December 6, 2018

iCAD Inc.
John Delucia
VP, Regulatory Affairs, Clinical Affairs and Quality Assurance
98 Spit Brook Rd.
Suite 100
NASHUA, NH 03062

Re: K182373
Trade/Device Name: PowerLook® Tomo Detection V2 Software
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological Computer Assisted Detection and Diagnosis Software
Regulatory Class: Class II
Product Code: QDQ
Dated: November 6, 2018
Received: November 7, 2018

Dear Mr. Delucia:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

for
Robert Ochs, Ph.D.
Director
Division of Radiological Health
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
*See PRA Statement below.*

510(k) Number *(if known)*
K182373

Device Name
PowerLook® Tomo Detection V2 Software

Indications for Use *(Describe)*
PowerLook® Tomo Detection V2 Software is a computer-assisted detection and diagnosis (CAD) software device intended to be used concurrently by interpreting physicians while reading digital breast tomosynthesis (DBT) exams from compatible DBT systems. The system detects soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D DBT slices. The detections and Certainty of Finding and Case Scores assist interpreting physicians in identifying soft tissue densities and calcifications that may be confirmed or dismissed by the interpreting physician .

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

**CONTINUE ON A SEPARATE PAGE IF NEEDED.**

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# **SECTION 1:** 510(K) Summary

**Date Prepared:** December 5, 2018

**Submitter:**

iCAD, Inc.
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**Contact Person:**

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**Submission Date:**

August 30, 2018

**Trade Name:**

PowerLook® Tomo Detection V2 software

**Common Name:**

Medical Imaging Software

**Classification Name/Regulation**

Radiological Computer Assisted Detection and Diagnosis Software
21 CFR 892.2090

**Product Code**

QDQ

**Device Classification**

Class II

**Legally Marketed Devices to Which Substantial Equivalence is Claimed**

PowerLook Tomo Detection (PLTD) V2 Software is substantially equivalent to the following legally marketed predicate device.

| Device Name | Manufacturer | FDA DEN Reference # | Decision Date |
|---|---|---|---|
| OsteoDetect | Imagen | DEN180005 | May 24, 2018 |

**Device Description**

PLTD V2 detects malignant soft-tissue densities and calcifications in digital breast tomosynthesis (DBT) image. The PLTD V2 software allows a interpreting physician to quickly identify suspicious soft tissue densities and calcifications by marking the detected areas in the tomosynthesis images. When the PLTD V2 marks are displayed by a user, the marks will appear as overlays on the tomosynthesis images. The PLTD V2 marks also serve as a navigation tool for users, because each mark is linked to the tomosynthesis plane where the detection was identified. Users can navigate to the plane associated with each mark by clicking on the detection mark. Each detected region will also be assigned a "score" that corresponds to the PLTD V2 algorithm's confidence that the detected region is a cancer (Certainty of Finding Score). Certainty of Finding scores are relative scores assigned to each detected region and a Case Score is assigned to each case regardless of the number of detected regions. Certainty of Finding and Case Scores are computed by the PLTD V2 algorithm and represent the algorithm's confidence that a specific finding or case is malignant. The scores are represented on a 0% to 100% scale. Higher scores represent a higher algorithm confidence that a finding or case is malignant. Lower scores represent a lower algorithm confidence that a finding or case is malignant.

**Key Outputs of PowerLook® Tomo Detection V2 Software**

**a. Lesion Detection**

PowerLook® Tomo Detection V2 software detects soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D digital breast tomosynthesis images. The PowerLook Tomo Detection V2 algorithm uses deep learning technology to process feature computations and uses pattern recognition to identify suspicious breast lesions appearing as soft tissue densities or clusters of calcifications. Each detected region in the tomosynthesis data is identified or represented by marking the contour of the lesion in the tomosynthesis slice where it was detected.

### b. Certainty of Finding and Case Scores

Certainty of Finding scores are relative scores assigned to each detected region and a Case Score is assigned to each case regardless of the number of detected regions. Certainty of Finding and Case Scores are computed by the PowerLook Tomo Detection V2 algorithm and represent the algorithm's confidence that a specific finding or case is malignant. The scores are represented on a 0% to 100% scale. Higher scores represent a higher algorithm confidence that a finding or case is malignant. Lower scores represent a lower algorithm confidence that a finding or case is malignant. The scores are based on a population with 50% prevalence of cancer and should be interpreted as the probability of the finding or case correctly being identified as malignant in a population of 50% cancers and 50% non-cancers. The scores serve as a guide to interpreting physicians to aid in determining if a suspicious finding or case needs further work-up. **These scores are not intended to be the clinically used "probability of malignancy"**. Certainty of Finding and Case Scores are not calibrated to the prevalence in the intended use population or to the prevalence in the pivotal reader study outlined in the Assessment of Clinical Performance Data section, and consequently, the Certainty of Finding and Case Scores are in general higher than the actual probability of malignancy in an intended use population with less than 50% prevalence. These scores represent a relative level of concern or level of suspicion because they do not represent an absolute clinical probability of malignancy.

## Supported Digital Breast Tomosynthesis Systems

The following Digital Breast Tomosynthesis systems have been tested and are compatible with PowerLook Tomo Detection V2 software:

- Hologic Selenia Dimensions
- GE Pristina

The PowerLook Tomo Detection V2 software is designed as a stand-alone executable operating within the larger software framework provided by PowerLook AMP[1].

## Intended Use / "Indications for Use"

*PowerLook® Tomo Detection V2 software is a computer-assisted detection and diagnosis (CAD) software device intended to be used concurrently by interpreting physicians while reading digital breast tomosynthesis*

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[1] iCAD PowerLook AMP is a Class I medical device exempt per 21 CFR § 892.2010 (Medical image storage device) and 21 CFR § 892.2020 (Medical image communications device). The PowerLook AMP is a device that provides electronic storage functions for medical images and also provides electronic transfer of medical image data between medical devices

*(DBT) exams from compatible DBT systems. The system detects soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D DBT slices. The detections and Certainty of Finding and Case Scores assist interpreting physicians in identifying soft tissue densities and calcifications that may be confirmed or dismissed by the interpreting physician.*

**Comparison with Predicate Device**

The Summary of Substantial Equivalence Table below details the similarities and differences between the subject device, PowerLook Tomo Detection V2, and the predicate device, OsteoDetect, classified under De Novo request DEN180005.

PowerLook Tomo Detection V2 and the predicate device have the same indication for use. Both devices are intended to aid in the detection, localization, and characterization of disease specific findings on acquired medical images, per 21 CFR 892.2090.

From a technology standpoint, PowerLook Tomo Detection V2 is the same as the predicate per 21 CFR 892.2090; both devices are radiological computer assisted detection and diagnostic software, intended to aid in the detection, localization, and characterization of disease specific findings on acquired medical images. The outputs of both devices serve as a concurrent read. The output is used to inform the clinical user (who themselves make the primary diagnostic and patient management decisions) and will not replace the clinical expertise and judgment of the clinical user. Where any differences may occur between the subject device and the predicate, special controls established for Radiological Computer Assisted Detection and Diagnosis Software are in place to further mitigate any risks in these differences.

**Summary of Indications for Use**

The subject device and the predicate device are both classified under the same classification name and number: Radiological Computer Assisted Detection and Diagnosis Software 21 CFR 892.2090. Both devices are intended to aid in the detection, localization, and characterization of disease specific findings on acquired medical images.

The subject device and the predicate may differ in their detection of disease specific findings however, special controls are in place to mitigate any risk for this difference.

**Summary of Technological Characteristic**

The technological characteristics of PowerLook Tomo Detection V2 are the same as the predicate OsteoDetect classified under De Novo request DEN180005. Per 21 CFR 892.2090, both devices are radiological computer assisted detection and diagnostic software intended to aid in the detection, localization, and characterization of disease specific findings on acquired medical

images. The outputs of both devices serve as a concurrent read. The output is used to inform the clinical user (who themselves make the primary diagnostic and patient management decisions) and will not replace the clinical expertise and judgment of the clinical user.

**General Safety and Effectiveness Concerns**

The device labeling contains instructions for use and any necessary cautions and warnings to provide for safe and effective use of this device. Risk management is ensured via a risk analysis which is used to identify and mitigate potential hazards. Any potential hazards are controlled via software development, verification and validation testing. In addition, general controls of the FD&C Act, and special controls established for Radiological Computer Assisted Detection and Diagnosis Software are in place to further mitigate any safety and or effectiveness risks.

**Assessment of Non-Clinical Performance Data**

PowerLook Tomo Detection V2 has been verified and validated according to iCAD's design control processes. All supporting documentation has been included in this 510(k) Premarket Notification. Verification activity included unit, integration, and system level testing.
Validation testing included standalone testing and performing a pivotal reader study to compare the clinical performance of radiologists using CAD detections and Certainty of Finding and Case Scores from the PLTD V2 CAD system with DBT images to that of radiologists using DBT without CAD

- **Standalone Performance on a Screening Population Dataset**

**Hologic DBT**

A standalone study, which evaluated the performance of PLTD without a radiologist, was conducted with a sample of 655 Hologic DBT cases, including 235 cancer cases with 242 malignant lesions. These 655 cases were used in the standalone study with PLTD V2. A stratified bootstrap procedure was used to estimate performance over a screening patient population. The bootstrap procedure limits the number of cases in a particular category when computing performance measures.

The purpose of the standalone study was to assess the standalone performance of PLTD V2 on a screening population.

Results from the standalone study showed that Case-Level Sensitivity, Lesion-Level Sensitivity, FP Rate in Non-Cancer Cases, and Specificity met design specifications. The detailed results are in the User Manual.

**GE DBT**

A standalone study, which evaluated the performance of PLTD V2, was conducted with a sample of 610 GE DBT cases, including 204 cancer cases with 221 malignant lesions. These 610 cases were used in the standalone study PLTD V2. A stratified bootstrap procedure was used to estimate performance over a screening patient population. The bootstrap procedure limits the number of cases in a particular category when computing performance measures.

The purpose of the standalone study was to assess the standalone performance of PLTD V2 on a screening population.

Results from the standalone study showed that Case-Level Sensitivity, Lesion-Level Sensitivity, FP Rate in Non-Cancer Cases, and Specificity met design specifications. The detailed results are in the User manual.

**Comparison of Performance Between GE DBT and Hologic DBT (Control Group)**

A comparison was made between the standalone performance of PowerLook Tomo Detection 2.0 on Hologic DBT images and PowerLook Tomo Detection 2.0 on GE DBT images. For this comparison, the performance on Hologic is considered the control group and performance on GE is the test group. The test is to determine if the difference between the control group and the test group is within the margin of non-inferiority for Sensitivity and AUC, and FPPI.

Standalone testing was performed for the control group and the test group individually. Key performance measures were then compared by subtracting the test group performance from the control group performance. This was done in a way to produce not just an estimate of the mean difference but also a distribution of the expected differences. In order to show statistical significance, the two-sided 95% confidence interval boundaries must be within the margin of non-inferiority.

Three measures were used to compare the performance of PowerLook Tomo Detection 2.0 with GE DBT images to PowerLook Tomo Detection 2.0 with Hologic images. Each of the three measures produced differences that were within the margin of non-inferiority. Therefore, in the areas of Sensitivity, FPPI, and AUC, PowerLook Tomo Detection 2.0 with the GE DBT system is not inferior to PowerLook Tomo Detection 2.0 with the Hologic DBT system.

**Assessment of Clinical Performance Data**

- **Pivotal Reader Study**

A pivotal reader study, which was a retrospective, fully-crossed, multi-reader, multi-case (MRMC) study of iCAD's PowerLook® Tomo Detection (PLTD) V2 computer-assisted detection (CAD) system, was conducted with 24 tomosynthesis radiologist readers and an enriched sample of 260 Hologic digital breast tomosynthesis (DBT) cases, including 65 cancer cases with 66 malignant lesions. The purpose of the pivotal study was to compare clinical performance of radiologists using CAD detections and Certainty of Finding and Case Scores from the PLTD V2 CAD system with DBT images to that of radiologists using DBT without CAD. The results of the pivotal study will support a regulatory submission for the PLTD V2 CAD system.

The objectives of this pivotal reader study were the following:

A. Co-primary objectives. The co-primary objectives were to determine:

1. Whether radiologist performance when using CAD with DBT images is non-inferior to radiologist performance when using DBT images without CAD and
2. Whether radiologist reading time when using CAD with DBT images is superior to (shorter than) radiologist reading time when using DBT images without CAD.

Radiologist performance was assessed by measuring case-level area under the receiver operating characteristic (ROC) curve (AUC) for the detection of malignant lesions, where malignant lesion localization was required for a reader to correctly detect cancer in a case.

B. Secondary objectives. The secondary objectives of the pivotal reader study included the following for radiologists when using CAD with DBT compared to using DBT without CAD:

1. Superiority of case-level AUC
2. Non-inferiority (with non-inferiority margin delta = 0.05) of sensitivity at the case level
3. Superiority of sensitivity at the case level
4. Non-inferiority (with non-inferiority margin delta = 0.05) of sensitivity at the lesion level
5. Superiority of sensitivity at the lesion level
6. Non-inferiority (with non-inferiority margin delta = 0.05) of specificity (case-level)
7. Non-inferiority (with non-inferiority margin delta = 0.05) of recall rate in non-cancers (case-level)

The pivotal study results showed that both co-primary endpoints were met. Specifically, the pivotal study showed that:

1. Radiologist performance using CAD with DBT was non-inferior to, and statistically significantly superior to, radiologist performance using DBT without CAD. Radiologists had superior per-subject average area under the receiver operating characteristic (ROC) curve (AUC) with CAD, 0.852, versus without CAD, 0.795. The average difference in AUC was 0.057 (95% CI: 0.028, 0.087; non-inferiority $p < 0.01$ for non-inferiority margin delta = 0.05, and $p < 0.01$ for test of difference).
2. Radiologist reading time when using CAD with DBT is superior to (shorter than) radiologist reading time when using DBT without CAD. Reading time improved 52.7% with CAD (95% CI: 41.8%, 61.5%; $p < 0.01$). *

* Interpreting physicians *reading times may vary based on the specific functionality of the viewing application used for interpretation.*

All pre-specified secondary endpoints also were met. In addition to superiority of case-level AUC, the pivotal study showed that:

- Radiologists had superior sensitivity at the case level with CAD. Average sensitivity increased by 0.080 (95% CI: 0.026, 0.134; non-inferiority $p < 0.01$ for non-inferiority margin delta = 0.05, and $p < 0.01$ for test of difference). Average case-level sensitivity was 0.770 without CAD and 0.850 with CAD.
- At the lesion level, radiologists also had superior sensitivity with CAD. Average per-lesion sensitivity across readers increased by 0.084 (95% CI: 0.029, 0.139; non-inferiority $p < 0.01$ for non-inferiority margin delta = 0.05, and $p < 0.01$ for test of difference), from 0.769 without CAD to 0.853 with CAD.
- Radiologists had non-inferior specificity with CAD. Specificity was 0.627 without CAD and 0.696 with CAD, for an average increase of 0.069 (95% CI: 0.030, 0.108; non-inferiority $p < 0.01$ for non-inferiority margin delta = 0.05).
- Finally, radiologists had non-inferior recall rate in non-cancer cases with CAD. In non-cancer cases, lower recall rates are better than higher recall rates. Average recall rate in non-cancer cases was 0.380 without CAD and 0.309 with CAD, for an average reduction of 0.072 (95% CI: 0.031, 0.112; non-inferiority $p < 0.01$ for non-inferiority margin delta = 0.05).

In this study the following were observed:

- Average sensitivity increased by 0.120 (SE=0.040) in the subgroup of 15 cancer cases with only calcifications.
- Average sensitivity increased by 0.068 (SE=0.031) in the subgroup of 50 cancer cases with at least one soft tissue density or mixed lesion.

- Average specificity decreased by 0.027 (SE=0.038) in the subgroup of 24 benign and recalled (non-cancer) cases with only calcifications.
- Average specificity increased by 0.079 (SE=0.028) in the subgroup of 62 benign and recalled (non-cancer) cases with at least one soft tissue density or mixed lesion.
- Average specificity increased by 0.084 (SE=0.021) in the subgroup of 109 non-cancer cases with no lesions.

**Conclusion:**

Based upon the information presented in this submission, it is concluded that PowerLook® Tomo Detection V2 is substantially equivalent to the named predicate device and that the nonclinical and clinical tests that demonstrate that the device is as safe, as effective, and performs as well as or better than the legally marketed device

## Summary of Substantial Equivalence:

| Features and Characteristics | Subject Device<br><br>iCAD Inc.<br>PowerLook® Tomo Detection V2 Software | Predicate Device<br><br>Imagen Inc.<br>OsteoDetect<br>DEN180005 | Discussion of Differences and Comments |
|---|---|---|---|
| **Regulation Number/Name** | 21 CFR 892.2090 / Radiological Computer Assisted Detection and Diagnosis Software. | Same | NA |
| **Regulation Description** | A radiological computer assisted detection and diagnostic software is an image processing device intended to aid in the detection, localization, and characterization of fracture, lesions, or other disease specific findings on acquired medical images (e.g. radiography, MR, CT). The device detects, identifies and characterizes findings based on features or information extracted from images, and provides information about the presence, location, and characteristics of the findings to the user. The analysis is intended to inform the primary diagnostic and patient management decisions that are made by the clinical user. The device is not intended as a replacement for a complete clinician's review or their clinical judgment that takes into account other relevant information from the image or patient history. | Same | NA |
| **Intended Use** | PowerLook® Tomo Detection V2 software is a computer-assisted detection and diagnosis (CAD) software device intended to be used concurrently by interpreting physicians while reading digital breast tomosynthesis (DBT) exams from compatible DBT systems. The system detects soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D DBT slices. The detections and Certainty of Finding and Case Scores assist interpreting physicians in identifying soft tissue densities and calcifications that may be confirmed or dismissed by the interpreting physician. | OsteoDetect analyzes wrist radiographs using machine learning techniques to identify and highlight distal radius fractures during the review of posterior-anterior (PA) and lateral (LAT) radiographs of adult wrists. | Both devices have the same intended use per 21 CFR 892.2090. |

| | | | |
|---|---|---|---|
| **Type of CAD Software** | Radiological computer assisted detection and diagnostic software | Same | NA |
| **Mode of Action** | Image processing device intended to aid in the detection, localization, and characterization of soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D DBT slices. | Image processing device intended to aid in identifying and highlighting distal radius fractures during the review of posterior-anterior (PA) and lateral (LAT) radiographs of adult wrists. | Both devices are intended to aid in the detection, localization, and characterization of disease specific findings on acquired medical images per 21 CFR 892.2090.<br><br>PLTD detects a different disease specific finding. However, special controls are in place to mitigate any risk for this difference. |
| **Clinical Output** | To inform the primary diagnostic and patient management decisions that are made by the clinical user. | Same | The outputs of both devices serve as a concurrent read. The output is used to inform the clinical user (who themselves make the primary diagnostic and patient management decisions) and will not replace the clinical expertise and judgment of the clinical user. |
| **Patient Population** | Symptomatic and asymptomatic women undergoing mammography. | Adult men and women undergoing radiographs of adult wrists. | PLTD is intended for a different patient population however special controls are in place to mitigate any risk for this difference. |
| **End Users** | Interpreting Physicians Radiologists | Clinicians | Same |
| **Image Source Modalities** | Digital breast tomosynthesis slices | 2D X-ray images | The Image Source Modalities are different. However, special controls are in place to mitigate any risk for this difference. |
| **Output Device** | Softcopy Workstation | Softcopy Workstation, PACS, RIS | NA |
| **Deployment** | Stand-alone computer | Same | NA |
| **Software Level of Concern** | Moderate | Moderate | NA |