Quantitative OCT Signal Analysis for Tumor Detection

Ton van Leeuwen

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Biomedical Optics/ Photonics

- Physics of
  - Interaction of light with tissue
  - Development of instrumentation
- Application of light
  - Therapeutic
  - Diagnostic
    - Monitoring / function
    - Imaging / morphology

Optical imaging and sensing of functioning biological systems

Relation between optical properties (μ_a, μ_s, g_n) or signals ($fluorescence, reflectance, \tau_{correlation}, ..$) and tissue status or type

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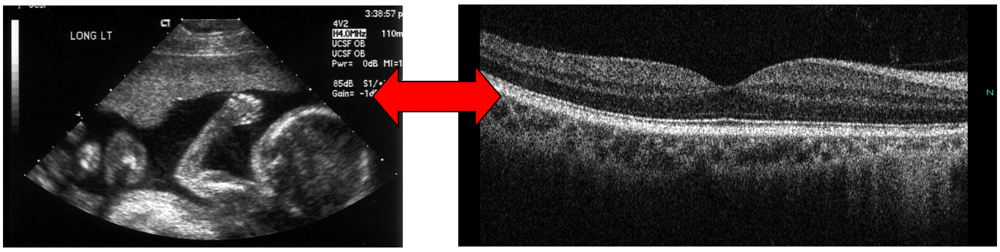
Optical Coherence Tomography (OCT)

Optical Coherence Tomography (OCT) is the optical analogue of ultrasound imaging



Contrast based on scattering properties of cells!

OCT enables μm-scale images of the morphology

applications in ophthalmology, cardiology, gastro-enterology, urology, ENT, dermatology, pulmonology, ….

Parametric imaging with OCT?

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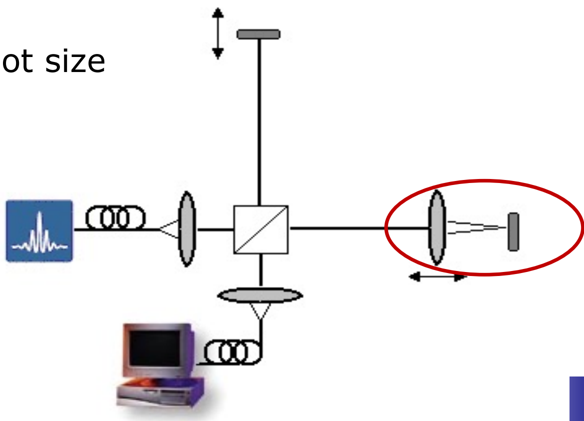
Optical Coherence Tomography (OCT)

- optical analogue of ultrasound imaging
- extension of confocal microscopy
- low coherence interferometry
- Axial resolution = coherence length of the light source
  $l_c = (2\ln 2/\pi)(\lambda_0^2/\Delta\lambda)$
- Lateral resolution ~ spot size



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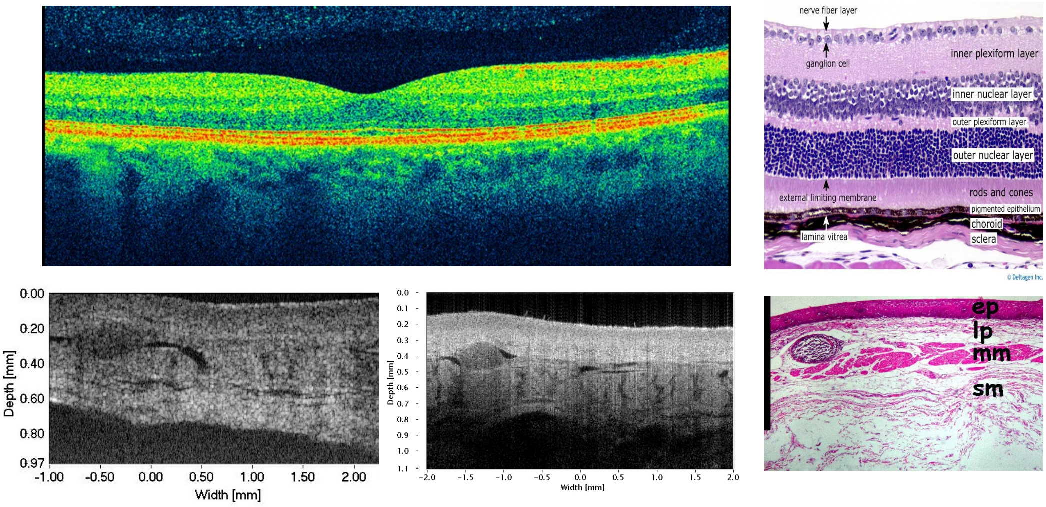
OCT images of retina and esophagus



λ_0 = 1300 nm,
$\Delta\lambda$ = 50 nm
l_c = 15 µm

λ_0 = 800 nm,
$\Delta\lambda$ = 125 nm
l_c = 3 µm

histopathology
resolution
~ 1 µm

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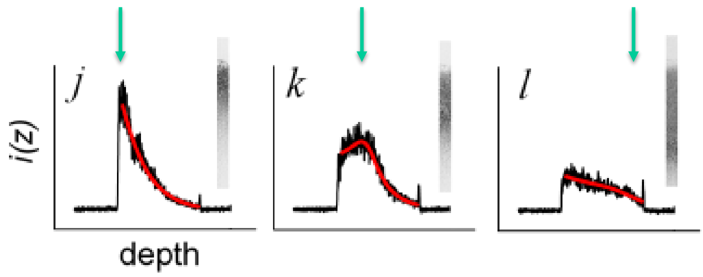
Single scattering approximation

- OCT signal dependent on:
  - Depth of focus
  - Position of the focus
  - Amount of back scattering
  - Attenuation coefficient

$$i_{\det}(z) = \eta \,\mathrm{Re}\left\{\gamma\left(\frac{2zn_{med}}{c}\right)\right\} \otimes h(z)\sqrt{P_{ref}P_{sample}}\sqrt{\mu_{b,NA}}\sqrt{\exp(-2\mu_s z)}$$



DJ Faber, et al. Optics Express 2004, 12: 4353-4365

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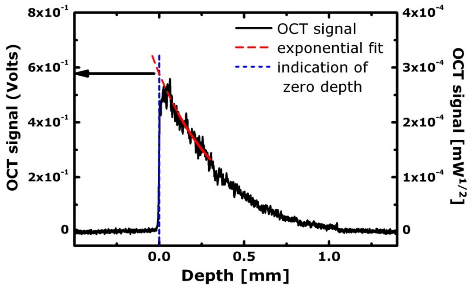
Single scattering approximation

- OCT signal dependent on:
  - Depth of focus
  - Position of the focus
  - Amount of back scattering (amplitude of the OCT signal)
  - Attenuation coefficient

$$i_{det}(z) = \eta \,\mathrm{Re}\left\{\gamma\left(\frac{2zn_{med}}{c}\right)\right\} \otimes h(z)\sqrt{P_{ref}P_{sample}}\sqrt{\mu_{b,NA}}\sqrt{\exp(-2\mu_s z)}$$



Kodach et al, Biomedical Optics express 2010, Optics Express 2011

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Single scattering approximation

introduction

OCT signals

tumor grading

outlook & conclusion

- OCT signal dependent on:
  - Depth of focus
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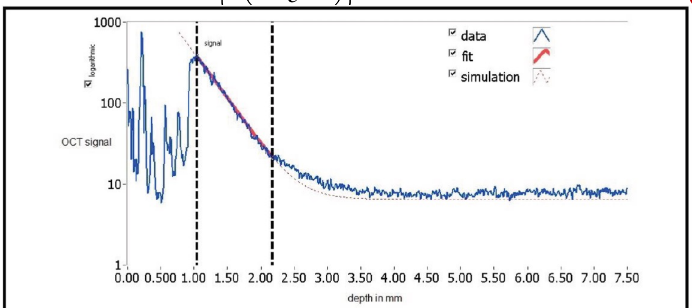
$$i_{det}(z) = \eta \,\mathrm{Re}\left\{\gamma\left(\frac{2zn_{med}}{c}\right)\right\} \otimes h(z)\sqrt{P_{ref}P_{sample}}\sqrt{\mu_{b,NA}}\sqrt{\exp(-2\mu_s z)}$$



JE Freund et al, Lasers Surg Medicine 2019: 2019;51:399-06

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Optical Coherence Tomography (OCT)

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OCT is the "Harlem Oil" of Biomedical Optics

See http://www.haarlemmerolie.nl

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Optical Coherence Tomography (OCT)

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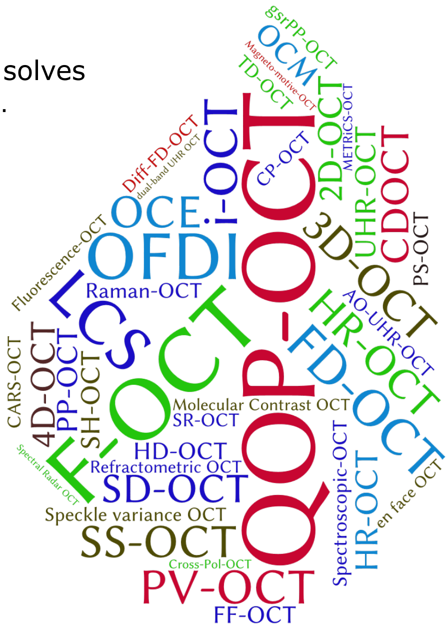
tumor grading

outlook & conclusion

One drop of OCT solves all the problems…



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Optical Coherence Tomography (OCT)

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One drop of OCT solves all the problems…

Optical Frequency Domain Imaging

Spectral Domain OCT

Swept Source OCT

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Time domain versus frequency domain OCT

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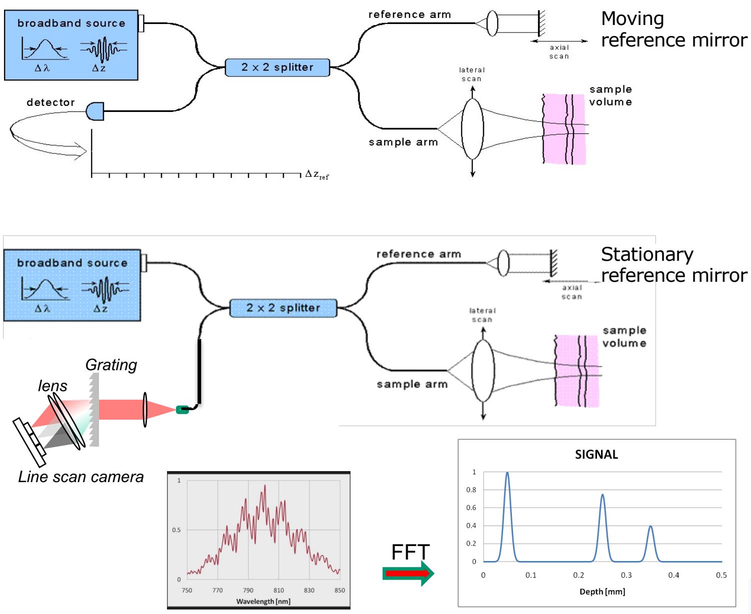

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JF de Boer, et al. OL 2003R Leitgeb et al, Optics Express 2003, Choma, et al., Optics.Express 2003

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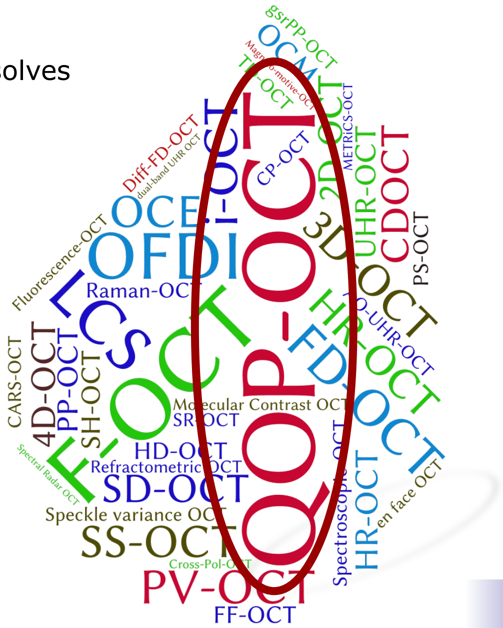
Optical Coherence Tomography (OCT)

introduction
[OCT signals]
tumor grading
outlook & conclusion

One drop of OCT solves all the problems…

Quantitative Optical Properties OCT



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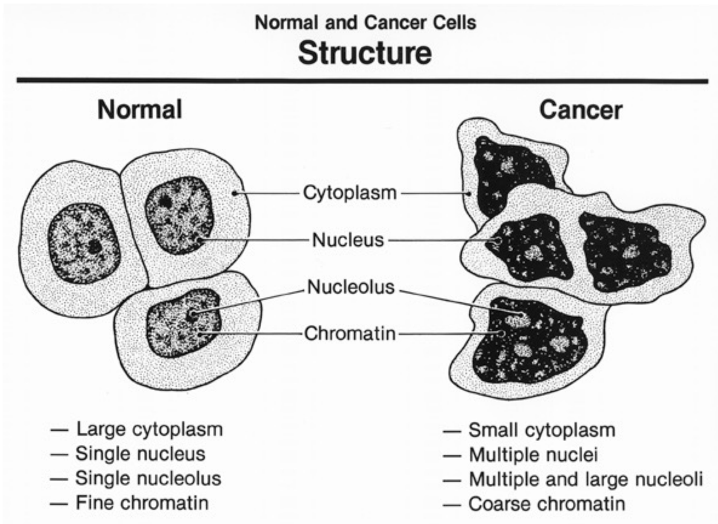
Hypothesis: Tumor detection based on the scattering coefficient

introduction
OCT signals
[tumor grading]
outlook & conclusion



Cellular changes of tumors induce increased scattering

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Tumor grading by OCT?

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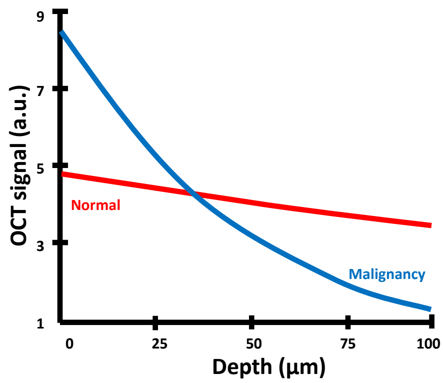
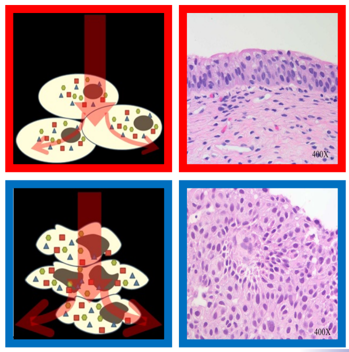
- OCT signals
- tumor grading
- outlook & conclusion

OCT can distinguish between benign and malignant tissues based on optical properties

McLaughlin et al xMICCAI 2009, Cauberg et al J Biomed Opt 2010, Tomlins et al J Biomed Opt 2010, Barwari et al J Endourol 2011 & BJU Int 2012, Wessels et al J Biomed Opt 2012, Bus et al. Jour of Uro 2013

Attenuation related to the grade of the tumor?





Xie et al (2002), Optics Express

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example 1: OCT of skin

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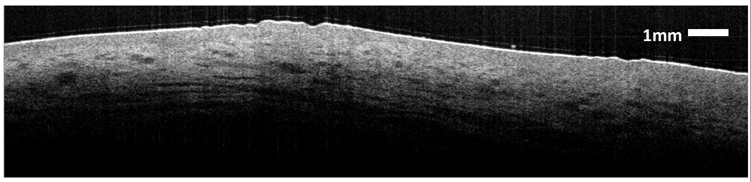
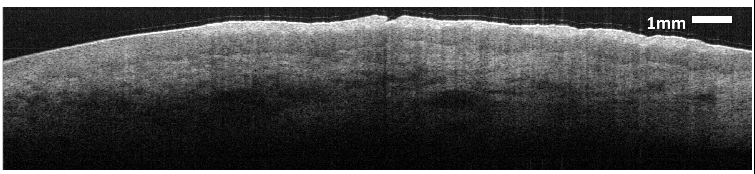
- tumor grading
- outlook & conclusion

Santec OCT system

healthy skin



neoplastic skin



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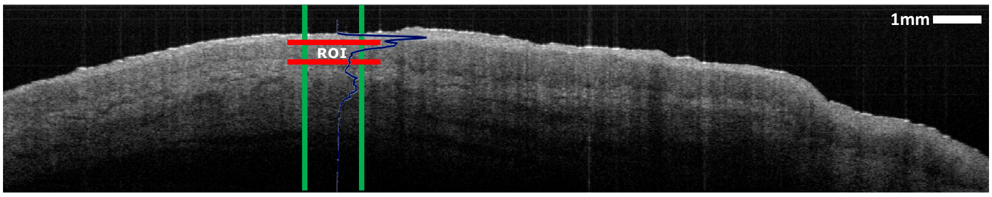
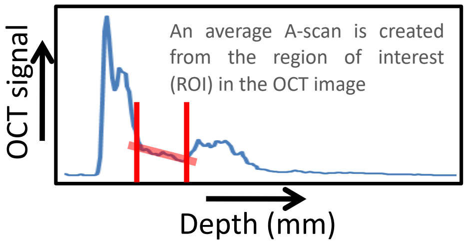
Fitting procedure

The OCT signal decreases with depth
Depends on scattering of the sample





$$i_d \propto \left[e^{-2\mu_t z}\right]^{\frac{1}{2}}$$

The **data** of the tissue part that is of interest can be fitted with single scattering model

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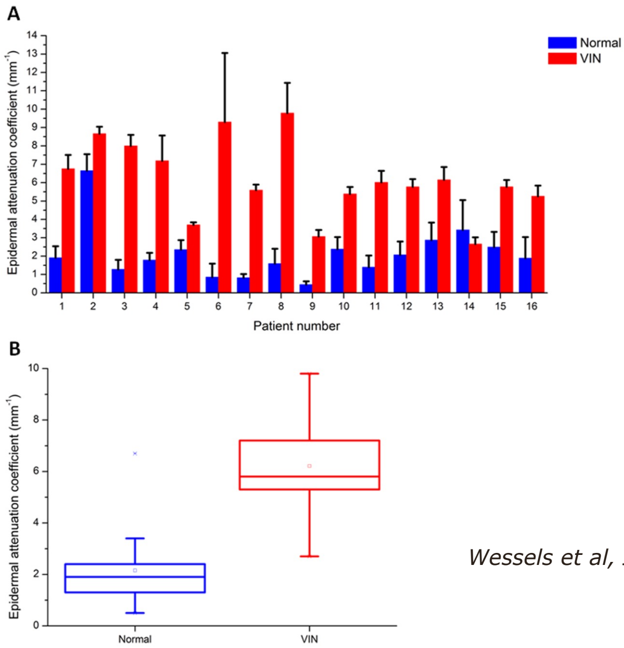
Quantitative analysis of OCT signals: μ_s



Wessels et al, J Biomed Optics 2012, 17: 11.6022

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example 2: OCT of ureter wall

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OCT signals

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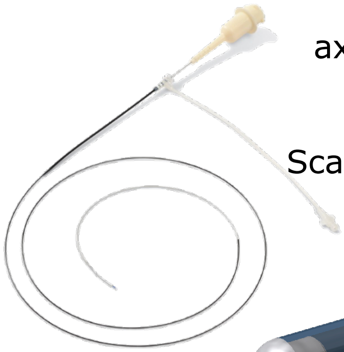
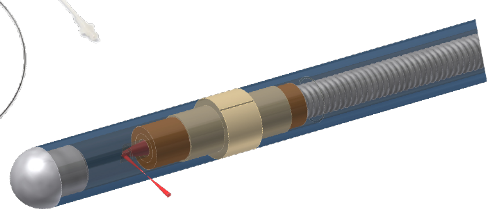


St Jude Illumien OCT system
Dragonfly imaging catheter
$\lambda_c \sim 1300$ nm
axial resolution = 15 μm
500 alines per frame
100 frames per second
Scan area is 52 by 10 mm



Catheter PSF and system role-off determined in 0.0002% IL

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OCT imaging during endoscopy

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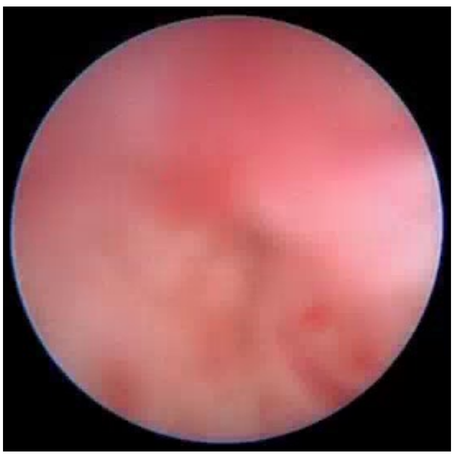

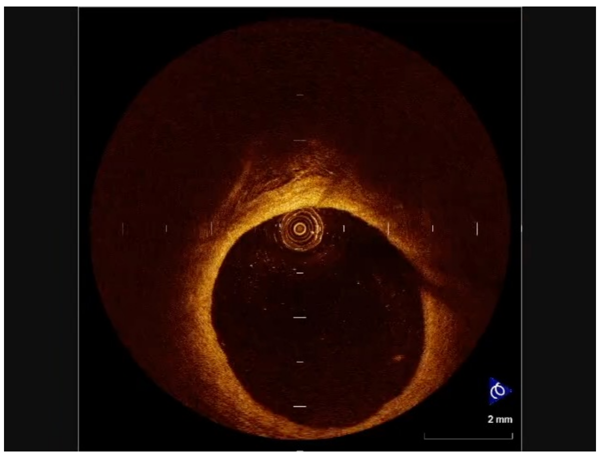

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3D volume reconstruction of normal appearing ureter

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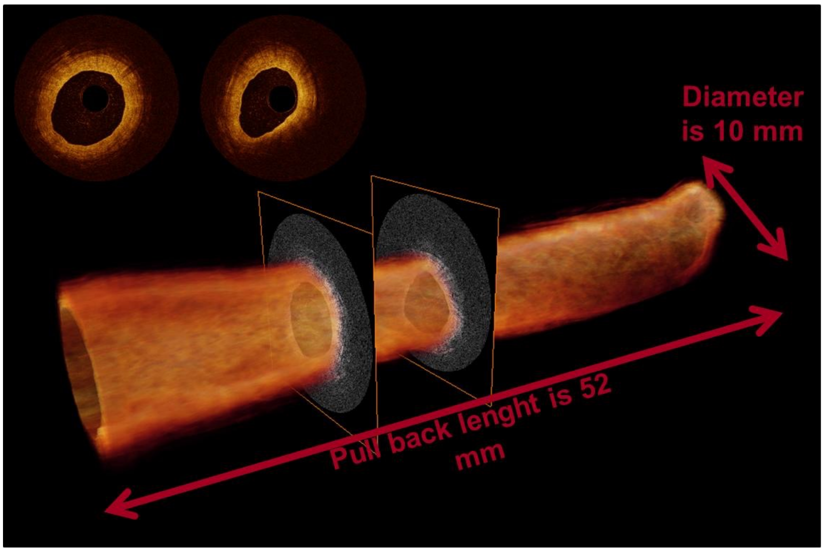

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3D visualization of lesions in ureter wall

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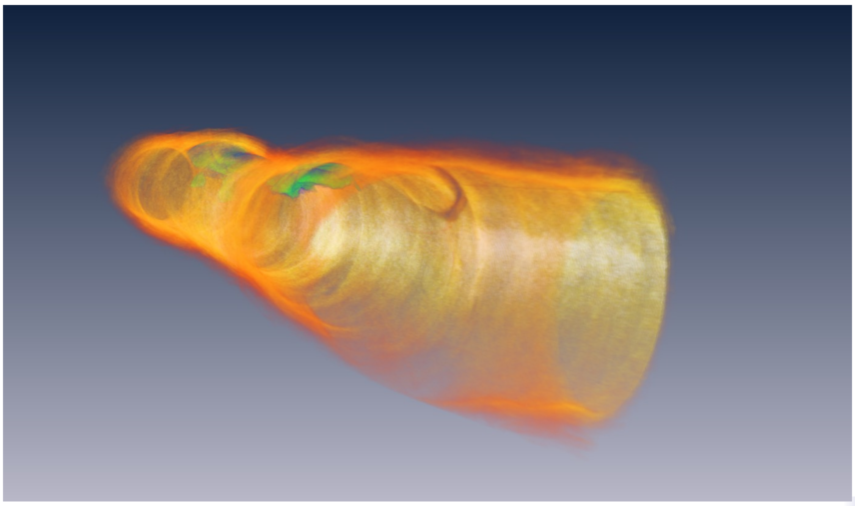

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examples OCT images of ureter wall lesions

Low grade tumors

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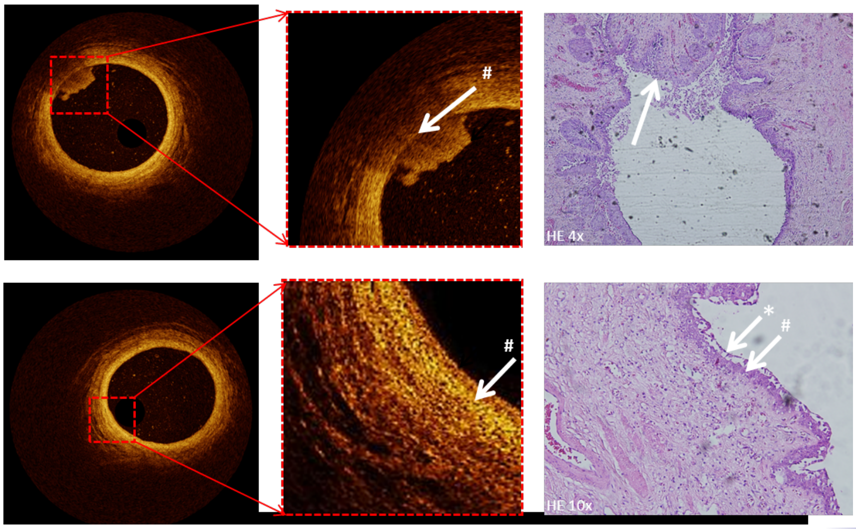

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Bus et al., Journal of Urology 2016, 196(6), 1749-1755

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examples OCT images of ureter wall lesions

High grade tumors

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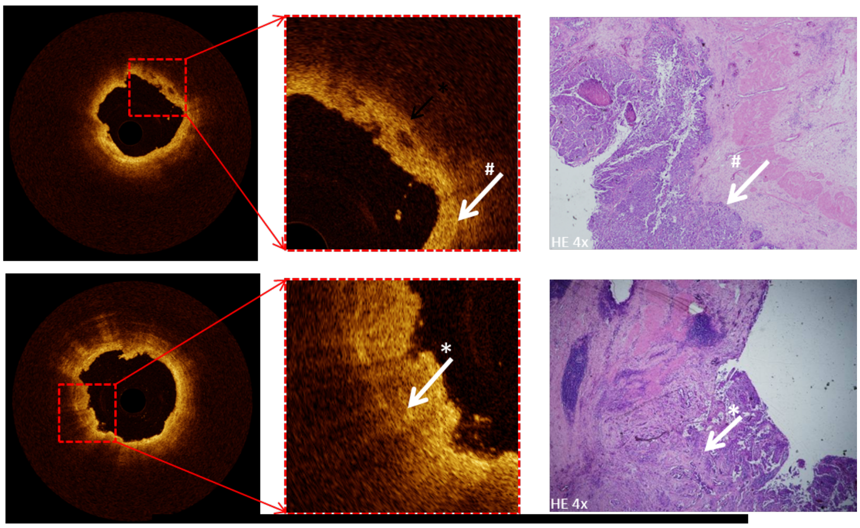

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Bus et al., Journal of Urology 2016, 196(6), 1749-1755

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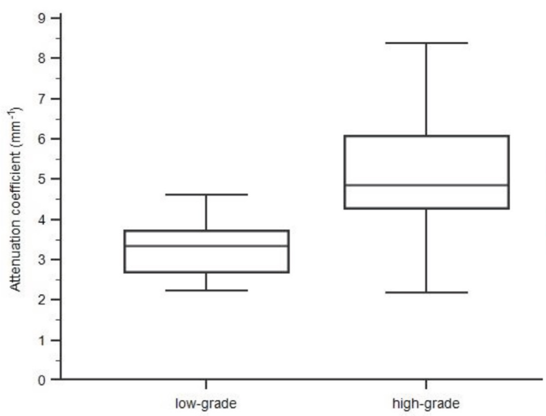
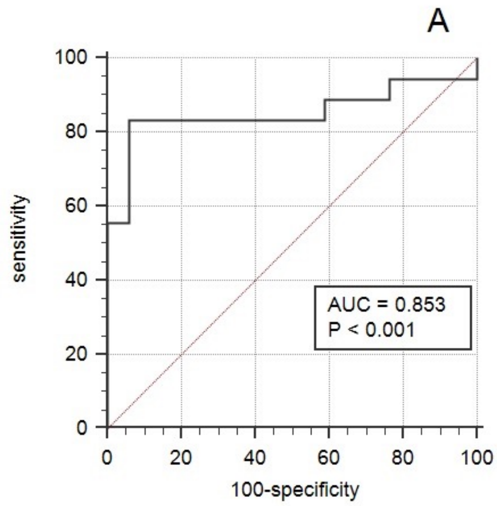
low versus high grade lesions in ureter wall





μ_{OCT} >4.0 mm^{-1}: sensitivity 83%, specificity of 94% for high-grade papillary UTUC

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Freund et al., Lasers Surg Med. 2019;51(5):399-06

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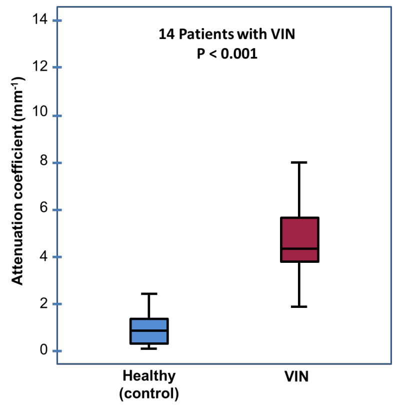
clinical studies based on the OCT attenuation coefficient

vulva	normal ↔ VIN
penis	normal ↔ PIN
skin	nevus ↔ melanoma
kidney	healthy ↔ RCC
bladder	*inconclusive*
prostate	*proof-of-principle*
ureter	low ↔ high grade
Barrett's esophagus	non- = dysplastic



ultimate goal: better detection, grading and staging of superficial tumors

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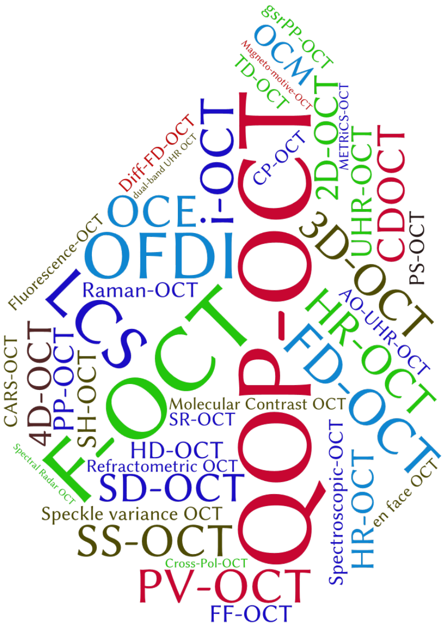
Optical Coherence Tomography (OCT)

One drop of OCT solves all the problems…

New developments & conclusions



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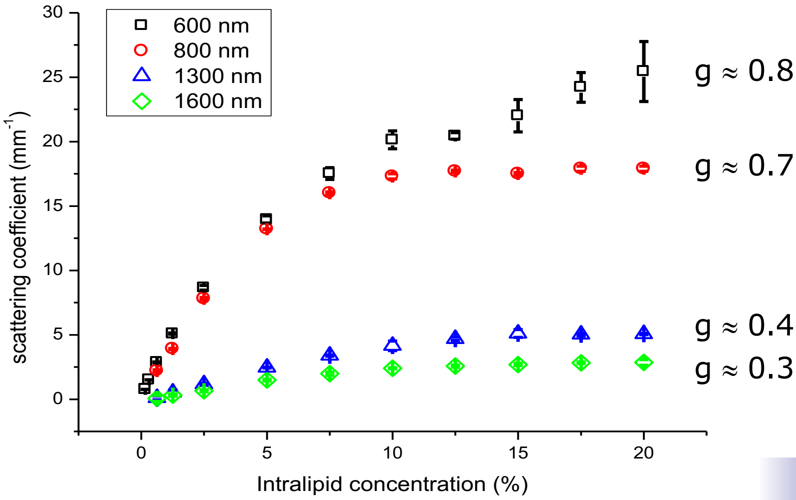
Developments

- Further understanding of OCT signals from multi-disperse media
  - OCT attenuation in Intralipid



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Scattering of many mono disperse spheres

- introduction
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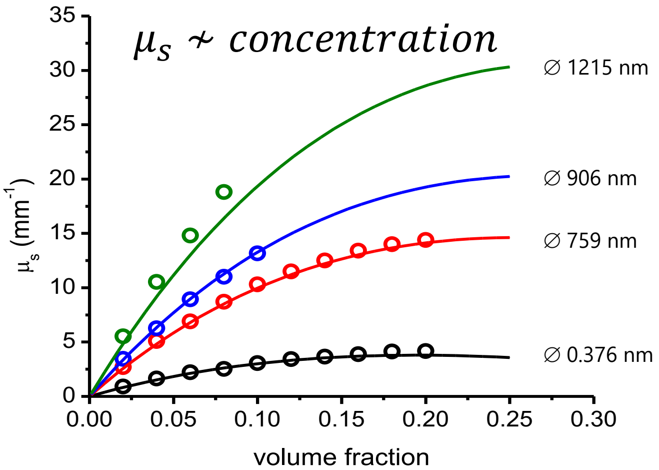
- tumor grading
- outlook & conclusion

$N \cdot 1 \neq N$: Dependent scattering for many beads



Corrected for dependent scattering with structure factor by Percus-Yevick model

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Nguyen et al Optics Express 2013

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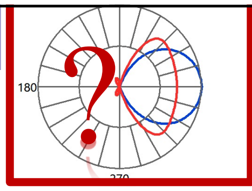
Scattering of many different spheres?



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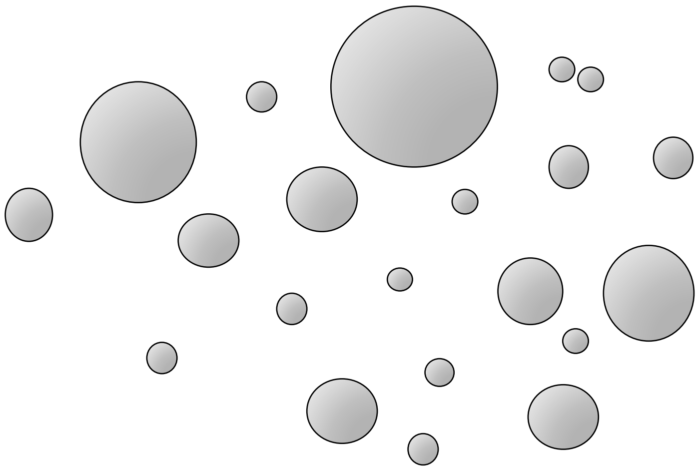
Non linear with concentration

$\mu_s, g_n??$



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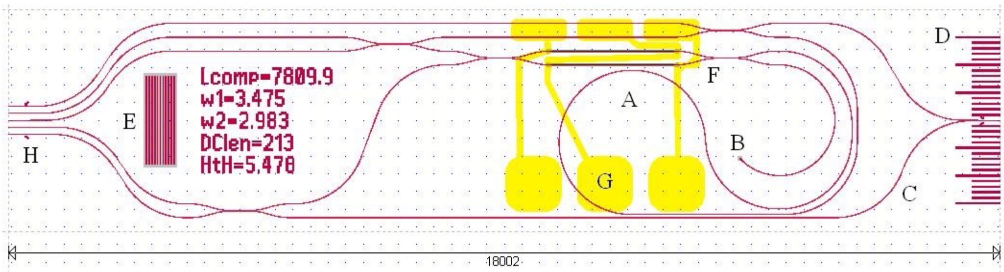
Developments

- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
  - Photonic integrated circuits



APEX TECHNOLOGIES Experts in next generation test equipment
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SMART PHOTONICS
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LioniX INTERNATIONAL
TU/e EINDHOVEN UNIVERSITY OF TECHNOLOGY
VTEC LASERS & SENSORS
BRIGHT Integrated PHOTONICS

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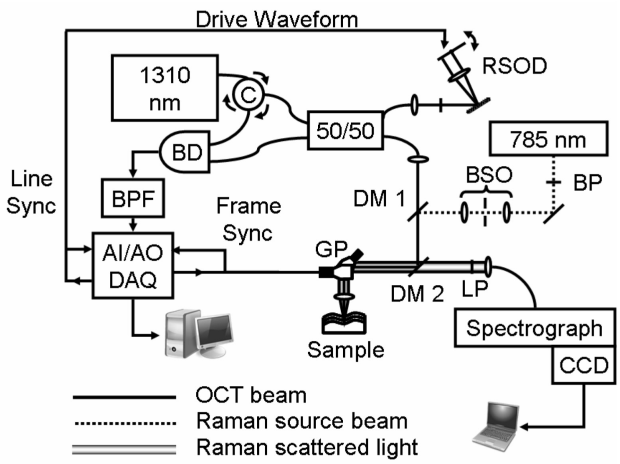
- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy



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C Patil et al,
Lasers Surg Medicine 2011, 43: 143–151

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- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence

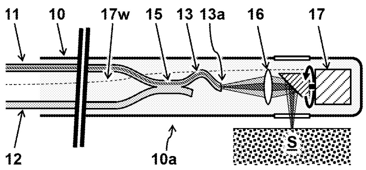

FIG 4C

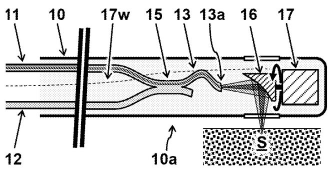

FIG 4D

patent F Feroldi, JF de Boer

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- Miniaturization of OCT systems
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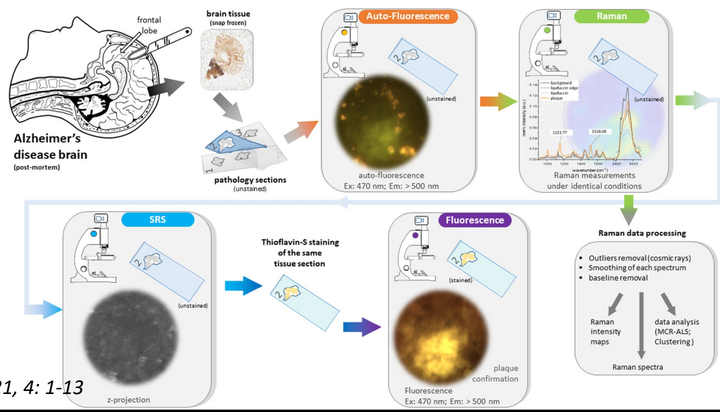
  - Raman microscopy
  - Fluorescence



B Lochocki, Biology Comm 2021, 4: 1-13

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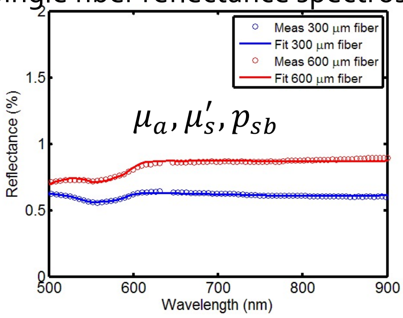
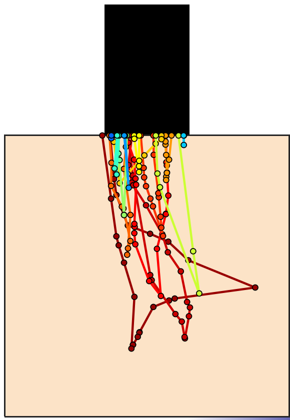
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence
  - Single fiber reflectance spectroscopy





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AL Post, J Biophotonics 2021, e202000351

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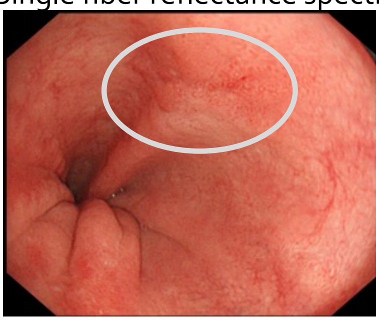
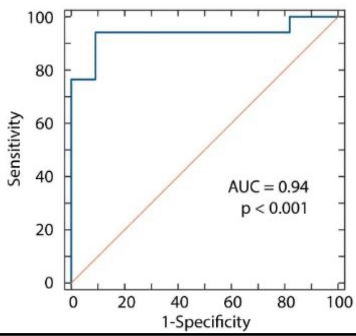
- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence
  - Single fiber reflectance spectroscopy: tumor versus Barret's esophagus





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AL Post, J Biophotonics 2021, e202000351

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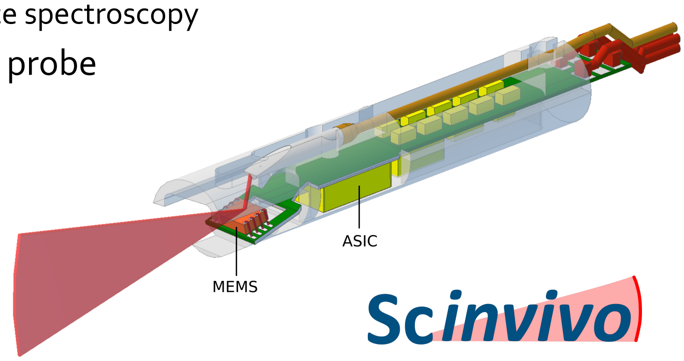
- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence
  - Single fiber reflectance spectroscopy
- Forward looking OCT probe



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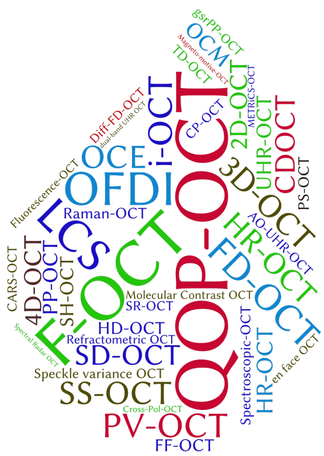
- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence
  - Single fiber reflectance spectroscopy
- Forward looking OCT probe

- Quantitative analysis of OCT signals:
  - attenuation coefficient
  - related to grade of the tumor
  - sometimes more contrast needed



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Optical Coherence Tomography (OCT)

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One drop of OCT solves all the problems…

THANK YOU

NWO Nederlandse Organisatie voor Wetenschappelijk Onderzoek

STW Nieuwe technologie mogelijk maken

CURE FOR CANCER

ZonMw

KWF

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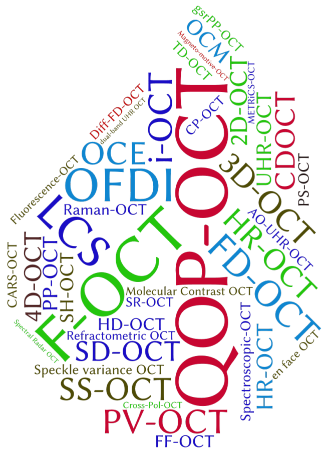

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Conclusions

introduction

OCT signals

tumor grading

outlook & conclusion

- Further understanding of OCT signals from multi-disperse media
- Miniaturization of OCT systems
- Combination with other imaging modalities
  - Raman microscopy
  - Fluorescence
  - Single fiber reflectance spectroscopy
- Forward looking OCT probe

- Quantitative analysis of OCT signals:
  - attenuation coefficient
  - related to grade of the tumor
  - sometimes more contrast needed

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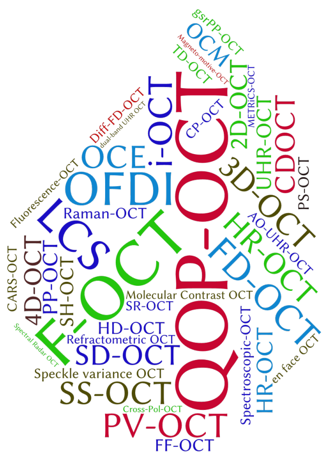

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