Author's response to reviews

Title: Retrospective analyses of optical coherence tomography in recurrent macular edema following intravitreal therapy in patients with retinal vein occlusion

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Author's response to reviews: see over
Dear Dr. Khanna,

We appreciate the rapid review of our manuscript entitled “Retrospective analyses of optical coherence tomography in recurrent macular edema following intravitreal therapy in patients with retinal vein occlusion” and the helpful comments of the reviewers. Specific questions and comments from the reviewers are shown in italics below with our responses to each immediately following.

Referee 1: Fiona Harris
Minor Essential Revisions

1. This study would be enhanced by the addition of raw data, in addition to the processed data already presented in graphical form. It would be interesting to see the numerical values for the increases in macular thickness, as well as the non-averaged percentage increases, for each of the macular areas under review.

It does not seem feasible for us to present raw data from 429 episodes of RME where thickness estimates were obtained from 5 macular fields and compared to a similar number of data points from earlier baseline measurements. We agree that analyzing data including each episode of RME for a given subject, in addition to averaged percentages, is warranted and of interest. We have done these additional analyses. Nevertheless, we believe the only feasible way these data can be presented is in graphical form (Figures 2 and 4) as the data set is far too large to present in tabular form. Individual baseline and retreatment (Day 95) thicknesses, however, are given for CST and 3H for the scans shown in Figure 5.

2. The definition of ‘resolution of macular oedema’ (p.6, line 9-10) may need to be clarified as the subsequent introduction of the concept of ‘pseudobaseline’ could imply that there is some residual or persistent macular oedema, with the treatment / retreatment cycles possibly constituting a saw-tooth effect of progressively increasing macular thickness.

We agree that the term “pseudobaseline” was confusing. We’ve rewritten that section (pg 6, lines 10-17) and removed this term. It should be noted that per our request and approval from the IRB, OCT data were only transcribed from patients’ records for the visit where the greatest decrease in ME was seen (baseline) and at the time of retreatment. In looking at data for those individuals with at least 5 instances of RME, baseline values more typically showed a downward trend or a stable pattern as opposed to a saw-tooth effect of increasing macular thickness (reported on pg 12, lines 6-10).

3. There appears to be a typo on p.8, line 9: perhaps 3Q should actually read 3H?

Typo was corrected.
Discretionary Revisions

1. It would be interesting to see the data divided into three separate groups, based on those treated with anti-VEGF agents, those treated with steroids, and those receiving a combination of intravitreal agents, to ascertain whether there is a significant difference in findings between these groups. It is agreed that this might be interesting; however, those data were not collected when patient records were reviewed for this study (and IRB approval was not requested to capture these data). We’ve included discussion on the unknown effect of different intravitreal agents on the development and resolution of RME on page 13 (lines 12-18).

2. There appears to be a typo on page 3, line 22: I believe 'RME' should have read 'recurrent macular edema (RME)'. This first reference to RME now has the abbreviation defined as recurrent macular edema. We thank the reviewer for catching this error.

3. The reader may find it helpful for interpretation of the results if the range of duration of follow up (p.5, lines 17-18) is stated. This information was not captured when patient records were reviewed and therefore cannot be stated.

4. It may be helpful to rephrase the sentence on lines 8-9 of page 9 (under 'Discussion') and clarify whether the 'macular' of RME refers to the 1.5mm diameter clinical macula, or the larger anatomical macula. This is clarified on page 10 (lines 10-12)

It may be worth bearing in mind that the findings of this paper may be of limited value to a UK audience, where it is common practice to examine the OCT in display mode when assessing macular oedema in CRVO and BRVO, rather than relying solely on CRT values. A discussion of quantitative information (thickness measurements) and qualitative information (display mode) is now included (page 13, line 19 to page 14, line 2).

Referee 2: Emily Han Shao

An interesting paper with some nicely reasoned arguments based on literature. Below are some comments to address under discretionary revisions:

1) A mention of how type II error is avoided by the study. Although the difference between increase in CST and other measures such as 3Q and 3H were noted by the author as not statistically significant, given CST still showed the largest increase; it would be helpful if the authors mentioned in the method how Type II errors are avoided in their study by the selection of their sample size, as otherwise it could potentially be argued that CST increases were not statistically significantly greater than other measures because the sample size is not big enough. Avoidance of type II error is often determined by what level alpha is set at. While we didn’t specify alpha (the level of probability which is needed to be reached to accept significant differences or reject
the null hypothesis), post hoc probabilities in comparing CST with 3Q/H were very high. This and other
discussion pertaining to type II error is provided on page 10, line 16 through page 11, line 5.

2) Interesting mention of the study by Arema et al in the discussion that RME tends to shift from
extrafoveal fields towards the fovea with time, was this something the authors noted in their own
patient cohort?
We discuss our data in light of the Arema et al study with regard to our data presented in Figure 5 (Page
12, lines 19-23).

Again we appreciate the reviewers’ helpful comments and hope that we have adequately answered
their questions and concerns. Please contact me if there are any questions with our paper. We look
forward to its publication in *BMC Ophthalmology*.

Best regards,
Christopher M. de Fiebre, Ph.D.