Artificial intelligence in medicine—dermatology compared to other medical specialties in FDA-cleared software as medical device

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Abstract

Artificial intelligence (AI) and machine learning (ML) have occupied the center stage in healthcare as research groups and institutions investigate their capabilities and risks. Dermatology is often cited as one of the medical specialties most ripe for disruption with AI technology due to the heavy incorporation of visual information into clinical decisions and treatments. Although the literature on AI in dermatology is rapidly growing, there has been a noticeable absence of mature AI solutions utilized by dermatology departments or patients. This commentary provides insight into the regulatory challenges facing AI solutions for the specialty of dermatology and the unique considerations that should be factored into AI development and deployment.

Keywords: artificial intelligence, dermatology, FDA regulation, machine learning, medical device

Introduction

Advancements in machine learning (ML) and artificial intelligence (AI) have paved the way for innovations across finance, transportation, security, education, and healthcare [1]. Funding has poured into companies and research teams that are building AI tools for a diverse set of industries as AI promises to increase efficiency, automate repetitive tasks, and reduce human error. Consequently, we have seen AI deliver self-driving cars, image-based security, and financial robo-advisors [1]. Although healthcare as a target of disruption has received much attention, there has been a relative lack of commercialization and integration into clinical workflows. One does not need to look far to find a plethora of potential barriers unique to healthcare that restrict AI innovation but regulatory hurdles are often cited among the most prominent of barriers [3].

Physician participation in the creation and governance of healthcare ML/AI is critical to its success but enabling physicians in this space requires knowledge of regulatory hurdles. Regulators are still trying to assess how to best manage and review digital innovations. Physician understanding of regulatory expectations and barriers for healthcare ML/AI can encourage physicians to lead efforts that set realistic expectations for ML/AI technology in a manner that delivers on its promises while still prioritizing clinical outcomes and the best interest of patients.

With a focus on the field of dermatology, we aim to enable more effective physician participation in the advancement of ML/AI for healthcare AI by 1) describing the current state of AI in dermatology and 2) providing an overview of special regulatory considerations that would be better navigated with engagement by dermatologists.

Discussion

Overview of FDA pathways for machine learning and artificial intelligence

Of the increasing number of ML/AI-based healthcare technologies, many are not subject to FDA review because they either do not meet the definition of a medical device or they pose negligible risk to patients [4,5]. Machine learning/AI functions that are not intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a disease or condition, such as workflow augmentation tools, scheduling applications, and data transfer and storage functions, do not meet the definition of a medical device and do not require FDA review prior to deployment. The FDA has also provided that, under their enforcement discretion, certain low risk medical device software functions, such as applications providing well-established general health and wellness recommendations, do not require FDA's active enforcement of the regulations at this time [6]. Other opportunities to use AI outside of FDA jurisdiction include meeting FDA's interpretation of clinical decision support (CDS) defined in the 21st Century Cures Act. Clinical decision support outside of FDA's jurisdiction does not apply when the AI is analyzing medical images (e.g., radiological imaging) or in vitro diagnostic signals (e.g., EKG) and requires that the basis for the recommendation is available so that the healthcare professional does not rely on the tool as the primary means of a diagnostic or treatment decision [5]. Healthcare ML/AI intended to drive medical decision-making, including many CDS systems with a meaningful clinical impact, may qualify as software as a medical device (SaMD) and be subject to FDA jurisdiction.

Although lower risk software that functions outside of FDA's active enforcement is undoubtedly an important part of patient care and requires fewer regulatory hurdles, the scope of innovation is limited when products must be narrowly tailored to avoid FDA regulations. The utility and impact of healthcare ML/AI will remain limited if physician innovators are not enabled to advance technology to the level of risk that implicates FDA regulations. With increased impact on patient care and a heightened level of regulatory scrutiny, enabling physician involvement with SaMD requires knowledge of the FDA pathway for SaMD summarized in **Figure 1**.

The current state of artificial intelligence in dermatology

Multiple medical specialties have successfully navigated FDA requirements for ML/AI-based medical devices software, with oncology, radiology, and cardiology leading the way [7,8]. Dermatology as a field has historically been a leader in innovation. However, with regard to FDA approval for SaMD, dermatology is notably lagging compared to other specialties in FDA-cleared ML/AI. Although there are numerous ML/AI-based dermatological applications currently available in the United States, very few have successfully navigated the FDA's pathway for medical device software.

In a search of the FDA database, there are only two claimed ML/AI-based dermatology medical devices—Melafind and Nevisense, both subjected to FDA's highest risk "Pre-Market Approval" pathway. This may be compared to 22 FDA-approved devices in radiology, five in cardiology, and six in oncology [3,9]. Melafind was the subject of the book *Innovation Breakdown*, describing the challenging process of obtaining FDA approval [10]. The MelaFind device, which analyzed images of skin lesions to aid dermatologists in determining whether a biopsy is necessary, never reached significant market adoption and in 2015, the MelaFind device was subjected to a voluntary recall after a finding that the user interface lacked FDA approval [11]. Nevisense, a device made by the company SciBase, uses electrical impedance spectroscopy and was approved by the FDA in 2017 for use by dermatologists to aid in the consideration of whether a biopsy is necessary [12,13]. Nevisense is intended to provide additional information about the "cellular characteristics" of cutaneous lesions with unclear clinical or historical signs of melanoma.

There is a paucity of FDA-approved devices in the field of dermatology relative to other specialties, but why? Undoubtedly, opportunities for ML/AI-based algorithm development in dermatology are robust, given the pattern-recognition-based and visually-oriented nature of the specialty. The potential

benefits in applying ML/AI-related technologies to the practice of dermatology are vast. With a shortage of dermatologists in the U.S., ML/AI has the potential to improve both access to care and quality of care [14]. Furthermore, literature reviews of ML/AI applications in dermatology show promise.

In 2017, Esteva et al. published that deep convolutional neural networks trained on 129,450 clinical images with biopsy-proven diagnoses led to equivalent diagnostic accuracy compared against 21 board-certified dermatologists with respect to two measures: keratinocyte carcinomas versus benign seborrheic keratosis and malignant melanomas versus benign nevi [15]. In addition to this study, there is a boom of ML/AI-based research in dermatology with thousands of publications, along with an explosion of ML/AI-driven tech start-ups targeting dermatologic diseases and skin care [16]. Most of these ML/AI applications, however, remain at the research stage or follow a path that is exempt from FDA jurisdiction. In a systematic review, Freeman et al. in *BMJ* 2020 demonstrated that algorithm-based smartphone applications (apps) available direct-to-consumers for skin cancer detection were unreliable [17].

Prior reviews have analyzed the literature on ML/AI in dermatology in various ways—by type of article, diseases targeted, and categories of barriers that impede ML/AI implementation [18-20]. Gomolin et al. astutely noted that whereas most of the literature included original research articles, few involved significant dermatologist collaboration in conceiving, designing, and interpreting those studies [18]. It should not be surprising that dermatologists' involvement in study design has led to datasets more representative of true clinical scenarios [21].

The ML/AI applications that have been developed and published are impressive with promising potential in improving dermatologic care. However, most of the publications require significant further technological and clinical validation studies. Arevalo et al., for example, presented an ML/AI that could analyze images of permanent section histopathology to classify basal cell carcinoma with 98.1% accuracy [22]. Nevertheless, to date there are still no FDA-cleared clinical diagnostics for basal cell carcinoma. Issues of trust by physicians and patients as well as liability for adverse outcomes limit absolute diagnostic reliability. In other words, a human decision can be explained but the decision made by ML/AI may not be interpretable [18]. In addition, machine learning models that are created must provide specific value to the physician, process, patient, or clinical flow. A meta-analysis of 70 studies found that ML/AI diagnostic algorithms were equivalent to human experts when it comes to diagnosing melanoma from images, with telemedicine being one of the first avenues to embrace ML/AI [23,24]. However, there is no comparison of how ML/AI performs compared to a dermatologist who has a face-to-face interaction in that meta-analysis, which is an important metric to consider knowing that face-to-face diagnostic accuracy exceeds that of teledermatology [25].

Dermatologists and physician leaders play a critical role in identifying areas in which the application of ML/AI can add value to the field. They play an equally important role in identifying the dangers of the inappropriate application of ML/AI and in assuring that patient safety, clinical needs, and feasibility of practice integration are all considered. Most dermatologists internationally support that ML/AI will improve dermatologic care (77.3%), yet few report an excellent understanding of ML/AI [26].

Special regulatory considerations for ML/AI in dermatology

Underlying the reviews of the current state of healthcare ML/AI in dermatology lies the answer to why dermatology is lacking FDA-cleared/approved SaMD. All specialities share many of the same deployment challenges. For example, medical device cybersecurity requirements must be met and account for human factors and usability engineering considerations that allow for the software to be used in the intended clinical setting. In addition, there are enormous challenges to accommodate multiple variables in the annotation of data [27,28]. However, dermatology faces many challenges that are unique to the specialty. Dermatologist awareness of these challenges and engagement in the solutions will help enable FDA approval for ML/AI systems applied to this field.

Diversity of data is one primary challenge for dermatology ML/AI. On the one hand, skin is easily accessible, but skin surfaces are highly variable across individuals. Color, texture, hydration level, hair quantity and distribution patterns, pore size, presence of rhytid, scars, tattoos are only part of the list of clinically assessable variables that ML/AI must consider. There are further data challenges associated with diversity of how data was collected, including lighting, distance, patient position, and equipment used. These additional data variables in dermatology increase the technical complexity of training ML/AI models. Providing clinical context to data scientists and product leaders is an opportunity for dermatologists to advance the field.

Another important consideration is spectrum of risk. Some of the "low hanging fruit" of ML/AI involve conditions in which the common false positive or false negative is low risk. For example, a condition in which a false positive is referral to a specialist (the standard of care) carries little to no risk. Conversely, if it can be shown that a common false negative is likely to be a slight variation on the severity of the same disease (e.g., no disease versus mild disease for a slowly progressing condition), the risk may remain low. However, the risk spectrum in dermatology is potentially highly variable. In a field in which nuances may be the difference between a melanoma and a dysplastic nevus, including history or other contextual clues from a full body skin examination, it is potentially more difficult to weigh the risks and benefits of a targeted ML/AI device. Dermatologist input on disease characteristics and risk of harm can help target ML/AI systems in which the benefits outweigh the risks.

One foundational consideration for the FDA is validating that the ML/AI works safely and effectively in the setting for which it is intended to be used [29]. This requires intimate knowledge of diagnostic decision-making and clinical workflows. As Gomolin et al. noted, few of the literature and research articles reviewed involved significant dermatologist collaboration [18]. This will not get algorithms far with the FDA because involvement of physicians is paramount for a number of reasons, including understanding clinical need, aligning to specialty standards of care, establishing clinical "gold standards" used for validating clinical decision support, and identifying and mitigating biases in design and implementation. Furthermore, clinical investigations conducted for the purpose of FDA clearance/approval are likely to require consideration of both technical and clinical workflows in addition to algorithm performance, which is lacking in most peer-reviewed studies.

Another foundational consideration is the difference between the setting of academic research ML/AI and the real world. For example, a research study may use skin imaging data provided by a dermatology department to train and test an ML/AI diagnostic. These images may be taken by professional photographers directed by the dermatologist to focus on particular areas of concern. In a real-world use case, however, the image may be captured by novices without professional direction. In addition, lack of standardization for how images are obtained across institutions creates more variability for the ML/AI model to accommodate, which could significantly change performance when placed outside of the environment in which it was trained and tested. For example, digital dermoscopy datasets may include data from different dermatoscopes, different lighting conditions, a range of distances from the skin, and other image quality issues, such as resolution and artifacts that are common considerations for ML/AI training. These challenges do not preclude the use of machine learning; rather, these are factors that need to be accounted for in the design, development, and validation of ML/AI tools that can best be understood and highlighted by the physician specialist. FDA review would expect that the circumstances under which the ML/AI device is tested matches the real-world circumstances under which the device is intended to be used, which emphasizes the importance of involving the physician in developing ML/AI algorithms.

Dermatology as a specialty is also distinguished in ways that may lead to more difficulty satisfying FDA review and clearance/approval requirements. For example, face-to-face interactions provide advantages and supplemental information that are

lost when dermatologists are asked to diagnose from images. These include 3-dimensional visual inspection, palpation, and contextual clues by full body examination and evaluation of unaffected skin. Machine learning/AI tools for cardiology and radiology, on the other hand, often have all the diagnostic information needed for the ML/AI to function in a two-dimensional digital image, which is one of the reasons these specialties are leading the way with application of ML/AI. Although a single skin lesion can be photographed, ML/AI algorithms that have learned based upon images of discrete lesions may be biased by not including other metrics important to dermatologists such as anatomic location, ethnicity, and duration. They also do not provide inspection of unaffected skin in the same individual for context. Ruling out disease is often just as important in dermatology as diagnosing disease; thus, the use cases may be limited since narrowing down to regions or lesions of suspect in and of itself may require clinical expertise. For example, a patient using a smart-phone app on one area of concern would not get the benefit of a full-body skin examination where surface areas as large as two squared meters are examined [30]. Further, in this scenario, the app relies on the risky assumption that patients (or consumers) can self-identify normal and abnormal skin findings for which to use their app. Thus, intent of use (primary care provider trained to identify concerning areas using the device versus patients using it in place of the standard full body skin examination) would be an important consideration for the FDA.

FDA review committees are also acutely aware of the clinical standard of care and its alignment with patient outcomes and ask applicants to justify how the ML/AI system will impact care. However, reference standards used to train ML/AI models often rely on proxies for patient outcomes, such as features in an image that correlate with disease. This can be especially difficult if diagnostic criteria involve information beyond what is available for the ML/AI to assess. For example, an ML/AI system to detect a disease or tumor may rely on images, but a clinical assessment may go beyond the image to include other information like change over time, patient history, and context. Justifying alignment of ML/AI with clinical evidence is further complicated by the lack of clarity regarding exactly how the ML/AI reached its conclusion (sometimes referred to as a "black box"). This leaves the ML/AI developer in the difficult position of justifying how the ML/AI aligns to clinical evidence, which can be especially complicated in cases where the ML/AI is unable to consider information material to the clinical standard of care. Alternatively, the developer could consider limiting the use of the ML/AI to circumstances under which trained dermatologists can independently validate results using clinical evidence, but this may detract from the utility of the ML/AI system. Another consideration for demonstrating alignment to the clinical standard of care is to conduct a clinical investigation that includes a study of patient outcomes, which could be a years-long and costly trial. Dermatologists have an opportunity to play a key role in ML/AI product strategy and deployment with their clinical expertise.

FDA-regulated ML/AI also requires multiple applications of formal risk analysis and management. One such risk consideration is bias. Bias has become a prominent concern for ML/AI applications across multiple industries, healthcare being no exception. There are, unfortunately, many examples of ML/AI propagating existing societal or creator bias rather than creating an impartial output [31]. Given that the quality of an algorithm's output is directly related to the quality of the inputs, special care must be given to the data used for training and validation. For example, if a diagnostic algorithm is trained on examples from light skin tones only, the generalizability of the algorithm to other skin tones would rightly be questioned. Additionally, if the reference standard when building and testing an ML/AI model comes from an expert human (i.e., dermatologist), implicit biases have the potential to be perpetuated in the algorithm. Furthermore, given the potential for an overreliance on ML/AI outputs, so-called "automation complacency," these biases may be less likely to be identified and corrected [32]. Although the promise of ML/AI-driven tools in the field of dermatology is profound, we must ensure that biases are not perpetuated and no patients are left to suffer the consequences.

Finally, racial and ethnic bias is an important barrier to generalization and external validation of ML/AI; well-designed clinical trials with input from dermatologists is critical for this reason. For example, training ML/AI on a homogenous dataset (e.g., Caucasians with Fitzpatrick skin type 1 or 2) has the potential for harm on already healthcare-vulnerable populations such as Black Americans. With regard to melanoma and squamous cell carcinoma in particular, outcomes are worse for people of color, which highlights the importance of having a representative dataset as inputs for ML/AI and the necessity of safe and reliable performance of the ML/AI for skin of color.

Conclusion

Dermatology as a field is no stranger to innovation or machine learning. However, we have yet to see examples of effective integration of this technology into daily practice. A review of FDA-approved ML/AI tools reveals that dermatology lags compared to many other specialties in this domain. Though there have been numerous non-FDA-approved ML/AI tools in dermatology, issues with accuracy and reliability, or lack of utility, prevent their adoption by physicians and health systems.

This commentary emphasizes the importance of dermatologist involvement in the design, refinement, and deployment of ML/AI systems to maximize their generalizability and alignment with clinical standards. All these factors have the effect of optimizing the ML/AI's path through FDA approval. Though a technical background is not a prerequisite for dermatologists getting involved, familiarity with foundational principles and common pitfalls of ML/AI would allow them to best leverage their medical expertise to guide ML/AI development.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. West DM, Allen JR. How artificial intelligence is transforming the world. 2018 April 24, 2018. Report No. Available from: https://www.brookings.edu/research/how-artificial-intelligence-is-transforming-the-world/. Accessed on January 16, 2022.
2. Panch T, Mattie H, Celi LA. The "inconvenient truth" about AI in healthcare. *NPJ Digit Med*. 2019;2:77. [PMID: 31453372].
3. Benjamens S, Dhunnoo P, Mesko B. The state of artificial intelligence-based FDA-approved medical devices and algorithms: an online database. *NPJ Digit Med*. 2020;3:118. [PMID: 32984550].
4. Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act - Guidance for Industry and Food and Drug Administration Staff. U.S. Food & Drug Administration, 2019 September 27, 2019. Report No. Available from: https://www.fda.gov/media/109622/download. Accessed on January 16, 2022.
5. Clinical Decision Support Software - Draft Guidance for Industry and Food and Drug Administration Staff. U.S. Food & Drug Administration, 2019 September 27, 2019. Report No. Available from: https://www.fda.gov/media/109618/download. Accessed on January 16, 2022.
6. Administration USFD. Policy for Device Software Functions and Mobile Medical Applications - Guidance for Industry and Food and Drug Administration Staff. U.S. Food & Drug Institution, 2019 September 27, 2019. Report No. Available from: https://www.fda.gov/media/80958/download. Accessed on January 16, 2022.
7. FDA Approvals for Artificial Intelligence-Based Algorithms in Medicine. In: The-Medical-Futurst-FDA-approved-AI-algorithms-in-medicine-2019-09. The Medical Futurist; 2019. Available from: https://cdn.medicalfuturist.com/wp-content/uploads/2019/06/The-Medical-Futurist-FDA-approved-AI-algorithms-in-medicine-2019-09.png. Accessed on January 16, 2022.
8. FDA-approved A.I.-based algorithms The Medical Futurist, [cited 2022]. Available from: https://medicalfuturist.com/fda-approved-ai-based-algorithms/. Accessed on January 16, 2022.
9. Medical Devices Database. U.S. Food & Drug Administration; 2021. Available from: https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/medical-device-databases/. Accessed on January 16, 2022.
10. Gulfo JV. Innovation Breakdown. Post Hill Press; 2014.
11. Class two Device Recall MelaFind U.S. Food & Drug Administration: 2015 [updated January 14, 2022; cited 2022]. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRes/res.cfm?ID=136172. Accessed on January 16, 2022.
12. Scibase [cited 2022]. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRes/res.cfm?ID=136172https://scibase.com/],. Accessed on January 16, 2022.
13. Premarket Approval (PMA) U.S. Food & Drug Administration, [updated January 10, 2022; cited 2022]. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150046. Accessed on January 16, 2022.
14. Jayakumar KL, Lipoff JB. Trends in the dermatology residency match from 2007 to 2018: Implications for the dermatology workforce. *J Am Acad Dermatol*. 2019;80:788-90. [PMID: 30744878].
15. Esteva A, Kuprel B, Novoa RA, et al. Dermatologist-level

classification of skin cancer with deep neural networks. *Nature*. 2017;542:115-8. [PMID: 28117445].
16. Lewinson RT, Vallerand IA. The Need for a National Strategy on Artificial Intelligence in Canadian Dermatology. *J Cutan Med Surg*. 2020;24:428-9. [PMID: 32363930].
17. Freeman K, Dinnes J, Chuchu N, et al. Algorithm based smartphone apps to assess risk of skin cancer in adults: systematic review of diagnostic accuracy studies. *BMJ*. 2020;368:m127. [PMID: 32041693].
18. Gomolin A, Netchiporouk E, Gniadecki R, Litvinov IV. Artificial Intelligence Applications in Dermatology: Where Do We Stand? *Front Med (Lausanne)*. 2020;7:100. [PMID: 32296706].
19. 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;21:41-7. [PMID: 31278649].
20. Schleissinger DI, Chhor G, Gevaert O, et al. Artificial intelligence and dermatology: opportunities, challenges, and future directions. *Semin Cutan Med Surg*. 2019;38:E31-E7. [PMID: 31051021].
21. Zakhem GA, Fakhoury JW, Motosko CC, Ho RS. Characterizing the role of dermatologists in developing artificial intelligence for assessment of skin cancer. *J Am Acad Dermatol*. 2021;85:1544-56. [PMID: 31972254].
22. Arevalo J, Cruz-Roa A, Arias V, et al. An unsupervised feature learning framework for basal cell carcinoma image analysis. *Artif Intell Med*. 2015;64:131-45. [PMID: 25976208].
23. Dick V, Sinz C, Mittlbock M, et al. Accuracy of Computer-Aided Diagnosis of Melanoma: A Meta-analysis. *JAMA Dermatol*. 2019;155:1291-9. [PMID: 31215969].
24. Young AT, Xiong M, Pfau J, et al. Artificial Intelligence in Dermatology: A Primer. *J Invest Dermatol*. 2020;140:1504-12. [PMID: 32229141].
25. Finnane A, Dallest K, Janda M, Soyer HP. Teledermatology for the Diagnosis and Management of Skin Cancer: A Systematic Review. *JAMA Dermatol*. 2017;153:319-27. [PMID: 27926766].
26. Polesie S, Gillstedt M, Kittler H, et al. Attitudes towards artificial intelligence within dermatology: an international online survey. *Br J Dermatol*. 2020;183:159-61. [PMID: 31953854].
27. Cybersecurity U.S. Food & Drug Administration, [updated December 22, 2021; cited 2022]. Available from: https://www.fda.gov/medical-devices/digital-health-center-excellence/cybersecurity. Accessed on January 16, 2022.
28. Applying Human Factors and Usability Engineering to Medical Devices - Guidance for Industry and Food and Drug Administration Staff. U.S. Food & Drug Administration, 2016. Available from: https://www.fda.gov/media/80481/download. Accessed on January 16, 2022.
29. Software as a Medical Device (SAMD): Clinical Evaluation - Guidance for Industry and Food and Drug Administration. U.S. Food & Drug Administration, 2017. Available from: https://www.fda.gov/media/100714/download. Accessed on January 16, 2022.
30. Mosteller RD. Simplified calculation of body-surface area. *N Engl J Med*. 1987;317:1098. [PMID: 3657876].
31. Gianfrancesco MA, Tamang S, Yazdany J, Schmajuk G. Potential Biases in Machine Learning Algorithms Using Electronic Health Record Data. *JAMA Intern Med*. 2018;178:1544-7. [PMID: 30128552].
32. Parikh RB, Teeple S, Navathe AS. Addressing Bias in Artificial Intelligence in Health Care. *JAMA*. 2019;322:2377-8. [PMID: 31755905].

Figure 1. *Potential Food & Drug Administration (FDA) pathways for software.*