AS-OCT quantification of anterior chamber inflammation – how close are we to a validated diagnostic tool?

Amal Minocha[1,2], Xiaoxuan Liu[3,4], Alastair K Denniston[3,4,5,6,7], Harry Petrushkin[2,5,8], Ameenat L Solebo[5,8,9,10]

1. University College London Medical School, London, UK

2. Moorfields Eye Hospitals NHS Foundation Trust, London, UK

3. Ophthalmology Department, University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

4. Academic Unit of Ophthalmology, Institute of Inflammation & Ageing, College of Medical and Dental Sciences, University of Birmingham, UK

5. NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, UK

6. Centre for Rare Diseases, Institute of Translational Medicine, Birmingham Health Partners, UK

7. Health Data Research UK, London, UK

8. Great Ormond Street Hospital for Children NHS Trust, London UK

9. Institute of Child Health, University College London, London, UK

10. National Institute for Health Research Biomedical Research Centre at UCL Great Ormond Street Institute of Child Health and Great Ormond Street Hospital, London UK

Corresponding address:

AL Solebo,

University College London Great Ormond Street Institute of Child Health

30 Guilford Street, London, WC1N 1EH, UK

No competing interests exist for any author.

Word count: 346/350

To the Editor:

We noted the recent use of anterior segment optical coherence tomography (AS-OCT) to quantify anterior chamber inflammation in a pilot study of intravitreal anti-vascular endothelial growth factor agents.(1) The authors reported an incidence of post-injection anterior chamber reaction of 30.5%, as detected on AS-OCT. This is more than 50 fold higher than previous clinical reports using slit lamp based examinations.

The perfect diagnostic tool is able to discriminate between subjects with and without disease. The current gold standard diagnostic for grading anterior chamber inflammation is slit lamp bio-microscopy using the Standardised Uveitis Nomenclature (SUN) inflammatory cell count scoring system. Under this system, "0" (a level denoting disease inactivity) represents no cells seen by the clinician within a 1mm beam of light at maximal intensity. Crucially, it does not denote the absence of anterior chamber cells.

We have derived the diagnostic accuracy measures, specifically sensitivity, specificity, negative and positive predictive values (NPV / PPV), from five of the key recent AS-OCT validation studies (Table 1).(2-6) Figure 1 shows the accuracy metrics of AS-OCT for active inflammation in each of these studies. The consistently high negative predictive values suggest that AS-OCT would be able to exclude anterior uveitis with high certainty. However, all studies reported detection of free floating cells in eyes which were 'clinically' free of inflammation. If one were to directly apply the thresholds provided by the SUN grading to AS-OCT, it would result in over-diagnosis and over-treatment. Further clinical validation and clinical utility work on normal and diseased cohorts is needed for us to understand the clinical relevance of imaging based cell counts.

Anterior uveitis is the most common form of uveitis world-wide, and is a common cause of attendance to emergency ophthalmology care. This disease burden, combined with a

worsening national shortfall of ophthalmologists represent a challenge to care provision. The use of virtual clinics has revolutionised the delivery of glaucoma and age related macular degeneration services. AS-OCT quantification of anterior chamber inflammation could, following further clinical validation work, emerge as a valuable tool for improving the quality and efficiency of clinical service provision.

References

1. Liao X, Jin C, Chen W, Zhang G, Cen LP, Ng DS, Chen H. Quantification of anterior chamber reaction after intravitreal injections of conbercept and ranibizumab: a pilot study. Eye (Lond). 2019 Jul 18. doi: 10.1038/s41433-019-0537-5

2. Invernizzi, A., Marchi, S., Aldigeri, R., Mastrofilippo, V., Viscogliosi, F., Soldani, A., Cimino, L. Objective Quantification of Anterior Chamber Inflammation. Ophthalmology (2017) 124(11):1670–1677. doi:10.1016/j.ophtha.2017.05.013.

3. Baghdasaryan, E., Tepelus, T.C., Marion, K.M, Huang, J, Huang, P, Sadda, SR, Lee, OL. Analysis of ocular inflammation in anterior chamber-involving uveitis using swept-source anterior segment OCT. (2018) Int Ophthalmology. doi:10.1007/s10792-018-1005-0.

4. Sharma, S., Lowder, C. Y., Vasanji, A., Baynes, K., Kaiser, P. K., & Srivastava, S. K. Automated Analysis of Anterior Chamber Inflammation by Spectral-Domain Optical Coherence Tomography. Ophthalmology (2015) 122(7):1464–1470. doi:10.1016/j.ophtha.2015.02.032..

5. Igbre, A. O., Rico, M. C., & Garg, S. J. High-speed optical coherence tomography as a reliable adjuvant tool to grade ocular anterior chamber inflammation: Retina (2014) 34(3):504–508. doi:10.1097/IAE.0b013e31829f73bd.

6. Li, Y., Lowder, C., Zhang, X., & Huang, D. Anterior Chamber Cell Grading by Optical Coherence Tomography. Investigative Opthalmology & Visual Science (2013) 54(1):258. doi:10.1167/iovs.12-10477