ORIGINAL RESEARCH

Patellar Skin Surface Temperature by Thermography Reflects Knee Osteoarthritis Severity

Anna E. Denoble[1], Norine Hall[1], Carl F. Pieper[2] and Virginia B. Kraus[1]

[1] Departments of Medicine, [2] Biometry and Bioinformatics, Duke University Medical Center, Durham, NC 27710, USA.
Corresponding author email: vbk@acpub.duke.edu

Abstract

Background: Digital infrared thermal imaging is a means of measuring the heat radiated from the skin surface. Our goal was to develop and assess the reproducibility of serial infrared measurements of the knee and to assess the association of knee temperature by region of interest with radiographic severity of knee Osteoarthritis (rOA).

Methods: A total of 30 women (15 Cases with symptomatic knee OA and 15 age-matched Controls without knee pain or knee OA) participated in this study. Infrared imaging was performed with a Meditherm Med2000™ Pro infrared camera. The reproducibility of infrared imaging of the knee was evaluated through determination of intraclass correlation coefficients (ICCs) for temperature measurements from two images performed 6 months apart in Controls whose knee status was not expected to change. The average cutaneous temperature for each of five knee regions of interest was extracted using WinTes software. Knee x-rays were scored for severity of rOA based on the global Kellgren-Lawrence grading scale.

Results: The knee infrared thermal imaging procedure used here demonstrated long-term reproducibility with high ICCs (0.50–0.72 for the various regions of interest) in Controls. Cutaneous temperature of the patella (knee cap) yielded a significant correlation with severity of knee rOA (R = 0.594, $P = 0.02$).

Conclusion: The skin temperature of the patellar region correlated with x-ray severity of knee OA. This method of infrared knee imaging is reliable and as an objective measure of a sign of inflammation, temperature, indicates an interrelationship of inflammation and structural knee rOA damage.

Keywords: osteoarthritis, infrared imaging, knee, inflammation, thermography

Introduction

An expanding array of imaging techniques is providing more options for diagnosis and monitoring of musculoskeletal diseases. Some imaging modalities, such as radiography, computed tomography, and magnetic resonance imaging, provide joint structural information. Other imaging modalities, such as bone scintigraphy and specialized forms of magnetic resonance imaging (delayed Gadolinium Enhanced Magnetic Resonance Imaging and sodium imaging or dGEMRIC) provide physiological or functional information. Infrared thermal imaging belongs to the functional imaging category; it provides a non-invasive and dynamic measure of the heat radiated from the superficial dermal microcirculation that resides 1–2 mm below the epidermal surface.[1] Regulation of the microcirculation and thermal radiation in human tissue is influenced by inflammatory, metabolic, and toxic factors, and is mediated through sympathetic tonus and vasoactive agents.[2] Many pathological processes in humans manifest themselves as local changes in heat production and also as changes in blood flow pattern at affected organs or tissues.[3] Owing to the blood flow and conductive transfer of heat from body depth to body surface regions, infrared images are believed capable of reflecting thermal processes deep in the body.[3] Infrared thermal imaging devices convert the infrared energy radiated by the human body into electrical impulses, which are then digitally indicated on a spatial temperature map.

Infrared thermal imaging has been used in a range of clinical applications in rheumatology including: the differentiation of primary and secondary Raynaud's phenomenon;[4] the monitoring of skin temperature elevations in scleroderma;[5] the assessment of autonomic functioning in reflex sympathetic dystrophy;[6] the evaluation of rheumatoid arthritis (RA),[7] juvenile idiopathic arthritis,[8] hand,[9] and knee OA;[10] and the objective assessment of the effects of anti-inflammatory arthritis therapies in human[11–18] and animal[19] clinical trials. Our goals were to standardize a method of knee infrared imaging, to test its reproducibility, and to explore which distinct knee region provides the highest correlation of local temperature with x-ray severity of knee OA.

Methods
Participants

Participants in this trial were enrolled in accordance with the policies of the Duke University Institutional Review Board and represented all participants enrolled at a single site (Duke University) of a multicenter observational study of women to evaluate the utility of magnetic resonance imaging for knee OA.[20,21] Informed consent was obtained from each subject. An equal number of female Controls (n = 15) and female knee OA Cases (n = 15) were enrolled. Cases and Controls were age-matched (to within 5 years), and all were 40 years or older. The entry criterion for OA participants were chosen with the goal of selecting a group with increased risk for knee OA progression and included definite x-ray evidence of knee OA of Kellgren-Lawrence (KL)[22] grade 2 or 3, frequent knee pain symptoms in the past year, body mass index (BMI) $\geq$ 30 kg/m^2, medial joint space widths $\geq$ 2 mm in the signal knee, and medial compartment greater than lateral compartment disease in the signal knee. The signal knee of OA participants was chosen on the basis of x-ray criteria and symptoms. Controls were required to have normal (KL0) knees bilaterally at baseline, no knee pain symptoms, and BMIs < 28 kg/m.[2] The right knee of Controls was automatically designated the signal knee. Medication use, including non-steroidal anti-inflammatory drugs (NSAIDs), was recorded at the time of infrared imaging. Participants were excluded for a history of signal knee surgery and intra-articular or oral steroid use in the preceding 6 months.

Radiographic imaging

Posteroanterior fixed flexion knee x-rays were obtained at baseline with a SynaFlexer™ Plexiglas positioning frame (Synarc, Inc., San Francisco, CA) with optimization of the horizontal alignment of the tibial plateau through the use of fluoroscopy for determining x-ray beam angle as previously described.[23] X-rays were read for KL grade blinded to the cutaneous temperature and clinical data by a single reader (VBK) with high reliability (Intraclass Correlation Coefficient for KL grade scoring 0.69).

Infrared thermal imaging
General considerations

In order to achieve the reproducibility desired for this clinical research, we aimed to minimize variability through standardization of a number of factors including: joint positioning; environmental temperature; distance of the limb from the infrared thermal

imaging device; and the regions of interest (ROIs) for acquisition of cutaneous temperature data.

Camera

A thermoelectrically cooled instrument with a stable internal reference point, the Meditherm Med2000™ Pro (Meditherm, Medical Monitoring Systems Pty Ltd., Beaufort, NC, USA) camera, was used in this knee study. The sensor of this camera is specifically designed to measure temperatures of the human body (10 °C to 40 °C). This instrument recorded a minimum of 64,000 measurements per image to an accuracy of 0.01 °C. The camera completed a single scan in 8 seconds. Each pixel of the image generated by the infrared camera was an individually referenced measurement avoiding the need for an external calibration target.

Positioning

Infrared images were obtained at the 6 month time point of the main study protocol for OA participants and at the 6 and 12 month time points for Controls. Participants were asked to sit with their signal knee exposed for ten minutes in a temperature controlled room set at 23.1 °C. Fluorescent lighting was used, as well as a black velvet wall-covering behind the participant to eliminate external infrared energy (emanating from such sources as outlets, electrical wires, and pipes). The positioning of the participant for infrared imaging recapitulated the foot positioning for the x-ray (15° external foot rotation). The magnification of the image was fixed by maintaining a constant distance of 76.2 cm between the knee and Meditherm Med2000™ Pro camera. The camera was placed on a mobile base and centered over a floor diagram with standardized right and left foot positions designated in colored tape. The height of the camera was adjusted for the individual, centering the camera at the patella.

Infrared imaging procedure

Infrared imaging was conducted in a room free of draughts, shielded from direct sunlight, and maintained at a constant temperature of 23.1 °C. Participants were asked to stand on the designated floor map and the camera was adjusted to their patellar height. Infrared thermal images of the signal knees were acquired in four configurations (anteroposterior,

posteroanterior, lateromedial, and mediolateral). The anteroposterior image was used for these analyses. Then, maintaining the same knee position, an anatomical marker (a 2 cm diameter silver sticker) was placed on the center of the patella to facilitate its precise subsequent localization in infrared images. A second anteroposterior view of the knee was acquired as a reference image.

Image analysis

The two anteroposterior images (one with and one without the patellar marker) were aligned side by side on the computer screen, and an acetate template indicating the ROIs was centered over the patella of the unmarked image, using the marked image as a guide (Fig. 1). Mean temperatures were extracted using WinTes thermal evaluation software (Compix, Lake Oswego, OR, USA) for the overall knee and the 5 regions of interest: medial, lateral, patellar, lower medial, and lower lateral regions.

Statistical analyses

Intraclass correlation coefficients (ICCs)[24] were used to assess the reproducibility of cutaneous temperature measurements from infrared images acquired 6 months apart in Controls (whose knee status was not expected to change). The association of temperature of the 5 regions of interest with radiographic OA (rOA) severity (global KL grade) were tested using Pearson correlation coefficients. Results were considered statistically significant at $P \leq 0.05$.

Results

Participants

The characteristics of the participants (Controls and Cases) are shown in Table 1. Of note, the overall knee mean temperature was similar for Cases and Controls (30.6 °C) with a larger standard deviation for Cases. The mean (SD) temperatures for different regions of the OA knees are provided in Table 2. It is notable but not surprising that they are well below the standard body core temperatures of 37 °C.

Reproducibility of knee infrared thermal imaging

At the start of the knee study, three sequential infrared thermal images of the knee for one participant were taken over the course of a few minutes. It was
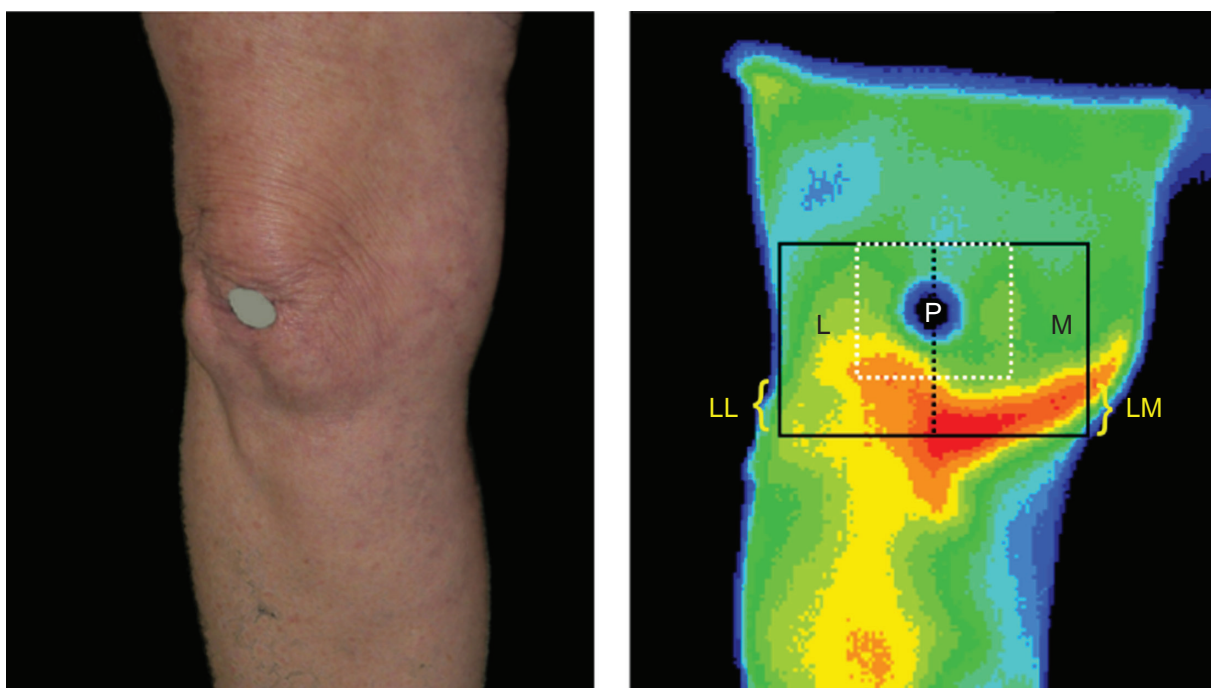
Figure 1. Infrared image analysis. To identify regions of interest on the infrared thermal images, it was necessary to localize the patella. For this purpose, two knee images were acquired, one without and subsequently one with a 2 cm anatomic marker (silver sticker) applied to the center of the patella (shown on left). This marker blocked temperature radiation and was readily recognized on the thermal images as a black circle (shown on right). This image facilitated alignment of an acetate diagram centered on the patella in order to quantify mean temperatures for specific regions of interest: P-patellar; M-medial; L-lateral; LM-lower medial; LL-lower lateral; and the overall knee.

found that the mean cutaneous temperature of the knee stabilized after three minutes of exposure to ambient temperature. Therefore, the use of a 10-minute equilibration period with the knee exposed was considered sufficient and this approach was followed for all subsequent imaging sessions. The reliability of infrared thermal imaging was assessed for the Controls whose knee status was not expected to change over the course of 6 months. The reliability was good with highest reliability observed for cutaneous temperature measurements of the lower medial and lower lateral regions of interest (Table 2).

Association of knee cutaneous temperatures with x-ray severity

Cutaneous temperature of one ROI, the patellar region of interest, was significantly associated with x-ray severity of knee OA ($P = 0.02$, Table 2, Fig. 2). The mean (SD) patellar ROI cutaneous temperature was 30.1 (1.05) for KL2 cases, and 30.5 (1.14) for KL3 cases. The knee OA cohort was chosen on the basis of medial compartment knee OA and there were borderline associations of medial knee temperatures (lower medial and combination of lower and upper medial knee temperatures) with knee rOA severity ($P = 0.06$). Although a total of 53% of OA participants used NSAIDs regularly (similar numbers in each OA subgroup), the mean temperatures for each ROI did not vary significantly by NSAID use.

Discussion

This study confirmed an association of joint cutaneous temperature at the patellar ROI with x-ray severity of OA. In work almost 40 years old related to rheumatoid arthritis, the cutaneous temperature of the patellar region was reported to reflect intra-articular temperature (recorded by a thermistor probe), and to accurately localize areas of inflamed synovial tissue verified at the time of surgical synovectomy (summarized by Collins),[17] and to correlate with scintigraphic measures of blood flow in the synovium.[25] Moreover, the patellar region was identified in a previous study as the region best reflecting changes of internal knee joint temperature after steroid injection in rheumatoid arthritis.[12]

Our previous infrared thermal imaging study involved hand OA[9] and demonstrated that joint surface temperature correlated in a phasic man-

Table 1. Characteristics of the study participants.

	Non-knee OA controls	Knee OA cases
Number (gender)	15 (female)	15 (female)
Age mean years ± SD (range)	61.9 ± 8.8 (48.0–75.6)	61.9 ± 9.2 (45.8–76.0)
Body mass index mean kg/m² ± SD (range)	23.7 ± 2.1 (21.3–27.7)	35.0 ± 4.0* (30.0–42.3)
Global knee cutaneous temperature mean ± SD (range)	30.6 ± 0.76 (29.5–32.2)	30.6 ± 0.86 (29.1–32.3)
Kellgren-Lawrence (KL) grade (number)	KL 0 (15)	KL 2 (8) KL 3 (7)
NSAID Use§	1 occasional 4 frequent	2 occasional 8 frequent

Notes: *$P < 0.0001$ between OA and control participants; §NSAID use was similar in the 2 OA subgroups: for both KL2 and KL3 there was 1 occasional user and 4 frequent users per group.
Abbreviation: SD, standard deviation.

ner with x-ray severity of OA. Higher joint surface temperatures characterized the earliest x-ray stages of OA, while the most severe x-ray stage of disease (KL4), was associated with sub-normal joint temperatures.[9] In this knee study we only observed positive associations of temperature and rOA severity. The difference in the two studies may in part be due to the exclusion of end-stage OA for the knee study, and might also relate to as yet unknown differences due to joint site.

This study was limited in power due to the small sample size and should therefore be considered an exploratory study in need of replication. The study protocol allowed ongoing use of regular medications including NSAIDs without a washout period that may have limited the power to detect stronger associations of temperature and knee rOA severity or associations of temperature with rOA severity at additional knee regions of interest. Of note, the ROI in which a significant association was seen between temperature and rOA severity (patellar) was the ROI, which displayed the lowest reliability (ICC = 0.50). Although the small sample size limited study power, it was nevertheless interesting in this sample of knee OA individuals selected for medial compartment predominant disease, that there was an indication of an association between temperature of the medial compartment and OA severity but the small sample size likely accounted for the inability to reject the null hypothesis at the $P = 0.05$ level. This finding would be worthy of follow-up study in a larger cohort. In summary, this method of infrared knee imaging is reliable and as an objective measure of a sign of inflammation, temperature, indicates an interrelationship of inflammation and structural knee rOA damage as measured by the Kellgren-Lawrence scale.

Acknowledgments

Table 2. Reliability of infrared imaging and associations of temperature with radiographic OA severity.

Region of interest	Reliability of infrared imaging in controls by ICC	Temperature in cases mean (SD)	Association of temperature with knee OA radiographic severity by KL grade R (*P* value)
Lower medial	0.70	30.4 (1.00)	0.494 (0.06)
Lower lateral	0.72	31.1 (0.76)	0.419 (0.12)
Patellar	0.50	30.3 (1.07)	**0.594 (0.02)**
Medial knee (upper and lower)	0.66	30.3 (0.90)	0.498 (0.06)
Lateral knee (upper and lower)	0.61	30.9 (0.80)	0.314 (0.25)

Abbreviations: ICC, Intraclass Correlation Coefficient; R, Pearson correlation coefficient; KL, Kellgren-Lawrence grade of radiographic osteoarthritis severity.
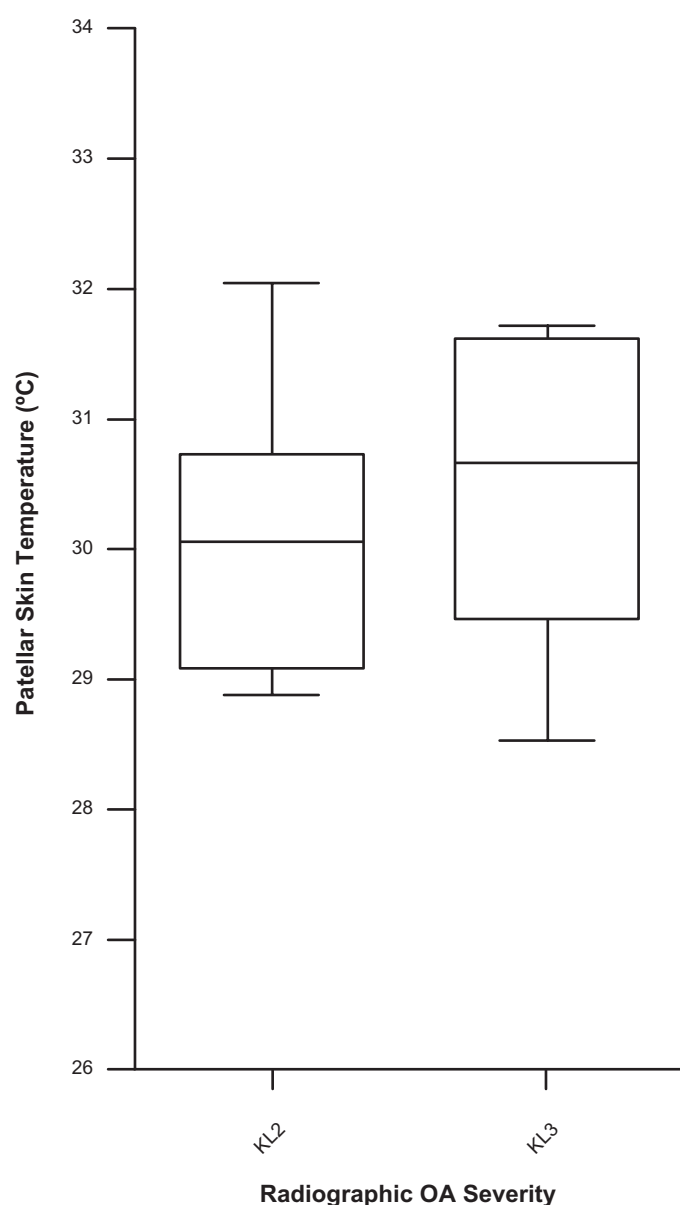
Figure 2. Patellar temperature and radiographic OA. Whisker and box plots depict the mean, 25th and 75th percentiles, minimum and maximum temperatures in the two osteoarthritis subgroups, Kellgren-Lawrence (KL2 and KL3) for the patellar region of interest.

Authors' Contributions

AE Denoble assisted with thermography, performed image and statistical analysis, and drafted the manuscript; N Hall served as study coordinator for all aspects of the study; CF Pieper supervised all statistical analyses, and VB Kraus designed and supervised all aspects of the study. All co-authors reviewed, edited, and approved the manuscript.

Disclosure

This manuscript has been read and approved by all authors. This paper is unique and not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

References

1. Braverman IM. The cutaneous microcirculation. *J Investig Dermatol Symp Proc*. 2000 Dec;5(1):3–9.
2. Bonelli RM, Koltringer P. Autonomic nervous function assessment using thermal reactivity of microcirculation. *Clin Neurophysiol*. 2000 Oct;111(10):1880–8.
3. Vainer BG. FPA-based infrared thermography as applied to the study of cutaneous perspiration and stimulated vascular response in humans. *Phys Med Biol*. 2005 Dec 7;50(23):R63–94.
4. Anderson ME, Moore TL, Lunt M, Herrick AL. The 'distal-dorsal difference': a thermographic parameter by which to differentiate between primary and secondary Raynaud's phenomenon. *Rheumatology (Oxford)*. 2007;46(3):533–8.
5. Maeda M, Kachi H, Ichihashi N, Oyama Z, Kitajima Y. The effect of electrical acupuncture-stimulation therapy using thermography and plasma endothelin (ET-1) levels in patients with progressive systemic sclerosis (PSS). *J Dermatol Sci*. 1998 Jun;17(2):151–5.
6. Bruehl S, Lubenow TR, Nath H, Ivankovich O. Validation of thermography in the diagnosis of reflex sympathetic dystrophy. *Clin J Pain*. 1996 Dec;12(4):316–25.
7. Devereaux MD, Parr GR, Thomas DP, Hazleman BL. Disease activity indexes in rheumatoid arthritis; a prospective, comparative study with thermography. *Ann Rheum Dis*. 1985 Jul;44(7):434–7.
8. Spalding SJ, Kwoh CK, Boudreau R, et al. Three-dimensional and thermal surface imaging produces reliable measures of joint shape and temperature: a potential tool for quantifying arthritis. *Arthritis Res Ther*. 2008; 10(1):R10.
9. Varju G, Pieper CF, Renner JB, Kraus VB. Assessment of hand osteoarthritis: correlation between thermographic and radiographic methods. *Rheumatology*. 2004;43(7):915–9.
10. Warashina H, Hasegawa Y, Tsuchiya H, et al. Clinical, radiographic, and thermographic assessment of osteoarthritis in the knee joints. *Ann Rheum Dis*. 2002 Sep;61(9):852–4.
11. Esselinckx W, Bacon PA, Ring EF, Crooke D, Collins AJ, Demottaz D. A thermographic assessment of three intra-articular prednisolone analogues given in rheumatoid synovitis. *Br J Clin Pharmacol*. 1978 May;5(5): 447–51.
12. Collins AJ, Cosh JA. Temperature and biochemical studies of joint inflammation. A preliminary investigation. *Ann Rheum Dis*. 1970 Jul;29(4): 386–92.
13. Dieppe PA, Sathapatayavongs B, Jones HE, Bacon PA, Ring EF. Intra-articular steroids in osteoarthritis. *Rheumatol Rehabil*. 1980 Nov;19(4):212–7.
14. Ring EF, Dieppe PA, Bacon PA. The thermographic assessment of inflammation and anti-inflammatory drugs in osteoarthritis. *Br J Clin Pract*. 1981 Jul–Aug;35(7–8):263–4.
15. Zazirnyi IM, Mahomedov OM, Drobotun OV, Ievseienko VH. [Effect of chondroprotectors in the treatment and prophylaxis of the knee joint osteoarthrosis]. *Lik Sprava*. 2000 Oct–Dec;(7–8):50–2.

16. Ring EF, Collins AJ, Bacon PA, Cosh JA. Quantitation of thermography in arthritis using multi-isothermal analysis. II. Effect of nonsteroidal anti-inflammatory therapy on the thermographic index. *Ann Rheum Dis*. 1974 Jul;33(4):353–6.

17. Collins AJ, Ring EF, Cosh JA, Bacon PA. Quantitation of thermography in arthritis using multi-isothermal analysis. I. The thermographic index. *Ann Rheum Dis*. 1974 Mar;33(2):113–5.

18. Bacon PA, Collins AJ, Ring EF. Letter: Treatment of acute gout. *Br Med J*. 1974 May 18;2(5915):387.

19. Um SW, Kim MS, Lim JH, Kim SY, Seo KM, Nam TC. Thermographic evaluation for the efficacy of acupuncture on induced chronic arthritis in the dog. *J Vet Med Sci*. 2005 Dec;67(12):1283–4.

20. Eckstein F, Buck RJ, Burstein D, et al. Precision of 3.0 Tesla Quantitative Magnetic Resonance Imaging of cartilage morphology in a multi center clinical trial. *Ann Rheum Dis*. 2008;67(12):1683–8.

21. Mazzuca SA, Hellio Le Graverand MP, Vignon E, et al. Performance of a non-fluoroscopically assisted substitute for the Lyon schuss knee radiograph: quality and reproducibility of positioning and sensitivity to joint space narrowing in osteoarthritic knees. *Osteoarthritis Cartilage*. 2008 Dec;16(12):1555–9.

22. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. *Ann Rheum Dis*. 1957 Dec;16(4):494–502.

23. Charles HC, Kraus VB, Ainslie M, Hellio Le Graverand-Gastineau MP. Optimization of the fixed-flexion knee radiograph. *Osteoarthritis Cartilage*. 2007 Nov;15(11):1221–4.

24. Fleiss J. *The Design and Analysis of Clinical Experiments*. New York: Wiley; 1986.

25. Cosh JA, Lindsay DJ, Davies ER, Ring FJ. The technetium scintigram as an indicator of syovial vascularity in rheumatoid arthritis: its comparison with the results of temperature measurement. *Ann Rheum Dis*. 1970 Nov;29(6):691.