Imaging with Fluorescein Angiogram to Quantify Diffusivity of Choroidal Neovascular Membrane

Aleksandra I. Pivovarova, MS[1] and Jacqueline Valadez[1]; Ram Peddada, MD, DSc[2]

[1]Alabama College of Osteopathic Medicine and
[2]Retina of Auburn & Metro-Columbus
RetinaDoc@SiteforSight.NET for Questions, Comments, Reprints

PURPOSE

The principal treatment strategy for wet age related macular degeneration (AMD) is intravitreal injection of anti-vascular endothelial growth factors (VEGF) in order to prevent further angiogenesis. It was previously hypothesized that the so-called slow responders to the treatment with anti-VEGF intravitreal injection are in fact rapid diffusers of VEGF in whom newly secreted and unbound VEGF following a treatment with anti-VEGF is able to rapidly diffuse through the Bruch's membrane (Peddada, 2014). According to that hypothesis, conversely, those patients who have a poor diffusivity of Bruch's membrane symptoms take longer to reoccur following a treatment. Therefore, diffusivity of Bruch's membrane may be an important predictor of the disease progression. In this report we demonstrate that the imaging of choroidal neovascular membrane (CNVM) in patients with AMD using fluorescein angiography presents an opportunity to quantitatively assess the permeability and estimate diffusivity of Bruch's membrane-CNVM complex *in vivo.*

METHODS

Hyperfluorescence of unmarked fluorescein angiograms of patients with wet AMD were retrospectively analyzed as a function of time. One good study with uninterrupted images and another study with fluctuations in hyperfluorescence (as in a less cooperative patient) were analyzed. Using ImageJ (imagej.nih.gov) gray scale index of the en face angiogram image within a test box circumscribed by the Bruch's membrane-CNVM complex was quantified as a function of time. The transient intensity of the leaking membrane was first obtained after adjusting for random variation in the intensity from one instant to the next by subtracting the adjacent background intensity. This transient intensity was normalized with respect to its range so that the smallest value was zero at time zero and the highest intensity value was 1. This data was fit to an exponential curve using three data points one at each end, i.e., time t = 0 and time of last data point, and a third data point approximately at midpoint of the angiogram. A time constant of the exponential curve was thus obtained.

RESULTS

The analysis yielded a time constant of 9.46 and 11.52 seconds, respectively for a stable angiogram and an erratic angiogram with fluctuations in the intensity. These values suggest that the time constant of growth of intensity of the hyperfluorescence of the images of the Fluorescein angiogram are robust measures deviating within 20% of each other despite random fluctuations in the intensity of the images during the course of the angiogram.

Figure 1. Test area (orange box) and Background area (yellow box) for measuring hyperfluorescence in (a) an angiogram with random fluctuations of fluorescence, perhaps due to frequent blinking and (b) a well conducted angiogram study.

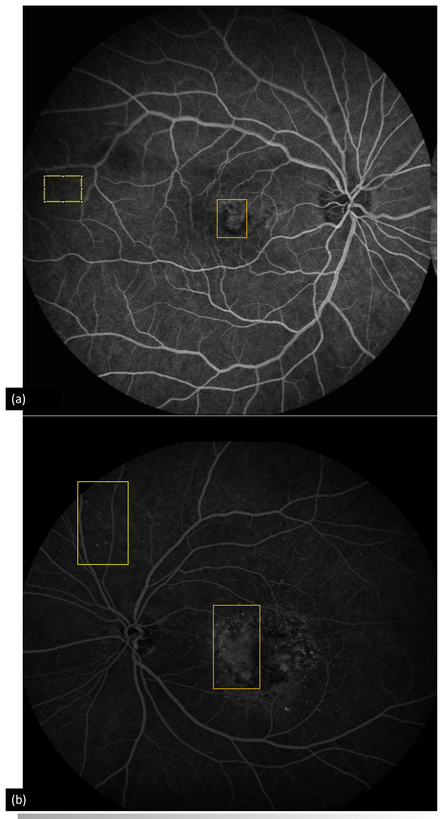
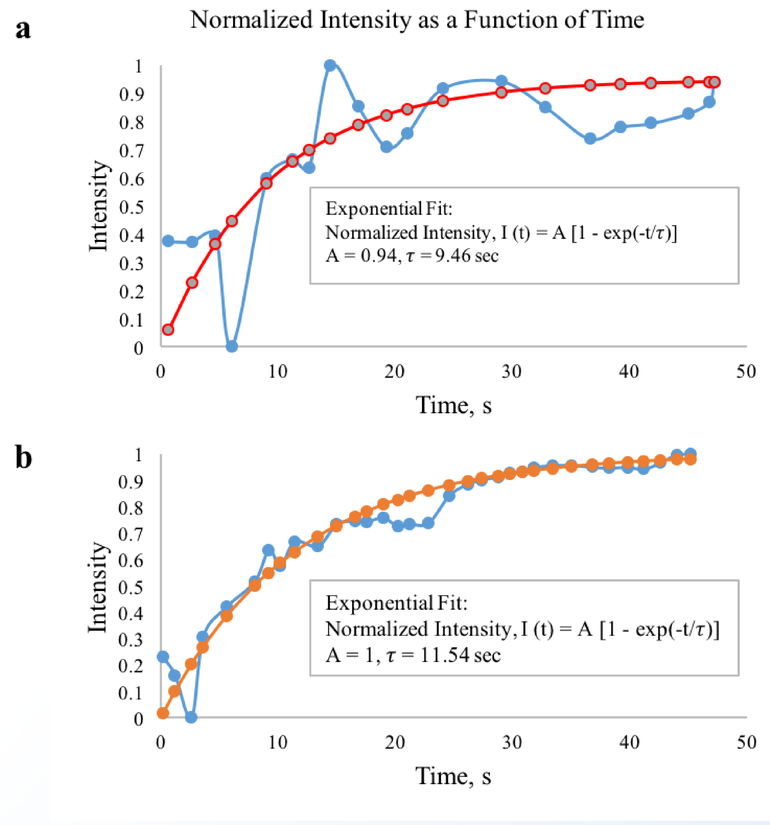


Figure 2. Intensity of hyperfluorescence normalized with the maximum intensity noted for the duration of the angiogram. (a) Study with random fluctuations (as may be due to frequent blinking of the subject), (b) Study with normal images (as in cooperative patient).



DISCUSSION

This study provides a method for estimation of the diffusivity or permeability of the Bruch's membrane-choroidal neovascular membrane complex. It is possible to measure the diffusivity of leaking membrane using fluorescein angiography by obtaining a time constant of the exponential curve. This parameter could be incorporated into a routine visit in order to give a better prediction of treatment for wet AMD and indicate a more precise prognosis.

REFERENCES

Peddada, R. Bruch's membrane diffusivity for vascular endothelial growth factors may explain variable response to wet age-related macular degeneration treatment: Clinical implications. Med Hypotheses. 2014 Dec;83(6):835-7.