Three Palm Software

CadOne™ User Manual

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1. CadOne™ System

1.1. Device Description

CadOne™ is a medical device which is designed to be used in mammography screening exams with a digital data source (e.g., FFDM or CR for mammography). The workflow (often referred to as “legacy” workflow) is that an acquisition device pushes the DICOM MG “For Processing” images from a mammography exam to CadOne via a DICOM storage service class. Then CadOne processes the images and generates a CAD report and pushes the report as a DICOM SR via a DICOM storage service to one or more destinations.

The CAD report that is output from CadOne is formatted as DICOM mammography SR, and it identifies two types of regions of interest: microcalcification clusters and density masses (including architecture distortion). The user may view the output using a commercial mammography workstation that displays DICOM MG “For Presentation” images with DICOM SR overlays.

1.2. Indication for Use

CadOne is a software product that analyzes digital mammography images and identifies regions that may warrant a further review by a radiologist. This device is intended to be used as an aid to the radiologists either after the initial reading has been completed, or used concurrently during the reading. The affected patient population is those patients who have presented for screening mammography.

1.3. Contraindications

There are no known contraindications for this device.

1.4. Warnings and Precautions

- **WARNING**: The recommended quality control procedure should be followed.
- **WARNING**: The device should be used with approved digital mammography acquisition systems. Images from un-approved mammography system may not meet the quality requirement for mammography. Therefore using such images may decrease CAD processing performance.
- **WARNING**: The images should be in a lossless format. Otherwise the detailed image information, such as, microcalcifications or spicules that are associated with a mass density may not be preserved for CAD process.
- **WARNING**: The CAD marks generated from the system should be used in the "second read" or “concurrent read” model, with the system simply being backup for the radiologist, not the source of a primary diagnosis.
- **WARNING**: Users should not make an assumption that the device identifies all regions that are either suspicious for cancer or indicative of cancer.
- **WARNING**: The device may not identify a region of interest in both views. Users should not take it as an indication that the region is less likely to be suspicious for cancer or indicative of cancer.

- **WARNING**: The device includes no serviceable hardware parts. For service assistance, contact the vendor who supplied the hardware.
- **CAUTION**: The device has not yet received FDA approval for sale in the US, so this device is available only for testing in the US. The device is limited by Federal (or United States) law to investigational use only.
- **CAUTION**: The device is not designed for use with non-mammography screening images, such as, implant exams, or diagnostic images.
- **CAUTION**: If the device is powered-off without a proper shutdown, the local system database may become corrupt. The device should be shutdown using Window's "Turn Off Computer" or "Shutdown" menu.

1.5. Residual Risks

The hazard analysis for CadOne has identified the following risks that are associated with this product. The risks and their controls are:

Hazard	Cause	Implemented control
H1. Patient is given over-diagnosis (i.e., unnecessary follow-up)	C1. System produces high false positive rate that may increases the radiologist's recall rate.	TPS continues to collect clinical data in order to retrain the system, so that performance can be improved, i.e., lower false positive and higher sensitivity. Such updates are tested and included in each release.
	C2. System produces low false positive rate that the radiologist comes to accept at suggested cancer without question.	CadOne output provides multiple operating points, so low false positive rate can be adjusted to increase sensitivity with cost of higher false positive. The same idea works for adjusting sensitivity.
H2. Patient is given under-diagnosis (i.e., does not receive appropriate follow-up)	C3. System failure results in missing report.	The system is designed to report to the user when it fails to produce CAD results. This is conveyed via a failed status in the exported SR.
	C4. System produces low sensitivity rate that may decrease the radiologist's recall rate.	TPS continues to collect clinical data in order to retrain the system, so that performance can be improved, i.e., lower false positive and higher sensitivity. Such updates are tested and included in each release.
	C5. System produces high sensitivity rate that the radiologist tends to ignore the studies with no markers.	CadOne output provides multiple operating points, so low false positive rate can be adjusted to increase sensitivity with cost of higher false positive. The same idea works for adjusting sensitivity.
	C9. Computer components or network links fail intermittently.	Installer/support will warn site to monitor hardware, and replaced as needed.
H4. Patient information exposed to unauthorized persons.	C7. Operating system defect allows unauthorized access.	Installer/support will warn customer to keep system patches current.
	C8. Site procedures do not control access to the software.	Installer/support will suggest to site IT that they implement appropriate physical and procedural security mechanisms.

1.6. Device Identification

CadOne has no user interface, as it runs in the background (often on a computer with no user logins), processing images to generate CAD reports. The user only sees any affect from this product when a CAD report is viewed along with the corresponding images, on a suitable mammography workstation. Information that identifies the product is thus not easily seen by the user – although it is available to support staff in the system logs. Information on the Manufacturer name, product name, version, production date, as well as the UDI information (as required by the FDA and EU MDR) is also encoded in the generated SR (and thus viewable on a workstation that can display that information from the DICOM object). Additional information such as the address of the manufacturer is available in section 6 of this document (which should also be made available to the user on the viewing workstation).

2. Principles of Operation

Early detection of breast cancer is the goal of mammography screening. With the rapid transition from film to digital acquisition and reading, more radiologists can benefit from advanced image processing and computational intelligence techniques when they are applied to this task. TPS's goal is to develop a next generation Computer Aided Detection (CAD) product that will be used as either a "second read" or a "concurrent read" tool for digital mammography screening – ultimately, this CAD product will be developed as a foundation for later TPS products that can be used as a "communicative read" tool for radiologists.

This system is for use in mammography screening, in particular, with digital (e.g., FFDM and CR for mammography) data sources. In current usage for digital mammography, the typical workflow is often referred to as "legacy" – the acquisition device pushes a case to CadOne (via a DICOM storage service class), CadOne processes the case and generates a CAD report, and then pushes that report (as DICOM SR) again via a DICOM storage service to one or more destinations as shown in Figure 1.

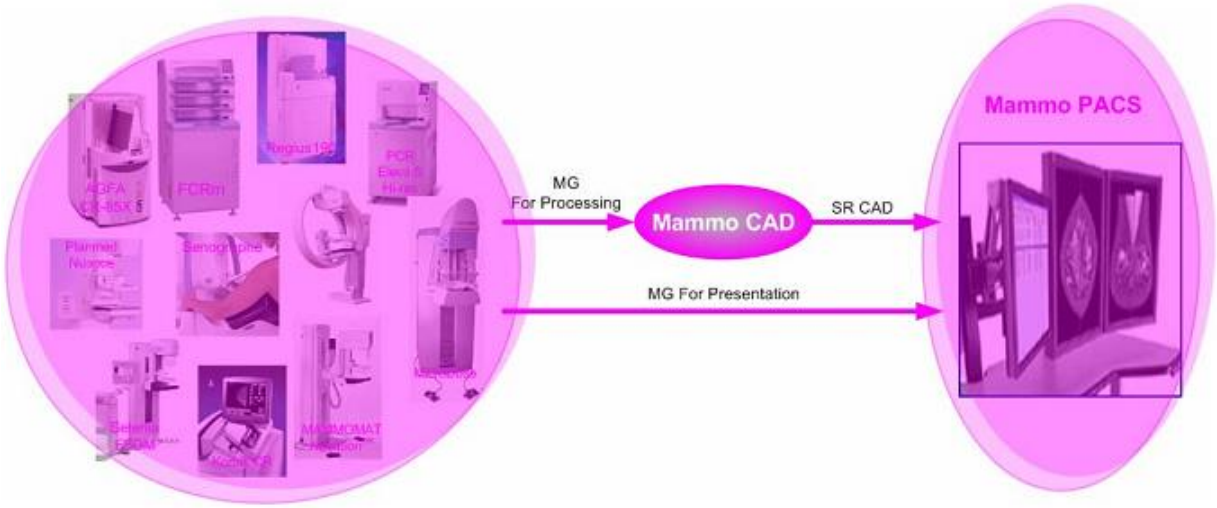

Figure 1. Mammography data flow including a CAD system

The technology embodied within the product consists of two main parts: (1) the infrastructure that is responsible for moving the source images and generated CAD reports using DICOM communications, and for managing the execution of algorithms, and (2) the specific algorithms that process the images to generate the reports that identify the presence of abnormal indicators – in particular microcalcification clusters and masses (including architectural distortion).

2.1. CAD Usage in Mammography Reading

As depicted in Figure 1, two types of digital DICOM mammography images are created at the digital imaging data source (e.g., FFDM or CR for mammography). A "For Processing" image is sent to CadOne for analysis, and a "For Presentation" image is sent to a PACS system and/or an image viewing workstation. CadOne automatically analyzes the image and sends the CAD information in the form of a DICOM Mammography CAD SR object to the PACS system and/or the image viewing workstation.

The CAD information is interpreted by a CAD-enabled workstation. The workstation will create and display overlays on the mammographic images explicitly indicating the CAD

findings as shown in Figure 2. These overlay findings as CAD markers designate areas which warrant further review by the radiologist.

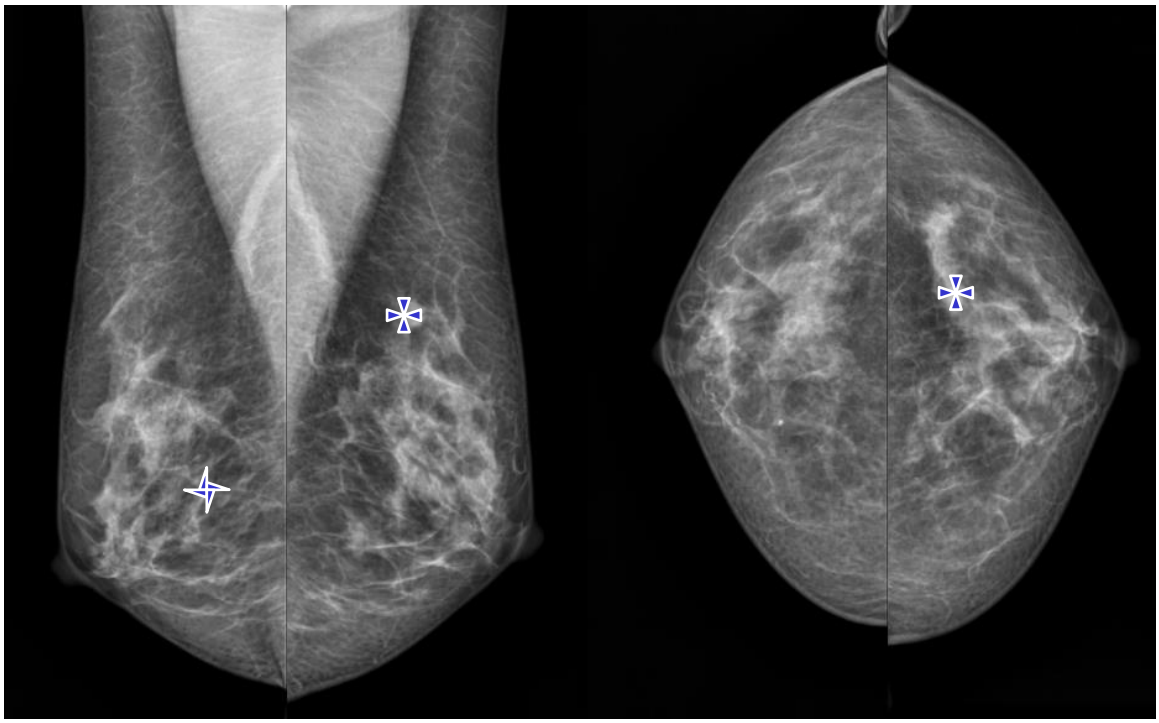

Figure 2. Example of CAD marker overlays on mammography images

There are two different types of CAD markers, microcalcification clusters and density masses. These are shown in Figure 3.

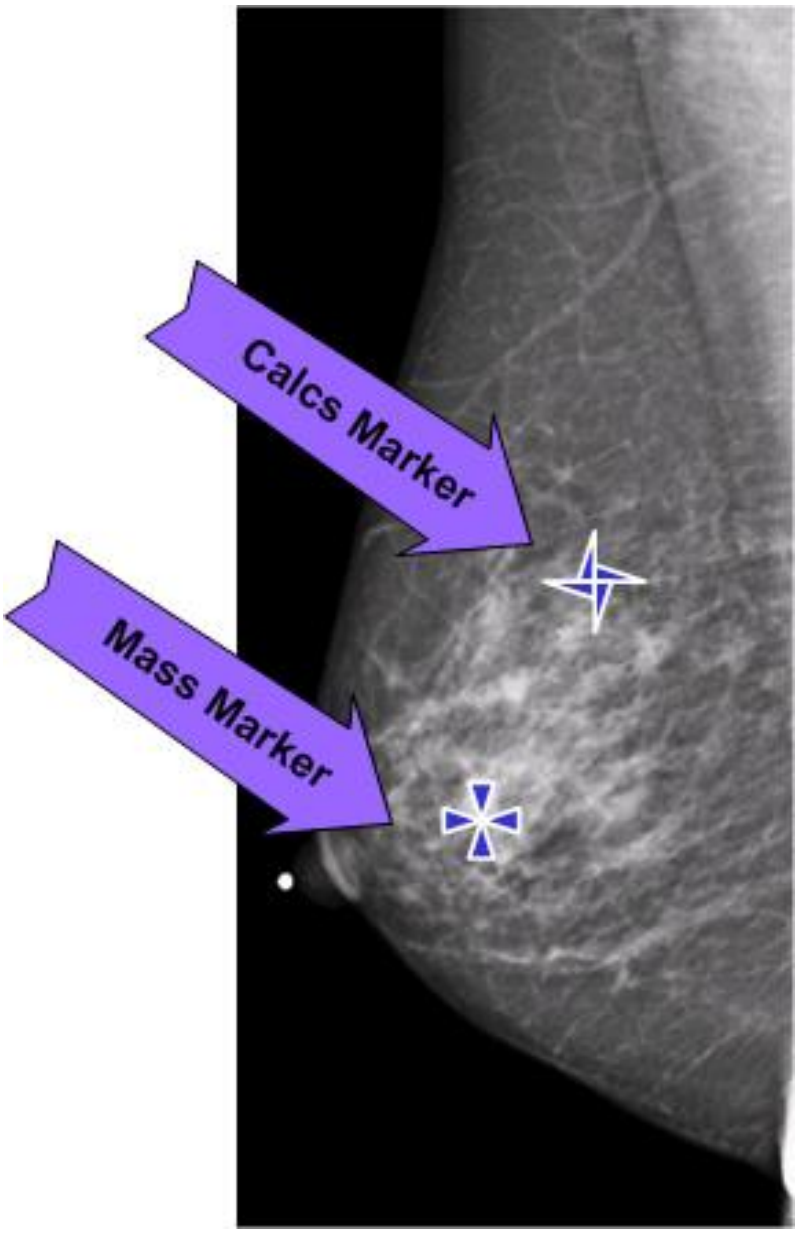

Figure 3. The two types of CAD markers, Calcs and Mass.

Calcs markers identify areas which may contain clusters of microcalcifications that indicate a possible abnormal condition. The Calcs marker graphic shape looks like a pinwheel. An example of the Calcs marker is shown in Figure 4.

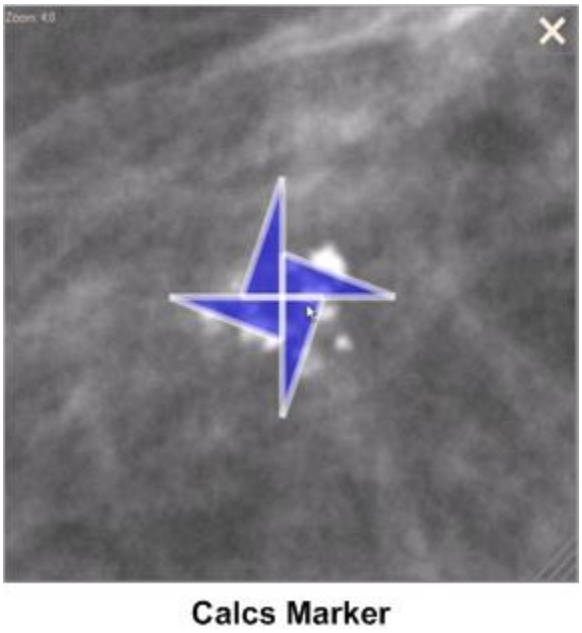

Figure 4. Example of a Calcs marker

Mass markers identify density areas that may appear suspicious for all reasons other than the appearance of microcalcification clusters. This includes the appearance of isolated masses, architectural distortions, and asymmetric densities. The Mass marker graphic shape looks like 4-petal flower. An example of the Mass marker is shown in Figure 5.

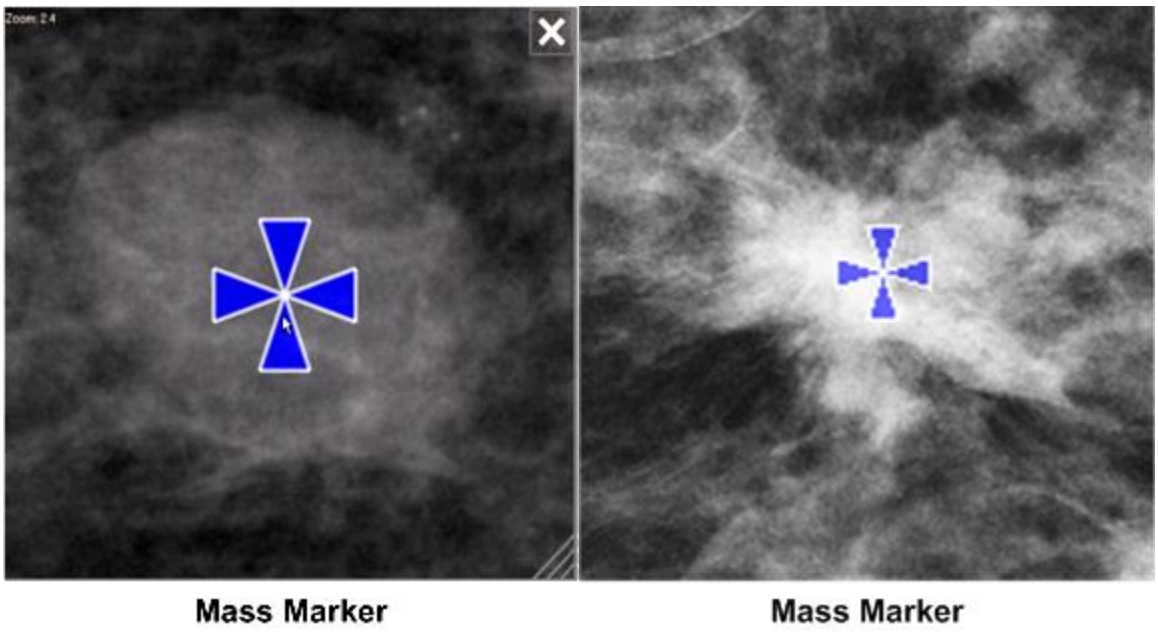

Figure 5. Example of Mass markers

2.2. Use of CAD Markers

Typically, the radiologist will first review the case. After making his decision regarding patient follow-up, the CAD output can be displayed overlaying the images. The radiologist should make sure that all of the areas identified by the CAD have been reviewed. If any areas were overlooked, they can be examined for potential abnormalities.

Although the technology inside CadOne is highly advanced and sophisticated, it is not perfect. Not all suspicious areas will be identified. CadOne will also sometimes mark areas which should be considered normal and require no further action.

Therefore, the CAD user should not rely on the CAD output to determine the areas of review. The entire breast must be examined independently. Also, areas with a CAD marker should not be worked up if the radiologist has already reviewed the area and determined it to be normal structures. The final decision should always be made by the radiologist using all available information in addition to the current mammographic images, including prior images, patient history, clinical information, and other imaging modalities.

Despite any imperfections, it has been shown that proper use of mammography CAD can increase the performance of the radiologist [1,2,3].

2.3. Multiple Operating Points

CadOne generates three operating points, called *Quiet*, *Medium* and *Zealous*. The Quiet point provide high specificity; the Zealous point provides high sensitivity; and the Medium point operates in between the Quiet point and Zealous point. The default operating point is usually configured to be the Quiet point.

An example of the Quiet point is shown in Figure 6.

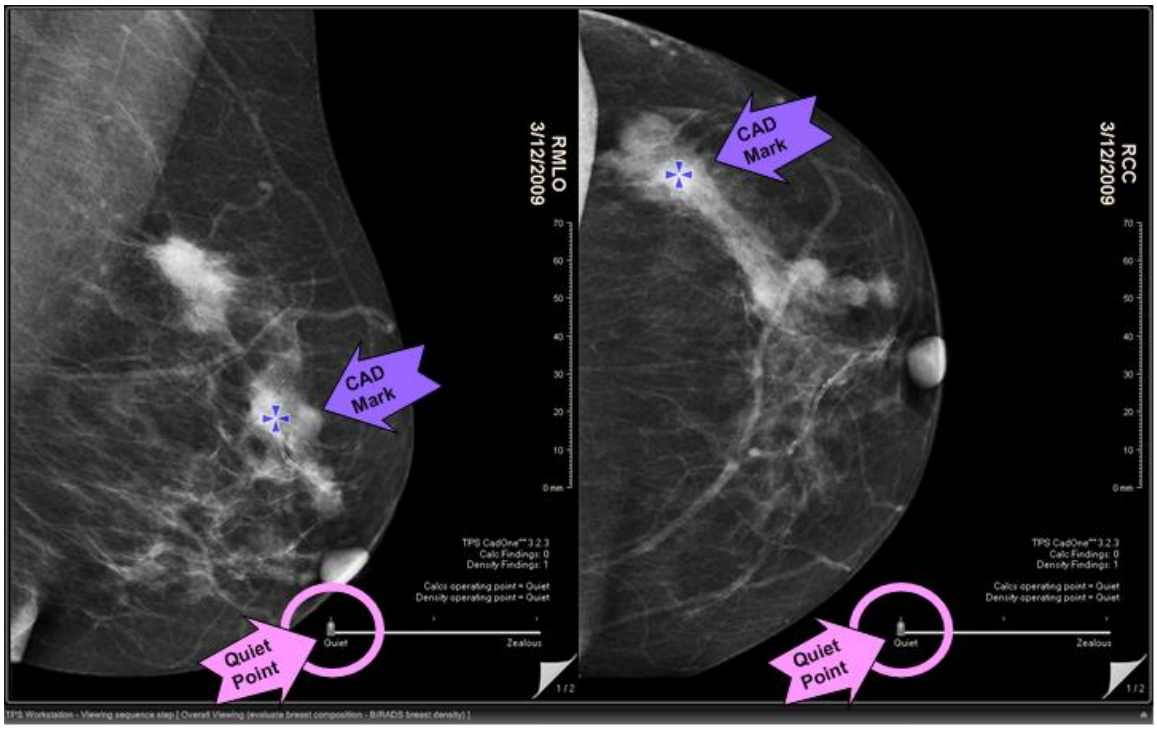

Figure 6. Example of multiple operating points with Quiet point selected

An example of the Zealous point is shown in Figure 7.

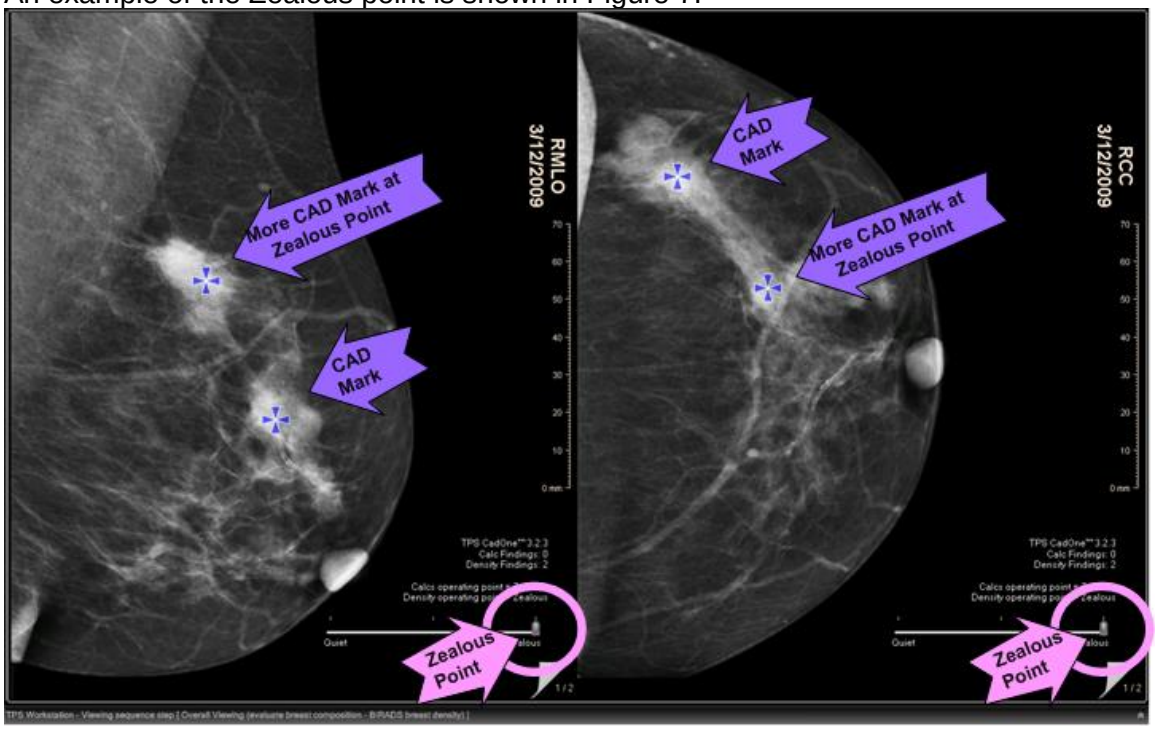

Figure 7. Example of multiple operating points with Zealous point selected

2.4. CAD Algorithm

The advanced image processing techniques developed for this product optimally combine both intensity and morphologic image processing methods at each step in the CAD algorithm – from image preprocessing and pseudo-modality normalization, to initial candidate selection and feature extraction for classification. The newer machine learning methods optimally integrate a statistical classifier, a kernel based classifier and traditional multilayer perceptron neural networks to demonstrate better training characteristics compared with the approaches used in most existing CAD systems.

The core of the CAD algorithm broadly can be categorized as having an initial pre-processing step, followed by separate processing paths for micro-calcification cluster and mass processing. Within each of the micro-calcification cluster and mass processing paths, the steps are parallel – initial segmentation to isolate a number of potential locations of interest (candidates), and for each such location, extraction of parameters (feature metrics) that categorize each, followed by classification of the generated feature vectors, with a resultant score of likelihood of being a cancer marker for each such candidate. Those candidates are finally grouped for the case using the scores (which can threshold to keep only the most “likely”) and other heuristics (like neighborhood, and maximum counts of each type per view, or per side, or per case), to arrive at a final combined report for the case which includes any potential micro-calcification cluster and mass findings.

2.5. Infrastructure

The CadOne System is comprised of the following major building blocks:

- Mammography CAD algorithm – the code that performs the mammography image specific processing. This code is hosted by the “algorithm service”, and is

given a set of images to process, and it generates a set of reports (the CAD results). The mammography CAD algorithm is discussed in previous section.

- Algorithm Service – this is a windows service that is installed on a hosting computer. It is configured to start on system startup, and runs in the background, accepting requests for computation from an “input queue” and passing them to algorithm(s) it hosts, and when those are completed, it sends a message to an “output queue”.
- DICOM Service - this is another windows service that is installed on the hosting computer. The algorithm service and DICOM service can be installed on the same computer, but the architecture supports other combinations (including models where there is no DICOM service – the initiator of CAD processing can be any software that can send a message to the input queue). The DICOM service essentially operates as a configurable DICOM router – it listens for associations, and in the simplest model provides a storage class provider for MG images that are pushed to it. On receipt of such images, it stores them to disk (in “part-10” format), and sends a request to the algorithm service (via the input queue) to process that case. Once the CAD is completed, the DICOM service receives a message from the “output queue”, and uses this to trigger the conversion of the CAD report into an export stream (typically DICOM SR) which is sent to configured destinations.
- Supporting services – there are two queues, which are implemented using MSMQ (so using operating system support). Status information which ties input jobs to returned output is also maintained by the system. Given that the architecture can be distributed across multiple computers, this repository is implemented as another service (called a “procedure log”), which is provided by TPS and installed as another windows service on a hosting computer.

2.6. Online User Manual

This manual can be accessed on Start menu under Three Palm Software sub-menu.

3. Hardware Configuration

The CadOne software can be installed on an off-the-shelf general-purpose computer. The general-purpose computer includes computer hardware, mouse, keyboard, network interface.

The recommended computer hardware includes platforms based on the Intel Core i7 or equivalent Xeon processor and later processors with at least 6GB RAM, running an x64 version of the Windows operating system.

4. References

The following documents are referenced by this manual:

1. Freer, T. et. al. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. *Radiology.* September 2001.
2. Couples, T. et. al. Impact of computer-aided detection in a regional screening mammography program. *AJR.* October 2005.
3. Birdwell, R. et. al. Computer-aided detection with screening mammography in a university hospital setting. *Radiology*. Aug 2005**.**

5. Conformance to Standards

Three Palm Software has obtained ISO 13485 certification for its quality management system. The quality management system has been certified by BSI. The accredited certification body has verified that the organization and all the functions of Three Palm Software fulfill the requirements stated in the standard ISO 13485:2016.

CadOne is a Class I device under the European MDR, and under the Health Canada Medical Device Regulations.

The product development for CadOne is in conformance with the following FDA recognized consensus standards:

1. NEMA PS 3.1 - 3.20, 2017c, Digital Imaging and Communications in Medicine (DICOM) Set

In accordance with the standards, the specification for CadOne system defines the DICOM Service Classes, Information Objects, Communications Protocols supported by this product.

6. Contact Information

For any questions or comments regarding this manual or CadOne, please contact:

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Phone: 1-408-356-3240
E-mail: support@threepalmsoft.com
16 Yankee Point Drive, Carmel, California 93923, USA

European Community Representative:

Wellkang Ltd t/a Wellkang Tech Consulting
Suite B, 29 Harley Street, London W1G 9QR, UK

Any serious incident that has occurred in relation to this device should be reported to the manufacturer, and to the competent authority of the Member State (of the EU) in which the user and/or patient is established.

A hardcopy (paper) version of this manual can be obtained by sending an email request to: support@threepalmsoft.com (include the serial number associated with the software in the request).

