University of Texas, MD Anderson Cancer Center   May 17, 2023
℅ Ms. Stella Tsai
Sr. Project Manager
1515 Holcombe Blvd.
HOUSTON TX 77030

Re: K222728
     Trade/Device Name: Radiation Planning Assistant (RPA)
     Regulation Number: 21 CFR 892.5050
     Regulation Name: Medical charged-particle radiation therapy system
     Regulatory Class: Class II
     Product Code: MUJ
     Dated: April 17, 2023
     Received: April 17, 2023

Dear Ms. Stella Tsai:

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,

Lora D. Weidner -S
Digitally signed by Lora D. Weidner -S
Date: 2023.05.17 07:14:45 -04'00'

Lora D. Weidner, Ph.D.
Assistant Director
Radiation Therapy Team
DHT8C: Division of Radiological Imaging
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Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number *(if known)*
K222728

Device Name
 Radiation Planning Assistant (RPA)

Indications for Use *(Describe)*
The Radiation Planning Assistant (RPA) is used to plan radiotherapy treatments for patients with cancers of the head and neck, cervix, breast, and metastases to the brain. The RPA is used to plan external beam irradiation with photon beams using CT images. The RPA is used to create contours and treatment plans that the user imports into their own Treatment Planning System (TPS) for review, editing, and re-calculation of the dose.

Some functions of the RPA use Eclipse 15.6. The RPA is not intended to be used as a primary treatment planning system. All automatically generated contours and plans must be imported into the user's own treatment planning system for review, edit, and final dose calculation.

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.

K222728

DATE PREPARED: 16 May 2023

1.   SUBMITTER

Manufacturer Name:	The University of Texas MD Anderson Cancer Center Department of Radiation Physics Division of Radiation Oncology 1515 Holcombe Blvd. Houston, TX 77030
Official Contact:	Stella Tsai, MHA, CCRA Sr. Project Director, IND Office The University of Texas MD Anderson Cancer Center 1515 Holcombe Blvd. Unit 1634 Houston, TX 77030 Telephone (713) 563-5464 swtsai@mdanderson.org

2.   DEVICE

Name of Device:	Radiation Planning Assistant (RPA)
Common or Usual Name:	System, Planning, Radiation Therapy Treatment
Classification Name:	21CFR 892.5050 - Medical charged-particle radiation therapy system
Regulatory Class:	II
Product Code:	MUJ

3.   PREDICATE DEVICE

Eclipse Treatment Planning System v15.6 (K181145)

4.   DEVICE DESCRIPTION

 Design Characteristics

The Radiation Planning Assistant (RPA) is a web-based contouring and radiotherapy treatment planning software tool that incorporates the basic radiation planning functions from automated contouring, automated planning with dose optimization, and quality control checks. The system is intended for use for patients with cancer of the head and neck, cervix, breast, and metastases to the brain. The RPA system is integrated with the Eclipse Treatment Planning System v15.6 software cleared under K181145. The RPA radiation treatment planning software tool was trained against hundreds / thousands of CT Scans of normal and diseased tissues from patients receiving radiation for head and neck, cervical, breast, and whole brain at MD Anderson Cancer Center.

5.   INDICATIONS FOR USE

The Radiation Planning Assistant (RPA) is used to plan radiotherapy treatments for patients with cancers of the head and neck, cervix, breast, and metastases to the brain.

The RPA is used to plan external beam irradiation with photon beams using computerized tomography (CT) images. The RPA is used to create contours and treatment plans that the user imports into their own Treatment Planning System (TPS) for review, editing, and re-calculation of the dose.

Some functions of the RPA use Eclipse 15.6. The RPA is not intended to be used as a primary treatment planning system. All automatically generated contours and plans must be imported into the user's own treatment planning system for review, edit, and final dose calculation.

6.   COMPARISON OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATE DEVICE

The Radiation Planning Assistant (RPA) is substantially equivalent to the Eclipse Treatment Planning System v15.6 (K181145) predicate device in the following respects:

Table 1:   **Comparison of the Technological Characteristics of the RPA with Predicate Device**

	Subject Device	Predicate Device
	Radiation Planning Assistant (RPA)	**Eclipse Treatment Planning System Version 15.6**
		K181145
CFR Citation	892.5050	892.5050
Product Code	MUJ	MUJ
Indications for Use	The Radiation Planning Assistant (RPA) is used to plan radiotherapy treatments for patients with cancers of the head and neck, cervix, breast, and metastases to the brain. The RPA is used to plan external beam irradiation with photon beams using computerized tomography (CT) images. The RPA is used to create contours and treatment plans that the user imports into their own Treatment Planning System (TPS) for review, editing, and re-calculation of the dose. Some functions of the RPA use Eclipse v.15.6. The RPA is not intended to be used as a primary treatment planning system. All automatically generated contours and plans must be imported into the user's own treatment planning system for review, edit, and final dose calculation.	The Eclipse Treatment Planning System (Eclipse TPS) is used to plan radiotherapy treatments for patients with malignant or benign diseases. Eclipse TPS is used to plan external beam irradiation with photon, electron, and proton beams, as well as for internal irradiation (brachytherapy) treatments.
Device Description	The Radiation Planning Assistant (RPA) is a web-based contouring and radiotherapy treatment planning software tool that incorporates the basic radiation planning functions from automated contouring, automated planning with dose optimization, and quality control checks. The system is intended for use for patients with cancer of the head and neck, cervix, breast, and metastases to the brain. The RPA system is integrated with the Eclipse Treatment Planning System v.15.6 software cleared under K181145.	The Varian Eclipse™ Treatment Planning System (Eclipse TPS) provides software tools for planning the treatment of malignant or benign diseases with radiation. Eclipse TPS is a computer-based software device used by trained medical professionals to design and simulate radiation therapy treatments. Eclipse TPS is capable of planning treatments for external beam irradiation with photon, electron, and proton beams, as well as for internal irradiation (brachytherapy) treatments.

Table 2:   Comparison of Functions of the Subject Device with Functions of the Predicate Device

	Comparison of the RPA System's Software Functions with Eclipse Treatment Planning System Version 15.6 (K181145)			
Software Function	**Description of Functions Available in Eclipse**	**Differences**	**Similarities**	**Rationale for Substantial Equivalence**
Software Contouring Functions	1. Organ-specific autocontouring algorithms. Eclipse v.15.6 includes the following organ-specific autocontouring algorithms for the following organs: spine, lung, brain, eye, bone. 2. Expert Segmentation. Eclipse v.15.6 includes an atlas-based contouring approach ("expert segmentation") for autocontouring of many structures, including: • Head / neck region: Body, bones, brainstem, cochlea, esophagus, eyes, mandible, oral cavity, various lymph nodes • Breast region: Body, heart, trachea, various lymph nodes • Pelvis: Body, bladder, femoral heads, pelvic bones, rectum, spinal canal The system calculates the anatomical points, image features, and similarity scores of the patient image and compares them with pre-stored expert cases. Rigid registration is used both for initializing the deformable registration algorithm and for displaying the expert case and patient image in aligned preview. The autocontouring approach depends on the selected structures. Either the structures are heuristically segmented from the patient image, or the structures are generated via deformable registration and structure propagation from the expert cases. If multiple expert cases are used, the propagated structures from the different atlases are fused by means of the simultaneous truth and performance level estimation (STAPLE) algorithm.	The RPA uses deep learning algorithms which Eclipse does not. <u>Use and function</u>: In Eclipse, the user edits the contours prior to planning. This is the same for complex planning in the RPA (VMAT planning for head / neck and cervix). It is different for simple plans, where the plan is generated before the user reviews the contours. If the user edits the contours in the RPA, they will have to delete the plan as well.	<u>Use and function</u>: The RPA provides autocontouring for a range of structures, including most of those listed here for Eclipse. <u>Performance data</u>: The algorithm for Expert Segmentation in Eclipse is very similar to the Multi-Atlas Contouring System (MACS) that is used to contour structures for the chest wall planning in the RPA. <u>Safety and effectiveness</u>: Both Eclipse and the RPA are designed to provide contours that the users review and edit.	Devices are Substantially Equivalent. Both devices provide autocontouring functions for the same anatomical regions. Both devices require user edits of contours with 'complex plans' prior to planning.
Eclipse, Other Plan Preparation	Automatic marker detection - Eclipse v.15.6 includes a function ('Calypso Beacon Detection') to automatically detect a specific type of marker (Calypso transponders) on CT images.	<u>Use and function</u>: The Eclipse function is for a specific type of marker that is different from the generic markers that the RPA is designed for.	<u>Use and function</u>: Both Eclipse and the RPA can automatically detect markers.	Devices are Substantially Equivalent. Both devices can automatically detect markers.

**Comparison of the RPA System's Software Functions with** the **Eclipse Treatment Planning System Version 15.6 (K181145)**				
Software Function	**Description of Functions Available in Eclipse**	**Differences**	**Similarities**	**Rationale for Substantial Equivalence**
Eclipse Automated Planning, VMAT	1. Photon Optimizer (PO) algorithm. This algorithm is used to optimize IMRT or VMAT plans based on DVH constraints / objectives. 2. Automated Optimization Workflow. Enabling this can automate the optimization workflow for IMRT planning so that, after optimization, the leaf motion calculation and final dose calculation are automatically initiated, and the results are then automatically saved. A similar feature exists for VMAT plans. 3. DVH Estimation Models for RapidPlan. DVH estimation models are created from information extracted from a set of previous treatment plans (called 'treatment plans'). The estimation models predict the DVH that is achievable from the current treatment plan (based on the geometry in the current plan), and also creates a set of optimization objects that can be based on the DVH estimates or fixed (i.e., not based on the DVH estimates).	Use and function: The main difference for VMAT planning is that Eclipse generally creates a plan that the user reviews, makes edits to the optimization constraints, and repeats the process to improve the plan quality. The RPA uses the same optimization tools (i.e., the tools in Eclipse), but the optimization objectives and constraints have been pre-set to give optimal plans for the majority of patients. The user is not able to easily edit the RPA VMAT plans so, if they do not approve the plan for clinical use, they must delete it and create one using their own routine processes (i.e., in their own treatment planning system).	Use and function: The RPA uses some Eclipse features, including DVH Estimates for RapidPlan and the Photon Optimizer for optimizing VMAT plans. The plans look very similar. Safety and effectiveness: Both Eclipse and the RPA are designed to create plans that the users then edit and review for clinical acceptability prior to use.	Devices are Substantially Equivalent. Both devices provide autoplanning features and create plans that the users then edit and review for clinical acceptability prior to use. Both devices provide Photon Optimizer, automated optimization workflow and DVH estimation models.
Autoplanning, Other	1. Beam Angle Optimization (BAO). This tool optimizes the number and angle of treatment beams. It optimizes the objective function, which is determined by DVH goals / constraints and a normal tissue objective (which falls off with distance from the PTV). BAO can be used for IMRT plans or as a starting point for conformal treatment plans. 2. Collimator Angle Optimization (CAO). This function optimizes collimator angle for each arc of a HyperArc plan such that, whenever possible, a given pair of MLC leaves delineates only one target in the beam's-eye-view. 3. Optimize collimator jaws. Adjusts the collimator jaws to best fit the MLC leaves to the structure. 4. Use recommended jaw positions. Adjusts the collimator jaw positions with an additional margin. 5. Optimize collimator rotation. Optimizes the collimator rotation around a structure.	Use and function: Autoplanning in Eclipse is mostly automation of individual tasks that are controlled by the user. The user does not control these tasks with the RPA. Use and function: Review and editing of 3D plans (cervix 4-field box, post-mastectomy breast plans, whole brain plans) for the RPA happens in the users' own treatment planning system.	Use and function: Many of the treatment plan details in Eclipse and RPA use functions with similar algorithms, such as optimizing the jaw positions. Safety and effectiveness: Both Eclipse and the RPA are designed to create plans that the users then edit and review for clinical acceptability prior to use.	Devices are Substantially Equivalent. Both devices create plans that the users then edit and review for clinical acceptability prior to use through the use of AI software. Both devices provide Beam Angle Optimization, Collimator Angle Optimization and collimator jaw optimization.

7. PERFORMANCE DATA

7.1 Non-Clinical Data

7.1.1 *Software Verification and Validation Testing*

Software verification and validation was conducted, and documentation was provided as recommended by the FDA's Guidance for Industry and FDA Staff, "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." The software for this device was considered as a "major" level of concern. Test results demonstrate conformance to applicable requirements and specifications.

No animal studies or clinical tests have been included in this pre-market submission.

The ground truth treatment plans were generated by the RPA by the primary 4-field box automation technique for cervical cancer by Kisling et al. (Kisling 2019) with beam apertures based on a patient's bony anatomy. Only the clinically acceptable plans were used for training (rated by physicians); their DRRs and corresponding beam apertures were the inputs for training (and just the DRRs for testing/prediction). No additional criteria were applied. The test set was generated in the same manner as the ground truth, but on previously unseen patients.

Initial software training for each anatomical location was successfully accomplished and is described in brief in Table 3 below.

Table 3 presents the initial testing performed for software training and testing. Multicenter performance testing is presented in Section 7.2.

Table 3:   Software Training for Anatomical Locations

Anatomical Location	Tissue Type(s)	Training Data Set	Test Data Independence
Head and Neck	Normal Tissue (primary)	3,288 patients (3,495 CT scans) who received radiation therapy at MD Anderson Cancer Center between September 2004 and June 2018. Any patient who received a simulation CT scan of the head/neck region in a head -first supine position was eligible.	174 CT scans were randomly selected from this group (and excluded for training) plus qualitative evaluation 24 CT scans from an external dataset.
	Normal Tissue (secondary)	160 patients who received radiation therapy at MD Anderson Cancer Center from 2018 to 2020. Any patient who received a simulation CT scan of the head/neck region in a head-first supine position was eligible.	Test patients were randomly selected and excluded from the training set.
	Lymph Node CTVs	61 patients who received radiation therapy at MD Anderson Cancer Center between 2010 and 2019. Any patient who received a simulation CT scan of the head/neck region in a head-first supine position was eligible.	These 71 cases were randomly placed in 3 groups: training (51 pts.), cross-validation (10 pts.) and final test (10 pts.).
Whole Brain	Whole Brain	The whole brain primary segmentation models used the same models as used for head and neck segmentation, described above, as well as an additional vertebral body localization and segmentation model (Vertebral Bodies model: spinal canal CNN: 1,966, VB labeling: 803, VB segmentation: 107, from 930 MDACC patients and 355 external patients). Patients who received spinal radiotherapy for spinal metastases (3DCRT and VMAT) at MD Anderson, or for whom data was publicly available (MICCAI challenge data).	Test patients were randomly selected from this group (and excluded for training).

Anatomical Location	Tissue Type(s)	Training Data Set	Test Data Independence
GYN	Normal Tissue (primary)	1,999 patients (2,254 CT scans) who received radiation therapy at MD Anderson from September 2004 and June 2018. Any patient who received a simulation CT scan of the pelvic region in a head-first supine position was eligible.	140 CT scans were randomly selected from this group (and excluded for training) plus qualitative evaluation with 30 cervical cancer patients from 3 centers in S. Africa.
	Normal Tissue (secondary)	192 patients (316 CT scans) who were treated for locally advanced cervical cancer between 2006 and 2020.	Test patients were randomly selected from this group (and excluded for training).
	CTVs (primary)	406 CT scans from 308 patients (UteroCervix), 250 CT scans from 201 patients (Nodal CTV), 146 CT scans from 131 patients (PAN), 490 CT scans from 388 patients (Vagina), 487 CT scans from 388 patients (Parametria) who received radiation therapy at MD Anderson Cancer Center between 2006 and 2020.	Test patients were randomly selected from this group (and excluded for training).
	Liver	Training data for GYN Liver (normal) comprised 119 patients (169 CT scans) who had received contrast-enhanced and non-contrast CT imaging of the liver at MD Anderson Cancer Center.	Test patients were randomly selected from this group (and excluded for training).
Chest Wall	Whole Body (secondary for chest wall)	Training data for whole body (secondary for chest wall) comprised 250 patients who were treated at MD Anderson between August 2016 and June 2021, with CT imaging in the thoracic region.	Test patients were randomly selected from this group (and excluded for training).

7.1.2   Standards Conformance

The subject device conforms in whole or in part with the following standards:

- IEC 62304 Medical device software - Software life cycle processes
- IEC 62083 Requirements for the safety of radiotherapy treatment planning systems

7.2   Clinical Data

A summary of the multicenter clinical data is presented in the tables below.

Table 4:   Demographics, Number of Patients, Number of Samples, and Clinical Sites

Characteristic	All Cervix VMAT	All Cervix 3D	All Chest Wall	All Head and Neck	All Whole Brain
No. of Unique Patients with RPA Plan(s)	50	47[a]; 45[b]	46	86	46
CT Scan Equipment					
Philips	x	x	x	x	x
Siemens	x	x	x	x	x
GE	x	x	x	x	x
No. of Clinical Sites	5	5	5	5	5
No. of Participating Physicians / Study Site					
Site 1	5	5	8	12	12
Site 2	1	1	2	3	2
Site 3	3	3	1	1	3
Site 4	3	3	8	1	6
Site 5	2	2	4	5	2
Clinical Subgroups and Confounding Factors					
By Study Site	None	None	None	None	None
By Equipment	None	None	None	None	None
Age Mean Min, Max	 51 26, 94	 50 26, 84	 51 31, 80	 62 27, 87	 60 14, 88
Sex Male Female Not Reported	 0.0% 100.0 0.0%	 0.0% 100.0% 0.0%	 2.2% 97.8% 0.0%	 79.3% 29.7% 0.0%	 39.1% 34.8% 26.1%
Race Asian Black/African American White Native Hawaiian or Pacific Islander British American Indian or Alaskan Native Other / not available	 9.8% 13.7% 39.2% 0.0% 7.8% 2.0% 27.5%	 2.1% 14.9% 78.7% 0.0% 0.0% 0.0% 4.3%	 26.1% 13.0% 32.6% 0.0% 0.0% 4.3% 23.9%	 5.4% 12.0% 73.9% 1.1% 0.0% 1.1% 6.5%	 6.5% 8.7% 54.3% 0.0% 0.0% 0.0% 28.3%
Ethnicity Hispanic or Latino Not Hispanic or Latino Other / not available	 25.5% 41.2% 33.3%	 10.6% 46.8% 42.6%	 8.7% 43.5% 47.8%	 7.6% 50.0% 42.4%	 6.5% 58.7% 34.8%

[a] 4-field box soft tissue plan
[b] 4-field box bony landmark plan

Table 5:   Summary of Statistical Results—Cervix

Criteria Number	Criteria	Results
1	Assess the safety of using the RPA plan for normal structures for treatment planning by comparing the number of patient plans that pass accepted dosimetric metrics when assessed on the RPA contour with the number that pass when assessed on the clinical contour. The difference should be 5% or less. When there are multiple metrics for a single structure at least one should pass this criterion.	$\leq$ 5% difference between RPA Plan and Clinical Plan for all bony structures and critical soft tissue structures with VMAT and 4 field box.*
2	Assess the effectiveness of the RPA plan for normal structures by comparing the dose to RPA normal structures for RPA plans and clinical normal structures for clinical plans. The difference in the number of RPA plans that pass accepted dosimetric metrics and the number of clinical plans that pass accepted dosimetric metrics should be 5% or less. When there are multiple metrics for a single structure at least one should pass this criterion.	$\leq$ 5% difference between RPA Plan and Clinical Plan for all bony structures and critical soft tissue structures with VMAT and 4 field box.**
3	Assess the effectiveness of the RPA plan for target structures by comparing the number of RPA plans that pass accepted dosimetric metrics (e.g., percentage volume of the PTV receiving 95% of the prescribed dose) when compared with clinical plans. The difference should be 5% or less. When there are multiple metrics used to assess a single structure, at least one coverage and one maximum criterion should pass this criterion.	$\leq$ 5% difference between RPA Plan and Clinical Plan for all assessed structures
4	Assess the geometric effectiveness of the RPA targets using recall. A low value for this metric represents under-contouring. The 25th percentile of the recall must be 0.7 or greater.	25th percentile for recall > 0.7
5	Assess the quality of body contouring generated by the RPA by comparing primary and secondary body contours generated by the RPA with manual body contours. Surface DSC (2mm) should be greater than 0.8 for 95% of the CT scans.	Surface DSC > 0.8 for 95% of CT scans
6	Assess the ability of the RPA to accurately identify the marked isocenter. This is achieved by comparing the automatically generated isocenters with manually generated ones. 95% of automatically generated marked isocenters (primary and verification approaches) should agree with manually generated marked isocenters within 3mm in all orthogonal directions (AP, lateral, cranial-caudal).	$\leq$ 3mm difference between RPA Plan and Clinical Plan for all orthogonal directions

* With the exception of bowel bag in the 4-field box plans, the RPA contour gives a more conservative result.
** RPA plan and clinical plan had 6% - 13% difference in passing rates using VMAT on right kidney, bladder, and bowel. The RPA Plan for rectum exceeded passing rates of the clinical plans in excess of 5%. However, when the RPA plan (which was created using the RPA normal contours) was assessed using the clinical normal contours, the passing rates for the clinical plan and RPA plan are within 5% for all normal structures. This is a result of the conservative nature of the RPA contours.

Table 6:   **Summary of Cervix Protocol**

Criteria Number	Inclusion Criteria	Exclusion Criteria	Sampling Method
1	CT scan of the female pelvic anatomy.	Poor Image Quality	Test datasets were chosen going forward in time until sufficient data were collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection was restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.
2	Clear CT image of the pelvic region without distortions.	-	
3	Test datasets consisted of CT images of patients previously treated for cervical cancer using radiotherapy following one of the following treatment schemes: • 4-field box (based on bony landmarks or soft tissue) • VMAT	-	
4	Scan was obtained with patient head-first, supine.	-	
5	The datasets included CT images, original clinical contours of anatomic structures and treatment targets, and the dose distributions used for patient treatment.	-	
6	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection could be restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.	-	
7	Testing datasets were unique, with no overlap with data used for model creation or in previous validation studies.	-	
8	CT scans included the manufacturer and model of the scanner used to obtain the CT image.	-	

Table 7:   Chest Wall Summary of Statistical Results

Criteria Number	Criteria	Results
1	Assess the safety of use of the RPA by comparing the number of patient plans that pass accepted dosimetric metrics when assessed on the RPA contour with the number that pass when assessed on the clinical contour. The difference should be 5% or less. When multiple metrics were used to assess a single structure at least one had to pass the criteria (similar to the manner in which doses are assessed in clinical practice).	$\leq$7% difference between RPA Plan and Clinical Plan for all assessed structures.
2	Assess the effectiveness of use of the RPA by comparing the number of RPA plans that pass accepted dosimetric metrics (e.g., mean dose to the organ-at-risk) when compared with clinical plans. The difference should be 5% or less. When multiple metrics were used to assess a single structure, at least one should pass this criterion (similar to the manner in which doses are assessed in clinical practice). This was considered on a structure-by-structure basis.	$\leq$5% difference between RPA Plan and Clinical Plan for all assessed structures.
3	Assess the quality of body contouring generated by the RPA by comparing primary and secondary body contours generated by the RPA with manual body contours. Surface DSC (2mm) should be greater than 0.8 for 95% of the CT scans.	Surface DSC > 0.8 for 95% of CT scans

Table 8:   Chest Wall Protocol Summary

Criteria Number	Inclusion Criteria	Exclusion Criteria	Sampling Method
1	CT scan of the breast (thorax) region.	Poor Image Quality	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection was restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.
2	Clear CT image of the breast (thorax) region without distortions.	-	
3	Test datasets must consist of CT images of patients previously treated for postmastectomy breast radiotherapy following one of the following treatment schemes: 　i.　Tangent fields with supraclavicular fields. Similar approaches, including those that also treat the intramammary lymph nodes are also acceptable.	-	
4	Scan was obtained with patient head-first, supine.	-	
5	The datasets must include CT images, original clinical contours of anatomic structures and treatment targets, and the dose distributions used for patient treatment.	-	
6	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection can be restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.	-	
7	Testing datasets must be unique, with no overlap with data used for model creation or in previous validation studies.	-	
8	CT scan must include the manufacturer and model of the scanner used to obtain the CT image or recorded separately.	-	

Table 9:   Head and Neck Summary of Statistical Results

Criteria Number	Criteria	Results
1	Assess the safety of use of RPA normal structures for treatment planning by comparing the number of patient plans that passed accepted dosimetric metrics (e.g., mean dose to the parotid) when assessed on the RPA contour with the number that passed when assessed on the clinical contour. The difference should be 5% or less. When multiple metrics were used to assess a single structure at least one should pass this criterion.	$\leq$5% difference between RPA Plan and Clinical Plan for the majority of assessed structures.
2	Assess the effectiveness of use of RPA normal structures for treatment planning by comparing the number of RPA plans that passed accepted dosimetric metrics (e.g., mean dose to the parotid) when compared with clinical plans. The difference should be 5% or less. When multiple metrics were used to assess a single structure, at least one should pass this criterion.	$\leq$5% difference between RPA Plan and Clinical Plan for the majority of assessed structures*.
3	Assess the effectiveness of the RPA plan for target structures by comparing the number of RPA plans that pass accepted dosimetric metrics (e.g., percentage volume of the PTV receiving 95% of the prescribed dose) when compared with clinical plans. The difference should be 5% or less. When there are multiple metrics used to assess a single structure, at least one coverage and one maximum criterion should pass this criterion.	$\leq$5% difference between RPA Plan and Clinical Plan for the majority of assessed criteria.
4	Assess the geometric effectiveness of the RPA targets using recall. A low value for this metric represents under-contouring and a potential risk of creating a plan that misses the target (although the user is expected to review and edit contours). The 25th percentile of the recall must be 0.7 or greater.	25th percentile for recall > 0.7
5	Assess the quality of body contouring generated by the RPA by comparing body contours generated by the RPA with manual body contours. Surface DSC (2mm) should be greater than 0.8 for 95% of the CT scans.	Surface DSC > 0.8 for >95% of CT scans
6	Assess the ability of the RPA to accurately identify the marked isocenter. This is achieved by comparing the automatically generated isocenters with manually generated ones. 95% of automatically generated marked should agree with manually generated marked isocenters within 3mm in all orthogonal directions (AP, lateral, cranial-caudal).	$\leq$3mm difference between RPA Plan and Clinical Plan for all orthogonal directions.

*RPA plan and clinical plan had 6% - 13% difference with the cochlea.

Table 10:   **Head and Neck Protocol Summary**

Criteria Number	Inclusion Criteria	Exclusion Criteria	Sampling Method
1	CT scan of head and neck anatomy.	Poor Image Quality	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection was restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.
2	Clear CT image of head and/or neck without distortions.	-	

3	Test datasets consisted of CT images of patients previously treated for head and neck cancer using radiotherapy following this treatment scheme:
	    i. VMAT or IMRT treatments
	    ii. 1-3 dose levels in the prescription
		-	

4	Scan was obtained with patient head-first, supine.	-	
5	The datasets included CT images, original clinical contours of anatomic structures and treatment targets, and the dose distributions used for patient treatment.	-	
6	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection could be restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.	-	
7	Testing datasets were unique, with no overlap with data used for model creation or in previous validation studies.	-	
8	CT scans included the manufacturer and model of the scanner used to obtain the CT image or were recorded separately.	-	

Table 11:   Whole Brain Summary of Statistical Results

Criteria Number	Criteria	Results
1	Assess the safety of using the RPA plan for normal structures by comparing the number of patient plans that pass accepted dosimetric metrics when assessed on the RPA contour with the number that pass when assessed on the clinical contour. The difference should be 5% or less. When there are multiple metrics for a single structure at least one should pass this criterion.	≤6% difference between RPA Plan and Clinical Plan for all assessed structures (Right and Left Lens)*.
2	Assess the effectiveness of the RPA plan for normal structures by comparing the number of RPA plans that pass accepted dosimetric metrics when compared with clinical plans. The difference should be 5% or less. When there are multiple metrics for a single structure at least one should pass this criterion.	≤9% difference between RPA Plan and Clinical Plan for all assessed structures (Right and Left Lens)**.
3	Assess the effectiveness of the RPA plan for target structures by comparing the number of RPA plans that pass accepted dosimetric metrics (e.g., percentage volume of the brain receiving 95% of the prescribed dose) when compared with clinical plans. The difference should be 5% or less. When there are multiple metrics used to assess a single structure, at least one coverage and one maximum criterion should pass this criterion.	≤5% difference between RPA Plan and Clinical Plan for all assessed structures.
4	Assess the quality of body contouring generated by the RPA by comparing primary and secondary body contours generated by the RPA with manual body contours. Surface DSC (2mm) should be greater than 0.8 for 95% of the CT scans.	> 0.8 difference between RPA Plan and Clinical Plan for all assessments.
5	Assess the ability of the RPA to accurately identify the marked isocenter. This is achieved by comparing the automatically generated isocenters with manually generated ones. 95% of automatically generated marked isocenters (primary and verification approaches) should agree with manually generated marked isocenters within 3mm in all orthogonal directions.	≤3mm difference between RPA Plan and Clinical Plan for all orthogonal directions.

* The RPA contours gave more conservative results, with lower passing rates than using clinical contours.
** Passing rates were higher for RPA plans than for clinical plans.

Table 12:   Whole Brain Protocol Summary

Criteria Number	Inclusion Criteria	Exclusion Criteria	Sampling Method
1	CT scan of the head/neck region.	Poor Image Quality	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection was restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.
2	Clear CT image of the head/neck region without distortions.	-	
3	Test datasets consisted of CT images of patients previously treated for whole brain radiotherapy following one of the following treatment schemes: i. Opposed laterals or slight obliques.	-	
4	Scan was obtained with patient head-first, supine.	-	
5	The datasets included CT images, original clinical contours of anatomic structures and treatment targets, and the dose distributions used for patient treatment.	-	
6	Test datasets were chosen going forward in time until sufficient data was collected, starting with CT scans collected on January 1, 2022. If insufficient patient scans were found, data collection could be restarted with January 1, 2021 (for patients treated in 2021) and so forth, until sufficient data was collected.	-	
7	Testing datasets were unique, with no overlap with data used for model creation or in previous validation studies.	-	
8	CT scans included the manufacturer and model of the scanner used to obtain the CT image.	-	

8.   CONCLUSIONS

The Radiation Planning Assistant (RPA) is substantially equivalent to the Eclipse Treatment Planning System v15.6 (K181145) predicate device. The intended use and indications for use are substantially equivalent. The major technological characteristics are substantially equivalent to the predicate devices, and the differences do not raise new questions of safety and effectiveness. The results of verification and validation as well as conformance to relevant safety standards demonstrate that the Radiation Planning Assistant (RPA) and the Eclipse Treatment Planning System v15.6 (K181145) meet safety and performance criteria and are substantially equivalent devices. The retrospective clinical data demonstrates that the device is safe and effective for its intended use as compared to the predicate device.

9.   REFERENCES

Kisling K, Zhang L, Simonds H, Fakie N, Yang J, McCarroll R, Balter P, Burger H, Bogler O, Howell R, Schmeler K, Mejia M, Beadle BM, Jhingran A, Court L. Fully Automatic Treatment Planning for External-Beam Radiation Therapy of Locally Advanced Cervical Cancer: A Tool for Low-Resource Clinics. J Glob Oncol. 2019 Jan;5:1-9. doi: 10.1200/JGO.18.00107. PMID: 30669457; PMCID: PMC6426517.