Effect of Accurate Segmentation on the Detection of Herniated Lumbar Spine Disc Using CAD System

Mamona Mumtaz [*a], **Munir Ahmad** [b], **Mirza Rahmat Baig** [c]

[a] Department of Physics, University of Management and Technology, Lahore, Pakistan

[b] Principal Scientist, Institute of Nuclear Medicine and Oncology (INMOL), Lahore, Pakistan

[c] Department of Physics, University of Lahore, Pakistan

[*] Corresponding Author: mamonamumtaz6@gmail.com

Abstract

The trend of using CAD systems has been increasing gradually and becoming the attention of many types of research nowadays. We consider the issue of building a CAD framework for the identification of the lumbar herniated circle from MRI sagittal outputs. Like other image-based CAD systems, we proposed a CAD system by introducing a new image segmentation technique (PCA-SIFT Segmentation) to detect the lumbar disc herniation. In this work, we enhance the region of interest of lumbar disc using SIFT-based features (PCA-SIFT). We proposed that accurate segmentation techniques give more accurate results as compared with manual segmentation. By using 30 patients data, and applying PCA-SIFT segmentation and manual segmentation with the help of implementing SVM classifier, we find that accurate segmentation (PCA-SIFT) gives more accuracy in detecting the disc herniation. With our CAD system, we achieve 94% accuracy.

Keywords: Computer-Aided Diagnostics, Lumbar Herniated Disc, PCA-SIFT Segmentation, Accurate Segmentation, Classification, SVM

Introduction

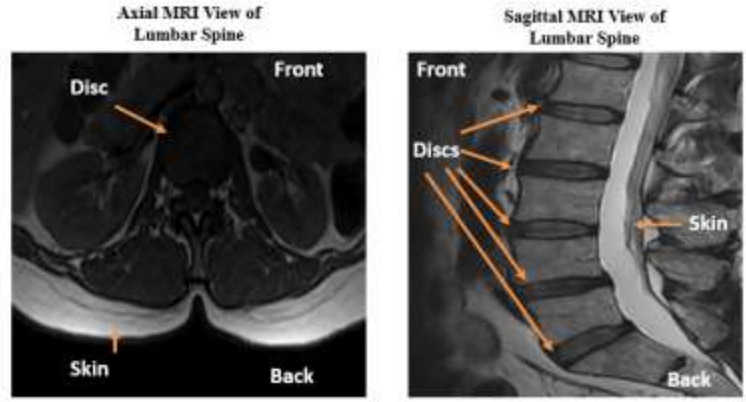
Lower back pain (LBP) is a common pain type that is influencing the lives of people around the world and is the most obvious purposes behind which many people see their clinical experts. It is an incessant disease since it impacts on the large part of the population and results in a huge socioeconomic burden. As indicated by Nurul, Haslinda, Saidi, Shamsul, and Zailina (2010) the recurrence of low back pain is prevalent more in developed countries than developing countries, for example, 42% and 35%. The prevalence of lower back pain causes significant levels of care use. Practically 80% of the population encountered a scene of lower back pain sooner or later during life (Rubin, 2007).

LBP is considered as the second most common disease after headache as a large no of patients are suffer from LBP and its treatment costs so much. A study shows that Americans spend nearly $50 billion each year on this type of medical treatment. The higher growth in the patients of lumbar herniated disc each year is about 8% as associated with the growth of radiologist which is 1%, validates seeking a Computer Aided Diagnostic (CAD) system for diagnostic of lumbar patients (Raja'S, Corso, Chaudhary, & Dhillon, 2010).

In past various researchers used different modalities for imaging the spine i.e. CT and MRI, and they found that MRI images are provided with the best support for the detection of abnormalities in the lumbar spine (Baert, 2007). The T2 weighted images give biological and morphological data to the disc tissue. The term biochemical tissue alludes to the disc's water content which is reflected in attractive reverberation signal power of T2 weighted images. The sagittal images show signal intensities while the Axil images show the deformation of the disc (Pfirrmann, Metzdorf, Zanetti, Hodler, & Boos, 2001).

There are two kinds of MRI images i.e., sagittal and axial, that are most widely used for diagnosis of lumbar disc herniation. Figure 1 shows the MRI images of sagittal and axial perspective on the lumbar spine. Our proposed CAD framework utilizes the sagittal MRI images on the lumbar spine with the end goal of detection of herniation. The explanation for utilizing the sagittal images on MRI is that sagittal view is generally used to decide whether the lumbar discs of various vertebrae are normal or not and can be utilized to find the herniated discs assuming any. The sagittal view contains entire lumbar spine see comprises of numerous discs. While axial perspective on MRI filters, as a rule, give more data about disc issues (Al-Ayyoub et al., 2018).

Figure 1: MRI views of the lumbar spine



Generally, CAD systems are based on the framework that analyzes and process different types of data about patients i.e., images of different parts of the human body to aid in finding the most accurate for diagnosis purpose. The Rationale behind building a CAD system is not to replace the radiologists but to assist them. The continuous increase in the patients with lower back pain in hospitals needs quick and efficient CAD systems which will provide radiologists with speedy and correct indications of disc herniation.

Keeping in view the importance of the detection of the lumbar herniated disc, the present study proposes a CAD system based on accurate segmentation technique i.e., PCA-SIFT Segmentation, for the detection of the lumbar herniated disc in MRI images. We claim that accurate segmentation results in higher accuracy in detecting the disc herniation. Further, we compared manual segmentation results with our proposed segmentation and found better accuracy using PCA-SIFT segmentation technique.

Many researchers applied different CAD systems for the detection of the lumbar herniated disc through MRI images. Previously, the researchers have used high-resolution surface coil imaging technique for a lumbar herniated disk and found the comparison of computed tomography (Unal, Polat, Kocer, & Hariharan, 2015). By analyzing the data of 17 patients, they found that surface coil MR imaging will become established as the process of choice for MRI imaging of lumbar disc disease, and MRI is the best alternative of CT and Myelography (Edelman et al., 1985). Van

Ginneken, Frangi, Staal, ter Haar Romeny, and Viergever (2002) apply the Active Shape Model segmentation technique with optimum features for the detection of the lumbar herniated disc. They use KNN classifiers for classification between normal and herniated discs.

Recently most of the researchers used intensity signals active shape model but in that, they utilized Gibbs distribution method for the analysis of herniated disc and also applied feature method (Raja'S, Corso, Chaudhary, & Dhillon, 2010). Ghosh, Raja'S, Chaudhary, and Dhillon (2011) conducted a study to investigate lumbar herniated disc detection through MRI images and applied five types of the classifier including (SVM, PCA + LDA, PCA + Naive Bayes, PCA +QDA and PCA+SVM) to find extract intensity and texture feature from each disc and to detect the disc herniation. Some researchers worked on the new technique they introduced PCA and LDA (Linear Discriminant analysis) method in MRI image of the herniated disc (Ghosh, Alomari, Chaudhary, & Dhillon, 2011). Michopoulou (2011) developed a model for the segmentation of MRI images of the lumbar spine and applied different classifiers to obtain the correctness of the CAD framework. Some authors detected the abnormalities in a lumbar disc with hybrid models and used two types of models in feature selection stage, F-score-based feature selection method and correlation-based feature selection method, to select the best discriminative feature (Huang et al., 2016).

The remainder of this study is constructed as follows. Next section of the study describes the proposed methodology and framework of study with an emphasis on the PCA-SIFT segmentation followed by results, conclusion and guideline for future research.

Methodology

We propose a CAD system that automatically diagnoses the lumbar herniated disc in MRI images. To make diagnoses, we proposed a system which considers many aspects of the lumbar spine images such as intensity values and texture values, and all these aspects are combined under machine learning mechanism. Our study includes the real-time lumbar herniated patient's data, collected from INMOL Hospital, Lahore, Pakistan. The dataset was in the original form of DCOM images. The dataset contains 30 patients' real-time data with patient names and ages.

The flowchart of our proposed system is presented in figure 2 comprising of four steps. In the first stage, we separate each lumbar spine patient's image into discs. We manually separate each disc from the whole image. There are 5 major discs in each lumbar spine image. Figure 3 shows the sample image of one patient that explains its five major discs. The first disc is called L1-L2 disc, the second one is L2-L3, the third one is L3-L4, forth one is L4-L5 and finally, the last disc is called L5-S1. In most of the cases, the disc herniation occurs in the last two types of discs as figure shows. In this figure disc L5-S1is herniated.

Figure 2: The flowchart of the proposed system

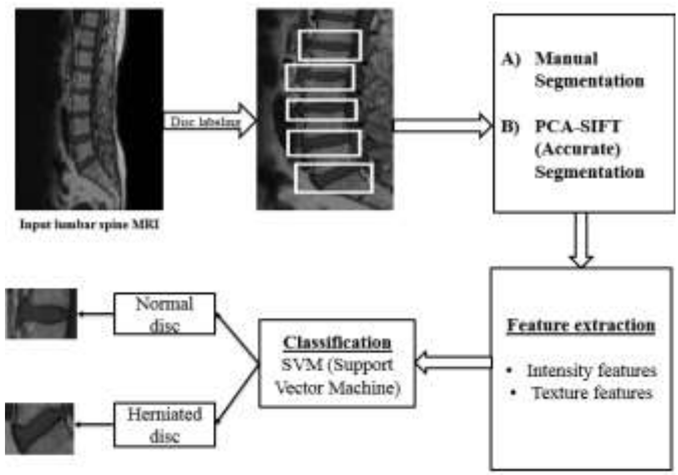


Figure 3: MRI Sagittal images of the lumbar spine

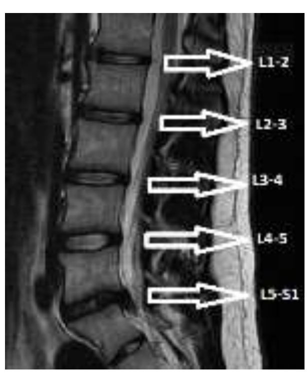


Image Segmentation Techniques

Image segmentation is among one of the most significant issues in the PC supported clinical imaging and it is utilized in the various sorts of utilization. Segmentation assumes an indispensable job in clinical images handling uniquely for guts organs variations from the norm location in MRI images and Computer Tomography (Abirami & Sheela, 2014).

The segmentation of clinical images includes three sorts of issues related to pictures. Firstly, pictures contain commotion, which can modify the force of a pixel and because of it, the grouping of that pictures gets dubious. Secondly, pictures show force non-consistency where the power level of a solitary tissue class differs progressively over the degree of the picture. Thirdly, pictures have limited pixel size and are dependent upon fractional volume averaging where singular pixel volumes contain a blend of tissue classes so the power of a pixel in the picture may not be reliable with any one class (Withey & Koles, 2007). These issues disclose to us that some level of vulnerability must be connected to the picture segmentation results.

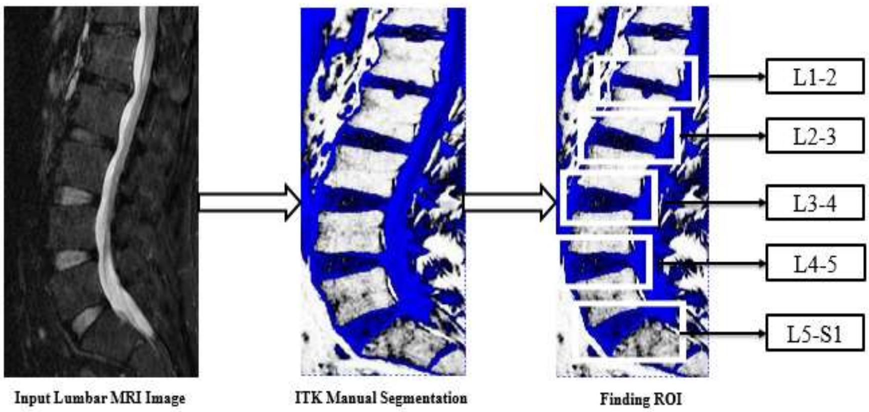
Manual Segmentation (ITK SNAP)

Manual segmentation is regularly utilized as the best quality level for the assessment of programmed segmentation (Tingelhoff et al., 2007). Manual segmentation is conceivable yet is a tedious errand and subject to administrator inconstancy. Replicating a manual segmentation result is troublesome and the degree of certainty attributed endures in like manner (Clarke et al., 1995).

We use ITK-SNAP software for manual segmentation of lumbar spine MRI images. The MRI data of images are in DICOM format and spatial resolution of 768*768 pixels of 8-bit greyscale. We applied threshold level segmentation to the MRI images using ITK-SNAP toolkit. The method of manual segmentation works by setting a pixel intensity range from ROI within an upper and lower-level threshold. For this purpose, a level set equation is applied. Where P is constrained connected- component surface based on a propagation term, where g is an input range, U and L are upper and lower thresholds (Todd, Kirillov, Tarabichi, Naghdy, & Naghdy, 2009). Figure 4 shows the manual segmentation results of MRI image using ITK SNAP. After manual segmentation of images, we separate each disc as shown in the figure.

$$P(X) = \begin{cases} g(x) - L & \text{if } g(x) < (U - L)/2 + L \\ U - g(x) & \text{otherwise.} \end{cases}$$

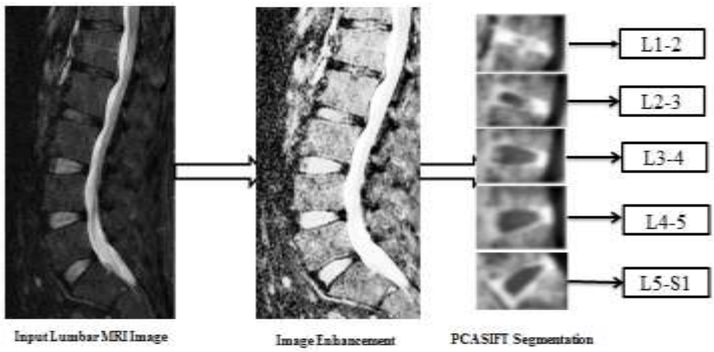
Figure 4: ITK Manual Segmentation of MRI Image



PCA SIFT Segmentation

Manual segmentation has numerous downsides, consequently, automatic segmentation strategies are best, be that as it may, huge issues must be defeated to accomplish segmentation via programmed means and it stays a functioning examination territory (Duncan & Ayache, 2000). PCA-SIFT segmentation system is a solo picture segmentation strategy which acknowledges indistinguishable contributions from the standard SIFT (Scale Invariant Feature Transform) descriptor. (Lowe, 2004) exhibited SIFT calculations for separating unmistakable invariant highlights from the pictures. It is broadly utilized in pictures mosaic, acknowledgement and recovery, and so on. The filter comprises of four significant stages, which are scale-space extrema recognition, key point restriction, direction task and key-point descriptor. Principle Component Analysis (PCA) is a method for dimensionality reduction, which is appropriate to speak to the key point's patches and empower us to straightly extend high dimensional examples into a low dimensional component space (Jolliffe, 2011). Figure 5 shows the PCA-SIFT segmentation of lumbar spine MRI pictures utilizing Matlab programming.

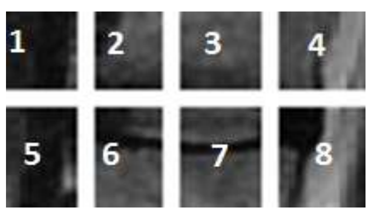
Figure 5: PCA-SIFT Segmentation of MRI Image



Features Extraction

The next step of our proposed system is to divide each segmented disc image into eight equal parts and find a region of interest (ROI) of an image that is affected by the disc herniation. Figure 6 shows the ROI of the disc images. The purpose of ROI is to extract the features of the disc images from the leftmost area (4, 8) in which disc herniation occurs. We use Matlab software for coding of our proposed system. We use intensity and texture features for feature extraction because these features give an accurate segmentation of the disc (Ghosh, Raja'S, et al., 2011).

Figure 6: ROI of disc



Most of the researchers focused on the intervertebral disc intensity levels along with the texture features for the CAD frameworks used for the detection of lumbar disc herniation from MRI images. The rationale behind using these features in our CAD system is, this makes detection dependent on accurate segmentation of the disc (Ghosh, Raja'S, et al., 2011). We focus intensity and texture features in our CAD system. The intensity features include features like maximum, minimum, mean intensity from the discs ROI. The formula used for calculating the intensity features is as follows.

$$\mathbf{X} = \{ \quad \frac{I(i)}{I(j)} \quad | \quad 1 \leq i, j \leq 8 \text{ and } i \neq j \}$$

(1)

Where I (i) is the average intensity of the ith part of the ROI and X = < xf >; $1 \leq f \leq 56$.

The texture features are calculated from the Gray-Level Co-occurrence Matrix (GLCM) of disc ROI. The mathematical representation of the GLCM matrix is as follows.

$$G_{\Delta x \Delta y}(i,j) = \sum_{p=1}^{n} \sum_{q=1}^{m} \begin{cases} 1, & \text{if } I(p,q) = i \text{ and} \\ & I(p+\Delta x, q+\Delta y) = j \\ 0, & otherwise \end{cases}$$

(2)

The G is presented by a $n*m$ image I and parameterized by an offset (Δx, Δy). GLCM gives us five well-known texture features, for example, energy, correlation, contrast, homogeneity, and entropy (Unal et al., 2015).

Classification Using Support Vector Machine (SVM)

The final step of our proposed methodology is the classification of the features extracted in the previous stage. The purpose of the classification process is to classify each disc features using PCA-SIFT segmentation and to find whether the disc is herniated or normal. For this purpose, we use a well-known classification technique which is the support vector machine (SVM). SVM was introduced in the early ’90s and today, its applications are found in many fields such as handwritten character recognition, time series prediction, data mining, medical diagnostics, bioinformatics, face detection, biomedical signal analysis and image classification.

SVM is capable of generalizing well in terms of accuracy as compared with many classifiers. SVM has become the choice of many researchers because it serves many advantages for real-world classification problems which are not found in many traditional classifiers (Suralkar, Karode, & Pawade, 2012). For instance (Ghosh, Raja'S, et al., 2011) designed a CAD system and compare many classifiers such as SVM, PCA+LAD, PCA+ Bayes, PCA+QDA, PCA+SVM, 5-NN for the detection of the lumbar herniated disc. They compare each classifier in terms of accuracy in detecting the lumbar herniated disc and found that SVM is the best and powerful classifier with 94.29% accuracy. To calculate the accuracy of the classification results, we use the three-fold cross-validation technique. In threefold classification, we divide our images data into 3 rounds. In the first round, we train the first 10 patients' images and test the remaining 20 patients' images. In the second round, we train next 10 patients' images and test remaining 20 images, and in the third round, we train the last 10 images and test the first 20 images. These results are calculated by comparing the results from classification with our gold standard radiologist report.

Results and Findings

We analyzed 30 lumbar MRI cases which have relating ground truth as radiologist report. We performed 3 fold cross-validation probes the two kinds of segmentation techniques with the assistance of SVM classifier and watch the precision. We performed a cross-validation test utilizing 30 cases to prepare and test our proposed technique. We performed three rounds and in each round, we trained 10 images and tested staying 20 images haphazardly. We checked the characterization exactness by contrasting our arrangement results and our highest quality level by characterizing the precision at each circle level *i* as:

$$\text{Accuracy}_i = \left(1 - \frac{1}{K}\sum_{j=1}^{K} |g_{ij} - n_{ij}|\right) \times 100\%$$

(3)

Where Accuracy $_i$ = denotes classification accuracy at disc level *i* and 1 ≤ I ≤ 5. Value of *K* denotes the number of cases in each testing, and g_{ij} is the gold standard binary assignment for disc *i* and n_{ij} is the resulting binary assignment for disc *i* from the inference in the model (Unal et al., 2015). Hence g_i and n_i are assigned the binary values the same way such that:

$$g_i = \begin{cases} 0 & \text{if disc } i \text{ is normal} \\ 1 & \text{if disc } i \text{ is abnormal} \end{cases}$$

(4)

We computed the accuracy at each level independently to show the detailed classification accuracy at each level and in this way have all the more comprehension of the circle levels and their effect on the classification accuracy. We acquired the clinical determination report for each case that contains a finding at each lumbar plate level. These reports are created by understanding inside our communitarian radiology focus. We think about these reports as the gold standard.

Table 1 shows the experiment results of manual segmentation. In this, we tested 20 images in three rounds using 3-fold cross-validation. We can see that the overall average accuracy of SVM classification is 82.33%. Results show that manual segmentation gives low accuracy in determining the lumbar herniated disc, especially as shown in the table having the accuracy of L5-S1 is only 39.33%. The lower two levels of the disc have the most variability in the lumbar area which misleads the manual segmentation and thus the error increases (Raja'S et al., 2010). The manual segmentation has many drawbacks such as slow up to 60 hours per scan and its results are variable up to 15% between experts (Warfield et al., 1995).

To overcome the problem of getting lower accuracy in determining the disc herniation, we used accurate segmentation which is PCA-SIFT segmentation technique. Table 2 shows the experiment result of PCA-SIFT segmentation with 3-fold cross-validation. Experiment results show that accurate segmentation gives more accuracy in detecting the lumbar disc herniation as it achieves the overall accuracy of 94%. We can see that its accuracy in detecting the lower section of the lumbar spine which is 91.67% and 86.67% is also greater than the manual segmentation results.

Every radiologist worries about giving a false positive reading. The retrospective error rate among radiologic examinations is approximately 30% (Lee, Nagy, Weaver, & Newman-Toker, 2013). Which means the lower limit of accuracy in determining disc herniation is 70% approximately and above this is considered as good accuracy of results using the CAD system. However, if the method achieves the accuracy of 90% in determining the lumbar disc herniation is considered as promising (Raja'S et al., 2010). Our proposed CAD system achieves 94% accuracy which is more than 90% accuracy that is promising as well. Many researchers used different segmentation techniques for the detection of a lumbar herniated disc such as (Ghosh, Malgireddy, Chaudhary, & Dhillon, 2014) used a supervised approach towards segmentation of MRI images and which gives an accuracy of 81% to 84%. Another study conducted by (Raja'S, Corso, Chaudhary, & Dhillon, 2009) used a probabilistic model on 80 clinical cases and achieves 91% accuracy in a cross-validation experiment. Since our CAD system has a unique segmentation technique and our calculated accuracy is based on only 20 trained cases, we achieve the highest accuracy in detecting lumbar herniated disc.

Table 1. SVM Results of Manual Segmentation

SVM - Manual Segmentation						
Cross-validation results: Each row tests 20 randomly selected cases						
Set	**L1-2**	**L2-3**	**L3-4**	**L4-5**	**L5-S1**	**Accuracy**
1	20	15	19	18	10	82
2	19	15	19	17	11	81
3	18	18	19	18	11	84
%	**95**	**80**	**95**	**88.33**	**53.33**	
Average Accuracy						**81.66**

Table 2. SVM Results of PCA-SIFT Segmentation

SVM - PCA-SIFT Segmentation (Accurate)						
Cross-validation results: Each row tests 20 randomly selected cases						
Set	**L1-2**	**L2-3**	**L3-4**	**L4-5**	**L5-S1**	**Accuracy**
1	19	19	19	19	17	93
2	20	20	20	18	17	95
3	20	19	19	18	18	94
%	**98.33**	**96.67**	**96.67**	**91.67**	**86.67**	
Average Accuracy						**94**

Table 3 shows the results of specificity and sensitivity of our methods. It describes the counts of false positive (FP), true positive (Tingelhoff et al.), false negative (FN) and true negative (Gupta, Nair, & Gogula) where:

$$Specificity = \frac{TN}{TN+FP} \quad (4)$$

$$Sensitivity = \frac{TP}{TP+FN} \quad (5)$$

$$\textit{Predictive value positive} = \frac{TP}{TP+FP} \tag{6}$$

$$\textit{Predictive value negative} = \frac{TN}{TN+FN} \tag{7}$$

The table describes that our results maintain the high levels of sensitivity and specificity around 95% and 96%.

Table 3. Sensitivity and Specificity

Sensitivity	**95%**
Specificity	**96%**
Predictive value positive	**96%**
Predictive value negative	**95%**

Conclusion

The current study proposed a CAD system to detect the lumbar herniated disc in MRI images using a unique accurate image segmentation technique. This study performs features extraction of segmented images and includes SVM classifiers to detect whether the disc is normal or herniated. The overall analysis shows that SVM classifiers give the optimum accuracy i.e. 94% in detecting the disc herniation using accurate segmentation technique. The analysis also shows that without accurate segmentation we cannot achieve desired and accurate results. The current study introduces a new segmentation technique that provides maximum accuracy. The advantage of using this technique is that it serves accurate segmentation and detects disc correctly with 94% accuracy with a small training dataset. If we apply it on the large dataset i.e. if we train more images then its accuracy in detecting the lumbar herniated disc becomes more than calculated accuracy. As an extension of the work, in future, our CAD system includes more dataset with different features for detecting the lumbar herniated disc.

References

Al-Ayyoub, M., Al-Mnayyis, N., Alsmirat, M. A., Alawneh, K., Jararweh, Y., & Gupta, B. B. (2018). SIFT based ROI extraction for lumbar disk herniation CAD system from MRI axial scans. *Journal of Ambient Intelligence and Humanized Computing*, 1-9.

Baert, A. (2007). *Spinal imaging: diagnostic imaging of the spine and spinal cord*: Springer Science & Business Media.

Clarke, L., Velthuizen, R., Camacho, M., Heine, J., Vaidyanathan, M., Hall, L., . . . Silbiger, M. (1995). MRI segmentation: methods and applications. *Magnetic resonance imaging, 13*(3), 343-368.

Duncan, J. S., & Ayache, N. (2000). Medical image analysis: Progress over two decades and the challenges ahead. *IEEE transactions on pattern analysis and machine intelligence, 22*(1), 85-106.

Edelman, R. R., Shoukimas, G. M., Stark, D. D., Davis, K. R., New, P., Saini, S., . . . Brady, T. J. (1985). High-resolution surface-coil imaging of lumbar disk disease. *American journal of roentgenology, 144*(6), 1123-1129.

Ghosh, S., Alomari, R., Chaudhary, V., & Dhillon, G. (2011). *Composite features for automatic diagnosis of intervertebral disc herniation from lumbar MRI.* Paper presented at the Conf Proc IEEE Eng Med Biol Soc.

Ghosh, S., Malgireddy, M. R., Chaudhary, V., & Dhillon, G. (2014). A supervised approach towards segmentation of clinical MRI for automatic lumbar diagnosis. In *Computational Methods and Clinical Applications for Spine Imaging* (pp. 185-195): Springer.

Ghosh, S., Raja'S, A., Chaudhary, V., & Dhillon, G. (2011). *Computer-aided diagnosis for lumbar mri using heterogeneous classifiers.* Paper presented at the Biomedical Imaging: From Nano to Macro, 2011 IEEE International Symposium on.

Gupta, A., Nair, A. P., & Gogula, R. (2003). Corporate governance reporting by Indian companies: A content analysis study. *The ICFAI Journal of Corporate Governance, 2*(4), 7-18.

Huang, Y., Liu, J., Zou, M., Zhang, Q., Chao, J., Zhao, W., . . . Wang, L. (2016). Colorimetric detection and efficient monitoring of a potential biomarker of lumbar disc herniation using carbon nanotube-based probe. *Science China Chemistry, 59*(4), 493-496.

Jolliffe, I. (2011). Principal component analysis. In *International encyclopedia of statistical science* (pp. 1094-1096): Springer.

Lee, C. S., Nagy, P. G., Weaver, S. J., & Newman-Toker, D. E. (2013). Cognitive and system factors contributing to diagnostic errors in radiology. *American Journal of Roentgenology, 201*(3), 611-617.

Lowe, D. G. (2004). Distinctive image features from scale-invariant keypoints. *International journal of computer vision, 60*(2), 91-110.

Michopoulou, S. (2011). *Image analysis for the diagnosis of MR images of the lumbar spine.* UCL (University College London),

Nurul, I., Haslinda, A., Saidi, M., Shamsul, B., & Zailina, H. (2010). Prevalence of low back pain and its risk factors among school teachers. *American Journal of Applied Sciences, 7*(5), 634-639.

Pfirrmann, C. W., Metzdorf, A., Zanetti, M., Hodler, J., & Boos, N. (2001). Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine, 26*(17), 1873-1878.

Raja'S, A., Corso, J. J., Chaudhary, V., & Dhillon, G. (2010). *Automatic diagnosis of lumbar disc herniation with shape and appearance features from MRI.* Paper presented at the Medical Imaging 2010: Computer-Aided Diagnosis.

Raja'S, A., Corso, J. J., Chaudhary, V., & Dhillon, G. (2009). Abnormality detection in lumbar discs from clinical MR images with a probabilistic model. *injury, 4,* 3.

Raja'S, A., Corso, J. J., Chaudhary, V., & Dhillon, G. (2010). Computer-aided diagnosis of lumbar disc pathology from clinical lower spine MRI. *International journal of computer assisted radiology and surgery, 5*(3), 287-293.

Rubin, D. I. (2007). Epidemiology and risk factors for spine pain. *Neurologic clinics, 25*(2), 353-371.

Suralkar, S., Karode, A. H., & Pawade, P. W. (2012). Texture image classification using support vector machine. *International Journal of Computer Applications in Technology, 3*(1), 71-75.

Tingelhoff, K., Eichhorn, K., Wagner, I., Westphal, R., Wahl, F., & Bootz, F. (2007). *Analysis of Manual Segmentation in Medical Image Processing.* Paper presented at the Aceppted at Thematic Conference on Computational Vision and Medical Image Processing ECCOMAS VIPIMAGE.

Todd, C., Kirillov, M., Tarabichi, M., Naghdy, F., & Naghdy, G. (2009). An analysis of medical image processing methods for segmentation of the inner ear.

Unal, Y., Polat, K., Kocer, H. E., & Hariharan, M. (2015). Detection of abnormalities in lumbar discs from clinical lumbar MRI with hybrid models. *Applied Soft Computing, 33*, 65-76.

Van Ginneken, B., Frangi, A. F., Staal, J. J., ter Haar Romeny, B. M., & Viergever, M. A. (2002). Active shape model segmentation with optimal features. *IEEE transactions on medical imaging, 21*(8), 924-933.

Warfield, S., Dengler, J., Zaers, J., Guttmann, C. R., Wells, W. M., Ettinger, G. J., . . . Kikinis, R. (1995). Automatic identification of gray matter structures from MRI to improve the segmentation of white matter lesions. *Journal of Image Guided Surgery, 1*(6), 326-338.

Withey, D. J., & Koles, Z. J. (2007). *Medical image segmentation: Methods and software.* Paper presented at the Noninvasive Functional Source Imaging of the Brain and Heart and the International Conference on Functional Biomedical Imaging, 2007. NFSI-ICFBI 2007. Joint Meeting of the 6th International Symposium on.