Safety and Effectiveness Information
for the QCA Plus Quantitative Coronary Arteriography Software

Introduction
Coronary arteriography is a medical procedure used to visualize the coronary arteries through the selective injection of contrast medium into the arteries and the use of x-ray equipment to create and record the images of the opacified arteries. Images are typically recorded on 35 mm cine film, although digital recording is also used. After the procedure, the opacified coronary arteries are viewed by a physician using a 35 mm cine projector or video monitor. Using these images, plus the results of patient history, physical examination and other laboratory tests, the physician makes qualitative judgements regarding the extent and severity of coronary artery disease and the need for and appropriate modality of treatment.

The purpose of quantitative coronary arteriography is to assist the physician by quantitatively measuring the dimensions of coronary artery segments. Using these dimensional data, additional parameters such as percent stenosis of the coronary artery segment can be calculated. Quantitative coronary arteriography has been shown by multiple investigators to be more accurate and reproducible than visual estimation of coronary artery dimensions and degree of stenosis.

Absolute measurements of coronary artery size require that the system be calibrated. Typically, the diameter of the coronary arteriographic catheter is used as the reference for calibration.

Quantitative coronary arteriography can be achieved by several techniques:
1. The use of calipers to measure the diameter of the vessel at one or more points.
2. Manually detecting and tracing the edges of an artery segment using a graphic digitizer, then calculating diameters along the segment.
3. Digitizing the image and using computerized edge detection to find the edges, then calculating diameters along the segment.
4. Digitizing the image and using densitometry to determine the diameters along the segment.

Method number three generally is believed to be the most accurate and reproducible, although this conclusion is still controversial. This is the method used by QCA Plus.
Hazard Analysis

Level of Concern
There is no substantial hazard of death or injury to the patient associated with using this software. The intended applications of the software are:

1. In clinical trials evaluating the effectiveness in treating coronary artery disease of therapies such as interventional devices, drugs or changes in lifestyle. Such trials incorporate data from many sources and are subject to intense scrutiny and statistical validation.

2. In diagnosing and evaluating the need for therapy of a patient with coronary artery disease. In such an application, the software provides data only and does not perform diagnosis. A decision regarding the need for therapy is multi-factorial, depending on patient symptoms, history and the results of multiple laboratory tests. The clinical judgement and experience of the physician is used to interpret and evaluate all of the data prior to making a diagnosis or therapy decision.

3. In evaluating the effectiveness of therapy for an individual patient. Again, the software provides data only and does not perform diagnosis. The effectiveness of the therapy in terms of symptomatic relief and the results of other laboratory tests are also evaluated by the physician in making a decision.

Analysis of Sources of Inaccuracy
Although it is believed that no hazard to the patient exists from this software, considerable attention has been given to sources of inaccuracy in the measurements and possible ways to avoid or detect inaccurate measurements. The following is a list of possible sources of inaccuracy that have been considered and ways they are avoided or detected:

1. Imaging problems:
   a. **Pincushion distortion**: This has been shown to be negligible in modern image intensifiers. Any distortion present will be at the edges of the image. The User Manual warns users against measuring images at the edge of the image.
   
   b. **Differences in magnification between the artery segment and calibration catheter**: This error occurs when the coronary artery segment and catheter are different distances from the image intensifier. This problem can be avoided by taking perpendicular views and performing a geometric correction. However, obtaining satisfactory perpendicular views is often not possible. There is typically only a one percent error per centimeter of difference and this error remains constant through serial measurements of the same segment. Therefore, it was considered best to warn the user of the problem in the User Manual and not attempt to correct it.
   
   c. **Differences in horizontal and vertical magnification in the video camera**: Most video cameras are not designed for use in quantitative systems. Therefore, the imaging geometry is not designed to produce "square pixels"; i.e., when digitized,
the image will have a different number of pixels per centimeter in the horizontal and vertical directions. QCA Plus incorporates a calibration routine for video cameras which allows both initial calibration and periodic checks of video camera magnification errors. A section of the User Manual entitled "How to Calibrate a Video Camera" is enclosed. QCA Plus allows multiple video cameras to be used through the use of a table of camera calibrations. If more than one camera calibration is in the table, the user is required to choose the appropriate entry from the table before any measurements can be made.

d. **Improper digitization of the video image:** The dynamic range of a video camera is considerably less than that of cine film. Therefore, it is very important that the exposure of the digitized cine image be adjusted to best encompass the density range of the coronary artery segment and its immediate surroundings. Depending on the cine projector and video camera, QCA Plus provides either automatic or semi-automatic adjustment of exposure for the Region of Interest in the cine image. A section of the user manual entitled "How to Digitize an Image" is enclosed.

2. **Edge detection errors:**

a. **Systematic errors in the detection of the edges of catheters and coronary arteries:** The function of the program is predicated upon its accuracy and consistency in detecting the edges of catheters and coronary artery segments under varying radiographic conditions. For this reason, its edge detection algorithm is based on a well established method developed by Reiber, et al, which uses the maximum of the sum of the first and second derivatives of the density gradient. Extensive validation of the program was performed using both *in vitro* and *in vivo* techniques. A copy of the manuscript "Coronary Artery Quantitation and Data Management System for Paired Cineangiograms" is enclosed. It describes this validation in considerable detail.

3. **Catheter calibration problems:**

a. **Errors in measuring the calibration catheter:** Almost all QCA programs that use the catheter as a calibrating object use a geometric measurement of either the outside or luminal diameter of the catheter. However, it has been shown that if a catheter is visualized radiographically and its *apparent* diameter is compared to the size of an independent standard such as a radiopaque grid, there will be significant differences in apparent diameters between catheters of different composition and construction. For this reason, QCA Plus allows standardization of catheter calibration factors using a radiopaque grid as the standard. A section of the user manual entitled "How to Calibrate a Catheter" is enclosed.

b. **An inappropriate calibration factor is entered by the user:** Almost all QCA programs allow the user to enter the calibration catheter size or calibration factor. Such entry is subject to multiple problems, such as transposition of digits or use of an inappropriate size. QCA Plus provides the user with a table containing the
names of all calibrated catheters. The user must choose the name of the appropriate catheter, and the appropriate calibration factor is provided automatically.

c. **The catheter is measured in one radiographic projection and the coronary artery segment is measured in a different view:** There is no way to automatically detect this error. However, when the catheter is measured, the user is required to provide the radiographic projection and may optionally provide precise angles. Each time a coronary artery segment is measured, the projection from which the calibrating catheter was measured is displayed to the user for verification. A section of the user manual entitled "How to Calibrate" is enclosed.

d. **The image quality is poor or the operator chooses an inappropriate frame:** Precise instructions on image quality frame selection are given to the operator in the User Manual. In addition, a statistical test is made to determine the validity of the calibration and an error message is displayed to the user if the calibration is suspect.

4. **Measurement problems:**
   
a. **The image quality is poor or the operator chooses an inappropriate frame:** There is no way to automatically detect these problems because of the variability of coronary artery geometry. Precise instructions on image quality and frame selection are given to the operator in the User Manual. A section of the user manual entitled "How to Measure a Coronary Artery Segment" is enclosed.

   b. **The operator misidentifies the segment:** There is no way to automatically detect this problem. However, the operator is required to identify the segment type and anatomic location before measurement can proceed. A section of the User Manual entitled "Working with Segments" is enclosed.

   c. **Edge detection errors due to image artifacts:** There is no way to automatically detect this problem. However, the operator is allowed to visually inspect and correct errors in the detected edges and calculated center line.

   d. **Incomparability of serial measurements of the same coronary artery segment:** QCA Plus has the ability to work with two cine projectors. This allows simultaneous display and measurement of the same segment from serial angiograms. Even without dual projectors, the results of a preceding measurement of the segment can be displayed alongside the current measurement for comparison.
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Re: K915542  
QCA Plus  
Dated: December 7, 1991  
Received: December 10, 1991  
Regulatory Class: II  
21 CFR 892.1600

Dear Mr. Sanders:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we have determined the device is substantially equivalent to devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments. You may, therefore, market the device, subject to the general controls provisions of the Federal Food, Drug, and Cosmetic Act (Act). General controls provisions of the Act include requirements for registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval) it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. In addition, the Food and Drug Administration (FDA) may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under the Radiation Control for Health and Safety Act of 1968, or other Federal Laws or Regulations.

This letter immediately will allow you to begin marketing your device as described. A FDA finding of substantial equivalence for your device to a legally marketed predicate device results in a classification for your device and permits your device to proceed to the market, but it does not mean that FDA approves your device. Therefore, you may not promote or in anyway represent your device or its labeling as being approved by FDA. If you desire specific advice on the labeling for your device, please contact the Division of Compliance Operations, Regulatory Guidance Branch (HFZ-323) at (301) 427-1116. Other general information on your responsibilities under the Act, may be obtained from the Division of Small Manufacturers Assistance at their toll free number (800) 638-2041 or at (301) 443-6597.

Sincerely yours,

Lillian Yin, Ph.D.  
Director, Division of Reproductive,  
Abdominal, Ear, Nose and Throat,  
and Radiological Devices  
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