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Human skin optical property modifications upon optical clearing agents estimated from spatially-resolved tissue optical spectroscopy

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INTRODUCTION & AIM OF THE STUDY

C Medical & scientific contexts

C Skin cancers (carcinomas)

- C Initiates in epidermis then spread deepward
- C Implies structural and biochemical modifications at cellular and tissular levels

C *In vivo* characterization for improving medical diagnosis performance

- C « Tissular optical biopsy » (clinically usable) approach
 - Multimodality: Diffuse Reflectance (DR) + AutoFluorescence (AF)
⇒ increasing detection Sensitivity (Se) and Specificity (Sp)
 - Spatially-Resolved (SR) spectroscopy
⇒ allowing tissue depth probing

C Optical Property (OP) estimation

- Modelling absorption, scattering and fluorescence
- Solving inverse problem

C Skin transparency enhancement

- Reducing absorption and scattering
- Using safe Optical Clearing Agent (OCA) + enhancer

C Aim of the present work

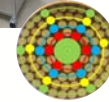
- C Investigating the impact of OCA on *ex vivo* skin's OP using SR-DR&AF spectroscopy



MATERIALS & METHODS (1/2)

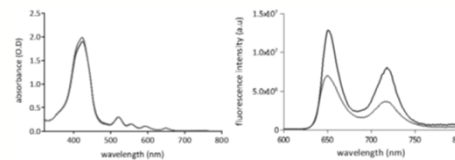
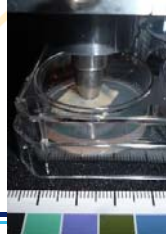
SR + multi-AF spectroscopy device

- DR acquisition spectral bandwidth 350-800 nm
- AF excitation peaks @ 365, 385, 395, 405 and 415 nm
- Multiple optical fiber - probe (SR)
 - Excitation/illumination fiber \varnothing : 600 μm
 - Collecting fibers \varnothing : 200 μm
 - 4 Distances between excitation and rings of collection fibers
 - $\Rightarrow D1 = 400 \mu\text{m}, D2 = 600 \mu\text{m}, D3 = 800 \mu\text{m}$ and $D4 = 1000 \mu\text{m}$



2-layer hybrid ex vivo model

- Top: ~440 μm thick skin strip
 - harvested ex vivo from arm inner side surgery wastes
- Bottom: ~5 mm thick gel
 - 1.5% agarose (w/w)
 - 500 μM AGuIX[®] nanoparticles Tb@P1: Terbium (Tb) + Porphyrin (P1)



CRAN

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October 28, 2017

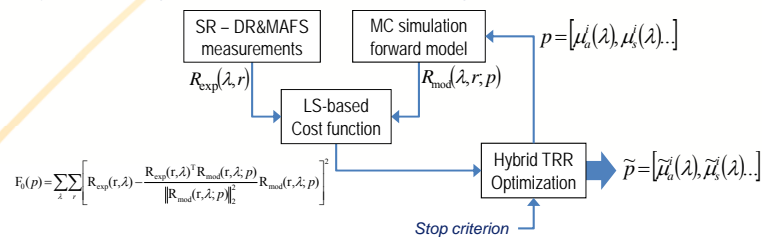
MATERIALS & METHODS (2/2)

OCA + enhancer

- Solution
 - 50% 3M-sucrose
 - 45% PolyEthylene Glycol 400 (PEG 400)
 - 5% Polypropylene Glycol (PG)
- Protocol
 - Skin immersion in 3 ml solution during 12, 24 and 36 minutes
 - Measurements at T_0 (no OCA), T_0+12 , T_0+24 and T_0+36

OP estimation and inverse problem solving

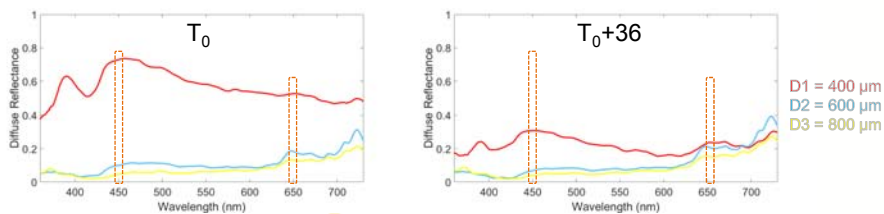
- Bi-layer model + probe geometry
- Estimation of absorption and scattering coefficients $\tilde{\mu}_a(\lambda)$ and $\tilde{\mu}_s(\lambda)$
 - Monte Carlo (MC) – based DR and AF simulation
 - Least-Square (LS) cost-function minimization
 - Hybrid Trust-Region-Reflective (TRR) optimization algorithm



RESULTS & DISCUSSION (1/3)

C Before OCA application (T_0) and after 36 minutes application (T_0+36)

C DR spectra



Distance D1

- ⇒ 2.35 x decrease @ 450 nm
- ⇒ 2.20 x decrease @ 655 nm

Distance D2

- ⇒ 1.40 x decrease @ 450 nm
- ⇒ 1.20 x increase @ 655 nm

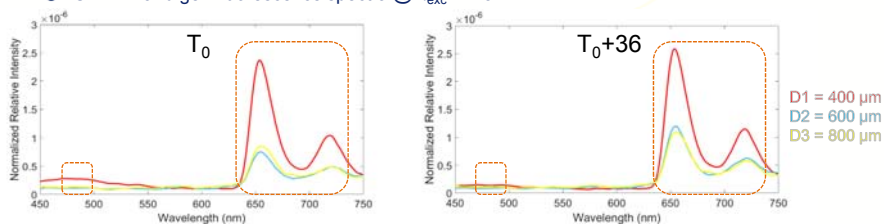
↓ skin absorption and scattering properties with OCA

- - - photons collected @ D1
- + photons collected @ D2 and D3 (longest λ , Tb-P1 bottom layer)

RESULTS & DISCUSSION (2/3)

C Before OCA application (T_0) and after 36 minutes application (T_0+36)

C Skin AF and gel Fluorescence spectra @ $\lambda_{exc} = 415$ nm



Distance D1

- ⇒ 2.0 x decrease @ 475 nm (skin AF emission peak)
- ⇒ 1.1 x increase @ 655 nm (Tb@P1 fluorescence emission 1st peak)

Distance D2

- ⇒ 1.60 x increase @ 655 nm (Tb@P1 1st peak)
- ⇒ 1.30 x increase @ 720 nm (Tb@P1 2nd peak)

Distance D3

- ⇒ 1.30 x increase @ 655 nm
- ⇒ 1.20 x increase @ 720 nm

↓ skin absorption and scattering properties with OCA

- - - skin AF photons (top layer) collected @ D1
- +++ Tb-P1 fluorescence photons (bottom layer) collected @ D2 and D3

RESULTS & DISCUSSION (3/3)

C Before OCA application (T_0) and after 36 minutes application (T_0+36)

Estimated values of skin layer $\tilde{\mu}_a(\lambda)$ and $\tilde{\mu}_s(\lambda)$

- C $\lambda = 450$ nm
 - ⇒ 1.80 x decrease in $\tilde{\mu}_a$
 - ⇒ 1.85 x decrease in $\tilde{\mu}_s$
- C $\lambda = 455$ nm
 - ⇒ 1.75 x decrease in $\tilde{\mu}_a$ ($0.4 \rightarrow 0.1$ cm⁻¹)
 - ⇒ 1.75 x decrease in $\tilde{\mu}_s$ ($225 \rightarrow 60$ cm⁻¹)
- C $\lambda = 720$ nm
 - ⇒ No change in $\tilde{\mu}_a$ (0.1 cm⁻¹)
 - ⇒ 1.49 x decrease in $\tilde{\mu}_s$ ($103 \rightarrow 53$ cm⁻¹)

C Conclusion & Perspectives

- C Preliminary results confirm potential in combining safe OCA and SR-DR&AFS depth sensitivity in the perspective of skin cancer surgical management
- C More results to be obtained and exploited
 - C Several AF excitations wavelengths
 - C Various thicknesses of skin samples



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Stanislas Place in Nancy, France

Thanks for your attention

Спасибо за внимание

谢谢你的关注

Merci pour votre attention

C Project members (CRAN, France)



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Marine Amouroux



Alain Delconte



Prisca Rakotomanga



Grégoire Khairallah



Frédéric Marchal

Collaborative members (WNLO-HUST, Chine)

Dan Zhu

Wei Feng

C Some of our references

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