iCAD, Inc.
% Ms. Heather Reed
Vice President, Quality Assurance
and Regulatory Affairs
98 Spit Brook Road, Suite 100
NASHUA NH 03062

October 4, 2019

Re: K191994
Trade/Device Name: ProFound™ AI Software V2.1
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer assisted detection and diagnosis software
Regulatory Class: Class II
Product Code: QDQ
Dated: July 24, 2019
Received: July 26, 2019

Dear Ms. Reed:

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/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); 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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). 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 (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-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

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
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)*
K191994

Device Name
ProFound™ AI Software V2.1

Indications for Use *(Describe)*
ProFound™ AI V2.1 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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K191994

510k Summary

Date Prepared: September 25, 2019

Submitter:
iCAD, Inc.
98 Spit Brook Road
Suite 100
Nashua, NH 03062

Contact Person:
Heather Reed
Vice President, Quality Assurance and Regulatory Affairs
Email: hreed@icadmed.com
Phone: (603) 309-1945
Fax: (603) 880-3043

Device Name:

Trade Name:	ProFound™ AI Software V2.1
Common Name:	Medical Imaging Software
Classification:	Radiological Computer Assisted Detection and Diagnosis Software
Product Code:	QDQ
Regulation Number:	21 CFR 892.2090
Review Panel:	

Predicate Device:

510k Number:	K182373
Manufacturer:	iCAD, Inc.
Device Name:	ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software

Device Description

ProFound AI V2.1 detects malignant soft-tissue densities and calcifications in digital breast tomosynthesis (DBT) images. ProFound AI V2.1 has the same performance with the DBT systems cleared for use with ProFound AI V2; furthermore, it provides support for additional DBT systems. The ProFound AI V.2.1 Software allows a radiologist to quickly identify suspicious soft tissue densities (masses, architectural distortions and asymmetries) and calcifications by marking the detected areas in the tomosynthesis images. When the ProFound AI V2.1 marks are displayed, the marks will appear as overlays on the 3D tomosynthesis images. For 3D tomosynthesis cases and depending on the functionality

offered by the viewing/reading application, the ProFound AI V2.1 marks may also serve as a navigation tool for users because each mark can be linked to the tomosynthesis slice where the detection was identified. Each detected region is also assigned a "score" that corresponds to the ProFound AI V2.1 algorithm's confidence that the detected region is malignant (certainty of finding). Each case is also assigned a case score that corresponds to the ProFound AI V2.1 algorithm's confidence that a case is malignant. The certainty of finding scores are represented as an integer in range of 0 to 100 to indicate the CAD confidence that the detected region or case is malignant. The higher the certainty of finding or case score, the more likely the detected region or case is to be malignant.

Technical Characteristics:

Lesion Detection

ProFound AI 2.1 Software detects soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D digital breast tomosynthesis or images. The ProFound AI 2.1 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 is identified or represented by marking the contour of the lesion in the 3D tomosynthesis slice or 2D digital mammography image where it was detected.

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 ProFound AI 2.1 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 the ProFound AI 2.1 software:
Supported 3D digital breast tomosynthesis systems:

- Hologic Selenia Dimensions
- GE Senographe SenoClaire
- GE Senographe Pristina
- Siemens Mammomat Inspiration
- Siemens Mammomat Revelation

Intended Use / "Indications for Use"
ProFound™ AI V2.1 is a computer-assisted detection and diagnosis (CAD) software device intended to be used concurrently by radiologists 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.

Comparison with Predicate Device

	***UNMODIFIED* Device ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software)**	***MODIFIED* Device ProFound™ AI V2.1**
Manufacturer	iCAD, Inc.	iCAD, Inc.
Classification Name	Radiological Computer Assisted Detection and Diagnosis Software	Radiological Computer Assisted Detection and Diagnosis Software

	***UNMODIFIED* Device ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software)**	***MODIFIED* Device ProFound™ AI V2.1**
Regulation Number	21 CFR 892.2090	21 CFR 892.2090
Product Code	QDQ	QDQ
510(k) #	K182373	Pending
Intended Use / Indication for Use	ProFound™ AI V2 (PowerLook® Tomo Detection V2) 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.	ProFound™ AI V2.1 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.
End User	Radiologists	Radiologists
Patient Population	Symptomatic and asymptomatic women undergoing mammography.	Symptomatic and asymptomatic women undergoing mammography.

	***UNMODIFIED* Device ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software)**	***MODIFIED* Device ProFound™ AI V2.1**
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 the detection, localization, and characterization of soft tissue densities (masses, architectural distortions and asymmetries) and calcifications in the 3D DBT slices.
Image Source Modalities	Digital breast tomosynthesis slices	Digital breast tomosynthesis slices
Output Device	Softcopy Workstation	Softcopy Workstation
Deployment	Standalone computer	Standalone computer
Supported Digital Breast Tomosynthesis Systems	ProFound AI V2 Software: • Hologic Selenia Dimensions • Ge Senographe SenoClaire • GE Senographe Pristina	Profound AI V2 Software: • Hologic Selenia Dimensions • Ge Senographe SenoClaire • GE Senographe Pristina ProFound AI V2.1 Software: • Siemens Mammomat Inspiration • Siemens Mammomat Revelation

Summary of Indications for Use:
The "Indications for Use" remain unchanged from the Predicate *UNMODIFIED* Device ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software).

Summary of Technological Characteristic
The technological characteristics of *Modified* Device, ProFound AI V2.1 remain unchanged from *Unmodified* Device ProFound™ AI V2 (PowerLook® Tomo Detection V2 Software) 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 secondary or concurrent read and not a primary 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

ProFound AI V2.1 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 regression testing was performed. Validation testing included System testing was performed according to Standalone Hologic Comparison Protocol 0074-5007A, which is the same protocol used to support the 510(k) clearance of the original ProFound AI V2 device. Lastly, ProFound AI V2.1 is deployed on a DICOM platform that has been successfully tested for clinical network integration.

Standalone Performance:

<u>ProFound AI for DBT V2.1 Siemens Standard Screening Population Dataset</u>

The ProFound AI for DBT V2.1 Siemens Standard Screening Population Standalone Study was executed to determine the performance of ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT images for comparison with the baseline performance of ProFound AI for DBT V2.0 with Hologic DBT images. Standalone testing was performed on tomosynthesis slices only. Sensitivity was measured on Cancer cases with at least 2 views per breast. Specificity and FP rates were measured on bilateral 2-view Non-Cancer cases (2 standard views for the left breast and 2 standard views for the right breast). Sensitivity, Specificity, and false positive rate per tomosynthesis image volume were measured at the operating point. The standalone data set consisted of a total of 694 Siemens Standard Reconstruction cases (238 cancer, 456 non-cancer) and were used to run the tests. 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 ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT 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.

ProFound AI for DBT V2.1 Siemens Empire Screening Population Dataset

The ProFound AI for DBT V2.1 Siemens Empire Screening Population Standalone Study was executed to determine the performance of ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT images for comparison with the baseline performance of ProFound AI for DBT V2.0 with Hologic DBT images. Standalone testing was performed on tomosynthesis slices only. Sensitivity was measured on Cancer cases with at least 2 views per breast. Specificity and FP rates were measured on bilateral 2-view Non-Cancer cases (2 standard views for the left breast and 2 standard views for the right breast). Sensitivity, Specificity, and false positive rate per tomosynthesis image volume were measured at the operating point. The standalone data set consisted of a total of 322 Siemens Empire Reconstruction cases (140 cancer, 182 non-cancer) and were used to run the tests. 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 ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT 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.

Standalone Hologic Comparison Test Results:

ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT

A comparison was made of the standalone performance of ProFound AI for DBT V2.0 with Hologic DBT images to the performance of ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT images. For this comparison, the performance on Hologic is considered the control group and performance on Siemens Standard 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 ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT images to ProFound AI for DBT V2.0 with Hologic DBT. Each of the three measures produced differences that were within the margin of non-inferiority. Therefore, in the areas of Sensitivity, FPPI, and AUC, ProFound AI for DBT V2.1 with Siemens Standard Reconstruction DBT system is not inferior to ProFound AI for DBT V2.0 with Hologic DBT system.

ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT

A comparison was made of the standalone performance of ProFound AI for DBT V2.0 with Hologic DBT images to the performance of ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT images. For this comparison, the performance on Hologic is considered the control group and performance on Siemens Empire 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 ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT images to ProFound AI for DBT V2.0 with Hologic DBT. Each of the three measures produced differences that were within the margin of non-inferiority. Therefore, in the areas of Sensitivity, FPPI, and AUC, ProFound AI for DBT V2.1 with Siemens Empire Reconstruction DBT system is not inferior to ProFound AI for DBT V2.0 with Hologic DBT system.

Conclusion:

Based upon the information presented in this submission, it is concluded that ProFound AI V2.1 is substantially equivalent to the named predicate device.