Policy Number	**OTH903.032**
Policy Effective Date	**02/15/2025**
Policy End Date	**12/31/2025**

Digital Imaging Software For Analyzing Time Series Retinal Images

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

Use of computer software to animate and analyze a time series of retinal images (e.g., MatchedFlicker®) is considered experimental, investigational and/or unproven for any indication, including but not limited to monitoring disease progression.

Policy Guidelines

There is no specific procedure code for computer software to animate and analyze a time series of retinal images (e.g., MatchedFlicker®) therefore, miscellaneous code 92499 might be used.

Description

The retina is a thin layer of tissue on the inside back wall of the eye, containing millions of light-sensitive cells and nerve cells that receive and organize visual information. The retina sends information to the brain through the optic nerve, enabling visual acuity. Retinal diseases can affect the area of the retina that serves the central vision. The goal of treatment for retinal disease is to stop or slow disease progression and preserve, improve or restore vision (1)

Computer-Aided Analysis of Time Series Retinal Images

MatchedFlicker® is a digital image, computer software program that is utilized to animate and analyze a time series of retinal images of the posterior segment of the eye. Images are taken at different points in time and then generated in a superimposed view. The analyses are performed by a side-by-side comparison of serial mono or stereo-photographs and the areas of change between the two images appear as a flickering motion. This technology was developed to aide in the evaluation and progression of retinal conditions such as glaucoma. (2) Currently the gold standard is analyses by a side-by-side comparison of serial mono or stereo-photographs. (3)

Regulatory Status

In 2009, the United States Food and Drug Administration (FDA) approved MatchedFlicker® imaging software (eyeIC, Narbeth, PA.) as a class II device under the 510(k)-clearance process. The MatchedFlicker® imaging software is FDA approved as a picture archiving and communications system and is substantially equivalent to other legally marketed digital imaging software, including but not limited to the following devices (2):

1. Nidek Advanced Vision Information System (NAVIS; K013694) manufactured by Nidek, Inc.;
2. Retasure (K071299) manufactured by Digital Healthcare, Inc.;
3. IMAGEnet (K082364) manufactured by Topcon Corp.

Product code NFJ. (2)

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function - including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable

intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Computer-Aided Analysis of Time Series Retinal Images

In 2009, Cymbor et al. evaluated the degree of concordance among examiners in judging glaucomatous progression between serial optic nerve head photos using digital image flicker comparison versus the traditional side-by-side photograph comparison method. The secondary comparison was to determine if flicker was quicker than side-by-side comparison. A total of 29 eyes were selected from patient records. Fourteen eyes showed various degrees of glaucomatous structural change among photos, while the remaining 15 eyes had no glaucomatous structural change. Three masked optometrists experienced in glaucoma management graded whether the photos represented glaucomatous change or no change when viewing photos randomly assigned to side-by-side or flicker comparison. Among multiple graders, flicker comparison gave moderate agreement, whereas side-by-side analysis gave fair agreement. The difference in time between the 2 methods was not statistically significant. The study concluded that flicker is a unique, easy to learn, and an accurate way to view serial optic nerve head photographs, although additional research is needed to determine if flicker comparison is a useful tool in the clinical management of structural glaucoma progression. (4)

In 2012, Myung and colleagues measured the accuracy and speed for detection of vascular progression in retinopathy of prematurity (ROP) from serial images. Two strategies were compared in a prospective comparative study: static side-by-side presentation and dynamic flickering of superimposed image pairs. Fifteen de-identified, wide-angle retinal image pairs were taken from infants. Image pairs representing vascular disease progression were taken ≥1 week apart, and control images without progression were taken on the same day. Dynamic flickering pairs were created by digital image registration. Ten experts independently reviewed each image pair on a secure website using both strategies and were asked to identify progression or state that images were identical. Accuracy and speed were measured, using examination date and ophthalmoscopic findings as a reference standard. Using static images, experts were accurate in a mean (%) ± standard deviation (SD) of 11.4 of 15 (76%) ± 1.7 image pairs. Using dynamic flickering images, experts were accurate in a mean (%) ± SD of 11.3 of 15 (75%) ± 1.7 image pairs. There was no significant difference in accuracy between these strategies (P = .420). Diagnostic speed was faster using dynamic flickering (24.7 ± 8.3 seconds) vs static side-by-side images (40.3 ± 18.3 seconds) (P = .002). Experts reported higher confidence when interpreting dynamic flickering images (P = .001). The study determined that retinal imaging provides objective documentation of vascular appearance, with potentially improved ability to recognize ROP progression compared to standard ophthalmoscopy. Speed of identifying vascular progression was faster by review of dynamic flickering image pairs than by static side-by-side images. There was no difference in accuracy. (5)

In 2012, Syed et al. believed optic disc hemorrhages are associated with active glaucomatous neurodegeneration and ongoing visual field loss. This study sought to determine whether automated alternation flicker enhances the detection of disc hemorrhages in serial images in patients with glaucoma compared to side-by-side photographic evaluation and single-image display. Serial sets of optic nerve photographs of 394 eyes from 234 patients followed for glaucoma at the authors' institutions were included in this study. Eyes with disc hemorrhages were graded for difficulty level and randomized along with non-disc hemorrhages. The images were controlled into one of three groups (automated alternation flicker, side-by-side or single image). Seven graders viewed all images and assessed for the presence or absence of disc hemorrhages. The sensitivity of automated alternation flicker for disc hemorrhages detection (0.878) was higher than side-by-side (0.705; p=0.002) and single photographs (0.757; p=0.01). There was no specificity difference between pairs of presentation groups (all p≥0.7). Syed and colleagues determined that automated alternation flicker is a more sensitive method for disc hemorrhage detection than the current clinical standard and may have an important role in the management of glaucoma. (6)

In 2014, Marlow et al. wanted to highlight changing features over time within a single static image through the auto-alignment and subtraction of serial optic nerve photographs. Subtraction maps were generated from auto-aligned (EyeIC, Narbeth, PA) baseline and follow-up images using Adobe Photoshop software. They demonstrated progressive retinal nerve fibre layer (RNFL) defects, optic disc hemorrhage (DH), neuroretinal rim loss (RL) and peripapillary atrophy (PPA). A masked glaucoma specialist identified features of progression on subtraction map first, then assessed feature strength by comparison with original images using alternation flicker. Control images with no progression and parallax-only images (as determined by flicker) were included. Eighty eyes of 67 patients were used to generate subtraction maps that detected glaucoma progression in 87% of DH (n = 28, sensitivity (Se) 82%, specificity (Sp) 98%) and 84% of PPA (n = 30, Se 80%, Sp 98%) cases. The lowest rate of detection was seen with RL at 67% (n = 31, Se 65%, Sp 100%). The subtraction technique was most sensitive for detecting parallax (n = 39, Se 98%, Sp 94%). Features of glaucoma progression appeared equally strong in flicker and subtraction images, but parallax was often enhanced on subtraction maps. Among control images selected for absence of features of glaucomatous change (n = 9) in original flicker images, no features were detected on subtraction maps. Auto-alignment and subtraction of serial optic nerve photographs reliably detect features of glaucoma progression with a single static image. Parallax identification may also be facilitated. Auto-alignment and subtraction of serial optic nerve photographs may prove especially useful in education and printed publications when dynamic imaging is not feasible. (7)

In 2016, Schaefer et al. compared the accuracy and speed of using the computerized MatchedFlicker software program to evaluate glaucomatous optic disc change against the traditional gold standard of manually examining stereoscopic disc photographs. Two resident ophthalmologists and 1 glaucoma fellow independently evaluated 140 image pairs from 100 glaucomatous/ocular hypertensive patient eyes using a handheld stereo viewer and the MatchedFlicker program. Fifty patients progressed to glaucoma as determined by the Ocular

Hypertension Treatment Study (OHTS) Optic Disc Reading Group and the OHTS Endpoint Committee in the OHTS, and 50 more had photographs taken a few minutes apart, which were negative controls with no progression. Twenty photograph pairs from each group were duplicated to determine reviewer variability. Photographs were examined in alternating blocks of 70 photograph pairs for each method, with the starting viewing method randomized. Reviewer accuracy and time to review for each method were measured. Using the handheld stereo viewer, the reviewers correctly identified progression or non-progression in 76.0% of the slide pairs. Using the MatchedFlicker software, 87.6% were correctly identified (P = .011). Evaluator speed averaged 34.1 seconds per image pair with the stereo viewer verses 24.9 seconds with the MatchedFlicker (P = .044). Overall, Flicker was significantly more specific but less sensitive than stereo slides. Trainees appeared more reluctant to identify glaucoma progression from slides than from Flicker. For the 2 less experienced trainees Flicker was significantly more accurate. The prospective evaluation concluded that the MatchedFlicker software had a greater accuracy and was quicker to perform than using a handheld stereoscopic viewer. (8)

In 2018, Schaefer et al. evaluated the accuracy and speed of trainees and experienced glaucoma specialists using the MatchedFlicker software against the manual examination of stereoscopic disc photographs for detecting glaucomatous optic disc change. Three experienced glaucoma specialists, two resident ophthalmologists and one glaucoma fellow from several institutions evaluated the same 140 image pairs from 100 glaucomatous/ocular hypertensive eyes using a handheld stereo viewer and the MatchedFlicker. Fifty had progression to glaucoma as determined by the Ocular Hypertension Treatment Study (OHTS) Optic Disc Reading Group and endpoint committee, and 50 more were negative controls for progression with photos taken a few minutes apart. Twenty photo pairs from each of the two groups were duplicated for reviewer variability analysis. The initial viewing method was randomized and then alternated for each group of 70 image pairs. Reviewer accuracy and evaluation time for each method were evaluated. The assessors averaged 8.6s faster per image pair (26%) with the MatchedFlicker than with the stereo viewer (p=0.0007). Evaluators correctly identified more image pairs when using the MatchedFlicker software over the stereo viewer (p=0.0003). There was no significant difference between the expert versus trainee group in speed or overall accuracy for either method. Experts were significantly more consistent than trainees with duplicate image pairs (p=0.029). Trainees appeared more reluctant to designate eyes as showing glaucoma progression than experts. Both expert glaucoma specialists and ophthalmologists in various training stages had greater accuracy and speed with the MatchedFlicker software than with a handheld stereoscopic viewer. Although this study is promising, additional larger, long-term RCTs are needed to establish impact on health outcomes using this technology. (9)

Professional Guidelines and Position Statements

There are no professional guidelines and position statements that recommend the use of MatchedFlicker in fundus photography analysis.

Summary of Evidence

The role of computer software to animate and analyze a time series of retinal images (e.g., MatchedFlicker®) to monitor disease progression of glaucoma and/or other retinal diseases has not been established. To date, there is insufficient evidence in the published, peer-reviewed scientific literature to establish improved health outcomes using this technology. Additional high quality randomized controlled trials (RCTs) with larger number of subjects are needed to evaluate the long-term safety and efficacy of this treatment modality and the impact on health outcomes.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	92499
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
12/31/2025	Document became inactive.
02/15/2025	Reviewed. No changes.
03/15/2024	Document updated with literature review. Coverage unchanged. No new references.
03/15/2023	Reviewed. No changes.
07/01/2022	Document updated with literature review. Coverage unchanged. No new references; others updated.
02/15/2021	Reviewed. No changes.
06/15/2020	Document updated with literature review. Coverage unchanged. Added reference 9.
11/01/2018	Reviewed. No changes.
12/15/2017	Document updated with literature review. Coverage unchanged.
12/01/2016	Reviewed. No changes.
01/01/2015	New medical document. Use of computer software to animate and analyze a time series of retinal images (e.g. Matchedflicker®) is considered experimental, investigational and/or unproven for any indication, including but not limited to monitoring disease progression.