# Digital Fluorescein Angiography

## VERT2

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## 1.0 Overview

This module is designed for clinics electing to use a digital capture system instead of film for the fluorescein angiograms. Please remember that color photographs that accompany the fluorescein angiogram may be taken using 35mm color slide film or color digital imaging.

Clinical sites using digital fluorescein angiography systems must obtain both photographer and digital camera system certification from the UW-FPRC *before initiating study photography*. Digital system software and hardware components will be evaluated and recorded as part of the system certification process. Submission of a completed **Digital Fluorescein Angiography System Certification Request Form** (see the FPRC Forms, Labeling & Shipping Information document) is required for each system used for this study. UW-FPRC digital system evaluation software may be run on the digital system as part of the certification process, *and periodically throughout the study,* to monitor system elements critical to accurate assessment of digital images.

It is strongly recommended that the digital system support "dial-in" access to allow system vendors and UW-FPRC technical staff access to the system throughout the study, to monitor settings or facilitate system maintenance. Any changes in the digital system that occur after the system is certified (including software or hardware changes) must be reported immediately after they are made to Dennis Thayer at 608-263-9858) and may require system re-certification.

## 2.0 Photographer Certification

Photographers taking digital angiograms must be certified for the relevant procedure(s), *before submitting actual patient photographs*. ***Only UW-FPRC certified photographers are allowed to take baseline (Screening Visit) photographs*** *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 the site does not have a certified photographer available to take the baseline photographs. *Only under extraordinary circumstances, may follow-up visit photographs be taken by an uncertified photographer (see Section 2.1 below).* Photographers electing digital angiography are still required to demonstrate the ability to perform color fundus photography on 35mm film. Certification for film-based angiograms does not qualify a photographer for digital angiography certification.

Photographer certification is study specific and each photographer requesting certification must submit a signed UW-FPRC certification request form to the UW-FPRC. Certification consists of (1) review of the study synopsis or study protocol and photography procedures and (2) demonstrated ability to perform the angiographic procedure by submission of digital images of acceptable quality. Digital angiograms must have been taken within the last 2 months. The second requirement may be waived if the photographer has prior certification at the UW-FPRC using a similar procedure, and has been active taking photographs, judged to be of good quality by the UW-FPRC, during the past year. Previously certified photographers who have been inactive for more that one-year may be asked to submit current sample photographs (often an abbreviated set) to become re-certified.

Photographers who are not eligible for certification on the basis of previous certification in another study should submit digital fluorescein angiograms *of two patients 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.* The digital files should be written to CD and the CD labeled as shown in Figure 3 (Section 7.0). Pre-printed labels may be

unavailable for labeling the CD; please hand label the CD using a permanent felt-tip marker. The CD should be labeled indicating the patient initials, photographer's name, date of photography and that the photographs are certification sets. **A signed UW-FPRC Request for Photographer Certification form is also required** (see the FPRC Forms, Labeling & Shipping Information document).

Photographers who meet certification criteria will receive confirmation of certification. Photographers who do not meet these criteria will receive feedback from the UW-FPRC photographic consultants, and will be required to submit additional angiograms. After three unsuccessful attempts for certification, no additional photographic submissions will be accepted until a plan for improving photographic quality has been developed in collaboration with the sponsor and principal investigator.

### 2.1 Uncertified Photographers (Follow-up visits only)

On rare occasions during follow-up visits, when a certified photographer is not available to take the angiograms, an uncertified photographer familiar with the procedure may perform the procedure. The uncertified photographer should review the procedure before performing angiography to be certain they understand and follow the procedures. The name of the uncertified photographer should be entered on the CD label.

### 3.0 Digital System Certification

System Requirements - Digital angiograms must be taken using Heidelberg HRA System, MRP OphthaVision®, OIS Winstation®, Escalon Medical Imaging (EMI), Topcon IMAGEnet®, Zeiss VISUPAC® or Digital Healthcare Classic digital systems using a three mega-pixel or larger image sensor. Each digital angiogram system must be certified by the UW-FPRC. This is accomplished by submitting the **"UW-FPRC Digital Color System Certification Request Form"** (see the *FPRC Forms, Labeling, Study Conventions Information* document). Copies of the digital system certification form are available on the UW-FPRC website or the EMMES website.

It is preferred that the digital system contains software and hardware that allows remote access and operation. The UW-FPRC or a manufacturer representative may inspect the digital camera system to assure that all capture settings are correct for accurate image analysis. This inspection may be performed via "dial-in" access or as part of a site visit. Inspection software may be used to verify and record system settings.

Certification Procedure - **Each digital system used for the study must be certified by the UW-FPRC before beginning study participant photography.** Certification begins with submission of the "UW-FPRC Digital Color System Certification Request Form" (see the *FPRC Forms, Labeling, Study Conventions Information* document). Each system you plan to use requires a separate form and certification. For digital systems not certified with the UW-FPRC, the system specific procedure outlined below should be followed. If the system is certified with the UW-FPRC but images have not been sent to the UW-FPRC within the previous 3 months, new images should be sent to the UW-FPRC to verify that they still match the certification settings. If the system was certified with the UW-FPRC but hardware or software changes have occurred since certification, a "Digital System Upgrade Form" should be completed and sent to the UW-FPRC. This form is located on the UW-FPRC website (http://eyphoto.ophth.wisc.edu). Depending on the upgrade, additional images may need to be sent with the form.

**Heidelberg HRA System** - The HRA Classic or HRA 2 systems used at the 30-degree setting are suitable. Eye Explorer® software, version 1.4.1.0 or higher, must be used and the system must have CD writing capability. Submit one angiogram saved using the .E2E file format (not as a movie image series).

**MRP OphthaVision® System**- System certification must be handled through MRP. Contact MRP's Matt Carnevale at 978-687-7979.

**OIS Winstation® System or Escalon Medical Imaging (EMI) or Digital Healthcare (DHC)** - Each system requires a calibration for certification. The calibration uses 10 color images, of 10 different eyes, at the acceptable image angle (determined by camera type). The color images should be centered on the posterior pole so that both the disc and macula are in view. If the center of the macula and the center of the disc are not clearly defined they can not be used for calibration. The UW-FPRC would prefer that OIS Winstation® systems have software version 10.0 or higher. EMI systems must have RC Prep software version 1.4 or higher. DHC Classic systems must have software version 4.22.06 or higher.

If there are any hardware or software changes made to the system 10 more color images may be required to recalibrate the system. This requirement can be abbreviated if one of the 10 eyes used in the initial calibration is from someone who can be photographed in the future (i.e. the same staff member's eye photographed under 2 different system perimeters). This way if the system changes, the patient can be re-photographed and the old and new photos can be sent to the UW-FPRC for calibration and recertification.

**Topcon IMAGEnet® System** - Run the Digital System Evaluation Software (DSES), which can be found on the web at http://eyephoto.ophth.wisc.edu/DSES.html or it can be mailed to you by contacting the UW-FPRC. Follow the directions included with the software and send the results to: Choices for Service in Imaging, Inc., 233 Rock Road #249, Glen Rock, NJ 07452. If you have any questions during the process please contact Tony Pugliese at 800-499-2291, tony@cfsimaging.com.

**Zeiss Visupac® System** – Send a completed "UW-FPRC Digital Color System Certification Request Form" to the UW-FPRC. Make sure the serial# of the Visupac® system and a phone number to access the system are included. Receipt of this form will initiate contact between the UW-FPRC and Carl Zeiss Meditec Inc. A representative from Carl Zeiss Meditec Inc. will in turn contact the site to arrange a time to go through the certification process.

Digital angiograms must be submitted on CD using only the standard methods existing in the software of the imaging system to isolate images for submission (do not use Windows Explorer to copy images to the CD). Images must not be compressed. The participant's name must be removed from the file so it is not displayed during image evaluation. When the participant's name is edited out of the file, the last name should be replaced with the words "System-Certification." The participant's first name should be replaced with the serial number of the fundus camera. Photographer certification photos may also be used for camera system certification.

The system certification process is considered successful after the UW-FPRC staff ensures that image files can be successfully viewed and analyzed and that each angiographic image (the red-free images are just sequentially numbered) contains a timing number (displayed in seconds). Additionally, the patient names should be removed from the images and replaced

with information as described above. Currently, the masking of patient information may not be possible with OIS systems.

## **4.0** Fundus **Camera Requirements**

The same model fundus camera used to take the stereo color fundus photographs should be used to perform the digital angiogram whenever possible. We realize that this is not possible when using the Heidelberg system and that a separate fundus camera will be needed to perform the stereo color photography. The 30° Zeiss FF4 and FF450-plus fundus cameras and the Topcon TRC-50 series (50VT, 50X, 50EX, 50IA, and 50IX or similar models) used at the 35° setting are suitable cameras. Additionally, the Canon UVi (or similar models) used at the 40° setting, and the Kowa, Nikon and Olympus camera models used at the 30° or 35° settings are suitable cameras for the study.

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 procedure, to the Fundus Photograph Reading Center, 406 Science Dr., Suite 400, Madison, WI 53711-1068, Attention: Photography Services. Photographer certification photographs may be used for camera approval. Cameras used to submit satisfactory certification photographs are considered suitable cameras for the study.

*Digital Image Exposures:* All images acquired during angiography should be saved and sent to the UW-FPRC. Please do not delete any images taken during the "early" sequence to obtain only the recommended number of exposures or to remove images thought to contain objectionable artifacts. It is very important that photographers minimize flash/gain changes to avoid digital image overexposure, which can cause the areas of hyperfluorescence to appear artificially bright and possibly larger than they really are. A gain above 12db should not be used, to avoid grainy effects in the images.

Many digital cameras have a wider range of flash/gain settings available to control image exposure. Some photographers may frequently adjust the flash or gain settings during the angiogram to improve image quality. While this is often a useful adjustment, we do not want areas of hyper fluorescence to become overexposed. To safeguard against this, we recommend that photographers start the angiogram series using a flash setting that avoids overexposure, increasing the flash setting *only if several underexposed frames are observed*. This technique is preferred over starting the series with a flash setting that may be too bright and reducing it only if overexposure is observed. For the Heidelberg systems, we recommend that photographers start the angiogram series using a sensitivity setting set at the 1 o'clock setting, decreasing the setting carefully throughout the transit phase to avoid overexposure. This technique should capture the early transit-filling phase. Monitoring the sensitivity setting will ensure that the images will not be overexposed.

*Heidelberg HRA Scanning Laser Considerations: The* laser intensity must be set to full power (setting 7). The mode selector is set to the "Red-Free" setting to take the stereo red-free photos and the sensitivity should be adjusted to provide a properly exposed image. When setting the sensitivity for the fluorescein images, it is recommended that the setting be approximately 10% higher than the setting typically used for acquiring IR images (IR images are optional and not required by this procedure). This will insure that the laser will be more sensitive at the time the fluorescein dye first appears, making capture of the transit phase more likely. Once the dye appears, the sensitivity may need further adjustment to

maintain good contrast without image overexposure. The scan depth should be set to "0.0". The focus setting should be adjusted on the fine retinal vessels.

When using the HRA for stereo images, the "stereo" button in the acquisition software should not be activated. We prefer that the stereo pairs are not "locked" as a single image icon.

## 5.0 Standard Fields (Figure 1)

The following descriptions of the standard fields assume that there are two cross hairs in the camera ocular (with the exception of the HRA system which does not contain a cross hair in the ocular), one vertical and the other horizontal intersecting in the center of the ocular.

**Field 1M** - Disc: Center the temporal edge of the optic disc at the intersection of the cross hairs in the ocular. When a cross hair is not available, as is the case with the HRA system, center the temporal edge of the optic disc in the center of the screen.

**Field 2** - Macula: Centered up to 1DD from the center of the macula, including all or most of the CNV lesion, if possible. A suitable position can often be obtained by rotating the camera temporally from the Field 1M position, without vertical adjustment. When a cross hair is not available, as is the case with the HRA system, center the macula in the center of the screen.

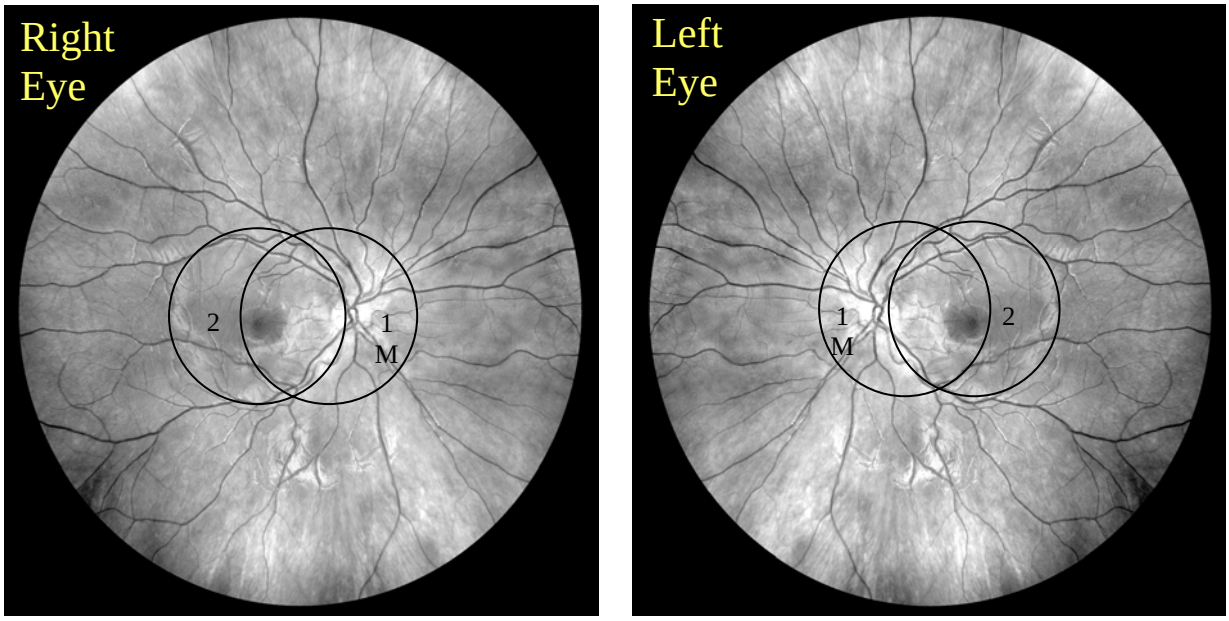



**Figure 1**

## 6.0 Fluorescein Angiography

The fluorescein angiogram contains stereoscopic views of 2 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. For Field 2, the camera should be centered on the center of the macula. If there is a central artifact in the fundus camera the center of the photo should be shifted up or down so that the artifact will not obscure the center. If necessary, in eyes with choroidal new vessel (CNV) lesions, in order to include all or most of the CNV lesion, the camera may be centered up to 2 DD from the center of the macula. In order to obtain stereo pairs that are correctly oriented on the computer monitor for stereoscopic viewing (i.e., do not have reversed stereoscopic effect), the photographer must be careful to shoot the members of each stereo pair in the proper sequence. For example, OIS systems may arrange the images on the monitor in rows, starting in the upper right-hand corner and therefore it is best that the right member of each pair be taken first, followed by the left member, as you would if you were preparing a film-based fluorescein angiogram. However, IMAGEnet® and Heidelberg systems arrange the images on the monitor in rows, starting in the upper left-hand corner and therefore it is best that the left member of each pair be taken first, followed by the right member.

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 photographs 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 anticubital or other convenient vein according to usual clinic procedures.

### 6.2 Timing

#### 6.2.1 Early Phase

The first photograph 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 constitute a stereo pair and are referred to as the "control" photographs. They serve to document the integrity of the interference filters. 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 sooner or delaying the initial exposures until fluorescence begins when a slow circulation time is expected). The usual result is 5 to 8 stereo pairs following the control pair, typically culminating about 40-45 seconds after the start of injection.

#### 6.2.2 Mid-Phase

After the early 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.

At this point the camera is positioned in front of the fellow eye and a stereo pair is taken of Field 2 at approximately 2 minutes. At this point, the camera is repositioned back to the study eye and a stereo pair of Field 2 is taken between 2 and 3 minutes.

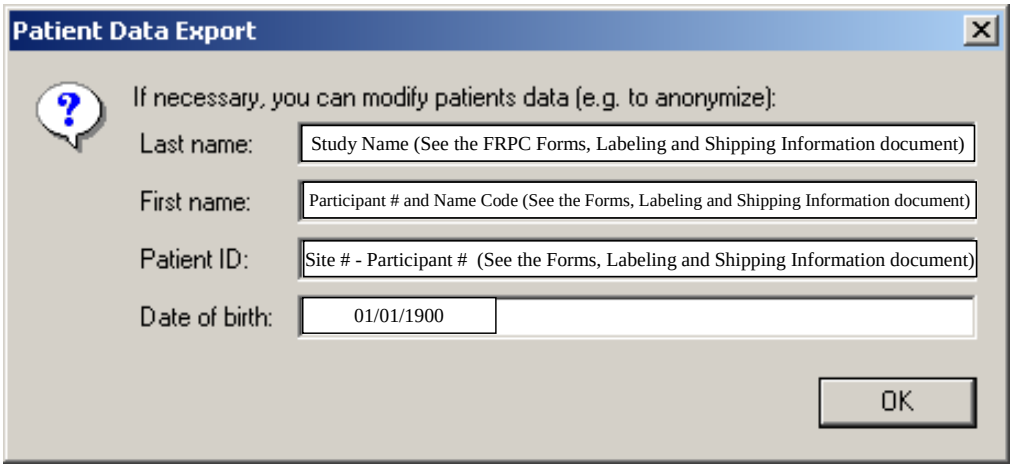
### 6.2.3 Late-Phase

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.

## 7.0 CD Preparation and Labeling & Fluorescein Angiogram Duplication

The entire angiogram should be written to CD using only the standard methods existing in the software of the imaging system to isolate images for submission to the UW-FPRC. *Do not use Windows Explorer® to copy images to the CD*. Before writing the CD, please replace the subject's ID number, last name and first name with study specific information, as outlined in the FPRC Forms, Labeling & Shipping Information document. Remember that the editing of patient information may not be possible with current OIS systems.

During the export of image files, a dialog box may appear allowing the operator to edit patient data. An example of the Patient Data Export dialog box from the Heidelberg system (Figure 2) as shown below:




Please no not compress the images and don't use re-writable CDs (CD-RWs). The images from only one participant should be written to each CD. Multiple visits from the same participant can be written to the same CD. Images should be sent promptly to the Reading Center. The CD should be labeled using a circular CD label. These labels will be provided and include the study name, name of the institution/investigator submitting the photographs, patient ID information, visit, date(s) of photography and photographer's name(s) and the serial number of the digital system used to perform the angiogram. A full resolution (not compressed) duplicate of the entire angiogram should be retained at the site. The circular CD label is shown in Figure 3.

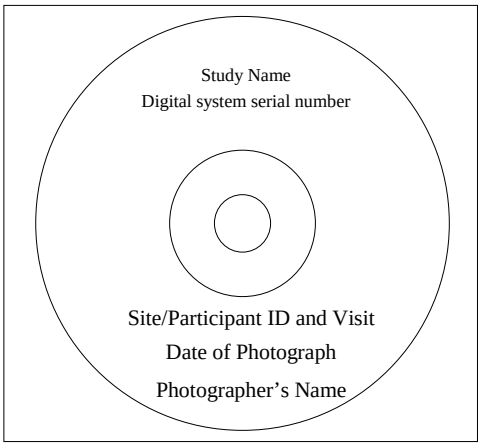



**Figure 3**

## 8.0 Transmission of Angiograms to the UW-FPRC

The digital angiographic file on CD and the original color transparencies should be sent together to the UW-FPRC within 10 working days (sooner if possible) after being taken.* The labeled CD should be placed inside a protective jewel case and the case placed inside a "bubble-wrap" or similar cushioned envelope to protect the media from damage. The completed **Transmittal Log** (see the FPRC Forms, Labeling & Shipping Information document) must accompany the shipment.