



FINAL REPORT FOR 2014 RETINA AUSTRALIA RESEARCH GRANT:

**Validation of Novel Outcome Measures for Use in
Vision Restoration Clinical Trials**

Investigators: Dr Lauren Ayton & Assoc/Prof Sharon Bentley

Date of report: 9 March 2015

1. Executive Summary

Until recently, there have been no possible treatments to restore vision in those with profound vision loss. However, progress in the field of vision restoration has led to the development of stem cells to replace damaged cells, gene therapy to correct genetic defects and visual prostheses to simulate vision for end stage diseases.¹⁻³ In this new era, it is necessary to accurately define what level of vision remains prior to any intervention, and then assess what will initially be small improvements in visual function. Visual acuity, measured using conventional tools (i.e. Snellen letter acuity charts) are not appropriate at these low levels of acuity and fail to capture improvement in functional vision (i.e. levels of vision that are useful in performing basic daily living tasks) or improvement in quality of life. Early clinical trials of some of these novel treatments have shown clinical efficacy⁴⁻⁶, but have also highlighted the difficulties in assessing vision at such a low level. At present, individual research teams use tests that best suit their needs, but there is no standardisation between groups. This means that it is currently not possible to compare the performance of different treatment devices and modalities, due to the lack of common validated outcome measures⁷.

Retina Australia supported our research project in 2014, which aimed to validate a set of novel outcome measures that were developed by our team of occupational therapists, orientation and mobility experts, ophthalmologists, optometrists and orthoptists at the Centre for Eye Research Australia. We are pleased to report that the study was a success, with the tasks being assessed in a group of 40 people with very poor visual acuity (less than 6/60; legal blindness) and/or severe visual field loss (less than 20° diameter) from retinitis pigmentosa.

2. Activities Undertaken & Findings

In this study, we enrolled a group of 40 individuals who had advanced retinitis pigmentosa. The majority of these people contacted us after receiving information about our work through the Retina Australia newsletter. The study consisted of a 3 to 4 hour visit, in which a number of vision tests and activities of daily living were completed. An occupational therapist completed a range of task assessments which involved people sorting clothes (grey, white and black items), searching for an object on a table or selecting specific items from a shelf. An orientation and mobility (O&M) specialist completed a number of O&M tests, including walking through an environment with obstacles, and using orientation skills to produce a map of a room setup.

The study provided us with a large dataset, from which we were able to make decisions about which tasks provided the most useful information. In particular, we were looking for tasks that could be used in vision restoration clinical trials, to inform which interventions are most beneficial. The resulting battery of tests has been named the LoVADA (Low Vision Assessment of Daily Activities).

The LoVADA has now been used in the world-first clinical trial of a suprachoroidal retinal prosthesis ("bionic eye") in Melbourne, and it is hoped that it will be used in international trials in the future. Dr Ayton and

Assoc/Prof Bentley are both involved in an International Task Force (called the Harmonization of Outcomes and Vision Endpoints in Vision Restoration, or the HOVER Task Force), which is aiming to develop standards of visual function testing in trials. This group of world-leading experts is developing guidelines that now include reference to the LoVADA protocols, and has led to a rapid international recognition of this novel tool. In addition, we are collaborating with the Wenzhou Medical University in China, who will be evaluating the use of the LoVADA protocol in a Chinese population.

3. Publications

The results of the LoVADA study have been published in one of the top-ranking vision journals, *Investigative Ophthalmology and Vision Science* (attached to this report):

1. Finger RP, McSweeney SC, Deverell LA, O'Hare F, Bentley SA, Luu CD, Guymer RH, Ayton LN. Developing an instrumental activities of daily living tool as part of the Low Vision Assessment of Daily Activities (LoVADA) protocol. *Invest Ophthal Vis Sci* 2014;55(12):8458-66.

Two additional publications on the LoVADA are currently under preparation or under review.

2. Ayton LN*, Finger RP*, Deverell L, O'Hare F, McSweeney SC, Luu CD, Fenwick EK, Keeffe JE, Guymer RH, Bentley SA. Developing a very low vision orientation and mobility test battery as part of the Low Vision Assessment of Daily Activities (LoVADA) protocol. Currently under review at *Invest Ophthal Vis Sci*.
3. Ayton LN, McSweeney SC, O'Hare F, Deverell L, McCarthy CD, Petoe MA, Barnes N, Finger RP, Bentley SA, Luu CD, Keeffe JE, Allen PJ, Guymer RH, for the Bionic Vision Australia Consortium. A prototype suprachoroidal retinal prosthesis improves performance on basic instrumental activities of daily living outcomes. Currently under preparation.

Finally, one additional manuscript on this subject cohort has recently been accepted by the journal *Ophthalmology*:

4. O'Hare F, Bentley SA, Wu Z, Guymer RH, Luu CD, Ayton LN. Charles Bonnet syndrome in advanced retinitis pigmentosa. Accepted by *Ophthalmology*, 7 March 2015.

4. Future Work and Conclusions

The results of this study were used as background information in a successful application to the National Health and Medical Research Council, and this further funding will allow us to continue our work into the Bionic Eye and vision restoration. As well as using the LoVADA protocol in this next bionic eye clinical trial, we also hope to test it in a larger population of people, particularly in those with non-retinal causes of vision loss (such as trauma). We believe that the learnings from this study will be used by many different research groups around the world, and are grateful for the support provided by Retina Australia.

5. References

1. Bainbridge JW, Smith AJ, Barker SS, et al. Effect of gene therapy on visual function in Leber's congenital amaurosis. *N Engl J Med* 2008;358(21):2231-9.
2. Schwartz SD, Hubschman JP, Heilwell G, et al. Embryonic stem cell trials for macular degeneration: a preliminary report. *Lancet* 2012;379(9817):713-20.
3. Rosenfeld PJ, Brown DM, Heier JS, et al. Ranibizumab for neovascular age-related macular degeneration. *N Engl J Med* 2006;355(14):1419-31.
4. Zrenner E, Bartz-Schmidt KU, Benav H, et al. Subretinal electronic chips allow blind patients to read letters and combine them to words. *Proc Biol Sci* 2011;278(1711):1489-97.
5. da Cruz L, Coley BF, Dorn J, et al. The Argus II epiretinal prosthesis system allows letter and word reading and long-term function in patients with profound vision loss. *Br J Ophthalmol* 2013(5):632-6.
6. Ayton LN, Blamey PJ, Guymer RH, et al. First-in-human trial of a novel suprachoroidal retinal prosthesis. *PLOS ONE* 2014;9(12):e115239.
7. Ayton LN, Rizzo JF. Psychophysical testing of visual prosthetic devices: A call to establish a multi-national joint task force. *J Neural Eng* 2014;11(2):020301.