Second Opinion®
CADe Software System - Client
Computer-Aided Detection for Intraoral Bitewing and Periapical Dental Radiographs

CLIENT USER MANUAL & LABELING

Software Version 2

Manufacturer - Pearl Inc.
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West Hollywood, CA 90069

UDI

Basic UDI-DI: ++D087SECONDOPINION2H8
UDI-DI – (01)00860003567920
Labeler Identification Code (LIC): D087
Model Identifier: SECONDOPINION2
Check Character: H8

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Table of Contents

1. Manual Information

1.1. Version

This manual is intended for correct and safe utilization of *Second Opinion*® v2. The GTIN Barcode denoting the version number of the software to which this manual pertains is displayed below:

1.2. Purpose

This manual provides instructions for operation of the *Second Opinion*® Client software device in accordance with its function and intended use.

1.3. Intended Audience

This manual is intended for any person who uses, maintains, or troubleshoots the *Second Opinion*® Client software device.

1.4. How to obtain a paper copy of this manual

To receive a paper copy of this manual, please send a request to Pearl Inc. at support@hellopearl.com that includes your organization name, full address, name of the product for which you are requesting a manual and its software version. Pearl Inc. will send a printed version of the manual to you via the postal service within seven business days of request receipt.

1.5. Regulatory Compliance

Second Opinion® complies with the regulatory requirements of the following:

- EN ISO 13485:2016 - Medical Devices – Quality Management Systems.
- Quality Management Systems Requirements for regulatory purposes, FDA 21 CFR Part 820 entitled Quality System Regulation (QSR).
- EU Medical Device Regulation (EU) 2017/745 of the European Parliament and

of the Council of 5 April 2017 on Medical Device (MDR)
- Australian Therapeutic Goods (Medical Devices) Regulations 2002
- Canadian Medical Devices Regulations SOR 98-282
- Medicines and Healthcare products Regulatory Agency (MHRA) UK MDR 2002 & Medicines and Medical Devices Act 2021
- Switzerland Medical Devices Ordinance (MedDO)
- Brazilian Health Regulatory Agency (ANVISA)
- The Health Insurance Portability and Accountability Act (HIPAA)
- General Data Protection Regulation (EU) 2016/679 (GDPR)

2. *Second Opinion*® Device Labeling

2.1. Brief Device Description

Second Opinion® is a computer-aided detection (CADe) software device intended to assist dental healthcare professionals review of intraoral radiographs. A proprietary software application, it has been designed to process intraoral radiographs and automatically detect presumptive evidence of five restorations (crowns, bridges, implants, root canals, fillings) and four pathologies (carries, notable margin, previously known as margin discrepancy, calculus, periapical radiolucency) which may present therein.

Second Opinion® consists of three components:

- In-office application or Client User Interface (“Client”)
- Application Programing Interface (“API”)
- Computer Vision Models (“CV Model”, “CV Models”)

The Client resides in the clinician’s office. The API and CV Models reside in a cloud computing platform hosted by Amazon Web Services Inc. (“AWS”), where radiograph processing takes place.

Results are displayed on a computer monitor in the clinician’s office for review by a dental practitioner. The user is instructed to first evaluate each radiograph in the conventional visual manner and then re-examine the radiograph utilizing *Second Opinion*® prior to making a final diagnosis.

2.2. Indications for Use

Second Opinion® is a computer aided detection ("CADe”) software to identify and mark regions in relation to suspected dental findings which include Caries, Discrepancy at the margin of an existing restoration, Calculus, Periapical radiolucency, Crown (metal,

including zirconia & non-metal), Filling (metal & non-metal), Root canal, Bridge and Implants.

It is designed to aid dental health professionals to review bitewing and periapical radiographs of permanent teeth in patients 12 years of age or older as a second reader.

2.3. Contraindications

Not to be used with patients under the age of 12 years.

2.4. Prerequisites

To operate *Second Opinion*® safely and according to its intended purpose, the following prerequisites must be met:

- The user has read and understood the Intended Use, Warnings, and Operating Instructions included in this User Manual.
- The user has a general understanding of how to use a personal computer that is running one of the compatible operating systems listed in the Reference Information section below.
- *Second Opinion*® has been correctly installed according to the instructions in Section 4 of this User Manual.

2.5. Warnings

The following warnings apply to the use of all *Second Opinion*® software:

- CAUTION: *SECOND OPINION*® IS NOT INTENDED TO OFFER A DIAGNOSTIC ASSESSMENT. Further clinical investigation of any detected potential pathologic and non-pathologic features that may appear in radiographs is always required.
- *Second Opinion*® is to be used with visual and tactile oral examination and patient risk assessment.
- Users should regularly confirm that the computer on which

the *Second Opinion*® Client software is operating is free of viruses or malware.

- Users should regularly confirm that the *Second Opinion*® Client software has been updated with the latest security patches.

- Do not use *Second Opinion*® software without proper training. Operator training and review of the *Second Opinion*® user manual is required prior to using the system.

- The *Second Opinion*® system may make a detection and highlight a region where no pathologic or non-pathologic feature exists. Users must always exercise their professional interpretative skills when reviewing the regions that have been detected by *Second Opinion*®.

- *Second Opinion*® may not detect or mark all regions that are indicative of a pathology. Users must always exercise their professional interpretative skills to determine whether any pathologic and non-pathologic features warranting clinical attention are present in radiographs processed by *Second Opinion*®.

- Effectiveness and safety have been established only for detections in bitewing and periapical radiographic images. Any features detected and highlighted on radiograph types other than bitewing and periapical cannot be used by the clinician to assist in radiographic evaluations. *Second Opinion*® deploys a CV model that classifies submitted radiographs into types: *bitewing*, *periapical* and *other*. If an image is categorized as *other*, the *Second Opinion*® Client will display a message to the user indicating that the image type is not supported.

- All images submitted for *Second Opinion*® processing must be JPEG, RVG, DCM, TIFF, PNG, and DIC. *Second Opinion*® may not function properly if an image in an unsupported format is submitted.

2.6. Adverse Effects

There are no known direct risks related to the use of the device to the safety or health of the user or the patient. Patients have no direct contact with the device. Indirect inherent risks are: (a) the device may not detect pathologic or non-pathologic features that present in radiographs (false negative detections); and (b) that the device may detect pathologic or non-pathologic features that do in fact present in radiographs (false positive readings). These possibilities are clearly explained in the warnings section included in the labeling of the device. Proper operation of the device is explained in the directions for use printed in this manual. The *Second Opinion*® output is one of several inputs that physicians employ in their decision making; final diagnostic decisions represent physicians' assessments and judgments derived from these several inputs.

2.7. Intended Use

The *Second Opinion*® is a cloud-based, stand-alone software that analyses radiograph images using machine learning techniques to detect, categorize, and highlight suspicious regions of interest (ROI). Any suspicious ROI detected by the *Second Opinion*® is assigned to one or more pathologic or non-pathological features. The device is intended for use as a concurrent reading aid for dental clinicians and should not be used as a standalone device.

2.8. Intended User Population

The intended users of *Second Opinion*® are dental health professionals in various settings including primary care (e.g., family dental practice, hospital-based dentistry, and dental service organizations), dental specialists, oral maxillofacial radiologists who review radiographs across these settings.

Second Opinion® is intended for installation at dental clinics, dental service organization offices and dental insurance providers on off-the-shelf computer systems running Microsoft Windows 7+ or through integration of an API with third-party practice management systems and X-ray sensor software.

2.9. Intended Patient Population

The device may be used to evaluate radiographs of dental patients, aged 12 and over, with permanent teeth.

2.10. Compatible Radiological Data Sources

Second Opinion® can process two types of intraoral radiographs: periapical and bitewing. These radiographs can be acquired on a wide range of dental radiograph systems from different manufacturers. The radiographs are stored on clinical office

network servers using digital storage systems. The system currently supports several common image formats, including JPEG, RVG, DCM, TIFF, PNG, and DIC.

Clinical studies of *Second Opinion*® were conducted by the manufacturer on more than 1,000 images from nine radiographic image acquisition devices. Five of the nine device categories contained a sufficient number of images for statistical testing: Carestream - Trophy Kodak RVG6100, Carestream -Trophy RVG6200, DEXIS Platinum, Kodak-Trophy - KodakRVG6100, and XDR - EV71JU213. The remaining four did not contain a sufficient number of images to allow for substantive conclusions based on analysis: Carestream - Trophy RVG5200, DEXIS, KaVo Dental Technologies - DEXIS Titanium, and the remaining without metadata to indicate device type.

Table 1 below summarizes outputs for the device subgroup in those clinical studies. All green fields represent statistically significant observations. “N/A” indicates that, for that *Second Opinion*® detectable feature, there were no images associated with the given device.

*Note – PR = Periapical Radiolucency; MD = Marginal Discrepancy, also known as Notable Margin.

Device	# of images	HIGH MRMC - FOMs
Carestream - Trophy Kodak RVG6100	322	Unaided Caries: 0.73 MD: 0.61 Calculus: 0.66 PR: 0.79 Aided Caries: 0.76 MD: 0.68 Calculus: 0.73 PR: 0.82
Carestream -Trophy RVG5200	18	Unaided Caries: 0.46 MD: 0.55 Calculus: N/A PR: 0.77 Aided Caries: 0.48 MD: 0.71 Calculus: N/A PR: 0.95
Carestream -Trophy RVG6200	328	Unaided Caries: 0.77 MD: 0.60 Calculus: 0.66 PR: 0.74 Aided Caries: 0.78 MD: 0.67 Calculus: 0.71 PR: 0.80
DEXIS	10	Unaided Caries: 0.69 MD: 0.71 Calculus: 0.68 Aided Caries: 0.77 MD: 0.72 Calculus: 0.80

		PR: 0.84	PR: 0.92
DEXIS Platinum	374	Unaided Caries: 0.72 MD: 0.62 Calculus: 0.67 PR: 0.75	Aided Caries: 0.72 MD: 0.71 Calculus: 0.73 PR: 0.79
KaVo Dental Technologies - DEXIS Titanium	53	Unaided Caries: 0.87 MD: 0.65 Calculus: 0.67 PR: 0.77	Aided Caries: 0.93 MD: 0.74 Calculus: 0.80 PR: 0.95
Kodak-Trophy - KodakRVG6100	493	Unaided Caries: 0.74 MD: 0.58 Calculus: 0.64 PR: 0.76	Aided Caries: 0.76 MD: 0.65 Calculus: 0.71 PR: 0.84
XDR - EV71JU213	357	Unaided Caries: 0.69 MD: 0.62 Calculus: 0.66 PR: 0.77	Aided Caries: 0.72 MD: 0.68 Calculus: 0.72 PR: 0.81
Remaining w/o metadata to indicate device type	55	Unaided Caries: 0.72 MD: 0.64 Calculus: 0.60 PR: 0.89	Aided Caries: 0.74 MD: 0.64 Calculus: 0.81 PR: 0.91

As an added safety provision, prior to detection processing, *Second Opinion*® deploys a CV Model that classifies submitted radiographs into types: *bitewing*, *periapical*, and *other*. If an image is categorized as Other, the *Second Opinion*® Client will display a message to the user indicating that the image type is not supported.

2.11. Hardware Requirements

Computer Requirements	
Processor architecture	Intel
Minimum processor	Pentium 4

Minimum internal memory	2 Gigabytes
Minimum disk space	250MB
Operating system	Microsoft ● Windows 7 32- or 64-bit ● Windows 8.1 Update 32- or 64-bit ● Windows 10 32- or 64-bit

The relationship of *Second Opinion*® to local and networked components within the dental office and cloud is illustrated in *Figure 1*, below.

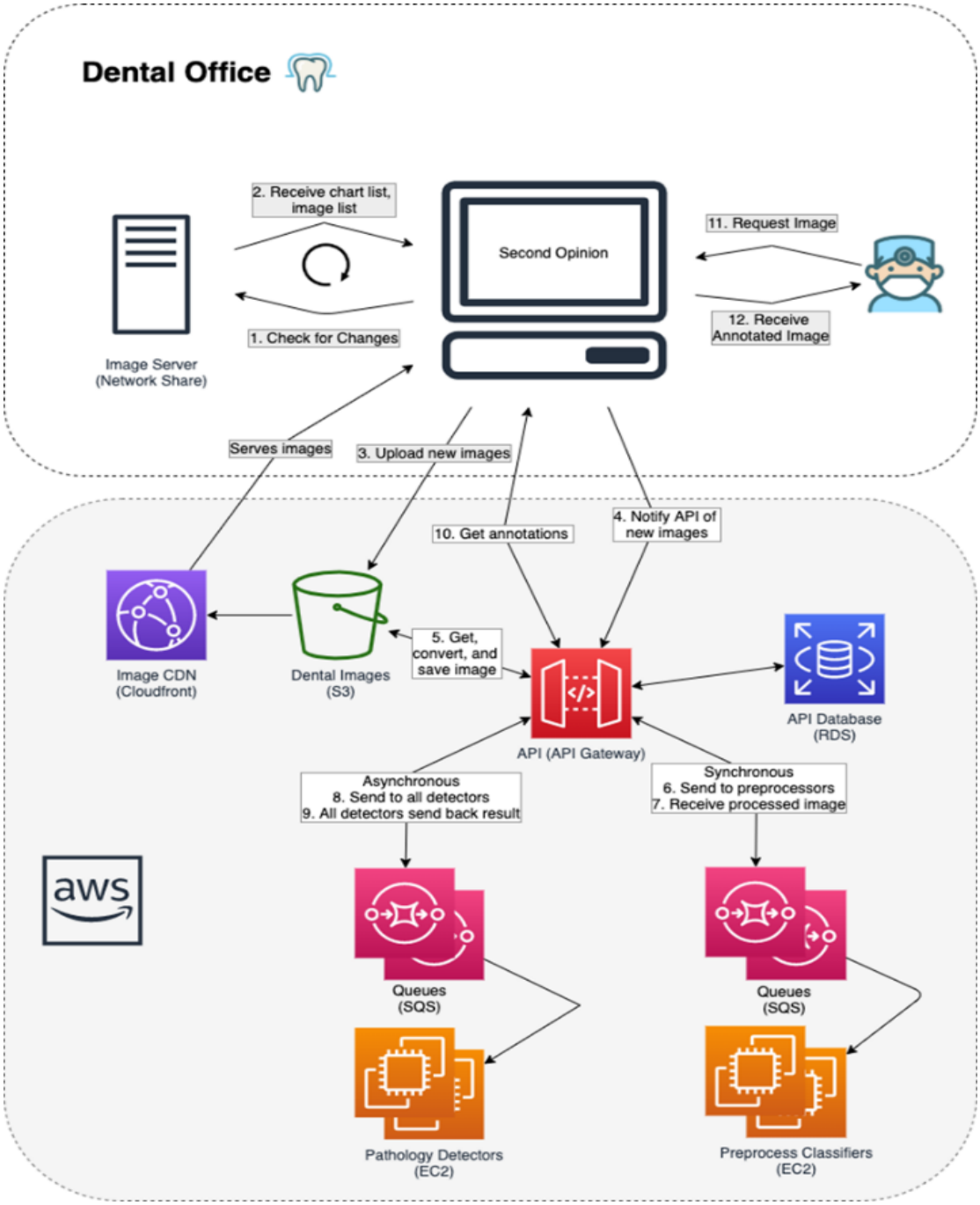


Figure 1. Second Opinion® workflow.

3. Product Information

3.1. Product Contents

Second Opinion® Client.

3.2. Principles of Operation

After installation, the *Second Opinion*® Client connects to the cloud based *Second Opinion*® API. To submit exams to the device, radiographic images are first selected in the *Second Opinion*® Client. To process the radiographs, *Second Opinion*® Client needs to be connected to the internet. The *Second Opinion*® Client sends the radiographs securely over the internet to cloud servers for processing. A result report and associated detections are then immediately generated by the API. The detections can then be viewed in the *Second Opinion*® Client user interface. To perform an analysis, the *Second Opinion*® Client must be authorized with valid account login credentials (username and password), which would have been configured at sign up.

4. *Second Opinion*® Installation Instructions

Warning: Pearl recommends that installation and system changes be performed by individuals familiar with the IT systems on which the *Second Opinion*® is running.

4.1. System Requirements

To use the *Second Opinion*® device you will need the following:

- A computer running Microsoft Windows 7 or newer.
- A working internet connection.

Specific computer hardware requirements can be found in Section 2.11 of this User Manual.

4.2. Installation

Download & configuration of the *Second Opinion*® installation package occurs at http://secondopinion.hellopearl.com

4.3. Registration

To use *Second Opinion*®, a username and password combination is required. Successful purchase of *Second Opinion*® will have resulted in account creation.

After installation, the *Second Opinion*® can be started by launching the "**Second Opinion Desktop.exe**" file in the installation folder.

The client will start up and ask for a valid username and password. Fill in the credentials in the appropriate fields then press "OK". An internet connection is required for the *Second Opinion*® Client to verify the credentials.

4.4. Updates

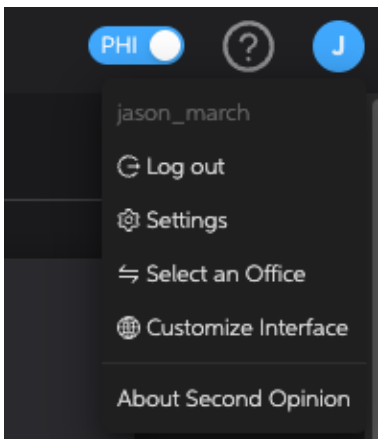
Every time the *Second Opinion*® Client starts, or every three minutes, the software checks if a software update is available. When an updated version of the software has been found, *Second Opinion*® Client will automatically download the new software and alert the user.

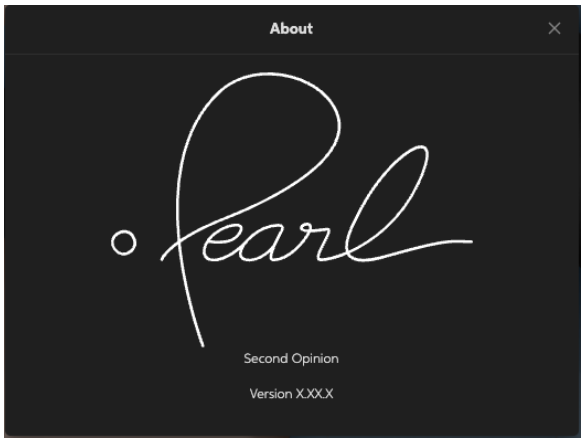
To install the update close and restart the application.

4.5. Accessing the manual and viewing the product label

Second Opinion® comes loaded with an up-to-date electronic copy of the user manual, which can be accessed by clicking the “Help” button in the application’s toolbar, located at the upper right corner of the application’s viewer. The “Help” button is denoted with a question mark icon inscribed in a circle.

Second Opinion® has an official product label that can be viewed from the user profile menu in the upper right-hand corner of the application, then by selecting “About *Second Opinion*®”.





5. *Second Opinion*® Operating Instructions

5.1. Description of User How *Second Opinion*® Operates

The *Second Opinion*® system consists of three parts: in-office application ("*Second Opinion*® Client*"*) or User Interface ("UI"), Application Programing Interface ("API"), and Computer Vision.

The *Second Opinion*® Client is continually monitoring a local (or networked) resource where dental radiographs (refer to Section 2.4 for list of supported image types) are stored. Once new imagery is discovered, the *Second Opinion*® Client invokes cloud-based APIs which submit the imagery to Computer Vision Models ("CV Model", "CV Models") for processing. The metadata that these CV Models produce describe the nature and location of detected pathologic or non-pathologic features that may appear in the radiographs.

This metadata information is then sent back to the *Second Opinion*® Client, which renders it for visual display and review within the Client's user interface. Any potential pathologic or non-pathologic features detected will appear inscribed within boundary boxes or segmentation masks overlaid on the original radiograph.

The entire process outlined above takes five to ten seconds to complete.

Second Opinion® CADe detects potential pathologic or non-pathologic features based on their visual appearance. Features are detected because they closely resemble known features present in the radiographs used to train the *Second Opinion*® CV Models.

The system can assist the clinician as a second reader by identifying regions that may warrant a more meticulous review.

The *Second Opinion*® software may be used only as an aid for detecting certain potential pathologic or non-pathologic features that can appear in dental radiographs. It is not for use as an aid in radiographic diagnosis or interpretation.

5.2. Getting Started

Follow the instructions below to begin using the *Second Opinion*® Client.

5.2.1. Launch Application

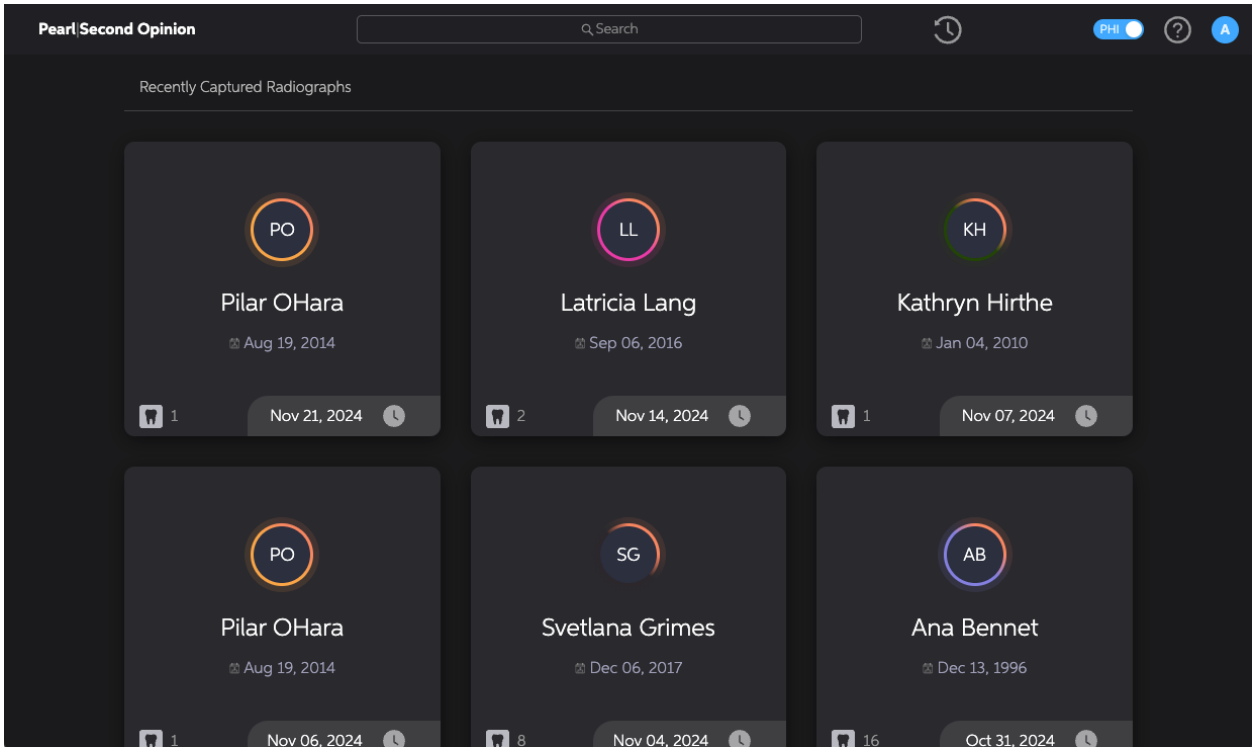
To launch the *Second Opinion*® Client, open the operating system's Start menu and click the All programs/All apps button to display a list of all installed applications. Click on the *Second Opinion*® application to open it.

5.2.2. Logging On

At the login window, enter Username and Password, then press Enter.
Note: For security reasons, the password is issued by the system administrator.

5.2.3. Opening Screen

When the application launches, the home screen will display in the user interface window.



To search for a patient's X-rays a search bar is provided. To return to recent radiographs, you may select the "Recents" icon (circular arrow) to the right of the search bar.

5.2.4. Customized Interface

The available language and date formats for the *Second Opinion*® application are located within the Customize Interface section, which is available from the user

profile dropdown when hovering over the user's initial in the upper right-hand corner of the application.

5.2.5. Navigating Patient Records

To load images from a patient visit, click on the patient record.

Charts are groups of images captured for a specific patient identifier on a specific date. The Chart List is populated in chronological order. Newly captured radiographs are accessible from the top left of the list. Images that are recognized as the same image type may be automatically stacked by the application when being imported into *Second Opinion*® on the FMX view.

5.2.6. Finding Specific Charts

The search bar above the Chart List can be used to search charts by patient identifier, date, or combination thereof.

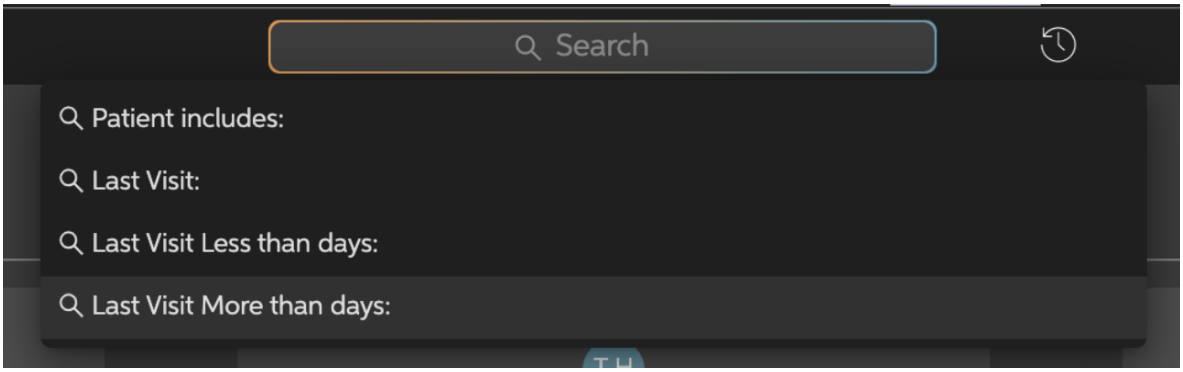


Image 4. Using search to find all radiographs for a specific patient identifier.

5.2.7. Typical Image Display

By default, the FMX view will open when a chart has been selected. You can deselect the FMX view, which will then display all of the radiographs in the left-hand column as a thumbnail filmstrip. The images will be grouped by date of radiographic capture. The first radiograph in the radiograph detection display screen will appear full size in the right-hand portion of the display.

Radiographs in the radiograph display pane will be scaled to fit within the pane. To the right of the radiograph display screen, the Conditions index presents a list of all potential pathologic and non-pathologic features that *Second Opinion*® has detected.

Within the radiograph display pane, annotated bounding boxes and/or segmentation masks are overlaid on the original radiograph to indicate regions where detected features appear. To highlight the region where a feature has been detected, the user can hover the cursor over the bounding box or segmentation mask.

Image 5. The Radiograph Detection Display screen

Users can limit which detected features are displayed and listed using the

pathology/non-pathology toggles above the conditions index, and the checkboxes adjacent the labels.

To quickly access and load a different chart, users can use the search bar, press the recent charts icon (to the right of the search bar) or press the back arrow adjacent the current chart's name to go back to prior results.

A vertical toolbar along the upper right side of the radiograph display pane includes five tools for manipulating the appearance of the radiograph in the radiograph display pane. Listed from top to bottom as they appear in the toolbar, these tools and their corresponding icons are:

- **Full Screen** (): Expand image to full viewport
- **Measurement Tool** (): Measure distance between two points
- **Tooth Parts** (): Toggle display of Tooth Parts overlay
- **Affected** (): Toggle display of Affected Tooth overlay
- **Brightness** (): Adjust brightness
- **Contrast** (): Adjust contrast
- **Invert** (): Invert colors
- **Rotate** (): Rotate image orientation
- **Flip** (): Flip image orientation
- **Zoom** (): Zoom in and out
- **Reset** (): Reset Image Controls
- **Edit Mode** (): Toggle Edit Mode
- **Pearl Enhanced View** (): Sharpen or unsharpen imagery

To access one of these tools, simply use the mouse to click on its icon using the mouse.

Section 5.2.12 of this User Manual explains these image adjustment functionalities in greater detail.

5.2.8. Comparison (A/B)

The comparison tool (A/B) allows the user to view two images from the same patient simultaneously (side by side) to compare for clinical analysis and education. When in comparison mode, you will have the capability of viewing and interacting with each individual image.

5.2.9. Image Selector Filmstrip

There is a toggle at the top to move from FMX view to Image Selector Filmstrip, when FMX is toggled off, the following occurs:

When a chart is loaded, all radiographs in the patient record are presented to the left of the radiograph display pane in a thumbnail filmstrip. Each date of radiographic capture serves as an expandable folder and notes the images captured on that date.

To select an image for display in the radiograph display pane, use the mouse to click on its thumbnail in the filmstrip. Users can also move between images by pressing the keyboard's up and down arrow keys.

5.2.10. How to Read Results

Second Opinion® applies bounding boxes or segmentation masks around all potential pathologic and non-pathologic features that it detects.

5.2.11. Selective Display of Potentials Detections

Located in the upper right-hand corner of the screen are two checkboxes labeled "Pathology" and "Non-Pathology." Users can select these checkboxes to show or hide detected features based on their pathologic or non-pathologic classification.

As detections are identified, a filled checkbox will appear next to the detection. Unchecking the box off will temporarily hide results of that class. If the box is inactive then there are no results of that class to hide or show.

5.2.12. How to Use Image Adjustment Controls

To improve the viewability of a radiograph in the radiograph display pane, *Second Opinion*® offers five image adjustment tools located in a toolbar on the upper right-hand side of the radiograph display pane. These tools can be used as follows:

- **Brightness** (): Use this slider to adjust image brightness. Move the slider to the left to decrease image brightness. Move the slider to the right to increase image brightness. Midpoint is default (and original) brightness.
- **Contrast** (): Use this slider to adjust image brightness. Move the slider to the left to decrease image contrast. Move the slider to the right to increase image contrast. Midpoint is default (and original) contrast.
- **Invert** (): Select this toggle button to invert coloration of the radiograph. Black regions of the original image will become white. White regions of the image will become black.
- **Rotate** (): Select this button to rotate the radiograph. Rotation can occur either clockwise or counterclockwise. Each time the button is clicked, the radiograph will rotate 90 degrees.
- **Zoom ():** Use this slider to zoom in and out of the image. When the slider is the far-left position, the full un-zoomed image fills the radiograph display pane; this is the default position. Moving the slider to the right will zoom in to magnify the image. When zoom is applied the image may be moved around via click and drag.
- **Pearl Enhanced View** (): Use this slider to deactivate or strengthen a sharpening of the image. Select 0 for no adjustments to the image or between 1-20 for increasing strength of sharpening.

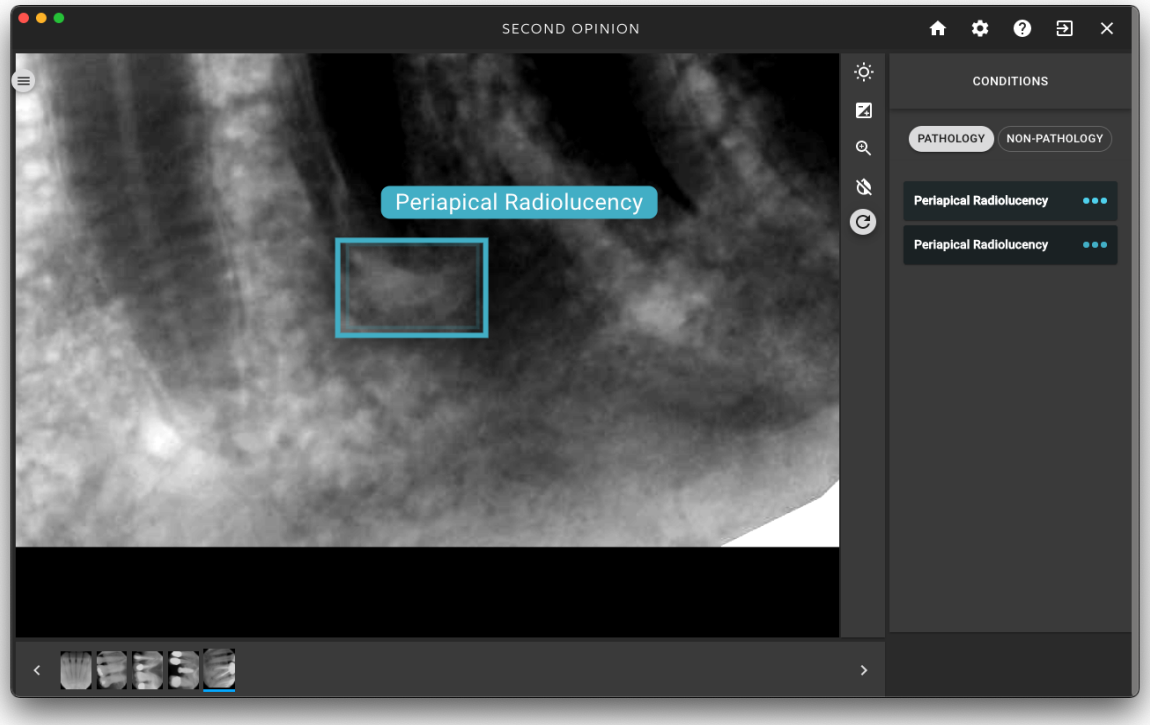


Image 8. Example of a radiograph with brightness and contrast increased, zoom applied and color inverted.

5.2.13. End User Controls to Add or Remove Detections

In order to provide the end user with ability to over-rule the AI detections, *Second Opinion*® employs a remove detections option and an edit mode. The option to remove detections will appear as an Eye icon when hovering on detections. Once a detection has been removed, it can be restored in Edit Mode.

Edit Mode is accessible via a pencil icon in the toolbar. Once activated, edit mode allows the user to restore an annotation (by way of the crossed-out Eye icon adjacent the label), or draw their own annotation (by way of click and drag a rectangle or trace the outline of detection tool using the outline edit tool) and provide it a label (by way of a drop-down selection). The status of a detection may be understood by iconography in the label.

- (AI) AI Detection without User Involvement
- (👤) User created annotation

- ( ) Eye Icon
- ( ) Crossed-Out Eye Icon

5.2.14. Tooth Parts Segmentation Overlay, Affected Overlay & Labeling of Caries

Second Opinion® makes use of AI Segmentation to ascertain the composition of a radiograph amongst ***tooth parts*** (e.g. Enamel, Dentin, Pulp, etc). The ***tooth parts*** overlay may be activated using the toggle at right of the radiograph providing a semi-transparent colored overlay and explanatory legend.

Second Opinion® displays an ***affected tooth*** percentage that is calculated by adding the portions of tooth composed of existing restorations and caries. Together, these are represented as a percentage of healthy crown. The ***affected tooth*** overlay may be activated using the toggle to the right of the radiograph. When active, colored radials will appear on each tooth with an ***affected tooth*** value. Additionally, a legend will display at the bottom with an explanation of each radial color and how calculations are made. There is also a disclaimer explaining usage limitations.

5.2.15. Bone Height Measurement

Second Opinion® provides estimated measurements from the CEJ to the bone crest. These are represented as line segments with millimeter measurements alongside for reference.

6. Summary of *Second Opinion*® Clinical Study Outcomes

To determine whether human readers' diagnostic accuracy improved when they used *Second Opinion*® to aid in their detection of certain pathologic and nonpathologic features that can appear in dental radiographs, *Second Opinion*® was clinically tested as a standalone device and in a fully-crossed multi-reader multi-case (MRMC) reader study.

The standalone studies evaluated readers' accuracy in detecting the nine dental features included in the *Second Opinion*® Indications for Use.

- Caries
- Margin Discrepancies
- Calculus
- Periapical Radiolucency

- Crowns
- Bridges
- Implants
- Root Canals
- Filling

The Weighted Alternative Free-Response Receiver Operating Characteristic (wAFROC) paradigm was used as the metric of efficacy for all studies. The ground truth (GT) was assessed using the consensus approach (based on agreement among at least three out of four expert readers) and based on the Jaccard Index of ≥ 0.4 for LL (Lesion Localization). Each GT reader independently marked areas on any radiograph wherein they marked (using the smallest possible rectangular bounding box to encompass the entire region identified) and identified the pathologic and/or non-pathologic features. All experts went through the training and reading of the images over the same period of time. The studies were conducted as retrospective, unblinded open-label, multi-site trials that produced clinically useful information on the potential application of this device in a dental office setting. 2,010 images reviewed by all four GT readers were used for the standalone and MRMC studies:

Feature	Caries	MD	Calculus	PR
# of normal radiographs	1,640	1,741	1,766	1,887
# of lesion-containing radiographs	370	269	244	123
Number of lesions	655	355	467	144
Average # of lesions/image	1.77	1.32	1.91	1.17

Table 2. Images reviewed by all four GT readers

Standalone Testing

In the standalone study, the *Second Opinion*® CADe exhibited comparable performance to unaided readers in detecting four pathologic features and five restorations.

Summary performance using the wAFROC-FOM accounting for multiplicity (represented by the “Adj. lower CI” column) is presented in the table below. The adjusted lower bound

of the 95% confidence interval was > 0.7, therefore meeting the primary endpoint for each of the four pathologies and five restorations.

	wAFROC-FOM [95% CI]	Adjusted Lower CI
Caries	0.76 [0.73, 0.79]	0.73
MD	0.75 [0.71, 0.78]	0.71
Calculus	0.82 [0.78, 0.85]	0.78
PR	0.79 [0.75, 0.84]	0.75
Crowns	0.89 [0.88, 0.9]	0.88
Bridges	0.96 [0.95, 0.98]	0.95
Implants	0.86 [0.83, 0.89]	0.83
Root Canals	0.95 [0.94, 0.96]	0.94
Fillings	0.85 [0.84, 0.87]	0.84

Table 3. wAFROC-FOM for the dental findings (Consensus methodology and Jaccard Index of ≥ 0.4)

Product's standalone sensitivity and false positive rate were also assessed. Sensitivity is defined as the number of dental pathologies (of a given type) detected as a percentage of the same type GT pathologies on a given slide. The false positive rate is defined as the number of false positive findings of a given type identified on a given slide and expressed in terms of FPPI (false positive per image).

The following sensitivity was documented for the individual dental pathologies (average values and 95% Confidence Interval):

- Caries – 89.77% [87.6%, 92.0%]
- MD – 80.57% [75.8%, 85.3%]
- Calculus – 87.79% [83.3%, 92.3%]
- PR – 76.39% [69.2%, 83.5%]

The false positive rate for the corresponding pathologies given in units of FPPI:

- Caries – 4.85 [4.66, 5.04]
- MD – 1.48 [1.37, 1.59]
- Calculus – 2.01 [1.88, 2.14]
- PR – 0.46 [0.42, 0.50]

Therefore, the standalone sensitivity of the product was in the range of 76.39% – 89.77% and the false positive rate was in the range of 0.46 – 4.85.

MRMC Testing and Results

Pearl conducted a fully-crossed multi-reader, multi-case (MRMC) retrospective reader study to determine the impact of *Second Opinion*® on reader performance in detecting four dental pathologies. The primary objective of the study was to determine whether the

detection accuracy of readers aided by *Second Opinion*® is superior to the detection accuracy of readers unaided by *Second Opinion*®.

Twenty-five readers were asked to determine the locations of all identified (i.e., classified) lesions, in a setting designed to increase user specificity in detection. Each reader to read a total of 2,010 images – 1,005 images unaided and 1,005 images aided (using *Second Opinion*®).

MRMC study results show that caries, MD, calculus, and PR showed significant improvement in reader averaged wAFROC-FOM comparing aided reads versus unaided readers. The reader averaged wAFROC-FOM and 95% CI for each modality and dental feature are shown in the table below:

	wAFROC-FOM [95% CI]			
	Unaided	**Aided**	**Difference (Aided-Unaided)**	**Adj. p-value**
Caries	0.74 (0.70, 0.78)	0.76 (0.72, 0.79)	0.0181 (0.01, 0.03)	0.0062
MD	0.61 (0.55, 0.66)	0.68 (0.64, 0.72)	0.0678 (0.04, 0.10)	0.0002
Calculus	0.66 (0.61, 0.71)	0.72 (0.68, 0.76)	0.0635 (0.04, 0.08)	< 0.0001
PR	0.76 (0.71, 0.81)	0.82 (0.78, 0.86)	0.0603 (0.04, 0.08)	< 0.0001

Table 4. wAFROC-FOM for the four dental pathologies (Consensus methodology and Jaccard Index of ≥ 0.4)

The performance of readers aided by the use of *Second Opinion*® demonstrated statistically significant improvement over the performance of unaided readers for caries, margin discrepancy, calculus, and periapical radiolucency.

Moreover, the improvement in sensitivity of a single dental finding was in the range of 0.9%– 11.7% and examination of the individual improvement in sensitivity documented that:

- 17/25 (68%) improved the sensitivity of detecting Caries
- 19/25 (76%) improved the sensitivity of detecting MD
- 22/25 (88%) improved the sensitivity of detecting Calculus
- 25/25 (100%) improved the sensitivity of detecting PR

The improvement in false positive rate of a single dental pathology was in the range of 0.008 – 0.136. Examination of the individual improvements in the rate of FPPI documented that:

- 23/25 (92%) improved the rate of FPPI for Caries
- 24/25 (96%) improved the rate of FPPI for MD
- 25/25 (100%) improved the rate of FPPI for Calculus
- 9/25 (36%) improved the rate of FPPI for PR

No statistically significant reductions in performance were observed when readers used *Second Opinion*® as an assistive aid. All pathologies met the pre-specified endpoints for the MRMC study.

The results have demonstrated that, in a significant portion of the target population, detection performances using the proposed device improved with statistical significance.

Analysis of study results for geographic region of image capture, patient age and patient sex confounders in the GT dataset demonstrated improvement in *Second Opinion*®-aided reader performance that was consistent with that observed across the studies in general. Furthermore, the overall study results were also observed for the image acquisition device subgroup. Specifically, results were similar across the five image acquisition devices with sufficient representation in the GT dataset to yield statistically meaningful results, as well as for the remaining four image acquisition devices with limited representation. In all cases, aided readers outperformed unaided readers and therefore, the *Second Opinion*® device shows result generalizability between imaging devices.

The statistically significant gains in aided reader performance using the *Second Opinion*® device, validate the efficacy of the device as an aid to dental health professionals in their detection of pathologic and non-pathologic features in radiographs of permanent teeth. Therefore, the proposed device could provide potential assistance for dentists in the review of dental pathologies found in intra oral radiographs when used as a second read.

7. *Second Opinion*® Troubleshooting

The information contained in this section provides steps that users may take to identify and solve basic problems that may occur while using the *Second Opinion*® Client. Any issues determined to be beyond the scope of these basic user troubleshooting instructions should be communicated to Pearl Customer Support.

A monitor, keyboard and mouse are required for troubleshooting.

Problem	Cause and Solution
Images or Results Fail to Load	Ensure that the computer is connected to the local network. Ensure that the local network is connected to the internet.

	Ensure that the networked image drive where radiographs are stored (if utilized) is connected to the network. Quit and restart *Second Opinion®* If the problem persists, contact *Second Opinion®* Customer Service.
Unable to Log In	Verify that credentials are correct. Ensure that the computer is connected to the local network. Ensure that the local network is connected to the internet. Quit and restart *Second Opinion®* Utilize forget password link to reset password.
Images Missing	Ensure that the date filter in the chart search function is configured correctly. Ensure that the computer is connected to the local network. Ensure that the local network is connected to the internet. Ensure that the networked image drive where radiographs are stored (if utilized) is connected to the network. Ensure that the radiograph storage file location settings are correctly configured (see

	Section 5.2.4 Settings Tab for configuration instructions)
Application Crashes	Restart application. Restart the computer. If the problem persists, contact *Second Opinion*® Customer Service.

8. Service and Maintenance

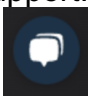
Second Opinion® is not independently user serviceable. When service is needed, Pearl will release an updated version of *Second Opinion*®. The update will be downloaded and installed automatically. See Section 4.4 of this User Manual for more information about software updates.

9. Technical Assistance

Second Opinion® Customer Service is available to answer questions about business, pricing, upgrades, customization and order status.

Technical Support is available to answer questions about technology, integration, and troubleshooting. Contact us at:

In-App: Users may receive support through the in-app chat tool in the bottom right corner of the *Second Opinion*® app. Clicking on the chat icon will open a live chat session with Pearl support.

- Support Chat Icon - 

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