Optical Coherence Tomography (OCT) Data Acquisition Manual

Version 2.0

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Dear Operator,

Retinal optical coherence tomography (OCT) allows detailed analysis of the retinal layers using low-coherent, near-infrared light. As for Magnetic Resonance Imaging (MRI) in clinical trials in Multiple Sclerosis (MS), a high level of precision in OCT assessment is needed. To ensure that the measurements are of high quality, there is a need for an independent reading of scans based on established quality criteria.

As the OCT operator is the only person who will see the live images during data acquisition he/she is a key figure to guarantee data quality. This OCT data acquisition manual, together with the training video that is available on our website, was put together to assist you achieve the best quality OCTs for the BENEFIT11 study. As soon as you are registered with the Zurich Reading Center, you will be asked to upload a certification scan. Should that scan meet the quality criteria, you will be certified to upload OCTs gathered from the BENEFIT11 patients of your centre.

We strongly recommend that you use this manual in conjunction with the tutorial video, which is available to view on our website after logging in with your personal details and password:

www.neuro-oct.com

The manual assumes throughout that the operator has previous experience of using the Heidelberg Spectralis OCT and/or Heidelberg Spectralis HRA + OCT.

We hope you will find this manuscript helpful and wish you every success in working with this exciting technology.

Yours,

Sven Schippling, MD
James Hanson, PhD

Zurich, July 2013
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INTRODUCTION

This manual summarises the retinal OCT acquisition procedures relevant for the BENEFIT11 OCT study. A certification scan, ideally performed on a healthy control subject matching one of the BENEFIT11 patients at your respective study centre, will be needed in order to become certified as a retinal OCT operator for the BENEFIT11 OCT study. Quality reading of the submitted scans will be based on: completeness of data acquired, correct labeling of the OCT files, and the OSCAR-IB quality criteria [Tewarie et al., 2012]. The quality reading criteria are described in more detail on page 29.

An instructional video, matching large parts of this manual, is available for online view on our website: www.neuro-oct.com

A separate manual is available to guide you through the process of uploading the OCT scan data to the central server.

This manual was written with the aim of illustrating the required procedures as clearly as possible. Please do not hesitate to contact us if any part of the manual remains unclear. Our contact information can be found at the end of the manual.
OCT HARDWARE

There are two OCT systems produced by Heidelberg Engineering:

- Spectralis OCT
- Spectralis HRA+OCT (also known as Spectralis Plus)

Both systems can be used interchangeably in this study. If you experience problems with the OCT hardware please contact Heidelberg Engineering directly (see contact details at the end of the manual).

SOFTWARE

After switching on the PC connected to the Spectralis, please start the Heidelberg Eye Explorer software as normal. At the time of writing the current version of the OCT hardware (Acquisition Module) is 5.6.4.0 and the current software (Viewing Module) is version 5.6.4.0. All data is stored in the “Heidelberg Eye Explorer” database version 1.7.1.0.

Please take a second to check which software versions your system has. To do so, click on “Help” at the menu bar and then click on “About...”. The new window will list all software versions, as shown in the screenshot below.
If your system has a software version older than that shown above (as indicated by a lower version number), please contact Heidelberg Engineering to arrange an upgrade (Mr. Sebastian Lukas; Support@HeidelbergEngineering.com). Because some features needed to obtain a certificate will require the software versions mentioned above, please have the upgrade performed before starting the study.
PATIENT NAMING PROTOCOL

Certification scans

Before performing scans on patients, each OCT operator must submit a scan on a healthy control subject (preferably matched in age and gender to a prospective patient in the study). This scan will be assessed in order to ensure that the operator is capable of obtaining scans of sufficient quality to be analysed in the study. When performing a scan to be submitted for certification, it is also important that no data that could identify the healthy control subject is provided. Therefore, please use the following proband data when preparing to record your certification scans:

Last name: BENEFIT11

First name: Country and site ID number (these are the first four digits of any of the six-digit PID numbers from your centre).

Title: to be left blank

Date of birth: 01.(true month).(true year).

Sex: enter female or male, as appropriate

Patient-ID: type ‘Certification’ followed by a space and your initials (not those of the control subject)

An example for operator JH, working at centre 01 in Switzerland (country33), and a male healthy control subject born in December 1975 is illustrated below:
Study scans

The OCT scan data submitted to the reading centre must not contain any data that enables a patient to be identified. Therefore it is important that the patient records are entered in the Heidelberg Eye Explorer database strictly according to the following protocol, in order to guarantee patient anonymity:

Last name: BENEFIT11

First name: to be left blank.

Title: to be left blank

Date of birth: 01.(true month).(true year).
**Sex:** enter female or male, as appropriate

**Patient-ID:** enter the unique six-digit PID given to the individual patient upon recruitment in the BENEFIT study, which enables identification of your country, site, and the individual patient. This will be in the format (XX/country code)(YY/centre code)(ZZ/patient number).

An example for male patient 01, born in December 1975 and registered at centre 01 in Switzerland (country 33), is illustrated below.
OCT IMAGING DATA ACQUISITION

Recording procedure

These instructions relate to the initial (baseline) examination. As Benefit11 is a cross-sectional study, only one OCT examination per patient is currently foreseen. However, OCT may also be an endpoint in future (as yet unplanned) studies.

Optic nerve head scans (ONHR-N preset)

After opening the measurement window, please ensure that under „Application & Structure“ the option “Axonal” is selected (see red box).

Select the preset „ONHR-N“ (1).

Using the focusing knob on the OCT device, select an initial focus of approximately 0.00 D.
Advise the patient to look nasally (i.e., to look left when measuring the right eye; to look right when measuring the left eye) at the blue fixation light. The patient should be allowed to blink as often as is necessary during scanning in order to optimize patient comfort and optical image quality.

Using the joystick, position the OCT camera so that both of the light-coloured reflexes visible in the fundus image (circled in red in the screenshot) overlap.
Move the camera slowly toward the patient, ensuring that the fundus image is evenly illuminated, until the two OCT images are visible on the right-hand side of the screen. The correct distance has been reached when the live cross-sectional OCT images are visible on the right-hand side of the screen. If necessary, adjust the focusing knob on the OCT acquisition module so that the retinal vessels are sharply focused (in the example below, a focus of -1.75D is required). The bar under the live OCT images should be blue in colour, which indicates adequate image quality. The greater the number displayed within the quality control bar (in the example below, 30), the greater the image quality.
Activate the eye tracker (Spectralis OCT: press and hold the button on the joystick for more than one second; Spectralis HRA & OCT/OCT Plus: press the black button on the touch panel).

Follow the specified steps carefully and precisely. Do NOT deviate from the following procedure in any way.

Position the Radial Scan marker over the centre of the optic nerve head (I)
To exactly define the position of the fovea, move the mouse to the centre of the macula region (II), then press and hold the left mouse button over the white dot visible on the live OCT image (shown on the screenshot below within the red circle). Using the live OCT image, mark the centre of the fovea using the vertical line and then release the mouse button.
Now define “Bruch's Membrane Opening” (BMO) using the two OCT images at the right of the screen. Bruch’s membrane is visible on the OCT scans as a bright horizontal line at the outermost aspect of the retina (i.e., the lowest brighty defined layer visible on the OCT image) which opens to allow the retinal nerve fibres to exit the eye as the optic nerve. The edges of Bruch’s membrane must be visualized and exactly defined. The easiest way to do this is by following the membrane from the edge of the screen until it ends. In the screenshot below, one of the four visible terminations of the membrane is shown by a red arrow.
To define BMO, click with the mouse on each of the four ends of Bruch’s membrane visible in the OCT images, one after the other. Once one of the ends has been defined, a vertical dashed red line will be visible on the OCT image at the defined location (see below).

Do NOT start the scan until all FOUR edges of Bruch’s membrane have been defined!

NOTE: it is possible that one or more of the edges which are first defined may lose their registration within the OCT software before all four edges are confirmed. In this case, simply click once more on the relevant end of Bruch’s membrane to define it once again. This is illustrated in the instructional video, which is viewable online at: www.neuro-oct.com.

The locations of BMO and the fovea that are defined at the initial scan will also be used for any subsequent scans, therefore any error made at the initial scan will also lead to all future scans being incorrectly centred. Please take great care to ensure accurate localization of BMO and the fovea at the initial scan!
When you are satisfied with your definitions of the fovea and BMO, start the scan by quickly (less than one second) pressing the joystick button (Spectralis OCT) or pressing ‘Acquire’ on the touchscreen (Spectralis Plus/ Spectralis HRA + OCT).

Four scans will now be automatically acquired without pause:

- A star scan centred on the optic nerve head (consisting of 24 radially-oriented line scans; see figure)
• Three ring/circle scans (diameter 12°, 14° and 16°) centred on the optic nerve head (example shown in figure). Note that each ring scan has a standard ART setting of 100. If this is not reached within a time limit, the procedure automatically moves on to the next scan (12° or 14° ring scans) or finishes the scan (16° ring scan). Only scans which reach an ART of 30 or more will be saved!

NOTE: because the star and circle scans are based on the location of BMO rather than the geometric centre of the visible optic nerve head, in some patients it may appear as though the scans are incorrectly centred; for example, in the following screenshot the centre of BMO lies slightly below the centre of the optic nerve head. However, this is no cause for concern as long as the BMO has been correctly located and defined.
During the scan process, please ensure that you keep control of the OCT with your hands at all times and monitor the live OCT image to ensure that the live OCT image is centred, evenly illuminated, and as close to horizontal as possible (correct beam placement; see OSCAR-IB criteria on page 28) in order to maximize image quality. Fine adjustments to the OCT device position will be necessary in order to acquire high-quality images.
When the star and circle scans have been acquired, the preset window is shown once again (see figure). The eye tracker is now inactive and the scan is no longer centred over the ONH and fovea.

**NOTE:** Please do NOT end the HEYEX software or switch to the other eye. If you do this, the BMO and foveal coordinates are lost and the entire process of defining BMO and the fovea as well as performing the star and circle scans must be repeated.

Now proceed to recording the scans in the PPoleN preset.
Posterior Pole scans (PPoleN preset)

The PPoleN preset consists of the following three scans, all centred on the fovea:

- 1x horizontal line scan (HS mode, 1 section, ART 2)
- 1x vertical line scan (HR mode, 19 sections, ART 25)
- 1x vertical line scan (HS mode, 61 sections, ART 15)

To record the PPoleN scans:

Firstly, click on the preset ‘PPoleN’ (2) immediately to the right of the ‘ONHR-N’ button (1) (see figure).

Advise the patient that the blue fixation light will now appear centrally rather than nasally, and that they should continue to fixate the blue light at all times whilst blinking whenever necessary.
The first scan of the PPoleN preset is a single horizontal line scan. This is to ensure registration of the previously-defined coordinates of BMO and the fovea, and will not be analysed.

When the eye tracker is engaged and the scan is centred on the fovea, press the joystick button briefly (Spectralis OCT) or touch the ‘Acquire’ button on the touch screen (Spectralis HRA & OCT/Spectralis Plus). The preset scans will now proceed without interruption until all are complete. As with the ONHR-N preset, please ensure at all times that the live OCT image is centred, evenly illuminated, and as close to horizontal as possible (correct beam placement; see OSCAR-IB criteria on page 28) in order to maximize image quality.
Following the single horizontal line scan, the first of the vertical volume scans commences automatically.
When the first *(high resolution)* vertical volume scan is complete, the second *(high speed)* scan commences automatically.
When the scans are finished, the eye tracker is disabled and the initial preset window is shown once again. At this stage you should move the OCT acquisition device to the other eye of the patient, and then repeat the procedure exactly as previously described, starting from page 9, on the other eye. When both eyes have been scanned, please exit the OCT acquisition window and save the scans by clicking on the \( \times \) symbol in the top right corner.
Please check that all of the scans have been successfully saved. Each eye should have seven scans visible in the database window.
The single horizontal line scan is no longer required and can safely be deleted. Assuming all three of the circle scans were successfully saved, the horizontal line scan should be the fourth of the seven scans (in the figure below, highlighted in red).
Finally, select all the remaining scans for the right eye, right click and select ‘Set reference’ from the menu. Repeat for the left eye.

Although BENEFIT11 is a cross-sectional study, it is important that in case of future clinical examination of the study patients, scans can be exactly replicated by performing Follow-Up scans.

Congratulations! You have now successfully completed the required scans. Please now upload the scans to the Reading Centre server by following the instructions in the upload manual.
OCT QUALITY CRITERIA: a brief overview

After upload of the data to the reading centre server (see separate Manual), all scans will be checked in order to ensure that they are of adequate quality. The primary quality criteria employed will be the OSCAR-IB criteria (Tewarie et al., 2012), which are briefly summarized in the table below. **Scans which do not meet one or more of the OSCAR-IB criteria will be rejected.**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Criteria</th>
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| O            | **Obvious** problems not covered by items below.  
  Please document for discussion + consensus agreement |
| S            | **Is the OCT signal sufficient?**  
  Signal strength > 15 (ring and volume scans) with appropriate averaging of multiple scans (ART activated). |
| C            | **Is the circle scan correctly centred?**  
  Post-hoc readjustment of the circle scan location is not possible. Readjustment is possible for the macular volume scan; however, if BMO and the fovea have been correctly defined, this should not be necessary. |
| A            | **Has the software algorithm functioned correctly?**  
  Red lines correctly identify the superior and inferior RNFL border (circle scan); red lines correctly identify the retinal borders (volume scan) |
| R            | **Is there retinal pathology which may impair the RNFL reading?**  
  A full list of excluding retinal pathology can be found in Tewarie et al., 2012. |
| I            | **Is the fundus well illuminated?**  
  Retinal structures should be visible (ring and volume scans) |
| B            | **Is the measurement beam placed centrally?**  
  Reflectivity of the ONL should be homogenous throughout the scans |


* At the time that the OSCAR-IB criteria were published, the ring scans were manually centred upon the optic nerve head rather than on BMO. As described on pages 18 & 19 and based on our own experience, in some patients the centre of BMO may not coincide exactly with the centre of the visible ONH. As long as BMO and the fovea have been correctly defined before commencing the scans, this is not a cause for concern.
Contact details

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