Application of OCT for osteonecrosis using an endoscopic probe based on an electrothermal MEMS scanning mirror

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ABSTRACT

Osteonecrosis becomes a more widespread problem as the population is getting older. Current osteonecrosis diagnosis not only requires invasive procedures but also often leads to surgical replacement. This paper reports a preliminary study of applying optical coherence tomography (OCT) for noninvasive diagnosis of osteonecrosis using an endoscopic probe based on a microelectromechanical (MEMS) scanning mirror. The endoscopic MEMS probe is only 2.5 mm in diameter and can scan a field of view of 24°. First a tissue sample of femoral head with osteonecrosis is scanned with the MEMS probe. The resultant OCT images can clearly delineate the necrosis region from the normal bone. Then in vivo experiments are carried out on an adult rabbit, in which the rabbit’s femoral head is scanned and imaged with the same MEMS probe and both three-dimensional (3D) structural images and blood flows are obtained. The OCT imaging experiments show that the femoral head of this rabbit does not have osteonecrosis and its blood flow is present, which is in agreement with the destructive diagnosis. The blood flow rates in the femoral head are extracted from the OCT images acquired in three cases: normal blood supply, partial ischemia and complete ischemia, which are 19.3 mm/s, 11.9 mm/s, and 1.88 mm/s, respectively. These experiments demonstrate that OCT can clearly distinguish between the osteonecrosis and normal bone and measure the blood flow rate in the bone, both with the cartilage present, showing great potential for non-invasive osteonecrosis diagnosis.

KEYWORDS

OCT; MEMS scanning mirror; osteonecrosis; osteonecrosis diagnosis

1. Introduction

Osteonecrosis is a clinical urgent problem, which often occurs after femoral neck fracture. With the accelerated aging of the population, the number of osteonecrosis incidences increases significantly in recent years[1]. Knowing the status of the blood supply in the femoral head is very important for determining if osteonecrosis occurs or not, especially in the surgical treatment of hip screw fixation. If the blood supply can be monitored noninvasively and the measured blood supply level is low, the treatment can be adjusted to direct hip replacement and the secondary surgery will be avoided. Therefore, to find a real-time noninvasive diagnostic method is critical for osteonecrosis treatment. Optical coherence tomography (OCT) is an imaging technique that uses the basic principle of low-coherence interferometry to detect various biological tissues, and it has been widely used in the...
diagnosis of ophthalmic and cardiovascular diseases\cite{2,3}. In recent years, OCT has been applied to many other medical fields, including urology, neurology and orthopedics\cite{4}. In the area of orthopedics, OCT is mainly used to detect degeneration of articular cartilage, and a large amount of articular cartilage degeneration observations have been reported in the literature\cite{5-8}. However, the application of OCT to assess blood flow in bones has not yet been reported. Currently, there are a variety of methods that can be used to evaluate bone blood flow rates, such as Dynamic Enhancement MRI\cite{9,10}, Laser Doppler Flowmetry (LDF)\cite{11}, Digital Subtraction Angiography (DSA)\cite{12}, Single-Photon Emission Computed Tomography (SPECT) and Positron Emission Tomography (PET)\cite{13}. However, Dynamic Enhancement MRI cannot be used during surgical operation; DSA is an invasive examination; and SPECT and PET are expensive and radioactive. LDF is real-time and easy to use, but it can only measure a small volume (typically within 1 mm$^3$), and it cannot measure the distribution of blood flow within the bone structure.

Doppler optical coherence tomography (D-OCT) is an important functional extension of OCT. D-OCT combines Doppler effect with OCT technology to detect distributed flow velocity in the depth direction of the sample\cite{14}. Due to its high spatial resolution and high velocity sensitivity, D-OCT is able to measure blood flow in blood vessels or even in microvasculatures. In this work, a common-path D-OCT system with a MEMS mirror-based endoscopic probe, abbreviated as ME-CPD-OCT, has been developed and employed for the preliminary study of applying D-OCT to measure the blood flow rate in the rabbit femoral head for noninvasive diagnosis of osteonecrosis. In this paper, first the ME-CPD-OCT system is described in Section 2, including the MEMS mirror and the MEMS endoscope probe design. Then, an OCT imaging experiment of a femoral head tissue sample with osteonecrosis, an in vivo ME-CPD-OCT imaging experiment, and the analysis of the experimental data are presented in Section 3.

## 2. Methodology: imaging system and imaging probe

### 2.1. ME-CPD-OCT

A swept source common-path Doppler optical coherence tomography system with a MEMS mirror based endoscopic probe, as shown in Figure 1, is developed based on a previous work\cite{15} with the balanced detector improved. A swept-source (SS) laser (SSOCT-1310, Axsun) sweeps in k-space at 50 kHz and generates a linear k clock sequence for the axial scan (A-san). The SS laser's center wavelength is 1310 nm and its full width half maximum (FWHM) bandwidth is about 80 nm. The maximum number of k clocks in each sweeping period is 1286. In this study, 1216 of the k points are selected for each A-scan, which are converted to 608 depth points that

![Figure 1. Schematic of the MEMS based endoscopic swept source common-path Doppler optical coherence tomography.](image-url)
correspond to a theoretical imaging depth of 5.4 mm in air. The laser beam from the SS laser passes through an optical circulator that then directs the laser into an endoscopic probe and circulates the optical signals returned from the sample to a Mach-Zander interferometer (MZI). A balanced photodiode (PDB460C, Thorlabs) converts the optical signals from the MZI into voltage signals that are subsequently acquired into a computer. After that, OCT structural images can be readily reconstructed through routine OCT data processing including digital filtering, numerical dispersion compensation and fast Fourier transform\[16\]. The depth resolution of this system is about 9 \(\mu\)m in the air and the resolution in the transverse direction is about 18 \(\mu\)m. The flow rate of blood in the sample can also be extracted through Doppler deconvolution\[17\].

2.2. MEMS mirror-based endoscopic probe

Figure 2(a) illustrates the 3D structural model of the proposed MEMS mirror-based common-path endoscopic probe. It is composed of a mount base, a gradient refractive index (GRIN) lens module, and a MEMS mirror. The outer diameter of an assembled probe is 2.5 mm, as shown in Figure 2(b). The diameter of most orthopedic drill is 3.5 mm, so the 2.5 mm probe is easy to be put in the hole considerate some residual bone debris. Figure 2(c) presents the core scanning engine MEMS mirror (MI-T05.1 WiO Technologies Co Ltd.), it has a 0.55 mm \(\times\) 0.55 mm active mirror plate coated with aluminum for high reflectivity. The chip size is 1.35 \(\times\) 1.44 \(\times\) 0.4 mm\(^3\). Figure 3(a) shows the SEM

![Figure 2](image1.png)

Figure 2. (a) Three-dimensional (3D) model of the probe; (b) photograph of the MEMS probe (c) photograph of MEMS mirror.

![Figure 3](image2.png)

Figure 3. (a) SEM image of MEMS mirror; (b) The MEMS mirror deflection angle as a function of driving voltage; (c) Frequency response of the MEMS mirror.
image of the MEMS mirror. The mirror is lifted by four electrothermal actuators and each actuator consists of three folded dual S-shape Al/SiO₂ bimorph structures[18] in series. A Ti heater is embedded in the bimorph actuator. The heater will heat the bimorph as a voltage applied on it, so that the actuator changes its displacement when temperature rises. Consequently, the MEMS mirror can achieve 2-axis large scan range at low drive voltage. Figure 3(b) shows the MEMS deflection angle as a function of voltage on one actuator. It can be seen that a 6° mechanical tilting angle is achieved with 6 V, so the optical scanning range is −12° to 12° for both x-axis and y-axis. The frequency response of the MEMS mirror with a 2 V sinusoidal driving signal is demonstrated in Figure 3(c). The figure shows a clearly decrease in deflection angle as the frequency higher than 30 Hz because of thermal response of the bimorphs. The resonant frequency of the MEMS mirror is 2377 Hz, which is higher than mirror in previous MEMS probe[19] for a high reliability. To generate linear raster scan patterns, the endoscopic probe is driven by a pair of triangular waveforms with the voltages varying from 0 to 5 V to scan at both x-axis and y-axis. The actuators in x-axis are driven at 50 Hz as the fast scan, while the actuators in y-axis are driven at 0.5 Hz as the slow scan. In this way, 3 D OCT images of the sample can be obtained. The 50 Hz fast-axis scan means 2 D OCT images are acquired in real time at 50 frames/s, or each B-scan takes 20 ms. Thus, 1000 A-lines are generated for each 2 D OCT image as the SS laser sweeps at 50 kHz. Thus, each 2 D OCT image, that is, a B-scan image, contains 500 A-lines. Finally, 100 B-scan images are recorded in 2 s for reconstructing one 3 D OCT image.

3. Experiments and discussion

3.1. OCT imaging of a tissue sample of femoral head with osteonecrosis

A sample of human femoral head with osteonecrosis from Zhongshan Hospital’s tissue bank was used in this experiment. The tissue sample was thawed and cut open to expose the necrotic regions. Then OCT imaging was performed on the necrotic regions using the ME-CPD-OCT system. The endoscopic probe was used to scan the osteonecrosis areas, as indicated in Figure 4(a).

Figure 4. (a) Sample of femoral head necrosis; (b) 3 D OCT of osteonecrosis; (c) 2 D OCT image of necrotic osteon; (d) Normal osteon. White scale bars in both horizontal and vertical directions represent 1 mm.
by the dash circles, from the articular surface. The corresponding 3D OCT image is shown in Figure 4(b), which clearly reveals that cartilage was absent on the surface of the necrosis area. Figure 4(c) and (d) are 2D OCT images of a necrotic bone and a normal osteon, showing that sparse and low scattering structures were observed in the necrotic bone.

3.2. In vivo imaging experiments

In vivo experiments are also performed using the ME-CP-DOCT system. An anesthetized rabbit is placed on a stage, and part of its femoral head is revealed, as shown in Figure 5(a). Then, the following steps are taken. First, the surface of the cartilage is scanned using the MEMS probe to find out whether OCT can distinguish between the cartilage and subchondral bone. Then the cartilage is removed, as shown in Figure 5(b). After that, the exposed subchondral bone is scanned with the MEMS probe. In the last step, D-OCT is performed on the subchondral bone at the same position in three periods: (1) at the normal blood supply condition, (2) at partial ischemia by blocking the ipsilateral femoral artery, and (3) at complete ischemia by terminating the rabbit. In order to eliminate the deviation introduced by the optical beam scan angle, the measured velocities are all converted to the direction along the surface of the sample.

3.3. Experimental results and data analysis

Figure 6(a–f) present the OCT images acquired from the surface of the cartilage. Figure 6(a) is a 3D OCT image combining blood flow signals with structure signals, where the color points represent blood flow signals. The 3D distribution of the blood flow in the bone is obtained via D-OCT and MEMS scanning[20]. In Figure 6(a), the red points represent flows moving towards the sample surface, while the blue ones represent the flows moving away from the surface. Note that the optical beam is scanned by the MEMS mirror at a range of angles. For a fluid flowing in parallel to the sample surface there is a fraction of the flow velocity present in the Doppler signals. Then even if the optical beam is perfectly perpendicular to the blood flow, due to the converging/diverging angle of the optical beam, the velocity still can be detected, with reduced signal-to-noise ratios. Figure 6(b) is the side-view stacking of all 100 OCT image frames in Figure 6(a), where we can see that the blood flow signals are concentrated in the subchondral bone, which matched well with the CD31 specific staining (which can stain vascular endothelial cells) result shown in Figure 6(f). In Figure 6(c), the white scale bars in both horizontal and vertical directions represent 1 mm and the dark line pointed by the white arrow represents the boundary of the cartilage and subchondral bone. The thickness of the cartilage is about 0.6 mm, which agrees with the
histological result shown in Figure 6(e). It can also be seen that the OCT imaging depths of the cartilage and bone both are about 2 mm. Note that D-OCT images successfully reveals the presence of the blood flow, which mainly exists at the boundary between the cartilage and subchondral bone. However, no blood vessels are clearly seen in D-OCT images. This is believed to be due to the small vessel sizes in this region which are beyond the resolution of the employed OCT system.

Figure 7 shows the OCT imaging experiment results for the femoral head without cartilage, where the three columns from left to right respectively represent the D-OCT images of the bone (1) at the normal blood supply condition, (2) at partial ischemia by blocking the ipsilateral femoral artery, and (3) at complete ischemia by killing the rabbit. Figure 7(a–c) is the reconstructed 3D structural OCT overlaid with their corresponding D-OCT images. Figure 7(d), (e–f) displays the superpositions of the 100 D-OCT images in Figure 7(a), (b) and (c), respectively. The color
points represent blood flow signals with the red for flowing toward the surface and the blue for flowing away from the surface. It can also be seen that the number of color points decreases remarkably when the blood vessels are changed from “normal” to “complete ischemia”. The average blood flow rates at the normal blood supply, partial ischemia and complete ischemia are 19.5 mm/s, 11.9 mm/s and 1.88 mm/s, respectively. Note that phase unwrapping algorithms are not applied here due to insufficient Doppler signals. If there are some phase wrapped Doppler signals, the mean value of the velocity in the normal blood supply or partial ischemia condition will be slightly smaller, but there will be very limited impact on the ischemia result.

3.4. Discussion

Though OCT has been used to image the structures of cartilage and bone for decades, the application of OCT to measure the blood flow in bones has not been reported. Interestingly, OCT combined with MEMS optical scanning has been used to miniature endoscopic probes that can realize precise velocity measurement. Thus, the effort of this work is to verify whether OCT with the help of MEMS optical scanning is a feasible method to evaluate blood flow rate in bones. Through in vivo animal experiments, we have found that the blood flow signals can be detected by combining the Doppler signals with the structural signals in OCT images, from which we can speculate the vascularity of the bone in 3D. It is also found that the blood vessels are mainly distributed in the subchondral bone, not in the cartilage. These results measured by OCT have been confirmed by the CD31 specific staining (Figure 5(f)). According to these findings, we can see that D-OCT has great potential to evaluate the blood flow rate of the subchondral bone, which has a close relationship with osteoarthritis[21].

Figure 7. Images acquired after removing the cartilage. First row ((a) (b) (c)): 3 D-OCT structural images overlaid with the blood flow distribution; the color points represent blood flow signals; Second row ((d) (e) (f)): 3 D plots of the blood signals.
In fact, D-OCT, detects not only the blood flow but also all moving matters in the bone. Although osteocytes or other structures in the bone may have small motions, they typically are much slower compared to the blood flow. Furthermore, when the femoral artery is throttled to reduce the blood flow velocity, the D-OCT image changes significantly, which confirms the correlation between the D-OCT image and blood flow velocity.

Also note that there is no clear evidence to show the presence of blood vessels. This is believed to be due to the sizes of the blood vessels in the subchondral bone. Subchondral bone is a special kind of cancellous bone, which is similar to cortical bone. Its blood vessels go in the haversian canals, whose diameters range from 25 to 125 μm (average 50 μm) in human[22]. The rabbit’s femoral head is about 1/25 volume of the human’s, so the haversian canals in the rabbit may be only a few micrometers in diameters[23]. In addition, in the subchondral bone, the blood vessels are usually capillaries, whose diameters are about 8 μm, and the vessel distribution is very complicated. The OCT system depth resolution is about 7.8 μm taken refractive index of blood into account, so it is hard to delineate blood vessels but only show some pixel dots in D-OCT images. A higher resolution OCT system may be needed for visualizing these blood vessels. OCT depth resolution depends on the bandwidth of laser source and the lateral resolution is decided by the probe. For depth resolution, dual bands of laser sources or more broadband laser source could be better. To improve the lateral resolution of probe and maintain good depth of focus is need to considerate, and holographic algorithm is also a good choice to compensate the resolution deteriorate off focus plane[24].

The femoral artery is the most important blood supply of the femoral head. If the femoral artery is blocked, OCT images can clearly show the blood flow rate in the femoral head decreases significantly. When the rabbit is terminated, the blood supply of the bone is completely blocked, and the velocity of the blood flow should be zero, but OCT images still show some flow signals in the bone. One possibility is that there is still some residual blood flow under the force of gravity, despite the fact that the heart has stopped pumping.

Currently, the OCT imaging depths of the cartilage and bone are both about 2 mm, but the thickness of the cartilage of the human femoral head is around 4 mm. So, the current OCT system may not be suitable clinically for directly obtaining the blood flow information of the subchondral bone from the surface of the cartilage. In the experiments, we have found that OCT can distinguish between the necrotic and normal regions of the femoral head, but more study is needed and the structural imaging and blood flow imaging of OCT should be combined to extract more information.

4. Conclusions

This study shows that OCT combined with Doppler and MEMS optical scanning is a feasible method to evaluate the blood flow in bones in vivo. In this method, OCT acquires 3D structural images, D-OCT provides a good sensitivity of blood flow rate in bones, and MEMS ensures small probe size and fast imaging speed. Though there are limitations of the imaging depth and resolution, this method can be used in many areas of orthopedics, such as arthroscopy, femoral head blood flow detection in operation, and risk evaluation of osteoarthritis. With the advances of the light source, photodetection, and image processing, this ME-CPD-OCT system surely has a bright future for clinical use in orthopedics.

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