HighRAD Ltd.
% John Smith
Partner
Hogan Lovells US LLP
555 Thirteenth St.
Washington, District of Columbia 20004

March 1, 2024

Re: K231690
Trade/Device Name: iCAS-LV
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: QIH
Dated: January 29, 2024
Received: January 29, 2024

Dear John Smith,

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 (the 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 available 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.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

Jessica Lamb, Ph.D.
Assistant Director, Imaging Software Team
DHT8B: Division of Radiologic Imaging
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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)*

K231690

Device Name

iCAS-LV

Indications for Use *(Describe)*

The iCAS -LV is intended to receive multi-phase volume datasets of reconstructed studies from PACS devices, to process them and to transfer the processing output to the PACS in DICOM format. It is a PC-based, self-contained, noninvasive image analysis software application. The device provides tools for visualization, measurements, segmentation, annotation, images registration, processing, and reporting.

The device is intended for use by trained physicians. Further, the iCAS-LV is indicated to support the physicians in visualization of CT reconstructed images and evaluation of physician-identified liver lesions. The combination of the visualization, interactive segmentation, measurements, automatic registration, and volumetric analysis, supports the physician in evaluation of the lesions in terms of size, shape, position and changes over time. The iCAS should not be used in isolation for diagnosis and making patient management decisions.

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

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

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

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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**K231690**

**510(k) SUMMARY**

**HighRad's iCAS-LV**

**Submitter**:

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**Phone:** +972-54-22-66660

**Contact Person**: Yossi Srour

**Date Prepared**: February 29, 2024

**Name of Device**: iCAS-LV

**Classification Name**: Medical image management and processing system

**Regulatory Class**: Class II

**Product Code**: QIH

**Regulation**: 21 CFR 892.2050

**Predicate Device:** IQQA-LIVER Software from EDDA Technology, Inc. (K061696)

**Device Description**

The iCAS-LV (iCAS hereafter) provides tools for interactive segmentation of radiologist-identified liver lesions, automatic lesion length (diameter) and lesion volume computation, supervised automatic liver registration of the prior and current contrast-enhanced CT (ceCT scans, henceforth CT scans), semi-automatic lesions matching between two scans, and automatic lesion length (diameter) and volume change over time computation. These software tools will enable the user to easily assess the individual lesions volume and length (diameter), the total lesions burden volume and their evolution over time. This may help save radiologists and clinicians significant time and effort and improve the comprehensiveness and reliability of their reporting. The processing of the CT scans by iCAS does not rely on nor use any CT scanner-specific data. The device is compatible with CT scanners of vendors and models that conform to DICOM requirements as specified in the device Labeling.

The output is a quantitative analysis of the liver lesions volumes and their locations in the prior and current CT scans and a quantitative analysis of the volumetric changes of these lesions over time. The pipeline process consists then of two validation/manual steps and four automatic/semi-automatic steps as follows:

1) Generate liver ROI of both Prior and Current scans.
2) Registration of liver ROIs using deformable registration.
3) Lesion segmentation using 3D U-Net models. Segmentations are not displayed to the user until lesions are identified in Step 4
4) Designation of the liver lesions by the radiologist in both prior and current scans, with the selection and validation of their computed segmentations, including, when needed, manual correction of these computed lesion segmentations.
5) Semi-automatic lesion matching of the identified lesions in the Prior and Current CT scans, including Labeling the lesions as existing, new or disappeared.
6) Lesions and lesions change quantification (volume and diameter), which can be extended to a complete longitudinal CT study analysis. The technique computes various quantitative lesion change measures and identifies key slices in each scan.

**Intended Use / Indications for Use**

The iCAS -LV is intended to receive multi-phase volume datasets of reconstructed studies from PACS devices, to process them and to transfer the processing output to the PACS in DICOM format. It is a PC-based, self-contained, noninvasive image analysis software application. The device provides tools for visualization, measurements, segmentation, annotation, images registration, processing, and reporting.

The device is intended for use by trained physicians. Further, the iCAS-LV is indicated to support the physicians in visualization of CT reconstructed images and evaluation of physician-identified liver lesions. The combination of the visualization, interactive segmentation, measurements, automatic registration, and volumetric analysis, supports the physician in evaluation of the lesions in terms of size, shape, position and changes over time. The iCAS should not be used in isolation for diagnosis and making patient management decisions.

**Performance Data**

The following testing was conducted for the iCAS-LV system with data included in the 510(k) document.

*Software Verification and Validation*

Software verification and validation were conducted for the iCAS-LV software to validate it for its intended use per the design documentation in line with recommendations outlined in General Principles of Software Validation, Guidance for Industry and FDA Staff. The iCAS-LV software demonstrated passing results on all applicable unit, integration, and requirements testing.

*Non-Clinical Performance Testing*

***Phantom Testing***

HighRAD performed a phantom study evaluating sphere volume, sphere volume difference, and related measures with estimates generated by the iCAS algorithm and by two expert radiologists using a dedicated CT liver phantom. The results demonstrated the algorithm performed well against the ground truth for volume (cc) estimation and in relation to the expert readers. Sphere diameter (mm)

estimates for the algorithm were slightly better than reader estimates in most cases, with readers similarly overestimating diameter. RECIST (mm) assessments were also collected as an additional assessment. The analysis of changes across locations on pairs of phantoms indicated the scanner was in line with reader performance for changes in location, volumes and invariance due to positioning.

Four scanners were evaluated; the performance was confirmed in all scanners with some small differences, as could be expected given the multiplicity of testing (GE, Philips, Siemens, and Canon). Hence, this phantom study supported the effectiveness of the algorithm for both volume and diameter estimation on multiple platforms.

***Standalone Performance Testing***

HighRAD conducted a clinical data analysis comparing lesion volume and length (diameter), as well as changes in lesion volume and length over time, using estimates generated by physician-assisted iCAS software, in comparison to ground truth determined by three radiologists. The analysis supports the utility of the iCAS algorithm based on DICE, ASSD, SHD, volume and RECIST measurements. The comparison results demonstrated that when used by a trained radiologist, the iCAS-LV assessment of lesions 3D volumetric agrees with the radiologist manual assessment.

The deep learning algorithm was tested using the following dataset:

- The retrospective multi-site data set consists of 108 patients (54 from Israel and Italy and 54 from the US) consists of 219 ceCT scans with 2,127 liver lesions. Of those, 1,942 lesions have a diameter >5mm (0.06cc), and 1,130 have a diameter >10mm (0.52cc). The mean number of lesions per scan is 9.7±13.1 with a mean lesion RECIST diameter of 13.97±12.41 mm and mean volume of 3.95±23.98cc.
- There were 51 females and 57 males with a mean age of 62 ±12 years (min 31 and max 92 years).
- For the volume changes over time calculation, the mean number of pairs of lesions per pairs of scans was 4.4±5.0.
- The clinical data used for the validation contained the following scanner manufacturers: GE Medical Systems, Philips, Siemens, Toshiba, Hitachi and some classified as “unknown”.
- The ground truthing process involved two experienced radiologists, one of whom is US board-certified, independently identifying and delineating liver metastases in abdominal ceCT scans. A third senior radiologist reviewed and compared their findings, with the final lesion delineations validated or modified by the third radiologist being considered as the Ground Truth for the study.

**Substantial Equivalence**

The predicate device, legally marketed IQQA-LIVER Software (K061696), and the iCAS-LV have the same intended use of communicating CT studies in DICOM format and of processing volumetric data.

Both the iCAS-LV and the predicate device are indicated for processing CT studies for visualization, evaluation and reporting of physician-identified liver lesions. Both devices support physicians in

evaluating physician-identified liver lesions by combining image processing, viewing and reporting tools.

The technological characteristics of the two devices are similar but different because of each device's unique software design. The verification and validation (V&V) process includes phantom testing, bench testing and clinical experimental study to address any safety and effectiveness concerns. The device performance was verified and validated in software and bench tests with 4 commercially available CT scanners by known vendors. The experimental clinical study was performed in conformance with the clinical environment using clinical studies from Israel, Italy and the US. Thus, the V&V process aimed to meet all the requirements of international standards and internal design control procedures. A comparison table is presented below.

| **Parameter** | **Subject Device**<br>**iCAS -LV** | **Predicate Device**<br>**IQQA-LIVER Software (K061696)** |
|---|---|---|
| Intended use | *The iCAS -LV is intended to receive multi-phase volume datasets of reconstructed studies from PACS devices, to process them and to transfer the processing output to the PACS in DICOM format. It is a PC-based, self-contained, noninvasive image analysis software application. The device provides tools for visualization, measurements, segmentation, annotation, images registration, processing, and reporting. The device is intended for use by trained physicians.* | *Indications for Use (intended use): The IQQA-Liver is a PC-based, self-contained, noninvasive image analysis software application for reviewing serial multi-phase CT acquisitions of the liver. Combining image viewing, processing and reporting tools, the software is designed to support physicians in the visualization, evaluation and reporting of liver and physician-identified liver lesions. The software supports a workflow based on automated image registration for viewing and analyzing multi-phase volume datasets. It also includes tools for interactive segmentation and labeling of liver segments and vascular structures. The software provides functionalities for manual or interactive segmentation of physician-identified lesions, and allows for regional volumetric analysis of such lesions in terms of size, shape, position and enhancement pattern, providing information for physician's assessment of lesion characterization. The software is designed for use by trained physicians. Image source: DICOM* |
| Indications for use | *Further, the iCAS-LV is indicated to support the physicians in visualization of CT reconstructed images and evaluation of physician-identified liver lesions. The combination of the visualization, interactive segmentation, measurements, automatic registration, and volumetric analysis, supports the physician in evaluation of the lesions in terms of size, shape, position and changes over time. The iCAS should not be used in isolation for diagnosis and making patient management decisions.* | |
| 21CFR section | 892.2050 | 892.2050 |
| Product Code | QIH | LLZ |
| Device nature | PC-based self-contained post processing SW package | PC-based self-contained post processing SW package |

| Parameter | Subject Device<br>iCAS -LV | Predicate Device<br>IQQA-LIVER Software (K061696) |
|---|---|---|
| Data inputs | CT reconstructed images in DICOM format | CT reconstructed images in DICOM format |
| SW Functions | The HighRAD uniquely designed SW, supports a workflow, which is based on automated image registration, manual or interactive segmentation of physician-identified liver lesions, for viewing and analysing multi-phase volume datasets, It also includes tools for Labeling and reporting. | Similar SW functions performed by EDDA unique design. |
| Graphical User Interface | A graphical user interface for users to interact with the software, to visualize CT data, to select tools and to drive the workflow | A graphical user interface for users to interact with the software, to visualize CT data, to select tools and to drive the workflow |
| Data outputs | CT images in DICOM format | CT images in DICOM format |

**Conclusions**

The iCAS-LV is as safe and effective as the predicate device. The device has the same intended use and similar indications, technological characteristics, and principles of operation as its predicate device. The minor differences in indications do not alter the intended use of the device and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences between iCAS-LV and its predicate devices raise no new issues of safety or effectiveness. Thus, the iCAS-LV is substantially equivalent.