Deep Learning Classification of Diabetes in Mice using OCT Angiography Images of the Pinna

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Introduction

- **Diabetes mellitus** (DM), a chronic metabolic disorder, is a major cause for vascular diseases.
- **Optical coherence tomography angiography** (OCTA) is a non-invasive imaging modality that can visualize the superficial vasculature in skin, providing a unique window into the condition of the vascular network in vivo.
- In recent years, **deep learning** has been shown to be a valuable tool in medical image analysis that is able to detect subtle differences in the specimen.

Methods

- Custom-built swept source OCT system at 1322 nm
- Type 2 diabetic mouse model and a healthy control (n = 6 each)
- Dataset of 24 stitched OCTA images with a size of approximately 8.2 x 8.2 mm covering nearly the full mouse ear.
- 50-layer **ResNet v2** convolutional neural network trained on random patches extracted from the OCTA images for classification of the samples as diabetic or healthy using 6-fold cross-validation.

Results

- For individual patches extracted from the OCTA images:
  - Cross-validated accuracy 0.925
  - Area under the receiver operating characteristic curve (AUC ROC) 0.974
- Averaging over all patches not exceeding the boundaries of each ear:
  - Correct results for all 24 ears (both accuracy and AUC ROC 1.000)

Table 1: Cross-validation results per patch and per image. Each fold consists of many small, overlapping patches extracted from two non-diabetic and two diabetic whole-ear OCTA images. Results are given both for individual patches as well as for whole images, i.e. using the averages over all patches of each image.

	Accuracy	ROC AUC	Accuracy	ROC AUC
	per patch		per image	
Total	0.925	0.974	1.000	1.000
Fold 1	0.907	0.983	1.000	1.000
Fold 2	0.913	0.984	1.000	1.000
Fold 3	0.980	0.999	1.000	1.000
Fold 4	0.908	0.972	1.000	1.000
Fold 5	0.982	0.998	1.000	1.000
Fold 6	0.865	0.899	1.000	1.000

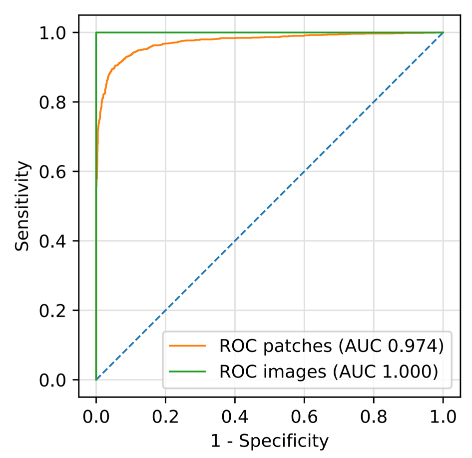
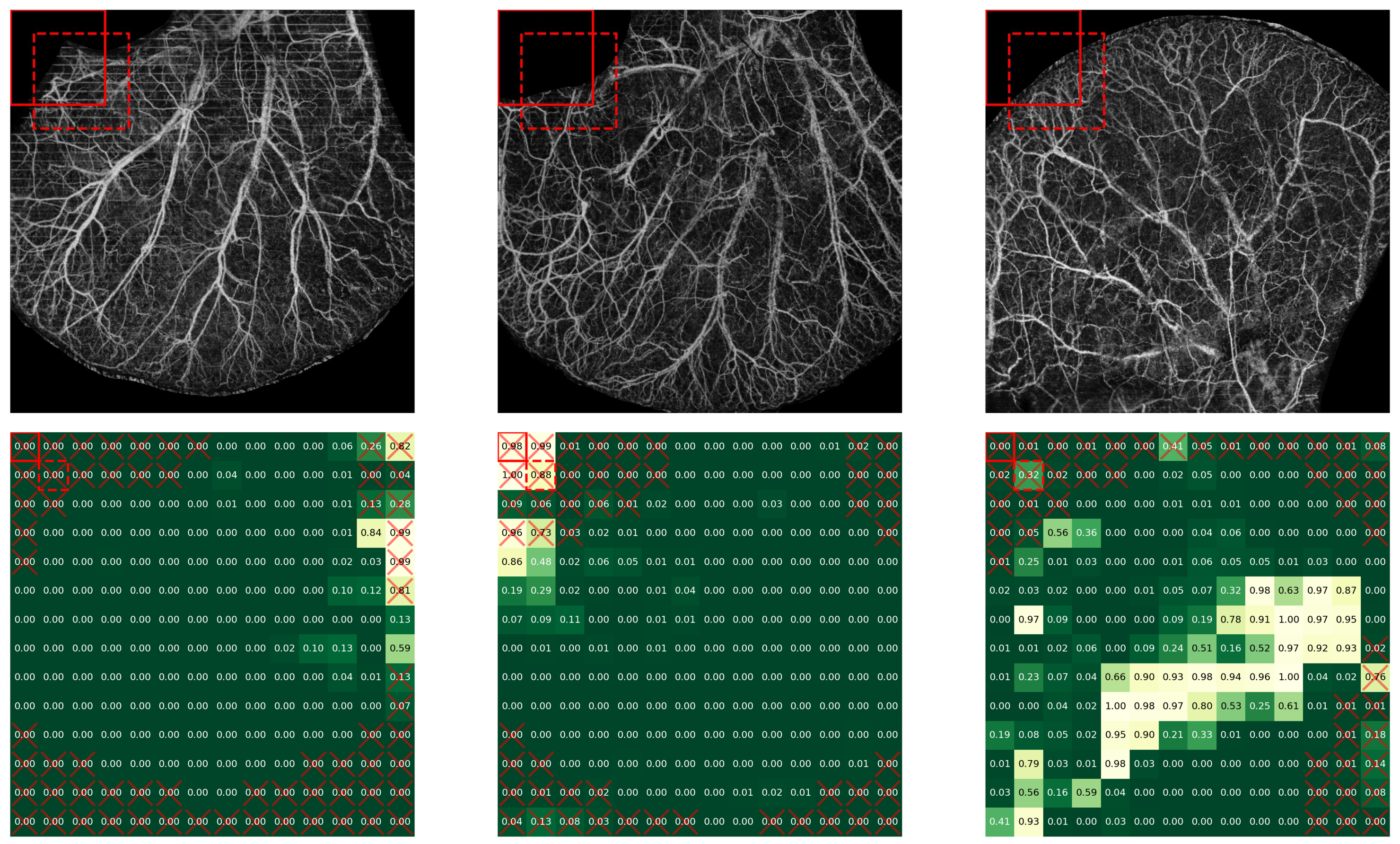


Figure 1: Receiver operating characteristic for the detection of diabetes. *ROC patches* gives the ROC curve for individual overlapping patches extracted from the acquired OCT images. *ROC images* gives the ROC curve after averaging over all usable patches of each image.

Non-diabetic animals:



Diabetic animals:

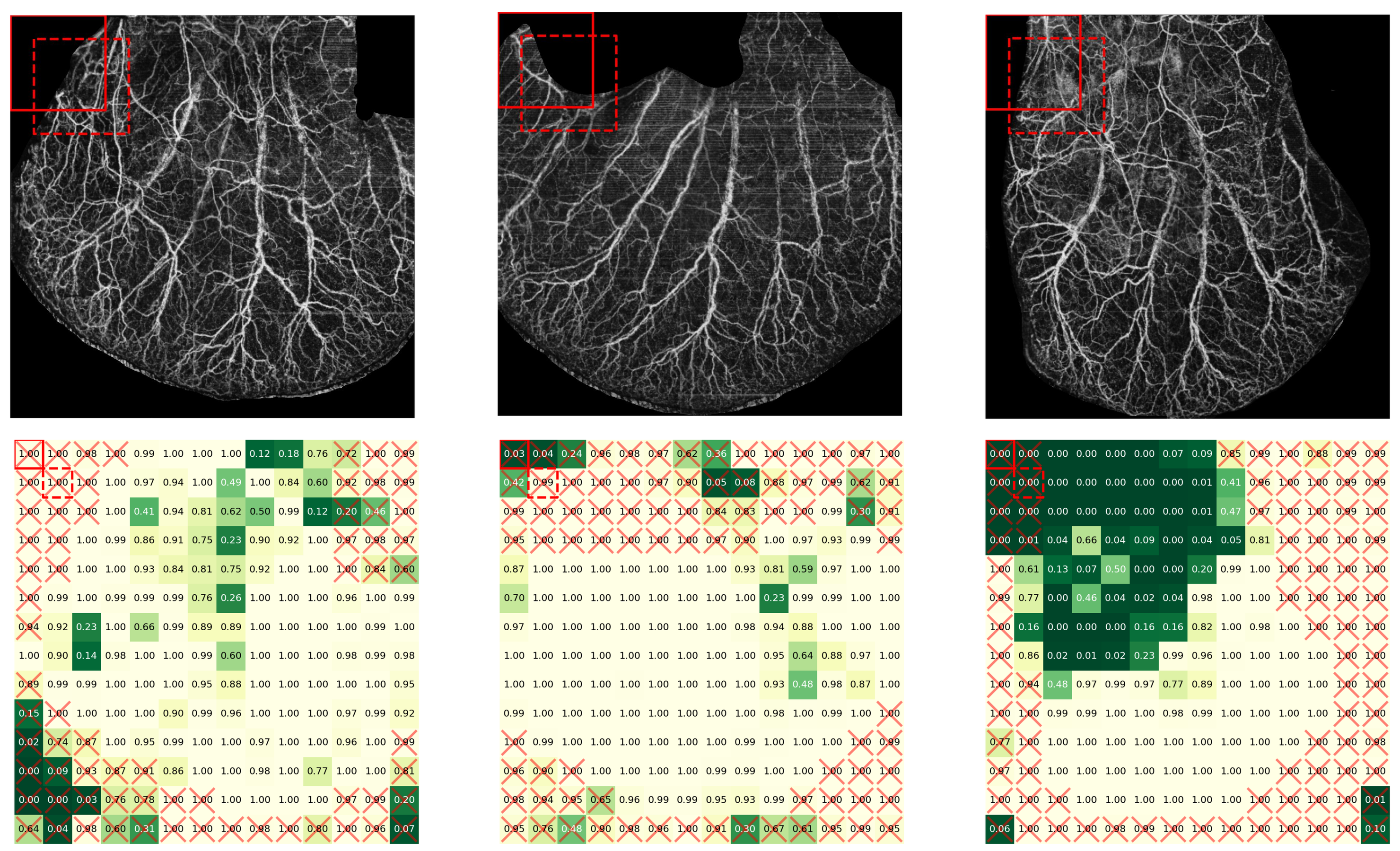


Figure 2: Example OCTA images with a size of approximately 8.2 × 8.2 mm with corresponding predictions of the convolutional neural network. As the network expects an input size of 2.09 × 2.09 mm (indicated by the red squares), inference was performed 196 times per image on overlapping patches of this size. Patches extending beyond the useful angiography image area were excluded from the average (indicated by red crosses). Numbers close to 1.0 represent CNN prediction of diabetic vascular changes. Top two rows non-diabetic mice, bottom two rows diabetic mice. Rightmost images are from those ears where the deep learning algorithm exhibited the worst performance. In all cases, the averaged prediction over all patches of an angiogram was correct.

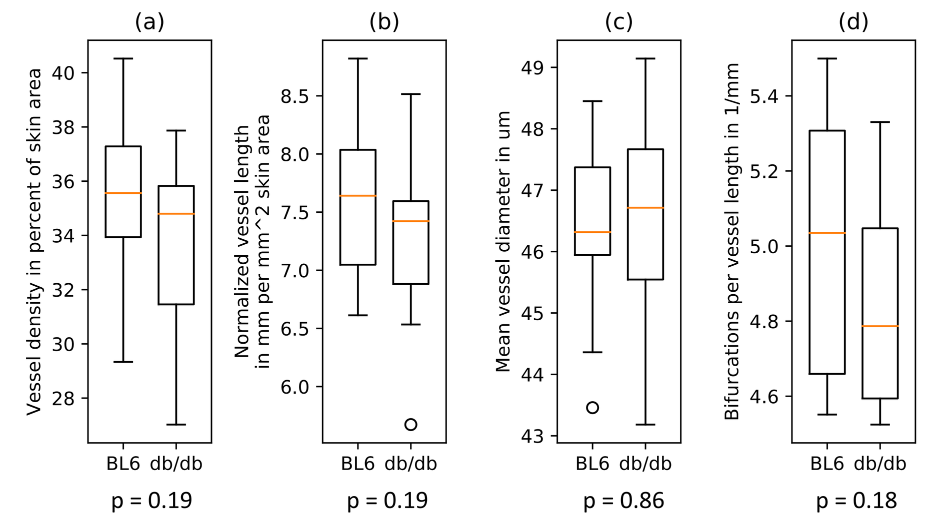


Figure 3: Quantitative analysis based on OCTA parameters of the vascular network in the ears of healthy (BL6) and diabetic (db/db) mice.

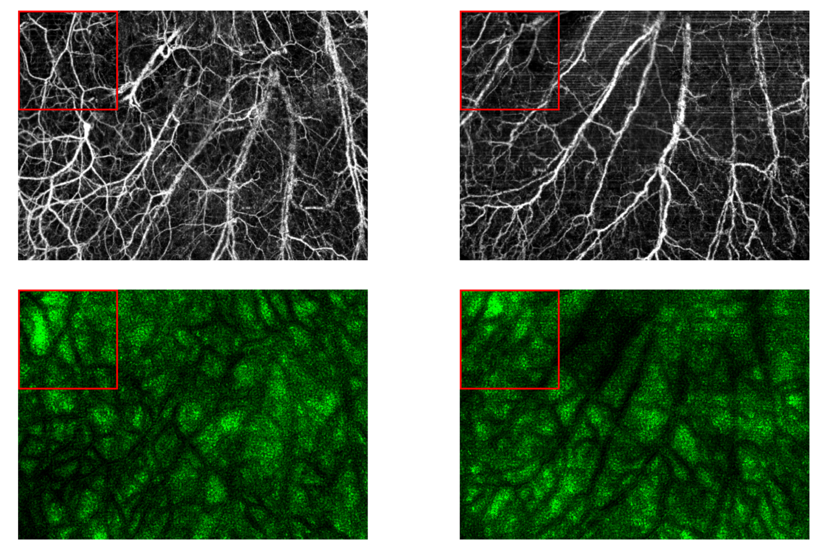


Figure 4: Gradient saliency maps stitched from many overlapping CNN predictions. Bright green areas represent regions the network is most influenced by when predicting diabetes-correlated vascular changes. Red squares indicate CNN input size.

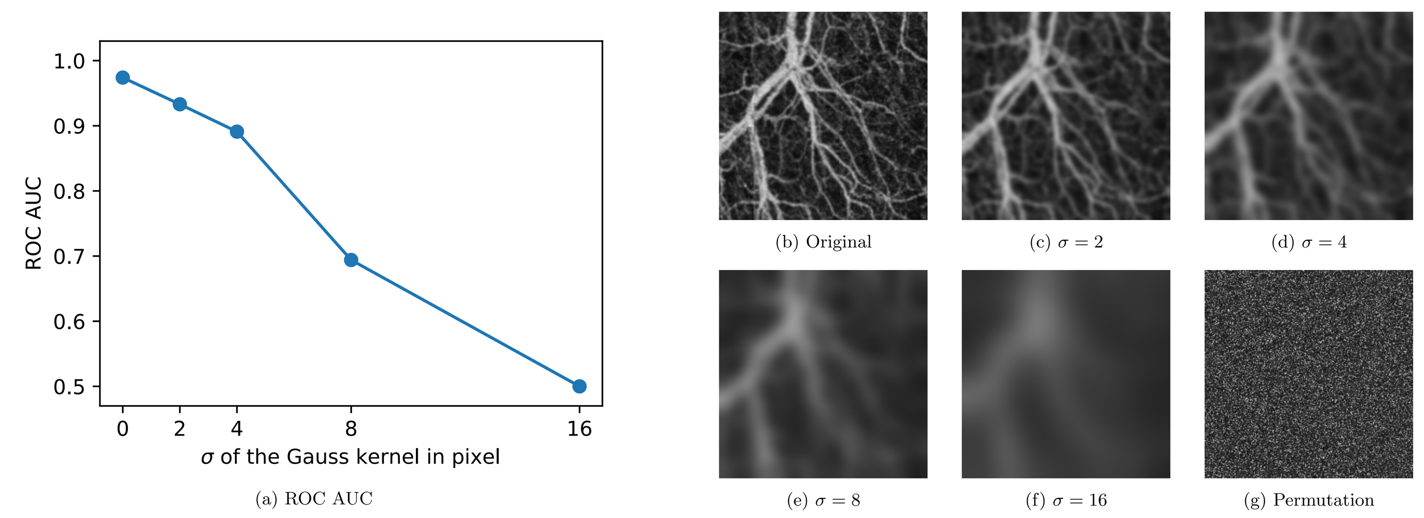


Figure 5: Effects of removing image information on the prediction of diabetes. (a) Impaired prediction due to the removal of high-frequency information with Gaussian blurring. (b) Sample CNN input image. (c-f) Same image with varying degrees of Gaussian blur applied. (g) Same image with randomly shuffled pixel position. For permuted images, an ROC AUC of 0.708 was obtained.

Discussion

We showed that a deep learning algorithm could successfully recognize DM based on changes in the vascular network of the ears. While the greater thickness of human skin might impede its use for OCTA analysis of diabetes-induced vascular damages, the retina can probably serve as an adequate alternative for a window into the state of vascular health in humans, warranting further research into deep learning analysis of diabetic OCTA images. In addition, chronic hyperglycemia, as caused by DM, is associated with long-term damage of the eye, ultimately resulting in diabetic retinopathy. Here, OCTA and deep learning might provide new biomarkers for the early detection of the disease.

References

Martin Pfister, Hannes Stegmann, Kornelia Schützenberger, Bhavapriya Schäfer, Christine Hohenadl, Leopold Schmetterer, Martin Gröschl, Rene M. Werkmeister, *Deep Learning Differentiates between Healthy and Diabetic Mouse Ears from Optical Coherence Tomography Angiography Images*, under review