Assessment of joint inflammation at the wrist of patients with rheumatoid arthritis: thermography findings closely mirror those from ultrasonography

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Abstract

Objective

To determine if thermography (in comparison with ultrasonography) may be helpful in detecting joint inflammation at the RA wrist categorised according to its clinical manifestations.

Methods

Four wrist groups were derived from the right wrist of RA subjects as follows: (1) swollen; tender (S1T1); (2) swollen; non-tender (S1T0); (3) non-swollen; tender (S0T1); (4) non-swollen; non-tender (S0T0). Thermographic parameters included the maximum (Tmax), average (Tavg) and minimum (Tmin) temperatures. Ultrasound parameters included the Total PD (TPD) and Total GS (TGS) scores. One-way ANOVA and Kruskal-Wallis test (for normally and non-normally distributed imaging parameters, respectively) and subsequent post-hoc tests were carried out for the comparative analysis of the wrist groups.

Results

A total of 70 wrist joints of 70 RA subjects were included in this cross-sectional study. For all imaging parameters (Tmax, Tavg, Tmin, TPD and TGS), statistically significant differences (all $p<0.05$) were detected (a) between the 4 wrist groups using either the one-way ANOVA or Kruskal-Wallis test and (b) for subsequent pairwise comparison of wrist group 1 (S1T1) vs. group 4 (S0T0) and group 2 (S1T0) vs. group 4 (S0T0). No significant differences (all $p>0.05$) were found for pairwise comparison of wrist group 3 (S0T1) vs. group 4 (S0T0) for all imaging parameters.

Conclusion

Thermography at the wrist appears promising in RA with its findings closely mirroring those from ultrasonography. Swollen joints (regardless of tenderness status) have higher joint surface temperatures and greater ultrasound-detected joint inflammation, findings which were not observed for tender only (non-swollen) joints.

Key words

thermography, ultrasonography, rheumatoid arthritis, synovitis, joints, inflammation

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Introduction

Thermography is an emerging imaging technique that is non-invasive and which offers a quick, contactless and objective joint surface temperature assessment in patients with rheumatoid arthritis (RA) (1, 2). Modern infra-red thermal cameras have high feasibility for use in that they are typically compact, highly portable and are simple to use (3). With remote assessment of RA patients on the rise in recent years, the application of thermography has also been postulated to help improve telemedicine consultations (whereby physicians are unable to perform physical examination on the patients) (4). Presently, for RA joint assessment, there are other more established imaging modalities available for use, such as magnetic resonance imaging (MRI) and ultrasonography (5-7). The last two decades have seen much progress made in the field of MRI and ultrasound as diagnostic, prognostic and outcome measurement tools (8-10) for RA joint assessment. In fact, both imaging modalities (MRI and ultrasound) have been recommended by the European Alliance of Associations for Rheumatology (EULAR) for use to help improve the certainty of a diagnosis of RA above clinical criteria alone when there is diagnostic doubt and both can help detect inflammation that can predict subsequent joint damage, even when clinical remission is present (11). Nonetheless, the use of MRI and ultrasound are not without limitations (12, 13). MRI facilities are generally expensive to set up, and there are magnet-related contraindications (such as pacemakers, implanted electronic devices, etc.). Ultrasonography, on the other hand, can be labour intensive and a considerable amount of training would be required to attain proficiency. The wrist joint, an important hand stabiliser, is selected in this present study as it is frequently affected in patients with RA, with 50% of RA patients having their wrist affected in the first two years of disease onset, increasing to more than 90% after 10 years (14). A recent small scale RA study using an extended 36-joint ultrasonography have identified the wrist joint (among the various joint sites assessed) as the joint sites most frequently displaying bone erosions (15). Unlike ultrasound imaging, there is presently a dearth of evidence supporting the clinical use of thermal imaging at the RA wrist. Rheumatologists routinely perform physical joint counts which include examining for joint swelling and tenderness as part of RA disease activity assessment (16). Hence, the rationale of the present study utilising thermal imaging to investigate the RA wrist categorised according to its clinical joint swelling and tenderness status. The aim of this present study is to test the use of thermography (alongside ultrasonography as the reference imaging method) to determine if thermal imaging may be helpful in detecting joint inflammation at the RA wrist categorised according to its clinical manifestations.

Materials and methods

In this cross-sectional observational study, RA subjects included in the study were either male or female patients aged from 21 to 99 years old who fulfilled the 2010 RA classification criteria (17), while pregnant subject(s) were excluded from the study. The patients were consecutively enrolled between December 2020 and March 2023 from a single study site, which is a local tertiary hospital's rheumatology unit. This study received approval in Sept 2020 from the SingHealth Centralised Institutional Review Board (CIRB) (2020/2669). It conforms to the relevant research ethnical guidelines and all subjects included in this study provided their informed consent prior to recruitment.

Clinical assessment

For each subject, the clinical, thermal and ultrasound imaging assessments were all performed on the same day during the same study visit. Clinical assessments including Disease Activity Score at 28 joints-erythrocyte sedimentation rate (DAS28-ESR) were performed by the unit's trained rheumatology nurses blinded to the findings from the imaging assessments. The rheumatology nurses received standardised training prior to performing clinical

assessments for the study. The laboratory test ESR (used in the calculation of DAS28-ESR) was performed using the Westergren method. Joint swelling and tenderness were recorded as either presence=1 or absence=0. For standardisation, only the right wrist of RA patients were used to derive the following four wrist groups: 1. swollen; tender (S1T1); 2. swollen; non-tender (S1T0); 3. non-swollen; tender (S0T1); 4. non-swollen; non-tender (S0T0).

Imaging assessment

Standardised ultrasound scanning was performed based on the published EULAR guidelines (18). Ultrasonography was carried out by a single rheumatologist experienced in musculoskeletal ultrasound imaging (a separate trained study team personnel performed the thermography while being blinded to the outcomes from the ultrasound imaging). Ultrasonography was carried out using the Mindray M9 machine with a L14-6Ns linear probe with ultrasound machine settings of pulse repetition frequency (PRF) of 700 Hz and Doppler frequency 5.7 MHz. Ultrasound grey-scale (GS) synovial hypertrophy and power Doppler (PD) were scored semi-quantitatively on a severity scale of 0 to 3 (0=normal, 1=mild, 2=moderate, 3=severe) using previously validated methods with acceptable inter- and intra-observer reliability (19, 20). The dorsal wrist joint was scanned by ultrasound at two recesses (*i.e*. the (a) distal radio-ulnar and (b) radio-carpal/ inter-carpal recesses) and the PD and GS synovial hypertrophy sub-scores at the two joint recesses of the right wrist joint of each subject were summed up to derive the respective Total PD (TPD) and Total GS (TGS) score. The rationale to sum up the PD and GS sub-scores at the two joint recesses of the wrist was to allow a more representative picture of ultrasound-detected joint inflammation of the entire wrist (as opposed to a more limited scanning of the wrist) for comparison with thermal imaging.

Thermography was conducted in a draft-free (windowless) room with a controlled temperature of approximately 23°C (21) using the FLIR T640 high performance portable thermal camera (with predefined emissivity value of 0.98 for skin, thermal sensitivity of <30 milli-Kelvin (mK) at 30°C and pixel resolution of 640 x 480). Thermal imaging was carried out based on previously established methods described in the literature (1, 21-22). To allow for acclimatisation, patients were rested for 15 minutes before the start of thermal imaging as per standard practice (21).

Physical objects such as watches obscuring the view of the thermal camera were removed. For standardisation, the hand of each subject was placed in a neutral position on a flat table top and its dorsal view captured as a thermal image with the thermal camera held 50cm above the hand. Thereafter, a region of interest (ROI) (1) was manually segmented by a trained study personnel (while blinded to the ultrasound scoring outcomes) using the grey-scale thermal image by placing a rectangular box over the targeted anatomical joint site (*i.e*. the right wrist area). Finally, the maximum (Tmax), average (Tavg) and minimum (Tmin) temperatures were recorded from each wrist ROI.

Statistical analysis

The normality of the imaging data was checked by the Shapiro-Wilk test. One-way ANOVA (for normally distributed imaging parameters) and Kruskal-Wallis test (for non-normally distributed imaging parameters) were used to test if any difference(s) exist between the 4 wrist groups for the following imaging parameters: Tmax, Tavg, Tmin, TGS and TPD. Where difference(s) existed between the 4 wrist groups, *post-hoc* tests were carried out correspondingly (with *p*-values adjusted for multiple testing) through the use of either Tukey's multiple comparison test or Dunn's test of multiple comparisons using rank sums. Manually segmented ROIs were obtained at two time points (at least 2 weeks apart) from a sample of 15 randomly selected wrist thermograms and the intra-class correlation coefficient (ICC) was used to calculate the intra-rater reliability (single rater) for the thermographic parameters (Tmax, Tavg and Tmin). The ICC results were interpreted as follows: <0.50 (poor); 0.50 to 0.75 (moderate); 0.75 to 0.90 (good); >0.90 (excellent) (23). The statistical analyses were performed using Stata 17 (StataCorp. 2021. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC).

Results

Subject baseline characteristics

A total of 70 right-sided wrist joints were studied from 70 RA patients with the following patient baseline characteristics: mean (SD) age of the subjects was 58.6 (12.1) years; majority (52 out of 70 subjects, 74.3%) were Chinese; majority (57 out of 70 subjects, 81.4%) were female; mean (SD) disease duration was 22.9 (44.6) months; mean (SD) DAS28-ESR was 3.65 (1.22); 47 out of 70 subjects (67.1%) were on oral prednisolone; all patients were on one or more of the following disease-modifying anti-rheumatic drugs (DMARDs): methotrexate, sulfasalazine, hydroxychloroquine and/or leflunomide.

Comparative analysis of thermal imaging parameters between wrist groups

For all thermal imaging parameters (Tmax, Tavg and Tmin), statistically significant differences (all $p<0.01$) were detected between the 4 wrist groups using the analysis via one-way ANOVA (Table I). *Post-hoc* analysis revealed statistically significant differences (all $p<0.05$) for subsequent pairwise comparison of wrist group 1 (S1T1) *versus* group 4 (S0T0) and group 2 (S1T0) *versus* group 4 (S0T0). No significant differences (all $p>0.05$) were found for pairwise comparison of wrist group 3 (S0T1) *versus* group 4 (S0T0) for all thermal imaging parameters (Tmax, Tavg and Tmin).

Comparative analysis of ultrasound imaging parameters between wrist groups

For all ultrasound imaging parameters (TGS and TPD), statistically significant differences (all $p<0.001$) were detected between the 4 wrist groups using the analysis via Kruskal-Wallis test (Table II). *Post-hoc* analysis revealed statistically significant differences (all

Table I. Comparative analysis between wrist groups for thermal imaging.

TI parameter	Wrist group 1: Swollen & tender (S1T1) n=13	Wrist group 2: Swollen & non-tender (S1T0) n=10	Wrist group 3: Non-swollen & tender (S0T1) n=10	Wrist group 4: Non-swollen & non-tender (S0T0) n=37	*p*-value[¥]	Pairwise comparisons	Difference in means (SD)	*p*-value[§]
Tmax, mean (SD)	33.4 (0.9)	33.4 (2.1)	32.5 (1.7)	31.8 (1.5)	0.002	For Tmax:		
						S1T1 *vs*. S0T0	1.6 (0.3, 2.9)	0.008
						S1T0 *vs*. S0T0	1.6 (0.2, 3.0)	0.02
						S0T1 *vs*. S0T0	0.7 (-0.8, 2.1)	0.62
Tavg, mean (SD)	32.4 (1.1)	32.5 (2.0)	31.3 (1.4)	30.9 (1.4)	0.002	For Tavg:		
						S1T1 *vs*. S0T0	1.5 (0.3, 2.8)	0.009
						S1T0 *vs*. S0T0	1.6 (0.2, 3.0)	0.02
						S0T1 *vs*. S0T0	0.4 (-0.9, 1.8)	0.84
Tmin, mean (SD)	31.1 (1.2)	31.3 (1.9)	30.1 (1.3)	29.9 (1.3)	0.008	For Tmin:		
						S1T1 *vs*. S0T0	1.3 (0.1, 2.5)	0.03
						S1T0 *vs*. S0T0	1.4 (0.1, 2.7)	0.03
						S0T1 *vs*. S0T0	0.2 (-1.1, 1.5)	0.98

TI: thermal imaging; Tmax: maximum temperature, Tavg: average temperature; Tmin: minimum temperature.
[¥]Analysis via one-way ANOVA; [§]*p*-values adjusted for multiple testing via Tukey's method.

Table II. Comparative analysis between wrist groups for ultrasound imaging.

Ultrasound imaging parameter	Wrist group 1: Swollen & tender (S1T1) n=13	Wrist group 2: Swollen & non-tender (S1T0) n=10	Wrist group 3: Non-swollen & tender (S0T1) n=10	Wrist group 4: Non-swollen & non-tender (S0T0) n=37	*p*-value[¥]	Pairwise comparisons	*p*-value[§]
TGS score, median (IQR)	4 (3-4)	4 (3-4)	2 (2-2)	2 (2-2)	<0.001	For TGS score:	
						S1T1 *vs*. S0T0	<0.001
						S1T0 *vs*. S0T0	0.002
						S0T1 *vs*. S0T0	0.45
TPD score, median (IQR)	4 (3-4)	3 (2-4)	1 (1-2)	1 (0-1)	<0.001	For TPD score	
						S1T1 *vs*. S0T0	<0.001
						S1T0 *vs*. S0T0	0.002
						S0T1 *vs*. S0T0	0.19

TGS: total grey-scale; TPD: total power Doppler; IQR: interquartile range.
[¥]Analysis via Kruskal-Wallis test; [§]*p*-values adjustedfor multiple testing via Holm's method.

Table III. Intra-rater reliability testing (thermography).

TI parameter	Intra-class correlation coefficient (95%CI)
Tmax	0.99988 (0.99965, 0.99996)
Tavg	0.99948 (0.99851, 0.99983)
Tmin	0.99930 (0.99794, 0.99976)

TI: thermal imaging; Tmax: maximum temperature; Tavg: average temperature; Tmin: minimum temperature.

$p<0.01$) for subsequent pairwise comparison of wrist group 1 (S1T1) *versus* group 4 (S0T0) and group 2 (S1T0) *versus* group 4 (S0T0). No significant differences (all $p>0.05$) were found for pairwise comparison of wrist group 3 (S0T1) *versus* group 4 (S0T0) for all ultrasound imaging parameters (TGS and TPD).

Intra-rater reliability testing

Table III summarises the ICC results for the thermographic parameters (Tmax, Tavg and Tmin). There was excellent intra-rater reliability for thermal imaging at the wrist of RA patients with the ICC results ranging from 0.99948 to 0.99988 for the studied thermographic parameters (Tmax, Tavg and Tmin).

Discussion

To the best of our knowledge, this present study is the first to apply both thermal and ultrasound imaging and systematically comparing the outcomes of wrist groups categorised according to the status of their clinical swelling and tenderness. There is presently a lack of data supporting the clinical use of thermal imaging for joint inflammation assessment at the RA wrist. The main findings from this present study addresses this current knowledge gap in the RA literature by demonstrating, for the first time, that findings from thermography at the wrist of RA patients closely mirror those from ultrasonography. Specifically, swollen joints (regardless of tenderness status) have higher joint surface temperatures and greater ultrasound-detected joint inflammation, findings which were not observed for tender only (non-swollen) joints. The findings from this present study suggest that joint swelling is more important than joint tenderness in reflecting underlying joint inflammation at the RA wrist. This is consistent with recent RA observational studies (24-27) demonstrating the relative importance of swollen joints *versus* tender joints in reflecting joint inflam-

mation (and the resultant damage). In a longitudinal imaging study involving 209 RA subjects with multiple joint sites (from both upper and lower limbs) scanned using ultrasonography, swollen joints, but not tender joints, had strong association with joint inflammation detected on ultrasound at both the joint and patient level (24). In a separate longitudinal study by Heckert *et al*. (25) involving 473 patients with RA, cumulative local joint swelling showed a stronger association with local radiographic joint damage progression in the same joint when compared with cumulative local joint tenderness without concurrent local joint swelling (β=0.14, 95% CI 0.13 to 0.15 *vs*. β=0.04, 95% CI 0.03 to 0.05, respectively). A recent cross-sectional study (26) involving 70 RA subjects demonstrated that swollen joint count, but not tender joint count, correlated significantly with both ultrasound PD joint inflammation (r=0.33) and ultrasound erosion score (r=0.69). Finally, in another study (27) involving 40 RA patients in clinical remission or low disease activity (*i.e*. 28-joint Disease Activity Score (DAS28) <3.2), swollen but not tender joints were shown to be associated with ultrasound PD joint inflammation.

Although less established than other imaging modalities such as MRI and ultrasound for joint assessment in RA, there has been an increase in interest of using thermal imaging for the evaluation of inflammatory and degenerative joint conditions in the past decade based on publication trends (28, 29). To date, a few observational studies have utilised both thermal and ultrasound imaging for assessment of joint inflammation in patients with RA (3, 30-31). In the study by Ahn *et al*. (30) involving 30 subjects (12 with RA and 18 with other forms of arthritis), high temperature of thermography at the knee was associated with positive PD signal at the para-patellar recess of the knee joint. In a separate small scale study involving 37 RA subjects with both thermal and ultrasound imaging performed at the bilateral wrist and hand joints, a significantly higher temperature at the joints was observed in the presence of ultrasound-detected PD and GS joint inflammation (2). Both thermal and ultrasound imaging of the foot were carried out in another study involving 81 RA subjects and 39 healthy controls (31). Among the feet joints assessed, it was observed that only the right first metatarsophalangeal joint (MTPJ) and the left second MTPJ showed a significance difference in the average temperature when comparing joints with or without ultrasound-detected joint inflammation, The above three studies (3, 30-31), along with this present study, suggest that the usefulness of thermal imaging may not be the same at different joint sites and more studies involving various joint sites will be required to help further clarify this aspect, and perhaps identify which joint site(s) may be more suited for thermography in the assessment of joint inflammation in patients with RA. A recent systematic review on the use of musculoskeletal ultrasound for treating RA to target revealed that ultrasonography is superior to clinical assessment in diagnosing joint involvement using MRI as a reference imaging modality (32). With this present study demonstrating that thermography at the wrist of RA patients closely mirror those from ultrasonography, two interesting questions that arise are as follows: (1) whether thermal imaging may similarly have some advantage(s) over clinical assessment and (2) whether thermography could have a place as an adjunctive tool in the routine assessment of joint inflammation in RA patients. More RA studies examining the use of thermal imaging at various clinical scenarios (*e.g*. active *vs*. disease remission, early *vs*. late stage disease, etc.) may shed light on potential clinical utility of thermography in joint inflammation assessment in RA patients.

This study is not without its limitations. The results from thermal and ultrasound imaging at the RA wrist were derived from a single time-point using a cross-sectional study design, and therefore, it is not known how well thermal imaging may perform when used for monitoring joint inflammation over time. This current study focuses on examining joint inflammation, without specifically looking at joint damage at the RA wrist. Therefore, future RA studies incorporating a longitudinal study design should include thermal imaging (along with other imaging modalities like conventional radiology, ultrasound and/or MRI for comparative analysis) performed serially at multiple time-points and ideally, include formal assessment of joint damage. As shown from this present study, there is excellent intra-rater consistency (single rater) for thermographic temperature measurements at the RA wrist although future thermal imaging studies incorporating more than one raters should additionally include analysis of inter-rater reliability.

In summary, the findings from this present study reveal that thermography at the wrist of RA patients closely mirror those from ultrasonography. Specifically, swollen joints (regardless of tenderness status) have higher joint surface temperatures and greater ultrasound-detected joint inflammation, findings which were not observed for tender only (non-swollen) joints. This represents an important step forward towards understanding the utility of thermal imaging at the RA wrist, and is likely to pave the way for future research looking at potential clinical application(s) of thermography for RA wrist inflammation assessment.

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