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Recognition of Ischaemia and Infection in Diabetic Foot Ulcers: Dataset and Techniques

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Abstract

Recognition and analysis of Diabetic Foot Ulcers (DFU) using computerized methods is an emerging research area with the evolution of image-based machine learning algorithms. Existing research using visual computerized methods mainly focuses on recognition, detection, and segmentation of the visual appearance of the DFU as well as tissue classification. According to DFU medical classification systems, the presence of infection (bacteria in the wound) and ischaemia (inadequate blood supply) has important clinical implications for DFU assessment, which are used to predict the risk of amputation. In this work, we propose a new dataset and computer vision techniques to identify the presence of infection and ischaemia in DFU. This is the first time a DFU dataset with ground truth labels of ischaemia and infection cases is introduced for research purposes. For the handcrafted machine learning approach, we propose a new feature descriptor, namely the Superpixel Color Descriptor. Then we use the Ensemble Convolutional Neural Network (CNN) model for more effective recognition of ischaemia and infection. We propose to use a natural data-augmentation method, which

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identifies the region of interest on foot images and focuses on finding the salient features existing in this area. Finally, we evaluate the performance of our proposed techniques on binary classification, i.e. ischaemia versus non-ischaemia and infection versus non-infection. Overall, our method performed better in the classification of ischaemia than infection. We found that our proposed Ensemble CNN deep learning algorithms performed better for both classification tasks as compared to handcrafted machine learning algorithms, with 90% accuracy in ischaemia classification and 73% in infection classification.

Keywords:

Diabetic foot ulcers, deep learning, ischaemia, infection, machine learning.

1 Introduction

Diabetic Foot Ulcers (DFUs) are a major complication of diabetes which can lead to amputation of the foot or limb. Treatment of Diabetic foot ulcers is a global major health care problem resulting in high care costs and mortality rate. Recognition of infection and ischaemia is very important to determine factors that predict the healing progress of DFU and the risk of amputation. Ischaemia, the lack of blood circulation, develops due to chronic complications of diabetes. This can result in gangrene of the diabetic foot ulcer, which may require amputation of the part of the foot or leg if not recognised and treated early. Detailed knowledge of the vascular anatomy of the leg, and particularly ischaemia enables medical experts make better decisions in estimating the possibility of DFU healing, given the existing blood supply [1]. In previous studies, it is estimated that patients with critical ischaemia have a three-year limb loss rate of about 40% [2]. Patients with an active DFU and particularly those with ischaemia or gangrene should be checked for the presence of infection. Approximately, 56% of DFU become infected and 20% of DFU infections lead to amputation of a foot or limb [3, 4, 5]. In one recent study, 785 million patients with diabetes in the US between 2007 and 2013 suggested that DFU and associated infections constitute a powerful risk factor for emergency department visits and hospital admission [6].

There are a number of DFU classification systems such as Wagner, University of Texas, and SINBAD Classification systems, which include information on the site of DFU, area, depth, presence of neuropathy, presence of

25 ischaemia, and infection [7, 8, 9]. SINBAD stands for S (Site), I (Ischaemia),
26 N (Neuropathy), B (Bacterial infection), A (Area), D (Depth). This paper
27 focuses on ischaemia and infection, which are defined as follow:

- 28 1. Ischaemia: Inadequate blood supply that could affect DFU healing.
29 Ischaemia is diagnosed by palpating foot pulses and measuring blood
30 pressure in the foot and toes. The visual appearance of ischaemia might
31 be indicated by the presence of poor reperfusion to the foot, or black
32 gangrenous toes (tissues death to part of the foot). From a computer
33 vision perspective, these might be important hints of the presence of
34 ischaemia in the DFU.
- 35 2. Bacterial Infection: Infection is defined as bacterial soft tissue or bone
36 infection in the DFU, which is based on the presence of at least two
37 classic findings of inflammation or purulence. It is very hard to de-
38 termine the presence of diabetic foot infections from DFU images, but
39 increased redness in and around ulcer and coloured purulent could pro-
40 vide indications. In the medical system, blood testing is performed as
41 the gold standard diagnostic test. Also, in the present dataset, the
42 images were captured after the debridement of necrotic and devital-
43 ized tissues which removes an important indication of the presence of
44 infection in DFU.

45 In related work, Netten et al. [10] find that clinicians achieved low validity
46 and reliability for remote assessment of DFU in foot images. Hence, it is clear
47 that analysing these conditions from images is a difficult task for clinicians.
48 In various image recognition applications, such as medical imaging and natu-
49 ral language processing tasks, machine learning algorithms performed better
50 than skilled humans including clinicians [11, 12, 13].

51 The previous state-of-the-art image-based computer-aided diagnosis of
52 DFU is composed of multiple stages, including image pre-processing, image
53 segmentation, feature extraction, and classification. Veredas et al. [14] pro-
54 posed the use of color and texture features from the segmented area and
55 multi-layer neural network to perform the tissue classification to distinguish
56 between healing-tissue and skin for healing prediction. Wannous et al. [15]
57 performed tissue classification from color and texture region descriptors on
58 a 3-D model for the wound. Wang et al. [16] used a cascaded two-stage
59 classifier to determine the DFU boundaries for area determination of DFU.
60 Major progress in the field of image-based machine learning, especially deep

61 learning algorithms, allows the extensive use of medical imaging data with
62 end-to-end models to provide better diagnosis, treatment, and prediction of
63 diseases [17, 18]. Deep learning models for DFU, predominantly led by works
64 from our laboratory have achieved high accuracy in the recognition of DFUs
65 with machine learning algorithms [19, 20, 21, 22].

66 The major issues and challenges involved with the assessment of DFU
67 using machine learning methods from foot images are as follows: 1) a major
68 time-burden involved in data collection and expert labelling of the DFU
69 images; 2) high inter-class similarity and intra-class variations are dependent
70 upon the different classification of DFU; 3) non-standardization of the DFU
71 dataset, such as distance of the camera from the foot, orientation of the image
72 and lighting conditions; 4) lack of meta-data, such as patient ethnicity, age,
73 sex and foot size.

74 Accurate diagnosis of ischaemia and infection requires establishing a good
75 clinical history, physical examination, blood tests, bacteriological study and
76 Doppler study of leg blood vessels. These tests and resources are not always
77 available to clinicians across the world and hence the need for a solution to
78 inform diagnosis, such as the one we proposed in this paper. Experts working
79 in the field of diabetic foot ulceration have good experience of predicting the
80 presence of underlying ischaemia or infection simply by looking at the ulcer.
81 We aim to replicate that in machine learning. To increase the reliability of
82 the annotation, two experts predict the presence of ischaemia and infection
83 from DFU images. Due to high risks of infection and ischaemia in DFU
84 leading to patient’s hospital admission, and amputation [23], recognition of
85 infection and ischaemia in DFU with cost-effective machine learning methods
86 is a very important step towards the development of complete computerized
87 DFU assessment system for remote monitoring in the future.

88 **2. DFU Dataset and Expert Labelling**

89 For binary classification of ischaemia and infection in DFU, we introduce
90 a dataset of 1459 images of patient’s foot with DFU over the previous five
91 years at the Lancashire Teaching Hospitals, obtaining ethical approval from
92 all relevant bodies and patients written informed consent. Approval was ob-
93 tained from the NHS Research Ethics Committee to use these images for this
94 research. These DFU images were captured with different cameras (Kodak
95 DX4530, Nikon D3300, and Nikon COOLPIX P100). The current dataset



Figure 1: Examples of foot images with DFU used for binary expert annotations for infection and ischaemia.

96 we received with the ethical approval from NHS did not contain any records
 97 or meta-data about these conditions or any medical classification.

98 Since there is no clinical meta-data regarding this DFU dataset, the ex-
 99 periment is performed on the images with handcrafted traditional machine
 100 learning and deep learning. This is the first time, recognition of ischaemia
 101 and infection in DFU is performed based on images, hence, there is no pub-
 102 licly available dataset. Here, we introduce the first DFU dataset with ground
 103 truth labels of ischaemia and infection cases. Expert labelling of each DFU

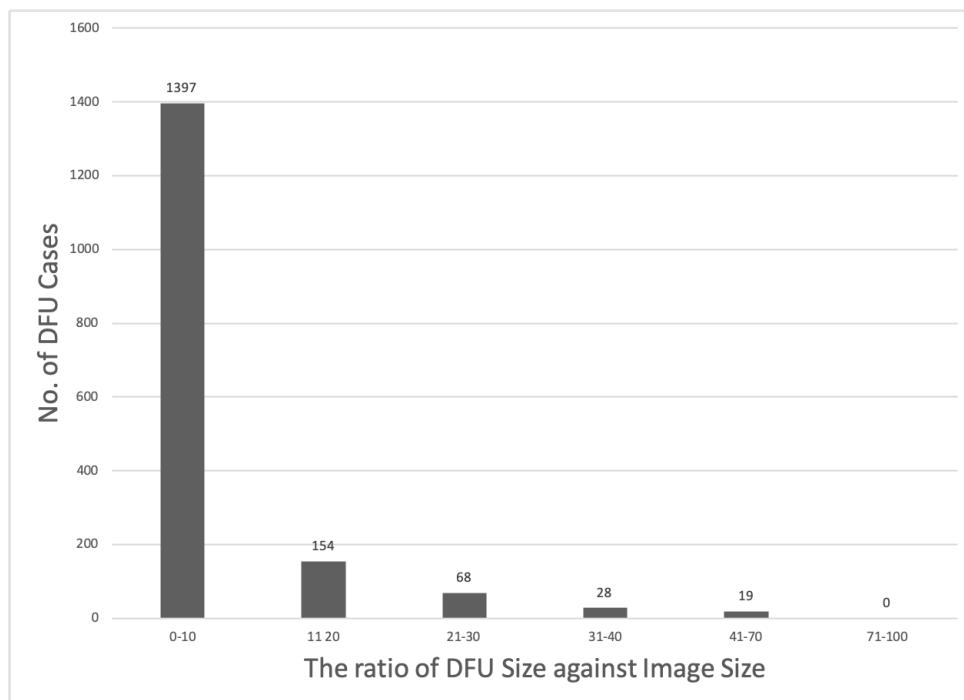


Figure 2: The number of DFU cases according to the area of DFU in full foot image of the DFU dataset.

104 according to the different conditions present in DFU according to the pop-
105 ular medical classification system on this DFU dataset is particularly im-
106 portant for this task. The ground truth was produced by two healthcare
107 professionals (consultant physicians with specialisation in the diabetic foot)
108 on the visual inspection of DFU images. Where there was disagreement for
109 the ground truth, the final decision was made by the more senior physician.
110 These ground truths are used for the binary classification of infection and
111 ischaemia of DFU. A few examples of foot images with DFU used for bi-
112 nary expert annotation are shown in Fig. 1. The complete number of cases
113 of expert annotation of each condition is detailed in Table 1. The dataset,
114 alongside its ground truth labels, will be made available upon acceptance of
115 this article.

116 **3. Methodology**

117 This section describes our proposed techniques for the recognition of is-
118 chaemia and infection of the DFU diagnosis system. The preparation of
119 a balanced dataset, handcrafted features, and machine learning methods
120 (handcrafted machine learning and deep learning approaches) used for bi-
121 nary classification of ischaemia and infection are detailed in this section.

122 *3.1. Natural Data-Augmentation Technique based on Deep Learning Algo-* 123 *rithm*

124 This section describes our proposed data augmentation method, called
125 Natural Data-augmentation, which is based on deep DFU localization algo-
126 rithm (Faster R-CNN).

127 In the DFU dataset, the images (size)varies between 1600×1200 and
128 3648×2736) depending on the cameras used to capture the data. In deep
129 learning, data augmentation is envisioned as an important tool to improve
130 the performance of algorithms. As shown in Fig. 2, approximately 92% of
131 DFU cases have area between 0% to 20% on foot images. In common data-
132 augmentation, the number of techniques used such as flip, rotation, random
133 scale, random crop, translation, and Gaussian noise to perform augment in
134 the dataset. Since DFU occupies a very small percentage of the total area
135 of foot images, there is a risk of missing the region of interests by using im-
136 portant augmentation technique such as random scale, crop, and translation.
137 Hence, Natural Data-augmentation is more suitable for the DFU evaluation
138 rather than common data-augmentation. This augmentation technique helps

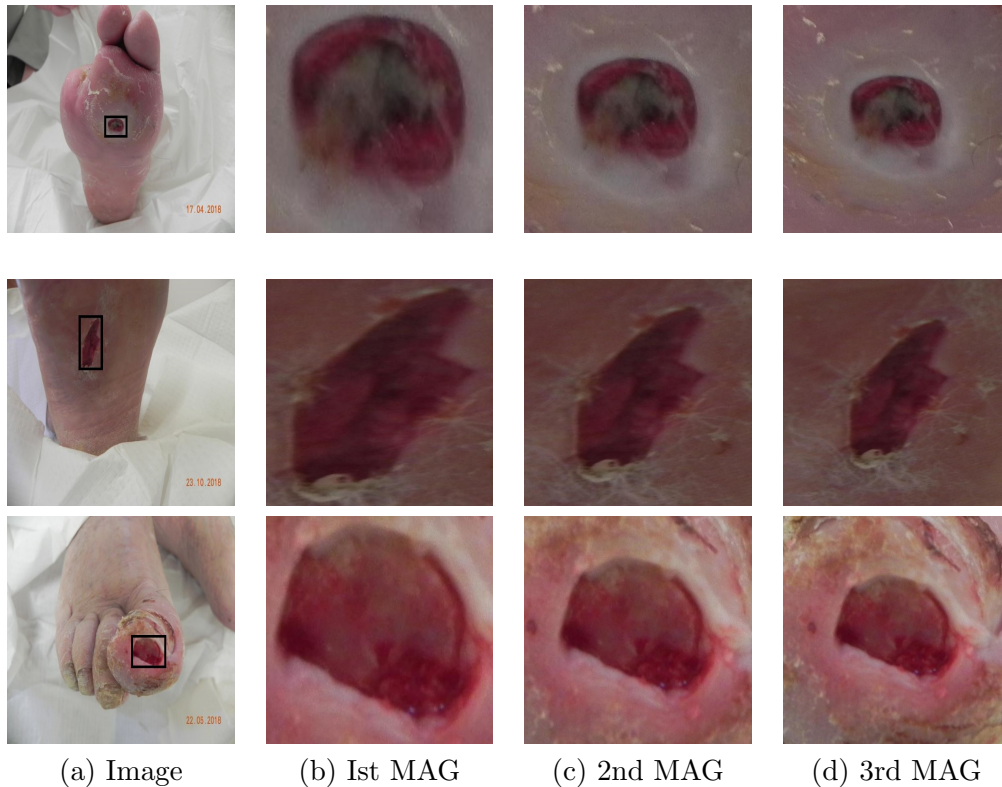


Figure 3: Natural Data-augmentation produced from the original image with different magnifications (three magnifications in this experiment). MAG refers to magnification

139 in assisting the machine algorithms to pinpoint ROI of DFU on foot images
 140 and focus on finding the strong features that exists in this area. We used
 141 the deep learning-based localization method, Faster-RCNN with Inception-
 142 ResNetV2, to get ROI of the DFU on foot images [24, 25]. Depending upon
 143 the size of DFU and image, the natural data-augmentation on the DFU
 144 dataset with different magnification is demonstrated in Fig. 3. Flexible pa-
 145 rameters can be used to choose the number of magnification factors (3 in
 146 this classification), as well as magnification distance, which can be adjusted
 147 from a single DFU image by natural augmentation. After magnification, fur-
 148 ther, data-augmentation is achieved with the help of angles, mirror, gaussian
 149 noise, contrast, sharpen, translation, shearing using our proposed methods
 150 as shown in Fig. 4.

151 As shown in Table 1, the number of DFU patches generated by crop-
 152 ping multiple DFU on foot images and augmented patches are generated

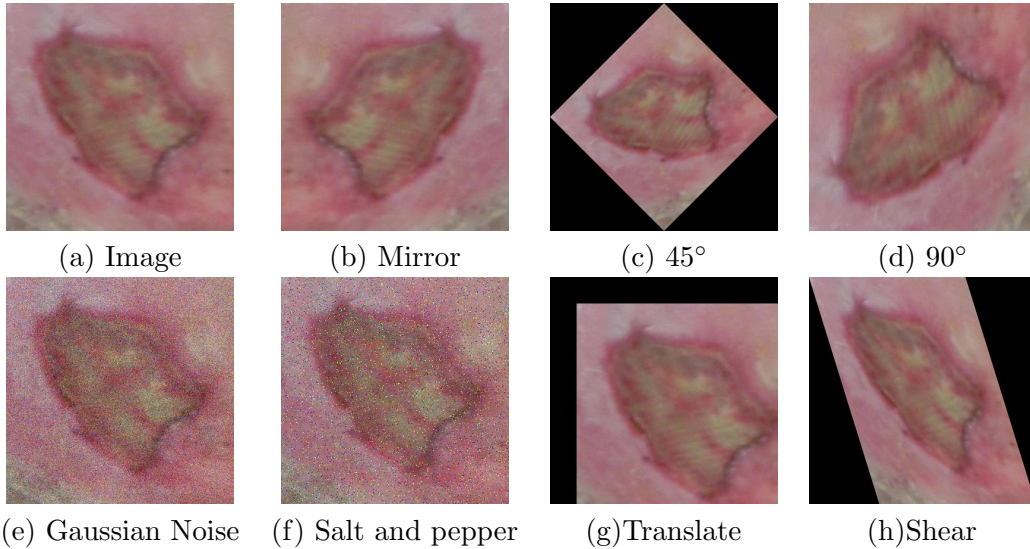


Figure 4: After magnification, different types of data-augmentation is achieved by the proposed Natural Data-augmentation

153 by natural data-augmentation (Fig. 3) and different data augmentations
 154 (Fig. 4). The total number of cases for ischaemia and non-ischaemia in this
 155 DFU dataset is imbalanced (1249 cases vs 210 cases) whereas infection (628
 156 cases) and non-infection (831 cases) are fairly balanced as shown in Table 1.
 157 We performed binary classification of ischaemia and infection with machine
 158 learning algorithms because for multi-class classification, this DFU dataset
 159 is imbalanced especially for cases (Ischaemia and No Infection) as shown in
 160 5.

161 3.2. Handcrafted Superpixel Color Descriptors

162 We investigated the use of human design features with traditional machine
 163 learning on the binary classification of infection and ischaemia. Our first
 164 attempt was experimenting with texture descriptors (Local Binary Patterns
 165 and Histogram of Gradient) and color descriptors as used in related works
 166 [19, 21]. However, we achieved very poor results for these binary classification
 167 problems. Hence, we propose a novel Superpixel Color Descriptors (SPCD)
 168 to extract the colors region of interest from DFU images that could be the
 169 important visual cues for the identification of ischaemia and infection in DFU.
 170 In the first step, we used a SLIC superpixels technique to produce superpixel
 171 over-segmentation of DFU patches based on pixel color and intensity values

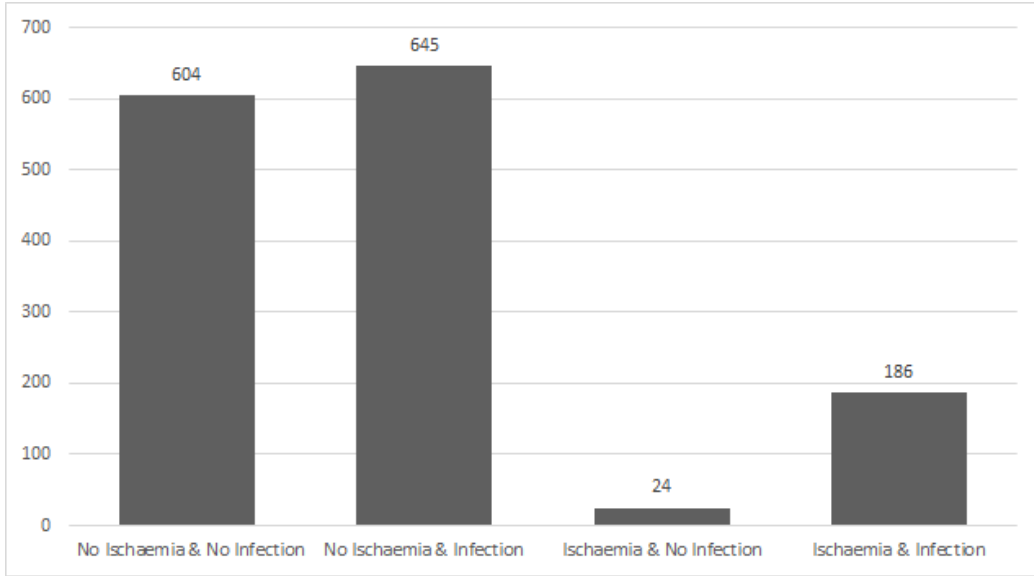


Figure 5: Distribution of ischaemia and infection cases as multi-class classification problem.

Table 1: The number of Infection and ischaemia cases, number of DFU patches and augmented patches using Natural Data-augmentation in DFU Dataset

Category	Definition	Cases	DFU patches	Augmented patches
Ischaemia	Absent	1249	1431	4935
	Present	210	235	4935
Total images		1459	1666	9870
Bacterial infection	None	628	684	2946
	Present	831	982	2946
Total images		1459	1666	5892

172 [26]. SLIC superpixels technique performs a localized k -means optimization
 173 in the 5-D CIELAB color and image space to cluster pixels as described by
 174 equations 1 - 4:

$$S = \sqrt{\frac{N}{k}} \quad (1)$$

$$D_s = d_{lab} + \frac{m}{S} d_{xy} \quad (2)$$

$$d_{lab} = \sqrt{(l_k - l_i)^2 + (a_k - a_i)^2 + (b_k - b_i)^2} \quad (3)$$

$$d_{xy} = \sqrt{(x_k - x_i)^2 + (y_k - y_i)^2} \quad (4)$$

175 where in eq. 1, S is the approximate size of a superpixel, N is the number
 176 of pixels and k is the number of superpixels; in eq. 2, D_s is the sum of the lab
 177 distance (d_{lab}) and the xy plane distance (d_{xy}); in eq. 3, l , a and b represent
 178 the lab colorspace; and in eq. 4, x and y represent the pixel positions.

179 In the second step, the mean RGB color value of each superpixel is com-
 180 puted and applied to each superpixel (S) denoted by:

$$S_i = \text{mean}(P(R, G, B)), i = 1, \dots, k \quad (5)$$

181 where in eq. 5, $P(R, G, B)$ is the pixel values of R,G,B channel in each i th
 182 position of S and k is total number of superpixels in the image.

183 Finally, with a different number of superpixels and threshold values from
 184 each color channel, we extracted regions of two particular colors of inter-
 185 est that are red and black from the DFU patches. For these classification
 186 tasks, we used the number of superpixels ($k=200$) and threshold values (T1:
 187 0.40,0.45,0.50,.055,0.60; T2: 0.15,0.20,0.25,0.30,0.35) to extract the color fea-
 188 tures from DFU patches of 256×256 . The threshold values are used to restrict
 189 the intensities of red and black pixels to be utilized as handcrafted features.
 190 Hence, we utilised a feature vector of 10 with SPCD algorithm along with
 191 texture descriptors (LBP, HOG) and color features (RGB, CIELAB) to train
 192 traditional machine learning approaches. The pseudocode for the SPCD al-
 193 gorithm is explained in Algorithm 1. The example of extracting color features
 194 using our novel SPCD algorithm is shown in Fig. 6.

195 For these classification problems, we experimented with a number of clas-
 196 sifiers with standard hyper-parameters on these color features. BayesNet,

Algorithm 1 Pseudocode for the Superpixel Color Descriptors Extraction

- 1: Over-segmentation of DFU patch with SLIC superpixel is performed;
 - 2: Mean RGB value of each superpixel is calculated and applied;
 - 3: Initialize variable S_Red & S_Black to 0
 - 4: **procedure** REDANDBLACKREGION
 - 5: **for** each Superpixel(S_i) **do**
 - 6: **if** $S_i(R) > T_1 * (S_i(R) + S_i(G) + S_i(B))$ **then return** S_Red=
S_Red + 1
 - 7: **if** $S_i(R) < T_2$ & $S_i(G) < T_2$ & $S_i(B) < T_2$ **then return**
S_Black= S_Black + 1
 - 8: $RedColorFeature = S_Red \div n$
 - 9: $BlackColorFeature = S_Black \div n$
-

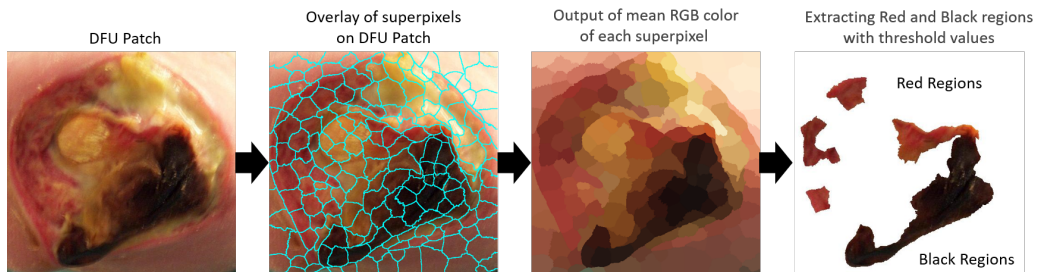


Figure 6: Example of extracting red and black regions from DFU patch with proposed Superpixel Color Descriptor algorithm which was then used to inform identification of ischaemia and infection. The k value of 200 for superpixel algorithm effectively overseg-mented the DFU patches.

197 Random Forest, and Multilayer Perceptron were selected and achieved the
198 highest accuracy among other machine learning classifiers.

199 *3.3. Deep Learning Approaches*

200 For comparison with the traditional features, deep learning algorithms
201 are used to perform binary classification to classify (1) infection and non-
202 infection; and (2) ischaemia and non-ischaemia classes in DFU patches. For
203 this work, we fine-tune (transfer learning from pre-trained models) the CNN
204 models, i.e. Inception-V3, ResNet50, and InceptionResNetV2 [27, 28, 29].
205 To train the CNN networks, we froze the weights of the first few layers of
206 the pre-trained networks for common features, such as edges and curves.
207 Subsequently, layers of networks are unfrozen to focus on learning dataset-
208 specific features.

209 Additionally, we utilized the Ensemble CNN method, which is a very
210 effective CNN approach to obtain very good accuracy on difficult datasets.
211 The Ensemble CNN model combines the bottleneck features from multiple
212 CNN models (Inception-V3, ResNet50, and InceptionResNetV2), and use
213 SVM classifier to produce predictions, as shown in Fig. 7.

214 **4. Results and Discussion**

215 Both infection and ischaemia datasets were split into 70% training, 10%
216 validation and 20% testing sets and we adopted the 5-fold cross-validation
217 technique. We utilized the natural data-augmentation technique for training
218 and validation sets in both traditional machine learning and deep learning
219 approaches. Hence, in this ischaemia dataset, we used approximately 11,564
220 patches, 1,652 patches, and 3,304 patches in training, validation, and test-
221 ing sets respectively whereas, in the infection dataset, we used 7,136 patches
222 (training), 1,019 patches (validation), and 2,038 patches (testing) from the
223 2611 original foot images. As mentioned previously, we used both hand-
224 crafted traditional machine learning (henceforth TML) models and CNN
225 models to perform the classification task and utilized 256×256 RGB images
226 as input for TML and InceptionV3, AlexNet, and ResNet50. For Inception-
227 ResNetV2, we resized the dataset to 299×299 . For this experiment, Tensor-
228 Flow is used for deep learning and Matlab is used for traditional machine
229 learning approaches.

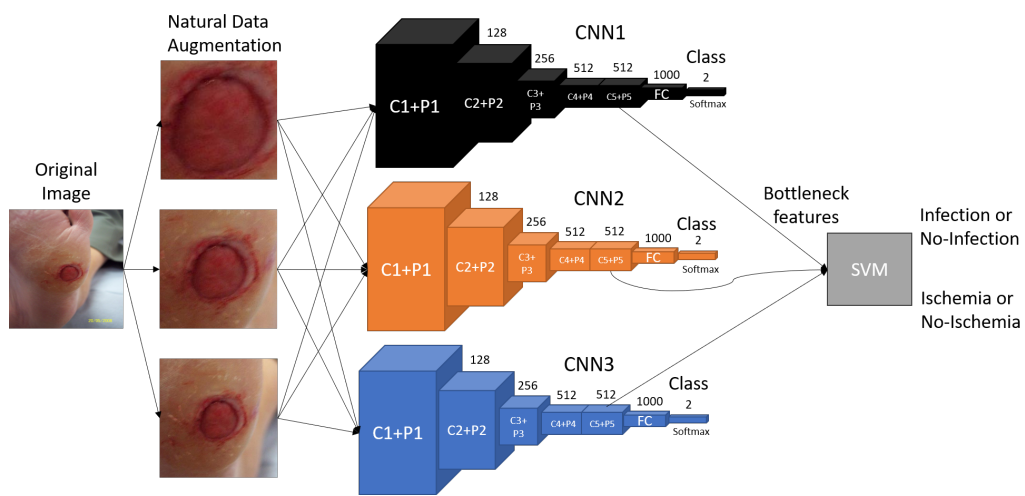


Figure 7: Extracting bottleneck features from CNNs and fed into SVM classifier to perform binary classification of ischaemia and infection, where C1-C5 are convolutional layers, P1-P5 are pooling layers and FC is fully connected layer. **Note: The CNNs in this figure are just representations of general CNNs architecture and do not represent the original CNN architectures of Inception-V3, ResNet50, and InceptionRes-NetV2.**

Table 2: The performance measures of binary classification of ischaemia by our proposed handcrafted traditional machine learning and CNN approaches.

	<i>Accuracy</i>	<i>Sensitivity</i>	<i>Precision</i>	<i>Specificity</i>	<i>F-Measure</i>	<i>MCC Score</i>	<i>AUC Score</i>
BayesNet	0.785±0.022	0.774±0.034	0.809±0.034	0.800±0.027	0.790±0.020	0.572±0.044	0.783
Random Forest	0.780±0.041	0.739±0.049	0.872±0.029	0.842±0.034	0.799±0.033	0.571±0.078	0.780
Multilayer Perceptron	0.804±0.022	0.817±0.040	0.787±0.046	0.795±0.031	0.800±0.023	0.610±0.045	0.804
InceptionV3 (CNN)	0.841±0.017	0.784±0.045	0.886±0.018	0.898±0.022	0.831±0.021	0.688±0.031	0.840
ResNet50 (CNN)	0.862±0.018	0.797±0.043	0.917±0.015	0.927±0.017	0.852±0.022	0.732±0.032	0.865
InceptionResNetV2 (CNN)	0.853±0.021	0.789±0.054	0.906±0.017	0.917±0.019	0.842±0.027	0.714±0.039	0.851
Ensemble (CNN)	0.903±0.012	0.886±0.035	0.918±0.019	0.921±0.021	0.902±0.014	0.807±0.022	0.904

Table 3: The performance measures of binary classification of Infection by our proposed handcrafted traditional machine learning and CNN approaches.

	<i>Accuracy</i>	<i>Sensitivity</i>	<i>Precision</i>	<i>Specificity</i>	<i>F-Measure</i>	<i>MCC Score</i>	<i>AUC Score</i>
BayesNet	0.639±0.036	0.619±0.018	0.653±0.039	0.660±0.015	0.622±0.079	0.290±0.070	0.643
Random Forest	0.605±0.025	0.608±0.025	0.607±0.037	0.601±0.069	0.606±0.012	0.211±0.051	0.601
Multilayer Perceptron	0.621±0.026	0.680±0.023	0.622±0.057	0.570±0.023	0.627±0.074	0.281±0.055	0.619
InceptionV3 (CNN)	0.662±0.014	0.693±0.038	0.653±0.015	0.631±0.034	0.672±0.019	0.325±0.029	0.662
ResNet50 (CNN)	0.673±0.013	0.692±0.051	0.668±0.023	0.654±0.051	0.679±0.019	0.348±0.028	0.673
InceptionResNetV2 (CNN)	0.676±0.015	0.688±0.052	0.672±0.015	0.664±0.039	0.680±0.024	0.352±0.031	0.678
Ensemble (CNN)	0.727±0.025	0.709±0.044	0.735±0.036	0.744±0.050	0.722±0.028	0.454±0.052	0.731

230 In Table 2 and 3, we report *Accuracy*, *Sensitivity*, *Precision*, *Specificity*, *F-*
231 *Measure*, *Matthew Correlation Coefficient (MCC)* and *Area under the ROC*
232 *curve (AUC)* as our evaluation metrics.

233 When comparing the performance of the computerized methods and our
234 proposed techniques, CNNs performed better in the binary classification
235 of ischaemia than infection despite more imbalanced data in the ischaemia
236 dataset, due to more cases of non-ischaemia in the dataset. The average per-
237 formance of all the models in terms of accuracy in the ischaemia dataset was
238 83.3% which is notably better than the average accuracy of 65.8% in infection
239 dataset. Similarly, *MCC Score* and *AUC Score* are considered to be viable
240 performance measures to compare the classification results. We obtained an
241 average *MCC Score* and *AUC Score* for ischaemia classification of 67.1% and

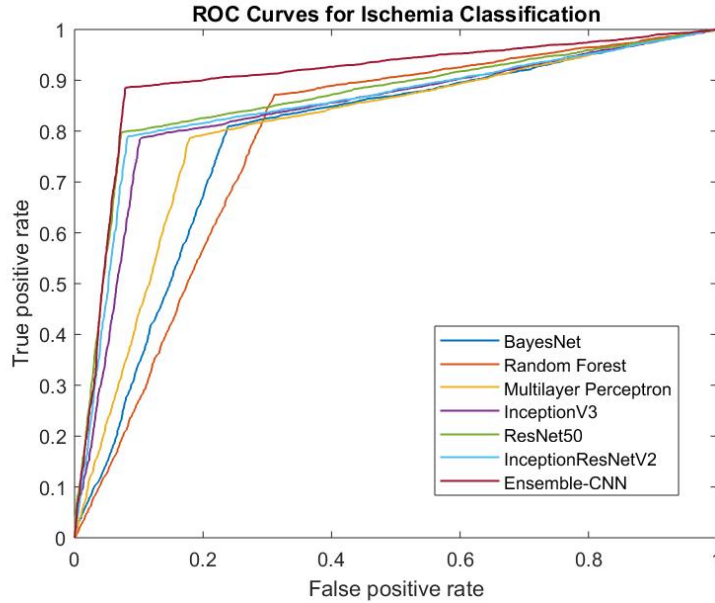


Figure 8: ROC curve for all TML and CNN methods for ischaemia classification.

242 83.2% respectively, as compared to the infection classification of 32.3% and
 243 65.8% respectively. The ROC curves for all the algorithms, including TML
 244 and CNNs for binary classification of ischaemia and infection, are shown in
 245 Fig. 8 and 9. When comparing the performances in ischaemia classification
 246 of TML and CNNs, CNNs (86.5%) performed better than the TML models
 247 (79%). Similarly, in infection classification, the accuracy of CNNs (68.4%)
 248 performed better than TML (62.1%) with a margin of 6.3%. Notably, En-
 249 semble CNN method achieved the highest score in all performance measures
 250 in both ischaemia and infection classification.

251 *Sensitivity* and *Specificity* are considered important performance mea-
 252 sures in medical imaging. The ensemble method yielded high *Sensitivity* for
 253 the ischaemia dataset with a margin of 6.9% from the second best perform-
 254 ing algorithm multilayer perceptron. Interestingly, a multilayer perceptron
 255 performed worst in the *Specificity* with a score of 79.5%. For *Specificity* in
 256 the ischaemia dataset, the ensemble method again obtained the highest score
 257 of 92.9% which is marginally better than ResNet50 (92.7%).

258 In infection classification, both TML and CNN methods received mod-
 259 erate scores in the performance measures. Again, CNN methods performed

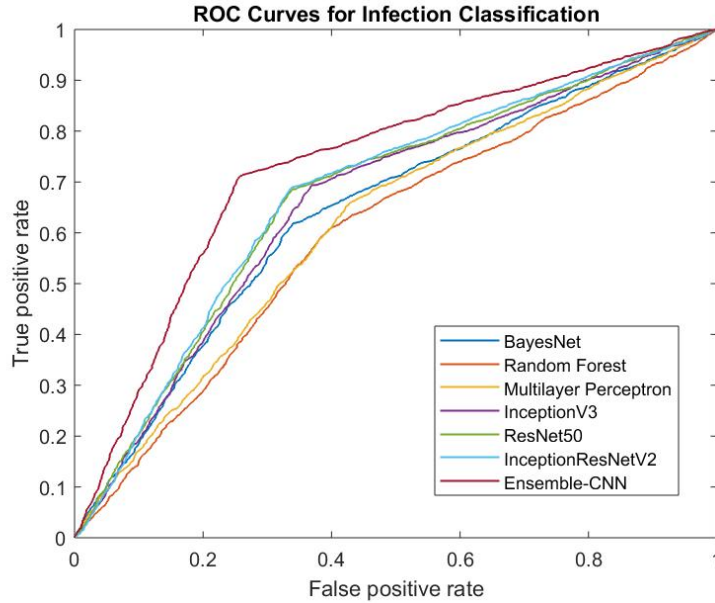


Figure 9: ROC curve for all TML and CNN methods for Infection classification.

260 better than TML methods achieving the highest score in all performance
 261 measures. The Ensemble CNN method performed better than other CNN
 262 classifiers especially for *Specificity* with a score of 74.4% in infection classi-
 263 fication with a notable margin of 8% than the second-best performing algo-
 264 rithm InceptionResNetV2(66.4%). For *Sensitivity*, all the CNNs performed
 265 marginally well with Ensemble method achieving the highest score of 70.9%.
 266 When comparing the performance of TML methods, Multilayer Perceptron
 267 (68.0%) performed well in *Sensitivity*, whereas BayesNet (66%) better in
 268 *Specificity*.

269 4.1. Experimental Analysis and Discussion

270 Assessment of DFU with computerized methods is very important for
 271 supporting global healthcare systems through improving triage and monitor-
 272 ing procedures and reducing hospital time for patients and clinicians. This
 273 preliminary experiment is focused on automatically identifying the important
 274 conditions of ischaemia and infection of DFU. The main aim of this exper-
 275 iment was to identify ischaemia and infection from images of the feet using
 276 machine learning. We have illustrated examples of correctly and incorrectly
 277 classified cases in both binary classifications of ischaemia (Fig. 10 and 11)

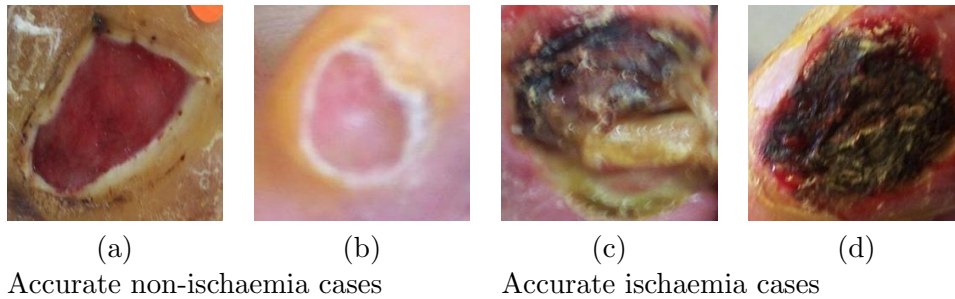


Figure 10: Examples of correctly classified cases by Ensemble-CNN on ischaemia dataset. (a) and (b) represent non-ischaemia cases. (c) and (d) represent ischaemia cases.

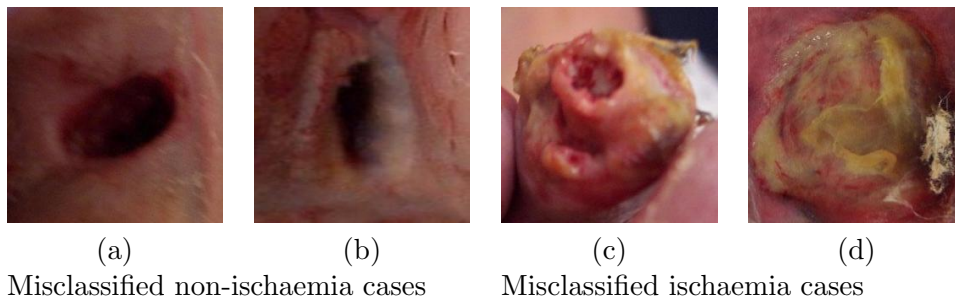


Figure 11: Examples of misclassified cases by Ensemble-CNN on ischaemia dataset. (a) and (b) represents non-ischaemia cases. (c) and (d) represents ischaemia cases.

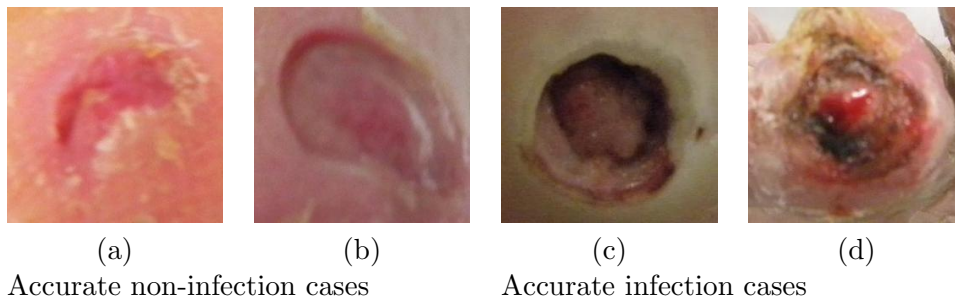


Figure 12: Examples of correctly classified cases by Ensemble-CNN on Infection dataset. (a) and (b) represents non-infection cases. (c) and (d) represents infection cases.

278 and infection (Fig. 12 and 13). As for the misclassified cases, there are huge
 279 intra-class dissimilarities and inter-class similarities between (1) infection and
 280 non-infection; (2) ischaemia and non-ischaemia cases in the DFU that make
 281 classifiers difficult to predict the correct class. Additionally, there are other

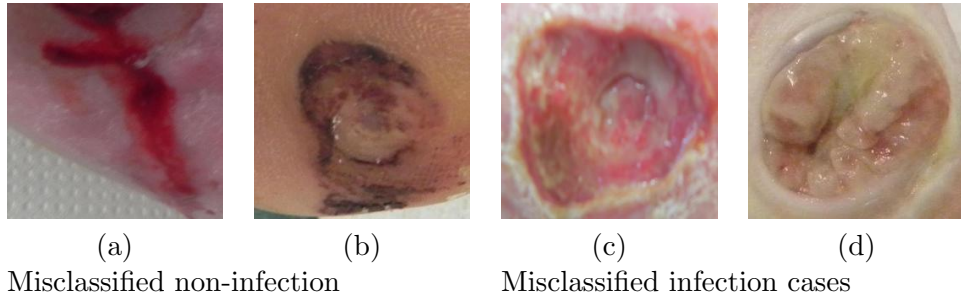


Figure 13: Examples of misclassified cases by Ensemble-CNN on Infection dataset. (a) and (b) represents non-infection cases. (c) and (d) represents infection cases.

282 influencing factors in the classification of these conditions such as lighting
 283 conditions, marks and skin tone. In misclassified cases of non-ischaemia as
 284 shown in Fig. 11, the cases (a) and (b) are hindered by the lighting condi-
 285 tion (shadow) respectively, whereas in the (c) and (d) misclassified ischaemia
 286 cases, the ischaemia features may be too subtle to be recognised from the
 287 images by the algorithm. Alternatively it is likely we needed a more sensitive
 288 objective measure of the ground truth from vascular assessments. We found
 289 that shadows are particularly problematic because machine learning algo-
 290 rithms can be deceived by shadows especially in determining the important
 291 conditions such as ischaemia. In Fig. 13, misclassified cases of non-infection,
 292 the presence of blood in the case (a), whilst case (b) belongs to one of the
 293 rare cases with the presence of ischaemia and non-infection. In misclassi-
 294 fied infection cases, the visual indicators of infection were likely too subtle,
 295 or we needed more sensitive objective ground truth provided through blood
 296 analysis.

297 In this work, we used the proposed natural data-augmentation with the
 298 help of DFU localisation to create DFU patches from full-size foot images.
 299 These patches are useful to focus more on finding the visual indicators for
 300 important factors of DFU such as infection and ischaemia. Then, we inves-
 301 tigated the use of both TML and CNNs to determine these conditions as
 302 binary classification. In this experiment, we received very good performance
 303 in terms of correctly classifying ischaemia despite the imbalanced cases in
 304 the DFU dataset. However, in the case of infection, the classifiers did not
 305 perform as well, since the condition of infection is hard to recognise from
 306 the foot images even by experienced medical experts specialized in DFU and
 307 therefore likely requires ground truth determined using objective blood tests

308 to identify bacterial infection.

309 Current research focuses on ischaemia and infection recognition in med-
310 ical classification systems, which requiring the guidance of medical experts
311 specialized in DFU. To develop a computer-aided tool for medical experts in
312 remote foot analysis, i.e. a remote DFU diagnosis system, the following are
313 challenges need to be addressed:

- 314 1. Recognition of the ischaemia and infection with machine learning al-
315 gorithms as an important proof-of-concept study for foot pathologies
316 classification. Further analysis of each pathology on foot images is
317 required according to the medical classification systems, such as the
318 University of Texas Classification of DFU [8] and SINBAD Classifica-
319 tion System [9]. This requires close collaboration with medical experts
320 specialized in DFU.
- 321 2. Deep learning algorithms need substantial datasets to obtain very good
322 accuracy, especially for medical imaging. This experiment included an
323 imbalanced DFU dataset (1459 foot images) for both ischaemia and in-
324 fection conditions. In the future, if these algorithms were to train with
325 a larger number of a more balanced dataset, it can possibly improve
326 the recognition of ischaemia and infection.
- 327 3. A study of the performance of algorithms on different types of cap-
328 turing devices is an important aspect of future work. This experi-
329 ment evaluates the performance of machine learning algorithms on the
330 DFU dataset collected with different cameras (heterogeneous sources of
331 data). This leads to more variability of image characteristics. Since the
332 algorithms have to deal with more heterogeneous patterns and charac-
333 teristics that are not intrinsic to the pathology itself. In this experi-
334 ment, we know that three types of devices were used, we do not have
335 the information on the association of images and the type of devices.
- 336 4. The current ground truth is based on visual inspection by experts only
337 and not supported by the medical notes or clinical tests (vascular as-
338 sessment for ischaemia and blood tests to identify the presence of any
339 bacterial infection). Furthermore, DFU images were debrided before
340 these images were captured. Hence, the debridement of DFU removes
341 important visual indicators of infection such as colored exudate. There-
342 fore, the sensitivity and specificity of these algorithms could be further
343 improved in the future, by feeding in ground truth from clinical tests
344 such as vascular assessments (ischaemia) and blood tests (to identify

- 345 the presence of any bacterial infection).
- 346 5. Current clinical practice obtains the foot photo using different camera
347 models, poses and illumination. It is a great challenge for a computer
348 algorithm to predict the depth and the size of the wound based on non-
349 standardized images. Standardized dataset, such as the data collection
350 method proposed by Yap et al. [30] will help to increase the accuracy
351 of the DFU diagnosis system.
 - 352 6. Dataset annotation is a laborious process, particularly for medical ex-
353 perts to label the foot pathologies into 16 classes according to the Uni-
354 versity of Texas classification system. To reduce the burden upon medi-
355 cal experts in the delineation and annotation of the dataset, there is
356 an urgent need to focus on developing unsupervised or self-supervised
357 machine learning techniques.
 - 358 7. Collecting the time-line dataset is crucial for early detection of key
359 pathologies. This will enable monitoring of foot health and changes lon-
360 gitudinally, where medical experts and computer algorithms can learn
361 the early signs of DFU. In the longer-term, the DFU diagnosis system
362 will be able to predict the healing process of ulcers and prevent DFU
363 before it happens.
 - 364 8. A smart-phone app could be developed for remote triage and moni-
365 toring of DFU. To scale-up the DFU diagnosis system, the application
366 should run on multiple devices, irrespective of the platform and/or the
367 operating system.

368 5. Conclusion

369 In this work, we trained various classifiers based on traditional machine
370 learning algorithms and CNNs to discriminate the conditions of: (1) is-
371 chaemia and non-ischaemia; and (2) infection and non-infection related to
372 a given DFU. We found high-performance measures in the binary classifi-
373 cation of ischaemia, compared to moderate performance by classifiers in the
374 classification of infection. It is vital to understand the features of both condi-
375 tions in relation to the DFU (ischaemia and infection) from a computer vision
376 perspective. Determining these conditions especially infection from the non-
377 standard foot images is very challenging due to: (1) high visual intra-class
378 dissimilarities and inter-class similarities between classes; (2) the visual in-
379 dicators of infection and ischaemia potentially being too subtle in DFU; (3)
380 objective medical tests for vascular supply and bacterial infection are needed

381 to provide more objective ground truth and further improve the classification
382 of these conditions; and (4) other factors such as lighting conditions, marks
383 and skin tone are important to incorporate into the prediction.

384 With a more balanced dataset and improved data capturing of DFU,
385 the performance of these methods could be improved in the future. Further
386 optimization in hyper-parameters of both deep learning and traditional ma-
387 chine learning methods could improve the performance of algorithms on this
388 dataset. Ground truths enhanced by clinical tests for the ischaemia and infec-
389 tion may provide further insight and further improvement of algorithms even
390 where there is no apparent visual indicator by eye. In the case of infection
391 even after debridement, ground truth informed by blood tests for infection
392 may yield improvements to sensitivity and specificity even in the absence of
393 overtly obvious visual indicators. This work has the potential for technology
394 that may transform the recognition and treatment of diabetic foot ulcers and
395 lead to a paradigm shift in the clinical care of the diabetic foot.

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