Accurate detection of white matter tracts: mapping of human brain eloquent areas with cross-polarization optical coherence tomography

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ABSTRACT

Optical coherence tomography (OCT) is a promising method for clarifying the boundaries of the infiltrative brain tumors within surrounding white matter. Since gliomas often tend to grow close to eloquent brain areas, the question of the proximity of the tumor to white matter tracts sharply arise during tumor resection to prevent their damage. Cross-polarization (CP) OCT is a so-called functional extension of OCT that seems to have benefits in visualization of myelin. It looks perspective not just to detect white matter, but also receive information about its condition – the myelination rate and presence of ordered fibers. The aim of this study was to visualize white matter organization of eloquent brain areas with CP OCT using post-processing methods. The ex vivo CP OCT images were collected from autopsy subjects of the human brain. The brain specimens contained white matter of different organization and localization: brainstem, corpus callosum, frontal and parietal tracts, subcortical white matter. Two optical coefficients (attenuation and inter-channel attenuation difference) were calculated for each A-scan and two types of color-coded maps based on them were built. No significant differences based on CP OCT attenuation and inter-channel attenuation difference coefficients were demonstrated between white matter from different brain areas. However, in vivo studies can show conversely results. The detection of white matter microstructure during surgery looks promising therefore additional CP OCT performance build-up can be considered.

Keywords: cross-polarization optical coherence tomography (CP OCT), white matter tracts, optical coefficients, myelin fiber orientation, eloquent brain areas, image processing

1. INTRODUCTION

Optical coherence tomography (OCT) is one of the most promising, innovative and rapidly emerging intraoperative imaging modalities for neurosurgical guidance during brain tumor surgery [1]. It can provide neurosurgeon with real-time high-resolution images clarifying the boundaries of the infiltrative brain tumors within surrounding tissues. OCT can provide differentiation between tumorous and non-tumorous tissues through both qualitative [2-5] and quantitative [6-8] assessment of the OCT signal by building color-coded maps.

OCT currently has difficulties in clearly distinguishing between the grey matter (both cortex, thalamus or basal ganglia) and tumorous tissue [3]. Therefore, further studies and technological refinement are needed to increase the diagnostic capabilities of OCT and to provide rapid and efficient detection of brain tumors during surgery. However OCT is seemed to be an excellent method of myelin visualization, that can be realized using so called OCT functional extension – polarization-sensitive (PS) OCT (and also polarization-sensitive optical coherence microscopy) [9-11] and cross-polarization (CP) OCT [6, 12]. These OCT modalities offer sensitivity to tissue birefringence providing contrasts imaging of myelinated and birefringent nerve fibers. PS OCT allows to visualize white matter tracts in the brain [9, 13] and moreover has demonstrated good cross-validation with diffusion tensor imaging (DTI) on a postmortem human medulla oblongata sample [14]. DTI is a noninvasive magnetic resonance imaging (MRI) modality which is widely used.

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in preoperative planning in brain tumor surgery providing the information about the location and orientation of white matter tracts in relation to the tumor mass [15]. Moreover DTI depicts the incorporation of white matter fibers within the infiltrative brain tumors, seen especially in low-grade tumors, and their destruction by the high-grade gliomas [16-18].

This data is crucial for neurosurgical planning in order to identify and prevent damaging of the eloquent white matter tracts. However, brain movement during tumor resection reduces the effectiveness of using preoperative images for intraoperative surgical guidance and therefore using additional methods for intraoperative definition of white matter state could be useful.

Taking this into account the PS/CP OCT seems to be a promising method for intraoperative assessment of white matter fibers surrounding tumor mass, myelination rate and presence of ordered fibers indirectly providing the information about in functional facilities to neurosurgeon.

Sampling during neurosurgical procedures is restricted by eloquent brain structures (e.g. brainstem, thalamus, capsula interna, basal ganglia, corpus callosum) and therefore the results of these studies are also limited. Moreover most of performed ex vivo studies have made no reckoning of the exact localization the brain specimen sampling. However, for routine use of OCT in brain tumor surgery the detailed OCT profiling of different brain areas is needed. The aim of this study was to receive and compare OCT signal parameters of completely intact white matter of different localizations.

2. METHODS

Tissue

The study was conducted on 8 fresh anatomical specimens (4 left and 4 right hemispheres) of the brain of adults aged 58 to 69 years, whose death was not caused by intracranial pathology. The white matter specimens were obtained from following brain areas: (1) cortical - U-shaped fibers; (2) subcortical - long-range association fibers; (3) corpus callosum; (4) brainstem. All specimens were delivered to the location of the OCT study, which took 10 minutes for each specimen. The study was approved by the Ethical Committee of the Privolzhsky Research Medical University, and informed consent was obtained from the legal representatives of a deceased persons. All methods were performed in accordance with the relevant guidelines and regulations.

CP OCT study and image analysis

The study was performed with a spectral-domain CP OCT device developed in the Institute of Applied Physics of the Russian Academy of Sciences (Nizhny Novgorod, Russia). The device has a 20,000 A-scan/s scanning rate and performs 2D lateral scanning with a range of 2.4 × 2.4 mm 2 to obtain a 3D distribution of backscattered light in the polarization parallel and orthogonal to the polarization of the probing beam. The contactless scanning and image processing were performed as it was described previously [7]. The distributions of the attenuation (\(u\)) and inter-channel attenuation difference (\(uD\)) coefficients calculated from three dimensional OCT data volume forms en-face color-coded maps [6]. In total, 58 white matter specimens were scanned and analyzed.

Histological study

Brain samples were fixed in 10% formalin for 48 hours and a series of histological sections were made. The histological sections were stained with hematoxylin and eosin (H&E) and Luxol fast blue stain with crezyl violet (to identify both myelinated fibers and the neuronal tissue structures).

Statistical analysis

The median value among all values of the optical coefficients calculated for each A-scan of a 3-D CP OCT image was used. The results are expressed as the Me [Q1; Q3] where Me is the median of the coefficient and [Q1; Q3] are the 25th and 75\(^{th}\) percentile values, respectively. To distinguish tissue types by each coefficient, we used the Mann-Whitney U-test with the hypothesis that there was no difference between the compared groups.

3. RESULTS AND DISCUSSION

Regardless of the localization of white matter, it appeared red and yellow on the attenuation maps (Fig. 1 1a-4a) and pale blue to red on the inter-channel attenuation difference maps (Fig. 1 1b-4b). However, several color-coded maps of corpus callosum look more intense red in comparison to others. In addition, both attenuation and inter-channel
attenuation difference coefficients showed no significant differences between white matter from different brain areas (Table 1).

Table 1. The attenuation ($u$) and inter-channel attenuation difference ($uD$) coefficients values of white matter from different brain areas.

|                          | U-shaped fibers (n=14) | Long-Range Association Fibers (n=24) | Corpus Callosum (n=9) | Brainstem (n=11) |
|--------------------------|------------------------|-------------------------------------|-----------------------|------------------|
| $u$ Me [Q1; Q3]$^1$      | 5.31 [5.07; 5.64]      | 5.34 [5.13; 5.56]                  | 5.30 [5.22; 5.49]     | 5.40 [4.74; 5.57] |
| $p^2$                    | 0.84                   | 0.82                               | 0.76                  |                  |
| $uD$ Me [Q1; Q3]$^1$     | 2.05 [1.66; 2.49]      | 1.92 [1.79; 2.12]                 | 1.79 [1.76; 1.85]     | 1.81 [1.66; 2.30] |
| $p^2$                    | 0.40                   | 0.29                               | 0.36                  |                  |

$p^*$ - Me [Q1; Q3]; Me – median; [Q1;Q3] – 25th and 75th percentiles values respectively, $2$ – both $D$ and $uD$ coefficients of different white matter areas were compared with $u$ and $uD$ of U-shaped fibers using U-test Mann-Whitney.
Therefore, CP OCT could be quite effective in distinguishing tumorous tissue or white matter regardless of tumor localization. However, the study was performed on ex vivo samples and the dehydration and loss of tissue perfusion could alter tissue structure [19] and the CP OCT contrast between different types of white matter tracts disappeared. Therefore, this data should be proved during in vivo studies, which can have conversely results.

Several MRI studies have shown that the longitudinal white matter tracts seem to contain larger fibers with increased axonal diameter and larger myelin sheaths that was shown on the cortico-spinal tract [20]. On the other hand, the white matter in the near cortical regions is constructed by a mixture of crossing fibers showing thinner myelin sheaths and smaller axon diameters as well as larger extracellular spaces [21, 22]. However, the variety of white matter microstructure across the brain could not be presented by current CP OCT resolution. The detection of white matter microstructure during surgery looks promising therefore additional CP OCT performance build-up can be considered.

The perfect contrast of bundled myelinated fibers related to the gray matter of the brain is demonstrated in the paper. Figure 2 shows attenuation and inter-channel attenuation difference maps of striatum slice. Bundles of white matter are characterized by higher optical coefficients compared to gray matter of the brain: 5.48 [5.12; 5.70] vs 1.28 [0.98; 1.31] for attenuation coefficient (p<0.001) and 1.80 [1.62; 2.24] vs 0.28 [0.22; 0.38] for inter-channel attenuation difference coefficient (p<0.001).

Detection of white matter bundles and tracts among cellular component of the brain is extremely important during micro-invasive operations when the surgeon’s field of vision is substantially limited or during stereotactic procedures on the brain (electrode placement navigation for deep brain stimulation in patients with Parkinson's disease).

4. CONCLUSIONS

No significant differences based on CP OCT attenuation and inter-channel attenuation difference coefficients were demonstrated between white matter from different brain areas. However, in vivo studies can show conversely results. The detection of white matter microstructure during surgery looks promising especially considering the high contrast of normal white and gray matter obtained by processing CP OCT data.
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REFERENCES

[1] Fan, Y., Xia, Y., Zhang, X., Sun, Y., Tang, J., Zhang, L., Liao, H., “Optical coherence tomography for precision brain imaging, neurosurgical guidance and minimally invasive theranostics,” BioScience Trends 12(1), 12-23 (2018).

[2] Yashin, K. S., Gubarkova, E. V., Kiseleva, E. B., Kuznetsov, S. S., Karabut, M. M., Timofeeva, L. B., Gladkova, N. D., Snopova, L. B., Moiseev, A. A., Medyanik, I. A., Kravets, L. Ya., “Ex vivo Visualization of Human Gliomas with Cross-Polarization Optical Coherence Tomography: Pilot Study,” Sovremennye tehnologii v medicine 8(4), 14-22 (2016).

[3] Yashin, K. S., Kiseleva, E. B., Gubarkova, E. V., Moiseev, A. A., Kuznetsov, S. S., Shilyagin, P. A., Gelikonov, G. V., Medyanik, I. A., Kravets, L. Ya., Potapov, A. A., Zagaynova, E. V., Gladkova, N. D., “Cross-Polarization Optical Coherence Tomography for Brain Tumor Imaging,” Frontiers in Oncology 9, (2019).

[4] Börhringer, H. J., Lankenau, E., Stelrmacher, F., Reusche, E., Hüttmann, G., Giese, A., “Imaging of human brain tumor tissue by near-infrared laser coherence tomography,” Acta Neurochirurgica 151(5), 507-517 (2009).

[5] Strenge, P., Lange, P., Grill, C., Draxinger, W., Danicke, V., Theisen-Kunde, D., Bonsanto, M., Huber, R., Brinkmann, R., “Ex vivo and in vivo imaging of human brain tissue with different OCT systems,” 49 (2019).

[6] Kiseleva, E. B., Yashin, K. S., Moiseev, A. A., Timofeeva, L. B., Kudelkina, V. V., Alekseeva, A. I., Meshkova, S. V., Polozova, A. V., Gelikonov, G. V., Zagaynova, E. V., Gladkova, N. D., "Optical coefficients as tools for increasing the OCT contrast for normal brain visualization and glioblastoma detection," Neurophotonics 6(3): 035003 (2019).

[7] Yashin, K. S., Kiseleva, E. B., Moiseev, A. A., Kuznetsov, S. S., Timofeeva, L. B., Pavlova, N. P., Gelikonov, G. V., Medyanik, I. A., Kravets, L. Ya., Zagaynova, E. V., Gladkova, N. D., “Quantitative nontumorous and tumorous human brain tissue assessment using microstructural co- and cross-polarized optical coherence tomography,” Scientific Reports 9(1), (2019).

[8] Kut, C., Chaichana, K. L., Xi, J., Raza, S. M., Ye, X., McVeigh, E. R., Rodriguez, F. J., Quiñones-Hinojosa, A., Li, X., “Detection of human brain cancer infiltration ex vivo and in vivo using quantitative optical coherence tomography,” Science Translational Medicine 7(292), 292ra100-292ra100 (2015).

[9] Wang, H., Akkin, T., Magnain, C., Wang, R., Dubb, J., Kostis, W. J., Yaseen, M. A., Cramer, A., Sakadžić, S., Boas, D., “Polarization sensitive optical coherence microscopy for brain imaging,” Optics Letters 41(10), 2213 (2016).

[10] de Boer, J. F., Hitzenberger, C. K., Yasuno, Y., “Polarization sensitive optical coherence tomography – a review [Invited],” Biomedical Optics Express 8(3), 1838 (2017).

[11] de Boer, J. F., Milner, T. E., Martin J. C. van Gemert, M. J. C., Nelson, J. S., “Two-dimensional birefringence imaging in biological tissue by polarization-sensitive optical coherence tomography,” Optics Letters 22(12), 934 (1997).

[12] Schmitt, J. M., Xiang S. H., “Cross-polarized backscatter in optical coherence tomography of biological tissue,” Optics Letters 23(13), 1060 (1998).

[13] Wang, H., Black, A. J., Zhu, J., Stigen, T. W., Al-Qaisi, M. K., Netoff, T. I., Abosch, A., Akkina, T., “Reconstructing micrometer-scale fiber pathways in the brain: Multi-contrast optical coherence tomography based tractography,” NeuroImage 58(4), 984-992 (2011).

[14] Wang, H., Zhu, J., Reuter, M., Vinke, L. N., Yendiki, A., Boas, D. A., Fischl, B., Akkina, T., “Cross-validation of serial optical coherence scanning and diffusion tensor imaging: A study on neural fiber maps in human medulla oblongata,” NeuroImage 100, 395-404 (2014).

[15] Dubey, A., Kataria, R., Sinha, V., “Role of diffusion tensor imaging in brain tumor surgery,” Asian Journal of Neurosurgery 13(2), 302 (2018).
[16] Jellison, B. J., Field, A. S., Medow, J., Lazar, M., Salamat, M. S., Alexander, A. L., “Diffusion tensor imaging of cerebral white matter: a pictorial review of physics, fiber tract anatomy, and tumor imaging patterns,” AJNR Am J Neuroradiol 25(3), 356-69 (2004).

[17] Witwer, B. P., Moftakhar, R., Hasan, K. M., Deshmukh, P., Haughton, V., Field, A., Arfanakis, K., Noyes, J., Moritz, C. H., Meyerand, M. E., Rowley, H. A., Alexander, A. L., Badie, B., “Diffusion-tensor imaging of white matter tracts in patients with cerebral neoplasm,” J Neurosurg 97(3), 568-75 (2002).

[18] Yen, P. S., Teo, B. T., Chiu, C. H., Chen, S. C., Chiu, T. L., Su, C. F., “White matter tract involvement in brain tumors: a diffusion tensor imaging analysis,” Surgical Neurology 72(5), 464-469 (2009).

[19] Kiseleva, E. B., Yashin, K. S., Moiseev, A. A., Sirotkina, M. A., Timofeeva, L. B., Fedoseeva, V. V., Alekseeva, A. I., Medyanik, I. A., Kravets, L. Ya., Gladkova. N. D., “Cross-Polarization Optical Coherence Tomography in Comparative in vivo and ex vivo Studies of the Optical Properties of Normal and Tumorous Brain Tissues,” Sovremennyye tehnologii y medicine 9(4), 177 (2017).

[20] Yagishita, A., Nakano, I., Oda, M., Hirano, A., “Location of the corticospinal tract in the internal capsule at MR imaging,” Radiology 191(2), 455-460 (1994).

[21] Groeschel, S., Hagberg, G. E., Schultz, T., Balla, D. Z., Klose, U., Hauser, T. K., Nägele, T., Bieri, O., Prasloski, T., MacKay, A. L., Krägeloh-Mann, I., Scheffler, K., “Assessing White Matter Microstructure in Brain Regions with Different Myelin Architecture Using MRI,” Plos One 11(11), e0167274 (2016).

[22] Herve, P. Y., Cox E. F., Lotfipour, A. K., Mougin, O. E., Bowtell, R. W., Gowland, P. A., Paus, T., “Structural properties of the corticospinal tract in the human brain: a magnetic resonance imaging study at 7 Tesla,” Brain Struct Funct 216(3), 255-62 (2011).