



August 21, 2024

Subtle Medical, Inc.
% Jared Seehafer
Regulatory Consultant
Enzyme Corporation
611 Gateway Blvd Ste 120
South San Francisco, California 94080

Re: K240290

Trade/Device Name: AiMIFY (1.x)
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: LLZ
Dated: July 18, 2024
Received: July 18, 2024

Dear Jared Seehafer:

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,

A handwritten signature in black ink, appearing to read "Douglas W. Fletcher".

Digitally signed by
Douglas W. Fletcher -S

for

Daniel M. Krainak, Ph.D.

Assistant Director

Magnetic Resonance and Nuclear Medicine Team

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

Indications for Use

510(k) Number (if known)

K240290

Device Name

AiMIFY (1.x)

Indications for Use (Describe)

AiMIFY is an image processing software that can be used for image enhancement in MRI images. It can be used to increase contrast-to-noise ratio (CNR), contrast enhancement (CEP), and lesion-to-brain ratio (LBR) of enhancing tissue in brain MRI images acquired with a gadolinium-based contrast agent. It is intended to enhance MRI images acquired using standard approved dosage per the contrast agent's instructions for use.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

AiMIFY 510(k) Summary

Table 1. Contact Details & Device Name

Date Summary Prepared:	2024-08-20
<u>Contact Details</u>	
Applicant Name:	Subtle Medical, Inc.
Applicant Address:	883 Santa Cruz Ave, Suite 205 Menlo Park, CA 94025 United States
Applicant Contact:	Ms. Ronny Elor
Applicant Contact Telephone:	(925) 324-8467
Applicant Contact Email:	ronny@subtlemedical.com
Correspondent Name:	Enzyme Corporation
Correspondent Address:	611 Gateway Blvd, Ste 120 South San Francisco, CA 94080 United States
Correspondent Contact:	Mr. Jared Seehafer
Correspondent Contact Telephone:	(415) 638-9554
Correspondent Contact Email:	jared@enzyme.com
<u>Device Name</u>	
Device Trade Name:	AiMIFY (1.x)
Common Name:	Medical image management and processing system
Classification Name:	System, Image Processing, Radiological
Regulation Number:	892.2050
Product Code:	LLZ
Device Class:	Class II
Legally Marketed Predicate Device:	Predicate #: K223623 Predicate Trade Name: SubtleMR Predicate Manufacturer: Subtle Medical

Device Description Summary

The AiMIFY device is a software as a medical device consisting of a machine learning software algorithm that enhances images taken by MRI scanners. AiMIFY consists of a software algorithm that improves contrast-to-noise ratio (CNR), contrast enhancement (CEP), and lesion-to-brain ratio (LBR) of Gadolinium-Based Contrast Agent (GBCA) enhanced T1-weighted images while maintaining diagnostic performance, using deep learning technology. It is a post-processing software that does not directly interact with the MR scanner and does not have a graphical user interface. It is intended to be used by radiologists in an imaging center, clinic, or hospital. The AiMIFY software uses T1 pre and post-contrast MR images acquired as part of standard of care contrast-enhanced MRI exams as the software input. The outputs are the corresponding images with enhanced contrast presence. AiMIFY enhances DICOM images.

AiMIFY image processing software uses a convolutional neural network based algorithm to enhance the AiMIFY-contrast images from pre-contrast and standard-dose post-contrast images. The image processing can be performed on MRI images with predefined or specific acquisition protocol settings as follows: gradient echo (pre- and post-contrast), 3D BRAVO (pre- and post-contrast), 3D MPRAGE (pre- and post-contrast), 2D T1 spin echo (pre- and post-contrast), T1 FLAIR/ inversion recovery spin echo (pre- and post-contrast).

The AiMIFY image is created by AiMIFY and sent back to the picture archiving and communication system (PACS) or other DICOM node by the compatible MDDS for clinical review.

Because the software runs in the background, it has no user interface. It is intended to be used by radiologists in an imaging center, clinic, or hospital.

Note, depending on the functionality of the compatible MDDS, AiMIFY can be used within the facility's network or remotely. The AiMIFY device itself is not networked and therefore does not increase the cybersecurity risk of its users. Users are provided cybersecurity recommendations in labeling.

Intended Use / Indications for Use

AiMIFY is an image processing software that can be used for image enhancement in MRI images. It can be used to increase contrast-to-noise ratio (CNR), contrast enhancement (CEP), and lesion-to-brain ratio (LBR) of enhancing tissue in brain MRI images acquired with a gadolinium-based contrast agent. It is intended to enhance MRI images acquired using standard approved dosage per the contrast agent's instructions for use.

Intended Use / Indications for Use Comparison

AiMIFY and SubtleMR are both intended to enhance 2D/3D T1 imaging data from MRI imaging systems.

Technological Comparison

The following table shows the similarities and differences between the technological characteristics of the predicate and subject devices.

Table 2. Summary of Technological Characteristics Comparison

Topic	Predicate Device	Subject Device
Physical Characteristics	Software package that operates on off-the-shelf hardware	Same
DICOM Standard Compliance	The software processes DICOM compliant image data	Same
Operating System	Linux	Same
Modalities	MRI	Same
User Interface	None – enhanced images are viewed on existing PACS workstations	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.	Same
Algorithm	SubtleMR implements an image enhancement algorithm using convolutional neural network based filtering. Original images are enhanced by running through a cascade of filter banks, where thresholding and scaling operations are applied. Separate neural network based filters are obtained for noise reduction and sharpness increase. The parameters of the filters were obtained through an image-guided optimization process.	AiMIFY implements an image enhancement algorithm using convolutional neural network based filtering. The model performs non-linear scaling of the contrast uptake between the pre- and post-contrast images to improve the visualization of the areas in the brain that have absorbed the contrast material.
Inputs	SubtleMR processes a single input image (with low SNR or low resolution) and outputs a single image with higher SNR or resolution.	AiMIFY processes two input images (T1 pre-contrast and T1 post-contrast) and outputs a single image with a higher relative CNR.
Processing	SubtleMR processes the input image slice by slice in a 2D fashion using a ResNET style neural network.	AiMIFY processes the input image in a 2.5D fashion using a UNet style neural network.

Fundamentally, both devices enhance images from input data provided by MR imaging systems. Though there are technological differences, they do not present different questions of safety and effectiveness, and the methods for assessing the safety and effectiveness of the subject device are substantively similar to those of the predicate device.

Predetermined Change Control Plan

AiMIFY has a Predetermined Change Control Plan for planned changes to improve the generalizability of the AiMIFY Artificial Intelligence/Machine Learning (AI/ML) model, to reduce processing time, and improve perceived image quality.

Improved generalizability of the AiMIFY AI/ML model is expected to affect the labeled limitations of AiMIFY, as the model will be more generalizable than the cleared version of the device. Improvements planned include additional training and/or performance data to add more gadolinium-based contrast agents, add additional patient ages (infants and children), add additional clinical conditions, and add additional scanner models. The AiMIFY AI/ML model is planned to be retrained with additional output channels to reduce processing time, and shall be subject to the same performance testing endpoints and acceptance criteria as the cleared version of the device.

Additionally, an optional pre-processing feature is planned that consists of an algorithm which will suppress vessel enhancement of the AiMIFY AI/ML model to reduce vessel conspicuity in the AiMIFY-enhanced images and resulting in improved perceived image quality. The vessel suppression algorithm shall be subject to the same performance testing performance testing endpoints and acceptance criteria as the cleared version of the device, along with the additional endpoints that lesions in AiMIFY-enhance images with vessel suppression should have equivalent CNR, LBR, CEP improvements than images without suppression and that the CNR, LBR, CEP around small and large blood vessels are lower in AiMIFY-enhance images with vessel suppression than without. The vessel suppression algorithm shall be subject to the same performance testing dataset used in the cleared version of the device, along with additional data containing lesions that appear like blood vessels to demonstrate that the vessel suppression algorithm doesn't incorrectly suppress enhancement of the lesion in this edge case situation.

All changes shall be performed as a part of Subtle Medical's Design Change Control process in a Quality Management System that is ISO 13485:2016 and MDSAP certified. All impacted design documentation, testing documentation, and labeling shall be updated appropriately for each change. None of the changes shall result in a change to the Indications for Use, Cautions, performance endpoints, or acceptance criteria of AiMIFY. Each change to AiMIFY shall be accompanied by a software version-specific Customer Release Notes describing the change along with software version-specific User Manual (with updated Limitations description if applicable) and other updated labeling.

Non-Clinical and/or Clinical Tests Summary & Conclusions

Dataset Characteristics:

The dataset used for the quantitative and qualitative tests consists of 95 T1 brain cases with a variety of protocols, contrast agent, MRI scanners, and patient demographics.

The images varied in acquisition including:

- T1 input protocols: BRAVO, MPRAGE+, FLAIR, FSE.
- Orientation: axial, sagittal, coronal
- Acquisition type: 2D, 3D

The images were acquired from various scanners:

- Field strength: 0.3T, 1.5T, 3.0T
- Vendors: GE, Philips, Siemens, Hitachi

The images were sourced from a variety of patients:

- Age: Relatively even distribution from age 7 to 86.
- Sex: Relative even distribution of females and males.
- Pathologies: Cerebritis, Glioma, Meningioma, Lymphoma, Metastases, Multiple Sclerosis, Neuritis, Inflammation, Other tumor related (resection / radiation necrosis / suspected cyst / etc.), other abnormalities
- Population Demographics*: California, USA; New York, USA; Nationwide, USA; Beijing, China

*Due to privacy practices, ethnicities of the training and testing data is unknown but can be inferred based on the population demographics from where they were sourced. The population demographics of data sources used for training and testing are as follows per the Census.gov July 2022 Estimates. In California, USA, the population of 39m people are distributed by race and hispanic origin as: White alone 70.7%, Black or African American alone 6.5%, American Indian and Alaskan Native alone 1.7%, Asian alone 16.3%, Native Hawaiian and Other Pacific Islander alone, percent 0.5%, Two or More Race 4.3%, Hispanic or Latino 40.3%, and White alone (not Hispanic or Latino) 34.7%. In New York, USA, the population of 20m people are distributed by race and hispanic origin as: White alone 68.6%, Black or African American alone 17.7%, American Indian and Alaskan Native alone 1%, Asian alone 9.6%, Native Hawaiian and Other Pacific Islander alone, percent 0.1%, Two or More Race 2.8%, Hispanic or Latino 19.7%, and White alone (not Hispanic or Latino) 54.2%. In the overall USA, the population of 333m people are distributed by race and hispanic origin as: White alone 75.5%, Black or African American alone 13.6%, American Indian and Alaskan Native alone 1.3%, Asian alone 6.3%, Native Hawaiian and Other Pacific Islander alone, percent 0.3%, Two or More Race 3%, Hispanic or Latino 19.1%, White alone (not Hispanic or Latino) 58.9%.

Quantitative Assessment (Bench Test):

In addition to software verification & validation, performance bench testing was conducted to demonstrate the safety and efficacy of applying AiMIFY to enhance contrasted images using a convolutional neural network on clinically acquired pre- and post-contrast brain images. To evaluate the performance of the software, Subtle quantitatively evaluated the 95 acquired studies recruited from clinical sites or hospitals. Of these cases, it was found during the Reader Study that 57 of them had lesions. The acquired studies include pre-contrast, post-contrast, and AiMIFY images from various sites, age ranges, manufacturers, scanner models, orientations, and magnitudes of field strengths. They were used to assess the superiority of the AiMIFY against the acquired post-contrast image using Contrast Enhancement Percentage (CEP), Contrast-to-Noise Ratio (CNR), and Lesion-to-Brain Ratio (LBR) to perform the analysis.

The **primary endpoint** of the quantitative test was that the CNR, LBR, and CEP of a selected region of interest (ROI) in each test dataset is on average improved by greater than or equal to 50% after AiMIFY enhancement compared to the traditionally acquired contrast images.

Two ROIs were drawn by a board-certified radiologist for each case to capture the enhancing lesion and brain parenchyma. An ROI was drawn at the superior sagittal sinus region without an enhancing lesion. The post-contrast image was labeled where the ROI was copied to the AiMIFY image with relevant metrics on the case. The ROI is designed to estimate the signal intensity value.

Contrast-to-Noise Ratio (CNR) was determined to be 559.94% across all 95 cases, and 831.70% for the 57 lesion-only cases. The CNR of the AiMIFY images is significantly higher (Wilcoxon signed-rank test, $p < 0.0001$) than that of the standard post-contrast images. The high increase of CNR of AiMIFY images compared to standard post-contrast images is due to the fact that both the contrast between a lesion and the normal parenchyma is increased by AiMIFY and also the noise of the images is reduced by the denoising module of AiMIFY.

Lesion-to-Brain Ratio (LBR) was determined to be 62.07% across all 95 cases, and 58.80% for the 57 lesion-only cases. The Contrast Enhancement Percentage (CEP) between the acquired post-contrast image and AiMIFY was determined to be 133.29% across all 95 cases, and 101.80% for the 57 lesion only cases. The LBR and the CEP metric of the AiMIFY images are both significantly better (Wilcoxon signed-rank test, $p\text{-value} < 0.0001$) than that of the standard post-contrast images. Both metrics are measuring the main effects of AiMIFY, which is the increase of signal intensity of enhancing tissue, measured as CEP and leading to higher LBR.

In summary, these results prove that the AiMIFY images are enhanced with the acquired post-contrast in terms of the signal intensity value from the brain parenchyma to the enhanced lesion.

Qualitative Assessment (Reader Study):

The AiMIFY Reader Study aimed to demonstrate image enhancement of contrasted MRI images by applying AiMIFY post-processing enhancement software using convolutional neural networks. Specifically, 3 board-certified neuro-radiologists evaluated the Perceived Visibility of anatomic features and lesions. The primary diagnostic categories were (1) Meningioma, (2) Glioma, (3) Lymphoma, (4) Metastases, (5) Infection, (6) Cerebritis, (7) Multiple Sclerosis, (8) Neuritis, (9) Other tumor-related (resection / radiation necrosis / suspected cyst / etc.), and (10) Other abnormality. The readers were presented with both the pre- and post-contrast input images and the AiMIFY enhanced image. Readers were asked to evaluate the Perceived Visibility of Lesion Contrast Enhancement, Lesion Border Delineation, and Lesion Internal Morphology on a 4-point Likert scale. Additionally, readers were asked to evaluate Perceived Image Quality, Artifact Presence, and Vessel Conspicuity on a 4-point Likert scale.

The **primary endpoint** of the qualitative test was the visibility of lesion features (lesion contrast enhancement, border delineation, and internal morphology) for cases with identified lesions in the test datasets should be statistically significantly better for AiMIFY processed images per the Wilcoxon signed rank test by $p < 0.05$.

Lesion Contrast Enhancement, Border Delineation, and Internal Morphology were significantly better than standard post-contrast by $p < 0.0001$. Therefore, results provide evidence that AiMIFY provides a significant improvement of lesion contrast enhancement, border delineation, and internal morphology visualization.

The **secondary endpoint** of the qualitative test was the visibility of perceived image quality and image artifacts for all cases in the test datasets for AiMIFY processed images should NOT be statistically significantly worse than standard post-contrast images per the Wilcoxon signed rank test by $p < 0.05$.

Perceived Image Quality and Artifact Presence And Impact On Clinical Diagnosis were significantly not worse than standard post-contrast by $p < 0.0001$. Additionally, two of three readers demonstrated that Perceived Image Quality is better than standard post-contrast by $p < 0.0001$. Therefore, these results provide evidence that AiMIFY does not have worse perceived image quality or artifacts that impact diagnosis, and may have higher perceived image quality.

In addition to the primary and secondary endpoints, the study contained several exploratory endpoints to characterize AiMIFY's performance.

Exploratory Endpoints:

Vessel Conspicuity

The first exploratory endpoint was the evaluation of user preference of vessel conspicuity for all cases in the test datasets for AiMIFY processed images to establish the limitations of AiMIFY.

Compared to 3.51% of standard post-contrast cases, 11.58% of AiMIFY cases were rated as likely to impact diagnosis due to vessel conspicuity. However, in 90% of cases vessel conspicuity was assessed as unlikely to impact or having no impact on diagnosis. This shows that the potential negative impact of the higher vessel conspicuity with AiMIFY is limited. Additionally, a further breakdown of results by reader revealed that there was significant variability in reader preference regarding vessel conspicuity.

False Lesion Analysis

The second exploratory endpoint was the evaluation of false lesion frequency, cause, and severity for all cases in the test datasets for AiMIFY processed images to establish a caution statement for AiMIFY.

73% of cases did not have false lesions, 4% of cases with false lesions did not have impact on diagnosis, 9% of cases with false lesions had minor impact on diagnosis, 14% of cases with false lesions had major impact on diagnosis (4% being due to false lesions that are introduced by AiMIFY, 2% due to quality of input images, and 8% being due to a combination of both causes). 100% of cases received scores from all readers that the Standard-of-Care image was sufficient to identify the false lesion(s).

Lesion Size

To establish the range of lesions that AiMIFY is validated to be used on the size of lesions in the 95 test subject validation datasets used for AiMIFY quantitative and qualitative assessment was performed.

AiMIFY has been validated with lesion sizes ranging from 1.23 cc to 7.08 cc with 95% CI, and has been tested on lesions as small as 0.02 cc and as large as 59.83 cc. AiMIFY processed images had greater lesion contrast enhancement than standard-of-care post-contrast images for both small lesions (<1cc: AiMIFY = 3.57 versus Original = 2.71) and large lesions (>1cc: AiMIFY = 3.77 versus Original = 3.23). This establishes the range of lesion sizes over which AiMIFY performance has been validated, and that enhancement is seen in both small (<1cc) and large (>1cc) lesions.

Radiomics

Radiomics analysis was performed to assess the similarity in the texture related features of the lesions as well as parenchyma tissue / healthy tissue, using the concordance correlation coefficient (CCC) as the metric, on 95 subject datasets (the same data from the AiMIFY Quantitative Assessment described above).

The similarity in the texture measured as Concordance Correlation Coefficient (CCC) between AiMIFY input and output images in seven radiomics feature classes were all ≥ 0.65 for lesion tissue. Specifically, the CCC in the seven radiomics feature classes ranged from 0.68 to 0.89, which are all ≥ 0.65 , for lesion tissue. Seven radiomics feature classes of SOC and AiMIFY-enhanced have a good correlation for lesion tissue.

The similarity in the texture measured as CCC between AiMIFY input and output images in seven radiomics feature classes were all ≥ 0.8 for parenchyma tissue / healthy tissue. Specifically, the CCC in the seven radiomics feature classes ranged from 0.82 to 0.92, which are all ≥ 0.8 , for parenchyma tissue / healthy tissue. Seven radiomics feature classes of SOC and AiMIFY-enhanced have a good correlation for parenchyma tissue / healthy tissue.

Dose Appearance

To assess whether AiMIFY-enhanced images have a high-dose-like appearance, the ‘dose concentration’ of AiMIFY-enhanced images to standard post-contrast images was compared using a physics-based formula. “BRAVO” sequence images were chosen for this evaluation due to the widely accepted signal evolution equation which is well established in the literature. On average, AiMIFY-enhanced images had 93% more dose concentration than standard post-contrast images, indicating they do have a high-dose-like appearance.

In addition, the training and validation datasets were compared in terms of CNR increase, where the training dataset compared CNR increase from low-dose to regular-dose post-contrast images while the testing dataset compared CNR increase from standard regular-dose post-contrast images and the AiMIFY-enhanced post-contrast images. Both datasets had significant increases in CNR increase.

SubtleMR

The AiMIFY device makes use of the SubtleMR device (K223623) as a denoising module in its post-processing engine. As the SubtleMR device was not previously tested or trained on AiMIFY-processed images, validation of SubtleMR using the validation tests described in K223623 was conducted to ensure performance of that device on this new type of input data.

When using SubtleMR in AiMIFY post-processing, average scores between the original and SubtleMR enhanced images are ≤ 0.5 Likert scale points for visibility of small structures. Specifically, the average score between original and SubtleMR enhanced images was 0.05 points. These results demonstrate that SubtleMR’s denoising does not over-smooth images processed by the AiMIFY algorithm.

When using SubtleMR in AiMIFY post-processing, average scores difference between the original and SubtleMR enhanced images are ≤ 0.5 Likert scale points for perceived SNR, Image Quality, Image

Artifact Scores. Specifically, the average SNR score difference between original and SubtleMR enhanced images was 0.05 for Septum Pellucidum, 0.08 for Cranial Nerves, and 0.07 for Cerebellar Folia. The average image quality/diagnostic confidence score difference between original and SubtleMR enhanced images was 0.11 for Septum Pellucidum, 0.04 for Cranial Nerves, and -0.05 for Cerebellar Folia. The average imaging artifacts score difference between original and SubtleMR enhanced images was 0.11 for Septum Pellucidum, 0.14 for Cranial Nerves, and 0.05 for Cerebellar Folia.

These results demonstrate that SubtleMR's denoising does not negatively impact perceived SNR, perceived image quality/diagnostic confidence, or imaging artifacts in images processed by the AiMIFY algorithm.

When evaluating for SNR improvement, the average SNR improvement was 14%, greater than the 5% acceptance criteria established in the SubtleMR validation, indicating that SubtleMR can denoise images processed by the AiMIFY algorithm.

Conclusion:

These results demonstrate that the AiMIFY is substantially equivalent to the predicate device.