December 5, 2022

Riverain Technologies, Inc.
% Jonathan Jackson
Director of Regulatory Affairs & Quality Assurance
3130 South Tech Blvd.
MIAMISBURG OH 45342

Re: K221612
Trade/Device Name: ClearRead CT
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: OEB, LLZ
Dated: October 31, 2022
Received: November 1, 2022

Dear Jonathan Jackson:

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,

Lu Jiang 2022.12.05 09:08:19 -05'00'

Lu Jiang, Ph.D.
Assistant Director
Diagnostic X-Ray Systems Team
DHT8B: Division of Imaging Devices
and Electronic Products
OHT8: Office of 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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K221612

Device Name
ClearRead CT

Indications for Use *(Describe)*
ClearRead CT is comprised of computer-assisted reading tools designed to aid the radiologist in the detection and characterization of pulmonary nodules during the review of screening and surveillance (low-dose) CT examinations of the chest on a non-oncological patient population. ClearRead CT requires both lungs be in the field of view and is not intended for monitoring patients undergoing therapy for lung cancer or limited field of view CT scans. ClearRead CT provides adjunctive information and is not intended to be used without the original CT series.

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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5.0 510(K) SUMMARY

Submission Date: December 1, 2022

Submitter Information:

Company Name: Riverain Technologies, Inc.

Company Address: 3130 South Tech Blvd.
Miamisburg, OH 45342-4860

Contact Person: Jonathan Jackson
Director of RAQA
Riverain Technologies, Inc.
937.531.5092
jjackson@riveraintech.com

Device Information:

Trade Name: ClearRead CT

Regulation Number: 21 CFR §892.2050

Regulation Name: Medical Image Management and Processing System

Regulatory Class: Class II

Product Code: OEB/LLZ

Device Description: **ClearRead CT Compare** is a post-processing application which processes a prior chest CT to determine whether a nodule detected in the current exam was present in the prior exam using the same detection algorithm used on the current exam. **ClearRead CT Compare** requires both lungs to be in the field of view. **ClearRead CT Compare** provides adjunctive information and is not intended to be used without the original CT series and is only invoked on those patients where a prior exam exists and if a nodule is detected in the current exam. **ClearRead CT Compare** receives images according to the DICOM® protocol, processes the Lung CT series, and delivers the resulting information through the same DICOM network interface in conjunction with results provided for the current exam, specifically whether the nodule is present on the prior exam and if so, the percent volume change between the current and prior exam along with the volume doubling time. Series inputs are limited to Computed Tomography (CT). The **ClearRead CT** Compare Processor processes each prior series received. The **ClearRead CT Compare**

output is sent to a destination device that conforms to the ClearRead CT DICOM Conformance Statement, such as a storage archive. **ClearRead CT Compare** does not support printing or DICOM media. **ClearRead CT Compare** is a product extension of our FDA cleared and marketed ClearRead CT device (K161201). The initial device contained ClearRead CT Vessel Suppress as well as ClearRead CT Detect.

ClearRead CT (the base system), includes normalization, segmentation, and characterization of nodules, and provides the following key features:

- **ClearRead CT Vessel Suppress** aids radiologists by suppressing normal structures in the input chest CT series.
- **ClearRead CT Detect** aids radiologists in the detection and characterizations of nodules in the input chest CT series.
- **ClearRead CT Compare** includes Scan Registration and Nodule Matching functions and adds the following key features:
  - **ClearRead CT Compare** aids radiologists in tracking nodule changes over time, providing additional characterizations per nodule, including percent nodule change and volume doubling time.

Indications for Use: **ClearRead CT** is comprised of computer-assisted reading tools designed to aid the radiologist in the detection and characterization of pulmonary nodules during the review of screening and surveillance (low-dose) CT examinations of the chest on a non-oncological patient population. **ClearRead CT** requires both lungs be in the field of view and is not intended for monitoring patients undergoing therapy for lung cancer or limited field of view CT scans. **ClearRead CT** provides adjunctive information and is not intended to be used without the original CT series.

Primary Predicate Device: **Riverain Technologies, Inc.**
(K161201)
ClearRead CT
Class II
21 CFR §892.2050

Secondary Predicate Device: **Philips Medical Systems Nederland B.V.**
(K162484)
Lung Nodule Assessment and Comparison Option (LNA)

Class II

Comparison to Predicate Device Technical Characteristics:

Riverain Technologies, Inc. is of the opinion that **ClearRead CT Compare** is substantially equivalent, both in intended use as well as to the technical characteristics of the listed predicate devices. Differences in the design and performance from the cited predicate device does not affect either the safety or the effectiveness of **ClearRead CT Compare** for its intended use. Table 5.1 shows the predicate devices listed along with the subject device, including the Product Code as well as the Indications for Use for each device.

	Primary Predicate: **ClearRead CT** (Riverain Technologies, Inc.) K161201	**Secondary Predicate:** **Lung Nodule Assessment and Comparison Option (LNA)** (Philips Medical Systems Nederland B.V.) K162484	**Subject Device:** **ClearRead CT, including ClearRead CT Compare** (Riverain Technologies, Inc.)
Product Code	OEB/LLZ	LLZ/JAK	OEB/LLZ
Indications for Use	ClearRead™ CT is comprised of computer assisted reading tools designed to aid the radiologist in the detection of pulmonary nodules during review of CT examinations of the chest on an asymptomatic population.	The Philips Medical Systems Lung Nodule Assessment and Comparison Option is intended for use as a diagnostic patient-imaging tool. It is intended for the review and analysis of thoracic CT images, providing quantitative and characterizing information about nodules in the lung in a single study, or over the time course of several thoracic studies. Characterizations include diameter,	ClearRead CT is comprised of computer-assisted reading tools designed to aid the radiologist in the detection and characterization of pulmonary nodules during the review of screening and surveillance (low-dose) CT examinations of the chest on a non-oncological patient population. ClearRead CT requires both lungs be in the field of view and is not intended for

		volume and volume over time. The system automatically performs the measurements, allowing lung nodules and measurements to be displayed.	monitoring patients undergoing therapy for lung cancer or limited field of view CT scans. ClearRead CT provides adjunctive information and is not intended to be used without the original CT series.
Intended User	Radiologist	Radiologists and Technologists	Radiologist
Modality	Thoracic CT Series	Thoracic CT Series	Thoracic CT Series
Anatomical Region	Chest	Chest	Chest
Clinical Condition	Lung Nodules	Lung Nodules	Lung Nodules
Nodule Types	Solid, Part-solid, Ground-glass	Solid, Part-solid, Ground-glass, Calcified	Solid, Part-solid, Ground-glass
ROI Segmentation	Yes	Yes	Yes
Automatic Calculation of Measurements for each Segmented Nodule	Yes	Yes	Yes
Temporal Comparison (Nodule Matching)	No	Yes, Semi-Automatic	Yes, Fully Automatic
Volume Doubling Time and % Change Calculation	No	Yes	Yes
Segmentation of Lung Airway,	Yes, Segmentation of the Lungs	Yes	Yes, Segmentation of the Lungs

Lungs, and Lung Lobes			
Alteration of Input Images	No	No	No
Average Diameter	No	Yes	Yes
Maximum Slice Thickness for Vessel Suppress	3mm	N/A	5mm
Micro-Nodule Filtering	No	No	Yes
Output Objects	Vessel Suppress Series, Detect Series	Interactive Viewing	Vessel Suppress Series, Detect Series, Summary Report

Table 5.1: Predicate Devices vs. Subject Device

Key features identified that differ from the predicate are discussed below.

Temporal Comparison
The purpose of ClearRead CT Compare is to augment ClearRead CT, without modification, by adding a nodule matching capability. The current scan is processed with the nodule detection algorithm as defined by ClearRead CT. If any regions are detected in the current scan, the system then processes the prior scan using the same automatic detection process. If regions were detected in the prior scan, alignment of the current and prior scans is carried out with a volume registration step.

Volume Doubling Time and % Change Calculation
Given an ROI from a current scan is matched with an associated ROI from the prior scan, the ClearRead CT Compare engine adds to the output nodule characteristics the percentage volume change and volume doubling time. These added measurements are derived quantities from existing validated measurements, namely the volume estimate of a region within the current and prior scans.

Average Diameter
The average diameter is derived by taking the average of the minimum and maximum diameters that were measured. These diameters are not new measurements as they were included in the predicate device, ClearRead CT.

5mm Slice Thickness for Vessel Suppress
The volume normalization step includes a process for normalizing slice thickness to 1mm. The module works for slice thickness values up to 5mm; however, it has only been utilized for 3mm and less. As there are sites processing thicker slice data, the module for CT scans with slice thickness values within the 3mm to 5mm range was evaluated. The same data that was previously used to assess the performance of vessel suppression for

slice thickness values ranging from 1mm to 3mm was used to evaluate the extended range. No changes were made to the vessel suppression module to accommodate the thicker slices.

While ClearRead CT may produce a vessel suppressed series for CT scans in the 3mm to 5mm range, the Detect component will not, however, be applied for slice thicknesses greater than 3 mm.

Micro-Nodule Filtering
ClearRead CT Detect locates nodules that are 5mm in diameter and above, while ClearRead CT Vessel Suppress allows visualization of nodules smaller than 5mm. We added a step to Vessel Suppression that will, optionally, remove objects whose approximate diameter is less than 5mm. This option can be turned on at the site, where the size for defining what constitutes a micro-nodule can be specified. However, the size threshold is not allowed to exceed 5mm to keep the performance of the system in line with existing label and product performance indicators.

In addition to the items listed in Table 5.1, several features and enhancements have been added to **ClearRead CT** since the initial release. A summary of these is provided below:

- Minor updates to improve performance and throughput
- Additional output options and interfaces to facilitate workflow, marker verification and 3rd party integrations
- Administrative and monitoring functions to streamline installations and application health monitoring

Testing Summary:

Non-clinical Testing

Non-clinical tests were conducted during the development process in accordance with the Riverain Technologies Design Control Process, which is compliant with the FDA Quality System Regulations, ISO 13485:2016 with MDSAP and the following standards.

- IEC 62304:2006/AMD1:2015, Medical devices – Software life cycle processes
- IEC62366-1:2015, Medical device – Part1: Application of usability engineering to medical devices
- ISO14971:2007, Medical devices – Application of risk management to medical devices (2nd Ed.)
- NEMA PS 3.1-3-20, Digital Imaging and Communications in Medicine (DICOM) Set 2016

Testing verified the requirements according to the **ClearRead CT** device specifications.

The ClearRead CT Risk Analysis for this update was reviewed and updated to Revision H, with risk control measures implemented to mitigate identified hazards. Documentation required for software with a Moderate Level of Concern is included as part of this submission. Device labeling, together with the results from verification and validation testing demonstrate that the device is safe and effective.

Target Nodule Match Rate was set to a minimum of 90% for each selected stratum based on a literature review of existing solutions. The hypotheses tested the performance of the matching routine to ensure that its performance is sufficiently high and that it does not depend on the size, attenuation, or location of the nodule. To this end, detected nodules were split into three categories based on their attenuation pattern: solid, part-solid, and ground glass.

Using a total of 900 nodules for assessment, Tables 5.2 and 5.3 below show ClearRead CT Compare matching performance for each nodule type (solid, part-solid, ground-glass) and each clinical location category (isolated, juxta-vascular, juxta-pleural). Match rate is consistent across nodule type and location, and far exceeds the intended performance benchmark of 90%.

Nodule Type	Match Rate	Mismatch Rate
Solid	0.961 (0.952,0.978)	0.033 (0.027,0.038)
Part-solid	0.957 (0.942,0.971)	0.039 (0.031,0.044)
Ground Glass	0.946 (0.934,0.965)	0.040 (0.033,0.046)

Table 5.2: Nodule Match Performance Estimates by Type.

Nodule Location	Match Rate	Mismatch Rate
Isolated	0.940 (0.934,0.947)	0.042 (0.035,0.047)
Juxta-Vascular	0.969 (0.963,0.975)	0.031 (0.024,0.035)
Juxta-Pleura	0.955 (0.949,0.961)	0.039 (0.033,0.044)

Table 5.3: Nodule Match Performance Estimates by Location

The computation of the Volume Doubling Time (VDT) and percentage volume change were checked against manual computation to ensure the accuracy of the implemented expression. The manual and automated calculations matched in every instance.

To evaluate the effect of using Vessel Suppress on slices up to 5mm, we used the same data that was previously used to assess the performance of vessel suppression for slice thickness values ranging from 1mm to 3mm. This process, in effect, extends the test. It is important to note that no changes were made to the vessel suppression module to accommodate the thicker slices.

The algorithm was run on 1mm data as a baseline, and across a set of 4 slice thickness values: 3.5, 4.0, 4.5, and 5.0, all in mm. By testing a span of thicker slice values, we ensured that vessel suppression performance is maintained up to 5mm. The data used for evaluation was not used in the development of the vessel suppression module.

Some noise in performance is to be anticipated, but a significant increase in residual is not: 10% was our predefined significance threshold for rejecting a test.

The data from residual analysis can be seen in Tables 5.4 and 5.5 below. As shown, the performance across different slice thickness values had little impact on performance, either for non-contrast or contrast scans.

Slice thickness	Interior Region	Exterior Region

3.5 mm	-2.3%	-0.1%
4.0 mm	0.4%	2.9%
4.5 mm	1.8%	2.9%
5.0 mm	-3.7%	3.8%

Table 5.4: The average performance for each indicator for **Non-Contrast Cases**

Slice thickness	Interior Region	Exterior Region
3.5 mm	-2.2%	1.1%
4.0 mm	-1.5%	3.3%
4.5 mm	-2.3%	2.7%
5.0 mm	-4.5%	4.6%

Table 5.5: The average performance for each indicator for **Contrast Cases**

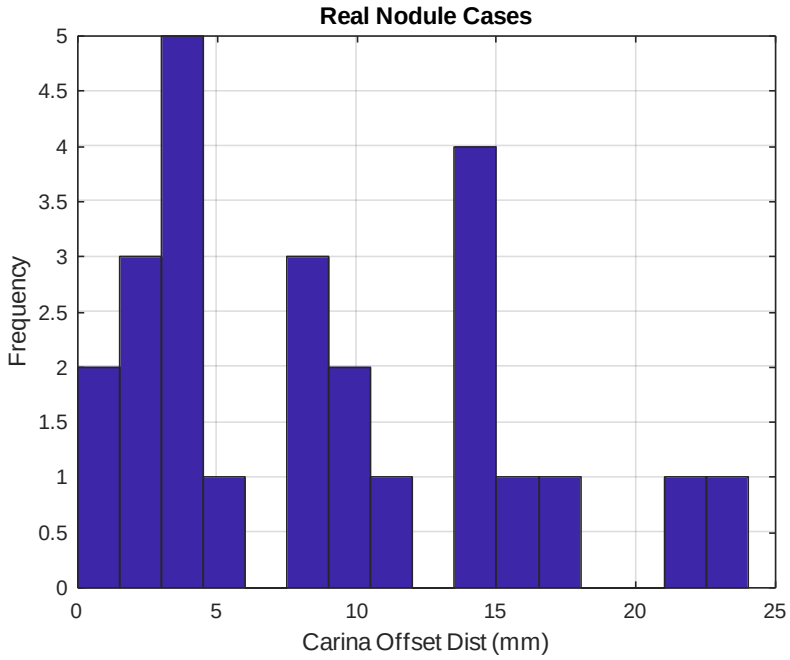
We added a step to Vessel Suppression, micro-nodule filtering, that will, optionally, remove objects whose approximate diameter is less than 5mm. This option can be turned on at the site, where the size for defining what constitutes a micro-nodule can be specified. However, the size threshold is not allowed to exceed 5mm to keep the performance of the system in line with existing label and product performance indicators.

Clinical Performance Testing

To complement non-clinical testing, 40 real nodules for a 25 patient cohort was assessed. The results are consistent with results derived from simulated data and are summarized below.

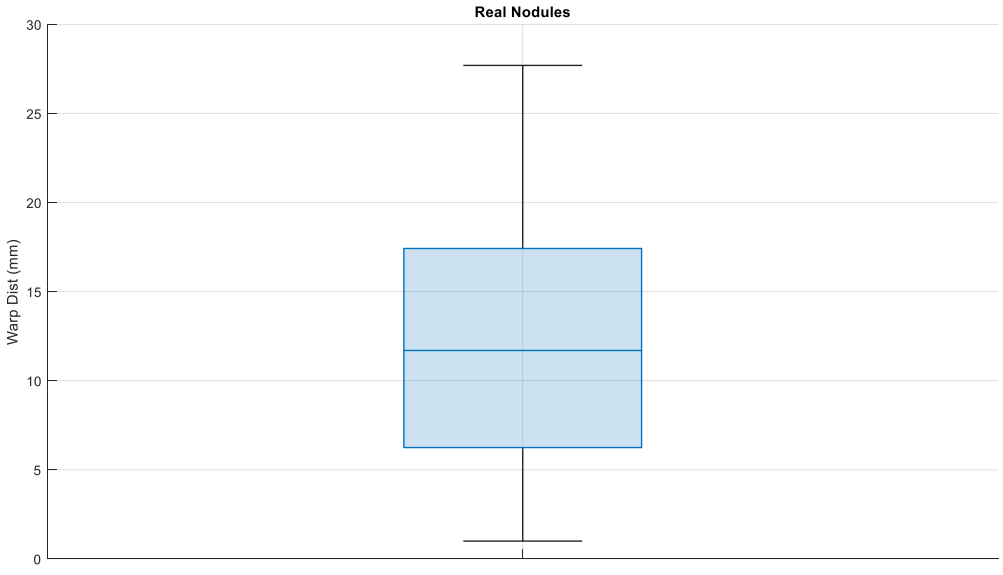
Over the 25 cases, a total of 42 actionable nodules were ground-truthed by the radiologist. Of the 42 nodules, 39 were found to have a corresponding region within the prior scan, leaving 3 nodules characterized as new nodules. All 39 nodules pairs were detected and correctly matched, while each of the 3 new ones was detected and correctly identified as new.

The frequency plot below shows the carina offset distance (between current and prior), in mm, for the scans containing real nodules.



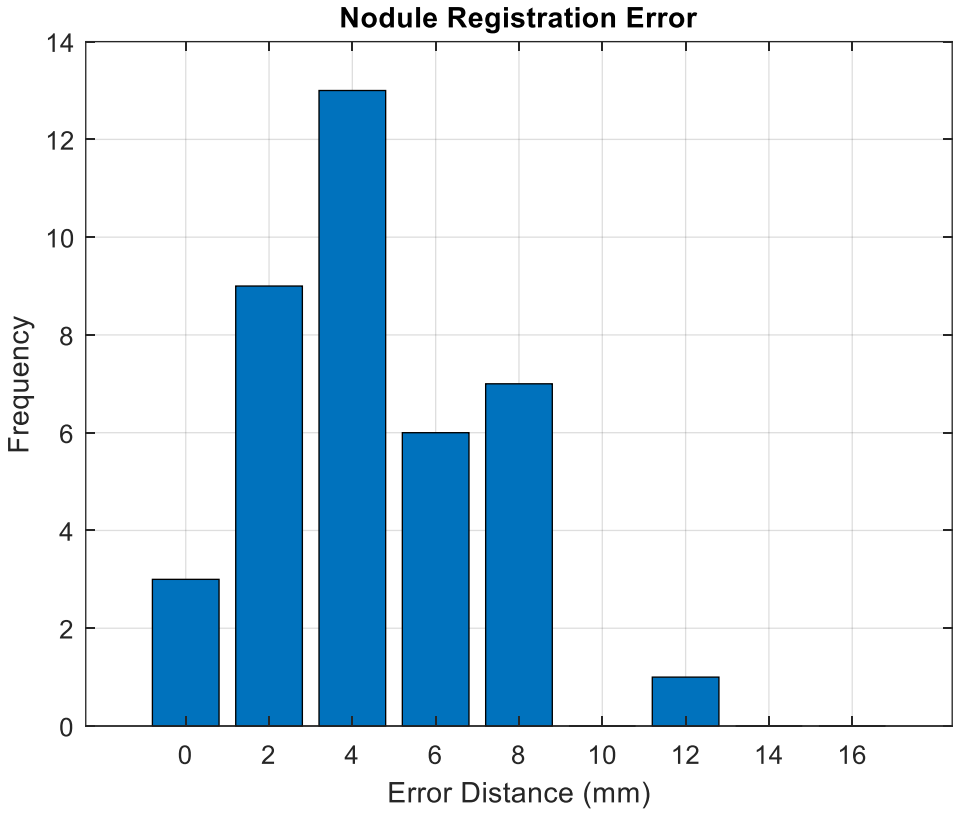
Carina offset distances for the real nodule cases

The box plot below shows the local displacement about matched nodules post affine alignment. These distances capture the needed amount of warp, in mm, to align the nodules after subtracting out the potentially large rigid (translational and rotational) effects.



Length of the warp required to align nodule centers, in mm, over the real cases

The registration, or alignment error (distance between post aligned nodule centroids), of each of the 39 real nodules successfully matched in the prior scan was performed. The figure below shows the distribution of error over all nodules.



Distribution of Nodule Registration Errors for Real Nodules

The average registration error was 4.46mm, with an associated standard deviation of 2.69mm. As shown, most nodules are aligned with high precision, well within our predefined 15mm tolerance.

ClearRead CT Compare is an extension of an existing, approved medical device. Nodule detection performance and measurements were validated as part of the initial submission of ClearRead CT (K161201). The current and prior scans are analyzed independently using the already cleared ClearRead CT Detect application.

Conclusion:

In preparing this 510(k) submission, Riverain Technologies has carefully considered the relevant statutory and regulatory requirements and believes that the information contained within satisfies the requirements for demonstrating substantial equivalence in terms of design features, fundamental technology, indications for use, and the safety and effectiveness of the device. Additionally, verification and validation testing demonstrate the safety and efficacy of the device to meet its intended use and specifications when operated as intended, with no detrimental impact upon the benefit / risk ratio of the device.