Mathematical Biosciences and Engineering

http://www.aimspress.com/journal/MBE

MBE, 18(6): 7759–7773.
DOI: 10.3934/mbe.2021385
Received: 06 July 2021
Accepted: 19 August 2021
Published: 08 September 2021

Research article

Thermal imaging in total knee replacement and its relation with inflammation markers

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Abstract: Total knee replacement is an end-stage surgical treatment of osteoarthritis patients to improve their quality of life. The study presents a thermal imaging-based approach to assess the recovery of operated-knees. The study focuses on the potential of thermal imaging for total knee replacement and its relation with clinical inflammatory markers. A total of 20 patients with bilateral knee replacement were included for thermal imaging and serology, where data was acquired on pre-operative day and five post-operative days. To quantify the inflammation, the temperature-based parameters (like mean differential temperature, relative percentage of raised temperature) were evaluated from thermal images, while the clinically proven inflammation markers were obtained from blood samples for clinical validation. Initially, the knee region was segmented by applying the automatic method, subsequently, the mean skin temperature was calculated and investigated for a statistical relevant relationship with inflammatory markers. After surgery, the mean skin temperature was first increased (> 2.15 °C for different views) then settled to pre-operative level by 90th day. Consequently, the mean differential temperature showed a strong correlation with erythrocyte sedimentation rate (r > 0.893) and C-reactive protein (r > 0.955). Also, the visual profile and relative percentage of raised temperature showed promising results in quantifying the temperature changes both qualitatively and quantitatively. This study provides an automatic and non-invasive way of screening the patients for raised levels of skin temperature, which can be a sign of inflammation. Hence, the proposed temperature-based technique can help the clinicians for visual assessment of post-operative recovery of patients.

Keywords: image analysis; inflammatory markers; non-invasive assessment; skin temperature; thermal imaging

1. Introduction

Total knee replacement (TKR) is an end-stage treatment of osteoarthritis (OA) patients to improve their quality of life. Normally, the surgery is followed by the inflammation that subsides with time, but it might be sustained in some cases [1]. Some studies suggest that the sustained inflammation of the post-operative knee may be a sign of infection [2,3]. The monitoring of serum levels of inflammatory markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and Interleukin-6 (IL-6) in the post-operative period after TKR has become the standard method for early detection of infection [4,5]. The inflammatory markers have shown high specificity and sensitivity for detecting post-operative infection in TKR [6,7]. Inflammation at the local site leads to increased vascularity due to vasodilation caused by mediators of inflammation. This increased vascularity leads to raised local skin temperature, which can be used as a surrogate to inflammatory marker and monitor the recovery of patient post-surgery; as reported by various studies [8–12].

The change in skin temperature can be monitored employing either a contact type thermometer or infrared radiation based thermal imaging, where the latter provides a non-ionizing and non-invasive solution for thermal measurement, called thermography [13]. For TKR, the use of thermography was firstly documented in 1981, where the authors reported the significant temperature difference between the knees with and without infection [14]. In another study, the temperature measurement was done with thermistors and observed that heat trauma created by cutting tool during TKR surgery may contribute to loosening of the tibial component [15]. In 2005, Mehra et al. examined the relationship between CRP and skin temperature of TKR patients post-operatively. They reported that CRP value settles to normal value by six weeks, but skin temperature may remain elevated till 18 weeks. In 2006, Haidar et al. recorded the thermal pattern of uncomplicated TKR and found that the mean differential temperature (MDT) peaks at 2.9 °C on the 7th post-operative day; and becomes almost zero after 24 months [16]. In another study, the changes in local knee skin temperature and serums like IL-6, ESR, and CRP of uncomplicated TKR patients were monitored [9]. Consequently, the authors suggested that the sustained elevation of these inflammatory markers and knee skin temperature may be early signs of complication. In a recent study, the advancement in classification and resolution enhancement of thermal images with the state of art deep learning has been reviewed by He et al. [17]. The authors reported that the deep learning algorithms are more frequently used for passive thermography rather than the active approaches. Till now, all the studies reported either a manual or semi-automatic segmentation technique for the extraction of the knee region. Further, none of the studies analyzed the temperature variation of different views of the knees. Moreover, none of the studies had reported the visual analysis method to assess the raised skin temperature.

In this study, an automatic segmentation technique is used to extract the knee region of high temperature. This work aims to quantify the inflammation of knee post TKR based on skin temperature assessment, where the various views of knee viz. medial, frontal and lateral were analyzed independently. More specifically, the thermal parameters yield the assessment of temperature changes in two ways: (a) quantitative analysis: MDT and relative percentage of raised temperature (RPRT) and (b) qualitative analysis: the visual profile of raised temperature (VPRT). The MDT and RPRT were used as an indicator of raised temperature to evaluate the post-operative recovery, where the reduction in value indicates the recovery. For further validation, the thermal parameters were correlated with clinically proven inflammation markers, viz. ESR and CRP.

2. Materials and methods

All patients who underwent bilateral TKR surgery for advanced-stage 4 osteoarthritis in the orthopedics department of the medical institute, from August 2019 to March 2020, were screened. The study was performed according to the guidelines of the Declaration of Helsinki [18]. The demographic details including age, sex, BMI, comorbidities and personal habits like smoking or alcohol, were noted (see Table 1). Patients with inflammatory arthritis, peripheral vascular disease, inflammatory skin diseases, autonomic dysfunction, etc., were excluded from the study. Further, all the patients were advised to avoid the intake of hot beverages and heavy meal 12 hours before the data acquisition. Ethical approval was obtained from the medical institute (INT/IEC/2018/000313). Prior informed consent was sought and obtained from all patients who were included in this study.

Table 1. Demographic details of patients.

Patient's demographics	
Number of patients	20
Age	62.55 ± 6.15 years
Gender	3M + 17F
BMI	29.98 ± 2.41 kg/m2
Alcohol/ smoking habit	No

The thermal images of the knee were obtained on the pre-operative day (PRD01), 2nd (POD02), 6th (POD06), 15th (POD15), 45th (POD45) and 90th (POD90) day post-operatively. A blood sample was collected on the days of thermal imaging for the calculation of ESR and CRP patterns. All surgeries were performed by a single experienced orthopedic surgeon using the medial parapatellar approach and posterior substituting the TKR implant of a single company.

The thermal images were captured with FLIR E60 thermal camera which has ± 2% accuracy, 60 Hz frame rate, and 0.05 °C thermal sensitivity. During data acquisition, the camera settings were kept as emissivity at 0.98 and reflected temperature at 20 °C. To get the stabilized performance, the camera was switched ON for at least 10 minutes before imaging [19]. The imaging trial was performed in an investigation room, where the ambient temperature was maintained between 23 ± 1 °C and humidity at 58 ± 2%. The humidity and temperature of the ambience were recorded by the digital hygrometer thermometer (model HTC-1). To ensure the patients' comfort, the images were captured in lying posture, where the knee region was unclothed and undressed for 10 minutes of acclimatization [11]. The undressing and cleaning of surgical wounds were done by clinicians, thereby decreases the risk of wound contamination. The camera was positioned approximately 0.6 meters away by focusing on the center of the knee to sufficiently capture the respective views. While capturing the medial view, the concerned knee was elevated to a suitable height using the cushion, thereby got the knee in the camera's field of view above the contralateral knee (see Figure 1).

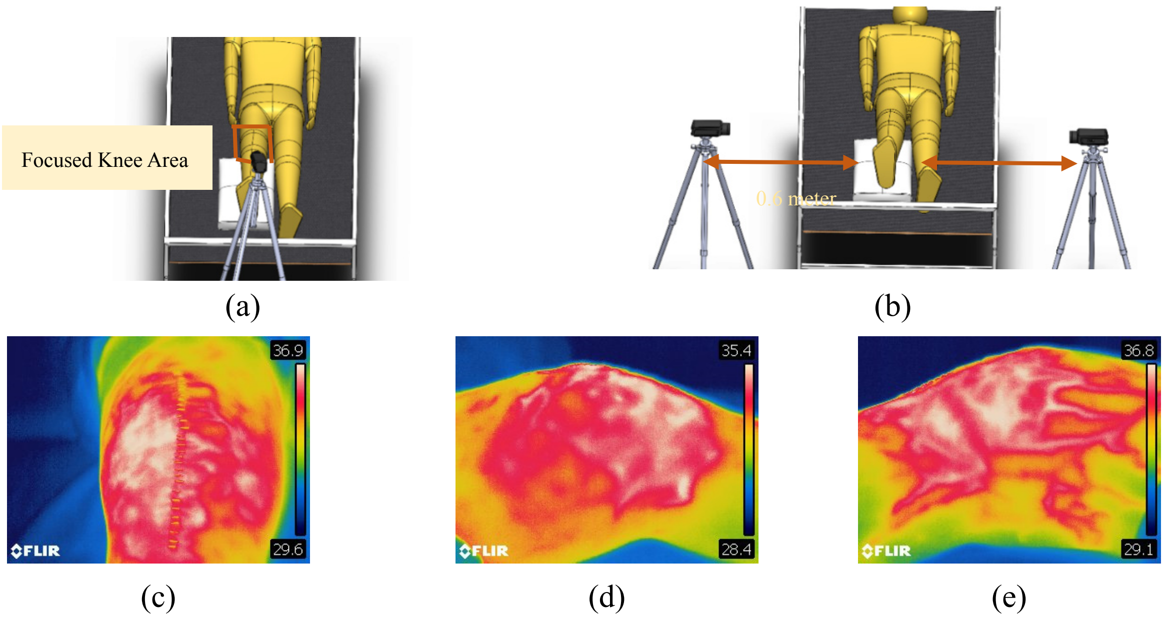

Figure 1. Image acquisition setup (a-b) and sample thermal images of (c) frontal, (d) medial and (e) lateral view.

In this way, the thermal images of 20 bilateral TKR patients (40 knees) were acquired, where each knee was captured with 3 different views (lateral, frontal, and medial projection). A total of 36 thermograms of each patient was collected over a follow-up period of 6 days. A graphical framework illustrating the steps involved is shown in Figure 2.

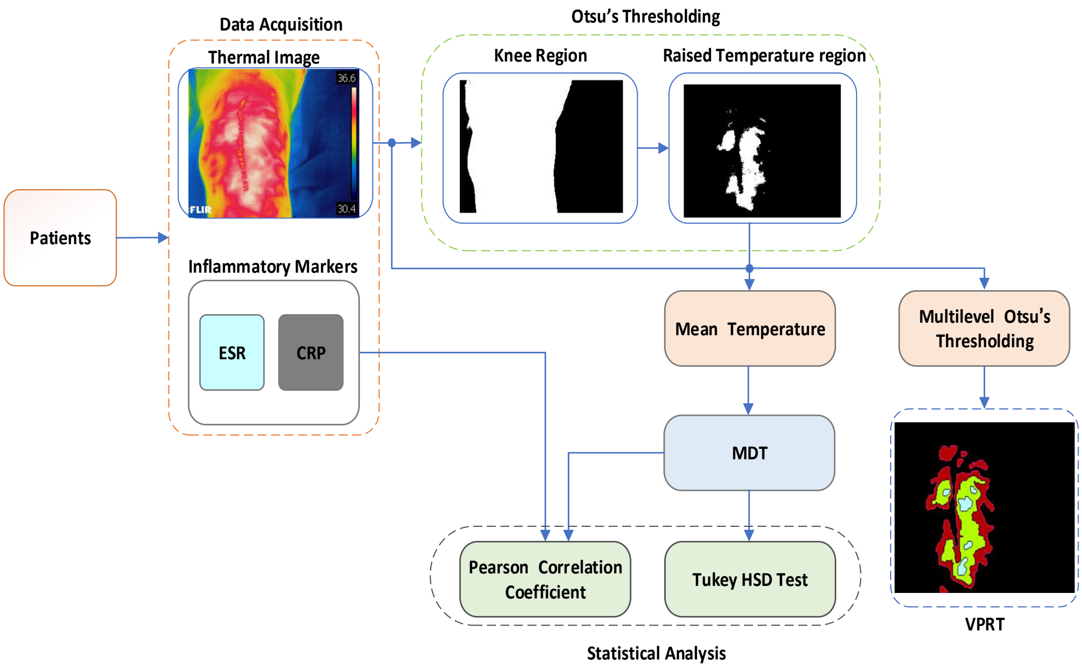

Figure 2. graphical framework.

In this study, the mean differential temperature (MDT) is taken as an intra-subject evaluation parameter to analyze the recovery of OA patients after surgery. To obtain the MDT values, the thermograms were first pre-processed by Otsu thresholding that separated the knee region from the background, then the mean temperature values of extracted knee regions were calculated [20]. The MDT is determined by subtracting the baseline temperature, i.e., the knee temperature at the pre-operative day from the knee temperature at all 5 post-operative days (see Eq (1)). As a result, the MDT values were separately calculated for each view of the knee and arranged in chronological order to analyze the thermal changes.

$$MDT_i = T_i - T_{pre-op}; \qquad For\ i = 1{:}n \tag{1}$$

where n is the number of sequential thermograms of a patient over the follow-up period, here n = 6, T_i is knee temperature on ith day, and T_{pre} is the knee temperature on pre-operative day.

Further, the relative percentage of raised temperature (RPRT) of the knee were calculated from the sequential thermograms to evaluate the post-operative recovery. RPRT was calculated by performing the three steps: (a) relative normalization, (b) thresholding, and (c) calculate pixels of the inflamed region and knee region. Firstly, the relative normalization was performed as follows:

$$I_{norm}(j) = \frac{T_j - T_{min}}{T_{max} - T_{min}}\ ; \qquad For\ j = 1{:}n \tag{2}$$

where n is the number of sequential thermograms of a patient over the follow-up period, here n =6 (the number of times a patients' thermal image was collected). T_{min} and T_{max} is the overall minimum and maximum temperature of a single view of the patient over a follow-up period respectively, and T_j is the temperature of jth thermal image.

Secondly, Otsu's thresholding was applied to extract the knee region to calculate the raised temperature from the normalized thermograms [20]. The proposed approach to calculate the RPRT is as follows:

$$RPRT = \frac{N_i}{N_k} \times 100\% \tag{3}$$

where, N_k is the total number of pixels in the extracted knee region and N_i is the number of pixels in the raised skin temperature region (s).

However, RPRT cannot depict the actual increased temperature, but it provides the relative profile of temperature over a follow-up period with respect to pre-operative day temperature, which can help the clinician to track the intra-subject recovery of a patient during the post-operative period.

Initially, the raised temperature region of the knee was extracted by applying the same method as used in RPRT i.e., Otsu's thresholding method. Then, the multi-level thresholding was applied to further classify the inflamed region, where the previously segmented region was again segmented to extract the higher temperature regions. This step is performed three times to get three different high temperature regions for a better visual analysis. VPRT illustrates the three regions with Pseudo-color representation viz. red, yellow, and white which were extracted by taking different thresholding values.

In this study, ESR and CRP were used for assessing the inflammation post-operatively. ESR is a non-specific marker, whereas CRP is one of the protein commonly referred as acute phase reactant. The ESR and CRP were calculated by the modified Westergren method and particle enhanced turbidimetric inhibition immunoassay (PETINIA) method, respectively.

2.1. Statistical analysis

The data normalcy was checked by the Anderson-Darling test, where $p < 0.05$ indicates that the data does not follow the normal distribution. In this case, $p = 0.763$ was obtained which indicates the high normalcy of data. Then, an ANOVA test with a post-hoc Tukey HSD test was performed to evaluate the intra-patient mean temperature variation. The test was considered statistically significant for $p < 0.05$ for the intra-knee group. The Pearson's Correlation Coefficients (r) between MDT and inflammatory markers were calculated. The correlation was considered as high positive if $r > 0.7$ [21]. The data were processed and analyzed using Python software on HP Z420 machine having 8 GB RAM.

3. Results

To analyze the thermal profiles of different views of the knees, the overall average of MDTs of all patients on a particular day with a standard deviation were calculated (see Table 2). The graphical representation of MDT profiles along with their p-value (obtained by ANOVA test) is illustrated in Figure 3. By analyzing the cumulative profiles, it was observed that the patients attained lower skin temperature on the 90th post-operative day after surgery when compared with pre-operative value. The MDT profiles increased to maximum on the 2nd or 6th day after surgery, then reached to pre-operative value on 45th or 90th post-operative day. The subgroup comparison was done via post-hoc Tukey HSD test to check the intra-patient temperature significance (see Table 4).

Table 2. Magnitude of average MDT over the follow-up period.

		Follow-up period				
		POD02	POD06	POD15	POD45	POD90
Average MDT ± s.d.	F_L	2.72 ± 1.10	2.79 ± 1.14	0.92 ± 1.31	–0.05 ± 1.49	–0.50 ± 1.44
	F_R	2.90 ± 1.15	2.86 ± 1.28	0.98 ± 1.34	0.14 ± 1.70	–0.22 ± 1.33
	M_L	2.62 ± 1.12	2.27 ± 1.00	0.32 ± 1.28	–0.55 ± 1.74	–0.89 ± 1.67
	M_R	2.66 ± 1.28	2.56 ± 1.31	0.38 ± 1.43	–0.36 ± 1.71	–0.76 ± 1.43
	L_L	2.3 ± 1.09	2.16 ± 1.09	0.32 ± 1.14	–0.47 ± 1.49	–1.19 ± 1.32
	L_R	2.19 ± 1.35	2.28 ± 1.27	0.40 ± 1.33	–0.23 ± 1.56	–0.63 ± 1.34

* POD- Post-operative day, * s.d. – Standard deviation. F_L, F_R, M_L, M_R, L_L, L_R are the frontal left, frontal right, medial left, medial right, lateral left, lateral right views of the knee respectively.

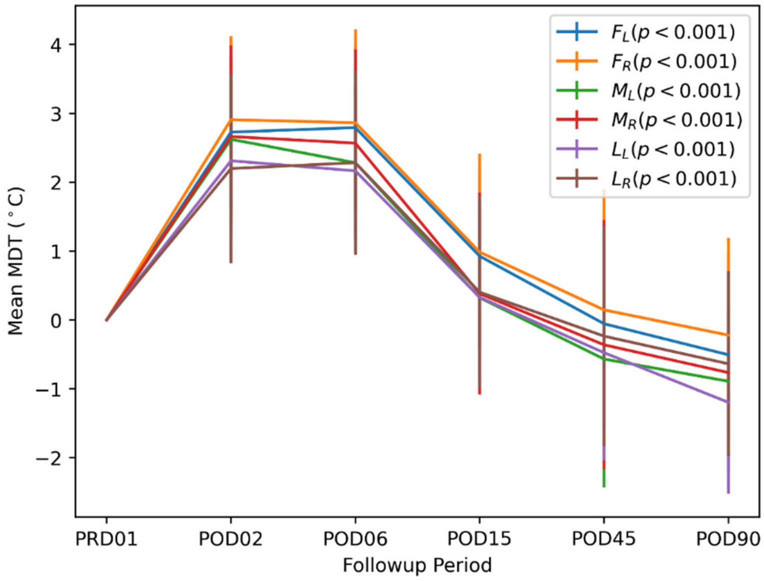

Figure 3. Mean MDT profiles of various views of knees (vertical bars indicate the standard deviation).

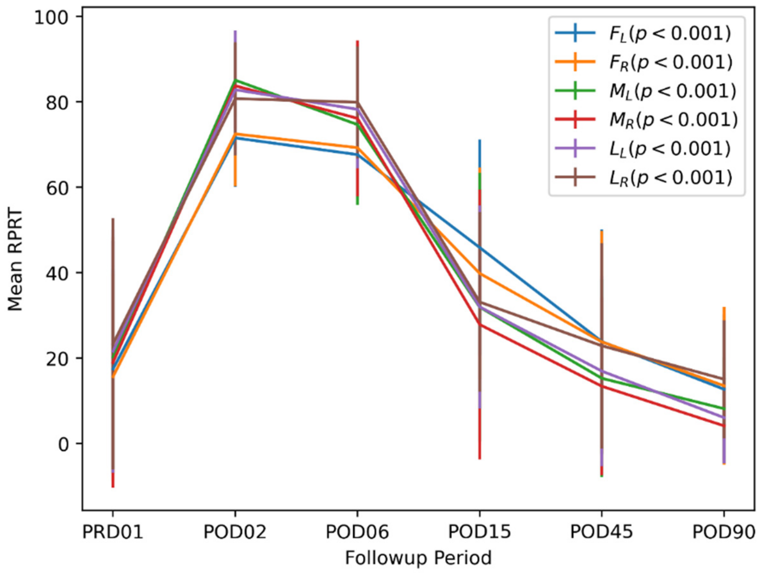

Figure 4. Illustrates the overall mean RPRT of various views of knees.

Consequently, similar profiles of inflammation had been observed for patients, however, with slight variation i.e., the maximum inflammation occurred on either POD02 or POD06 (see Figures 6 and 7). As a fact, the profile of RPRT correlates highly with the profile of MDT, where both profiles indicated the post-operative recovery as the inflammation subsided with time.

VPRT indicates the changes in skin temperature during the post-operative days based on false-color representation, as shown in Figure 5. In contrast to quantitative analysis, it yields the temperature profile visually which provides ease to the doctors and clinicians for better evaluation of recovery.

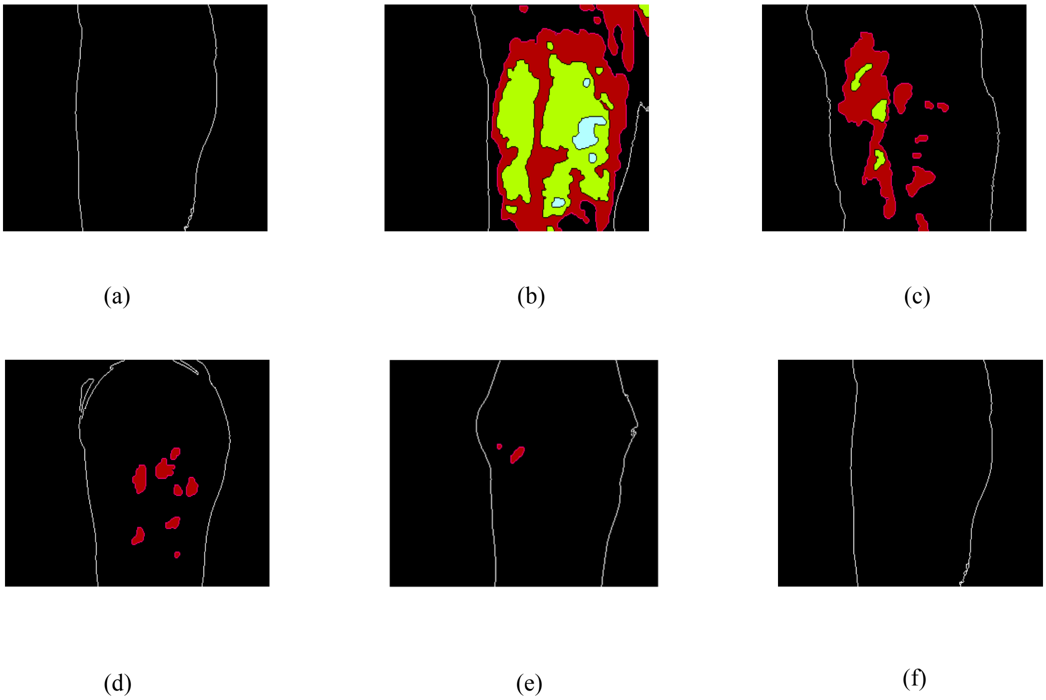

Figure 5. Illustrates the skin temperature on the frontal view of the operated knee of a single patient on (a) PRD01, (b) POD02, (c) POD06, (d) POD15, (e) POD45, and (f) POD90. (Colors represent the various levels of raised temperature on intra-subject normalized images; temperature of white & blue region > yellow & green region > red region).

The skin temperature profile is observed as (a) normal temperature on pre-operative day, (b) highest temperature rise on POD02, and (c) raised temperature decreases with time and settled to pre-operative value till POD45 or POD90 (Figure 4). In brief, the temperature first increases until the maximum value, then starts decreasing and disappears till the 90th day. Hence, VPRT closely follows the changes in MDT and RPRT profile.

The average ESR value on the pre-operative day was 23.85 ± 10.93 mm/hr (Table 3). The peak of serum ESR value in post-operative day was on POD02 and POD06 (68.4 ± 9.43 mm/hr) and thereafter gradually settling down to near normal value by POD90 (21.33 ± 17.62 mm/hr) as shown in Figure 6. Similarly, the average CRP value on the pre-operative day was 2.9 ± 1.97 mg/L. We observed an increase in CRP value post-operatively attaining peak at POD02 (301 ± 85.98 mg/L), decreasing thereafter, and reaching to a value less than or equal to the pre-operative value on POD45 day (9.23 ± 8.05 mg/L) as shown in Figure 7. However, there was a wide variation in the level of CRP during the early post-operative period up to POD15. The normal range for ESR and CRP was considered 25 mm/hr and 10 mg/L respectively. The initial increase in the values of ESR and CRP in post-operative period was a sign of inflammation which subsided with time and reached to pre-operative value by POD90.

Table 3. ESR and CRP values of the follow-up period.

		Follow-up period					
		PRD01	POD02	POD06	POD15	POD45	POD90
Inflammatory markers	ESR	23.85 ± 10.93	66.35 ± 17.38	68.4 ± 9.43	48.72 ± 22	33.22 ± 24	21.33 ± 17.62
	CRP	2.9 ± 1.97	301 ± 85.98	157.95 ± 69	51.48 ± 70.01	9.23 ± 8.05	3.81 ± 2.49

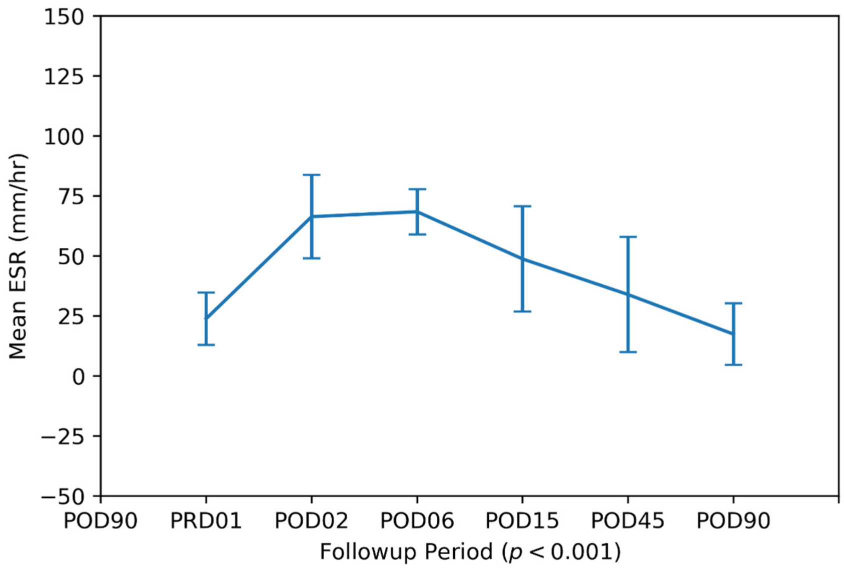

Figure 6. Illustrates the overall average ESR values over a follow-up period.

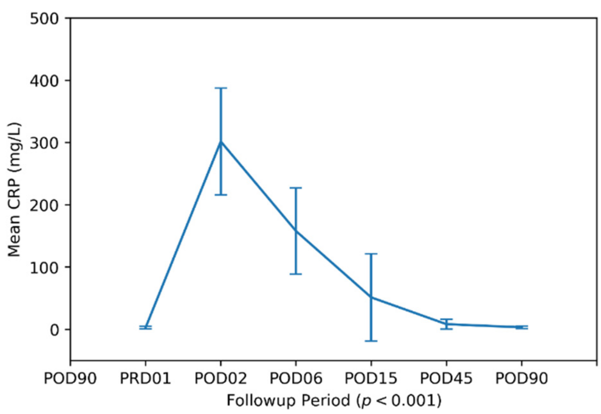

Figure 7. Illustrates the overall average CRP values over a follow-up period.

The ANOVA test was applied to check the significant difference in temperature values at a different time during follow-up and found a p-value < 0.001 for all the views of the knee (see Figures 3, 4, 6 and 7). Further, the post-hoc Tukey HSD test is applied to find the statistically significant difference between the different combinations of pre-operative and post-operative days for various views of knees (Table 4). The table clearly showed that the test had an insignificant p-value for a different combination of PRD01, POD45, and POD 90 which indicates that the raised temperature has settled to pre-operative value with time, while other combinations of test groups showed a highly significant p-value.

Table 4. Correlation among pre-operative and post-operative days using the Tukey HSD test.

Group1	Group2	p-value					
		FL	FR	IL	IR	LL	LR
PRD01	POD02	0.001	0.001	0.001	0.001	0.001	0.001
PRD01	POD06	0.001	0.001	0.001	0.001	0.001	0.001
PRD01	POD15	0.0188	0.0465	0.7004	0.8369	0.5606	0.5817
PRD01	POD45	0.9	0.8562	0.3196	0.1217	0.7357	0.7709
PRD01	POD90	0.9	0.1269	0.001	0.0025	0.1142	0.3572
POD02	POD06	0.9	0.9	0.9	0.9	0.9	0.9
POD02	POD15	0.001	0.001	0.001	0.001	0.001	0.001
POD02	POD45	0.001	0.001	0.001	0.001	0.001	0.001
POD02	POD90	0.001	0.001	0.001	0.001	0.001	0.001
POD06	POD15	0.001	0.001	0.001	0.001	0.001	0.001
POD06	POD45	0.001	0.001	0.001	0.001	0.001	0.001
POD06	POD90	0.001	0.001	0.001	0.001	0.001	0.001
POD15	POD45	0.0042	0.0013	0.0099	0.0044	0.0397	0.0517
POD15	POD90	0.0016	0.001	0.001	0.001	0.001	0.0062
POD45	POD90	0.9	0.7057	0.1886	0.7449	0.7987	0.9

By applying the Pearson's Correlation test, the correlation coefficients (r) obtained for both CRP and ESR with MDT which characterize the strength of correlation between the skin temperature and inflammatory markers (see Table 5). Thirty-two knees out of 40 showed a very strong correlation ($r \geq 0.8$) between CRP and MDT in all views of knees. Six knees showed a strong correlation with $0.8 > r \geq 0.6$ and 2 knees showed a moderate correlation with $0.6 > r \geq 0.3$. Similarly, the 22 knees show a very strong correlation and 8 knees show a strong correlation between ESR and MDT. Further, the 6 knees show moderate correlation and only 4 knees have poor correlation ($r \sim 0$). Also, similar findings of correlation have been observed in all views of knees.

Table 5. Pearson's correlation coefficient between the groups CRP-MDT and ESR-MDT.

Correlation groups	Pearson's correlation coefficient, *r*					
	F_L	F_R	I_L	I_R	L_L	L_R
CRP-MDT	0.893	0.91	0.936	0.918	0.908	0.899
ESR-MDT	0.976	0.966	0.955	0.957	0.98	0.964

In brief, most of the knees show a good correlation between CRP and MDT, whereas only 4 knees show a poor correlation between ESR and MDT. Overall, the MDT shows a very strong correlation with CRP ($r > 0.893$, $\sim 0.91 \pm 0.015$) and ESR ($r > 0.955$, $\sim 0.966 \pm 0.01$), as tabulated in Table 5.

4. Discussion

Table 6. Comparative MDT analysis with previously reported studies.

Authors (References)	Measurement method or equipment	Segmentation Technique	Temperature (˚C) around 1 week	Temperature (˚C) around 90th day	Correlation
Haidar et al. [16]	Contact method	Not applicable*	2.5	1.2	–
Romano et al. [12]	Thermal camera	Manual Segmentation using an elliptical shape	2.6	0.9	–
Yishake et al. [11]	Thermal camera	Manual Segmentation using a rectangular shape	4.2	1.8	–
Zeng et al. [10]	Infrared thermometer	Not applicable*	2.4	1.3	Low positive
Our study	Thermal camera	Multilevel Otsu (Automatic)	2.79	0.50	Very High

* Not applicable as the contact-based method is used.

This study aimed to explore the potential of thermography in assessing the post-operative recovery of TKR patients. It was found that the MDT value peaks at either 2nd or 6th day after surgery and settled to pre-operative values by day 90, which followed a similar pattern as that of inflammatory markers. Further, a very high Pearson's correlation was observed between MDT and the inflammatory markers (see Table 5).

To calculate the MDT value, all studies in literature used the mean temperature difference between contralateral and operated knee. But in our case, both knees of the patient were operated; hence MDT was calculated with pre-operative mean temperature. The maximum rise in temperature has been observed on the 3rd and 5th day by Romano et al. and Zeng et al. respectively, while Yishake et al. and Haidar et al. observed the peak changes on the 7th day [10,11,16,27]. Similarly, in this study, MDT peaked on the 6th post-operative day for frontal view. The MDT value reached almost pre-operative value at POD90. The MDT values of various researchers along with other important parameters, are shown in Table 6.

Previously, six studies have reported the use of ESR and CRP either individually or combinedly as inflammatory markers along with thermography. These studies reported the peak value of ESR and CRP value in the first-week post-surgery. The average settling time of ESR is around 13 weeks, while for CRP, it is around 6 weeks [8–10,12,28]. Similarly, in the current study, the ESR and CRP values settled to pre-operative value by 90th and 45th day respectively (Table 6).

Only one study calculated the correlation coefficient between the inflammatory markers and skin temperature [10]. They found a strong correlation between the parameters similar to our study. Although a high overall correlation was found in our study, except for 2 patients which showed poor correlation. This may be due to fever and infection in the early post-operative period. A strong correlation can also be an indicator that skin temperature may be helpful in the diagnosis of inflammation of TKR patients post-operatively. As the ESR and CRP value follows a similar pattern as that of MDT and it is found statistically correlated with these markers, MDT can be considered for assessing the inflammation and recovery of the patient. Similarly, RPRT and VPRT may also be useful to the clinician in assessing the raised knee temperature. Consequently, the recovery of the patient can be assessed both qualitatively and quantitatively. To the best of our knowledge, this is the first study that provides the quantification of inflammation in terms of raised temperature using thermography.

Two types of methods are used for the thermal measurement a) contact-based method and b) non-contact method. Ammer observed that the contact-based method would have a higher value than the imaging-based method, but the difference between the healthy and unhealthy patients becomes more visible in the case of the imaging-based method [29]. In the contact-based method, measurement is totally manual and site-specific as used by the researcher. While non-contact based thermal imaging method for TKR patients was used by various other studies which used either manual or semi-automatic segmentation technique for ROI extraction and most of them explored only the frontal side for their assessment [11,12,30]. Romano et al. used an elliptical shape to extract the ROI, which is a manual segmentation technique and error-prone as the inflammation region does not follow any specific shape. Similarly, Yishake et al. and Windisch et al. also used a rectangular shape for the calculation of the raised knee skin temperature. Manual segmentation is a very time-consuming technique and not feasible for large dataset. In contrast, the current study used an automatic segmentation technique for ROI extraction and all three views of knees were analyzed using the same approach, which provided promising results. Although all the views showed the elevated temperature post-operatively, the frontal side took much more time in normalizing the skin temperature (Figures 3 and 4).

The small sample size in the current study is a limitation; however, this represents an early attempt at exploring the role of thermal imaging during the post-operative period of total knee replacement. Further, other researchers such as Mehra et al., Haidar et al., Romano et al., Yishake et al. had used 20, 32, 40, 31 knees respectively in their operated group for their study [8,11,12,16].

Moreover, As the results are promising, we are looking to enroll more patients along with other clinical parameters. Furthermore, we did not use the interleukin-6 (IL-6) marker due to cost constraints.

5. Conclusions

The study presents the potential of a thermography-based approach to evaluate the post-operative recovery of TKR patients. Based on statistical analysis, it is observed that the skin temperature may be used in the diagnosis of inflammation in TKR patients. In contrast to serology, it provides an automatic, non-invasive, time-saving and cost-effective solution. The proposed approach provides the VPRT and RPRT, which may assist the clinicians in better evaluation of post-operative recovery.

Acknowledgments

The cooperation of all the participants is duly acknowledged.

Conflict of interest

There is no conflict of interest to declare.

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