



University of Wisconsin
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

Fundus Photograph Reading Center

Non-study Specific Standard Digital Fluorescein Angiography (FA-D)

(Adapted from the Early Treatment Diabetic Retinopathy Study (ETDRS), Macular Photocoagulation Study (MPS) and the Age-Related Eye Disease Study (AREDS),
Manuals of Operations^{1, 2, 3})

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1. Overview

The following is the University of Wisconsin-Fundus Photograph Reading Center's (UW-FPRC's) Standard Digital Fluorescein Angiography procedure (FA-D). Please refer to the documents specific to this study to determine if additional imaging procedures apply to this trial.

All clinical sites using this procedure must take images using a digital system that is UW-FPRC certified for black and white fluorescein angiography capture capability. This typically requires a one mega pixel or higher resolution image capture system. For details about how to certify a digital system refer to the UW-FPRC's "Digital System Certification" document or view the FPRC website <http://eyephoto.opth.wisc.edu/index.html>.

Only UW-FPRC certified photographers are allowed to take Qualifying Visit (baseline) images unless an exception to this rule is granted (on a case-by-case basis) by the study sponsor. The sponsor may suspend patient enrollment if a site does not have a certified photographer available to take the qualifying images. Only under extraordinary circumstances may follow-up visit images be taken by an uncertified photographer (see Section 3 below).

Clinical sites are strongly encouraged to have a minimum of two, but no more than three, certified photographers. Photographers are encouraged to contact the UW-FPRC's imaging consultants, Dennis Thayer thayer@rc.opth.wisc.edu, Pamela Vargo vargo@rc.opth.wisc.edu or Hugh Wabers wabers@rc.opth.wisc.edu (608-263-9858) with any photography related questions. Pointers on imaging technique may be found in Section 10.

2. Photographer Certification

Photographers taking photographs (or digital images: the terms will be used interchangeably in this procedure) for studies evaluated by the UW-FPRC must be certified for the relevant procedure(s), *before submitting actual patient images*.

Photographer certification is specific for each study and each photographer requesting certification must submit a signed "UW-FPRC Photographer Certification Request Form" for each study. This form can be found at the end of this document. A copy of the form may also be available on the UW-FPRC website: <http://eyephoto.opth.wisc.edu>: access may require a username and password. One form will be used for all imaging procedures associated with a given study. System certification requires a separate study specific form *for each system* being used.

Certification consists of (1) review of study synopsis/protocol and imaging procedures and (2) demonstrating the ability to perform the imaging procedure by submission of images of acceptable quality. The second requirement may be waived if the photographer has prior certification at the UW-FPRC using **an identical procedure**, and has been active taking images, judged to be of good quality by the UW-FPRC, during the past 12 months. Photographers who are certified for **a similar procedure** may be asked to submit sample photographs to become certified.

Photographers who are not eligible for certification on the basis of previous UW-FPRC certification should submit two fluorescein angiograms taken using this procedure. *The angiograms may be taken of patients with any retinal or choroidal disorder in whom*

angiography is being carried out for clinical purposes Photographers previously certified for this procedure on film (FA-F) electing to perform this procedure digitally (FA-D) must submit one fluorescein angiogram. This allows us to check image quality (stereo effect, exposure, filter integrity, and image resolution) and to determine whether we can open the CD/DVD and archive the images.

Photographers are encouraged to send complete submissions for each procedure that they are requesting certification (i.e. if two FA-Ds are required for certification please send both in one submission).

Photographers who meet certification criteria will receive confirmation of certification. Those who do not meet these criteria will receive feedback from the UW-FPRC imaging consultants, and may be required to submit additional sets of images. A plan for improving image quality may be necessary after three complete unsuccessful certification submissions.

Once a photographer is certified for a specific study they are certified for the duration of that specific study, even if they are inactive for more than one year.

3. Uncertified Photographers (Follow-up Visits Only)

On rare occasions during **follow-up** visits, when a certified photographer is not available, an uncertified photographer familiar with this procedure may take the images. The uncertified photographer should review the imaging procedure before performing photography to be certain they understand and follow the procedure. The name of the uncertified photographer should be identified on the CD/DVD, as well as any other study documentation requiring photographer name. A brief description should be entered on the transmittal log explaining the reason an uncertified photographer took the images.

4. Fundus Cameras

The Topcon TRC-50 series (50VT, 50X, 50EX, 50IA, 50IX, and 50DX) used at the 35° setting, and the Zeiss FF450-plus, FF4, and Visucam, camera models used at the 30° settings are suitable cameras. The Canon fundus cameras (UVi or similar models) used at the 40° setting is also suitable. Additionally, some models of Kowa, Nikon fundus cameras and the Heidelberg scanning laser system with 30° or 35° settings may be used.

Cameras other than these may be substituted upon approval of the UW-FPRC. Approval may be obtained by submitting sample photographic sets, taken according to this procedure, to the Fundus Photograph Reading Center, Attention: Imaging Services, 406 Science Dr., Suite 400, Madison, WI 53711-1068.

5. Fluorescein Angiography Fields

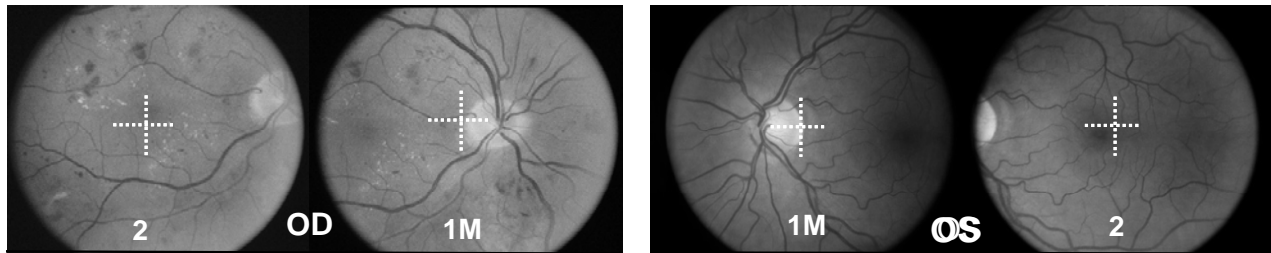


Figure 1

The following field descriptions assume that there are two cross hairs in the camera ocular, one vertical and the other horizontal intersecting in the center of the ocular. Fields 1M and 2 of a left eye and right eye are illustrated in Figure 1.

Field 1M-Disc: Center the temporal edge of the optic disc in the intersection of the cross hairs. The optic nerve will be off center providing a view of the macula. When a cross hair is not available, center the temporal edge of the optic disc in the center of the screen.

TIP: The optic nerve is not centered in this field.

Field 2-Macula: Center the macula near the intersection of the cross hairs. A suitable position can often be obtained by rotating the camera temporally from the Field 1M position, with slight vertical adjustment.

6. Fluorescein Angiography

The fluorescein angiogram contains stereoscopic views of two fields at specified times after injection. These fields include the macula (Field 2) of both eyes and the disc field (Field 1M) of the study eye. Field 2, the camera should be centered near the center of the macula but not exactly on it, so that the artifact that is present in some fundus photographs will not obscure the center. If necessary, in trials investigating choroidal new vessels (CNV) Field 2 can be shifted by one disc diameter to include as much of the lesion as possible.

Stereo pairs should be taken shooting the left member of the pair first, followed by the right member of the pair. This sequence should be followed throughout the angiogram

Please do not delete any images taken during the fill phase (0sec-50sec). The UW-FPRC would prefer that all red-free images and images acquired between 1min-10min be edited to include only the stereo pairs described in this section.

Stereoscopic red-free photographs are taken of Field 2 in each eye prior to the injection of the fluorescein dye.

6.1. Fluorescein Injection

After the red-free images of both eyes have been taken, the camera is positioned for Field 2 of the study eye. Fluorescein is injected rapidly (less than 5 seconds if possible) into the antecubital or other convenient vein according to usual clinic procedures.

6.2. Timing (See Appendix A)

6.2.1. Early Phase

The first image of the early phase is taken at time "0"; that is, at the moment injection of the fluorescein dye begins. The second photograph is taken at the moment the injection is complete. These photographs are referred to as the "control" photographs. They serve to document the integrity of the interference filters (exciter and barrier). The time shown on the second frame documents the rate of injection.

Ideally, the control photographs are followed by a series of 10 to 16 exposures taken at 1 to 2 second intervals, beginning about 15 seconds after the start of fluorescein injection (sooner if fluorescein appears before 15 seconds or delaying the series if a slow circulation time is expected or the dye doesn't appear). The usual result is 5 to 8 stereo pairs following the control pair, typically culminating about 40-45 seconds after the start of injection. Remember not to delete any of these early phase images.

6.2.2. Mid-Phase

After the early-phase photographs are completed the photographer takes stereo pairs of Field 2 and then of Field 1M of the study eye at approximately 60 to 90 seconds. Next, a stereo pair of Field 2 is taken of the fellow eye at approximately 2 minutes. Then, the camera is positioned back to the study eye and a stereo pair of Field 2 is taken between 2 and 3 minutes. Remember that the UW-FPRC would prefer that images taken during the mid and late phases be edited to include only necessary stereo pairs.

6.2.3. Late-Phase

A stereo pair of Field 2 in the study eye is taken at 5 minutes. Two final stereo pairs are taken of Field 2 in both eyes at 10 minutes.

7. Exporting and Labeling of Digital Images

Digital images should be saved to CD/DVD using no compression or lossless compression. Lossy compressed (standard .jpg) images may be accepted but will be evaluated by the UW-FPRC on a case-by-case basis.

Only the standard methods existing in the capture software of the imaging system should be used to isolate images for submission. Specific image handling procedures are outlined in the UW-FPRC's "Digital System Certification" document or the UW-FPRC website, <http://eyephoto.opth.wisc.edu/>. Digital images should be "burned" to CD/DVD before being archived on the computer system (a process that often compresses the images for storage). We recommend confirming that the images were successfully burned to CD/DVD by checking the CD/DVD on another computer.

For *certification images* please comply with HIPPA regulations by masking patient identifiers on the digital files. If pre-printed labels are not available for labeling the CD/DVD, please hand-label using a permanent felt-tip marker. The CD/DVD label must indicate the fundus camera

head serial number, patient identifier, photographer's name, date of photography, and that the images are certification sets.

For *submissions of study participants* please comply with HIPPA regulations by replacing the subject's ID number, last name, and first name with study specific information (as shown in Figure 2), (for OIS systems editing is only possible with specific versions of Winstation®).

Replace	With	Study Specific
Patient's ID#	Site#, Screening #	STUDY SPECIFIC INFO
Patient's Last Name	Study Name	STUDY SPECIFIC INFO
Patient's First Name	Subject #, (space) Name code	STUDY SPECIFIC INFO
Patient's Date of Birth	01/01/1900	STUDY SPECIFIC INFO

Figure 2

For *study submissions* the CD/DVD should be labeled using a circular CD/DVD label (as shown in Figure 3). These labels are typically provided by the UW-FPRC and include the study name, site ID, patient ID and visit information (sites may need to manually enter information for initial visits). The CD/DVD label also includes a space for date of photography, the photographer's name(s) and the serial number of the fundus camera used (located on the head of the fundus camera). A duplicate set of images of each submission should be retained at the site.

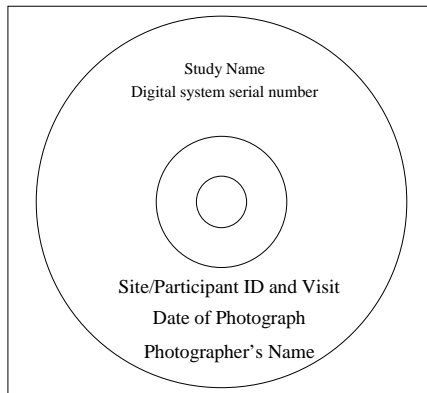


Figure 3

The CD/DVDs should be prepared and labeled as described above. The sets of images should be sent together with the completed Transmittal Log (see *UW-FPRC Labeling and Shipping Instructions* section of the study specific documents) to the UW-FPRC as soon as possible after being taken.

8. Retakes

The fluorescein images should be evaluated for quality by the *principal investigator and/or photographer* (unless prohibited by Study Protocol) before submission to the UW-FPRC. If quality is not adequate for assessment of key features of the study eye, such as extent of macular edema, and if no irremediable cause of inadequate quality is present (such as lens opacities or a pupil that will not dilate adequately), the images should be retaken before submission to the UW-

FPRC. When images are considered upgradable because of poor quality, the UW-FPRC may issue a retake request.

9. Evaluation of Image Quality

Fluorescein angiogram images are reviewed and assigned a grade for overall quality. Feedback will be provided to the photographers as needed to help with resolution of any problems. Special attention will be given to photographers having difficulty meeting study photo quality standards. If a certified photographer consistently fails to meet study standards, certification may be suspended.

10. Pointers on Imaging Technique

10.1. General

Stereo pairs should be taken shooting the left member of the pair first, followed by the right member of the pair. All digital images should be reviewed for quality at the time of photography and the photographer should select the best stereo pairs for each field, deleting extra, unnecessary images, except in the 0 sec. to 40-45 sec. fill phase.

10.2. Patient Cooperation

Photography of the photophobic subject can be very challenging for the photographer and uncomfortable for the subject. Minimizing the number of flashes and the length of time the eye is exposed to a bright viewing lamp are two things that can help make the photography procedure more comfortable. Additionally, keeping the view lamp as low as possible (maybe even dimming the room lights) can help make the photography procedure more tolerable. Patients should be asked to blink to help keep the cornea clear.

If the subject has great difficulty tolerating the screening visit photography procedure and the photographer thinks this will lead to a problem at follow-up visits, the situation should be discussed with the principle investigator and/or coordinator and consideration should be given to not enrolling the subject in the study.

10.3. Focus/Clarity

Remember that the best image quality can be acquired if corneas are not disturbed by prior examination with a diagnostic contact lens.

Constant attention must be paid to keeping the cross hairs in the camera ocular in focus; otherwise the images will be out of focus. Proper camera-to-eye distance should be maintained to avoid haziness and artifacts.

If it is not possible to get the entire photographic field in crisp focus, the photographer should concentrate on getting the center of the field in focus, sacrificing a bit on the periphery if necessary.

When the photographer moves to Field 2, having just taken Field 1M, **he/she should refocus on retinal vessels near the center of the field.** *Failure to do so results in images that shows the foveal area to be slightly out of focus while the periphery is in focus.*

A common problem is focusing below the surface of the retina. Images which include the optic nerve (Fields 1M and often Field 2) sometimes show clear focus on the bottom of the cup, while the retina is slightly out of focus. Some photographers use the lamina cribrosa (at the bottom of the cup), the disc margin, or the granular pattern of the pigment epithelium for focusing. Instead, it is preferable to focus on fine retinal vessels. Since the depth of focus is greater posterior to the plane of absolute focus than anterior to it, it makes sense to err on the side of focusing slightly above the retina rather than too deep. This should keep both the anterior surface of the retina and the pigment epithelial background in focus. Such a strategy is of special importance when macular edema is present.

10.4. Stereoscopic Effect

Dilation of the pupil to at least 6mm is important to permit good quality stereo photography. If the pupils cannot be dilated to at least 4mm for the screening visit, the subject should not be entered into the study.

The technique described by Allen⁴ is used for taking non-simultaneous stereo fundus images. The camera **should not be rotated or pivoted for stereo images**; instead, it should be moved laterally from left to right with the joystick (or by sliding the camera base on its table, if preferred). About 2mm is the minimum separation between members of the stereo pair to be aimed for when moving the joystick or sliding the camera.

Stereo pairs should be taken shooting the left member of the pair first, followed by the right member of the pair. When obtaining stereo pairs, care should be taken that at least one member of the pair is of good technical quality with crisp focus. In many cases, it will be possible to obtain good quality in both members of the pair, but if this is not the case, *the aim should be to obtain good quality in one member and **some** stereo separation between the members, accepting **somewhat** poorer quality in the second member of the pair, if necessary.*

10.5. Exposure, Gain, and Flash

It is very important that photographers utilize flash, gain and gamma changes to obtain optimal exposure. It is important to avoid severe over or under exposure to avoid loss of image detail. We recommend that photographers become familiar with using the camera and software controls available to insure optimal exposure and contrast. The FPRC Imaging staff is available to assist in recommending acceptable settings.

Most digital systems have a wide variety of image enhancement tools to adjust image contrast, brightness or sharpness after image capture. Enhancement tools should not be used at the clinical site to adjust image quality after imaging has taken place. Careful attention must be paid to obtaining optimum exposure and image sharpness so that enhancements are not necessary.

11. References

1. Early Treatment Diabetic Retinopathy Study Research Group, Manual of Operations. Chapter 13. Baltimore: ETDRS Coordinating Center, University of Maryland. Available from: National Technical Information Service, 52285 Port Royal Road, Springfield, VA 22161; Accession No. PB85 223006/AS Chapter 13.
2. Macular Photocoagulation Study Group, Macular Photocoagulation Study: Manual of Procedures. MPS Coordinating Center, Baltimore, MD. Available from National Technical Information Service, 5285 Port Royal Road, Springfield, VA 22161; Accession No. PB90-207903.
3. Age Related Eye Diseases Research Group, Manual of Operations. Chapter 8. Potomac, MD: AREDS Coordinating Center, EMMES Corporation, 11325 Seven Locks Road, Suite 214, Potomac, MD 20854.
4. Allen L. Ocular fundus photography. *Am J Ophthalmol* 1964; 57:13-28.

12. Appendix A

Fluorescein Angiogram Timing

Timing	Study Eye (SE) or Fellow Eye (FE)	Field
Start injection = 0sec	SE	F2
Stop injection ~5sec		
Transit 15-45sec (~5-8pairs)		
60-90sec		
60-90sec	SE	F1M
2min	FE	F2
2-3min	SE	F2
5min		
10min		
10min	FE	F2

13.Approvals

The following signatures indicate approval of this document.

13.1. Document Control

Jason Eberhardy
Technical Writer, Document Control

Date

13.2. Author

Pamela Vargo
Photographic Consultant

Date

13.3. Review

Hugh Wabers
Senior Imaging Consultant

Date

Dennis Thayer
Ophthalmic Imaging Specialist

Date

13.4. Approval

Michael Neider
Associate Director, Imaging

Date