Advantis Medical Imaging Single Member P.C.
℅ Paris Ziogkas
COO
Eleftheriou Venizelou Avenue 99 Nea Smirni
Athens, 17123
GREECE

October 14, 2021

Re: K202808
Trade/Device Name: Brainance MD
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: LLZ
Dated: September 21, 2021
Received: September 27, 2021

Dear Paris Ziogkas:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for

devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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

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

Sincerely,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K202808

Device Name
Brainance MD

Indications for Use *(Describe)*
Brainance MD provides analysis and visualization capabilities of dynamic MRI data of the brain, presenting the derived properties and parameters in a clinically useful context.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

Submitter

Submitter Name : Advantis Medical Imaging Single Member P.C.

Submitter Address: Eleftheriou Venizelou Avenue 99, Nea Smirni, Athens, Greece, 17123

Phone : +302109329558

Contact Person : Paris Ziogkas (pz@advantis.io)

Date prepared : September 21st 2021

Device

Device Trade Name : Brainance MD

Device Common Name : PACS

Device : System, Image Processing, Radiological

Classification Name : Medical image management and processing system

Classification Regulation: 21 CFR 892.2050

Class : II

Panel : Radiology

Product Code : LLZ

Predicate Device

Primary Predicate : K163324, nordicBrainEx

This predicate has not been subject to a recall.

Reference Device Name 1 : K090546, nordicICE Software

This reference device has not been subject to a recall.

Reference Device Name 2 : K162513, Arterys Software v2.0

This reference device has not been subject to a recall.

Device Description

Brainance MD is a web-accessible medical viewing and post-processing software application. Brainance MD offers comprehensive functionality for dynamic image analysis and visualization of brain MRI data which are acquired through DICOM compliant imaging devices and modalities.

The following algorithms provide the main functional analyses of the software application.

- BOLD: BOLD fMRI analysis is used to highlight small magnetic susceptibility changes in the human brain in areas with altered blood-flow resulting from neuronal activity.
- DTI: Diffusion analysis is used to visualize local water diffusion properties from the analysis of diffusion-weighted MRI data. Fiber tracking utilizes the directional dependency of the diffusion to display the white matter structure in the brain.
- DSC Perfusion: Calculations of perfusion related parameters that provide information about the blood vessel structure and characteristics. Examples of such maps are blood volume, blood flow, time to peak, mean transit time and leakage.

Apart from the aforementioned functionalities, Brainance MD offers general visualization tools, a data handling database, data upload, data download and a reporting feature.

Intended use

Brainance MD is an advanced visualization and processing software, with specific focus on providing algorithms designed to analyze brain MRI data. The software is web-accessible and can be used with data and images acquired through DICOM compliant imaging devices and modalities.

The software is intended to be used by medical personnel, including but not limited to radiologists and medical technicians, trained in the methods provided by the application.

Indications for Use

Brainance MD provides analysis and visualization capabilities of dynamic MRI data of the brain, presenting the derived properties and parameters in a clinically useful context.

Comparison of Technological Characteristics with the Predicate Device

	Subject Device	Primary Predicate Device	Reference Device 1	Reference Device 2	Differences
Device Name	Brainance MD	nordicBrainEx	nordicICE	Arterys Software v2.0	-
510(k)Number	K202808	K163324	K090546	K162513	-
Manufacturer	Advantis Medical Imaging Single Member P.C.	NordicNeuroLab AS	NordicNeuroLab AS	Arterys Inc.	-
Regulation Number	892.2050	892.2050	892.2050	892.2050	No difference
Device Classification Name	System, Image Processing, Radiological	System, Image Processing, Radiological	System, Image Processing, Radiological	System, Image Processing, Radiological	No difference
Product Code	LLZ	LLZ	LLZ	LLZ	No difference
Development Framework	Web development framework	Embarcadero C++ Builder XE2	Embarcadero C++ Builder XE2	Web development framework	Difference - Note 1
Operating Environment	Client-server	“Off-the-shelf” windows PC workstation	“Off-the-shelf” windows PC workstation	Client-server	Difference - Note 2
Input data	DICOM compliant MR data, Nifti	DICOM compliant MR data	DICOM compliant MR data ,RAW, Analyze, Nifti	-	Difference - Note 3
Organ/Area	Brain	Brain	Brain	-	No difference
General Functionality	2D MPR visualization, 3D Visualization, Volumes of interest, Measurement tools, DICOM compliant node, Reporting tool	2D MPR visualization, 3D Visualization, Volumes of interest, Measurement tools, DICOM compliant node, Reporting tool	2D MPR visualization, 3D Visualization, Regions of interest, Measurement tools, DICOM compliant node	-	No difference

	Subject Device	Primary Predicate Device	Reference Device 1	Reference Device 2	Differences
Dynamic Analyses	BOLD, DTI, DSC	BOLD, DTI, DSC, DCE	-	-	Difference - Note 4
Analyses of BOLD fMRI	Note 5	Note 6	-	-	No difference
Analyses of DTI	Note 7	Note 8	-	-	No difference
Analyses of DSC	Note 9	Note 10	-	-	Difference - Note 11
Environment of Use	Intended for use in clinical/hospital environment	Intended for use in clinical/hospital environment	Intended for use in clinical/hospital environment	Intended for use in clinical/hospital environment	No difference

Notes

Note 1

The subject device and reference device 2 are developed using web frameworks while primary predicate device and reference device 1 are developed using Embarcadero C++ Builder XE2. The aforementioned difference does not raise any safety or performance issues.

Note 2

The subject device and reference device 2 make use of the client server model while primary predicate device and reference device 1 operate on “Off-the-shelf” windows PC workstations. The aforementioned difference does not raise any safety or performance issues.

Note 3

The subject device and reference device 1 can accept and proccess input data of both DICOM and Nifti format while the primary predicate device can only accept and process DICOM data. The comparison with reference device 2 in this field is not applicable. The aforementioned difference does not raise any safety or performance issues.

Note 4

Regarding dynamic analyses the subject device is designed to analyse BOLD, DTI, and DSC sequences while the primary predicate device can also be used for the analysis of DCE apart from the other three aforementioned sequences. The aforementioned difference does not raise any safety or performance issues.

Note 5

Possibility for importing, creating or editing BOLD design files including: BOLD paradigm and contrasts, Preprocessing steps (Slice time correction, Motion correction, smoothing, High-Pass filtering), BOLD analysis with the General Linear Model, 2D/3D visualization or activations overlaid structural datasets, Combined 3D visualization of BOLD activations and white matter fiber tracts from Diffusion Tensor Imaging studies, Interactive thresholding of statistical maps, Automated co-registration of functional and structural datasets, Possibilities for saving statistical maps and 3D snapshots to various file formats.

Note 6

Possibility for importing, creating or editing BOLD design files including: BOLD paradigm and contrasts, Preprocessing steps (Slice time correction, Motion correction, smoothing, High-Pass filtering), BOLD analysis with the General Linear Model, 2D/3D visualization or activations overlaid structural datasets, Combined 3D visualization of BOLD activations and white matter fiber tracts from Diffusion Tensor Imaging studies, Interactive thresholding of statistical maps, Automated co-registration of functional and structural datasets, Possibilities for saving statistical maps and 3D snapshots to various file formats.

Note 7

Possibility of processing DTI files including: Co-registration between DTI series and structural datasets, Automatic attempt to extract diffusion gradient configuration from DICOM header, Custom configuration possible, including uploading from file, Fast generation of parametric maps (Color-coded DTI, Fractional anisotropy (FA), Apparent diffusion coefficient/Mean diffusivity (ADC), Tensor eigenvalues (λ1, λ2 and λ3)), 3D tractography using seed/target approach, Optimize tracking results by selection of termination criteria (FA-value, tract

turning angle and minimum fiber length), 3D visualization of white matter fiber tracts superimposed on various underlay volumes (structural, FA, color-coded eigenvector maps etc.), Interactive selection of specific white matter fiber bundles using Region-of-Interest tools, Superimposing of 3D BOLD fMRI activations, Saving parametric maps and 3D snapshots to various file formats.

Note 8

Possibility of processing DTI files including: Co-registration between DTI series and structural datasets, diffusion gradient configuration, Automatic attempt to extract diffusion gradient configuration from DICOM header, Custom configuration possible, including uploading from file, Fast generation of parametric maps (Color-coded DTI, Fractional anisotropy (FA), Apparent diffusion coefficient/Mean diffusivity (ADC), Trace weighted, Tensor eigenvalues (λ1, λ2 and λ3)), 3D tractography using seed/target approach, Optimize tracking results by selection of termination criteria (FA-value, tract turning angle and minimum fiber length), 3D visualization of white matter fiber tracts superimposed on various underlay volumes (structural, FA, color-coded eigenvector maps etc.), Interactive selection of specific white matter fiber bundles using Region-of-Interest tools, Superimposing of 3D BOLD fMRI activations, Saving parametric maps and 3D snapshots to various file formats.

Note 9

The module includes perfusion analysis of T2 first-pass effects, contrast agent leakage correction to extravascular space, “One-button” perfusion analysis using predefined settings for the computation of the following maps: Relative blood flow (rBF), Relative blood volume (rBV), Mean transit time (MTT), Leakage map. The module also includes: Optional automatic normalization to automatically segmented white matter, Visual inspection of dynamic curves for one or multiple ROIs, Methods for leakage correction, Gamma-variate fitting of input function and tissue curves, Easy image fusion (drag & drop) of perfusion maps and structural images.

Note 10

The module includes perfusion analysis of both T1 and T2 first-pass effects, various methods for corrections for contrast agent leakage to extravascular space, “One-button” perfusion analysis using predefined settings for the computation of the following maps: Relative blood flow (rBF), Relative blood volume (rBV), Mean transit time (MTT), Time to peak (TTP)/Delay, Leakage map (apparent contrast agent permeability (Ktrans) map), Chi-square map, Multiple additional output maps for advanced analysis and quality control. The module also includes: Optional automatic normalization to automatically segmented white matter, grey matter or both, Choice of manual or fully automatic (slice-wise or whole volume) selection of arterial input function (AIF), or population based AIF, Visual inspection of dynamic curves from AIF-pixels/ROI, Methods for leakage correction, Vessel segmentation, Optional gamma-variate fitting of input function and tissue curves, Integrated motion correction, Easy image fusion (drag & drop) of perfusion maps and structural images.

Note 11

In the analysis of DSC perfusion, the subject device includes a single method for correction of contrast agent leakage while the primary predicate device offers multiple methodologies. The subject device does not compute ktrans and Chi-square map while the primary predicate device does. The subject device applies normalization to automatically segmented white matter while the primary predicate device applies normalization to automatically segmented white matter, grey matter or both. The subject device does not compute the Arterial Input Function (AIF) while the primary predicate device does. The subject device does no vessel segmentation while the primary predicate device does. The aforementioned difference does not raise any safety or performance issues.

Comparison of Intended Use

Apart from the Technological Characteristics it is noteworthy that the subject device and the primary predicate device have the same Intended Use and Indications for Use.

Brainance MD: is an advanced visualization and processing software, with specific focus on providing algorithms designed to analyze brain MRI data. The software is web-accessible and can be used with data and images acquired through DICOM compliant imaging devices and modalities. The software is intended to be used by medical personnel, including but not limited to radiologists and medical technicians, trained in the methods provided by the application.

nordicBrainEx: is an advanced visualization and processing software, with specific focus on providing algorithms designed to analyze functional MR data of the brain. The software runs on a standard “off-the-shelf” PC workstation and can be used with data and images acquired through DICOM compliant imaging devices and modalities. The software is intended to be used by medical personnel, such as radiologists or medical technicians, trained in the methods provided by the application. In order to best accommodate this group of users, it is specifically designed to have an easy to use and streamlined workflow, as well as an intuitive graphical user interface.

Comparison of Indications for Use

Brainance MD: Brainance MD provides analysis and visualization capabilities of dynamic MRI data of the brain, presenting the derived properties and parameters in a clinically useful context.

nordicBrainEx provides analysis and visualization capabilities of dynamic MRI data of the brain, presenting the derived properties and parameters in a clinically useful context.

Software

Brainance MD was successfully validated and verified against the requirements specification and its intended use. The results from the validation and verification activities justify that Brainance MD meets the product requirement specifications and intended use, which is deemed to be substantially equivalent to the predicate.

Validation and verification activities were conducted in a controlled environment and in compliance with IEC 62304, ISO 13485:2016 and 21 CFR 820. Brainance MD is also in compliance with the DICOM standard.

The verification and validation activities conducted demonstrate that Brainance MD is at least as safe and effective as the predicate device and does not introduce any new risks.

Performance

The performance testing conducted demonstrates that Brainance MD is as safe and as effective to use as the predicate device and does not introduce any new risks.

More specifically, apart from the standard software verification and validation testing conducted and documented in compliance with the FDA Guidance, “Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices”, a detailed comparative study was performed between the subject device and the primary predicate device on the basis of the core functionalities.

Performance Testing Summary

A comparative study was conducted in order to validate the equivalence of results computed by Brainance MD and the primary predicate device regarding the processing of DSC Perfusion, fMRI and DTI sequences. Towards this direction two sequences that were part of two different exams/subjects (either healthy control or diseased) were selected for the comparison conducted for each modality. The subjects selected were all adults and either healthy controls or diseased diagnosed with metastasis or glioblastoma multiforme.

The two sequences selected for each modality were processed with each one of the software (Brainance MD and primary predicate device) using the exact same processing protocol and parameters for each user defined function.

The maps that resulted from the processing were compared using ICC & Bland-Altman analysis on all valid pixel values for every subject in the dataset. The fiber tracts that resulted were compared using Mean Relative Difference (MRD) as Percentage across each tract, which is the mean across samples of the absolute difference divided by the maximum absolute value.

The final results matched the criteria of acceptance/approval priorly set by the manufacturer and thus equivalency between the two devices on a result level was proven.

Discussion Summary

According to the comparisons between the subject device and predicate device, we can conclude that the subject device does not raise any new potential safety risks when compared to the chosen predicate device and performs in accordance with its intended use.

The subject device is substantially equivalent to the predicate device. Substantial equivalence is based on the following observations:

- The indications for use and intended uses of both the subject device and predicate device are equivalent
- The subject and predicate devices consist of software applications which visualize and analyze brain MR data
- The subject and predicate device are both standalone software applications to facilitate the import and visualization of MR data sets
- The subject and predicate device offer similar visualization and processing functionalities and incorporate well known and extensivelly tested methodologies
- Both the subject and predicate device are intended to be used in the same environment and by trained healthcare professionals
- Performance testing demonstrates that the subject device performs at least as safely and effectively as the predicate device

Conclusion

Based on the information submitted in this premarket notification, and based on the indications for use, technological characteristics, performance testing and technological comparison to the predicate devices, Brainance MD raises no new risks of safety and effectiveness and is substantially equivalent to the predicate devices.