

Digital Imaging and Communications in Medicine (DICOM)

Supplement 143

DICOM SR Template for Reporting of Macular Grid Thickness and Volume

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Scope and Field of Application

5 This Supplement to the DICOM Standard introduces a DICOM SR template for reporting of macular grid thickness and volume values derived from ophthalmic images, such as OPT images. This is part of an ongoing program by DICOM WG9 to create a comprehensive set of DICOM supplements for the full range of ophthalmic instruments.

10 Clinicians would employ such a report in routine care of patients with macular disease. This is also of interest for clinical trial workflow, to allow standardized reporting from different brands of OPT devices to reading centers. Defining a standard report will allow data to be compared more efficiently from eyes imaged by various OPT machine types. This is critically important in clinical research, where data from scans from multiple instrument makers will need to be pooled for analysis and for longitudinal study of eyes where baseline scans may come from one machine but later data comes from another.

15

Changes to NEMA Standards Publication PS 3.2-2008
Digital Imaging and Communications in Medicine (DICOM)
Part 2: Conformance
Conformance

20

Item: Add to table A.1-2 categorizing SOP Classes:

The SOP Classes are categorized as follows:

25

Table A.1-2
UID VALUES

| UID Value | UID NAME | Category |
|-------------------------------------|---|-----------------|
| ... | ... | ... |
| <u>1.2.840.10008.5.1.4.1.1.79.1</u> | <u>Macular Grid Thickness and Volume Report Storage SOP Class</u> | <u>Transfer</u> |
| ... | ... | ... |

Changes to NEMA Standards Publication PS 3.3-2008
Digital Imaging and Communications in Medicine (DICOM)
Part 3: Information Object Definitions

30

Update PS3.3 Annex A to include Macular Grid Thickness and Volume Report

A.1.4 Overview of the Composite IOD Module Content

Table A.1-2
COMPOSITE INFORMATION OBJECT MODULES OVERVIEW - NON-IMAGES

| IODs Modules | Macular Grid Thickness and Volume Report |
|----------------------------------|---|
| Patient | <u>M</u> |
| Clinical Trial Subject | <u>U</u> |
| General Study | <u>M</u> |
| Patient Study | <u>U</u> |
| Clinical Trial Study | <u>U</u> |
| General Equipment | <u>M</u> |
| Enhanced General Equipment | <u>M</u> |
| Clinical Trial Series | <u>U</u> |
| SR Document Series | <u>M</u> |
| SR Document General | <u>M</u> |
| SR Document Content | <u>M</u> |
| SOP Common | <u>M</u> |

35 **Add the following to Ophthalmic Measurements IODs PS 3.3 Annex A**

A.35.x Macular Grid Thickness and Volume Report Information Object Definition

A.35.x.1 Macular Grid Thickness and Volume Report Information Object Description

The Macular Grid Thickness and Volume Report IOD is used to represent the macular grid thickness and volume values derived from ophthalmic images.

40 **A.35.x.2 Macular Grid Thickness and Volume Report IOD Entity-Relationship Model**

The E-R Model in Section A.1.2 of this Part applies to the Macular Grid Thickness and Volume Report IOD. Table A.35.x.3-1 specifies the Modules of the Thickness and Macular Volume Report IOD.

A.35.x.3 Macular Grid Thickness and Volume Report IOD Module Table

45 Table A.35.x.3-1 specifies the Modules of the Macular Grid Thickness and Volume Report IOD.

**Table A.35.x.3-1
MACULAR GRID THICKNESS AND VOLUME REPORT IOD MODULES**

| IE | Module | Reference | Usage |
|-----------|----------------------------|-----------|-------|
| Patient | Patient | C.7.1.1 | M |
| | Clinical Trial Subject | C.7.1.3 | U |
| Study | General Study | C.7.2.1 | M |
| | Patient Study | C.7.2.2 | U |
| | Clinical Trial Study | C.7.2.3 | U |
| Series | SR Document Series | C.17.1 | M |
| | Clinical Trial Series | C.7.3.2 | U |
| Equipment | General Equipment | C.7.5.1 | M |
| | Enhanced General Equipment | C.7.5.2 | M |
| Document | SR Document General | C.17.2 | M |
| | SR Document Content | C.17.3 | M |
| | SOP Common | C.12.1 | M |

A.35.x.3.1 Macular Grid Thickness and Volume Report IOD Content Constraints

50 **A.35.x.3.1.1 Value Type**

Value Type (0040,A040) in the Content Sequence (0040,A730) of the SR Document Content Module is constrained to the following Enumerated Values (see Table C.17.3-1 for Value Type definitions):

55 TEXT
 IMAGE
 NUM
 CONTAINER
 CODE
 PNAME

60 UIDREF
DATE

A.35.x.3.1.2 Relationship Constraints

65 Relationships between Content Items in the content of this IOD shall be conveyed in the by-value mode. See Table C.17.3-2 for Relationship Type definitions.

Note: Relationships by-reference are forbidden. Therefore, Referenced Content Item Identifier (0040,DB73) is not present in any of the Content Items within the SR Document Content Module.

70 Table A.35.x.3.1.2-1 specifies the relationship constraints of this IOD.

**Table A.35.x.3.1.2-1
RELATIONSHIP CONTENT CONSTRAINTS FOR MACULAR GRID THICKNESS AND
VOLUME REPORT IOD**

| Source Value Type | Relationship Type (Enumerated Values) | Target Value Type |
|-------------------|--|---|
| CONTAINER | HAS OBS CONTEXT | CODE, PNAME, TEXT, UIDREF, DATA, NUM |
| CONTAINER | CONTAINS | CONTAINER, NUM, TEXT, CODE |
| any type | HAS CONCEPT MOD | CODE |
| NUM | HAS OBS CONTEXT | TEXT |
| NUM | INFERRED FROM | IMAGE |

75 A.35.x.3.1.3 Template Constraints

The document shall be constructed from TID 2100 Macular Grid Thickness and Volume Report invoked at the root node.

Changes to NEMA Standards Publication PS 3.4-2008

80

Digital Imaging and Communications in Medicine (DICOM)

Part 4: Service Class Specifications

Add Macular Grid Thickness and Volume Report SOP Classes to PS3.4 Annex B

B.3.1.4 Related General SOP Classes (A-ASSOCIATE-RQ)

85

| SOP Class Name | Related General SOP Class Name |
|---|--------------------------------|
| <u>Macular Grid Thickness and Volume Report</u> | <u>Enhanced SR</u> |

B.5 Standard SOP Classes

Table B.5-1
STANDARD SOP CLASSES

| SOP Class Name | SOP Class UID | IOD (See PS 3.3) |
|---|-------------------------------------|---|
| <u>Macular Grid Thickness and Volume Report</u> | <u>1.2.840.10008.5.1.4.1.1.79.1</u> | <u>Macular Grid Thickness and Volume Report</u> |

90

B.5.1.5 Structured Reporting Storage SOP Classes

The requirements of Annex O apply to the following SOP Classes:

95

- Basic Text SR
- Enhanced SR, and SOP Classes for which it is the Related General SOP Class
- Comprehensive SR, and SOP Classes for which it is the Related General SOP Class
- Mammography CAD SR
- Chest CAD SR
- Procedure Log
- X-Ray Radiation Dose SR
- Spectacle Prescription Report
- Macular Grid Thickness and Volume Report

100

105

110

Add Macular Grid Thickness and Volume Report Storage SOP Class to PS3.4 Annex I

I.4 MEDIA STANDARD STORAGE SOP Classes

Table I.4-1
Media Storage Standard SOP Classes

115

| SOP Class Name | SOP Class UID | IOD (See PS 3.3) |
|---|-------------------------------------|---|
| <u>Macular Grid Thickness and Volume Report</u> | <u>1.2.840.10008.5.1.4.1.1.79.1</u> | <u>Macular Grid Thickness and Volume Report</u> |

I.4.1.2 Structured Reporting Storage SOP Classes

120 The requirements of Annex O apply to the following SOP Classes:

- Basic Text SR
- Enhanced SR, and SOP Classes for which it is the Related General SOP Class
- 125 • Comprehensive SR, and SOP Classes for which it is the Related General SOP Class
- Mammography CAD SR
- 130 • Chest CAD SR
- Procedure Log
- X-Ray Radiation Dose SR
- 135 • Spectacle Prescription Report
- Macular Grid Thickness and Volume Report

Changes to NEMA Standards Publication PS 3.6-2008

140

**Digital Imaging and Communications in Medicine (DICOM)
Part 6: Data Dictionary**

Add the Macular Grid Thickness Report UIDs to PS3.6 Annex A:

145

Annex A (Normative): Registry of DICOM Unique Identifiers (UID)

| UID Value | UID NAME | UID TYPE | Part |
|-------------------------------------|---|------------------|------------|
| ... | | | |
| <u>1.2.840.10008.5.1.4.1.1.79.1</u> | <u>Macular Grid Thickness and Volume Report Storage</u> | <u>SOP Class</u> | <u>3.4</u> |

Add new rows to PS 3.6 Annex A Table A-3

150

**Table A-3
CONTEXT GROUP UID VALUES**

| Context UID | Context Identifier | Context Group Name |
|------------------------------|--------------------|---|
| ... | | |
| <u>1.2.840.10008.6.1.819</u> | <u>4220</u> | <u>Visual Fixation Quality During Acquisition</u> |
| <u>1.2.840.10008.6.1.820</u> | <u>4221</u> | <u>Visual Fixation Quality Problem</u> |
| <u>1.2.840.10008.6.1.821</u> | <u>4222</u> | <u>Ophthalmic Macular Grid Problem</u> |

Changes to NEMA Standards Publication PS 3.16-2008
Digital Imaging and Communications in Medicine (DICOM)
Part 16: Content Mapping Resource

155

Item: Add to PS3.16 Section 2 Normative References:

ETDRS ETDRS Report Number 10, Grading Diabetic Retinopathy from Stereoscopic Color Fundus Photographs- An Extension of the Modified Airlie House Classification. *Ophthalmology*, May 1991, vol98 (p786-805), Supplement

160

Item: Add Macular Template to PS3.16:

TID 2100 Macular Grid Thickness and Volume Report

The Macular Grid Thickness and Volume Report is a structured report encoding the macular grid thickness and volume values derived from ophthalmic images, such as ophthalmic OPT images. This may encode measurements of either or both eyes.

165

The macular grid conveyed by this report is based upon the grid employed by the Early Treatment of Diabetic Retinopathy Study (ETDRS) to measure area and proximity of macular edema to the anatomic center (fovea) of the macula. See *ETDRS Report Number 10*.

170

TID 2100
Macular Grid Thickness and Volume Report
Type: Extensible

| | NL | Rel with Parent | VT | Concept Name | VM | Req Type | Condition | Value Set Constraint |
|---|----|-----------------|-----------|--|----|----------|---------------------|---|
| 1 | | | CONTAINER | EV (111690, DCM, "Macular Grid Thickness and Volume Report") | 1 | M | | |
| 2 | > | HAS CONCEPT MOD | INCLUDE | DTID (1204) Language of Content Item and Descendants | 1 | M | | |
| 3 | > | HAS OBS CONTEXT | INCLUDE | DTID (1001) Observation Context | 1 | M | | |
| 4 | > | CONTAINS | INCLUDE | TID (2101) Macular Grid Thickness and Volume Measurement | 1 | MC | IF Row 5 is absent. | \$Laterality = EV (G-A100,SRT, "Right") |
| 5 | > | CONTAINS | INCLUDE | TID (2101) Macular Grid Thickness and Volume Measurement | 1 | MC | IF Row 4 is absent. | \$Laterality = EV (G-A101,SRT, "Left") |

TID 2101 Macular Grid Thickness and Volume Measurement

This Template encodes the macular grid thickness and volume measurements for a single eye.

175

| Parameter Name | Parameter Usage |
|----------------|-----------------|
| \$Laterality | Which eye |

TID 2101
Macular Grid Thickness and Volume Measurement
Type: Extensible

| | NL | Rel with Parent | VT | Concept Name | VM | Req Type | Condition | Value Set Constraint |
|----|----|-----------------|-----------|--|----|----------|-----------|---------------------------------------|
| 1 | | | CONTAINER | EV (121070,DCM, "Findings") | 1 | M | | |
| 2 | > | HAS CONCEPT MOD | CODE | EV (G-C0E3, SRT, "Finding Site") | 1 | M | | EV (T-AA000, SRT, "Eye") |
| 3 | >> | HAS CONCEPT MOD | CODE | EV (G-C171, SRT, "Laterality") | 1 | M | | \$Laterality |
| 4 | > | CONTAINS | NUM | EV (57108-3, LN, "Macular Grid.Center Point Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 5 | > | CONTAINS | NUM | EV (57109-1, LN, "Macular Grid.Center Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 6 | > | CONTAINS | NUM | EV (57110-9, LN, "Macular Grid.Inner Superior Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 7 | > | CONTAINS | NUM | EV (57111-7, LN, "Macular Grid.Inner Nasal Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 8 | > | CONTAINS | NUM | EV (57112-5, LN, "Macular Grid.Inner Inferior Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 9 | > | CONTAINS | NUM | EV (57113-3, LN, "Macular Grid.Inner Temporal Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 10 | > | CONTAINS | NUM | EV (57114-1, LN, "Macular Grid.Outer Superior Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 11 | > | CONTAINS | NUM | EV (57115-8, LN, "Macular Grid.Outer Nasal Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 12 | > | CONTAINS | NUM | EV (57116-6, LN, "Macular Grid.Outer Inferior Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 13 | > | CONTAINS | NUM | EV (57117-4, LN, "Macular Grid.Outer Temporal Subfield Thickness") | 1 | M | | UNITS=EV(um, UCUM, "micrometer") |
| 14 | > | CONTAINS | NUM | EV (57118-2, LN, "Macular Grid.Total Volume") | 1 | M | | UNITS=EV(mm3, UCUM, "mm3") |
| 15 | > | CONTAINS | NUM | EV (111691, DCM, "Number of Images Used for Macular Measurements") | 1 | M | | UNITS = EV ((images), UCUM, "images") |

| | | | | | | | | |
|----|----|-----------------|---------|--|-----|---|--|--|
| 16 | > | CONTAINS | NUM | EV (111692, DCM, "Number of Samples Used per Image") | 1 | M | | UNITS = EV({samples}), UCUM, "samples") |
| 17 | > | CONTAINS | NUM | EV (111693, DCM, "Analysis Quality Rating") | 1 | M | | UNITS = EV({0:100}), UCUM, "range:0:100") Value = 0 – 100 |
| 18 | >> | HAS OBS CONTEXT | INCLUDE | DTID (2102) Quality Rating Identification | 1 | M | | |
| 19 | > | CONTAINS | NUM | EV (111694, DCM, "Image Set Quality Rating") | 1 | M | | UNITS = EV({0:100}), UCUM, "range:0:100") Value = 0 – 100 |
| 20 | >> | HAS OBS CONTEXT | INCLUDE | DTID (2102) Quality Rating Identification | 1 | M | | |
| 21 | > | CONTAINS | NUM | EV (111029, DCM, "Image Quality Rating") | 1-n | U | | UNITS = EV({0:100}), UCUM, "range:0:100") Value = 0 – 100 |
| 22 | >> | INFERRED FROM | IMAGE | No purpose of reference | 1 | M | | |
| 23 | >> | HAS OBS CONTEXT | INCLUDE | DTID (2102) Quality Rating Identification | 1 | M | | |
| 24 | > | CONTAINS | CODE | EV (111696, DCM, "Visual Fixation Quality During Acquisition") | 1 | U | | DCID (4220) Visual Fixation Quality During Acquisition |
| 25 | >> | HAS CONCEPT MOD | CODE | EV (111697, DCM, "Visual Fixation Quality Problem") | 1-n | U | | DCID (4221) Visual Fixation Quality Problem |
| 26 | > | CONTAINS | CODE | EV (111698, DCM, "Ophthalmic Macular Grid Problem") | 1-n | U | | DCID (4222) Ophthalmic Macular Grid Problem |
| 27 | > | CONTAINS | TEXT | EV (121106, DCM, "Comments") | 1 | U | | |

180

TID 2102 Quality Rating Identification

This template specifies the algorithm (and parameters) used to create a quality rating for an image or image set.

185 It is expected that the identified algorithm will create a consistent quality rating when analyzing a given image. If the algorithm allows change to its parameters which would alter the quality rating created, the specific parameters used should be specified.

TID 2102 QUALITY RATING IDENTIFICATION Type: Non-Extensible

190

| | NL | Rel with Parent | VT | Concept Name | VM | Req Type | Condition | Value Set Constraint |
|---|----|-----------------|------|--|-----|----------|-----------|----------------------|
| 1 | | | TEXT | EV (111001, DCM, "Algorithm Name") | 1 | M | | |
| 2 | | | TEXT | EV (111003, DCM, "Algorithm Version") | 1 | M | | |
| 3 | | | TEXT | EV (122405, DCM, "Algorithm Manufacturer") | 1 | M | | |
| 4 | | | TEXT | EV (111002, DCM, "Algorithm Parameters") | 1-n | U | | |

Add the following to PS3.16 Annex C:

CID 4220 Visual Fixation Quality During Acquisition

Context ID 4220

Visual Fixation Quality During Acquisition

195

Type: Extensible

Version: 20090917

| Coding Scheme Designator (0008,0102) | Code Value (0008,0100) | Code Meaning (0008,0104) |
|---|-----------------------------------|-------------------------------------|
| SRT | G-A555 | Steady |
| SRT | G-A556 | Not Steady |
| SRT | G-A385 | Indeterminate |

CID 4221 Visual Fixation Quality Problem

Context ID 4221

Visual Fixation Quality Problem

200

Type: Extensible

Version: 20090917

| Coding Scheme Designator (0008,0102) | Code Value (0008,0100) | Code Meaning (0008,0104) |
|---|-----------------------------------|-------------------------------------|
| DCM | 110518 | Patient Movement |
| SRT | F-02FA4 | Eccentric Fixation |
| DCM | 110519 | Operator Error |
| DCM | 110501 | Equipment failure |

CID 4222 Ophthalmic Macular Grid Problem

Context ID 4222

Ophthalmic Macular Grid Problem

205

Type: Extensible

Version: 20090917

| Coding Scheme Designator (0008,0102) | Code Value (0008,0100) | Code Meaning (0008,0104) |
|---|-----------------------------------|-------------------------------------|
| <i>Include CID 4221 Visual Fixation Quality Problem</i> | | |
| SRT | F-0123A | Constricted Pupil |
| SRT | DA-73402 | Lens Opacity |
| SRT | DA-75300 | Corneal Opacity |
| SRT | DA-7931D | Vitreous Opacity |
| SRT | R-20839 | Poor Visual Fixation |
| SRT | DA-76000 | Eyelid Disease |

| | | |
|-----|----------|-----------------------------|
| DCM | 111695 | Interfering Tears or Drops |
| SRT | DA-74100 | Refractive Error |
| DCM | 111209 | Patient Positioning Problem |
| SRT | F-F1722 | Dry Eyes Problem |

210

Add to PS3.16 – Add To Annex D DICOM Controlled Terminology Definitions (Normative)

| Code Value | Code Meaning | Definition | Notes |
|------------|--|---|-------|
| ... | | | |
| 110518 | Patient Movement | A movement of the patient affecting test quality | |
| 110519 | Operator Error | An error of the operator affecting test quality | |
| ... | | | |
| 111690 | Macular Grid Thickness and Volume Report | A macular grid thickness and volume report for a patient. The macular grid is an analytic tool described in PS3.17 Annex X. | |
| 111691 | Number of Images Used for Macular Measurements | Number of images used for the macular grid measurement. | |
| 111692 | Number of Samples Used per Image | Number of samples used per Image for analysis | |
| 111693 | Analysis Quality Rating | A numeric rating of the quality of the entire analysis with respect to grading and diagnostic purposes. Higher numbers indicate greater quality. | |
| 111694 | Image Set Quality Rating | A numeric rating of the quality of an entire image set with respect to grading and diagnostic purposes. Higher numbers indicate greater quality. | |
| 111695 | Interfering Tears or Drops | Tear film or drops affecting test quality | |
| 111696 | Visual Fixation Quality During Acquisition | The assessment of the centricity and persistence of the visual fixation (direction of gaze) during the acquisition | |
| 111697 | Visual Fixation Quality Problem | The reason why the patient's visual fixation was not steady or was indeterminate | |
| 111698 | Ophthalmic Macular Grid Problem | The reason why the macular grid measurements may be questionable | |

Changes to NEMA Standards Publication PS 3.17-2008
Digital Imaging and Communications in Medicine (DICOM)
Part 17: Explanatory Information

215

| |
|--|
| Add to PS3.17 – Add Use Cases for Macular Grid Thickness and Volume Reports |
|--|

**Annex X Macular Grid Thickness and Volume Report Use Cases
(Informative)**

220 **X.1 Introduction**

Ophthalmologists use OPT data to diagnose and characterize tissues and abnormalities in transverse and axial locations within the eye. For example, an ophthalmologist might request an OPT of the macula, the optic nerve or the cornea in either or both eyes for a given patient. Serial reports can be compared to monitor disease progression and response to treatment. OPT devices produce two categories of clinical data: B-scan images and tissue measurements.

X.2 Use of B-scan Images

Prior to interpreting an OPT B-scan (or set of B-scans), users must first determine if the study is of adequate quality to answer the diagnostic question. Examples of inadequate studies include:

- 230 1. The pathology that needs to be visualized does not appear within the field of the scan
2. The image quality is not sufficient to see the tissue layers of interest (i.e. media opacity, blink, etc)
3. The scans are not in the expected anatomic order (i.e. due to eye movements)

235 In some cases, inadequate images can be corrected by capturing another scan in the same area. However, in other cases, the patient's eye disease interferes with visualization of the tissues of interest making adequate image quality impossible. Ideally, when choosing between multiple scans of the same tissue area, physicians would have access to information about the above questions so they can select only the best scan(s).

240 The physician may then choose to view and assess each B-scan in the dataset individually. When assessing OPT B-scans, ophthalmologists often identify normal or expected tissue boundaries first, then proceed to identify abnormal interfaces or structures next. The identification of pathology is both qualitative (i.e. does a structure exist) and quantitative (i.e. how thick is it). If previous scans are present for this patient, the physician may choose to compare the most recent scan data with prior visits. Due to workflow constraints, it may be difficult for B-scan interpretations to happen on the same machine that captures the images. Therefore, remote image assessment, such as image viewing in the examining room with the patient, is optimal.

245

X.3 Use of Tissue Measurements

250 In addition to viewing B-scan image data, clinicians also use quantitative measurements of tissue thicknesses or volumes extracted automatically from the OPT images. As with image quality, the accuracy of automated segmentation must be assessed prior to use of the numerical

255 measurements based on these boundaries. This is typically accomplished by visual inspection of boundary lines placed on the OPT images but also can be inferred from analysis confidence measurements provided by the device software. In addition to segmentation accuracy, it is also important to determine if the region of interest has been aligned appropriately with the intended sampling area of the OPT.

260 The analysis software application segments OPT images using the raw data of the instrument to quantify tissue optical reflectivity and location in longitudinal scan or B-scan images. Many boundaries can be identified automatically with software algorithms, see Figure x.3-1.

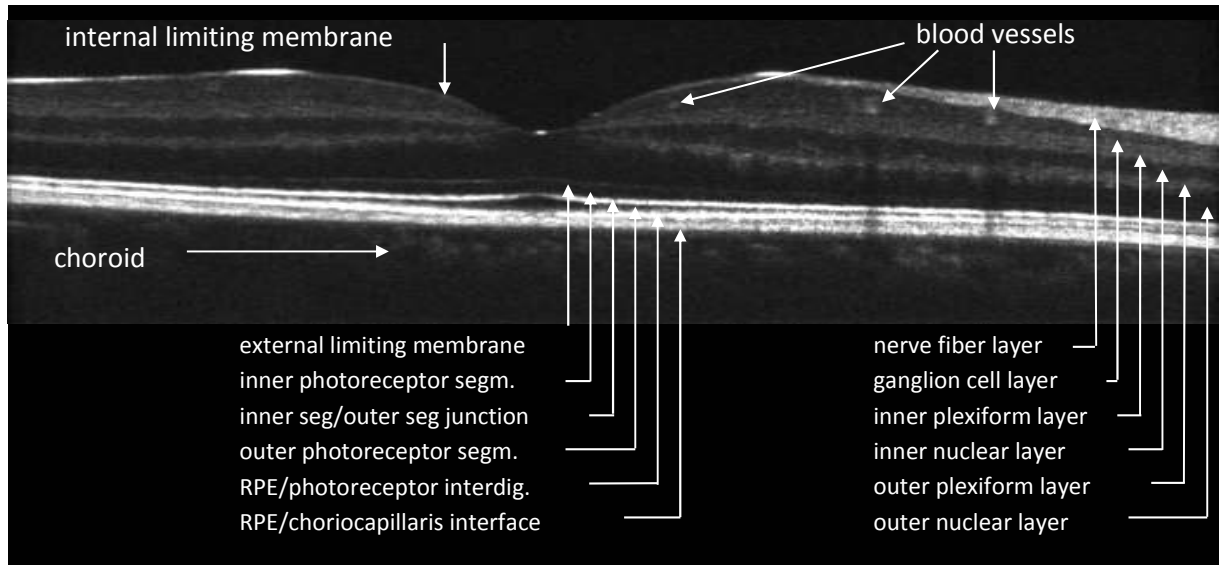


Figure X.3-1 OPT B-scan with Layers and Boundaries Identified

X.4 Axial Measurements

265 The innermost (anterior) layer of the retina, the internal limiting membrane (ILM) is often intensely hyperreflective and defines the innermost border of the nerve fiber layer. The nerve fiber layer (NFL) is bounded posteriorly by the ganglion cell layer and is not visible within the central foveal area. In high quality OPT scans, the sublamina of the inner plexiform layer may be identifiable. The external limiting membrane is the subtle interface between the outer nuclear layer and the photoreceptors. The junction between the photoreceptor inner segments and outer segments (IS/OS junction) is often intensely hyperreflective and in time domain OPT systems, was thought to represent the outermost boundary of the retina. Current thought, however, suggests that the photoreceptors extend up to the next bright interface, often referred to as the retinal pigment epithelium (RPE) interdigitation. This interface may be more than 35 micrometers beyond the IS/OS junction. When three high intensity lines are not present under the retina, however, this interdigitation area may not be visible. The next bright region typically represents the RPE cell bodies which consist of a single layer of cuboidal cells with reflective melanosomes oriented at the innermost portion of the cells. Below the RPE cells is a structure called Bruch's membrane which is contiguous with the outer RPE cell membrane.

280 The axial thickness and volume of tissue layers can be measured using the boundaries defined above. For example, the nerve fiber layer is typically measured from the innermost ILM interface to the interface of the NFL with the retina. Time domain OPT systems measure retinal thickness as the axial distance between the innermost ILM interface and the IS/OS junction. However, high resolution OPT systems now offer the potential to measure true retinal thickness (ILM to

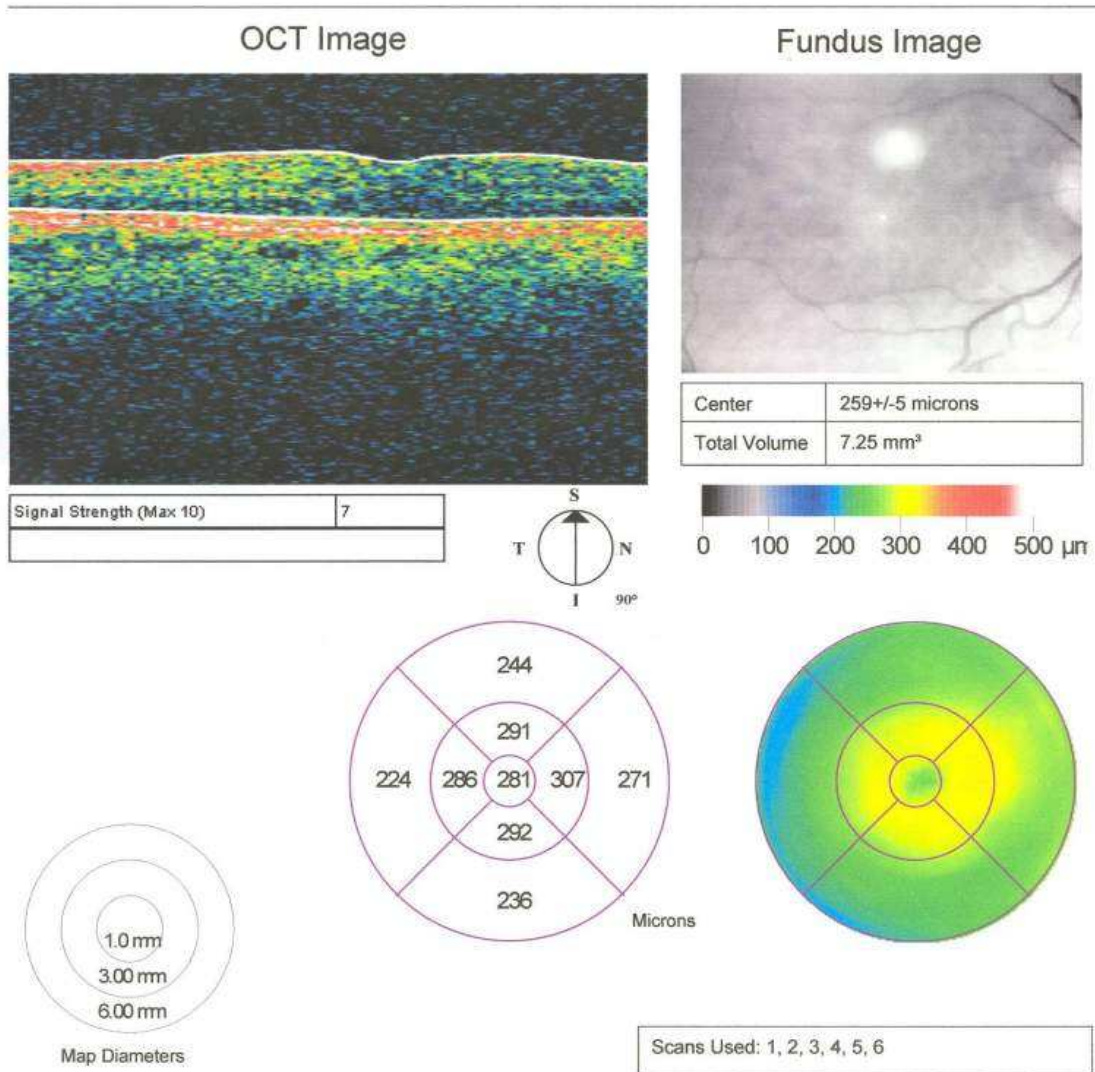
285 outermost photoreceptor interface) in addition to variants that include tissue and fluid that may
intervene between the retina and the RPE. The RPE layer is measured from the innermost
portion of the RPE cells, which is the hyper reflective melanin-containing layer to the outermost
highly reflective interface. Pathologic structures that may intervene between normal tissue layers
290 may obscure their appearance but often can be measured using the same methods as normal
anatomic layers.

X.5 En Face Measurements

The macular grid is based upon the grid employed by the Early Treatment of Diabetic
Retinopathy Study (ETDRS) to measure area and proximity of macular edema to the anatomic
center of the macula, also called the fovea. This grid was developed as an overlay for use with
295 32mm film color transparencies and fluorescein angiograms in the seminal trials of laser
photocoagulation for the treatment of diabetic retinopathy. Subsequently, this grid has been in
common use at reading centers since the 1970s, has been incorporated into ophthalmic camera
digital software, and has been employed in grading other macular disease in addition to diabetic
retinopathy. This grid was slightly modified for use in Time Domain OPT models developed in the
300 1990s and early 2000s in that the dimensions of the grid were sized to accommodate a 6 mm
diameter sampling area of the macula.

The grid for macular OPT is bounded by circular area with a diameter of 6 mm. The center point
of the grid is the center of the circle. The grid is divided into 9 standard subfields. The center
subfield is a circle with a diameter of 1 mm. The grid is divided into 4 inner and 4 outer subfields
305 by a circle concentric to the center with a diameter of 3 mm. The inner and outer subfields are
each divided by 4 radial lines extending from the center circle to the outermost circle, at 45, 135,
225, and 315 degrees, transecting the 3 mm circle in four places. Each of the 4 inner and 4 outer
subfields is labeled by its orientation with regard to position relative to the center of the macula –
superior, nasal, inferior, and temporal. For instance, the superior inner subfield is the region
310 bounded by the center circle and the 3 mm circle the 315 degree radial line, and the 45 degree
radial line. The nasal subfields are those oriented toward the midline of the patient's face,
nearest to the optic nerve head. The grids for the left and right eyes are reversed with respect to
the positions of the nasal and temporal subfields – in viewing the grid for the left eye along the
antero-posterior (Z) axis, the nasal subfields are on the left side and in the right eye the nasal
315 subfields are on the right side (nasal as determined by the location of the subfield closest to the
nose).

The OPT macula thickness report consists of the thickness at the center point of the grid, and the
mean retinal thickness calculated for each of the 9 subfields of the grid. In the context of the
macular disease considered for the diagnosis, and qualitative interpretation of morphology from
320 examination and OPT and/or other modalities, the clinician uses the macula thickness report to
determine if the center and the grid subfield averages fall outside the normative range.
Monitoring of macular disease by serial grid measurements allows assessment of disease
progression and response to intervention. Serial measurements are assessed by comparing
OPT thickness or volume reports, provided that the grids are appropriately centered upon the
325 same location in the macula for each visit.



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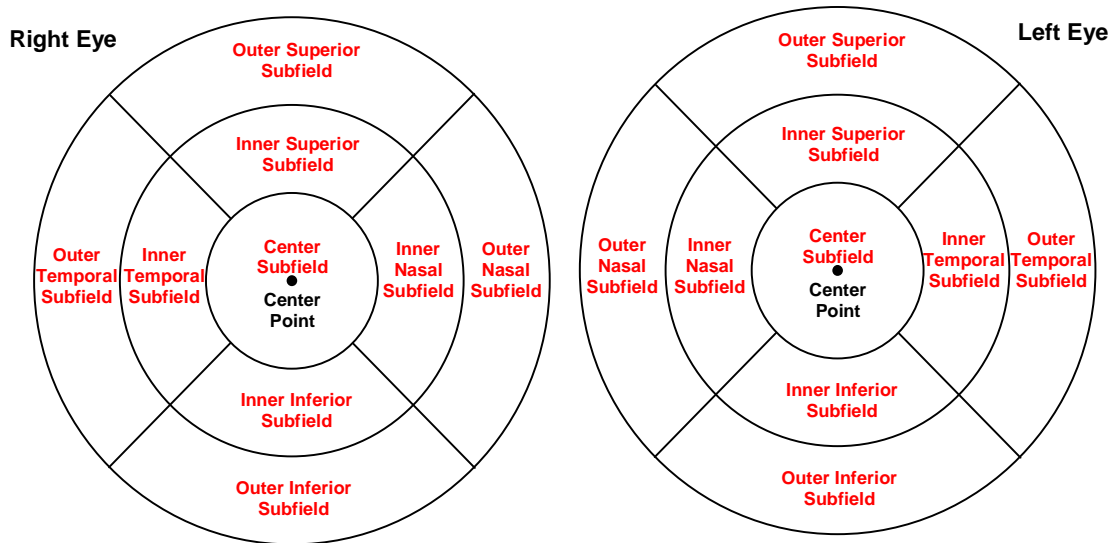
Figure X.5-1 Macular Grid Thickness Report Display Example

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The center point of the grid should be aligned with the anatomic center of the macula, the fovea. This can be approximated by having the patient fixate upon a target coincident with the center of the grid. However, erroneous retinal thickness measurements are obtained when the center of the grid is not aligned with the center of the macula. This may occur in patients with low vision that cannot fixate upon the target, or in patients that blink or move fixation during the study. To determine the expected accuracy of intervisit comparisons, clinicians would benefit from knowing the alignment accuracy of the OPT data from the two visits. Ophthalmologists may also want to customize locations on the fundus to be monitored at each visit.

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The following figure illustrates how the content items of the Macular Grid Thickness and Volume Report are related to the ETDRS Grid. Figure shown is not drawn to scale.



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Figure X.5.2 – ETDRS GRID Layout

X.6 Interpretation of OPT

The process of evaluation of diabetic macular edema will help illustrate the role of the OPT macula thickness report. In diabetic macular edema there is a breakdown in the blood retina barrier which can lead to focal and/or diffuse edema (or thickening) of the macula. The report of the thickness of each subfield area of the macula grid will help direct treatment. For instance, laser treatment to a specific thickened quadrant would be expected to reduce the thickness of retina in the treated zone. Serial comparisons of OPT thicknesses should demonstrate a reduction in thickness in the successfully treated zone. A zone that subsequently became thicker on follow-up scans may warrant further treatment. In addition to an expected local response to specific zonal treatment such as laser, there are treatments with drugs and biologics which are less localized. For instance, the injection of intravitreal drugs in a successfully treated eye would be expected to have a global reduction of thickness in all zones with DME. Patients with severe retinal disease may lose the ability to fixate making the acquisition of OPT images to represent a specific zone less reliable.

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