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Article

Cross-polarization optical coherence tomography probes for intraoperative application in neurosurgery

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Abstract: Optical coherence tomography (OCT) is one of the most promising, innovative and rapidly emerging intraoperative imaging modalities for neurosurgical guidance in brain tissue imaging, "optical biopsy", brain cerebral vascular detection, nerve fibers and white matter tracts detection. In this article, we provide a short survey of cross-polarization OCT and different types of OCT probes that can be used in routine neurosurgical practice. Through different types of probes there are multiple applications where OCT can play a highly complementary role in offering the real-time microscopic assessment and imaging of normal and pathological brain tissues. The biopsy-needle based probe for CP OCT was shown to be an effective instrument for brain tissue mapping and express estimation of tissue status as well as for detecting large blood vessels to prevent causing bleeding during biopsy sampling. The folded CP OCT probe for intraoperative use for brain tissue examination was shown as a potentially efficient sensor head for CP OCT. The probe demonstrated high lateral resolution in diffractive limited probing beam quality. The length of dismountable probe tip allows using the probe under operating microscope. Due to the designed family of specialized probes CP OCT fills in the niche of devices for express brain tissue examination *in situ*.

Keywords: cross-polarization optical coherence tomography (CP OCT); cross-scattering; probes; brain tumors; stereotactic biopsy; neurosurgical guidance

1. Introduction

Optical coherence tomography (OCT) is one of the most promising, innovative and rapidly emerging intraoperative imaging modalities for neurosurgical guidance in brain tissue imaging, "optical biopsy", brain cerebral vascular detection, nerve fibers and white matter tracts detection [1]. OCT imaging has some advantages in the field of intraoperative technologies in neurosurgery: high-resolution, high-speed, low-cost, label free, non-invasiveness, and convenience performance. Several studies have shown that OCT can provide differentiation between tumorous and non-tumorous tissues through both qualitative [2,3] and quantitative assessment [4,5] of the OCT signal by building color-coded maps. Moreover, OCT seems to be an excellent method of myelin visualization, that can be realized using so-called OCT functional extensions – polarization-sensitive (PS) OCT and also polarization-sensitive optical coherence microscopy [6,7] and cross-polarization

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(CP) OCT [2]. These OCT modalities provide contrast imaging of myelinated fibers due to their sensitivity to tissue birefringence. Thus, PS OCT allows visualizing white matter tracts in the brain.

There are several scenarios how OCT can be implemented in neurosurgery: (1) OCT can be used intraoperatively for brain imaging and provide real-time feedback to the surgeons, e.g. clarifying the boundaries of the infiltrative brain tumors within surrounding tissues; (2) OCT can be used for emergency biopsy by neuropathologist; (3) OCT can aid in stereotactic procedures for verifying target for deep brain stimulation or guiding biopsy overcoming challenges both with requirement of multiple sampling and hemorrhagic complications.

According to these scenarios, possible implementations of OCT scanner designs have been proposed: (1) hand-held imaging probes [2,8], surgical instrumentation (e.g. biopsy needle) [9–11], microscope-integrated systems [3,12,13] and nonportable stationary OCT systems [5,14]. However, considering multifunctionality of OCT in neurosurgery, a multipurpose device with a particular set of OCT probes can be preferred. Moreover, all of the proposed probes need to comply with optimal surgical ergonomics, current neurosurgical protocols and other surgical devices in the operating room.

In this article, we provide a short survey of cross-polarization OCT and different types of OCT probes that can be used in routine neurosurgical practice. In addition, we present a concept of dismountable sterilizable contact-type OCT probe designed to avoid overlapping of surgeons field of view using operating microscope.

2. Cross-polarization OCT in brain tumor surgery

2.1. Cross-polarization OCT as a variant of polarization-sensitive OCT

Intensity-based OCT has demonstrated significant results in detecting pathological changes in tissues with layered structure, such as those in the eye. In case of structureless tissue types (brain, breast) the advanced contrast OCT imaging can be achieved by using PS OCT [15]. This technique can detect a number of characteristics of the matter caused by optical anisotropy of its constituent elements, that provides the possibility to generate tissue-specific contrast [15,16] in OCT images. Based on the polarization anisotropy of the tissue structure, PS OCT provides better visualization of elongated structures and therefore offers advanced imaging of myelinated fibers in peripheral nerves and the brain [17]. CP OCT has been shown as a simplified variant of PS OCT providing not only conventional OCT imaging but also allowing visualization of those locations in object where the initial polarization state of the probing light alters into orthogonal state due to birefringence or/and cross-scattering in biological tissues [18]. This OCT modality enables recording two co-registered images common scattering (conventional OCT image or so-called image in co-polarization) and anisotropic (image in cross-polarization) that detects tissue backscattering producing polarization state orthogonal to the incident one. The last is obtained through the use of the orthogonally polarized backscattered light, which is mutually coherent with the incident one, what contributes to the cross-polarized OCT image. The origin of such “coherent backscattering” includes random polarization during light propagation in the media, depolarization during the backscattering process, and “regular” polarization changes associated with propagation back and forth in birefringent media [19].

2.2. Cross-polarization OCT devices

Since 2002, several generation of CP OCT devices with cross-polarization detection were developed in the Institute of Applied Physics of the Russian Academy of Sciences (Nizhny Novgorod, Russia) and produced for custom use by Biomedtech LLC (Nizhny Novgorod, Russia) [20,21], as shown in Figure 1 a,b.

The early studies were performed with the time-domain (TD) CP OCT device “OCT-1300U” (1310 nm wavelength, 200 A-scans per second line rate). The device belongs to a family of endoscope compatible systems, which was approved for clinical use (product license №FCP 2012/13479 from 30 May 2012). It is characterized by number of features that are sufficient for solving the majority of

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endoscopic tasks, e.g. express estimation of tissue state in small areas. However, its imaging rate and scanning protocol (only the 2D scanning is rational to be used due to low line rate) do not meet modern requirements and are insufficient for the tasks like angiography, elastography, or tissue structure orientation imaging [22,23]. The CP OCT image includes both images: (1) cross-polarization (upper part); (2) co-polarization (lower part), as shown in Figure 1 c6.

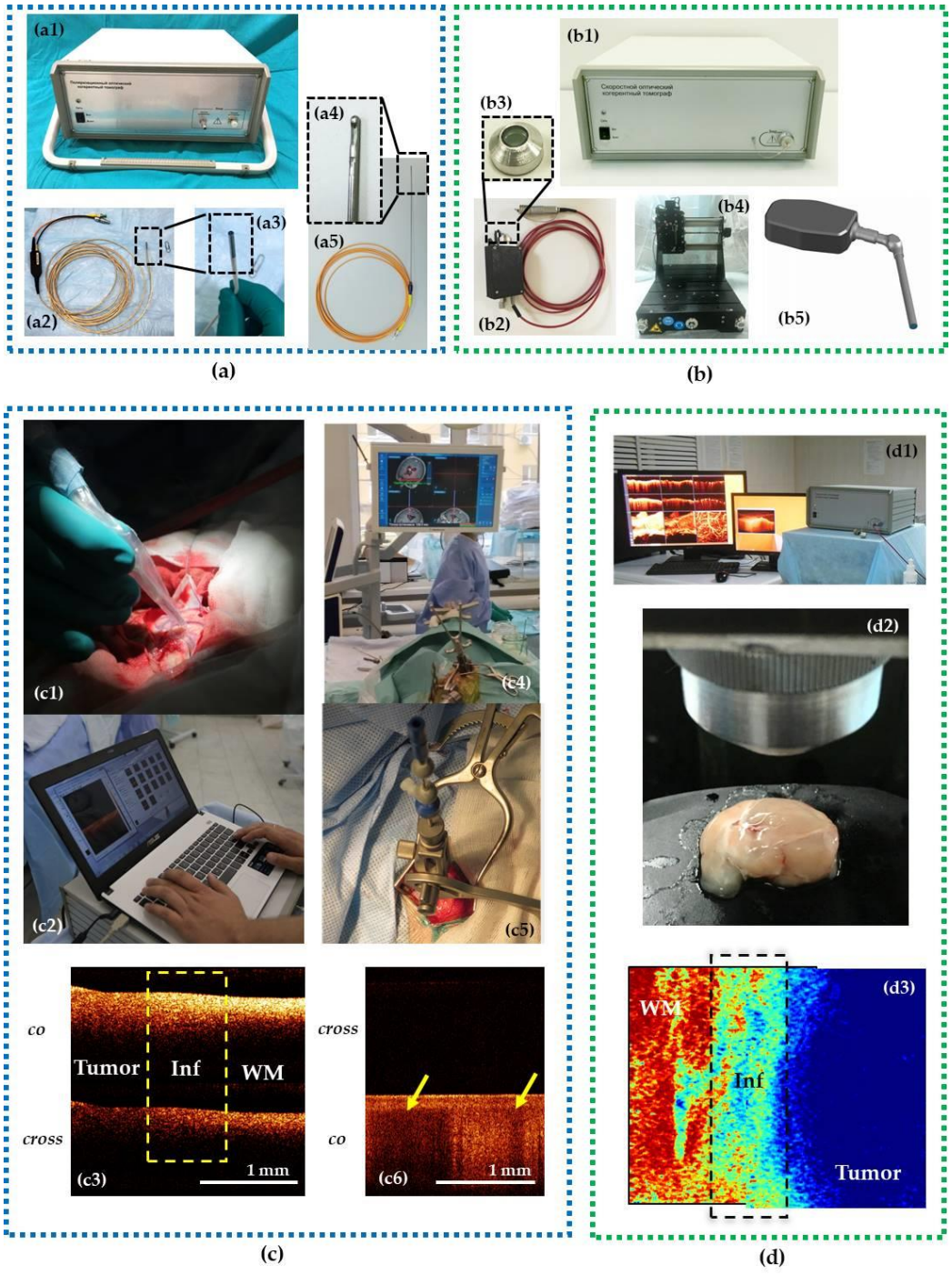

Figure 1. Different CP OCT devices with compatible probes (**a, b**) are presented with corresponding types of the CP OCT images in co-polarization and cross-polarization (**c3), (c6**) and optical coefficient color-coded map (**d3**). (**c3), (d3**) CP OCT images demonstrate clear signal differences between tumor and white matter (WM), yellow and black dotted rectangles indicate infiltration zone (Inf) of white matter. (**a**) Time-domain certified CP OCT device "OCT-1300U" with 2 probes: (**a2**), (**a3**) forward-flexible hand-held probe for intraoperative use (**c1), (c2**) providing 2D images (**c3**); (**a4**), (**a5**) needle-like probe for stereotactic biopsy providing 1D imaging (**c6**) (yellow arrows are showing the blood vessels) and its possible application during frameless stereotactic biopsy using

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neuronavigation system (**c4), (c5**). (**b**) Spectral-domain OCT device (**b1), (d1**) with flexible contactless multifunctional CP OCT probes for 3D scanning (**b2**), (**b3**), (**d2**) that can provide user with color-coded maps (**d3**); (**b4**) rigid attachment of a probe on a special positioner mount for large area scanning; (**b5**) the end part of the probe is constructed in curve shape for intraoperative use in the field of an operating microscope.

The spectral-domain (SD) OCT engine for CP OCT imaging was developed in IAP RAS preserving optical characteristics of probing light (central wavelength 1300 nm, output power 5 - 15 mW). The probing beam bandwidth is little higher than in previously used TD CP OCT device, which causes the lateral resolution of 15 um in air. The device was designed to provide 20 000 A-scan/s line rate using linear photodiode array SU-512LDB-1.7T1 (Goodrich), 1200 lpmm diffractive grating T-1200-1310 (LightSmyth) and double prism corrector made from custom crafted elements (Nanyang Jingliang optical technology corp, China). This allowed to avoid any polarization anisotropy in the spectrometer. To realize uniform optimal conditions for cross-polarization studies of biological tissue the device was equipped with a system of active maintenance of circular polarization of a probing wave in common path OCT setup [24]. The resulting CP OCT image also includes both co-and cross- images but in reverse order to the ones in TD OCT: (1) co-polarization (upper part); (2) cross-polarization (lower part), as demonstrated in Figure 1c3. The image acquisition can be performed in a contact or contactless mode (probe dependent).

Table 1. Cross-polarization OCT devices.

	Time-domain OCT-1300U	**Spectral-domain CP OCT system**
Technical		
Wavelength	1310 nm	1310 nm
Spectrum width	100 nm	120 nm
Axial resolution	15 um	10 um
Scanning rate	200 A-scans/s	20,000 A-scan/s
Probing beam polarization state	random	circular
Acquisition time	2 sec (2D)	0.05 sec (2D), 26 sec (3D for multimodal)
Image modalities		
2D	yes	yes
3D	no	yes
OCT angiography	no	yes
OCT elastography	no	yes
OCT image analysis		
qualitative	yes	yes
quantitative	only for co-channel, 1 optical coefficient	for co- and cross- channels, several optical coefficients
Approval for clinical use	since 2005	in progress

2.3. Cross-polarization OCT image analysis

Numbers of studies demonstrate that OCT images assessment can be performed through three main approaches: (1) qualitative (visual); (2) quantitative (using optical coefficients calculation), and (3) combined based on building color-coded maps.

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Qualitative assessment is based on visual analysis of light attenuation profile in the tissue in cross-sectional OCT images. Using this method, tumorous and non-tumorous tissues are differentiated based on signal intensity parameter as the most powerful criteria [2,3]. The tumorous tissue is characterized by low signal level and white matter - by high-intensity signal, as shown in Figure 1c3. The key structural element of white matter influencing features of the received CP OCT signal is the presence of myelin fibers - highly elongated conducting objects. They are responsible for high depolarizing properties demonstrated by white matter in case of fibers chaotic arrangement on the scale of the probing beam while ordered arrangement of myelin fibers causes the origin of linear birefringence and polarizing properties. The qualitative approach provided high sensitivity of (82–85%), specificity (92–94%), and diagnostic accuracy (87–88%) for distinguishing white matter from tumor tissue [2].

The quantitative approach based on some optical coefficients calculation appears to be a more objective and accurate method for OCT data analysis. Different strategies for numerical data obtaining were developed, however, it still requires further studies [4,5]. The most widespread optical coefficient being used for quantitative processing of OCT signal received from various brain tissues is attenuation coefficient. The sensitivity and specificity of quantitative approach is approximate 100% [4,5].

The combined approach includes building of contrast color-coded maps of the tissue. The maps offer an en-face view of the tissue. The color codes represent the value distribution of the tissue throughout the image [4,5]. In case of gliomas, the color codes demonstrate clear differences between tumorous tissue and white matter. Figure 1d3 presents an appropriate illustration. This approach appears more promising for clinical use especially by neurosurgeons due to its combination of quantitative accuracy and user-friendliness for evaluation.

2. Cross-polarization OCT probes for neurosurgery

The main part of each sensor device is its distal component, which transfers probing radiation (near IR light in the case of OCT) and receives the signal wave. In OCT this role is played by optical probes, which diversity is very wide. In this paper, we will focus on the description of four different CP OCT probes which demonstrated the most valuable clinical applicability. Table 2 presents a comparison between these CP OCT probes. The first probe is a flexible hand-held CP OCT probe for detecting brain tumor margins, supplied as a standard for TD CP OCT device “OCT-1300U”. The second is a side-view modification of the flexible hand-held CP OCT probe, designed for the use in conjunction with a stereotactic biopsy needle for “optical biopsy” and detection of blood vessels in the region of interest directly following surgical procedure. The third probe was developed as a part of fast SD OCT system, which can be used for fundamental studies and emergency pathomorphological examinations. It was applied for obtaining a large amount of human post-mortem and animal specimens’ images and was widely used in experimental studies. The last probe design highlighted here is a dismountable hand-held curved device intended to be used in an operating room equipped with an operating microscope.

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Table 2. The performance comparison of CP OCT probes.

	Characteristics	Standard CP OCT probes		Specialized CP OCT probes	
		Flexible hand-held probe	**Contactless multifunctional CP OCT probe**	**Stereotactic needle-type probe**	**Dismountable curved hand-held probe**
1.	CP OCT device	Time-domain OCT-1300U	Spectral-domain OCT system	Time-domain OCT-1300U	Spectral-domain OCT system
2.	Probe type	forward-looking	forward-looking	side-looking	forward-looking
3.	Contact/ Contactless	contact	contactless with contact option	contact	contact
4.	Outer diameter of the probe	2.7 mm	8 mm	1.65 mm	8 mm
5.	Lateral resolution	25 μm	15 μm	25 μm	15 μm
6.	Lateral image size	2D: 1.3x1.4 mm or 200x256 pixels (width x height)	3D: 2.4x2.4x1.35 mm or 512x512x256 pixels (width x length x height)	2D: from 2 to 200 mm length of the single scan	3D: 2.4x2.4x1.35 mm or 512x512x256 pixels (width x length x height)
7.	Portability	yes	no	yes	yes
8.	Intraoperative use	yes	no	yes	yes
9.	Application	"optical biopsy" - differentiation between tumorous and non-tumorous tissues	fundamental studies and emergency pathomorphological examination	"optical biopsy" - blood vessels and tissue type detection	"optical biopsy" - differentiation between tumorous and non-tumorous tissues

2.1. Flexible hand-held CP OCT probe

The flexible hand-held CP OCT probe (Figure 1 a2, a3, c1) was constructed at early stages of common-path OCT development. The 5 m-long fiber probe was realized in few modifications with intendent the outer diameter of a scanning head varying from 1.6 mm to 2.7 mm. The probing beam driving mechanism was described in details in [25]. The probe head design is compatible with most of commercially available endoscopes, but it may also be used independently.

The small head size makes it possible to use the probe in any environment and previously studies have demonstrated its applicability for tumorous tissue detection during brain cancer resection using described qualitative (visual) CP OCT criteria [2]. However, the positioning of the probe can face several problems due to its flexibility. A possible solution to this problem is the development of a dismountable curved hand-held probe that will be described below.

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2.2. Stereotactic needle-type probe

Intensity-based OCT has demonstrated significant results in detecting pathological changes in tissues with layered structure The probe was designed for the use in conjunction with TD CP OCT device "OCT-1300U" to provide the navigation guidance during taking a biopsy. The probe head was created in a side-view mode using previously described ideas [9-11, 26].

One of the first ideas of obtaining brain imaging through a needle-type OCT probe was published in 2011 and the forward-looking imaging needle implementation to brain imaging was described [10]. The approach demonstrates high usability, but it is not applicable for biopsy guidance.

Pichette J. et al. reported on the biopsy-needle based design of OCT probe in 2015 [9]. They set multiple OCT channels on the outer surface of the needle, making it possible to perform OCT visualization directly during the biopsy sampling. The disadvantage of the method lies in its merit – the sampling stylet window is located in a blind zone of the probe (which may be overcome by the main needle rotation) and the outer part becomes very complex in production.

The most valuable design of the biopsy needle compatible probe was provided by David D. Sampson's group [11,27]. The biopsy sampling protocol includes the use of a standard biopsy needle cover and two inner items consequently induced into its hole: an OCT probe to detect safety-sampling area and a standard inner stylet to extract the sample.

We constructed a device based on the same principles: the standard biopsy needle tube was used as a probe head body and a system of GRIN lens, spacer and beam reflecting prism was used to project the fiber tip into the tissue under investigation. The main differences in our design are the use of the actual inner stylet as a body of the OCT probe, which exit window is filled with optically transparent glue, and abandoning mechanized scanning during the examination. In addition, to redirect radiation towards the exit window, a microprism (item 66-767 from Edmund Optics) was glued to the exit end of the spacer instead of an angled polishing of the spacer fiber. Moreover, since the OCT engine is used with a probe, it was made as a common-path OCT with long length of Fiseau interferometer (the distance between the fiber tip and the outer lens surface of the Flexible hand-held CP OCT probe is 10 mm in air), the same distance was preserved between the fiber tip and the outer needle tube surface in a needle-type OCT probe. The latter produces several difficulties in probe constructing, but it afforded the probe interchangeability with the flexible hand-held CP OCT probe.

The lateral scanning ability was rejected for this probe. The scanning procedure is performed through manual driving of the scanner along the needle axis and allows recording almost an infinite length of the scan. The last gives the opportunity to map the brain from its surface to the target area and be sure that biopsy window is located exactly in the tumor area. At this stage of investigations, we believe that preservation of manual driving of the probe is the most appropriate option due to the possibility of varying the velocity of the probe movement (and lateral direction scale on the OCT image). The image shadow analysis also provides the possibility of detection of large vessels, which should not be a subject of damage during biopsy taking.

Although several scientific groups have already presented stereotactic biopsy needles [9–11], there is no common lens concerning point of its application – vessel detection and preventing hemorrhage or "optical biopsy" of studied tissue. In our opinion, OCT is an excellent technology for both tasks and can improve the results of a stereotactic biopsy. The "optical biopsy" performed immediately during the procedure can dramatically decrease the risk of the acquisition of non-informative diagnostic samples outside from the viable tumor volume (such as necrotic/gliosis or normal white matter), which has been reported in up to 24% of stereotactic biopsy series [28–30]. Currently, a neurosurgeon needs to perform intratumoral serial biopsies followed by intraoperative neuropathological assessment [30,31]. It can improve the diagnostic value and accuracy but is associated with an increased risk of intracranial hemorrhages, which have been reported in 0.3–59.8% of cases [28,32,33] and considerably contribute to the reported mortality of 3,9% (28,30,32). Stereotactic OCT probe provides information on blood vessel presence in the biopsy point; thereby, surgeon can change the needle position to avoid vessel damage.

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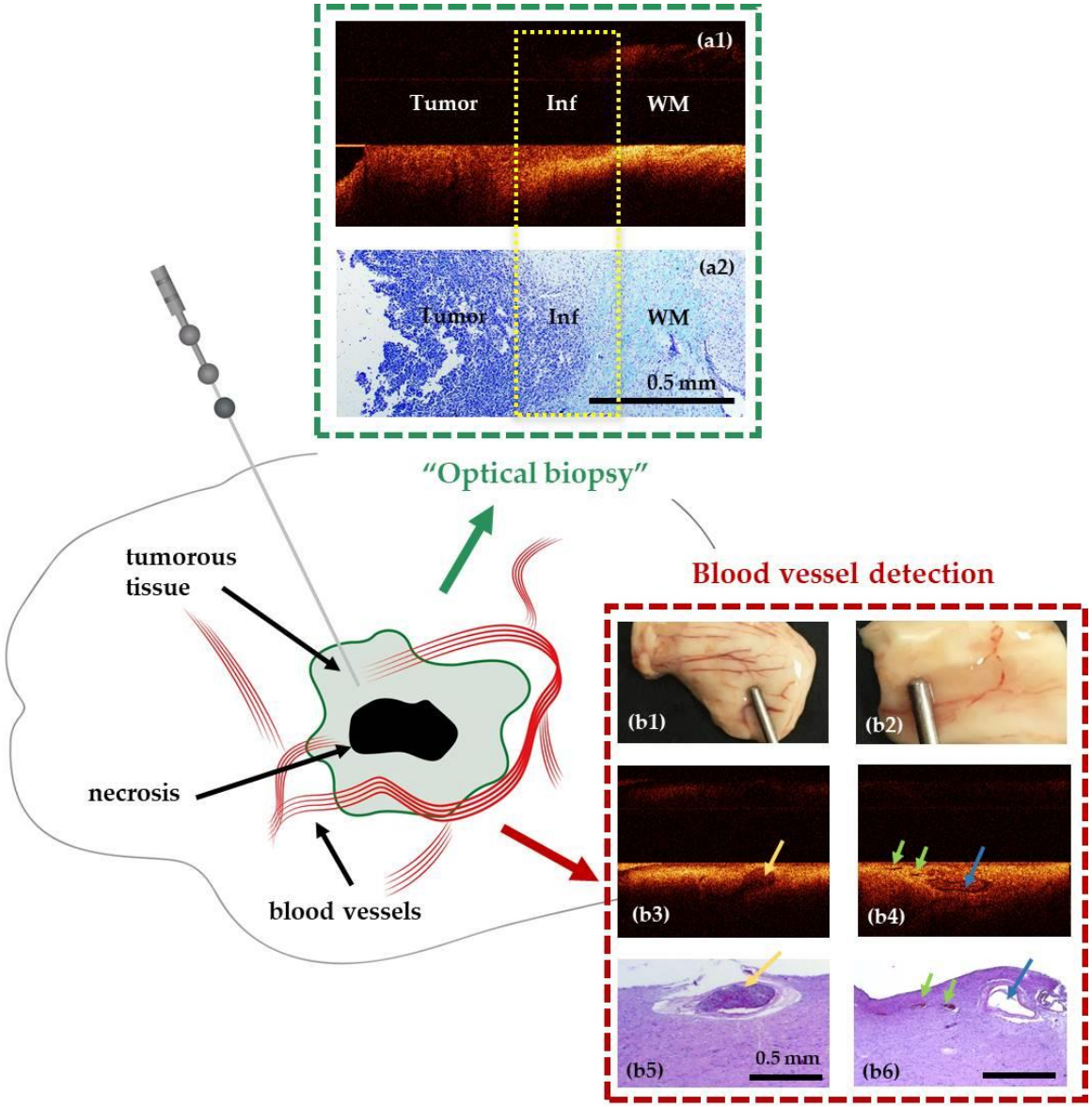

Figure 2. Stereotactic needle-type OCT probe for vessel detection (**b3**), (**b4**) and preventing hemorrhage and "optical biopsy" of studied tissue (**a1**). The CP OCT images were obtained from rats with astrocytoma 101.8. (**a1**) Structural CP OCT image demonstrates clear signal differences between tumor and white matter (WM), yellow dotted rectangle indicates infiltration zone (Inf) of white matter. The arrows on the CP OCT images and corresponding histological slices show typical CP OCT signs of vessels.

2.3. Contactless multifunctional CP OCT probe

This probe design does not have any principal differences in comparison with the most of modern 3D MEMS-based OCT probes: it consists of a two-axis fast scanning (resonant frequency 340 Hz) MEMS mirror (A8L18.3-4200AU-TINY48.4-B/TP by Mirrorcle Technologies, Inc.) and a simple telecentric scanning lens. The lens is characterized by a relatively short working distance, which allows using the probe in both contact and contactless regimes. The probe body was made to provide compatibility with motorized stage for large area imaging during experiments on animal models or post-mortem samples. The probe demonstrated high potential of 3D CP OCT imaging in brain-targeted applications, but its design does not allow using the probe in operating room due to two main factors. Firstly, it is characterized by small length of potentially interchangeable and serializable distal head, which prohibit the use of sterile covers. Secondly, housing profile of the probe is too big for avoiding the overlap of the field of view of the operating microscope. While the

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first problem may be solved by the use of an elongated probe head, the second one requires the development of other approaches in constructing the probe.

This type of probes are widely used in many experimental studies in the field of neurooncology, performed both *in vivo* and *ex vivo* on animals and on patients' samples [5,14,34–36]. This type of probe has potential to be a part of optical digital pathomorphological systems with advanced label-based and label-free photonic technologies together along with advances in artificial intelligence, machine learning and computer-aided diagnosis algorithm [37]. In particular for neuropathologist, OCT can have a powerful impact in the following clinical situations: (1) when excisional biopsy is hazardous and fast real-time feedback for neurosurgeon is required such as following a stereotactic biopsy; (2) when pathologists need guidance to select areas of tumor mass in large tissue specimens for histological evaluation, such as following temporal lobectomy for diffuse astrocytoma.

2.4. Hand-held curved CP OCT probe

Currently two main competitive concepts of using OCT during open neurosurgical procedures have been suggested. On the other hand, the OCT integration into a surgical microscope appears to be the most obvious and comfortable option for surgeons because it provides wide-OCT imaging directly in oculars [3,12,13]. However, realization of this idea requires the reconstruction of production-release design and building of a so-called "OCT-ready" surgical microscope by the developer company. The hand-held imaging probes [2,8,30] do not need such technical advances and can be used jointly with microscope for intraoperative assessment of tissues. In brain tumor surgery OCT can be used for in situ detection of cancer tissue via "optical biopsy". However, most of suggested systems are not comfortable in clinical use due to their size, shape, flexibility etc.

The bayonet-shaped CP OCT probe presented in this paper seems to be most favorable option since this construction is familiar for surgeon and preserves field of view, as shown in Figure 3a. The probe consists of two detachable parts – the scanning head with long flexible cable and a group of focusing optics with folded axis contained in a stainless steel tube of a complex shape. The focusing optics group is designed from telecentric scanning group (1) and 1:1 translator (3) (Figure 3b) combined with equilateral prism, which entrance and exit sides are orthogonal to the chief ray of probing beam. The prism glass (BK7) refractive index and the angle of incidence to the reflecting side (60 degrees) cause total internal reflection from this face, therefore, this element does not induce optical losses into the optical path of the device. To minimize flare-blinding effects the exit window of the probe is made of curved inner shape, the outer surface has small tilt (2 degrees) to the optical axis of the probe. In addition to flare repression, the tilted outer surface helps to prevent the appearance of air bubbles when touching an uneven elastic surface by squeezing the latter over the edge of the window.

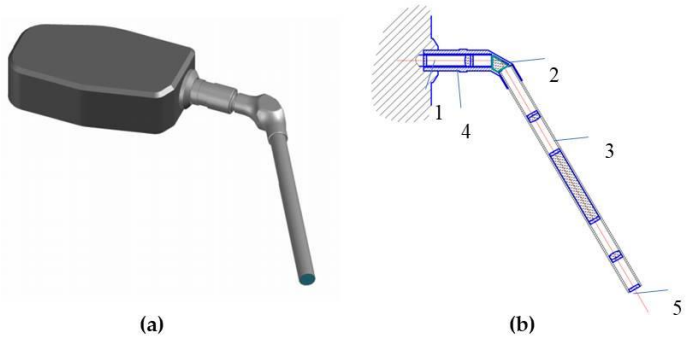

Figure 3. Optical setup of bayonet-shaped probe for CP OCT: (**a**) external view; (**b**) schematic view. 1 – telecentric scanning lens group, 2 – probe folding, 3 – replaceable sterilizeable optical beam translator, 4 – standard LEMO's® coupling, 5 – main optical axis.

Long focal lens using in the optical setup provides paraxial beam propagation and causes diffraction limited quality of the beam in its focal plane. The optical setup provides 15 um axial

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resolution while the Rayleigh length is about 0.5 mm. The system is achromatized for 1250-1350 nm optical range, the image distortion does not exceed 0.5% value.

The optic group connection is made based on LEMO's® Push-Pull Self-Latching Connection System (not shown in detail of Figure 3), well known by most clinicians. The length of dismountable probe tip is 150 mm that is enough to provide the possibility to use it conjunctly with an operating microscope.

Due to the use of LEMO's® connection the distal part of the probe may be easily dismounted and then sterilized using one of standard protocols based on chemical solutions or gas methods applicable for endoscope systems including STERRAD. The prohibited sterilizing methods include usage of solutions containing hydrogen peroxide (concentration 6% or more), formic acid and other strong oxidants, incl. ozone. With all methods of disinfection and sterilization, the temperature should not exceed 100 degrees Celsius, sudden changes in temperature are also not allowed. The probe scanning head with its flexible connection cable may be treated with disinfectant solutions, but it should be enclosed in a sterile cover while in the operating room.

5. Conclusions

Recent studies demonstrated that OCT has a great potential in neurosurgery the best known in brain tumor surgery. As described here, through different types of probes there are multiple applications where OCT can play a highly complementary role in offering the real-time microscopic assessment and imaging of tissues during brain tumor surgery, stereotactic biopsy and in the pathology laboratory. The biopsy-needle based probe for CP OCT was shown as an effective instrument for brain tissue mapping and express estimation of tissue status as well as for detecting large blood vessels to prevent causing bleeding during biopsy sampling. The folded CP OCT probe for intraoperative use for brain tissue examination was shown as a potentially efficient sensor head for CP OCT. The probe demonstrated high lateral resolution in diffractive limited probing beam quality. The length of dismountable probe tip allows using the probe under operating microscope. The designed family of specialized probes allows CP OCT to occupy a niche of devices for express brain tissue examination in situ after obtaining approval for clinical use process.

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