Vysioneer Inc
% Chiu S. Lin
Consultant
33 Rogers Street, # 308
CAMBRIDGE MA 02142

March 19, 2021.

Re: K203235
Trade/Device Name: VBrain
Regulation Number: 21 CFR 892.2050
Regulation Name: Picture archiving and communications system
Regulatory Class: Class II
Product Code: QKB
Dated: February 9, 2021
Received: February 10, 2021

Dear Chiu Lin:

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)*
K203235

Device Name
VBrain

Indications for Use *(Describe)*
VBrain is a software device intended to assist trained medical professionals, during their clinical workflows of radiation therapy treatment planning, by providing initial object contours of known (diagnosed) brain tumors (i.e., region of interest, ROI) on axial T1 contrast-enhanced brain MRI images.

VBrain uses an artificial intelligence algorithm (i.e., deep learning neural networks) to contour (segment) brain tumor on MRI images for trained medical professionals' attention, which is meant for informational purposes only and not intended for replacing their current standard practice of manual contouring process. VBrain does not alter the original MRI image, nor does it intend to be used to detect tumors for diagnosis. VBrain is intended only for generating Gross Tumor Volume (GTV) contours of brain metastases, meningiomas, and acoustic neuromas on axial T1 contrast-enhanced MRI images; It is not intended to be used with images of other brain tumors. The user must know the tumor type when they use VBrain. VBrain is intended to be used on adult patients only.

Medical professionals must finalize (confirm or modify) the contours generated by VBrain, as necessary, using an external platform available at the facility that supports DICOM-RT viewing/editing functions, such as image visualization software and treatment planning system.

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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Section 5 510(k) Summary

5.1 Submitter

Vysioneer Inc.

33 Rogers St. #308, Cambridge, MA 02142

Contact Person:	Jen-Tang Lu, PhD (Chief Executive Officer)
Phone:	609-865-8659
Email:	jt@vysioneer.com
Date Summary Prepared:	February 09, 2021

5.2 Device Name

Trade Name:	VBrain
Common Name:	Radiological Image Processing Software for Radiation Therapy
Regulation Number / Product Code:	21 CFR 892.2050 / QKB

5.3 PREDICATE DEVICE

Primary Predicate #1: AccuContour™, K191928, Xiamen Manteia Technology LTD

Primary Predicate #2: MIM - MRT Dosimetry, K182624, MIM Software Inc.

5.4 Intended Use / Indications for Use

VBrain is a software device intended to assist trained medical professionals, during their clinical workflows of radiation therapy treatment planning, by providing initial object contours of known (diagnosed) brain tumors (i.e., the region of interest, ROI) on axial T1 contrast-enhanced brain MRI images.

VBrain uses an artificial intelligence algorithm (i.e., deep learning neural networks) to contour (segment) brain tumor on MRI images for trained medical professionals' attention, which is meant for informational purposes only and not intended for replacing their current standard practice of manual contouring process. VBrain does not alter the original MRI image, nor does it intend to be used to detect tumors for diagnosis. VBrain is intended only for generating Gross Tumor Volume (GTV) contours of brain metastases, meningiomas, and acoustic neuromas on axial T1 contrast-enhanced MRI images; It is not intended to be used with images of other brain tumors. The user must know the tumor type when they use VBrain. VBrain is intended to be used on adult patients only.

Medical professionals must finalize (confirm or modify) the contours generated by VBrain, as necessary, using an external platform available at the facility that supports DICOM-RT viewing/editing functions, such as image visualization software and treatment planning system.

5.5 Device Description

VBrain is a software device indicated for use in the analysis of brain MRI images. The device consists of image preprocessing, deep learning neural networks, and postprocessing components, and is intended to assist trained medical professionals, during clinical workflows of radiation therapy treatment planning, by highlighting and contouring known (diagnosed) brain tumors on the axial T1 contrast-enhanced MRI images. The software is configured to work on a PACS network. Upon user's request, it will pull patient scans or users can send corresponding MR images, and the device will utilize deep learning neural networks to generate contours for the detected/diagnosed brain tumors and export the results as DICOM-RT objects (using the RT Structure Set ROI Contour attribute, RTSTRUCT) back to the network. The medical professionals must finalize (confirm and modify) the contours produced by VBrain as necessary using an external platform that supports RT DICOM viewing/editing, such as a treatment planning system.

5.6 Comparison with Predicate Devices

VBrain is substantially equivalent to a combination of the primary predicate devices AccuContour™ (K191928) and MIM - MRT Dosimetry (K182624).

The proposed device, VBrain, and the primary predicates, AccuContour™ (K191928) and K182624 (MIM - MRT Dosimetry), are all software devices intended to be used in the workflow of radiation therapy by providing tools of segmenting (contouring) of tumors and/or organs on MRI and/or CT images. Both the proposed device and AccuContour™ (K191928) are AI-based (deep learning) software regulated under the Product Code QKB (Radiological Image Processing Software For Radiation Therapy). On the other hand, both the proposed device and K182624 (MIM - MRT Dosimetry) provide tools for tumor contouring. The only difference is that VBrain uses deep learning (neural networks) to automatically generate tumor contours as a starting point for user's review and edit, while K182624 (MIM - MRT Dosimetry) provides a semi-automatic

tool (propagation tool) that requires user's input to start the image segmentation (contouring) process.

Although the proposed new device, VBrain, uses a data-driven deep learning-based algorithm for contouring of known brain tumors, the primary predicate MIM - MRT Dosimetry (K182624) uses a semi-automatic algorithm that requires user's input to start the contouring process. The specific design of the proposed device does not raise different questions of safety and effectiveness, because the new device only provides initial object contours of known (diagnosed) brain tumors for the medical professionals' attention, which are meant for informational purposes only and not intended for replacing their current standard practice of manual contouring process. Medical professionals must use VBrain in conjunction with appropriate software to review and edit results generated automatically by VBrain. In addition, VBrain does not alter the original MRI image, nor does it intend to be used to detect tumors for diagnosis. The medical professionals must know the tumor type when they use VBrain. Consequently, the new device does not change any medical professionals' workflow planning procedure and therefore does not raise different questions of safety and effectiveness.

Please see Table 5-1 comparing the intended use and key technological characteristics of the proposed device and the predicate devices.

Table 5-1. Comparison with the Predicate Devices.

Company	**Vysioneer Inc.**	**Xiamen Manteia Technology LTD. (Primary)**	**MIM Software Inc. (Primary)**
Device Name	VBrain	AccuContour™	MIM - MRT Dosimetry
510k Number	Pending	K191928	K182624
Regulation No.	21CFR 892.2050	21CFR 892.2050	21CFR 892.2050
Classification	II	II	II
Product Code	QKB	QKB	LLZ
Intended Use/Indication for Use	VBrain is a software device intended to assist trained medical professionals, during their clinical workflows of radiation therapy treatment planning, by providing initial object contours of known (diagnosed) brain tumors (i.e., the region of interest, ROI) on axial T1 contrast-enhanced brain MRI images.	It is used by radiation oncology department to register multimodality images and segment (non-contrast) CT images, to generate needed information for treatment planning, treatment evaluation and treatment adaptation. The product has two image process functions: (1) Deep learning contouring: it can automatically contour	MIM software is used by trained medical professionals as a tool to aid in evaluation and information management of digital medical images. The medical image modalities include, but are not limited to, CT, MRI, CR, DX, MG, US, SPECT, PET and XA as supported by ACR/NEMA DICOM 3.0.

	VBrain uses an artificial intelligence algorithm (i.e., deep learning neural networks) to contour (segment) brain tumor on MRI images for trained medical professionals' attention, which is meant for informational purposes only and not intended for replacing their current standard practice of manual contouring process. VBrain does not alter the original MRI image, nor does it intend to be used to detect tumors for diagnosis. VBrain is intended only for generating Gross Tumor Volume (GTV) contours of brain metastases, meningiomas, and acoustic neuromas on axial T1 contrast-enhanced MRI images; it is not intended to be used with images of other brain tumors. The user must know the tumor type when they use VBrain. VBrain is intended to be used on adult patients only. Medical professionals must finalize (confirm or modify) the contours generated by VBrain, as necessary, using an external platform available at the facility that supports DICOM-RT viewing/editing functions, such as image visualization software and treatment planning system.	the organ-at-risk, including head and neck, thorax, abdomen and pelvis (for both male and female), (2) Automatic Registration, and (3) Manual Contour. It also has the following general functions: (1) Receive, add/edit/delete, transmit, input/export, medical images and DICOM data; (2) Patient management; (3) Review of processed images; (4) Open and Save of files.	MIM assists in the following indications: • Receive, transmit, store, retrieve, display, print, and process medical images and DICOM objects. • Create, display and print reports from medical images. • Registration, fusion display, and review of medical images for diagnosis, treatment evaluation, and treatment planning. • Evaluation of cardiac left ventricular end-diastolic volume, end-systolic volume, and ejection fraction. • Localization and definition of objects, such as tumors and normal tissues in medical images. • Creation, transformation, and modification of contours for applications including, but not limited to, quantitative analysis, aiding adaptive therapy, transferring contours to radiation therapy treatment planning systems, and archiving contours for patient follow-up and management. • Quantitative and statistical analysis of PET/SPECT brain scans by comparing to other registered PET/SPECT brain scans.

			• Planning and evaluation of permanent implant brachytherapy procedures (not including radioactive microspheres). • Calculating absorbed radiation dose as a result of administering a radionuclide. When using device clinically, the user should only use FDA approved radiopharmaceuticals. If using with unapproved ones, this device should only be used for research purposes. Lossy compressed mammographic images and digitized film screen images must not be reviewed for primary image interpretations. Images that are printed to film must be printed using an FDA-approved printer for the diagnosis of digital mammography images. Mammographic images must be viewed on a display system that has been cleared by the FDA for the diagnosis of digital mammography images. The software is not to be used for mammography CAD.
Segmentation (Contouring) Technology	Deep learning	Deep learning	Atlas-based algorithm and propagation tools (requiring user's input to

			start the image segmentation process)
Operating System	Linux operating system	Microsoft Windows	Microsoft Windows and Apple macOS operating systems
User Population	Trained medical professionals including, but not limited to, radiologists, oncologists, physicians, medical technologists, dosimetrists, and physicists.	It is used by radiation oncology department.	Trained medical professionals
Supported Modalities	Axial T1 contrast-enhanced MRI images	Segmentation Features: Non-Contrast CT Registration Features: CT, MRI, PET	CT, MRI, CR, DX, MG, US, SPECT, PET and XA as supported by ACR/NEMA DICOM 3.0.
Localization and Definition of Objects (ROI)	Qualified brain tumors - brain metastases, meningiomas, and acoustic neuromas	Organ-at-risk, including head and neck, thorax, abdomen and pelvis (for both male and female)	Tumors and normal tissues
Performance Testing & Software V & V	To support the intended use of the VBrain AI software for brain tumor contouring (segmentation) performance, Vysioneer conducted a retrospective, blinded, multicenter, multinational study with the VBrain software. The test data sets consisted of 116 cases acquired from 4 different institutions (3 US and 1 non-US). Five metrics are evaluated: (1) lesion-wise sensitivity, (2) false-positive rate, (3) lesion-wise Dice coefficient, (4) average Hausdorff distance, and (5) average centroid distance between	Segmentation performance test The segmentation performance test was performed on proposed device and predicate device to evaluate the automated segmentation accuracy. Two separate tests were performed. One test involved images generated in healthcare institutions in China using scanner models available in China covering three major vendors. The other involved images generated in healthcare institutions in US using scanner models available in US covering three major vendors. The three major vendors were GE,	MIM Software Inc. has conducted performance and integration testing on MIM - MRT Dosimetry software with a comparison to a commercially available solution for internal radionuclide dosimetry. Standard quality control phantoms, simulated phantoms based on the NEMA IEC Body Phantom, simulated phantoms based on patient data, and clinical patient data were used for verification testing. All tests were performed using standard clinical acquisition and reconstruction protocols. The accuracy of planar corrections for

	VBrain's segmentation and clinicians' segmentation. All the metrics were demonstrated to pass the performance goals. 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" for software devices identified as Major Level of Concern related to radiation therapy treatment planning.	Siemens and Philips. For each body parts, all intended organs were included in images of the US and China. Ground truthing of each image was generated from the consensus of at least three licensed physicians. DICE similarity coefficients (DSC) was used for evaluation. DSC values were calculated on two sets of images for test group and control group, respectively. According to the results, it could be concluded that the DSC of proposed device was non-inferiority compared with that of the predicate device. Registration performance test The registration performance test was performed on proposed device and predicate device to evaluate the automated registration accuracy. Two separate tests were performed. One test involved images generated in healthcare institutions in China using scanner models available in China covering three major vendors. And the image registration feature is tested on multi-modality image sets from same patients. The other involved most images generated in healthcare institutions in U.S. All fixed image and	attenuation, scatter, and background were verified in simulated phantoms. The average errors were less than 12% for all regions except for the smallest region (2.6 cm) with 21% error for Lu-177 and 17% error for I-131 where the partial volume effect lowered accuracy as expected. In all cases, the software passed its performance requirements and met specifications The accuracy of area-under-the curve (AUC) calculations were verified for different fitting options using simulated data with differences less than 3.1% compared to manual AUC calculations which met predefined acceptance criteria when considering the presence of Poison noise in the image data. The accuracy of the generation of CT-derived physical density maps were verified in clinical patient data and compared to published results with less than 5% difference for soft tissue regions and less than 10% difference for bone regions. The difference for lung density fell within the range of expected density values. The accuracy dose calculations using MIM

		most moving images came from U.S and a small amount of moving images adopted from online database were originally from non-US sources. All the scanner models covered three major vendors. And the image registration feature is only tested on multi-modality image sets from different patients. Both tests covered various modalities, including CT/CT, CT/MR and CT/PET. The Normalized Mutual Information (NMI) was used for evaluation. NMI values were calculated on two sets of images for both the proposed device and predicate device, respectively. The NMI value of proposed device was compared with that of the predicate device. According to the results, it could be concluded that the NMI of proposed device was non-inferiority compared with that of the predicate device.	- MRT Dosimetry was verified in simulated phantoms and clinical patient data for I-131 and Lu-177. The acceptance criterion for MIM - MRT Dosimetry is a difference of mean dose of smaller or equal to 20% in comparison to a commercially available solution after correction of the standard phantoms in the commercial solution to match the mass of the patient data. Additionally, comparison of the Voxel S Value method in MIM - MRT Dosimetry to Local Deposition Model values for Lu-177 showed a difference less than 1% for all organs tested. In all cases the software demonstrated acceptable agreement between the different dose methods.

5.7 Performance Data

Vysioneer conducted a retrospective, blinded, multicenter, multinational study with the proposed device VBrain with the primary endpoint to evaluate the software's performance on identifying axial T1 contrast-enhanced MRI scans containing brain metastases, acoustic neuromas, or meningiomas. The test dataset was an independent dataset consisting of 116 cases with 238 tumors acquired consecutively and retrospectively from 4 different institutions (3 US and 1 non-US). The ground truth of each tumor contours was generated from the consensus of three board-certified radiation oncologists. Five metrics are evaluated: (1) lesion-wise sensitivity, (2) false-positive rate,

(3) lesion-wise Dice coefficient, (4) average Hausdorff distance, and (5) centroid distance between VBrain's segmentation and ground-truth segmentation. VBrain meets all performance goals.

Specifically, lesion-wise sensitivity of VBrain was observed to be 90.3% (95% CI: 86.1-93.7%) and the false-positive rate was observed to be 0.681 tumors/case (95% CI: 0.500-0.879) tumors/case). In addition, segmentation performance was measured with the lesion-wise Dice similarity coefficient (DSC) and average Hausdorff distance between VBrain's segmentation and ground-truth segmentation in terms of lesion size. They were observed to be lesion-wise DSC: 0.793 (95% CI: 0.775-0.811) and average Hausdorff distance in terms of lesion size: 5.0% (95% CI: 4.4-5.6%). Centroid distance between VBrain's segmentation and ground-truth segmentation was measured in terms of lesion size and was observed to be 5.6% (95% CI: 5.0-6.2%).

5.8 Software Verification and Validation

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" for software devices identified as Major Level of Concern related to radiation therapy treatment planning.

5.9 Conclusion

In conclusion, Vysioneer Inc. has conducted performance testing on VBrain. In all the cases, the software passed its requirements for safety and effectiveness and does not introduce any new potential safety risks. It demonstrates that VBrain is substantially equivalent to and performs at least as safely and effectively as the listed predicate devices.