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Computer-aided diagnosis of early knee osteoarthritis based on MRI T2 mapping

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Abstract. This work was aimed at studying the method of computer-aided diagnosis of early knee OA (OA: osteoarthritis). Based on the technique of MRI (MRI: Magnetic Resonance Imaging) T2 Mapping, through computer image processing, feature extraction, calculation and analysis via constructing a classifier, an effective computer-aided diagnosis method for knee OA was created to assist doctors in their accurate, timely and convenient detection of potential risk of OA. In order to evaluate this method, a total of 1380 data from the MRI images of 46 samples of knee joints were collected. These data were then modeled through linear regression on an offline general platform by the use of the ImageJ software, and a map of the physical parameter T2 was reconstructed. After the image processing, the T2 values of ten regions in the WORMS (WORMS: Whole-organ Magnetic Resonance Imaging Score) areas of the articular cartilage were extracted to be used as the eigenvalues in data mining. Then, a RBF (RBF: Radical Basis Function) network classifier was built to classify and identify the collected data. The classifier exhibited a final identification accuracy of 75%, indicating a good result of assisting diagnosis. Since the knee OA classifier constituted by a weights-directly-determined RBF neural network didn't require any iteration, our results demonstrated that the optimal weights, appropriate center and variance could be yielded through simple procedures. Furthermore, the accuracy for both the training samples and the testing samples from the normal group could reach 100%. Finally, the classifier was superior both in time efficiency and classification performance to the frequently used classifiers based on iterative learning. Thus it was suitable to be used as an aid to computer-aided diagnosis of early knee OA.

Keywords: Knee OA, MR T2 mapping, RBF neural network, computer-aided diagnosis

1. Introduction

The technique for early diagnosis of osteoarthritis of the knee is a hot research topic in clinical medicine, medical imaging and other fields. However the pathogenesis of this disease is not clear, and

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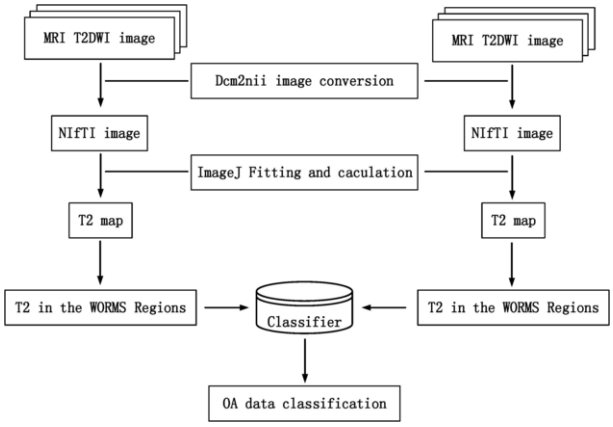

Fig. 1. Diagram of the implementation of specific research work

the irreversible and difficult-to-treat condition force the patients to suffer long-term pain and seriously harming the quality of their life [1]. Thus Early detection, diagnosis, and intervention are highly desired to conquer this disease.

Recent researches in OA clinical pathology have found that the matrix of articular cartilage has already changed before the morphological damage of cartilage. The main changes include the loss of PGs (proteoglycans), the damaged collagen lattice structure, and the higher water content [2]. The quantatitive changes in the biochemical components of articular cartilage can directly reflect the development of OA. MR T2 mapping is a MR technique to evaluate the osteoarthritis through quantitative analysis of the data about the articular cartilage's components. A number of clinical trials have demonstrated that the T2 values reflect good sensibility, specificity, and repeatability of the OA magnetic resonance rating [3]. Especially in the WORMS system, there is a strong correlation between T2 and OA.

The computer-aided diagnosis(CAD) technique [4,5] could be used to perform the MR T2 mapping on an offline general computer platform. The data mining was implemented based on the eigenvalues, i.e. the T2 values of ten regions in the WORMS (WORMS: Whole-organ Magnetic Resonance Imaging Score) areas of the articular cartilage. Then a RBF classifier was built to classify the data about the knee OA via consulting the result of clinical imaging dignosis and the sample training. Figure 1 shows the technology roadmap.

MR T2 mapping, which obtains T2 map from original T2WI image, is one of the widely-used MR physiologic imaging techniques for cartilage [6]. T2 map is a map of the values of physical parameter T2 showing the transverse relaxation time of the observed tissue or structure. Through the quantitative measurement of T2 values in regions of interest of the tissue and then analysis of the relationships between the values and the biochemical components of the tissue, the quantitative evaluation of variation in the biochemical components of the tissue could be achieved [7].

At present, the MRI Recht rating method is usually employed in the clinical rating of cartilage injury. Taking the most serious injury in the sagittal image of articular cartilage as the input criteria, the injury can be divided into five grades from normal to abnormal. In the revised WORMS system for the tibia and femoral cartilage, the knee cartilage was divided into ten regions for observation. Many scholars have revealed that there is a widespread and strong correlation between the T2 values of cartilage and the WORMS values in each subregion, particularly in the central load-bearing regions (MFc, MTc and LTc) - the T2 values increase as the disease worsens. This highlights the gradual process of cartilage degeneration [8,9].

The emphasis of this study was the data mining based on the WORMS areas. Given the small number of samples, the cartilage injury was divided into such three groups of normal, mild OA, and serious OA in clinical diagnosis in practice as suggested by clinical diagnostician. The Recht Grade 0 and Grade I represented mild OA (Group OA1), Grade II and III represented serious OA (Group OA2); Grade IV denoted a widespread full-thickness loss of cartilage, in which case the T2 values were relatively hard to calculate and thus excluded in the study.

2. Materials and methods

2.1. Materials and tools

More than five echo times (the range of echo time: $5 \leq \text{TE} \leq 70$ ms) in the same SE sequence were chosen for the scanning of the MRI images of the knee joints obtained. The lower edge of patella was at the center of each image, and the cross section should include the medial and lateral condyles of the lower part of femur. Eight echo times - 8.9, 17.8, 26.7, 35.6, 44.5, 53.4, 62.3 and 71.2 (ms) were arranged in the echo time chain for T2 mapping. After MRI scanning, the image data were kept in new files in a sequence of check of use, normally in the format of DICOM (Digital Imaging and Communications in Medicine).

ImageJ software is a Java-based public image processing and analysis program developed by Professor Wayne Rasband at NIH (National Institutes of Health). It supports image stacks, a series of images that share a single window in image processing, it is multithreaded. This is a basis for estimating the T2 values through fitting of multiple images.

2.2. Methods

2.2.1. Collection of the T2 values of knee joints

Selecting different images of the same thin layer at different echo times separately, then an image stack of the T2-weighted images of the thin layer at different echo times was generated (See Figure 2).

The image processing must be performed on the images of the same thin layer at different echo times, and no changes in their relative positions were allowed. As the draw slip for browsing the image stack was moved from left to right, the luminance of the images exhibited a gradient variation from brightness to darkness, resulting in the T2 map of the cross section of the relevant knee joint. The T2 map in the

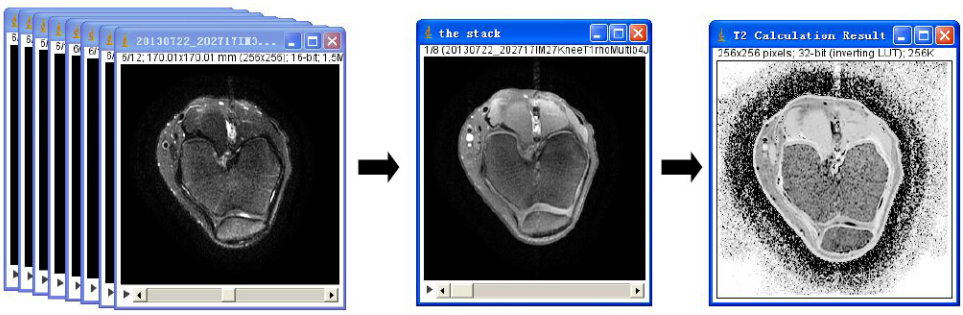

Fig. 2. A T2 map from 8 images of the same thin layer at different echo times

format of grayscale displayed the spatial distribution of the T2 values of cartilage, and each pixel denoted a T2 value.

According to the function of MR transverse relaxation time T2:

$$M_{xy} = M_0 e^{-\frac{t}{T_2}} \tag{1}$$

the T2 value of each pixel in at least two T2WI images at the same imaging position could be calculated:

$$T_2 = \frac{TE_2 - TE_1}{In(S_1/S_2)} \tag{2}$$

Designating the signal strength at the time of t as $S(t)$, then the following formula was yielded through calculating the logarithm for both sides of the formula above:

$$InS(t) = InS_0 + \frac{1}{T_2} \times t \tag{3}$$

Eq.(3) was a linear equation. Through calculating the logarithm of the signal strength S of the corresponding pixel in various images as well as the combined linear fitting with the corresponding TE values, InS0 and T2 values were obtained.

A ROI (ROI: Region of Interest) (x=150, y=180, T2=37.58ms) in the image stack was picked out randomly. The signal strength of 8 imges at different echo times was measured separately (the corresponding results: 1354.0, 1306.0, 945.0, 813.0, 632.0, 489.0, 338.0 and 354.0), then the T2 decay curve of this ROI was calculated using Excel, as shown in Figure 3. The result of curve fitting showed a relatively good fit to the randomly selected data points, indicating that the calculation through fitting of T2 map was characterized by good stability and strong R2 correlation. Therefore, the acuracy of the measurement of T2 values was ensured.

Because human eyes are not sensitie to the grayscale, the pseudo-color image processing technique was used so that the T2 map could display outstanding contrast ratio of knee cartilage, as shown in Figure 4.

According to WORMS partition method, the femur and tibia in a sagittal image of a knee joint has three areas - the anterior, central, and posterior areas, respectively. Three times of sampling were conducted

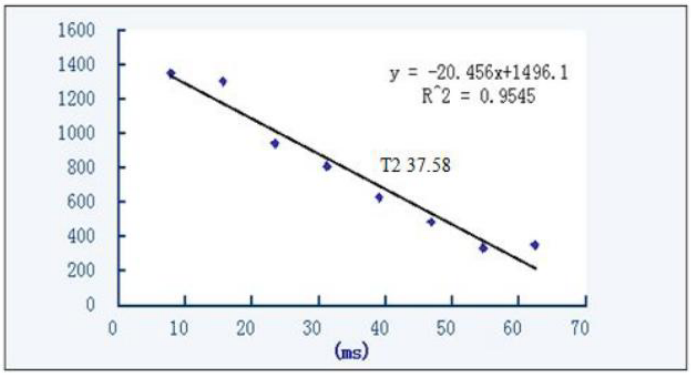

Fig. 3. Decay curve of T2 of a pixel in a specific region of the tissue

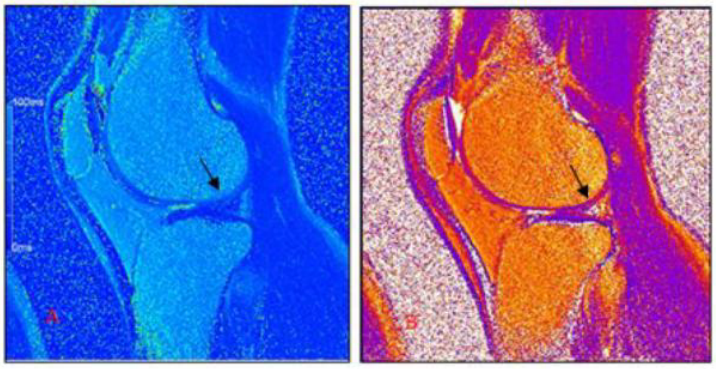

Fig. 4. A comparison between the images of the same thin layer after the pseudo-color processing respectively in the online Workstation and offline computer. Figure 4(A) is the pseudo-color T2 map created by the processing in an online workstation after magnetic resonance, and Figure 4(B) is the pseudo-color T2 map created by the processing on an offline computer platform. The comprison of the two images shows that Figure 4(B) displays more distinct artilage (as indicated by the arrow) and better effect of layering, in which three layers of the tissue can be observed clearly.

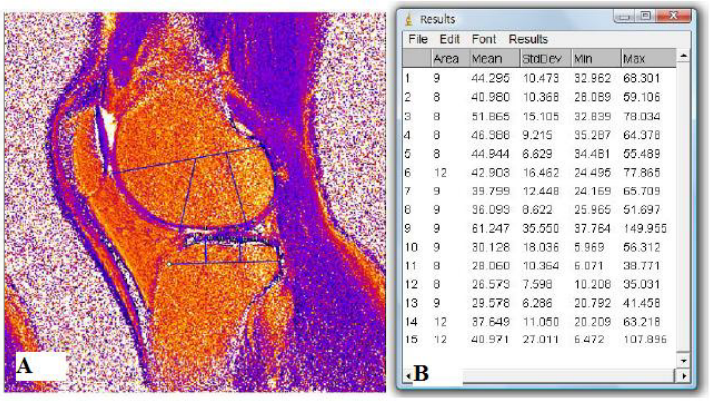

Fig. 5. Measurement of the T2 values in the sagittal image of the knee joint. Figure 5(A) shows the window for measurement of the lateral knee joint. It is divided into 6 areas according to WORMS, and each area (with an exception of the anterior femur area) is further partitioned into three regions of interest. Figure 5(B) dislays the record of the 15 regions of interest in the lateral joint knee

respecively in these areas except for the anterior femur. The data from A a total of 15 samples of each thin layer were collected, as shown in Figure 5.

The recorded data were accurate to the second decimal place. The OA injury was divided into such three groups of normal, mild OA, and serious OA in accordance with clinical diagnosis. Based on the sample data in Figure 5 as the input object, together with the data of the 15 ROIs in the medial area, a whole data set of the T2 values of the ten regions in the WORMS areas was obtained, as listed in Table 1. Finally, the data of 30 samples in total were obtained.

2.2.2. T2 data classification based on RBF neural network

RBF neural network is an efficient feedforward neural network model of a single hidden layer widely used in data mining. It has the best approximation performance and global optimal characteristics that were absent in other feedforward networks [10]. The constructed neural network classifier also has good performane in T2 data classification.

Table 1
T2 values of the WORMS areas of the knees of adults in the normal group (in ms)

area	MFc			MFp			MTa			MTc			MTp		
ROI	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
T2	50.37	45.98	47.94	45.55	37.23	39.19	53.35	28.99	21.97	26.38	27.92	32.93	36.93	35.55	46.44
area	LFc			LFp			LTa			LTc			LTp		
ROI	1	2	3	1	2	3	1	2	3	1	2	3	1	2	3
T2	44.47	53.00	44.38	57.50	47.10	36.43	88.54	50.64	70.29	22.00	37.90	32.38	28.58	27.35	32.88

In a normalized nneural network model, the input vector of all the training samples was the center of the Gaussian excitation function of the hidden neurons in the network, and the common Gaussian function was used to excite the hidden neuron i [11]:

$$r_i(x) = \exp(-\frac{||x - I_i||^2}{2\sigma_i^2}), \quad x, I_i \in R^M, \sigma_i > 0 \tag{4}$$

where I_i was the center of the Gaussian RBF (also the corresponding input vector of the training sample i) and had the same number of demensions as the input x of the neural network. σ_i was the variance of the Gaussian excitation function and determined the width of the function from the central point.

The sample set was expressed as $\{I_i, O_i\}_{i=1}^N$. Inputing the training sample I_k, $(k = 1, 2, \cdots, N)$ into the network, the expected output vector should be O_k, but the actual output of the network was $y_k = [y_{k1}, y_{k2}, \cdots, y_{kJ}]^T$, which could be given as

$$y_{kj}(I_k) = \sum_{i=1}^{N} w_{ij} r_{ki}(I_k) = \sum_{i=1}^{N} w_{ij} \exp\left[-\frac{1}{2\sigma_i^2} \sum_{m-1}^{M} (I_{km} - I_{im})^2\right]$$

where $j = 1, 2, \cdots, J, w_{ij} (i = 1, 2, \cdots, N; j = 1, 2, \cdots, J)$ represented the connection weights from the neuron i in the hidden layer to the neuron i in the output layer, and σ_i was the variance of Gaussian excitation function of the neuron i.

In the structure of the classifier constituted by the RBF neural network of T2 values, the input layer had $M = 8$ neurons, the hidden layer had $N = 38$ neurons, and the output layer had $J = 3$ neurons. RBF neural network classifier was supposed to master the determination of two network parameters: the variance of the Gaussian excitation function of the hidden neurons and the connection weights between related neurons.

The variance formula below was used in the calculation and determination of each variance $\sigma_i (i = 1, 2, \cdots, N)$:

$$\sigma = \sigma_1 = \sigma_2 = \cdots = \sigma_N = \frac{L_{m\alpha}}{\sqrt{2N}} \tag{5}$$

where $L_{m\alpha}$ was the maximum distance between centers (i.e. the maximum norm distance between the column vectors of I).

Based on the concept of matrix pseudoinversion the connection weights $w_{ij} (i = 1, 2, \cdots, N; j = 1, 2, \cdots, J)$ in the RBF neural network were determined:

$$W = \Gamma^+ O^T \tag{6}$$

Where W represented the weight of w_{ij} in the column N and the row J of the matrix ($i = 1, 2, \cdots, N; j = 1, 2, \cdots, J$). Then the excited matrix $\Gamma = [r_{ki}] \in R^{N \times N}$ was input, in which

$$r_{ki} = \exp\left[\frac{||I_k - I_j||^2}{2\sigma^2}\right], \quad k_i \in \{1, 2, \cdots, N\} \tag{7}$$

In a normalized RBF neural network, if $\Gamma \in R^{N \times N}$ was a non-singular matrix, the pseudoinversion of the matrix Γ^+ could be considered as the inversion of matrix Γ^{-1} directly, i.e the $W = \Gamma^{-1}O^T$; or the pseudoinversion of the matrix Γ^+ would remain with $W = \Gamma^+ O^T$ [12].

Having input the data of sample I_i that was not studied or tested, the RBF neural network output was generated via RBF neural network calculation as follows:

$$y_i = [y_{i1}, y_{i2}, \cdots, y_{iJ}]^T \tag{8}$$

Then the network output y_i was normalized in this way: if $y_{ij} = m\alpha\{y_{i1}, y_{i2}, \cdots, y_{iJ}\}$, set $y_{ij} = 1$, or set $y_{ij} = 0$, $j = 1, 2, \cdots, J$.

The class of an unknown sample I_i was determined according to the result of the normalization. Since the T2 data sets were made up of a series of character class identifier, it was not advisable to implment direct processing using the RBF neural network. Therefore, [1, 0, 0], [0, 1, 0] and [0, 0, 1] were set as the numerical class identifiers of the three classes of normal, mild OA, and serious OA respectively. If the normalized output of a studied RBF neural network was [1, 0, 0], the related sample should be classified as a normal sample. If the normalized output was [0, 1, 0], the related sample should belong to the class of mild OA. If the normalized output was [0, 0, 1], there was occurrence of serious OA in the related sample.

Taking T2 values as the eigenvalues, a normalized RBF neural network model classifier based on the weights-directly-determined method was built. The T2 data set includes three classes of output, i.e. the normal, mild OA, and serious OA. A total of thirty input data corresponded to the values of the ten regions (known as MFc, MFp, MTa, MTc, MTp, LFc, LFp, LTa, LTc, and LTp respectively, in ms) of each class. A total of thirty output corresponded to the input data of the ten regions (known as MFc, MFp, MTa, MTc, MTp, LFc, LFp, LTa, LTc, and LTp respectively, in ms) of each class. The test had used the data of 46 samples in total, among which 25 were in the normal class, 14 were in the mild OA class and 7 in the serious OA class. Then, 21, 12 and 5 samples were randomly picked out from the three classes respectively, to establish a training sample set ($N = 21 + 12 + 5 = 38$), while the rest formed a testing sample set.

3. Results

In this research, 128 pieces of image data about the diagnosis of knee OA were collected from the platforms for scientific communication with various domestic medical institutions, among which 46 pieces of high-quality MRI images were selected as the data sources for T2 mapping. A total of 1380 T2 values of the regions of interest were measured successfully, and then tested by spss16.09. The results are displayed in Table 2.

The test finally succeeded in generating a normalized RBF neural network based on the T2 eigenvalues through the study and training of the data from 38 samples, the training accuracy for neurons was 100%,

Table 2
T2 values of each region of the normal and abnormal groups

		Normal	Mild OA		Serious OA	
No.	Feature	Average (ms)	Average (ms)	P value	Average (ms)	P vaule
1	MFc	47.54	58.08	0.002	129.75	0.000
2	MFp	46.13	47.14	0.697	49.17	0.321
3	MTa	44.34	46.69	0.510	77.67	0.000
4	MTc	39.82	41.20	0.665	60.69	0.015
5	MTp	42.95	43.10	0.956	47.99	0.171
6	LFc	45.67	55.26	0.014	153.11	0.000
7	LFp	44.06	45.20	0.679	54.58	0.012
8	LTa	45.54	50.32	0.151	66.01	0.001
9	LTc	37.49	38.34	0.742	51.11	0.007
10	LTp	40.24	45.54	0.059	39.38	0.793

the training time was 0.0038s, the testing accuracy was 75%, and the total neuron number was 38. Among the 8 samples tested by the classifier, four normal samples of knee joints were classified correctly, demonstrating a classification accuracy of 100% for the normal group's data. However, one of the mild OA samples was classified into the normal group, and one of the serious OA samples was classified into the mild OA group.

On the one hand, the test proved that the MRI T2 mapping of knee joints was sensitive to the variation in the T2 values during the early degeneration of articular cartilage. On the other hand, it demonstrated the effectiveness of the RBF neural network classifier in the classification of data about knee OA. On the basis of matrix inversion and pseudoinversion, the classifier utilized the the center vector, variance, and weights-direct-determination methods instead of any iterations. Moreover, it was superior both in time efficiency and classification performance to the frequently used classifiers based on iterative learning - the testing of eight samples took only about 0.0038s. This further demonstrated that the RBF was suitable to be used as an aid to computer-aided diagnosis of early knee OA.

4. Discussion

The measurements of the T2 values of knee cartilage were similar to the relevant reports at home and abroad [13]. The average T2 value of knee cartilage is normally around 43.37ms. The T2 values of the central load-bearing regions in the OA groups were relatively high, possibly due to the effect of stree. The central regions of the WORMS areas were the sensitive observation areas for the early diagnosis of knee OA and the evaluation of treatment effect. Some samples showed little difference in the sum of the T2 values, but they belonged to different classes according to diagnostic results. It was primarily because the locations of data layering in different regions were not the same. Besides, the three classes defined in the classification in this study may be too rough, and the weight of the effect of OA on different WORMS areas may differ for each individual due to the anatomical and physiological characteristics of knee cartilage.

The T2 values of the OA groups were significantly higher than those of the normal group, consistent with the result by Dunn [14]. This result also supports the conclusion that early degradation of cartilage is caused by the damage of collagenous fiber, the loss and displacement of collagenous tissue and the resulting increase in the water content in cartilage tissue.

The normalized RBF neural network model constructed based on the T2 values exhibited an mediocre accuracy in OA classification, possibly due to the following reasons:

1. The numbers of samples were relatively small. There were only 12 training samples of mild OA and 5 training samples of serious OA, impacting the significance of statistical difference to a large degree. Therefore, via larger-scale testing and training of more samples, the identification accuracy of the classifier could be improved.
2. The data source was too simple. The T2 values as the only eigenvalues were inadequate. If some other features, such as the gender, age, BMI (Body Mass Index), hormone levels, human morphology of each sample, were added to form a multidimensional parametric data set according to the clinical diagnosis of OA, the performance of the classifier could be greatly enhanced.
3. The classes defined in the classifier were too rough. The three classes based on the MR Recht rating method failed to correlate the WORMS areas and WORMS scores, resulting in the wrong classification. Furthermore, what the T2 values reflected was the variation in the tissue's biochemical information, inconsistent with the morphological diagnostic criteria to some extent.

However, simply the T2 values could ensure an OA classification accuracy of only 75%, which no doubt demonstrates the sensitivity of the T2 values of cartilage to OA from another point of view. This is because the T2 values are the values of a pure parameter obtained via the fitting, and processing of the collected image data based on the MRI principle, rather than a kind of simple image texture data. So the T2 values can directly reveal the internal biochemical information of the tissue that significantly correlates the OA disease. From the perspective of simple classifier design, it should be a good choice to adopt T2 value as the eigenvalue for OA diagnosis.

5. Conclusion

In general, a simple, non-invasive, efficient and accurate detection scheme for early knee OA has always been a pursuit in the medical field. The combination of computer technology and the advanced T2 mapping technique to assist diagnosis eliminates the influence of the subjective factors in traditional morphological diagnosis with OA images, thus avoiding the great difference in diagnostic results caused by differences in knowledge and experience. It can detect the existing risk of OA before the occurrence of morphological changes and thus can produce more accurate results of OA diagnosis and treatment effect evaluation.

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References

[1] C.Y. Xiao, Q.L. Lin and M. Li, Progress in the research on the mechanism of subchondral bone lesions of OA, Medical Information **23** (2010), 1767-1769.

[2] E. Quaia, R. Toffanin, G. Guglielmi, M. Ukmak, A. Rossi, B. Martinelli and M.A. Cova, Fast T2 mapping of the patellar articular cartilage with gradient and spin-echo magnetic resonance imaging at 1.5T: validation and initial clinical experience in patients with osteoarthritis, Skeletal Radiol **37** (2008), 511-517.
[3] G. Blumenkrantz and S. Majumdar, Quantitative magnetic resonance imaging of articular cartilage in osteoarthritis, Eur Cells Mater **13** (2007), 75-86.
[4] C.M. Chen, Y.H. Chou, C.S.K. Chen, J.Z. Cheng, Y.F. OU, F.C. Yeh and K.H. Chen, Cell-competition algorithm: a new segmentation algorithm for multiple objects with irregular boundaries in ultrasound images, Ultrasound in medicine and Biology **31** 2005, 1647-1664.
[5] J.Z. Cheng, Y.H. Chou, C.S. Huang, Y.C. Chang, C.M. Tiu, K.W. Chen and C.M. Chen, Computer-aided US Diagnosis of breast lesions by using cell-based contour grouping, Radiology **255** (2010), 746-754.
[6] S. Apprich, G.H. Welsch, T.C. Mamisch, P. Szomolanyi, M. Mayerhoefer, K. Pinker and S. Trattnig, Detection of degenerative cartilage disease: comparison of high-resolution morphological MR and quantitative T2 mapping at 3.0 Tesla, Osteoarthritis and Cartilage, **18** (2010), 1211-1217.
[7] E. Lammentausta, P. Kiviranta, M.J. Nissi, M.S. Laasanen, I. Kiviranta, M.T. Nieminen and J.S. Jurvelin, T2 relaxation time and delayed Gadolinium-enhanced MRI of cartilage(dGEMRIC) of human patellar cartilage at 1.5T and 9.4T: relationships with tissue mechanical properties, J Orthop Res, **24** (2006), 366-374.
[8] K. Woertler, M. Strothmann, B. Tomhach and P. Reimer, Detection of articular cartilage lesions: experimental evaluation of loe-and high-field strength MR imaging at 0.18 and 1.0T, J Magn Reson Imaging **116** (2000), 678-685.
[9] M.P. Recht, D.W. Piraino, G.A. Paletta, J.P. Schils and G.H. Belhobek, Accuracy of fat-suppressed three-dimensional spoiled gradient-echo FLASH MR imaging in the detection of patellofemoral articular cartilage abnormalities, Radiology **198** (1996), 209-212.
[10] Y.N. Zhang, K.N. Li and N. Tan, An RBF neural network classifier with centers, variances and weights directly detemined, Computing Technology and Automation **28** (2009), 5-9.
[11] Y.N. Zhang, W.E. Leithead and D.J. Leith, Time-series gaussian process regression based on toeplitz computation of O(N^2) operation and O(N) - level storage. Proceedings of the 44th IEEE Conference on Decision and Control, 2005, 3711-3716.
[12] Y.N. Zhang, W. Li, C. Yi and K. Chen, A weights-directly-determined simple neural network for nonlinear system identification, Proceedings of IEEE International Conference on Fuzzy Systems, 2008, 455-460.
[13] C.G. Peterfy, A. Guermazi, S. Zaim, P.F. Tirman, Y. Miaux, D. White, M. Kothari, Y. Lu, K. Fye, S. Zhao and H.K. Genant, Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis, Osteoarthritis Cartilage **12** (2004), 177-190.
[14] T.C. Dunn, Y. Lu, H. Jin, M.D. Ries and S. Majumdar, T2 relaxation time of cartilage at MR imaging: comparision with severity of knee osteoarthritis, Radiology **232** (2004), 592-598.