

Sleep Apnea Study Retinal Photography Protocol

1. INTRODUCTION

The Wisconsin Sleep Cohort (WSC) is an epidemiological research study of the major factors related to the incidence and progression of sleep disordered breathing (SDB) and its relation to subclinical and clinical cardiovascular disease (CVD), type 2 diabetes, and the metabolic syndrome involving 1,523 men and women aged 30-60 years of age employed at one of 5 Wisconsin State agencies. Sleep Apnea Eye study is an extension of WSC and seeks to determine the relationship of retinal microvascular disease to their relationship between SDB and the metabolic syndrome.

Specifically, Sleep Apnea Eye Study will examine 650 subjects during the on-going WSC cohort examination beginning June 15, 2004. Examinations will be conducted at the General Clinical Research Center, University of Wisconsin-Madison Medical School.

In Sleep Apnea Eye Study, retinal photographs of both eyes of the study participants will be obtained. These photographs will be graded at the Ocular Epidemiology Reading Center (OERC) at the University of Wisconsin-Madison for retinal microvascular characteristics, including focal arteriolar narrowing, arterio-venous nicking and retinopathy (e.g., microaneurysms, retinal hemorrhages). In addition, generalized arteriolar narrowing will be quantified using a computer-based measure of retinal vascular caliber. Other significant retinal conditions will also be noted, such as retinopathy or vascular occlusions in people with and without diabetes. One important feature of the retinal photography in the Sleep Apnea Eye Study compared to the previous population-based studies like ARIC, MESA, etc. is that the current study includes taking pulse synchronized retinal photographs with a view to reduce the variability of retinal vessel measurements with the pulse cycle.

2. EQUIPMENT AND SUPPLIES

2.1. The camera

A Canon CR6-45NM fundus camera equipped with a digital Canon 10D camera back will be used for this project. A laptop computer, supported by an articulating arm, will contain image acquisition and archive software EyeQSL, provided by Digital Healthcare Inc. The fundus camera and computer are mounted on a motorized instrument table to allow maximum subject comfort and optimum camera alignment. Both photographer and subjects have pneumatically adjustable stools with a backrest.

2.2. The trigger module

The retinal photography trigger module will be used to automatically trigger the camera switch for photography at 30 percent of ear lobe pulse-to-pulse interval, which is estimated to be approximately equal to 0.625 of the ECG-based R-R interval. This module is composed of:

- a. Ear clip pulse rate monitoring system
- b. Microchip PIC16F819 microprocessor
- c. Front panel switch settings

The ear clip pulse rate monitoring system is used to detect the ear lobe pulse. This signal is then fed to a Micro Chip PIC16F819 microprocessor that does the following: (a) automatically adjusts the gain applied

to the pulse signal to ensure adequate signal amplitude for the microprocessor, (b) detects the peaks of the pulse waveform, (c) measures the peak to peak time interval, (d) computes the appropriate delay based upon the front panel switch settings and the inherent latency in the Canon camera, and (e) outputs a pulse to trigger the photoflash. The function of this trigger module is to time the camera shutter to operate at desired particular delays during the cardiac cycle. The camera trigger can be set to any integer percent of the pulse-to-pulse interval. Based on previous research that identified the least variable point in pulse-to-pulse interval for retinal photography, the camera trigger is currently set to 30 percent of the pulse-to-pulse interval. The connection to the camera is permanent, but allows both computer generated and independent camera operation, as well as pausing at any time during the sequence. Setting the front panel switch to "30" will preset the retinal photography trigger module to trigger the camera at 30 percent of the ear lobe pulse-to-pulse interval. Also, the trigger unit has an LED on it. When it begins to blink steadily (at the patient's heart rate), photos can be taken. When the LED is off or on constantly, the automatic gain circuit is searching for a signal.

2.3. Supplies

An inventory of supplies for the University of Wisconsin Medical School GCRC where retinal photography will be performed, assuming an average participation of 715 subjects (10% over-estimate) is as follows:

- | | |
|--|--------------------------------|
| a. Lens cotton (long-grain sterile cotton batting) | One 4 oz. box |
| b. Lens cleaning alcohol | One 8oz. bottle (100% alcohol) |
| c. Facial tissues | Six boxes (200 tissues/box) |
| d. Spare view lamp (#BH3-3277) | One |
| e. Canon camera fuses (125V, 4 amp) | Two |
| f. CDs and CD labels | 250 |

3. EQUIPMENT SET-UP

The fundus camera should be placed in a room that can be completely darkened during the photography procedure. This is because no dilating drops will be used and we rely on the natural dilation of the pupil that occurs in the dark to perform the fundus photography. The camera should be placed in the room so that the patient has easy access to the examination stool and so that the photographer has ready access to the room light switch. A small reading lamp located near the camera, equipped with red light, may be used to help the photographer see to navigate and write during the procedure. This lamp should be turned off during photography to reduce the risk of pupil constriction. Light from the computer screen may need to be adjusted to minimize pupil constriction.

The fundus camera will be set on the motorized instrument table and the laptop computer will be attached to the articulating arm located above the camera's video display monitor. The pneumatic stools are positioned on opposite sides of the fundus camera.

The retinal photography trigger module will be located on the motorized table next to the camera. The trigger module will remain covered when not in use, and will not be removed from the room. All cable connections between these units themselves and the camera should remain permanent, apart from the power supply main cord. Any question or problem arising with their function should be directed to Dan Yee or David Markovitch at (608) 262-1326

3.1. Daily Set-Up Procedure

The camera dust cover and lens cap should be removed at the beginning of the day and the lens inspected and cleaned (see section 3.2) as necessary. Dust is the greatest enemy, producing the majority of artifacts on the photographs. When the camera is not in use, the lens cap should be in place and the special dust cover must remain on the camera.

3.2. Camera Lens and Body Care

Before each photograph, the camera lens must be inspected and, if dirty, cleaned with the brush and air bulb to remove debris. Should more extensive cleaning of the lens be required, the lens can be fogged with your breath or moistened with absolute alcohol and then cotton should be used in a circular polishing motion until no dirt or oily film is visible on the lens when it is viewed from the front with the alignment lens removed and the view lamp on and turned up to its near maximum intensity (see page 28 in the Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual). The body of the camera should be kept clean and free of dirt with a soft cloth and water or a common spray cleaner. The forehead rest may be cleaned with alcohol.

3.3. Instrument Table and Stools

The instrument table and stools can be kept clean by wiping with a common spray cleaner and a soft cloth. Occasionally the castors on the table and stools may squeak requiring a drop of light oil. The electric motor on the table requires no lubrication. The motor is protected by fuses, which may need to be replaced should excessive current blow them out. The power rating of the fuse will be indicated near the instrument table fuse holder.

3.4. Flash, View and Split Lamp Concerns

The Canon cameras are equipped with new lamps at the beginning of the study. It is not anticipated that the flash lamp will fail during the study. The view and split lamp should last approximately one to two years and are easily replaced as needed. The flash lamp has a life of at least 5,000 flashes, enough to complete the study. Since the view lamps are relatively inexpensive bulbs, one spare should be ordered from Canon USA, Inc. and kept at the site. Clinic staff in the field can replace the view lamp. Remember to keep all oil from your fingers off these lamps during replacement. The flash and split lamp should be replaced by a qualified technician. Both lamps can be ordered from Canon USA, Inc. when needed for overnight delivery.

As the flash lamp ages, the light output can diminish, producing progressively darker photographs. This can temporarily be over-ridden by an adjustment of the transformer output, though ultimately the lamp should be replaced. The decision to replace the lamp, due to dark photos, will be made with the Photography Consultant following routine review of the digital photographs. The flash lamp requires careful handling during installation (the burnt out lamp may be hot, and the new lamp must be properly aligned. Replacement should be attempted only by a field center staff trained to do this.

3.5. Camera Malfunctions or Errors

Since the camera requires virtually no other maintenance, any malfunction will need to be investigated first by the photographers, when necessary, via telephone with the OERC staff. Trouble-shooting tests can be performed in consultation with the OERC staff to diagnose any malfunction. Because the photographer can see the digital images immediately after they are taken, he or she will be alerted to problems not evident until the processed films are reviewed with conventional film-based fundus cameras. This includes problems with transformer power settings, problems with a dirty objective lens; improperly focused images or missed images caused by a patient's blink or other software/hardware malfunctions.

Some camera malfunctions or photographer errors may not be evident to clinic staff during photography and will not be discovered until the digital images are reviewed at the OERC. This includes unusual image artifacts or problems related to the camera or software. For this reason, prompt transmission of images to the OERC is important and we anticipate that images will be archived and transmitted to the reading center once each week. Additionally, a telephone should be available in the camera room so that the site photographers and the OERC photography consultants can speak should a malfunction be discovered during photography or should the photographers have a problem or question needing immediate attention. The photography consultants, Michael Neider, Hugh Wabers and Anne Goulding can be reached at 608-263-9858.

Service information can also be obtained directly from Canon USA, Inc., Irvine, California or Itasca, Illinois. Our contacts there are Tom Penkala, Canon USA, Inc., 100 Park Blvd., Itasca, Illinois, (telephone number: 630-250-6230, e-mail: tpenkala@cusa.canon.com) or Mark Scheckle, 15955 Alton Parkwa, Irvine California, telephone number: 949-753-4193, e-mail: mscheckel@cusa.canon.com),

4. SUBJECT PHOTOGRAPHY OVERVIEW

Digital images will be transferred into a table mounted laptop computer, archived to CD, and transmitted weekly to the OERC in Madison, Wisconsin, via FTP protocol for analysis. Before the first patient of the day is photographed, the photographer prepares for the photography session by first turning on the power to the Canon 10D camera back. The power is then turned on for the Canon CR6-4NM fundus camera and to the Dell laptop computer. The photographer escorts the patient into the photography room, positioning them before the fundus camera, and explains the procedure. The EyeQSL software program is initiated and subject ID and photographer information is entered into the appropriate computer screens and the software is set to acquire images.

A total of 5 photographs will be taken from both eyes of each participant centered around two specific eye fields. Field 1 will be centered on the optic nerve and Field 2 on the macula. A diagram of the location of these two fields can be seen below in Figure 1. The retinal photography sequence is given below:

Photograph number	Eye	Field	Photography details
1	Study eye	Field 1	Ear pulse synchronized
2	Study eye	Field 1	Unsynchronized
3	Study eye	Field 2	Unsynchronized
4	Fellow eye	Field 1	Unsynchronized
5	Fellow eye	Field 2	Unsynchronized

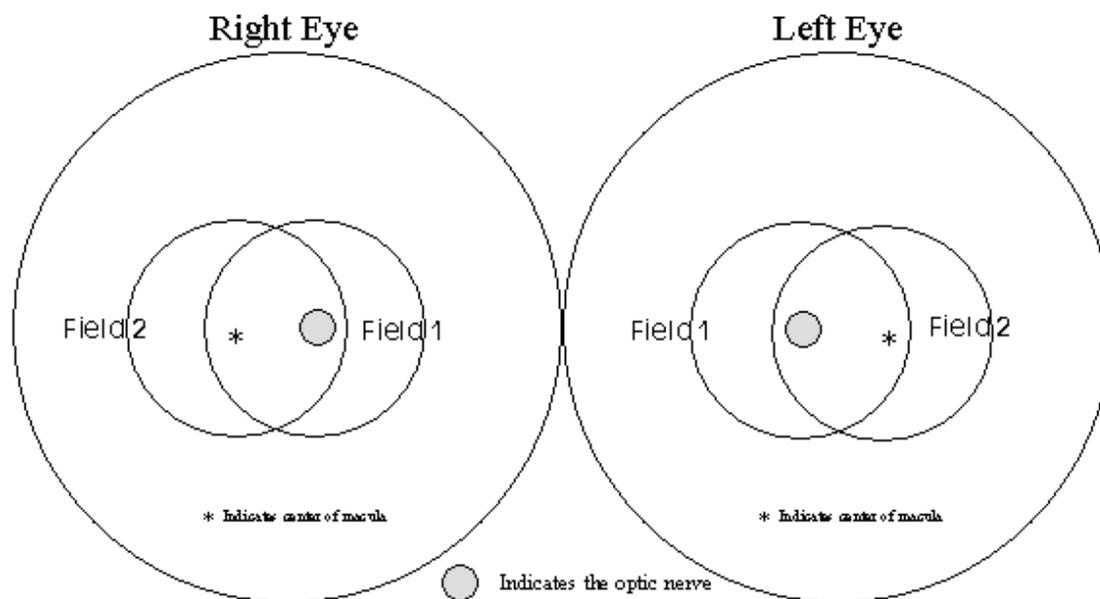


Figure 1

The study eye will be selected based on the subject's ID number. When the value of the ID number is even, the right eye will be photographed first, and when it is odd; the left eye will be photographed first. If the eye specified by this algorithm is considered too difficult to photograph with adequate photographic quality, only the opposite eye should be photographed, and an explanatory note entered in the Sleep Apnea-Eye Study Photography Completion form. Conditions falling into this category are (based upon the technician's judgment): eye missing, inability to dilate at least 4 mm, inability to fixate adequately for proper photographic fields, and opacities of the media preventing a reasonably clear view of the retinal vasculature and resulting in unreadable digital images.

4.1. Subject Exclusion

The photographer will attempt photography on subjects with poor visual acuity who may be unable to direct their gaze so that their optic nerve or macula is properly positioned on the camera monitor (as may be the case where both eyes are blind or when the subject is deaf and communication with them is impossible). In these cases, the photographer should get the best field definition possible. If, in the photographer's judgment, no acceptable photograph can be taken of either eye, the subject will be excused from photography.

The photographer should attempt photography on those subjects who are physically disabled, to the point that they can be comfortably positioned at the camera. To facilitate this, the subject may remain in a wheel chair positioned before the motorized camera table lowered to the appropriate height. Care should be taken when lowering the camera table to avoid pressing against the subject's legs. If, in the photographer's estimation, the subject cannot be comfortably positioned, no photography will be performed.

4.2. Pre-examination Procedure

Before attempting photography, the photographer should become very familiar with the camera through a training session and by learning the terminology on pages 4 and 5 of the Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual. This Retinal Photography Protocol uses terminology from the Operation Manual and it is recommended that the entire manual be reviewed by each photographer before performing photography.

The retinal camera and trigger unit should remain covered when not in use. High humidity or temperatures must be avoided. Dusty conditions mean that the camera will need frequent cleaning. The objective lens should be checked and cleaned with the air bulb if necessary before each subject is photographed. A more extensive cleaning is required to remove grease, smudges or stubborn spots from the lens. This cleaning requires removal of the lens "boot" and external alignment lamp ring and should be referred to the chief photographer at each field center.

4.7. Subject Explanation

Photography begins with a complete explanation of the procedure by the photographer. A color illustration may be useful to show what the retina looks like. It is important to reassure the subject that no retinal damage is caused by this procedure. The subject should know to expect several flashes. The pictures will include the macula (area of central vision) and it is normal to experience a blue or red tint to vision immediately following the flash. This disappears within five to seven minutes. No dilation drops will be used for this examination, and the eyes will not be touched. A sample script of a typical retinal photography explanation (suitable for use as written material for deaf or interested subjects) follows:

We will be taking several photographs of the inside of the back of both of your eyes (the retina) so we can study the blood vessels and look for any unusual changes. We will not be touching your eyes or be giving you any eye drops to take the pictures. Instead, you will be asked to sit in a darkened room before a special camera with your chin in a chin rest. We darken the room so that your pupils will dilate and we can align and focus the camera on your retina. While your pupils are dilating, we may ask you some questions about your vision and the health of your eyes. During the aligning process you will only be aware of some small red lights and a blinking green box and red bars visible in the camera lens. We will ask you to follow the blinking green box as we move it. Just before we take the picture, we will ask you to blink your eyes and then open them real wide. The camera will flash a light from within the camera lens as each picture is taken.

Just after the picture is taken, you may see a blue or red circular spot before the eye photographed. This will disappear within 5-7 minutes and causes no damage to the eye. Please remember that we are only taking pictures (not an x-ray) of a small portion of the back of your eyes and that this picture will not substitute as an eye examination. You will certainly be notified should we notice anything requiring immediate attention. Please continue to see your eye doctor on a regular basis for your complete eye examinations.

4.7. Completing the Sleep Apnea Eye Study Vision History Form

While the subject's eyes are dilating, the photographer will complete the Sleep Apnea Eye Study Vision History Form, which concerns the subject's ophthalmic history. The time taken to complete the form will be used to sufficiently dilate the subject's eyes for photography. This will depend upon adequacy of ambient light for the photographer (to be able to read questions and record answers) and upon the time required to answer the questions). For logistical reasons, this form may be completed as a paper form, and later entered into the computer system.

4.7. The Sleep Apnea Eye Study Photography Completion Form

The Sleep Apnea Eye Study Photography Completion Form records the circumstances of the photographic session, and can only be completed as the session begins. The participant's ID number should be filled in at the top right hand corner of the form. The last digit of this number will determine the

study eye (right eye if even, left eye if odd); this eye should be photographed first. Before beginning the photography session, the photographer records his or her initials, the photography date and the date that the Vision History Questionnaire was completed. If either eye cannot be photographed for a reason gathered during the ophthalmic history (e.g., that eye has been enucleated) or for a reason that emerges during the first part of the session (one eye does not dilate sufficiently well to be photographed), the photographer should record this in the comments section. The flash setting (2 unless re-adjusted by the photographer) and the estimated diameter of the pupil at the time of the first photograph of each eye should be recorded. The photographer is encouraged to comment on anything unusual such as artifacts, pathology or other problems encountered during the session. When the photography session is over and the photographer is reviewing the images in the contact strip, the eye and fields photographed should be marked. If extra images were taken, mark "other" and record the reason for extra images in the comments section. When the final images for each have been decided upon by the photographer, he/she can record the total number of images taken of each eye. Photocopies of this form will be mailed along with the images to the OERC in Madison.

4.8 Preparing the Camera

The Canon 10D digital camera back must be turned on first. This is done using the small dial located on the back left side of the camera body. This must precede turning on the Canon fundus camera or computer since the camera "looks" for the 10D camera body during start up. The Canon CR6-45NM video display is activated when the power switch on the side of the main unit is turned on. If no photography or switch operations are performed for 10 minutes, a power saving mode is activated, turning the lamps and display off to prevent unnecessary wear. During this power saving mode a green "ready" lamp blinks on the monitor. Pressing any button below the monitor will reactivate the system.

Notice that the flash power setting (located on the lower right-hand corner of the monitor) blinks when the main unit is switched on. This indicates the system is charging up. Do not attempt to take photographs until the blinking stops, indicating a fully charged flash.

The camera contains an internal clock and the date will automatically change each day. The photographer must manually change the date if this clock should fail or if the camera is left unplugged for a long period of time. The date is displayed on the fundus camera monitor and is changed through the menu located in the "Set 3" screen (see p. 154 in the Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual). The date format will read Month-Day-Year. The Canon 10D camera body should be attached to the main unit and set with the following settings:

Shutter speed	60
Mode Dial	Manual
White Balance	Flash
Quality	Large/Normal
Red Eye	Off
AEB	0-
ISO	400
Beep	Off
Auto power off	Off
Review	On
Review Time	8 seconds
LCD	Normal (three bars)

The camera should remain ON until the end of the day

4.9 Technical checks for the retinal photography trigger module:

a. Trigger module is plugged into CR6 camera base.

b. A 5-minute warm-up time was allowed for the trigger module.

Front panel switch has been set to "30" (30 percent of the pulse-to-pulse wave in the ear lobe)

5. EXAMINATION PROCEDURE

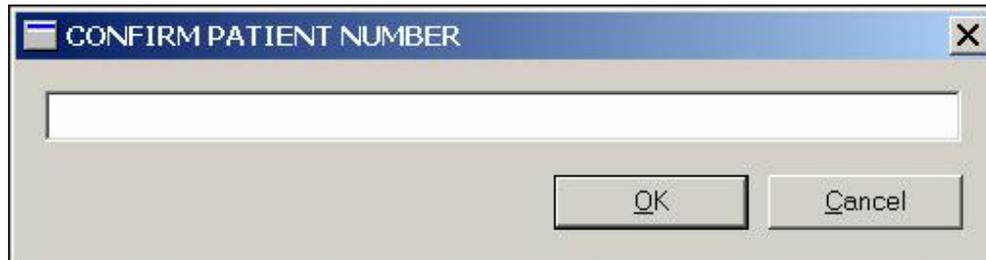
5.1. Subject Positioning and ID Entry

The subject and photographer are seated on the appropriate sides of the retinal camera. The subject is positioned so that he/she is comfortable with chin and forehead in the headrest. Chin height should be adjusted so that the eyes are approximately level with the height adjustment mark on the face rest pole. The room is darkened to the level where a newspaper can barely be read (equal to about 5 lux). The camera room door is closed. The only light in the room should come from the display monitors. If a lamp is used to aid the examiner during administration of the questionnaire, it must be turned off when photography is performed.

The subject should have the trigger monitor ear clip attached to the left ear lobe. A short baseline pulse wave tracing will be produced. When the LED is off or on constantly, the automatic gain circuit is searching for a signal. The photographer should wait for a steady signal from the LED on the trigger unit. When it begins to blink steadily (at the patient's heart rate), photos can be taken.

While the subject begins to dilate, the photographer begins the image capture procedure by double clicking the desktop Digital Healthcare Client icon and selecting the EyeQSL program. A "Login" screen will appear in which the name and password for that computer are entered. An "Unarchived Visits" screen will appear containing images from any patients who have not yet been archived. Select the "Next" button on this screen to open the "Identify a Patient" screen.

The photographer then enters the patient's unique 4-digit subject ID number in the Patient Number. The first letter of the ID number should be entered into the Acrostic field, and the photographer's initials into the Photographer # field. These fields must be filled in before the photographer is able to begin capturing images. Additional information may be entered into fields as indicated in the study protocol. The "Next" button is clicked until the "Confirm Patient number" box appears, at this point, the patient number is re-entered and the "OK" button is selected. A "Visual Acuity" box will appear, then click "Cancel".



The photographer is ready to begin taking photographs when the 4-panel split screen and timer box appear. The timer box displays the time the photograph was taken and also the current photo number.



When the photographer takes a picture, the timer stops and the image will briefly appear on a screen located on the digital camera back. It will then take a few seconds for the image to transfer from the camera to the computer screen. The timer will restart after the image appears on the screen. The photographer will review the image for quality and may take another image if they believe a better quality image can be obtained or they may accept the image by simply taking the next photograph when the patient is ready and the pupil is adequately dilated.

At the time the photographer has completed the patient's photographs, he/she will select the "End" button located on the timer box. The photographs that have been taken will then appear on the computer screen in a "Contact Strip" box. The photographer reviews all of the images in the contact strip and may delete any unwanted images at this time. This is done by left clicking on the image to be deleted, making the gray border around the image turn purple. Select "Delete from..." on the menu that appears. Select "Delete from Visit." The photographer may then elect to continue the photography session, if they wish to retake a particular field. Once the technician is satisfied with the photographs, he or she can select "Quit" to end the photography session. At this point, a new subject may begin being photographed by filling in the new patient information and repeating the steps stated above. If no other participants are to be seen, the photographer can "Quit" the program.

5.2. Pupil Size and External Camera Alignment

The camera stage holding knob is unlocked, the alignment switch is turned on and the stage is moved to center the eye to be photographed horizontally and the height adjustment ring is used to position the eye vertically. The pupil should appear on the TV screen coinciding with the central circle on the monitor. The camera joystick is moved forwards or backwards until the pupil appears perfectly round. At this

point, proper external alignment has been achieved. A pupil larger than the central 4mm circle on the monitor is required for adequate photography. If the eye does not dilate to at least 4mm after a 5-minute waiting period, the fellow eye should be examined for pupillary dilation as well. If dilation of the fellow eye is larger, the photographer will photograph the fellow eye first. At this point, the pupil size is measured using the alignment circle on the monitor as a gauge. This measurement is estimated to the nearest 1mm and it is recorded on the Sleep Apnea Photography Completion form.

5.3. Internal Eye Alignment

Once proper external pupil alignment is achieved, the alignment switch is pressed to provide a view of the fundus, split focusing lines, corneal reflection dots, and the fixation light. If no split lines are seen, the height or left/right adjustment is improper, the "Split" (split lines) setting is set to "off" (Set 1, Split/FCD), or the diopter compensating slider is pulled out. The split lines may fade in and out if the pupil is too small, the alignment of the camera is not centered on the pupil, or if the eyelashes or lids eclipse the light. If no corneal reflection dots are seen, the forward/backward adjustment is improper. The best photographs are obtained when the eye is well dilated, fixation is on the target; and lids and lashes are held wide open.

5.4. Alignment, Focus and Proper Fixation of Fundus Photographs

While viewing the fundus image on the screen, the photographer carefully adjusts the fixation target control button to locate Fields 1 and 2 correctly on the screen. Field 1 is always photographed first.

Any fine adjustment of fixation is made by moving the fixation lever and instructing the subject to look into the lens of the camera at the green target box. In the event that the subject sees no fixation light with the eye being photographed, the photographer must carefully instruct the subject to make micro movements (fine movements up, down, left or right) until the protocol fields are located.

Once the fixation is confirmed, the photographer must constantly adjust and position the camera to maintain the correct position of the corneal reflection dots. It is important that these dots be properly positioned at the three and a nine o'clock positions before the picture is taken. This will ensure the correct distance from the eye and will allow capture of a sharp digital image. Focus is done manually by dialing either of the focus knobs located on the side of the fundus camera. Proper focus is obtained by aligning the two horizontal focus bars visible on the fundus camera monitor (see p. 12 of the Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual). Good focus is critical for grading photographs.

The photographer will instruct the subject to blink once or twice just before the picture is taken. This blinking will insure a moist (and subsequently clearer) cornea and will safeguard against unwanted blinks at the moment of exposure. Once alignment is satisfactory, the shutter release, located in the tip of the joystick, is depressed and the exposure is made. The quality of the digital image is evaluated by the examiner and ungradable images, which in the opinion of the photographer may be improved, may be retaken. Once the best quality image is obtained, the second field is photographed and the photographer conducts the same image evaluation procedure.

6. PHOTOGRAPHIC CHALLENGES

6.1. Photography Through Small Pupils

The photographer will experience much more difficulty attempting photography through small (less than 4mm) pupils because all of the camera light doesn't enter through the smaller pupil. This usually results in uneven illumination (seen as dark shadows) on the monitor. In this situation, the photographer must make careful camera adjustments to position the shadows as far away from the optic nerve in the Field 1 photo and away from the macula on the photograph of Field 2.

A small percentage of subject's eyes will not dilate to the minimum 4mm required for adequate photography. Certain medication may prevent any dilation and the pupil size observed on the monitor may be 2-3mm, inadequate for the photographer to appreciate all retinal landmarks on the viewing monitor. In this case it is recommended that the photographer introduce the small pupil aperture located on the left side of the fundus camera body (see p.10 of the Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual). This function adjusts the illumination to concentrate more of the retinal illumination into a smaller area providing more even illumination to the center of the field while sacrificing illumination at the field perimeter. If after introducing the small pupil function only one focus line is visible, it might be necessary to adjust the camera position either vertically or horizontally to bring the second line into view so that accurate focus can be set. However, there may be circumstances that prevent the second line from appearing, even when the camera adjustments are made. In these cases it may be helpful to remove the small pupil function momentarily while searching for the second line and adjusting focus, and reintroducing the small pupil function before taking the photograph.

If no retinal landmarks are visible, often the case with ≤ 2 mm diameter pupils, the photographer should adjust the camera slightly to position the corneal reflection dots slightly above or below their optimum position. This technique allows a portion of the illumination light (which falls on the iris when the pupil is small) to enter the eye. If any retinal landmarks become visible with this technique, a picture should be taken. However, if no retinal landmarks are visible, no picture is taken. The photographer notes the problem on the Photography Completion form.

6.2. Exposure Compensations for Dark or Light Retinas

The normal flash output used in this study will be flash number 2. The flash output can be increased or decreased by first pressing the "DA" button followed by the +/- buttons located under the main video display screen of the fundus camera monitor. Higher numbers increase flash output and produce brighter images while lower numbers decrease flash output and produce darker images. A one number increase or decrease in flash intensity is usually all that is needed. Photography through small pupils, media opacities or of darkly pigmented retinas (Black or Asian) will require increased flash output (to flash 3) to avoid underexposed pictures. Photography of lightly pigmented retinas (blond, albino or Scandinavian) will require decreased flash output (to flash 1) to avoid overexposed pictures. The photographer should check the color saturation of the first image taken of each participant, and adjust the flash if necessary before proceeding.

6.3. Focus with High Myopia or Hyperopia

The diopter compensation slide should be set to the "0" position for most eyes. This is the only setting in which the focus bars are active and allows photography of eyes with refractions between -12 and +15 diopters. In the event that the eye photographed falls outside this range and focus cannot be achieved, as in the case of aphakia or high myopia, the diopter compensation slider must be adjusted for the clearest focus to the "+" or "-" position and the focusing knob is then turned manually to provide the

sharpest image as seen on the monitor. Obtaining a brighter retinal image by increasing the view light intensity can facilitate this. The normal setting for the view light intensity adjustment is 4.

Standard TV monitor functions can be adjusted for the photographer's viewing comfort (including contrast and brightness) by opening the access door below the TV monitor. These are standard controls similar to those found on a home TV set and only effect viewing. They do not affect final photo quality.

7. Inventory form

At the end of each week, all Sleep Apnea Eye Study Photography Completion forms will be given to the person who will archive the images. Whomever archives the images should compare the completion forms to the “unarchived” images before archiving the images to confirm that all visits are present. Once the images have been archived, the contents of the CD (patients’ ID, photo date, eye and fields photographed) should be recorded on the Sleep Apnea Eye Study Non-Myd Digital Photograph Image Inventory Form. The date the images were archived and the 10 digit CD number (assigned by the EyeQSL software during the archiving process) should be recorded on the inventory form, as well as the name of the person preparing the CD and transmitting the images and the batch number. If a second person would like to have confirmation of OERC receipt of images, their name and email address should be written beneath the person preparing the shipment. Comments about the archiving process, inconsistencies between the Sleep Apnea Eye Photography Completion Forms and Sleep Apnea Study Non-Myd Digital Image Inventory Form, or other deviations from protocol should be recorded in the comments box on the shipping manifest.

8. DIGITAL FILE HANDLING

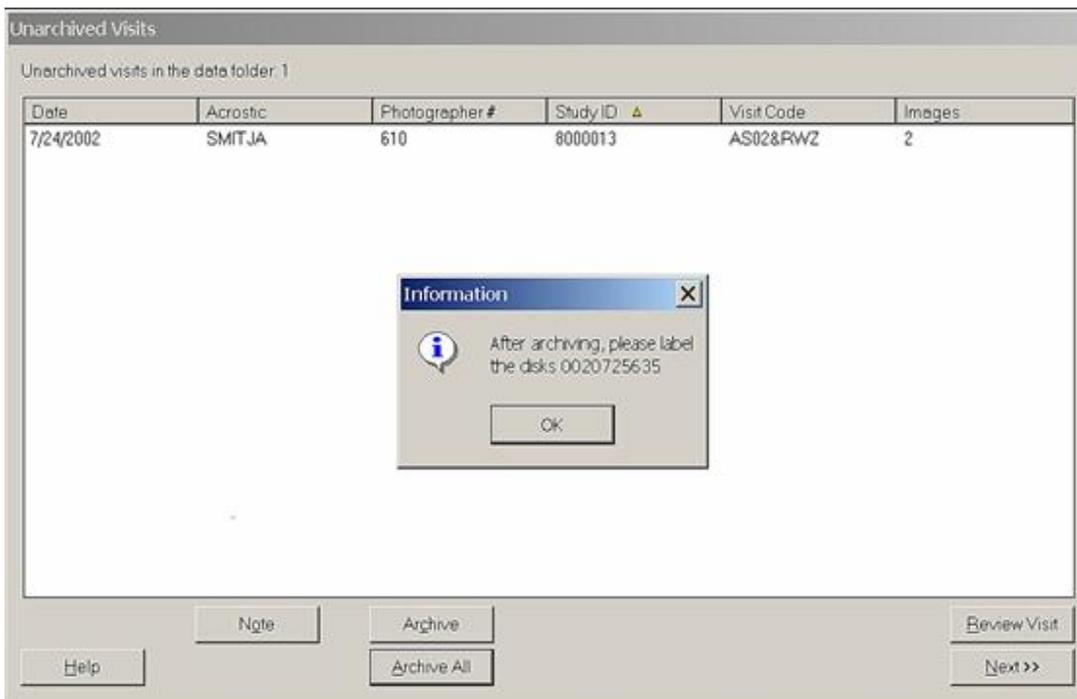
8.1. Archive Procedure

The archiving process will be completed at the end of each week after the final participant has been photographed. The photographer is required to make one archive copy. The first step in the archiving process involves formatting the CD. A blank CD is placed into the CD drive on the laptop computer. After a few seconds the “Roxio EZ CD Creator 5.0”, a CD writing program, should appear on the screen. If it does not, the CD writing program can be selected from the Start Menu/Programs.

When prompted, select “data” and then “Direct CD”. Next, select “Format CD”. When prompted to type a label for the disc, leave the space blank and click “start format”. The program will begin formatting. When finished, select “OK” and close the CD writing program. You will be unable to pre-format them as the CDs will need to be “closed” before ejecting them (see next paragraph).

Once the CD has been formatted, the photographer may then proceed to the “Identify a Patient” screen and select the “Archive” button. All of the visits for the week that have not already been archived will appear on the “Unarchived Visits” screen.

The photographer has the option of selecting the “Archive All” button or selecting or highlighting individual visits and clicking on the “Archive” button separately. Note that only ten participants can be saved onto a CD. If more than ten visits are unarchived, select the first fifteen and hit “Archive”. Record the information for these visits on the inventory form. An information box will appear before the archiving process begins, which prompts the photographer to label the disk with a specific code number. **This number must be written on the CD and on the inventory form.**



Once this information is taken note of, press “OK” and the computer will begin archiving. This may take several minutes depending on how many images are being archived.

Eject the CD by pressing on the eject button located on the front of the CD drive. There will be options on how to save the information. Select “Close and read on any computer,” also check the box for protecting the CD from being written to again.



8.2. CD labeling

The archived CDs should be labeled as shown:

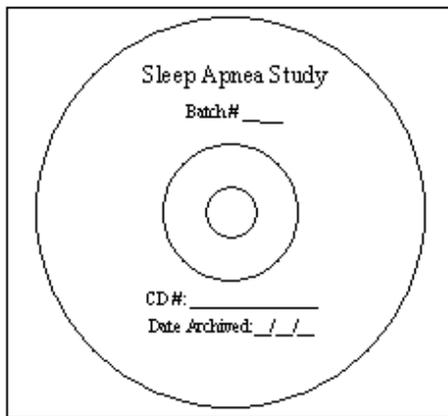


Figure 2

The person creating the CD should record the study name, date the CD was archived and the **10 digit CD number** assigned by the EyeQSL software. The CD should be placed in a jewel case and stored safely on site for image back up.

8.3. Image Transmission

Once the labeling of the CD is complete, the CD should be placed back in the CD drive for transmission. The photographer should then hit the "Upload" icon on the desktop. A dialog box entitled <Image Uploader> will appear, and messages reporting the status of the program will be listed. When the transmission is complete, the statement "Status: Successfully Sent" will appear. Hit "exit" to end the process. If an error message appears, contact the tech support at the OERC.

9. PHOTOGRAPHER CERTIFICATION

9.1. Obtaining Certification

Each examiner taking fundus photographs will need to become certified before taking photographs for the study. The initial group of photographers will receive didactic and hands-on training at the University of Wisconsin. The Reading Center Photographic Consultant, Michael Neider, will conduct this training, which will involve training on equipment set up. Following the training, each photographer will practice taking photographs and will prepare photographic sessions for submission to Michael Neider for certification via image transmission to the OERC. Certification begins with the completion of the Photographer Certification Request Form (Attachment 2). This form is submitted along with photographs of 10 eyes (5 right eyes and 5 left eyes) photographed following the study protocol. A photographer is fully certified after submitting satisfactory quality photographs of 10 eyes taken on non-study volunteers. These photographs must show proper field definition (Fields 1 and 2 of each eye, 20 images total), proper exposure, alignment and focus. Photography certification subjects should be assigned study ID numbers using a sequential 3 digit number, starting with 101. The acrostic for all certification subjects will be "CERTIFY", and the photographer's initials. For example:

Study ID: 101 (102, 103, ect.)

Acrostic: CERTIFY

Photographer: AAA

The photographs must be archived to CD, completely labeled and transmitted according to protocol. A separate CD should be submitted for each technician. Once certification is complete, the photographer's information will be entered into the database and notification of certification will be forwarded to the photographer.

9.2. Certification of New Photographers

As additional personnel need training to become certified, a certified photographer at that center will provide complete instruction and copies of the Ocular Epidemiology Photography Protocol and Canon Non-Mydriatic Retinal Camera CR6-45NM Operation Manual. The trainee photographer will practice on volunteers and, when ready, prepare and submit photographs of 10 eyes for consideration for certification.

9.3. Certification Maintenance Requirements

In order to maintain certification, photographers must complete photograph a minimum of 6 eyes per month and 75% of their photographs must be gradable. This will be determined from the monthly photo quality report generated by the study coordinator. If a photographer fails to meet either of these requirements, he or she will be contacted and given feedback by a photography consultant. During the following month, the photographer will be allowed to continue to take photographs of study participants only if supervised by a fully compliant certified photographer. If the photographer does not meet these standards of quantity or quality of their photographs for three consecutive months, certification will be revoked. The technician will not be able to take study photographs until he/she has submitted a new set of acceptable certification photographs.

10. QUALITY CONTROL

10.1. Photograph Quality

Photographers will provide the first assessment of photo quality, a big advantage of digital imaging. This "on the spot" review of images allows for the immediate assessment of image quality and the opportunity to retake the images before the patient leaves the camera photography area. Additionally, Reading Center staff will continuously monitor photographic quality throughout the study. Initially all photographs will be reviewed by reading center staff and feedback will be provided to the photographers in cases that warrant critique. A telephone call, e-mail or letter will be used detailing problems and suggesting improvements. Once the study is underway and the photographers sufficiently trained, data on quality will be generated from the photograph readers' evaluations of all photographs. The Photography Consultant will review a small percentage of the photographs, and feedback will be provided to the photographers in cases that warrant critique. In cases where problems with photo quality persist, the additional training may be arranged at the Ophthalmic Photography Learning Center (OPLC) located in Madison, Wisconsin.

11. COMMUNICATION CHANNELS

It is vital that proper and frequently used channels of communication be established for the effective exchange of questions and information between all staff members. Following is a listing of names, addresses, and telephone numbers to facilitate this exchange:

Ocular Epidemiology Reading Center
610 North Walnut Street, 4th Floor WARF
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Barbara EK Klein, MD, MPH (608) 263-0276
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Anoop Shankar, MD, MSc., MPH (608) 265-0027
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Stacy Meuer (608) 263-8835
Senior Grader meuers@epi.ophth.wisc.edu

Fundus Photograph Reading Center
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