

Supplementary Online Content

Burlina PM, Joshi N, Pacheco KD, Liu TYA, Bressler NM. Assessment of deep generative models for high-resolution synthetic retinal image generation of age-related macular degeneration. *JAMA Ophthalmol*. Published online January 10, 2019. doi:10.1001/jamaophthalmol.2018.6156

Figure 1. Parts A through C (top row) and D through F (bottom row)

eTable. Showing Exact Number of Images Used for Training/Validation/Testing for the Various GANs and DCNNs

eFigure 2. The Figure Shows the Nearest Neighbors' Analysis for Real AREDS Images for Non-Referable Cases

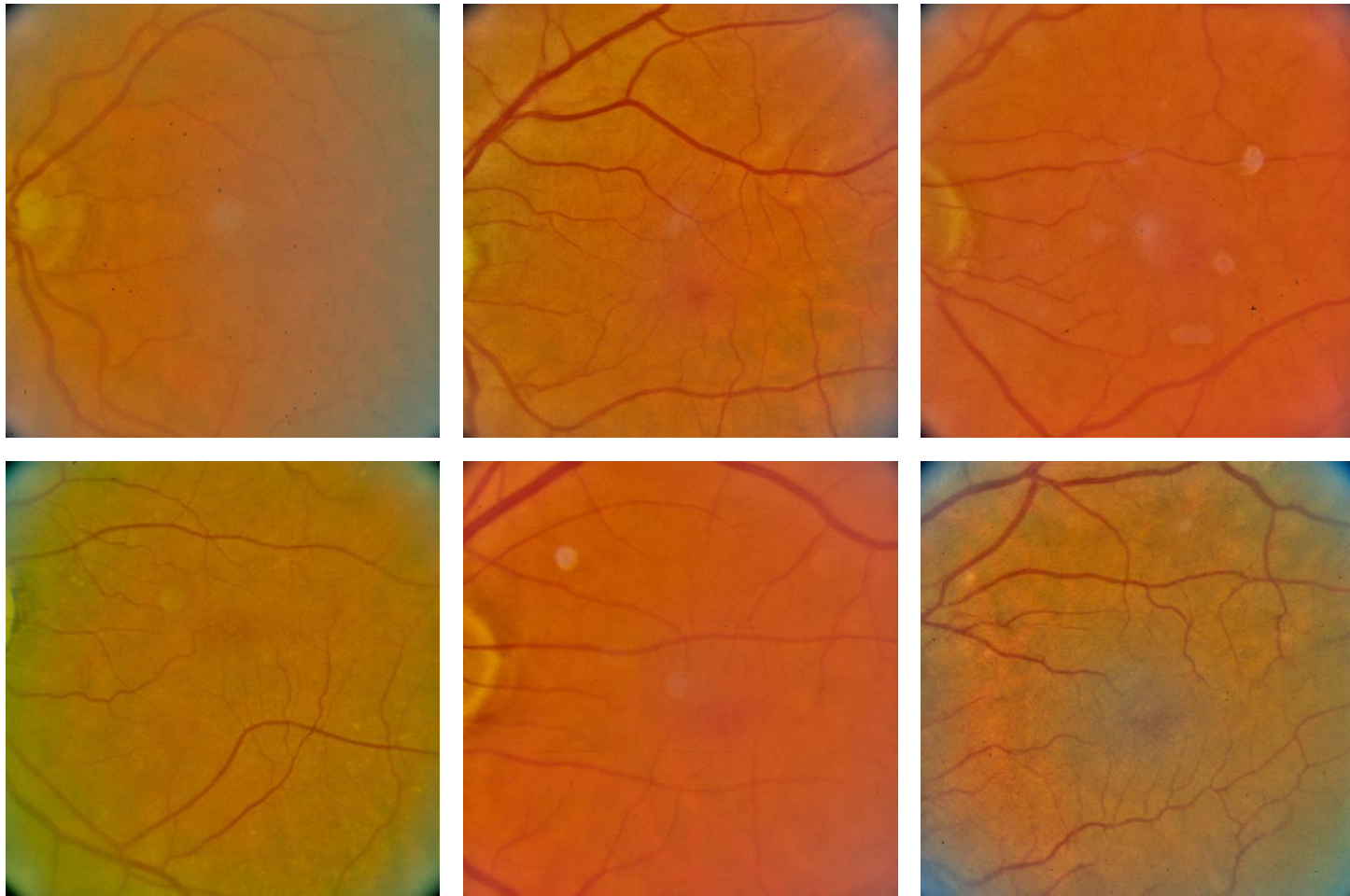
eFigure 3. Showing the Nearest Neighbors' Analysis for Real AREDS Images for Referable Cases

eAppendix.

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

Image Preprocessing. All images used in this study were first preprocessed using the previously reported⁷ method consisting of detecting the outer boundaries of the retina, cropping images to the inscribed square, and resizing to 512x512 for training ProGANs. When such images are used later in diagnostic DCNNs, these images were resized to 224x224.

eFigure 1. Parts A through C (top row) and D through F (bottom row)



Answer to eFigure 1 as to which images are real and which are synthetic: The real images without referable age-related macular degeneration (AMD), i.e., with no AMD or with early AMD as defined in the Age-Related Eye Disease Study, are images A, D, and E. The synthetic images without referable AMD are images B, C, and F.

eTable: Showing exact number of images used for training/validation/testing for the various GANs and DCNNs.

	Number of training images	Numbers of validation images	Number of testing images	Number of images generated by the GAN kept for training DCNN-S	Number of images generated by the GAN kept for validation of DCNN-S
GAN-NR	66,308	N/A	N/A	66,308	826
GAN-R	52,782	N/A	N/A	52,782	603
DCNN-S	66,308 ^(A) +52,782 ^(B)	826 ^(A) +603 ^(B)	7267 ^(C) + 6035 ^(D)	N/A	N/A
DCNN-R	66,308 ^(C) + 52,782 ^(D)	826 ^(C) +603 ^(D)	7267 ^(C) + 6035 ^(D)	N/A	N/A

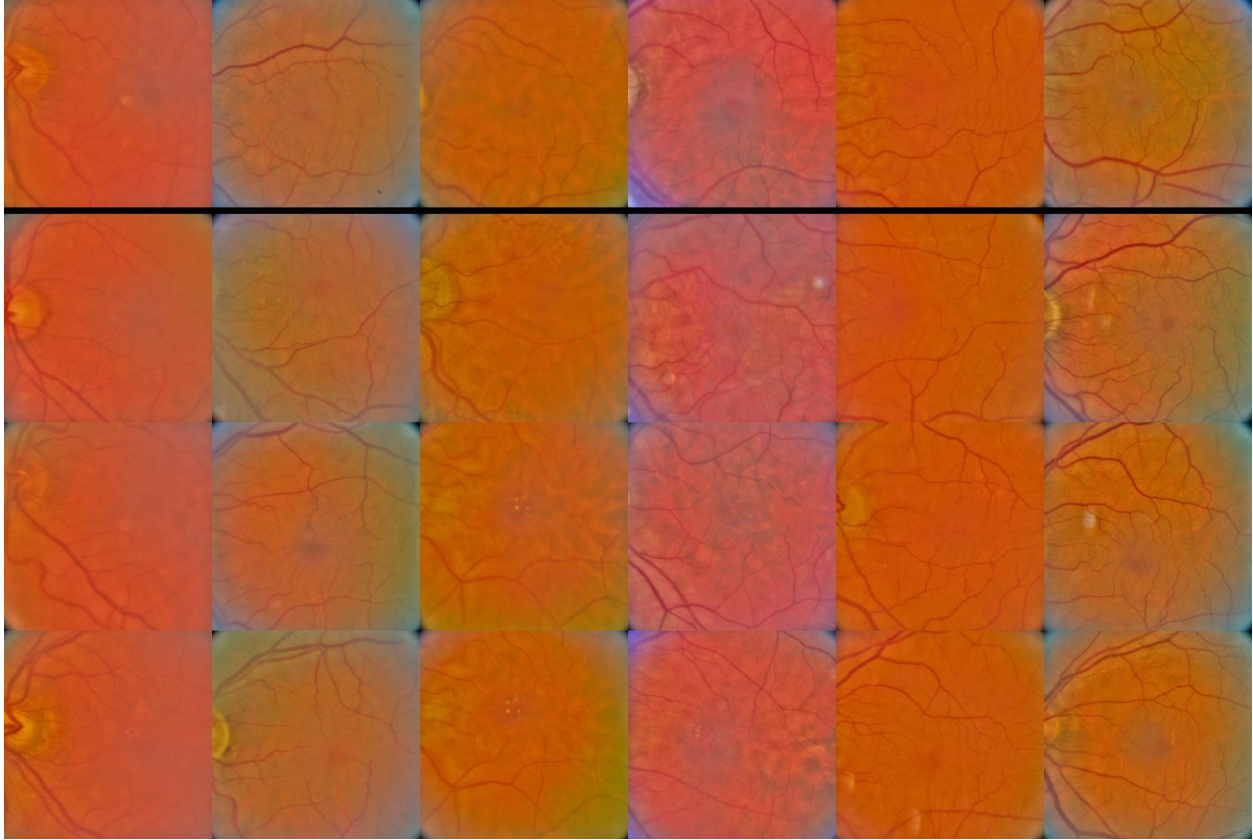
Note for Supplemental Table S1

The following notes apply to the images used:

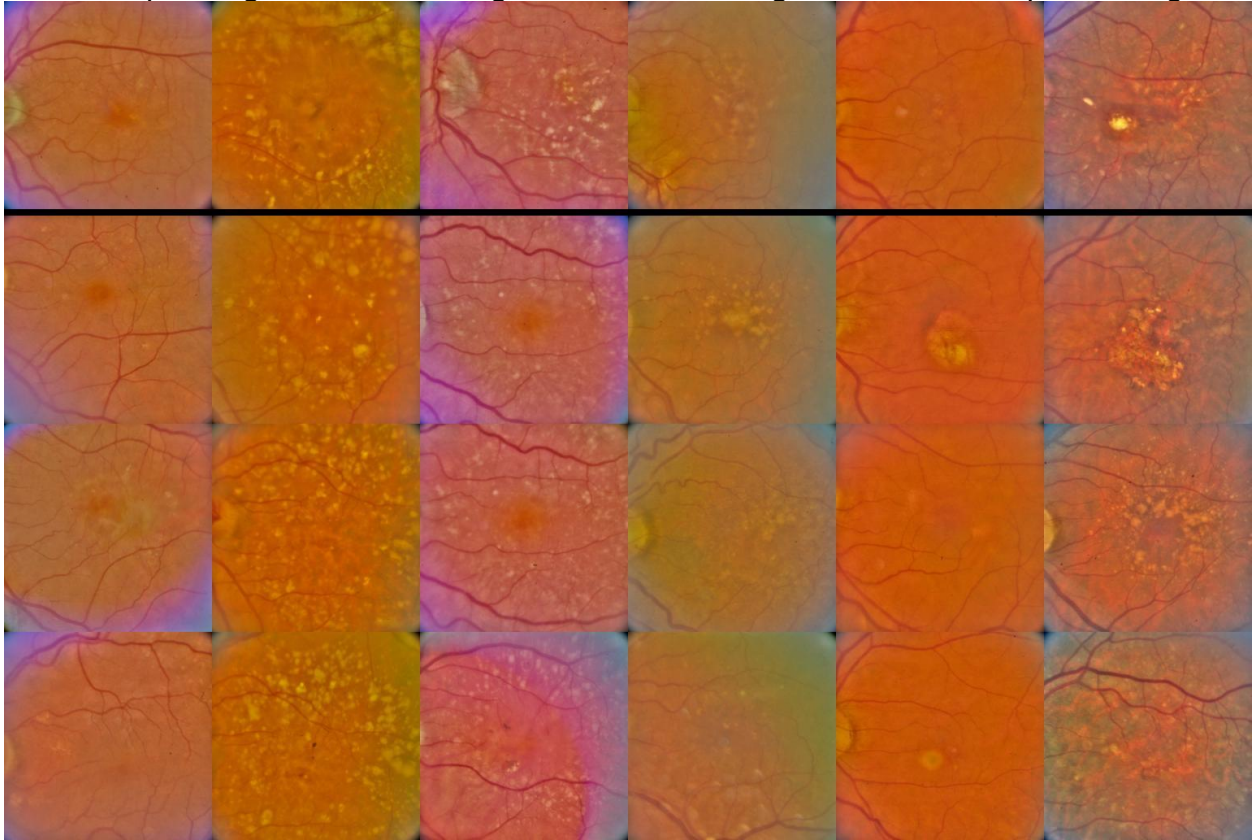
- (A) These images are generated from GAN-NR.
- (B) These images are generated from GAN-R.
- (C) These images are taken from the original/real AREDS images and are of class NR.
- (D) These images are taken from the original/real AREDS images and are of class R.
- Stereo pairs are kept within the same partition (training, validation, or testing).
- Images that the GANs was trained on are not used for testing the DCNN-R or DCNN-S.
- Patient partitioning is used: patients used in training, validation and testing are distinct.

Nearest Neighbor Analysis

eFigure 2: The figure shows the nearest neighbors' analysis for real AREDS images for non-referable cases. The top row shows synthetic images and second through fourth rows show the corresponding real nearest neighbors in the training dataset to the top row image.



eFigure 3: showing the nearest neighbors' analysis for real AREDS images for referable cases. Top row shows synthetic images and second through fourth rows show the corresponding real nearest neighbors in the training dataset to the top row image.



This analysis demonstrates that synthetic images and their real nearest neighbors' images are distinct from each other, therefore highlighting the ability of GANs to generate datasets of images that are distinct and are not close copies of training dataset images.

eAppendix

Two class Referable vs Non-referable AMD Classification

This study focuses on a 2-class classification problem which was derived from the original 4-step AREDS enrollment scale, where referable AMD was defined as the intermediate or advanced stage of AMD, and non-referable AMD was defined as no or early AMD.⁹ The original 4-step AREDS eligibility scale is single eye-based and grading is performed using the following criteria: eyes with no or only small drusen ($DS < 63 \mu\text{m}$) and no abnormal pigmentation are classified *normal*; when presenting multiple small drusen, or medium-sized drusen ($63 \mu\text{m} \leq DS < 125 \mu\text{m}$) and/or pigmentation abnormalities, eyes are classified *early AMD*; when presenting with large drusen ($DS \geq 125 \mu\text{m}$) or numerous medium-sized drusen and pigmentation abnormalities, eyes are classified *intermediate AMD*; finally, eyes with choroidal neovascularization or geographic atrophy lesions such as retinal pigment epithelial detachment, subretinal pigment epithelial hemorrhage, are deemed *advanced AMD*, if the fellow eye does not have central geographic atrophy or choroidal neovascular AMD.