Project Details	
Project Code	MRCNMH26Ca Redmond
Title	Novel area-modulation stimuli for identifying changes in visual field sensitivity in Age-related Macular Degeneration (AMD)
Research Theme	NMH
Project Type	Dry lab
Summary	Age-related macular degeneration (AMD) is one of the world's leading causes of sight loss. Traditional measures of vision in AMD are of gross loss and do not adequately describe vision that is most important for everyday tasks. We recently discovered a functional biomarker for AMD through basic psychophysics research and have developed a novel visual stimulus to more accurately measure vision clinically. The PhD (aligned with the REVAMP Study) aims to understand the extent to which our novel method offers improvements over standard methods in identification of visual loss in AMD and how they relate to changes in retinal structure.
Description	Age-related macular degeneration (AMD) is one of the world's leading causes of sight loss. Approximately 500,000 people in the UK are visually impaired due to AMD, with numbers projected to rise to 1.23 million by 2050 with population ageing. AMD presents in two main forms: (1) 'wet', which causes rapid, severe vision loss but is treatable with anti-VEGF injections; and (2) 'dry', which progresses more slowly, is currently untreatable, and is the focus of a growing number of clinical trials. Advances in Optical Coherence Tomography (OCT) allow clinical observation of detailed retinal and RPE changes associated with AMD. However, patients are more concerned with how their vision is affected, which OCT and other imaging techniques cannot measure. Clinically, vision loss in AMD is assessed with visual acuity charts which test foveal vision. This approach does not adequately assess vision across the wider macular region, which is important for daily tasks. Microperimetry is sometimes used to address this, but its scientific basis is limited, and it is likely insensitive to all but moderate-to-severe vision loss. Microperimetry involves presenting small light stimuli (Goldmann III, "GIII") of varying brightness to central visual field locations while tracking gaze, requiring patients to press a button when they see a stimulus. Aside from gaze-tracking, this is essentially the same method used for standard perimetry in glaucoma. Many parameters in microperimetry were adopted wholesale from traditional glaucoma testing; not because they are optimised for AMD, but due to clinical familiarity/interpretability. These parameters originated ~50 years ago from Goldmann kinetic perimetry and were designed before underlying mechanisms of glaucoma or AMD were understood. Successive generations of perimetric tests have inherited these outdated design choices, despite their limitations being well-documented. The GIII stimulus does not target glaucoma- or AMD-specific functional biomarkers. High measurement variability also undermines detection of early or progressive vision loss, contributing to the often-cited challenge in glaucoma that several years of testing are required to confirm moderate decline. Redesigned perimetric techniques informed by modern understanding of visual neuroscience and clinical science are a major unmet need.

	We propose to investigate the utility of Area-Modulated Perimetry (AMP) in patients with AMD. AMP uses stimuli with fixed brightness that vary in size, designed to directly measure changes in spatial summation; a psychophysical attribute identified by our group as a functional biomarker for AMD. AMP therefore departs fundamentally from microperimetry, which relies on outdated GIII stimuli and is well-positioned to offer improved diagnostic utility over existing tests like microperimetry. AMP-derived functional measures may also correlate more closely with structural changes in the retina than GIII-derived measures. This proposal builds directly on our prior success in glaucoma, where we demonstrated superiority of AMP over standard perimetry in the Research and Evaluation of Area-Modulation Perimetry (REVAMP) Study. REVAMP is a UK-wide, multi-site, academic-led research programme funded by the MRC DPFS (MR/V038516/1), to translate AMP from laboratory to clinic. The proposal is a direct and logical extension of our previous glaucoma work into AMD. It is therefore relatively low-risk yet allows development of scientific skills, and has high potential for translational impact. Research question: Do area-modulated stimuli offer greater signal/noise ratio than conventional GIII stimuli in investigation of visual loss in AMD? Objective-1: Determine and compare signal/noise ratio for area-modulated and GIII stimuli in a cohort of patients with AMD. 'Signal' will be calculated as the pointwise difference between measured visual thresholds and those predicted for age-similar controls (REVAMP normative database). 'Noise' will be the variance in these differences over 5 repeat visits. Objective-2: Investigate the relationship between AMP thresholds and underlying retinal/RPE structure. Pointwise correlations between function (AMP, GIII thresholds) and structure (RPE thickness, whole retinal thickness) will be performed. AMD will be stratified by severity. Spatial concordance between locations with similar levels of structural and functional damage (separately for each stimulus) will be quantified with the Dice similarity coefficient. Objective-3: Validate a model for converting GIII thresholds to AMP equivalents. We previously developed a model to convert legacy GIII data to AMP, enabling incorporation of legacy data for clinical continuity as AMD testing is translated to clinics. Data from glaucoma patients and healthy individuals informed the model, and the student will determine if it remains appropriate for AMD. If not, the student's data will inform an AMD-specific model. Patients will be recruited from the Macular Research Group participant database (Cardiff University). Taking ownership: In Y1, the student will prepare an ethics amendment to REVAMP to include the PhD study, update the protocol, and develop SOPs. They will receive training in eye-tracking (with Dr Lee McIlreavy) and self-guided MATLAB training to adapt code for experiments. Progress will be reviewed regularly, supporting independent learning. If the student proposes an improved, realistic, achievable alternative

	method to address a research objective, they will be encouraged to lead its development and execution, with supervisory support.
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