Siemens Medical Solutions USA, Inc.
% Ms. Veronica Padharia
Regulatory Affairs Specialist
2501 N. Barrington Road
HOFFMAN ESTATES IL 60192

October 11, 2020

Re: K202213
Trade/Device Name: syngo.CT Neuro Perfusion
Regulation Number: 21 CFR 892.1750
Regulation Name: Computed tomography x-ray system
Regulatory Class: Class II
Product Code: JAK
Dated: August 5, 2020
Received: August 6, 2020

Dear Ms. Padharia:

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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K202213

Device Name
syngo.CT Neuro Perfusion

Indications for Use *(Describe)*
The syngo.CT Neuro Perfusion software package is designed to evaluate areas of brain perfusion. The software processes images or volumes that were reconstructed from continuously acquired CT data after the injection of contrast media.

It generates the following result volumes:
- Cerebral blood flow (CBF)
- Cerebral blood volume (CBV)
- Local bolus timing (time to start (TTS), time to peak (TTP), time to drain (TTD))
- Mean transit time (MTT)
- Transit time to the center of the IRF (TMax)
- Flow extraction product (permeability)
- Temporal MIP
- Temporal Average
- Baseline Volume
- Modified dynamic input data

The software allows the calculation of mirrored regions of interest and the visual inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and to calculate Hypoperfused Area and Mismatch Ratio in the brain tissue affected by acute stroke.
Areas of decreased perfusion appear as areas of changed signal intensity:
- Lower signal intensity for CBF and CBV
- Higher signal intensity for TTP, TTD, MTT, and TMax

A second application is to visualize blood brain barrier disturbances by modeling extra-vascular leakage of blood into the interstitial space. This additional capability may improve the differential diagnosis of brain tumors and may be helpful in therapy monitoring.

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
FOR
SYNGO.CT NEURO PERFUSION

I. Identification of the Submitter

Importer/Distributor
Siemens Medical Solutions USA, Inc.
40 Liberty Boulevard
Malvern, PA 19355
Establishment Registration Number
2240869

Manufacturing Site
Siemens Healthcare GmbH
Siemensstr 1
D-91301 Forchheim, Germany

Establishment Registration Number
3004977335

Submitter Contact Person:
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II. Device Name and Classification

Product Name:	syngo.CT Neuro Perfusion
Propriety Trade Name:	syngo.CT Neuro Perfusion
Classification Name:	Computed Tomography X-ray System
Classification Panel:	Radiology
CFR Section:	21 CFR §892.1750
Device Class:	Class II
Product Code:	JAK

III. Predicate Device

Predicate Device

Trade Name:	syngo.CT Neuro Perfusion
510(k) Number:	K163284
Clearance Date:	03/01/2017
Classification Name:	Computed Tomography X-ray System
Classification Panel:	Radiology
CFR Section:	21 CFR §892.1750

Device Class:	Class II
Product Code:	JAK

Reference Device

Trade Name:	iSchemaView RAPID
510(k) Number:	K182130
Clearance Date:	12/27/2018
Classification Name:	System, Image Processing, Radiological
Classification Panel:	Radiology
CFR Section:	21 CFR § 892.2050
Device Class:	Class II
Product Code:	LLZ

IV. Device Description

The syngo.CT Neuro Perfusion software allows the quantitative evaluation of dynamic CT data of the brain acquired during the injection of a compact bolus of iodinated contrast material. It mainly aids in the early differential diagnosis of acute ischemic stroke. Blood-brain-barrier (BBB) imaging feature supports the diagnostic assessment of brain tumors.

By providing images of e.g. cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP), and Mean Transit Time (MTT) from one set of dynamic CT images or volumes, syngo.CT Neuro Perfusion allows a quick and reliable assessment of the type and extent of cerebral perfusion disturbances, including fast evaluation of the tissue at risk and non-viable tissue in the brain. The underlying approaches for this application were cleared as part of the predicate device and remain unchanged in comparison to the predicate device

syngo.CT Neuro Perfusion allows simultaneous multi-slice processing and supports the workflow requirements in a stroke workflow. The availability of flow extraction product imaging extends the option to the diagnosis of brain tumors. A listing of device modifications as part of the new software version VB50 of syngo.CT Neuro Perfusion is as follows:

Additional Parameters *Hypoperfused Area* and *Mismatch Ratio*:
These parameters are calculated based on NVT (non-viable tissue) and TAR (tissue at risk). Hypoperfused Area is calculated based on the sum of NVT and TAR while the Mismatch Ratio is calculated by dividing Hypoperfused Area by NVT.

V. Indications for Use

The syngo.CT Neuro Perfusion software package is designed to evaluate areas of brain perfusion. The software processes images or volumes that were reconstructed from continuously acquired CT data after the injection of contrast media.

It generates the following result volumes:

- Cerebral blood flow (CBF)
- Cerebral blood volume (CBV)
- Local bolus timing (time to start (TTS), time to peak (TTP), time to drain (TTD))
- Mean transit time (MTT)
- Transit time to the center of the IRF (TMax)
- Flow extraction product (permeability)
- Temporal MIP

- Temporal Average
- Baseline Volume
- Modified dynamic input data

The software allows the calculation of mirrored regions of interest and the visual inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and to calculate Hypoperfused Area and Mismatch Ratio in the brain tissue affected by acute stroke.

Areas of decreased perfusion appear as areas of changed signal intensity:

- Lower signal intensity for CBF and CBV
- Higher signal intensity for TTP, TTD, MTT, and TMax

A second application is to visualize blood brain barrier disturbances by modeling extra-vascular leakage of blood into the interstitial space. This additional capability may improve the differential diagnosis of brain tumors and may be helpful in therapy monitoring.

VI. Comparison of the IFU Statement and Technological Characteristics with the Predicate Device

This section compares the IFU statement as well as the technological characteristics with the predicate device, syngo.CT Neuro Perfusion (K163284), and the reference device, iSchemaView RAPID (K182130).

IFU Comparison:

Subject Device **Siemens syngo.CT Neuro Perfusion** ***SOMARIS/8 VB50***	**Predicate Device** **Siemens syngo.CT Neuro Perfusion** ***SOMARIS/8 VB20, K163284***	**Reference Device** **iSchemaView RAPID** ***K182130***
The syngo.CT Neuro Perfusion software package is designed to evaluate areas of brain perfusion. The software processes images or volumes that were reconstructed from continuously acquired CT data after the injection of contrast media. It generates the following result volumes: • Cerebral blood flow (CBF) • Cerebral blood volume (CBV) • Local bolus timing (time to start (TTS), time to peak (TTP), time to drain (TTD)) • Mean transit time (MTT) • Transit time to the center of the IRF (TMax) • Flow extraction product (permeability) • Temporal MIP • Temporal Average • Baseline Volume • Modified dynamic input data The software allows the calculation of mirrored regions of interest and the visual inspection of time attenuation curves. One clinical	The syngo.CT Neuro Perfusion software package is designed to evaluate areas of brain perfusion. The software processes images or volumes that were reconstructed from continuously acquired CT data after the injection of contrast media. It generates the following result volumes: • Cerebral blood flow (CBF) • Cerebral blood volume (CBV) • Local bolus timing (time to start (TTS), time to peak • (TTP), time to drain (TTD)) • Mean transit time (MTT) • Transit time to the center of the IRF (TMax) • Flow extraction product (permeability) • Temporal mip • Temporal average • Baseline volume • Modified dynamic input data The software also allows the calculation of mirrored regions or volumes of interest and the visual	iSchemaView's RAPID is an image processing software package to be used by trained professionals, including but not limited to physicians and medical technicians. The software runs on a standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis of images. Data and images are acquired through DICOM compliant imaging devices. The iSchemaView RAPID provides both viewing and analysis capabilities for functional and dynamic imaging datasets acquired with CT Perfusion (CT-P), CT Angiography (CTA), and MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI and CT). The DWI Module is used to visualize local water diffusion properties from

application is to visualize the apparent blood perfusion and to calculate Hypoperfused Area and Mismatch Ratio in the brain tissue affected by acute stroke. Areas of decreased perfusion appear as areas of changed signal intensity: • Lower signal intensity for CBF and CBV • Higher signal intensity for TTP, TTD, MTT, and TMax A second application is to visualize blood brain barrier disturbances by modeling extra-vascular leakage of blood into the interstitial space. This additional capability may improve the differential diagnosis of brain tumors and may be helpful in therapy monitoring.	inspection of time attenuation curves. One clinical application is to visualize the apparent blood perfusion and the parameter mismatch in brain tissue affected by acute stroke. Areas of decreased perfusion appear as areas of changed signal intensity: • Lower signal intensity for CBF and CBV • Higher signal intensity for TTP, TTD, MTT, and TMax A second application is to visualize blood brain barrier disturbances by modeling extravascular leakage of blood into the interstitial space. This additional capability may improve the differential diagnosis of brain tumors and be helpful in therapy monitoring.	the analysis of diffusion weighted MRI data. The Dynamic Analysis Module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume. RAPID CT-Perfusion and RAPID MR-Perfusion can be used by physicians to aid in the selection of acute stroke patients (with known occlusion of the intracranial internal carotid artery or proximal middle cerebral artery) for endovascular thrombectomy. Instructions for use of contrast agents for this indication can be found in Appendix A of the User's Manual. Additional information for safe and effective drug use is available in productspecific iodinated CT and gadolinium-based MR contrast drug labeling. In addition to the RAPID imaging criteria, patients must meet the clinical requirements for thrombectomy, as assessed by the physician, and have none of the following contraindications or exclusions. Contraindications/Exclusions: • Bolus Quality: absent or inadequate bolus. • Patient Motion: excessive motion leading to artifacts that make the scan technically inadequate. • • Presence of Hemorrhage.

<u>Comparison of the IFU statement related to the Predicate Device syngo.CT Neuro Perfusion (K163284):</u>

The IFU statement of the subject device includes both parameters Hypoperfused Area and Mismatch Ratio due to the significance in decision-making during the AIS clinical workflow. The sentence is as follows: *"One clinical application is to visualize the apparent blood perfusion and to calculate* ***Hypoperfused Area*** *and* ***Mismatch Ratio*** *in the brain tissue affected by acute stroke".* This is the relevant difference as compared to the predicate device.

Comparison of the IFU statement related to the Reference Device iSchemaView RAPID (K182130)

The IFU Statement of the reference device is principally divided in eight sections. To simplify the comparison process, a comparison of each section of the reference device against the subject device's IFU statement is provided next:

The first two sections as listed in the table (right column) above describe the type of the medical device (image respectively post-processing software application), the target group ("trained professionals") as well as the system environment where the software runs on. We describe the target group and the system environment in our user manual but not in our IFU statement.

1. *iSchemaView's RAPID is an image processing software package to be used by trained professionals, including but not limited to physicians and medical technicians.*
2. *The software runs on a standard off-the-shelf computer or a virtual platform, such as VMware, and can be used to perform image viewing, processing and analysis of images. Data and images are acquired through DICOM compliant imaging devices.*

The third and fourth section refer to the modality and the modality-specific feature "DWI Modules" which refers to the MR acquisition mode only. Our subject device conducts post-processing on CT data only as described in the second sentence of our IFU statement. The subject device is not intended to work on MR data.

3. *The iSchemaView RAPID provides both viewing and analysis capabilities for functional and dynamic imaging datasets acquired with CT Perfusion (CT-P), CT Angiography (CTA), and MRI including a Diffusion Weighted MRI (DWI) Module and a Dynamic Analysis Module (dynamic contrast-enhanced imaging data for MRI and CT).*
4. *The DWI Module is used to visualize local water diffusion properties from the analysis of diffusion weighted MRI data.*

The fifth section refers to the analysis of dynamic imaging data of the blood flow. The assessment of dynamic image data is realized by cerebral blood flow (CBF) and cerebral blood volume (CBV) as listed in our IFU statement.

5. *The Dynamic Analysis Module is used for visualization and analysis of dynamic imaging data, showing properties of changes in contrast over time. This functionality includes calculation of parameters related to tissue flow (perfusion) and tissue blood volume.*

The sixth section describes which specific medical procedure (endovascular thrombectomy) can be applied using the reference device. Our IFU statement does not provide such specific information.

6. *RAPID CT-Perfusion and RAPID MR-Perfusion can be used by physicians to aid in the selection of acute stroke patients (with known occlusion of the intracranial internal carotid artery or proximal middle cerebral artery) for endovascular thrombectomy.*

The seventh section provides specific information concerning the use of a contrast agent. Our IFU statement explains that the subject device processes images or volumes after the injection of contrast media. Specific information concerning the contrast agent are communicated to the end-user in the user manual.

7. *Instructions for use of contrast agents for this indication can be found in Appendix A of the User's Manual. Additional information for safe and effective drug use is available in productspecific iodinated CT and gadolinium-based MR contrast drug labeling.*

The eighth section describes the contraindications. Such information is listed in the user manual of the subject device.

8. *In addition to the RAPID imaging criteria, patients must meet the clinical requirements for thrombectomy, as assessed by the physician, and have none of the following contraindications or exclusions.*

   Contraindications/Exclusions:
   - *Bolus Quality: absent or inadequate bolus.*
   - *Patient Motion: excessive motion leading to artifacts that make the scan technically inadequate.*
   - *Presence of Hemorrhage.*

Additionally, the subject device is able to evaluate brain tumors while the reference device does not provide such functionality. This functionality, the evaluation of brain tumors, is already part of the predicate device (syngo.CT Neuro Perfusion, VB20) as listed in the IFU statement comparison table.

Comparison of Technological Characteristics

The only modification made to syngo.CT Neuro Perfusion VB50 software is the addition of the Hypoperfused Area and Mismatch Ratio parameters. All remaining features are unchanged. Please refer to the table below for a high-level overview of features within Neuro Perfusion:

Feature	Subject Device	Predicate Device	Reference Device	Comments
	syngo.CT Neuro Perfusion *(SOMARIS/8 VB50)*	syngo.CT Neuro Perfusion *(SOMARIS/8 VB20, K163284)*	iSchemaView RAPID (K182130)	
Tissue at risk and non-viable tissue visualization	The flexible penumbra analysis mode allows highlighting of areas as Non-viable Tissue (NVT) and Tissue-At-Risk (TAR) according to certain user defined thresholds. Thresholds of two different Perfusion maps, e.g. CBF, CBV, MTT, TTP can be used. Results can be smoothed to reduce artefacts. Relative thresholds can be used for CBV and CBF. The visualization is done as color coded overlay on temporal MIP. Additional TAC and statistical values are displayed. Hypoperfused Area (sum of existing parameters TAR and NVT) and Mismatch Ratio parameters (division of Hypoperfused Area by NVT or (TAR+NVT)/NVT) have been added.	The flexible penumbra analysis mode allows highlighting of areas as Non-viable Tissue (NVT) and Tissue At Risk (TAR) according to certain user defined thresholds. Thresholds of two different Perfusion maps, e.g. CBF, CBV, MTT, TTP can be used. Results can be smoothed to reduce artefacts. Relative thresholds can be used for CBV and CBF. The visualization is done as color coded overlay on temporal MIP. Additional TAC and statistical values are displayed	According to both publications Bathla et al. 2019 and Bathla et al. 2020 the definition of the Hypoperfused Area and Mismatch Ratio parameters is considered substantially equivalent to how these parameters are utilized within the reference device, iSchemaView RAPID (K182130).	**Modified** **Addition of *Hypoperfused Area* and *Mismatch Ratio* parameters.** Both parameters derive from already cleared parameters NVT and TAR. The subject device provides the additional parameters Hypoperfused Area (sum of TAR and NVT) and Mismatch Ratio (division of Hypoperfused Area by NVT or (TAR+NVT) / NVT). The reference device, iSchemaView RAPID (K182130) was used as a comparison marketed software in order to determine how modifications to the thresholds of these parameters resulted in comparable measurements.
Purpose of the application	Visualization of tissue perfusion using rapid sequences collected after the administration of contrast medium	Visualization of tissue perfusion using rapid sequences collected after the administration of contrast medium	Visualization of tissue perfusion using rapid sequences collected after the administration of contrast medium	Same; No change between the primary predicate and device subject to this review.
Acquisition	Patient scan following administration of contrast media	Patient scan following administration of contrast media	N/A	No change between the primary predicate and device subject to this review.
CT Scanning Mode	Scanning at a single table position or using spirals with the same scan range	Scanning at a single table position or using spirals with the same scan range	N/A	No change between the primary predicate and device subject to this review.
Motion Correction	Rigid motion correction which can be used in brain datasets	Rigid motion correction which can be used in brain datasets	N/A	No change between the primary predicate and device subject to this review.

Feature	Subject Device	Predicate Device	Reference Device	Comments
	syngo.CT Neuro Perfusion *(SOMARIS/8 VB50)*	syngo.CT Neuro Perfusion *(SOMARIS/8 VB20, K163284)*	iSchemaView RAPID (K182130)	
Time Point Removal	On user request time points and time ranges (time point volumes) can be removed from the current evaluation if they show strong patient or organ movement.	On user request time points and time ranges (time point volumes) can be removed from the current evaluation if they show strong patient or organ movement.	N/A	No change between the primary predicate and device subject to this review.
4D Noise Reduction	Noise reduction with preservation of time-attenuation information can be performed to improve the image quality of noisy input images and to allow for robust image evaluation	Noise reduction with preservation of time-attenuation information can be performed to improve the image quality of noisy input images and to allow for robust image evaluation	N/A	No change between the primary predicate and device subject to this review.
Brain Segmentation	The task can apply the brain segmentation algorithm	The task can apply the brain segmentation algorithm	N/A	No change between the primary predicate and device subject to this review.
HU Segmentation	Removes all pixels that lie outside the Min HU and Max HU thresholds	Removes all pixels that lie outside the Min HU and Max HU thresholds	N/A	No change between the primary predicate and device subject to this review.
Reference Vessel Definition	Automatic identification of the reference vessel with simple interactive override if the user does not accept automatic detection	Automatic identification of the reference vessel with simple interactive override if the user does not accept automatic detection	N/A	No change between the primary predicate and device subject to this review.
Vessel and Arteries Definition	Automatic identification of the brain vessels and arteries with simple interactive override possibility	Automatic identification of the brain vessels and arteries with simple interactive override possibility	N/A	No change between the primary predicate and device subject to this review.
Hemisphere Plane Definition	Automatic hemisphere plane definition which can be manually corrected	Automatic hemisphere plane definition which can be manually corrected	N/A	No change between the primary predicate and device subject to this review.
Normalization	Normalization of CBF and CBV values based on a histogram analysis of the non-ischemic hemisphere	Normalization of CBF and CBV values based on a histogram analysis of the non-ischemic hemisphere	N/A	No change between the primary predicate and device subject to this review.
Result Storage	Storage of all result images in the database as DICOM CT grayscale, color RGB, Enhanced CT	Storage of all result images in the database as DICOM CT grayscale, color RGB, Enhanced CT	N/A	No change between the primary predicate and device subject to this review.
ROI (region of interest) evaluation	ROI (region of interest) measurements with calculation of mean value, standard deviation and area for detailed analysis of specific ischemic areas	ROI (region of interest) measurements with calculation of mean value, standard deviation and area for detailed analysis of specific ischemic areas	N/A	No change between the primary predicate and device subject to this review.

Feature	Subject Device	Predicate Device	Reference Device	Comments
	syngo.CT Neuro Perfusion *(SOMARIS/8 VB50)*	syngo.CT Neuro Perfusion *(SOMARIS/8 VB20, K163284)*	iSchemaView RAPID (K182130)	
ROI mirroring	Mirroring of the ROIs at the hemisphere plane and output of statistical parameters like mean value, standard deviation and area	Mirroring of the ROIs at the hemisphere plane and output of statistical parameters like mean value, standard deviation and area	N/A	No change between the primary predicate and device subject to this review.
TAC display	Parallel display of several time attenuation curves	Parallel display of several time attenuation curves	N/A	No change between the primary predicate and device subject to this review.
Automatic Stroke calculation	Automatic calculation of all steps, visualization of all intermediate results allowing a final result check	Automatic calculation of all steps, visualization of all intermediate results allowing a final result check	N/A	No change between the primary predicate and device subject to this review.
Sending of Images to PACS	Automatic sending of result images to PACS including quality control images. Possibility to do the evaluation manually.	Automatic sending of result images to PACS including quality control images. Possibility to do the evaluation manually.	N/A	No change between the primary predicate and device subject to this review.

As outlined in the table above, the change in the VB50 release of Neuro Perfusion is the addition of the Hypoperfused Area and Mismatch Ratio parameters.

The calculation of these values are from already existing parameters NVT (non-viable-tissue) and TAR (tissue at risk) within the commercially available syngo.CT Neuro Perfusion SOMARIS/8 VB20 release (K163284):

- Hypoperfused Area is calculated based on the sum of NVT and TAR
- Mismatch Ratio is calculated by dividing Hypoperfused Area by NVT

Equivalence of the parameters "Hypoperfused Area" and "Mismatch Ratio" with the reference device iSchemaView RAPID (K182130) was shown mainly by Bathla et al. 2020[1]. This study also contains all patients of Bathla 2019[2].

Testing population used in the study
Patients presenting with AIS between January 2017 and December 2018 were screened. For the MT group, consecutive patients were included who underwent MT (mechanical thrombectomy) and met the following criteria: AIS presenting between 6 and 24 hours since last known normal, presence of ICA or M1-MCA occlusion and availability of a CTP study. For the NMT group, the inclusion criteria were: AIS presenting between 6 and 24 hours of last known normal, no endovascular therapy and presence of a confirmed acute stroke on follow-up imaging. In total 74 patients were in the MT group, of these 9 did not have complete perfusion data, 3 patients had motion artifacts, 62 were included in the final analysis. 73 patients were in the NMT group, complete perfusion data was not available for 12 patients, 5 had motion artefact, so 56 patients were included.

[1] Bathla et al. (2020): *"Comparing the Outcomes of Two Independent CT Perfusion Softwares and Their Impact on Therapeutic Decisions in Acute Ischemic Stroke"*
[2] Bathla et al. (2019): *"Achieving comparable perfusion results across vendors. The next step in standardizing stroke care: a technical report"*

Methodology of the study

The values for core infarct and hypoperfused area were compared between the two groups using Bland–Altman plots and Wilcoxon signed rank test. Correlation between the core infarct and hypoperfused area was evaluated using intraclass correlation coefficient (ICC). Individual patient triage between MT and NMT groups were evaluated based on a combination of perfusion outputs alone, and after considering additional neuroimaging eligibility criteria as defined in DEFUSE III, to determine if the final clinical decision, based on a combination of factors, would remain the same regardless of eligibility determined based on perfusion imaging.

Summary of the findings and their clinical importance/implications

From the point of view of 'go versus no-go' for MT, the core infarct volume, mismatch ratio and hypoperfused area only were considered initially. This yielded concordance in 60/62 cases between the two packages in the MT group. When low ASPECTS (defined as <6 in DEFUSE III) was also considered, one additional patient (in retrospect) would not have qualified regardless of the discrepancy in perfusion outputs. The second patient would qualify based on package A (Subject Device), but not package B (Reference Device). In the NMT group, concordant results were noted in 49/56 patients when perfusion criteria alone were considered. Of the seven patients for whom the results differed, five patients would additionally qualify based on package A and two patients based on package B alone. Of these, however, three patients did not have any vascular occlusion on the angiogram images, while two patients had M2/M3-MCA occlusions. Two patients had low ASPECTS scores. Therefore, none of these patients would additionally qualify when all DEFUSE III criteria were considered. Overall, there was high concordance when perfusion outputs were considered in isolation (110/118, 93.2%), which improved even further when additional imaging criteria (site of vessel occlusion and ASPECTS) were also considered (117/118, 99.1%).

Discussion on the limitations of the use of the subject device

The discussion on the limitations is identical in content to Bathla et al. 2020. The results show that despite differences in perfusion post-processing techniques, high agreement between perfusion softwares in term of 'go versus no-go' for MT can be achieved in real-world settings when patients are triaged based on imaging inclusion and exclusion criteria as defined in DEFUSE III. Similarly, we did not find any significant differences in the core and hypoperfused area in the NMT group and between the core volumes in the MT group. Even though the hypoperfused area in the MT group showed good correlation between the two packages (ICC: 0.79), the difference in calculated volumes was significant as discussed below. The use of Tmax to reliably define hypoperfusion has been demonstrated. Hypoperfusion is defined as Tmax>6 s for both packages. However, we noted a mean difference in hypoperfused area to be about 12.75 mL for the NMT group and 17.3 mL for the MT group. For the MT group, this translated to a difference of about 11.6% overestimation in mean volume (8.7% for median volumes) using package B when compared with package A.

Appropriate criteria to achieve comparable results

Limitations of the study include the retrospective nature, a small sample size and a single center experience.

High concordance in terms of proceeding or not proceeding with MT in AIS patients is achievable between syngo.via and RAPID, and increases even further when additional neuroimaging criteria (ASPECTS and site of occlusion) are also considered. Both packages show similar core volume estimations in both the MT and NMT groups. The penumbral volumes in patients in the MT group may be overestimated with RAPID but do not appear to impact eligibility for MT.

Fundamental scientific technology

The fundamental scientific technology of syngo.CT Neuro Perfusion SOMARIS/8 VB50 is the same compared to the commercially available predicate device. The post-processing software functionality remains unchanged from the predicate device with the exception of the feature modifications listed

above. Siemens believes that the feature modifications subject to this syngo.CT Neuro Perfusion application are substantially equivalent to the predicate device.

VII. Performance Data / Safety and Effectiveness

The following performance data has been provided in support of the substantial equivalence determination:

Bench Testing
Verification and Validation activities demonstrate continued conformance with special controls for medical devices containing software, including assurance that functions work as designed, performance requirements and specifications have been met, and that all hazard mitigations have been fully implemented. Integration and Functional testing were conducted for syngo.CT Neuro Perfusion during product development. In addition, testing was performed to ensure the feature modifications within this submission meet the predetermined acceptance values.

It is in Siemens' opinion that the results of these test activities demonstrate that the subject device performs as intended and the results were found acceptable to support the claim of substantial equivalence.

Traceability of requirement and functional specifications is ensured during component integration, software validation and system testing

Validation Summary of the Parameters (Hypoperfused Area and Mismatch Ratio)
Performance data was provided in the form of Verification and Validation to support the substantial equivalence determination. In addition to the V&V testing, both the Hypoperfused Area and Mismatch Ratio parameters have been evaluated in publications as described in both papers Bathla et el. 2019 and Bathla et al. 2020. The summary of these publication is shown above in section VI of the 510(k) Summary.

Risk Analysis
Risk Management has been ensured via the risk analysis in compliance with ISO 14971 to identify and provide mitigation to potential hazards beginning early in the design cycle and continuing throughout the development of the product.

For this submission, the risk analysis was performed to ensure the risk control was implemented to mitigate identified hazards. The testing results support that all the software specifications have met the acceptance criteria. Testing for verification and validation of the device was found acceptable to support the claims of substantial equivalence. Siemens adheres to recognized and established industry standards for development including ISO 13485 and IEC 62304.

FDA Recognized Standards
Siemens hereby certifies that syngo.CT Neuro Perfusion will meet the following voluntary standards covering electrical and mechanical safety listed below, prior to introduction into interstate commerce:

Recognition Number	Product Area	Title of Standard	Date of Recognition	Standards Development Organization
12-300	Radiology	Digital Imaging and Communications in Medicine (DICOM) Set; PS 3.1 – 3.20	06/27/2016	NEMA
13-79	Software	Medical Device Software - Software life-cycle processes [including Amendment 1 (2016)]; 62304:2006/A1: 2016	01/14/2019	AAMI, ANSI, IEC
5-40	Software/ Informatics	Medical Devices - Applications of risk management to medical devices; 14971:2007/(R)2010	06/27/2016	ANSI, AAMI, ISO

5-129	General I (QS/RM)	Medical devices - Part 1: Applications of usability engineering to medical devices; 62366-1 Edition 1.1 Consolidated Version	07-06-2020	IEC

VIII. Conclusion

There are no differences in the Indications for Use or Fundamental Technology Characteristics of the syngo.CT Neuro Perfusion software as compared to the currently commercially available software (K163284).

The modifications made (in regard to the addition of the Hypoperfused Area and Mismatch Ratio parameters) in this submission were previously withdrawn (K192052).

The feature modifications made within the VB50 release of Neuro Perfusion do not raise any new issues of safety and effectiveness as compared to the predicate device. Modifications made fall within already existing fundamental scientific technology which remains within previously cleared specification. Based on this information—as well as documentation in support of modifications made—it is Siemens' opinion that the syngo.CT Neuro Perfusion software is substantially equivalent to the predicate device.