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Mikhail Kirillin
Olga Panteleeva
Ekaterina Yunusova
Ekaterina Donchenko
Natalia Shakhova

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Mikhail Kirillin,[a] Olga Panteleeva,[b] Ekaterina Yunusova,[c] Ekaterina Donchenko,[d] and Natalia Shakhova[a,c]
[a]Institute of Applied Physics RAS, 603950, Ulyanov Street, 46, Nizhny Novgorod, Russia
[b]Clinical Hospital of the Russian Railways, 603011, Lenin Avenue, 18, Nizhny Novgorod, Russia
[c]Nizhny Novgorod Medical Academy, 603000, Minin Square, 10/1, Nizhny Novgorod, Russia
[d]Research Institute of Traumatology and Orthopedics, 603155 Verhne-Voljskaya Naberejnaya, 18, Nizhny Novgorod, Russia

Abstract. An increase of infertility and chronic pelvic pains syndrome, a growing level of latent diseases of this group, as well as a stably high percentage (up to 25% for infertility and up to 60% for the chronic pelvic pains syndrome) of undetermined origin raises the requirement for novel introscopic diagnostic techniques. We demonstrate abilities of optical coherence tomography (OCT) as a complementary technique to laparoscopy in diagnostics of fallopian tubes pathologies. We have acquired OCT images of different parts of fallopian tubes in norm and with morphologically proven pathology. Based on comparative analysis of the OCT data and the results of histological studies, we have worked out the subjective OCT criteria for distinguishing between unaltered and pathologic tissues. The developed criteria are verified in blind recognition tests. Diagnostic efficacy of OCT diagnostics in the case ofpelvic inflammatory diseases has been statistically evaluated, and high diagnostic accuracy (88%) is shown. Basing of the subjective criteria, an attempt to develop independent criteria aimed for automated recognition of pathological states in fallopian tubes is undertaken. Enhanced diagnostic accuracy (96%) of the developed independent criteria is demonstrated. [DOI: 10.1117/1.JBO.17.8.081413]

Keywords: optical coherence tomography (OCT); recognition; histogram analysis; laparoscopy; fallopian tubes; pelvic inflammatory diseases (PID).

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1 Introduction

In spite of the rapid advance in medical sciences, problems concerned with revealing causes of infertility and chronic pelvic pains are still of great significance. According to data from the World Health Organization (WHO), in addition to low birthrate, the level of infertile marriages grew from 12% to 18% worldwide in the recent two to three decades. The WHO classification of infertility forms includes the so-called "unexplained infertility," when there are no visible objective causes of impairment of reproductive function.[1]

On the one hand, diagnosis "unexplained infertility" is associated with current prevalence of asymptomatic and subclinical forms of female pelvic diseases. Thus subclinical pelvic inflammatory diseases (PID) amount 60% of all PID cases, which allows us to introduce the term of "silent" or unrecognized inflammations.[2] At the same time, PID among women below 30 amount to 37% to 48%, being one of the main factors for infertility development risk.[3]

On the other hand, appearance of such terms as "unexplained infertility" and "unrecognized PID" are explained by imperfection of traditional diagnostic techniques, which could be applied for diagnostics of PID. These techniques include transvaginal ultrasound (TVUS), computed tomography (CT), and magnetic resonance imaging (MRI). Transvaginal ultrasound is effective in diagnosing of acute PID and complications of PID such as tubo-ovarian abscess.[4] Combination of TVUS with color Doppler flowmetry allows to assess vascularity and pulsatility indices,[5] which improve the diagnostic efficacy. Computed tomography is informative when PID is accompanied by reactive inflammation of surrounding pelvic and abdominal organs.[6] MRI proved its superiority to TVUS and CT in diagnostics of PID providing sensitivity of 95% and specificity of 89%[7]; however, its application is limited by economic reasons and high requirements to infrastructure. Currently invasive laparoscopic examination is considered as the preferred method for diagnostics of PID, although it ensures sensitivity of only 27% and a specificity of 92%.[8]

In order to increase diagnostic accuracy of laparoscopic examination, we propose the method combining laparoscopy and OCT imaging for detection of morphological changes in fallopian tubes in the case of chronic inflammation. Previously OCT study of fallopian tubes *ex vivo* was reported by Herrmann et al.,[9] who show that OCT probably allows identification of tubal causes of infertility. We report the results of the *in vivo* study performed in a clinical environment. This study allowed us to work out subjective criteria for distinguishing OCT images of normal and pathologic cases. The developed criteria further underwent blind recognition test.

However, the problem of independent criteria for OCT diagnostic data evaluation is still of high importance. Such criteria could be useful when OCT scanning provides a video stream and a clinician is not able to analyze the obtained frames in real time. An approach toward automatic recognition of area boundaries in OCT images was developed by Bazant-Hegemark et al.[10,11] Another approach is sonification of OCT images when a specific sound is generated, depending on the features of an

Address all correspondence to: Mikhail Kirillin, Ulyanov str. 46, Nizhny Novgorod, 603950, Russia. Tel: 7 831 4164619, Fax: 7 831 4363792. E-mail: mkirillin@yandex.ru

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obtained OCT image.[12] Due to structural difference of OCT images of norm and pathology, the corresponding sound signals vary significantly, which allows a clinician to distinguish them. An alternative approach for OCT image recognition is histogram analysis, which has been recently successfully applied in OCT of ovarian tissue.[13] In our study we use this approach in OCT diagnostics of fallopian tubes.

2 Materials and Methods

The capabilities of OCT for diagnosing subacute inflammations were studied in two steps: first we developed the distinguishing criteria for OCT images of the objects of interest, and second, we applied OCT with the image distinguishing procedure as a diagnostic tool for patients with under-recognized diagnosis. About 165 female patients were enrolled in the study. The inclusion criteria were the following: reproductive age (18 to 45) and indications for laparoscopy, such as infertility, endometriosis, PID, and the CPP syndrome. All the patients signed the informed written consent in conformity with the WMA Declaration of Helsinki. The study was authorized by the Human Research Ethics Committee (Protocol No. 8 of 03.11.2009).

OCT imaging was performed during standard laparoscopy (laparoscope "Olympus Winter & Ibe GmbH," Germany) using "OCT-1300U" modality (IAP RAS, BioMedTech Ltd., Nizhny Novgorod, Russia). It is a compact portable device ($15 \times 40 \times 40$ cm in size, 10 kg weight), which needs no supplementary equipment or special operating conditions. OCT device characteristics are as follows: radiation wavelength is 1280 nm, in-depth resolution is 15 μm, lateral resolution is 30 μm, imaging rate is eight to 10 frames per second, probing depth is up to 2 mm, and replaceable endoscopic probe diameter is 2.7 mm.

The diagnostic procedure is shown in Fig. 1. In standard laparoscopic examination, an endoscope is inserted through an incision and a trocar, which allows for control of operations inside abdominal cavity. OCT-probe is inserted into abdominal cavity through an additional trocar and a special holder. OCT-probe surface is attached with a slight compression for 1 to 2 s to the serous membrane of fallopian tube in the middle (isthmic) part. Uterine end of a fallopian tube is embedded into uterine wall (muscular layer), which prevents OCT-study because imaging depth is limited by 2 to 3 mm. The length of the isthmic part where the OCT examination is performed is 1 to 3 cm.

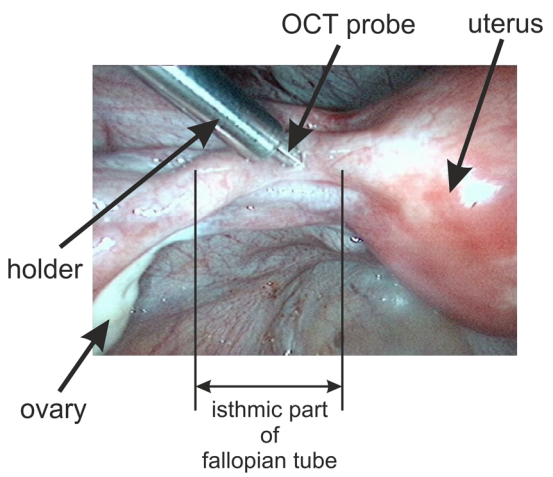

Fig. 1 Laparoscopic image of the diagnostic procedure.

The OCT studies were carried out first on patients without PID, but with indications for surgical treatment (benign tumors), and further on PID patients with planned removal of fallopian tubes as a preparatory stage to supplementary reproductive technologies. Histological analysis of the surgical material was used as a reference for interpreting the OCT data. We obtained typical OCT images of tissue in norm and pathology verified morphologically, which enabled us to develop the distinguishing criteria of the studied pathology for comparative analysis of OCT and histological data (54 cases). At the next step (OCT studies on 118 patients), we used the developed criteria to assess their diagnostic efficacy in blind recognition with subsequent statistical evaluation of results of the tests.

3 Results and Discussion

3.1 *OCT Images of PID*

A fallopian tube is a paired tubular organ connecting the uterine cavity in the region of its upper corner with the abdominal cavity at the ovary site. The fallopian tubes comprise four parts: infundibulum of uterine tube, ampulla of uterine tube, isthmus of uterine tube, and the uterine (interstitial) part. Morphological and/or functional alterations of fallopian tubes are known as the most frequent causes of female infertility. Chronic inflammatory diseases of fallopian tubes change the structure of the tubes' muscular wall, impairing the function of this organ and leading to dysperistalsis. The current prevalence of latent forms of inflammation often makes diagnostics of such changes difficult. We used OCT to study internal structure of the muscular membrane of fallopian tubes. OCT images were acquired during standard laparoscopy, where an OCT probe was put to the fallopian tube from the serous membrane side. Due to anatomical features, the interstitial part of the tube is inaccessible for OCT examination.

At the first stage we acquired OCT images of different parts of unaltered fallopian tubes in female patients of different age groups and at different phases of menstrual cycle. This study was undertaken to obtain a reference image of unaltered fallopian tubes. OCT images of the infundibulum and ampulla of uterine tube were greatly variable depending on age and phase of menstrual cycle, which makes these images unacceptable as a reference. Reproducible OCT images were obtained for the isthmus of uterine tube. This part is located immediately near the uterine; it has the length of no more than 3 to 4 cm, the internal diameter of about 2 to 3 mm, and the wall thickness comparable to the internal diameter. OCT images of the wall of unaltered fallopian tube in this part are unstructured, with moderate signal level and signal intensity gradually decreasing in-depth. The upper border of tissue in OCT images is even; the rate of signal intensity decrease is uniform [Fig. 2(a)]. The unstructured character of images is explained by the anatomy of this part of the tube: small height of the outer serous membrane epithelium (less than 20 μm) and homogeneous muscular layer with compactly located fibers. The features of the obtained OCT images were verified by results of histology.

In the case of PID the two different types of OCT images of fallopian tubes were obtained [Fig. 2(b) and 2(c)]. Images of the first type were inhomogeneous with dominating transverse striations and alternating areas of low- and high-signal level. Areas with low-signal level were relatively large, of variable size, irregular contours, round, or oval in shape. Comparison with the results of histology demonstrates that these areas

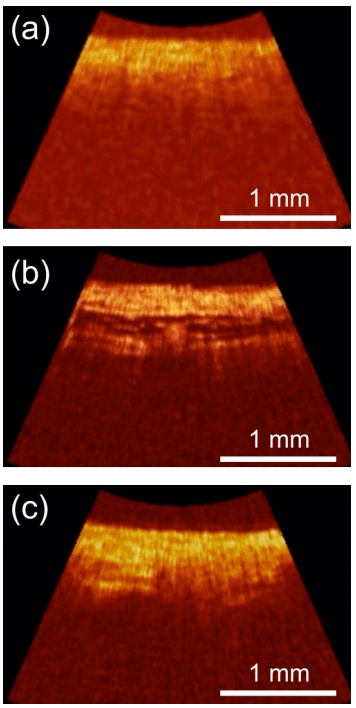

Fig. 2 Typical OCT images of fallopian tubes: (a) without inflammation, (b) with prevalence of edema, and (c) chronic alterations with fibrosis.

correspond to disintegration of the muscular layer of the fallopian tube due to edema typical for subacute inflammation. In addition to low-signal areas, we encountered small areas with high-signal intensity. The rate of OCT signal decrease varies over the image [Fig. 2(b)]. In OCT images of the second type, the areas with high-signal level prevail, which morphologically correspond to fibrosis of the muscular layer of fallopian tube [Fig. 2(c)]. Comparative analysis of OCT and histology data shows that images of the first type correspond to subacute inflammation accompanied by edema, and images of the second type to chronic inflammation with fibrosis.

Thus we have worked out the following subjective criteria for distinguishing between OCT images of normal and pathological organ. Typical features of OCT images of unaltered fallopian tubes are lack of structure and uniform in-depth signal decrease. In the presence of inflammation, the alternating areas with low- and high-signal level appear in an OCT image. Prevalence of areas with low-signal intensity morphologically corresponds to edema with disintegration of muscular fibers of the fallopian tube wall. The presence of areas with high-signal intensity in OCT images corresponds to fibrosis of the muscular wall of the fallopian tube.

To prove the adequacy of the developed criteria, we have performed a blind test on recognition of inflammatory changes in fallopian tubes by means of OCT. Eight respondents were enrolled, 376 recognitions were made. Results of the tests demonstrated that the sensitivity of OCT diagnostics is 90%, specificity 81%; and diagnostic accuracy 88%, resulting in kappa value of 0.63; positive and negative predictive values are 94% and 70%, correspondingly. The obtained data confirm that OCT is capable of detecting the signs of inflammation with high probability (90%) and allows us to exclude inflammatory changes with considerable certainty (higher than 80%) with substantial interobserver agreement.

3.2 *Development of Criteria for Automated Recognition of Pathology Cases in OCT Images*

The development of independent criteria for distinguishing norm from inflammation with edema or inflammation with fibrosis using OCT images is based on subjective criteria, which we previously worked out and tested in a blind recognition test. Since our subjective criteria deal with such characteristics as signal level, uniformity, and presence of alternating areas, we chose classical histogram image analysis as an approach to develop the independent criteria. The images were extracted as frames from a video captured by OCT during laparoscopy procedure and were further converted to 8-bit grayscale images. A rectangular area covering an informative part of the frame was selected, and the intensity histogram of this area was analyzed. A set of 37 OCT images, including eight images of norm and 29 images of an organ with inflammation (both with edema and fibrosis), was used a reference group for developing independent distinguishing criteria. These images were selected from those with histological verification of diagnosis. The histograms shown in Fig. 3(a) through 3(c) correspond to the three types of OCT images presented in Fig. 2(a) through 2(c). The range of low-intensity signal in a histogram is mostly related to OCT noise, which absolute magnitude can vary due to limited dynamical range of OCT device. To overcome these variations, the first maximum of each histogram corresponding to average noise level is taken as a reference level and is set to 0.

The essential difference between histograms of unaltered tissue (norm) and chronic alterations with fibrosis cases is manifested by the width of the first maximum and higher counts for higher signal values in the case of fibrosis. Higher counts for higher signal level correspond to previously found subjective criteria that high-signal level prevails in OCT images of chronic alterations with fibrosis. Smaller width of first maximum in this case indicates that the in-depth signal decay is more rapid compared with normal cases, so the number of low-signal counts is small. From Fig. 3(b) one can see that the case of edema can be classified as a transition from norm to fibrosis: the first maximum is wider compared with the case of fibrosis and narrower compared with norm, while the number of high-signal counts is larger than that for norm and smaller than the one for fibrosis.

The two described histogram features were used to develop the criterion for distinguishing norm from inflammation accompanied by fibrosis. The score S_1 corresponding to this criterion is calculated according to the formula:

$$S_1 = N_{110} + \frac{1000 - N_7}{5},$$

where N_7 is the number of counts for signal level of 7 (high for norm, low for fibrosis), and N_{110} is the number of counts for signal level of 110 (high for fibrosis, low for norm). It is constructed to result below 100 for norm and above 100 for fibrosis. From analysis of the values in the reference group, we found that N_{110} is more sensitive to presence of fibrosis so we decided to make its weight in criterion higher than that of N_7 Values of S_1 for OCT images presented in Fig. 2 are summarized in Table 1.

The value of S_1 for the case of inflammation with edema is 113, which is higher than the value expected for norm, but it is not far from the boundary value of 100. Minimal and maximal

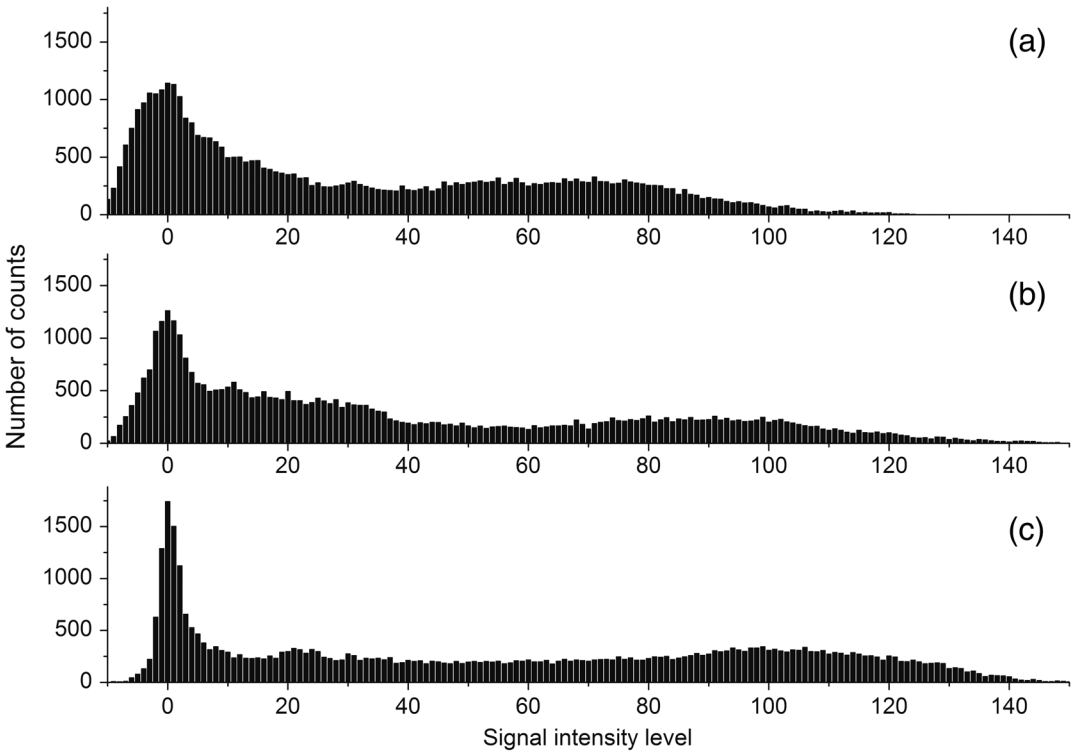

Fig. 3 Typical histograms of OCT images of fallopian tubes: (a) unaltered tissue, (b) with prevalence of edema, and (c) chronic alterations with fibrosis.

values of S_1 for different types of OCT images from the reference group of 37 images are summarized in Table 2. As one can see, groups for norm and edema have some overlay, which does not allow for clear distinguishing. Therefore we developed another criterion allowing to separate norm from inflammation with edema in OCT images.

The subjective criterion proposed in this study describes images of edema as inhomogeneous with dominating transverse striations and alternating areas of low- and high-signal level while images of norm are characterized by monotonous decay of signal level. In this respect we propose another score S_2 based on the sum of positive values of OCT signal first derivative over in-depth axis exceeding empirically defined threshold, which allows to exclude speckle noise effect on this value:

$$S_2 = \frac{\sum_i \sum_{j, f_{j+2} - f_2 > 10} f_{i,j+1} - f_{i,j}}{10},$$

where indices i and j represent pixel numeration over transversal and in-depth axes, respectively, $f_{i,j}$ is OCT signal value. The score was also normalized to provide value below 100 for norm and above 100 for inflammation.

The S_2 values for OCT images presented in Fig. 2 are also shown in Table 1. The value of S_2 for images of inflammatory states significantly exceeds that for norm. Minimal and maximal values of S_2 for reference group of 37 OCT images are presented in Table 2. It is evident that the score S_2 allows one to separate norm from inflammation with signs of edema. Scores S_2 versus S_1 for the reference group of 37 images are plotted in Fig. 4(a). Each point in the parameter plane represent a particular OCT image; its position is defined by the scores S_1 and S_2 as coordinates. In the figure, the area corresponding to norm (values below 100 for both scores) is indicated by a rectangle, which clearly separates the points characterizing normal tissue from those characterizing inflammation. This fact allows us to conclude that the developed quantitative criteria are valid to distinguish between OCT images of normal and abnormal states.

In order to verify the developed criteria, we have selected another test set of 21 OCT images, including two norm and 19 inflammation cases from the images with histological verification of diagnosis. The results obtained by applying the developed independent criteria to this group [Fig. 4(b)] approve the validity of the developed criteria.

Table 1 Independent criteria scores for OCT images presented in Fig. 2.

	OCT image type (diagnosis)		
Score	Without inflammation [Fig. 2(a)]	Inflammation with edema [Fig. 2(b)]	Inflammation with fibrosis [Fig. 2(c)]
S_1	45	113	206
S_2	8.8	507	889

Table 2 Minimal/maximal independent criteria scores for reference group of 37 OCT images.

	OCT image type (diagnosis)		
Score	Without inflammation	Inflammation with edema	Inflammation with fibrosis
S_1	38/88	20/198	112/308
S_2	8.8/85	177/610	31/2413

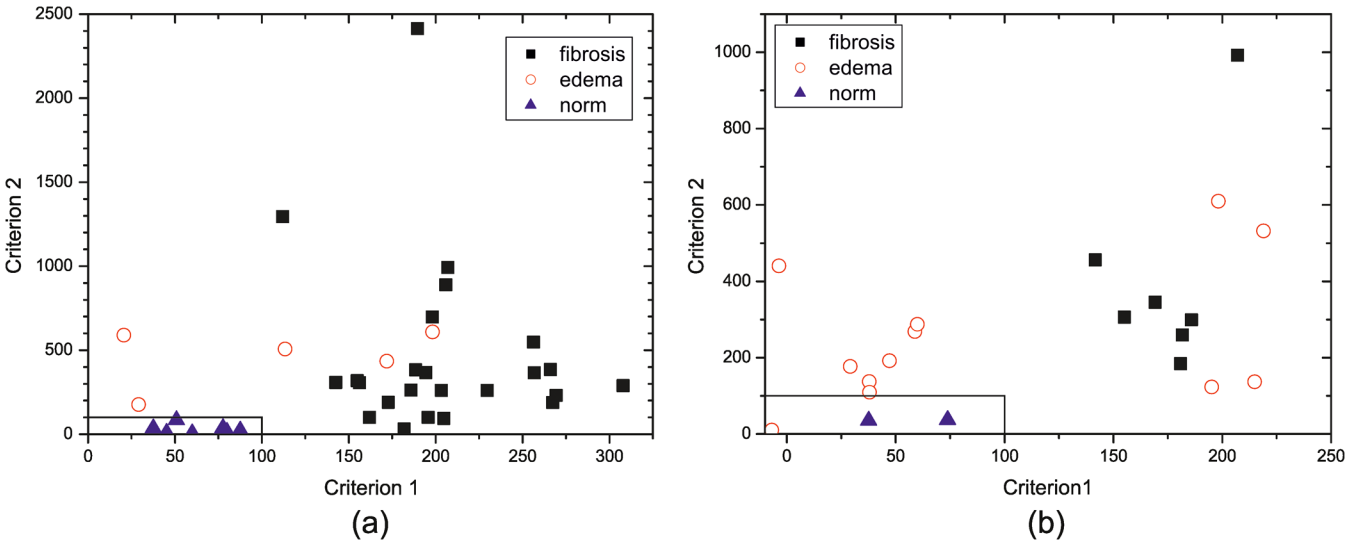

Fig. 4 Characterization of norm and pathology OCT images by independent criteria scores for reference (a) and test (b) groups. Rectangular zone demonstrates area indicating norm.

Summarizing data for both reference and test groups the proposed distinguishing method based on independent criteria resulted in the following statistical characteristics: sensitivity is 96%, specificity is 100%; diagnostic accuracy is 96%; positive and negative predictive values are 100% and 83%, respectively. These values are higher than those obtained from application of subjective criteria confirming additional diagnostic value of the developed independent criteria.

4 Conclusion

In the present work, we show abilities of OCT in diagnostics of fallopian tubes pathologies. Being an introscopic technique, OCT can become an alternative to biopsy and morphological verification. The obtained data on diagnostic efficacy under subjective recognition of OCT images (sensitivity 90%, specificity 81%; diagnostic accuracy 88%) indicate high potential of OCT in detecting PID. Introduction of independent criteria allowed to additionally increase diagnostic value (sensitivity 96%, specificity100%; and diagnostic accuracy 96%). In perspective these criteria can be employed for automatic recognition of OCT images and processing of video-stream.

We demonstrate that OCT data can be used not only for diagnosing inflammation, but also for more accurate determination of the character of morphological alterations: prevalence of edema or fibrosis. This information is important for more precise classification of the inflammatory process phase, for disease prognosis and choosing treatment strategy. We suppose that the use of OCT as a supplement to laparoscopy will allow us to optimize diagnosis of latent forms of PID and to more accurately evaluate the morphological form of the disease by taking into consideration the specific features of each clinical case and thus providing more adequate and personified treatment.

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