Impact case study (REF3b)

Institution: University College London

Unit of Assessment: 1 - Clinical Medicine

Title of case study: The Moorfields Regression Analysis improves the management of glaucoma

1. Summary of the impact

Prevention of blindness caused by glaucoma requires an early diagnosis, for which we have developed new clinical techniques. The Moorfields Regression Analysis (MRA) is an algorithm that we developed for the Heidelberg Retina Tomograph, an imaging device for glaucoma diagnostics. The MRA made it possible, for the first time, to accurately quantify structural damage caused by glaucoma. The MRA allows earlier diagnosis of glaucoma, and has been adopted worldwide.

2. Underpinning research

Research conducted at UCL since 1994 has improved the clinical management of glaucoma, a disorder characterised by optic nerve damage and progressive visual field (VF) loss. The major risk factor for this condition is high intraocular pressure (IOP), and the prevention of blindness caused by glaucoma requires an early diagnosis. In glaucoma management, both functional and structural examinations are used to confirm and monitor the disease.

For functional examinations, it is fundamental that VF tests are conducted to identify vision loss but VF measurements are highly variable and, as shown by work done by our group, frequent monitoring is therefore needed. In collaboration with Dalhousie University (Halifax, Canada), Garway-Heath worked on practical recommendations for measuring the rates of VF change in glaucoma **[1]**. Clear guidance was given to clinicians on how many VF tests they need to acquire within a certain period of time to identify rapid deterioration of the disease. The work was very quickly adopted worldwide and has been widely cited.

Structural examinations can be performed by examining changes in the optic nerve head (ONH), which can be detected by examining the ONH with a slit lamp microscope, the most frequently used instrument by ophthalmologists, or with high-resolution photography (stereoscopic photography). These techniques, however, are subjective and they cannot be used to adequately quantify the amount of damage. Because of these limitations, structural examinations in glaucoma have not been used optimally and glaucoma management has mostly relied on VF testing. The introduction of automated imaging techniques laid the foundations for objective analysis of the ONH. However, these techniques lacked an adequate algorithm to enable the accurate quantification of ONH damage. To address this need, Garway-Heath and his team developed the Moorfields Regression Analysis (MRA), for one of the earliest and best-established imaging devices, the Heidelberg Retina Tomograph (HRT) **[2]**. The HRT measures the amount of neural tissue present in the ONH, which is reduced by glaucoma. The MRA enabled the classification of ONH damage and revolutionised the use of imaging in the clinical management of glaucoma **[3, 4]**. In a recent Europe-wide study, the MRA was validated further: it performed better than general ophthalmologists and most glaucoma specialists in identifying glaucomatous optic nerves **[5]**.

It is important that clinicians and researchers appreciate how functional and structural defects in glaucoma are related, so that the agreement of outputs from different diagnostic test modalities (structural and functional) can be assessed. The 'Garway-Heath Map' was developed to facilitate this understanding and it shows the anatomical relationship between VF test points and regions of the ONH. The MRA output classifies regions of the optic nerve head as within or outside normal limits; the map helps to correlate vision loss with the pattern and extent of damage to the optic nerve **[6]**.

3. References to the research

[1] Chauhan BC, Garway-Heath DF, Goñi FJ, Rossetti L, Bengtsson B, Viswanathan AC, Heijl A.

Practical recommendations for measuring rates of visual field change in glaucoma. Br J Ophthalmol. 2008 Apr;92(4):569-73. http://dx.doi.org/10.1136/bjo.2007.135012

[2] Heidelberg Engineering website, showing how the Moorfields Regression Analysis is used in their software: http://www.heidelbergengineering.co.uk/products/hrt/hrt-glaucoma/moorfields-regression-analysis/

[3] Garway-Heath DF, Hitchings RA. Quantitative evaluation of the optic nerve head in early glaucoma. Br J Ophthalmol. 1998 Apr;82(4):352-61. http://dx.doi.org/10.1136/bjo.82.4.352

[4] Wollstein G, Garway-Heath DF, Hitchings RA. Identification of early glaucoma cases with the scanning laser ophthalmoscope. Ophthalmology. 1998 Aug;105(8):1557-63. http://dx.doi.org/10.1016/S0161-6420(98)98047-2

[5] Reus NJ, Lemij HG, Garway-Heath DF, Airaksinen PJ, Anton A, Bron AM, Faschinger C, Holló G, Iester M, Jonas JB, Mistlberger A, Topouzis F, Zeyen TG. Clinical assessment of stereoscopic optic disc photographs for glaucoma: the European Optic Disc Assessment Trial. Ophthalmology. 2010 Apr;117(4):717-23. http://dx.doi.org/10.1016/j.ophtha.2009.09.026

[6] Garway-Heath DF, Poinoosawmy D, Fitzke FW, Hitchings RA. Mapping the visual field to the optic disc in normal tension glaucoma eyes. Ophthalmology. 2000 Oct;107(10):1809-15. http://dx.doi.org/10.1016/S0161-6420(00)00284-0

4. Details of the impact

Glaucoma is known as 'the silent thief of sight' because most people with glaucoma have no early symptoms or pain. By the time a patient is aware of vision loss, the disease is usually quite advanced. Late diagnosis is one of the most important risk factors for glaucoma blindness. Left undiagnosed and untreated, glaucoma can lead to irreversible blindness. If the condition is detected early enough, it is often possible to halt its development or delay its progression with medical or surgical treatment **[a]**. Diagnostic and monitoring techniques, therefore, play a pivotal role in glaucoma management. The research in this case study has contributed to the improvement of glaucoma healthcare by providing new diagnostic tools and evidence for the required frequency of monitoring the VF.

The diagnostic and predictive power of the MRA has led to the worldwide acceptance that imaging of the ONH should be performed in addition to VF monitoring, in order to characterise glaucomatous damage to the eye **[b]**. The MRA has also become a 'reference standard' for establishing the performance of other imaging devices in establishing whether or not glaucoma is present **[c]** and in predicting its development in patients with high IOP **[d]**. The worldwide scale of use of this technology is substantial. At Moorfields Eye Hospital, all newly referred glaucoma patients are now imaged using the HRT, which means that around 32,500 patients in this hospital alone have been benefited from this technique for the period 2009–2013 **[e]**. Nationwide and worldwide, this number is much higher.

The pre-eminence of the MRA is further illustrated through its use as the technique of choice in glaucoma imaging (scanning laser ophthalmoscopy) diagnostics worldwide, with more than 6,500 HRT devices having been sold, mostly since the incorporation of the MRA into the device's software in 1999. For more than 15 years, the MRA has remained a robust indicator of structural change, which has contributed to the success of the HRT and its adoption by clinicians worldwide. Heidelberg Engineering have confirmed that "*The inclusion of the Moorfields Regression Analysis developed with Professor Garway-Heath has been one of the contributing factors to the adoption and success of the HRT within the glaucoma community. MRA has become synonymous with HRT and is considered one of the most important single tests for the early diagnosis of glaucoma*" **[f]**.

The development of a map that correlates structural findings with functional loss is another key achievement in the field of glaucoma management. As a result of this research, it is now possible

for clinicians to understand the link between vision loss and damage to the optic nerve that transmits visual information from the eye to the brain. The anatomical map known as the 'Garway-Heath Map' was developed to help establish this correlation and is now used worldwide for the evaluation of glaucoma patients and in clinical research in glaucoma and other ocular conditions **[g]**. In the diagnostics industry, it is incoprporated into widely-used diagnostic software such as in the Heidelberg Eye Explorer **[h]**. It has recently been incorporated into FORUM Glaucoma Workplace (Carl Zeiss) **[i]**, software for the presentation of diagnostic test results, allowing clinicians to visualise simultaneously functional and structural outcomes of patients. Heidelberg Engineering and Carl Zeiss are the market leaders in glaucoma diagnostics and the 'Garway-Heath map' has become central to the display of the diagnostic results.

The significance of our research and publications on imaging is evident from their extensive referencing in European management guidelines **[j]** and their citation as Suggested Reference Texts in American Preferred Practice Pattern (PPP) Guidelines **[k]**. The widespread success of the HRT since the incorporation of the MRA into its software has boosted research and development in this field. This, in turn, has led to widespread use of imaging devices in the clinic as confirmed in the European Glaucoma Society (EGS) guidelines **[l]**. Using our publications as the basis for its evidence, the EGS recommends the use of imaging in the diagnosis of glaucoma and in monitoring its progression. Likewise, the American PPP Guidelines recommend the use of imaging devices as diagnostic tools, and recognise their increasing clinical importance **[m]**. Our work on imaging has also been used as the basis for evaluating the evidence for the use of imaging devices in screening for glaucoma **[n]**. Our work on the frequency of VF testing required to identify patients at risk of lifetime visual impairment has been used by the EGS in its guidelines to recommend the optimal frequency of VF testing in glaucoma management **[j].**

5. Sources to corroborate the impact

[a] Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M; Early Manifest Glaucoma Trial Group. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002 Oct;120(10):1268-79. http://dx.doi.org/10.1001/archopht.120.10.1268

[b] Medved N, Cvenkel B. Diagnostic accuracy of the Moorfields Regression Analysis using the Heidelberg Retina Tomograph in glaucoma patients with visual field defects. Eur J Ophthalmol. 2007 Mar-Apr;17(2):216-22. http://www.ncbi.nlm.nih.gov/pubmed/17415695

[c] Leung CK, Ye C, Weinreb RN, Cheung CY, Qiu Q, Liu S, Xu G, Lam DS. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography a study on diagnostic agreement with Heidelberg Retinal Tomograph. Ophthalmology. 2010 Feb;117(2):267-74. http://dx.doi.org/10.1016/j.ophtha.2009.06.061.

[d] Weinreb RN, Zangwill LM, Jain S, Becerra LM, Dirkes K, Piltz-Seymour JR, Cioffi GA, Trick GL, Coleman AL, Brandt JD, Liebmann JM, Gordon MO, Kass MA; OHTS CSLO Ancillary Study Group. Predicting the onset of glaucoma: the confocal scanning laser ophthalmoscopy ancillary study to the Ocular Hypertension Treatment Study. Ophthalmology. 2010 Sep;117(9):1674-83. http://dx.doi.org/10.1016/j.ophtha.2010.03.044.

[e] Source: Moorfields Eye Hospital, Outpatients and Diagnostics Department. Copy of data available on request.

[f] Testimony provided by Heidelberg Engineering. Copy available on request.

[g] Kupersmith MJ, Anderson S, Durbin M, Kardon R. Scanning laser polarimetry, but not optical coherence tomography predicts permanent visual field loss in acute nonarteritic anterior ischemic optic neuropathy. Invest Ophthalmol Vis Sci. 2013 Aug 15;54(8):5514-9. http://dx.doi.org/10.1167/iovs.13-12253.

[h] Heidelberg Engineering's information on the Heidelberg Eye Explorer, with reference to the 'Garway-Heath map':
http://www.innovamed.com/sites/default/files/hrthepbrochureengllowres.pdf

[i] Carl Zeiss website with information on FORUM Glaucoma Workplace "*RNFL segmental deviation maps are combined with pattern deviation results from HFA visual fields using a methodology published by Garway-Heath et al.*":
http://meditec.zeiss.com/meditec/en_de/products/ophthalmology/forum.html#inpagetabs-2

[j] The work by Garway-Heath on imaging has been incorporated by the European Glaucoma Society (EGS) into its Terminology and Guidelines for Glaucoma, 3rd edition. *See page 83 (references 28, 31, 32, 34, 37, 38, 40, 41), page 87 (reference 6).*
http://www.eugs.org/eng/EGS_guidelines.asp.

[k] The work by Garway-Heath on imaging and structure/function correlation has been cited in the Suggested Reference Texts of the American Academy of Ophthalmology Preferred Practice Pattern Guidelines (Weinreb RN, Greve EL, eds. Glaucoma Diagnosis: Structure and Function. World Glaucoma Association Consensus Series - 1. The Netherlands: Kugler Publications; 2004). http://one.aao.org/preferred-practice-pattern/primary-openangle-glaucoma-suspect-ppp--october-20.

[l] Burr JM, Mowatt G, Hernández R, Siddiqui MA, Cook J, Lourenco T, Ramsay C, Vale L, Fraser C, Azuara-Blanco A, Deeks J, Cairns J, Wormald R, McPherson S, Rabindranath K, Grant A. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. Health Technol Assess. 2007 Oct;11(41):iii-iv, ix-x, 1-190. Review. http://dx.doi.org/10.3310/hta11410