Application of Phase Optical Time Domain Reflectometry in Brain Tumor Surgery

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ABSTRACT

Maximum removal of brain tumors and maximum neuroprotection of the brain are the keys to brain tumor surgery. In order to solve such problems as inaccurate positioning, long positioning period, high cost in traditional brain tumor detection assistance, using a new spectral imaging technology to detect brain tumors to assist the brain surgery has become a hot topic in the current researches. This article first introduces the relevant background of the direction of brain tumor research, explains the principle and steps of filtering method based on wavelet threshold, finally studies the application effect of phase optical time domain reflectometry in brain tumor surgery, and verify its effect through experiments on mice. The experimental results show that the recognition and positioning of brain tumor can be realized effectively by using the phase optical time domain reflectometry, which can provide highly accurate and instant assistance for brain tumor surgery in the form of images. The research in this paper provides a supplement to the practical application of advanced spectroscopy in brain tumor surgery and is of great significance in guiding the scientific development of brain tumor surgery techniques.

Key Words: Phase Optical Time Domain Reflectometry, Brain Tumor, Wavelet Threshold, Experiment on Mice, Spectroscopy

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Introduction

Brain tumor is the most common malignant disease of neurosurgery, and removal of brain tumor is the most effective method to cure malignant tumor in clinic, in which the biggest difficulty lies in the positioning of tumors and the distinction between the boundaries of tumors and normal tissues. To provide guidance to brain surgeons by means of different auxiliary means is the research topic of removing brain tumors and protecting brain nerves to the greatest extent (Bondy *et al*., 2008).

Ultrasound was first applied to brain neurosurgery in 1980, to determine the location and volume of the tumor through ultrasound imaging. The emergence of real-time CT (iCT) and MRI (iMRI) improves the accuracy of brain tumor detection for brain tissue displacement. Diffusion tensor imaging (DTI) and other new magnetic resonance imaging techniques can be used to quantify the infiltration of brain tumors into the peripheral tissues (Fan *et al*., 2004). Magnetic resonance spectroscopy (MRS) and multi-voxel Bop are all complementary to magnetic resonance imaging (MRI) in the detection of brain tumors. In addition, guided fluorescence resection is a method to position brain tissue through marker technology, which effectively improves the overall resection rate of brain tumors. The above traditional methods of assisted tumor positioning have a certain effect on brain tumor surgery, but they have the disadvantages of long positioning time, side effects of chemical substances, accuracy, and long postoperative recovery cycle (Keenanand Shorter, 2004). Imaging spectroscopy, as an accurate, rapid and highly

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sensitive detection technology, has been widely used in the medical fields, deepening in surgery, pathological diagnosis, cell analysis, and other aspects (Carovac *et al*., 1972).

Phase optical time domain reflectometry is an advanced detection technique in spectral imaging, which reduces the noise in the environment and improves the signal-to-noise ratio through wavelet threshold filtering (Wang *et al*., 2015). In this paper, with mouse as animal experimental models, the phase optical time domain reflectometry is used for imaging analysis to realize spectral data analysis, and the boundary of the tumor tissue is finally presented to the surgeon in the form of images. The research in this paper is an extension of the application of phase optical time domain reflectometry in the medical field, which has a positive effect on the development of clinical brain tumor technology.

Imaging Spectroscopy and Phase Optical Time Domain Reflectometry

Imaging spectroscopy

Hyperspectral imaging technology is developed based on multi-spectral remote sensing technology, which contains spatial, image, and spectral information (Bendor *et al*., 2009). Biological tissues have low absorption and high scattering characteristics in the visible and near-infrared bands. Photon absorption mainly comes from melanin, hemoglobin and water, and tissue scattering depends on the structure characteristics of organism, such as shape, volume, density of cell and nucleus, nuclear-cytoplasmic ratio, interstitial composition, etc. (Ustin *et al*., 2004). Different substances have different reflection spectrum curves, due to their differences in absorption and scattering properties. Through extraction of narrow band spectra by processing hyperspectral imaging data, different substances can be detected or identified, and the spatial distribution of different materials can be understood (Emslie *et al*., 2008). In the research, spectral data were mainly processed by three methods, i.e., the hemoglobin spectrum curve, different scattering properties, hyperspectral and spatial dimension data.

The clinical application of imaging spectroscopy in clinical medicine has developed to a certain extent at home and abroad. The scholars from University of Tokyo have successfully applied this technique to distinguish arteries and veins of blood vessels. At the same time, foreign scholars have developed an on-line hyperspectral imaging surgical system made up of halogen lamp, PGP imaging spectrometer, scanning device, control system, data display and processing system, and conducted a spectral scanning of abdominal cavity with animals as experimental objects, which has made a certain achievement.

At present, imaging spectroscopy and the development of related instruments have provided a complete set of data acquisition and data processing software and hardware, which has been widely used in clinical blood vessels, tumor pathological diagnosis and detection. Figure 1 is a flow chart of acquisition, preprocessing and output of hyperspectral data.

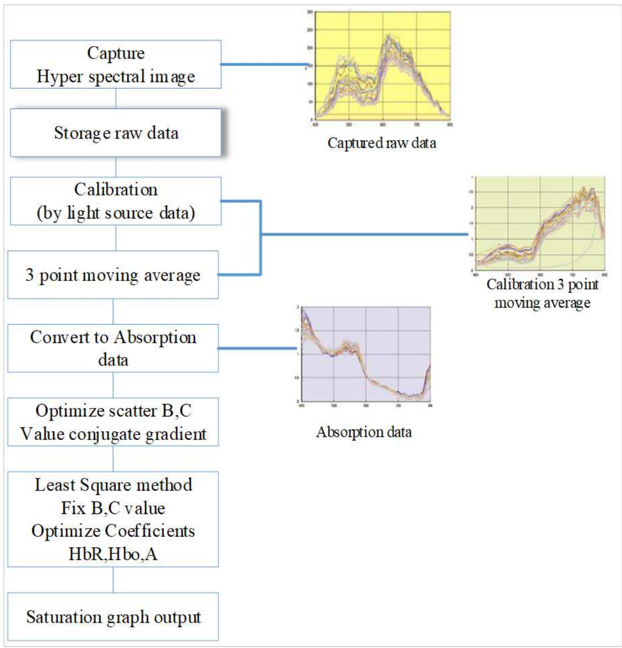

Figure 1. The hyperspectral imaging technology data processing flow

The application of imaging spectroscopy in medicine has been developed in the direction of multi-modality, shared spectrum database and surgical intelligent database, providing more and more technical support for brain tumor technology.

Phase optical time domain reflectometry

Phase optical time domain reflectometry is a new sensor imaging technology developed with the development of optical fiber technology and communication technology. Due to the influence of external interference during the detection process, the noise signal needs to be removed to achieve the maximum signal to noise ratio through different filtering methods (Zhang *et al*.,

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2001), including superposition average method, the wavelet transform and the wavelet threshold filtering method. Although the superposition average method can suppress the noise to a certain extent, but its long filtering time will affect the real-time performance of the system. The wavelet threshold method can effectively identify the interference signal and is more suitable for signal recognition based on phase optical time domain reflected light.

The wavelet transform is the inner product of x (t) of the signal to be analyzed at a different scale a after the function of a mother wavelet performs a displacement b, as shown in Formula 1:

$$WT_x(a,b) = \frac{1}{\sqrt{a}}\int_{-\infty}^{+\infty} x(t)\psi\frac{(t-b)}{a}dt \qquad (1)$$

Where, $WT_x(a,b)$, the result of wavelet transform, is a binary function about a and b. $\psi(t)$ is a mother wavelet, and the binary function changes with it. b reflects the displacement, scale factor a realizes the telescopic transformation of the mother wavelet (Madeiro *et al*., 2007). The adjustment of the position and width of the band-pass filtering intermediate frequency is achieved by the change of a. Wavelet transform has the characteristics of adaptive analysis. For the low-frequency components of the signal that needs low time resolution and high frequency resolution, a will automatically become smaller; for high-frequency signals, a will automatically become larger, and as b changes, the signals can be gradually analyzed.

Wavelet threshold filtering is to decompose the original signal with noise into different scales by wavelet, then remove the noise in different scales, reconstruct the wavelet, and finally realize the reconstruction of the signal. The flow chart is as follows:

During the denoising process of wavelet threshold, the wavelet base, threshold, number of decomposition levels, function threshold, etc. will affect the denoising effect. Selecting the most suitable wavelet base according to the experimental results is beneficial to the smoothness and denoising effect of the signal processing later. The phase optical time domain reflectometry based on wavelet threshold filtering has been applied in practice, and the time domain reflector has been gradually developed in the medical field. Based on this technique, the spectral imaging function of reflector is used to provide experimental instrument for mouse experiment.

Preparation of Phase Optical Time Domain Reflectometry Experiment

Experimental materials and instruments

There are37 healthy mice for the experiment, with 17 males and 20 females, weighing 200-260 g. The C6 neuroma cell line is used as the culture source of brain tumor cells. Other experimental materials include: 10% newborn calf serum, RPMI1640 culture powder, 25uL microsyringe, alcohol, physiological saline, chloral hydrate, sterile gauze, sterile gloves and so on. The experimental instruments mainly include VS-1300-V super clean bench, I-typed stereotaxic instrument, 307-2B typed table dental electric drill (Li *et al*., 2007; Garini *et al*., 2006).

Experimental methods

(1) Culture of brain tumor in mice

First, the mice are anesthetized in an aseptic state, and their parietal bone is fully exposed in the brain incision 5-6 minutes after they are anesthetized. A bone window with a diameter of about 0.5 cm is drilled with an electric drill without damaging the cerebral dura mater. Then a microsyringe is used to inject C6 suspension of 1×10^6/uL at a concentration of 10 uL. After the injection, the brain window is sealed with sterile bone wax, and then the incision is sutured, after washing with physiological saline (Bydlon *et al*., 2010).

(2) Mouse model of brain tumor

After C6 injection, mice return to normal diet after 2 days, most of them show abnormal excitability after 7 days, their body weight decreases and their fur began to shed after 12 days, and their eating and drinking is reduced after 14 days.

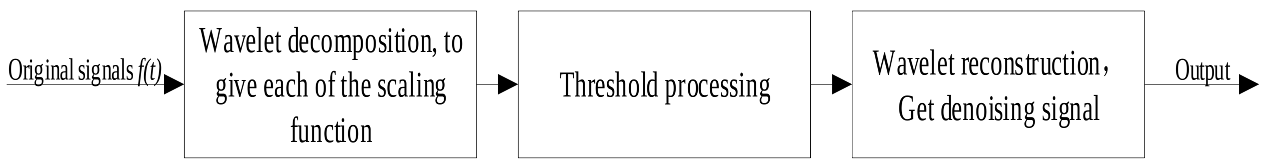

Figure 2. Wavelet domain denoising process

Through the final observation, 31 out of 37 mice have successfully developed brain tumors, with a success rate of 83%.

During the culture process, in order to avoid the diffusion of tumor cells along the needle tract, the inserting stitch of 6 mm and back stitch of 1mm are adopted. The stereotaxic instrument helps to position the needle accurately and ensure its depth. The brain tumor characteristics of the mouse model prepared by the above method are similar to those of the human brain, with high differentiation degree, abundant microvessels, and fast growing rate, which can be an ideal animal model for brain tumor surgery (Schuerger *et al*., 2003).

Phase optical imaging spectrometer

In order to meet the comprehensive requirements of qualitative, quantitative, timing and positioning analysis of brain tumor surgery, certain achievements have been made in researches on optical disk analyzers based on phase optical time domain reflectometry. The medical imaging spectrometer with navigation features is used in the experimental study of this paper. Table 1 shows the parameters of the phase optical imaging spectrometer.

Table 1. The parameters of the medical imaging spectrometer

Technical indicators	Value
Spectral range	400-900nm
Spectral resolution	Better than 5nm
Spatial distribution rate	Better than 1mm
Spectral channel number	Bigger than 100
Quantitative digits	12bit
Volume	Less than300mm×50mm×50mm
Weight	Less than3kg
Single scan time	Less than 60s

Optical system imaging adopts the same optical path design of the medical microscope. The entrance slit of the spectroscopic system and the medical microscope are in a confocal plane to ensure that the visual view field is consistent with the view field of the imaging spectrometer, so as to realize the synchronization of clinical diagnosis process and spectral data acquisition, meeting the requirement of real-time measurement.

In order to ensure the effect of spectral imaging, the experimental instrument is first tested for spectral line bending and color distortion. Spectral line bending is the standard that defines the image generated by the spectrometer and the ideal image. The color distortion is due to the fact that the difference in magnification results in inconsistent image heights of spectral images with different wavelengths. A test curve is obtained by detecting waveforms of three wavelengths, 400 nm, 600 nm and 800 nm respectively, as shown in Figure 3, where the solid line is the actual test curve and the dotted line is the ideal spectral curve. It can be seen from the figure that the spectral curve is only 0.09% and the color distortion is only 0.6%, which meets the requirements of the instrument.

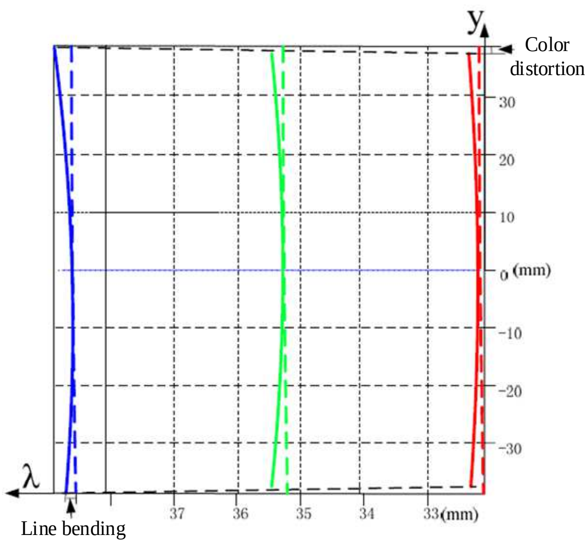

Figure 3. Spectral line bending and color distortion test curve

After the preparation of the experiment, a spectral imager based on phase optical time domain reflectometry is used to assist in the clinical experiment of mouse brain tumor resection.

Clinical Experiment of Phase Optical Time Domain Reflectance Spectrometer

The mouse models prepared in Chapter 3 are used for data acquisition and data analysis, and the application of phase light time-domain reflectance spectroscopy in positioning brain tumor is verified.

Experimental methods

The removal process of tumor cells is similar to the implantation process. After general anesthesia is performed on the mice, sterile gloves, iodine, alcohol, scalpels, hemostatic forceps and other experimental tools are prepared. The mouse is fixed on the spectrometer, and the primary incision for culturing tumor cells is selected for glass bone wax, and then the bone window is expended to fully expose brain tumor of the mouse for experiments. The experimental device after fixation is shown in Figure 4.

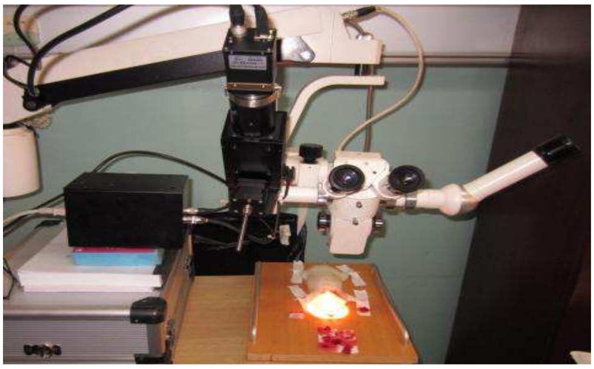

Figure 4. Spectral data acquisition experiment device

Experimental data

(1) Brain tumor imaging

The wavelet threshold method is used to preprocess the collected signals and to reduce the influence of random noise so as to improve the signal to noise ratio. Spectral imaging of brain tumors in experimental mice is shown in Figure 5.

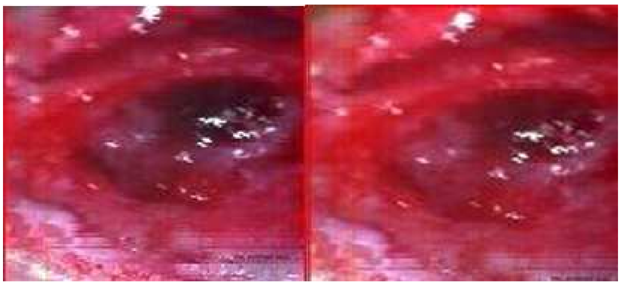

Figure 5. Brain Tumor Spectral Imaging

It can be seen from the Figure that the image quality obtained by the phase optical time domain reflectometry is high, ready for further quantitative analysis of biological tissues.

(2) Spectral image feature analysis

Based on the collected hyperspectral image of the brain tumor, the center position of the brain tumor can be clearly found in the spectral image of the 100-band brain tumor. However, the boundary between the brain and normal tissue is fuzzy, thus points A, B and C of normal tissue are selected in the center and periphery of the tumor for spectral reflectance analysis. Figure 6 shows the curve of the three-point spectral reflectance.

It can be seen from the Figure that the reflectance at points B and C is higher than that at point A. There are different degrees of difference in different wavelength ranges; some areas are more obvious, while some are not. At the center with a wavelength of 715 nm, the characteristic peak appears at point A, and the absorption peak appears at point B. The spectral reflectance curves of points A and C are similar in the range of 450-570 nm. In the follow-up pathological analysis, point A is defined as the brain tumor tissue of the mouse, and points B and C are normal brain tissue. The accuracy of spectral imaging has been verified.

Experiments have proved that spectral imaging technology based on phase optical time domain reflectometry can effectively provide spectral images of mouse brain tumors, and the differentiation of reflectance at different points can be effectively added to the division of tumor tissue boundaries, which can precisely cope with the problem of indistinguishable boundary caused by the tumor tissue growth, providing support and guidance for clinicians. Spectral imaging of phase optical time domain reflectometry not only has the characteristics of accurate positioning, but also can meet the real-time display requirements owing to the faster data processing speed of the wavelet threshold. After scanning the brain tumors, spectral imaging and reflectance can effectively achieve a win-win situation in classification speed and classification accuracy based on the position of the tumor.

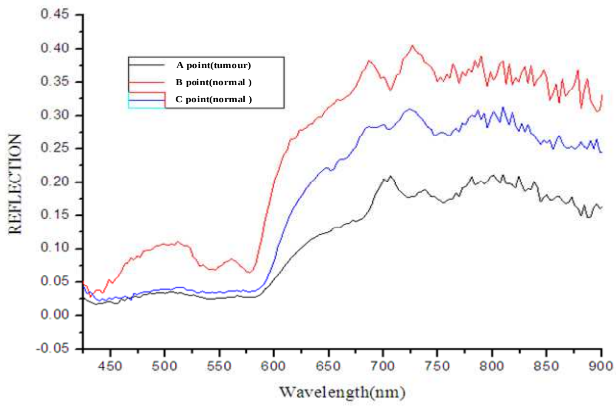

Figure 6. Three-point spectral reflectance comparison curve

Conclusions

As a kind of advanced detection technology, phase optical time domain reflectometry combines with spectroscopy to be applied to clinical medicine, which has created a new direction for the research of brain tumors. This article first introduces the development status of the brain tumor surgery and the problems to be solved, and then explains the principles of the phase optical time domain reflectometry and the wavelet threshold and the data processing flow. The integration of the two is applied to the experiment of brain tumor surgery using mice as objects. The experimental results have validated the good effect of phase optical time domain reflectometry in tumor resection. Based on the experimental research of phase optical time domain reflectometry in brain tumor surgery, the main research contents and significance of this article are as follows:

(1) It has designed a detailed experimental procedure for mouse brain tumor implantation and tumor resection and created good experimental materials for spectral imaging experiments.

(2) The experimental application of phase optical time domain reflectometry and spectroscopy in brain tumors has laid a theoretical and experimental foundation for human clinical application studies.

(3) The experimental results show that the spectral image generated by the spectral imaging technique can clearly show the brain tumor area, and the difference of reflectance can effectively help to identify the tumor tissue and the normal tissue, providing real-time and accurate guidance to the surgeon.

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