Koios Medical, Inc.
% Patricia Setti-Laperch
Director of Regulatory Compliance and Quality
242 West 38th Street, 14th Floor
NEW YORK NY 10018

December 16, 2021

Re: K212616
Trade/Device Name: Koios DS
Regulation Number: 21 CFR 892.2060
Regulation Name: Radiological computer-assisted diagnostic software for lesions suspicious of cancer
Regulatory Class: Class II
Product Code: POK, QIH
Dated: November 12, 2021
Received: November 15, 2021

Dear Patricia Setti-Laperch:

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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K212616

Device Name

Koios DS

Indications for Use *(Describe)*

Koios DS is an artificial intelligence (AI)/machine learning (ML)-based computer-aided diagnosis (CADx) software device intended for use as an adjunct to diagnostic ultrasound examinations of lesions or nodules suspicious for breast or thyroid cancer.

Koios DS allows the user to select or confirm regions of interest (ROIs) within an image representing a single lesion or nodule to be analyzed. The software then automatically characterizes the selected image data to generate an AI/ML-derived cancer risk assessment and selects applicable lexicon-based descriptors designed to improve overall diagnostic accuracy as well as reduce interpreting physician variability.

Koios DS may also be used as an image viewer of multi-modality digital images, including ultrasound and mammography. The software includes tools that allow users to adjust, measure and document images, and output into a structured report.

Koios DS software is designed to assist trained interpreting physicians in analyzing the breast ultrasound images of adult (>= 22 years) female patients with soft tissue breast lesions and/or thyroid ultrasounds of all adult (>= 22 years) patients with thyroid nodules suspicious for cancer. When utilized by an interpreting physician who has completed the prescribed training, this device provides information that may be useful in recommending appropriate clinical management.

Limitations:
• Patient management decisions should not be made solely on the results of the Koios DS analysis.
• Koios DS software is not to be used for the evaluation of normal tissue, on sites of post-surgical excision, or images with doppler, elastography, or other overlays present in them.
• Koios DS software is not intended for use on portable handheld devices (e.g. smartphones or tablets) or as a primary diagnostic viewer of mammography images.
• The software does not predict the presence of the thyroid nodule margin descriptor, extra-thyroidal extension. In the event that this condition is present, the user may select this category manually from the margin descriptor list.

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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K212616

510(k) Summary of Safety and Effectiveness

This 510(k) summary of safety and effectiveness information is submitted as part of the Premarket Notification in accordance with the requirements of 21 CFR Part 807, Subpart E and Section 807.92.

1. Identification of Submitter:

Submitter:	Koios Medical Inc.
Address:	242 West 38th Street, 14th Floor New York, NY 10018
Phone:	732-529-5755
Fax:	732-529-5757
Contact:	Patricia Setti-Laperch
Title:	Director of Regulatory Compliance and Quality
Phone:	732-529-5755
Fax:	732-529-5757
Summary Date:	December 16, 2021

2. Identification of Product:

Device Name:	Koios DS, Version 3.0
Device Common Name:	Radiological Computer-Assisted Diagnostic Software
Device Classification:	21 CFR 892.2060, Class II, POK (primary) 21 CFR 892.2050, Class II, QIH (secondary)
Classification Name:	Radiological Computer-Assisted Diagnostic Software (CADx) for Lesions Suspicious for Cancer
Manufacturer:	Koios Medical, Inc.

3. Marketed Devices

In terms of safety and performance, this software medical device is substantially equivalent to the devices listed below:

Model:	Koios DS for Breast
Manufacturer:	Koios Medical, Inc.
510(k) Number:	K190442

4. Device Description

Koios DS is a software application designed to assist trained interpreting physicians in analyzing breast and thyroid ultrasound images. The software device is a web application that is deployed to a Microsoft IIS web server and accessed by a user through a compatible client. Once logged in and granted access to the Koios DS application, the user examines selected breast or thyroid ultrasound DICOM images. The user selects Regions of Interest (ROIs) of orthogonal views of a breast lesion or thyroid nodule for processing by Koios DS. The ROI(s) are transmitted electronically to the Koios DS server for image processing and the results are returned to the user for review.

Breast Functionality:
Koios DS software automatically classifies breast lesions suspicious for cancer based on image data into one of four ACR BI-RADS® Atlas[1,2] or European U1-U5[3] Classification System-aligned categories (Benign, Probably Benign, Suspicious or Indeterminate, or Probably Malignant) and also displays a continuous graphical Confidence Level Indicator depicting where the lesion falls within its respective category and its relation to neighboring categories. The software automatically classifies the shape (Round, Oval, Irregular) and orientation (Parallel, Not Parallel) of the selected lesion.

Thyroid Functionality:
Koios DS is a software medical device used to analyze ultrasound data to classify user-selected regions containing thyroid nodules suspicious for cancer. The software generates a set of user-editable sonographic nodule descriptor recommendations (Composition, Echogenicity, Shape, Margin, Echogenic Foci) along with an optional, deep-learning derived cancer risk assessment of the suspected nodule from two orthogonal views. Nodule descriptor recommendations are subsequently mapped to a categorical assessment and risk level rating via the ACR TI-RADS ATLAS™[4,5] or American Thyroid Association (ATA)[6] risk stratification systems (RSSs) based on user preference. The software's direct, non-descriptor-based cancer risk assessment is presented as the Koios "AI Adapter" that, when used in conjunction with the ACR TI-RADS or ATA guidelines for nodule risk stratification, is shown to improve overall diagnostic performance of both systems. The AI Adapter operates as an optional lexicon-specific input used to modify the final categorization in the ACR TI-RADS and ATA RSSs. The AI adapter positively impacts performance through either a point-based modification (either positive or negative) or a risk-shift modification (either positive or negative) for ACR TI-RADS and the ATA systems,

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[1] BI-RADS® ATLAS is a registered trademark of American College of Radiology. All Rights Reserved.

[2] ACR BI-RADS Atlas: https://www.acr.org/-/media/ACR/Files/RADS/BI-RADS/US-Reporting.pdf

[3] European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis (Health & Consumer Protection Directorate – General). Fourth Edition. Editors: N. Perry, M. Broeders, C. de Wolf, S. Törnberg

[4] TI-RADS™ ATLAS is a trademark of American College of Radiology. All Rights Reserved.

[5] ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. Tessler, Franklin N. et al. Journal of the American College of Radiology, Volume 14, Issue 5, 587 - 595

[6] 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Haugen, Alexander, et al., Thyroid. Jan 2016, 26(1): 1-133.

respectively. This process creates an AI-augmented categorization that is meant to be used with no other modifications to the decision-making pathway of either RSS. A trained interpreting physician may choose to incorporate or exclude the Koios AI Adapter from the overall assessment when finalizing their diagnostic interpretation.

Koios DS enables the following functionality:

- Breast and Thyroid diagnostic core AI engines enabled by state-of-the-art computer vision and machine learning techniques capable of reading, interpreting, analyzing, classifying and generating findings from ultrasound image data resulting in an automated risk assessment for breast lesions and thyroid nodules suspicious for cancer
- Automatic classification of thyroid nodules aligned to both TI-RADS and ATA descriptors of: Composition, Echogenicity, Shape, Margin, and Echogenic Foci based on user-selected regions of interest (ROIs)
- Automatic classification of breast lesion BI-RADS and U1-U5 Descriptors Shape and Orientation based on user-selected or confirmed regions of interest (ROIs)
- Annotation and description of ultrasound images based on ACR BI-RADS Breast Imaging Atlas and U1-U5 for Koios DS Breast
- Annotation and description of ultrasound images based on and ACR TI-RADS Atlas and ATA classification guidelines for Koios DS Thyroid
- Reporting forms for breast lesion or thyroid nodule identification and tracking in the Electronic Health Record
- Smart Calipers - extraction of user-supplied ROI data (alternately referred to as Calipers) embedded in DICOM SR files from the ultrasound modality
- Smart Click (Breast only) - generation of automated ROI based on user-supplied position (click on a lesion) within the image
- Ability to save findings to PACS
- Ability to export findings to reporting software
- Remote analysis interface to generate and view results within compatible software (e.g. ultrasound equipment or PACS workstation software)
- Installer and Configuration Wizard
- Single Sign-on (SSO) Windows and LDAP Authentication
- Operating system and platform-agnostic usage
- Zero-footprint web-based HTML5 DICOM image viewer with image manipulation and annotation tools

User Profile:

Koios DS is for use by trained professionals only. Koios DS is not for use by patients. Users must have appropriate medical professional competence, such as trained sonographers and interpreting physicians.

Use Environment:
Koios DS is a software application for use within a healthcare setting for the examination and assessment of breast lesions or thyroid nodules using ultrasound. It is a platform-agnostic web application that queries and accepts DICOM compliant digital medical files from any compliant device subject to the specified DICOM Conformance Statement for Koios DS. Processing of the image(s) occurs in conjunction with a trained interpreting physician's typical diagnostic case read. The output of the system is a digital display to be used as a concurrent read and report input that may be added as an addendum to the DICOM series selected for processing or exported directly into a patient's draft report.

Operating Principle:
Koios DS is an ASP.NET web application deployed to a Microsoft IIS web server inside a Windows operating system environment accessed by a user through a compatible client. The application provides image-derived data via web triggering and remote analysis.

Once logged in and granted access to the Koios DS application, the user examines selected breast and thyroid ultrasound DICOM images. The user selects or confirms up to two ROIs, from up to two orthogonal views that represent a single breast lesion for processing by the system. For thyroid functionality, two ROIs are required for analysis by the system. The first ROI must be drawn on the transverse view, with the second on the longitudinal view of the nodule. For breast functionality, bench testing has verified a single ROI does not significantly decrease system AUC performance. The ROI(s) are transmitted electronically to the Koios DS server by the Koios DS Breast or Koios DS Thyroid software for image processing and the results are returned to the user for review in the respective interface. Images and data can be stored, communicated, processed, and displayed within the system and/or across computer networks at distributed locations.

The software does not require any specialized hardware to return a diagnostic output, but the time to process ROIs will vary depending on the hardware specifications.

Koios DS contains two distinct AI/ML engines to characterize breast lesions and thyroid nodules. Based on the structured data that exists within the DICOM header for a patient study, the Koios DS system calls the corresponding engine for analysis of the identified lesion or nodule. Each system uses computer vision and machine learning techniques embedded within an engine capable of reading, interpreting, analyzing, and generating findings from ultrasound data. The underlying breast and thyroid engines draw upon knowledge learned from a large database of known cases, tying image features to their eventual diagnosis, to form a predictive model.

Koios DS results can be saved or transferred in three separate ways: in-transit transmission, saving to Picture Archiving and Communication System (PACS), and exporting results to third-party reporting software. In-transit transmission may be utilized when users wish to share analyses across viewing workstations. Results can be stored in in-transit memory for a preset period of time defined by a system administrator. After that preset period of time, all results are wiped from the local memory. Another method of saving is storing a report in the patient study on the PACS. After single or multiple lesion or nodule analyses have been performed and ultimately accepted by a trained interpreting physician, Koios DS can export a summary report to PACS as an

addendum to the DICOM study that was selected for processing. This report serves as future reference and aid in the comparison of cases requiring follow up. This functionality is strictly reserved for approved users and must be configured by a site administrator.

Koios DS also supports exporting results to third-party reporting software to facilitate the reporting process. Saving or exporting preferences can be configured by the system administrator and user.

5. Indications for Use

Koios DS is an artificial intelligence (AI)/machine learning (ML)-based computer-aided diagnosis (CADx) software device intended for use as an adjunct to diagnostic ultrasound examinations of lesions or nodules suspicious for breast or thyroid cancer.

Koios DS allows the user to select or confirm regions of interest (ROIs) within an image representing a single lesion or nodule to be analyzed. The software then automatically characterizes the selected image data to generate an AI/ML-derived cancer risk assessment and selects applicable lexicon-based descriptors designed to improve overall diagnostic accuracy as well as reduce interpreting physician variability.

Koios DS may also be used as an image viewer of multi-modality digital images, including ultrasound and mammography. The software includes tools that allow users to adjust, measure and document images, and output into a structured report.

Koios DS software is designed to assist trained interpreting physicians in analyzing the breast ultrasound images of adult (>= 22 years) female patients with soft tissue breast lesions and/or thyroid ultrasounds of all adult (>= 22 years) patients with thyroid nodules suspicious for cancer. When utilized by an interpreting physician who has completed the prescribed training, this device provides information that may be useful in recommending appropriate clinical management.

Limitations:

• Patient management decisions should not be made solely on the results of the Koios DS analysis.
• Koios DS software is not to be used for the evaluation of normal tissue, on sites of post-surgical excision, or images with doppler, elastography, or other overlays present in them.
• Koios DS software is not intended for use on portable handheld devices (e.g. smartphones or tablets) or as a primary diagnostic viewer of mammography images.
• The software does not predict the presence of the thyroid nodule margin descriptor, extra-thyroidal extension. In the event that this condition is present, the user may select this category manually from the margin descriptor list.

6. Substantial Equivalence Chart

Product	Koios DS for Breast (K190442)	Koios DS (subject device)
Physical Characteristics	Software Package Operates on off-the-shelf hardware	Software Package Operates on off-the-shelf hardware
Storage	Storage not supported	Storage not supported
Image Input	DICOM	DICOM
Characteristics	Decision support device used to assist in the assessment and characterization of breast lesions using US image data.	Decision support device used to assist in the assessment and characterization of breast lesions and thyroid nodules using US image data.
Intended Use/Indications for Use	Koios Decision Support (DS) for Breast is a software application designed to assist trained interpreting physicians in analyzing the breast ultrasound images of patients with soft tissue breast lesions who are being referred for further diagnostic ultrasound examination. Koios DS for Breast is a machine learning-based decision support system, indicated as an adjunct to diagnostic ultrasound for breast cancer. Koios DS for Breast automatically classifies user-selected region(s) of interest (ROIs) containing a breast lesion into four BI-RADS-aligned categories (Benign, Probably Benign, Suspicious, Probably Malignant), and displays a continuous graphical confidence level indicator of where the lesion falls across all categories. Koios DS for Breast also automatically classifies lesion shape and orientation according to BI-RADS descriptors. The software requires a user to select up to two ROIs, from up to two orthogonal views, that represent a single lesion to be selected and processed. When utilized by an interpreting physician who has completed the prescribed training,	Koios Decision Support (DS) is an artificial intelligence (AI)/machine learning (ML)-based computer-aided diagnosis (CADx) software device intended for use as an adjunct to diagnostic ultrasound examinations of lesions suspicious for breast or thyroid cancer. Koios DS allows the user to select or confirm regions of interest (ROIs) within an image representing a single lesion or nodule to be analyzed. The software then automatically characterizes the selected image data to generate an AI/ML-derived cancer risk assessment and selects applicable lexicon-based descriptors designed to improve overall diagnostic accuracy as well as reduce interpreting physician variability. Koios DS software may also be used as an image viewer of multi-modality digital images, including ultrasound and mammography. The software includes tools that allow users to adjust, measure and document images, and output into a structured report. Koios DS software is designed to assist trained interpreting physicians in analyzing the breast ultrasound images of adult (>= 22 years) female patients with soft tissue breast lesions and/or thyroid ultrasounds of all adult (>= 22 years) patients with thyroid nodules suspicious for cancer.

	this device provides information that may be useful in rendering an accurate diagnosis. Patient management decisions should not be made solely on the results of the Koios DS for Breast analysis. This device is intended to help trained interpreting physicians improve their overall accuracy as well as reduce inter- and intra-operator variability. Koios DS for Breast may also be used as an image viewer of multi-modality digital images, including ultrasound and mammography. The software includes tools that allow users to adjust, measure and document images, and output into a structured report.	When utilized by an interpreting physician who has completed the prescribed training, this device provides information that may be useful in recommending appropriate clinical management.
Target Population **(subset of above for comparison purposes)**	Koios Decision Support (DS) for Breast is a software application designed to assist trained interpreting physicians in analyzing the breast ultrasound images of patients with soft tissue breast lesions who are being referred for further diagnostic ultrasound examination.	Koios DS software is designed to assist trained interpreting physicians in analyzing the breast ultrasound images of adult (>= 22 years) female patients with soft tissue breast lesions and/or thyroid ultrasounds of all adult (>= 22 years) patients with thyroid nodules suspicious for cancer.
Limitations for Use **(subset of above for comparison purposes)**	Limitations: Koios DS for Breast is not to be used on sites of post-surgical excision, or images with doppler, elastography, or other overlays present in them. Koios DS for Breast is not intended for the primary interpretation of digital mammography images. Koios DS for Breast is not intended for use on mobile devices.	Limitations: • Patient management decisions should not be made solely on the results of the Koios DS analysis. • Koios DS software is not to be used for the evaluation of normal tissue, on sites of post-surgical excision, or images with doppler, elastography, or other overlays present in them. • Koios DS software is not intended for use on portable handheld devices (e.g. smartphones or tablets) or as a primary diagnostic viewer of mammography images. • The software does not predict the presence of the thyroid nodule margin descriptor, extra-thyroidal extension. In the event that this condition is present, the user may select this category manually

		from the margin descriptor list.
Modality Used for Analysis	Breast Ultrasound Data	Breast Ultrasound Data Thyroid Ultrasound Data
Input	Medical images provided in a DICOM format	Medical images provided in a DICOM format
ROI Requirements	The software requires a user to select up to two ROIs, from up to two orthogonal views, that represent a single lesion to be selected and processed.	Breast The software requires a user to select up to two ROIs, from up to two orthogonal views, that represent a single lesion to be selected and processed. Thyroid Two ROIs that represent a single lesion to be selected and processed are required for analysis. The first ROI is drawn on the transverse view of the nodule. The second is drawn on the longitudinal view.
Output (Breast)	Koios defined categorical and continuous outputs (confidence level indicator) that align to BI-RADS and auto-classified shape and orientation	Koios DS Breast defined categorical and continuous outputs (confidence level indicator) that align to BI-RADS, U1-U5, and auto-classified shape and orientation.
Output (Thyroid)	N/A	Koios DS Thyroid software automatically classifies thyroid nodules suspicious for cancer based on image data generating an output aligned to either the TI-RADS or ATA classification guidelines. The system automatically generates user-modifiable nodule descriptors (Composition, Echogenicity, Shape, Margin, Echogenic Foci) and a direct, image-derived cancer risk assessment that is translated into an optional lexicon-specific modifier.
Comparative Clinical Performance Testing (Breast)	Metric: AUC Cases: 900 Readers: 15	Metric: AUC Cases: 900 Readers: 15
Comparative Clinical Performance Testing (Thyroid)	N/A	Metric: AUC Cases: 650 Readers: 15

7. Description of Similarities and/or Differences

Intended Use/Indications for Use (IFU)

Comparing the IFU of the predicate device Koios DS Breast (K190442) and Koios DS, there are several key similarities and differences outlined below:

Both devices are intended to be utilized as diagnostic aids that operate on user-supplied Regions of Interest (ROIs). Koios DS Thyroid functionality requires two ROIs representing a single lesion to be selected and processed for analysis. The first ROI is drawn on the transverse view of the nodule. The second is drawn on the longitudinal view.

The Koios DS system also contains the Smart Click (breast only) and Smart Caliper functionalities for streamlining the previously manual ROI selection process. The Smart Click functionality enables the user to click on the center of a lesion in order to activate a system-generated region of interest surrounding the selected lesion for the user. The Smart Calipers functionality ingests caliper data from compatible ultrasound devices with the capability to use a calculation package when drawing calipers on lesions. Koios DS can automatically generate ROIs and resulting analyses for the user based on this caliper data. Both Smart Click and Smart Caliper-generated ROIS can be edited or deleted by the user and have been demonstrated to have no adverse impact on the diagnostic outputs of the Koios DS engines.

The intended use and indications for use statements have been updated from those of the predicate device in order to enhance labeling clarity and to detail the additional breast and thyroid cancer decision support functionality and limitations. These differences do not affect the safety and effectiveness of the device when used as a labeled Computer-Assisted Diagnostic software for lesions suspicious for cancer.

Target Patient Population

Both the Koios DS Breast predicate and the subject device are software applications designed to assist trained interpreting physicians in analyzing the ultrasound images of patients with soft tissue lesions who are being referred for further diagnostic ultrasound examination.

Additional detail has been included to clarify the Koios DS Breast product indications for females, as well as to exclude pediatric use for Koios DS Breast and Koios DS Thyroid.

Technological Characteristics

Modality

Koios DS shares the ultrasound modality requirements of Koios DS Breast and provides additional functionality for Thyroid ultrasound images.

Input

Per the respective device descriptions of Koios DS Breast and Koios DS, the input to each consists of medical images provided in a DICOM format. The technical implementation for ingesting images for processing occurs via the same DICOM-based interface. Based on the structured data that exists within the DICOM header for a patient study or a user selection, the Koios DS system calls the appropriate corresponding engine (Breast or Thyroid) for analysis of the identified lesion or nodule. The Koios DS system also contains the Smart Click and Smart Caliper functionalities for streamlining the previously manual ROI selection process. Regarding Region of Interest image input data, Koios DS Thyroid functionality requires two ROIs representing a single lesion to be selected and processed for analysis, whereas this is optional for breast.

Output

When comparing breast functionality, the predicate and subject devices differ only in the additional optional output display in alignment with the European U1-U5 Classification system for enhanced usability in international markets. Direct comparison with the Koios DS Breast v2.0 predicate engine's categorical output performance determined there is a significant increase in AUC (5%), no significant change in sensitivity, and a significant increase (24%) in specificity. Koios DS retains the identical descriptor outputs and performance for the assessment of shape and orientation.

Koios DS software contains functionality for automatically classifying thyroid nodules suspicious for cancer. Similar to Koios DS Breast, this is based on image data. The system generates an output aligned to either the TI-RADS or ATA classification guidelines (in comparison with BI-RADS and U1-U5 for breast). The system automatically generates user-modifiable thyroid nodule descriptors (Composition, Echogenicity, Shape, Margin, Echogenic Foci), analogous to the Shape and Orientation descriptors present in the breast functionality, and a direct, image-derived cancer risk assessment that is translated into an optional lexicon-specific (TI-RADS or ATA) modifier. Clinical data demonstrates that this provides a significant improvement in overall reader performance when utilizing Koios DS for the interpretation of thyroid ultrasound studies.

Performance Testing

To compare the performance of the subject device to the predicate device (K190442), a clinical study was conducted in order to assess the performance of the thyroid functionality of the subject device and bench testing was conducted on the updated breast functionality. As in the predicate device, ground truth for all breast analysis was determined by pathology or 1-year follow-up for cases that were not biopsied, whereas for thyroid it was determined exclusively via histo/cyto-pathology and/or surgical excision. The breast and thyroid engine validation sets are composed of 900 lesions from 900 different patients and 650 lesions from 650 different patients, respectively. Each was set aside from the systems' training data for the purpose of validating performance.

While operating on identical modalities, but different body regions (breast versus thyroid), similar primary endpoints were utilized in the clinical validation studies of the subject and predicate devices. Both clinical studies evaluated an Area Under the Curve (AUC) shift when comparing the performance of users alone versus users utilizing the respective software platform with a 1-month washout period. The number of cases evaluated in the predicate study was 900, while the subject device study evaluated a total of 650 cases which were both

determined via power estimates utilizing pilot study estimates for effect size. The number of interpreting physicians utilized in both studies was 15 readers. Additionally, bench testing was conducted to assess the standalone performance, as measured by AUC, on identical breast validation datasets.

The results of the subject device's clinical study evaluating its impact on the diagnostic performance of thyroid lesion classification successfully met all primary endpoints demonstrating a 0.083 (0.066, 0.099 95% CI) improvement in parametric AUC on the overall dataset along with a stratified analysis of United States (US)-based readers on US-based cases demonstrating an improvement of 0.074 (0.051, 0.098 95% CI) in parametric AUC. The absolute improvement in AUC on the US-only stratification demonstrated a larger mean shift than seen in the predicate device's study (0.074 versus 0.037).

Previous clinical study evaluations reported in K190442 have demonstrated significant AUC improvements for readers utilizing Koios DS Breast. The subject device's updated breast classification engine was compared to the predicate device on the same 900 case validation set and demonstrated a statistically significant shift in AUC to 0.929 (0.913, 0.945 95% CI) from 0.882 (0.857, 0.907 95% CI). An additional 50 new cases were added to the set and evaluated to test the subject device for robustness to dataset drift. This additional test generated a resulting AUC of 0.930 [0.914, 0.946 95% CI], demonstrating there is no degradation in performance attributable to dataset drift.

In conclusion, the subject device has demonstrated substantially equivalent performance to the predicate by showing statistically significant results against similar success criteria in both clinical and bench testing comparisons.

8. Performance Testing – Bench/Non-Clinical

Breast Engine

Malignancy Risk Classification:
Bench testing was performed on the updated breast engine to ascertain the degree of concordance with trained interpreting physicians. Ground truth for malignancy risk classification was determined by pathology or 1-year follow-up for cases that were not biopsied. The system was analyzed on 900 lesions from 900 different patients set aside from the system's training data for the purpose of validating performance. Each lesion was represented by two orthogonal images (e.g. radial and anti-radial), providing a total of 1800 images. System performance on the 900 cases reported an AUC of 92.9%, with a Sensitivity of 0.97 [0.96, 0.99] and a Specificity of 0.61 [0.57, 0.66].

Direct comparison with the prior (Koios DS Breast v2.0 predicate) engine's performance determined there is a significant increase in AUC (5%), no significant change in sensitivity, and a significant increase (24%) in specificity.

In summary, a comprehensive evaluation of the breast engines was conducted across key performance metrics and bench testing demonstrated that the system exceeds physician performance measured by AUC, sensitivity,

and specificity. The engine's shape and orientation predictions have not been modified from the previously cleared device (which demonstrated the required level of agreement with the subjective categorizations assigned by physicians). Testing characterizes the system's sensitivity to shifts in the selected region of interests (ROI) and transducer frequency. Testing characterizes the system's Positive Predictive Value (PPV), Negative Predictive Value (NPV), Positive Likelihood Ratio (PLR) and Negative Likelihood Ratio (NLR) in comparison with physicians. Testing demonstrates that the performance of the engine does not demonstrate degradation when regions of interest are provided by the Smart Click system, as compared to manually drawn regions of interest. In all tests, the Breast engine met or exceeded performance requirements.

Thyroid Engine

Bench testing was performed on the thyroid engine to ascertain the degree of concordance with trained interpreting physicians utilizing both the ACR TI-RADS and ATA classification systems. Ground truth for malignancy risk classification was determined by pathology results only. The system was analyzed on 500 lesions from 500 different patients set aside from the system's training data for the purpose of validating performance. Each lesion was represented by two orthogonal images (e.g. radial and anti-radial), providing a total of 1000 images.

When applied to diagnoses made using ACR TI-RADS guidelines, the AI Adapter and descriptor predictors achieved an AUC of 79.8%, demonstrating a significant increase over the average physician AUC. When recommending biopsy, the system's sensitivity is 0.644 [0.545, 0.744] and specificity is 0.612 [0.566, 0.658]. When recommending follow-up, the system's sensitivity and specificity are 0.879 [0.812, 0.946] and 0.495 [0.446, 0.544], respectively. In both scenarios, bench testing of the system demonstrates a non-significant improvement in sensitivity and a significant improvement in specificity over the physician average.

Tests demonstrating AI Adapter impact on ATA classifications yielded similarly improved performance. With application of the AI Adapter, physician AUC demonstrates a significant increase of 9.135% [5.975, 12.294]. Sensitivity shows a non-significant increase of 0.511% [-5.182, 6.204], while specificity shows a significant increase of 18.741% [9.885, 27.596].

Bench testing included verification of standalone performance, performance with TI-RADS and ATA outputs, as well as performance when compared to a separate data set including data from independent sites (separate and apart from the sites/data used to train and tune the algorithm).

In summary, a comprehensive evaluation of the thyroid engine was conducted across key performance metrics and bench testing demonstrated that application of the Koios DS AI Adapter exceeds physician performance as measured by AUC, sensitivity, and specificity. Descriptor predictions were tested objectively – against ground truth pathology. Testing demonstrated that performance requirements were met under ACR TI-RADS and ATA reporting systems as well as when compared against independent site data. Outputs were additionally tested subjectively and met the requirements for agreement with readers' descriptor categorizations. Testing characterized the sensitivity of the system with respect to shifts in the region of interest and variation in performance between high and low transducer frequencies. System performance on data acquired from

independent sites meets performance requirements. In all tests, the Thyroid engine met or exceeded performance requirements.

9. Performance Testing – Clinical

Breast

A clinical study was previously executed (K190442) to determine the effect of Koios DS Breast on reader performance. As discussed in the prior section, the prior device's performance has been met or significantly improved across all measured metrics by the subject device. This data continues to apply to the breast functionality within the subject device, with the understanding that its performance is superior, and it would therefore provide an equivalent or greater benefit. The below summary of the clinical study data has been included for ease of reference.

The study objective was to determine the impact on Interpreting Physician (Reader) performance as defined by the area under the Receiver Operating Characteristic (ROC) Curve (AUC) when Koios DS Breast and an ultrasound examination are combined (USE + DS), compared to USE Alone in patients that present with a soft tissue breast lesion through any form of imaging or physical examination and are referred for diagnostic ultrasound.

The study consisted of 15 readers with varying levels of training and experience providing analysis on a randomized set of 900 patient cases presented with USE + DS and USE Alone in two reading periods separated by a 1-month wash-out, totaling 1800 cases analyzed per reader. The reader set and dataset were distributed in accordance with FDA guidance and are explained in detail below:

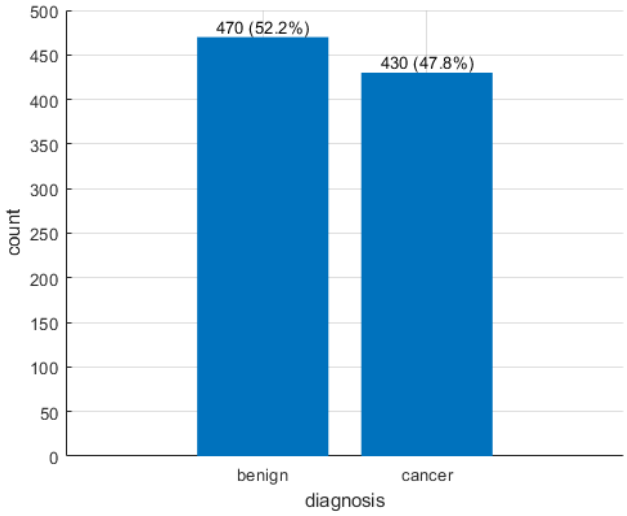
Reader Background

Reader ID	Board Certification/ Specialty	Breast Fellowship Trained and/or Dedicated Breast Imager	Years of Experience – Mammography and/or Breast Ultrasound	Academic Institution Affiliation (Yes/No)	MQSA Qualified Interpreting Physician
1	Diagnostic Radiology	No	13 years	No	Yes
2	Diagnostic Radiology	No	4 years	No	No
3	Diagnostic Radiology	Yes	7 years	Yes	Yes
4	Breast Surgeon	No	0 years	No	No
5	OB/GYN	No	20 years	No	No
6	Diagnostic Radiology	No	13 years	Yes	No
7	Diagnostic Radiology	No	3 years	Yes	No
8	OB/GYN	No	0 years	No	No
9	Diagnostic Radiology	Yes	15 years	No	Yes
10	Diagnostic Radiology	No	13 years	No	No
11	Diagnostic Radiology	Yes	30 years	No	Yes
12	Diagnostic Radiology	Yes	10 years	Yes	Yes
13	Diagnostic Radiology	No	0 years	No	No
14	Interventional Radiology	No	4 years	No	No
15	Breast Surgeon	No	25 years	Yes	No

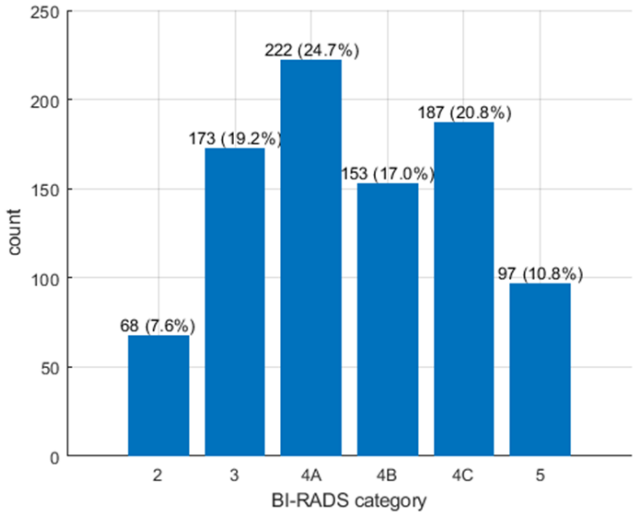
Dataset Demographic Information

The Koios DS Breast engine was tested on images sourced from a wide variety of ultrasound hardware and data with the following patient demographics to ensure the system performance is generalizable to and representative of diverse populations. Patient demographic distribution was based upon data from the Breast Cancer Surveillance Consortium (2006-2009)[7].

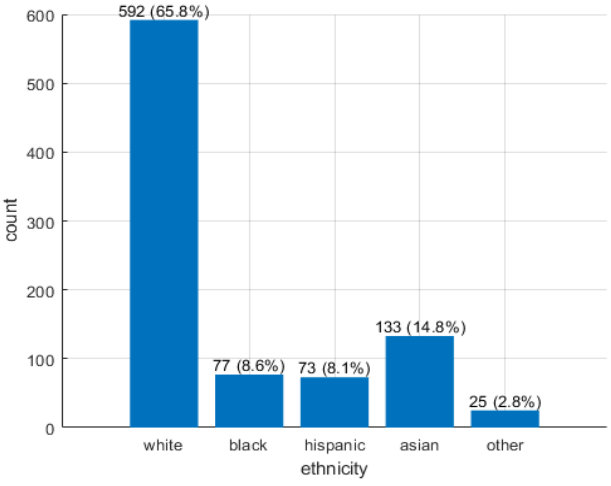
The following figures represent the final validation dataset (900 cases):



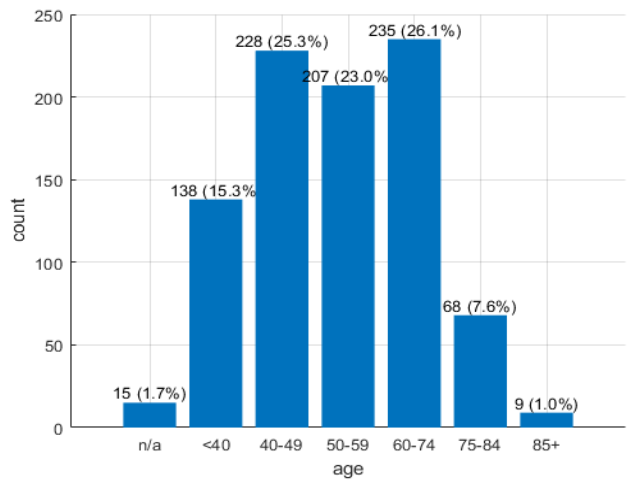
Distribution of Malignancy in Final Validation Set



Distribution of BI-RADS Category in Final Validation Set

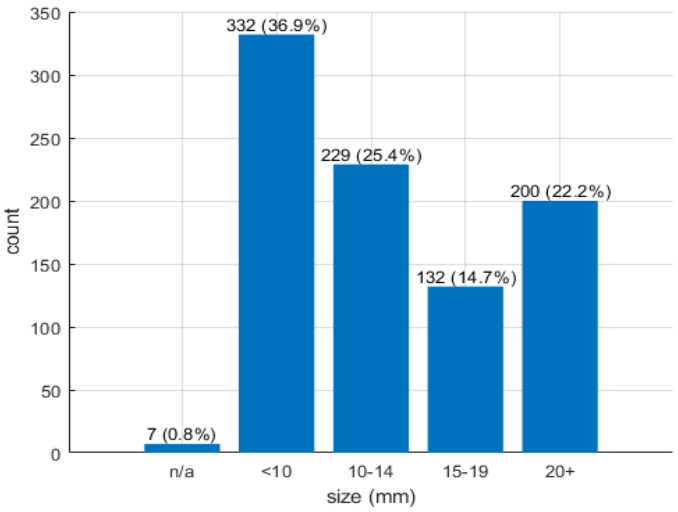


Distribution of Ethnicity in Final Validation Set

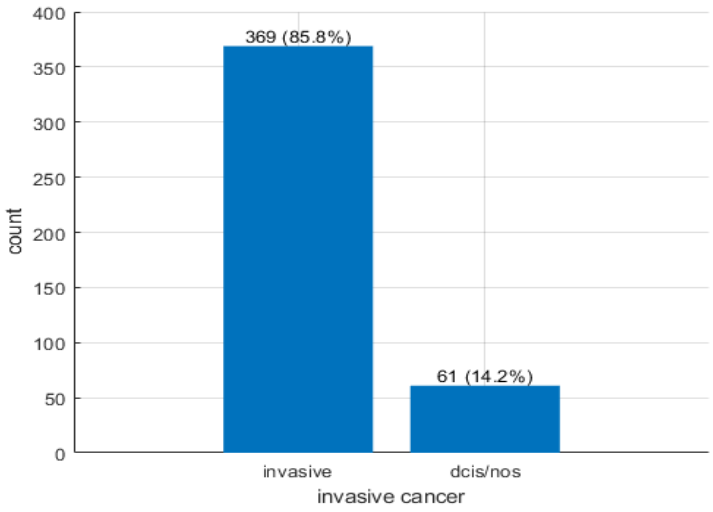


Distribution of Age in Final Validation Set

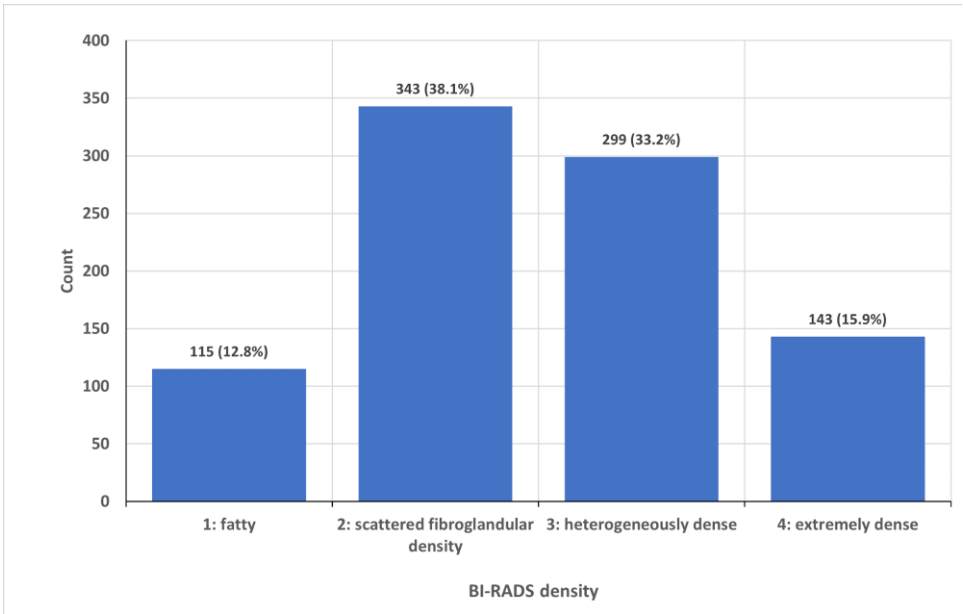
[7] Data were obtained from the Breast Cancer Surveillance Consortium, funded by the National Cancer Institute (HHSN261201100031C). From the Breast Cancer Surveillance Consortium website, http://www.bcsc-research.org/



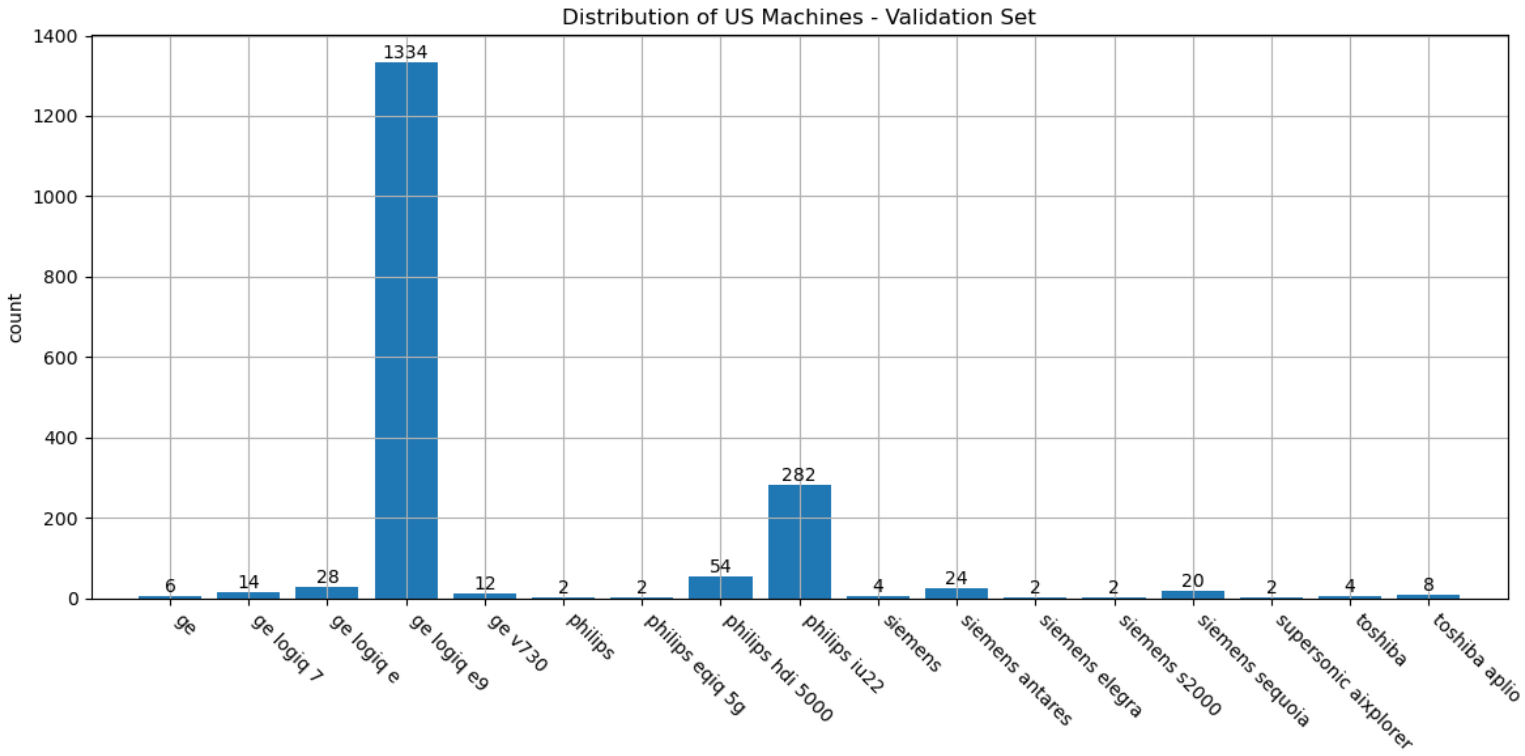
Distribution of Lesion Size in Final Validation Set



Distribution of Invasive Cancer in Final Validation Set



Distribution of BI-RADS Density in Final Validation Set



Distribution of US Machines in Final Validation Set

Per the primary endpoint of the study, ROC curves were generated and analyzed. All AUCs were computed via the trapezoidal approximation. Based on the standard error measurements, the error can be propagated to estimate the mean performance interface and 95% confidence interval. This was found to be 0.0370 (0.030, 0.044) at $\alpha = .05$, satisfying the success criteria for the primary endpoint.

To characterize the effect of Koios DS (USE + DS) system on inter-operator variability, the Kendall Tau-B correlation coefficient was computed in a pairwise manner for all readers. The metric is > 0 for all reader pairs. The standard error for USE + DS and USE Alone was computed to assess if the shifts in the metric were significant. The average Kendall Tau-B of USE Alone was .5404 (.5301, .5507) and the average Kendall Tau-B of USE + DS was .6797 (.6653, .6941) with 95% CI demonstrating a significant increase in the metric ($\alpha = .05$).

Also assessed was the effect of Koios DS on intra-operator variability leveraging 150 reads that did not switch from USE Alone to USE + DS across the washout session in the reader study (75 each). USE Alone class switching rate was 13.6% and the USE + DS class switching rate was 10.8% ($p = 0.042$), demonstrating a statistically significant reduction in intra-reader variability when using USE + DS.

Thyroid

An observational case-controlled, Multi-Reader, Multi-Case (MRMC) retrospective clinical trial (CRRS-3) was executed to determine the effect of Koios DS Thyroid on reader performance.

Effect on performance was defined by measuring the area under the Receiver Operating Characteristic (ROC) Curve (AUC) when Koios DS and an ultrasound examination were combined (USE + DS), compared to unassisted TI-RADS based Reader performance (USE Alone). All data analysis cases consisted of USE Alone and USE + DS image readings in patients that presented with a thyroid abnormality through any form of imaging or physical examination and were referred for diagnostic ultrasound where a nodule was subsequently discovered.

Data analysis in the CRRS-3 study was based on 650 retrospectively collected cases that were assigned a TI-RADS Assessment Category 1 through 5 at the time of initial review at study entry based upon the interpreting physician of the ultrasound evaluation. The study consisted of 15 readers reviewing and interpreting 650 cases twice (1300 total cases per reader). All data analysis was based on two randomized evaluations of each case with and without the assistance of Koios DS software with a 1-month washout period between corresponding presentations of the case and interpretations by physicians.

The study design called for a mixed population of physician readers (11/15 or 73% US based) and cases (500 or 77% US based) coming from both the US and Europe. Readers with a current medical license who met inclusion criteria and completed the study training protocol were considered trained interpreting physicians for study purposes. Readers possessed varying levels of training and experience, as detailed below:

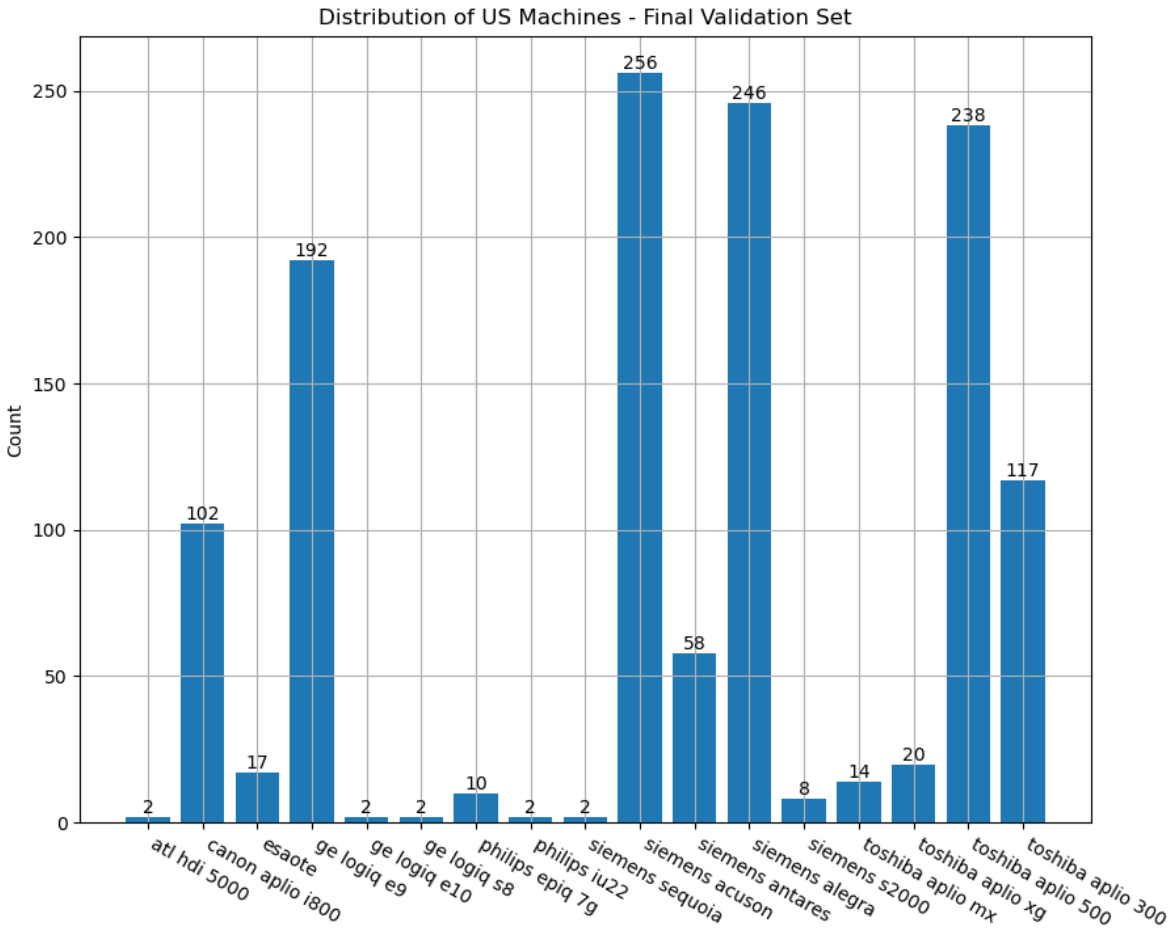
Reader Experience

Reader ID	Reader Category	Experience (post-residency)
R1	**Domestic Endocrinologist (End)**	< 10 years
R2	**Domestic Radiologist (Rad)**	≥ 20 years
R3	**Domestic Rad**	≥ 20 years
R4	**Domestic Rad**	≥ 10 and < 20 years
R5	**Domestic Rad**	≥ 10 and < 20 years
R6	**Domestic Rad**	≥ 10 and < 20
R7	**Domestic Rad**	≥ 20 years
R8	**Domestic Rad**	< 10 years
R9	**Domestic Rad**	≥ 20 years
R10	**Domestic Rad**	≥ 20 years
R11	**Domestic End**	< 10 years
R12	**European Rad**	≥ 20 years
R13	**European Rad**	≥ 20 years
R14	**European End**	≥ 20 years
R15	**European End**	≥ 20 years

Dataset Demographic Information

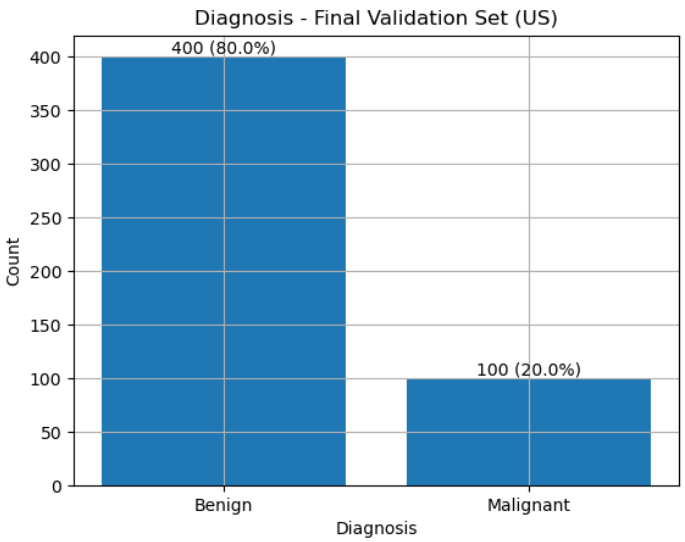
The Koios DS thyroid engine was tested on images sourced from a wide variety of ultrasound hardware and data with the following patient demographics to ensure the system performance is generalizable to and representative of diverse populations.

The following ultrasound hardware represents the final validation dataset (650 cases).

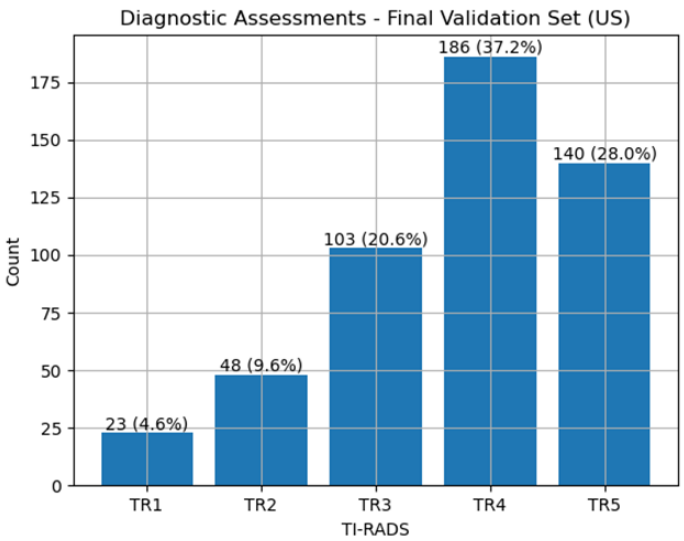


Distribution of ultrasound machine models in the final validation set, by image

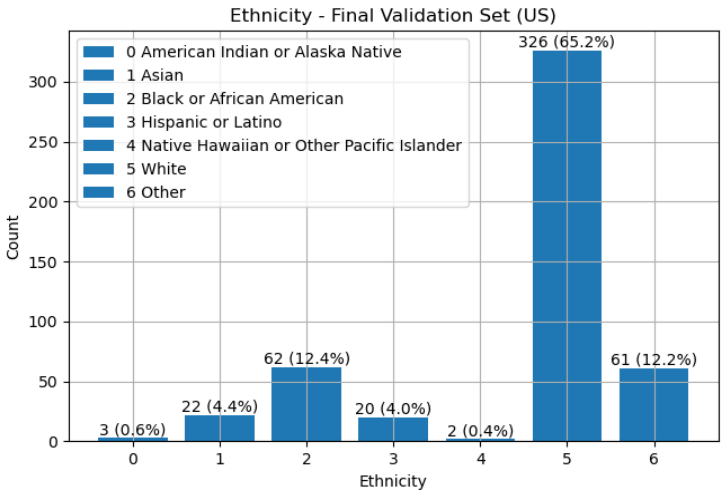
The final validation set data is divided into 2 subsets; 500 cases from United States locations and 150 cases from European locations. The following figures represent the United States patient demographics:



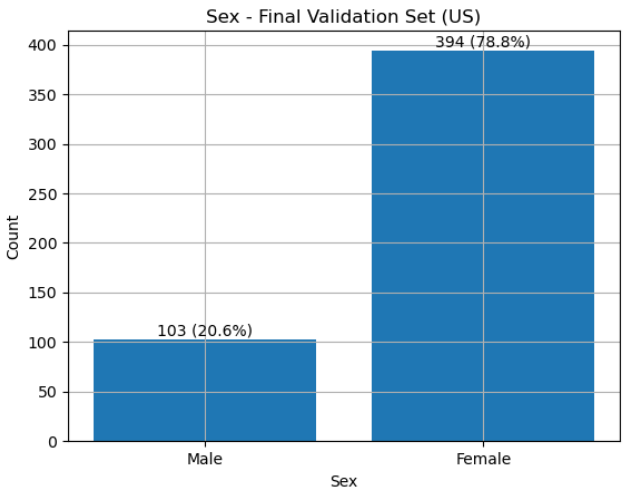
Distribution of Malignancy in the Final Validation Set (United States)



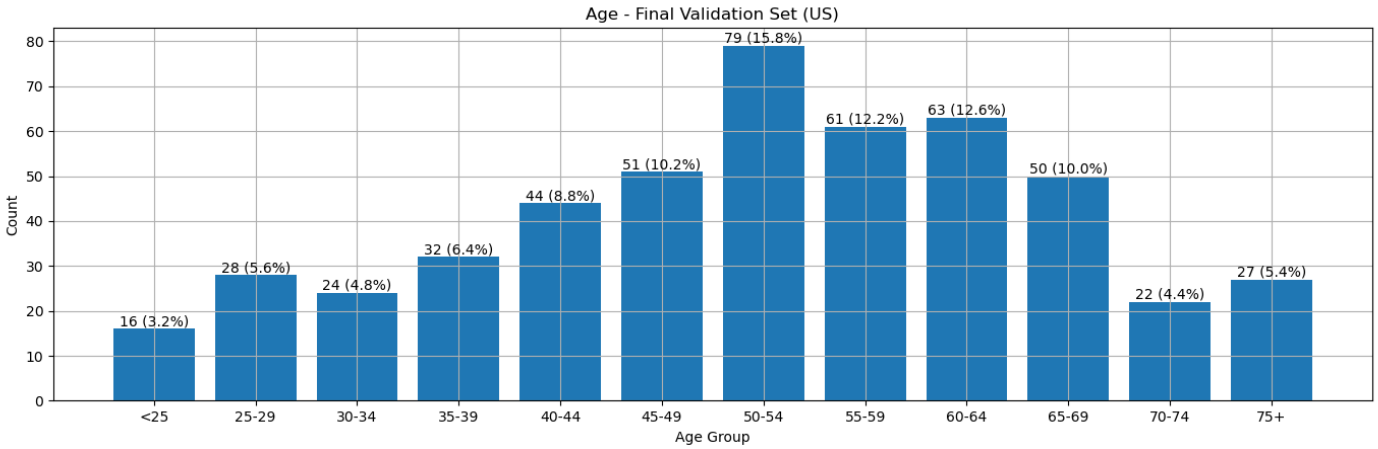
Distribution of TI-RADS Assessment in the Final Validation Set (United States)



Distribution of Patient Ethnicity in the Final Validation Set (United States)

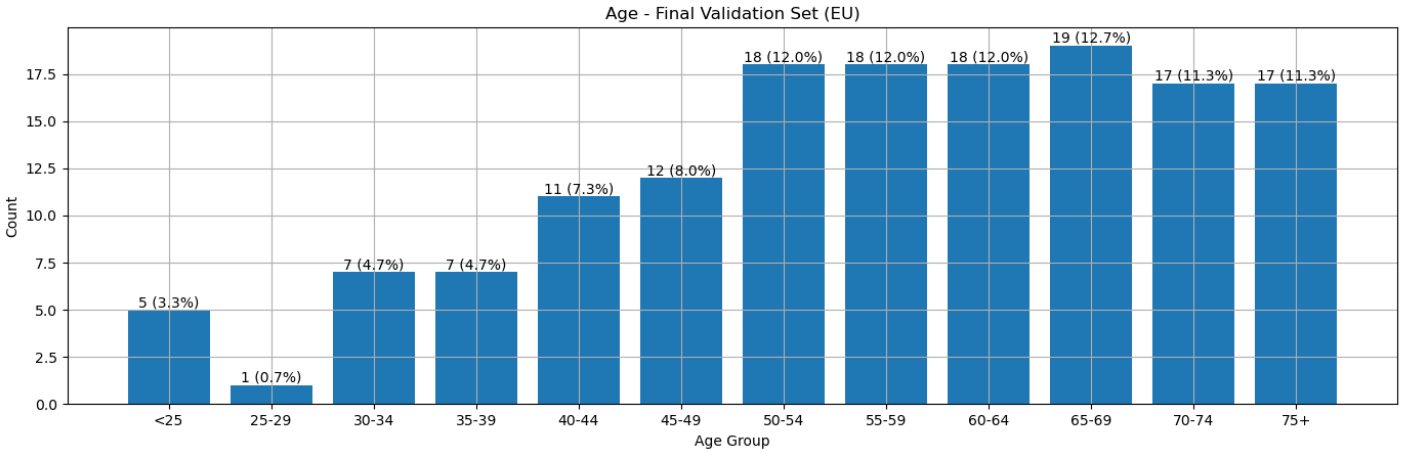


Distribution of Patient Sex in the Final Validation Set (United States)

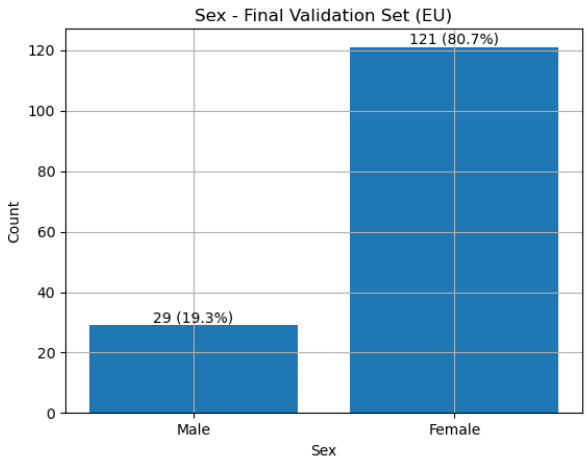


Distribution of Patient Age in the Final Validation Set (United States)

The following figures represent the European patient demographics:



Distribution of Patient Age in the Final Validation Set (European)



Distribution of Patient Sex in the Final Validation Set (European)

The primary CRRS-3 analysis was performed on the Readers' TI-RADS point total gradings from their review of the USE Alone and their review of the USE + DS for the Non-Cancer Case Set and Cancer Case Set. For each Reader, two ROC curves (Sensitivity vs. 1 – Specificity) were plotted using the USE Alone and the USE + DS primary analysis cases. Reader-specific AUC values for the primary analysis were derived from the trapezoidal approximation, whereas the mean AUC values and associated standard errors within- and between-modality across all Readers were derived from the DBM (Dorfman-Berbaum-Metz ANOVA after jackknife) method. This approach captures both reader variability and case variability and is the standard methodology for comparing AUCs in MRMC studies. All ROC curve analysis was done with respect to cyto-/histological or excisional pathology.

Summary of All Primary Study Endpoints and Secondary Analyses (US data in bold)

Analysis	Overview	Result
Primary Endpoint 1	Change in average AUC with Koios DS (all readers, all data)	+0.083 [0.066, 0.099] (parametric) +0.079 [0.062, 0.096] (non-parametric)
Primary Endpoint 2	**Change in average AUC with Koios DS (US readers, US data)**	**+0.074 [0.051, 0.098] (parametric)** **+0.073 [0.049, 0.096] (non-parametric)**
Secondary Analysis 1	Change in average Sensitivity and Specificity of FNA with Koios DS (all readers, all data)	+ 0.084 [0.054, 0.113] (sensitivity) + 0.140 [0.125, 0.155] (specificity)
	Change in average Sensitivity and Specificity of FNA with Koios DS (US readers, US data)	**+ 0.058 [0.017, 0.098] (sensitivity)** **+ 0.130 [0.110, 0.151] (specificity)**
	Change in average Sensitivity and Specificity of FNA with Koios DS (EU readers, EU data)	+0.125 [0.014, 0.237] (sensitivity) +0.171 [0.109, 0.233] (specificity)
Secondary Analysis 2 -– excluding cases recommended for FNA	Change in average Sensitivity and Specificity of Follow-up with Koios DS (all readers, all data)	+ 0.092 [0.043, 0.141] (sensitivity) + 0.242 [0.220, 0.264] (specificity)
	Change in average Sensitivity and Specificity of Follow-up with Koios DS (US readers, US data)	**+ 0.087 [0.023, 0.151] (sensitivity)** **+ 0.206 [0.176, 0.235] (specificity)**
	Change in average Sensitivity and Specificity of Follow-up with Koios DS (EU readers, EU data)	+0.084 [-0.133, 0.300] (sensitivity) +0.350 [0.267, 0.434] (specificity)
Secondary Analysis 2a – including cases recommended for	Change in average Sensitivity and Specificity of Follow-up with Koios DS (all readers, all data)	+0.060 [0.040, 0.080] (sensitivity) +0.206 [0.192, 0.219] (specificity)

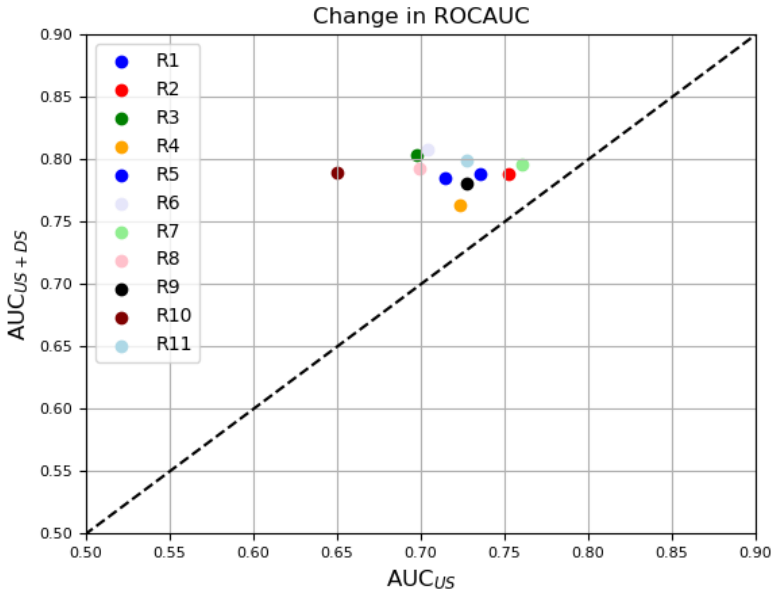
FNA	**Change in average Sensitivity and Specificity of Follow-up with Koios DS (US readers, US data)**	**+0.053 [0.026, 0.080] (sensitivity)** **+0.180 [0.161, 0.198] (specificity)**
	Change in average Sensitivity and Specificity of Follow-up with Koios DS (EU readers, EU data)	+0.060 [-0.009, 0.129] (sensitivity) +0.296 [0.238, 0.354] (specificity)
Secondary Analysis 3	Change in average AUC with Koios DS (EU Readers, EU Data)	+ 0.079 [0.024, 0.134] (parametric) + 0.066 [0.014, 0.118] (non-parametric)
Secondary Analysis 4	Inter-Reader Variability measuring the association of TI-RADS points assigned with and without decision support Difference (Relative Change %)	40.7% (all readers, all data) **37.4% (US readers, US data)** 49.7% (EU Readers, EU Data)
Secondary Analysis 5	Impact on Interpretation Time	-23.6% (all readers, all data) **-22.7% (US readers, US data)** -32.4% (EU Readers, EU Data)
Secondary Analysis 6	Change in average AUC with Koios DS descriptor classifiers only (without AI Adapter) (parametric)	+0.022 [0.005, 0.039] (all readers, all data) **+0.017 [-0.007, 0.041]** **(US readers, US data)** +0.010 [-0.051, 0.071] (EU Readers, EU Data)
	Change in average AUC with Koios DS descriptor classifiers only (without AI Adapter) (non-parametric)	+0.019 [0.001, 0.037] (all readers, all data) **+0.015 [-0.010, 0.039]** **(US readers, US data)** +0.004 [-0.054, 0.062] (EU Readers, EU Data)
	Change in average sensitivity and specificity of FNA with Koios DS descriptor classifiers only (without AI Adapter)	<u>Sensitivity:</u> +0.052 [0.022, 0.081] (all readers, all data) **+0.026 [-0.014, 0.066]** **(US readers, US data)** +0.109 [-0.004, 0.221] (EU Readers, EU Data)

		<u>Specificity</u> -0.009 [-0.024, 0.006] (all readers, all data) **-0.001 [-0.022, 0.019]** **(US readers, US data)** -0.032 [-0.095, 0.031] (EU Readers, EU Data)
	Change in average sensitivity and specificity of Follow-up with Koios DS descriptor classifiers only (without AI Adapter) – excluding cases recommended for FNA	<u>Sensitivity</u> 0.079 [0.031, 0.128] (all readers, all data) **0.072 [0.008, 0.135]** **(US readers, US data)** 0.133 [-0.068, 0.334] (EU Readers, EU Data) <u>Specificity</u> 0.015 [-0.010, 0.040] (all readers, all data) **0.012 [-0.021, 0.045]** **(US readers, US data)** 0.010 [-0.093, 0.113] (EU Readers, EU Data)
	Change in average sensitivity and specificity of Follow-up with Koios DS descriptor classifiers only (without AI Adapter) – including cases recommended for FNA	<u>Sensitivity</u> +0.047 [0.026, 0.067] (all readers, all data) +0.037 [0.009, 0.065] (US readers, US data) +0.067 [0.000, 0.134] (EU Readers, EU Data) <u>Specificity</u> +0.000 [-0.013, 0.012] (all readers, all data) +0.003 [-0.014, 0.019]

		(US readers, US data) -0.012 [-0.065, 0.041] (EU Readers, EU Data)

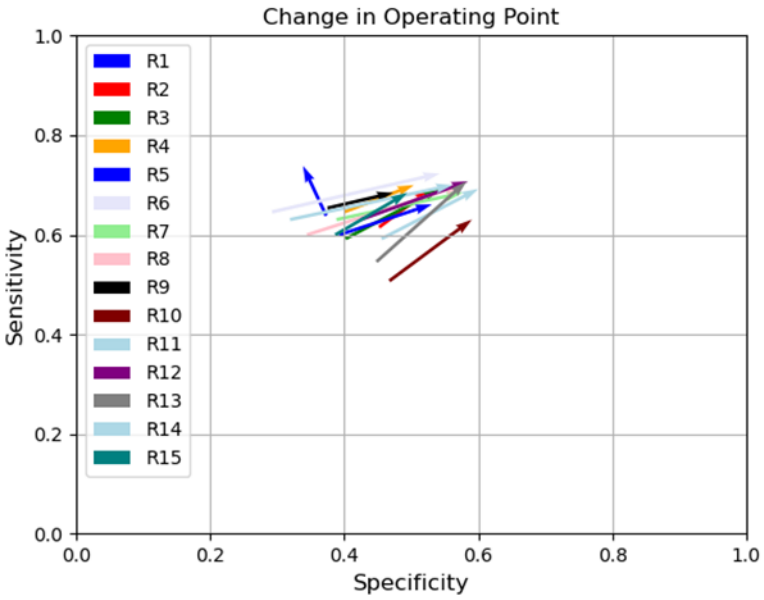
Summary of System Clinical Performance Using TI-RADS RSS

	All Readers, All Data	**US Readers, US Data**	**EU Readers, EU Data**
Change in average Sensitivity/Specificity of FNA			
TI-RADS categorization w/AI Adapter + size criteria	+0.084 [0.054, 0.113] (sensitivity) +0.140 [0.125, 0.155] (specificity)	+0.058 [0.017, 0.098] (sensitivity) +0.130 [0.110, 0.151] (specificity)	+0.125 [0.014, 0.237] (sensitivity) +0.171 [0.109, 0.233] (specificity)
TI-RADS categorization + size criteria	+0.052 [0.022, 0.081] (sensitivity) -0.009 [-0.024, 0.006] (specificity)	+0.026 [-0.014, 0.066] (sensitivity) -0.001 [-0.022, 0.019] (specificity)	+0.109 [-0.004, 0.221] (sensitivity) -0.032 [-0.095, 0.031] (specificity)
Change in average Sensitivity/Specificity of Follow-up			
TI-RADS categorization w/AI Adapter + size criteria	+0.060 [0.040, 0.080] (sensitivity) +0.206 [0.192, 0.219] (specificity)	+0.053 [0.026, 0.080] (sensitivity) +0.180 [0.161, 0.198] (specificity)	+0.060 [-0.009, 0.129] (sensitivity) +0.296 [0.238, 0.354] (specificity)
TI-RADS categorization + size criteria	+0.047 [0.026, 0.067] (sensitivity) +0.000 [-0.013, 0.012] (specificity)	+0.037 [0.009, 0.065] (sensitivity) +0.003 [-0.014, 0.019] (specificity)	+0.067 [0.000, 0.134] (sensitivity) -0.012 [-0.065, 0.041] (specificity)



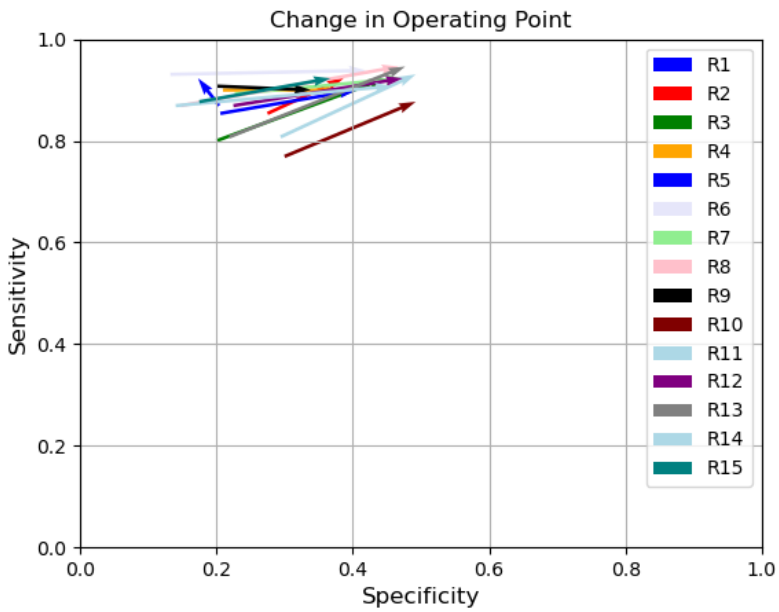
Reader US (TI-RADS categorization) vs. US+DS (TI-RADS categorization w/AI Adapter)

Per reader non-parametric AUC comparing US to US+DS. The dashed line represents equivocal results with all points above this line demonstrating an improvement for the US+DS reading condition.



Reader US (TI-RADS categorization + size criteria) vs. US+DS (TI-RADS categorization w/AI Adapter + size criteria) Change in Operating Point (FNA)

Change in Sensitivity and Specificity of FNA Recommendations for all data for all readers. The base of the arrow represents the initial operating point, while the arrowhead represents the sensitivity and specificity of US+DS



Reader US (TI-RADS categorization + size criteria) vs. US+DS (TI-RADS categorization w/AI Adapter + size criteria) Change in Operating Point (Follow-up)

Change in Sensitivity and Specificity of Follow-Up Recommendations for all data for all readers. The base of the arrow represents the initial operating point, while the arrowhead represents the sensitivity and specificity of US+DS

Primary endpoints were successfully met, demonstrating a **statistically significant improvement of 0.074 [0.051, 0.098] (95% confidence interval)** in overall reader performance of US-based readers when utilizing Koios DS for the interpretation of US-based thyroid ultrasound studies.

10. Special Controls

Design verification and validation and product labelling include all requirements proscribed in the 21 CFR 892.2060 Special Controls.

11. Conclusion

Non-clinical and clinical performance tests demonstrate that the Koios DS software device is as safe, as effective, and performs as well as or better than the legally marketed predicate Koios DS Breast software. It has similar intended use, indications for use, technological characteristics, and principles of operation as its predicate device. The Koios DS product is substantially equivalent to K190442.