Supplementary Online Content

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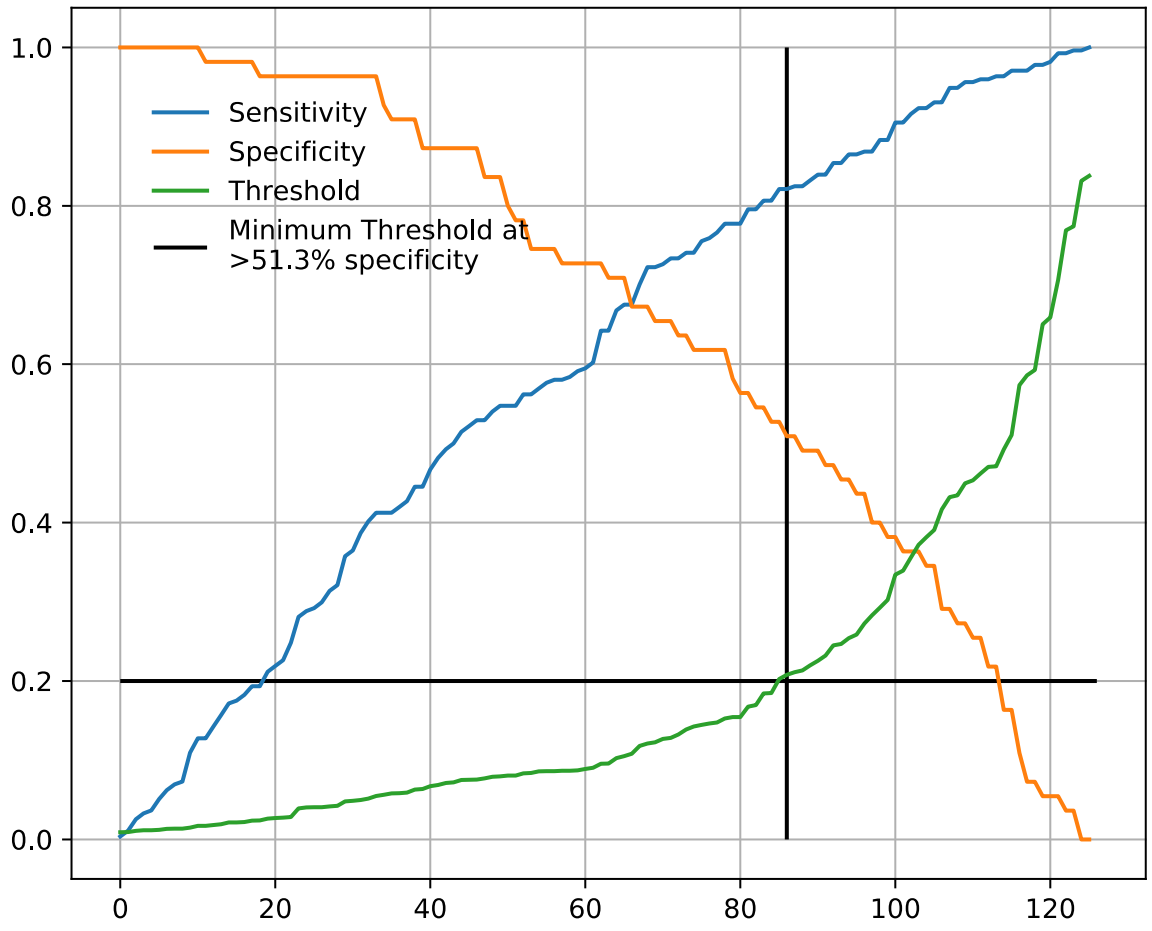
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Sensitivities (Blue) and Specificities (Orange) at Different Threshold Cutoffs (Green) of the Combined Classifier Evaluated on the Validation Set

A threshold cut at 0.2 (black) is found for a minimum of 51.3% specificity.



eAppendix. Neural Network Training

We compared multiple architecture and training hyperparameter combinations in a grid-search fashion, and used only the single best performing network for dermoscopic and close-up images, based on validation accuracy, for further analyses. We trained four different CNN architectures (InceptionResNetV2, InceptionV3, Xception, ResNet50) and used model definitions and ImageNet pretrained weights as available in the Tensorflow (version 1.3.0)/ Keras (version 2.0.8) frameworks. We removed the top layer of all networks and sent the flattened output vector through two fully connected (”dense”) layers with 10 softmax activated units as an output (8 for the close-up image dataset). We implemented dropout to the first fully connected layer to avoid overfitting. Weights were updated in all layers during training. Training was performed using the Adam optimizer (weight decay 1e-06) and crossentropy loss with logarithmic weighting to adjust for data imbalance. Learning rates were initialized at 1e-05 or 1e-06 and divided by 10 (down to a minimum of 1e-08) if validation loss did not improve for 2 epochs. Training was conducted for a maximum of 50 epochs but stopped early if there was no improvement in validation accuracy for 7 epochs. We used common augmentation techniques on image inputs: Random horizontal and vertical flipping, width- and height shift with empty pixels filled by the value of their nearest neighbor, and random shearing and zooming.

eTable 1. Complete List of Diagnoses and Their Frequencies Within the Test-Set

Abbreviation	Group	Included Diagnoses	n
akiec	Malignant	Actinic Keratosis; Intraepithelial Carcinoma / Bowen disease; In Situ Squamous Cell Carcinoma	335
bcc	Malignant	Basal Cell Carcinoma	720
fibroxanthoma, atypical	Malignant	Atypical Fibroxanthoma	1
kaposi	Malignant	Kaposi Sarcoma	1
mcc	Malignant	Merkel Cell Carcinoma	1
mel	Malignant	Melanoma	35
melmet	Malignant	Melanoma Metastases	9
morbus paget	Malignant	Morbus Paget	1
neurofibrosarcoma	Malignant	Neurofibrosarcoma	1
scc	Malignant	Keratoacanthoma; Invasive Squamous Cell Carcinoma	368
sebaceous carcinoma	Malignant	Sebaceous carcinoma	1
syringoid carcinoma	Malignant	Syringoid carcinoma	2
trichilemmal carcinoma	Malignant	Trichilemmal carcinoma	1
angiofib-fp	Benign	Fibrous papule; Angiofibroma	8
angioma	Benign	Angioma; Angiokeratoma	51
bkl	Benign	Inverted Follicular Keratosis; Lichen Planus-like Keratosis; Seborrheic Keratosis	241
cca	Benign	Clear Cell Acanthoma	10
chromoblastomycosis	Benign	Chromoblastomycosis	1
cnh	Benign	Chondrodermatitis nodularis helicis	5
collagenoma	Benign	Collagenoma	1
cyst	Benign	Cyst	18
dermatitis	Benign	Dermatitis	7
df	Benign	Dermatofibroma	15
eccrine poroma	Benign	Eccrine poroma	1
epidermolytic acanthoma	Benign	Epidermolytic acanthoma	1
fibrokeratoma	Benign	Acral fibrokeratoma	1
folliculitis	Benign	Folliculitis; Perifolliculitis	12

granuloma	Benign	Granuloma	6
hidradenoma-s-c	Benign	Cylindroma; Hidradenoma; Spiradenoma	4
lsc	Benign	Lichen sclerosus	4
mastocytosis	Benign	Mastocytosis	2
molluscum contagiosum	Benign	Molluscum contagiosum	4
morphea	Benign	Morphea	1
neurofibroma-nl	Benign	Neurofibroma; Neurilemmoma	8
nevus	Benign	Nevus	73
pilomatrixoma	Benign	Pilomatrixoma	3
porokeratosis	Benign	Porokeratosis	6
prurigo nodularis	Benign	Prurigo nodularis	3
pseudolymphoma	Benign	Pseudolymphoma	1
psoriasis	Benign	Psoriasis	4
pyogenic granuloma	Benign	Pyogenic granuloma	34
scar	Benign	Scar	24
sebaceous-benign	Benign	Sebaceous epithelioma; Sebaceous hyperplasia; Sebaceous adenoma	6
skintag-s-f	Benign	Skin tag; Fibroma	8
syringocystadenoma	Benign	Syringocystadenoma	1
trichilemmoma	Benign	Trichilemmoma	1
tricho-benign	Benign	Trichoepithelioma; Trichoblastoma	7
tungiasis	Benign	Tungiasis	1
vascular-malformation	Benign	Vascular malformation; Venous lake	2
viral wart	Benign	Viral wart	18
xanthogranuloma	Benign	Xanthogranuloma	3

eTable 2. Education of Users According to Their Experience Group

	Beginner (n=31)	**Intermediate (n=28)**	**Expert (n=36)**
Dermatology Resident	32.3% (n=10)	3.6% (n=1)	2.8% (n=1)
Dermatology Specialist	41.9% (n=13)	78.6% (n=22)	75.0% (n=27)
General Practitioner	22.6% (n=7)	14.3% (n=4)	14.3% (n=5)
Medical Student	3.2% (n=1)	-	-
Nurse	-	-	5.6% (n=2)
Oncologist	-	3.6% (n=1)	2.8% (n=1)

eTable 3. Percent of Correct Prediction of the Malignancy Status for Specific Diagnoses of a CNN Using Either Close-up or Dermatoscopic Images

Diagnosis	Close-Up CNN	Dermatoscopy CNN
AKIEC	0.587 (95% CI: 0.540-0.633)	0.779 (95% CI: 0.738-0.817)
Angioma	0.878 (95% CI: 0.811-0.927)	0.799 (95% CI: 0.722-0.862)
BCC	0.572 (95% CI: 0.540-0.603)	0.906 (95% CI: 0.886-0.924)
BKL	0.709 (95% CI: 0.679-0.738)	0.574 (95% CI: 0.542-0.605)
DF	0.780 (95% CI: 0.624-0.894)	0.415 (95% CI: 0.263-0.579)
Mel	0.229 (95% CI: 0.188-0.275)	0.505 (95% CI: 0.454-0.556)
Nevus	0.794 (95% CI: 0.731-0.848)	0.698 (95% CI: 0.630-0.761)
SCC	0.703 (95% CI: 0.659-0.744)	0.769 (95% CI: 0.728-0.807)