Journal Article Review

Identifying features of early and late AMD: A comparison of MultiColor versus traditional color fundus photography

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Background and Purpose

Color fundus photography (CFP) has long been used to identify and document pathological hallmarks of age-related macular degeneration (AMD). While it remains the gold standard in AMD imaging, there have been numerous technological advances that may offer additional clinical information beyond CFP. While new technologies have been qualitatively described, a quantitative approach is required to validate alternative imaging techniques. Accordingly, this study compares the sensitivity and specificity of CFP to SPECTRALIS® MultiColor (MC) technology for detecting and grading of the following features of AMD: hard drusen, soft drusen, reticular pseudodrusen, pigment clumping, non-geographic atrophy (GA) pigmentation, atrophy, hemorrhage, and fibrosis.

Methods

A total of 59 patients were included from participating hospital clinics and the Northern Ireland Cohort for the Longitudinal study of aging (NICOLA) dataset. 105 eyes with gradable images on both modalities were included. A Canon CX-1 Digital Fundus Camera was used for 50° field-of-view CFP, while the SPECTRALIS device captured a single 30° MC image, centered on the macula. The MC modality generates a composite image from blue (486 nm), green (518 nm), and infrared (IR, 815 nm) wavelengths. The user can then choose to view any of the individual channels, or a pseudocolor composite of all three. Participants also had spectral-domain optical coherence tomography (SD-OCT) images taken as an additional imaging modality. CFP, MC, and OCT images were anonymized and unlinked for grading at the NetwORC UK reading center. The authors systematically graded the images for the relevant features. Sensitivity and specificity were calculated between CFP and MC, and when there was a disagreement between modalities, OCT scans were used as an adjudicator.

Discussion

The authors describe the appearance and detection of each of the AMD features on both CFP and MC.

- All drusen subtypes (hard, soft, and reticular) were detected more frequently with MC, while the drusen edges were better defined with MC (Fig. 1). The higher detection rate of reticular pseudodrusen (19.8% on MC compared to 7% with CFP), a drusen subtype associated with increased risk for developing advanced AMD, suggests that MC is potentially important in the monitoring of AMD (Fig. 2).
- Focal GA could be easily distinguished on MC, as these areas had sharply delineated margins, and the interior of these areas appeared orange in color on the MC composite (Fig. 3). This important finding may help physicians identify foveal sparing with MC.
- Areas of hemorrhage appeared “dark red and occasionally brown/black” on MC, in comparison to the brighter red seen with CFP (Fig. 4). This is the one late AMD feature which is better visualized on CFP than on MC images; the authors noted that CFP was good for detecting small hemorrhages in particular.
- On MC, pigment clumping appeared either as “dark brown-black” in cases with RPE hypertrophy or as bright orange/red in other pigment clumping cases. Pigment clumping was detected more frequently on CFP than MC. Non-GA hypopigmentation had a “less striking color with undefined margins” on MC, and corresponded to areas of diffuse atrophy on the CFP.
- Fibrous tissue appeared as “bright lime-green or yellowish areas” on MC, and the margins of the fibrosis were “sharply delineated.” (Fig. 5). This indicates the utility of MC for detecting changes in fibrotic areas over time and may aid in assessing this important potential pharmaceutical target.

When comparing the two modalities directly for early AMD features, MC detected all features more frequently than CFP, with the largest difference seen in reticular pseudodrusen. For advanced AMD signs, MC detected more fibrosis and atrophy compared to CFP (Fibrosis: 24.2% on MC and 15.6% on CFP; Atrophy: 33.7% on MC and 27.1% for CFP).The authors also looked at the three different channels that make up the MC composite images and found that different channels were optimal for different features of AMD: IR was ideal for hard drusen and non-GA hypopigmentation, while hemorrhages and fibrosis were best visualized in the green channel.

Finally, the specificity and sensitivity were compared directly for CFP and MC. With CFP as the basis for analysis, MC identified soft drusen (85%), reticular drusen (83%), atrophy, and fibrosis (100%). When MC was instead used as the basis, CFP was less sensitive identifying soft drusen (58%), reticular drusen (28%), atrophy (83%), and fibrosis (68%). When discrepancies arose between MC and CFP, the OCT scans most often confirmed the MC findings for hard drusen (14 of 17 discrepancies), soft drusen (8 of 10), reticular drusen (12 of 14), atrophy (3 of 5), and fibrosis (6 of 8). Hemorrhages and non-GA hypopigmentation were more concordant with CFP on OCT (2 of 2 for hemorrhages and 6 of 8 discrepancies for non-GA hypopigmentation).

Conclusion

This study shows that “for most of the early and late AMD lesion features, MultiColor demonstrated greater sensitivity than CFP, especially for the detection of reticular drusen.” These findings demonstrate the clinical utility of this advanced imaging modality, as it provides a new form of focused information to study features of AMD. The study illustrates that MultiColor images show distinct structures at different depths within the retina. From a practical clinical standpoint, the authors also note that the SPECTRALIS imaging platform allows capture of eye-tracked OCT images and MC images on the same machine, which allows the patient to remain seated at a single device instead of moving between devices. Additionally, as imaging biomarkers become more widely accepted clinical trial endpoints, techniques like MultiColor will offer more specific detection of important AMD features. The SPECTRALIS MultiColor three-wavelength imaging approach will aid in feature grading and the assesment of various forms of retinal pathology.

Fig 1. Soft drusen in AMD.

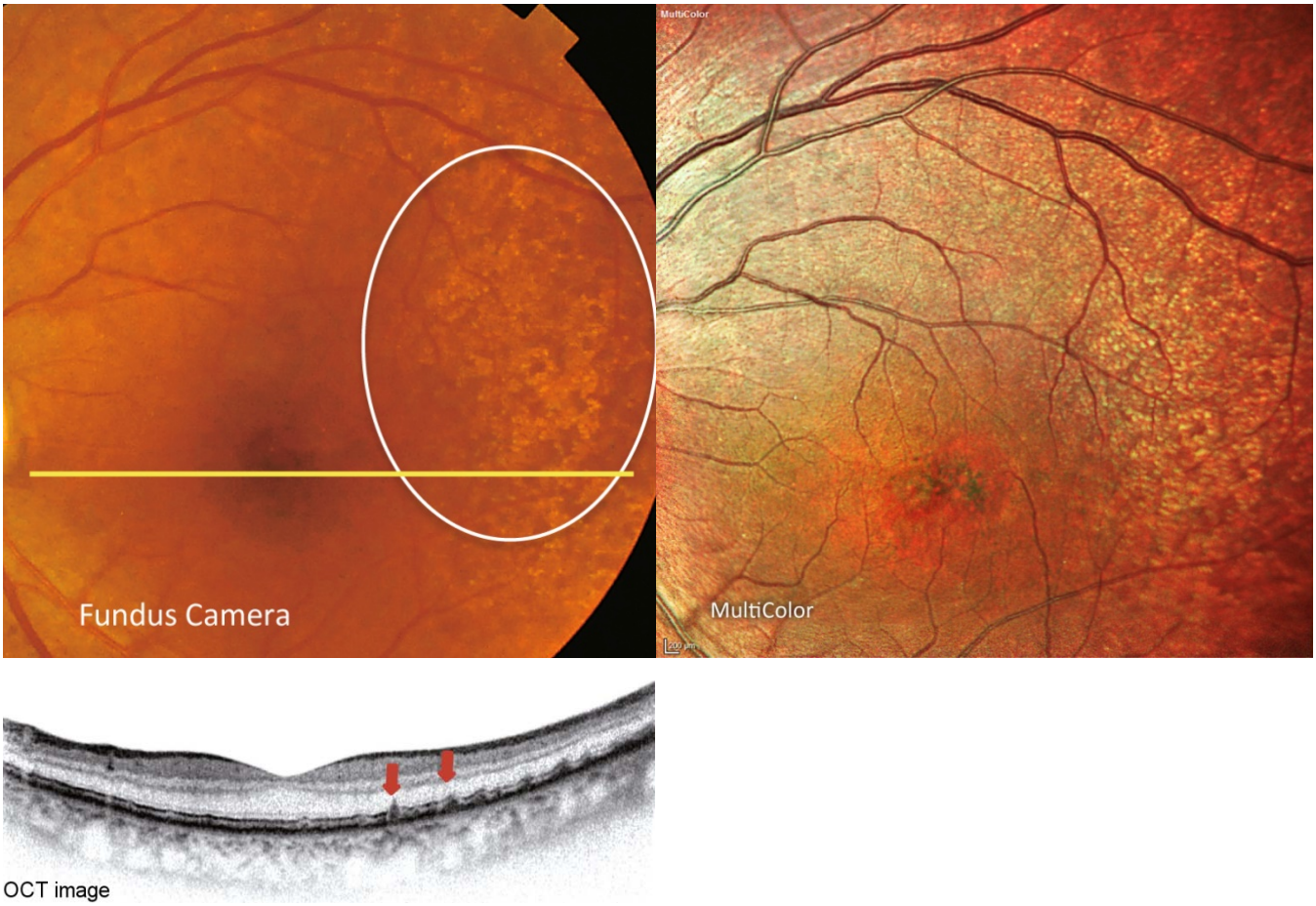

Fig 2. Reticular pseudodrusen in AMD (courtesy of Dr. Sonoda, Kagoshima University).

Fig 3. Geographic atrophy in AMD.

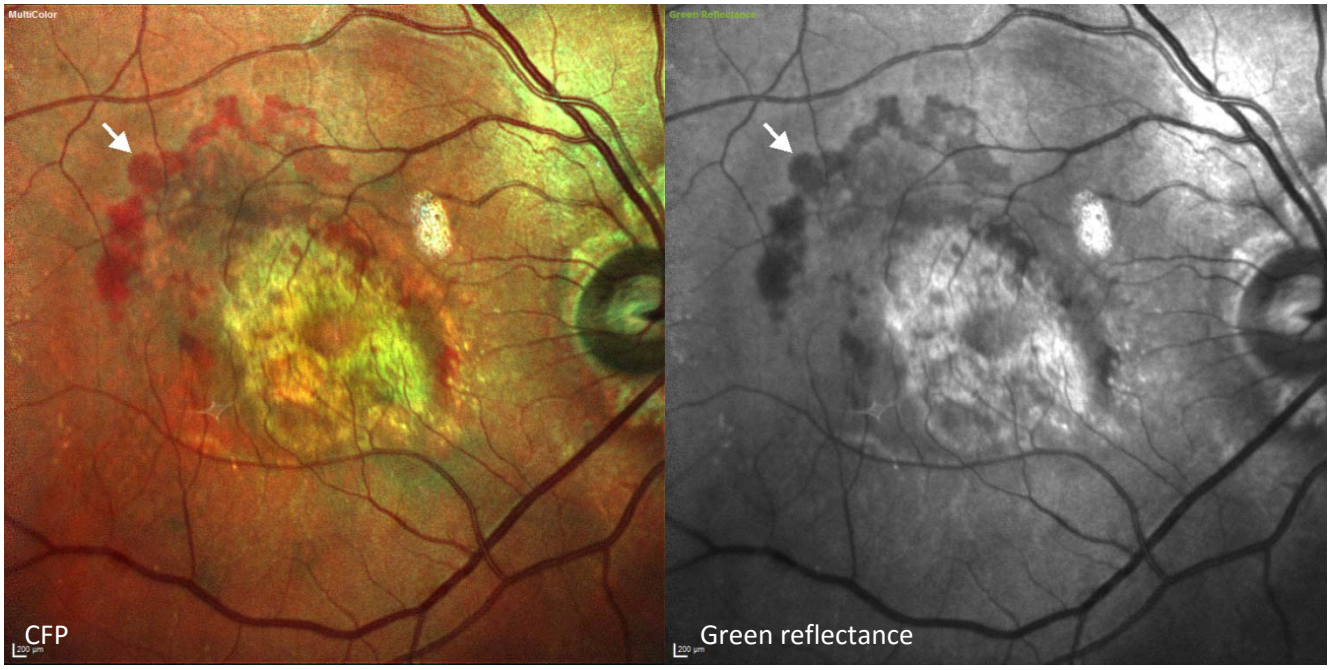

Fig 4. CNV with hemorrhages in AMD. Note the strong absorbance of green light in the green reflectance image (right, arrow).

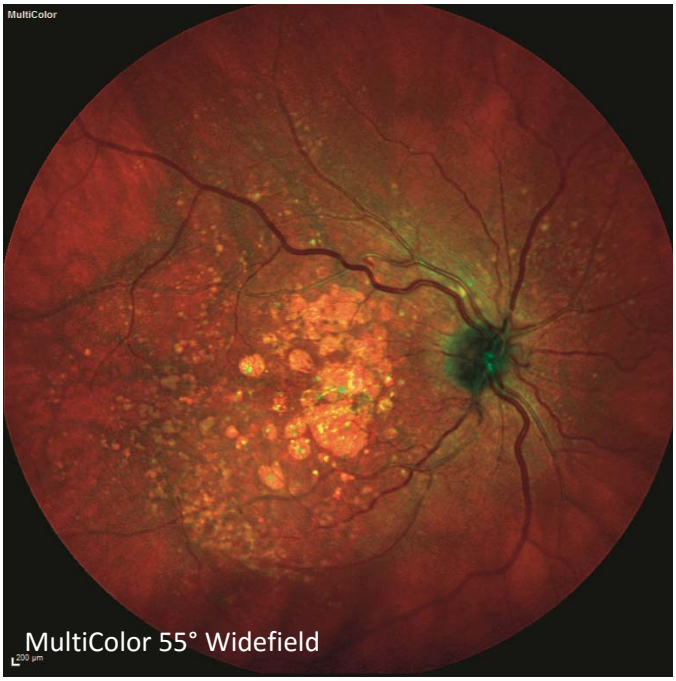

Fig 5. Areas of geographic atrophy with subretinal fibrosis (green areas within GA).