See-Mode Technologies Pte. Ltd.
% Sadaf Monajemi
Co-founder and Director
32 Carpenter Street, #03-01
Singapore, 059911
Singapore

September 9, 2024

Re: K240697
Trade/Device Name: See-Mode Augmented Reporting Tool, Thyroid (SMART-T)
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological Computer Assisted Detection And Diagnosis Software
Regulatory Class: Class II
Product Code: QDQ, QIH
Dated: August 2, 2024
Received: August 2, 2024

Dear Sadaf Monajemi:

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.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

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
DHT 8B: Division of Radiological Imaging
Devices and Electronic Products
OHT 8: 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: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K240697

Device Name

See-Mode Augmented Reporting Tool, Thyroid (SMART-T)

Indications for Use *(Describe)*

See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is a stand-alone reporting software to assist trained medical professionals in analyzing thyroid ultrasound images of adult (>=22 years old) patients who have been referred for an ultrasound examination.

Output of the device includes regions of interest (ROIs) placed on the thyroid ultrasound images assisting healthcare professionals to localize nodules in thyroid studies. The device also outputs ultrasonographic lexicon-based descriptors based on ACR TI-RADS. The software generates a report based on the image analysis results to be reviewed and approved by a qualified clinician after performing quality control.

SMART-T may also be used as a structured reporting software for further ultrasound studies. The software includes tools for reading measurements and annotations from the images that can be used for generating a structured report.

Patient management decisions should not be made solely on the basis of analysis by See-Mode Augmented Reporting Tool, Thyroid.

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.

This "510(k) Summary" was prepared per section 807.92(c).

1. ADMINISTRATIVE INFORMATION

Date of Preparation: September 5, 2024
Prepared by: Sadaf Monajemi, PhD. Co-founder and Director
Manufacturer: See-Mode Technologies Pte. Ltd.
32 Carpenter Street #03-01
Singapore 059911
SINGAPORE
Email: sadaf@see-mode.com
Tel: +61 415 952 782
www.see-mode.com

Official Contact: Dr. Sadaf Monajemi, PhD, Co-founder and Director
See-Mode Technologies
32 Carpenter Street #03-01
Singapore 059911
SINGAPORE
Email: sadaf@see-mode.com
www.see-mode.com

2. DEVICE NAME AND CLASSIFICATION

Trade/Proprietary Name: See-Mode Augmented Reporting Tool, Thyroid (SMART-T)
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological computer-assisted detection and diagnosis software
Classification Name: System, Image Processing, Radiological
Review Panel: Radiology
Regulatory Class: Class II
Product Code: QDQ/QIH

3. INTENDED USE

Localization and characterization of thyroid ultrasound images.

4. INDICATIONS FOR USE

See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is a stand-alone reporting software to assist trained medical professionals in analyzing thyroid ultrasound images of adult (>=22 years old) patients who have been referred for an ultrasound examination.

Output of the device includes regions of interest (ROIs) placed on the thyroid ultrasound images assisting healthcare professionals to localize nodules in thyroid studies. The device also outputs ultrasonographic lexicon-based descriptors based on ACR TI-RADS. The software generates a report based on the image analysis results to be reviewed and approved by a qualified clinician after performing quality control.

SMART-T may also be used as a structured reporting software for further ultrasound studies. The software includes tools for reading measurements and annotations from the images that can be used for generating a structured report.

Patient management decisions should not be made solely on the basis of analysis by See-Mode Augmented Reporting Tool, Thyroid.

5. DEVICE DESCRIPTION

See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is a stand-alone, web-based image processing and reporting software for localization, characterization and reporting of thyroid ultrasound images.

The software analyzes thyroid ultrasound images and uses machine learning algorithms to extract specific information. The algorithms can identify and localize suspicious soft tissue nodules and also generate lexicon-based descriptors, which are classified according to ACR TI-RADS (composition, echogenicity, shape, margin, and echogenic foci) with a calculated TI-RADS level according to the ACR TI-RADS chart.

SMART-T may also be used as a structured reporting software for further ultrasound studies. The software includes tools for reading measurements and annotations from the images that can be used for generating a structured report.

The software then generates a report based on the image analysis results to be reviewed and approved by a qualified clinician after performing quality control. Any information within this report can be changed and modified by the clinician if needed during quality control and before finalizing the report.

The software runs on a standard “off-the-shelf” computer and can be accessed within the client web browser to perform the reporting of ultrasound images. Input data and images for the software are acquired through DICOM-compliant ultrasound imaging devices.

The data produced by the software is intended to be used by trained medical professionals, including but not limited to physicians and medical technicians. The software is not intended to be used as an independent source of medical advice or to determine or recommend a course of action or treatment for patients.

6. SUBSTANTIAL EQUIVALENCE

6.1. Predicate Device

Manufacturer: TaiHao Medical Inc.
Trade Name: BU-CAD
510(k) Identifier: K210670
Regulation Number: 21 CFR 892.2090
Regulation Name: Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer
Classification Name: Radiological Computer Assisted Detection/Diagnosis Software For Lesions Suspicious For Cancer
Classification Panel: Radiology
Regulatory Class: Class II
Product Code: QDQ, LLZ
Date Cleared: December 21, 2021

6.2. Tabular Comparison of Features and Specifications of the Subject Device, Predicate Device, and Reference Device

	Subject Device See-Mode Augmented Reporting Tool, Thyroid (SMART-T) (K240697)	**Predicate Device BU-CAD (K210670)**	**Reference Device Koios DS (K212616)**
Administrative information			
Regulation	21 CFR 892.2090 Radiological computer-assisted detection and diagnosis software for lesions suspicious for cancer	21 CFR 892.2090 Radiological computer-assisted detection and diagnosis software for lesions suspicious for cancer	21 CFR 892.2060 Radiological computer-assisted diagnostic software for lesions suspicious of cancer
Regulatory Class	Class II	Class II	Class II

	Subject Device **See-Mode Augmented Reporting Tool, Thyroid (SMART-T)** **(K240697)**	**Predicate Device** **BU-CAD (K210670)**	**Reference Device** **Koios DS (K212616)**
Product Code	QDQ, QIH	QDQ, LLZ	POK, QIH
510(k) Number	K240697	K210670	K212616
Intended Use			
Indications for Use	See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is a stand-alone reporting software to assist trained medical professionals in analyzing thyroid ultrasound images of adult (>=22 years old) patients who have been referred for an ultrasound examination. Output of the device includes regions of interest (ROIs) placed on the thyroid ultrasound images assisting healthcare professionals to localize nodules in thyroid studies. The device also outputs ultrasonographic lexicon-based descriptors based on ACR TI-RADS. The software generates a report based on the image analysis results to be reviewed and approved by a qualified clinician after performing quality control. SMART-T may also be used as a structured reporting software for further ultrasound studies. The software includes tools for reading measurements and	BU-CAD is a software application indicated to assist trained interpreting physicians in analyzing the breast ultrasound images of patients with soft tissue breast lesions suspicious for breast cancer who are being referred for further diagnostic ultrasound examination. Output of the device includes regions of interest (ROIs) and lesion contours placed on breast ultrasound images assisting physicians to identify suspicious soft tissue lesions from up to two orthogonal views of a single lesion, and region-based analysis of lesion malignancy upon the physician's query. The region-based analysis indicates the score of lesion characteristics (SLC), and corresponding BI-RADS categories in user-selected ROIs or ROIs automatically identified by the software. In addition, BU-CAD also automatically classifies lesion shape, orientation, margin, echo pattern, and posterior features according to BI-RADS descriptors.	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

	Subject Device **See-Mode Augmented Reporting Tool, Thyroid (SMART-T)** **(K240697)**	**Predicate Device** **BU-CAD (K210670)**	**Reference Device** **Koios DS (K212616)**
	annotations from the images that can be used for generating a structured report. Patient management decisions should not be made solely on the basis of analysis by See-Mode Augmented Reporting Tool, Thyroid.	BU-CAD 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 (SR). Patient management decisions should not be made solely on the basis of analysis by BU-CAD.	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.
Intended Population	Patients with thyroid nodules who are being referred for ultrasound scan (Prescription only)	Patients with soft tissue breast lesions who are being referred for ultrasound interpreting (Prescription only)	Patients with thyroid nodules suspicious for cancer (Prescription only)
Image Source	Ultrasound images	Ultrasound images	Ultrasound images
Rx only?	Yes	Yes	Yes
Technological Characteristics			

	Subject Device **See-Mode Augmented Reporting Tool, Thyroid (SMART-T)** **(K240697)**	**Predicate Device** **BU-CAD (K210670)**	**Reference Device** **Koios DS (K212616)**
Application Description	The subject device is a stand-alone, web-based image processing and reporting software for localization, characterization and reporting of thyroid ultrasound images. The software analyzes thyroid ultrasound images and uses machine learning algorithms to extract specific information. The algorithms can identify and localize suspicious soft tissue nodules and also generate lexicon-based descriptors, which are classified according to ACR TI-RADS (composition, echogenicity, shape, margin, and echogenic foci) with a calculated TI-RADS category according to the ACR TI-RADS chart. The software then generates a report based on the image analysis results to be reviewed and approved by a qualified clinician after performing quality control. Any information within this report can be changed and modified by the clinician if needed during quality control and before finalizing the report.	BU-CAD is a software system designed to assist users in analyzing breast ultrasound images including identification of regions suspicious for breast cancer and assessment of their malignancy. BU-CAD consists of a viewer, a lesion identification module, and a lesion analysis module. The lesion identification module identifies regions of interest (automated ROIs) of a single suspicious soft tissue lesion in up to two orthogonal views of breast ultrasound images for assisting users in detecting soft tissue lesions. Additionally, the lesion identification module generates an ROI and a lesion contour on each breast ultrasound image. The lesion analysis module analyzes given ROIs of a breast lesion on ultrasound images, and generates a score of lesion characteristics (SLC) in terms of malignancy or benignity of a lesion, BI-RADS category, and BI-RADS descriptors.	Koios DS is a 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. Koios DS software contains functionality for automatically classifying thyroid nodules suspicious for cancer. The system generates an output aligned to either the TI-RADS or ATA classification guidelines. The system automatically generates user-modifiable thyroid nodule descriptors (Composition, Echogenicity, Shape, Margin, Echogenic Foci) and a direct, image-derived cancer risk assessment that is translated into an optional lexicon-specific (TI-RADS or ATA) modifier.
Anatomical Location	Thyroid	Breast	Thyroid and Breast
Input	Medical images provided in a DICOM format	Medical images provided in a DICOM format	Medical images provided in a DICOM format

	Subject Device **See-Mode Augmented Reporting Tool, Thyroid (SMART-T)** **(K240697)**	**Predicate Device** **BU-CAD (K210670)**	**Reference Device** **Koios DS (K212616)**
Output	ROIs placed on thyroid nodules TI-RADS lexicon descriptors TI-RADS category according to the ACR TI-RADS chart	ROIs and lesion contours placed on suspicious soft tissue lesion BI-RADS lexicon descriptors A region-based score of lesion malignancy BI-RADS category	**<u>Thyroid</u>** TI-RADS lexicon descriptors based on user-selected ROIs TI-RADS category according to the ACR TI-RADS chart A direct, deep-learning derived cancer risk assessment that is translated into an optional lexicon-specific modifier. The software's direct, non-descriptor-based cancer risk assessment is presented as the Koios "AI Adapter" that can be used in conjunction with the ACR TI-RADS or ATA guidelines for nodule risk stratification **<u>Breast</u>** Categorical and continuous outputs (confidence level indicator) that align to BI-RADScategories Auto classification of BI-RADS lexicon descriptors (shape and orientation)
Operating Platform	Client-server technology.	Client-server technology	Client-server technology
Image Format	DICOM	DICOM	DICOM
2D viewing capabilities	Yes	Yes	Yes
Image storage and report generation	Yes	Yes	Yes

6.3. Comparison with Predicate and Reference Devices

Similarities

- **Intended Use**: The intended use of SMART-T is the same as that of the legally marketed predicate device, BU-CAD. Both are intended to be used by clinicians interpreting radiological images to help them localize and characterize soft tissue lesions. SMART-T and the predicate device are both intended to be used concurrently with the reading of images and are not intended as a replacement for the review of a clinician or their clinical judgment.

- **Target Population:** SMART-T, BU-CAD, and Koios DS share the same intended population. All devices are intended to be used for assisting trained interpreting clinicians in analyzing patients with soft tissue lesions or suspicious nodules that are being referred for diagnostic ultrasound examination.

- **Localization and Characterization:** See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is similar to BU-CAD, the legally marketed predicate device, in its intent to localize soft tissue lesions in ultrasound images. While the reference Koios DS device analyzes thyroid lesions, it relies on users to manually identify the nodules, whereas the subject device automatically localizes the nodules.

  Additionally, similar to the predicate and reference devices, the subject device characterizes nodules based on lexicon descriptors. The subject device (SMART-T), predicate device (BU-CAD), and reference device (Koios DS) all use established classification systems for their ultrasonographic lexicon descriptors. They all use the American College of Radiology Systems for describing soft tissue lesions or nodules. The ACR atlases provide standardized imaging terminology, report organization, assessment structure, and a classification system, which enables radiologists to communicate results clearly and consistently. The predicate BU-CAD device uses ACR BI-RADS for breast ultrasound images. Both SMART-T and the reference Koios DS device use ACR TI-RADS for analyzing and reporting thyroid ultrasound images.

  Both BU-CAD and SMART-T automatically localize soft tissue findings, with the findings classified in line with lexicon descriptors. Similar to BU-CAD, our subject device provides automatic regions of interest (ROIs), rather than manually selected, to localize thyroid nodules. The ROI highlights the bounding box around the detected nodules for the user to easily review and make their own assessment.

- **Performance Testing**: When comparing clinical validation between SMART-T, BU-CAD and Koios DS, the devices were evaluated using similar endpoints in their clinical studies. The Area Under the Curve (AUC) shift was used when comparing the performance of users with and without the aid of the device.

The number of cases evaluated in the MRMC reader study for BU-CAD was 628, the number of cases for Koios DS was 650 and the reader study for SMART-T included 600 cases. The number of readers included in the BU-CAD reader study was 16 (14 radiologists and 2 breast surgeons), the number of readers for Koios DS was 15 (14 radiologists and 1 endocrinologist) and the number of readers for SMART-T was 18 (all radiologists).

Following the primary endpoint, the AUC shift between predicate and subject device was similar. Similarly, the MRMC for BU-CAD showed an improvement of readers' determination of BI-RADS descriptors (Shape, Orientation, Margin, Echo Pattern, and Posterior Features) for at least one or more subcategories for each descriptor. The MRMC study for SMART-T, however, showed reader improvement in all TI-RADS descriptors (Composition, Echogenicity, Shape, Margin and Echogenic Foci).

The SMART-T MRMC reader study demonstrated substantially equivalent performance to BU-CAD and Koios DS by showing similar study design, success criteria and performance.

Differences

- **Anatomical Regions:** BU-CAD is specifically focused on breast ultrasound images, whereas See-Mode Augmented Reporting Tool, Thyroid (SMART-T) analyzes thyroid ultrasound images. This is aligned with our reference device, Koios DS, which assesses and characterizes both breast lesions and thyroid nodules using ultrasound image data. SMART-T localizes thyroid nodules and characterizes the nodule with their lexicon descriptors (composition, echogenicity, shape, margin, echogenic foci) in line with ACR TI-RADS.

- **Modality**: Contrary to BU-CAD and Koios DS, SMART-T only interprets ultrasound images. SMART does not analyze mammography images or other multi-modality digital images.

The technological characteristics of the subject device and its predicate and reference device have been evaluated to determine equivalence. Upon reviewing and comparing intended use, design, materials, principle of operation, and overall technological characteristics, the subject device is determined to be substantially equivalent to predicate and reference devices.

Both devices (subject device and predicate) have the same intended use and are indicated for the same use. The subject device uses standard principles of operation, methods, and algorithms for processing, measurement, and quantification of the images and is intended to be used by trained professionals, which is similar to the predicate and reference devices.

The comparison of technological characteristics, non-clinical performance data, clinical data, and software validation data demonstrate that See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is as safe and effective when compared to the predicate and reference devices that are currently marketed for similar intended use and indications for use. The table above provides a comparison between the proposed subject device, the predicate device, and the reference device.

7. PERFORMANCE DATA - CLINICAL AND BENCH TESTING

The performance of our device has been validated both in an MRMC reader study and standalone, as described below:

- Standalone Study: To evaluate the standalone performance of our device, where the output of the models are directly compared against ground truth labels.

- Multi-reader Multi-Case (MRMC) Study: To compare the performance of expert readers (radiologists) with and without the aid of our device. The study evaluated the readers' localization and characterisation of thyroid nodules in scenarios both unaided and aided. In the MRMC study, we had 18 radiologists read 600 cases from 600 patients twice, once with the aid of the device and once without. There was a one-month washout period in between the two reads.

To ensure the generalizability and satisfactory performance of our models on new, unseen data, all cases in our MRMC study were sourced from institutions or sources not part of the model training or development datasets. The preceding results of this study, demonstrating the models' success with data from novel institutions, have been presented.

The performance of the device was evaluated across different sub-groups of patient sex, patient age, nodule size, ultrasound machine, data sources (US vs. Non-US), reader category (US vs. Non-US), and reader experience.

Data Selection

The dataset has been collected retrospectively from thyroid ultrasound images of patients who have been referred for an ultrasound examination. The study consisted of 600 cases from unique patients with 74% of the data acquired from the US. The age range is respective of the target population with an 81.5% female cohort. The ethnicity distribution in our dataset is representative of the broader US population.

The cases in the dataset contained both negative and positive biopsy results with all TI-RADS levels represented. The data is sampled such that the distribution of the data accounts for patient sex, age, nodule size, malignancy, a priori clinical ACR TI-RADS level and a minimum sample is present for each subgroup. The data was curated from images sourced from accepted ultrasound systems, such as GE Healthcare, Philips Medical Systems and Siemens Medical Systems.

The patient distribution of the dataset:

- Patient sex
    - Female: 489 cases
    - Male: 111 cases
- Patient age
    - <30 years: 29 cases
    - 30-49 years: 131 cases
    - 50-69 years: 320 cases
    - 70+ years: 120 cases

Reader Selection

The study consisted of 18 board-certified radiologists with experience ranging from 0 to 11 + years. All readers were trained and used the American College of Radiology guidelines for interpreting thyroid ultrasound studies. Each reader was asked to identify the nodule, select TI-RADS lexicon descriptors, select TI-RADS category, and a nodule suspicion score with and without the aid of the subject device.

Establishing ground truth

In both the standalone and the MRMC study we evaluated the performance of our software on localisation, TI-RADS descriptors, and FNA outcomes. The ground truthing approach for each is described below:

- Ground truth labels of benign or malignant status were assigned to the nodule for each case, sourced from the reference standard of FNA or 2 year follow-up for benign status.

- The ground truth labels for localisation, ACR TI-RADS lexicon descriptors, and TI-RADS level agreement were based on the labels of two expert US-board certified radiologists and an adjudicator (also US-board certified radiologist with the most years of experience). This allowed for evaluating the accuracy of the readers in aided

and unaided fashion, as well as evaluating the standalone performance of the device in localisation and classifying nodules against ground truth labels.

Performance improvement with LROC

Given that our device is intended for both localisation and characterisation, LROC analysis together with AULROC and LROC curves are essential for evaluating the performance of our device.

The results of the LROC analysis are shown in the table below. We have considered IOU > 0.5 as the criterion for successful location detection in the LROC analysis. In this analysis, the malignant cases where the detection IOU is below or equal to 0.5 are penalised as false negative.

IOU Criteria	Average Aided AUC (95% CI)	Average Unaided AUC (95% CI)	Standalone (95% CI)
IOU > 0.5	0.758 (0.711, 0.803)	0.736 (0.693, 0.780)	0.703 (0.642, 0.762)

To provide a comprehensive analysis and evaluate the performance of our device with various IOU thresholds, we have obtained AULROCs for different IOU thresholds ranging from 0.5 to 0.8 with 0.1 increments as shown in the table below. It was observed that the use of the device results in an improved AULROC performance for the readers across different IOU thresholds. Specifically, AULROC is improved significantly when applying more rigorous IOU criteria (>0.6, >0.7, and >0.8), showing the promise of the device to improve readers' performance.

	Average Reader AUC (95% CI)		
Analysis	**Aided**	**Unaided**	**Difference (Aided – Unaided)**
AURLOC			
IOU > 0.5	0.758 (0.711, 0.803)	0.736 (0.693, 0.780)	0.022 (-0.012, 0.056)
IOU > 0.6	0.734 (0.682, 0.781)	0.682 (0.632, 0.730)	0.052 (0.008, 0.093)
IOU > 0.7	0.686 (0.629, 0.740)	0.548 (0.490, 0.610)	0.138 (0.082, 0.195)
IOU > 0.8	0.593 (0.529, 0.658)	0.356 (0.293, 0.423)	0.237 (0.168, 0.307)

Identification and localisation of nodules

To evaluate the localisation performance of the device, we calculated the average accuracy of the readers on localisation in aided and unaided scenarios, as well as the standalone performance. Localisation accuracy for each reader is calculated as the number of cases

where the reader's bounding box has an overlap greater than 0.5 with the ground truth, divided by the total number of cases.

	Average Aided (95% CI)	Average Unaided (95% CI)	Standalone (95% CI)
Localisation Accuracy	95.6% (94.1, 97.0)	93.6% (92.1, 95.0)	95.1%

As demonstrated in the table above, the aid of our device results in superior performance of the readers for localising thyroid nodules. It was also observed that the results of the algorithm are consistent across different sub-groups.

Thyroid lexicon descriptors

Aside from localisation, the other output of our device is characterisation of thyroid nodules according to ACR TI-RADS lexicon descriptors. In the table below, we have calculated the accuracy of the readers in determining each of the ACR TI-RADS descriptors (composition, echogenicity, shape, margin, and echogenic foci). We have also evaluated the standalone performance of the device on TI-RADS lexicon descriptors. As described above, the ground truth for the TI-RADS descriptors is the consensus labels of two expert US-board certified radiologists and an adjudicator (also US-board certified radiologist with the most years of experience).

TI-RAD Descriptor	Average Aided (95% CI)	Average Unaided (95% CI)	Standalone (95% CI)
Composition	84.9% (82.2, 87.5)	80.4% (77.3, 83.4)	86.7%
Echogenicity	77.4% (74.4, 80.3)	70.0% (67.0, 72.8)	68.2%
Shape	90.8% (88.2, 93.1)	86.4% (83.7, 88.8)	93.4%
Margin	73.5% (70.2, 76.7)	57.3% (53.3, 61.2)	58.4%
Echogenic Foci	75.2% (71.9, 78.5)	71.1% (67.1, 74.9)	70.3%

As can be seen from the table above, the device provides significant improvement and achieves superiority for characterizing all lexicon descriptors according to ACR TI-RADS. It

was also observed that the results of the algorithm are consistent across different sub-groups.

Attaining superiority across all TI-RADS descriptors is a strong proof point for the performance of our device, as it aligns with its primary function and intended use according to the ACR TI-RADS guideline.

TI-RADS level agreement

The accuracy of TI-RADS (TR) levels is critical as it directly informs clinical decisions regarding patient management according to the ACR TI-RADS guideline. To evaluate the impact of our device on TR level agreement, we have compared the overall TR level agreement percentage of each of the readers against the ground truth in both aided and unaided scenarios. As described above, the ground truth for the TI-RADS descriptors and, therefore the TR level, is based on the consensus labels of two expert US-board certified radiologists and an adjudicator (also US-board certified radiologist with the most years of experience).

To further evaluate the level of agreement, we also calculated the agreement for each TR level (TR-1 to TR-5). The agreement percentage for each TR level for each reader is calculated by dividing the number of cases where a reader's TR level matches the ground truth TR level by the total number of cases with that specific TR level. The average TR level agreement is then calculated as the average over all the readers.

TI-RADS	Average Aided (95% CI)	Average Unaided (95% CI)	Standalone (95% CI)
Overall	60.0% (56.8, 63.3)	51.1% (47.8, 54.5)	63.8 (60.0, 67.7)
TR-1	59.0% (42.3, 74.9)	52.9% (37.3, 68.3)	61.9 (40.0, 82.6)
TR-2	38.1% (31.1, 45.6)	31.2% (24.6, 38.1)	41.1 (31.7, 50.4)
TR-3	68.9% (62.6, 74.9)	58.8% (52.2, 65.4)	71.7 (64.9, 78.3)
TR-4	61.4% (56.5, 66.3)	52.1% (47.2, 57.0)	65.5 (59.1, 71.6)
TR-5	71.3% (61.8, 80.5)	62.0% (52.2, 71.5)	77.0 (66.1, 87.3)

The table above highlights a significant improvement in TR level agreement among readers with the use of the device. It is important to note that TR level agreement has been improved across all TR levels, from TR-1 to TR-5, with particularly significant gains at higher TR levels (TR-3, TR-4, and TR-5). Notably, these higher TR levels (TR-3 to TR-5) are the levels that are of high clinical importance with follow-up or FNA considerations. It was also observed that the results of the algorithm are consistent across different sub-groups.

Subgroup analysis

Subgroup analysis of patient sex (female, male), patient age (<30, 30-49, 50-69, 70+), nodule size (<10mm, 10-15mm, 15-20mm, 20-25mm, >=25mm), ultrasound machine (GE, Philips, Samsung, Siemens, Canon/Toshiba), reader category (US/Canada, Non-US/Canada), reader experience (0-3 years, 4-7 years, 8-10 years, >=11 years), and source of data (US, non-US) from the MRMC reader study were performed. The readers aided by SMART-T achieved consistent performance across all of the subgroups.

Conclusion

The results of our MRMC reader study shows improvement in reader performance with the aid of our device. Based on these results it was observed that the use of the device results in superior performance of the readers on nodule localisation, TI-RADS lexicon characterisation, and TR level agreement. The use of the device can also improve the performance of the readers with regards to malignancy and benignity status.

The standalone performance of the device is also on-par with the aided use of our device, indicating the validity of our algorithms. The outputs of our study are in line with the intended use of See-Mode Augmented Reporting Tool, Thyroid.

8. NON-CLINICAL DATA

The design and development of SMART-T has been implemented according to recognised standards. See-Mode Technologies has performed software verification and validation testing for the subject device according to the FDA's guidance document "Content of Premarket Submissions for Device Software Functions," as well as "IEC 62304:2006/AC: 2015 - Medical Device Software - Software Lifecycle Processes". Special Controls were added according to 21 CFR 892.2090, "DEN180005 Evaluation of automatic class III designation for OsteoDetect – Decision summary with special controls".

The risk analysis was completed and the hazard risk analysis has been submitted as part of this application. It has been observed that all the risks identified with the subject device are acceptable and have been reduced as far as possible in accordance with ISO 14971:2019 Medical devices - Application of risk management to medical devices.

9. CONCLUSIONS

A detailed analysis has been conducted between See-Mode Augmented Reporting Tool, Thyroid (SMART-T) and its predicate and reference devices. It is noted that no new additional questions of safety and effectiveness are raised by these technologies. Through reviewing the similarities and differences of the intended use, technological characteristics and principles of operation, as well as assessing the clinical and non-clinical performance data, See-Mode Augmented Reporting Tool, Thyroid (SMART-T) is as safe, as effective and performs as well as the predicate and reference devices.