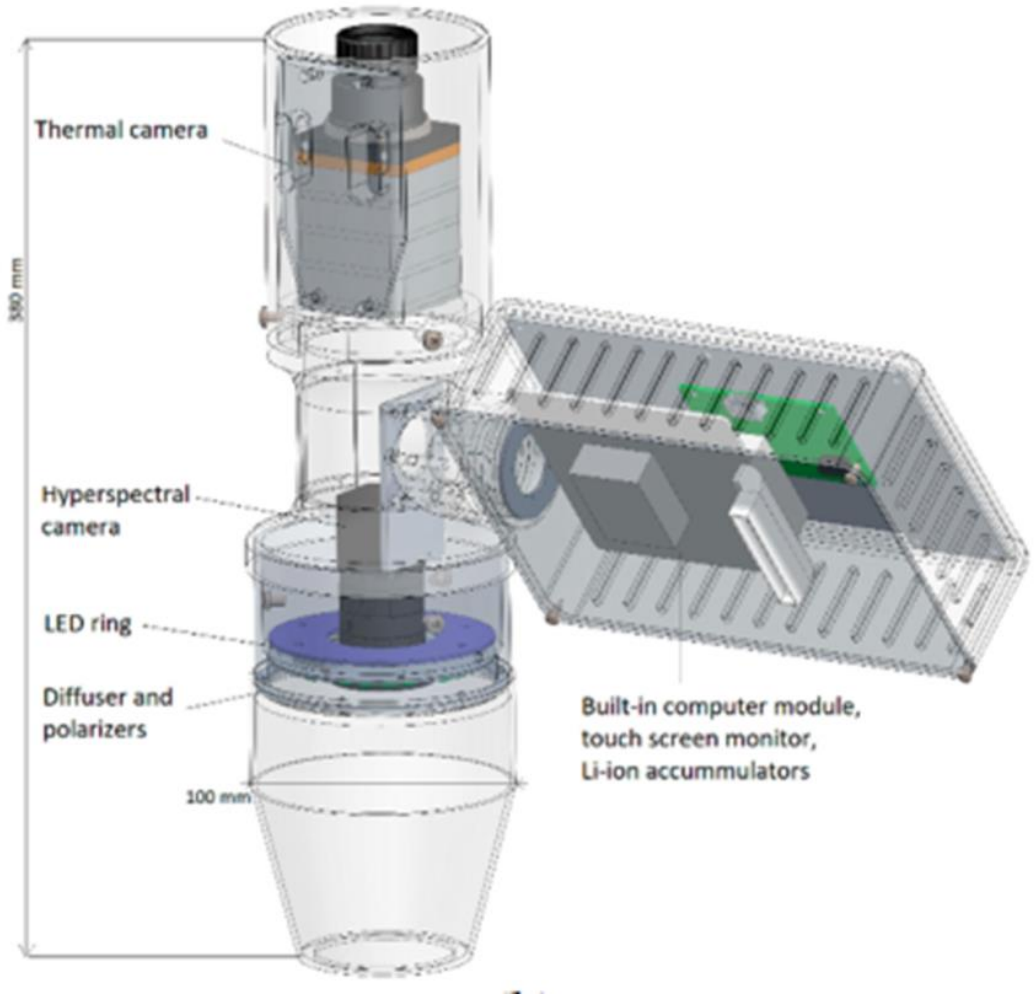


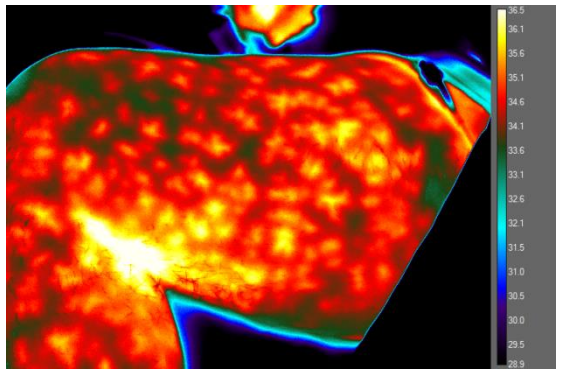

Results' viewing
Prototype #1
Prototype #2
Prototype #N
LEDs:
405nm,
535nm,
660nm,
940nm
5 Mpix camera
3G + WiFi
Cloud
Matlab fullfeatured
Scripts processing servers
CHECK YOUR SKIN

Multispectral & thermal skin imager for sepsis diagnostics (2019)

with Ximea 16-band mosaic camera, white @ green LEDs







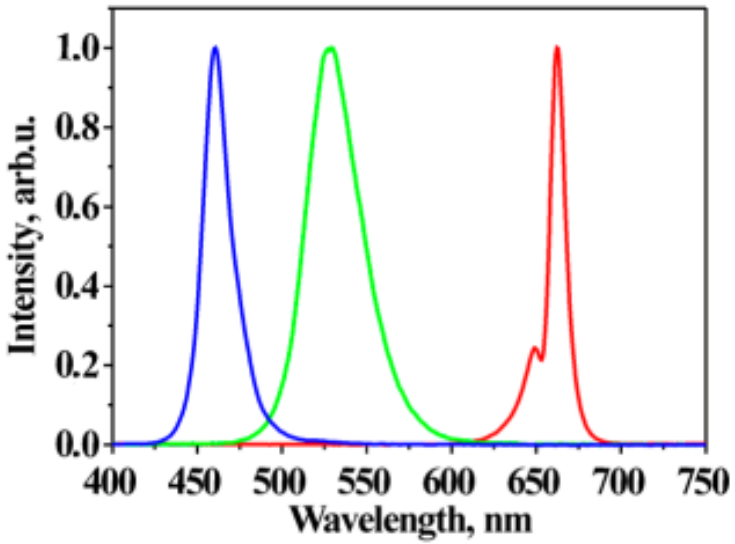
U.Rubins et.al., «Multimodal device for real-time monitoring of skin oxygen saturation and microcirculation function», *Biosensors,* 9, 97 (2019).

Multi-spectral-line imaging:

>100x improved spectral selectivity, single snapshot

Conventional:

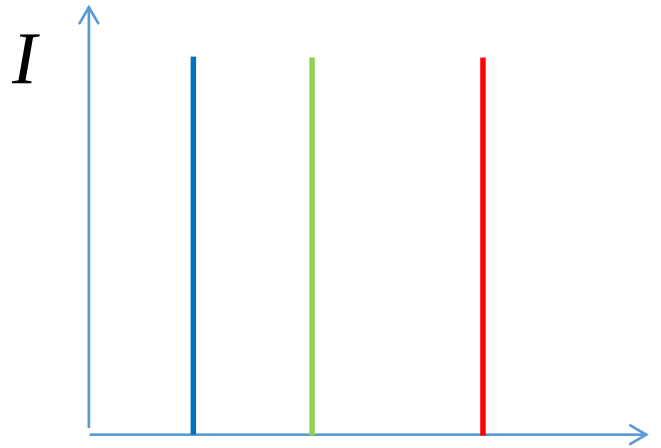
Spectral **band** images



Sequential (t>>0)

Novel:

Spectral **line** images



Single snapshot (t→0)

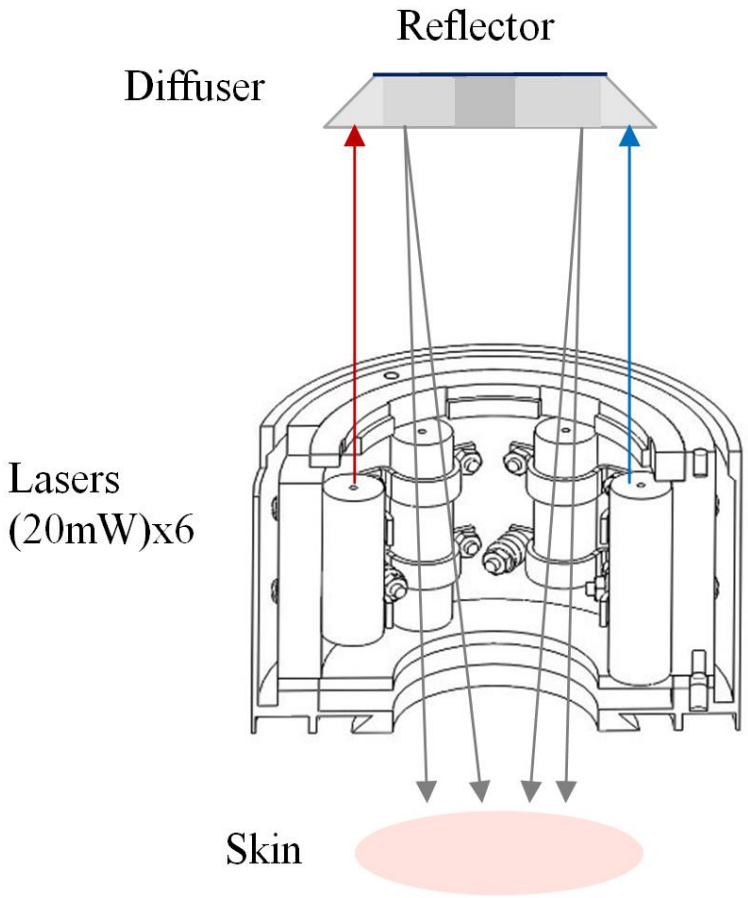
n =3 → n > 3

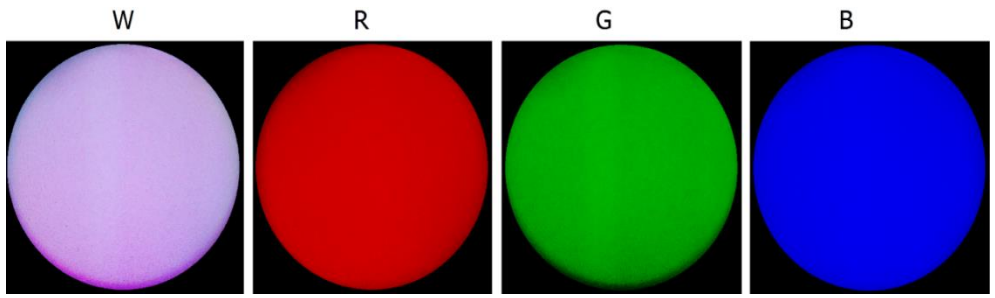
Benefits:

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

WO2013135311 (A1), 2012. Method and device for imaging of spectral reflectance at several wavelength bands (J.Spigulis. L.Elste).

Triple-wavelength laser add-on (2015)

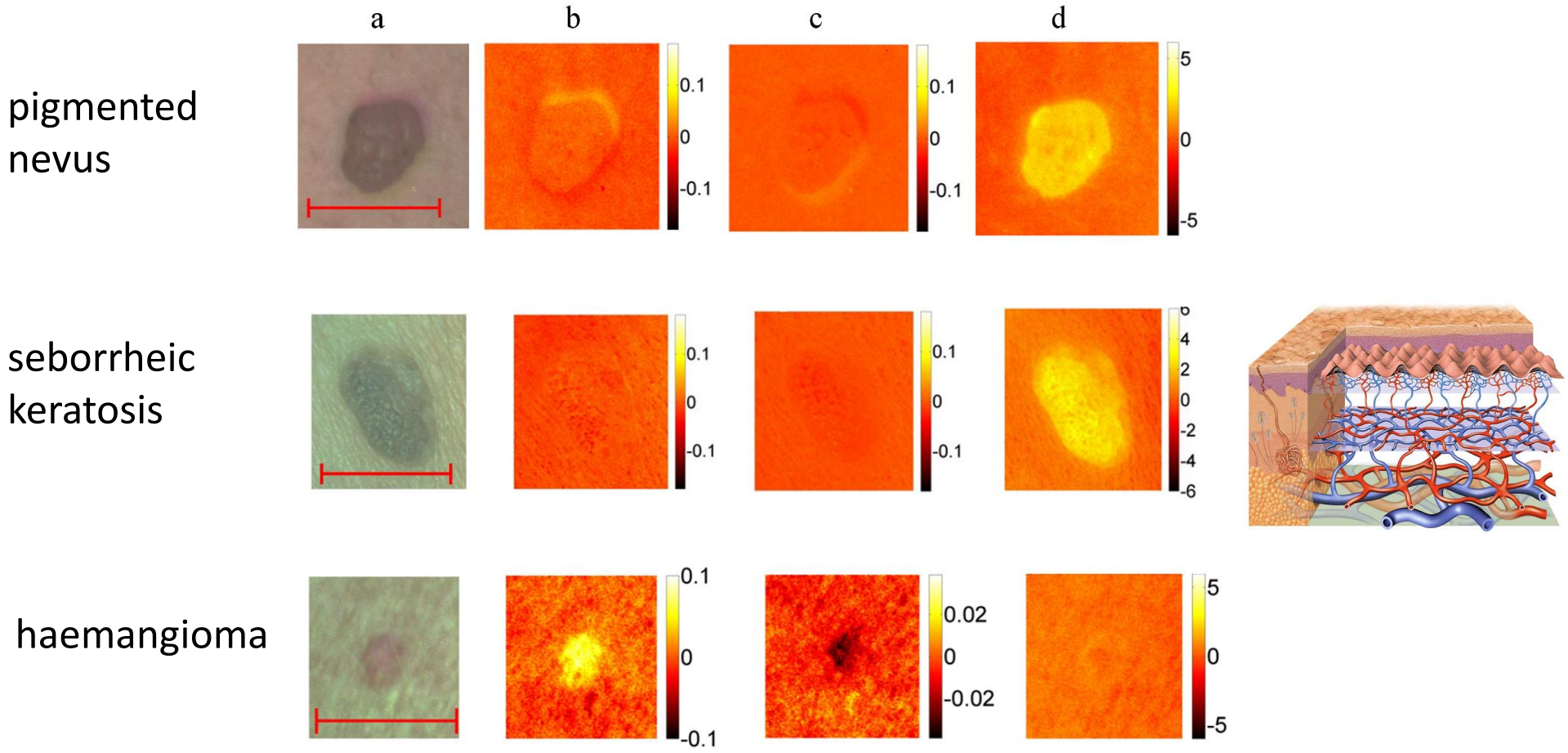




659 nm 532 nm 448 nm

J.Spigulis, et al., “Smartphone snapshot mapping of skin chromophores under triple-wavelength laser illumination”, *J.Biomed.Opt.*, **22**(9), 091508 (2017).

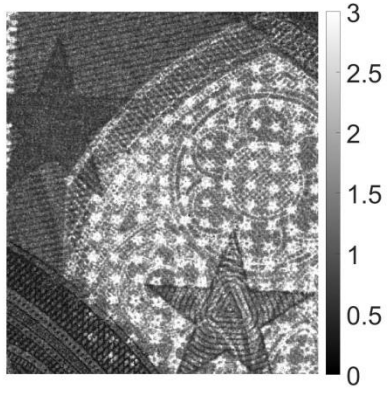
RGB images (a) and maps of chromophore content changes: b – oxy-haemoglobin, c – deoxy-haemoglobin, d – melanin.

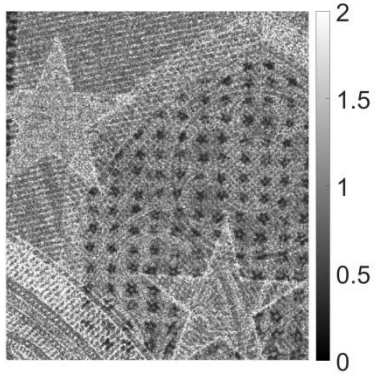


Spigulis J., et al. Smartphone snapshot mapping of skin chromophores under triple-wavelength laser illumination. *J.Biomed.Opt.*, **2017**, 22(9): 091508.

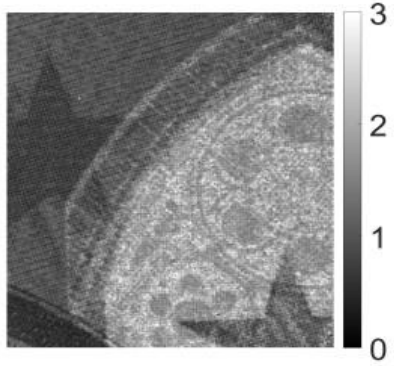
LATVIJAS BANKA

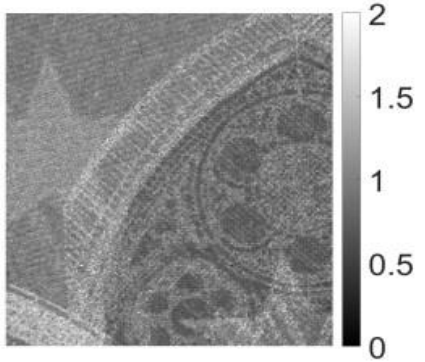
Another potential application: forgery detection





Real





Fake

RGB

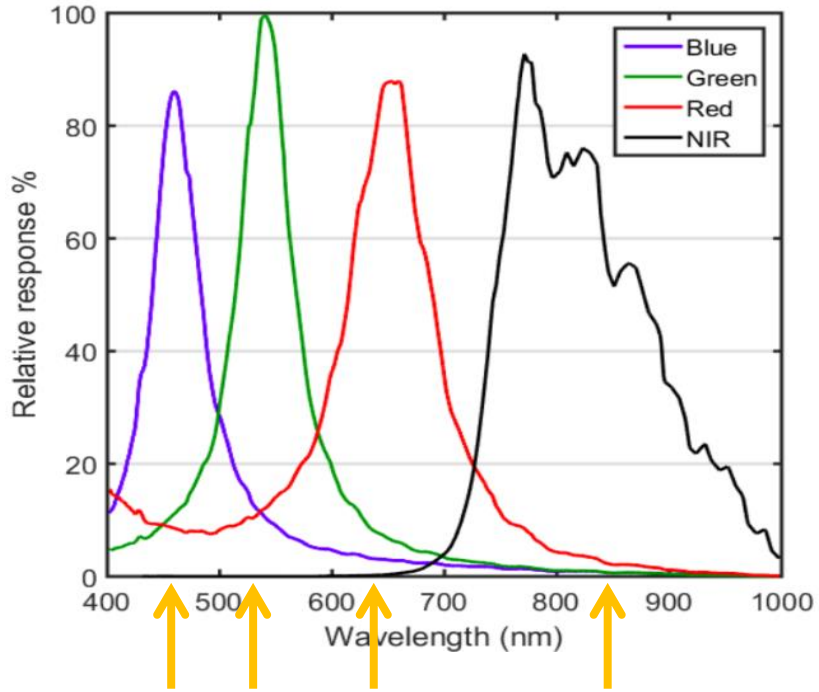
659/448nm

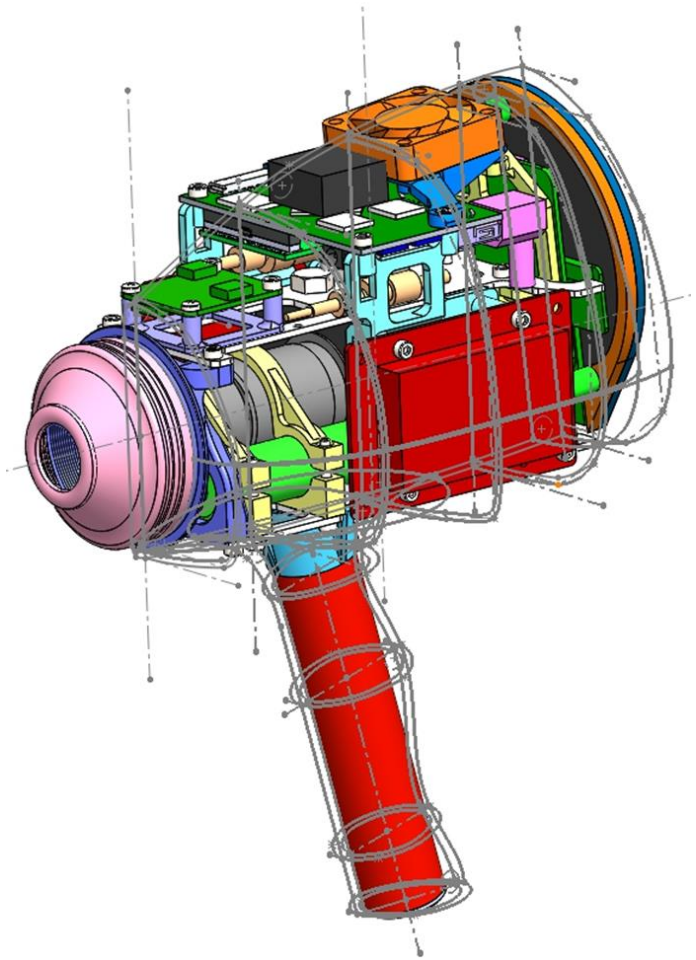
448/532nm

The four laser line single camera prototype (2020)

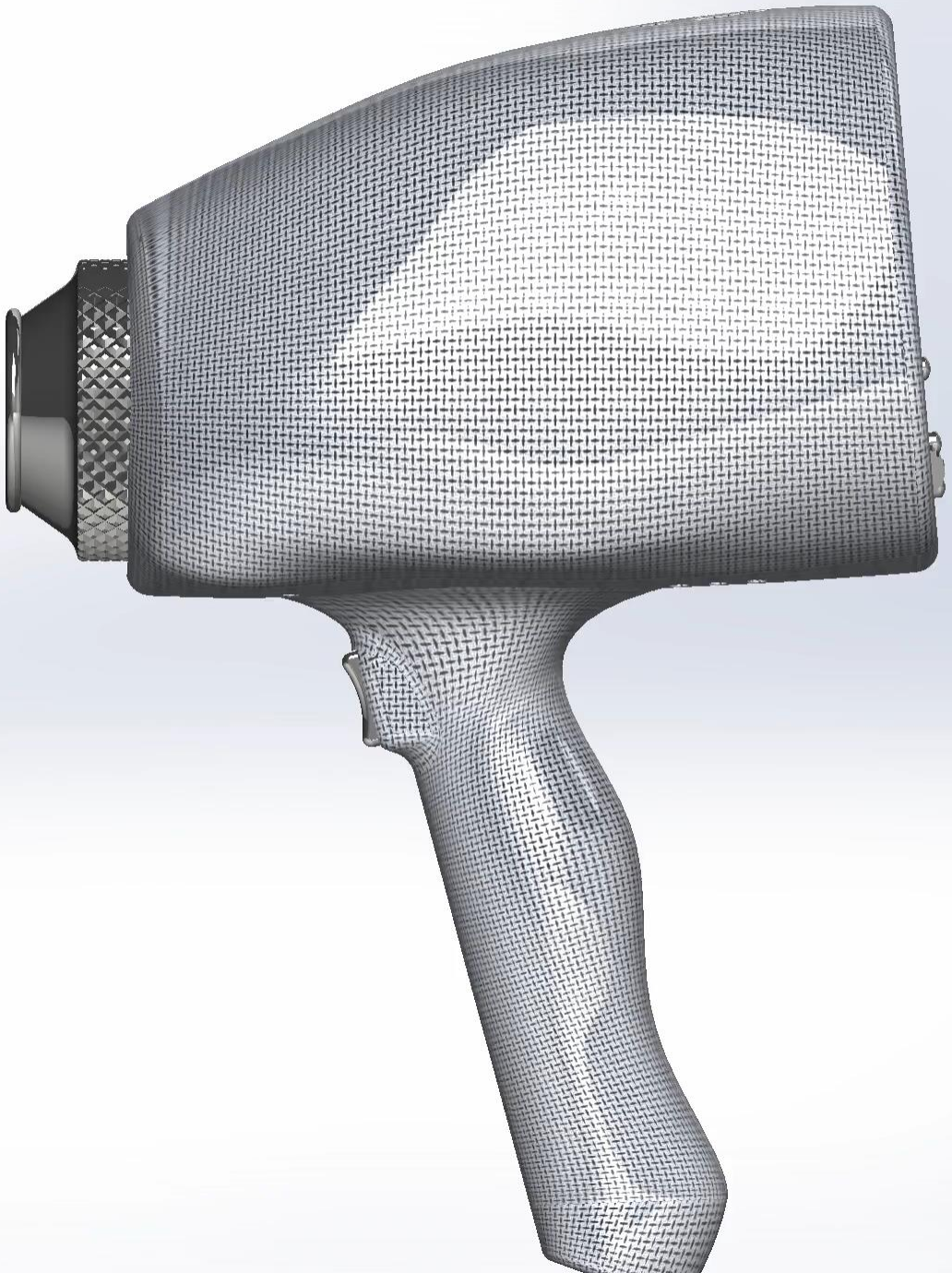
405+450/523/638/850 nm

Four-band camera spectral sensitivities →

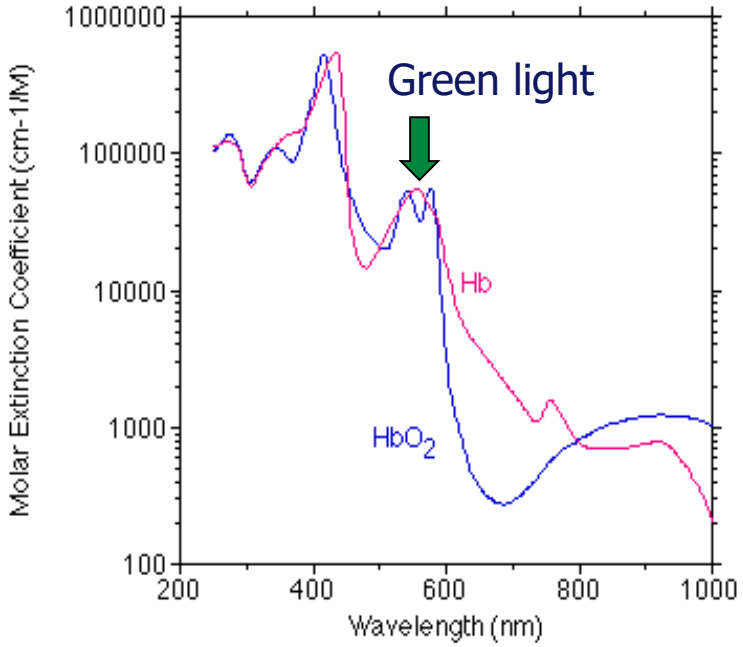


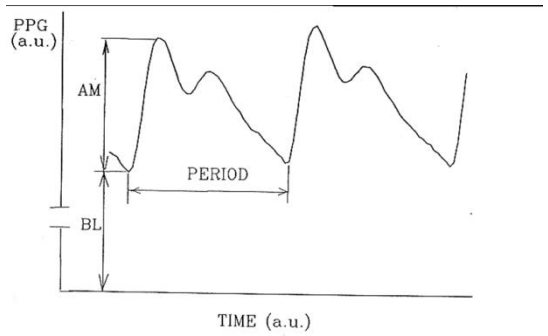


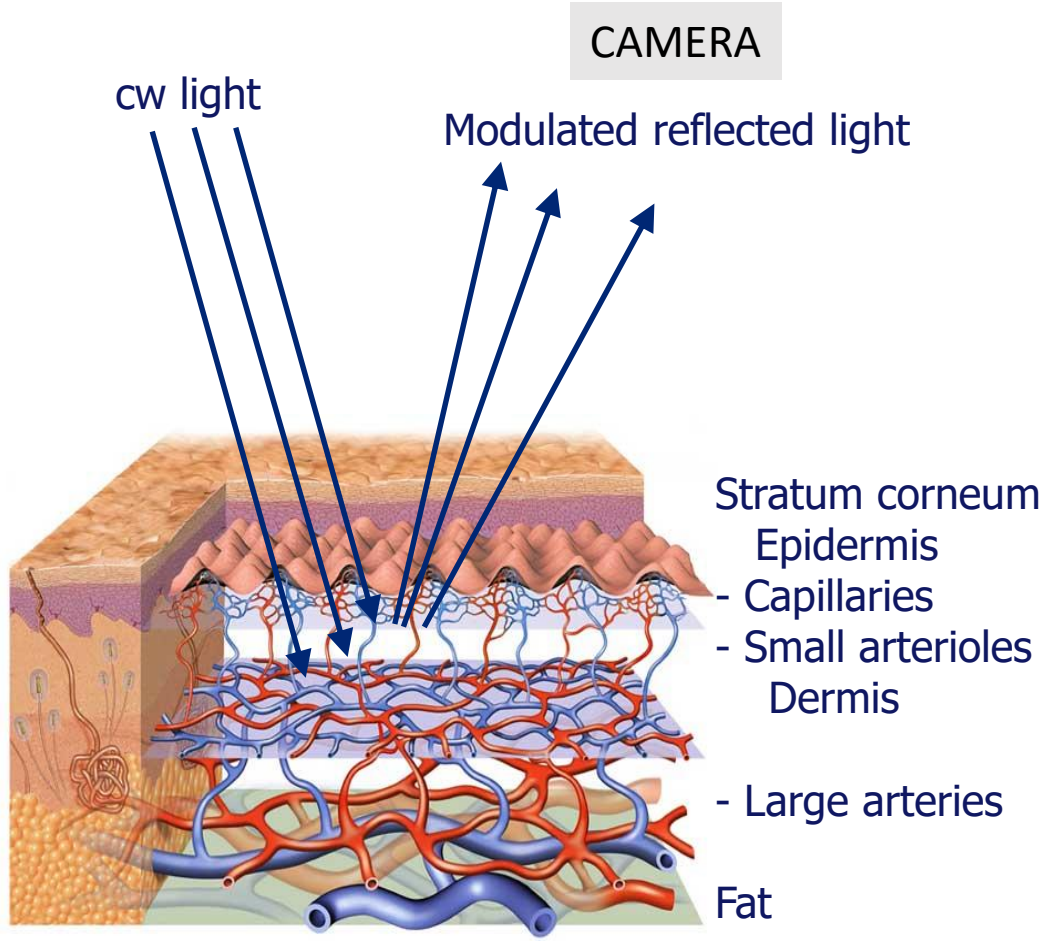
J.Spigulis, et al., “Spectral line reflectance and fluorescence imaging device for skin diagnostics”, *Appl. Sci.* **10**, 7472 (2020).



Photoplethysmography imaging: principle

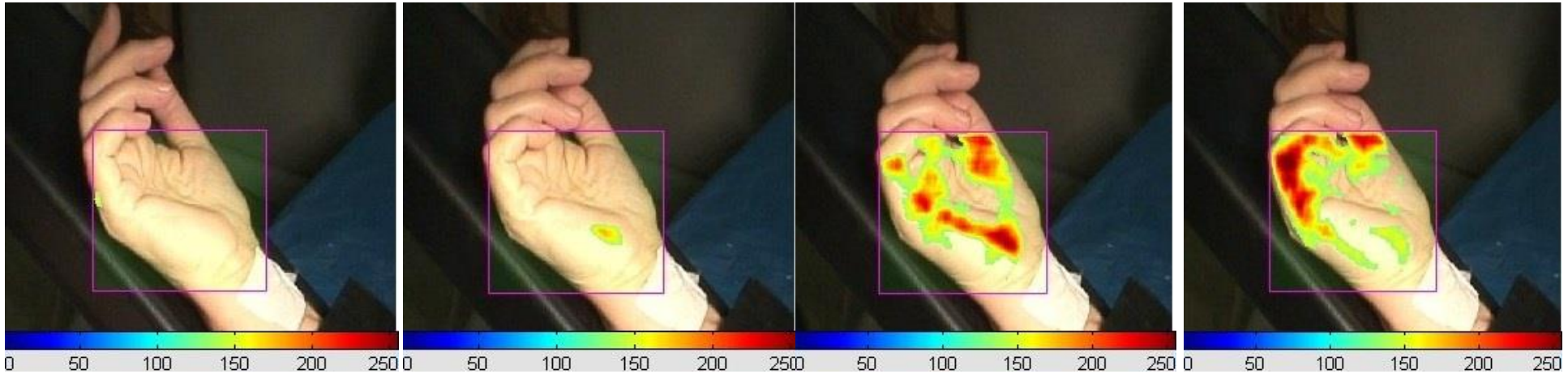




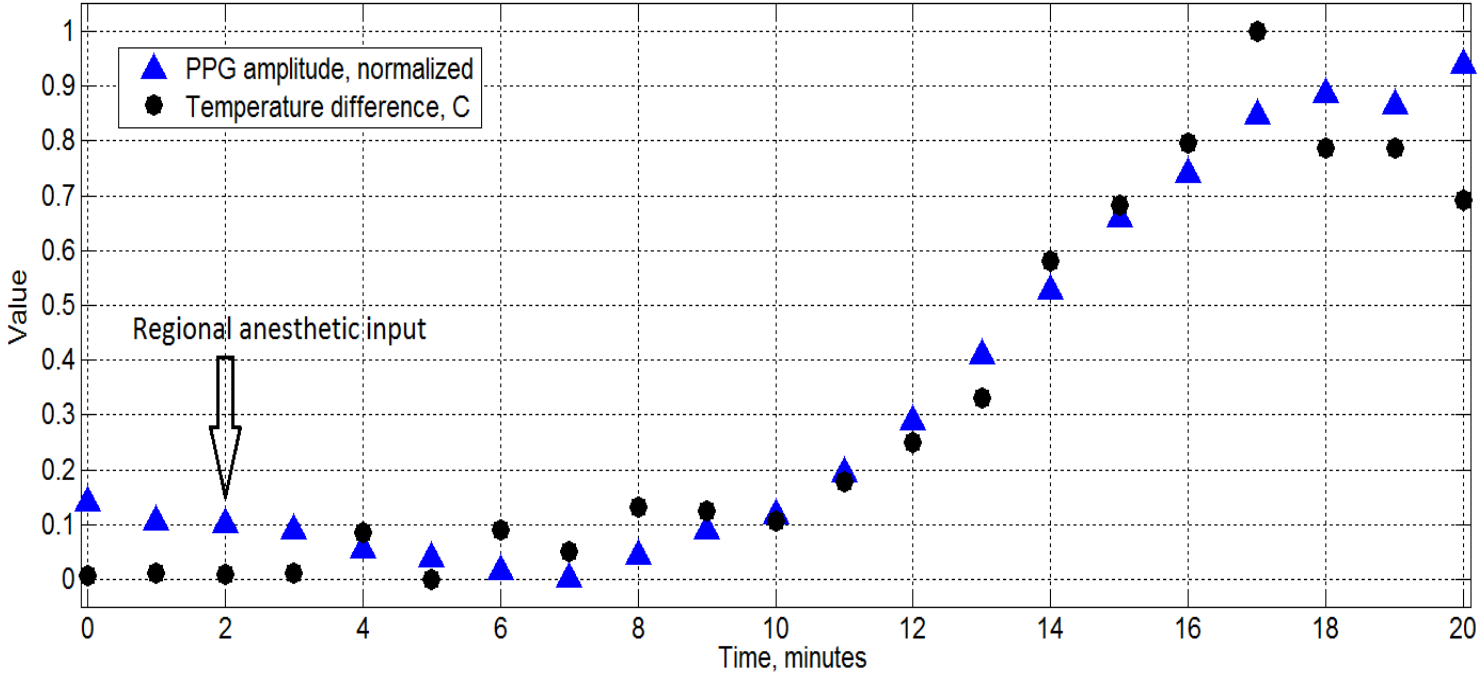


PPGI: non-contact technique for detection of arterial blood pulsations

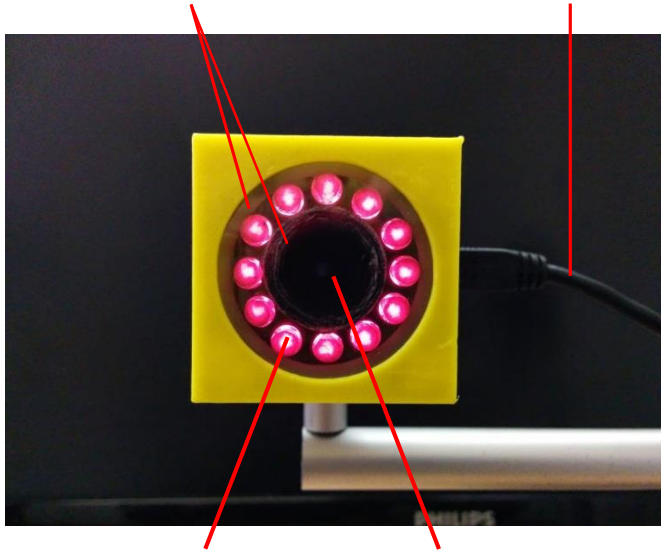
Remote anaesthesia control: perfusion monitoring

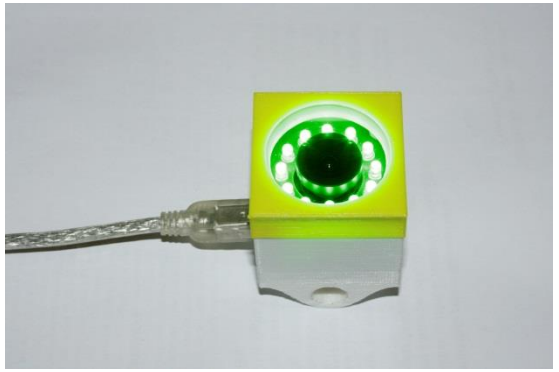


RA injection 8 minutes 12 minutes 16 minutes



Compact 4x4x4 cm prototype for PPGI measurements (2016)

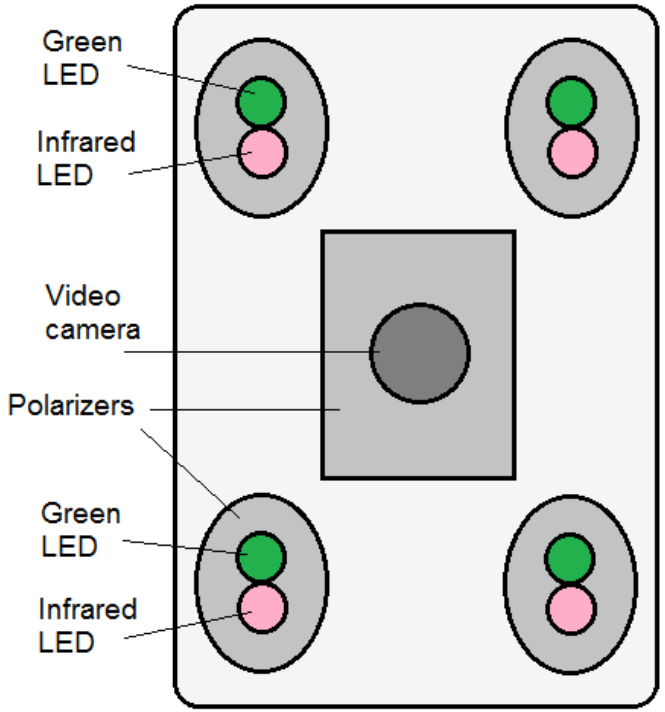




IR LED (760nm) – for measurements of deeper blood vessels;
Green LED (540nm) – for measurements of upper blood vessels

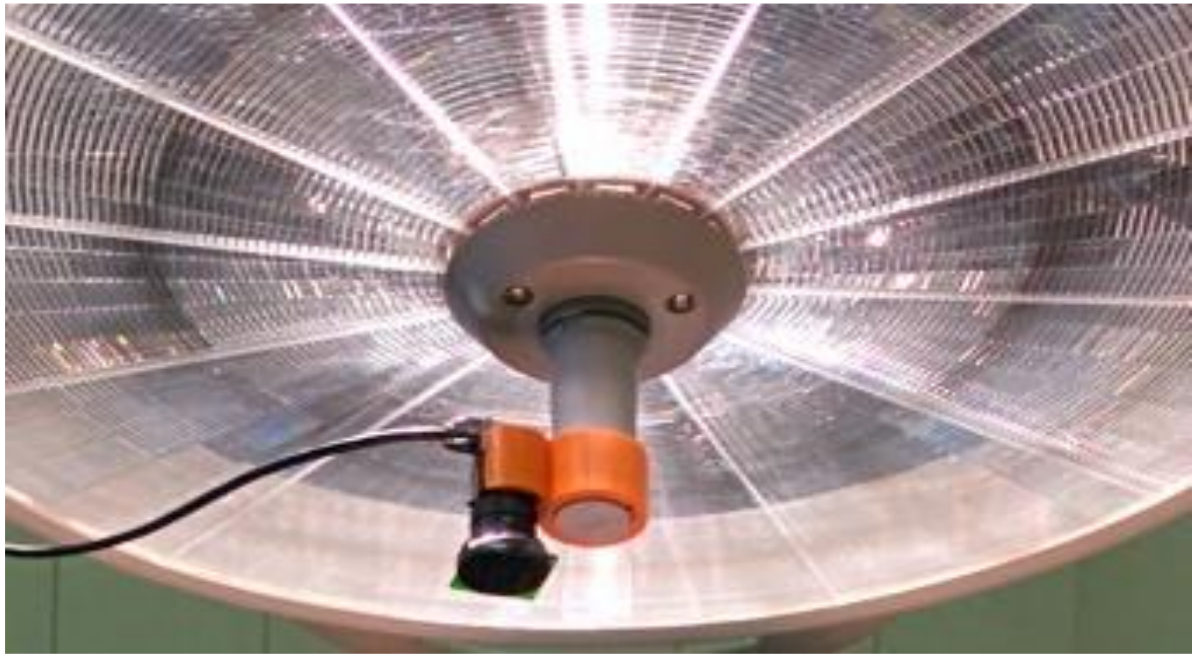
The prototype for hand PPGI measurements (2017)

1. The device has vacuum pillow for fixing of palm in steady position.
2. Four bispectral illuminators perform uniform illumination of skin.



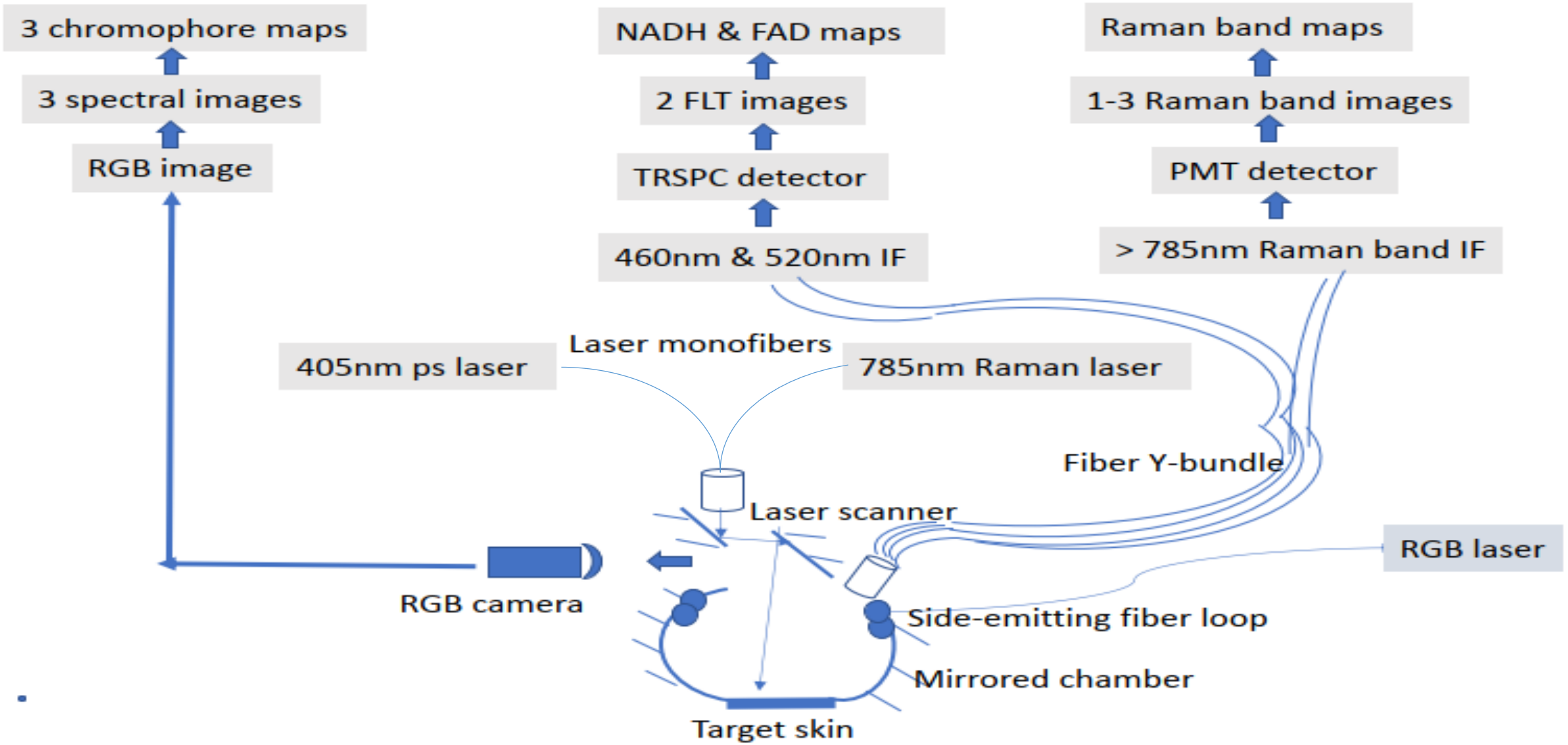
IR LED (810nm) – for measurements of deeper blood vessels;
Green LED (530nm) – for measurements of upper blood vessels

Anaesthesia monitoring before/during surgeries by PPG-imaging: installed in Riga Hospital of Traumatology and Orthopaedics (2017)

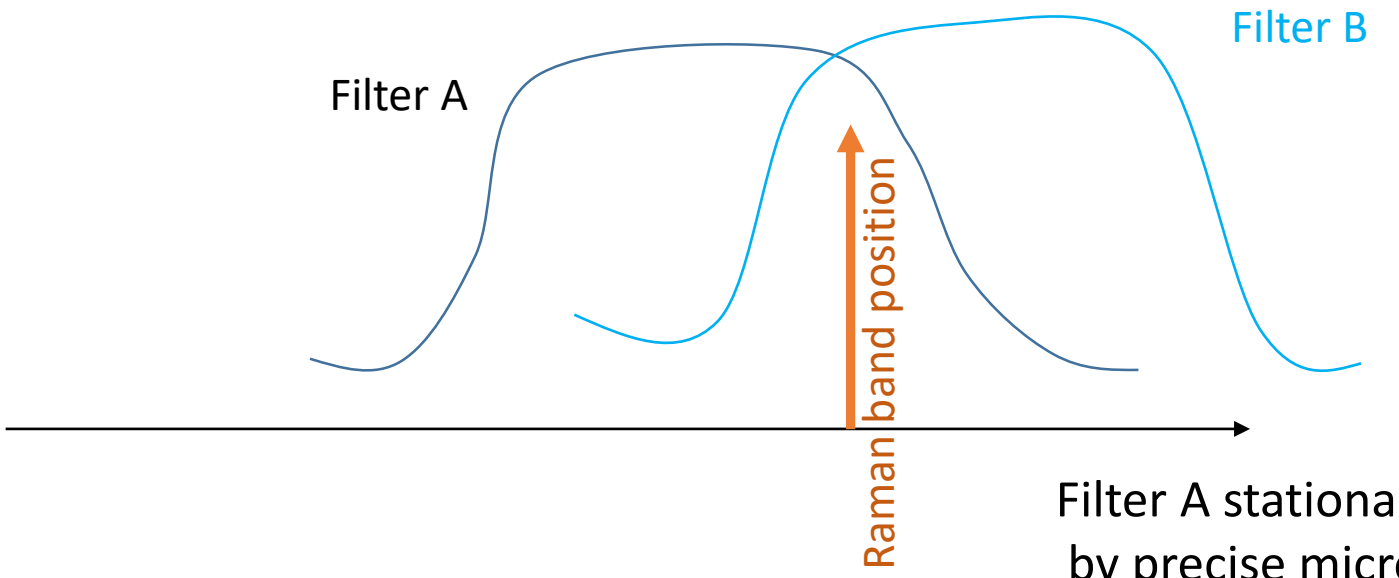


Standard operation lamp used as the light source, only camera with green band filter attached, with cable connection to PC

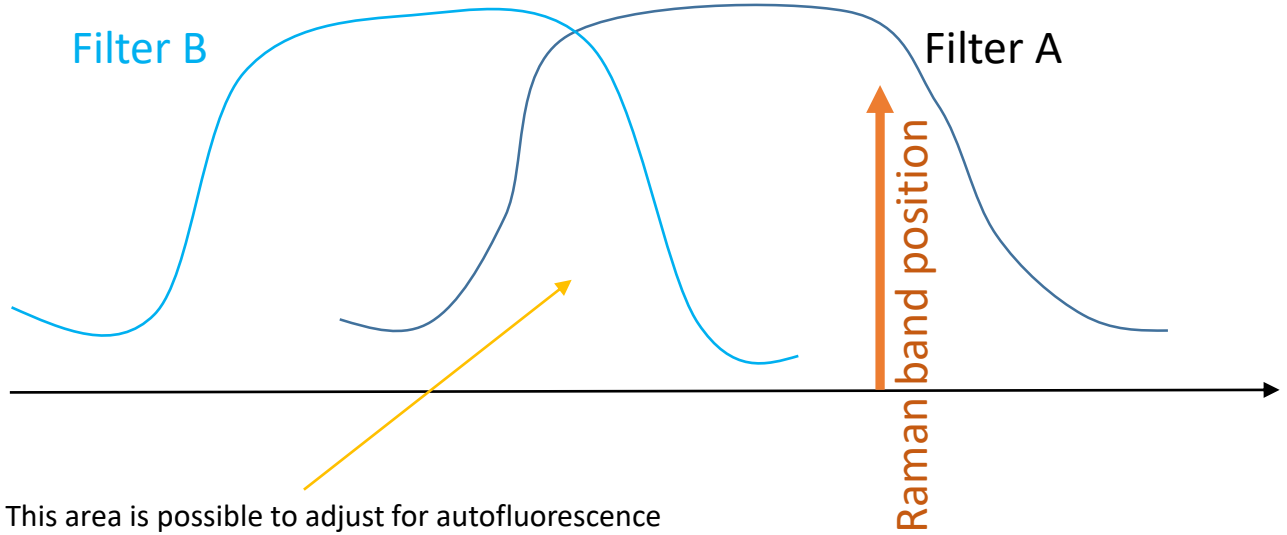
Tri-modal skin imaging project: concept scheme



Double-filter separation of a Raman band to be imaged



Filter A stationary; Filter B rotated by precise micrometer step-screw.



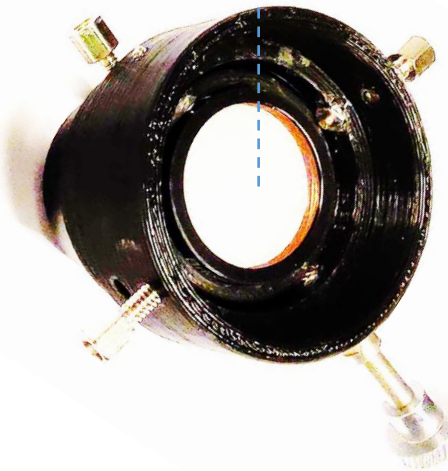
This area is possible to adjust for autofluorescence compensation if AF increase is distorting the Raman image

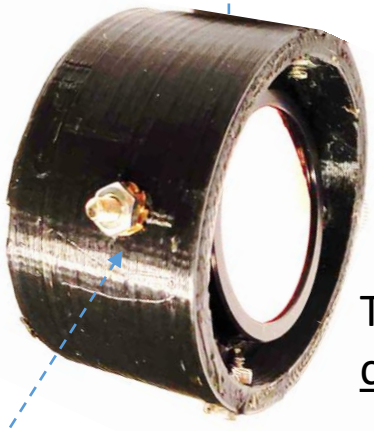
FILTER COMPARTMENT

785 ex. rejection filter

Exchangeable narrow band-pass filter F#1 or F#2

Wide band-pass filter, F#0 (inside compartment)

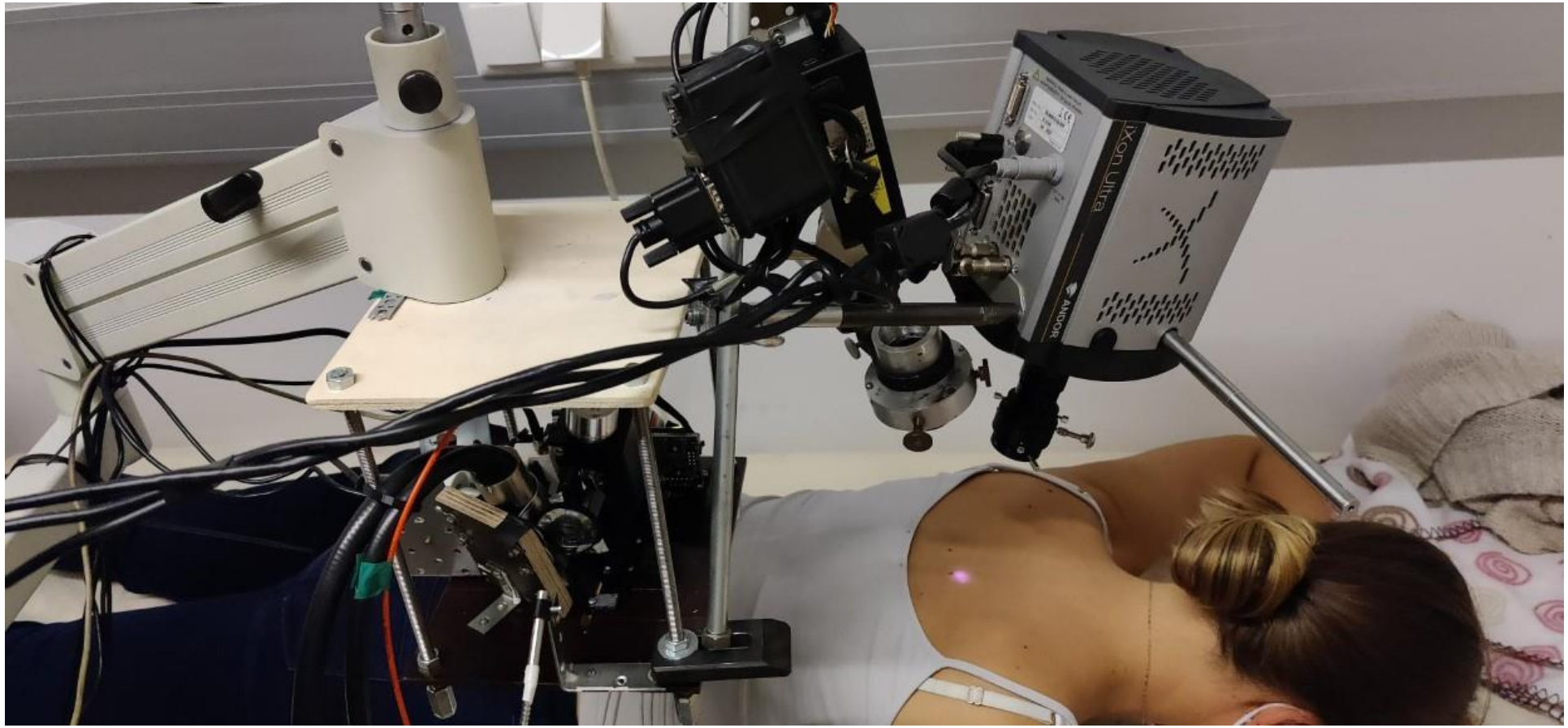




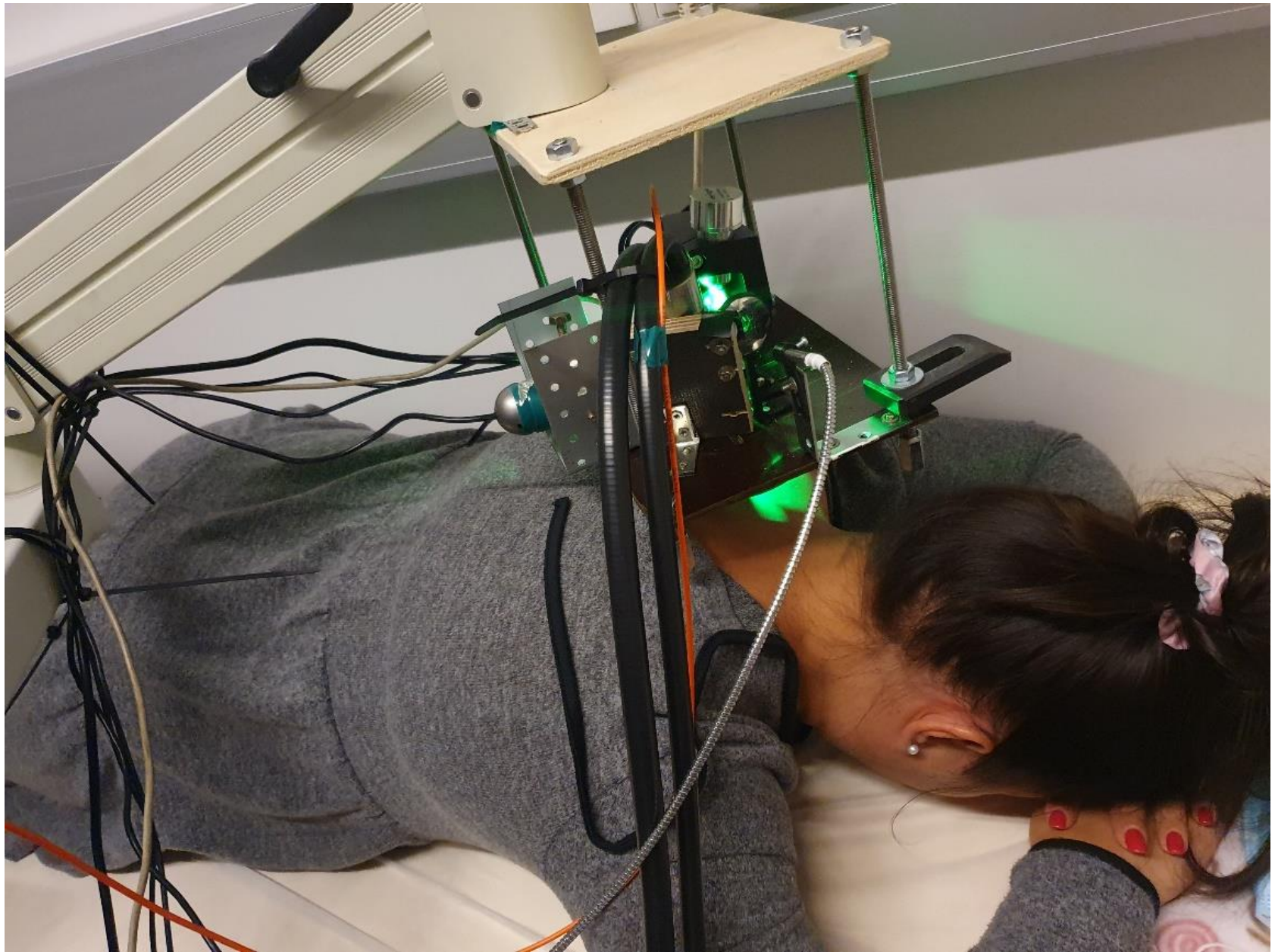
Tilting angle calibrated

Filter rotation handles

Camera-based Raman band imaging of skin



Bi-modal RGB-FLIM imaging of skin



SUMMARY

- A family of camera-based prototype devices for non-contact optical assessment of *in-vivo* skin has been designed, assembled and clinically tested:

➢ multimodal imaging concept-device „SkImager“

➢ three smartphone-based devices with spectrally specific illumination units

➢ four spectral line imaging device for skin chromophore mapping

➢multispectral-thermal imaging device for early sepsis diagnostics

➢ multispectral-fluorescence imaging device for skin melanoma screening

➢ photoplethysmography imaging devices for remote monitoring of anaesthesia efficiency during surgeries

- A prototype device for multimodal (RGB multispectral / AF lifetime / Raman band) skin imaging is under development
- The bottleneck: hundreds of clinical measurements are needed to collect sufficient statistics for permission to use as routine medical tools in hospitals, clinics and family doctor’s offices; too expensive so far, the current state: **experimental demo-devices**

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Thank You!

- janispi@latnet.lv
- http://home.lu.lv/~spigulis