ARIC Neurocognitive Study

ARIC Vessel Measurement System

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ARIC NCS Vessel Measurement System

1. DESCRIPTION

The VMS is a semi-automated system used to measure retinal vessel widths from a digital retinal image.

The automated components include placement of the overlying grid centered on the optic disc, vessel type identification, and width measurements for vessels. The color blue is used to denote venules and the color red is used to denote arterioles in the screen displays. The data table on the control window displays the mean width and standard deviation for each measured vessel and locates each vessel by its clockwise angle in degrees. The vessels are automatically typed as arteriole or venule; in the case of uncertainty, the vessel is typed as an arteriole.

The manual components include the option to override any of the initial automated decisions or measurements. This would include adjusting the placement of the grid, changing the vessel type, deleting vessels, re-measuring vessels, and adding significant vessels missed in the initial automation.

The VMS is operated off of a 2-monitor workstation with the image files organized by reading lists. The location of the application is C:\PROGRAM FILES\VASCULAR MEASUREMENT\ and the location of the images is on the server at \\EYESEE10\ARIC\VESSEL IMAGES\IMAGES\rlNNNN,…*.TIF (tagged image file format). The file C:\PROGRAM FILES\VASCULAR MEASUREMENT\ \VESSELDATAPARAMS.DAT contains input parameters including the allowable range of reading lists and pixel conversion factors. The pixel conversion factor should be 5.11. The data is saved on the server at \\EYESEE10\ARIC\VESSEL IMAGES\IMAGES\rlNNNN \RESULTS.CSV (comma separated values) and is formatted in an Excel spreadsheet.

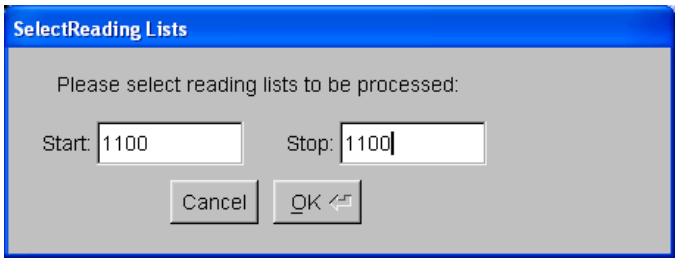
The Modified ARIC grid is composed of 3 concentric circles which demarcate an average optic disc, Zone A defined as the region from the disc margin to 1/2 disc diameter from the disc, and Zone B defined as the region from ½ disc diameter to 1 disc diameter from the disc. All retinal vessels are measured in Zone B.

Only the width data from the 6 largest venules and 6 largest arterioles are required to calculate the AV ratio using the Knudtson formula. No branch (daughter) width data are required.

2. PROCEDURE

Log onto workstation with network name and password. This will automatically identify the graders number code in the output table.

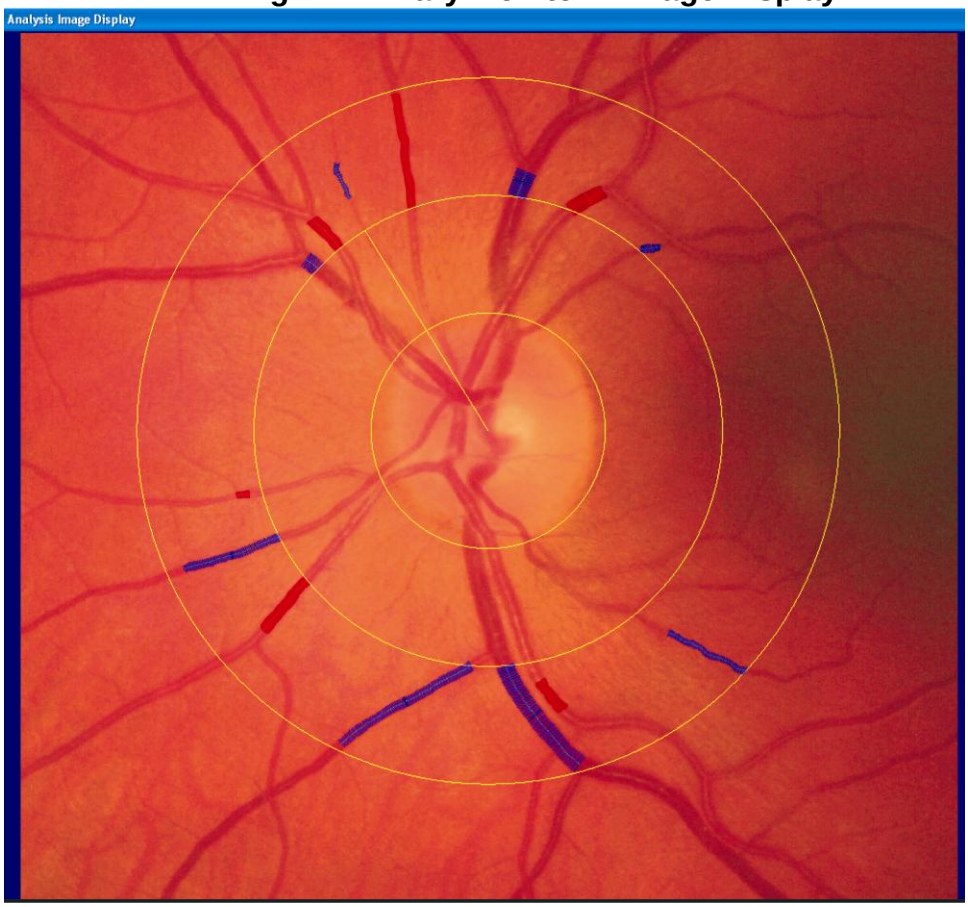
1. Select range of reading lists



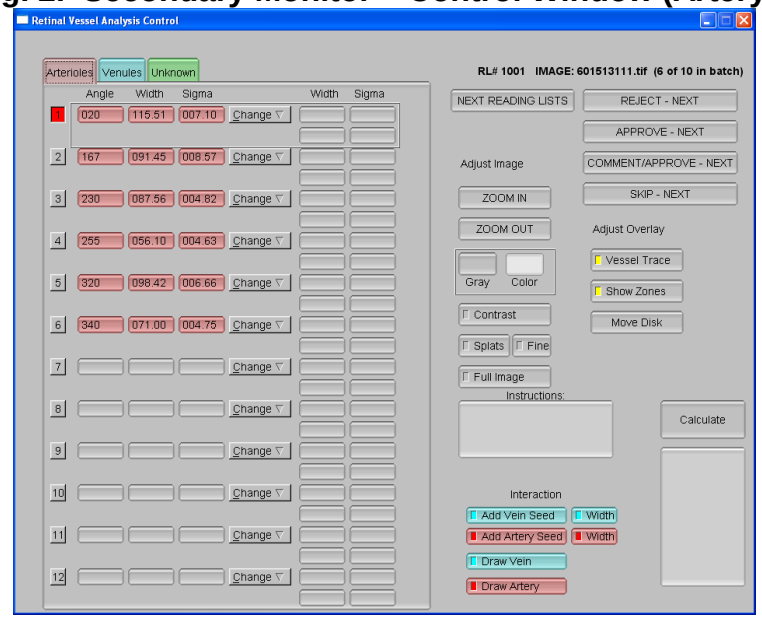
The application opens on the primary monitor with 3 windows: the image display window, the control window, and the vessel data parameters file.

2. Drag control window from behind image window to secondary monitor. The image display should be kept on the larger primary monitor. The vessel data parameters file is left hidden below the image display.

2.1 Fig. 1. Primary Monitor – Image Display



2.2 Fig. 2. Secondary Monitor – Control Window (Artery View)



3. ADJUST IMAGE TOOLS (See examples on following pages)

Zoom In/Zoom Out – zoom in to incrementally magnify a selected area of the image or zoom out to display the entire cropped image (figs. 3h, 3i)
Gray/Color – choose red-free or color image display (figs. 3a, 3b)
Contrast – equalizes color contrast; especially useful for eliminating choroidal pattern (toggle) (fig. 3g)
Splats – displays computer model of image with "splat" units; useful in determining likelihood of an accurate measurement in a specific area (toggle) (fig. 3d)

Fine – displays a more detailed visual of splat units (toggle) (fig. 3e)

Full Image – pops-up original (uncropped) F1 image; useful for vessel identification (toggle) (fig. 3c)

Vessel Trace – hides vessel width overlay for unobstructed view of vessels; toggles back to display same overlay (fig. 3b)

Show Zones – hides grid overlay for unobstructed view of image; toggles back to display same grid (fig. 3f)

Move Disc – brings up control window that allows incremental movement of grid overlay by clicking directional arrows; center OK button saves grid placement and refreshes vessel measurements. Red Cancel button restores original grid placement and vessel measurements

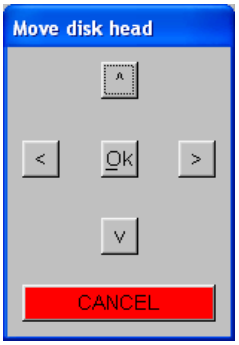
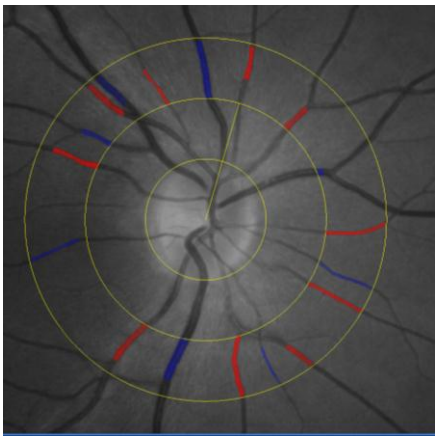
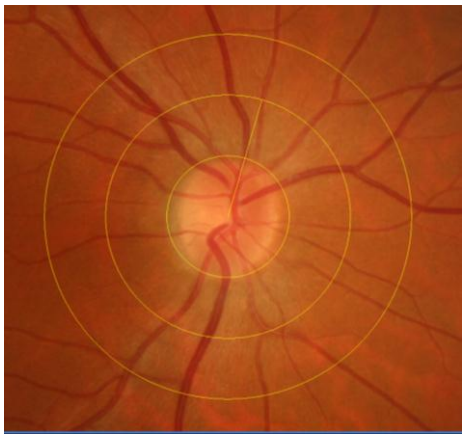


Fig. 3. Adjust- Image Tools Examples

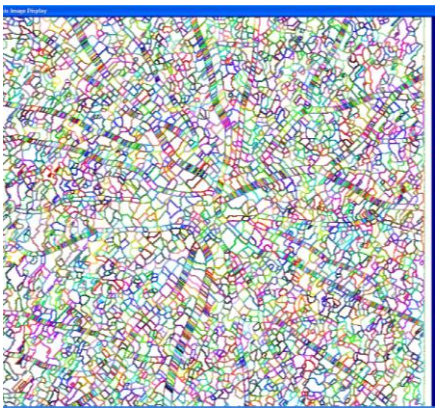


3.1 3a. Gray

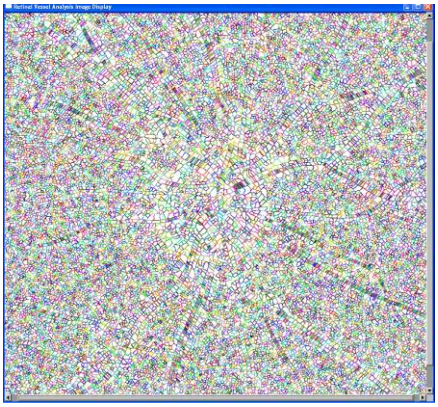


3.2 3b. Color – Vessel Trace

3.3 3c. Full Image



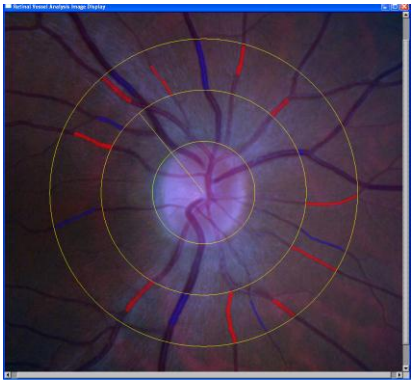
3.4 3d. Splats



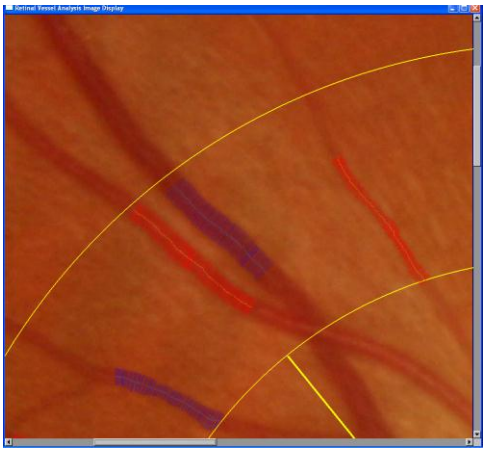
3.5 3e. Fine Splats

Fig. 3. Adjust-Image Tools Examples (cont'd.)

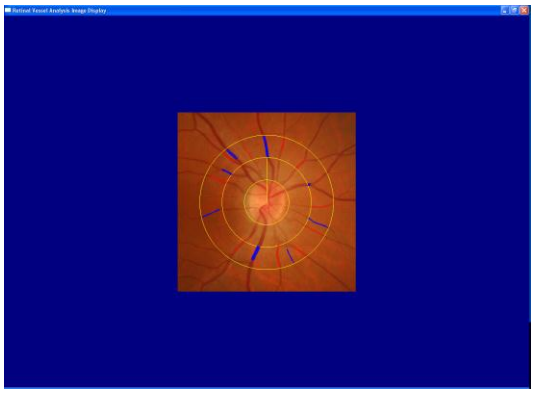
3.6 3f. Show Zones



3.7 3g. Contrast



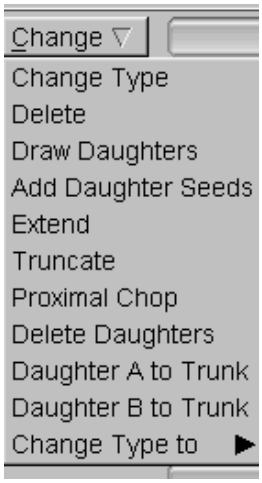
3.8 3h. Zoom In



3.9 3i. Zoom Out

4. VESSEL MEASUREMENT TOOLS – CHANGE MENU

To make the following changes to vessels, the vessel must first be accessed. Vessels are accessed by clicking on the seed point (the proximal end of the vessel trace) on the image display or by clicking on the vessel number button on the data table. Both access methods highlight the vessel trace, direct the pointer to the vessel trace seed point (and angle location), and highlight the data for the accessed vessel on the data table. In this way, the visual vessel trace and the data (angle, width, Sigma) for each vessel are easily correlated.



Change Menu

Change Type – automatically switches vessel type and updates vessel trace color and type on data table.

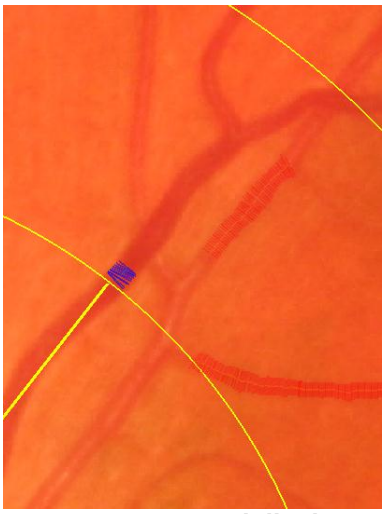
Delete – deletes vessel trace from display and vessel measurement and type from data table. The vessel data is then listed as type Unknown in the data table.

Extend – to add on a second segment distal to the original (bypasses unmeasurable area); the Extend segment is added by seeding a start point with 2 clicks along the vessel. The data table regenerates the mean and standard deviation based on the combined segments. (Fig. 4)

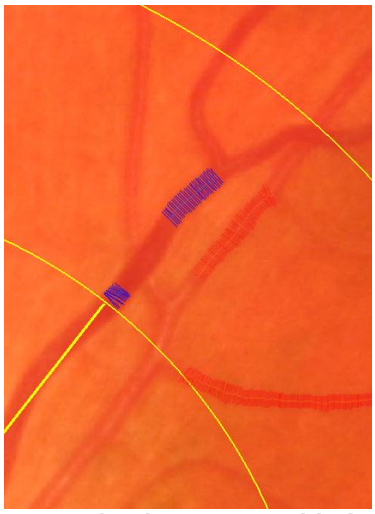
Truncate – make a single click at a point on the vessel to terminate the distal segment before a branching or crossing or measurement discrepancy. (Figs. 5 and 6)

Proximal Chop – make a single click at a point on the vessel to terminate the proximal segment. (Fig. 6)

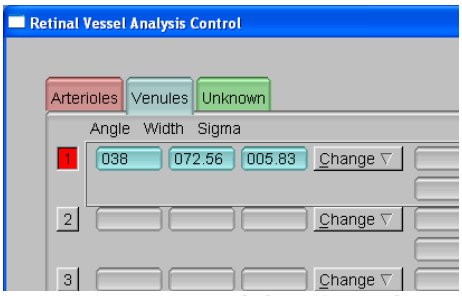
4.1 Fig. 4. Extend Example



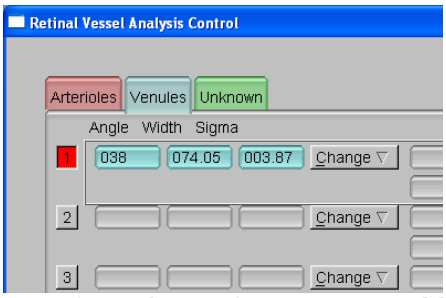
Automated display



Distal segment added with Extend



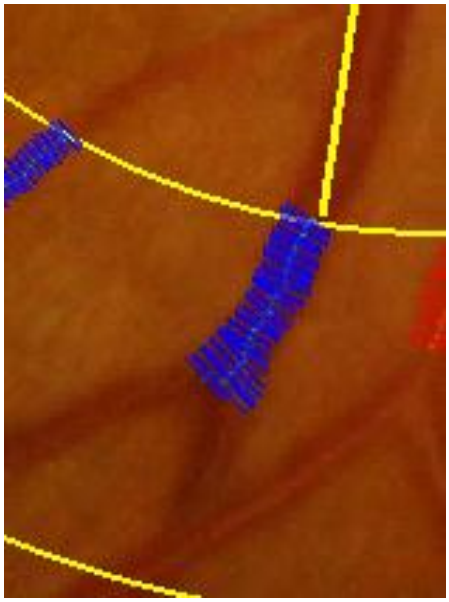
Automated data for Vein #1



Data for Vein #1 after segment added with Extend

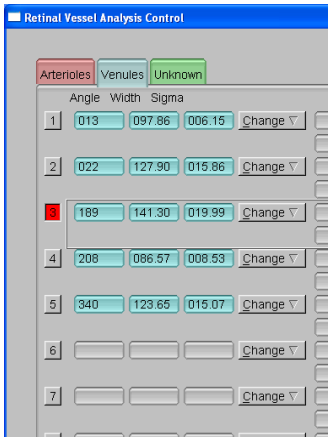
The extend tool is used to produce a longer representative measured segment. If the extended measured length is considered visually accurate by the grader, it should be accepted regardless of the effect on the mean and Sigma since it includes the natural variability of the vessel width in Zone B.

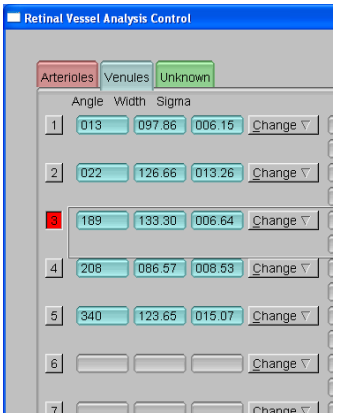
4.2 Fig. 5. Truncate Example



Automated trace

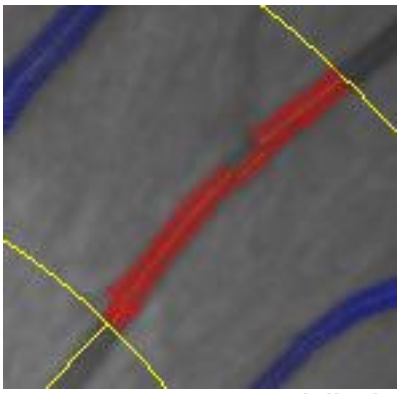
Venule truncated before branching



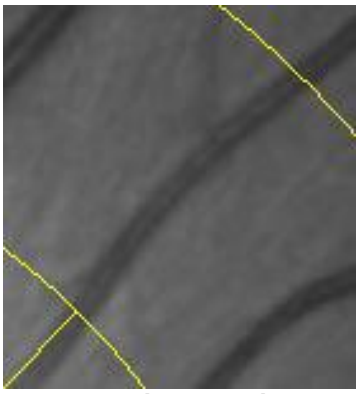


Note the effect of truncating the automatic venule measurement before the branch on the width and standard deviation of Venule #3.

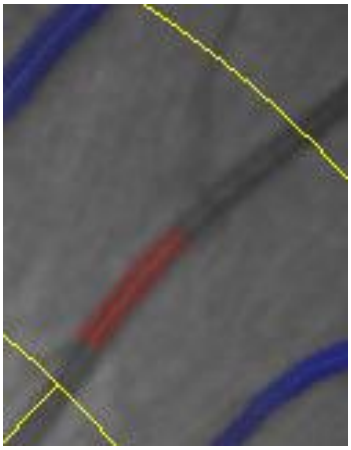
4.3 Fig. 6. Proximal Chop / Truncate Example



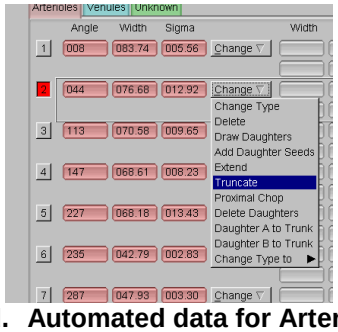
6a. Automated display



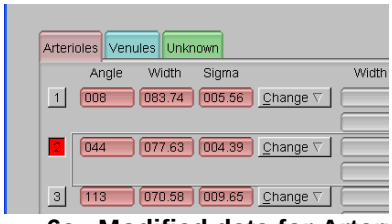
6b. Vessel trace removed



6c. Final measurement using proximal chop and truncate



6d. Automated data for Artery #2

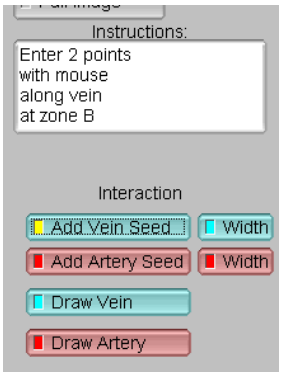


6e. Modified data for Artery #2

The automated display of Artery #2 has outliers at the proximal and distal ends (Fig. 6a), the reasons for which are more clear in Fig. 6b. The outlier segments are removed by using Proximal Chop and Truncate and the vessel trace appears accurate (Fig. 6c). As shown in Figs. 6d and 6e, the mean width was not affected significantly by these corrections, but the Sigma value was improved and with the visual accuracy of the vessel trace is an assurance of credible data.

5. VESSEL MEASUREMENT TOOLS - INTERACTIONS

The **Instructions** window displays the mouse click requirements for each of the following vessel measurement tools:



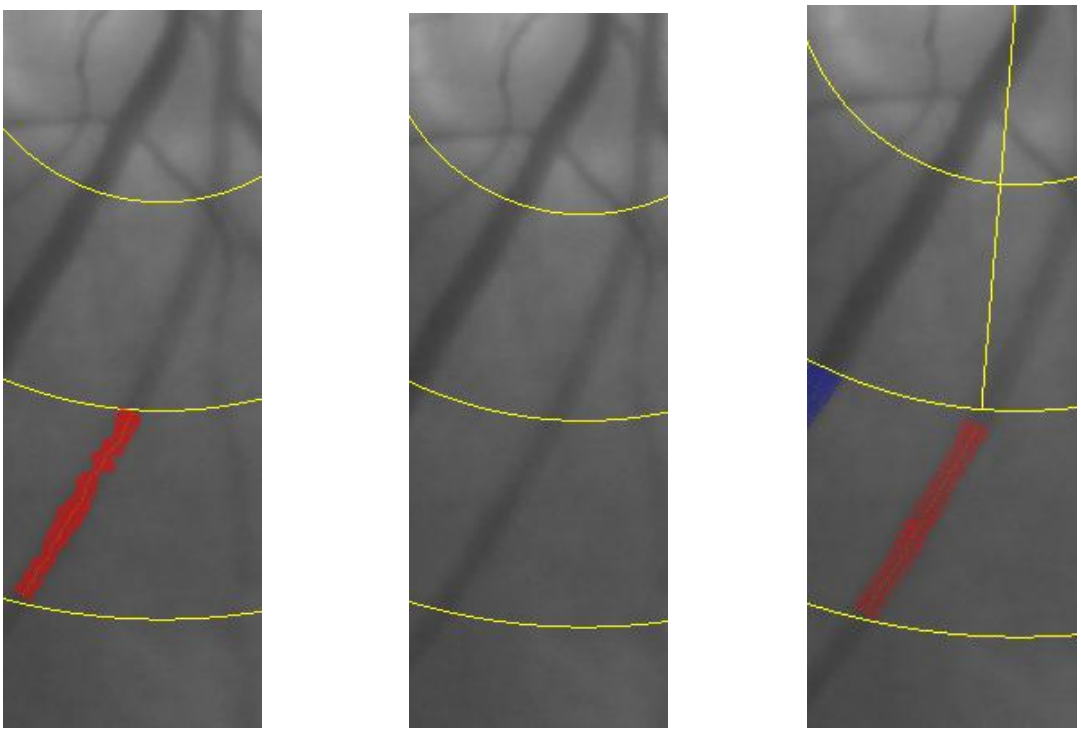
Instructions for Add Vein Seed

Add Vein/Artery Seed – enter mouse click at desired starting point of segment and second mouse click along the direction of the vessel; automated measured segment will display and may need further modification with Change Tools.

Draw Vein/Artery – enter first mouse click at desired starting point and enter 4 more mouse clicks along vessel to be measured with intent to include as much as Zone B as possible; measured segment will display and may need further modification with Change Tools.

Widths – enter 1 mouse click along edge of vessel and second mouse click at opposite width edge as perpendicular as possible; automated measured segment will display and may need further modification with Change Tools. This tool is especially useful for vessels with central light reflex. (Figs. 7a-7c)

5.1 Fig. 7 Width Tool Example



7a. **7b.** **7c.**

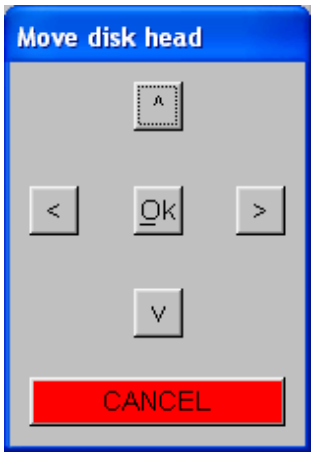
The automated measure (Fig. 7a) has obvious outliers due to the softly focused vessel edges (Fig 7b). Seeding or drawing the arteriole produces the same pattern. Using the Width tool produces a visually accurate trace that smoothes out the vessel edges (Fig. 7c).

6. GRADER INTERACTIONS

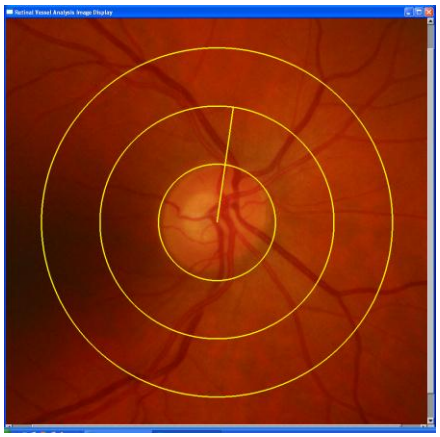
The grader is responsible for visual evaluation of the automated display and modifying as necessary. This includes approving the placement of the grid, correcting vessel types, and modifying vessel measurements according to the following guidelines.

6.1 Grid Placement

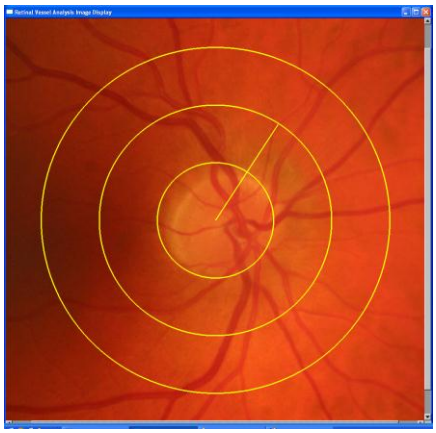
The grader will visually determine if the inner circle is *acceptably* centered on the optic disc. Acceptable is defined as within 5 or fewer incremental clicks in any *one* direction from the optimal position (not a total of >5 clicks in multiple directions). If the original grid placement is acceptable, CANCEL should be clicked to restore the original position. If the placement should be changed, OK should be clicked. The vessel measurements will automatically recalculate according to the new Zone B.



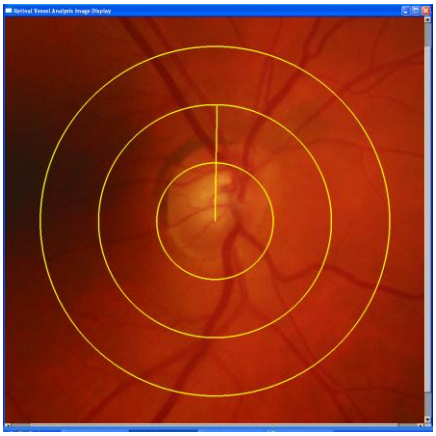
6.2 Fig. 8 Grid Placement Examples



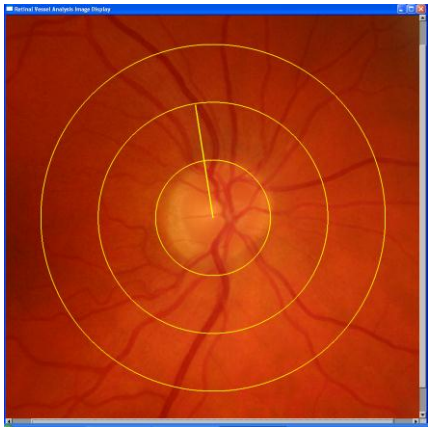
8a. Acceptable – 1left and 1 up click



8b. Acceptable – 5 right clicks



8c. Unacceptable – 8 up clicks



8d. Acceptable – 3 right 2 up clicks

6.3 Identification of Arterioles and Venules

The grader identifies each vessel within Zone B as either an arteriole or a venule and makes changes as necessary. Most vessels with a caliber greater than or equal to 50u can be identified as either arterioles or venules from the digital image. For smaller vessels, the option to view the entire uncropped image may be helpful or referring back to the images in the EyeQ database may be necessary. Only the data from the largest 6 venules and largest 6 arterioles are necessary so if the largest 6 are easily determined the smaller vessels can be deleted without further considerations. If more than 6 are automatically and correctly displayed, no deletions are necessary because the calculating process will ignore the unnecessary values.

The grader uses the guidelines below to identify each vessel:

(1) Color on digital image. Arterioles are a lighter orange-red color with a strong central light reflex. However, the central light reflex may not always be apparent, especially in arterioles less than 50u in caliber. Veins are a darker purple-red color with little or no central light reflex.

(2) Course. Arterioles tend to be straighter and smoother in outline; they are more regular in both path and outline. Venules are generally more tortuous, and more irregular in outline and diameter. Venules are broader in diameter at the disc margin than the corresponding arterioles.

(3) Alternating vessels. In principle, arterioles alternate with venules. Therefore, if the grader has measured a distinct venule, the next vessel is more likely to be an arteriole.

(4) Crossing. As a general rule, arterioles do not cross arterioles and venules do not cross venules. This is a reliable guideline more than 1 DD from the disc margin (but may not always be true on or near the disc). Therefore, if a vessel of unknown identity crosses a venous branch within or distal to Zone B, then the unknown vessel is an arteriole. If it crosses an arteriolar branch within or distal to Zone B, then it is a venule. This rule is crucial in identifying small vessels.

(5) Parent vessel. Smaller branches can be identified by tracing them proximally to their branching from a parent vessel, the identity of which may be evident from the first two guidelines. Angles between vessels may be useful in differentiating crossings and branchings. Crossings are frequently almost perpendicular (90^o) or, if the two vessels are coursing in parallel, the angle of the crossing may be very shallow (less than 30^o). Branchings are usually somewhat less than perpendicular (with the angle between the two branches from 30^o to 45^o).

7. VESSEL MEASUREMENT GUIDELINES

The grader determines the validity of a measurement by the visual display and the width and standard deviation values. More significance should be given to the visual display.

An acceptable measurement is required to have the following:

1. The visual vessel trace should have no obvious outliers from the visible edges of the vessel.
2. The length of the measured segment should be as long as possible through Zone B for each particular vessel. A reasonable length will depend on the branching of the vessel and the photographic quality of the digital image.

All measurements must be taken proximal to all visible branching regardless of the length of the trunk or the length of the measured segment. If the trunk length in Zone B is short, it may be difficult to get a reliable measurement. In this case, a Comment should be added to the saved data indicating the location of the possibly suspect vessel width. *If the trunk is ungradable, then both branches should be measured instead of the trunk. The saved data should then be saved with the comment (check box) Ungradable Arteries/Veins (6 largest).*

The grader should not always attempt to optimize the automated measurement since it may be difficult to agree on what segment represents a “normal” width. Perceived variations in vessel edges should be allowed, especially if the measured segment is relatively long through Zone B, but only if the variation is not what should be considered an outlier. Variations may be due to normal anatomical variation of the vessel, undulations of the vessel, or minor image quality issues.

If it is clear that a vessel width is affected by a crossing (e.g. arterio-venous nicking) or obscured by nerve fiber, then those affected segments should be deleted and the grader should determine the most representative segments to be measured.

More than 6 vessels of each type may be measured and saved; the formula will automatically be based on the 6 largest measurements of each vessel type.

To maintain consistency and reproducibility, it is necessary to keep grader interactions to a minimum. The following priority order should be used when correcting the initial automated display:

Grader Interaction Order of Priority

1. No interaction; accept the automated measure through Zone B
2. Automated measure **truncated** and/or **proximal chopped** before a branching, or a crossing if necessary, or an area of outlying measurements.

Automated measure deleted (if displayed) and:

3. Vessel **seeded**. The starting point of the seed should be as close to the inner gridline of Zone B as possible to produce as long a measured length as possible. If the seed is unsuccessful, the splat view may be used to indicate the appropriate measuring area.
4. Vessel **drawn** in a similar manner as the seed. Vessel Draw is often a more expedient and accurate way to measure problematic vessels.
5. **Width** tool used to seed problematic vessels, e.g., larger vessels with central reflex or vessel edges affected by image quality.

The **Extend** tool should be used if it is possible to produce a longer measured segment for any of the measurements obtained by the above methods.

Special Cases

If the splat display indicates only limited measurable areas along a significant vessel, then the grader should use all available tools to obtain a visually accurate width, if possible. The measured segment may be partially or totally outside the grid only if the measurement appears accurate and representative of the entire vessel. The decision to take a measurement inside or outside the grid in these special cases is based on where the grader determines the most accurate and representative measurement is obtainable. All measurements outside the grid must be taken by using the draw tool.

A record of the special case must be entered under the Save with Comment menu by checking the “Other” button and adding a comment indicating the location (angle degree) of the vessel and the grading limitation (i.e., O/G).

All grading decisions made by the grader that are not covered in the grading guidelines, should be documented as Other and a detailed comment should be entered. Examples of detailed comments may include the following:

Other

A148 O/G (*arteriole located at 148º measured outside Zone B)*

V18 Q *(questionable i.e., unreliable measurement for vein located at 18º)*

Note:

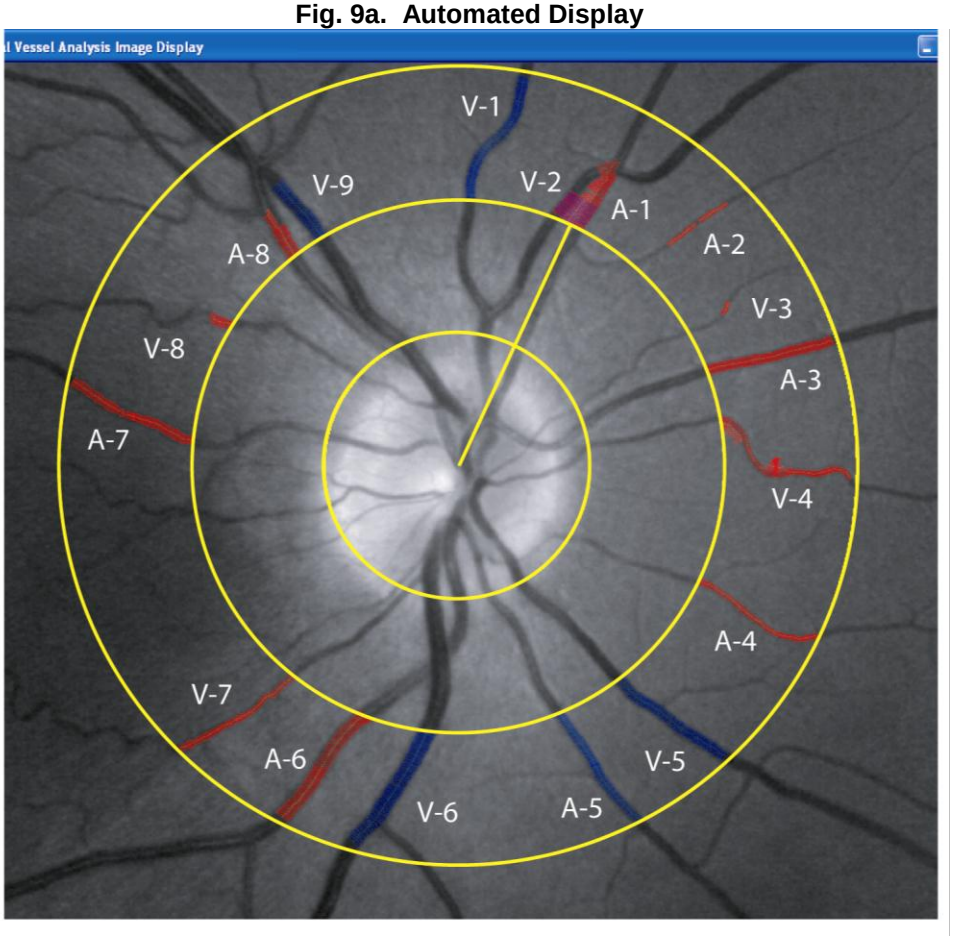
Errors introduced by the grader may significantly affect the calculated results or reproducibility of the data. For this reason, it is important to adhere to the grading guidelines and to give special attention to the following:

- Grid placement
- Vessel typing
- Measuring trunk vs. branches
- Deleting all automated “garbage” values
- Not overlooking significant vessels
- Potential for more than one automated measure on one vessel
- Typing and measuring small vessels in order to get 6 largest vessels of each type

It is recommended that the grader completely review all the vessel traces and corresponding vessel data on the control window before saving.

7.1 COMPLETE GRADING EXAMPLE

Fig. 9a. Automated Display



Grader Operations

A1 – delete/artery seed/truncate (before branch)
A2 – no change
crossing)
A3 – no change
A4 – truncate (before branch)
(outliers)
A5 – change type/truncate (before branch)
A6 – no change
A7 – no change
A8 – truncate (before outlier)

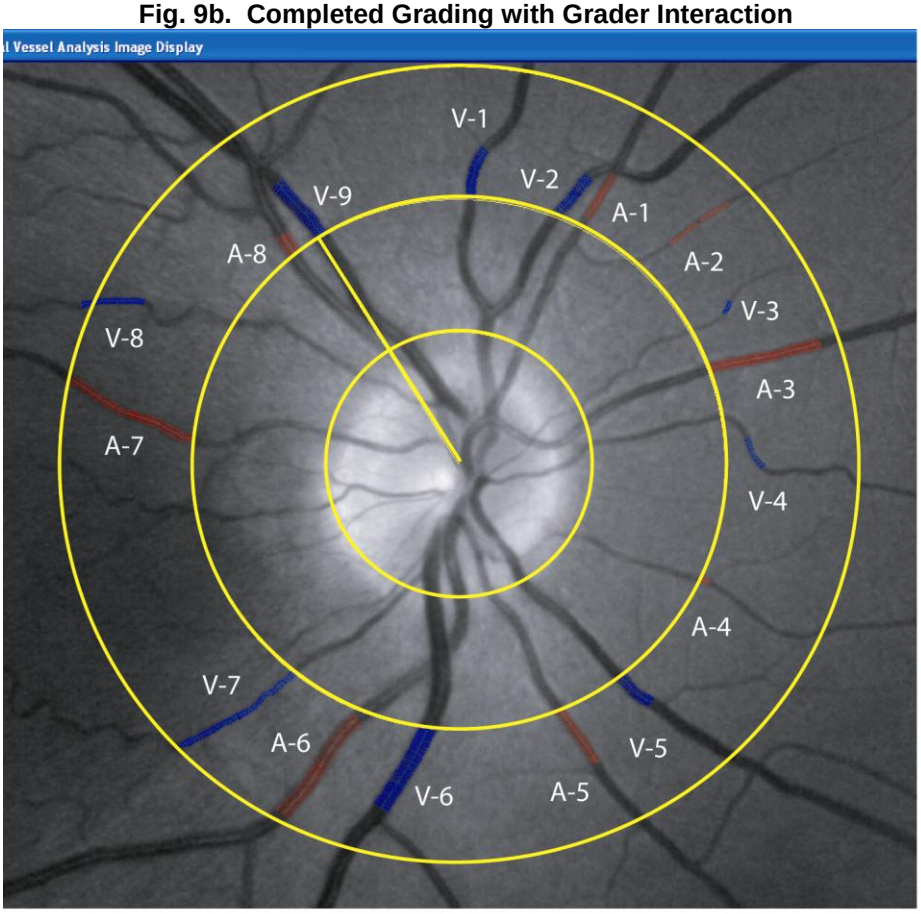
V1 – truncate (before branch)
V2 – delete/vein seed/truncate (before

V3 – change type
V4 – change type/proximal chop/truncate

V5 – truncate (before branch)
V6 – truncate (before branch)
V7 – change type
V8 – delete /vein seed
V9 – no change

COMPLETE GRADING EXAMPLE

Fig. 9b. Completed Grading with Grader Interaction



COMPLETE GRADING EXAMPLE

Fig. 9c. Final Artery Data

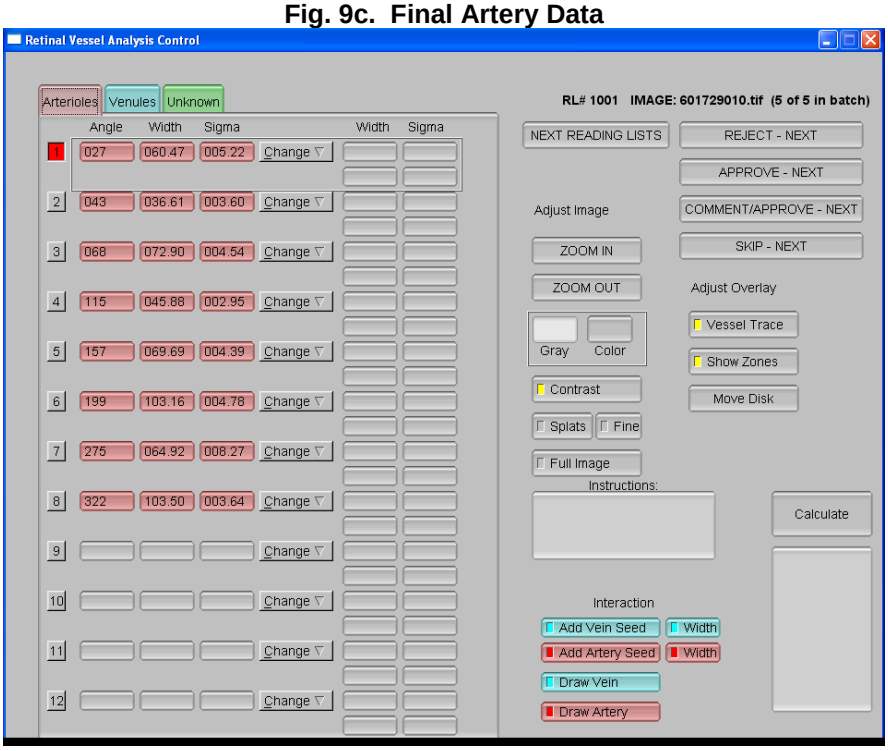
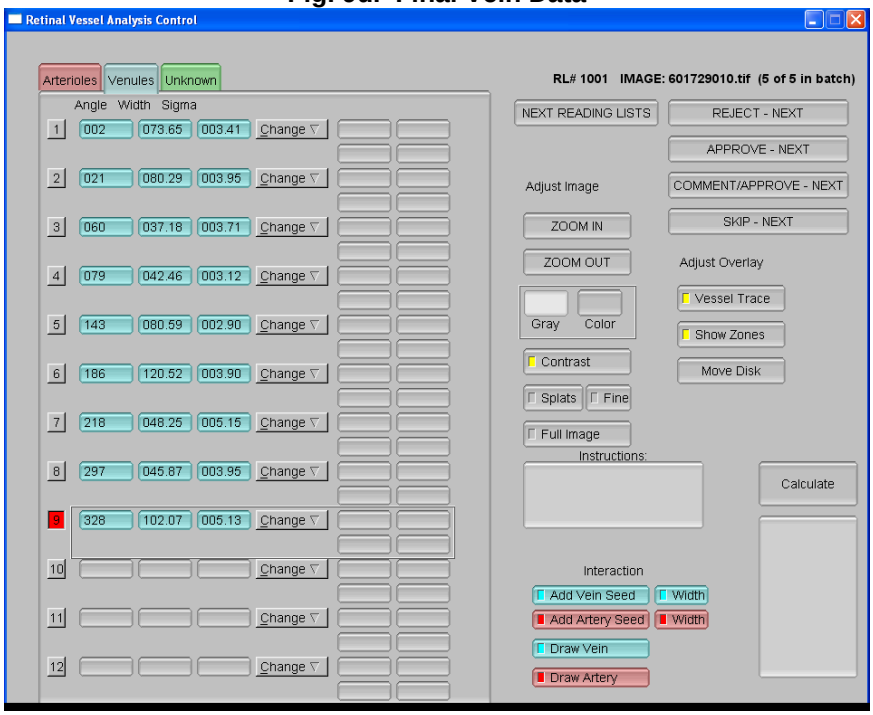
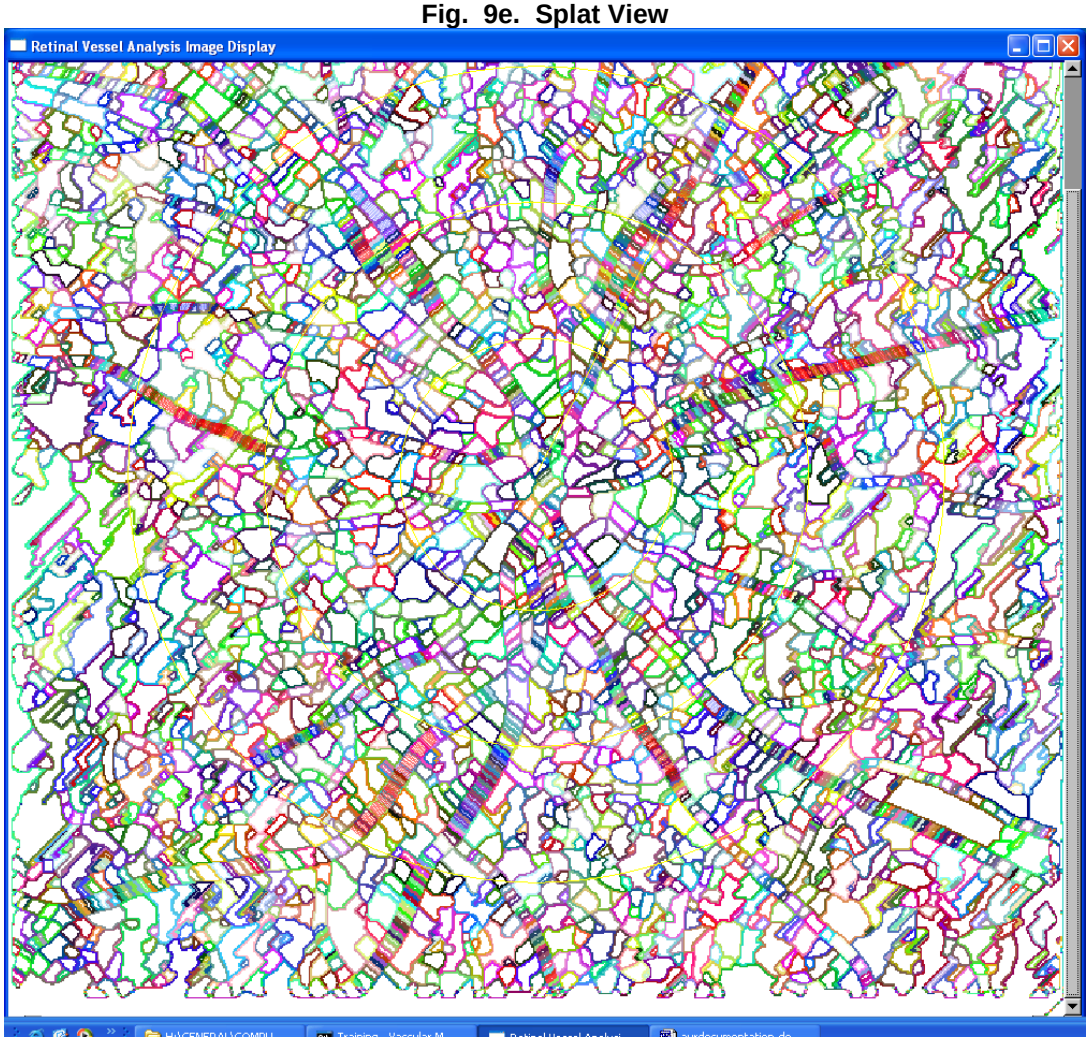


Fig. 9d. Final Vein Data



COMPLETE GRADING EXAMPLE

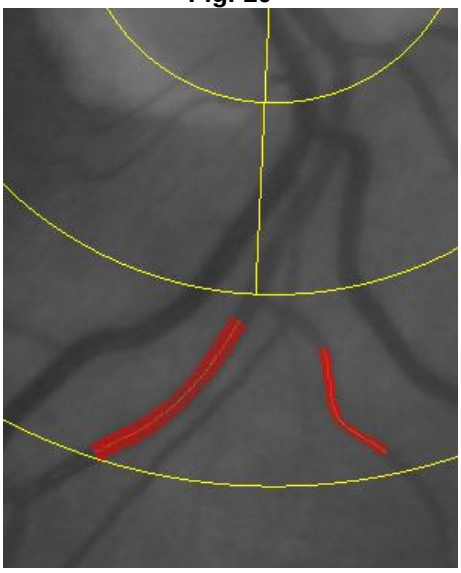
Fig. 9e. Splat View



With practice, the grader can discern the vessel pattern and the feasibility of accurate measurements from viewing the splat model.

7.2 BRANCHING EXAMPLES

Fig. 10



When the Zone B gridline falls at the point of branching (see Fig. 10), then the vessel branches should be measured as trunks.

Fig. 11a

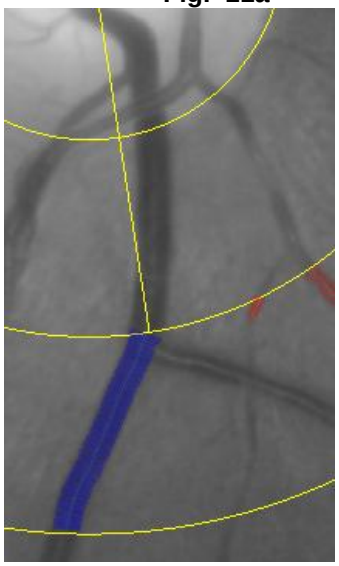
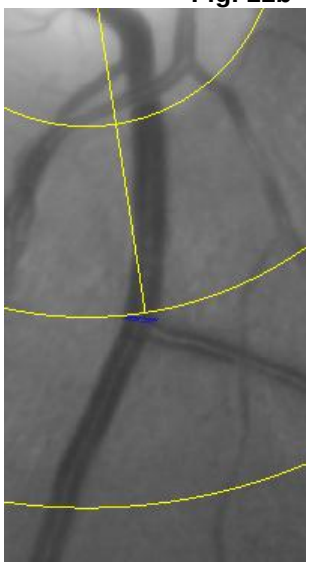


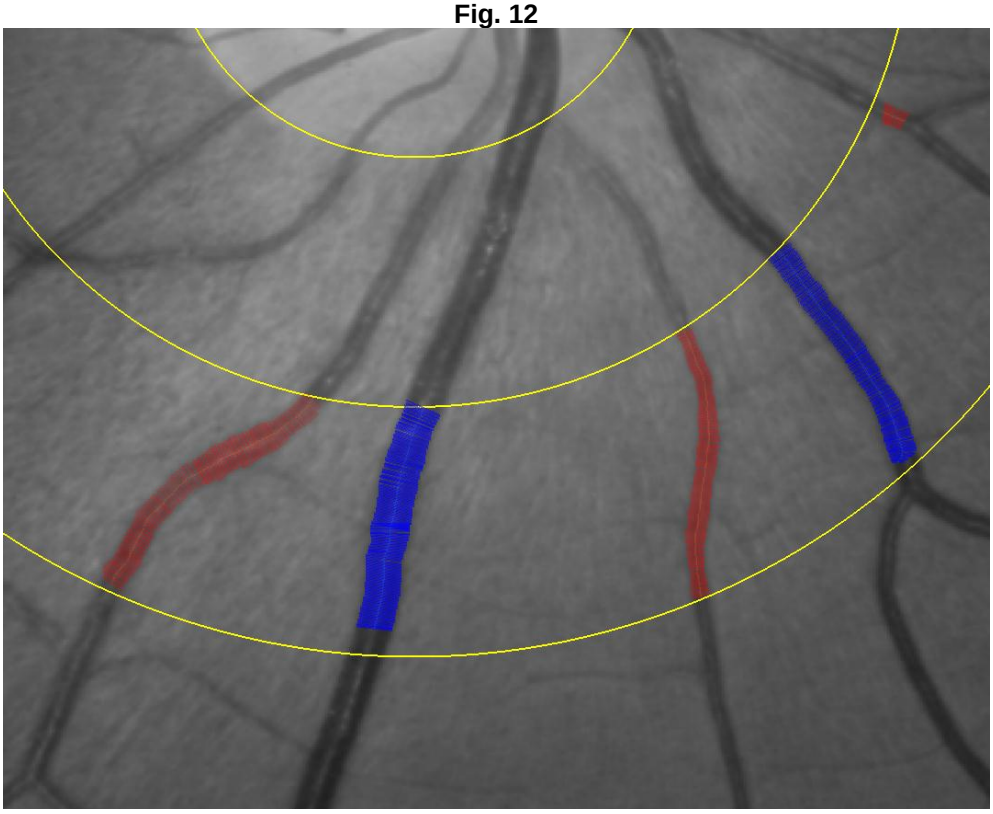
Fig. 11b



All trunks should be measured before branching even if the measured segment is very short. The automated vessel trace in Fig. 11a is truncated before the branch to produce the very short but acceptable measured segment in Fig. 11b. If the measurement is of questionable reliability, a comment should be added identifying the vessel.

BRANCHING EXAMPLES

Fig. 12



If suspected branches are impossible to identify with certainty and are of small size, then the grader should not truncate the vessel and instead measure as long a segment as possible. (see Fig. 12)

8. DATA SAVING OPTIONS

The SKIP – NEXT button is used to move through a reading list without saving data to the Excel file. This should be used when the grading has already been completed for an eye and the grader needs to advance to a subsequent image in the reading list.

The NEXT READING LISTS button brings up the Select Reading List window and allows the grader to leave the current reading list. This option does not save the current data.

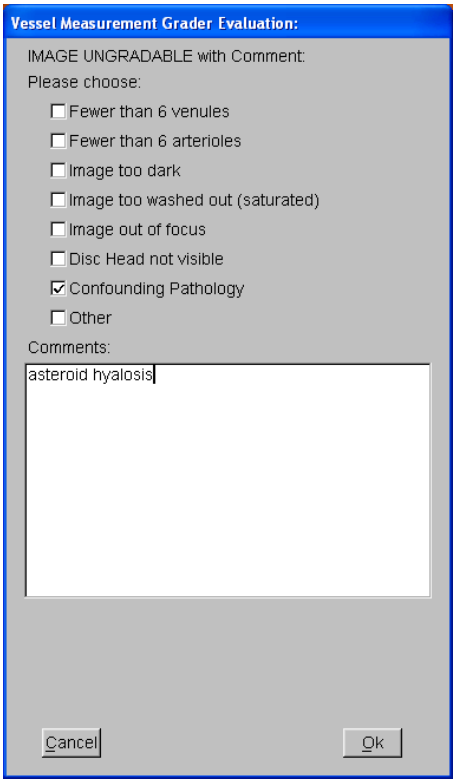
Saving of Data

At the completion of grading, there are 3 options for saving the data and automatically continuing to the next image in the reading list:

1. REJECT – NEXT
2. APPROVE – NEXT
3. COMMENT/APPROVE - NEXT

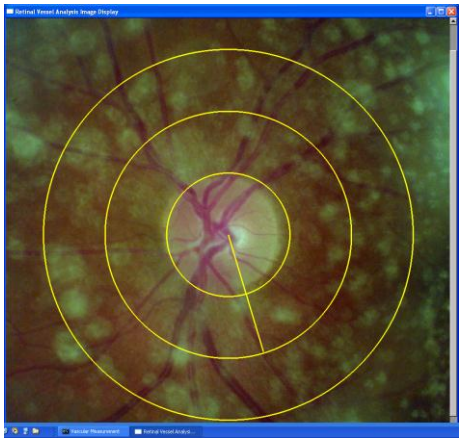
The APPROVE-NEXT option is used for images that are gradable and no comment is necessary.

The REJECT-NEXT option is used for images that are ungradable. Images that are ungradable very often will have no acceptable automated vessels on the initial display and the grader will have difficulty discerning any vessels due to the reasons listed in the menu. The splat view will also confirm the likelihood of acceptable measurements. **Eyes that have <4 acceptable measurements of either vessel type will be considered ungradable.** The grader enters one or more reasons for rejecting the image.

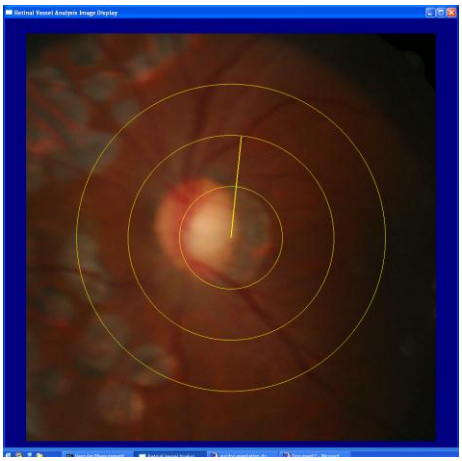


REJECT-NEXT

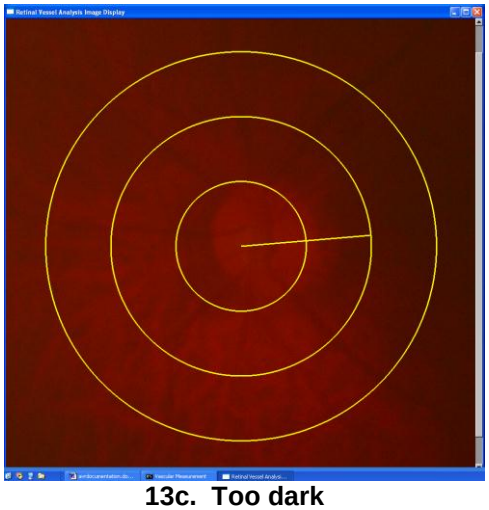
8.1 REJECT-NEXT EXAMPLES



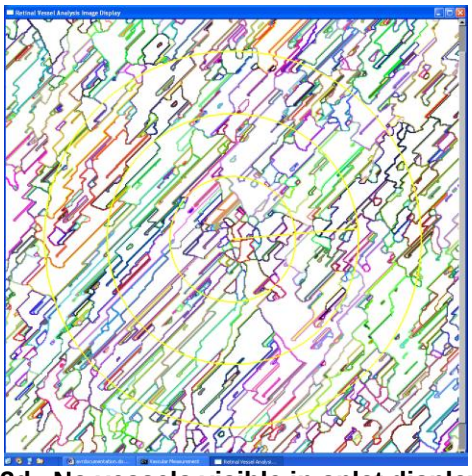
13a. Confounding pathology



13b. Out of focus/too dark/other



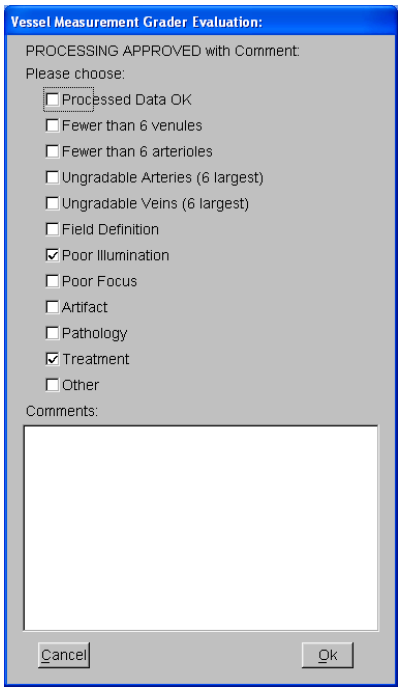
13c. Too dark



13d. No vessels visible in splat display

Pathologies like asteroid hyalosis (Fig. 13a) may obscure vessels and compromise measurements. Eyes with narrowed and sheathed arterioles clearly due to a pathology other than a cardiovascular condition, e.g. retinitis pigmentosa, should be rejected. Poor illumination may cause the image to be too dark for automated measures or too dark for the grader to visually validate the vessel trace (Figs. 13b and 13c). Vessels affected by laser treatment should always be documented in the Other-Comments (Fig. 13b). Gradability is easily determined by the splat display (Fig. 13d).

The COMMENT/APPROVE-NEXT option is used for images that are gradable but had grading discrepancies that may affect the consistency of the data. These comments will be evaluated by the statisticians. All special case grading decisions made by the grader will be documented using the Other button and entering a detailed comment.

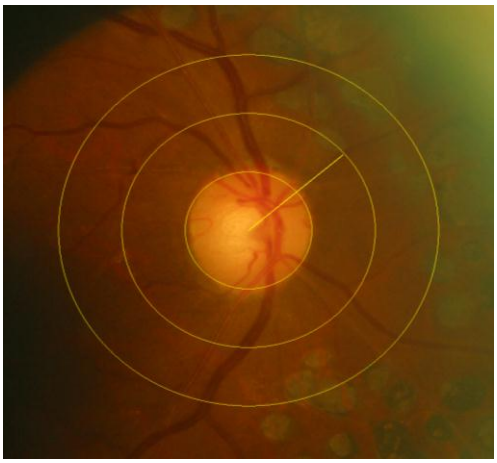


COMMENT/APPROVE-NEXT

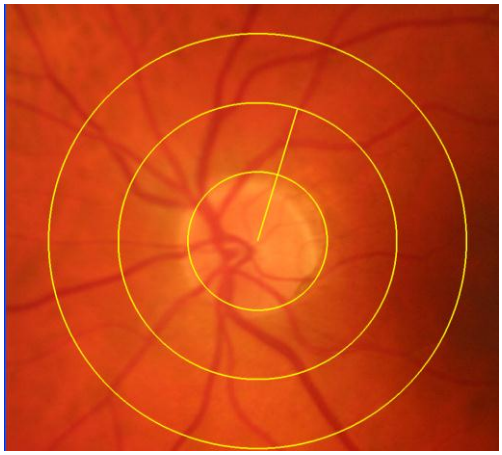
Fewer than 6 venules/arterioles refers to eyes that anatomically have less than 6 vessels of one or both types.

Ungradable arteries/veins (6 largest) refers to eyes that have ungradable vessels among the 6 largest. It is important to record the location of the missing vessel(s) in the comments.

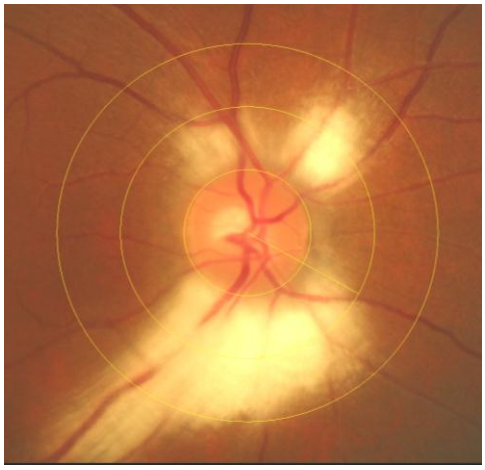
8.2 Approve with Comment Examples



14a. Poor illumination with treatment



14b. Poor focus



14c. Pathology/Ungradable arteries-veins

Affects of laser treatment on vessels should be documented with a comment (Fig. 14a). Poor focus often blurs the edges of vessels and causes falsely large measurements (Fig. 14b). Anatomical conditions such as myelinated nerve fiber may obscure significant vessels. The example shown in Fig 14c has more than one ungradable largest arteriole and venule and would not qualify for data analyses.