



**Second Opinion® 3D**

## USER MANUAL & LABELING

Software Version 3

Document Revision 1.0.0

Rx Only



**Manufacturer - Pearl Inc.**

9200 Sunset Blvd, STE 430

West Hollywood, California 90069 US



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## 1. Manual Information

### 1.1. Version

This manual is intended for the correct and safe utilization of *Second Opinion*® 3D v3. The GTIN Number denoting the version number of the software to which this manual pertains is 198715016079.

### 1.2. Purpose

This manual provides instructions for the operation of the *Second Opinion*® 3D 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*® 3D 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](mailto:support@hellopearl.com) that includes your organization's 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.

### 1.5. Regulatory Compliance

*Second Opinion*® 3D 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).
- Canadian Medical Devices Regulations SOR 98-282
- The Health Insurance Portability and Accountability Act (HIPAA)
- General Data Protection Regulation (EU) 2016/679 (GDPR)
- IEC 82304-1:2016-10 (en-fr) — Health software — Part 1: General requirements for product safety

## 2. *Second Opinion*® 3D Device Labeling

### 2.1. Brief Description

*Second Opinion*® 3D is a CBCT radiological automated image processing software device that uses machine learning to detect and localize anatomies on CBCT scans and radiographs. The device aids in the detection of individual teeth (including implants and bridge pontics), the skull, mandible, inferior alveolar canal and mental foramen, maxillary sinus, nasal space, and airway, as well as



impactions and sinus radiopacity. The output is a visual overlay on the input scan indicating these anatomies and findings.

The device is not intended as a replacement for a complete dentist's review or clinical judgment that considers other relevant information from the image, patient history, or in vivo clinical assessment. The API and CV models reside in a cloud computing platform hosted by Amazon Web Services (AWS), where scan processing takes place. Results are displayed on a computer monitor in the clinician's office for review by a dental practitioner, who is instructed to first evaluate each scan in the conventional visual manner and then re-examine it using *Second Opinion*® 3D prior to making a final diagnosis.

## **2.2. Indications for Use**

*Second Opinion*® 3D is a radiological automated image processing software device (including computer-aided detection, "CADe") intended to assist dentists in identifying, marking, and visualizing clinically relevant anatomy, suspected impacted teeth, regions of increased radiodensity within the paranasal sinuses, and restorative findings (including pulp space, implants, and root canals) on cone beam computed tomography (CBCT) images.

The device does not classify, characterize, or diagnose pathology. It should not be used in lieu of a full patient evaluation or as the sole basis for making or confirming a clinical decision or diagnosis. It is designed to support trained health professionals in reviewing CBCT scans of 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*® 3D safely and according to its intended purpose, the following prerequisites must be met:

- 2.4.1. The user has read and understood the Intended Use, Warnings, and Operating Instructions included in this User Manual.
- 2.4.2. 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.



## 2.5. Warnings

CAUTION: *SECOND OPINION*® 3D IS NOT INTENDED TO OFFER A DIAGNOSTIC ASSESSMENT. Further clinical investigation of any region of interest (ROI) is necessary.

- *Second Opinion*® 3D 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*® 3D software is operating is free of viruses or malware, and that the software has been updated with the latest security patches.
- Indirect inherent risks result from user errors in type or resolution of imagery, or over-reliance on AI.
- Do not use *Second Opinion*® 3D software without reviewing the *Second Opinion*® 3D user manual.
- The *Second Opinion*® 3D system may detect and highlight a region where no feature exists. Users must always exercise their professional interpretative skills when reviewing the regions detected by *Second Opinion*® 3D.
- Effectiveness and safety have been established only for detections in CBCT radiographic images. Any features detected and highlighted on radiograph types other than CBCT cannot be used by the clinician to assist in radiographic evaluations. *Second Opinion*® 3D deploys a CV Model that classifies submitted radiographs into particular anatomies.
- All images submitted for *Second Opinion*® 3D processing must be DICOM, NII, or .NII.GZ. *Second Opinion*® 3D may not function properly if an image in an unsupported format is submitted.
- *Second Opinion*® 3D is not intended to instruct providers to take CBCT scans, but rather is designed to analyze CBCT radiographs already acquired as part of care.

## 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 result from user errors in type or resolution of imagery, or over-reliance on AI. Proper operation of the device is explained in the directions for use printed in this manual. The *Second Opinion*® 3D 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**

*Second Opinion*® 3D is a radiological automated image processing software device intended to assist dentists in identifying, marking, and visualizing clinically relevant anatomy, suspected impacted teeth, regions of increased radiodensity within the paranasal sinuses, Carotid Artery Calcification (CAC), temporomandibular disorder, or implants and restorative findings (including pulp space, implants, and root canals) on CBCT scans, by highlighting regions of interest for further review.

It does not classify, characterize, or diagnose pathology, and should not be used in lieu of a full patient evaluation or as the sole basis for making or confirming a clinical decision or diagnosis. It is designed to support trained health professionals in reviewing CBCT scans of patients 12 years of age or older as a concurrent, second reader.

## **2.8. Intended User Population**

The intended users of *Second Opinion*® 3D are dentists in various settings including primary care (e.g., family dental practice, hospital-based dentistry and dental service organizations), dental specialists, and oral maxillofacial radiologists who review radiographs across these settings. *Second Opinion*® 3D is intended for dental clinics, dental service organization offices and dental insurance providers on off-the-shelf computer systems.

## **2.9. Intended Patient Population**

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

## **2.10. Compatible Radiological Data Sources**

*Second Opinion*® 3D can process cone-beam computed tomography (CBCT) image data. CBCT datasets may be acquired from a range of dental CBCT systems from different manufacturers and are typically stored on clinical office network servers using digital storage systems. The system supports import of 3D



image volumes in DICOM format (CT image series) and, where applicable, NIfTI volume formats (.nii and .nii.gz).

## 2.11. Hardware Requirements

The application is web-based; therefore, the hardware requirements are dictated by users meeting the requirements for Chrome version 97+ or over. Chrome 97+ recommended hardware including:

- Intel Pentium 4 processor or later that's SSE3 capable
- MacOS Big Sur 11 or later
- Linux
- 64-bit Ubuntu 18.04+, Debian 10+, openSUSE 15.5+, or Fedora Linux 39+

## 3. Product Information

### 3.1. Product Contents

*Second Opinion® 3D*

### 3.2. Principles of Operation

To submit exams to the device, CBCT radiographic images are first uploaded into *Second Opinion® 3D*. As *Second Opinion® 3D* is a browser-based product, in order to process the CBCT radiographs, the users' computer needs to be connected to the internet. A result report and associated detections are then immediately generated by the API. The detections can then be viewed in the *Second Opinion® 3D* user interface. To perform an analysis, the *Second Opinion® 3D* must be authorized with valid account login credentials (username and password), which would have been configured at sign up.

## 4. *Second Opinion® 3D* Access Instructions

### 4.1. System Requirements

To use the *Second Opinion® 3D* device you will need the following:

- A computer running with Chrome version 97+
- A working internet connection.

### 4.2. Accessing

*Second Opinion® 3D* can be started by launching <http://secondopinion.hellopearl.com>.

### 4.3. Updates

Every time *Second Opinion® 3D* is opened or refreshed via the web application, the application updates in the background. The user interface does not notify the user when an update is available as there is no data being stored by *Second Opinion® 3D*.



In order for the user to be on the most current version, *Second Opinion*® 3D will need to be refreshed daily.

#### **4.4. Accessing the manual and viewing the product label**

*Second Opinion*® 3D has access to an up-to-date electronic copy of the user manual, which can be accessed by hovering over the User Avatar at the lower left, clicking “About Second Opinion”, and then clicking “View user manual here”.

### **5. *Second Opinion*® 3D Operating Instructions**

#### **5.1. Description of How *Second Opinion*® 3D Operates.**

*Second Opinion*® 3D consists of three parts: User Interface ("UI"), Application Programming Interface ("API"), and a Computer Vision / Machine Learning processing layer ("CV Models" / "ML Modules").

Once new imagery is uploaded, the cloud-based API submits the imagery to the CV/ML Models for processing. These models produce metadata describing the nature, location, and extent of: anatomical structures (teeth, skull, mandible, inferior alveolar canal and mental foramen, maxillary sinus, nasal space, and airway); suspected impacted teeth and regions of increased radiodensity within the paranasal sinuses; and restorative findings, including dental pulp chambers, root canal fillings, and dental implants, Carotid Artery Calcification, temporomandibular joint, temporomandibular disorder, identified in the CBCT scan. This metadata is sent back to *Second Opinion*® 3D, which renders it for visual display and review within the user interface. Any anatomies, impactions, sinus radiopacity, pulp chambers, root canal fillings, Carotid Artery Calcification, temporomandibular joint, temporomandibular disorder, or implants detected will appear inscribed within color-coded segmentations overlaid on the original scan.

The time this process takes depends on the user's network connection; the resolution of the CBCT scan being uploaded can also affect processing time.

*Second Opinion*® 3D detects and segments these anatomies, findings, and restorations based on their visual appearance, because they closely resemble known features present in the scans used to train its CV/ML Models. The system can assist the dentist or radiologist by reducing the time and effort associated with manually segmenting these structures and by minimizing observational oversights, allowing for more efficient and thorough review of the CBCT scan.

The *Second Opinion*® 3D software may be used only as an aid for detecting and visualizing anatomies, suspected impactions, sinus radiopacity, Carotid Artery



Calcification, temporomandibular joint, temporomandibular disorder, and restorative findings (pulp chambers, root canal fillings, implants) in CBCT scans. It is not for use as an aid in diagnosis or interpretation. It does not classify, characterize, or diagnose pathology, does not provide measurements or volumetric quantification, and should not be used in lieu of a full patient evaluation or as the sole basis for clinical decision-making.

## **5.2. Getting Started**

Follow the instructions below to begin using the *Second Opinion*® 3D.

### **5.2.1. Launch Application**

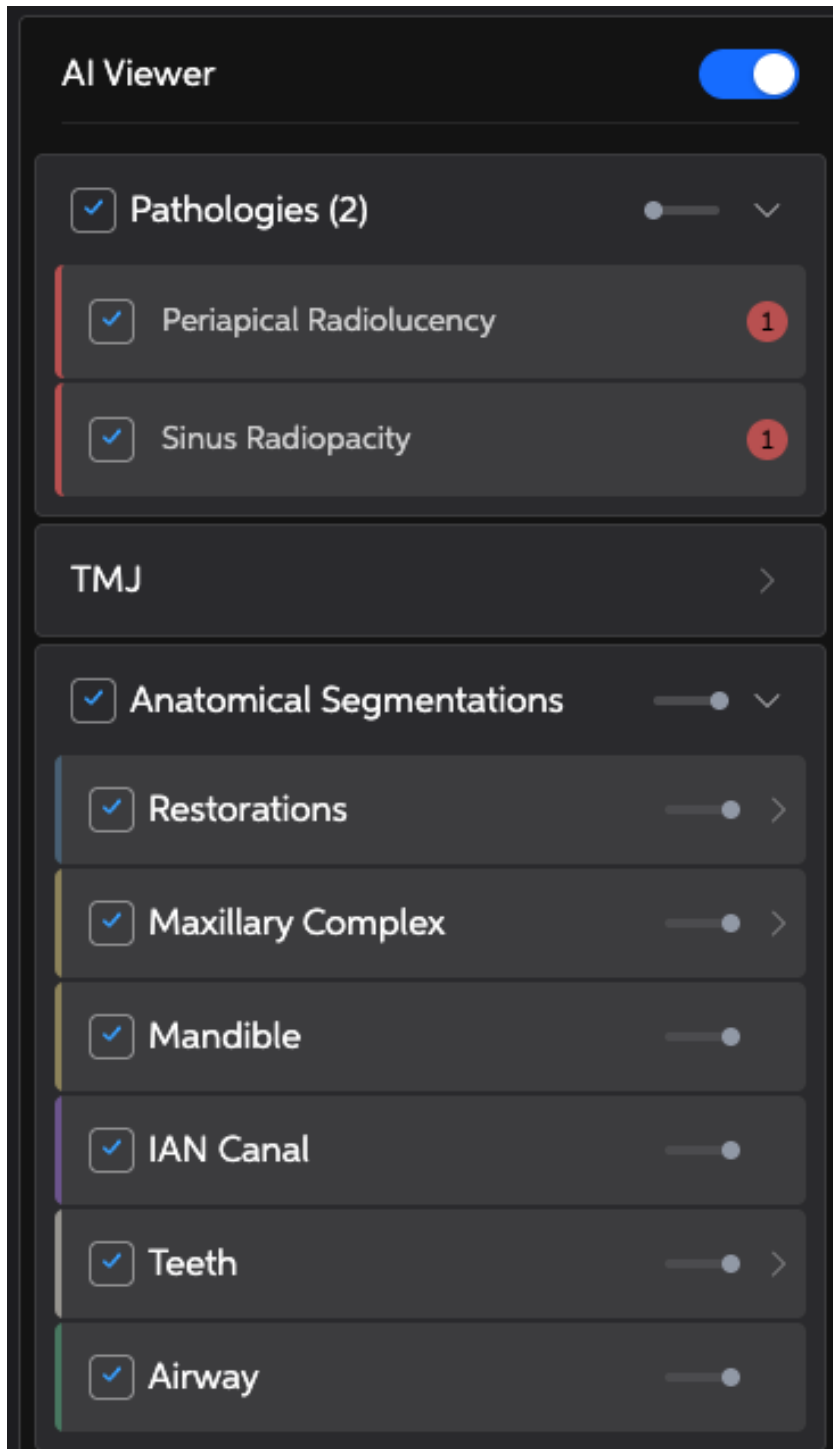
To launch the *Second Opinion*® 3D, visit the following website:  
<http://secondopinion.hellopearl.com>.

### **5.2.2. Opening Screen**

When the web application launches, the home screen will display in the user interface window. CBCT radiographs in the previously listed file types (section 2.10) will be uploaded into the web application.

### **5.2.3. Typical Image Display**

CBCT scans in the viewer will be scaled to fit within the pane. The left portion of the display will contain multiple views of the scan. The right side will contain all of the image controls, including the ability to select and deselect the display of detections





Within the CBCT scan display pane, masks are overlaid on the original CBCT scan to indicate regions where detected structures appear. In the display plane, four views are associated with the CBCT scan: one 3D view and three 2D views. The four views can be arranged in different layouts depending on the user's preference, which is controlled by the "Layout" option in the control menu.

The 3D and 2D views include controls for zooming in/out, camera reset (returning to the default configuration), a switch to invert (left-to-right or top-to-bottom, depending on the view), pan, rotation, density shift, brightness, contrast, and a slicer to navigate through the volume and its masks. The 2D Views are Axial, Sagittal, and Coronal. All of the 2D views are synchronized with the masks displayed in the 3D view.

The image control icons are listed below:

- **Zoom** (  ): Zoom in and out
- **Reset View** (  ): Reset Image Controls
- **Pan** (  ): Allows the user to pan the image
- **3D Rotate** (  ): Control the 3D image
- **Rotate** (  ): Allow rotation of the 2D images
- **Layout** (  ): Change the image layout on the display
- **3D Density Shift** (  ): Changes the density view of the 3D image
- **Invert** (  ): Reverses the image's light and dark values
- **Brightness** (  ): Changes the image brightness
- **Contrast** (  ): Changes the image contrast

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

This User Manual explains these image adjustment functionalities in greater detail later.



#### **5.2.4. Slice Control**

When a file is uploaded, the 2D views panel has the ability to move in between the slices for the Axial, Sagittal, and Coronal views. In those views, each of the items listed in the Structures index can be adjusted. In addition, the name of the anatomy can be altered and will be updated for each view for the 2D view.

#### **5.2.5. How to Use Image Adjustment Controls**

To improve the viewability of a CBCT radiograph in the radiograph display pane, *Second Opinion*® 3D offers image adjustment tools located in a toolbar on the right-hand side of the display pane or directly in the 2D view pane. These tools can be used as follows:

- **Zoom:** Use this slider to zoom in and out of the image. When the slider is in 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.
- **Toggle Pan:** This feature allows users to move an image around without resizing it. The user can click and drag the image to navigate to different areas while maintaining the current zoom level.
- **Reset view:** This feature allows users to quickly restore an image to its original position and zoom level. If the image has been panned, rotated, or zoomed in, clicking the reset view button recenters the image and returns it to its default scale and orientation.
- **Mask View:** This function allows users to selectively hide or show sections of the anatomy for focused viewing.
- **Mask Color:** This feature allows users to change the color of a section of the anatomy.
- **Opacity Toggle:** This feature allows users to adjust the transparency of an anatomy, making it more or less visible as needed. Users can slide the control to decrease opacity, making the image more transparent, or increase it to restore full visibility.
- **Invert:** Select this toggle button to invert the orientation of the CBCT radiograph. This allows for users to flip an image horizontally or vertically, effectively mirroring its orientation. Users can toggle back to the original orientation as needed.

#### **5.2.6. Virtual Pano**

A virtual rendering of a panoramic view created from the 3D scan also known as Vpano. Some clinicians refer to a panorex as an “OPG” so this could also be called a “virtual OPG”. This happens automatically, while in many competing software applications, the user needs to do manual work to generate it.



## 6. *Second Opinion*® 3D Performance Testing

Bench testing was performed on *Second Opinion*® 3D to clinically validate the different anatomical structures in CBCT radiographs of permanent teeth. The software modification is intended to assist dentists with their manual comparison by identifying and marking clinically relevant anatomy in CBCT radiographs. The effectiveness of *Second Opinion*® 3D was gauged via bench performance testing to determine the segmentation accuracy of *Second Opinion*® 3D in identifying different anatomical structures in CBCT radiographs of permanent teeth of patients 12 years of age or older.

The bench performance testing included 25 images of the following anatomies: dentition, maxilla, mandible, IAN space, sinus, nasal space, and airway. These anonymized images represent patients across the United States with permanent teeth and shall be representative of the intended patient population. The success criteria for this study have been defined as follows: a clinically meaningful measure of accuracy is assumed to be a mean of 0.70 (i.e., if the lower bound of the 95% CI exceeds 0.70) (Albano D., et al., 2024). In the table below, the results of the anomalies with corresponding statistical analysis can be observed:

**Table 1: Standalone for Anatomy for Overall Dice**

| AnatomyID | Anatomy Name | Mean (95% CI)     | Median [Min., Max.] | Std.dev. | one-sample t-test (p_value) |
|-----------|--------------|-------------------|---------------------|----------|-----------------------------|
| 1         | Dentition    | 0.81 (0.74, 0.87) | 0.93 [0.0, 0.97]    | 0.27     | <0.000001                   |
| 2         | Maxilla      | 0.9 (0.87, 0.92)  | 0.92 [0.71, 0.94]   | 0.06     | <0.000001                   |
| 3         | Mandible     | 0.96 (0.95, 0.98) | 0.97 [0.83, 0.98]   | 0.03     | <0.000001                   |
| 4         | IAN space    | 0.76 (0.72, 0.81) | 0.79 [0.36, 0.87]   | 0.11     | 0.010675                    |
| 5         | Sinus        | 0.97 (0.95, 0.98) | 0.97 [0.86, 0.99]   | 0.03     | <0.000001                   |
| 6         | Nasal space  | 0.88 (0.84, 0.91) | 0.91 [0.67, 0.94]   | 0.08     | <0.000001                   |
| 7         | Airway       | 0.93 (0.89, 0.97) | 0.96 [0.45, 0.98]   | 0.1      | <0.000001                   |

The following anatomies had a mean of above 0.70: Dentition, Maxilla, Mandible, IAN space, Sinus, Nasal space, and airway. The *Second Opinion*® 3D device has therefore been determined to accurately segment the identified anatomies based on the analysis of results with p-values



below 0.05, showing statistically significant accuracy at a 95% confidence interval.

### **Implant, pulp space, and root canal**

Standalone performance testing was conducted on *Second Opinion*® 3D to clinically validate three additional restorative and anatomical structures (implant, pulp space, and root canal) in CBCT radiographs of permanent teeth. The software modification is intended to assist dentists with their manual comparison by identifying and segmenting these structures in CBCT radiographs. The effectiveness of *Second Opinion*® 3D was gauged via retrospective standalone performance testing to determine the segmentation and detection accuracy of the device in identifying implant, pulp space, and root canal findings in CBCT radiographs of permanent teeth of patients 12 years of age or older.

Each study used a de-identified dataset drawn from five U.S. geographic regions, independent of model training data (39 images for implant, 237 images for pulp space, and 61 images for root canal). Ground truth was established by two U.S.-licensed dentists, with adjudication by a licensed maxillofacial radiologist. The primary endpoint for each finding was segmentation accuracy, measured by the Dice Similarity Coefficient (DSC), tested against a null hypothesis threshold drawn from published literature (Erdoğan Kibcak et al., 2025 for implant; Sherwood et al., 2021 for pulp space and root canal). Implant and root canal also carried prespecified secondary endpoints of sensitivity and specificity. Results are summarized below:

**Table 2: Standalone for anatomical structures for Overall Dice**

| Finding    | N   | DSC, Mean (95% CI)      | H0 Threshold | p-value | Sensitivity (95% CI)    | Specificity (95% CI)    |
|------------|-----|-------------------------|--------------|---------|-------------------------|-------------------------|
| Implant    | 39  | 0.8667 (0.8546, 0.8787) | $\leq 0.83$  | <0.0001 | 0.9474 (0.8899, 0.9757) | 0.9852 (0.9743, 0.9915) |
| Root Canal | 61  | 0.7732 (0.7608, 0.7856) | $\leq 0.76$  | 0.0185  | 0.9096 (0.8600, 0.9428) | 1.0000 (0.9973, 1.0000) |
| Pulp Space | 237 | 0.7739 (0.7655, 0.7823) | $\leq 0.76$  | 0.0006  | not applicable          | not applicable          |

For all three findings, the observed DSC exceeded its respective null hypothesis threshold, and the null hypothesis was rejected at the prespecified significance level ( $\alpha = 0.05$ ). Implant and root canal also met their secondary sensitivity and specificity endpoints, each exceeding the literature-derived reference thresholds. Enrollment for implant (39 of a 40 target) and root canal (61 of a 67 target) came in modestly under the protocol-specified target, but this did not affect



study conclusions, as both enrolled samples substantially exceeded the statistically required minimum. The *Second Opinion*® 3D device has therefore been determined to accurately segment and detect implant, pulp space, and root canal based on the analysis of results with p-values below 0.05, showing statistically significant accuracy at a 95% confidence interval.

### **Standalone Performance Assessment for Sinus Radiopacity and Impactions**

The effectiveness of *Second Opinion*® 3D was evaluated in a standalone performance assessment to validate the inclusion of sinus radiopacity and impaction detections in patients 12 years of age and older.

Across the impactions study dataset (N = 270 images; 127 abnormal and 143 normal by ground truth), *Second Opinion*® 3D demonstrated strong detection performance. Sensitivity was 0.9454 (95% CI: 0.9131, 0.9661;  $p < 0.0001$ ). Specificity was 0.9924 (95% CI: 0.9901, 0.9942;  $p < 0.0001$ ). The study also demonstrated favorable segmentation and localization accuracy on detected lesions, with a Dice of 0.8622 (95% CI: 0.8550, 0.8694) and a Jaccard of 0.7618 (95% CI: 0.7528, 0.7708), supporting that correct detections were generally well-localized relative to expert annotations.

Across the sinus radiopacity study dataset (N = 316 images; 217 abnormal and 99 normal by ground truth), *Second Opinion*® 3D demonstrated strong detection performance. Sensitivity was 0.8757 (95% CI: 0.8386, 0.9052;  $p < 0.0001$ ) and specificity was 0.8583 (95% CI: 0.8100, 0.8958;  $p = 0.0001$ ). The study also demonstrated favorable segmentation and localization accuracy on detected lesions, with a Cumulative Dice of 0.8152 (95% CI: 0.7879, 0.8425) and a Jaccard of 0.6880 (95% CI: 0.6493, 0.7267), supporting that correct detections were generally well-localized relative to expert annotations.

Performance for both impactions and sinus radiopacity was explored across subgroups of interest, including age group, gender, geographic area, and imaging device manufacturer. Results were generally consistent across subgroups, supporting generalizability across demographics and acquisition conditions. Certain subgroup strata contained small sample sizes (for example, some device manufacturers and regions), resulting in wide confidence intervals and limiting interpretability; therefore, subgroup findings should be considered exploratory and not used to support definitive claims of performance differences between strata.

The studies included cases with real-world technical confounding factors (such as motion blur, beam hardening, edge haze, and resolution limitations) to evaluate robustness under degraded image quality conditions that may be encountered in the expected use environment. While the study was not powered specifically for these confounding-factor strata, the results provide supportive evidence that performance remains high in the presence of common artifacts, with some expected degradation in segmentation/localization metrics in more challenging conditions.



Based on these findings, *Second Opinion*® 3D – Advanced Detections demonstrates clinically meaningful standalone performance for the detection and localization of impacted teeth and sinus radiopacities in CBCT images.

### **MRMC Clinical Reader Study Results for Sinus Radiopacity and Impactions**

In addition to standalone testing, two retrospective multi-reader multi-case (MRMC) clinical reader studies were conducted to characterize the clinical utility of *Second Opinion*® 3D – Advanced Detections. In each study, 28 independent clinical readers (general dentists, dental specialists, and oral radiologists, all independent from model development and ground truth processes) evaluated a set of de-identified CBCT scans under both unaided and aided conditions, with a four-week washout period between sessions. The primary endpoint was the reader-average weighted Alternative Free-Response Receiver Operating Characteristic Area Under the Curve (wAFROC-AUC), analyzed using the Dorfman-Berbaum-Metz (DBM) ANOVA with jackknife covariance estimation under the Random Reader Random Case (RRRC) assumption. Ground truth was established by two independent, blinded DDS/DMD dentists, with adjudication by a board-certified oral maxillofacial radiologist.

### **Sinus Radiopacity MRMC Study**

The sinus radiopacity MRMC study enrolled 316 de-identified CBCT scans (217 abnormal [68.7%] containing sinus radiopacity findings; 99 normal [31.3%]), representing 307 individual sinus radiopacity instances across five U.S. geographic regions. The reader-average wAFROC-AUC was 0.8269 (95% CI: 0.79, 0.87) in the aided condition and 0.6815 (95% CI: 0.63, 0.73) in the unaided condition. The difference of 0.1454 (95% CI: 0.1220, 0.1687) was statistically significant ( $p < 0.00001$ ). Aided reading also demonstrated substantially improved sensitivity: 0.802 (95% CI: 0.7942, 0.8095) aided versus 0.534 (95% CI: 0.5248, 0.5439) unaided, a difference of 0.268. Specificity was 0.8518 aided versus 0.8600 unaided (difference  $-0.0082$ ;  $p = 0.9558$ ), confirming that the aided condition did not introduce a meaningful false positive burden. The HR-ROC AUC improved from 0.7535 (unaided) to 0.8755 (aided), a difference of 0.122 ( $p < 0.00001$ ). Subgroup analyses demonstrated statistically significant improvements across most age groups and gender subgroups.

**Table 3: Sinus Radiopacity MRMC – Overall Detection Accuracy (Primary and Secondary Endpoints)**

| <b>Metric</b> | <b>Aided Estimate<br/>(95% CI)</b> | <b>Unaided Estimate<br/>(95% CI)</b> | <b>Difference<br/>Aided – Unaided<br/>(95% CI)</b> | <b>p-value</b> |
|---------------|------------------------------------|--------------------------------------|----------------------------------------------------|----------------|
| wAFROC-AUC    | 0.8269<br>(95% CI: 0.79, 0.87)     | 0.6815<br>(95% CI: 0.63, 0.73)       | 0.1454<br>(95% CI: 0.1220, 0.1687)                 | $p < 0.00001$  |

|             |                                |                                |                                   |           |
|-------------|--------------------------------|--------------------------------|-----------------------------------|-----------|
| Sensitivity | 0.802<br>[0.7942, 0.8095]      | 0.534<br>[0.5248, 0.5439]      | 0.268                             | p<0.00001 |
| Specificity | 0.8518<br>[0.8434, 0.8598]     | 0.8600<br>[0.8519, 0.8678]     | -0.0082                           | p=0.9558  |
| HR-ROC AUC  | 0.8755<br>(95% CI: 0.84, 0.91) | 0.7535<br>(95% CI: 0.71, 0.80) | 0.122<br>(95% CI: 0.0993, 0.1447) | p<0.00001 |

### Impactions MRMC Study

The impactions MRMC study enrolled 270 de-identified CBCT scans (127 abnormal [47.0%]; 143 normal [53.0%]) from five U.S. geographic regions. The reader-average wAFROC-AUC was 0.928 (95% CI: 0.90, 0.96) in the aided condition and 0.9274 (95% CI: 0.90, 0.95) in the unaided condition. The observed difference of 0.0006 (95% CI: -0.0090, 0.0103; p=0.9569) was not statistically significant, reflecting that both aided and unaided readers already demonstrated high diagnostic accuracy. The lack of statistical significance reflects high baseline unaided performance rather than a lack of clinical utility; the point estimate is positive (aided > unaided), consistent with a modest benefit of device assistance. Reader-average sensitivity was 0.8967 (95% CI: 0.8899, 0.9032) aided versus 0.8871 (95% CI: 0.8800, 0.8939) unaided; specificity was 0.9948 aided versus 0.9958 unaided. Subgroup analyses across age, gender, geographic region, and imaging device manufacturer demonstrated consistently high performance in both aided and unaided conditions, supporting generalizability of device performance.

**Table 4: Impactions MRMC – Overall Detection Accuracy (Primary and Secondary Endpoints)**

| Metric      | Aided Estimate<br>(95% CI)     | Unaided Estimate<br>(95% CI)   | Difference<br>Aided – Unaided<br>(95% CI) | p-value  |
|-------------|--------------------------------|--------------------------------|-------------------------------------------|----------|
| wAFROC-AUC  | 0.928<br>(95% CI: 0.90, 0.96)  | 0.9274<br>(95% CI: 0.90, 0.95) | 0.0006<br>(95% CI: -0.0090, 0.0103)       | p=0.9569 |
| Sensitivity | 0.8967<br>[0.8899, 0.9032]     | 0.8871<br>[0.8800, 0.8939]     | 0.0096                                    | N/A      |
| Specificity | 0.9948<br>[0.9945, 0.9951]     | 0.9958<br>[0.9955, 0.9960]     | -0.0010                                   | p=1.0    |
| HR-ROC AUC  | 0.9547<br>(95% CI: 0.93, 0.98) | 0.9562<br>(95% CI: 0.94, 0.98) | -0.0015                                   | p=0.8818 |



Taken together, the standalone and MRMC evidence demonstrates that *Second Opinion*® 3D – Advanced Detections provides clinically meaningful detection performance for impacted teeth and sinus radiopacities in CBCT images. The device supports its intended use as a second reader aid, consistent with FDA expectations for CADe devices.



## 7. Cybersecurity

*Second Opinion*® 3D is a standalone, browser-based software system. All data required to power the device is transmitted from the user through the *Second Opinion*® 3D user portal. All data received by the system is temporarily stored within the Amazon Web Services cloud environment. Databases and temporary file stores, which represent data-at-rest, all reside within Amazon Web Services S3 and are protected using the 256-bit Advanced Encryption Standard (“AES-256”). Data flow between the user and *Second Opinion*® 3D system’s cloud components is encrypted using AES-256 through Transport Layer Security version 1.2 (TLS 1.2). Vulnerability scanning is conducted within Amazon Web Services using managed security services to detect malware or malicious software.

To access *Second Opinion*® 3D, users must authenticate using an email and password. Password strength criteria must be met to successfully create a valid *Second Opinion*® 3D account. Multi-factor authentication (MFA) is available for all users of the *Second Opinion*® 3D platform and is strongly recommended for enhanced security.

Authentication with *Second Opinion*® 3D is managed by Auth0 (Okta). Auth0 protects against cybersecurity attacks in several ways:

- Bot Detection
- Suspicious IP Throttling
- Brute-force Protection

The *Second Opinion*® 3D system may automatically disable any accounts that exhibit potentially malicious behavior.

To ensure security, users are recommended to take the following precautions:

- Harden the environment(s) where the users are accessing *Second Opinion*® 3D
- Enforce the use of antivirus software on all endpoints within the office network
- Ensure all software on office endpoints is up to date with the latest security patches
- Monitor threat exchanges to stay informed about new forms of cybersecurity attack including phishing, spoofing, and impersonation
- Exercise vigilance when engaging with unknown phone numbers or email addresses. Pearl email will always come from the [hellopearl.com](mailto:hello@pearl.com) domain
- Immediately report any suspicious behavior observed with respect to your



- Second Opinion® 3D software to Pearl support: [support@hellopearl.com](mailto:support@hellopearl.com)
- Immediately report any breach of office network to Pearl support: [support@hellopearl.com](mailto:support@hellopearl.com)

## 8. Second Opinion® 3D Troubleshooting

### Pearl, Inc.

#### Customer Support

<https://hellopearl.atlassian.net/servicedesk/customer/portal/1>

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*® 3D. 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 | <p>Ensure that the computer is connected to the internet.</p> <p>Ensure that the image type is correct</p> <p>Quit and restart <i>Second Opinion</i>® 3D</p> <p>If the problem persists, contact <i>Second Opinion</i>® Customer Service.</p> |
| Unable to Log In               | <p>Ensure that the computer is connected to the internet.</p> <p>Quit and restart <i>Second Opinion</i>®</p> <p>Utilize forget password link to reset password.</p>                                                                           |



|                     |                                                                                                                              |
|---------------------|------------------------------------------------------------------------------------------------------------------------------|
| Application Crashes | Restart application. Restart the computer.<br><br>If the problem persists, contact <i>Second Opinion</i> ® Customer Service. |
|---------------------|------------------------------------------------------------------------------------------------------------------------------|

## 9. Service and Maintenance

*Second Opinion*® 3D is not independently user serviceable. When service is needed, Pearl will release an updated version of *Second Opinion*® 3D. See Section 4.3 of this User Manual for more information about software updates.

### 9.1. Termination of Service

To terminate your *Second Opinion*® 3D subscription or service account, please contact your Customer Success representative or reach out to our support team directly. Our team will guide you through the offboarding process and ensure your account is properly closed.

## 10. Reporting AI Performance Concerns

### 10.1 Reporting AI Performance Concerns

If you believe that a *Second Opinion*® 3D AI output contributed to or could have contributed to harm to a patient, or if you observe a pattern of AI performance that concerns you, please report this to Pearl directly.

### 10.2 Contact for AI performance reporting:

- Email: [support@hellopearl.com](mailto:support@hellopearl.com) (include "AI Performance" in the subject line)
- Online: <https://pages.hellopearl.com/customer-support>

#### When reporting, please include:

- A description of what *Second Opinion*® 3D detected (or failed to detect)
- The image type and confidence level shown
- Your clinical assessment of the correct finding
- Whether patient care was or could have been affected

Where required under EU MDR or EU AI Act serious incident reporting obligations, Pearl will escalate to the relevant competent authority. You do not need to determine whether a regulatory report is required before contacting Pearl.



### 10.3 What Pearl does with performance data

Pearl continuously monitors the *Second Opinion*® 3D AI performance in real-world use, including review of feedback from the "Tell us about this image" feature, analysis of aggregated detection trends, review of safety reports, and periodic re-evaluation of the AI models against updated clinical benchmarks. Where performance changes in a clinically meaningful way, Pearl will issue updated guidance or a software update.

## 11. Technical Assistance

*Second Opinion*® 3D 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:

Online: <https://hellopearl.atlassian.net/servicedesk/customer/portal/1>

Email: [support@hellopearl.com](mailto:support@hellopearl.com)

Mail:

Pearl Inc.  
8605 Santa Monica Blvd  
PMB 58456  
West Hollywood, California 90069-4109  
USA