OCT phantoms with known attenuation

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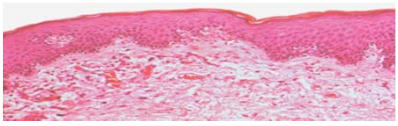
Tissue mimicking phantoms

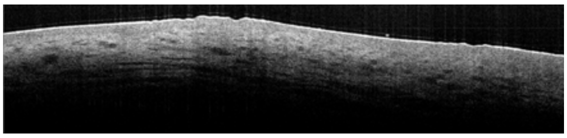
- Morphology
- Scattering (and absorption)

- Understanding *in vivo* measurements
  - OCT signal
  - Scattering properties of phantoms
  - Retinal phantom test

Skin: histology and OCT images

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion

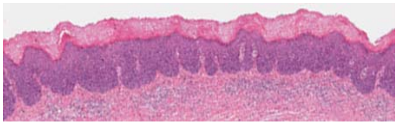


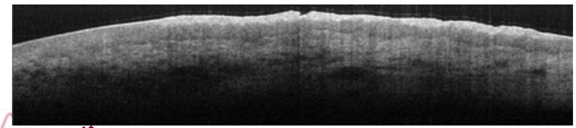


healthy epidermis

mean 0.5 mm

Wilkinson. Atlas of Vulvar Disease 2008





VIN epidermis

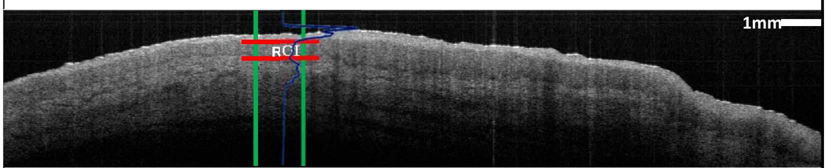
0.35- 1.66 mm, mean **0.93 ± 0.37**mm

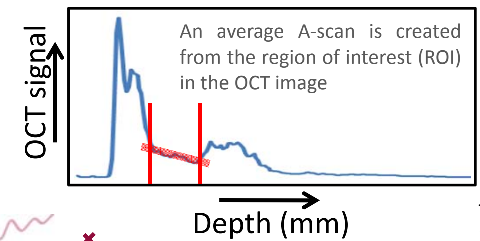
Baggish. Obstet Gynecol 1989

Fitting procedure

introduction
OCT signal
Phantoms:
silicon
liquid
conclusion

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

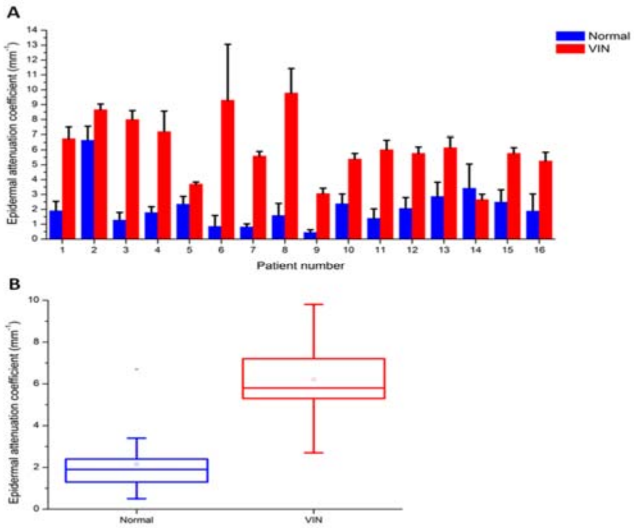




$$i_d \propto \left[e^{-2\mu_{oct}z}\right]^{\frac{1}{2}}$$

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

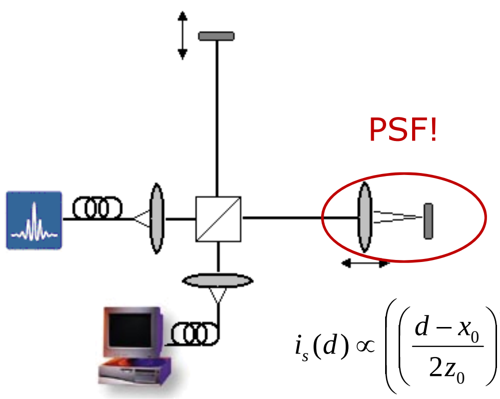
Quantitative analysis of OCT signals: μ_t



Cauberg et al, JBO 2010, ex-vivo Bladder cancer
Barwari et al, Journ of EndoUro, 2011, ex-vivo kidney tumor
Barwari et al, BJU int, 2012, in-vivo kidney tumor
Wessels et al, JBO 2012, in-vivo vulvar neoplasia
Bus et al, J Urol 2013, in vivo ureters

Optical Coherence Tomography (OCT)

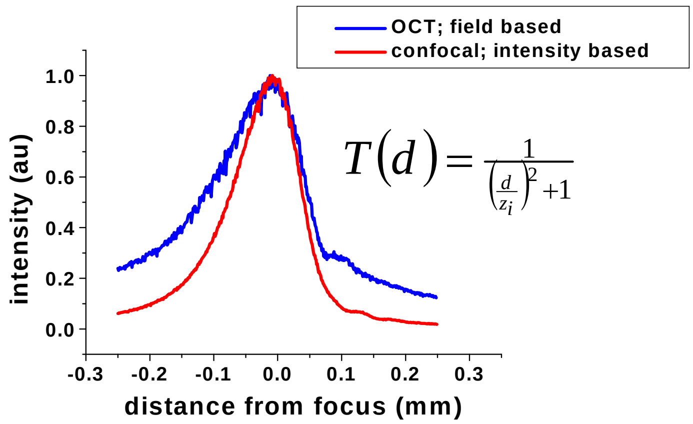
- Path length is known
- Can we measure μ_s by OCT signal analysis?
- Theory:
  - Single scattering model
  - OCT = extension of confocal microscope



$$i_s(d) \propto \left(\left(\frac{d-x_0}{2z_0}\right)^2+1\right)^{-1/2}\cdot\exp(-\mu_t d)$$

confocal layout

Transfer function mirror reflection



$$T(d) = \frac{1}{\left(\frac{d}{z_i}\right)^2 + 1}$$

retrieving μ_t

introduction

OCT signal

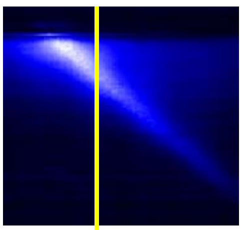
Phantoms:

silicone

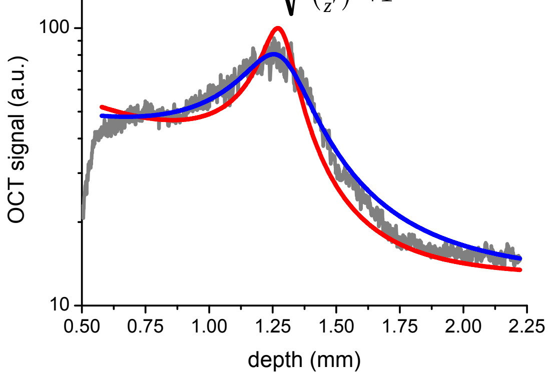
liquid

conclusion

vertical section



$$i(d) = \sqrt{\frac{1}{\left(\frac{d}{z'}\right)^2 + 1} e^{-2\mu d}}$$



z' = 63 μm; μ = 2.3 ± 0.6 mm^{-1}

z' = 126 μm; μ = 1.6 ± 0.3 mm^{-1}

calibrated samples from Lund

introduction

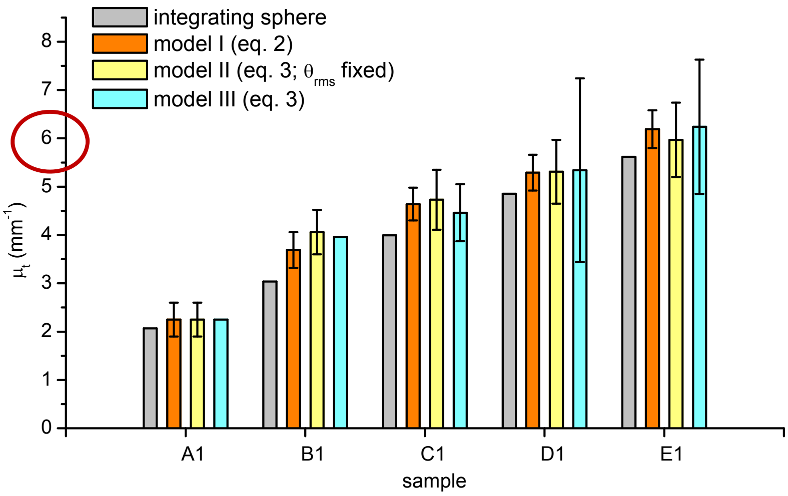
OCT signal

Phantoms:

silicone

liquid

conclusion



'glass' slides, limited choice in optical properties

TG van Leeuwen et al. IEEE J.Sel.Top.Quant.Elec. 2003, 9: 227-233.

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

Journal of Biomedical Optics 15(2), 025001 (March/April 2010)

introduction

OCT signal

Phantoms:

silicone

liquid

conclusion

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Optical phantoms of varying geometry based on thin building blocks with controlled optical properties

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Abstract. Current innovations in optical imaging, measurement techniques, and data analysis algorithms express the need for reliable testing and comparison methods. We present the design and characterization of silicone elastomer-based optical phantoms. Absorption is included by adding a green dye and scattering by adding TiO_2 or SiO_2 particles. Optical coherence tomography measurements demonstrate a linear dependence of the attenuation coefficient with scatterer concentration in the absence of absorbers. Optical transmission spectroscopy of the nonscattering absorbing phantoms shows a linear concentration dependent absorption coefficient. Both types of samples are stable over a period of 6 months. Confocal microscopy of the samples demonstrates a homogeneous distribution of the scatterers, albeit with some clustering. Based on layers with thicknesses as small as 50 μm, we make multifaceted structures resembling flow channels, (wavy) skin-like structures, and a layered and curved phantom resembling the human retina. Finally, we demonstrate the ability to incorporate gold nanoparticles within the phantoms. In conclusion, our phantoms are easy to make, are based on affordable materials, exhibit well-defined and controllable thickness, refractive index, absorption, and scattering coefficients, are homogeneous, and allow the incorporation of novel types of nanoparticle contrast agents. We believe our phantoms fulfill many of the requirements for an "ideal" tissue phantom, and will be particularly suited for novel optical coherence tomography applications.

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Keywords: biomedical optics; imaging systems; optical properties; scattering; absorption.

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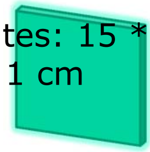
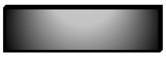
De Bruin et al. JBO. 2010

Kitchen Hardware

Glass plates: 15 * 15 * 1 cm





Spacers: >= 50 µm

Tissue homogenizer

Vacuum pump

Ultrasonic bath

Mixer

De Bruin et al. JBO. 2010

Ingredients 1

Sylgard ® 184 Silicone Elastomer
DOW/Corning

Silicone: 9 parts

Elastomer: 1 part

http://www.dowcorning.com/

- Optical 'clear' material
- Thermal conductivity: 0.17 W /mK (soft tissue range)
- Elongation at break : 140%
- Density: 0.97 kg/l

De Bruin et al. JBO. 2010

Ingredients 2

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion

Titanium dioxide (TiO_2)
Sigma Aldrich
Refractive index 2.49 (anatase form)
Mean radius ~50 nm (unknown distribution)

Glass particles (SiO_2)
Kisker biotech
Refractive index 1.37
Mean radius: 500±58 nm

→ **Scattering**

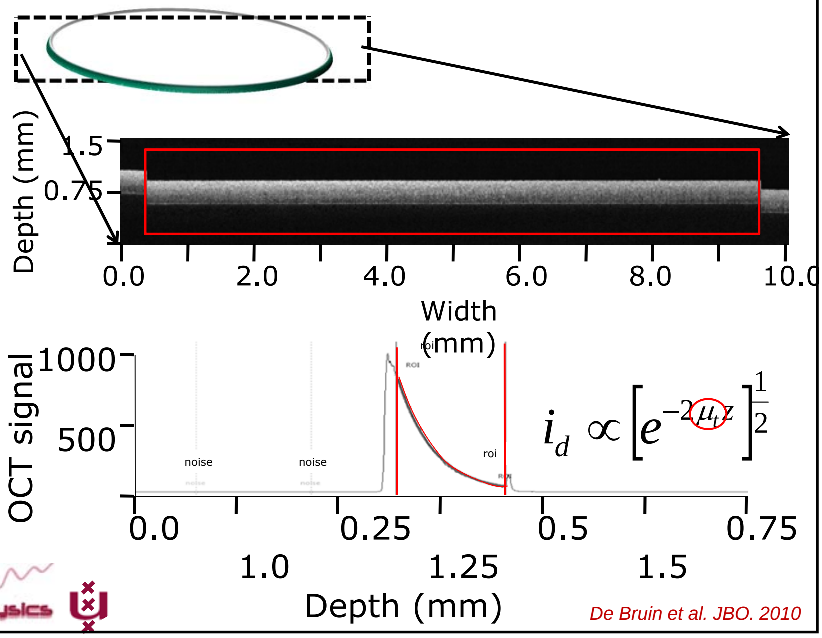
Absorber ABS 551
Exciton

→ **Absorption**

De Bruin et al. JBO. 2010

Thin Layered Phantoms

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion



De Bruin et al. JBO. 2010

Scattering TiO2 (OCT data @ 800 nm)

introduction

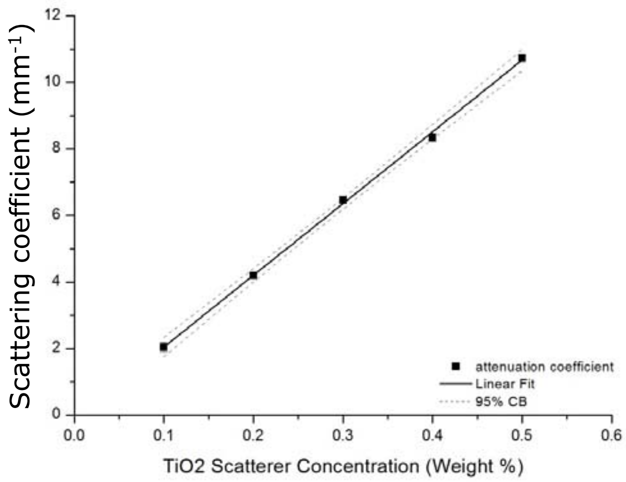
OCT signal

Phantoms:

silicone

liquid

conclusion



BME & Physics

De Bruin et al. JBO. 2010

Scattering SiO2 (OCT data @ 800 nm)

introduction

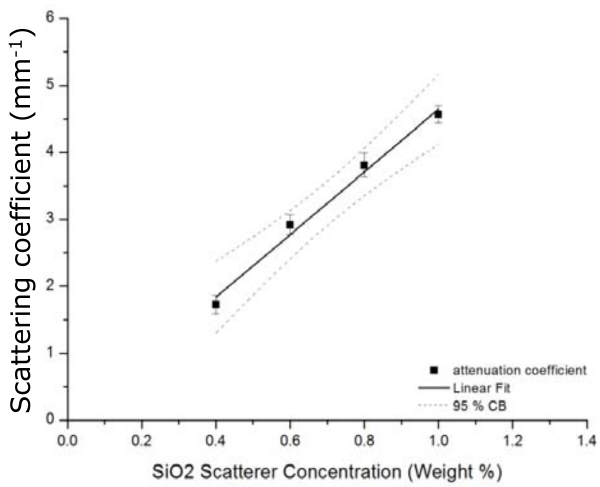
OCT signal

Phantoms:

silicone

liquid

conclusion



BME & Physics

De Bruin et al. JBO. 2010

Macroscopic Homogeneity

introduction

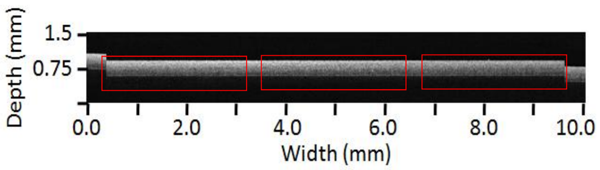
OCT signal

Phantoms:

silicone

liquid

conclusion



OCT at 850 nm					
Concentration weight %	μ_t roi1 mm^{-1}	μ_t roi2 mm^{-1}	μ_t roi3 mm^{-1}	Mean $\mu_t \pm$ SD mm^{-1}	$\Delta\ \mu_t$ %
0.1	1.75	2.00	1.93	1.89±0.16	8.5
0.2	4.25	5.15	5.17	4.86±0.08	1.6
0.3	7.50	7.64	6.73	7.29±0.21	2.9
0.4	8.21	8.29	8.75	8.42±0.29	3.4
0.5	10.00	11.30	11.6	10.97±0.38	3.4

De Bruin et al. JBO. 2010

Microscopic Homogeneity

introduction

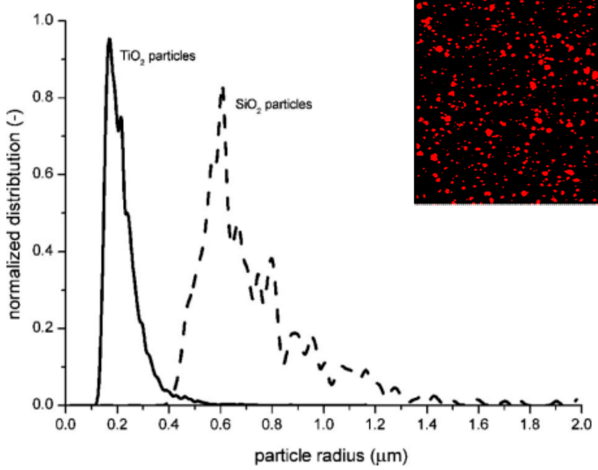
OCT signal

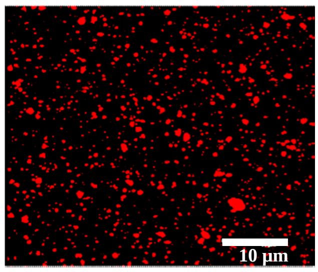
Phantoms:

silicone

liquid

conclusion





De Bruin et al. JBO. 2010

Thin Layered Phantom Stack

introduction

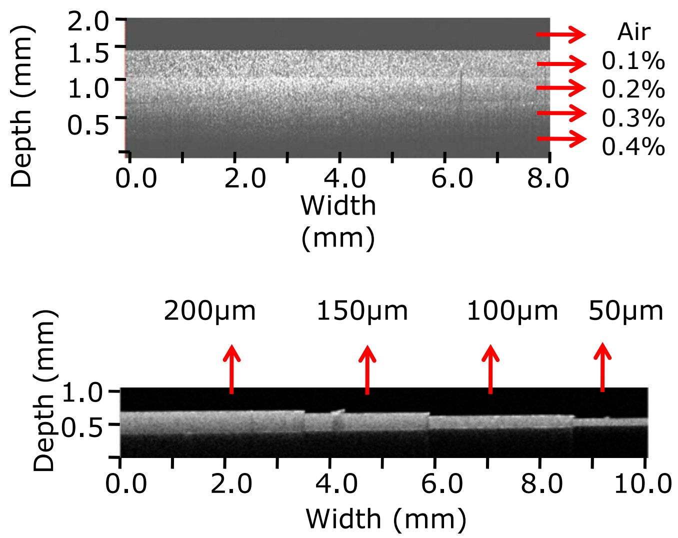
OCT signal

Phantoms:

silicone

liquid

conclusion



De Bruin et al. JBO. 2010

Skin simulating phantom

introduction

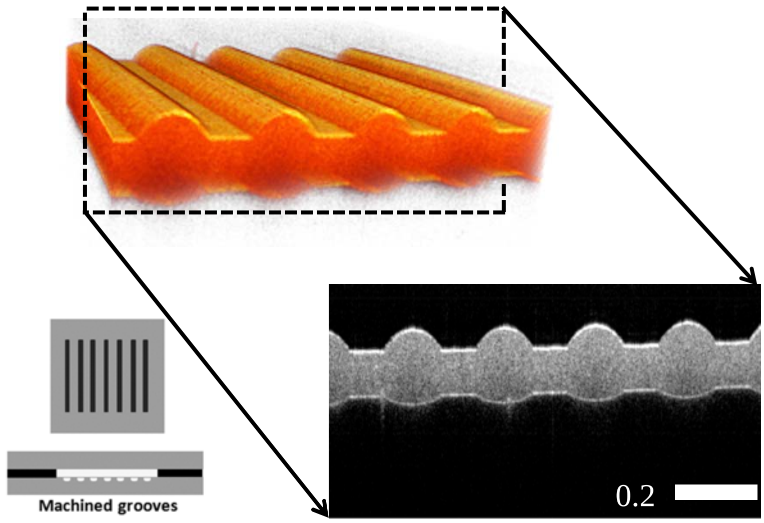
OCT signal

Phantoms:

silicone

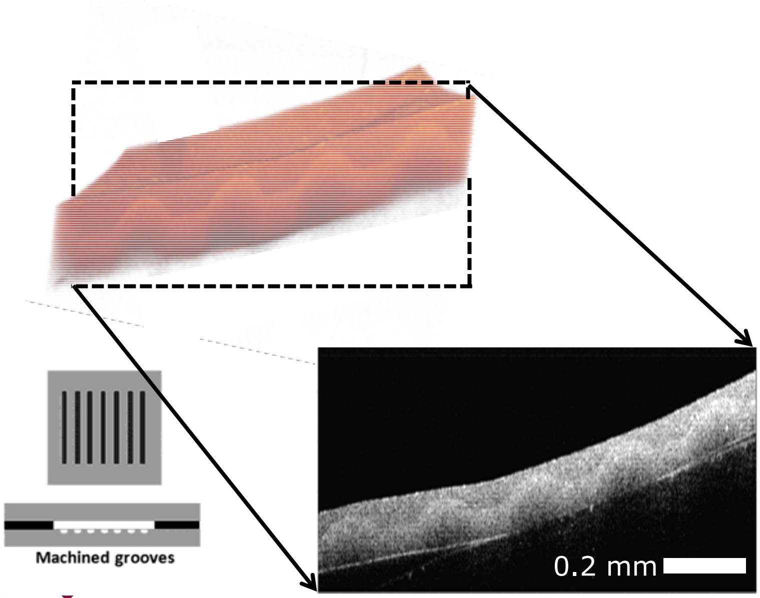
liquid

conclusion



De Bruin et al. JBO. 2010

Skin simulating phantom



De Bruin et al. JBO. 2010

Vessel Simulating Phantom

introduction

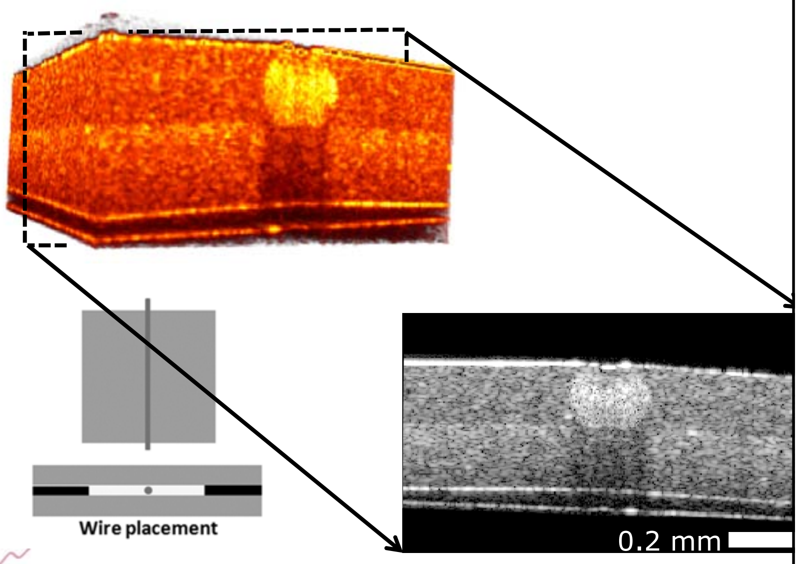
OCT signal

Phantoms:

silicone

liquid

conclusion



De Bruin et al. JBO. 2010

Retina Simulating Phantom

introduction

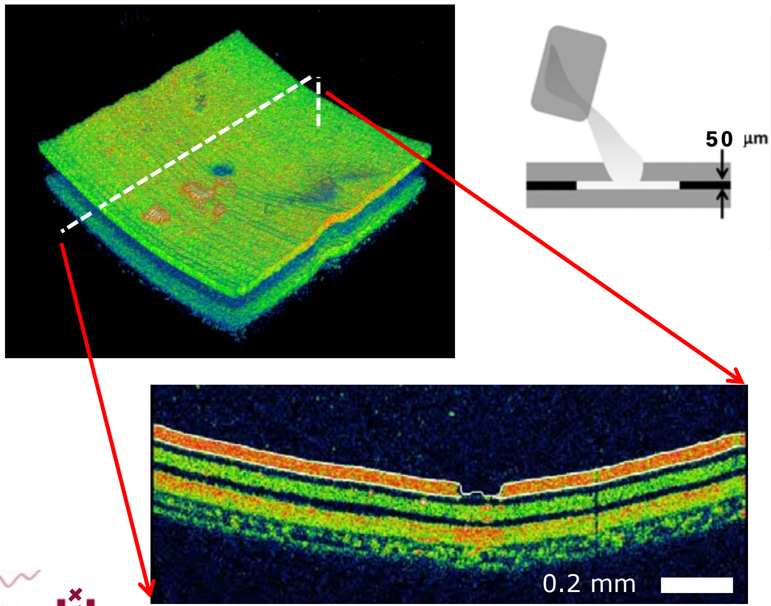
OCT signal

Phantoms:

silicone

liquid

conclusion



De Kinkelder et al. J Bio-Photonics 2013

Retina Simulating Phantom

introduction

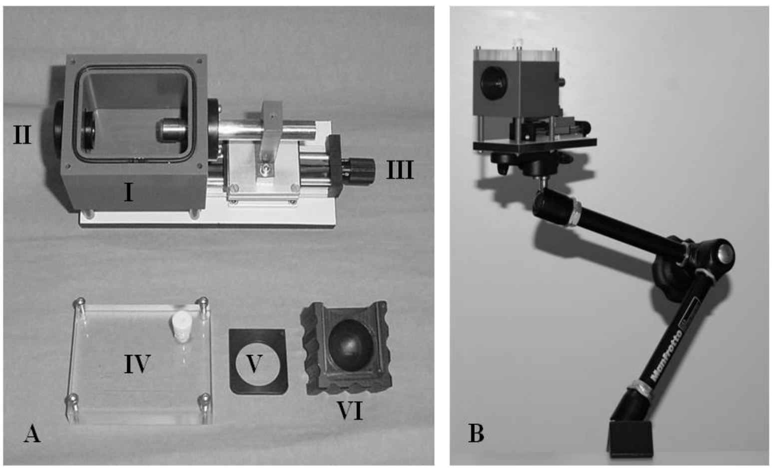
OCT signal

Phantoms:

silicone

liquid

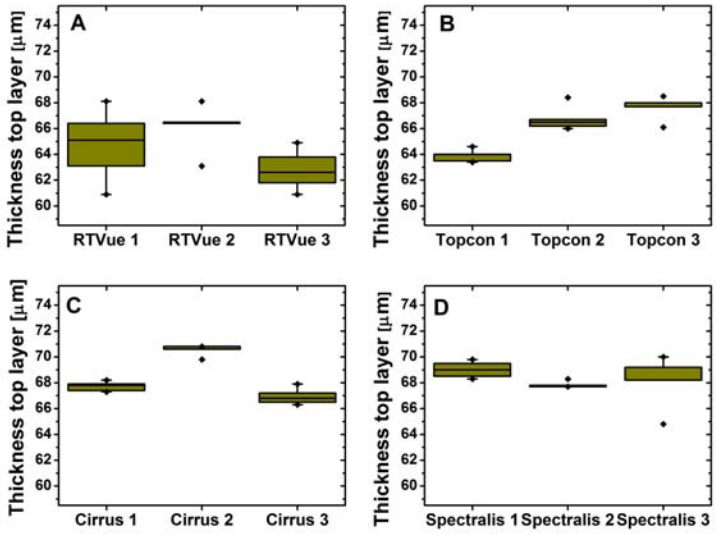
conclusion



De Kinkelder et al. J Bio-Photonics 2013

Comparison of OCT systems

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion



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De Kinkelder et al. J Bio-Photonics 2013

So….

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion

Durable phantoms **(~14 % stability in 6 months)**

Concentration dependent scattering and absorption **(2~11 mm^{-1})**

Tissue comparable index of refraction **(1.42 ±0.01)**

Advanced ´tissue mimicking´ geometry **(skin, retina, channels)**

Homogeneity **(> 8 %)**

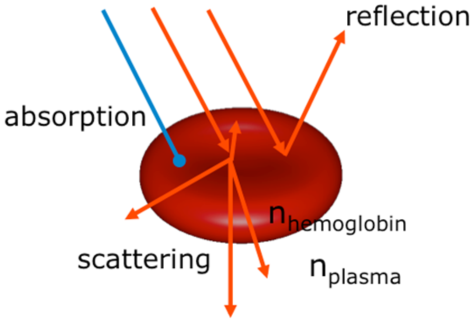
Relatively cheap **(~$3 for TiO_2)**

Liquid phantoms?

BME & Physics

Interaction: light-RBC

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion



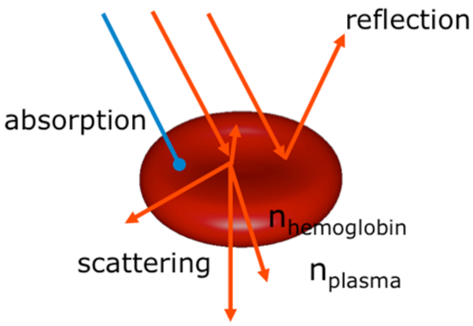
effects of scattering with concentration?

$\mu_s = \sigma_s \bullet \leftarrow$

BME & Physics

Interaction: light-RBC

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion



non linear effects of scattering with concentration

$\mu_s \neq \sigma_s \bullet \leftarrow$ above 1 vol%

For whole blood: $\mu_{S,blood} = (1-hct)^2 \dfrac{hct}{V_{RBC}} \sigma_{S,RBC}$

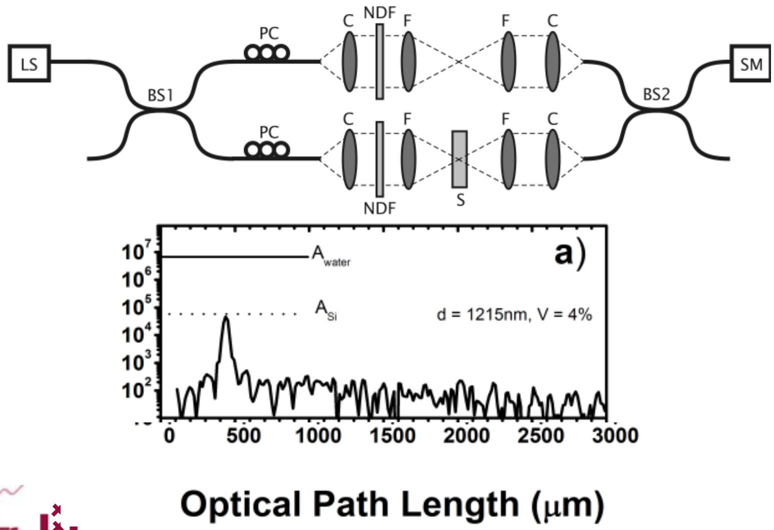
Bosschaart et al Lasers Med Sc 2014

BME & Physics

μ_s for high concentrations?

- transmission OCT measurements

(1300 nm spectral domain home built system, coherence length 12 µm)



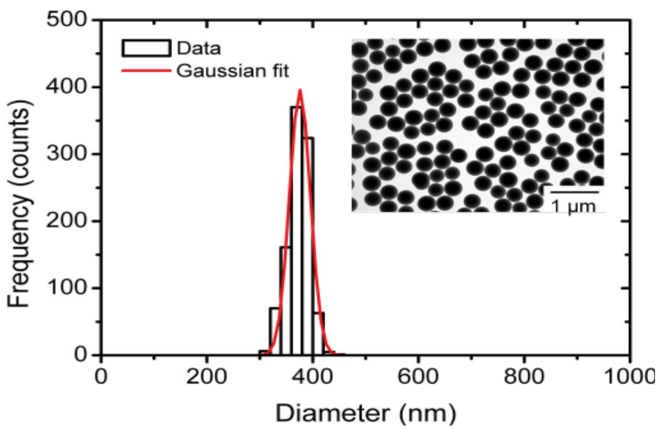
Nguyen et al Optics Expresss 2013

μ_s for high concentrations

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion

Silica beads (0.5, 0.8, 1.0 and 1.5 µm)

Size distribution by EM measurements



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μ_s for high concentrations

Silica beads

- introduction
- OCT signal
- Phantoms:
  - silicone
  - liquid
- conclusion

Mie calculations (1300 nm, silica, *n=1.447* in water, *n=1.32*)

Cat. #	Diameter (SD) (nm)	Scattering Cross section (μm^2)	Anisotropy factor	Max. Vol. (%)
Psi-0.5	376 (20)	0.0012451	0.253	20
Psi-0.8	759 (14)	0.031297	0.742	20
Psi-1.0	906 (17)	0.069361	0.781	10
Psi-1.5	1215 (18)	0.24026	0.869	10

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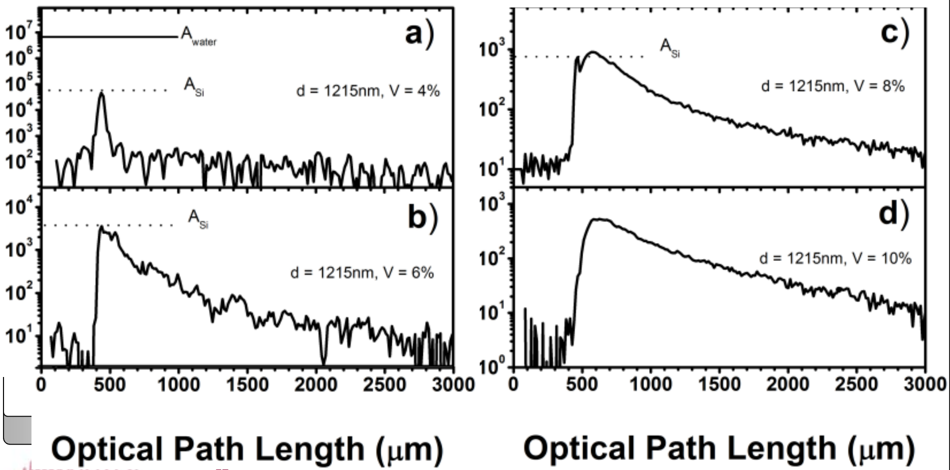
μ_s for high concentrations

Transmission results for 1215 nm silica beads at 4, 6, 8 and 10 vol%



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μ_s for high concentrations

introduction

OCT signal

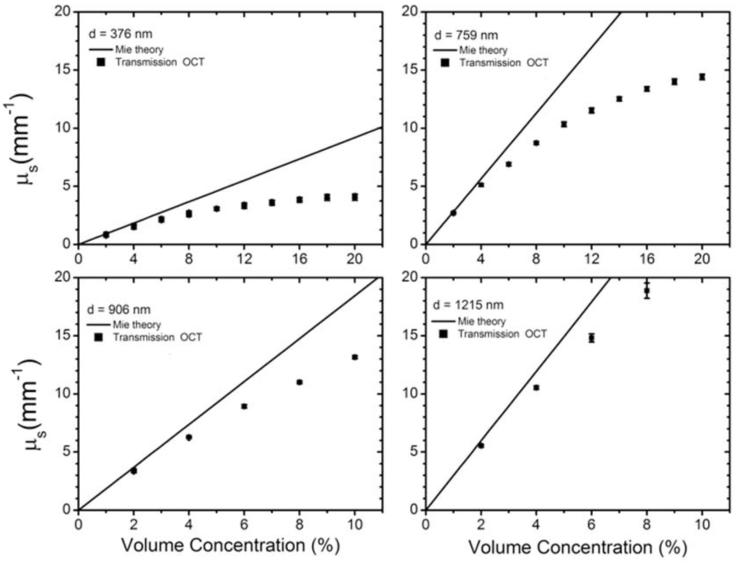
Phantoms:

silicone

liquid

conclusion

- Transmission results for all beads



μ_s for high concentrations

introduction

OCT signal

Phantoms:

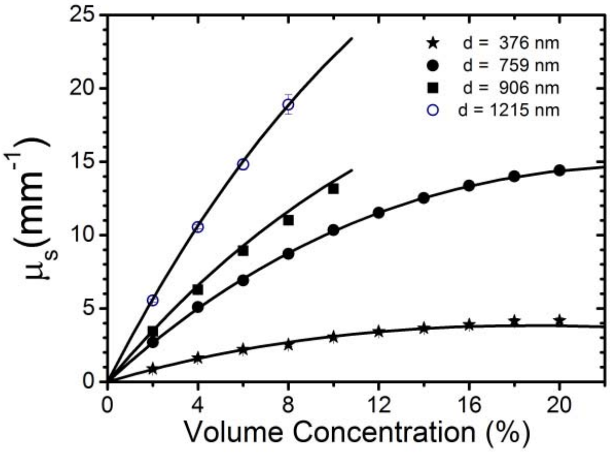
silicone

liquid

conclusion

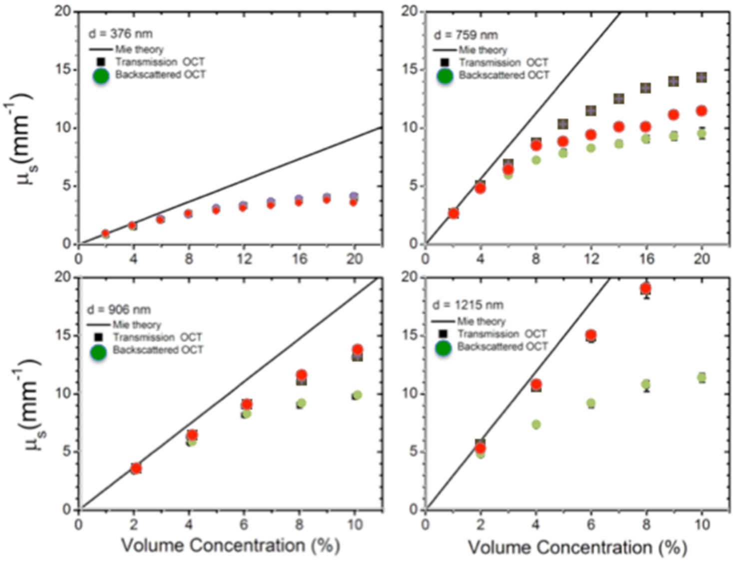
Dependent scattering for all beads

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



Nguyen et al Optics Expresss 2013

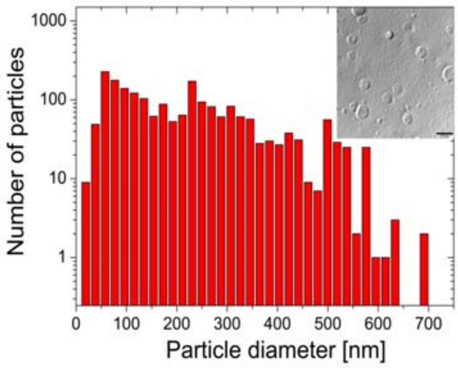
OCT: multiple versus dependent scattering



EHF results: Under restricting conditions for theta$_{RMS}$ (g)

Dependent scattering for IL

How about Intralipid?



Kodach et al. Optics Express, 2011, Vol. 19, pp. 6131-6140

Dependent scattering for IL

introduction

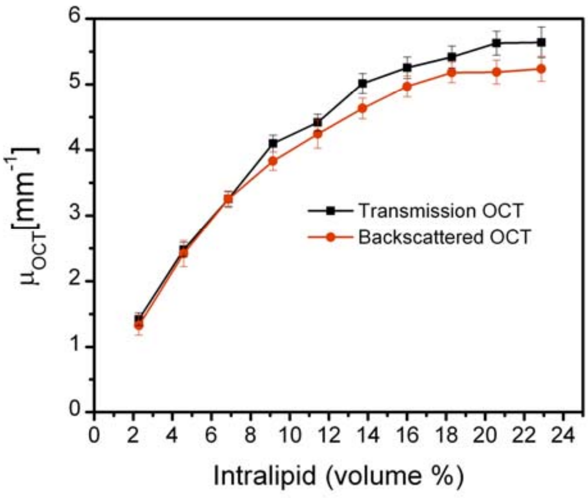
OCT signal

Phantoms:

silicone

liquid

conclusion



Different OCT systems

introduction

OCT signal

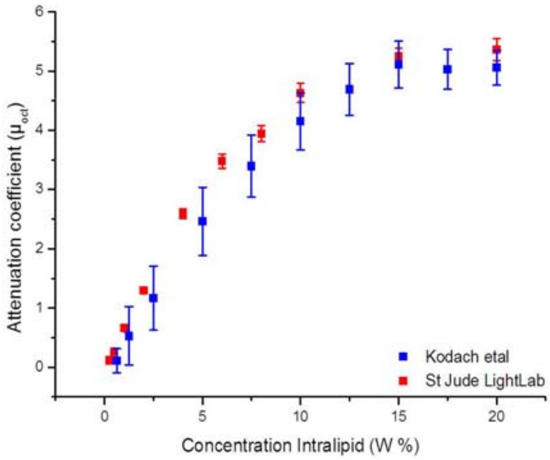
Phantoms:

silicone

liquid

conclusion

After probe calibration, @ 1300 nm: maximal attenuation in IL is ~ 5 mm^{-1}



Kodach et al. Optics Express, 2011, Vol. 19, pp. 6131-6140

Conclusions: scattering measured by OCT

introduction
OCT signal
Phantoms:
silicone
liquid
conclusion

OCT signal analysis give insight in fundamental and in vivo scattering properties

- Stable tissue mimicking phantoms
- Dependent scattering (> 1 vol%)
- Attenuation determination *in vivo*

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

- How is the signal processed?
- Lateral resolution?

BME & Physics