

Peer Review File

Article information: <http://dx.doi.org/10.21037/atm-20-4355>

Abstract

Comment 1: Lines 8-9: remove caps for “Optical Coherence Tomography”

Reply 1: This has been changed as suggested (lines 8-9)

Introduction

Comment 2: Line 28: listed references are for animal studies. Please include relevant reference for human studies.

Reply 2: Four clinical references were added, this changes is highlighted in red font and not by "track changes" due to the use of Sciwheel reference software that does not allow "track changes" (line 45)

Comment 3: Line 35: change “a clinical setting” to “ human clinical trials”

Reply 3: This has been changed as suggested (line 52)

Comment 4: Line 36: change to “The normal transparency of the anterior ...”

Reply 4: This has been changed as suggested (line 53)

Comment 5: Lines 42: change “adopted from the clinic” to “are used currently in clinical practice to evaluate human retina, the results of these animal studies using in vivo retinal imaging may be directly ...”

Reply 5: This has been changed as suggested (lines 58-60)

Comment 6: Lines 44 to 47: consider adding references

Reply 6: We added the text "as detailed in this review" as majority of the references mentioned in the review describe the use of imaging techniques in translational animal studies (lines 65-66).

Comment 7: Line 57: please add that DARC is being considered for human use in clinical trial.

Reply 7: This has been changed as suggested (lines 72-73)

Color Fundus Photography:

Comment 8: Line 71: suggest rewording to “..in humans and animals, both large and small, and is a key...”

Reply 8: This has been changed as suggested (line 91)

Comment 9: Lines 77-79: suggest rewording to “...and the resulting bleb of elevated retina following subretinal injection and the eventual resolution can be visualized by color fundus photography.”

Reply 9: This has been changed as suggested (lines 98-100)

Comment 10: Line 80: suggest rewording to “..retina grafts or retinal pigment epithelial cells grown on scaffold...”

Reply 10: This has been changed as suggested (line 102)

Comment 11: Line 82: suggest rewording to “...safety of intraocular injection of viral vectors or cells and for evaluating the potential regenerative effects of various therapies on the retina.”

Reply 11: This has been changed as suggested (lines 105-106)

Near IR Imaging:

Comment 12: Line 97: Suggested rewording as “Retinal imaging using NIR-FAF was..”

Reply 12: This has been changed as suggested (line 120)

Fluorescent fundus imaging:

Comment 13: Line 156: add references including the following as example of EGFP-labeled cells in rd1 mice eyes: Moisseiev E, Smit-McBride Z, Oltjen S, Zhang P, Zawadzki RJ, Motta M, Murphy C, Cary W, Annett G, Nolte J, Park SS. Intravitreal administration of human bone marrow CD34+ stem cells in a murine model of retinal Degeneration. **Invest Ophthalmol Vis Sci** 57: 4125-4135, 2016

Reply 13: Done (Lines 181-183)

OCT:

Comment 14: Line 218: edit to “edema” to “retinal edema or thinning”

Reply 14: This has been changed as suggested (line 243)

Comment 15: Line 225: edit to “OCT imaging enabled retinal structural changes to be demonstrated longitudinally in various animal models of retinal disease including mouse model...?”

Reply 15: This has been changed as suggested (lines 250-252)

Comment 16: Lines 229-31: reword as follows: “..for using OCT imaging for evaluating safety and efficacy of novel intervention using a fewer number of study animals. Disease progression analysis can be done using serial imaging of the same animal.”

Reply 16: This has been changed as suggested (lines 256-260)

Comment 17: Lines 238-242: reword as follows: “Some published translational studies were able to obtain high resolution OCT images of the retina in animal eyes by using commercially available clinical grade OCT instruments equipped with eye tracking to prevent image signal disturbance from animal breathing. Some of these instruments are also equipped to improve OCT image resolution by using an automated software that rescans the same area of the retina and averages multiple images.”

Reply 17: The text has been changed as suggested (lines 267-276)

OCT Angiography:

Comment 18: Line 254: please add here: “In addition, retinal vascular diseases, such as diabetic retinopathy, is associated with changes in retinal vasculature”

Reply 18: This has been changed as suggested (lines 288-290)

Comment 19: Lines 257-8: change to “...changes in retinal and choroidal circulation noninvasively in human and animal eyes” and add the following references:

Reply 19: The text was revised. The references that the reviewer wanted to include are missing. We added 3 references describing OCTA analysis in human, moques and rat eyes (line 293-294).

Comment 20: Line 260: change “choroidal blood vessels” to “retinal and choroidal circulation.”

Reply 20: This has been changed as suggested (line 296)

Comment 21: Lines 260-263: change sentence to “However, these angiographic methods are invasive and provide only two-dimensional imaging of the retinal and choroidal circulation. With fluorescein angiography, visualization of the choroidal circulation is limited by the overlying retinal pigment epithelium. In contrast, OCTA provides a three-dimensional image of the retinal and choroidal circulation by detecting the movement of blood cells in rapid sequential OCT imaging of the same region of the retina. Thus, OCTA images can be obtained using OCT instrumented equipped with the appropriate software. It is relatively fast.”

Reply 21: This has been changed as suggested (lines 296-307)

Comment 22: Line 275: Suggest adding that OCTA has been used to study the protective effects of novel intervention in rodent models of retinal vasculopathy: reference--Moisseiev E, Anderson J, Oltjien S, Goswami M, Zawadzki RJ, Nolta JA, Park SS. Protective Effect of Intravitreal Administration of Exosomes derived from Mesenchymal Stem Cells on Retinal Ischemia. **Curr Eye Res** 42(10): 1358-1367, 2017.

Reply 22: Done (lines 319-320)

Comment 23: Line 277: suggest change “retinal degeneration progression” to “retinal disorders”

Reply 23: This has been changed as suggested (line 323)

Adaptive Optics:

Comment 24: Line 284: change “visualization of the retina” to “visualization of the retina at a cellular level.”

Reply 24: This has been changed as suggested (line 329-330)

Comment 25: Lines 308-319: Rather than summarize the results of this study, please be more specific about how AO was useful or not useful for this study.

Reply 25: This paragraph was revised (lines 354-363).

DARC:

Comment 26: Line 359: Include that DARC is being explored in clinical trial as a novel method for detecting changes in the ganglion cells of the retina associated with glaucoma.

Reply 26: Done, and the NCT number was added (lines 416-418).

FIGURES 1 and 2

Comment 27: Provided images appear to be modified images of previous publication (ref 53), please site reference in figure legend and obtain permission to publish from journal with copyright if necessary

Reply 27: Figure 2 is a new figure. Figure 1 contains panels from our previous publication in TVST (reference 57 in revised manuscript). Following TVST Journal Policies: "If you would like to reuse a figure or table from an article that you previously published in *TVST*, you do not need written permission. When reprinting the *TVST* material, however, please include a full article citation." (<https://tvst.arvojournals.org/ss/forauthors.aspx>).

The reference is cited in the revised figure legend (lines 889-890)