Journal of Information Hiding and Multimedia Signal Processing ©2014 ISSN 2073-4212
Ubiquitous International Volume **5**, Number **3**, July **2014**

Non-invasive Knee Osteoarthritis Diagnosis via Vibroarthrographic Signal Analysis

Wei-Chun Lin, M.D.[ab*], Tsair-Fwu Lee, Ph.D.[c*§], Shu-Yuan Lin, M.D.[d]
Li-Fu Wu[c], Hung-Yu Wang, Ph.D.[e], Liyun Chang, Ph.D.[f], Jia-Ming Wu[gh]
Jing-Chuan Jiang[c], Chiu-Ching Tuan, Ph.D.[i], Mong-Fong Horng, Ph.D.[e]
Chin-Shiuh Shieh, Ph.D.[e], Pei-Ju Chao, Ph.D.[j§]

[a] Department of Institute of Photonics and Communications
National Kaohsiung University of Applied Sciences,Kaohsiung, Taiwan
[b] Department of Orthopedic, Kaohsiung Municipal Min-Sheng Hospital, Taiwan
[c] Medical Physics and Informatics Laboratory, Department of Electronics Engineering
National Kaohsiung University of Applied Sciences, Kaohsiung, Taiwan
[d] Department of Plastic Surgery, Kaohsiung Municipal Min-Sheng Hospital, Taiwan
[e] Department of Electronics Engineering, National Kaohsiung University of Applied Sciences, Kaohsiung, Taiwan
[f] Department of Medical Imaging and Radiological Sciences, I-Shou University, Kaohsiung, Taiwan
[g] Department of Information Engineering, I-Shou University, Taiwan
[h] Department of Radiation Oncology, E-Da Hospital, Kaohsiung, Taiwan
[i] Department of Electronics Engineering, National Taipei University of Technology,Taipei, Taiwan
[j] Department of Radiation Oncology, Kaohsiung Chang Gung Memorial Hospital and
Chang Gung University College of Medicine, Kaohsiung, Taiwan
* These authors contributed equally to this work.
§ Corresponding authors: Tsair-Fwu Lee, Ph.D., and Pei-Ju Chao, Ph.D

Received November, 2013; revised March, 2014

Abstract. *Crepitus is a prominent sign during the knee joint undergoing a range of motion which can be detected to form the vibroarthrographic (VAG) signals. These signals can be used as useful indicators of osteoarthritis (OA) status for supplementing conventional X-ray imaging in the diagnosis of knee OA. In this study, a non-invasive knee OA diagnosis system was conducted via VAG signal analysis.This system included a goniometer to provide an analog reference signal for positioning, an electronic stethoscope to detect knee VAG signals and an FPGA signal processing system as a system kernel. Power spectra of the signals provided by the Fourier transform were obtained and partition indices calculated. Discriminant functions were built with distribution parameters constructed from the partition indices. The processed VAG signals were compared with X-ray images in OA diagnosis to explore the differences between predicted and observed results. System model performance was evaluated using measures for discriminative ability, including the area under the receiver operating characteristic curve (AUC). The negative predictive value (NPV) was checked for the rate of correctly predicting the absence of OA. The positive predictive value (PPV) is the proportion of patients with OA who are correctly diagnosed.System performance was validated using the receiver operating characteristic curve. The classification result illustrated a sensitivity of 89.52% and a specificity of 67.50%, with a total accuracy rate of 81.52%. The AUC values obtained were 0.68 (95% CI 0.61-0.74). The rates of correctly predicting the lack of OA were approximately 78.6% (NPV) and the proportions of patients with OA who are correctly diagnosed were approximately 82.8% (PPV), respectively.VAG analysis in OA diagnosis provides an economic alternative to X-ray examination in osteoarthritic patients.*
Keywords: Osteoarthritis (OA); Crepitus; Vibroarthrographic signals; Kellgren-Lawrence grading; Fourier transform

1. **Background.** Osteoarthritis (OA) is a major common joint disease worldwide. It is a progressively degenerative process and involves low-grade inflammation, mainly affecting the elderly. It is a highly prevalent disease and causes substantial disability in late life in most developed countries. About 10% of the total world population and more than half of the people aged over 50 years suffer from OA [1,2]. It causes pain, swelling and reduced motion in joints. Healthy cartilage, which is the slippery tissue that covers the ends of the bones in a joint, absorbs the shock during movements. In OA, this cartilage breaks, leading to the bones rubbing together. Knee OA disturbs about 30% of those over 65 years old. Its pathological features include joint space narrowing, osteophyte formation and joint angulation [3, 4]. It gradually worsens with time and there are currently no cures. However, OA therapies do exist that can relieve pain and help patients remain active.

The knee is the most common part of the body to be affected by arthritic degeneration. Injured knees resulting from a variety of traumatic causes are well-known. The very common non-traumatic causes of knee OA include chondromalacia patella, in which the articular cartilage softens, fibrillates and is shed from the undersurface of the patella [5, 6]. One of the major problems during the examination of the causes or progression of these conditions is the difficulty in detecting articular cartilage changes until they become gross, either anatomically or symptomatically. Image-based techniques such as X-ray imaging, computed tomography (CT) and magnetic resonance imaging (MRI) can detect major cartilage pathologies, but fail to characterize the functional integrity of the cartilage, such as its softening, stiffness or fissuring [7].

To diagnose cartilage pathology, arthroscopy is the gold standard method for evaluating cartilage status. The grading system provided by arthroscopy plays an important role in the prognosis and treatment of knee osteoarthritis. However, arthroscopy is an invasive procedure and carries some risks related to anesthesia. Furthermore, arthroscopy is not practical in being repeated in the same patient [8, 9]. Therefore, several researchers have continued to look for alternative tools, such as joint auscultation, to overcome these drawbacks of imaging and arthroscopy.

Crepitus in the knee is often noted during clinical examination of OA patients. This physical examination is performed with one hand of the examiner being placed on the patella during a passive range of motion (ROM). However, it is a subjective assessment and cannot be recorded and analyzed for comparison. Moreover, its interpretation is dependent on the examiner and requires a lot of personal experience. This knee sound signal, generated during knee ROM, represents the acoustic and vibrational signals caused by the joint surfaces rubbing together. It is associated with cartilage pathological conditions such as roughness, softening, breakdown or cartilage loss, and may be a useful index of the osteoarthritic status [10].

Many studies have reported the feasibility and usefulness of this technique for the non-invasive diagnosis of articular dysfunctions via the analysis of knee sounds obtained by an auscultation. Chu et al. devised strategies to reduce the skin friction and ambient noise during recording and to classify the knee sound signals into various categories, such as rheumatoid arthritis, degenerative arthritis and chondromalacia patella, using their auto-correlation function [11, 12]. Kernohan et al. reported that 86% of patients with meniscal injuries produced characteristic signals and that the changes in the normal joint crepitus could be a useful indicator of early cartilage degeneration [13]. They found that the signal was the largest on the affected side, had a large displacement and appeared repetitively at the same knee angle in cycles. McCoy et al. showed the possibility of identifying

chondromalacia patella, meniscus lesions and arthritis using knee sound analysis, based on the division of the sound peaks into frequency groups [14]. Rangayan et al. reported that meniscal lesions demonstrated sharp bursts in the sound signal, which appeared as short energy durations in the range of 0 to 200 Hz in the spectral contour plots, while mild chondromalacia exhibited sound signals as long durations in the frequency range of 0 to 300 Hz [15]. The signals associated with severe chondromalacia were observed to be of relatively low frequencies (0-100 Hz), as expected, due to the loose cartilage tissue existing between the rubbing surfaces. Another report by Nagata et al. discussed the procedures for reducing noise in the recordings of knee joint sounds and the potential of frequency analysis of the sound signals using a narrow band spectrum analyzer in diagnosing osteoarthritis [16]. Reddy et al. demonstrated that the mean power of the acceleration signal in the range of 100 to 500 Hz was significantly different for OA patients compared to rheumatoid arthritis patients [17].

Regarding the signal processing of knee sounds, various techniques have been tested for classifying normal and abnormal knees according to the articular pathology, such as autoregressive [18, 19], least square [20], linear prediction modeling [21], time-frequency analysis [22] and wavelet decomposition [23,24]. In this study, we analyzed knee sound signals using the Fourier domain method. Fourier spectral analysis is widely used in acoustic signal analysis; however, the spectral power partition has not been characterized as features for knee sound analysis yet. Moreover, we explored the set-up of the signal acquiring system in this study. Previous papers on sound characteristics did not compare their results to those from X-ray imaging in the diagnosis of joint pathology.

The objective of this paper was to characterize the Fourier spectral features obtained from normal and abnormal knee sounds. Correlations with X-ray images were made and discriminant functions were then built from the feature model space to see whether knee sound analysis could be used in diagnosing knee OA.

2. **Materials and Methods.**

2.1. **Demographic data.** Fifty-nine cases of patients with degenerative arthritis and 85 cases with no history of knee injury or discomfort were enrolled. Their demographic data including sex, age and disease status were recorded. Every OA patient had undergone knee X-rays for anterior-posterior and lateral views for disease grading with Kellegren-Lawrence (KL) scores [25]. The KL grades were given by two independent orthopedic surgeons and recorded at three compartments of the knee joint: medial, lateral and patellofemoral (PF). The KL grading scale is for classifying the status of OA into one of five grades, with 0 representing normal and 4 the most severe disease:

Grade 0: none (definite absence of OA)

Grade 1: doubtful (doubtful narrowing of joint space and possible osteophyte)

Grade 2: minimal (definite osteophytes and possible narrowing of joint space)

Grade 3: moderate (moderate osteophytes, definite narrowing of joints space, some sclerosis and possible deformity of bone contour)

Grade 4: severe (Large osteophytes, marked narrowing of joint space, severe sclerosis and definite defor- mity of bone contour).

This study was approved by the Medical Ethics Committee of the Kaohsiung Municipal Min-Sheng Hospital (KMMH-IRB10101) and all participants gave informed written consent.

2.2. **Experimental protocol.** An electro-stethoscope was made by assembling a conventional stethoscope with a high-efficiency microphone. The microphone was connected

to the line-in port of a PC. The sound signals were transferred to a PC through an integrated audio card. The recorded signals were then digitized with a sampling rate of 44100 Hz and 16 bits per sample. A flexible electro-goniometer used to measure the knee joint angle was placed on the lateral aspect of the knee, with the axis of rotation at the joint line. Since the knee sound signals might be changed by the pressure between the skin and the bell of the stethoscope, a specially fitted knee brace was used to hold the stethoscope in front of the patella as in Fig. 1a. An overview of the VAG signals recording system flowchart was given in Fig. 1b.

The contact area selected for auscultation was the medial condyle on the patella, to take into consideration the physiological structure and position that could best remove interference from muscle contraction. The knee position in flexion was defined as 90 degrees, while the knee in full extension was defined as 0 degrees. One ROM cycle consisted of one passive extension and one passive flexion over an approximate angle range of $90^\circ \rightarrow 0^\circ \rightarrow 90^\circ$ in 2 seconds.

Prior to the experiment, the subject was warmed up passively to keep the speed of knee flexion and extension constant. After a training session of several ROM cycles in the sitting position, each subject underwent a passive ROM cycle for 20 s, keeping a constant angular velocity as much as possible. During data collection, the passive ROM cycle was kept to nearly 2 s per cycle. If the period is not exactly of the desired length, the variation in the knee angular velocity might affect the frequency characteristics of the sound signals, resulting in errors of the acquired signals. Therefore, to minimize this possibility, the sound signals obtained during one cycle were segmented according to the knee joint angle recorded by the goniometer. The sound signals were aligned simultaneously with the goniometric data. The sound signals collected during 25 to 75 degrees of flexion were taken for further analysis. The signals obtained during 0 to 25 degrees and 75 to 90 degrees, corresponding to the start and end stages of the knee ROM, were discarded due to noise. From a physioanatomical point of view, during the start and end stage of the knee range of motion, the patella is not in full contact with the femur surface. Moreover, a lot of ambient noise related to acceleration/deceleration of the knee joint is more prominent during this period. Therefore, only segments from 25 to 75 degrees of flexion were retained. The ascending signal limb was labeled "up" and the descending limb "down". The ascending limb corresponded to knee extension, while the descending limb corresponded to knee flexion. A difference was observed in these two limbs despite the same tracking path of the patella on the femur surface.

2.3. **Signal processing and feature selection.** The sound signal was input as a standard vector form in the time domain for computer analysis. Fast Fourier transformation of the signal was then performed. We designed a ratio index (R) to characterize the power spectrum property of the signals:

$$R = \frac{\int_{l1}^{u1} f(x)^2 dx}{\int_{l}^{u} f(x)^2 dx} \tag{1}$$

In equation 1, the denominator is the partial sum of the signal power spectra in the frequency domain. In this study, the lower limit l for integration was set at 5 and the upper limit u at 500 [26]. The lower limit l cannot be 1 for two reasons: baseline wandering and the fact that the first four low frequency components may interfere with the cycle of knee range of motion. Therefore, it is necessary to start the partial sum of the power spectra from l=5. On the other hand, the choice of the upper limit u is more flexible

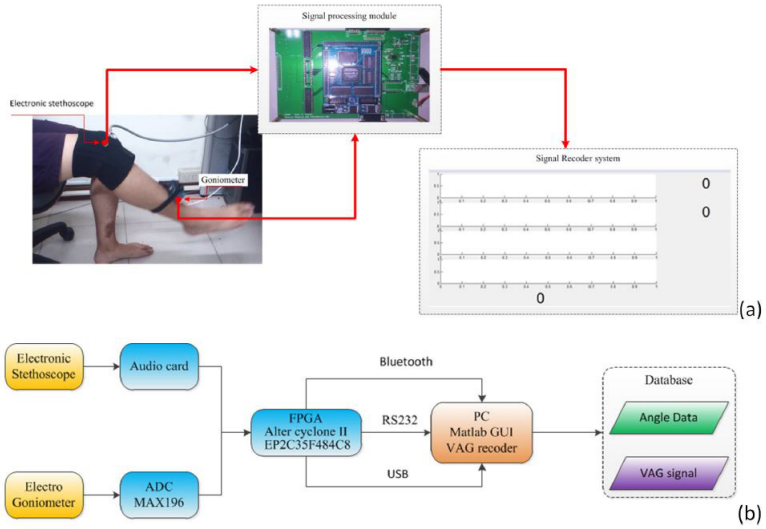

FIGURE 1. (a) Knee flexed (90°) and fully extended (0°) in a sitting position as measured with a goniometer. (b) An overview of the VAG signals recording system flowchart.

due to the fact that Fourier spectrum energy is more concentrated over the low frequency region.

In Eq.1, the denominator is designed to represent the signal variability between normal and OA knee. In this study, the lower limit l1 of this integration was set at 20 and the upper limit u1 at 100.

In addition to the power spectral partial sum ratio R, four statistical parameters were also obtained to complete the feature space characterization. The mean parameter was calculated as:

$$m = \sum_x (x - m) x P(x) \tag{2}$$

Variance of signal was calculated as follows:

$$m = \sum_x (x - m)^2 P(x) \tag{3}$$

Skewness was calculated as:

$$S = \frac{\frac{1}{n}\sum_{i=1}^{n}(x_i - x)^3}{\left(\sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - x)^2}\right)^3} \tag{4}$$

Kurtosis as:

$$K = \frac{\frac{1}{n}\sum_{i=1}^{n}(x_i - x)^4}{\left(\sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - x)^2}\right)^4} \tag{5}$$

The patient data were randomly divided into two groups: the training data group (with 40 patients) and the test data group (with the remaining 104 patients). The training data group had 20 patients with OA and 20 patients without OA. The test data group had 39 patients with OA and 65 without OA.

A VAG discriminant function was used as the predictive feature which can be written as

$$\mathrm{VAG} = \mathrm{A}\,|m - m_{test}| + \mathrm{B}\,|v - v_{test}| + \mathrm{C}\,|S - S_{test}| + \mathrm{D}\,|K - K_{test}| \tag{6}$$

In equation (6), A, B, C and D represent the weightings for each absolute-valued term, respectively. Standard deviation was assigned as 10 and substituted into equation (7), which is known as the Moore- Penrose pseudoinverse of matrix. Therefore, the weightings were obtained as follows:

A=-0.8203, B=1.1960, C=-159.6932 and D=156.5432.

$$\begin{bmatrix} 10 \\ 10 \\ 10 \\ 10 \end{bmatrix} = \begin{bmatrix} A \\ B \\ C \\ D \end{bmatrix} * \begin{bmatrix} m_1 & \dots & m_n \\ v_1 & \ddots & v_n \\ S_1 & & S_n \\ K_1 & \cdots & K_n \end{bmatrix} \tag{7}$$

Four parameters calculated from equations (2) to (5) and the normalized parameters, e.g.,xtest=x+Ntest ,were substituted into equation (6) to evaluate VAG values of normal and OA conditions. If VAGnormal was greater than VAGOA, it was categorized into the OA group.

2.4. **Statistical analysis.** To validate the use of VAG signals in identifying OA, the negative predictive value (NPV) was checked for the rate of correctly predicting the absence of OA. The positive predictive value (PPV) is the proportion of patients with OA who are correctly diagnosed. The equations used to determine the PPV and NPV are listed in (8) and (9). System model performance was also evaluated using measures for discriminative ability, including the area under the receiver operating characteristic curve (AUC). An AUC of 1 corresponds with a perfect prediction and an AUC of 0.5 with no discriminatory power at all. Cutpoint was obtained by using Youden's index method(Youden's index =sensitivity+specicity-1). All analyses were performed using SPSS 17.0.

$$\mathrm{PPV} = \frac{\text{senitivity} \times \text{prevalence}}{\text{senitivity} \times \text{prevalence} + (1 - \text{senitivity}) \times (1 - \text{prevalence})} \tag{8}$$

$$\mathrm{NPV} = \frac{\text{specificity} \times (1 - \text{prevalence})}{\text{specificity}(1 - \text{prevalence}) + (1 - \text{senitivity}) \times \text{prevalence}} \tag{9}$$

3. **Results.** The demographic data of the 144 samples with/without OA are listed in Table 1, the training set (with 40 patients) and the testing set (with the remaining 104 patients). The training set had 20 patients with OA and 20 patients without OA. Fig. 1 shows our recording system. In this study, the patellofemoral KL grade was taken as the only grade for building the discriminant model. The KL grades of three compartments were recorded and their correlation relationship explored in Table 2. Using the non-parametric Spearman's rho test, all three KL variables achieve statistical signi

cance at alpha level of 0.01.

As shown in Fig. 2, the sound signals are aligned simultaneously with the goniometer data. The sound signals collected during 25-75 degrees of exion are taken for further analysis. Fig. 3(a) shows VAG signals from one normal knee and (b) shows sound signals of abnormal knee.

The classier as equation (6) is built using twenty OA and twenty control samples; the remaining 104 data samples are used for validation. The scatter-plot of the study samples

was shown in Fig.4. The red Os along the top of the graph show the individual patient with osteoarthritis. The green Xs along the bottom show the patients without knee osteoarthritis. The discriminant function built from equation (6) has better separating ability than pure R value.

TABLE 1. Demographic data

			patellofemoral	medial	lateral
Spearman's rho	patellofemoral	Correlation Coefficient	1.000	.558*	.534*
		Sig. (2-tailed)		<.001	<.001
	medial	Correlation Coefficient	.558*	1.000	.575*
		Sig. (2-tailed)	<.001		<.001
	lateral	Correlation Coefficient	.534*	.575*	1.000
		Sig. (2-tailed)	<.001	<.001	

Abbreviation: KL: *Kellegren-Lawrence scores;*
*. Correlation is significant at the 0.01 level (2-tailed).

TABLE 2. Correlation between the KL grades

			patellofemoral	medial	lateral
Spearman's rho	patellofemoral	Correlation Coefficient	1.000	.558*	.534*
		Sig. (2-tailed)		<.001	<.001
	medial	Correlation Coefficient	.558*	1.000	.575*
		Sig. (2-tailed)	<.001		<.001
	lateral	Correlation Coefficient	.534*	.575*	1.000
		Sig. (2-tailed)	<.001	<.001	

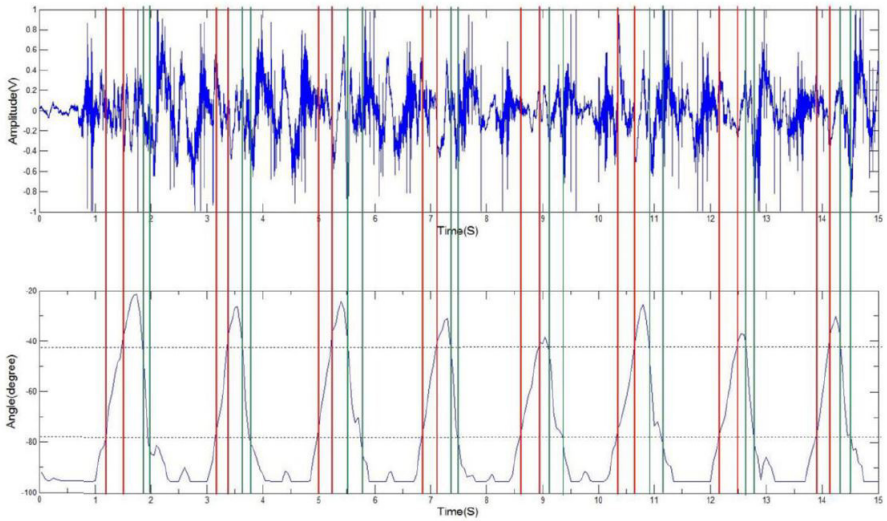

FIGURE 2. Knee sound signals segmented"up" and "down" during 25° to 75° of flexion.

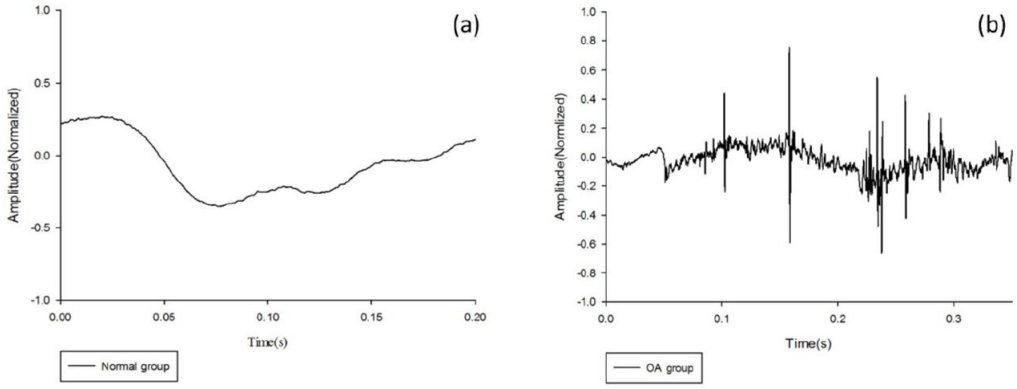

FIGURE 3. (a) VAG signals from one normal knee and (b) sound signals from abnormal knee. The recording system used was set in the same condition for recording these two signals. Abbreviation: VAG: vibroarthrographic;

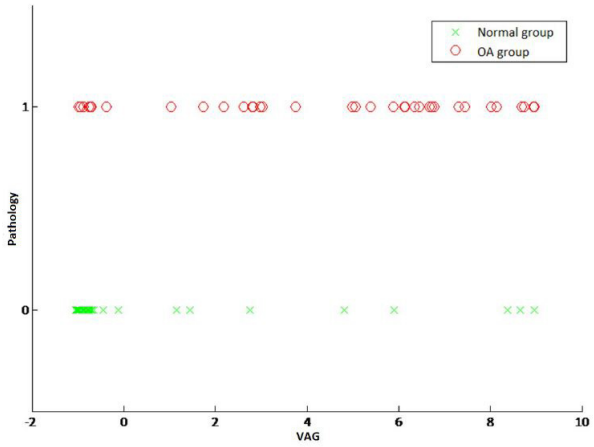

FIGURE 4. The scatter-plot of the study samples. The red Os along the top of the graph show the individual patient with osteoarthritis. The green Xs along the bottom show the patients without knee osteoarthritis.

TABLE 3. Test Result

Performance measure	(%)
Specificity	67.5
Sensitivity	89.5
PPV	82.8
NPV	78.6
AUC	80.7

Abbreviation: PPV: positive predictive value; NPV: negative predictive value; AUC: area under the receiver operating characteristic curve;

The classification results are shown in Table 3. The sensitivity rate was 89.52% and specificity rate 67.50%. The total accuracy rate was 81.52%. According to Table 3, the AUC values obtained were 0.864 (95% CI 0.791-0.937) with a standard error (SE) of 0.037, as illustrated in Fig. 5. The rates of correctly predicting the lack of OA were

approximately 78.6% (NPV) and the proportions of patients with OA who are correctly diagnosed were approximately 82.8% (PPV), respectively.

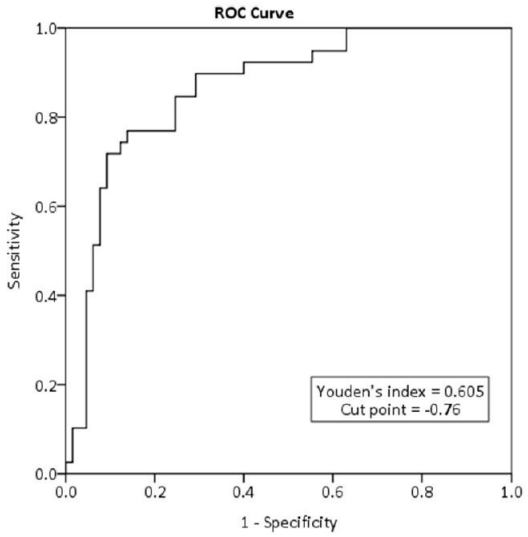

FIGURE 5. The receiver operating characteristic curve analysis for prediction of with/without knee osteoarthritis. Cutpoint was obtained by using Youdens index method.

4. **Discussion.** Nowadays, X-ray remains the gold standard for diagnosing OA. Although auscultation of the knee is non-invasive, it is still not widely prevalent in clinical practice. The crepitus sounds generated during knee ROM are non-stationary and involve multiple components. Due to the potential harmful irradiation effects of X-ray and its cost, the non-invasive knee sound auscultation therefore provides a useful alternative to routine X-ray examination. In this study, the grading of osteoarthritis by X-ray was compared to the signal properties of VAG.

For every patients X-ray, three KL grades were assigned. The KL grades were recorded as medial, lateral and patellofemoral compartment respectively. There exists statistical significant correlation between these grades as shown in table 3. Therefore, in this study, the patellofemoral KL grade was taken as the only grade for building the discriminant model. From the pathophysiological point of view, the patellofemoral joint plays a more important role than the other two compartments. For aging patients, the patellofemoral OA change always compares to medial compartment change, while the lateral compartment is least involved. The phenomenon may be linked to two observations: the patellofemoral joint is the major friction surface during knee flexion-extension exercise, and the human center of gravity lies in middle of body so the medial compartment has higher stress than lateral compartment. However, if an intricate model can combined the three KL grades, it will be of great use to explore the relationships between the three KL grades and obtained a better discriminant model.

We used a conventional microphone with the line-in cable connected to a personal computer. The microphone was then connected to a stethoscope plastic tube. This innovative device can work well in acquiring sound signals with good quality and ease. In the setting up of the equipment for data acquisition, the goniometer is of vital important and accompanies the stethoscope. As shown in Fig.2, goniometric data can provide information on the knee position and facilitate data segmentation. We used the VAG signals during 25 to 75 degrees of flexion, while signals during the start and end stages of knee ROM were discarded.

Regarding the variability of each cycle length, Fourier analysis was adopted. Since the precise control of each cycle time length is not feasible, the analysis method should be robust to the variability in signal lengths. We believe that the fundamental frequency behavior is more constant in this respect. Indeed, high frequency components were more prominent than low frequency ones (Fig.3). However, to compare the normal and OA groups, differences in the frequency spectral power must be represented as a single index. Hence, we designed the partition ration R as described by Eq.1.

In equation 1, the denominator was chosen for normalization of the sound intensity. The lower limit of the denominator integration must not contain less than five low frequency components. As mentioned previously, the first low frequency component is DC and represents the offset effect, while the other low frequency components may interfere with the knee range of motion. The choice of the upper limit is more flexible because the higher frequency power is more diminished in the Fourier domain.

The choice of the numerator integration limits should emphasize the high frequency differences between normal and osteoarthritic knees. In this study, the lower and upper limits chosen corresponded to the 10 to 50 Hz region, comparable to previous studies.

Figure 4 shows the scatter-plot of the study samples with wider distribution of OA knees signals. This wider variability explained the multi-factorial nature of knee crepitus sounds. On the other hand, it also represents the heterogeneity of the patient group. The normal knee group represented a more homogenous collection of healthy subjects. There was a substantial overlap between the two groups representing normal and OA knees respectively. We believe this overlap contributes to misclassification. However, it was still possible to obtain good classification using VAG signals.

5. **Conclusions.** In this study, knee sound signals were obtained by an innovative stethoscope device used together with a goniometer. The sound signals were input into a personal computer and segmented according to the goniometric data. Fourier transformation of the signals was performed to obtain power spectrum and calculate partition indices. Distribution parameters were obtained and the optimum classification threshold then decided. Our results showed good sensitivity and specificity rates. As the result, we find that VAG analysis of the knee provides an economical alternative to X-ray examination in osteoarthritic patients, which can also monitor of knee joint pathology at an early stage.

Competing interests: Part of this study was presented on the International Conference on Genetic and Evolutionary Computing (ICGEC 2012).

Acknowledgment. This study was supported financially, in part, by grants from NSC-101-2221-E-151-007-MY3, and NSC-102-2221-E-151-032.

REFERENCES

[1] D. T. Felson, and Y. Zhang, An update on the epidemiology of knee and hip osteoarthritis with a view to prevention, *Arthritis & Rheumatism*, vol. 41, no. 8, pp. 1343-1355, 2004.

[2] L. Shamir, S. M. Ling, W. W. Scott, A. Bos, N. Orlov, T. J. Macura, et al., Knee X-ray image analysis method for automated detection of Osteoarthritis, *IEEE Trans. on Biomedical Engineering*, vol. 56, no. 2, pp. 407-415, 2009.

[3] J. W. Prescott, M. Pennell, T. M. Best, M. S. Swanson, F. Haq, R. Jackson, et al., *An automated method to segment the femur for osteoarthritis research*, pp. 6364-6367, 2009.

[4] E. Yelin, and L. F. Callahan, Special article the economic cost and social and psychological impact of musculoskeletal conditions, *Arthritis & Rheumatism*, vol. 38, no. 10, pp. 1351-1362, 1995.

[5] C. B. Frank, R. M. Rangayyan, and G. D. Bell, Analysis of knee joint sound signals for non-invasive diagnosis of cartilage pathology, *IEEE Engineering in Medicine and Biology Magazine*, vol. 9, no. 1, pp. 65-68, 1990.

[6] J. M. Grenier and M. A. Wessely, Knee MRI. Part II: MR imaging of common internal derangements affecting the knee, *Clinical Chiropractic*, vol. 7, no. 3, pp. 131-140, 2004.
[7] T. Neogi, M. Nevitt, J. Niu, L. Sharma, F. Roemer, A. Guermazi, et al., Subchondral bone attrition may be a reflection of compartment-specific mechanical load: the MOST Study, *Annals of the rheumatic diseases*, vol. 69, no. 5, pp. 841-844, 2010.
[8] B. V. Berg, F. Lecouvet, B. Maldague, and J. Malghem, MR appearance of cartilage defects of the knee: preliminary results of a spiral CT arthrography-guided analysis, *European radiology 2004*, vol. 14, no. 2, pp. 208-214,2004.
[9] I. V. Breuseghem, Ultrastructural MR imaging techniques of the knee articular cartilage: problems for routine clinical application, *European radiology*, vol. 14, no. 2, pp. 184-192, 2004.
[10] C. C. Jiang, J. H. Lee, and T. T. Yuan, Vibration arthrometry in the patients with failed total knee replacement, *IEEE Trans. Biomedical Engineering*, vol. 47, no. 2, pp. 219-227, 2000.
[11] M. Chu, I. Gradisar, and R. Mostardi, A noninvasive electroacoustical evaluation technique of cartilage damage in pathological knee joints, *Medical and Biological Engineering and Computing*, vol. 16, no. 4, pp. 437-442, 1978.
[12] M. L. Chu, I. A. Gradisar, M. R. Railey, and G. F. Bowling, Detection of knee joint diseases using acoustical pattern recognition technique, *Journal of Biomechanics*, vol. 9, no. 3, pp. 111-114, 1976.
[13] W. G. Kernohan, D. E. Beverland, G. F. Mccoy, S. N. Shaw, R. G. Wallace, G. C. Mccullagh, et al., The diagnostic potential of vibration arthrography, *Clinical orthopaedics and related research*, vol. 210, pp. 106-112, 1986.
[14] G. F. McCoy, J. D. McCrea, D. E. Beverland, W. G. Kernohan, and R. Mollan, Vibration arthrography as a diagnostic aid in diseases of the knee. A preliminary report, *Journal of Bone & Joint Surgery, British Volume*, vol. 69, no. 2, pp. 288-293, 1987.
[15] R. Rangayyan, C. Frank, G. Bell, and R. Smith, Analysis of knee joint sound signals, *Proc. of the Annual International Conference of Engineering in Medicine and Biology Society*, pp. 712-713, 1988.
[16] Y. Nagata, Joint-sounds in gonoarthrosisXclinical application of phonoarthrography for the knees, *J UOEH*, vol. 10, pp. 47-58, 1988.
[17] N. P. Reddy, B. M. Rothschild, E. Verrall, and A. Joshi, Noninvasive measurement of acceleration at the knee joint in patients with rheumatoid arthritis and spondyloarthropathy of the knee, *Annals of biomedical engineering*, vol. 29, no. 12, pp. 1106-1111, 2001.
[18] J. H. Lee, C. C. Jiang, and T. T. Yuan, Vibration arthrometry in patients with knee joint disorders, *IEEE Trans. Biomedical Engineering*, vol. 47, no. 8, pp. 1131-1133, 2000.
[19] S. Tavathia, R. M. Rangayyan, C. B. Frank, G. Bell, K. Ladly, and Y. T. Zhang, Analysis of knee vibration signals using linear prediction, *IEEE Trans. Biomedical Engineering*, vol. 39, no. 9, pp. 959-970, 1992.
[20] Z. M. Maussavi, R. M. Rangayyan, G. D. Bell, C. B. Frank, and K. Ladly, Screening of vibroarthrographic signals via adaptive segmentation and linear prediction modeling, *IEEE Trans. Biomedical Engineering*, vol. 43, no. 1, pp. 15, 1996.
[21] S. Krishnan, R. Rangayyan, G. Bell, C. Frank, and K. Ladly, Adaptive filtering, modelling and classification of knee joint vibroarthrographic signals for non-invasive diagnosis of articular cartilage pathology, *Medical and Biological Engineering and Computing*, vol. 35, no. 6, pp. 677-684, 1997.
[22] R. M. Rangayyan ,and Y. Wu, Screening of knee-joint vibroarthrographic signals using statistical parameters and radial basis functions, *Medical and Biological Engineering and Computing*, vol. 46, no. 3, pp. 223-232, 2008.
[23] Y. Shen, R. Rangayyan, G. Bell, C. Frank, Y. Zhang, and K. Ladly, Localization of knee joint cartilage pathology by multichannel vibroarthrography, *Medical engineering & physics*, vol. 17, no. 8, pp. 583-594, 1995.
[24] K. Umapathy, and S. Krishnan, Modified local discriminant bases algorithm and its application in analysis of human knee joint vibration signals, *IEEE Trans. Biomedical Engineering*, vol. 53, no. 3, pp. 517-523, 2006.
[25] H. J. Park, S. S. Kim, S. Y. Lee, N. H. Park, J. Y. Park, Y. J. Choi, et al., A practical MRI grading system for osteoarthritis of the knee: Association with Kellgren-Lawrence radiographic scores, *European Journal of Radiology*, vol. 82, no. 1, pp. 112-117, 2012.
[26] T. F. Lee, W. C. Lin, L. F. Wu, and H. Y. Wang, Analysis of Vibroarthrographic Signals for Knee Osteoarthritis Diagnosis, *Proc. of the 6th International Conference on Genetic and Evolutionary Computing*, pp. 223-228, 2012.