Appendix S1. Test set images

All included images in the test set as displayed to the dermatologists. The exact same images (i.e., same image resolutions) were used for evaluating the CNN models. This image file is submitted separately.

Case number	True label	Breslow thickness (mm)
1	Invasive melanoma >1.0 mm	1.2
2	In situ melanoma	
3	In situ melanoma	
4	In situ melanoma	
5	Invasive melanoma >1.0 mm	1.1
6	Invasive melanoma ≤1.0 mm	0.6
7	Invasive melanoma ≤1.0 mm	0.5
8	In situ melanoma	
9	Invasive melanoma ≤1.0 mm	0.4
10	In situ melanoma	
11	In situ melanoma	
12	In situ melanoma	
13	Invasive melanoma ≤1.0 mm	0.8
14	In situ melanoma	
15	Invasive melanoma ≤1.0 mm	0.3
16	Invasive melanoma ≤1.0 mm	0.4
17	In situ melanoma	
18	In situ melanoma	
19	Invasive melanoma ≤1.0 mm	0.4
20	In situ melanoma	
21	In situ melanoma	
22	In situ melanoma	
23	Invasive melanoma ≤1.0 mm	0.4
24	In situ melanoma	
25	In situ melanoma	
26	In situ melanoma	
27	Invasive melanoma ≤1.0 mm	0.5
28	Invasive melanoma ≤1.0 mm	0.2
29	In situ melanoma	
30	In situ melanoma	
31	In situ melanoma	
32	In situ melanoma	
33	In situ melanoma	
34	In situ melanoma	
35	In situ melanoma	
36	Invasive melanoma >1.0 mm	2
37	Invasive melanoma ≤1.0 mm	0.4
38	Invasive melanoma ≤1.0 mm	0.5

39	In situ melanoma	
40	In situ melanoma	
41	Invasive melanoma ≤1.0 mm	0.7
42	Invasive melanoma ≤1.0 mm	0.5
43	In situ melanoma	
44	Invasive melanoma >1.0 mm	1.2
45	In situ melanoma	
46	Invasive melanoma >1.0 mm	2.4
47	In situ melanoma	
48	Invasive melanoma ≤1.0 mm	0.7
49	Invasive melanoma ≤1.0 mm	1
50	Invasive melanoma ≤1.0 mm	0.6
51	In situ melanoma	
52	In situ melanoma	
53	In situ melanoma	
54	Invasive melanoma ≤1.0 mm	0.8
55	In situ melanoma	
56	In situ melanoma	
57	In situ melanoma	
58	In situ melanoma	
59	Invasive melanoma ≤1.0 mm	0.5
60	Invasive melanoma ≤1.0 mm	0.3
61	In situ melanoma	
62	In situ melanoma	
63	In situ melanoma	
64	Invasive melanoma ≤1.0 mm	1
65	Invasive melanoma ≤1.0 mm	0.7
66	Invasive melanoma ≤1.0 mm	0.7
67	Invasive melanoma ≤1.0 mm	0.6
68	In situ melanoma	
69	Invasive melanoma ≤1.0 mm	0.4
70	Invasive melanoma ≤1.0 mm	0.6
71	Invasive melanoma ≤1.0 mm	0.6
72	Invasive melanoma ≤1.0 mm	0.5
73	In situ melanoma	
74	In situ melanoma	
75	Invasive melanoma ≤1.0 mm	0.4
76	Invasive melanoma ≤1.0 mm	0.4
77	In situ melanoma	
78	In situ melanoma	
79	In situ melanoma	
80	In situ melanoma	
81	Invasive melanoma ≤1.0 mm	0.4
82	Invasive melanoma ≤1.0 mm	0.7
83	In situ melanoma	
84	Invasive melanoma ≤1.0 mm	0.5

85	In situ melanoma	
86	Invasive melanoma ≤1.0 mm	0.7
87	Invasive melanoma >1.0 mm	1.6
88	In situ melanoma	
89	Invasive melanoma ≤1.0 mm	0.6
90	In situ melanoma	
91	In situ melanoma	
92	In situ melanoma	
93	Invasive melanoma ≤1.0 mm	0.8
94	Invasive melanoma >1.0 mm	1.1
95	Invasive melanoma ≤1.0 mm	0.3
96	In situ melanoma	
97	In situ melanoma	
98	Invasive melanoma >1.0 mm	1.7
99	In situ melanoma	
100	In situ melanoma	
101	In situ melanoma	
102	Invasive melanoma >1.0 mm	1.7
103	Invasive melanoma ≤1.0 mm	0.8
104	Invasive melanoma >1.0 mm	1.2
105	In situ melanoma	
106	In situ melanoma	
107	Invasive melanoma ≤1.0 mm	0.9
108	Invasive melanoma >1.0 mm	3.5
109	Invasive melanoma >1.0 mm	1.6
110	In situ melanoma	
111	In situ melanoma	
112	In situ melanoma	
113	Invasive melanoma ≤1.0 mm	0.6
114	In situ melanoma	
115	Invasive melanoma ≤1.0 mm	0.3
116	In situ melanoma	
117	In situ melanoma	
118	Invasive melanoma ≤1.0 mm	0.3
119	In situ melanoma	
120	Invasive melanoma ≤1.0 mm	0.8
121	In situ melanoma	
122	In situ melanoma	
123	In situ melanoma	
124	In situ melanoma	
125	In situ melanoma	
126	In situ melanoma	
127	In situ melanoma	
128	Invasive melanoma ≤1.0 mm	0.5
129	Invasive melanoma ≤1.0 mm	0.4
130	In situ melanoma	

131	In situ melanoma	
132	In situ melanoma	
133	Invasive melanoma ≤1.0 mm	0.2
134	In situ melanoma	
135	In situ melanoma	
136	In situ melanoma	
137	Invasive melanoma ≤1.0 mm	0.5
138	In situ melanoma	
139	In situ melanoma	
140	Invasive melanoma >1.0 mm	2.5
141	Invasive melanoma >1.0 mm	3
142	Invasive melanoma ≤1.0 mm	0.4
143	Invasive melanoma ≤1.0 mm	0.5
144	Invasive melanoma ≤1.0 mm	0.7
145	In situ melanoma	
146	In situ melanoma	
147	Invasive melanoma ≤1.0 mm	0.9
148	In situ melanoma	
149	Invasive melanoma ≤1.0 mm	0.4
150	In situ melanoma	
151	In situ melanoma	
152	Invasive melanoma ≤1.0 mm	0.4
153	In situ melanoma	
154	Invasive melanoma ≤1.0 mm	0.4
155	Invasive melanoma >1.0 mm	1.1
156	Invasive melanoma >1.0 mm	1.6
157	In situ melanoma	
158	In situ melanoma	
159	Invasive melanoma >1.0 mm	1.5
160	In situ melanoma	
161	In situ melanoma	
162	Invasive melanoma ≤1.0 mm	0.8
163	In situ melanoma	
164	Invasive melanoma ≤1.0 mm	0.5
165	Invasive melanoma >1.0 mm	>=4
166	Invasive melanoma >1.0 mm	>=4
167	In situ melanoma	
168	Invasive melanoma >1.0 mm	1.9
169	Invasive melanoma ≤1.0 mm	0.3
170	In situ melanoma	
171	Invasive melanoma >1.0 mm	1.4
172	Invasive melanoma ≤1.0 mm	0.5
173	Invasive melanoma ≤1.0 mm	1
174	Invasive melanoma ≤1.0 mm	0.4
175	In situ melanoma	
176	Invasive melanoma ≤1.0 mm	0.8

177	Invasive melanoma ≤1.0 mm	0.8
178	Invasive melanoma >1.0 mm	3.4
179	In situ melanoma	
180	In situ melanoma	
181	Invasive melanoma ≤1.0 mm	0.7
182	Invasive melanoma ≤1.0 mm	0.6
183	In situ melanoma	
184	Invasive melanoma ≤1.0 mm	0.6
185	In situ melanoma	
186	In situ melanoma	
187	Invasive melanoma ≤1.0 mm	0.8
188	Invasive melanoma ≤1.0 mm	0.5
189	Invasive melanoma ≤1.0 mm	1
190	In situ melanoma	
191	In situ melanoma	
192	In situ melanoma	
193	In situ melanoma	
194	In situ melanoma	
195	In situ melanoma	
196	Invasive melanoma >1.0 mm	1.6
197	In situ melanoma	
198	In situ melanoma	
199	Invasive melanoma ≤1.0 mm	0.3
200	Invasive melanoma ≤1.0 mm	0.6
201	In situ melanoma	
202	In situ melanoma	
203	Invasive melanoma >1.0 mm	1.4
204	In situ melanoma	
205	Invasive melanoma ≤1.0 mm	0.4
206	Invasive melanoma ≤1.0 mm	0.3
207	Invasive melanoma >1.0 mm	1.4
208	Invasive melanoma >1.0 mm	1.2
209	In situ melanoma	
210	In situ melanoma	
211	Invasive melanoma >1.0 mm	1.1
212	Invasive melanoma ≤1.0 mm	1
213	In situ melanoma	
214	Invasive melanoma ≤1.0 mm	0.6
215	Invasive melanoma ≤1.0 mm	0.7
216	Invasive melanoma >1.0 mm	1.3
217	In situ melanoma	
218	In situ melanoma	
219	In situ melanoma	
220	Invasive melanoma ≤1.0 mm	0.5
221	In situ melanoma	
222	In situ melanoma	

223	In situ melanoma	
224	In situ melanoma	
225	Invasive melanoma ≤1.0 mm	1
226	In situ melanoma	
227	In situ melanoma	
228	In situ melanoma	
229	In situ melanoma	
230	Invasive melanoma >1.0 mm	>=4
231	Invasive melanoma ≤1.0 mm	0.5
232	In situ melanoma	
233	In situ melanoma	
234	In situ melanoma	
235	In situ melanoma	
236	In situ melanoma	
237	Invasive melanoma ≤1.0 mm	0.9
238	In situ melanoma	
239	In situ melanoma	
240	In situ melanoma	
241	In situ melanoma	
242	In situ melanoma	
243	In situ melanoma	
244	In situ melanoma	
245	Invasive melanoma ≤1.0 mm	0.7
246	Invasive melanoma ≤1.0 mm	0.5
247	Invasive melanoma ≤1.0 mm	0.4
248	In situ melanoma	
249	In situ melanoma	
250	Invasive melanoma ≤1.0 mm	0.9
251	Invasive melanoma ≤1.0 mm	0.7
252	In situ melanoma	
253	In situ melanoma	
254	In situ melanoma	
255	Invasive melanoma >1.0 mm	3
256	Invasive melanoma ≤1.0 mm	0.7
257	Invasive melanoma ≤1.0 mm	0.3
258	Invasive melanoma >1.0 mm	3.8
259	In situ melanoma	
260	Invasive melanoma >1.0 mm	1.7
261	In situ melanoma	
262	In situ melanoma	
263	In situ melanoma	
264	In situ melanoma	
265	Invasive melanoma >1.0 mm	3.4
266	In situ melanoma	
267	Invasive melanoma ≤1.0 mm	0.6
268	Invasive melanoma >1.0 mm	3.4

269	In situ melanoma	
270	Invasive melanoma ≤1.0 mm	0.4
271	Invasive melanoma >1.0 mm	1.3
272	In situ melanoma	
273	Invasive melanoma >1.0 mm	1.8
274	Invasive melanoma ≤1.0 mm	0.8
275	In situ melanoma	
276	Invasive melanoma ≤1.0 mm	0.9
277	In situ melanoma	
278	In situ melanoma	
279	Invasive melanoma ≤1.0 mm	1
280	Invasive melanoma ≤1.0 mm	0.6
281	Invasive melanoma >1.0 mm	1.2
282	Invasive melanoma ≤1.0 mm	0.4
283	In situ melanoma	
284	Invasive melanoma >1.0 mm	>=4
285	In situ melanoma	
286	In situ melanoma	
287	Invasive melanoma >1.0 mm	>=4
288	Invasive melanoma ≤1.0 mm	0.7
289	In situ melanoma	
290	Invasive melanoma ≤1.0 mm	0.4
291	Invasive melanoma ≤1.0 mm	0.5
292	In situ melanoma	
293	In situ melanoma	
294	In situ melanoma	
295	Invasive melanoma ≤1.0 mm	0.6
296	Invasive melanoma ≤1.0 mm	0.4
297	In situ melanoma	
298	In situ melanoma	
299	Invasive melanoma ≤1.0 mm	0.7
300	Invasive melanoma >1.0 mm	1.4

Appendix S2. R source code for model definition and training.

```
target_size <- c(600, 600)
cat_list <- c("In_situ". "Invasiv")



###### DATA AUMENTATION FOR TRAINING SET ######

train_data_gen <- image_data_generator(
  rescale = 1/255
)

validation_data_gen <- image_data_generator(
  rescale = 1/255
)


###### DEFINE BATCH SIZES FOR TRAINING AND VALIDATION SET ######

train_image_array_gen <- flow_images_from_directory(train_image_files_path,
                                                    train_data_gen,
                                                    target_size = target_size,
                                                    classes = cat_list,
                                                    batch_size = 10,
                                                    class_mode = "binary")


validation_image_array_gen <-
flow_images_from_directory(validation_image_files_path,
                                                         validation_data_gen,
                                                         target_size = target_size,
                                                         classes = cat_list,
                                                         batch_size = 10,
                                                         class_mode = "binary")
```

```
########### MODEL DEFINITION #############

MERGED_INPUT <- layer_input(shape = c(1200, 600, 3), name = "MERGED_INPUT")

CLIN_INPUT <- layer_cropping_2d(MERGED_INPUT, cropping =
                                  list(c(0, 600), c(0, 0)), name="CLIN_INPUT")

DERM_INPUT <- layer_cropping_2d(MERGED_INPUT, cropping =
                                  list(c(600, 0), c(0, 0)), name="DERM_INPUT")


OUTPUT_FROM_CLIN_CONV <- CLIN_INPUT %>%

  layer_conv_2d(filters = 16, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 32, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 64, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2), name="LASTMAXPOOL_CLIN") %>%

  layer_flatten(name="FLATTENED_FROM_CLIN_CONV")


OUTPUT_FROM_DERM_CONV <-  DERM_INPUT %>%

  layer_conv_2d(filters = 16, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 32, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 64, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%
```

```
  layer_max_pooling_2d(pool_size = c(2, 2)) %>%

  layer_conv_2d(filters = 128, kernel_size = c(3, 3), activation = "relu") %>%

  layer_max_pooling_2d(pool_size = c(2, 2), name="LASTMAXPOOL_DERM") %>%

  layer_flatten(name="FLATTENED_FROM_DERM_CONV")



MAIN_OUTPUT <-

  layer_concatenate(c(OUTPUT_FROM_CLIN_CONV, OUTPUT_FROM_DERM_CONV)) %>%

  layer_dropout(rate = 0.5) %>%

  layer_dense(units = 256, activation = "relu") %>%

  layer_dense(units = 1, activation = "sigmoid", name="MAIN_OUTPUT")



model <- keras_model(
  inputs  = c(MERGED_INPUT),
  outputs = c(MAIN_OUTPUT)
)

############# COMPILE THE MODEL #############

model %>% compile(
  loss = "binary_crossentropy",
  optimizer = optimizer_rmsprop(lr = 5e-5),
  metrics = c("acc", tf$keras$metrics$AUC(name="auc"))
)


############# TRAIN THE MODEL #############

history <- model %>% fit_generator(
  train_image_array_gen,
  steps_per_epoch = 108,
  epochs = 30,
  validation_data = validation_image_array_gen,
  validation_steps = 20,
  class_weight = list("0"=1, "1"=(581/497)),
  callbacks = list(
    callback_csv_logger(filename=paste0(logspath, modelnamebest, ".txt"),
                        append=TRUE, separator="\t"),
    callback_model_checkpoint(filepath=paste0(logspath, modelnamebest,
                              ".h5"),
                              save_best_only=TRUE,
                              monitor="val_auc",
                              mode="max")
  )
)
```

Appendix S3. Model summary.

```
Layer (type)                 Output Shape              Param #   Connected to
==================================================================================================
MERGED_INPUT (InputLayer)    [(None, 1200, 600, 3 0
__________________________________________________________________________________________________
CLIN_INPUT (Cropping2D)      (None, 600, 600, 3)  0           MERGED_INPUT[0][0]
__________________________________________________________________________________________________
conv2d_26 (Conv2D)           (None, 598, 598, 16) 448         CLIN_INPUT[0][0]
__________________________________________________________________________________________________
max_pooling2d_22 (MaxPooling2 (None, 299, 299, 16) 0          conv2d_26[0][0]
__________________________________________________________________________________________________
DERM_INPUT (Cropping2D)      (None, 600, 600, 3)  0           MERGED_INPUT[0][0]
__________________________________________________________________________________________________
conv2d_27 (Conv2D)           (None, 297, 297, 32) 4640
max_pooling2d_22[0][0]
__________________________________________________________________________________________________
conv2d_33 (Conv2D)           (None, 598, 598, 16) 448         DERM_INPUT[0][0]
__________________________________________________________________________________________________
max_pooling2d_23 (MaxPooling2 (None, 148, 148, 32) 0          conv2d_27[0][0]
__________________________________________________________________________________________________
max_pooling2d_28 (MaxPooling2 (None, 299, 299, 16) 0          conv2d_33[0][0]
__________________________________________________________________________________________________
conv2d_28 (Conv2D)           (None, 146, 146, 64) 18496
max_pooling2d_23[0][0]
__________________________________________________________________________________________________
conv2d_34 (Conv2D)           (None, 297, 297, 32) 4640
max_pooling2d_28[0][0]
__________________________________________________________________________________________________
max_pooling2d_24 (MaxPooling2 (None, 73, 73, 64)   0          conv2d_28[0][0]
__________________________________________________________________________________________________
max_pooling2d_29 (MaxPooling2 (None, 148, 148, 32) 0          conv2d_34[0][0]
__________________________________________________________________________________________________
conv2d_29 (Conv2D)           (None, 71, 71, 128)  73856
max_pooling2d_24[0][0]
__________________________________________________________________________________________________
conv2d_35 (Conv2D)           (None, 146, 146, 64) 18496
max_pooling2d_29[0][0]
__________________________________________________________________________________________________
max_pooling2d_25 (MaxPooling2 (None, 35, 35, 128)  0          conv2d_29[0][0]
__________________________________________________________________________________________________
max_pooling2d_30 (MaxPooling2 (None, 73, 73, 64)   0          conv2d_35[0][0]
__________________________________________________________________________________________________
conv2d_30 (Conv2D)           (None, 33, 33, 128)  147584
max_pooling2d_25[0][0]
__________________________________________________________________________________________________
conv2d_36 (Conv2D)           (None, 71, 71, 128)  73856
max_pooling2d_30[0][0]
__________________________________________________________________________________________________
max_pooling2d_26 (MaxPooling2 (None, 16, 16, 128)  0          conv2d_30[0][0]
__________________________________________________________________________________________________
max_pooling2d_31 (MaxPooling2 (None, 35, 35, 128)  0          conv2d_36[0][0]
__________________________________________________________________________________________________
conv2d_31 (Conv2D)           (None, 14, 14, 128)  147584
max_pooling2d_26[0][0]
__________________________________________________________________________________________________
conv2d_37 (Conv2D)           (None, 33, 33, 128)  147584
max_pooling2d_31[0][0]
__________________________________________________________________________________________________
max_pooling2d_27 (MaxPooling2 (None, 7, 7, 128)    0          conv2d_31[0][0]
__________________________________________________________________________________________________
max_pooling2d_32 (MaxPooling2 (None, 16, 16, 128)  0          conv2d_37[0][0]
__________________________________________________________________________________________________
conv2d_32 (Conv2D)           (None, 5, 5, 128)    147584
max_pooling2d_27[0][0]
__________________________________________________________________________________________________
```

```
conv2d_38 (Conv2D)              (None, 14, 14, 128)  147584
max_pooling2d_32[0][0]
_____________________________________________________________________________
LASTMAXPOOL_CLIN (MaxPooling2 (None, 2, 2, 128)    0          conv2d_32[0][0]
_____________________________________________________________________________
LASTMAXPOOL_DERM (MaxPooling2 (None, 7, 7, 128)    0          conv2d_38[0][0]
_____________________________________________________________________________
FLATTENED_FROM_CLIN_CONV (Fla (None, 512)          0
LASTMAXPOOL_CLIN[0][0]
_____________________________________________________________________________
FLATTENED_FROM_DERM_CONV (Fla (None, 6272)         0
LASTMAXPOOL_DERM[0][0]
_____________________________________________________________________________
concatenate_2 (Concatenate)   (None, 6784)         0
FLATTENED_FROM_CLIN_CONV[0][0]

FLATTENED_FROM_DERM_CONV[0][0]
_____________________________________________________________________________
dropout_2 (Dropout)             (None, 6784)         0          concatenate_2[0][0]
_____________________________________________________________________________
dense_2 (Dense)                 (None, 256)          1736960    dropout_2[0][0]
_____________________________________________________________________________
MAIN_OUTPUT (Dense)             (None, 1)            257        dense_2[0][0]
=============================================================================
Total params: 2,670,017
Trainable params: 2,670,017
Non-trainable params: 0
_____________________________________________________________________________
```