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Evaluation of Rheumatoid Arthritis using Thermography and Colour Doppler Ultrasound

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Abstract: Rheumatoid arthritis (RA) is a common systemic autoimmune disease characterised by chronic inflammation of several joints. The main symptoms are morning stiffness, joint swelling, inflammation, neovascularisation and synovial hyperplasia. Early detection helps to minimise disease progression, however, there is no single test for the diagnosis for RA. A series of test, namely, radiography, subjective clinical variables like 28 disease activity score (DAS-28), swollen joint count and a series of laboratory tests are used to diagnose RA. However, sensitivity of these tests is limited in the earlier stage. According to Eular task force (2016), there is a need for cost-effective as well as safer techniques for the diagnosis of RA. Therefore, this study focuses on the application of non-invasive, radiation-free, cost economic technique, namely, thermography and colour Doppler ultrasound (CDUS) in the diagnosis of early stage RA. The main aim of this case study is to correlate thermographic and CDUS knee features in RA patients using clinical and functional assessment as golden standard. The present study depicts various steps involved in thermographic and CDUS evaluation of RA from normal subjects. Thermographic investigation of RA involves image acquisition, region of interest (ROI) selection, image segmentation and feature extraction. In this study, Gray-level cooccurence matrix (GLCM) features are used to classify normal and abnormal RA thermal images. Knee joint effusion and perfusion are employed to diagnose RA using CDUS images. ImageJ is used to analyse the intensity of perfusion. Semi-quantitative grading scoring is used to grade knee joint effusion and perfusion. The results of the present study reveal that IR thermography correlates well with clinical findings than CDUS. To the author's knowledge, this is the first study to compare thermography with CDUS using clinical findings as golden standard.

Keywords: Rheumatoid arthritis, Thermography, Colour Doppler ultrasound, Imagej, image segmentation.

Abbreviations used:

RA	Rheumatoid Arthritis
CDUS	Colour Doppler Ultrasound
ESR	Erythrocyte Sedimentation Rate
DAS-28	Disease Activity Score-28
EULAR	European League Against Rheumatism Task Force
GLCM	Gray-level cooccurence matrix

1. INTRODUCTION

Rheumatoid arthritis (RA) is a degenerative, multifactorial systemic disease that affects around 1% – 2% of the Indian population, especially among women in the age group of 50 [1]. It causes pain, disability and degenerative loss of function. Early screening or diagnosis of RA allows better treatment and prevention. RA is commonly diagnosed using radiography, subjective clinical variables like 28 disease activity score (DAS-28), swollen joint count and a series of laboratory tests. However, sensitivity of these tests is limited in the diagnosis of RA in the earlier stage. A number of studies have focused to explore efficient diagnosis criteria for the earlier screening of RA [2–4]. The combination of modern imaging and treatment methods

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is necessary for the early diagnosis which will improve the quality of life of RA patients, in spite of worldwide rise in its incidence.

In accordance with evidence-based recommendations of European League Against Rheumatism (Eular) task force [5], there is a need for the application of non-invasive and cost economic diagnostic techniques for RA, especially in the early stage. Earlier stage diagnosis helps in the better treatment procedures and improved quality of life. Moreover, in the earlier stage, the disease exhibits increased metabolic activity [6]. Hence, proper diagnosis and treatment minimises structural damage. MRI is widely used in the detection of early stage RA. However, the use of this system is limited by its inherent high cost factor and less availability. On the other hand, ultrasound and thermography play a promising role in the detection of early stage RA as it is cost effective, easy accessible and non-invasive for mass screening. During the early stage, the high metabolic activity of the disease results in temperature differences, and hence the use of thermography is justified in the diagnosis of RA. Hildebrandt [7] and Brenner et al. [8] performed thermographic research studies to assess a series of joint diseases, especially RA and osteoarthritis (OA). In addition, Denoble [9] correlated skin surface temperature at the joint with arthritis activity. Likewise, Frize et al. [10] diagnosed RA using IR thermography and determined that knees and metacarpophalangeal joints (mcp) of the 2nd and 3rd fingers are the best-suited joints to image. In a recent study, Lasanen et al [11] correlated IR thermography results with clinical assessment using 58 children affected with juvenile RA.

In the same way, the increased blood flow in the synovial membrane can be characterized by colour Doppler ultrasound (CDUS). In addition, Eular task force recommended the importance of ultrasound, in the evaluation of RA. Moreover, CDUS has successfully proven to quantify intrasynovial blood flow and acts as an indicator of synovial membrane inflammation [12]. Beitinger et al. [13] performed standardized CDUS examinations using 111 knee joints and indicated the potential of CDUS in differentiating RA from other arthritis. Similarly, a positive correlation between CDUS and biochemical tests, namely, erythrocyte sedimentation result (ESR) and C-reactive protein (CRP) was suggested. In addition, an association between RA and disease activity markers, such as 28-joint disease activity score (DAS) and swollen joint count have been proposed [14, 15].

Thus, there have been number of studies to evaluate the potential of IR thermography and CDUS individually in the detection of RA. However, to the author’s knowledge, there have been no previous studies comparing the two techniques in the detection of RA.

This study investigates the role of non-invasive and cost-effective techniques, namely, IR thermography and CDUS in the diagnosis of earlier stage RA. The main aim of this study is to correlate thermographic and colour Doppler ultrasonographic knee features in RA patients using clinical and functional assessment as golden standard. This study provides an insight on the various steps involved in the thermographic and CDUS evaluation of RA.

2. PATIENTS AND METHODS

This study deals with 10 RA subjects and 10 healthy volunteers from SRM Medical college Hospital and Research Center. The present study is approved by SRM Institutional Ethical Committee (Ethical clearance certificate: 855/IEC/2015). Informed consent has been obtained prior to the study. All RA patients are having a diagnosis of adult-onset RA as defined by Indian Rheumatology Association (2008) [16] and modified Indian Health assessment criteria for the classification of RA. In addition, clinical disease severity assessment is done for all patients using Health Assessment Questionnaire (HAQ) and disease activity score 28 (DAS28). Furthermore, biochemical test, namely, erythrocyte sedimentation rate (ESR; determined by Westergren method) was done to confirm the presence of RA.

3. IR THERMOGRAPHIC EVALUATION

Thermographic detection of RA is done by the following steps as shown in the (Figure 1). The steps involved in IR thermal image diagnosis are as follows:

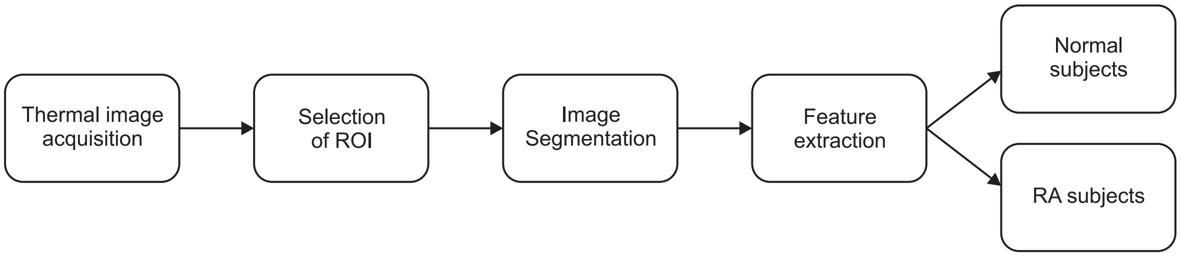


Figure 1: Steps involved in thermographic determination of RA and healthy subjects

A. Thermal Image Acquisition

Thermographic IR knee images are obtained using a thermal imaging camera. Before image acquisition, all subjects were asked to sit with their legs uncovered for 15–20 minutes in a temperature-controlled room (20° C) to regulate the knee joint temperature. Care has been taken to maintain the distance between subject and the camera at 1 m. IR images are captured both in sitting (knees flexed at 90°) and standing position. FLIR software version 1.2 (FLIR Systems Inc., Wilsonville, OR) and Matlab version 7.5.0 (64-bit version R2007b; The MathWorks, Natick, MA) were used for image analysis and processing, respectively. The resulting thermogram shows uniform and symmetric temperature variations for normal subjects (Figure 2a), whereas, abrupt temperature variations represent RA condition (Figure 3a).

B. Image Preprocessing

In the second step, the thermal image is cropped to remove the undesired body parts (Figure 2b) from the region of interest.

C. Image Segmentation

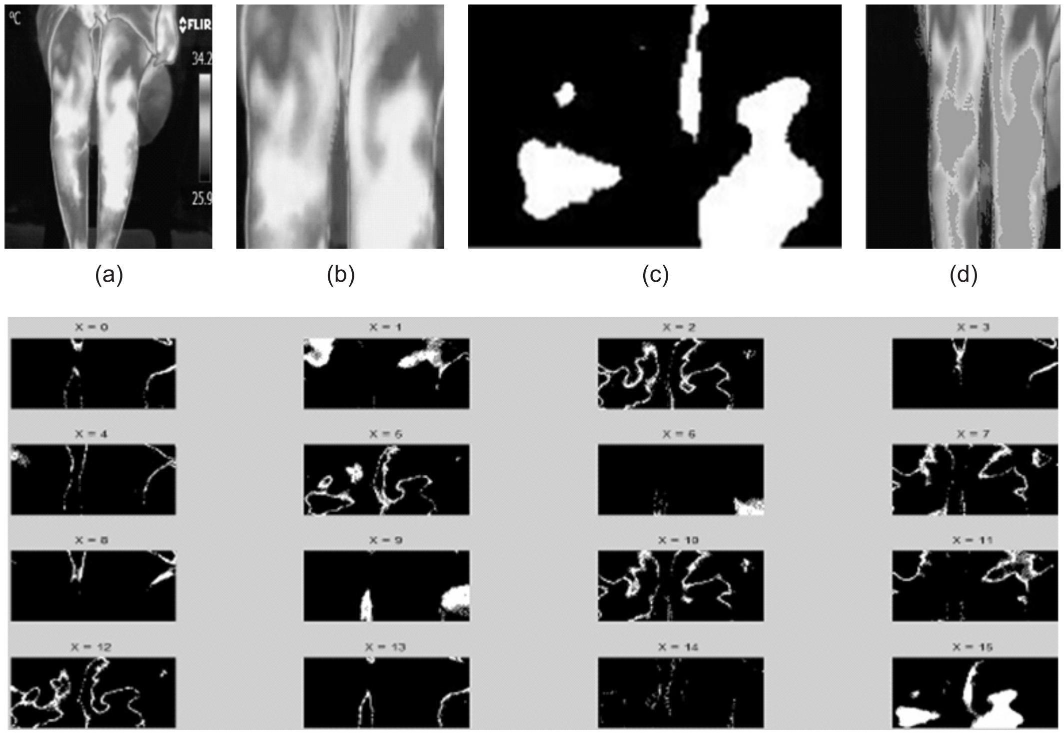
Figures 2(a) and 3(a) represent thermographs of RA and normal subjects. Normal thermograph is characterized by symmetric, uniform temperature regions, whereas, RA thermograph is characterized by the presence of asymmetric, higher temperature pattern, namely, white regions (hot spot region). Hence, the main aim of image segmentation is to effectively segment the hot spot region.

D. Colour Image Segmentation

This is a type of threshold-based image segmentation in which an optimal threshold value is manually selected by trial and error method and based on that hot spot region is segmented . The major steps involved in colour image segmentation are given in Figure 4. The thermal image is quantized into 16 colours and binary mask of each index is given in Figure 2(e). The segmentation mask is developed by combining indices which have maximum components of ROI and the image is segmented (Figure 2(c)). Superimposition of the segmented image is done by reconstructing the individual colour channels into RGB image (Figure 2(d)).

E. Feature Extraction

The feature describes the significant characteristics and specifies certain quantifiable property of an image. These can be either low or high level features that is used to differentiate various characteristics of an image. The features provide characteristic properties of an IR thermogram that is used to classify abnormal from normal subjects. In this case study, GLCM features namely contrast, correlation, energy, homogeneity for both healthy subjects and control are measured.



(e)

Figure 2: Colour image segmentation of RA subjects: (a) Thermographic image of RA subject, (b) cropped image, (c) Segmented image, (d) Superimposed image and (e) binary mask (X = 15)

4. COLOUR DOPPLER ULTRASONOGRAPHIC EVALUATION

Colour Doppler ultrasonographic examination was done in 5 RA patients and 2 control subjects. CDUS examination was done after clinical and thermographic investigation. Conventional gray scale US is used to investigate the knee joint starting at lateral joint space, then to lateral, medial, central, and suprapatellar recess, and medial joint space. Both longitudinal and transverse US images were taken.

The following US parameters were measured:

1. Existence of effusion
2. Anterior posterior diameter of suprapatellar recess to determine effusion extent.
3. Intensity of perfusion on CDUS images.

The extent of effusion is measured by the semi-quantitative grading system based on Fiocco et al. [17]

Grade 0: <2 mm

Grade 1: 2–5 mm

Grade 2: 6–8 mm

Grade 3: >8 mm

For each patient, the scan with maximum colour Doppler activity is used to determine perfusion intensity. Based on the study by Schmidt et al. [18], the degree of perfusion is semi-quantitatively graded using a scale of 0–3.

Grade 0: no colour Doppler signal (no perfusion)

Grade 1: 1–3 colour pixels (mild perfusion)

Grade 2: 3–10 colour pixels (moderate perfusion)

Grade 3: >10 colour pixels (intense perfusion)

Results of Thermal Image Examination

Figure 2 shows the results of colour image segmentation of RA thermogram. Figure 2(a)–(e) represents thermogram of RA subjects, cropped image, segmented image and superimposed image, respectively. The manual segmentation output of RA subjects reveals hot spot (white) region (Figure 2(c)) indicating abnormality, whereas for normal subjects it shows dark image (Figure 3(c)). Thus, colour image segmentation is implemented successfully to differentiate normal and RA subjects using thermography.

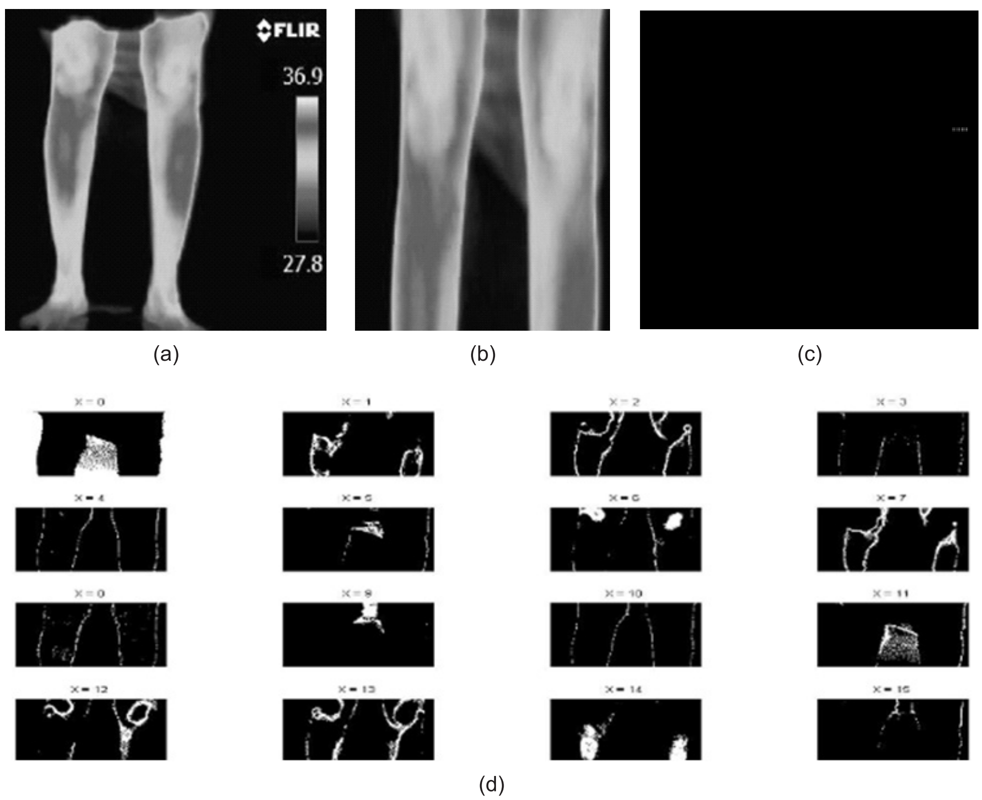


Figure 3: Colour image segmentation of normal subjects: (a) Thermographic image of RA subject, (b) cropped image, (c) Segmented image and (d) binary mask (X = 15)

Feature Extraction

Table 1 provides the thermographic feature extraction data for both healthy subjects and RA patients. From the Table 1, it is clear that the major features namely contrast, correlation, energy and homogeneity are higher for abnormal than the normal subjects. Thus, GLCM features can be used to classify normal and abnormal RA subjects using IR thermography.

Results of CDUS Examination

ImageJ is used to analyse the color Doppler ultrasound images to determine the intensity of perfusion. ImageJ is a Java-based, open source, freely available, platform independent image processing and analysis program developed by National Institutes of Health (NIH), USA [19].

Table 1
Feature extraction results of thermographic data (*n* = 10 RA subjects and 10 controls)

S.No	*Parameters*	*Normal (Mean ± SD)*	*Abnormal (Mean ± SD)*
1.	Contrast	0.106 ± 0.03	0.2447 ± 0.124
2.	Correlation	0.431 ± 0.04	0.86238 ± 0.04
3.	Energy	0.76 ± 0.07	0.98 ± 0.03
4.	Homogeneity	0.80 ± 0.162	0.98 ± 0.006

The steps involved in segmenting the colour pixels from CDUS images are as follows:

1. *Selection of ROI*: After the US image is loaded in ImageJ platform, the ROI is selected using the in-built function available in ImageJ. The ROI is traced in the synovium tissue which is characterised by the hypoechoic mass near the joint covering the bony surfaces. The image is then cropped to remove the unwanted regions (Figure 4(a)).
2. *Smoothing*: Smoothing is done to eliminate the problems caused by the cell boundaries. Median filter is used to remove the noise (Figure 4(b)).
3. *RGB colour transformation*: The image is split into R, G, B colour channels and the image with best contrast is selected.
4. *Thresholding*: The colour pixels are segmented using autothreshold method given in ImageJ (Figure 4(c)).

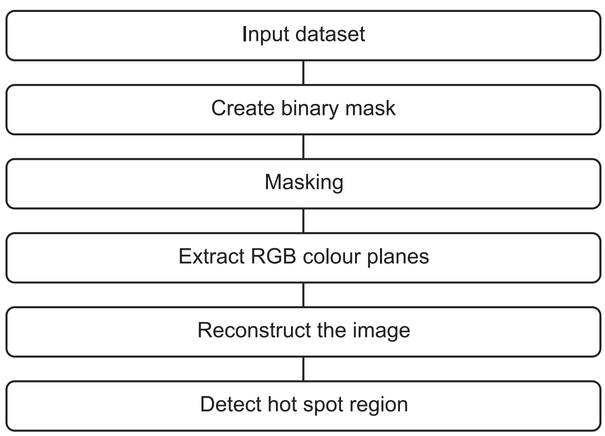


Figure 4: Steps involved in colour image segmentation

Figure 5 represents the CDUS image of the control subject. In the control subjects, there are no knee joint effusions and perfusions. Figure 5 reveals no signs of perfusion, hence it is not processed by Image j program.

The Table 2 reveals the colour Doppler findings of healthy and control subjects. Out of the 5 RA patients, knee joint effusion and perfusion is found only in 4 patients. Likewise, 2 control subjects do not reveal any signs of knee joint effusion and perfusion. Mild degree of knee joint effusion and perfusion was found in 3 images out of 4 RA positive CDUS images. Only one RA subject revealed moderate degree of perfusion and knee joint effusion in the CDUS findings.

Table 2
CDUS results of 5 RA subjects and 2 controls

S.No	*Patients ID*	*Effusion (Y/N)*	*Anterior posterior diameter*	*Extent of effusion*	*Intensity of perfusion*
1	IR0026	Y	6.3 mm	2	2
2	IR0001	Y	3.0 mm	1	1

S.No	*Patients ID*	*Effusion (Y/N)*	*Anterior posterior diameter*	*Extent of effusion*	*Intensity of perfusion*
3	IR0012	Y	2.3 mm	1	1
4	IR003	y	3.0 mm	1	1
5	IR0004	N	0	NA	NA
6	CR001	N	NA	NA	NA
6	CR002	N	NA	NA	NA

Effusion grading: AP diameter of the suprapatellar recesses

Grade 0: <2 mm; Grade 1: 2–5 mm; Grade 2:6–8 mm; Grade 3: >8 mm

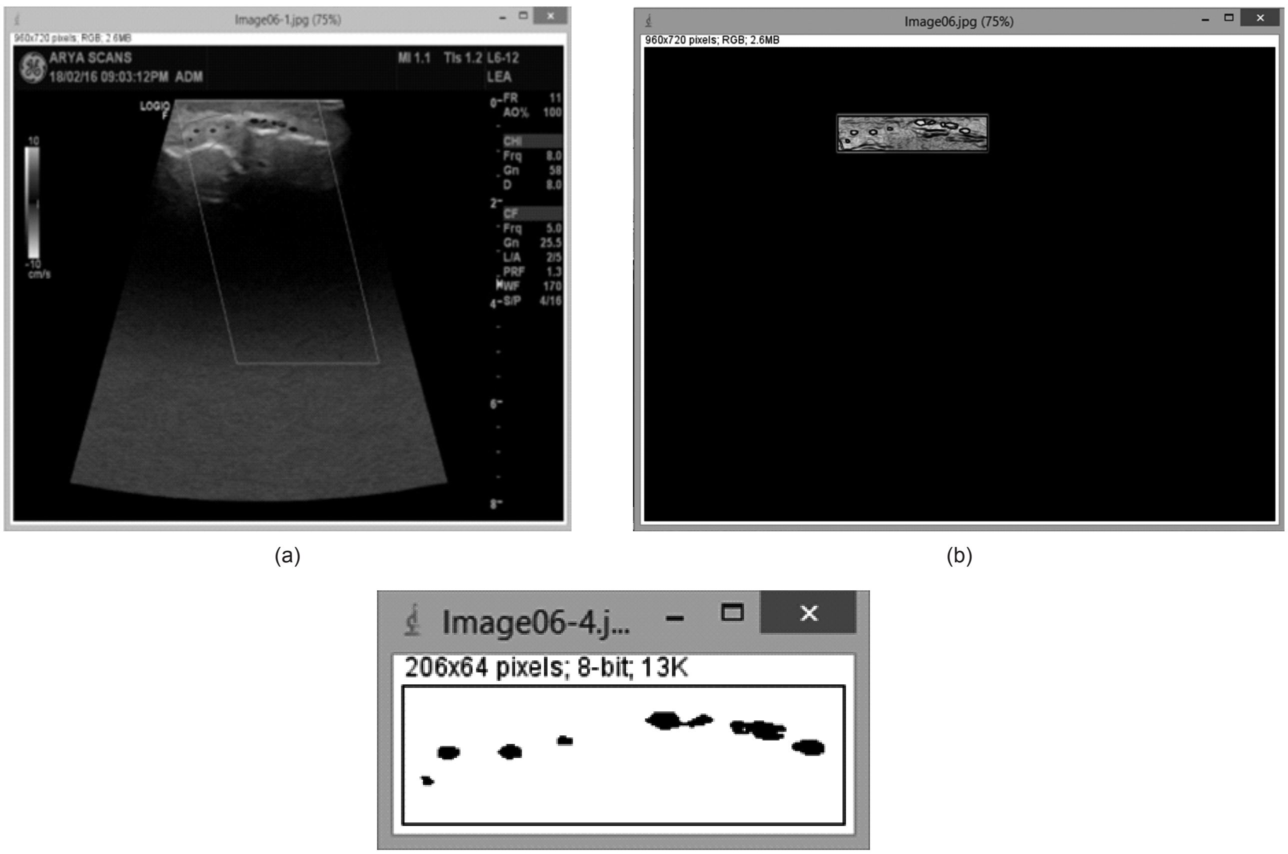
Perfusion grading:

Grade 0: no colour Doppler signal (no perfusion)

Grade 1: 1–3 colour pixels (mild perfusion)

Grade 2: 3–10 colour pixels (moderate perfusion)

Grade 3: >10 colour pixels (intense perfusion)



(a) (b) (c)

Figure 5: CDUS image of RA subjects: (a) Selection of ROI, (b) Filtered and cropped image and (c) Segmented image

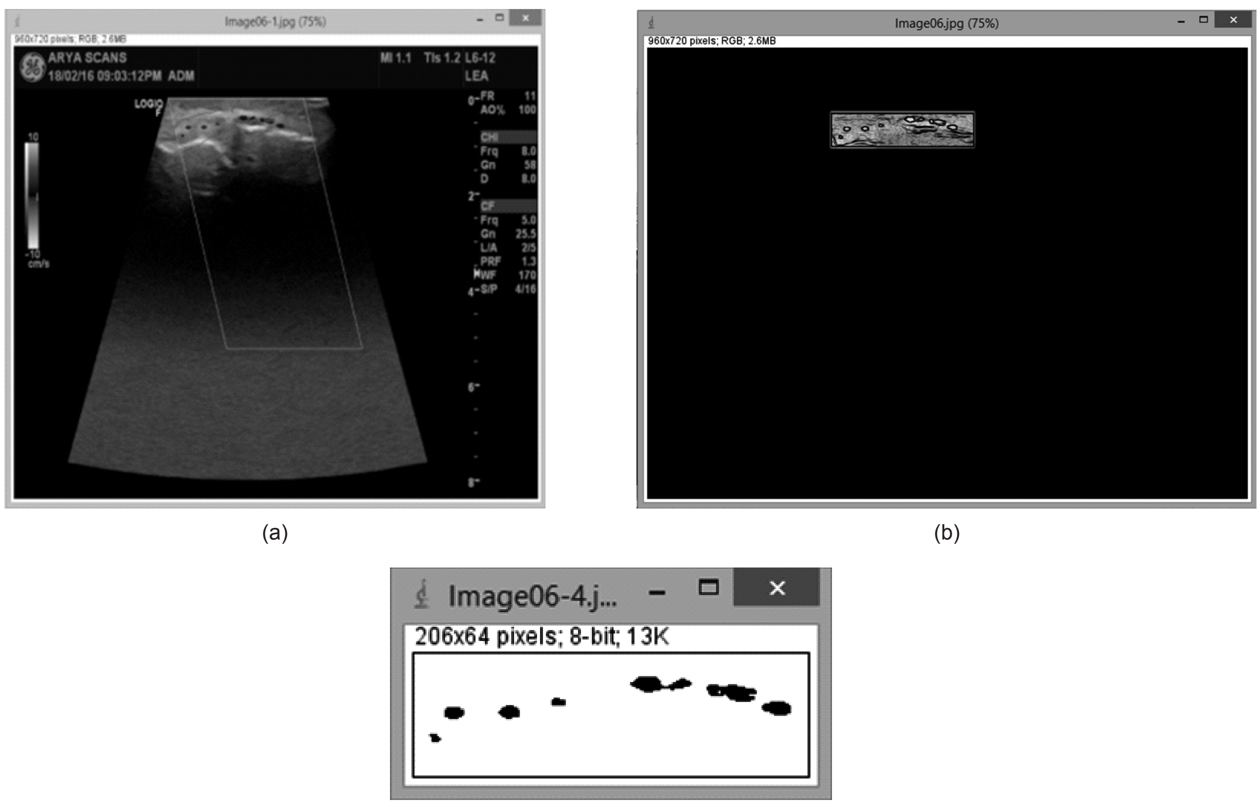
Comparison of clinical, thermographic and CDUS findings

The Table 3 compares the results of clinical, thermographic and CDUS findings of five RA patients. The thermographic results of five RA subjects were in-line with the clinical findings. On the other hand, out of the five CDUS images, the results of four subjects correlated with clinical findings. The four CDS images provided positive findings for RA. However, only one CDUS image does no correlate with the clinical findings. The clinical findings revealed a positive result for RA, whereas the CDUS results provided a negative finding result for RA. Thus, from this study, it is revealed that clinical findings correlated well with thermographic results than CDUS results.

Table 3
Comparative data of clinical, thermographic and CDUS

S.No	*Patients ID*	*Clinical examination*	*Thermographic results*	*CDUS results*
1	IR0026	+	+	+
2	IR0001	+	+	+
3	IR0012	+	+	+
4	IR003	+	+	+
5	IR0004	+	+	–
6	CR001	–	–	–
6	CR002	–	–	–

Legend: + indicates RA; – indicates Normal.



(a) (b) (c)

Figure 5: CDUS image of RA subjects: (a) Selection of ROI, (b) Filtered and cropped image and (c) Segmented image

5. DISCUSSION

This study attempts to evaluate the use of non-invasive, cost economic and easily accessible diagnostic techniques in the evaluation of early stage RA. To the author's knowledge, this is the first study, to compare thermography and CDUS findings by correlating clinical findings. The present study provides a deep insight on the various steps involved in the IR thermal and CDUS evaluation of normal and RA subjects. From the results of the present study, it is evident that IR thermal imaging has a potential in the diagnosis of RA in the early stage. The results of the present study are in line with the results of previous studies indicating that IR thermography is a promising tool in the diagnosis of RA. A number of clinical studies [2, 4, 5] have suggested that heat distribution as a quantitative measure of disease activity, however, in the present study, the presence of RA is correlated with the image processing based methodology, viz. the presence of hot spot region.

From the present study, it is revealed that GLCM features hold good for the classification of normal and RA subjects. In-line with the results of the present study, Kapoor et al. [20] employed texture features to diagnose abnormal breast images from normal breast thermal image. Conversely, several previous studies have employed statistical features to classify normal and abnormal RA subjects [3,9,10]. Hence, future studies should employ both GLCM and statistical features for the classification of RA and normal subjects.

From the results of the present study, it was found that clinical and functional assessment score correlates highly with IR thermal image analysis than CDUS. Out of the five CDUS images, the results of 4 images are comparable to the clinical findings. However, the result of 1 CDUS image does not correlate with clinical findings. However, the results of the present study contradict with the previous studies [10, 11,13] in which Doppler ultrasound was efficient in determining synovitis and effusions. Similarly, in the study by Qvistgarrd et al. [21] CDUS correlated well with ESR scores using 18 RA joints. Hence, no definite conclusions can be drawn from this study, as the results of the ultrasound image analysis are operator- as well as instrument- depended. Hence, the present study warrants further investigation with large sample size of data.

According to the results of present study, both IR thermal imaging and CDUS offers a better diagnostic potential in detecting early stage RA than CDUS. Future studies should compare these two diagnostic techniques using large sample size and appropriate study design.

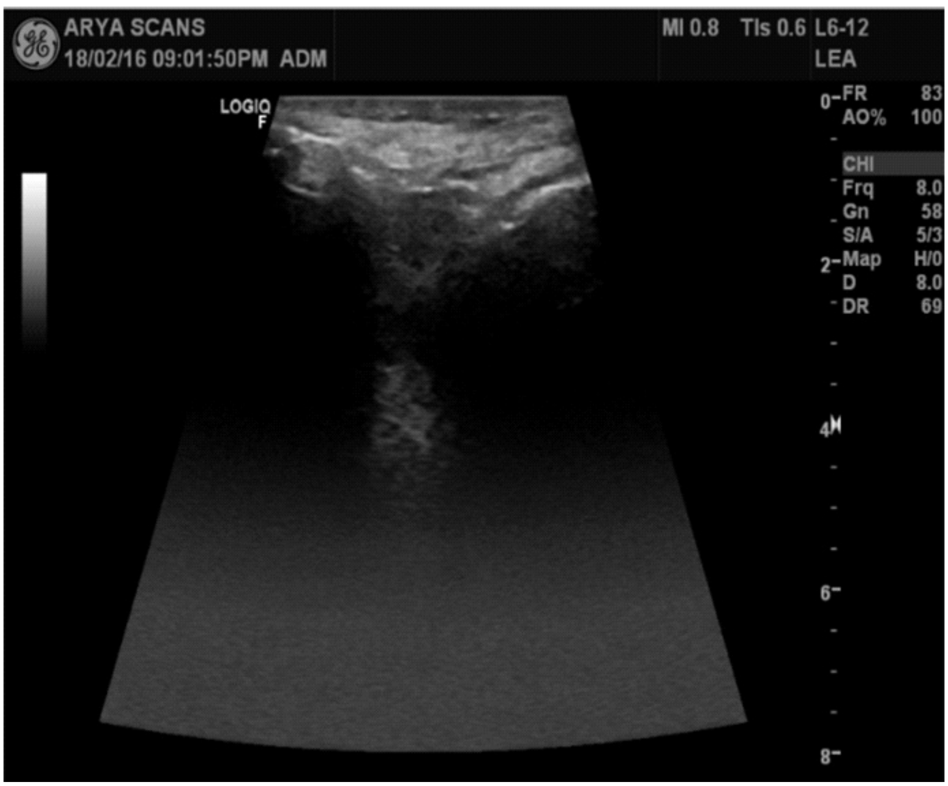


Figure 6: CDUS image of control subjects

6. LIMITATIONS AND RECOMMENDATIONS

- The results of the present study are limited by the study design. Since, the sonographers were not blinded to the clinical information there would have been a certain observer bias. Hence, randomized blinded control study should be adopted in future to eliminate observer bias.
- CDUS examination is subjected to artifacts and false-positives, hence standardization of CDUS is necessary.

- Body or room temperature, physical activity, food habits before examination can influence thermal and CDUS findings. Hence, future studies should consider these factors.

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