likely that GLUT1 inhibitors can only be applied topically owing to the strong glucose requirement of other tissues. In addition, the possibility that blockade of GLUT1 may have more severe effects on human skin than on mouse skin, particularly when the inhibitors are used for a prolonged period and on multiple body sites, must be considered.

In spite of these open questions, the study by Zhang et al.[2] highlights the importance of glucose metabolism in keratinocytes and the potential of these cells for metabolic reprogramming upon glucose deprivation. In particular, it opens new avenues for the treatment of psoriasis and other inflammatory and/or hyperproliferative skin diseases. ❐

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Competing interests

The authors declare no competing interests.

MACHINE LEARNING

# AI for medical imaging goes deep

An artificial intelligence (AI) using a deep-learning approach can classify retinal images from optical coherence tomography for early diagnosis of retinal diseases and has the potential to be used in other image-based medical diagnoses.

Daniel S. W. Ting, Yong Liu, Philippe Burlina, Xinxing Xu, Neil M. Bressler and Tien Y. Wong

Deep learning is a new AI machine-learning technique[1], and its medical applications have generated much interest over the past few years. It is designed to mimic the layers of neurons in the human brain to process and extract information, allowing computers to learn without being explicitly programmed. This technique can also be potentially used to detect diseases, including retinal diseases from fundus images[2–4], tuberculosis from chest radiographs[5,6] and malignant melanoma from skin images[7]. More recently, deep learning has been utilized to identify risk factors associated with cardiovascular diseases (for example, blood pressure, smoking and body mass index) from retinal photographs[8]. In a recent February issue in *Cell*, Kermany et al.[3] present an AI approach for detecting several medical conditions, including diabetic macular edema (DME), choroidal neovascularisation (CNV), drusen and pediatric pneumonia, from patient images, with promising diagnostic performance.

Population-level screening of patients with diabetes for identification of retinal comorbidities is a major public health strategy that aims to allow early access to tertiary eye care services to affected individuals for early treatment[9]. In the United States, for example, it is currently neither practical nor economical to have trained health care providers screen all 20 million individuals with diabetes to identify the 1 million or so with DME. Patients with diabetes are usually asymptomatic but should be monitored so they can be appropriately treated (for example, with lasers or anti–vascular endothelial growth factor) before visual loss occurs[10]. Similarly, it may not be feasible to screen all 65 million people in the United States over the age of 50 years to identify and monitor the 8 million asymptomatic individuals with signs of early AMD (i.e., drusen) or those with onset of signs of late AMD (i.e., CNV). Treatment of these asymptomatic individuals is very effective in preserving vision.

There have been substantial developments in deep-learning techniques using convolutional networks (ConvNets) over the last few years. Transfer learning, as used by Kermany et al.[3], is a method for building an AI system using ConvNets that have already been pretrained using a large data set in the public domain. For example, transfer learning allows the knowledge gained during the training process to recognize animals in images to be used in recognizing retinal diseases from optical coherence tomography (OCT) images. A ConvNet consists of multiple layers of neurons with trainable weights that are thus able to learn features and patterns. Inspired by the biology of the visual cortex in the brain, each neuron in a ConvNet is connected to a local region of inputs to learn specific features of an image. In medical imaging, many publicly available ConvNet models (VGGNet, ResNet, Inception V3 and DenseNet) have been used thus far[2,11].

Kermany et al.[3] showed promising diagnostic applications for deep learning and transfer learning techniques in detection of three major retinal conditions, namely DME, CNV and drusen, from images captured using OCT, a technique that employs a retinal-imaging device that uses infrared light and low-coherence interferometry to scan through the retinal layers[3]. In this study, the authors trained the deep learning framework on 37,000 images of CNV, ~11,000 images of DME, ~9,000 images of drusen and ~51,000 images from unaffected individuals using Inception V3; images were obtained from 4,686 individuals in total. This was followed by validation on 1,000 images, consisting of 250 images of CNV, 250 images of DME, 250 images of drusen and 250 normal images. The authors evaluated the AI performance in three models—multiclass comparison, limited model and binary classifiers. For the multiclass comparison, the authors used the AI to individually differentiate images of CNV, DME and drusen from images of healthy patients.



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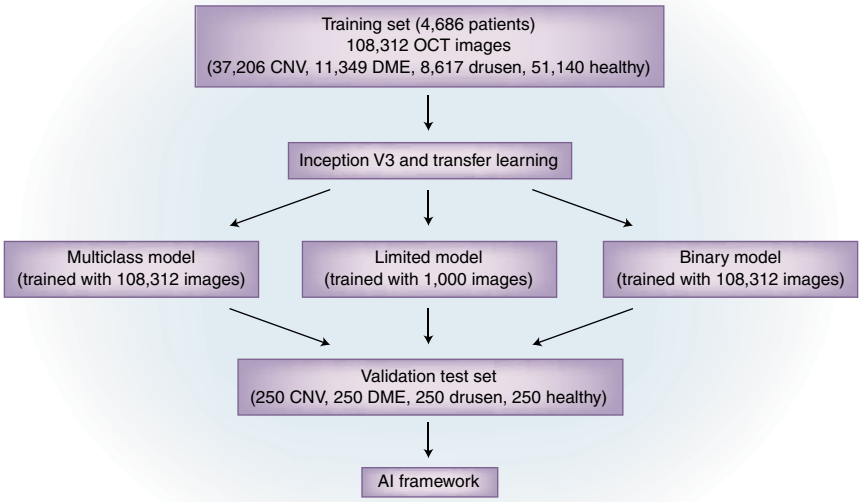


**Fig. 1 | Transfer learning can be applied to classify retinal optical coherence tomography images for early diagnosis of retinal diseases.** Kermany et al.[3] developed an AI framework for detecting of CNV, DME and drusen from OCT images. Their AI framework used the transfer learning approach Inception V3 on a training set and was repeated for 100 iterations using three different approaches, as indicated. The approach was able to diagnose disease with 90% accuracy.

For the limited model, only 1,000 images (250 CNV, 250 DME, 250 drusen and 250 normal) were used, and the number of images in these training sets was much smaller than the original training data set (116,000 images). For the binary classifier, the authors divided the OCT images into CNV versus normal, DME versus normal and drusen versus normal to test the individual AI algorithm for each condition (Fig. 1).

The diagnostic performance of deep learning for all three models was >90% accuracy in differentiating CNV, DME, drusen and normal images, with the best outcome achieved in the binary classifiers model (an accuracy of >98%) (Fig. 1). Although it had a slight drop in accuracy, the limited model was able to achieve an accuracy of >90% even though the training set was 100 times smaller than the full data set. In comparison to six human experts, the deep learning system showed similar outcomes in identifying individuals requiring urgent referral as determined on the basis of their OCT images. Further validation of the effectiveness of the authors' deep learning approach for medical diagnoses was conducted on a set of children chest X-rays (CXR) consisting of 5,232 training images from 5,826 patients (2,538 bacterial pneumonia, 1,345 viral pneumonia and 1,349 healthy) and 624 images (234 healthy and 390 pneumonia) from 624 patients. They achieved an accuracy of 92.8%.

Before the approach progresses to the clinic, it is important to consider the following points. To further validate the authors' approach, it would be useful to carry out a direct comparison of their results with existing deep learning systems to weigh relative merits, limitations, performance, efficiency and ease of use. In addition, with respect to using the approach in other applications, the authors carried out occlusion testing, which was successful in identifying the areas in the ConvNet that are important for making a diagnosis. This, however, may not be easily applicable to diseases with variable abnormal areas or other imaging modalities (for example, CXR). Also, it is important to consider where this approach could be best applied: would it be for screening the general population in the primary healthcare setting or in aiding ophthalmologists in making diagnoses in tertiary care settings? Lastly, and more generally, future studies might address challenges in medical imaging, such as how and/or when machines and human adjudication differ, and design methods that quantitatively and qualitatively assess and explain sources of error for both humans and machines.

In conclusion, Kermany et al.[3] have shown that a deep learning system has excellent diagnostic performance in detecting DME, CNV and drusen on OCT images and pediatric pneumonia on CXR. They also highlighted the application of transfer learning in conditions with small datasets. Many areas in deep learning for medical imaging analysis, however, still have questions that remain unanswered. Thus, it is critical for machine learning and medical communities to collaborate closely not only to facilitate the development and validation of deep learning techniques[12], but also to strategically deploy these technologies for patient care. ❐

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## Competing interests

D.S.W.T. and T.Y.W. are co-inventors of a patent on a deep learning system in detection of retinal diseases. N.M.B. and P.B. are co-inventors of a patent on a deep learning system in detection of age-related macular degeneration.



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