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REVIEW ARTICLE

Therapeutic application of machine learning in psoriasis: A Prisma systematic review

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Abstract

Dermatology, being a predominantly visual-based diagnostic field, has found itself to be at the epitome of artificial intelligence (AI)-based advances. Machine learning (ML), a subset of AI, goes a step further by recognizing patterns from data and teaches machines to automatically learn tasks. Although artificial intelligence in dermatology is mostly developed in melanoma and skin cancer diagnosis, advances in AI and ML have gone far ahead and found its application in ulcer assessment, psoriasis, atopic dermatitis, onychomycosis, etc. This article is focused on the application of ML in the therapeutic aspect of psoriasis.

KEYWORDS
artificial intelligence, dermatology, machine learning, psoriasis

1 | INTRODUCTION

Psoriasis, a genetically determined immune-mediated disease, severely impacts the quality of life and is associated with a significant risk of psoriatic arthritis and major cardiometabolic comorbidity.[1,2] Most of these associations can be mitigated by early and correct diagnosis.

While AI is aimed to simulate human intelligence, ML is a subset of AI that enables the goals of AI to be achieved. It is the study of algorithms and statistical models that the computer uses to perform a task. This results in the analysis of data, which the machine uses to automatically learn tasks.

Among the many types of ML, deep learning is a subset, which applies artificial neural networks to make predictions.[3] It consists of multiple layers of "neuron" that have adjustable weights (mathematical function). These neural networks pass input data through a series of interconnected nodes (viz. analogous to biological neurons). This helps the machine to execute intricate tasks. Thus, it has the ability to process what has been learnt by itself.

Like other dermatological conditions, assessment of a patient is via visual diagnosis and evaluation-based severity scoring systems, which is assessor dependent. These results in variation in diagnosis and severity of the disease assessed for the same patient at the same time by different dermatologists. This emphasizes the importance of

user-independent systems, which results in accurate diagnosis and uniform assessment of systems.

Multiple systems are developed which identify psoriatic lesions and differentiate them from other common differential diseases.[4,5,6] Many computer vision methods are developed like which automatically assesses area for PASI scoring.[7] With actual comparison done between machine learning methods and human eye by Savolainen et al. [8] Meienberger et al. compared psoriasis lesion detection by different types of neural networks. One type was trained with unweighted objective function and the other one with penalty factor on false predictions of diseased regions to the manually marked psoriasis lesions using accuracy, F1 score, and difference in the area.[9]

Recently, the application of machine learning has become specified by its usage in the treatment and therapeutic aspect of psoriasis.

2 | METHODS

A PUBMED search was done for a systematic review of the literature using "Psoriasis" [All fields] AND "Therapeutics" [All fields]/ "Treatment" [All fields] with multiple keywords [All fields] added with the "AND" operator. The multiple keywords used were "machine learning," "artificial intelligence," "deep learning," "computer vision," "neural network," "supervised learning," "unsupervised learning," "natural language processing," "segmentation," and "reinforcement learning."

3 | RESULTS

In all, total of 273 articles were found. After the removal of duplicates, 149 articles were present. Finally, based on the relevance, 8 articles were chosen. All the articles were selected by SBL and NSS, which were definitively included in the systematic review. All the articles were reviewed by senior author VRS (Figure 1 and Table 1).

4 | DISCUSSION

Schleusener et al.'s SORS-SERDS, a fiber probe-based Raman spectroscopy, in combination with machine learning algorithms, has been used to evaluate for non-invasive in vivo determination of the treatment efficiency of psoriasis. This helps in preventing relapses due to inadequate treatment.[10] An in-house software was used for controlling the spectroscope parameters, data acquisition, and integration. In this study, two spectra each from three different depths at a single site were captured at two different excitation wavelengths by the Shamrock 303i Czerny-Turner spectrometer. All the spectra were pre-processed using an in-house script for de-spiking, wavenumber calibration, and intensity normalization. The spectra from two different wavelengths at a single depth were integrated to obtain a fluorescence-free Raman spectrum. Thus, 3 fluorescence-free Raman spectrum were obtained for each site corresponding to 3 depths. After vector normalization (i.e., $(\omega i)=I(\omega i)||I(\omega)||$), the spectra from a single point were reconstructed into a single spectral waveform, which now enables classification of psoriatic lesions based on the information obtained from three different depth levels.

These reconstructed data were used to distinguish normal from the psoriatic spectra. This integration was based on principal component analysis (PCA, from R package "stats") and linear discriminant analysis (LDA, from R package "MASS"). A "spectra-level prediction" was made using 5 spectra from each patient at visit 1 and visit 2. However, the model was largely determined from the spectra from the first visit. The

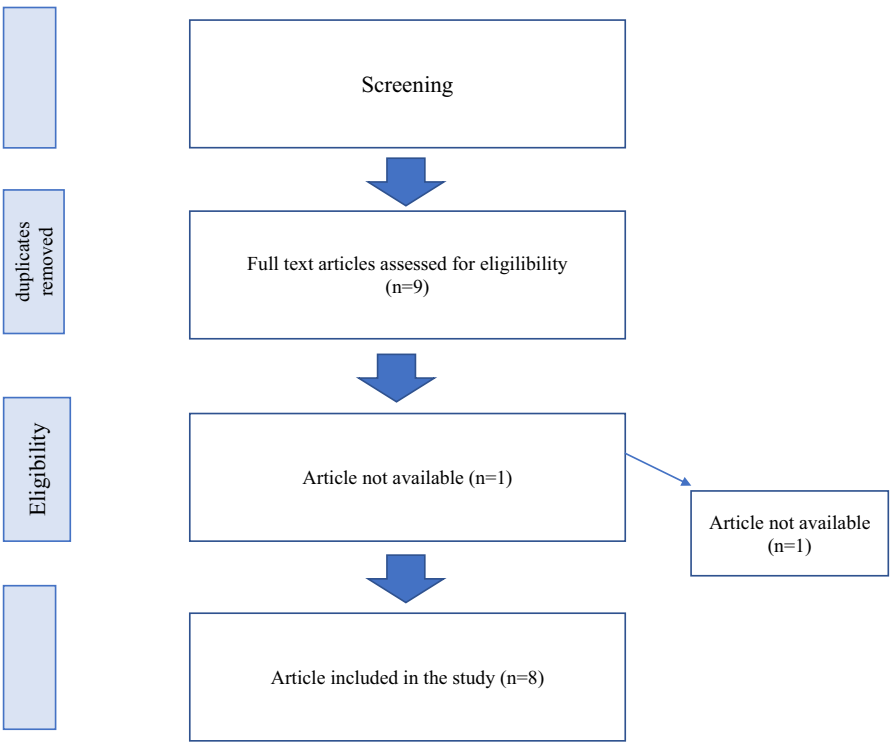

FIGURE 1 Systematic review flowchart based on the PRISMA framework

TABLE 1 Articles included in the study

PMID	Title	Authors	Journal	Year
33680562	Fiber-based SORS-SERDS system and chemometrics for the diagnostics and therapy monitoring of psoriasis inflammatory disease in vivo	Schleusener J, Guo S, Darvin ME, Thiede G, Chernavskaia O, Knorr F, Lademann J, Popp J, Bocklitz TW.	Biomed Opt Express	2021
33733038	Machine Learning Applications in the Evaluation and Management of Psoriasis: A Systematic Review	Yu K, Syed MN, Bernardis E, Gelfand JM.	JPsoriasis Psoriatic Arthritis	2020
33346505	Predicting Secukinumab Fast-Responder Profile in Psoriatic Patients: Advanced Application of Artificial-Neural-Networks (ANNs)	Damiani G, Conic RRZ, Pigatto PDM, Carrera CG, Franchi C, Cattaneo A, Malagoli P, Uppala R, Linder D, Bragazzi NL, Grossi E.	J Drugs Dermatol	2020
31705874	Early Quantification of Systemic Inflammatory Proteins Predicts Long-Term Treatment Response to Tofacitinib and Etanercept	Tomalin LE, Kim J, Correa da Rosa J, Lee J, Fitz LJ, Berstein G, Valdez H, Wolk R, Krueger JG, Suárez-Fariñas M.	J Invest Dermatol	2020
31278649	Artificial Intelligence in Dermatology—Where We Are and the Way to the Future: A Review	Hogarty DT, Su JC, Phan K, Attia M, Hossny M, Nahavandi S, Lenane P, Moloney FJ, Yazdabadi A.	Am J Clin Dermatol	2020
30953507	Anti-TNF-α treatment-related pathways and biomarkers revealed by transcriptome analysis in Chinese psoriasis patients	Liu L, Liu W, Zheng Y, Chen J, Zhou J, Dai H, Cai S, Liu J, Zheng M, Ren Y.	BMC SystBiol	2019
30395877	Understanding and exploiting prediction errors minimization within the brain in pharmacological treatments	Puviani L, Rama S	Behav Brain Res	2019
9833051	Comparison of actual psoriasis surface area and the psoriasis area and severity index by the human eye and machine vision methods in following the treatment of psoriasis	Savolainen L, Kontinen J, Alatalo E, Röning J, Oikarinen A.	Acta Derm Venereol	1998

spectra for each patient were predicted by the model built on spectra of the other patients at the first visit. Hence, five "spectra-level predictions" were obtained for each patient. Also, a "patient-level prediction" was obtained through a majority vote from the five spectral predictions of the same patient and patient was assigned as psoriasis if 3 or more spectra were predicted as "psoriasis." These predictions applied at subsequent visits are capable of determining treatment efficacy and the disease resolution and recurrence.[10]

Damiani et al did a unique study where they made a predictive model using artificial neural networks (ANNs) on patients treated with secukinumab and hence creating a semantic map for three main profiles: responders, non-responders, and an intermediate model, thus resulting in prediction of secukinumab fast responders.[11] An auto contractive map (Auto-CM), an unsupervised ANN, was used feed 15 continuous variables like body surface area (BSA), CBC, Hb, platelets, and liver function tests, which were classified into two variable classes—high and low. These variables are assigned an order based on the correlation distance and an MST creates a comprehensive semantic map of only relevant associations representing the global vision of variation patterns. Irrespective of the number of iterations, the auto-CM neural network is capable of producing perfect graphical representation. In this way, the algorithm determines the mutual relationships among the variables as defined by the disease.

Nevertheless, in order to evaluate subset of variables most closely associated with a response to secukinumab, a supervised neural network algorithm called Training with Input Selection and Testing, or TWIST was applied. Here, datasets with 7 variables, which were closely related to the disease at baseline, were selected from the original dataset as input and two variables—fast responder and non-responder—were assigned as output.

Linear multivariate statistics and multiple regression analysis were of limited value in determining complex variance and correlation of blood parameters with disease and treatment efficacy. By contrast, ANNs-based approaches may prove to be efficient in solving complex biostatistics and therapeutic problems.[11]

Tomalin LE et al. developed a machine learning model that predicted treatment outcome of etanercept and tofacitinib using longitudinal serum profiles for 92 inflammatory markers and 65 proteins representing cardiovascular disease measured at baseline and 4 weeks of initiation. The machine learning algorithms were used to predict treatment response using several biochemical markers. Classifier algorithms in 7 different languages were applied using both W0 (baseline) and W4 (4 weeks post-treatment) profiles. Predictive algorithms were developed using linear discriminant analysis (LDA) projection for inflammatory proteins (INF) alone ($n = 92$) and in combination with cardiovascular disease proteins (INF + CVD) ($n = 157$). The dataset was segregated into training set (80%), testing set (20%), and validation set for developing predictive model in each classifier. Bootstrap aggregate (bagging) was used on the predictive models built on the basis of training data for selection of the most robust (selection frequency > 70% quantile) predictive protein signature to build the final model. Final models from

multiple classifiers were combined into ensembles of all possible combinations of the final models, which had a better predictive accuracy than single model.

Tofacitinib core signatures predicted several proteins ($n = 7$) like IL-17C, IL-20, and S100A12 (ENRAGE) involved in the IL-17 pathway in both the W0 and W0 and W4. These proteins were significantly altered in patients responding to tofacitinib treatment.

The etanercept core protein signatures at W0 and W4 also included proteins involving IFNγ, CCL20, CXCL10, and IL-12 receptor B-mediated mechanisms and included CVD proteins like GAL and LEP.[12]

This is similar to experiment done by Liu et al where to understand the molecular mechanism of anti-TNF alpha agent's global gene expression profile were analyzed from monocytes at 6th and 12th week of treatment. A total of 176 differentially expressed genes (DEGs) were identified from the gene signals. Then, a gene co-expression module was constructed utilizing weighted correlation network analysis (WGCNA), which identified 22 co-expression modules that correlated significantly with treatment response. 79 of these 176 DEGs were members of the co-expression modules. The algorithms were further used to identify 30 pathways whose overall gene expression activities were significantly associated with the treatment response. 19 DEGs were members of these 30 pathways, whose functionality was related to TNF-α-mediated pathways. Additional novel pathways like heparan sulfate proteoglycan metabolic process and vascular endothelial growth factor (VEGF) synthesis were also implicated in treatment response.[13]

Savolainen L et al conducted a comparison study on computer image analysis (CIA) of psoriatic lesions with human investigator, where human investigator tended to overestimate the involved body surface area, leading to higher PASI scores. However, it pointed out how the method demands high image photography and was technically demanding and time-consuming.[14]

Patrick et al developed a system to identify drugs that can be repurposed in the treatment of psoriasis. They used "word embedding" to summarize findings from >20 million articles and confirm the drugs effective in psoriasis. The potential candidate drugs were compared with the effective drugs using matrix factorization technique to obtain accurate performance. This approach predicted the use of budesonide and hydroxychloroquine in the treatment of psoriasis, probably due to their anti-inflammatory properties. The top drugs with the potential to treat psoriasis as predicted by the algorithm were Leflunomide, Mesalamine, Cyclophosphamide, Mercaptopurine, Balsalazide, Glatiramer, Latanoprost, and Bimatoprost. Another finding of interest was that differentially expressed gene targets of the top 10 drug predictions for psoriasis were substantially up-regulated among psoriasis patients.[15]

Zang et al. used SemMedDB, a structured knowledge database extracted from all MEDLINE citations to develop a system that identifies the drug–drug interactions based on semantic predictions. The methodology involved two novel ways: (a) utilization of data from MEDLINE database (via semantic predications extracted by SemRep); and (b) utilization of biological functions, as defined by the UMLS, in the definition of drug effects, in order to detect possible interactions that would go unnoticed if only a single gene or protein effect was considered. The use of SemMedDB predications expands the range of genes and drugs considered to all drugs contained in the UMLS and all genes and proteins within either the UMLS or Entrez Gene. The predications in SemMedDB are extracted from the complete set of biomedical citations contained in MEDLINE, and they are based on actual assertions in the text, not co-occurrence or similarity functions. The wide-open approach to drug list, gene list, and drug interaction target offers more flexibility in finding potential interactions. In this study after assessing each drug pair from the medication lists of all 22 patients, authors elicited 19 known and 62 unknown drug–drug interactions. It predicted the likelihood of severe psoriasis when Lisinopril administered with Sertraline.[16]

Emam et al examined whether ML could help in prediction of long-term responses to biologics.[17,18] Here, data from 681 psoriatic patients from Danish registry cohort, DERMBIO. Six different modeling techniques were considered. These included prediction approaches: (i) generalized linear model (GLM), (ii) support vector machine, (iii) decision tree, (iv) random forest, (v) gradient-boosted trees, and (vi) deep learning. Also patient variables were taken into consideration along with Dermatology Life Quality Index (DLQI) and PASI. Drug discontinuation was taken as a surrogate measure of treatment failure.

They found that GLM model outperformed other models in terms of accuracy. At the same time, GLM model performed better in classifying the reason for discontinuation and reason for discontinuation. Also, another GLM model was produced to calculate the expected length of treatment. They predicted that characteristics of patients continuing treatment were (i) ≥23 years old at the time of diagnosis, (ii) ≤49 years old at the time of treatment, (iii) receiving ustekinumab rather than a tumor necrosis factor inhibitor, (iv) not diagnosed with psoriatic arthritis, (v) baseline DLQI ≥16, (vi) baseline PASI ≥9.4, (vii) no previous history of biologic failure and (viii) weight ≤98.9 kg.

Many studies are conducted which predict the risk the comorbidities in psoriatic patients. Patrick et al introduced a computational pipeline that predicted psoriatic arthritis in psoriasis patients. They uniquely combined statistical genetics and machine learning approaches to assess the risk.[19] Munger et al used random forest algorithm to determine the top predictors of non-calcified coronary burden using coronary computational tomography angiography.[20]

5 | LIMITATION

This study was limited to PUBMED search only. We have not included conducted search from other databases (EMBASE, GOOGLE SCHOLAR, SCOPUS etc.). Usage of Boolean search with "AND" "Therapeutics" [All fields]/"Treatment" [All fields] resulted in limited search results.

6 | CONCLUSION

Artificial intelligence is developing at lightning speed in dermatology. We can expect the use of AI in dermatology clinics in coming years. At the same time, the use of AI in therapeutic aspect of psoriasis will play a significant role especially in assessing the drug interactions and responsiveness to treatment. Dermatology Life Quality Index (DLQI) of these patients can be significantly improved by timely analysis and targeted approach using AI.

AUTHOR CONTRIBUTION

Snehal Balvant Lunge, **Nandini Sundar Shetty**, **Vidyadhar R. Sardesai**, **Priyanka Karagaiah**, **Paul S. Yamauchi**, **Jeffrey M. Weinberg**, **Leon Kircik**, and **Mario Giulini** wrote and revised the manuscript. **Mohamad Goldust** performed conception, writing, review, and revising the manuscript.

CONFLICT OF INTEREST

None.

DISCLAIMER

"We confirm that the manuscript has been read and approved by all the authors, that the requirements for authorship as stated earlier in this document have been met and that each author believes that the manuscript represents honest work."

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

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REFERENCES

1. Dogra S, Yadav S. Psoriasis in India: prevalence and pattern. *Indian J DermatolVenereolLeprol*. 2010;76:595-601.
2. Dubreuil M, Rho YH, Man A, et al. Diabetes incidence in psoriatic arthritis, psoriasis and rheumatoid arthritis: a UK population-based cohort study. *Rheumatology*. 2014;53(2):346-352.
3. Puri P, Comfere N, Drage LA, et al. Deep learning for dermatologists: part II. Current applications. *J Am Acad Dermatol*. 2020;16:30918-X
4. Hsiao YP, Chiu CW, Lu CW, et al. Identification of skin lesions by using single-step multiframe detector. *J Clin Med*. 2021;10(1):144.
5. Dash M, Londhe ND, Ghosh S, Shrivastava VK, Sonawane RS. Swarm intelligence based clustering technique for automated lesion detection and diagnosis of psoriasis. *Comput Biol Chem*. 2020;1(86):107247.
6. Kim S, Kim J, Hwang M, et al. Smartphone-based multispectral imaging and machine-learning-based analysis for discrimination between seborrheic dermatitis and psoriasis on the scalp. *Biomed Opt Express*. 2019;10(2):879-891.
7. Ihtatho D, Fadzil MA, Affandi AM, Hussein SH. Area assessment of psoriasis lesion for PASI scoring. *2007 29th Annual International Conference of the IEEE Engineering in Medicine and Biology Society 2007 Aug 22*. IEEE;2009:3446-3449.
8. Savolainen L, Kontinen J, Alatalo E, Röning J, Oikarinen A. Comparison of actual psoriasis surface area and the psoriasis area and severity index by the human eye and machine vision methods in following the treatment of psoriasis. *Actadermato-Venereologica*. 1998;28:78(6)-467.
9. Meienberger N, Anzengruber F, Amruthalingam L, et al. Observer-independent assessment of psoriasis-affected area using machine learning. *J Eur Acad Dermatol Venereol*. 2020;34(6):1362-1368.
10. Schleusener J, Guo S, Darvin ME, et al. Fiber-based SORS-SERDS system and chemometrics for the diagnostics and therapy monitoring of psoriasis inflammatory disease in vivo. *Biomed Opt Express*. 2021;12(2):1123-1135.
11. Damiani G, Conic RR, Pigatto PD, et al. Predicting Secukinumab fast-responder profile in psoriatic patients: advanced application of artificial-neural-networks (ANNs). *J Drugs Dermatol*. 2020;19(12):1241-1246.
12. Tomalin LE, Kim J, da Rosa JC, et al. Early quantification of systemic inflammatory proteins predicts long-term treatment response to tofacitinib and etanercept. *Journal of Investigative Dermatology*. 2020;140(5):1026-1034.
13. Liu L, Liu W, Zheng Y, et al. Anti-TNF-αtreatment-related pathways and biomarkers revealed by transcriptome analysis in Chinese psoriasis patients. *BMC Syst Biol*. 2019;13(2):29.
14. Savolainen L, Kontinen J, Röning J, Oikarinen A. Application of machine vision to assess involved surface in patients with psoriasis. *Br J Dermatol*. 1997;137(3):395-400.
15. Patrick MT, Raja K, Miller K, et al. Drug repurposing prediction for immune-mediated cutaneous diseases using a word-embedding–based machine learning approach. *J Investigative Dermatol*. 2019;139(3):683-691.
16. Zhang R, Cairelli MJ, Fiszman M, et al. Using semantic predictions to uncover drug-drug interactions in clinical data. *J Biomed Inform*. 2014;49:134-147.
17. Hogarty DT, Su JC, Phan K, et al. Artificial intelligence in dermatology—where we are and the way to the future: a review. *Am J Clin Dermatol*. 2020;21(1):41-47.
18. Emam S, Du AX, Surmanowicz P, Thomsen SF, Greiner R, Gniadecki R. *Predicting the long-term outcomes of biologics in psoriasis patients using machine learning*. arXiv Preprint arXiv:1908.09251. 2019.
19. Patrick MT, Stuart PE, Raja K, et al. Genetic signature to provide robust risk assessment of psoriatic arthritis development in psoriasis patients. *Nat Comm*. 2018;9(1):4178.
20. Munger E, Choi H, Dey AK, et al. Application of machine learning to determine top predictors of non-calcified coronary burden in psoriasis: an observational cohort study [published online ahead of print October 31, 2019]. *J Am AcadDermatol*. 2019;83(6):1647-1653.

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