Diffuse Reflectance Spectroscopy with Infrared Thermography for Accurate Prediction of Cellulitis

Adam B. Raff[1,6], Antonio Ortega-Martinez[2,6], Sidharth Chand[3,7], Renajd Rrapi[3,7], Carina Thomas[4], Lauren N. Ko[3], Anna C. Garza-Mayers[3], Allison S. Dobry[3], Blair Alden Parry[5], Richard Rox Anderson[3,4] and Daniela Kroshinsky[1]

Cellulitis is frequently misdiagnosed owing to its clinical mimickers, collectively known as pseudocellulitis. This study investigated diffuse reflectance spectroscopy (DRS) alone and in combination with infrared thermography (IRT) for the differentiation of cellulitis from pseudocellulitis. A prospective cohort study at an urban academic hospital was conducted from March 2017 to March 2018. Patients presenting to the emergency department with presumed cellulitis were screened for eligibility, and 30 adult patients were enrolled. Dermatology consultation conferred a final diagnosis of cellulitis or pseudocellulitis. DRS measurements yielded a spectral ratio between 556 nm (deoxyhemoglobin peak) and 542 nm (oxyhemoglobin peak), and IRT measurements yielded temperature differentials between the affected and unaffected skin. Of the 30 enrolled patients, 30% were diagnosed with pseudocellulitis. DRS revealed higher spectral ratios in patients with cellulitis ($P = 0.005$). A single parameter model using logistic regression on DRS measurements alone demonstrated a classification accuracy of 77.0%. A dual parameter model using linear discriminant analysis on DRS and IRT measurements combined demonstrated a 95.2% sensitivity, 77.8% specificity, and 90.0% accuracy for cellulitis prediction. DRS and IRT combined diagnoses cellulitis with an accuracy of 90%. DRS and IRT are inexpensive and noninvasive, and their use may reduce cellulitis misdiagnosis.

JID Innovations (2021);**1:**100032 doi:10.1016/j.xjidi.2021.100032

INTRODUCTION

Cellulitis is a common infection of the skin and skin-associated structures that typically presents with redness, warmth, and pain in the affected area (Arakaki et al., 2014; Levell et al., 2011; Raff and Kroshinsky, 2016; Strazzula et al., 2015). Pseudocellulitis comprises several different diagnoses that can mimic the clinical appearance of cellulitis, such as lipodermatosclerosis and acute deep vein thrombosis (Raff and Kroshinsky, 2016). Difficulty in distinguishing cellulitis from its mimickers leads to misdiagnosis in over 30% of cases (Strazzula et al., 2015) and results in an estimated 130,000 unnecessary admissions and $515 million in avoidable healthcare spending in the hospital setting (Weng et al., 2017). Reducing unnecessary antibiotic coverage is also important in decreasing the emergence of drug-resistant organisms, antibiotic-associated side-effects, and costs (Jenkins et al., 2010).

Although dermatology and infectious disease consultations are considered the clinical gold standard for diagnosis of cellulitis (Arakaki et al., 2014; David et al., 2011; Jain et al., 2017; Levell et al., 2011; Strazzula et al., 2015), specialty access remains limited (Kimball and Resneck, 2008), and there exists a need to develop objective diagnostic modalities to assist clinicians. Infrared thermography (IRT) provides quantitative measurements of skin temperature and has previously been shown to aid in the differentiation of cellulitis from pseudocellulitis (Ko et al., 2018b). The average maximum temperature of the skin with cellulitis is 3.7 °C warmer than unaffected skin, and a temperature difference $\geq$0.47 °C conferred a 96.6% sensitivity and 82.4% positive predictive value for diagnosing cellulitis (Ko et al., 2018b).

This study investigated the utility of diffuse reflectance spectroscopy (DRS) for the prediction of cellulitis. DRS obtains quantitated color measurements of the skin and other exposed tissues and has previously demonstrated utility in the diagnosis of irritant contact dermatitis and gingivitis (Kollias et al., 1995; Zakian et al., 2008). In a DRS measurement, a broad spectrum of light penetrates the tissue and is scattered back to a detector that measures the intensity of reflected light at each wavelength, which is dependent on the color absorption properties of various substances present in the

[1]Department of Dermatology, Beth Israel Lahey Health, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, USA; [2]Neurophotonics Center, Boston University, Boston, Massachusetts, USA; [3]Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; [4]Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; and [5]Department of Emergency Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

[6]These authors contributed equally to this work.

[7]These authors contributed equally to this work.

Correspondence: Daniela Kroshinsky, Department of Dermatology, Massachusetts General Hospital, Havard Medical School, 50 Staniford Street, 2nd Floor, Boston, Massachusetts 02114, USA. E-mail: dkroshinsky@partners.org

Abbreviations: CI, confidence interval; DRS, diffuse reflectance spectroscopy; IRT, infrared thermography

Received 25 February 2021; revised 22 April 2021; accepted 29 April 2021; accepted manuscript published online 8 June 2021; corrected proof published online 31 August 2021

Cite this article as: JID Innovations 2021;1:100032

skin (Kollias et al., 1995). Both DRS and IRT are simple, inexpensive, and noninvasive modalities that can be deployed in portable devices readily accessible in multiple patient care settings. This prospective study specifically evaluated the utility of DRS alone and that of combined IRT and DRS for enhanced discrimination of uncomplicated cellulitis from pseudocellulitis.

RESULTS

A total of 30 patients met eligibility criteria and consented to participation (Figure 1). Examination of the study population revealed heterogeneous demographics with mean patient age of 54 years (SD = 18 years) and a 3:2 representation of male-to-female ratio (Table 1). Dermatology evaluation ascribed a diagnosis of cellulitis to 21 patients (70.0%) and that of pseudocellulitis to 9 patients (30.0%). Two patients with pseudocellulitis had bilateral lesions on the lower extremities necessitating IRT measurements of temperature differentials between the affected area and an unaffected area on the proximal lower extremity. At the predetermined follow-up time, no adverse events were noted, and no patients had their final diagnosis reclassified. Patients diagnosed with cellulitis were significantly younger than those diagnosed with pseudocellulitis ($P = 0.013$).

DRS measurements revealed significantly higher spectral ratios in comparing deoxyhemoglobin with oxyhemoglobin absorption ($P = 0.005$). The single parameter model for prediction of cellulitis with DRS alone by logistic regression demonstrated an optimal threshold value of 1.012, with spectral ratios above this value corresponding to a 50% probability of cellulitis (Table 2, Figure 2). This classification yielded a sensitivity of 86% (95% confidence interval [CI] = 64–97%), a specificity of 56% (95% CI = 14–79%), a positive predictive value of 82% (95% CI = 60–95%), a negative predictive value of 63% (95% CI = 24–91%), and an accuracy of 77% (95% CI = 58–90%). The dual parameter model for prediction of cellulitis with DRS and IRT combined by linear discriminant analysis demonstrated a sensitivity of 95% (95% CI = 76–100%), a specificity of 78% (95% CI = 40–97%), a positive predictive value of 91% (95% CI = 71–99%), a negative predictive value of 88% (95% CI = 47–100%), and an accuracy of 90% (95% CI = 73–98%) (Table 3, Figure 3). Validation of the dual parameter model on 215,460 combinations of training and validation sets estimated future accuracy of 87% (95% CI = 74–100%).

DISCUSSION

Cellulitis is a common illness whose diagnosis is often confounded by mimicking conditions, necessitating the development of objective diagnostic tools. Misdiagnosis of cellulitis is frequent, as represented by the 30% pseudocellulitis rate occurring in this study population, consistent with the findings of previous studies (Arakaki et al., 2014; Levell et al., 2011; Weng et al., 2017). This study investigated the performance of DRS alone and in combination with IRT for the objective diagnosis of cellulitis. A previous study showed that IRT set to a temperature differential of 0.47 °C in a dermatology consult cohort showed 97% sensitivity and 83% accuracy for cellulitis detection (Ko et al., 2018b). This study reported comparable performance for DRS alone with an 86% sensitivity and 77% accuracy for cellulitis detection. The use of DRS and IRT in combination performed better than the use of either technique alone and resulted in a 95% sensitivity and 90% accuracy for cellulitis detection. These technologies both benefit significantly from their simplicity, noninvasiveness, rapidity, inexpensiveness, and portability. Another major advantage of this study is its execution in a real emergency department clinical setting without the disruption of workflow. Used together, they present an opportunity to augment clinical decision making and potentially decrease the misdiagnosis rate.

DRS relies on intuitive quantitative measurements of skin changes, representing a significant advantage for the objective diagnosis of cellulitis. DRS has been used previously to quantify vascular oxygenation as a prognostic tool in breast and oral cancers (Brown et al., 2009; Mallia et al., 2010) and has shown value in the diagnosis of other dermatologic conditions, such as irritant contact dermatitis (Kollias et al., 1995). In the context of this study, DRS constituted a robust method for the quantification of color changes in the skin that

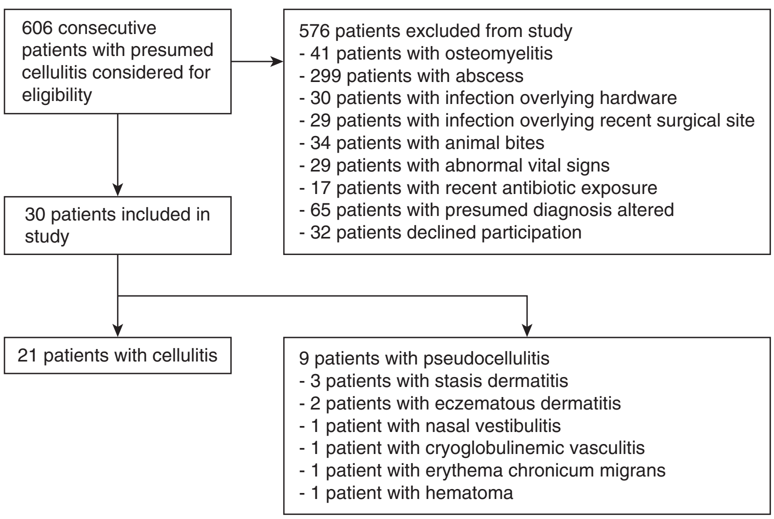

Figure 1. Screening and enrollment of the study. This flowchart shows study screening and enrollment.

Table 1. Baseline Patient Demographics

Characteristic	Total (n = 30)	Cellulitis (n = 21)	Pseudocellulitis (n = 9)	*P*-value
Age, y, mean ± SD	54 ± 18	48 ± 17	66 ± 16	0.013
Gender, n (%)				0.051
Male	18 (60)	15 (71)	3 (33)	
Female	12 (40)	6 (29)	6 (67)	
Race, n (%)				0.590
White	25 (84)	17 (81)	8 (89)	
Asian or Pacific Islander	1 (3)	1 (5)	0 (0)	
American Indian	0 (0)	0 (0)	0 (0)	
Black	1 (3)	1 (5)	0 (0)	
Hispanic	3 (10)	2 (9)	1 (11)	
Body area affected, n (%)				—
Head and neck	3 (10)	2 (10)	1 (11)	
Upper extremity	3 (10)	3 (14)	—	
Lower extremity	24 (80)	16 (76)	8 (89)	
Lesion laterality, n (%)				—
Unilateral	28 (93)	21 (100)	7 (78)	
Bilateral	2 (7)	—	2 (22)	

Baseline demographics for patients with cellulitis and pseudocellulitis.

is typically scrutinized in the clinical diagnosis of cellulitis. Considering that higher spectral ratios suggest increased presence of oxyhemoglobin, DRS likely detected increased dermal perfusion with highly oxygenated blood resulting from an acute inflammatory response to infection as occurs in cellulitis. In contrast, DRS likely registered lower spectral ratios for common pseudocellulitis diagnoses marked by venous congestion of poorly oxygenated blood, such as stasis dermatitis or deep vein thrombosis. Furthermore, DRS can be readily deployed at any site affected by cellulitis, as evidenced in the diverse clinical presentations included in this study.

IRT provides quantitative measurements of skin changes distinct from those provided by DRS, thus presenting an opportunity for enhanced discrimination of cellulitis as evidenced by the improved performance of these technologies in combination. IRT represents an appropriate method for the quantification of skin warmth that is typically considered in the clinical diagnosis of cellulitis (Ko et al., 2018b). Whereas DRS can be affected by optical absorption characteristics of substances other than hemoglobin that are present varyingly in the skin, such as water, lipids, and melanin, IRT is likely less impacted by this variability. This advantage is especially important for the diagnosis of cellulitis in darker skin types where the perception of underlying erythema can be obscured by melanin content, which can reduce the overall reflectance of the skin. The impact of melanin content has been recently conjectured to interfere with even commonly used photometric methods such as pulse oximetry (Sjoding et al., 2020). Interestingly, in addition, the full spectrum registered by DRS may encode helpful information about confounding optical features of the examined skin, such as melanin content, which may be amenable to extrication in future studies by more sophisticated algorithmic methods for improved diagnostic performance. Although this study took place at an institution with a predominately white patient population, 16% of patients had the skin of color. IRT may augment diagnostic accuracy in darker skin types where

Table 2. Spectral Ratios for Patients with Cellulitis and Pseudocellulitis

Ratio of 556/542 nm	Cellulitis	Pseudocellulitis
Mean	1.0736	1.0159
SD	0.0472	0.0473
n	21	9

The mean of the spectral ratio between 556 nm (deoxyhemoglobin peak) and 542 nm (oxyhemoglobin peak) was calculated for the affected skin in patients with cellulitis and pseudocellulitis. The mean spectral ratios were compared using a two-sided Student's *t*-test with a calculated *P*-value of 0.0048.

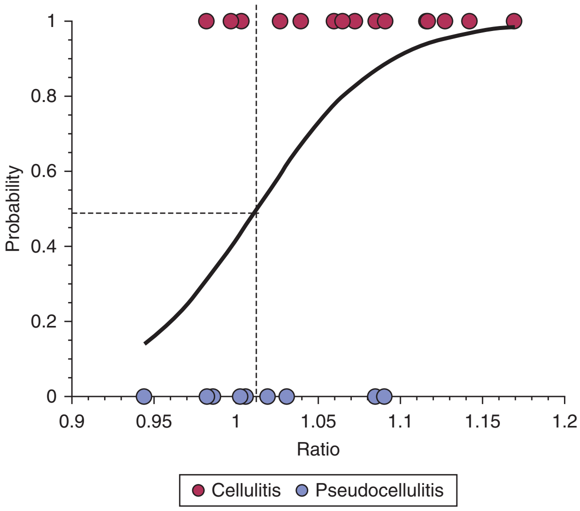

Figure 2. Spectral ratio predictive model. Using logistic regression, we determined the probability of cellulitis on the basis of the spectral ratio (556/542 nm) of the affected skin. Red circles indicate patients with cellulitis, and blue circles indicate patients with pseudocellulitis. The 50% threshold corresponds to a spectral ratio of 1.012.

Table 3. Estimation of Prediction Performance for Dual Parameter Model

Statistic	Mean	Confidence Interval (2.5−97.5%)
Accuracy	0.8681	0.7401−1.0000
Sensitivity	0.9138	0.7791−1.0000
Specificity	0.7766	0.4976−1.0000
Positive predictive value	0.9054	0.7888−1.0000
Negative predictive value	0.8611	0.6430−1.0000

Combinatorial resampling was used to predict the generalizability of the dual parameter model. A total of 215,460 different training and validation sets were used. The average classification performance is presented as a mean and confidence interval.

accuracy also reduces unnecessary costs; a comparison of the false positive rate of the combined DRS and IRT method in this study with current misdiagnosis rates estimates savings of $284 million annually in the United States (Peterson et al., 2017). Furthermore, the improved accuracy of these combined technologies can help elucidate pseudocellulitis that may require significantly different evaluation and management as evidenced by the cases of cryoglobulinemic vasculitis and erythema chronicum migrans correctly discriminated in this study. These combined technologies can be quickly and inexpensively deployed without necessitating dermatology consultation, thus improving cellulitis management and costs possibly in a wide variety of clinical settings.

subtle erythema may be obscured by melanin content. Future multicenter studies assessing this technology in more diverse populations are needed to validate the accuracy of both methods combined. Thus, combined DRS and IRT measurements may be generalizable to patients of all skin types for highly accurate diagnosis of cellulitis, especially in comparison with clinical examination alone.

DRS and IRT are both inexpensive technologies that present an opportunity for further cost savings in the form of improved diagnostic accuracy leading to reduced unnecessary admissions and antibiotic treatments. Dermatology expertise is currently considered as one of the gold standards for management (Ko et al., 2018a; Li et al., 2018) but is not always readily available. Rather, cellulitis is commonly managed by primary care, emergency medicine, or internal medicine physicians (Arakaki et al., 2014; David et al., 2011; Jain et al., 2017; Levell et al., 2011; Strazzula et al., 2015), and an interview study among health care providers showed substantial challenges in diagnosis and variability in practice among these providers (Patel et al., 2020). Improved diagnostic

MATERIALS AND METHODS

This study recruited patients presenting with presumed cellulitis for the obtainment of IRT and DRS measurements and was approved by the Partners Institutional Review Board. Adult patients aged >18 years seen in the emergency department at Massachusetts General Hospital (Boston, MA) with a presumed diagnosis of cellulitis as assessed by emergency department physicians were included after written informed consent was obtained. Patients were not considered if pregnant, incarcerated, or decisionally impaired. To minimize confounders, patients were excluded if they had clinical or radiographic evidence of abscess or osteomyelitis, if they had complicated infection sites such as those involving surgical sites <4 weeks from operation, if they had underlying hardware such as orthopedic implants and intravenous access lines, or if they had animal or human bites. Patients with abnormal vital signs, specifically temperature >100.4 °F or tachycardia >100 beats per minute, or with exposure to intravenous antibiotics for more than 24 hours were also excluded. Enrolled patients received specialty consultation by an attending dermatologist with the conferral of a final diagnosis of cellulitis or pseudocellulitis. During consultation, the attending dermatologist was blinded to any infrared thermograms or

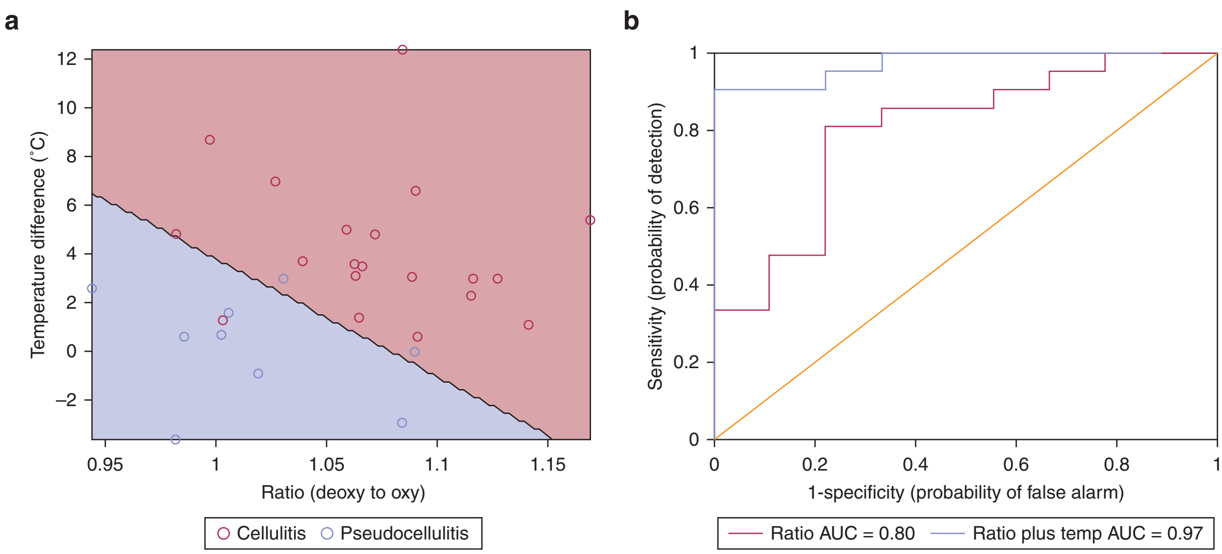

Figure 3. Dual parameter predictive model and ROC curve. (**a**) A linear classifier was calculated for the thermal differences and the spectral ratios using a linear discriminant analysis technique. By changing the intercept of the line, optimal sensitivity and specificity of the classifier can be selected. We show a sensitivity of 95% (95% CI = 76–100%), specificity of 78% (95% CI = 40–97%), PPV of 91% (95% CI = 71–99%), NPV of 88% (95% CI = 47–100%), and accuracy of 90% (95% CI = 73–98%). (**b**) ROC curve for predicting cellulitis in using spectral ratio predictive model alone and dual parameter predictive model. AUC, area under the curve; CI, confidence interval; deoxy, deoxyhemoglobin; NPV, negative predictive value; oxy, oxyhemoglobin; PPV, positive predictive value; ROC, receiver operating characteristic.

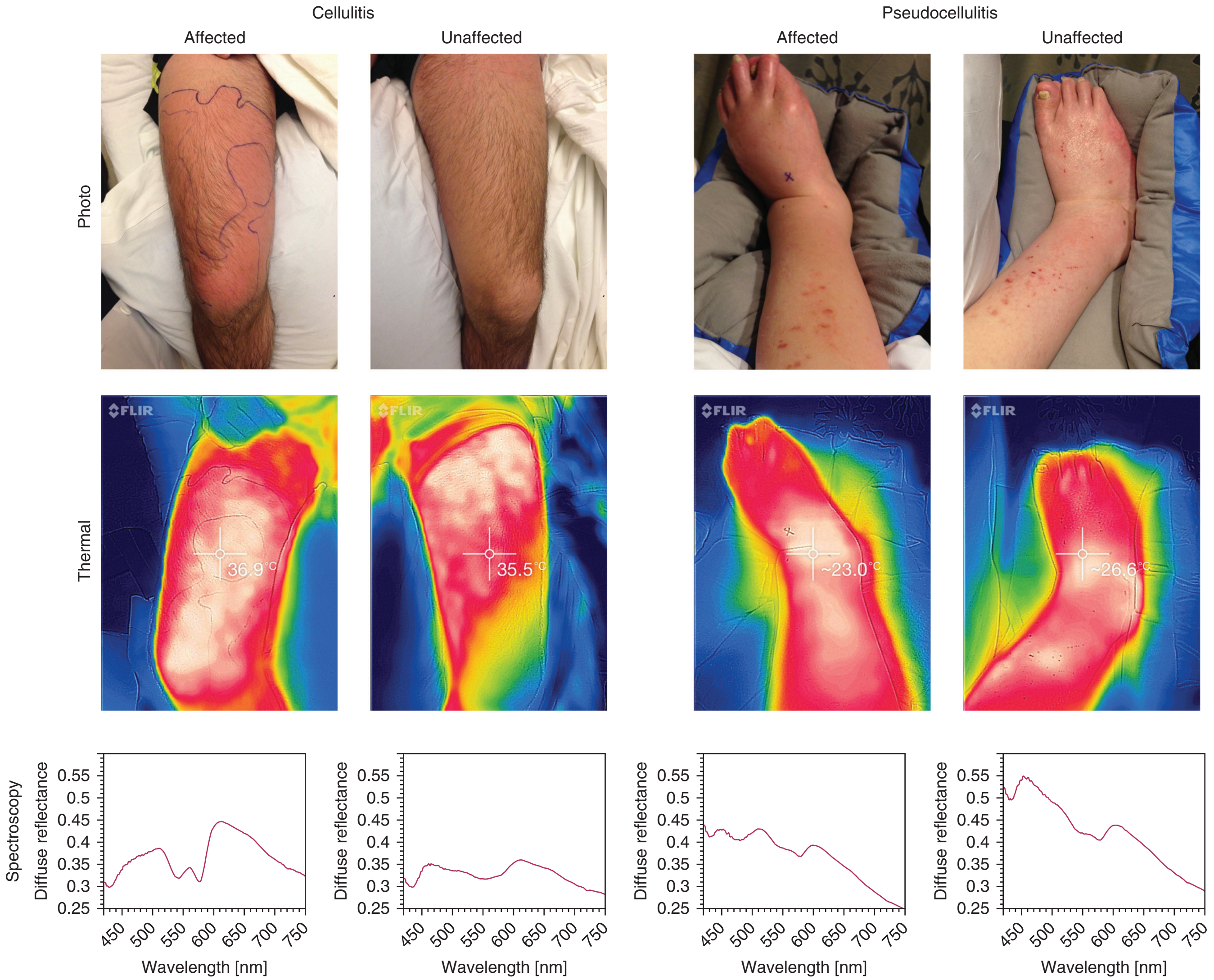

Figure 4. Clinical imaging, thermal imaging, and diffuse reflectance spectroscopy of representative patients. Representative data for the affected and unaffected areas of skin. For the patient with cellulitis, the temperature difference (between the affected and the unaffected skin) was 1.4 °C. For the patient with pseudocellulitis, the temperature difference was −3.6 °C. Patients consented to the publication of their clinical images.

diffuse reflectance spectra obtained. Included patients also received follow-up in the form of a phone call or clinic visit to assess for disease resolution and accuracy of the final diagnosis. Relevant information on patient history and clinical course for included patients was recorded from direct medical history or chart review and was securely managed using Research Electronic Data Capture tools (Nashville, TN) (Harris et al., 2009).

DRS measurements for included patients returned a spectral ratio comparing deoxyhemoglobin-to-oxyhemoglobin absorption in the affected skin (Figure 4). The DRS apparatus consisted of a handheld optic fiber spectrometer equipped with a probe made of six broadband illumination fibers and one reflectance detection fiber. DRS measurements were obtained by placing the probe directly on the affected skin without downward pressure. To standardize the reflectance intensity for each measurement, acquired spectra were normalized to the spectrum of the illuminating light source captured using a spectralon reflectance standard. Spectral ratio was calculated as the ratio of the deoxyhemoglobin absorption peak at 556 nm to the oxyhemoglobin absorption peak at 542 nm. The DRS apparatus was made of components supplied by Ocean Optics (Largo, FL) and included the optic fiber spectrometer (USB2000), broadband light source (HL-2000), reflectance fiber probe (QR600-7-SR-125F), and spectralon reflectance standard (WS-1-SL).

IRT measurements for included patients returned a temperature differential between the affected and the unaffected skin (Figure 4). The IRT apparatus consisted of a forward-looking infrared camera capable of capturing live and still images with a temperature measurement range of −20 °C to 120 °C in increments of 0.1 °C. Live thermographic images were captured by roving a forward-looking infrared camera approximately 30 cm from the skin surface. Affected skin temperature was identified as the maximum skin temperature measured in the affected area, and unaffected skin temperature was identified as the skin temperature measured on the corresponding contralateral body area for unilateral cellulitis or on the ipsilateral proximal body area for bilateral cellulitis. This bilateral comparison was designed to account for global factors that can affect skin temperature such as ambient room temperature, body mass index, and anatomical characteristics of the affected site. Temperature differential was calculated as the temperature difference between the affected and the unaffected skin. The IRT apparatus was supplied by FLIR Systems (Wilsonville, OR) and included the FLIR Generation One camera.

Statistical analysis was performed to characterize the study population and predict cellulitis on the basis of DRS alone and DRS and IRT combined. Categorical variables are reported as counts with percentages, and continuous variables are reported as means with SD or as medians with first and third quartiles, dependent on the distribution. Differences between categorical variables were compared using Pearson's χ^2 test of independence, and differences between continuous variables were compared using Student's *t*-test if confirmed to be normally distributed through Kolmogorov–Smirnov test of normality at a significance threshold of $P < 0.05$ or otherwise using the Mann–Whitney U test. Significance tests were all two-tailed at $P < 0.05$. A single parameter model for the prediction of cellulitis using DRS alone was created using logistic regression on spectral ratios obtained. A dual parameter model for the prediction of cellulitis using DRS and IRT combined was performed using linear discriminant analysis on the pairs of temperature differentials and spectral ratios obtained. A receiver operating characteristic curve was generated for both models to characterize the performance of optimal classification. The exact CIs for performance characteristics in both the single and dual parameter models were calculated using the Clopper–Pearson method. The dual parameter model was further validated for future generalizability using a cross-validation procedure consisting of a combinatorial resampling method (stratified leave-*P*-out cross-validation). All possible partitions of the measurement pairs into training and validation sets at a 4:1 ratio with proportional representation of pseudocellulitis in training and validation sets were generated, and a linear classifier was computed from each training set to predict cellulitis in each corresponding validation set. A mean confusion matrix for optimal classifications was calculated with corresponding estimates of performance characteristics and their variances. Analysis was conducted in MATLAB, version 7.1, and R, version 3.2.

Given that this investigation was a study for proof of technological concept, its stringent eligibility criteria resulted in a small set of included patients. In particular, the study population was recruited from the emergency department at a single academic medical center and thus may not generalize readily to outpatient presentations of cellulitis. Future studies are needed to validate these technologies more broadly in the skin and skin-associated structure infections. In particular, future studies should account for additional patient factors that may have a physiological impact on skin temperature such as recent medication intake. A larger study population will be necessary for more robust validation of these models before clinical implementation.

Spectral ratios from DRS and temperature differentials from IRT can differentiate cellulitis from pseudocellulitis more accurately than clinical examination. These technologies are both noninvasive, inexpensive, and easy to use and may be amenable to combination in the form of a single device. The dual parameter model for the prediction of cellulitis reported in this study may help to reduce misdiagnosis rates, unnecessary hospitalization, antibiotic overuse, and healthcare costs. Further studies are needed to validate this diagnostic method in larger cohorts and varied clinical settings.

Data availability statement

Datasets related to this article can be found at https://doi.org/10.17632/bwsvw6drw5.1, hosted at Mendeley.

ORCIDs

Adam B. Raff: http://orcid.org/0000-0002-3389-5096
Antonio Ortega-Martinez: http://orcid.org/0000-0003-3296-4341
Sidharth Chand: http://orcid.org/0000-0002-5725-6600
Renajd Rrapi: http://orcid.org/0000-0001-9795-2865
Carina Thomas: http://orcid.org/0000-0002-6802-6886
Lauren N. Ko: http://orcid.org/0000-0002-6281-2421
Anna C. Garza-Mayers: http://orcid.org/0000-0002-4553-1927
Allison S. Dobry: http://orcid.org/0000-0003-0309-173X
Blair Alden Parry: http://orcid.org/0000-0002-6230-5286
R. Rox Anderson: http://orcid.org/0000-0003-4966-3035
Daniela Kroshinsky: http://orcid.org/0000-0002-4781-9676

AUTHOR CONTRIBUTIONS

Conceptualization: ABR, AOM, RRA, DK; Data Curation: ABR, AOM, SC, RR, CT, LNK, ACGM, ASD, BAP, DK; Formal Analysis: ABR, AOM, SC, RR, LNK, ACGM, ASD, DK; Investigation: ABR, AOM, SC, RR, DK

ACKNOWLEDGMENTS

This work was funded by the National Institutes of Health, Advancing Innovation in Dermatology, and Dermatology Foundation. This study was reviewed and approved by Partners Institutional Review Board, with approval number 2012P000752.

CONFLICT OF INTEREST

ABR, AOM, RRA, and DK filed a patent for the development of diffuse reflectance spectroscopy and thermal imaging technology.

REFERENCES

Arakaki RY, Strazzula L, Woo E, Kroshinsky D. The impact of dermatology consultation on diagnostic accuracy and antibiotic use among patients with suspected cellulitis seen at outpatient internal medicine offices: a randomized clinical trial. JAMA Dermatol 2014;150:1056–61.

Brown JQ, Wilke LG, Geradts J, Kennedy SA, Palmer GM, Ramanujam N. Quantitative optical spectroscopy: a robust tool for direct measurement of breast cancer vascular oxygenation and total hemoglobin content in vivo. Cancer Res 2009;69:2919–26.

David CV, Chira S, Eells SJ, Ladrigan M, Papier A, Miller LG, et al. Diagnostic accuracy in patients admitted to hospitals with cellulitis. Dermatol Online J 2011;17:1.

Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81.

Jain SR, Hosseini-Moghaddam SM, Dwek P, Gupta K, Elsayed S, Thompson GW, et al. Infectious diseases specialist management improves outcomes for outpatients diagnosed with cellulitis in the emergency department: a double cohort study. Diagn Microbiol Infect Dis 2017;87:371–5.

Jenkins TC, Sabel AL, Sarcone EE, Price CS, Mehler PS, Burman WJ. Skin and soft-tissue infections requiring hospitalization at an academic medical center: opportunities for antimicrobial stewardship. Clin Infect Dis 2010;51:895–903.

Kimball AB, Resneck JS Jr. The US dermatology workforce: a specialty remains in shortage. J Am Acad Dermatol 2008;59:741–5.

Ko LN, Garza-Mayers AC, St John J, Strazzula L, Vedak P, Shah R, et al. Effect of dermatology consultation on outcomes for patients with presumed cellulitis: a randomized clinical trial. JAMA Dermatol 2018a;154:529–36.

Ko LN, Raff AB, Garza-Mayers AC, Dobry AS, Ortega-Martinez A, Anderson RR, et al. Skin surface temperatures measured by thermal imaging aid in the diagnosis of cellulitis. J Invest Dermatol 2018b;138:520–6.

Kollias N, Gillies R, Muccini JA, Uyeyama RK, Phillips SB, Drake LA. A single parameter, oxygenated hemoglobin, can be used to quantify experimental irritant-induced inflammation. J Invest Dermatol 1995;104:421–4.

Levell NJ, Wingfield CG, Garioch JJ. Severe lower limb cellulitis is best diagnosed by dermatologists and managed with shared care between primary and secondary care. Br J Dermatol 2011;164:1326–8.

Li DG, Xia FD, Khosravi H, Dewan AK, Pallin DJ, Baugh CW, et al. Outcomes of early dermatology consultation for inpatients diagnosed with cellulitis. JAMA Dermatol 2018;154:537–43.

Mallia RJ, Narayanan S, Madhavan J, Sebastian P, Kumar R, Mathews A, et al. Diffuse reflection spectroscopy: an alternative to autofluorescence spectroscopy in tongue cancer detection. Appl Spectrosc 2010;64:409–18.

Patel M, Lee SI, Levell NJ, Smart P, Kai J, Thomas KS, et al. An interview study to determine the experiences of cellulitis diagnosis amongst health care professionals in the UK. BMJ Open 2020;10:e034692.

Peterson RA, Polgreen LA, Cavanaugh JE, Polgreen PM. Increasing incidence, cost, and seasonality in patients hospitalized for cellulitis. Open Forum Infect Dis 2017;4:ofx008.

Raff AB, Kroshinsky D. Cellulitis: a review. JAMA 2016;316:325–37.

Sjoding MW, Dickson RP, Iwashyna TJ, Gay SE, Valley TS. Racial bias in pulse oximetry measurement. N Engl J Med 2020;383:2477–8.

Strazzula L, Cotliar J, Fox LP, Hughey L, Shinkai K, Gee SN, et al. Inpatient dermatology consultation aids diagnosis of cellulitis among hospitalized patients: a multi-institutional analysis. J Am Acad Dermatol 2015;73:70–5.

Weng QY, Raff AB, Cohen JM, Gunasekera N, Okhovat JP, Vedak P, et al. Costs and consequences associated with misdiagnosed lower extremity cellulitis. JAMA Dermatol 2017;153:141–6.

Zakian C, Pretty I, Ellwood R, Hamlin D. In vivo quantification of gingival inflammation using spectral imaging. J Biomed Opt 2008;13:054045.