Correlation between Optical Coherence Tomography Images and Histological Features in Female Reproductive Tract Lesions

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Abstract: Female reproductive tract lesions are diverse, ranging from benign inflammation to malignant tumors, all of which seriously threaten women's health. Early accurate diagnosis is crucial for improving prognosis. As the "gold standard" for diagnosis, histopathological examination is difficult to meet the needs of clinical screening and dynamic monitoring due to limitations such as invasiveness and sampling restrictions. Optical Coherence Tomography (OCT), as a non-invasive, real-time, and high-resolution imaging technology, can clearly display the microstructure of biological tissues, known as "optical biopsy", and shows promising application prospects in the diagnosis of female reproductive tract lesions. This article systematically reviews the basic principles of OCT technology, the research progress on the correlation between OCT image features and histological features in lesions of different parts of the female reproductive tract such as the cervix and endometrium, analyzes the diagnostic efficacy, advantages and limitations of OCT technology, and prospects its future development direction, aiming to provide a reference for the clinical application of OCT technology in the diagnosis of female reproductive tract diseases.

Keywords: Optical Coherence Tomography (OCT); Histopathology; Cervical cancer; Endometrial cancer

1. Introduction

The female reproductive tract includes multiple organs such as the cervix, vagina, endometrium, and fallopian tubes, with various types of lesions, including inflammation, intraepithelial neoplasia, benign tumors, and malignant tumors. Among them, cervical cancer and endometrial cancer are common malignant tumors in women worldwide. According to the statistics of the World Health Organization, there were approximately 604,000 new cases of cervical cancer and 342,000 deaths worldwide in 2020, while there were about 417,000 new cases of endometrial cancer and 97,000 deaths [1]. Early diagnosis and intervention can significantly improve the cure rate

and survival rate of such diseases. For example, the 5-year survival rate of stage I cervical cancer can reach more than 90%, while that of advanced stage is only about 17% [2]. Therefore, finding an efficient and non-invasive early diagnostic method is of great significance for the prevention and treatment of female reproductive tract lesions.

At present, the clinical diagnostic methods for female reproductive tract lesions mainly include gynecological physical examination, imaging examinations (ultrasound, CT, MRI, etc.), laboratory examinations (HPV testing, TCT screening, etc.), and histopathological examination. Among them, histopathological examination clarifies the nature and grade of lesions by observing the morphological and structural changes of tissue cells, and is the "gold standard" for diagnosis. However, this examination is an invasive procedure, with defects such as sampling bias, long examination cycle, and inability to perform real-time monitoring, which limits its application in large-scale screening and dynamic evaluation of lesions. Although ultrasound examination is non-invasive and convenient, its resolution is low, making it difficult to clearly display the microstructure of tissues; CT and MRI examinations have high resolution, but have problems such as radiation exposure (CT), long examination time, and high cost, which cannot meet the clinical needs for accurate, rapid, and non-invasive diagnosis of lesions [3].

Optical Coherence Tomography (OCT) is a non-invasive imaging technology based on the principle of low-coherence light interference developed in the 1990s. Its axial resolution can reach 1–10 μm, close to the level of histopathology, and can real-time obtain cross-sectional microstructure images of biological tissues *in vivo* [4]. Since its advent, OCT technology has been widely used in ophthalmology, cardiovascular system, digestive system and other fields, playing an important role in the early diagnosis, treatment guidance and prognosis evaluation of diseases. In recent years, with the continuous development of OCT technology and the research and development of special endoluminal probes, the application research of OCT in the diagnosis of female reproductive tract lesions has gradually increased. Numerous studies have confirmed that OCT image features have a good correlation with histopathological features, and it is expected to become an important auxiliary method for non-invasive diagnosis of female reproductive tract lesions. This article reviews the research progress on the correlation between OCT technology and histological features in female reproductive tract lesions, aiming to provide a reference for clinical application.

2. Research on the correlation between OCT images and histological features of lesions in different parts of the female reproductive tract

The histoanatomical structures of different regions in the female reproductive tract vary, and the corresponding OCT imaging features of lesions in these regions also differ accordingly. At present, research on the correlation between OCT imaging features and histological characteristics has mainly focused on the cervix, vagina, endometrium and other sites (**Figure 1**), while there are relatively few studies on the fallopian tubes, ovaries and other regions.
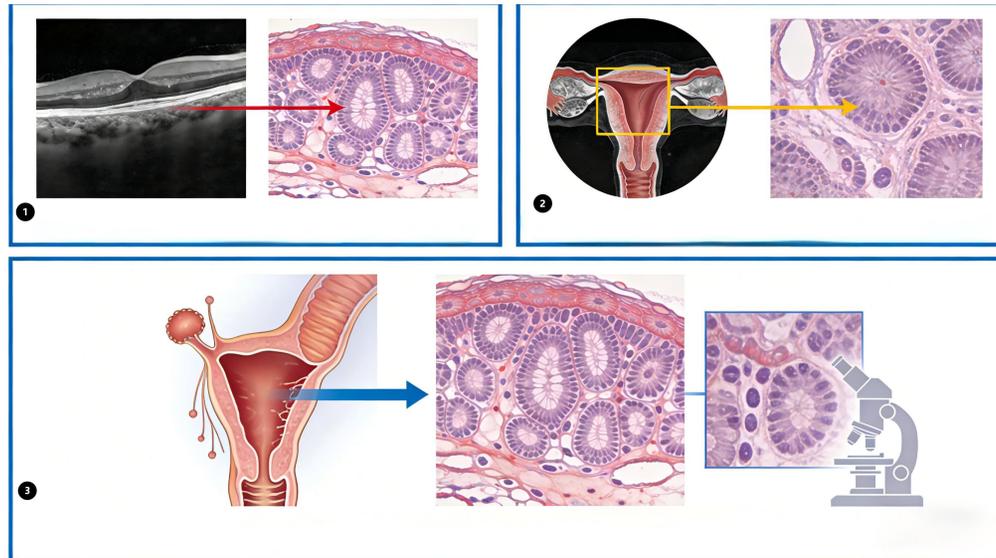
Figure 1. Case studies on the correlation between OCT images of the reproductive tract and histological features. (1) Cervical canal: OCT shows epithelial thickness, which is consistent with histopathological measurement values. (2) Endometrial polyps: OCT reveals high-signal lesion boundaries, and histopathological examination confirms benign polyps. (3) Cervical transformation zone: OCT images show the metaplastic epithelium transition zone, which is consistent with the histological verification of this area.

2.1. Cervical lesions

Cervical lesions are one of the most common lesions in the female reproductive tract, including cervicitis, cervical intraepithelial neoplasia (CIN), and cervical cancer. Among them, CIN is a precancerous lesion of cervical cancer, and timely detection and treatment of CIN can effectively prevent the occurrence of cervical cancer. The histological structure of the cervix from the inside to the outside is the mucosal layer, muscular layer, and serosal layer. The mucosal layer is composed of the epithelial layer and lamina propria. The epithelial layer is stratified squamous epithelium or columnar epithelium, and the lamina propria is connective tissue containing abundant blood vessels and glands. Normal cervical tissue and cervical lesions of different degrees have typical features in OCT images, which are highly correlated with histological features.

The OCT image of normal cervical mucosa shows a clear 4-layer structure [5]. The first layer is the epithelial superficial layer, presenting a hypoechoic band with uniform thickness, corresponding to the superficial cells of stratified squamous epithelium in histology; the second layer is from the epithelial basement membrane to the spinous layer, presenting a moderately hyperechoic band with clear texture, corresponding to the basement membrane and spinous layer cells; the third layer is the lamina propria, presenting a hypoechoic band with a few regular blood vessel shadows, corresponding to the connective tissue and blood vessels in histology; the fourth layer is the muscular layer, presenting a hyperechoic band, corresponding to the cervical muscular tissue. This image feature is completely consistent with the histological structure of the normal cervix and can be used as a benchmark for judging whether the cervical tissue is normal.

The main OCT image features of cervicitis are thickening of the mucosal layer, especially the epithelial layer and lamina propria, unclear or blurred layered structure, mild to moderate uneven echo intensity, scattered punctate hyperechoic or hypoechoic areas, increased number of blood vessels, and dilation of some blood vessels [6]. Histologically, cervicitis is mainly manifested by congestion and edema of the mucosal layer, inflammatory cell infiltration, and hyperplasia or dilation of glands. The features such as thickening, uneven echo, and abnormal

blood vessels in OCT images are the reflection of these histological changes. Studies have shown that the OCT image score of cervicitis is positively correlated with the degree of histological inflammation, and the severity of inflammation can be evaluated through OCT image features [7].

The OCT image features of cervical cancer are more typical, mainly manifested by complete destruction of the layered structure, disappearance of the normal tissue structure, diffuse hyperechoic or mixed echo, severe uneven echo intensity, a large number of irregular hyperechoic nodules or hypoechoic necrotic areas, blurred or unidentifiable lesion boundaries, extensive infiltration into surrounding tissues, significant abnormal blood vessel morphology, a large number of abnormally proliferated new blood vessels with disordered and tortuous courses and irregular vessel walls [8]. Histologically, cervical cancer is manifested by cancer cells breaking through the basement membrane, infiltrating into deep tissues to form irregular cancer nests. The cancer cells have significant pleomorphism, with large and hyperchromatic nuclei, increased nuclear-cytoplasmic ratio, accompanied by necrosis and neovascularization. The features such as structural destruction, abnormal echo, and significant vascular abnormalities in OCT images accurately reflect these histological changes. Multiple studies have confirmed that the sensitivity, specificity, and accuracy of OCT in diagnosing cervical cancer are 88–95%, 92–96%, and 90–94% respectively, with high diagnostic efficacy, and it can be used as an important auxiliary method for screening and diagnosing cervical cancer [9].

2.2. Endometrial lesions

Endometrial lesions include endometritis, endometrial hyperplasia, and endometrial cancer. Among them, endometrial hyperplasia is a precancerous lesion of endometrial cancer, and early diagnosis is crucial for improving the prognosis of patients. The cyclical changes of the histological structure of the endometrium and the changes after lesions can be reflected in OCT images.

The OCT image features of normal endometrium vary in different menstrual cycles. The OCT image of the proliferative phase endometrium shows a 2–3 layer structure: the epithelial layer is a hypoechoic band, the lamina propria is a hypoechoic band with a few blood vessels, and the overall thickness is relatively thin; the thickness of the secretory phase endometrium increases, the boundary between the epithelial layer and the lamina propria is unclear, the echo is uneven, and scattered hyperechoic points can be seen, corresponding to glandular secretion and glycogen deposition in histology; the layered structure of the menstrual phase endometrium is blurred, the echo is disordered, and irregular hypoechoic areas can be seen, corresponding to endometrial shedding and bleeding in histology [10]. These OCT image features are consistent with the cyclical histological changes of the normal endometrium and can be used to evaluate the physiological state of the endometrium.

The main OCT image features of endometritis are thickening of the endometrium, blurred layered structure, uneven echo, scattered punctate hyperechoic or hypoechoic areas, increased number of blood vessels, and abundant blood flow signals [11]. Histologically, endometritis is manifested by congestion and edema of the endometrium, inflammatory cell infiltration, and dilation or hyperplasia of glands. The features such as thickening, uneven echo, and abnormal blood vessels in OCT images are the reflection of these histological changes. Studies have shown that OCT can accurately identify endometritis through image features, with a diagnostic sensitivity and specificity of about 90% [12].

The OCT image features of endometrial cancer are complete destruction of the endometrial layered structure, disappearance of the normal tissue structure, diffuse hyperechoic or mixed echo, uneven echo, hypoechoic necrotic areas, blurred lesion boundaries, infiltration into the muscular layer, significant abnormal blood vessel morphology,

and a large number of abnormally proliferated new blood vessels [5]. Histologically, endometrial cancer is manifested by cancer cells breaking through the basement membrane, infiltrating into deep tissues to form cancer nests. The cancer cells have significant pleomorphism, accompanied by necrosis and neovascularization. The OCT image features accurately reflect these histological changes. Studies have found that the sensitivity and specificity of OCT in diagnosing endometrial cancer are 85–92% and 90–95% respectively, and it can be used as an auxiliary diagnostic method for endometrial cancer [13].

3. Clinical application value of OCT technology

Based on its good diagnostic efficacy and technical characteristics, OCT technology has important value in the clinical application of female reproductive tract lesions, mainly reflected in the following aspects:

(1) Lesion screening

OCT technology is non-invasive, convenient, and fast, and can be used for large-scale screening of female reproductive tract lesions, especially further screening of high-risk groups such as HPV-positive and TCT-abnormal groups. It can effectively reduce unnecessary biopsies and improve screening efficiency. A multicenter study further verified the value of the in vivo OCT imaging system in evaluating cervical lesions: the accuracy, sensitivity, and specificity of OCT screening versus HPV combined with TCT screening were 83.7% vs 64.9% ($\chi^2 = 128.82$, $p < 0.001$), 77.8% vs 64.5% ($\chi^2 = 39.01$, $p < 0.001$), 91.8% vs 65.4% ($\chi^2 = 98.12$, $p < 0.001$), respectively, with statistically significant differences [14]. This study showed that for HPV-positive but TCT-normal populations, OCT examination can be used to evaluate whether there are occult lesions in the cervical tissue, avoiding missed diagnosis or excessive biopsy.

(2) Diagnosis and grading

OCT images can clearly reflect the histological features of lesions, helping to clarify the nature and grade of lesions and provide a basis for clinical diagnosis. For lesions that are difficult to be clearly diagnosed by conventional examinations, such as atypical hyperplasia and microinvasive carcinoma, OCT examination can provide more diagnostic information and improve diagnostic accuracy.

(3) Guiding biopsy and surgery

OCT technology can perform real-time imaging, accurately locate the scope and boundary of lesions during the examination, guide biopsy sampling, and improve the positive rate of biopsy [15]. In surgical treatment, OCT can be used to evaluate whether the surgical margin is clean, avoid residual lesion tissue, and reduce the recurrence risk. For example, in cervical conization, OCT can be used to real-time monitor the OCT image features of the margin tissue to judge whether there are residual CIN or cancer cells, ensuring the thoroughness of the surgery.

(4) Monitoring of treatment effect and follow-up

OCT technology is non-invasive and can be repeated, making it suitable for dynamic monitoring after treatment of female reproductive tract lesions, evaluating the treatment effect, and timely detecting recurrence [16]. For example, after physical therapy or surgical treatment of CIN patients, regular OCT examinations can be performed to observe whether the OCT image features of the cervical tissue return to normal. If abnormal image features appear, it indicates possible recurrence, and further treatment measures need to be taken in time.

4. Future prospects of OCT technology

Aiming at the limitations of OCT technology, future improvements and developments can be carried out in the following aspects to further improve its application value in the diagnosis of female reproductive tract lesions:

(1) Technological improvement

Develop OCT equipment with high imaging depth and large field of view to improve the display ability of deep lesions and large-scale lesions. For example, by improving the light source and probe design, the imaging depth can be increased to 3–5 mm, and the scanning field of view can be expanded to more than 10 mm, reducing missed diagnosis and misdiagnosis. At the same time, further improve the imaging speed and resolution, reduce motion artifacts, and improve image quality.

(2) Standardization of diagnostic criteria

Conduct large-sample, multicenter clinical studies to establish a unified OCT image diagnostic standard and scoring system, and improve the consistency and accuracy of diagnosis. At the same time, develop a computer-aided diagnosis (CAD) system, use artificial intelligence technology to automatically analyze and identify OCT images, reduce human error, and improve diagnostic efficiency.

(3) Expansion of multi-field applications

In addition to diagnosis and monitoring, explore the application of OCT technology in the treatment of female reproductive tract lesions, such as real-time monitoring of treatment effects in minimally invasive treatments such as photodynamic therapy and laser therapy, guiding the adjustment of treatment parameters, and improving the accuracy and effectiveness of treatment [17].

5. Conclusion

As a non-invasive, real-time, and high-resolution imaging technology, OCT can clearly display the microstructure of female reproductive tract tissues, and its image features have a good correlation with histopathological features. In the diagnosis of lesions such as the cervix and endometrium, OCT technology has high diagnostic efficacy and can be used for lesion screening, diagnosis, grading, guiding biopsy, and monitoring treatment effects, with important clinical application value. Although OCT technology still has limitations such as limited imaging depth, small field of view, and ununified diagnostic criteria, with the continuous improvement of technology and in-depth research, its application prospect in the diagnosis of female reproductive tract lesions will be broader. In the future, by further optimizing equipment performance, standardizing diagnostic criteria, and expanding research scope, OCT technology is expected to become an important tool for the diagnosis and management of female reproductive tract lesions, providing better protection for women's reproductive health.

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