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Automatic Focusing and Robotic Scanning Mechanism for Precision Laser Ablation in Neurosurgery

Hongen Liao, *IEEE Member*, Masafumi Noguchi, Takashi Maruyama, Yoshihiro Muragaki, Hiroshi Iseki, Etsuko Kobayashi, Ichiro Sakuma, *IEEE Member*

Abstract— **We have developed an laser ablation system with an automatic focusing (AF) and robotic scanning mechanism for precision malignant gliomas resection in neurosurgery. A 5-aminolevulinic acid (5-ALA)-induced fluorescence based intra-operative tumor diagnosis technique has been incorporated into the robotic laser ablation system. The system enables an intra-operative identification of the position of a tumor with fluorescence illuminated by a laser excitation. The AF and robotic scanning mechanism assists in tracking the surface of the malignant brain tumors, and provides position information for both laser scanning in 5-ALA fluorescence identification and laser ablation in tumor resection. Experimental results showed the automatic focus device had a precision of 0.5 mm and the mechanism could track the brain surface with a movement caused by pulsation and respiration.**

Index Terms— **Medical robotics, automatic focus, laser ablation, neurosurgery, fluorescence.**

I. Introduction

In current neurosurgery, surgeon resects most tumors with an accuracy millimeters using a combination of a computer-aided navigation system with diagnostic images, such as magnetic resonance (MR), ultrasound (US), and computed tomography (CT) images, and conventional surgical instruments, such as electric cautery and suction device [1-2]. In craniotomy procedure, cerebrospinal fluid leakage and surgical interventions deform the brain tissue. In some cases, brain shift reaches to up to tens of millimeters and continuously increases during the procedure, which strongly requires an accurate and precise image-guided surgical navigation based on intraoperative imaging. Several advanced surgical tools and imaging techniques have been developed and are becoming widely used to guide surgeons in tumor resection. The combination use of open magnetic resonance imaging (MRI) devices enables the intra-operative identification of remaining tumor tissue during the operation [1]. Most malignant gliomas can be resected in microscope-based surgery with an accuracy of millimeter, however, the level achieved depends on the skill of the surgeon. Furthermore, the extent of the resection remains controversial because malignant gliomas are difficult to be completely resected using conventional surgical techniques, especially in a complex area.

5-aminolevulinic acid (5-ALA)-induced protoporphyrin IX (PpIX) fluorescence has been introduced in intra-operative identification of tumor [3]. 5-ALA elicits synthesis and induces the synthesis of PpIX as a metabolic precursor in the haem biosynthesis pathway. Since 5-ALA leads to accumulation of fluorescent porphyrins in malignant glioma tissue, the gliomas can be detected using 5-ALA-induced porphyrin fluorescence. The use of 5-ALA for intra-operative visualization of malignant glioma tissue enables greater completeness of tumor removal [4]. Studies have shown that the intra-operative use of this guiding method may also reduce the residual tumor volume and prolong progression-free survival in patients suffering malignant glioma [5].

Treatment for malignant gliomas depends on the location, cell type and grade of the malignancy. Usually, the treatment is a combined approach using surgery, radiation therapy, and chemotherapy. However, it is difficult to know the exact boundary between tumor and normal tissue, and excessive process of the normal brain tissue will damage its function. A non-contact therapeutic approach is a good way to improve ablation accuracy because conventional surgery tends to deform the brain. An example of such an approach is laser ablation with photocoagulation under the guidance of an MRI navigation system [6]. Most auto-focusing systems are used for video camera [7-8]. This approach can be also used for tracking the surface of targeted objects. However, camera image based auto-focusing sensor is time-cost due to image processing and not suitable to be used in high-speed auto-focusing mechanism.

In this study, we developed a robotically control laser ablation system for precise treatment that combined an automatic tumor identification technique to improve treatment accuracy. The boundary between tumorous and nontumorous tissue is identified using 5-ALA-induced PpIX fluorescence, and the tumor is accurately ablated with the micro laser [9]. A manipulation with high-speed automatic focusing (AF) and automatic stage mechanism was developed to guide both the excitation laser module for fluorescence identification and the laser beam onto the lesion for ablation,

H. Liao is with Department of Bioengineering, Graduate School of Engineering, and Translational Systems Biology and Medicine Initiative, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan. (e-mail: liao@bmpe.t.u-tokyo.ac.jp).

M. Noguchi, E. Kobayashi, and I. Sakuma are with Department of Precision Engineering, Graduate School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan.

Y. Muragaki, T. Maruyama, H. Iseki are with Graduate School of Medicine, Tokyo Women's Medical University, 8-1 Kawada-cho, Shinjuku-ku, Tokyo 162-8666 Japan.

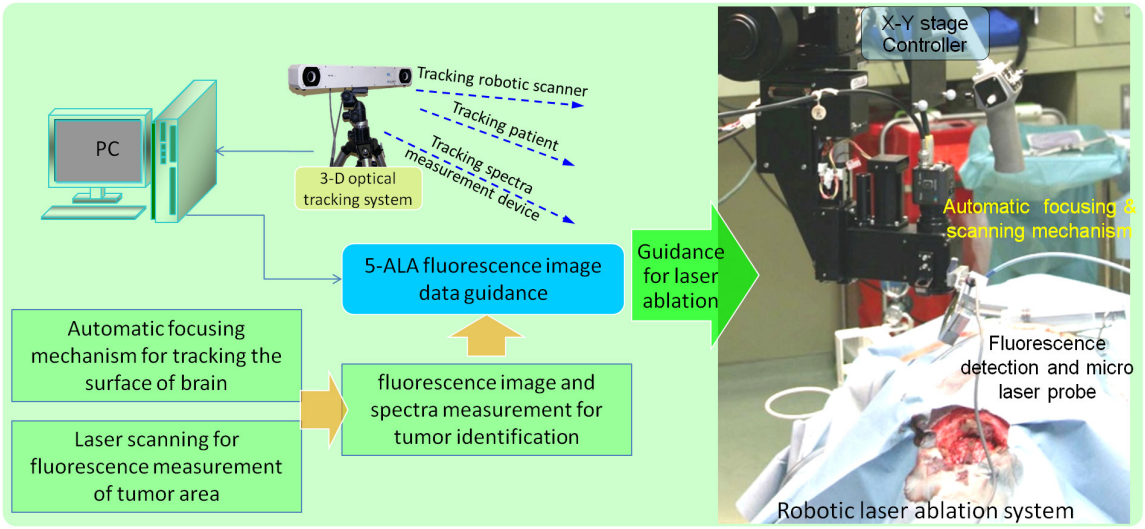


Fig. 1. Laser ablation system with automatic focus mechanism and tumor identification device

resulting in tumor ablation with a high accuracy. The automatic focusing mechanism enables the focus point to be adjusted at XYZ direction and the tumor to be completely scanned. The performance of the AF and robotic scanning system was evaluated using a set of phantom experiments, and the 5-ALA induced fluorescence guided laser ablation system was evaluated by a dissected porcine brain.

II. System and Methods

A. System configuration

Our automatic focusing and robotic scanning mechanism for precision laser ablation system includes a 5-ALA-induced PpIX fluorescence tumor detection navigation, a micro laser module, and an automatic focusing and robotic scanning mechanism. As shown in Fig. 1, the fluorescence detection probe and micro laser probe are attached to the automatic focusing system. The brain surface is tracked by an AF mechanism and an automatic XY-stage scanning mechanism. The XY-stage mechanism is positioned on a plane perpendicular to the AF axis and used to determine the spatial position of the tumor. A spectral photometer is used to collect the spectra data of the fluorescence. The spectra are collected by a spectral photometer, and the data is analyzed and used for assisting intraoperative detection of the brain tumor and its boundaries. Switching between micro-lasing and scanning with the step-driven stage is controlled by the PC. The prototype is characterized by positioning of the irradiation beam by observing the target using a charge coupled device (CCD) camera and by ablation of the lesion surface by evaporation etching. A micro laser is used to photocoagulate the brain tissue, enabling precise ablation at the boundary between the tumor and normal tissue.

The laser scanning and tumor ablation procedure includes three steps: 1) scan the tumor and measure the spectra of the fluorescence; 2) segment the analyzed fluorescence area and identify the tumors; 3) perform laser ablation on the target.

B. Automatic Focusing Mechanism

Requirements for 5-ALA induced fluorescence guided laser ablation treatment in neurosurgery are as follows: 1) The system enables 5-ALA-induced fluorescence measurement and spectra analysis; 2) The auto focusing and surface scanning device have a precision of sub millimeter; 3) The AF axis works in conjunction with XY stage; 4) Both surgical area and laser ablation can be viewed from a video camera; 5) Viewing area is more than 15 mm in diameter. 6) The device can be mounted on a surgical microscopy device. The overview of the automatic focusing mechanism and robotic scanning mechanism are shown in Fig. 2. Both the fluorescence detection probe and the micro laser probe have each working distance, which require an AF mechanism, constantly maintaining the distance from the target surface.

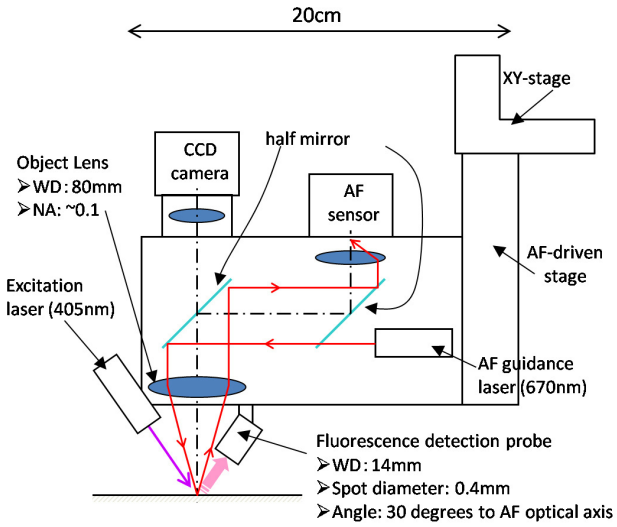


Fig. 2. Automatic focusing and scanning mechanisms.

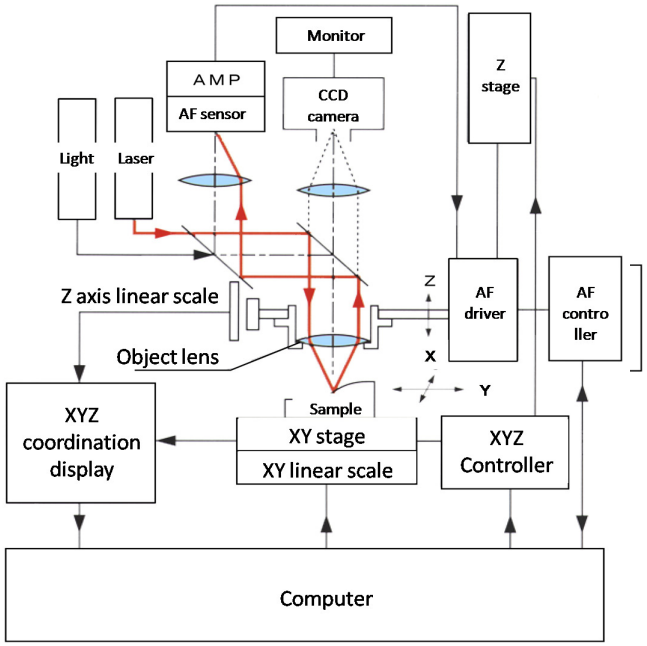


Fig. 3. System configuration of AF and XY scanning.

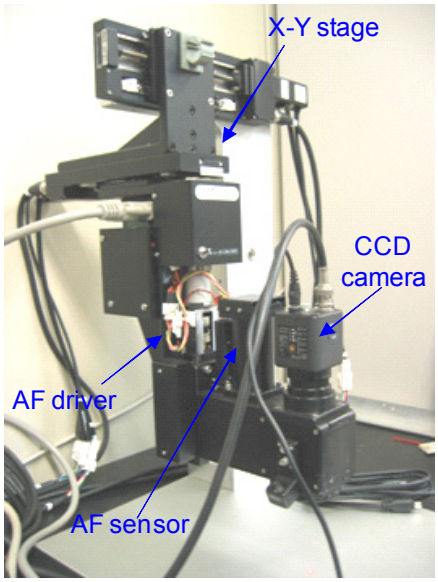


Fig. 4. Prototype of laser ablation device with automatic focus mechanism and tumor identification instrument.

The AF system is designed based on the three-dimensional measurement system. In this system, position measurement is performed using a confocal optical mechanism using a guide laser and a split photodiode, enabling a focusing with an accuracy of micrometers. Two half mirrors are integrated into the optical mechanism: one is used for fusion of AF senor and AF guidance laser; the other is used for fusion of CCD camera image viewing and AF scanning. The surgical viewing field is observed by a CCD camera coaxially incorporated in the AF system. This system is coupled with 2-axial (XY) automatic stepping drive stage and can make a robotic scanning on the surface of the brain.

The mechanism and control for the AF measurement system is shown in Fig. 3. The object lens is mounted on a linear scale, which can be moved around the Z-axis. The guidance laser is carried out through an offset lens in optic axis. A reflected laser light is made to carry out image formation on a two division type photo-diode (AF sensor). The laser spot image comes in the center of AF sensor when it is adjusted to the focusing point, while the position of spot is displaced right and left at the time of defocusing, which require a feedback for the differential output of a sensor to AF drive mechanism. Moreover, the CCD camera optical system is included in the coaxial system, and the object can be observed due to the co-focus. In addition to the AF system, the mechanism also includes a manual control function. A prototype of laser ablation device with automatic focus mechanism and tumor identification instrument is shown in Fig. 4.

C. Surface Scanning Mechanism Scanning Procedure

Surface scanning mechanism is controlled by the XY-stage. First, the operator defines the measurement area in the CCD camera view of the AF system with guidance from surgical navigation system. The area is sectioned into a grid pattern with a grid interval of 0.2 mm. Measurement is performed at the central point in each grid square using step scanning. As the measurement at each point requires more than a few hundred milliseconds for integration of the spectral photometer, the measurement speed is about a few second for a square of mm^2. Second, the system segments the fluorescent area and saves the coordination data of the grid. The fluorescence intensity is calculated from the spectral data, and binarization is performed using Otsu's thresholding method [10]. After the system finishes identifying the fluorescence area relative to the tumor, the micro ablation laser uses surface scanning and automatic focusing mechanism to ablate the area. The ablation speed is 1 mm/s, and the pitch is 0.1 mm.

D. 5-ALA-induced Fluorescence-guided Micro Laser Ablation

During fluorescence detection, the patient's tumor is illuminated by a guide laser diode (405 ± 5 nm; Digital Stream Co., Ltd., Kanagawa) connected to an incoherent light system emitting blue-violet light. The laser beam diameter is 1 mm; the output is set to 0.7 mW to reduce photo bleaching of surrounding areas. The fluorescence is collected by a detection probe and guided into a spectrometer through an optical multi-mode fiber and then into a PC for spectral analysis [9]. The spectra of brain tissues were acquired in vivo, and promising optical filters were selected through simulation using these spectra. The regions in which the fluorescent properties were uniform were identified by analyzing the image intensity of the fluorescence.

Since light with a wavelength around 3 μm is strongly absorbed by water, the laser is effective only on the surface of living tissue. Furthermore, the laser can perform a precise

ablation at low output (0.5 W or less). We choose an infrared continuous-wave laser with a wavelength of 2.8 μm. The beam is output by a microchip solid-state laser on the tip of the microlaser probe. The pumping light source for the laser is a near-infrared laser diode with a wavelength of 970 nm, and the light is guided through a quartz optical fiber to the laser probe. A prototype of laser ablation device with automatic focus mechanism and tumor identification instrument is manufactured. The vectors of the fluorescence detection probe, the ablation laser probe, and the excitation laser module are intersected into the position of the focus point of AF system.

III. Experimental Setup and Results

We combined 5-ALA-induced PpIX fluorescence into the tumor detection system, and integrated the system with a micro ablation laser module for treatment. The performance of the AF and the robotic scanning system was evaluated using a set of combination experiments using a biomedical stimulant material (phantoms) and a porcine brain. The experiments include repetition test of the performance of the AF system, measurement range evaluation, pulsation and respiration tracking experiment

A. Repetition Evaluation of AF Mechanism

A repetition test for evaluation of the performance of the AF mechanism was implemented. Our focusing lens includes two types: 1-time zoom lens and the 0.5-time zoom lens. We set the offset to 2.5 mm, and tested the offset of each up and down direction around the focus position. The position of the object lens in the state where AF settled down was measured by using a laser displacement meter (LB-02, LB-62, resolution: 2μm, Keyence Co., Ltd., Japan). Measurement was respectively performed 10 times. Table.1 shows the average and standard deviation in the position of the object lens. For the 1-time zoom lens and the 0.5-time zoom lens, the gap of 9 μm and 15 μm were measured, respectively. Standard deviation was 5 μm for 0.5-time lens from up, and it was 2 μm in the case of others. The total standard deviation from the up and down direction was 5μm and 8μm for the 1-time zoom lens and 0.5-time zoom lens, respectively.

B. Focusing Range Measurement

We evaluated the focusing range of the AF system by measuring how much the defocusing of the AF system can be shifted from its focal position (Fig. 5). The focus plane of the AF device was moved from a horizontal plane to an inclination plane. The measured object is set with an inclination plane of 75 degree. We test the device from four directions, including forward, backward, left and right shift. Since the guide laser of AF is prepared and irradiated to the optic axis to the forward direction, it is used to observe the difference in the inclination plane. We limit the movement range of defocus to 12 mm and set the interval to 0.5 mm for each step. The results for zoom lens of 1-time and 0.5-time were listed in Table 2. Both lenses have a focusing range of more than 12 mm in horizontal direction. For the inclination test, the lens with 0.5 time zoom showed a better focusing range then that with 1-time zoom. The lens with 1-time zoom only has a focusing range of 4.5 mm~5.0 mm when the inclination is higher in forward direction.

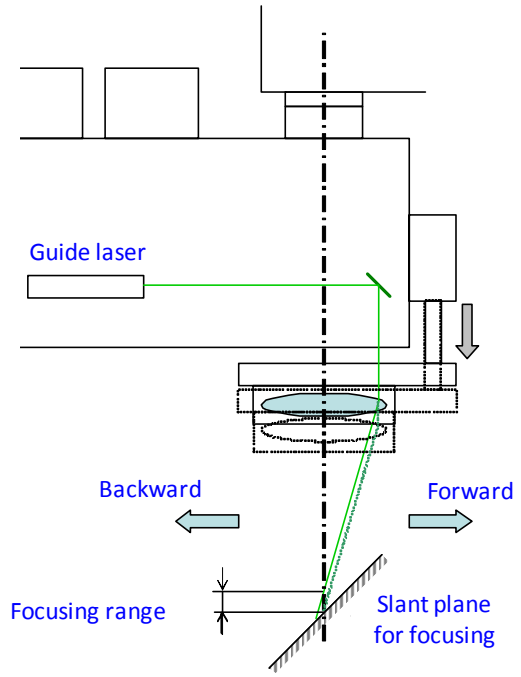


Fig. 5. Focusing range measurement from different directions using a slant plane with inclination of 75 degree.

Table 1. Repetition test for auto focusing mechanism.

Lens	Direction	Avg.(μm)	S.D. (μm)	Total (μm)
1-time	Up	--	2	5
	Down	-9	2	
0.5-time	Up	--	5	8
	Down	-15	2	

Table 2. Measurement of auto focusing range using a slant plane.

		Focusing range (mm)	
Lens	Inclination	up	Down
1-time	Horizontal	12+	12+
	Higher in forward direction	4.5	5.0
	Higher in backward direction	12+	12+
	Higher in left direction	10.5	11.5
	Higher in right direction	10.5	11.5
0.5-time	Horizontal	12+	12+
	Higher in forward direction	12+	12+
	Higher in backward direction	12+	12+
	Higher in left direction	12+	12+
	Higher in right direction	12+	12+

C. *Pulsation and respiration tracking experiment*

The pulsation and respiration of the patient may cause movement of brain. During the treatment in neurosurgery, the periodical movement of the tissue can be observed due to the change of the pressure caused by the pulsation of the vessel and respiration. To evaluate the system on following each cycle of the movement, we used a motor-controlled phantom to simulate the pulsation and the respiration of human being. A test object was connected by a cam with its axis pass in the shifted position from a circular center, so that the movement of the object became continuation in a sine wave (Fig.6). We set the amplitude for pulsation as 0.5 mm with two frequencies of 1 Hz and 1.5 Hz, which can be achieved by choosing the minor and major axis of the cam. The amplitude for respiration was 2 mm and the frequency was 0.25 Hz. We used a laser displacement meter (LB-02, LB-62, Keyence Co., Ltd., Japan) to measure the movement of the object. Figure 7 shows one of the experimental results for pulsation simulation test (with a frequency of 1 Hz, observed by 0.5-time lens). Figure 8 shows one of the experimental results for respiration evaluation (a respiration frequency of 0.25 Hz, observed by 1-time zoom lens).

The tracking results showed a latency of the displacements between the measured and the lens. The latency was too small to affect the accuracy of the laser ablation.

D. *Brain Phantom Test and in-vivo Animal Implementation*

We used a brain phantom to validate the feasibility of the AF and robotic scanning system (Fig.9 (a)). Experiments showed the system could track the surface of the brain automatically, and the tacking procedure could be conducted in real-time.

An in-vivo brain tumor tracking and laser ablation was also performed (Fig.9 (b) and (c)). The scanning was done using a laser irradiation power of 0.36 W and a beam spot diameter of 0.16 mm at 3 mm/s for on the outline and at 8 mm/s inside the outline. With either velocity, the surface of the brain was laser ablated uniformly and shallowly, and the surface was laser scanned at 0.1 mm spacing. The laser ablation was performed after obtaining the fluorescence data of the tumor. Figure 9 (b) shows an image of the tissue taken before laser ablation, and (c) shows an image taken after the ablation. During the laser ablation, a guidance laser for identifying the focus point was integrated into the CCD image.

IV. Discussion and Conclusion

We developed an automatic focusing and robotic scanning mechanism for precision laser ablation in neurosurgery. The system has automatic focusing and a robotic scanning mechanism and was designed for laser treatment. The ablation is performed using fluorescence information with spatially robotic position control.

With our current system, the entire tumor is first scanned and the tumor area is indentified. Laser ablation is performed after fluorescence spectral analysis. Since deformation and movement of the brain tissue occurs during the procedure, the auto focusing and scanning system was designed for tracking the movement. Our future works will combine the spectral analysis and laser ablation to enable diagnosis and therapy to be performed simultaneously.

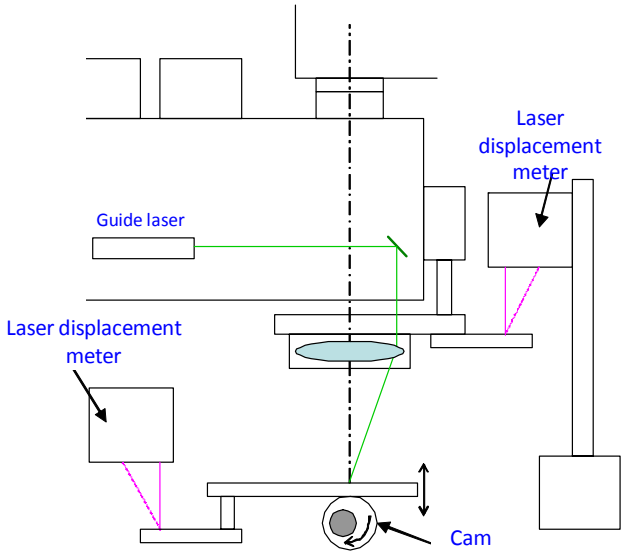


Fig. 6. Pulsation and respiration tracking experiment

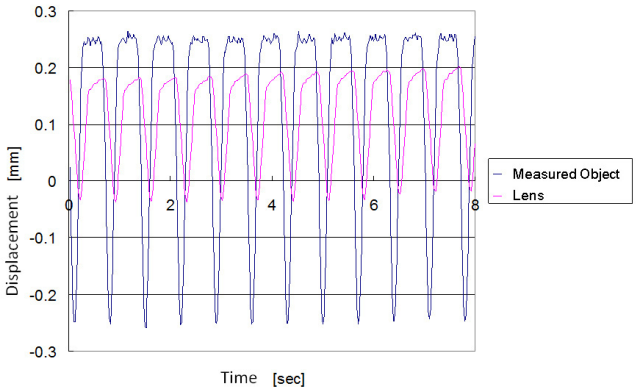


Fig. 7. Tracking results of AF system with a pulsation simulation test of a pulsation frequency of 1 Hz, observed by 0.5-time zoom lens.

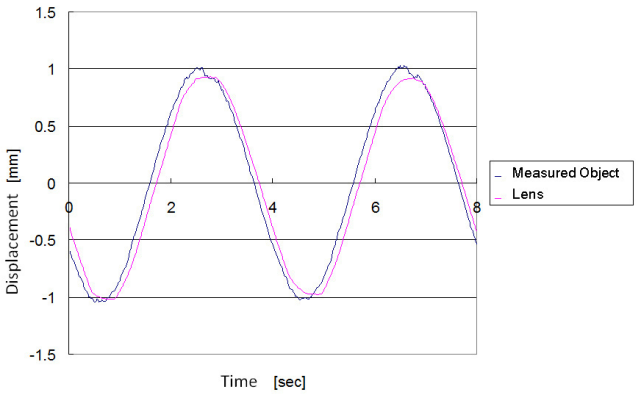
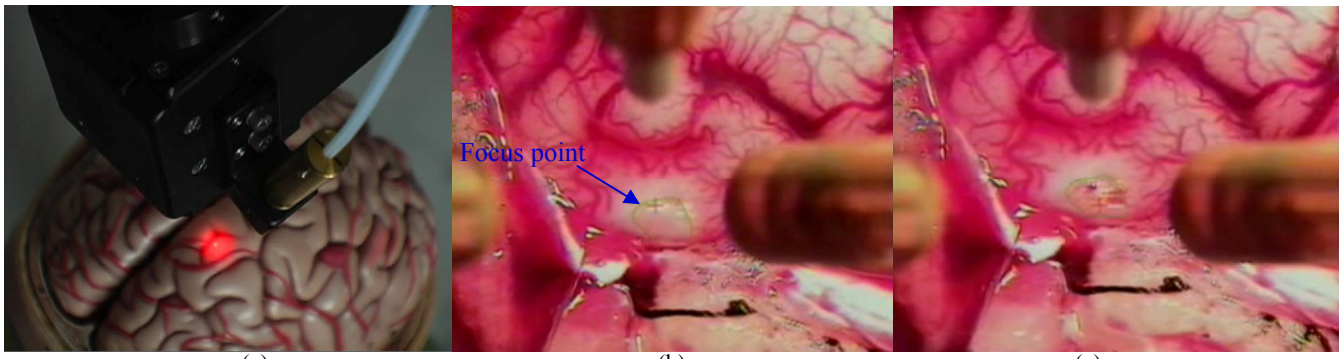


Fig. 8. Tracking results of AF system with a respiration simulation test of a respiration frequency of 0.25 Hz, observed by 1-time zoom lens.



(a) (b) (c)

Fig. 10. Phantom test and in-vivo laser ablation experiment: (a) brain phantom to validate the feasibility of the AF and robotic scanning system; (b) and (c) in-vivo laser ablation trial with automatic focusing and robotic scanning mechanisms. (b) Before the laser ablation; (c) During the laser ablation.

Compared with discrimination using a camera and optical filters, discrimination using spectral analysis is affected less by the reflectance properties of the targets, which depend on the scattering factor and the target's geometry. It is more effective for brain tissue, which has much undulation and is composed of several kinds of tissue with different optical properties.

Although the latency would not affect the accuracy of the laser ablation, improvement of the auto-focusing speed is still required to track an active object. The AF sensor and the AF driver can be made more sensitively and more reactively.

The integration system combines tumor detection using 5-ALA-induced PpIX fluorescence and precise ablation using a micro-laser with an automatic focusing and robotic mechanism for scanning the brain surface. In this study, ablation is performed using fluorescent information and AF / robotic scanning mechanisms for position control. The area is sectioned into a grid pattern and measurement is performed at the central point in each square using scanning. A target area is selectively irradiated with the micro ablation laser. The experimental results showed that the system could track the surface of the tumor automatically and the ablation system could be automatically guided by the 5-ALA-induced fluorescence guided system.

V. Acknowledgment

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