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Peng Chen

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Laser-based gas absorption spectroscopy in decaying hip bone: water vapor as a predictor of osteonecrosis

Delong Chen,[a,b,†] Wansha Li,[c,†] Wei He,[b,d,e] Hao Zhang,[c] Qingwen Zhang,[b,d,e] Huiying Lin,[c] Sune Svanberg,[c,f] Katarina Svanberg,[c,f,*] and Peng Chen[d,e,*]

[a]Guangzhou University of Chinese Medicine, First Clinical Medicine School, Guangzhou, China
[b]Guangzhou University of Chinese Medicine, Laboratory of Orthopedics and Traumatology of Chinese Medicine, Lingnan Medical Research Center, Guangzhou, China
[c]South China Normal University, South China Academy of Advanced Optoelectronics, Center for Optical and Electromagnetic Research, Guangzhou, China
[d]Guangzhou University of Chinese Medicine, Orthopedics Department, First Affiliated Hospital, Guangzhou, China
[e]Guangzhou University of Chinese Medicine, Hip Center, Guangzhou, China
[f]Lund University, Lund Laser Center, Lund, Sweden

Abstract. Affluent blood flow through a complicated net of vessels supplies skeletal bone tissue with oxygen and nutrients. Due to accidental events or physiological processes, the blood supply might be deficient or even disrupted, and the healthy bone decays in a process that, for the hip location, is denoted as osteonecrosis of the femoral head (ONFH) or avascular femoral head necrosis. Early diagnosis is important for the prognosis. X-ray-based imaging, such as CT or MRI, is not of much value for the early detection. As the decay theoretically is associated with the development of gas-filled pores, gas analysis should have diagnostic value. We have introduced gas in scattering media absorption spectroscopy, as a complementary modality. Eighteen extracted femoral joint heads, diseased as well as normal, were investigated. Diseased samples are associated with clear signals due to water vapor, whereas the normal ones largely lack such features. The results suggest that free water vapor could serve as an early indicator of pore development and thus as a promising predictor of ONFH pathological changes, once the technique has been fully refined. [DOI: 10.1117/1.JBO.24.6.065001]

Keywords: free water vapor; predictor; osteonecrosis of the femoral head; laser spectroscopy.

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1 Introduction

Oxygen and nutrients to the skeletal bone tissue in humans are transported through a complicated vascular system, representing 10% of the total cardiac output.[1] The main blood stream to the larger bone structures in the body, such as to the long, almost cylindrical femoral or thigh bone, runs through a main artery penetrating directly to the central medulla of the bone supporting the blood hematopoiesis. Connected to this artery are separate smaller vessels supplying the outer periost of the bone structure with a flow direction from the inner location at the central medulla to the surface.[1] Osteonecrosis or avascular necrosis is a condition related to the disruption of the blood supply, and even if it can affect all bones in the body, the hip is the most common location.[2,3] Osteonecrosis of the femoral head (ONFH) is a process and develops in several stages, from normal to a flattened caput, which eventually will collapse.[4,5] The incidence of ONFH has been increasing steadily every year all over the world and especially in China.[6] Apart from the result of accidental fractures, which have been surgically treated with metal nails or other osteosynthesis materials, or of smoking or excessive alcohol use, the etiology of ONFH is not fully understood. Some of the mechanisms behind the development of the disease involve fat hypertrophy, fat emboli, and intravascular coagulation. Other potential risk factors are disease-related, such as diabetes, inflammation of the pancreas, and Crohn's disease, but also medications, such as high dose corticosteroids and bisphosphonates, can induce the disease.[7]

Normally, the viable spongy bone in the femoral head is filled with blood. Once ischemia occurs with deficient blood supply, the pathological process in the femoral head starts with the development of sclerosis, flattening, sequestrum formation, and secondary osteoarthritis (OA).[8] Our findings from a recent study,[9] that the decaying bone develops enclosed pores filled with gas including water vapor, are possibly related to earlier knowledge of increased tissue volume.[8] Our findings are also partly supported by the use of one of the few therapy options that are applied—core decompression.[4] This procedure involves drilling channels transdermally through the trochanter part to the head for relieving high pressure in the femoral head, originating from increased tissue volume.[4]

Gas in decaying tissue most probably consists of methane, carbon dioxide, and hydrogen, typical for decaying tissue. However, none of these gases can optically be detected *in situ* since their absorption bands fall outside the so-called tissue optical window (700 to 1300 nm), where the absorption from, e.g., blood and liquid water is reduced. However, water vapor would also always be present in the gas-filled pores since the environment is moist, and thus 100% relative humidity at 37°C would

*Address all correspondence to Peng Chen, E-mail: docchen777@gmail.com; Katarina Svanberg, E-mail: Katarina. Svanberg@med.lu.se

†These two authors contributed equally to this paper.

pertain in the clinical case. The free water vapor concentration is given by the temperature only, through the Arden–Buck relation, yielding about 6% of the pore gas being water vapor.[10] Gas in scattering media absorption spectroscopy (GASMAS), a high-resolution laser spectroscopy method, critically takes advantage of the fact that free gases exhibit very sharp optical absorption lines, which can be detected by sensitive electronics when superimposed on the much broader absorption structures of the surrounding solid or liquid medium.[11,12] Water vapor exhibits characteristic absorption lines, e.g., in the 820- and the 935-nm regions. Soon after its invention, the GASMAS technique was introduced to detect water vapor gas in enclosed cavities in human tissue, such as in the facial sinus cavities, in the lungs and intestines of newborn babies, and in a middle-ear phantom.[13–17] We have also employed the technique in various food safety studies.[18]

As mentioned, we applied GASMAS in orthopedic application within the field of ONFH,[9] and this study represents a follow-up. Due to nonavailability, the earlier study did not include normal bone tissue, and therefore we could not compare normal and diseased conditions, which now was possible in this study. Another more technical aspect we wanted to clarify was the possible influence of the handling of the excised samples regarding the immediate freezing after the surgical extraction. This important issue was investigated in detail in another orthopedical study;[19] we found that the handling procedure did not influence the outcome and this knowledge is now transferred to this case. This study is thus much more comprehensive than the preliminary study[9] while still confirming the preliminary findings. Further, a small, technical signal offset present in our experimental setup and discovered in Ref. 19 could now be accounted for.

Early diagnosis is important for the prognosis of the patients. X-ray-based imaging, such as CT, is not of much value for early detection. MRI has shown potential for detection of the border between healthy and necrotic bones.[4] GASMAS might be a complementary diagnostic modality for early detection and in particular if it is combined with laser-Doppler for tissue perfusion monitoring.[20]

2 Earlier GASMAS Monitoring of Femoral Bone

Encouraged by the earlier promising results using GASMAS in biomedical applications,[11–17] we included orthopedics as a clinical field, where there are still open questions to be investigated, such as small-scale anatomical or morphological changes in the development of OA.[9] Initially, a test on a dry femoral bone was performed; a bone structure used for demonstration purposes at the hospital. As expected, prominent gas signals were obtained from the dry porous structure. As a second step, *in-vitro* experiments on femoral heads were performed. These samples were extracted from patients scheduled for total hip arthroplasty (THA), and gas-filled voids could be demonstrated in samples with two types of disease: ONFN and OA. The earlier study[9] suffered from the fact that no normal samples were available for comparison, but for the diseased ones, it was clearly shown that gas signals were present and that the detected gas originated from pores inside the bone, by making a demonstration of gas exchange.[9] Based on the encouraging results, a follow-up and more complete study was pursued, and the results are reported in this paper.

3 Materials and Methods

3.1 *Sample Collection*

Eighteen femoral heads were retrieved from the same number of patients undergoing THA surgical procedures at the Orthopedics Department, First Affiliated Hospital, Guangzhou University of Chinese Medicine. As shown in Tables 1 and 2, among the 18 bone samples, 11 samples were affected by ONFH and the others were related to acute femoral neck fracture and thus defined as the control group with regard to possible porosity. All patients were monitored with x-ray and MRI imaging before THA and met the diagnostic criteria of ONFH or femoral neck fracture.[6,21,22] The 11 patients in the ONFH group had a mean age of 60 years with a standard deviation (SD) of ±4 years and the control had a mean age of group 59 years and an SD of ±5 years. This means that the two groups were very similar concerning the age distribution. From the gender point of view, the ONFH group included seven males and four females and the control group included four males and three females. Both

Table 1 Patients' information.

No.	Sex	Age (years)	Diagnosis	Other disease
01	M	59	Osteonecrosis of femoral head (left)	—
02	F	62	Osteonecrosis of femoral head (right)	—
03	M	64	Osteonecrosis of femoral head (bilateral)	Hypertension
04	F	56	Osteonecrosis of femoral head (bilateral)	Hypertension
05	F	67	Osteonecrosis of femoral head (left)	—
06	M	55	Osteonecrosis of femoral head (bilateral)	—
07	M	55	Osteonecrosis of femoral head (bilateral)	—
08	M	53	Osteonecrosis of femoral head (left)	Hypertension
09	M	64	Osteonecrosis of femoral head (bilateral)	—
10	M	61	Osteonecrosis of femoral head (left)	—
11	F	64	Osteonecrosis of femoral head (left)	—
12	M	55	Femoral neck fracture (right)	Hypertension
13	M	58	Femoral neck fracture (left)	—
14	M	53	Femoral neck fracture (left)	—
15	M	68	Femoral neck fracture (left)	Hypertension
16	F	55	Femoral neck fracture (right)	—
17	F	64	Femoral neck fracture (left)	—
18	F	57	Femoral neck fracture (right)	—

Table 2 Patient demographics and clinical profiles.

Diagnostic category	N	Mean age ± SD	Sex	
			M	F
ONFH	11	60.00 ± 4.45	7	4
Control	7	58.57 ± 5.04	4	3
Total	18	59.44 ± 4.74	11	7

Notes: ONFH: Osteonecrosis of femoral head; control group is the patient with femoral neck fracture.

groups included a small number of hypertension patients (three in the ONFH group and two in the control/fracture group). The samples were immediately frozen to −80°C and then thawed to room temperature for 5 h prior to GASMAS investigation. The study was approved by the Ethics Review Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine (No. ZYYECK[2017]028), and written informed consents were obtained from patients.

3.2 *Experimental Setup*

A schematic diagram of the experimental setup available at the Center for Optical and Electromagnetic Research, South China Normal University, Guangzhou, is shown in Fig. 1. A distributed feedback diode laser, operating at the wavelength of 937 nm, was used as the light source driven by the combination of current and temperature controllers. The superposition of two analog waves from a LabVIEW-controlled unit were used to modulate the laser output, where a current ramp with a frequency of 5 Hz was used to scan the wavelength to obtain the gas absorption imprint, and a sinusoidal wave with a frequency of 9015 Hz was used to modulate the wavelength to allow so-called lock-in signal detection for optimal recording of the weak signals. The modulated laser output was delivered to the sample through an optical fiber, and the scattered light from the samples was collected with a photodiode. Then the current signal from the photodiode passed through a low-noise current amplifier and was subsequently converted to a voltage signal. The signal was fed to a computer via a data acquisition (DAQ) card. A more technical description of the technique and the digital lock-in detection employed for signal enhancement is given in Refs. 11 and 23–27.

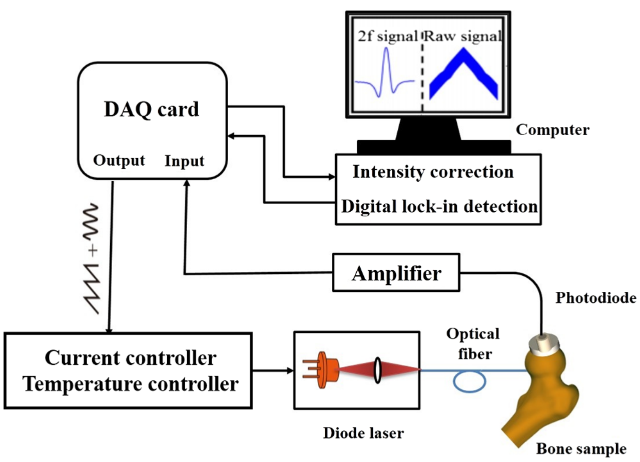

Fig. 1 The experimental setup for GASMAS measurements of water vapor in pores inside the femoral head.

As human tissue exhibits strong light scattering, the commonly used Beer–Lambert law is not directly applicable to extract the gas concentration from the absorption imprint. Therefore, an equivalent mean path length L_{eq} was introduced, which is the distance in a reference gas (typically the ambient air) that the light needs to pass through to experience the same absorption imprint as when traveling through the sample. The details of the data evaluation procedure can likewise be found in previous reports.[23,26,27]

4 Measurements and Results

GASMAS measurements were performed on all 18 excised femoral heads after they were thawed for 5 h to reach room temperature conditions. Results are shown in Fig. 2. Figure 2(a) shows the experimental arrangement of the light injection fiber and the detector in close contact with the femoral head. A typical registration curve is shown in Fig. 2(b). The red, smooth curve is a fitted reference signal for the same water vapor absorption line recorded under ideal conditions over a path length of 1300 mm distance in air with known water vapor relative humidity. To extract the equivalent mean path length L_{eq} through the bone sample with 100% relative humidity (saturation conditions), the reference signal is fitted with appropriate scaling. We used a distance of 40 mm between the fiber-optic light injection point and the center of the detector in all the measurements. This choice was based on a special study on one of the ONFH samples as illustrated in Fig. 3, where we examined the influence of the injection site—detector.[9] As expected from experiment and theory on porous media studied by GASMAS,[11] the L_{eq} value increases with increasing separation for uniform samples. The points D and H had a similar distance to the detector, whereas the L_{eq} of the water vapor signal at point D was much larger than that at point H. This seemed to be caused by the higher severity of the OA around the H point of the femoral head, as observed in visual inspection, which indicated a promising potential of the GASMAS technique as a diagnostic tool. Since the signal-to-noise conditions become worse for large separations, due to the strong reduction of the amount of light reaching the detector, a trade-off regarding distance must be reached. The data for all 18 femoral head samples as represented in Fig. 2(c) were all taken for the same separation of 40 mm. All the measurements were individually repeated three times, and the data are expressed as the average of the observed values to get the mean value (mean) of the observations with the SD to quantify the dispersion of data recordings and presented as mean ± SD. A t-test reveals a p value of <0.05, which indicates a significant difference between the two groups. We have subtracted an offset water vapor signal corresponding to 2.0 mm in the data shown in Fig. 2(c). This water vapor signal is related to free air-space due to spurious ambient oxygen present internally in the experimental setup, related to the coupling of the laser light into the fiber. We noted that there is a significant difference between the ONFH and normal samples, as clearly shown in Fig. 2(d) on showing the averaged data for the two sample groups, with clear evidence of free gas in the diseased samples, whereas the non-ONFH samples basically show a close-to-zero result. An exception is sample 9, which has a particularly low value, and also samples 3, 4, and 6 could be confounded with normal

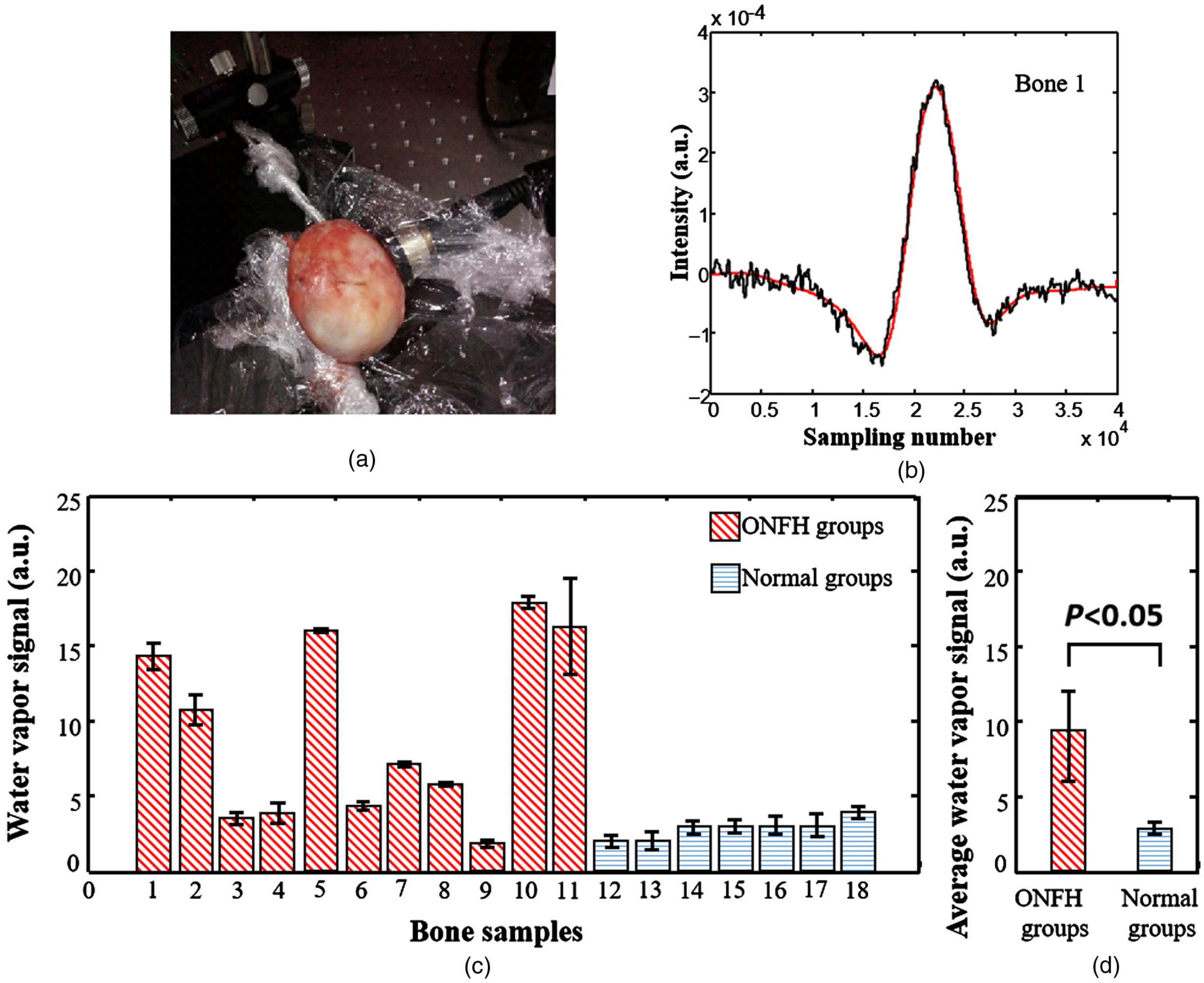

Fig. 2 The experimental setup and the results for the 18 femoral heads. (a) GASMAS measurement arrangement, (b) water vapor signal from one sample, and (c) data for all 18 samples. ONFH samples are indicated in red whereas normal femoral head samples are indicated in blue. The mean values and SD of the two groups are shown in (d) with a p value <0.05.

samples. Samples 1, 2, 5, 10, and 11 all have very high values, around 15 mm. In view of the results shown in Fig. 3 and discussed above in that context, this might indicate particularly severe cases of necrosis. However, at the present time, no detailed pathological comparison was made.

5 Discussion

ONFH, also called avascular bone necrosis, is a common disorder of the hip. Ischemia or deficient blood supply plays an essential role in the development of ONFH. We were, in our earlier study,[9] able to show that degenerating femoral heads contained gas-filled pores, possibly also indicating an increased volume related to high pressure in the *in-vivo* case, which is in line with published literature.[4] The recent study demonstrated that there is a clear morphological difference in between ONFH and normal femoral bone structure as monitored with the GASMAS technique. The t-test performed on the results showed a significant difference between the two groups with a p value <0.05. The demographic and clinical distribution of the two groups showed very similar statistics. Also from the point of view of other diseases, it is very similar conditions with few cases of hypertension in both groups. This means that there is no specific bias that could influence the results.

As we also have investigated the handling procedure with the immediate deep freezing and slow thawing, we knew that the handling procedure did not induce any artificial changes that could influence the result.[19] A challenging topic is whether other joints in the human body behave similarly when developing arthrosis. We investigated arthrosis in the tibia condylar bone of the knee joint, but found no gas-filled voids in that location, at least not at the time of surgery.[19] The reason for this might be that the indication for surgical intervention is when the cartilage layer is worn down, which happens before the bone starts to degenerate. So, in principle, the tibial bone we were investigating could be looked upon as "normal" samples at a stage comparable to the normal femoral heads in this study. The case of knee arthrosis has a different biological background than that for ONFH, where the bone structure itself is affected.[28] The presence of the small offset gas signal discussed above concerning the ambient spurious oxygen was first studied in detail in connection with the tibia bone study[19] and allowed us to also make the small correction for this effect in the earlier data,[9] now presented together with the new data for nonaffected femoral heads.

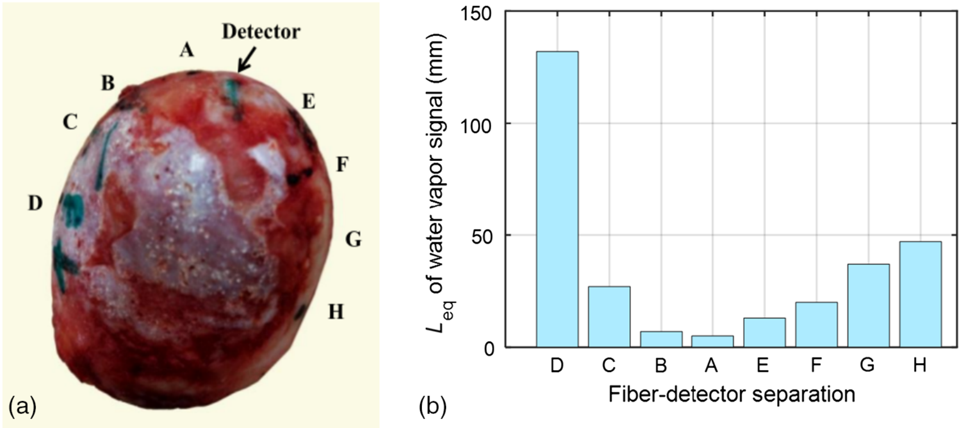

Fig. 3 GASMAS monitoring of water vapor of a diseased femoral head, where some parts of the sample is more affected by ONFH (seen as color changes even at the surface). (a) Different light injection positions on the femoral head and (b) the L_{eq} of the water vapor signal at each position (adapted from Ref. 9).

The measurements on the human femoral heads *in vitro* suggest that GASMAS could provide a powerful tool for studies of the human femoral head *in vivo* and thus be useful for the diagnostics of caput necrosis. This paper strongly complements our preliminary account on femoral heads, where no comparison to unaffected samples could be done,[9] and where the small instrumental offset was not applied. We could further ascertain that the sample handling procedure with freezing and thawing did not affect the results.[19] The mere fact that the identically treated diseased and nondiseased samples were found to differ strongly regarding gas content, which further corroborates this conclusion.

At present, we are planning to perform measurements *in vivo*. A special fiber-optic probe can be integrated in an arthroscope to allow GASMAS measurements *in situ* as discussed in Ref. 9. Just like the design of an optical probe used for detection of gas in the middle-ear cavity,[16] the probe consists of multiple fibers to be used to transmit and collect the light. To allow larger injection-detection separations, light injection using an optical fiber, inserted through a syringe needle, can be used with the fiber tip in contact with the periosteum of the bone structures under study, and the collected scattered light could be transmitted through the arthroscope. This procedure is of course more invasive than other conventional diagnostic techniques, such as x-ray-based CT or MRI. On the other hand, the use of an arthroscope with transdermal application is a conventional technique both for diagnosis and therapy of the hip.[4] The arthroscopic technique is considered as minimally invasive and used as a standard modality for biopsy sampling for various diseases in the hip, such as in pigmented villonodular synovitis or even for the therapy of arthrosis-related pain with core decompression. As such, it is considered much less invasive than open incisions to reach the hip structures.[4,29]

In addition, considering the changes of blood perfusion inside the femoral head related to ONFH, we are planning to apply the laser-Doppler technique[20] to measure the blood perfusion around and inside the femoral head. Then only an optical heterodyne detection module would be added to the electronics while the rest is the same. As a supplementary method, the laser-Doppler technique might also be used to distinguish ONFH from normal femoral head conditions and may improve the diagnostic accuracy of caput necrosis, especially when combined with the GASMAS technique.

Disclosures

The authors have no relevant financial interests in this article and no potential conflicts of interest to disclose.

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Delong Chen is an MD candidate at the First Clinical Medicine School, Guangzhou University of Chinese Medicine. His major is in Chinese medicine, orthopedics, and traumatology. His research focuses on the basic and clinical study of hip and knee joint diseases, especially the osteonecrosis and osteoporosis.

Wansha Li received her bachelor's degree in physics from Jiangxi Normal University in 2015. She finished her MSc studies at the Center for Optical and Electromagnetic Research, the South China Normal University (SCNU), Guangzhou, in 2018. Her research interests include laser spectroscopy applied to food safety and biomedical topics.

Wei He obtained his PhD from Guangzhou University of Chinese Medicine in 2001. He has been working in the First Affiliated Hospital of Guangzhou University of Chinese Medicine since 1988. As a professor, he devotes himself to the study of osteonecrosis of the femoral head (ONFH) and has treated more than 10,000 ONFH cases. His interests concern clinical and basic research on ONFH.

Hao Zhang received his bachelor's degree in physics from the East China Institute of Technology, Nanchang, in 2011. His major field was optical engineering. He received his PhD from the Center for Optical and Electromagnetic Research, SCNU, Guangzhou, in 2016, and is now a postdoc at the Henan Agricultural University, Zhengzhou. His research interests concern applications of laser spectroscopy to the biophotonics and agricultural fields.

Qingwen Zhang received his master's degree from Guangzhou University of Chinese Medicine in 2006. He has been working at the First Affiliated Hospital of Guangzhou University of Chinese Medicine since 1993. As a professor, he devotes himself to the study of osteonecrosis of the femoral head and knee injuries. His interests concern clinical and basic research on knee injuries.

Huiying Lin received her bachelor's degree from the Guangdong University of Technology, Guangzhou, in 2014. She finished her MSc studies at the Center for Optical and Electromagnetic Research, SCNU, Guangzhou. Her research interests include laser spectroscopy applied to biomedical and food safety topics.

Sune Svanberg obtained his PhD from the University of Gothenburg in 1972; since 1980, he has been a professor of physics at Lund University, Lund, Sweden. For 30 years, he was the head of the Atomic Physics Division, and for 20 years, he was the director of the Lund Laser Centre. Since 2011, he has also been a distinguished professor at SCNU, Guangzhou. His research interests include laser spectroscopic applications to the environmental, food safety, and biomedical fields.

Katarina Svanberg obtained her PhD from Lund University in 1989. She is affiliated with the Department of Oncology, Lund University Hospital, where she has been active as chief consultant and professor of oncology for more than 25 years. Since 2011, she has also been a distinguished professor at the SCNU, Guangzhou. Her research interests concern applications of laser spectroscopy to the biomedical and biophotonics fields.

Peng Chen obtained his PhD from Guangzhou University of Chinese Medicine in 2014. From 2012 to 2014, he was at the Medical School of the University of California at Davis as a joint training PhD candidate. As a surgeon, he works at the First Affiliated Hospital of Guangzhou University of Chinese Medicine where he has been active since 2015. His research interests concern the biomarkers in ONFH and in osteoarthritis.