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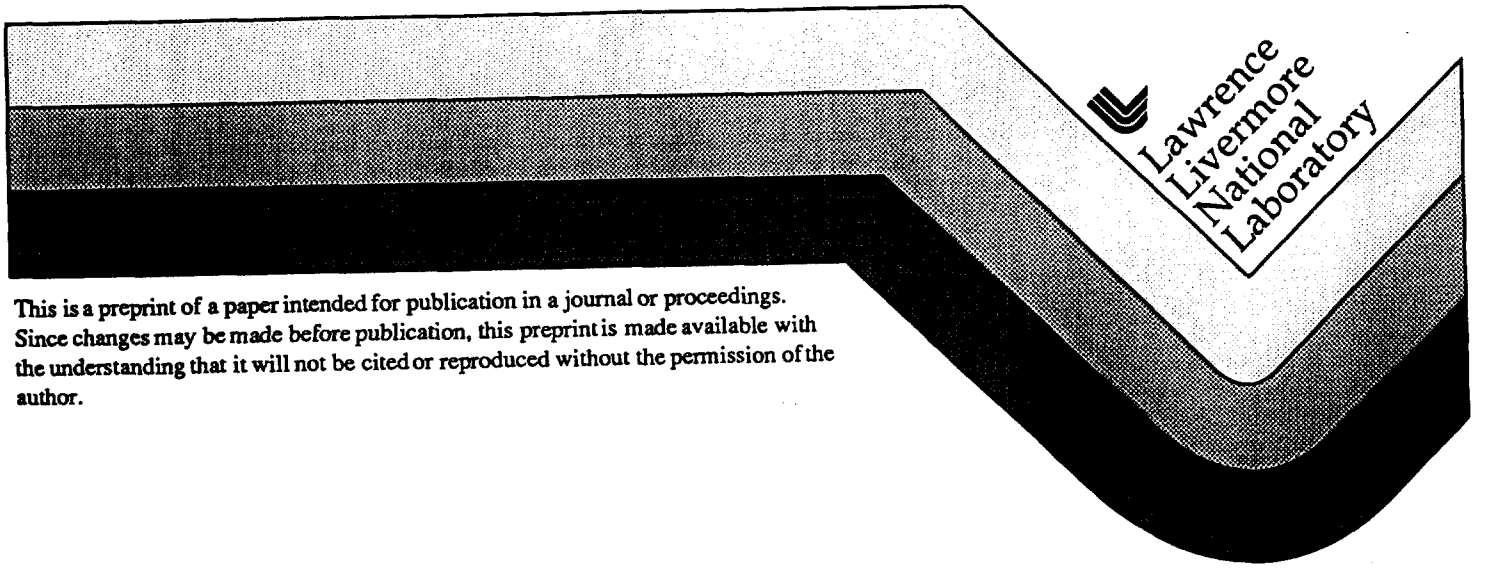

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Optical Feedback Signal for Ultrashort Laser Pulse Ablation of Tissue

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Abstract

An optical feedback system for controlled precise tissue ablation is discussed. Our setup includes an ultrashort pulse laser (USPL), and a diagnostic system utilizing analysis of either tissue fluorescence or plasma emission luminescence. Current research is focused on discriminating hard and soft tissues such as bone and spinal cord during spinal surgery using either technique. Our experimental observations exhibit considerable spectroscopic contrast between hard and soft tissue, and both techniques offer promise for a practical diagnostic system.

Keywords

Ultrashort pulse laser, tissue ablation, plasma luminescence, tissue fluorescence, optical feedback system

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Introduction

Since the first use of lasers in the medical field, considerable effort has been made to replace conventional surgical tools with lasers. To be a practical alternative, clinical lasers have to be easy to control, safe, and effective in cutting and removing tissue with limited collateral damage. Ultrashort pulse lasers (< 1 psec) are of significant interest to clinicians and researchers due to precise and highly effective ablation capabilities (~1 μm/pulse) accompanied by minimal collateral thermal/mechanical damage [1]-[5]. Thermal damage is minimized for two reasons. First, USPL has a high ablation efficiency, i.e. less energy is required per pulse compared to the nanosecond pulses. For example, the ablation threshold is less than 1 J/cm^2 for 0.35 psec pulses vs. 20 J/cm^2 for 1 ns pulses for tooth ablation [2]. Second, most of the energy that is deposited is taken away by the expanding plasma and ejected meterial. Mechanical damage is also not significant since due to the above reason and the short deposition time, the shockwave into the material experiences a rapid decay [6]. In Fig. 1, we show the results of drilling a human tooth with 350 fsec laser pulses [7]. The smooth ablation surface and absence of mechanical cracking is characteristic of USPL ablation. These characteristics of USPL tissue ablation led to its use in ophthalmology [8]-[11] and preliminary dental trials [4], [12]-[13] where precise ablation is needed. Additionally, it has potential for use in the areas of midear bone ablation, bone incision, microperforation etc. [2]. The present work focuses on the clinical application of bone ablation for spinal surgery.

An USPL operating at 1 kHz will remove on the order of 1 mm of material per second. This makes an automatic feedback and control system necessary for microsurgical applications such as spinal surgery or angioplasty to prevent accidental ablation of surrounding tissue. Fluorescence [14], [15] and plasma luminescence [16]-[18] have been used for detection of calcified atherosclerotic plague with high sensitivity in angioplasty. A major drawback of using fluorescence spectroscopy is interference with blood clots and need for additional diagnostic light source [14], [17]. Plasma luminescence during pulsed

laser ablation leads to a characteristic spectrum determined by tissue composition. A major disadvantage for longer pulse ablation system in using luminescence spectra in tissue diagnosis is that it requires an ablative laser fluence which might not be well-suited since it causes significant thermal/mechanical damage to the surrounding tissue. The present research is focused on fluorescence and luminescence spectral analysis to distinguish bone from soft tissue. We test the principle of using such spectra in real-time feedback signal during spinal surgery where the spinal cord must remain undamaged while bone is rapidly removed or drilled.

Methods and Results

A fresh piece of porcine spine was cut either axially or transversely to expose the spinal cord and bone cross sections. The cross sections were sprayed with saline occasionally to prevent dehydration. These tissues were irradiated by UV light generated by a tunable Optical Parametric Oscillator laser (Spectra Physics, Model # 730) and the corresponding fluorescence was measured using a scanning double grating spectrometer with a photomultiplier tube (PMT). The PMT signal is gated and integrated during the fluorescence lifetime and multiple signals were accumulated at each wavelength. The whole sequence was computer controlled.

The excitation-emission matrix (EEM) measurement on bone and spinal cord was performed in the excitation range of 300 to 500 nm. It was found that an excitation wavelength of 325 nm generates the most distinct spectra between the two types of tissue. Fig 2. shows the fluorescence spectra for the two tissues excited at 325 nm. Both spectra were calibrated for the grating efficiency over wavelengths. The spinal cord displays fluorescence peaks at 395 nm and 465 nm while the bone fluorescence has a featureless spectrum with a wide plateau between 390 nm and 420 nm. In this figure, the total magnitude of fluorescence is stronger with spinal cord than with bone. However, this overall magnitude can change dramatically depending upon slight changes in coupling

efficiency between fluorescence source (tissue surface) and the detector. In a similar measurement not shown in this paper, the fluorescence intensity of bone was sometimes quite comparable with that of spinal cord. This observation implies that an absolute fluorescence intensity measurement can be misleading. It is desirable to have a different optical signature which will give us a more reliable contrast between the two tissues independent of the fluorescence intensity. One solution is to take the ratio of intensities at two different appropriately chosen wavelengths. Fig. 3 shows the fluorescence ratio between wavelengths of 395 nm and 495 nm for the two tissue types. The ratio is 0.79 for bone and 1.75 for spinal cord. Therefore, the fluorescence contrast ratio between the two tissues is about 2.2 and a two channel system with appropriate filters could be used for active laser control.

Our ultrashort pulse laser ablation system is equipped with four separate lasers. An 82 MHz Ti-Sapphire actively mode-locked laser (Spectra Physics, Model # 3960) is pumped by a 5 W, frequency doubled Nd:YAG laser (Spectra Physics Model : Millenia) running at 532 nm. The mode-locked laser pulse has duration of 100 fsec. Its power is, in turn, amplified by another Ti-Sapphire regenerative amplifier (Positive Light, Model : Spitfire) through a chirped pulse amplification (CPA) process. This amplifier is pumped by a 10 W, 527 nm Nd:YLF laser (Positive Light, Model : Merlyn). The final pulse duration is about 150 fsec running at 1 kHz and its amplified energy is more than 1 mJ/pulse.

These 150 fsec pulses were focused onto the tissue to generate the plasma luminescence. The luminescence signal was collected by a 1 mm diameter optical fiber and was delivered to the spectrometer and charged coupled device (CCD) camera. The source light was normally incident onto the tissue and the fiber was placed 20° from the normal direction and 5 mm away from the tissue surface. The source light shutter and CCD shutter were controlled by a pulse generator.

Typical plasma luminescence signals for bone and spinal cord are shown in Fig. 4. The tissues were irradiated by 150 fsec, 1 mJ pulses running at 1 kHz and the luminescence was recorded by spectrometer and CCD for 1 sec. The bone luminescence spectrum displays many strong Ca lines with some Na, Mg, and P lines. The strongest peak appears near 615 nm where several Ca lines are close together. On the other hand, the spinal cord luminescence spectrum contains a Na line at 589 nm with no noticeably strong lines elsewhere. For a similar reason as in the fluorescence case, it is desirable to take an intensity ratio between two wavelengths to discriminate between the tissue types. The intensity ratio at 615 nm and 575 nm is approximately 6 for bone and 1.5 for spinal cord thus producing a contrast ratio of 4 for these tissues.

It remains to be shown that one can discriminate bone and spinal cord over a wide intensity range of luminescence. Fig. 5 shows the temporal changes of the averaged luminescence signal for every 0.1 second since the onset of the laser irradiation. Again, the laser was running at 1 kHz. Therefore, each datum corresponds to the averaged luminescence over 100 shots. The bone luminescence diminishes exponentially with time as the ablation front propagates through the tissue. This observation presumably results from the decreasing amount of material ejected as the laser drills a hole into the tissue as shown in Fig. 1. Furthermore, the distance between the ablation front and the detector becomes larger as the hole becomes deeper. However, as shown in Fig. 6, the ratio between two wavelengths (615 and 575 nm) is still stable for bone and spinal cord regardless of the intensity of luminescence. The spinal cord luminescence does not seem to decrease with time supposedly because this soft tissue moves due to shockwave during ablation resulting in multiple ablation spot. The ratio for bone is 4.8 which is about 3.4 times stronger that that of spinal cord which is only 1.4.

Discussion

One of the major advantages of using fluorescence spectra in feedback control is that one can determine the tissue type before ablating the tissue. On the other hand, for luminescence feedback it is necessary to ablate a small amount of tissue. However, the luminescence spectroscopy technique does not need an additional light source which is required for fluorescence analysis. The requirement of inducing ablation to perform luminescence spectroscopy can probably be acceptable since most tissues can tolerate microns of ablation. Therefore, if the tissue can be discriminated within approximately 10 microns (i.e. about 10 pulses), serious damage to the tissue can be avoided.

We have shown that both tissue fluorescence and luminescence spectra can be effectively used to discriminate between hard and soft tissues. The contrast ratio between bone and spinal cord was 2.2 with the fluorescence technique and 3.4 - 4 with the plasma luminescence technique. Ultimately, by setting an appropriate threshold ratio between bone and spinal cord signals, we can create an effective on/off feedback control.

From Fig. 4, one might conclude that overall intensity of luminescence would provide a better signature to discriminate the tissue types since the intensity of bone luminescence is much greater that that of spinal cord luminescence. However, as demonstrated in Fig. 5, luminescence intensity decreases exponentially as ablation proceeds and after 0.5 second, the overall bone luminescence intensity becomes comparable with the spinal cord intensity (Fig. 5). Additionally, the luminescence signal collection efficiency can vary significantly depending upon the detector position during a clinical procedure. Therefore, a relative measurement is more reliable. By taking the ratio between two different wavelengths, a highly stable signal is found despite variations in the detection efficiency.

We found that plasma luminescence spectroscopy generates better contrast between bone and spinal cord. Furthermore, it was shown that luminescence can be measured very consistently over a wide range of the absolute intensity. With fluorescence, it might be

difficult to deliver the excitation beam and collect a good fluorescence signal from the ablation front because the hole diameter decreases as ablation proceeds as shown in Fig. 1. Luminescence spectroscopy does not have this problem because the luminescence is collected from the ejected plume. Therefore, a feedback system utilizing luminescence appears preferable.

Summary and Future Studies

Tissue fluorescence and plasma luminescence of bone and spinal cord were investigated as the basis for a real-time optical feedback system. The intensity ratio between two different wavelengths produces a contrast ratio of 2.2 with fluorescence and 3.4 with luminescence for hard and soft tissues. The luminescence spectral analysis is preferable because it generates a better contrast for the two tissue types, and produces more stable results regardless of luminescence intensity.

A real-time controlled ultrashort pulse laser ablation system is now being assembled and an appropriate delivery system is also under investigation.

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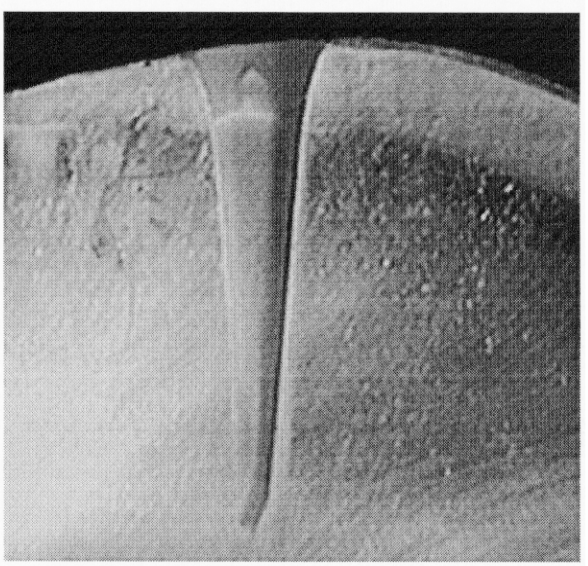

Fig. 1. Cross section of a conical hole drilled in tooth by 350 fsec laser system. With no thermal shock, there is no collateral damage to adjacent tissue.

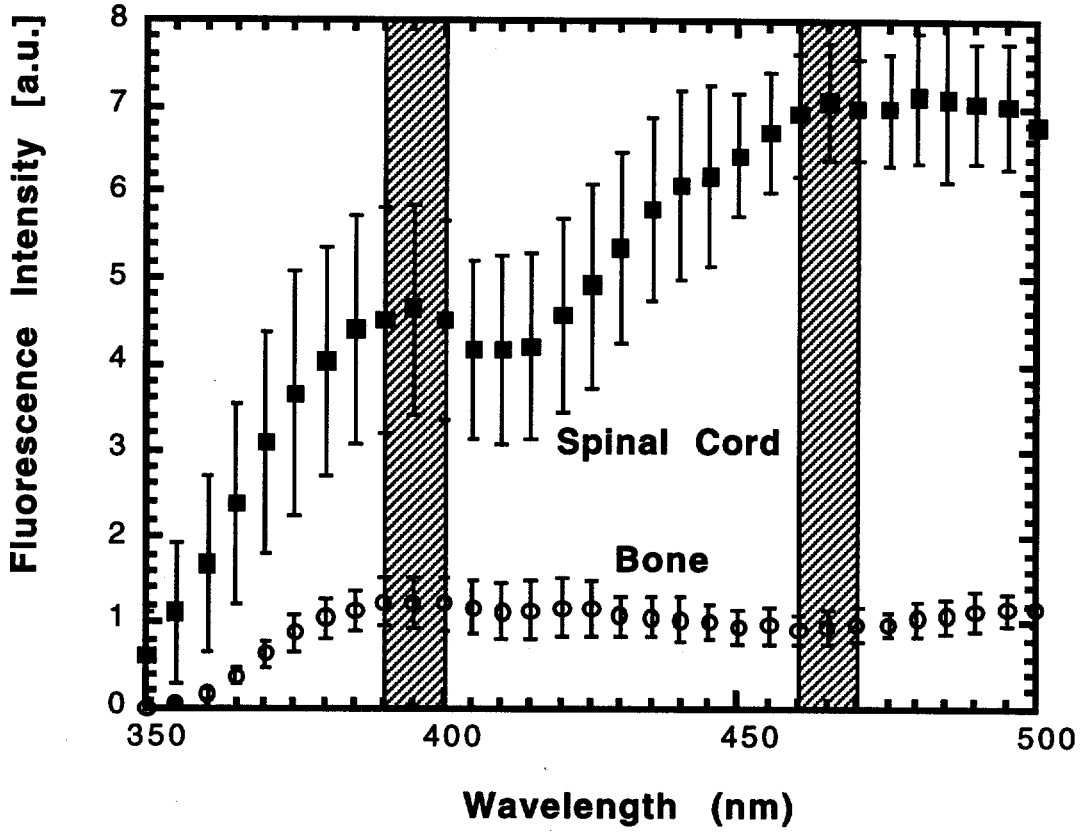

Fig. 2. Fluorescence spectra for bone and spinal cord. The spinal cord displays fluorescence peaks at 395 nm and 465 nm while the bone fluorescence has relatively monotonous spectrum with wide plateau between 390 nm and 420 nm.

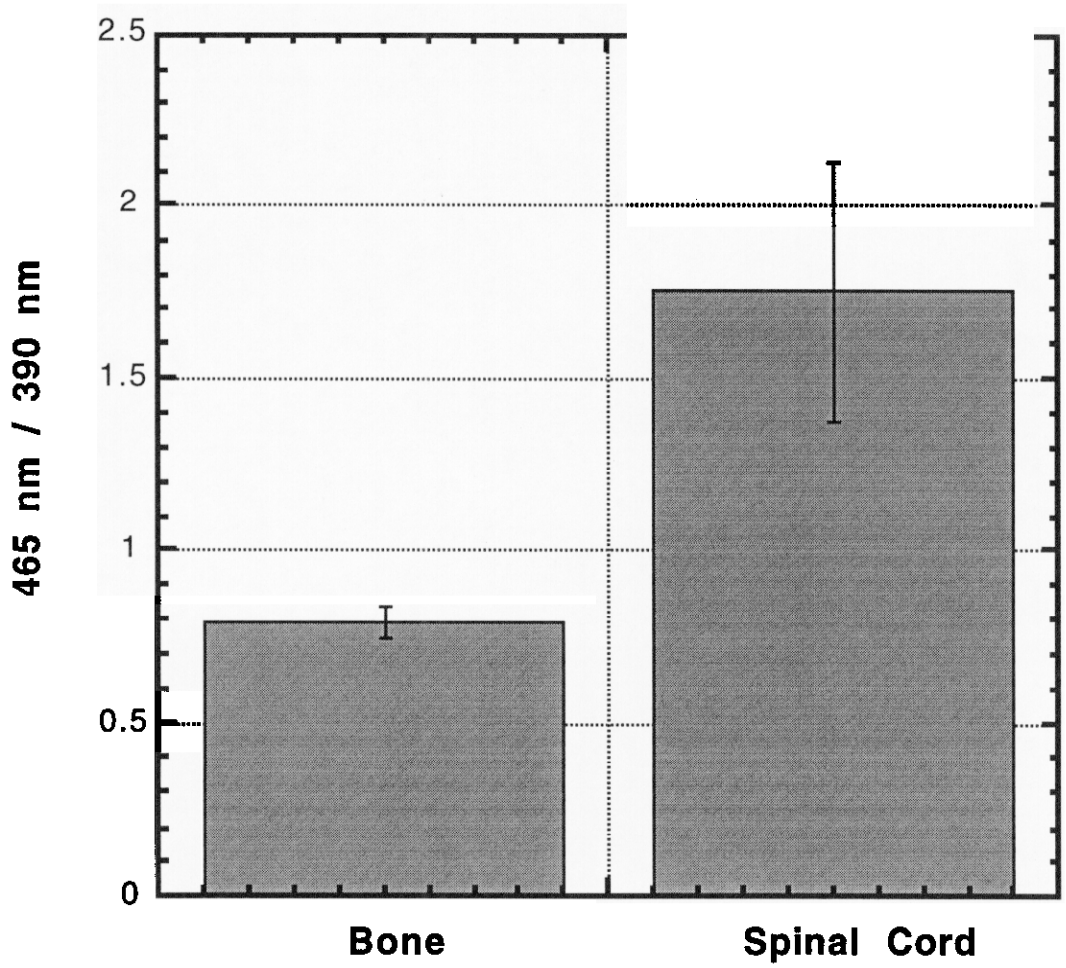

Fig. 3. Ratio 465 nm / 390 nm is 0.79 for bone and 1.75 for spinal cord. Laser will be automatically turned off if the ratio for bone rises above a threshold of 1 - 1.3.

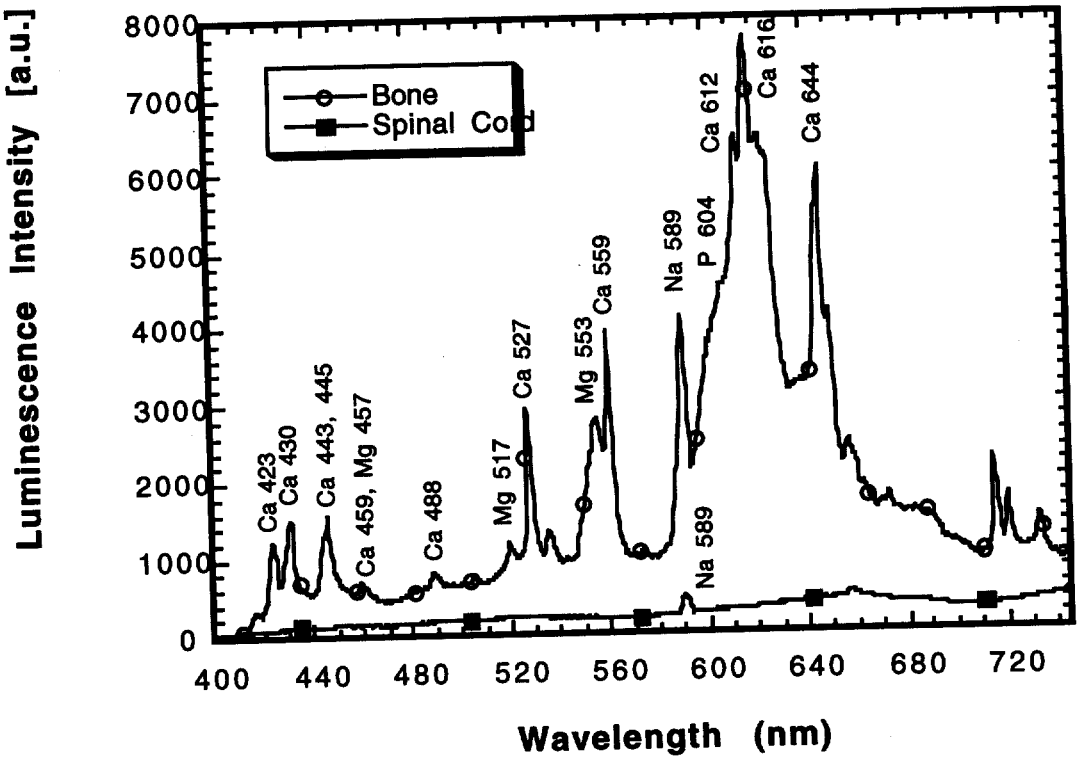

Fig. 4. Plasma luminescence spectra of bone and spinal cord. Strong Ca lines are shown in the visible range. By measuring S_{615}/S_{575}, we will be able to discriminate between bone and spinal cord.

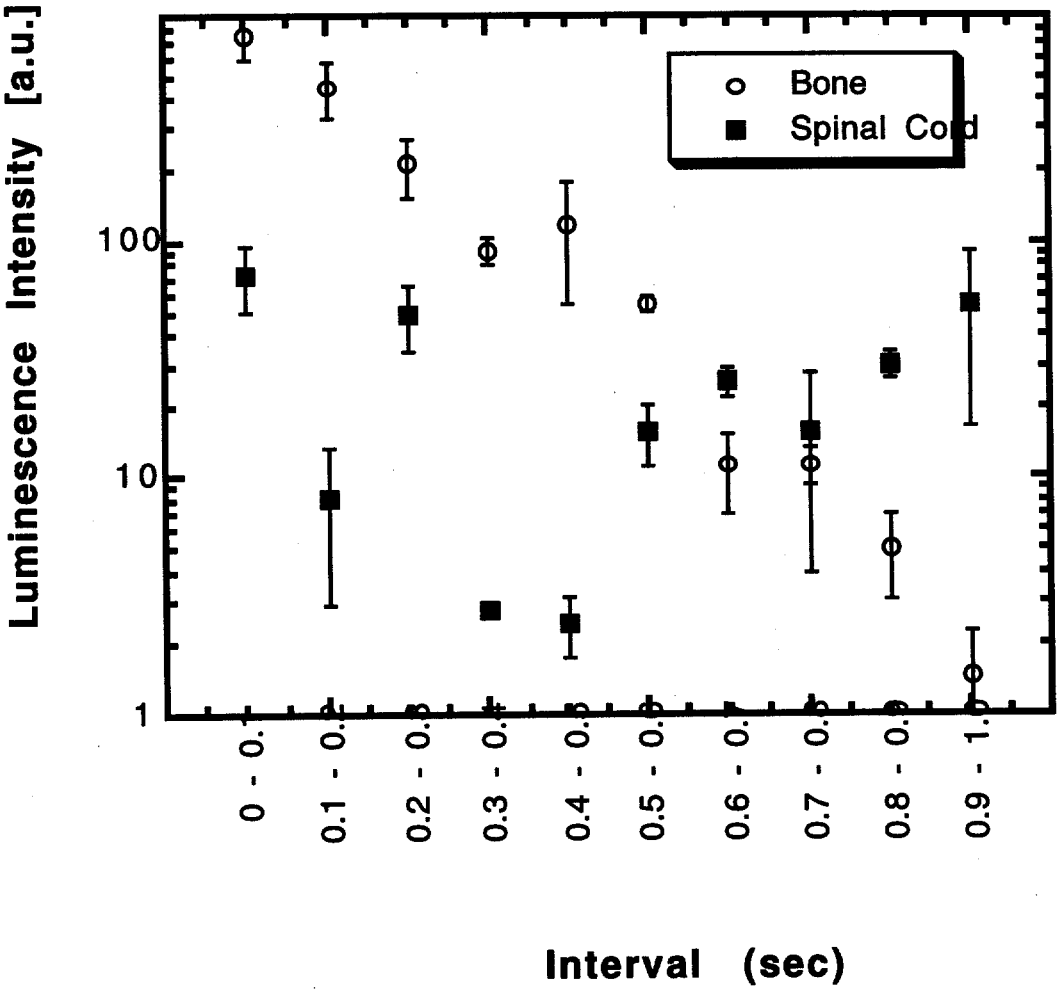

Fig. 5. While Drilling a Hole, the Luminescence Signal Becomes Weaker because Less material is ablated as the hole becomes deeper. Each value includes averaged luminescence signal over 100 shots (Total # of shots = 1000). Rep rate = 1 kHz.

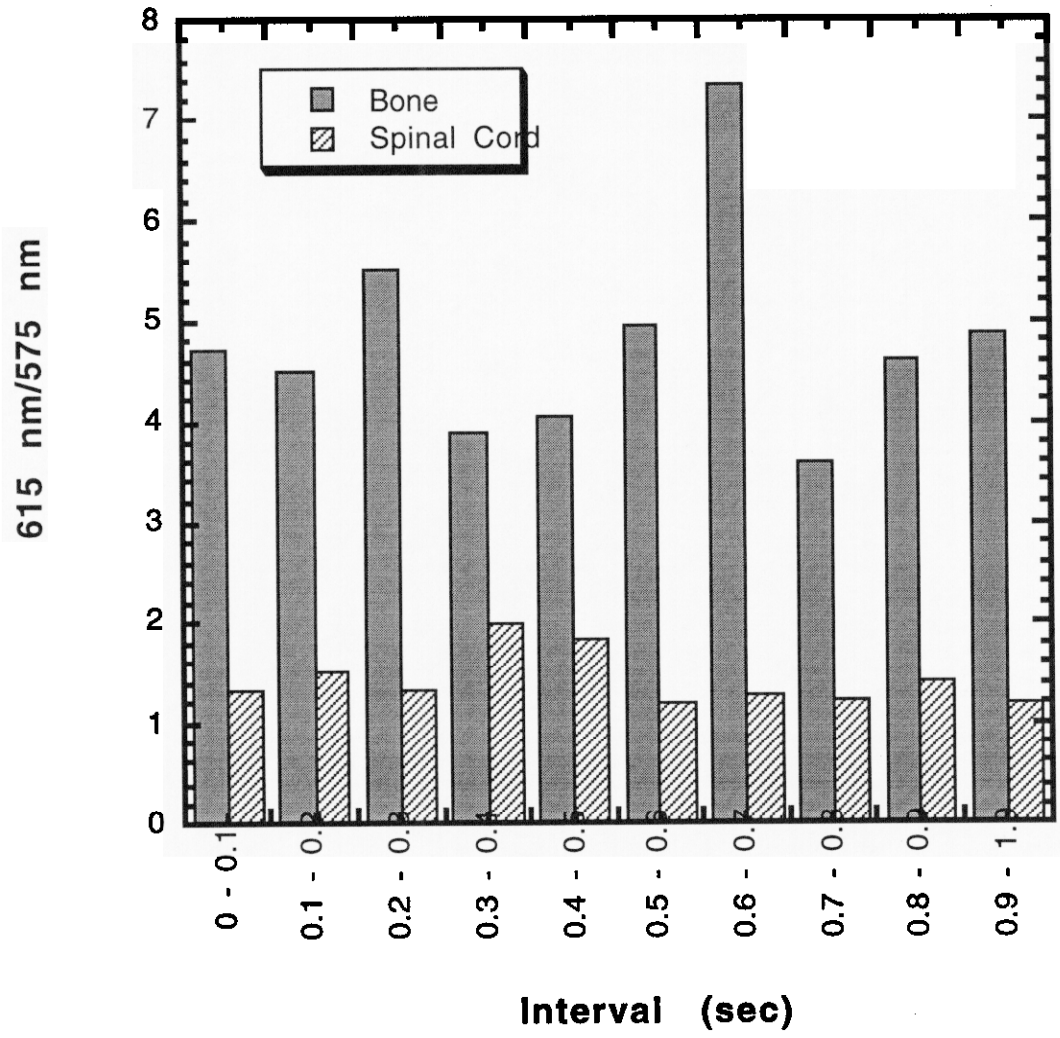

Fig. 6. Average wavelength ratio (615 nm/575 nm) is 4.8 for bone and 1.4 for Spinal Cord. The ratio is consistent regardless of the luminescence intensity. By setting the threshold ratio at 2.5 - 3, we can create the on/off feedback control

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