CONCENTRATION INFLUENCE ON CONTRAST AGENTS PROPERTIES IN OPTICAL COHERENCE TOMOGRAPHY

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Abstract: This work deals with contrast agents for optical coherence tomography (OCT). The experiment for testing properties of two substances (Intralipid and polystyrene based magnetic microparticles) in optical coherence tomography is described. A basic statistical analysis is presented – the concentration dependence of intensity mean values and intensity histograms fitting by probability distributions. The results help to better understand the light properties of different media under OCT scanning from statistical point of view.

Keywords: Optical coherence tomography, contrast agents, Intralipid, Polystyren magnetic based microparticles, optical properties, statistical distributions

1. INTRODUCTION

Optical coherence tomography is a non-invasive imaging technique producing high-resolution cross-sectional images of living tissues as an optical scattering medium. It is based on interferometric principle, using the interference between a split and later re-combined broadband optical field, usually infrared. Achieved resolution highly depends on the properties of the light source, micrometer and sub-micrometer resolution is possible. This technique enables to gain information about structural and functional tissue properties [1].

The first application of OCT was in ophthalmology, but there is a wide spectrum of other applications due to advances in OCT technology [2]. In ophthalmology, OCT is mainly used for investigation of the posterior part of the eye; however, imaging of the anterior segment is also possible. Another application can be an optical biopsy. It enables an access to the tissue and cell function and morphology *in situ*. This is very promising especially for tumor diagnostics, monitoring its progression or evaluation of treatment effect.

Recently, there has been interest in techniques for enhancement OCT contrast. This can be achieved by (for example) application of some contrast agents – passive or targeted to specific cells and tissues. Such agents are known already in MRI or CT modalities. As contrast agents for OCT, many types of materials can be used, for example, air-filled microbubbles, engineered microspheres, near-infrared fluorescent dyes and plasmon-resonant nanoparticles [3].

This paper presents experiments for testing two different substances - Intralipid (fat emulsion) and polystyrene based magnetic microparticles (PSM) and the statistical analysis of measured intensities (e.g. finding suitable statistical distribution).

2. THEORETICAL BACKGROUND

2.1. OPTICAL COHERENCE TOMOGRAPHY

Basic OCT systems were based on a Michelson interferometer (Figure 1). The split field travels in a reference path and in a sample path, reflecting from a reference mirror or from multiple layers within a sample respectively. Interference between the optical fields is observed when the reference and sample arm optical path lengths are matched. Interference pattern corresponds to variations of refractive index in the sample. A time domain systems obtain the interference pattern by translation of the reference mirror to change the path length and match different sample layers. There are also frequency domain systems which derive the depth information from measurements of the output spectrum and its Fourier transformation. This two possibilities can be evident from equation (1) of the sample response function $H(\omega)$, which describes the overall reflection from all sample structures in the *z* direction [1]:

$$H(\omega)=\int_{-\infty}^{\infty} r(\omega,z)e^{i2n(\omega,z)\omega z/c}dz\,, \tag{1}$$

where the function $r(\omega,z)$ is the backscattering coefficient from the sample structural features and $n(\omega,z)$ frequency and depth dependent refractive index.

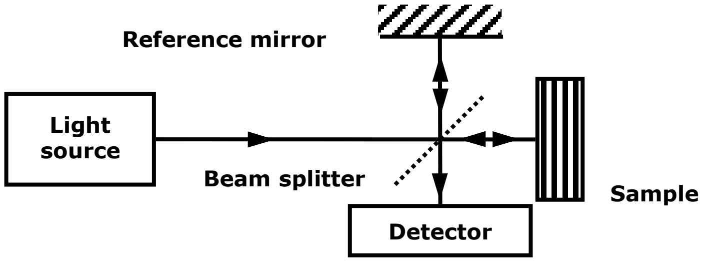


Figure 1: Basic principle of simple OCT system (adapted from [1])

2.2. LIGHT SCATTERING

Light beam illuminating a material with dielectric constant different from unity will be absorbed, scattered or both, depending on the light wavelength and the optical properties of the material. Scattering is observed only when a material is heterogeneous (due to local density fluctuations or dispersed particles). Scattering intensity depends on refractive indexes of materials and their surroundings, particle size (with respect to light wavelength), shape, concentration and other material properties [5].

2.3. SELECTED STATISTICAL DISTRIBUTIONS

Several statistical distributions were used to fit histograms obtained in experimental part.

The Weibull distribution is a generalization of the exponential distribution and its application is in various failure situations. The probability density function (PDF) is

$$f(x)=\lambda\gamma(\lambda x)^{\gamma-1}e^{-(\lambda x)^{\gamma}}\,,\; x\geq 0\,,\; \lambda,\gamma>0\,, \tag{2}$$

where λ and γ are called scale and shape parameters. [4]

The Gamma distribution is frequently used as a model for industrial reliability and human survival. It has PDF with similar scale and shape parameters [4]

$$f(x)=\frac{\lambda}{\Gamma(\gamma)}(\lambda x)^{\gamma-1}e^{-\lambda x}\,,\; x,\lambda,\gamma>0\,, \text{ where } \Gamma(\gamma)=\int_{0}^{\infty} x^{\gamma-1}e^{-x}dx \tag{3}$$

The Log-logistic distribution is special type of logistic distribution. Its PDF is [4]

$$f(x)=\frac{\alpha\gamma x^{\gamma-1}}{\left(1+\alpha x^{\gamma}\right)^{2}}\,,\; x\geq 0\,,\; \alpha,\gamma>0\,, \tag{4}$$

The Nakagami distribution was proposed to model the fading of radio signals. It has PDF

$$f(x)=\frac{2}{\Gamma(\mu)}\left(\frac{\mu}{\omega}\right)^{\mu}x^{2\mu-1}e^{\left(-\frac{\mu}{\omega}x^{2}\right)},\ x,\omega>0,\ \mu\geq 0.5, \quad (5)$$

where ω and μ are scale and shape parameters. [5]

3. EXPERIMENTAL DESIGN

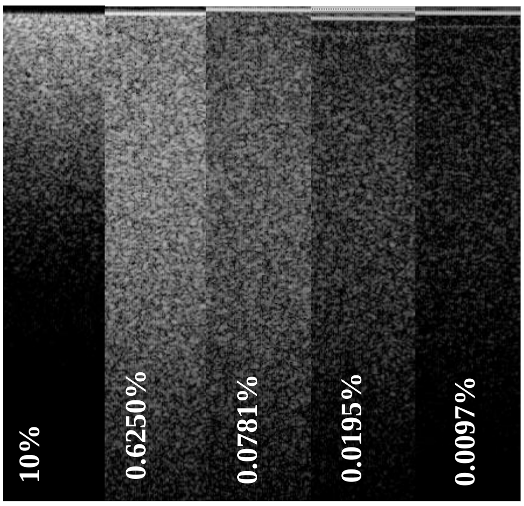
Two types of contrast agents were examined in this work – Intralipid (Fresenius Kabi) and polystyrene based magnetic microparticles (Sigma-Aldrich, diameter 1 μm). Intralipid is a fat emulsion which can serve as a simulation of homogenous medium in flow phantom. On the contrary, PSM can serve as particle based contrast agent.

Each of these substances was mixed with distilled water in various concentrations in geometric progression with common ratio 0.5 in range 20-0.005% for Intralipid and 1.66-0.0008% for PSM. Liquid sample of every mixture was imaged by Swept Source OCT system (Thorlabs, OCS1300SS) with center wavelength 1325 nm. Raw volume data were saved from device. Subsequent processing was done in MATLAB.

Whole raw data file contains headers with information about imaging settings and raw data frames (interference signal from detector). These frames were processed by standard procedures – simple inverse discrete Fourier transform (IDFT) and absolute value was carried out to obtain reflected intensities. Half of obtained image was taken as an output, because the IDFT result is symmetrical. These reflection images were used for analysis described below. For visualization purpose, the images intensities were modified to logarithmic range according to $B=\log(A/\max(A))\cdot a+b$, where *A*, *B* are input and output images, respectively; *a* and *b* are constants defined by required contrast, brightness and dB range.

4. RESULTS AND DISCUSSION

Examples of obtained images are in Figure 2. The influence of absorption is significant for the first cutouts with high concentration of both substances. This concentration dependence of penetration depth is clearly visible in Figure 2 for PSM. Intralipid is a fat emulsion and therefore lower backscattering manifests in the depth for decreasing concentration.



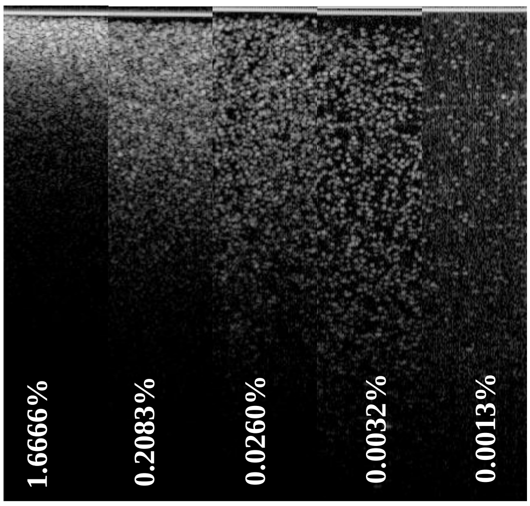


Figure 2: Intralipid (left) and PSM images for selected concentrations in descending order (displayed depth 3 mm)

To minimize the influence of attenuation effect, small rectangular regions near the surface (approximately 175 μm thick) were selected and analyzed. Mean values of these regions were computed to estimate the mean light intensities reflected by examined sample. These values are displayed in

Figure 3 as a function of concentration together with rational regression function

$$f(x)=\frac{(p_1x+p_2)}{(x^2+q_1x+q_2)}. \qquad (6)$$

The range of low concentrations was also successfully fitted with linear function, because it has been expected that there will be possibility for quantitative measurement due to low influence of *inter-scattering* interaction between particles. This can be seen from Figure 3, particularly for PSM.

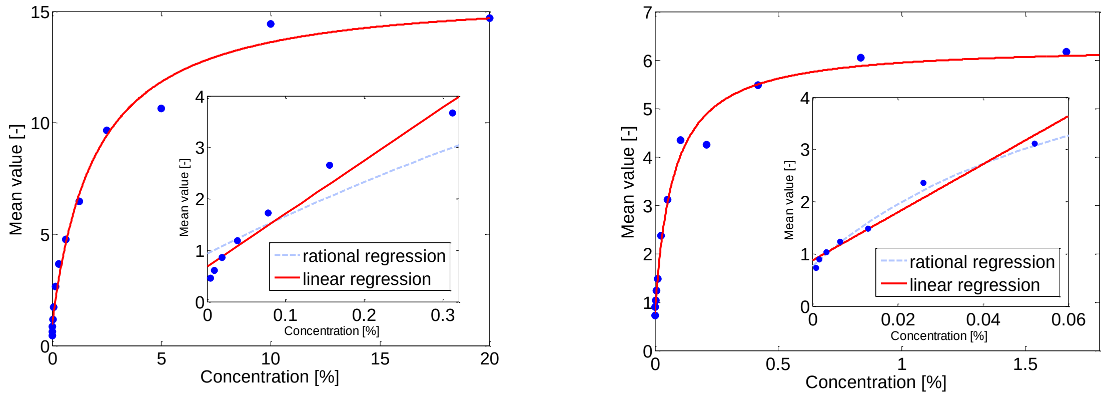


Figure 3: Mean intensity values vs. percent concentration of Intralipid (left) and PSM. The rational regression fit is shown for whole concentration range and linear regression for small concentration.

The histograms of pixel intensities, as an estimation of probability density functions (PDF), were analyzed for the same regions. Several theoretical PDFs were fitted for both substances and all concentrations. Distribution parameters were estimated by standard MATLAB function. The best results (according to mean square error (MSE), Figure 6) were achieved with Nakagami and Weibull distribution. Fitting results with Nakagami PDF are shown in Figure 4. Both distributions fitted well for whole concentration range.

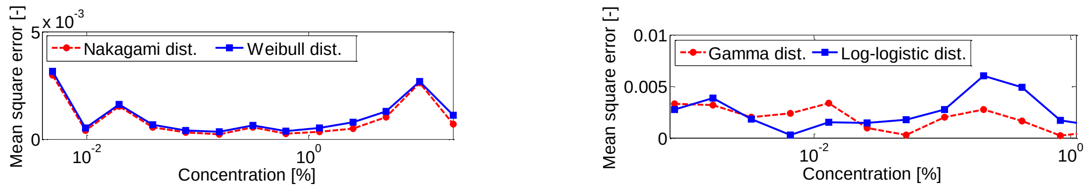


Figure 4: Concentration dependence of MSE for Intralipid (left) and PSM

The situation was different for PSM. No tested distribution fitted well enough for whole concentration range. Best results (according to MSE, Figure 6) were achieved with Log-logistic distribution for lower concentrations and Gamma distribution for higher concentrations (Figure 5).

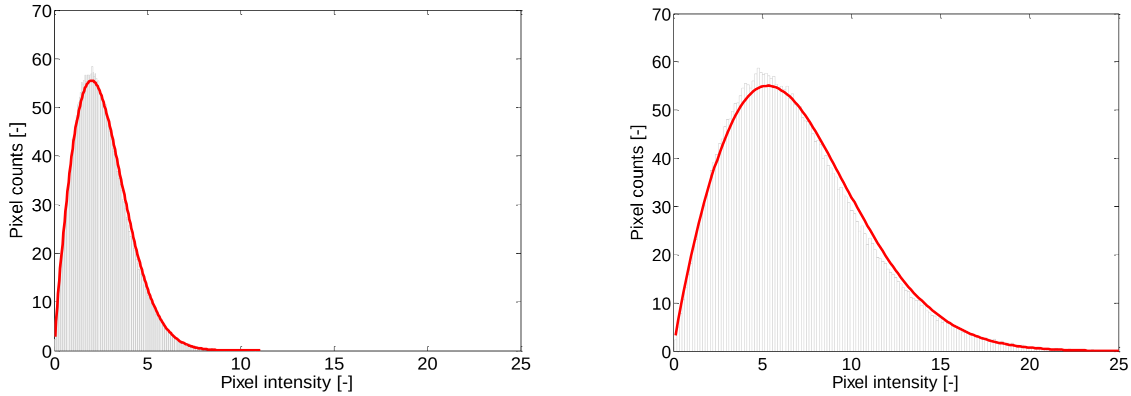


Figure 5: Histograms of Intralipid images with fitted Nakagami distribution for concentration 0.15625% (left) and 1.25%

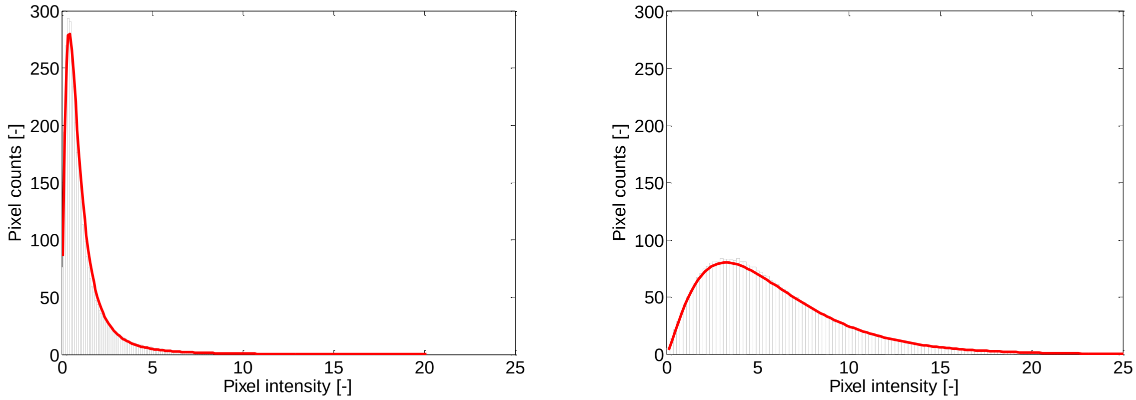


Figure 6: Histograms of PSM images with fitted Log-logistic distribution for concentration 0.00651% (left) and Gamma distribution for 0.833%

5. CONCLUSION

In this work, two substances (Intralipid and polystyrene based magnetic microparticles) were tested to determine their properties in optical coherence tomography. The results were visualized in plain images for empirical evaluation. Concentration dependence of mean values of image intensities was displayed and fitted with nonlinear rational regression function. Lower concentrations can be approximated with linear function if necessary. The best statistical distributions were found to fit image histograms – Nakagami and Weibull distribution for Intralipid, Log-logistic and Gamma distribution for polystyrene microparticles. Future work will focus on testing other substances and nanoparticles as a possible contrast agents and design of flow phantom for optical coherence tomography.

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