March 1, 2024

MRIguidance B.V
℅ Sujith Shetty
Executive Vice President
Maxis Medical
3031 Tisch Way
Suite 1010
San Jose, California 95128

Re: K233030
Trade/Device Name: BoneMRI
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: QIH
Dated: January 17, 2024
Received: January 22, 2024

Dear Sujith Shetty:

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.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

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

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn

(https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Daniel M. Krainak, Ph.D.
Assistant Director
DHT8C: Division of Radiological Imaging
and Radiation Therapy Devices
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K233030

Device Name
BoneMRI

Indications for Use *(Describe)*
BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with increased contrast with respect to the surrounding soft tissue.
It is to be used in the pelvic region, which includes the bony anatomy of the sacrum, hip bones and femoral heads; and the spine, which includes the bony anatomy of the cervical, thoracic, lumbar, and S1 vertebrae. BoneMRI is indicated for use in patients 12 years and older.

BoneMRI is not to be used for diagnosis or monitoring of (primary or metastatic) tumors. BoneMRI images are not intended to replace CT images in general but can be used to visualize 3D bone morphology, tissue radiodensity and tissue radiodensity contrast.

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

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510(k) Summary

1. 510(k) Information

510(k) Number:	K233030
Date Prepared:	February 26, 2024
510(k) Submitter:	MRIguidance B.V. Maliesingel 23, 3581 BG Utrecht, the Netherlands
510(k) Submitter Contact Person:	David Sparks Head of Regulatory Affairs MRIguidance B.V. Email: david.sparks@mriguidance.com Tel: +31 681741711
Correspondent Contact Person:	Dr. Sujith Shetty EVP Maxis Medical 3031 Tische Way, Suite 1010 San Jose, CA 95128 USA Email: sjshetty@maxismedical.com

2. Device Information

Device Trade Name:	BoneMRI
Device Common Name:	MRI image enhancement software
Device Classification Name:	Medical image management and processing system (21 CFR 892.2050)
Device Classification:	Class II
Product Code:	QIH

3. Predicate Device

Device Trade Name:	BoneMRI
Manufacturer:	MRIguidance B.V.
Device 510(k) Clearance:	K230197
Device Classification Name:	Medical image management and processing system (21 CFR 892.2050)
Device Classification:	Class II
Product Code:	QIH

4. Device Description

The BoneMRI application is a standalone image processing software application that analyses 3D gradient echo MRI scans acquired with a dedicated MRI scan protocol. From the analysis of the gradient echo MRI scan, 3D tomographic radiodensity contrast images, called BoneMRI images, are constructed.

The BoneMRI images can be used to visualize the bone structures in MR images with enhanced contrast with respect to the surrounding soft tissue. The application is designed to be used by imaging experts, such as radiologists or orthopedic surgeons, typically in a physician's office.

The BoneMRI application is a server application running on the clinic or hospital networks. It is available as fully on-premise software with specific GPU hardware requirements, or partly running as a managed cloud service, for which the environment in which the managed modules run is controlled by MRIguidance. The on-premise software is fully controlled by the clinic or hospital, and as such, no protected health information (PHI) will leave the clinic or hospital network. All data sent to the managed cloud server will be de-identified before it leaves the clinic or hospital network, and as such, the managed cloud service will not receive PHI.

Within the hospital network, the application communicates with a DICOM compatible imaging archive (e.g., a PACS) to receive input MRI and to return BoneMRI images. Reading of the resulting BoneMRI images is performed using regular DICOM compatible medical image viewing software.

The BoneMRI application uses an algorithm to detect bone images from MRIs obtained using a specific gradient echo acquisition sequence. The algorithm training sets included images from multiple clinical sites, multiple anatomies, and multiple scanners to ensure that the trained algorithm was robust with respect to the approved indications for use. None of the data used in the training dataset was used subsequently in the validation dataset.

5. Indications for Use

BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with increased contrast with respect to the surrounding soft tissue. It is to be used in the pelvic region, which includes the bony anatomy of the sacrum, hip bones and femoral heads; and the spine, which includes the bony anatomy of the cervical, thoracic, lumbar, and S1 vertebrae. BoneMRI is indicated for use in patients 12 years and older.

BoneMRI is not to be used for diagnosis or monitoring of (primary or metastatic) tumors. BoneMRI images are not intended to replace CT images in general but can be used to visualize 3D bone morphology, tissue radiodensity and tissue radiodensity contrast.

6. Comparison of Technological Characteristics with the Predicate Device

A comparison of the intended use, indication for use, and technological characteristics of the subject BoneMRI application to the predicate device (BoneMRI v1.6, K230197) is presented below. We have included the attributes suggested in the July 2018 Guidance *"The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications"* for this comparison.

Table 1 Predicate device comparison

	Predicate Device (BoneMRI K230197)	Subject Device (BoneMRI)	Comment
Intended use			
Intended Use	BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with enhanced contrast with respect to the surrounding soft tissue.	BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with enhanced contrast with respect to the surrounding soft tissue.	The same
21CFR Section	829.2050	829.2050	The same
Product Code	QIH	QIH	The same
Target Population	Adults	Adolescents and Adults	Different
Indications for Use	BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with enhanced contrast with respect to the surrounding soft tissue. It is to be used in the pelvic region, which includes the bony anatomy of the sacrum, hip bones and femoral heads; and the lumbar spine region, which includes the bony anatomy of the vertebrae from L3 to S1. BoneMRI is not to be used for diagnosis or monitoring of (primary or metastatic) tumors. Warning: BoneMRI images are not intended to replace CT images.	BoneMRI is an image processing software that can be used for image enhancement in MRI images. It can be used to visualize the bone structures in MRI images with increased contrast with respect to the surrounding soft tissue. It is to be used in the pelvic region, which includes the bony anatomy of the sacrum, hip bones and femoral heads; and the spine, which includes the bony anatomy of the cervical, thoracic, lumbar, and S1 vertebrae. BoneMRI is indicated for use in patients 12 years and older. BoneMRI is not to be used for diagnosis or monitoring of (primary or metastatic) tumors. BoneMRI images are not intended to replace CT images in general but can be used to visualize 3D bone morphology, tissue radiodensity and tissue radiodensity contrast.	Similar

Technological Characteristics			
Device Nature	Software package	Software package	The same
Operating System	Linux	Linux	The same
Data Input	MRI images in DICOM format	MRI images in DICOM format	The same
Data Output	MRI images in DICOM format	MRI images in DICOM format	The same
Processing Algorithms	MRIguidance software implements an image enhancement algorithm using convolutional neural network. Original images are enhanced by running them through a cascade of filter banks, where thresholding and scaling operations are applied. Separate neural network-based filters are obtained to assign a Hounsfield Unit (HU) value to a single volume element, based on intensity and contextual information. The parameters of the model were obtained through an algorithm development pipeline.	MRIguidance software implements an image enhancement algorithm using convolutional neural network. Original images are enhanced by running them through a cascade of filter banks, where thresholding and scaling operations are applied. Separate neural network-based filters are obtained to assign a Hounsfield Unit (HU) value to a single volume element, based on intensity and contextual information. The parameters of the model were obtained through an algorithm development pipeline.	The same
User Interface	None – enhanced images are viewed on existing PACS workstations.	None – enhanced images are viewed on existing PACS workstations.	The same
Workflow	The software operates on DICOM files on the file system, enhances the images, and stores the enhanced images on the file system. The receipt of original DICOM image files and delivery of enhanced images as DICOM files depends on other software systems. Enhanced images co-exist with the original images.	The software operates on DICOM files on the file system, enhances the images, and stores the enhanced images on the file system. The receipt of original DICOM image files and delivery of enhanced images as DICOM files depends on other software systems. Enhanced images co-exist with the original images.	The same

7. Summary of Changes

The changes to the BoneMRI application from the predicate device (BoneMRI v1.6, K230197) to the subject device are detailed in the table below.

Table 2 Summary of changes for the BoneMRI application

Change	Change Description
Software architecture	Refactor of the application workflow; introducing multi-tenancy capabilities; and improving scalability of cloud deployment.
Validation strategy	Revision of the validation strategy to support the validation of a multi-vendor, multi-field strength algorithm.
Intended patient population	The intended patient population of BoneMRI is extended to include adolescents. The algorithm for the application has not been changed.
Predetermined Change Control Plan	Addition of a Predetermined Change Control Plan to support an iterative development approach for the machine learning models in the BoneMRI application.
Algorithm for the Spine region	The algorithm for the Spine region has been re-trained. With additional data for training and testing, the anatomical region of the algorithm was extended to include the Cervical Spine and the Thoracic Spine in addition to the Lumbar Spine.
Algorithm for the Pelvic region	No changes are made to the algorithm for the Pelvic region. Updates have been made to improve statistical testing of the algorithm and to test the algorithm on additional subgroups.

8. Predetermined Change Control Plan

The BoneMRI application uses an algorithm derived from machine learning (ML) to detect bone images from MRIs obtained using a specific gradient echo acquisition sequence. The algorithm training sets included images from multiple clinical sites, multiple anatomies, and multiple scanners to ensure that the trained algorithm was robust with respect to the approved indications for use. MRIguidance will make future algorithm improvements under a Predetermined Change Control Plan (PCCP). In that plan, a protocol is provided to mitigate the risks of the algorithm changes leading to changes in the device's technical specifications or negatively affecting performance specifications directly associated with the indications for use of the device. Changes made under this PCCP are detailed in the table below. In accordance with the PCCP, all algorithm modifications will be trained, tuned, and locked prior to release of the application.

Table 3 Summary of changes under a Predetermined Change Control Plan

Modification	Rationale
1. Re-training to improve ML model performance with additional training data	Re-training of the ML model with additional data to increase the safety and performance of the device in any of the following categories: • Increased accuracy; • Increased performance for challenging cases such as rare pathologies or artifacts; • Increased robustness and generalization of the model.
2. Validation of additional scanner support	Validation of the ML model (either with or without additional re-training of the ML model) in order to validate an additional MRI vendor or field strength.

9. Performance Data

The following performance testing has been performed on BoneMRI:

1. Software verification and validation testing
2. Studies that utilized retrospective clinical data to demonstrate the software enhanced imaging quality in MR images via an enhancement of bone validated with CT.

Software Verification and Validation Testing

Software verification and validation testing were conducted, and documentation was provided as recommended by FDA's Guidance for Industry and FDA Staff, "*Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*" dated June 14, 2023.

Performance Validation

A quantitative voxel-by-voxel validation of BoneMRI was performed on imaging data from 76 patients (pelvic region) and 117 patients (spine region), consisting of the BoneMRI and CT of the same patient in the same anatomical region, acquired using standard of care bone imaging protocols during previously conducted clinical investigations. Test data are acquired at different medical sites, departments or within different clinical studies than training data, and test data is unseen data that was not used in any way during developments. The validation was conducted by MRIguidance based on an algorithm to detect bone images from MRIs obtained using a specific gradient echo sequence. The demographics and performance data, including subgroup analysis of the patient population are described in the table below.

Table 4 Validation data demographics and performance testing. All statistical testing was with a significance level of p <0.05.

Subgroup		N	Gender	Age	Data origin	Cortical delineation error (mm)	Mean deviation in all tissue and bone (HU)	Correlation coefficient in bone
Total	**Pelvis**	76	75% M 25% F	53 ± 26	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Spine	117	49% M 51% F	48 ± 23	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
Adults	**Pelvis**	57	93% M 7% F	66 ± 17	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Spine	94	51% M 49% F	59 ± 16	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
Adolescents	**Pelvis**	19	21% M 79% F	17 ± 3	US	< 1 mm	< 25 HU < 55 HU	> 0.75
	Spine	23	22% M 78% F	15 ± 2	EU	< 1 mm	< 25 HU < 55 HU	> 0.75

US	**Pelvis**	25	24% M 76% F	18 ± 4	US	< 1 mm	< 25 HU < 55 HU	> 0.75
	Spine	23	33% M 67% F	64 ± 10	US	< 1 mm	< 25 HU < 55 HU	> 0.75
EU	**Pelvis**	51	100% M 0% F	71 ± 80	EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Spine	91	46% M 54% F	49 ± 23	EU	< 1 mm	< 25 HU < 55 HU	> 0.75
BMI	**Obese**	11	64% M 36% F	51 ± 16	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Over-weight	17	60% M 40% F	52 ± 18	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Healthy	18	22% M 78% F	29 ± 22	US, EU	< 1 mm	< 25 HU < 55 HU	> 0.75
	Under-weight	10	20% M 80% F	17 ± 3	EU	< 1 mm	< 25 HU < 55 HU	> 0.75

The objective was to validate the quantitative accuracy of BoneMRI using rigorous, objective, and unbiased statistical tests comparing bone morphology, radiodensity, and radiodensity contrast in BoneMRI and CT images. The endpoints of the testing were the metrics that describe the accuracy of 3D bone morphology, radiodensity, and radiodensity contrast versus co-registered CT scans in terms of voxel-by-voxel HUs and standard deviations around these HU values. Subgroup analyses for different MRI vendors, field strengths, age ranges, geographical locations and BMI was performed as part of the testing. The results demonstrated clinically acceptable accuracy on each of these endpoints.

The data provided demonstrate that BoneMRI application can:

- accurately reconstruct the 3D bone morphology with a mean absolute cortical delineation error below 1.0 mm on average;
- accurately reconstructs the tissue radiodensity, with a mean deviation below 25 HU on average and a mean deviation below 55 HU specifically for bone;
- accurately reconstructs the tissue radiodensity contrast, with a mean HU correlation coefficient above 0.75 specifically for bone.

The BoneMRI application demonstrates accurate bone morphology, radiodensity, and radiodensity contrast to qualitatively and quantitatively assess the bony anatomy of the pelvic and spine regions.

10. Substantial Equivalence Conclusion

The subject BoneMRI application has the same intended use and a similar indication as the identified predicate device, its predecessor (BoneMRI, K230197). The technological features of the BoneMRI application are the same as the identified predicate device. Therefore, we conclude that the BoneMRI application is substantially equivalent to the identified predicate device.