Selective OCT imaging of cells using magnetically-modulated optical contrast agents

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Abstract: Changes in optical scattering of ferromagnetic contrast agents are detected using optical coherence tomography. By modulating an applied magnetic field, we demonstrate selective imaging of cells in culture containing phagocytosed hematite particles.

OCIS codes: (170.0110) Imaging systems; (170.1650) Coherence imaging; (170.4500) Optical coherence tomogrraphy

1. Introduction

Contrast agents have been employed in virtually every imaging modality to site-specifically label cells and tissues to enhance diagnostic capabilities. Recently we reported a new class of *in vivo* contrast agents for optical coherence tomography that are ferromagnetic [1]. These agents may be useful for targeting tissues by means of surface-modification of the protein coat that encapsulates optically scattering particles. Using optical coherence tomography (OCT), mechanical movement was detected within an embedded agarose layer doped with ferromagnetic contrast agents. This was observed by comparing consecutive axial scans of the agarose while varying an applied magnetic field.

In this work we report the ability to selectively image magnetic particles with OCT. This is accomplished by applying a modulated magnetic field to the sample while scanning with a standard OCT system. The detected backscatter signal is then filtered about the modulation frequency to construct an image. Ferromagnetic particles present within the sample undergo mechanical movement in response to the gradient of the magnetic field. Since these particles are also highly optically scattering, OCT is sensitive to this movement. The modulated magnetic field therefore induces modulated mechanical motion of the particles which is subsequently detected as modulation of the OCT scattering signal.

This technique is applied to an *in vitro* cell culture to demonstrate increased contrast in cells that have successfully phagocytosed ferromagnetic particles. This is accomplished by comparing a purely structural OCT image to a magnetic-specific OCT image. Using contrast agents targeted to specific tissues, this technique has the potential to label *in vivo* tissue of diagnostic interest on the cellular level.

2. Experiment

An OCT system was used with galvanometers for scanning in the axial and transverse directions. Transverse and axial resolutions were 4μm and 5μm, respectively. High axial resolution was obtained using pulses from a femtosecond titanium:sapphire oscillator launched into an ultra-high numerical aperture fiber [2]. For magnetic imaging, a solenoid with 1cm inner diameter was placed underneath the sample. The magnetic field immediately above the surface of the solenoid was ~300G at the peak current. The solenoid power supply was modulated at 1kHz with a 10% duty cycle.

Macrophages (ATCC #TIB-67) were incubated overnight in the presence of hematite (Fe_2O_3) particles which were taken up via phagocytosis. The particles were aggregated into micrometer-sized clusters. Cell counts indicate no detrimental effects of the hematite to cell growth. A cell dish containing the aqueous growth media was then placed directly atop the solenoid in the sample arm of the OCT system.

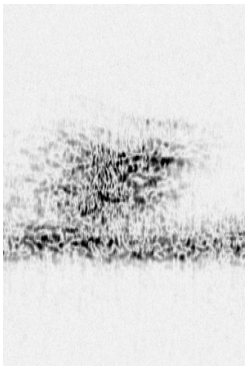

Fig. 1. Structural OCT image (300μm tall × 200μm wide) of macrophage cells. No structure was obtained from a control dish containing growth media without cells.

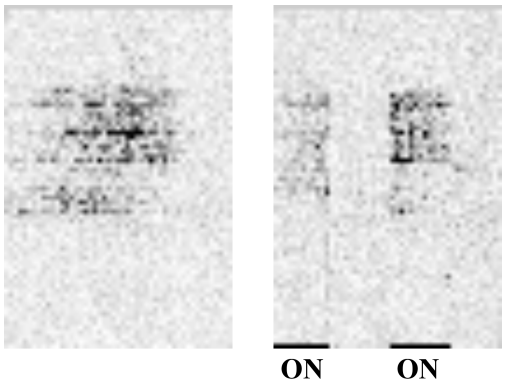

Fig. 2. Selective OCT imaging of macrophage cells (300μm tall × 200μm wide) using magnetic contrast. The images were acquired over the same scan region as in Fig. 1. The image in the right panel was acquired with the solenoid power supply on only for portions of the image indicated. This clearly indicates improved contrast in the presence of the magnetic field.

Figure 1 illustrates a typical structural OCT image of the macrophage cells. In light of recent evidence [3], it is likely that each cell naturally contains several discrete scattering regions. In addition, light microscopy confirms that the hematite is also highly visible within the cell. After structural imaging the samples were imaged using magnetic-specific detection. While modulating the solenoid current, the detected output from the OCT interferometer was analyzed with a lock-in amplifier for each position of the galvanometers during the scan. The resulting image is shown in Figure 2. A dish containing cells without hematite was also imaged as a control, and although a large structural OCT signal was observed, no magnetic-specific signal was obtained.

3. Conclusion

In conclusion, we have demonstrated the ability to magnetically label *in vitro* cells in culture and detect labeled cells using OCT. In combination with tissue-targeting technology for optical contrast agents, this new technique offers a potential method for labeling, imaging, and diagnosing abnormal tissue.

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4. References

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