Skin Analytics

Instructions For Use
Deep Ensemble for Recognition of Malignancy (DERM)

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Instructions for Use

Deep Ensemble for Recognition of Malignancy (DERM)

DERM is a standalone software device that employs artificial intelligence (AI)-based algorithms to analyse a dermoscopic image of a skin lesion and return a suspected diagnosis and referral recommendation for the lesion. The device is intended to be integrated with a third party client software system through which images are transmitted to and results are displayed from DERM. Only images captured by approved dermoscopic hardware systems are permitted for submission to DERM for analysis.

DERM is primarily intended to be used by healthcare organisations as an automated clinical management tool to help screen, triage or assess patients presenting with one or more lesions where there is a concern of skin cancer. In such cases, the outputs from DERM may be used to issue management instructions without a second read from a human clinician, such as 'refer', 'discharge' or 'monitor'.

1. Manufacturing Information

DERM is manufactured by Skin Analytics Limited, Smithfield Business Centre 2nd Floor, 5 St John's Lane, London, EC1M 4BH, United Kingdom.

This device fulfils the provisions of the UK Medical Device Regulation 2002 (as amended), EU Medical Device Regulation 2017/745 and New Zealand Medicines (Database of Medical Devices) Regulations 2003. This device has been developed in accordance with Skin Analytics' ISO 13485:2016 certified Quality Management System.

For questions or help, please contact Skin Analytics Support at support@skinanalytics.co.uk

2. Intended Use and Indication for Use

DERM is an artificial-intelligence (AI)-based skin lesion analysis device intended for use in the screening, triage and assessment of skin lesions suspicious for skin cancer. DERM will analyse a dermoscopic image of a skin lesion and return a suspected diagnosis and, if applicable, a referral recommendation for the lesion.

DERM is indicated for use on dermoscopic images of cutaneous lesions where there is a suspicion of skin cancer in patients aged 18 years or over in any body location except where specific exclusions apply.

DERM does not provide a definitive diagnosis for skin cancer.

DERM has been tested on images of skin lesions that represent the population of patients and lesions DERM may be used on, in powered prospective studies, run in the UK, US and Italy. Given the prevalence of the disease in the general population, DERM has primarily been evaluated on patients with Fitzpatrick skin types I-IV. DERM should be used with caution on lesions of other skin types.

DERM is intended to be used by primary care clinicians / providers (e.g. general practitioners, nurse practitioners) and secondary care clinicians / providers (e.g. dermatologists). These users may use DERM and its outputs as an automated clinical management tool or to augment other clinical data points to support clinical decision-making.

Medical photographers and patients may be authorised to capture images to submit to DERM but are not intended to be users of the outputs generated by DERM.

3. Contraindications

DERM should not be used on:

- Patients under the age of 18
- Assessing skin conditions where the concern is not of skin cancer (e.g. rashes, eczema, infectious diseases, lupus)
- Monitoring treatment
- Staging of disease
- Images other than dermoscopic images of skin lesions
- Images of skin lesions from a subject other than the identified patient
- Open or ulcerated skin lesions
- Skin lesions unable to be entirely imaged within the dermoscopic device used
- Skin lesions obscured by hair, tattoos or scars
- Skin lesions beneath nails, in eyes or on mucosal surfaces or on soles of feet or palms of hands
- Skin lesions which have previously been biopsied

4. Document Information

Purpose

This document contains the instructions necessary to use DERM in accordance with its function and intended use.

This Instructions for Use document is intended for use by:

- Healthcare Providers (customer organisations) considering the use of DERM by their healthcare professionals as a decision support tool in the screening, triage and assessment of skin lesions suspicious for skin cancer
- Healthcare Providers (customer organisations) considering the use of DERM as an automated clinical management tool to screen or triage patients presenting to clinicians with lesions suspicious for skin cancer
- Healthcare Professionals who are using DERM in the screening, triage and assessment of skin lesions suspicious for skin cancer
- Patients or healthcare professionals who are taking and submitting dermoscopic images to DERM for analysis

The latest version of this Instructions For Use, provided in pdf format, can be downloaded from the website (https://skin-analytics.com/derm-medical-device-resources-for-healthcare-organisations/).

How to obtain a paper copy of this document

To obtain a paper copy of this document, send an email to support@skinanalytics.co.uk. Please include in your email your organisation name, full address, the product for which you are requesting a manual and the version of the software. Skin Analytics aims to send a paper copy within 7 days of a request at no additional cost.

Definitions

Term	Definition
AI	Artificial Intelligence
API	Application Programming Interface
AK	Actinic Keratosis
AN	Atypical Nevus
BCC	Basal Cell Carcinoma
Camera Device	An image capture device, such as a smartphone, that is used in conjunction with a Dermoscope to take an image of a skin lesion to send to DERM for analysis
Client System	Third party client software able to send requests to DERM for analysis and retrieve the outputs from DERM
User	A healthcare professional, non-medical clinical user or patient using a client system via a clinical organisation.
Connection Kit	A clip that attaches the Dermoscope to the Camera Device
Dermoscope	A specialised lens that is used in conjunction with a Camera Device to take an image of a skin lesion to send to DERM for analysis
False Negative	A malignant lesion classified as a benign lesion
False Positive	A benign lesion classified as a malignant lesion
Healthcare Provider	See “Organisation”
IEC	Intraepidermal Carcinoma/Bowen’s disease

Image Capture Hardware	Combination of Camera Device, Dermoscope and Connection Kit, which together are validated for use with DERM
Input Image	The image taken by the User and submitted to DERM for analysis. This should be a Dermoscopic image of a Skin Lesion.
Lesion Priority	The prioritisation logic that allows DERM to return the label of the more severe condition in the event that a lesion exceeds the Threshold for multiple classification labels.
Lesion Classification	The Clinical term for the Lesion Classification returned by DERM e.g. possible Melanoma, probable BCC, etc
Organisation	Network of hospitals or clinics purchasing the use of DERM. Examples include a Hospital Trust, or a Clinical Commissioning Group from the NHS
OUS	Out of United States
SCC	Squamous Cell Carcinoma
Sensitivity	The percentage of positive cases that DERM finds as positive
Specificity	The percentage of negative cases that DERM finds as negative
Reference Sensitivity	Minimum acceptable sensitivity DERM achieves for each lesion type.

Glossary of Symbols used in DERM Labelling

Consult instructions for use or consult electronic instructions for use

Manufacturer

Date of Manufacture

UK Conformity Assessed

EU Conformity Assessed

EU Authorised Representative

EU Importer

Model Number

Caution

Medical Device

Unique Device Identifier

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5. Warnings and Precautions

Precautions

- All Users must follow the instructions for use, including the intended use and indications for use (Section 2) and the safety and cautionary information (this section).
- DERM must be integrated with a Client System, so that Users of the Client System can submit dermoscopic images of skin lesions for analysis by DERM, receive the outputs of the analysis performed by DERM, and/or enable automated clinical management activities to be triggered by DERM outputs via the client system (such as patient referral letters). The integration must be completed according to the instructions set out in the DERM API User Manual. Skin Analytics operates an Onboarding process to enable and support integration of Client Systems. For further details, please contact support@skinanalytics.co.uk.
- In order to assure that DERM operates with the stated sensitivity and specificity, the images submitted to DERM for analysis must be captured using approved dermoscopic Image Capture Hardware. Images must be captured using a Camera Device connected to a Dermoscope using a Connection Kit. For details of the latest approved hardware, please refer to the Skin Analytics website: https://skin-analytics.com/derm-medical-device-resources-for-healthcare-organisations/
- Users should regularly ensure that the Client System is operating on a computer that is free of viruses and malware and compliant with local cybersecurity policies.

Warnings

DERM is to be used only by prescription of a healthcare professional or by a clinical organisation's client system in the screening, triage and assessment of skin lesions suspected of skin cancer.

DERM does not provide a definitive diagnosis.

When deployed as part of an automated clinical management system, the DERM classification output may be used to trigger an automated clinical management response via a clinical organisation's client system. The content and format of the response, such as a referral letter, is created under the responsibility of the commissioning clinical organisation. Where applicable, the organisation is expected to take into account the explicit clinical safety warnings for automation detailed in the "Pathway Responsible Owner User Manual" and in this section.

When DERM is used to augment other clinical data points, or support a clinical decision on a patient, the result provided should be viewed alongside all other clinical information before issuing a clinical management decision.
If DERM is unavailable, clinical users should continue a patient assessment following existing clinical practice (traditional teledermatology or face-to-face review).

DERM should not be used for cases or excluded lesions listed in the 'Contraindications' section.

DERM does not screen for any lesions not listed in the "Product Information - Device Inputs and Outputs" section (e.g. rare malignant lesions such as Merkel Cell Carcinoma).

DERM should be used with caution on Fitzpatrick skin types V - VI. DERM has been tested on skin lesions representative of the incidence of skin cancer in a powered prospective studies run in the UK, US and Italy. Given the prevalence of the disease in the general population, DERM has been evaluated mostly on Fitzpatrick skin types I-IV. DERM should be used with caution on lesions of other skin types.

DERM will check that an image is a dermoscopic image of a skin lesion, and that it is of sufficient quality for assessment (i.e. not too dark or blurred). Good image-taking technique is therefore an important prerequisite for successful use of DERM. For information on how to take good images for DERM analysis, please refer to "Hardware, Image Capture, Exclusions & Consent" manual, the latest version of which, provided in PDF format, can be downloaded from the website - Guidance on image capture (https://skin-analytics.com/derm-medical-device-resources-for-healthcare-organisations/).

The dermoscopic images sent to DERM should not be captured with the use of an immersion fluid as immersion fluid may introduce image artefacts that could adversely impact the performance of DERM.

The dermoscopic image sent to DERM should not contain any other external objects or markers within the image and/or obscuring the lesion, e.g. felt-tip marker, sticker, ruler, as this could adversely impact the DERM assessment.

DERM will only analyse the dermoscopic image that has been submitted to it. Make sure that the dermoscopic image is of the correct lesion of concern.

DERM only assesses dermoscopic images of skin. The Client System used to access DERM may also capture other information pertinent to the patient or the lesion (e.g. age, lesion location, change, or context (non-dermoscopic images)). This additional data is not included in the assessment of DERM. If more than one dermoscopic image has been submitted for assessment by DERM, each image will be assessed in isolation and independent of the others.

The rate of false positives and false negatives produced by DERM is dependent on the configured operating parameters used (as set out in "Configuration - Operating Parameters" Section). High sensitivity settings to minimise false negatives necessarily means that there will be some positive classifications which turn out to be benign.

Care should be taken when giving results to patients in order to minimise anxiety.

6. Product Information

How does DERM work?

DERM is a standalone software device that employs artificial intelligence (AI)-based algorithms to analyse a dermoscopic image of a skin lesion and return a suspected diagnosis and referral recommendation for the lesion. The device is intended to be integrated with a third party client software system through which images are transmitted to and results are displayed from DERM. Only images captured by approved dermoscopic hardware systems are permitted for submission to DERM for analysis. DERM can return a suspected diagnosis and, if applicable, a referral recommendation[1] for the following conditions:

- Melanoma
- Squamous Cell Carcinoma (SCC)
- Basal Cell Carcinoma (BCC)
- Intraepidermal Carcinoma (IEC)
- Actinic Keratosis (AK)
- Atypical Naevus (AN)
- Benign (this includes Benign Vascular Lesion, Seborrheic Keratosis, Dermatofibroma, Solar Lentigo and Melanocytic Benign Nevus)

DERM is primarily intended to be used by healthcare organisations as an automated clinical management tool to help screen, triage or assess patients presenting with one or more lesions where there is a concern of skin cancer. In such cases, the outputs from DERM may be used to issue management instructions without a second read from a human clinician, such as 'refer', 'discharge' or 'monitor'. However, depending on an organisation's clinical governance requirements / procedures for managing patients in a skin cancer pathway, some organisations may opt to use the device's output to augment other clinical datapoints, support a clinical decision, or require that the outputs from DERM are read by a second (human) reader before issuing a clinical management decision.
DERM is intended to be deployed in healthcare organisations who have the necessary clinical governance procedures in place to establish and oversee a skin cancer pathway. Prior to implementation, all pathways are required to be approved by both Skin Analytics and the healthcare organisation to ensure that DERM is deployed per its intended use.

DERM operates a sequential, 3-step process.

Step 1: Identification of dermoscopic image

DERM checks whether the submitted image corresponds to a dermoscopic image of the skin or not. This ensures that accidentally submitted images that are not a dermoscopic image are not further processed. DERM returns an error message if it identifies the image as a non-dermoscopic image of the skin.

[1] See Page 13 for a list of default labels. The wording of the labels may be modified, under a controlled and risk assessed process, to suit a healthcare providers specific clinical pathway

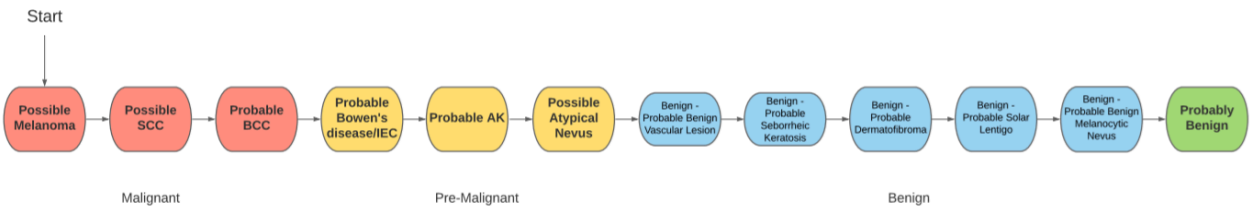
Step 2: Image quality assessment

If the image is identified as a dermoscopic image of the skin (Step 1), DERM assesses the quality of the image, ensuring that it is neither too blurry nor too dark. If the image fails the quality assessment, DERM does not process the image and outputs an error message indicating the reason for the failure (i.e. too dark or too blurry).

Step 3: Image analysis

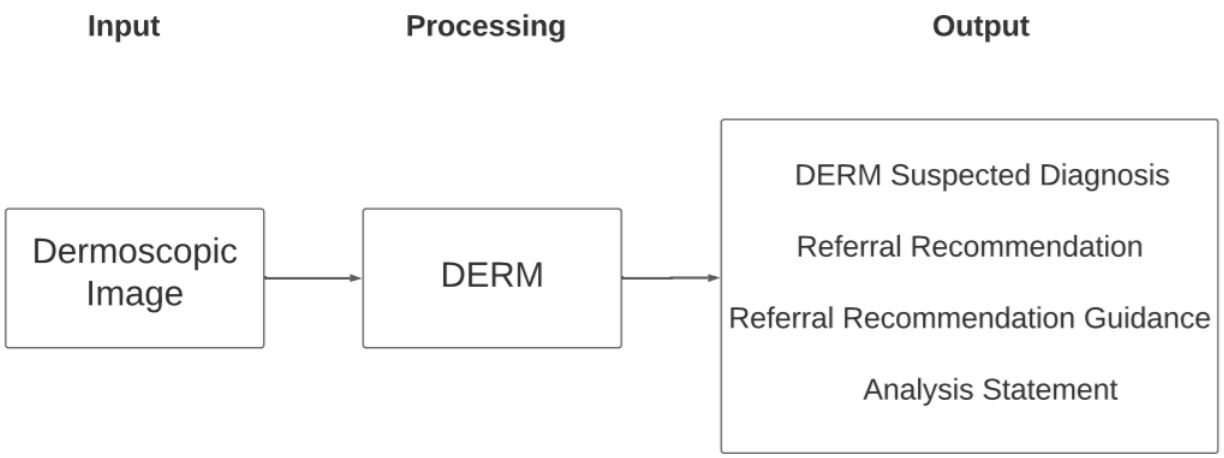
If the image is a dermoscopic image of the skin and presents an acceptable level of quality, DERM proceeds to analyse the image, where the image is labelled with a suspected diagnosis (e.g. possible melanoma; probable BCC). In order to label the image, DERM first identifies the skin lesion within the image (but note that DERM will not detect whether the dermoscopic image contains the whole lesion or not). If more than one skin lesion is identified within the image, DERM outputs a suspected diagnosis for each of the lesions identified. Despite this behaviour, DERM uses the entire image to calculate the suspected diagnosis for each lesion.

When a lesion exhibits features of more than one lesion type, DERM prioritises the riskier skin conditions over benign conditions by implementing a risk hierarchy in its final analysis. This order of processing (shown below with priority running from left to right) is used to ensure that DERM always returns the more severe suspected diagnosis.



Device Inputs and Outputs

The inputs and outputs of the device are shown in the schematic below.



Please note: Referral Recommendation and Referral Recommendation Guidance are optional fields and may not be shown under your configuration.

The device inputs are described in the table below:

Input	Description
Image	Dermoscopic image submitted to DERM through the API.

The device outputs are described in the table below:

Output Field	Description	Default Output(s)
DERM Suspected Diagnosis	DERM's suspected diagnosis for a given skin lesion.	• Possible Melanoma • Possible Squamous Cell Carcinoma (SCC) • Probable Basal Cell Carcinoma (BCC) • Probable Bowen's Disease / Intraepidermal Carcinoma (IEC) • Probable Actinic Keratosis (AK) • Possible Atypical Nevus • Benign - Probable Benign Vascular Lesion • Benign - Probable Seborrheic Keratosis • Benign - Probable Dermatofibroma • Benign - Probable Solar Lentigo • Benign - Probable Benign Melanocytic Nevus

		• Probably Benign
Analysis Statement	Text describing whether the request has been successfully processed, or if an error has occurred. If the image is not a dermoscopic image of the skin, or if it's too blurry or too dark, the message will appear here.	• Skin lesion detected and successfully processed • Image Quality failed - too dark • Image Quality failed - too blurry • Image not a dermoscopic image of the skin • System Error
Referral Recommendation (optional)	An associated text supplementing DERM's Suspected Diagnosis, indicating the recommended next step in the patient management pathway. This content is configurable at the request of the clinical organisation / user commissioning use of DERM.	• Urgent Suspected Cancer Referral • Refer according to local pathway • Manage according to local pathway • Manage as Atypical Nevus • Discharge and give safety netting advice Where the specific referral recommendations are not implemented, a generic safety-net statement can be configured.
Referral Recommendation Guidance (optional)	An associated text supplementing DERM's Referral Recommendation	• Refer on urgent suspected cancer pathway for specialist review. • Consider urgent referral pathway if there is a particular concern that a delay may have a particular impact such as site or size. See NICE guidance. • Follow local pathway for Actinic Keratosis. • Manage as Atypical Nevus • Discharge patient, recommend self-monitoring and further GP review if there are any changes or they remain concerned. If you are concerned despite this result consider referral Where the specific referral recommendations are not implemented, a generic safety-net statement can be configured.

Notes:

- Additional outputs, not displayed to the Clinical User, are provided for technical and administrative purposes and are detailed in the DERM API User Manual.
- Whether probable or possible is used is determined using the Positive Predictive Value (PPV). 'Probable' is used when a PPV for that lesion is >30% and 'Possible' for lesions with a PPV of <30%.

Product Lifetime

Skin Analytics defines the lifetime of DERM as 10 years.
Skin Analytics will continue to support DERM for at least one year after the latest version update.

7. Installation and Configuration

Installation

As DERM is an online hosted service, no installation is necessary. To use DERM, requesting Organisations must register for a DERM account with Skin Analytics.

Configuration

DERM is deployed with a set of default settings which have been selected and optimised by Skin Analytics across the development of the device. Any changes from the default settings will be agreed by Skin Analytics and your organisation following a defined procedure before being implemented.

DERM configuration relates to two aspects of the analysis:

Operating parameters – the settings which determine the trade-off between the false positives and false negatives of DERM. The settings consist of a single sensitivity value for each of the conditions identified by DERM.

Analysis result wording - the words used to explain the results of the analysis. Analysis result wording is agreed for the following DERM Outputs:

a. DERM Suspected Diagnosis. Only changes consistent with the product's intended use will be permitted; for example, replacing the term 'possible melanoma' with 'suspicious lesion'.

b. DERM Referral Recommendation: Only changes consistent with the product's intended use will be permitted, but there may be some local configuration to align with the clinical pathway where DERM is implemented. Examples and options of possible outputs are given in the Device Outputs table above.

c. DERM Referral Recommendation Guidance: Further detail on the referral recommendation, which may be tailored to the local pathway where DERM is implemented, but following a rigorous approval process to ensure it is in line with the intended use. Examples and options of possible outputs are given in the Device Outputs table above.

Operating Parameters

The analysis performance of DERM can be configured to suit the clinical context and pathway. For each lesion type, the trade-off between sensitivity and specificity can be tuned. For example, it may be more desirable to have a high sensitivity for melanoma to minimise the chance of false negatives. Alternatively, a higher specificity may be preferred when the burden of potential over-referrals is a consideration. Skin Analytics onboards all organisations with a set of default settings, which ensure the minimum sensitivity levels observed in the table below are achieved for each lesion type.

Lesion Priority	Lesion Type	Reference Sensitivity
1	Melanoma	95%
2	Squamous Cell Carcinoma (SCC)	95%
3	Basal Cell Carcinoma (BCC)	90%
4	Bowen's disease / Intraepidermal Carcinoma (IEC)	90%
5	Actinic Keratosis (AK)	90%

Analysis result wording

For each lesion assessment, the results returned by DERM include:

- DERM's Suspected Diagnosis
- Referral Recommendation
- Referral Recommendation Guidance
- Analysis Statement

Submitting Images for Analysis

Once the DERM account is set up and configured, and the Client System is integrated, please refer to the instructions for your Client System to submit images to DERM for analysis. DERM is expected to complete an image analysis result in less than 20 seconds.

Updates

Updates to the DERM service will be managed by Skin Analytics. Updates which alter the connection between DERM and the Client System will only become available to the Client System once it is updated to connect to the new DERM connection.

Decommission and Disposal

Once DERM is deployed into service, the device will continue to operate until it is either upgraded to a new version, or retired from service. In the event of decommissioning or upgrade, requirements for data retention and transfer will align with EN 82304-1 standards and applicable regulatory requirements.

Skin Analytics will manage the decommissioning process. When decommissioning the software, Skin Analytics will create a backup of DERM data and store the backup in the company's electronic storage facility. Once the backup is completed, Skin Analytics will shutdown the cloud infrastructure / account hosting the DERM software following the AWS guidelines.

8. Legal

The terms related to your use of DERM will be set out in the contract between Skin Analytics Ltd and your organisation.

To review the Privacy Policy, please refer to the Skin Analytics website for the latest version: https://skin-analytics.com/privacy-policy/

9. Troubleshooting

This section covers the most common problems encountered by users who are submitting images and receiving results from DERM. If, after reading this section, you still have doubts on what to do next, please email support@skinanalytics.co.uk.

I have submitted an image but I can only see "Image not a dermoscopic image of the skin"

When DERM displays "Image not a dermoscopic image of the skin" message it means that the initial step (Step 1 Described in Product Information 'How does DERM Work') has determined that the image does not correspond to a dermoscopic image of the skin and that further processing has not been completed. This usually happens because a context (non-dermoscopic) image has been submitted or because the dermoscope has not been attached to the smartphone. Make sure that the dermoscope is firmly attached to the smartphone and that you are taking a picture with the skin lesion in the centre. Then retake the image and resubmit.

On rare occasions, the original image will be a dermoscopic image of the skin but DERM will output this message. This is due to the accuracy of DERM in detecting dermoscopic images being slightly lower than 100%. Simply retake the image and resubmit if this happens.

I have submitted an image but I only receive “Image Quality failed - image too dark”

When DERM displays “Image Quality failed - image too dark” message it means that the quality assessment step (Step 2 Described in Product Information ‘How does DERM Work’) has determined that the image is too dark to be analysed and further processing has not been completed. This usually happens because the dermoscope does not have the light turned on. Make sure that the dermoscope’s light is switched on then retake the image and resubmit.

On rare occasions, the original image will be taken with the dermoscope’s light switched on, but DERM will output this message. This is due to the accuracy of DERM in detecting dark images being slightly lower than 100%. Simply retake the image and resubmit if this happens.

I have submitted an image but I only receive “Image Quality failed - image too blurry”

When DERM displays “Image Quality failed - image too blurry” message it means that the quality assessment step (Step 2 Described in Product Information ‘How does DERM Work’) has determined that the image is too blurry to be analysed and further processing has not been completed. This usually happens because the dermoscope is not firmly pressed against the skin, or the photo was taken before the camera was able to focus on the lesion. Make sure that the dermoscope is firmly pressed against the skin as detailed in “Submitting images for analysis”. Then retake the image and resubmit.

Some lesions are located on a part of the body where it is difficult to achieve a fully in-focus image, such as when the lesion is on the tip of an ear, or bony prominence. In this case, it may not be possible to take an image that will be accepted by DERM.

On rare occasions, the original image will be fully focused, but DERM will output this message. This is due to the accuracy of DERM in detecting blurry images being slightly lower than 100%. Simply retake the image and resubmit if this happens.

I have submitted an image but I only receive “System error”

When DERM displays the “System error” message it means that an internal error in the communication between the Client System and DERM has occurred. This is usually due to authentication issues or due to a bug in the integration between the two softwares and is independent of the submitted image. Contact your local IT department and the organisation responsible for the maintenance of the Client System if you see this message.

I have submitted an image but I do not receive anything back

A lack of response after submitting an image for analysis usually implies a drop in your Internet connection or that the submit button may not have been clicked. Ensure that the Client System is connected to the Internet and that any local firewalls in your local system are not preventing the image from being submitted. Contact

your local IT department and the organisation responsible for the maintenance of the Client System if you see this message.

My kit (dermoscope, smartphone, connection kit (clip)) is damaged. What should I do?

If you are concerned that the damage is affecting the quality of images that you are capturing, stop submitting cases to DERM. You should speak to the organisation that supplied your kit to arrange for a replacement, or repair as necessary.

I don't have an Internet connection. What should I do?

The Client System will require an Internet connection in order to send the image to DERM and to transmit the results. Contact your local IT department to restore the connection in order to use DERM.

I can't log in/I have forgotten my password. What should I do?

DERM does not have any login details from a clinical user perspective. Users access DERM via a Client System. Please contact your local Client System administrator to retrieve your login details for accessing the Client System.

I don't agree with DERM's output, what should I do?

DERM is intended to be used by, or under, the direction of healthcare professionals or by a clinical organisation's client system in the screening, triage and assessment of skin lesions suspected of skin cancer.

When DERM is used as a decision support?

DERM does not provide a definitive diagnosis. The output provided by DERM should be viewed alongside other clinical information when making decisions on patient management, and care should be taken when giving results to the patient in order to minimise anxiety.

When DERM is used as an automated clinical management tool?

DERM's sensitivity settings are configured to find the right balance between minimising both false positives and false negatives, but in some occasions DERM will produce a false positive (i.e classify a lesion as malignant when it is not) or a false negative (i.e. classify a lesion as benign when it is malignant). It is the responsibility of the Pathway Responsible Owner to make the decision on patient management based on DERM's output.

If you are concerned about the performance of DERM against expected performance, please contact Skin Analytics' help desk or your point of contact so that we can look into it. In the UK, you can also report any adverse events to the MHRA using the yellow card scheme: https://yellowcard.mhra.gov.uk/. If the adverse events occur in the EU, you can report the event to the national competent authority of the relevant member state in which the event occurred.

What happens when a failure to maintain security is detected?

DERM is continuously monitored for security incidents. In the event that a failure to maintain security is detected, Skin Analytics will communicate the impact of and actions needed to address the security incident with all affected users and organisations. Failure to detect a security breach may result in a loss of service, or - at worst - corrupted DERM outputs. Skin Analytics operates a ISO 27001-certified information security management system and has implemented robust cybersecurity controls in the device to limit the occurrence and impact of a security incident.

10. Clinical Evaluation of DERM

Skin Analytics performs clinical evaluation activities to ensure that there is sufficient clinical evidence to confirm the devices' clinical benefit and its compliance with the relevant essential requirements for safety and performance when utilised in accordance with its Instructions for Use.

Clinical Benefits

- DERM will detect skin cancer, pre-malignant and benign lesions with an accuracy similar to or greater than dermatologists.
- DERM will detect skin cancer with a sensitivity similar to or higher than dermatologists.
- DERM will drive a reduction in the number of lesions needed to biopsy to identify skin cancer.
- DERM will reduce urgent referrals and biopsy requests for non-malignant lesions compared to teledermatologists.

Performance Characteristics

The performance of DERM has been evaluated through numerous clinical studies. The device has been established in the UK market for several years. The DERM risk benefit profile, in the intended use population for the detection of skin cancer, is shown to be acceptable based on state-of-the-art determination and clinical evidence which include clinical validation studies and post market surveillance data. DERM's performance has been investigated using a range of different image capture hardware combinations.

Summary of Clinical Data from Conducted Clinical Investigations

DERM-003 Clinical Investigation: Effectiveness of an image analysing algorithm (DERM) to diagnose non-melanoma skin cancer (NMSC) and benign skin lesions compared to gold standard clinical and histological diagnosis

The DERM-003 study was a prospective, multi-center, single-arm, masked clinical validation study that aimed to demonstrate the effectiveness of an AI as a Medical Device (AIaMD) ("DERM") to identify Squamous Cell Carcinoma (SCC), Basal Cell Carcinoma (BCC), pre-malignant and benign lesions from dermoscopic images of suspicious skin lesions (Clinicaltrials.gov NCT04116983)(1). The co-primary endpoints were the Area Under the Receiver Operating Characteristic Curve (AUROC) of the DERM result for SCC and BCC of biopsied lesions, using histopathological-confirmed diagnosis as ground truth

diagnosis. Secondary endpoints included diagnostic measures for malignant and non-malignant lesions of both the DERM output and clinical diagnosis.

The AUROC for SCC and BCC produced by DERM on images of biopsied lesions captured on the iPhone 6S were 88.9% and 89.5%, respectively, 88.5% and 89.6% for images captured on the iPhone 11, and 84.9% and 87.2% for images captured on the Samsung 10. The AUROCs for BCC and SCC, when calculated on all lesions, were >90% except for SCC in images captured on the Samsung 10 camera, where the AUROC was 87%. The DERM AUROC for benign lesions was 85% on non-biopsied lesions and 81% for all lesions with images captured by the iPhone 11. The AUROCs produced by DERM using all lesions were higher than those calculated from the dermatologists' assessment of lesions for all lesion types, except AK (all image capture hardware) and Atypical nevi when imaged by the Samsung 10. Using pre-determined diagnostic thresholds on images of all lesions taken on the iPhone 6S the AIaMD achieved a sensitivity and specificity of 95.4% (95% CI 83.3-99.2%) and 44.7% (95% CI 40.4-49.1%) for SCC; and 94.9% (95% CI 90.6-97.4%) and 41.6% (95% CI 36.2-47.2%) for BCC. All 16 lesions diagnosed as melanoma in the study were correctly classified by DERM.

The results from the DERM-003 study showed that DERM accurately identifies non-melanoma skin cancer and defined benign conditions, and that taking the images was a quick and well tolerated process.

DERM-005 Clinical Investigation: Impact of an Artificial Intelligence Platform (DERM) on the Healthcare Resource Utilisation (HRU) Needed to Diagnose Skin Cancer When Used as Part of a United Kingdom-based Teledermatology Service

DERM-005 was a prospective, single-centre, single-arm, masked, non-inferiority, study that aimed to demonstrate that the performance of DERM has the potential to reduce urgent referrals and biopsy requests for non-malignant lesions compared to teledermatologists (Clinicaltrials.gov NCT04123678) (2). The primary endpoint was the rate of unnecessary referrals of non-cancerous lesions reviewed by teledermatology or DERM for the same cancer detection rate between Standard of Care (SoC) and DERM.

Using both sensitivity settings, DERM achieved a significantly higher rate of identifying pre-malignant and benign lesions that did not need a biopsy or urgent referral (specificity) compared to SoC (p-value = 0.001) with comparable sensitivity for skin cancer. Of the 8 histology-diagnosed melanomas, seven were correctly labelled as melanoma by both SoC and DERM; of the 13 histology-confirmed SCCs, 11 were labelled SCC and 2 were labelled BCC by DERM; and of the 46 histology-confirmed BCCs, 31 were labelled as BCC, 10 as melanoma or SCC, and 5 as premalignant or benign by DERM.

The results from the DERM-005 study demonstrate DERM has a high specificity for skin cancer, and that taking the images was a quick and well tolerated process.

DERM-006 Clinical Investigation: A clinical validation study to demonstrate the effectiveness of an Artificial Intelligence algorithm (DERM) to identify skin cancer in patients undergoing a skin biopsy

DERM-006 was a prospective, international, multi-centre, single-arm, cross-sectional, masked, clinical validation study that aimed to demonstrate the performance of DERM when used to identify malignant skin lesions from dermoscopic images of skin lesions (Clinicaltrials.gov NCT5126173). The co-primary

endpoints were the specificity and sensitivity of detecting malignant lesions, while secondary endpoints included the sensitivity and specificity of DERM to identify melanoma, SCC and BCC lesions.

DERM achieved a sensitivity of 97.5% and specificity 31.1% with images captured by the iPhone 11 + DL200HR hardware combination, while it achieved a sensitivity of 93.4% and specificity 31.6% with the iPhone 11 + DL1 combination. In addition, DERM showed a high level of accuracy in detecting individual lesion conditions, in particular with images taken by the iPhone 11 + DL200HR lens combination. Specifically, DERM demonstrated a sensitivity of 94.3% and a specificity of 62.8% in detecting melanoma, a sensitivity of 92.5% and a specificity of 44% in detecting SCC, and a sensitivity of 98.7% and a specificity of 31.1% in detecting BCC.

The results from the DERM-006 study demonstrate DERM has a high sensitivity and specificity for skin cancer, and that taking the images was a quick and well tolerated process.

Summary of Other Clinical Data

DERM-007 IPD Meta-Analysis: The Diagnostic Accuracy of an Artificial Intelligence algorithm (DERM). A Prospective, Individual Patient Data (IPD) meta-analysis based on a synthesis of data from 3 prospective clinical studies across 21 sites in 3 countries

DERM-007 was a prospective, individual patient data meta-analysis based on a synthesis of data from 3 prospective clinical studies across 21 sites in 3 countries, which was designed to demonstrate the diagnostic accuracy of DERM across all lesion types. The co-primary endpoints were the sensitivity and specificity of DERM to detect pre-malignant lesions (SCC in situ (IEC / Bowen's Disease), AK and Atypical Nevus), while secondary endpoints included the sensitivity and specificity of DERM to identify each individual lesion types. Exploratory endpoints included performance of DERM to detect malignant lesions.

The three clinical studies, DERM-003, DERM-005 and DERM-006, recruited patients with at least one suspicious skin lesion. Lesions were imaged with an iPhone 11/X smartphone with a DermLite DL1 Basic dermoscopic lens.

Using a random effects model on a data set of images captured by the iPhone 11/X with the DL1 lens, the sensitivity and specificity of DERM to detect premalignant lesions was estimated to be 81.5% (95% CI: 75.1-87.1%) and 49.0% (95% CI: 21.8-76.4%), respectively. DERM demonstrated a sensitivity of above 90% for IEC and AK lesions, and above 65% for Atypical Nevi and specificity above pre-defined success criteria. In addition, the sensitivity of DERM to detect melanoma was 87.2% (95% CI: 80.6% - 92.8%), and SCC was 95.1% (95% CI: 90.3% - 98.5%).

The results from the DERM-007 study demonstrate DERM has a high sensitivity and specificity for pre-malignant lesions.

Real-World Performance of DERM, Cumulative Data Collected at UK Clinical Sites between April 2022 and September 2023

Real-world data from deployments are reviewed on a periodic basis to confirm that the performance of DERM remains at or above target pathway sensitivities. All available data in the UK since April 2022 has been evaluated as part of the service evaluation for DERM. The most recent performance report, issued in December 2023, presents performance data on DERM for over 21,218 lesions, assessed between April 2022 and Sept 2023, derived from deployments at 11 clinical sites across the UK. DERM achieves a pathway sensitivity of >95% for melanoma and SCC, and over 90% for BCC, IEC and AK in a population which includes patients aged 18-102 and with all skin types represented.

Lesion Type	Pathway sensitivity (95% CI interval)
Malignant	97.1% (96.5-97.6%)
Melanoma	95.2% (93.3-96.6%)
SCC	98.2% (97.2-98.9%)
BCC	97.4% (96.6-98.0%)

April 2022 - September 2023 DERM Performance on Malignant Lesions, UK Clinical Deployments

Frontiers in Medicine Publication: Real-world post-deployment performance of a novel machine learning-based digital health technology for skin lesion assessment and suggestions for post-market surveillance

Data from real-world performance from deployment of DERM within skin cancer pathways at two UK hospitals (University Hospitals Birmingham, West Suffolk Foundation Trust) between July 2021 and October 2022 were published. Two versions of DERM were deployed during this period, separated by time: DERM-version A (DERM-vA) (July 2021 to April 2022), and version B (DERM-vB) (April 2022 to October 2022). Each version used fixed sensitivity thresholds. DERM was accessible to adults of all ages (18–100 years) and was used to assess potential malignant skin lesions in all Fitzpatrick skin types I–VI. Both versions of DERM achieved a pathway sensitivity for skin cancer of >96%, and for melanoma >95% (3).

Hardware

Performance data that supports the use of DERM with different approved hardware combinations primarily comes from clinical studies, which have shown that the hardware can have an impact on DERM performance. DERM should therefore only be used with images captured on the hardware that has undergone testing to validate acceptable performance.

Device usage

Post-Market surveillance data demonstrates the feasibility of using the device in the clinic. Of the 29,543 cases due for DERM assessment across deployments at 11 NHS sites between April 2022 and November 2023, only 1.1% of cases (316/29,453) were excluded from DERM analysis due to being unable to capture a dermoscopic image, and 3.9% of cases (1158/29,453) were excluded due to technical (network / connectivity) issues. As the patient will automatically be referred for dermatologist review in these cases, the risk of missed cancer from a failure of DERM to return a prediction is minimal.

References

1. Marsden H, Morgan C, Austin S, DeGiovanni C, Venzi M, Kemos P, Greenhalgh J, Mullarkey D and Palamaras I (2023). Effectiveness of an image analyzing AI-based Digital Health Technology to identify Non-Melanoma Skin Cancer and other skin lesions: results of the DERM-003 study. Front. Med. 10:1288521. doi: 10.3389/fmed.2023.1288521

2. Marsden H, Kemos C, Venzi M, Noy M, Maheswaran S, Francis N, Hyde C, Mullarkey D, Kalsi D, Thomas L (2024) Accuracy of an Artificial Intelligence as a medical device as part of a UK-based skin cancer teledermatology service. Front. Med. 11:1302363. doi.org/10.3389/fmed.2024.1302363

3. Thomas L, Hyde C, Mullarkey D, Greenhalgh J, Kalsi D and Ko J (2023) Real-world post-deployment performance of a novel machine learning-based digital health technology for skin lesion assessment and suggestions for post-market surveillance. Front. Med. 10:1264846. doi: 10.3389/fmed.2023.1264846

Summary of DERM v4 *In Silico* Technical Test Performance[2]

- DERM can detect Actinic Keratosis (AK) with a high degree of sensitivity across multiple configuration settings, and above a target pathway sensitivity of 90% for AK.
- DERM can detect Atypical Nevus (AN) with an acceptable degree of sensitivity across multiple configuration settings.
- DERM can detect Basal Cell Carcinoma (BCC) with a high degree of sensitivity across multiple configuration settings, and above a target pathway sensitivity of 90% for BCC.
- DERM can detect Bowen's disease / Intraepidermal Carcinoma (IEC) with a high degree of sensitivity across multiple configuration settings, and above a target pathway sensitivity of 90% for IEC.
- DERM can detect Melanoma Skin Cancer with a high degree of sensitivity across multiple settings, and above a target pathway sensitivity of 95% for melanoma.
- DERM can detect Squamous Cell Carcinoma (SCC) Skin Cancer with a high degree of sensitivity across multiple settings, and above a target pathway sensitivity of 95% for SCC.

The latest information on the research supporting the use of DERM can be found at https://skin-analytics.com/performance/, or for further information please contact Skin Analytics for a summary of evidence.

[2] Data held on file