Hippocampal Limited Sparing Enhanced Coverage Whole Brain (HLS-EC-WB) Model Description

Purpose:

This document describes the context in which the Hippocampal Limited Sparing Enhanced Coverage Whole Brain (HLS-EC-WB) Model should be used, as well as how it was configured and validated. All instruction needed to use this model in your clinic can be found when you **read the first five pages of this document**.

Applicability:

Note *RapidPlan knowledge-based planning and its models are not intended to replace clinical decisions, provide medical advice or endorse any particular radiation plan or treatment procedure. The patients' medical professionals are solely responsible for and must rely on their professional clinical judgment when deciding how to plan and provide radiation therapy.*

Note *The performance of the HLS-EC-WB model may vary depending on the contouring and planning guidelines. Each site should validate the model with institution-specific contouring and planning guidelines before clinical use.*

Note *You should validate every DVH estimation model before using it clinically. This applies to any model, whether Varian provided, peer provided or the models you create yourself.*

- This model is designed to be used for RapidArc treatment plans for whole brain utilizing a hippocampal sparing technique. This model was created using 4 arc Halcyon plans calculated with AcurosXB but has also been validated with multiple (coplanar and non-coplanar) beam geometries on TrueBeam. (See Annex C for quantification of performance for each method).

- This HLS-EC-WB model differs from prior v2.0 model in that this model is preconfigured for **20Gy Rx with greatly reduced sparing to the Hippocampus. Unless you are sure to be treating to 20Gy with reduced hippocampal sparing, it is recommended to use either HMS-EC-WB or HSWBv2.**

Intent	20Gy/5fx-only **L**imited **S**paring **E**nhanced **C**overage H**LS**-**EC**-WB	30Gy Scalable Rx **M**oderate **S**paring **E**nhanced **C**overage (H**MS**-**EC**-WB)	30Gy Scalable Rx Aggressive Sparing HSWBv2
Hippocamus Dmin	7.6Gy (**38% Rx**) ALARA	9Gy (30% Rx) ALARA	9Gy (30% Rx) ALARA
Hippocamus D0.03cc	13Gy (**65% Rx**)	16Gy (53.3% Rx)	16Gy (53.3% Rx) **ALARA**
PTV Rx dose coverage	20Gy @ 98%-99%	30Gy @ 98%-99%	30Gy @ ≥95%

- The model is intended to be used in conjunction with a **MU objective** with a **strength of 80** and **minimum MU 1000 (1600 for 6X-FFF) and maximum MU of 2500**. This MU objective **must be added manually each time**.

- The "**Automatic Intermediate Dose**" function of the Photon Optimizer was utilized with **MR3** return and **convergence mode: extended** selected in the calculation options. These **settings should be changed prior to starting the optimization or plan quality will be compromised.** Also, to reach desired homogeneity goals, **consider an additional intermediate dose optimization: "2xMR3"** (See Annex C)

- The model is intended for whole brain with hippocampal sparing without a simultaneous integrated boost (SIB) to gross disease. If SIB is intended to be utilized for boost volume, clinical validation of model performance is necessary. The model was not generated or fully validated for SIB clinical cases (See Annex D).

Target and OAR contouring and planning guidelines:

The HLS-EC-WB model was created using the following guidelines. Every patient must have a planning CT. The CT simulation scan must encompass the entire head to include the most superior aspect of the patient through the entire head. Axial slice thickness should not exceed 2.5mm and smaller axial cuts are recommended. The use of MRI guided contouring is also recommended. The MRI axial slice thickness should match the CT slice thickness as much as possible. It is recommended to obtain gadolinium-enhanced studies to include three-dimensional spoiled gradient (SPGR), magnetization-prepared rapid gradient echo (MP-RAGE), or turbo field echo (TRF) axial MRI scans with axial slice thickness not greater than 1.5mm. Standard axial and coronal gadolinium contrast-enhanced T1-weighted sequence and axial T2/FLAIR sequence scans should be acquired with no greater than 2.5mm slice thickness.

The planning target volumes (PTV) and the organs at risk (OARs) are contoured on the planning CT.

Target contouring guidelines:

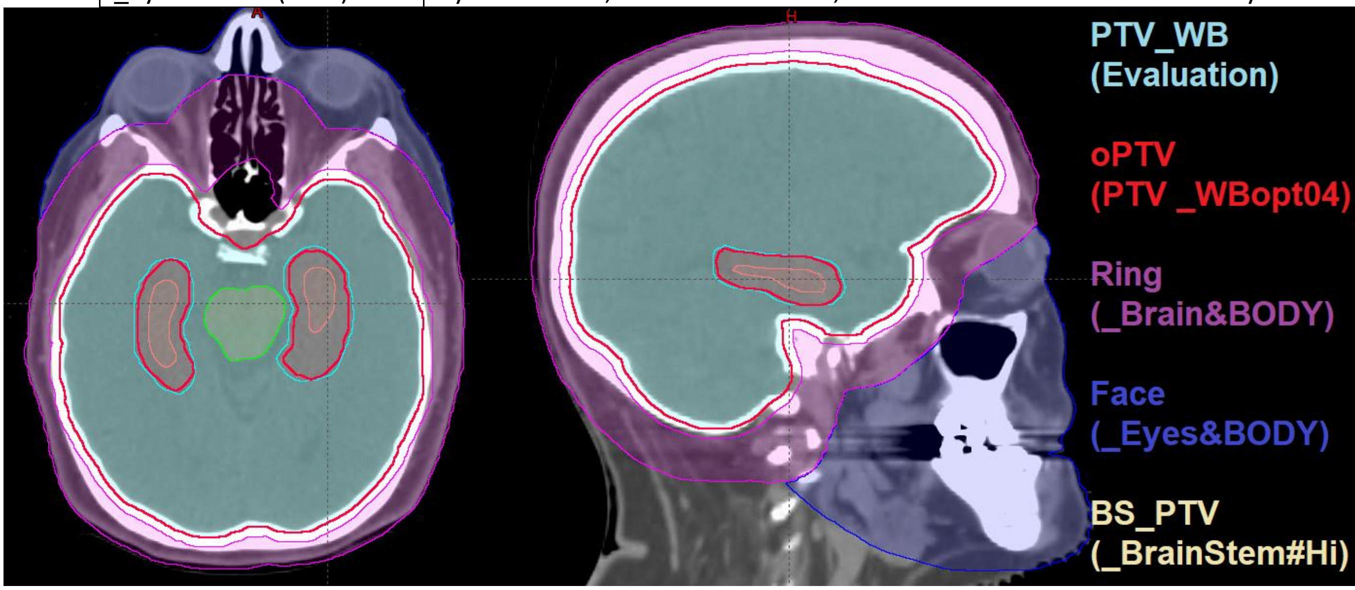
Target name	Guidelines
CTV (or Brain)	Whole brain parenchyma through the foramen magnum
PTV_WB	CTV + 2mm setup margin added in this model, but 0-3mm are valid (institutional preference) excluding the hippocampal avoidance region

OAR contouring guidelines:

OAR name	Guidelines
Hippocampus(R+L)	Bilateral hippocampal contours (contoured in one structure); will be generated from the CT simulation image set fused to MRI image sets <u>Average Total Volume of this structure was 4.5cc</u> in training set cases. The largest volumes seen in the training set were ~7cc (>7.5cc were excluded).
Brainstem	Best generated on MRI image set and verified on CT simulation image set. Inferior aspect at the level of foramen magnum (should be at the interface of CTV inferior aspect) and superiorly to include midbrain
Spinal Canal	Superior aspect to begin at the distal edge of the brainstem through inferior aspect of the image set
Lens(R/L)	Use CT image set only for creation; bilateral contoured separately
Optic Nerve (R/L)	Use CT image set only for creation; bilateral contoured separately
Eye(R/L)	Best generated from CT simulation image set; delineate the entire globe of the eye; bilateral contoured separately
Optic Chiasm	Structure best visualized on MRI image set and confirmed on CT image set; located above the pituitary fossa which is located within the sella turcica
Lacrimal Gland(R/L)	Structure sits superior and lateral to the globe of the eye; best generated on CT simulation image set and verified on MRI; bilateral contoured separately

Optimization structure Guidelines*

Hippocampus+05(R+L)	Avoidance used to create PTV_WB for evaluation only (not trained in this model)
PTV_WBopt04	PTV excluding hippocampi +4mm additional margin from hippocampus structure. Reduced margin in optimization to achieve Rx @ 99% PTV_WB).
_Brain&BODY (Ring)	+20mm from the brain, SUB +5mm from brain, removed from outside body
_Brainstem#Hi (BS_PTV)	Brainstem SUB Hippocampus + 5mm
_Eyes&BODY (Face)	Eyes +100mm, SUB brain +20mm, removed from outside of the body



* Optimization structures can be automatically created with ESAPI PlanScoreCard tool (Annex B3)

Treatment planning guidelines:

All cases used to train and to validate the model were planned using head-first supine position with head positioned in a neutral position. All patients were immobilized with an aquaplast mask. A four arc VMAT technique was utilized with four full coplanar arcs on Halcyon with MLC in SX2 mode (standard mode on all Halcyon D / Drive and above configurations). Arcs had alternating clock-wise and counter clock-wise gantry rotations with collimator positions set at 315, 0, 45 and 90. The coplanar arcs had 359.8 degrees of arc rotation for each field. Arcs were positioned at a single isocenter located in the center of the target.

Full validation with different number of arcs, geometries and dose calculation methods on TrueBeam (M120 MLC) can be seen in Annex C, including a quantification of the relative dosimetric performance of each method.

The following dose prescription and planning guidelines were used for the cases to train and validate the model.

Target

PTV_WB	20Gy in 5 fractions
coverage	D100% at 99%; D98% > 20Gy; D2% < 21Gy (normalization to D100% >=99%)

OARs

Chiasm	D0.03cc < 21Gy
Brainstem	D0.03cc < 22Gy
Cord	D0.03cc < 22Gy
Optic Nerve	D0.03cc < 21Gy
Eye	Mean dose < 2Gy; Max dose <11Gy
Lacrimal Gland	Mean dose < 4Gy
Lens	D0.03cc < 3Gy
Hippocampus	D0.03cc <13Gy; Mean dose < 9Gy; D100% < 7.6Gy

References for contouring and planning guidelines:

Roberge D, Chan M, Gondi V. **CCTG CE. 7: Stereotactic Radiosurgery Compared With Hippocampal-Avoidant Whole Brain Radiotherapy (HA-WBRT) Plus Memantine for 5 or More Brain Metastases** https://www.ctg.queensu.ca/public/brain/brain-disease-site
(HLS-EC-WB-2023 https://medicalaffairs.varian.com/wholebrain-limited-hippocampalsparing-20gy-vmat2)

Liu H, Clark R, Magliari A, Foster R, Reynoso F, Schmidt M, Gondi V, Abraham C, Curry H, Kupelian P, Khuntia D, Beriwal S. **RapidPlan hippocampal sparing whole brain model version 2-how far can we reduce the dose?** Med Dosim. 2022 Autumn;47(3):258-263. doi: 10.1016/j.meddos.2022.04.003. https://www.meddos.org/article/S0958-3947(22)00039-5/fulltext
(HSWBv2-2022 https://medicalaffairs.varian.com/wholebrain-hippocampalsparing-vmat2)

Magliari V, Magliari A, Foster R. **Hippocampal Sparing Whole Brain: Rapid Plan ModelFollowing the NRG-CC001 Protocol**. *AAMD Conf Poster Present*. https://medicalaffairs.varian.com/download/PosterPresentationAAMD2017RapidplanHCSWB.pdf
(HSWBv1-2016 http://medicalaffairs.varian.com/wholebrain-hippocampalsparing-vmat1)

Brown P, Gondi V **NRG-CC001: A Randomized Phase III Trial of Memantine and Whole-Brain Radiotherapy With or Without Hippocampal Avoidance in Patients with Brain Metastases** https://www.nrgoncology.org/Clinical-Trials/NRG-CC001

Prokic V, et al **Whole Brain Irradiation with Hippocampal Sparing and Dose Escalation on Multiple Brain Metastases: A Planning Study on Treatment Concepts** http://dx.doi.org/10.1016/j.ijrobp.2012.02.036

Physicians with considerable experience in treating patients under the **CCTG CE.7 protocol**, additional planning goals and contouring consistency were completed to their clinical preference.

Structure codes:

To ensure robust structure matching between new cases and the structures defined in the model, it is recommended to use the following structure code assignment:

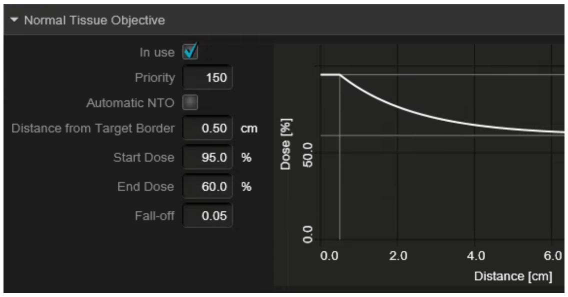
Structure name example	Structure name in model	Structure code(s) in model
PTV_WBopt04mm	PTV_WBopt	(PTV_High,PTV_Int Target)
Hippocampus_Totl	Hippocampus(R+L)	(275020)
Chiasm	OpticChiasm	(62045)
Brainstem	Brainstem	(79876)
Spinal Cord	SpinalCanal	(9680, 7647)
LOptic	OpticNerve(R/L)	(50878, 50875)
ROptic	OpticNerve(R/L)	(50878, 50875)
LEye	Eye(R/L)	(12515, 125124)
REye	Eye(R/L)	(12515, 125124)
LLacrimal	Lacrimal(L/R)	(59103, 59102)
RLacrimal	Lacrimal(L/R)	(59103, 59102)
LLens	Lens((R/L)	(58243, 58242)
RLens	Lens((R/L)	(58243, 58242)
NS_Ring	_Brain&BODY	(Control Region)
BrainstemPTV	_Brainstem#Hi	(Control Region)
Face	_Eyes&Body	(Control Region)

Optimization objectives and settings:

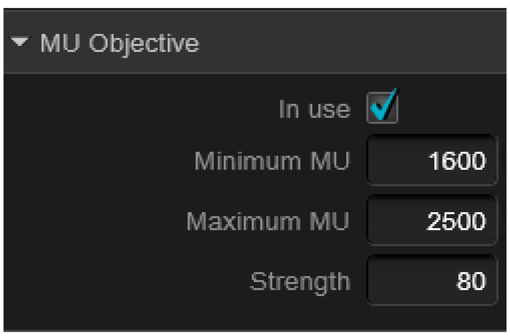
The following optimization objectives were defined in the model and will be generated when the model is applied to a new case:

Target	ID	Vol [%]	Dose	Priority	gEUD a
Yes	_BRAINSTEM#HI (Control)				
	Lower	99.9	100.5 %	210	
Yes	PTV_WBopt4 'TV_High, PTV_Intermediate)				
	Upper	0.0	105.0 %	400	
	Upper	1.5	103.5 %	190	
	Upper	12.0	102.4 %	175	
	Lower	99.5	101.6 %	260	
	Lower	99.7	100.5 %	280	
	Lower	100.0	95.7 %	200	
	Upper gEUD		101.8 %	115	40.0
	_BRAIN&BODY (Control)				
	Upper	0.0	99.0 %	350	
	_Eyes&BODY (Control)				
	Mean		Generated	85	
	Line (preferring OAR)	Generated	Generated	110	
	Brainstem (79876)				
	Upper	0.0	101.0 %	175	
	Eye(R/L) (12515, 12514)				
	Upper (fixed vol., generated dose)	0.0	Generated	125	
	Mean		Generated	95	
	Line (preferring target)	Generated	Generated	85	
	Hippocampus(R+L) (275020)				
	Upper (fixed vol., generated dose)	99.0	Generated	230	
	Upper (fixed vol., generated dose)	0.0	Generated	185	
	Mean		Generated	120	
	Line (preferring target)	Generated	Generated	135	
	Lacrimal(L/R) (59103, 59102)				
	Mean		Generated	65	
	Line (preferring target)	Generated	Generated	80	
	Lens(R/L) (58243, 58242)				
	Upper (fixed vol., generated dose)	0.0	Generated	110	
	Mean		Generated	68	
	Line (preferring target)	Generated	Generated	74	
	OpticChiasm (62045)				
	Upper	0.0	100.5 %	160	
	OpticNerve(R/L) (50878, 50875)				
	Upper	0.0	100.5 %	160	
	Line (preferring target)	Generated	Generated	30	
	SpinalCanal (9680, 7647)				
	Upper	0.0	100.5 %	160	

Applying the model will also set the following parameters for the NTO:



MU objective is also recommended for planning with the following parameters:



Minimum 1600 for 6X-FFF, 1000 for 6X

******* MUST be added manually *******

Model Training:

This Hippocampal Limited Sparing Enhanced Coverage Whole Brain (HLS-EC-WB) model was trained with the same final 42 case multi-institution CT dataset from the HSWBv2, structures were modified as needed. Each case was simulated with aquaplast mask immobilization and neutral head position.

All cases were initially re-planned to 20Gy in 4Gy fractions with 6X-FFF energy on a Varian Halcyon with SX2 MLC mode.

All cases utilized VMAT technique. Arcs had alternating clockwise and counterclockwise gantry rotations with collimator positions set at 315, 0, 45 and 90 degrees. The coplanar arcs had 359.8 degrees of arc rotation and were positioned with isocenter located in the center of the target.

The recursive method of model creation was utilized to generate a RapidPlan model with very consistent, high-quality plans developed with tight DVH prediction bands allowing for finely balanced hippocampal sparing, target coverage and homogeneity optimization objectives to be used. HLS-EC-WB uses plans created from HSWBv2 (which was, in-turn, created from HSWBv1 model released in 2016) as its starting point leveraging the Rx scaling feature (30Gy->20Gy). These initial plans were created without the HSWBv2 hippocampal DVH prediction line objectives and instead DVH point objectives were generated along the hippocampus line objectives. These objectives were then offset by fixed percentages toward higher dose levels to account for the dose gradient shifting toward the hippocampal structures in order to achieve the desired target coverage goal (Rx dose covering 99% of PTV_WB). A modified version of the V2.0 scorecard was created which adjusted previous metrics and added additional metrics to capture CE. 7 and it's author's clinical preference (aggressive target coverage and maximal homogeneity). The free PlanScoreCard ESAPI scoring tool was not only utilized to score plans (scores which guide tuning the model's automatically generated optimization objective priorities), but was also used to automatically create optimization structures (see Annex B3).

Those initial plans created from HSWBv2 model scaled to 20Gy and with offset hippocampal sparing objectives became the training set for the initial HLS-EC-WB model. A recursive model creation process was employed to ensure the final HLS-EC-WB training set consisted, exclusively, of plans generated from the initial HLS-EC-WB model. Evaluating plan scores at each step in the process informed multiple iterations of re-tuning the optimization objective set.

Model Validation:

The HLS-EC-WB model was validated using the 42 cases included in the final model training set. See the table on the next page to better understand the model creation / validation and scores achieved throughout the process.

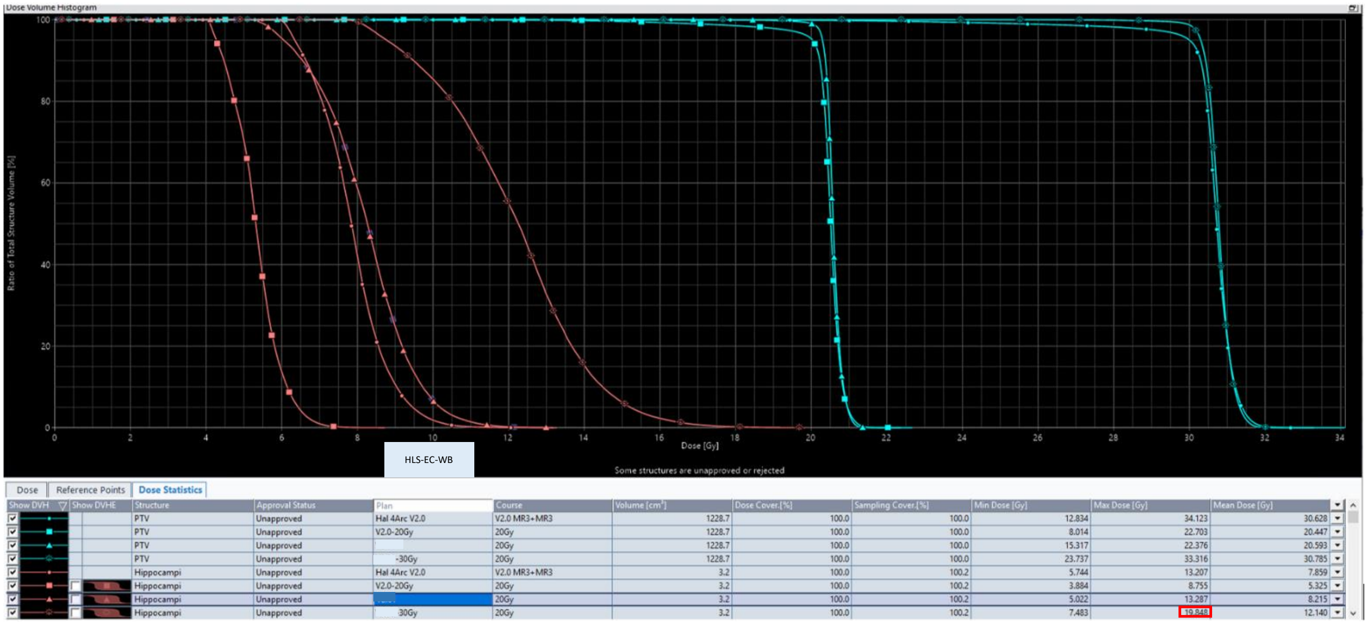
Five additional validation cases not included in the model training set are explored, in detail, in the Annex. Those cases are scored with various arc geometries (both coplanar and non-coplanar) on both Halcyon and TrueBeam (Millennium120 MLC) with differing numbers of intermediate dose optimizations, with a quantification of the relative dosimetric performance (score) of each method. Further validation including differing beam energies, dose calculation methods and convergence mode options, are available in the clinical description included with the HSWBv2 RapidPlan Model.

	V2.0 Scorecard=142	HLS-EC-WB Scorecard = 158.5 Total points		
	Final Result	created by modV2.0 model	created by initial HLS-EC-WB	Final Result
Patient	Final V2.0 Model	Training Set for initial HLS-EC-WB	Training Set for final HLS-EC-WB	Final HLS-EC-WB Model
Patient 1	132.35	141.86	145.71	145.44
Patient 3	132.47	145.2	144.86	143.44
Patient 4	137.17	147.19	147.07	149.02
Patient 5	129.81	142.07	147.21	147.2
Patient 8	132.53	140.78	143.11	142.5
Patient 9	132.6	140.45	141.33	142.38
Patient 11	132.32	133.87	138.56	140.29
Patient 13	131.92	144.49	145.4	145
Patient 16	136.6	141.81	143.81	146.68
Patient 19	134.64	139.96	138.36	142.39
Patient 20	131.66	135.18	140.46	140.36
Patient 21	131.36	133.19	134.17	139.98
Patient 23	134.14	145.68	146.29	144.43
Patient 24	133.82	137.54	143.45	141.3
Patient 25	134.88	145.97	146.43	146.63
Patient 27	133.96	146.26	146.81	145.79
Patient 28	131.32	139.94	141.11	140.14
Patient 30	133.23	140.83	140	143.21
Patient 34	131.16	141.55	143.28	143.15
Patient 35	132.72	144.64	145.4	145.29
Patient 44	129.91	137.45	135.43	140.17
Patient 45	129.64	139.56	141.95	143.56
Patient 47	133.63	145.21	145.85	146.5
Patient 48	135.3	145.59	146.16	146.85
Patient 49	134.7	144.78	146.3	145.5
Patient 50	131.7	144.62	144.8	144.11
Patient 52	132.01	138.99	142.36	141.31
Patient 54	134.41	145.38	143.13	145.87
Patient 55	132.49	135.02	135.9	140
Patient 57	134.69	140.16	140.75	145.58
Patient 60	131.74	134.59	131.7	135.36
Patient 64	134.42	141.49	146.32	145.41
Patient 65	133.45	143.75	143.68	143.29
Patient 66	132.58	136.49	138.8	140.33
Patient 68	132.24	134.1	143.46	144.42
Patient 69	130.8	131.62	126.21	135.51
Patient 70	133.5	135.17	139.71	140.47
Patient 71	132.54	141.31	143.41	143.58
Patient 72	132.72	140.79	138.28	142.04
Patient 77	131.67	142.35	144.01	142.5
Patient 80	134.76	147.27	147.11	146.36
Patient 85	135.24	144.27	140.82	145.73
Average	**132.9714286**	**140.9147619**	**142.1180952**	**143.3111905**

Annex Directory

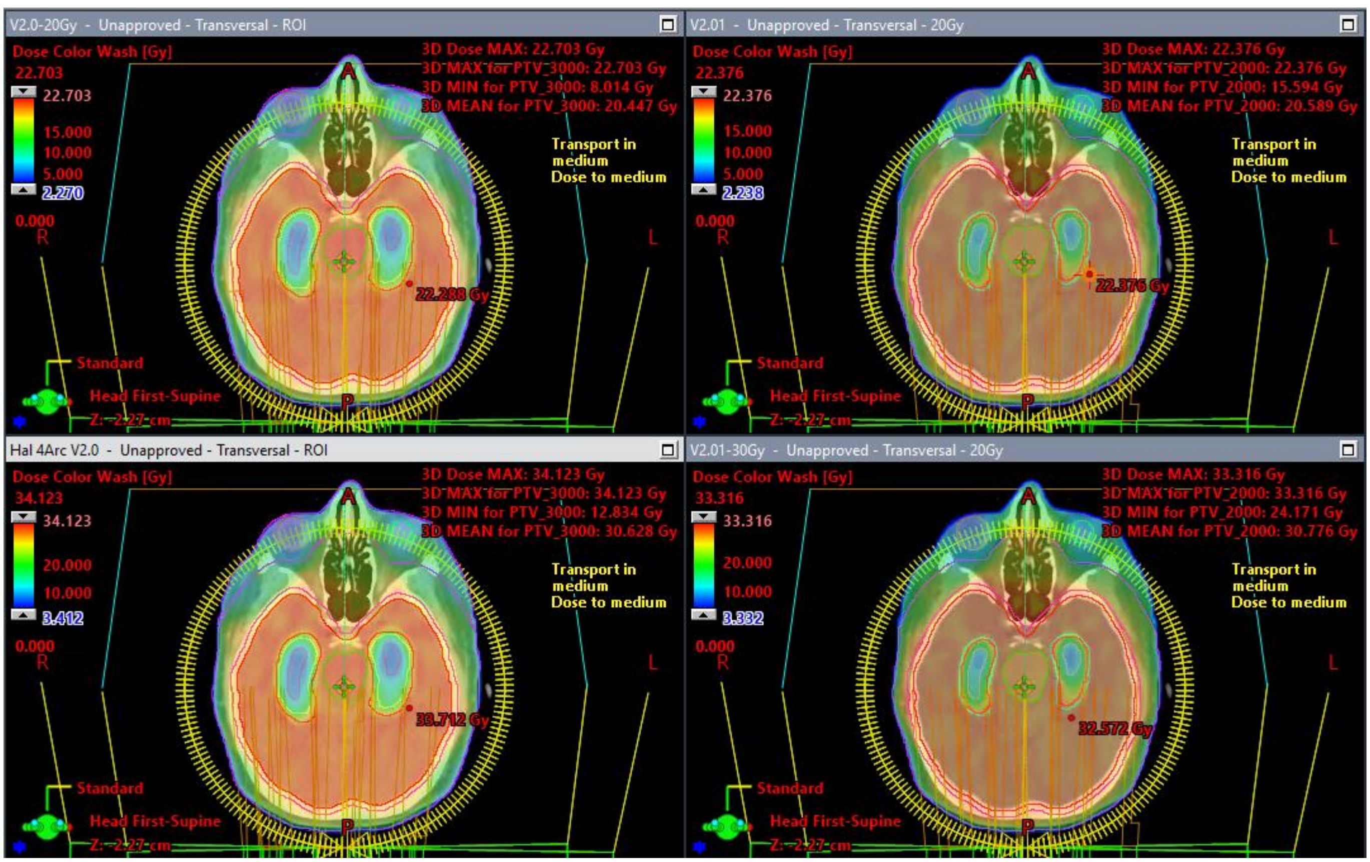
Annex A: Comparison of **HLS-EC-WB / HSWBv2: different tradeoffs** (coverage vs sparing)

A1 DVH comparison-HSWBv2 & HLS-EC-WB models reoptimized to 20Gy & 30Gy (patient 36)



Show DVH	Show DVHE	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
☑		PTV	Unapproved	Hal 4Arc V2.0	V2.0 MR3+MR3	1228.7	100.0	100.0	12.834	34.123	30.628
☑		PTV	Unapproved	V2.0-20Gy	20Gy	1228.7	100.0	100.0	8.014	22.703	20.447
☑		PTV	Unapproved		20Gy	1228.7	100.0	100.0	15.317	22.376	20.593
☑		PTV	Unapproved	-30Gy	20Gy	1228.7	100.0	100.0	23.737	33.316	30.785
☑		Hippocampi	Unapproved	Hal 4Arc V2.0	V2.0 MR3+MR3	3.2	100.0	100.2	5.744	13.207	7.859
☑	☐	Hippocampi	Unapproved	V2.0-20Gy	20Gy	3.2	100.0	100.2	3.884	8.755	5.325
☑	☐	Hippocampi	Unapproved		20Gy	3.2	100.0	100.2	5.022	13.287	8.215
☑	☐	Hippocampi	Unapproved	30Gy	20Gy	3.2	100.0	100.2	7.483	19.848	12.140

A2 Isodose comparison-HSWBv2 & HLS-EC-WB models reoptimized to 20Gy & 30Gy (patient 36)



For reference only:

HLS-EC-WB should not be scaled to 30Gy, D.03cc hippocampus dose will be too high!

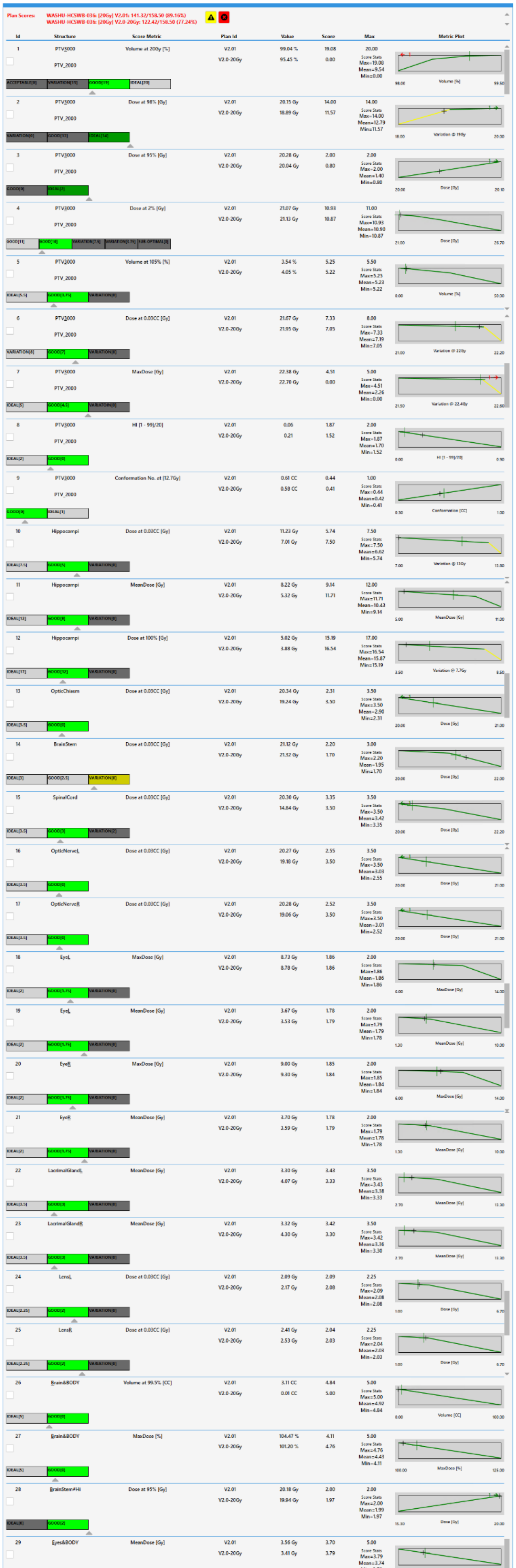
Annex B: **Dosimetric scorecard** and **PlansScoreCard** ESAPI tool

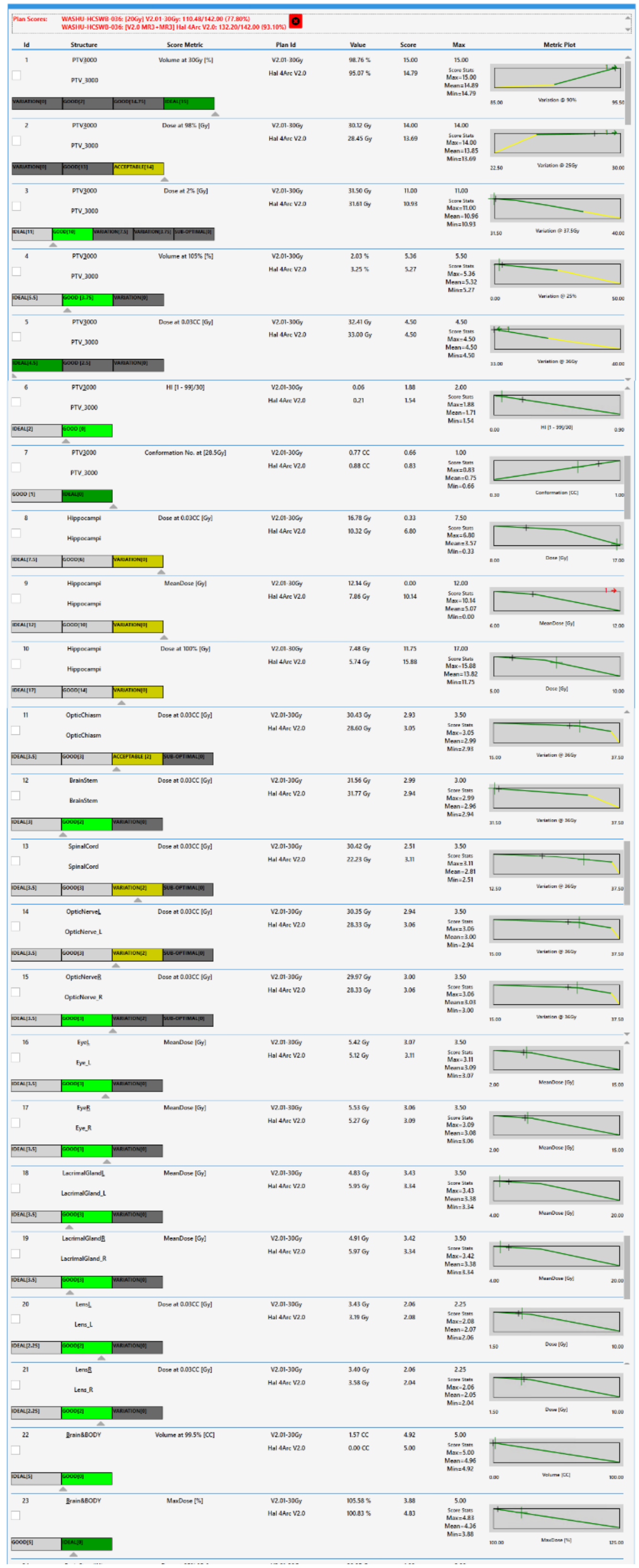
B1 **Score comparison of HSWBv2/HLS-EC-WB:** expressing intent with precision

Plan Score Comparison								
	V2.0 Scorecard 30Gy (142 total points)				HLS-EC-WB Scorecard 20Gy (158.5 total points)			
Patient	v2.0 model		HLS-EC-WB model@30Gy		v2.0 model@20Gy		HLS-EC-WB model	
36	132.08	93.01%	110.48	77.80%	123.42	81.07%	141.32	90.81%
37	133.24	93.83%	112.35	79.12%	128.49	73.64%	143.93	90.42%
39	132.17	93.08%	117.58	82.80%	116.72	72.34%	143.31	86.62%
40	133.39	93.94%	116.68	82.17%	114.66	78.08%	137.3	89.30%
41	131.82	92.83%	112.31	79.09%	123.76	76.60%	141.54	89.26%
Average	**132.54**	**93.34%**	**113.88**	**80.20%**	**121.41**	**76.35%**	**141.48**	**89.28%**

For reference only:

HLS-EC-WB should not be scaled to 30Gy, D.03cc hippocampus dose will be too high!



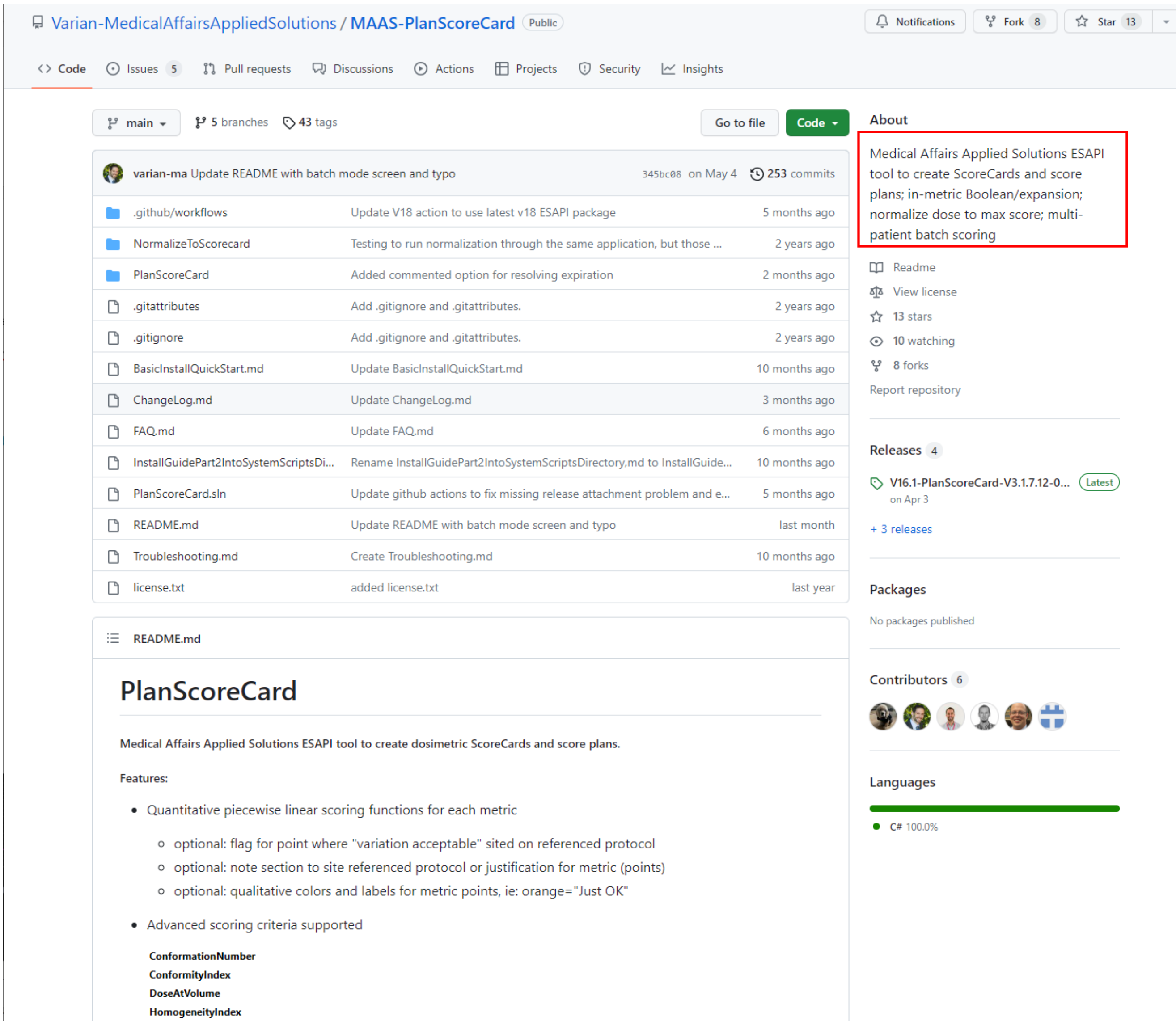


ScoreCard Comparison HLS-EC-WB(left) and HSWBv2(right) both RP models reoptimized to both 20Gy & 30Gy (patient 36) Note: HSWBv2 plan fails HLS-EC-WB Scorecard target coverage and Dmax, while HLS-EC-WB plan fails HSWBv2 scorecard for hippocampal mean dose (red arrow = 0pts/FAIL)

Annex B: **Dosimetric scorecard** and **PlansScoreCard** ESAPI tool

B2 PlanScoreCard ESAPI tool: where to find

[Varian-MedicalAffairsAppliedSolutions](https://github.com/Varian-MedicalAffairsAppliedSolutions) (https://github.com/Varian-MedicalAffairsAppliedSolutions/MAAS-PlanScoreCard)



Currently, the source code is shared on the Varian Innovation Center GitHub where it can be downloaded and complied with Visual Studio 2022 (including with the free community edition), now in the releases section users can find precompiled binaries ready to run in all compatible versions of Eclipse (v15.6+). PlanScoreCard is made available under the Varian Limited Use Software License Agreement.

Annex B: Dosimetric scorecard and **PlansScoreCard** ESAPI tool

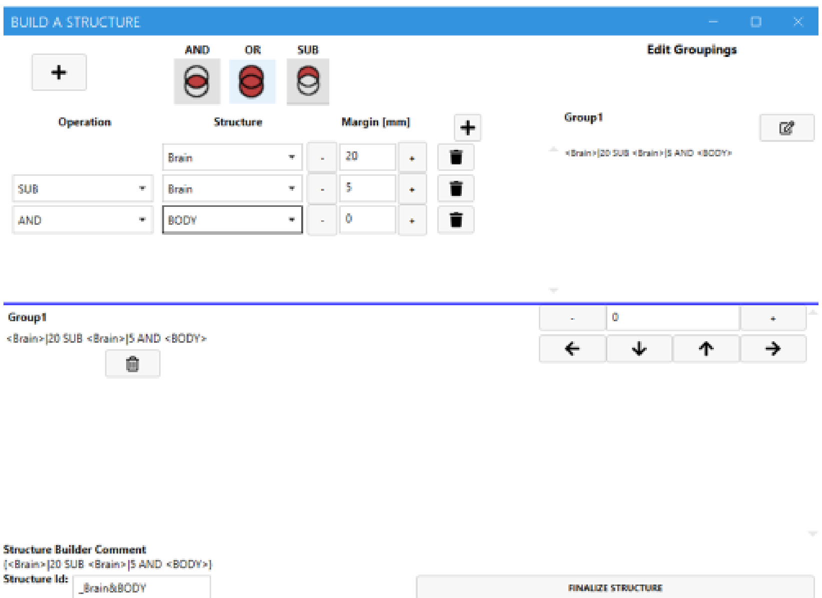
B3 PlanScoreCard ESAPI tool: automatically generate derived structures

The PlanScoreCard tool has a feature where derived structures (made with Boolean and expansion tools) can be created automatically. These structures can be created temporarily (to be used for scoring the plan but never saved back to the database) or (if the ESAPI tool has been approved for writing) the PlanScoreCard tool's configuration file can be edited so these generated structures are saved.

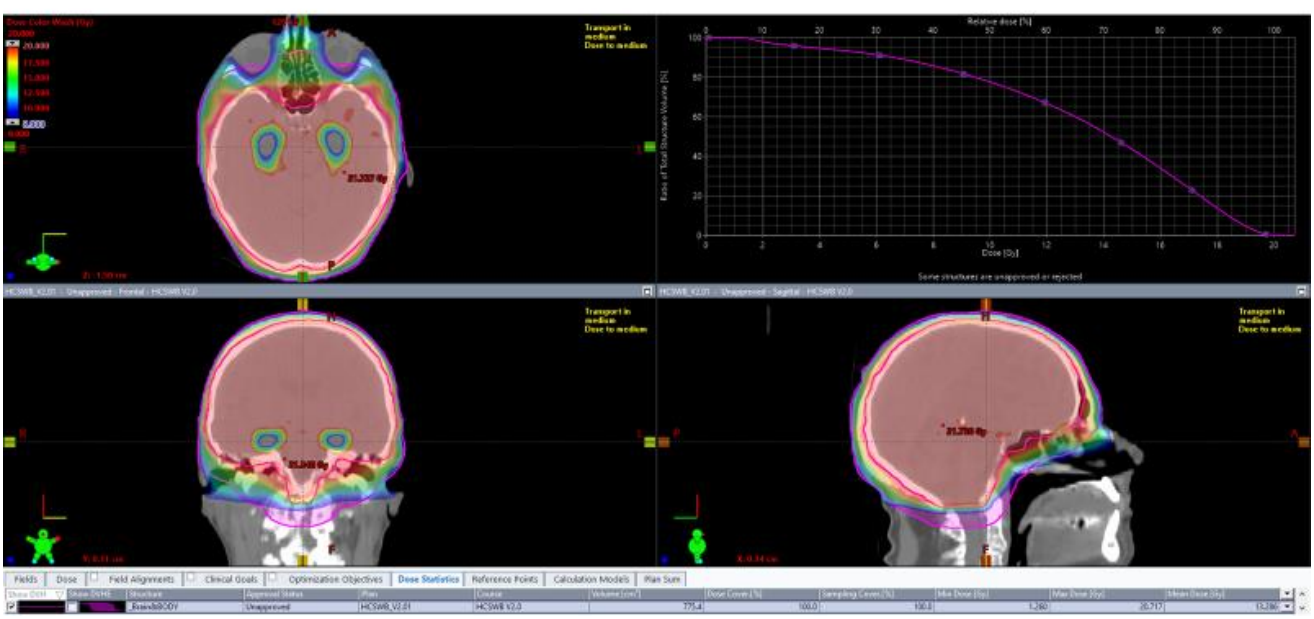
Below are screen captures showing how to build structures

Ring Structure Generation

+20mm from the brain, SUB +5mm from the brain, and removed from outside of the body



Ring Structure

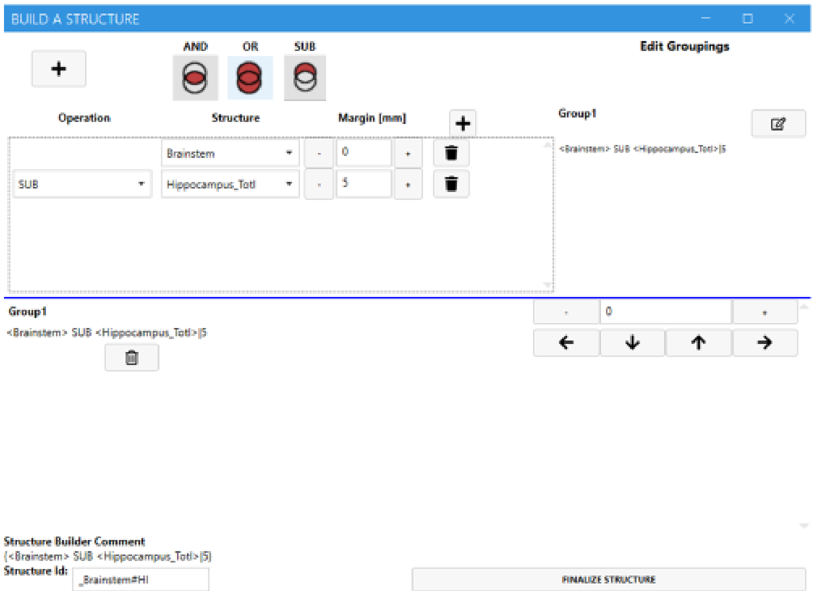


Annex B: Dosimetric scorecard and **PlansScoreCard** ESAPI tool

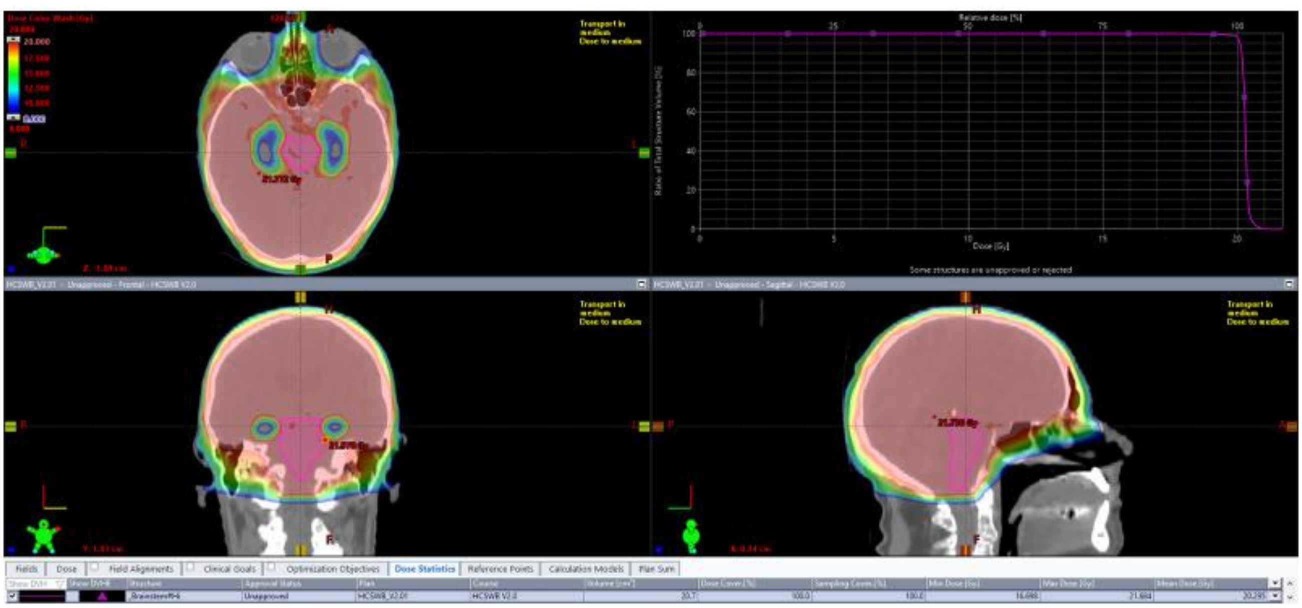
B3 PlanScoreCard ESAPI tool: automatically generate derived structures

Brainstem Target Structure Generation

Brainstem SUB Hippocampi + 5mm



Brainstem Target Structure

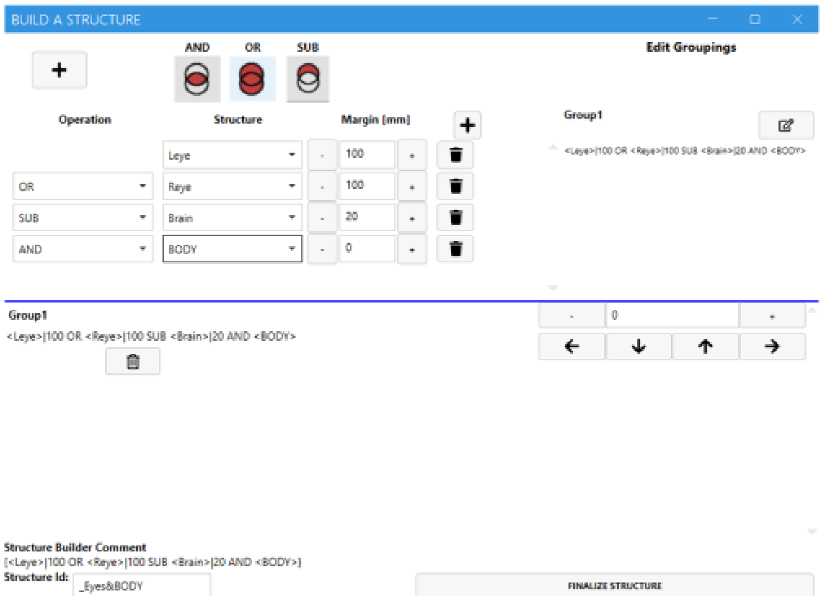


Annex B: Dosimetric scorecard and **PlansScoreCard** ESAPI tool

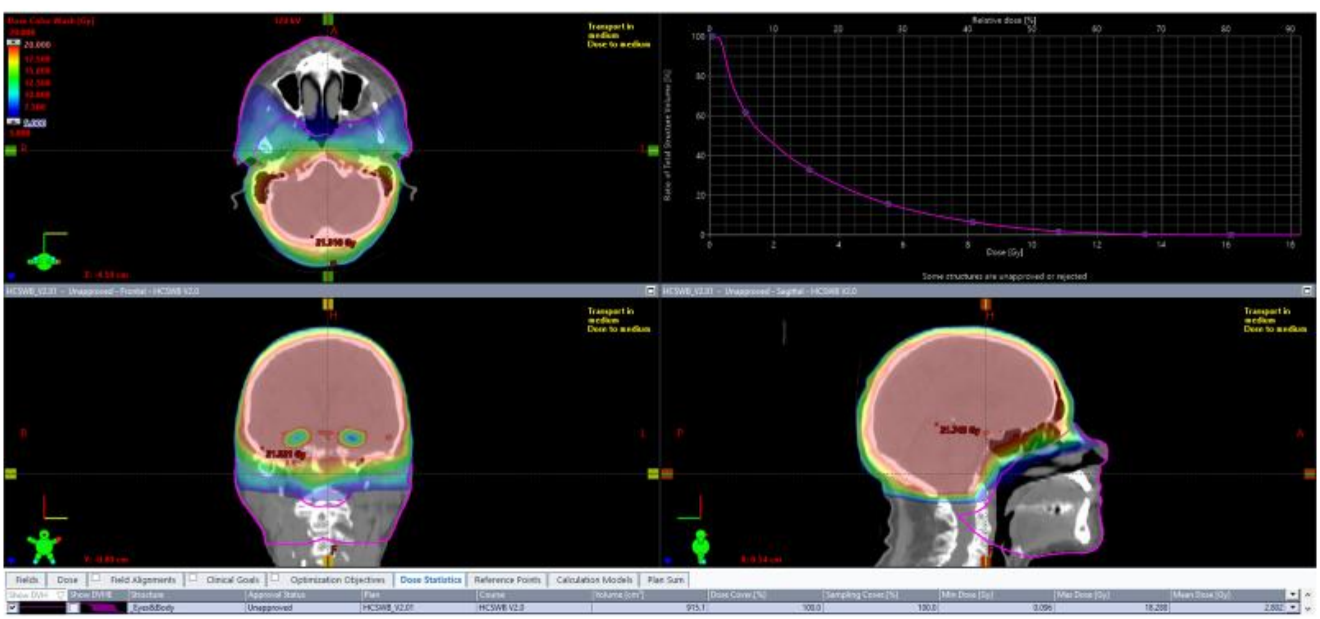
B3 PlanScoreCard ESAPI tool: automatically generate derived structures

Face Structure Generation

Eyes + 100mm, SUB Brain +20mm, and removed from outside of the body



Face Structure

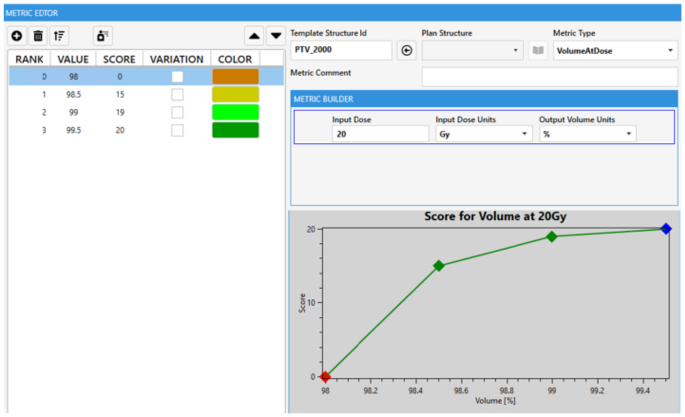


Annex B: Dosimetric scorecard and PlansScoreCard ESAPI tool

B4 Scorecard modifications HLS-EC-WB from HSWBv2

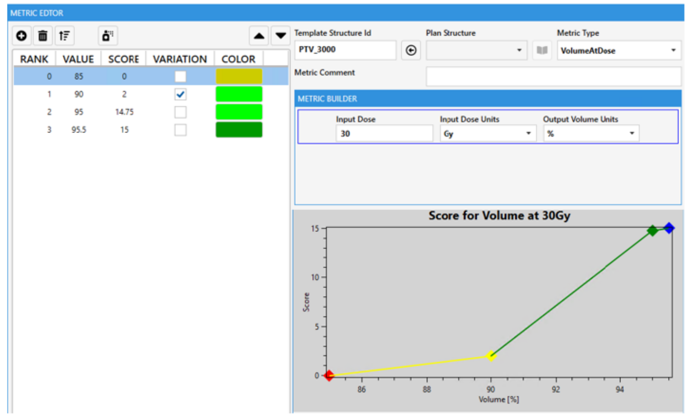
PTV Brain – **Volume at 20Gy (customized-not scaled)**

HLS-EC-WB



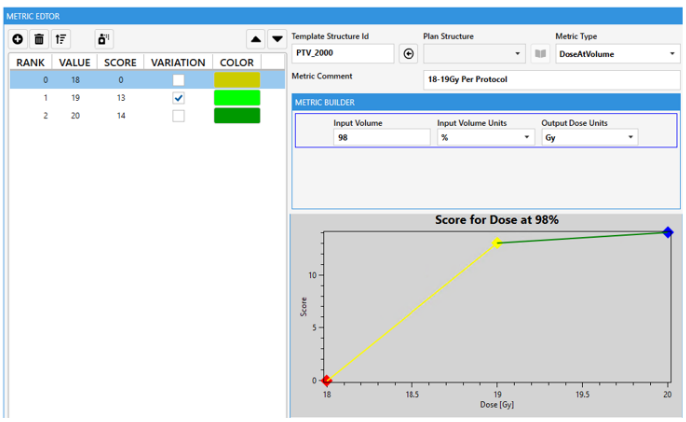
PTV Brain – **Volume at 30Gy**

HSWBv2

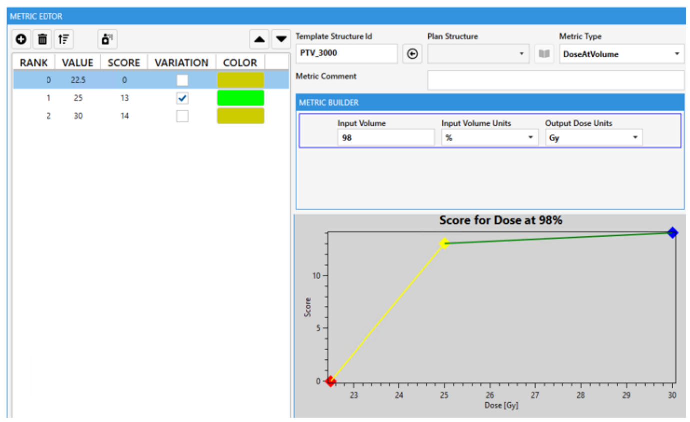


PTV Brain – **Dose at 98% (scaled)**

HLS-EC-WB

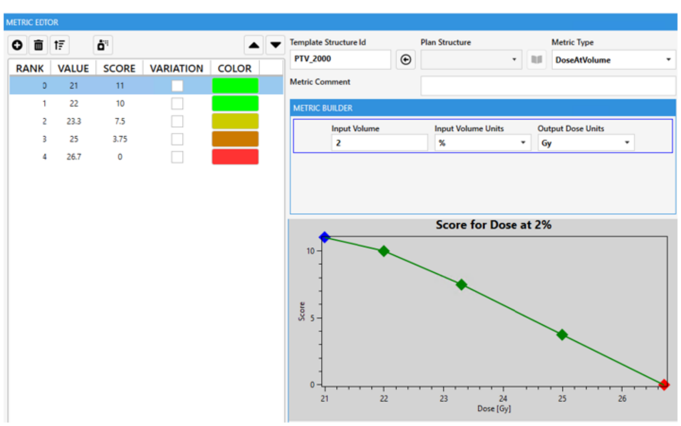


HSWBv2

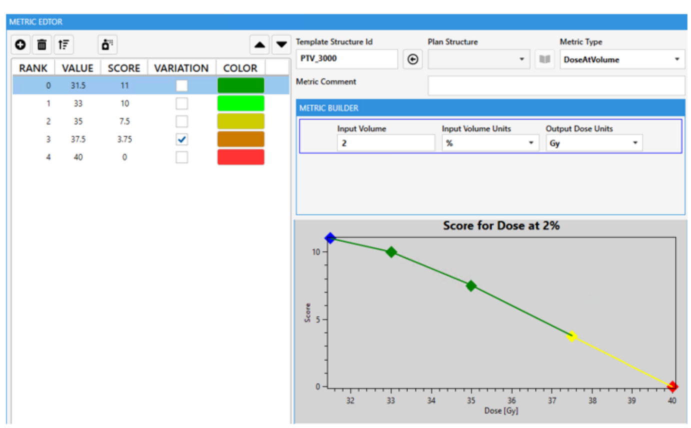


PTV Brain – **Dose at 2% (scaled)**

HLS-EC-WB



HSWBv2

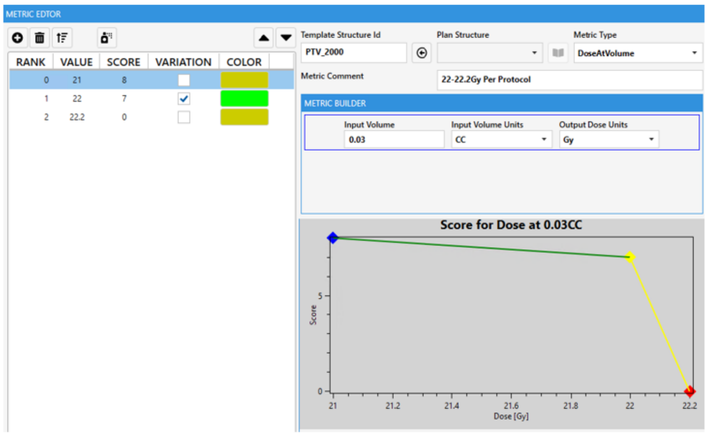


Annex B: Dosimetric scorecard and **PlansScoreCard** ESAPI tool

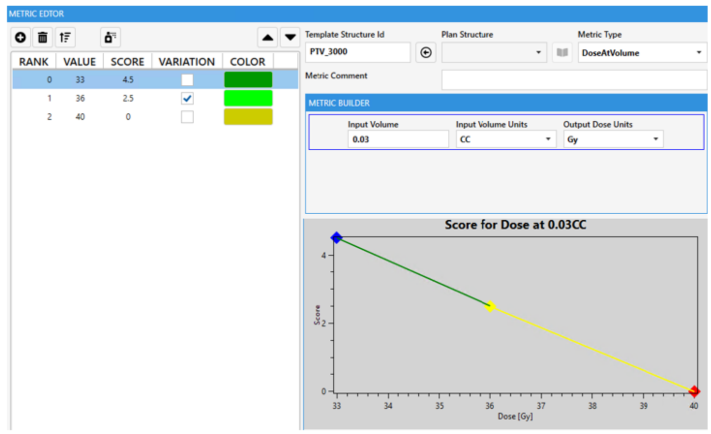
B4 Scorecard modifications HLS-EC-WB from HSWBv2

PTV Brain – **Dose at 0.03cc (customized-not scaled)**

HLS-EC-WB

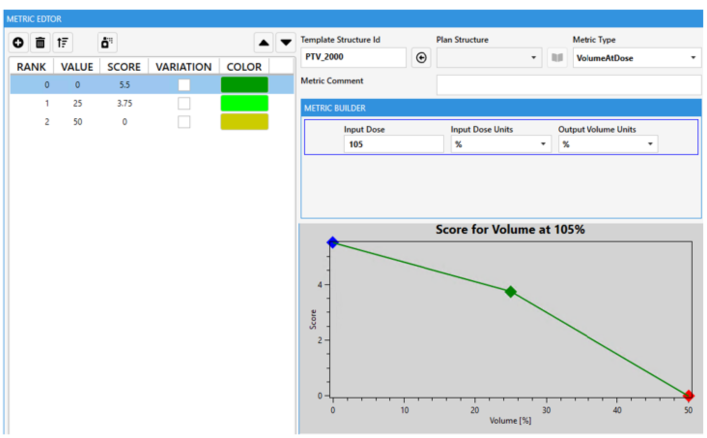


HSWBv2

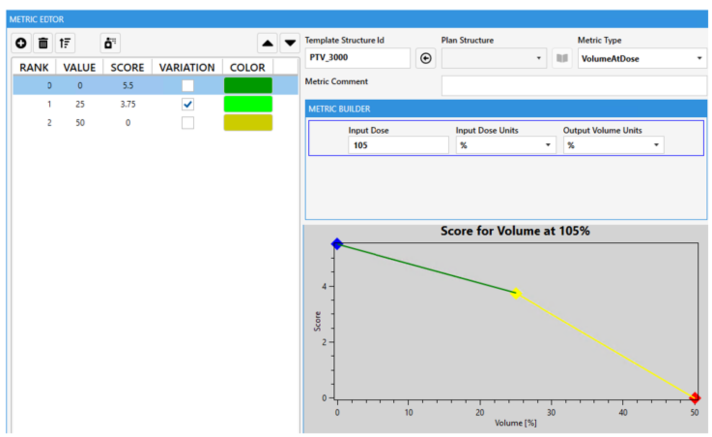


PTV Brain – **Volume at 105%**

HLS-EC-WB



HSWBv2

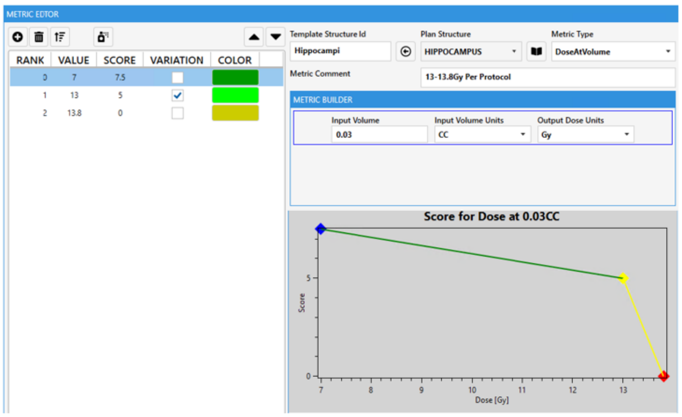


Annex B: Dosimetric scorecard and PlansScoreCard ESAPI tool

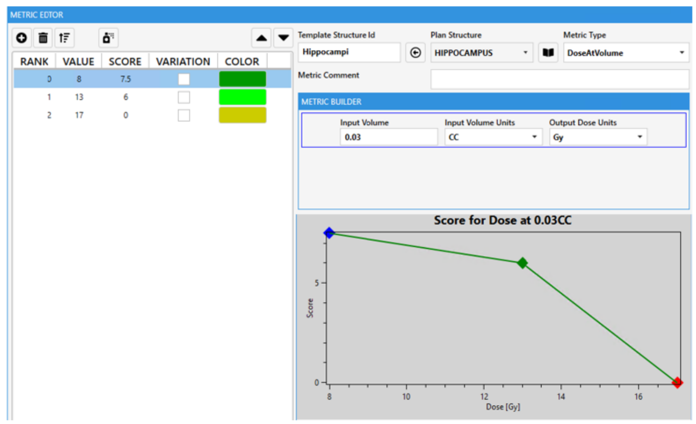
B4 Scorecard modifications HLS-EC-WB from HSWBv2

Hippocampus– **Dose at 0.03cc (customized-not scaled)**

HLS-EC-WB

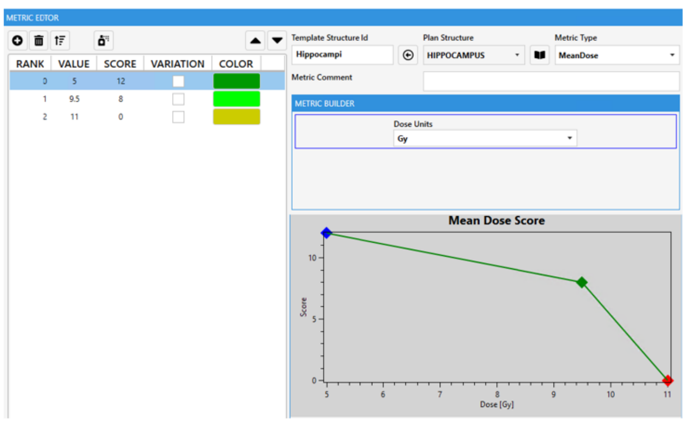


HSWBv2

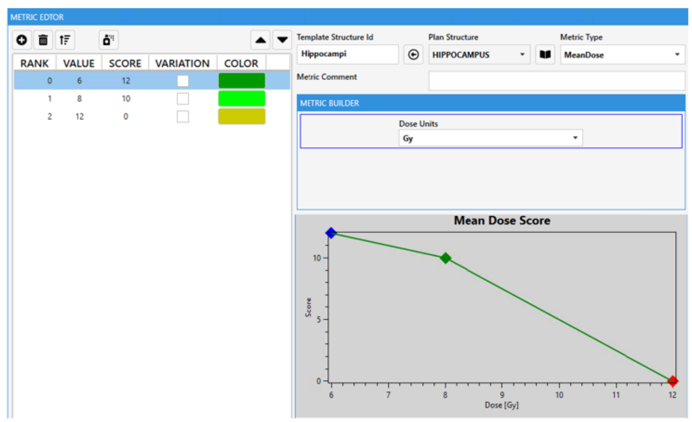


Hippocampus– **Mean Dose (customized-not scaled)**

HLS-EC-WB

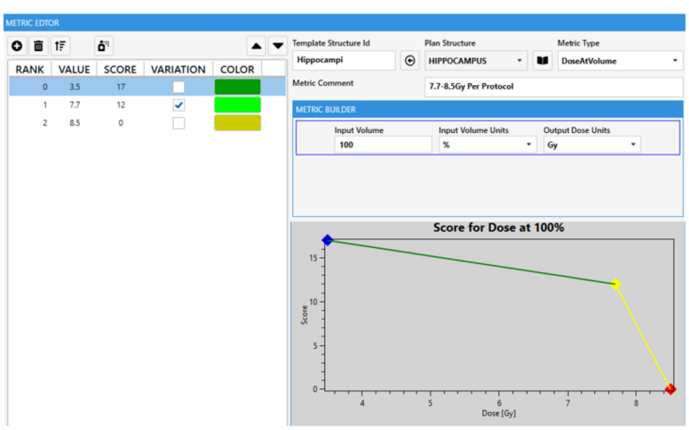


HSWBv2

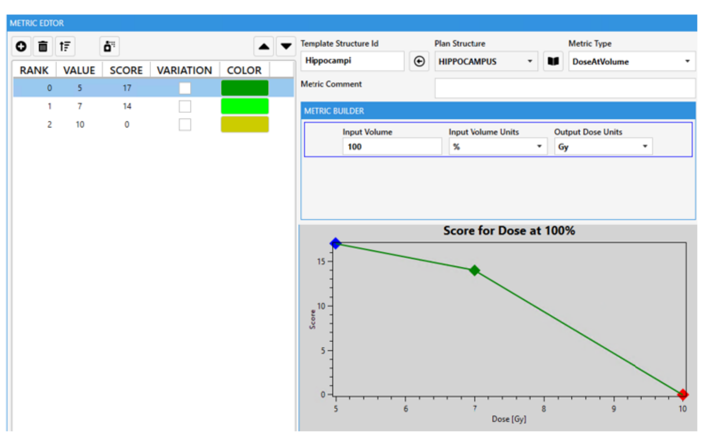


Hippocampus– **Dose at 100% (customized-not scaled)**

HLS-EC-WB



HSWBv2

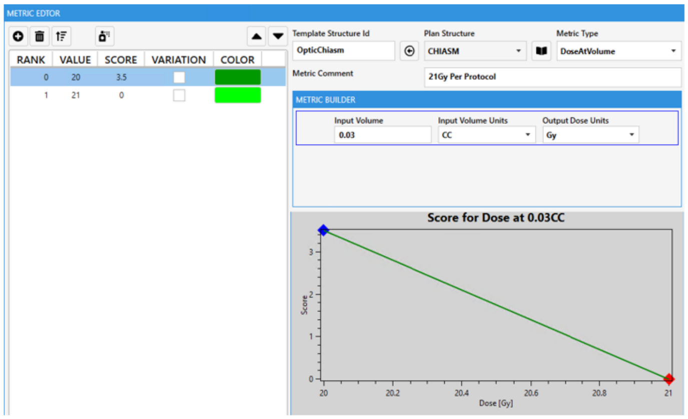


Annex B: Dosimetric scorecard and PlansScoreCard ESAPI tool

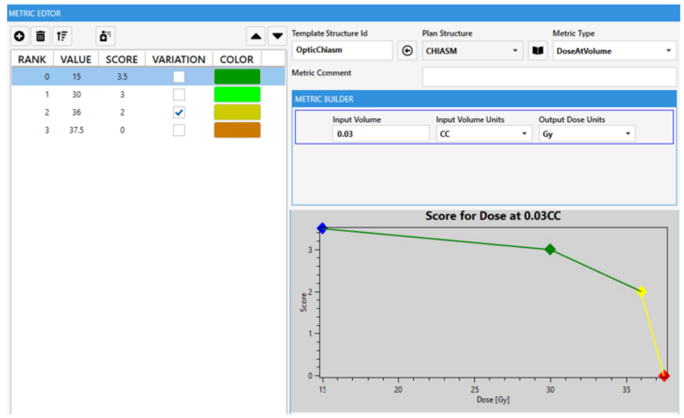
B4 Scorecard modifications HLS-EC-WB from HSWBv2

Optic Nerves and Chiasm– **Dose at 0.03cc (customized-not scaled)**

HLS-EC-WB

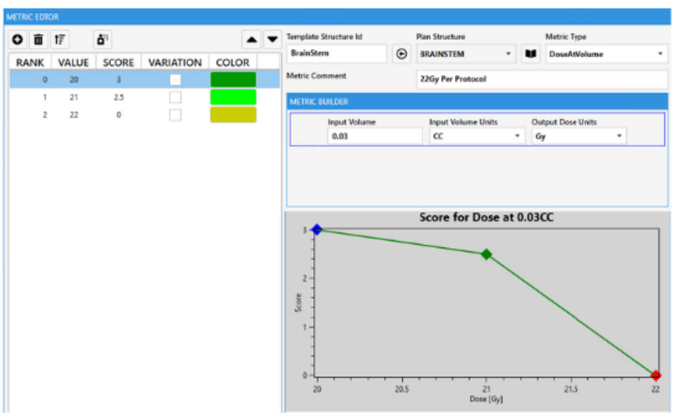


HSWBv2

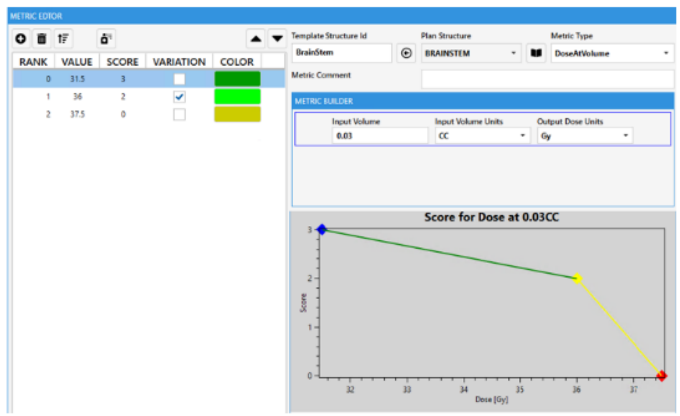


Brainstem– **Dose at 0.03cc (customized-not scaled)**

HLS-EC-WB

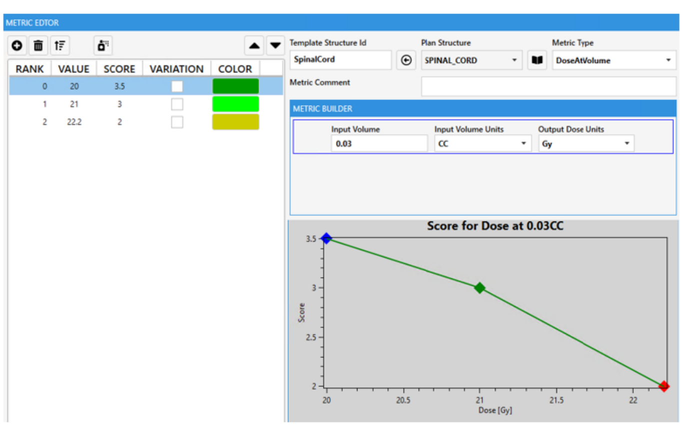


HSWBv2

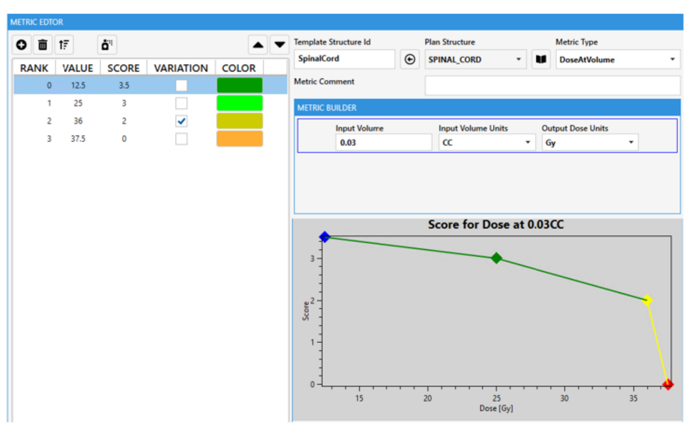


Spinal Cord– **Dose at 0.03cc (customized-not scaled)**

HLS-EC-WB



HSWBv2

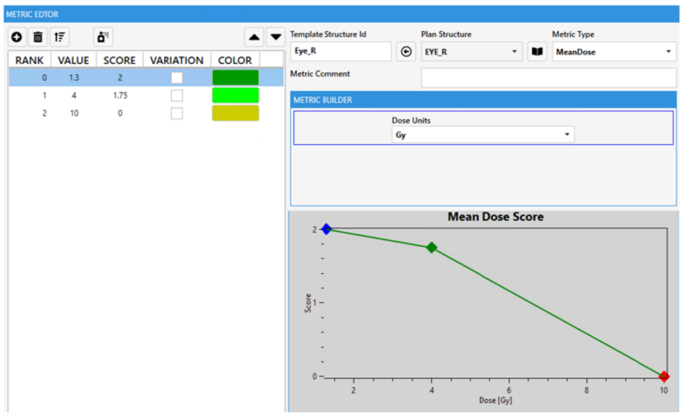


Annex B: **Dosimetric scorecard** and **PlansScoreCard** ESAPI tool

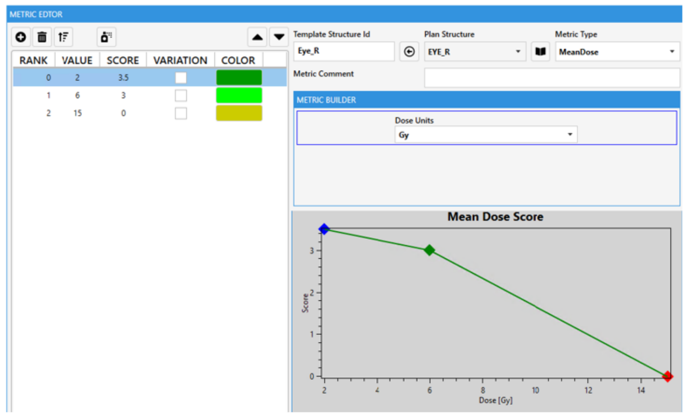
B4 Scorecard modifications HLS-EC-WB from HSWBv2

Eyes – **Mean Dose (scaled)**

HLS-EC-WB

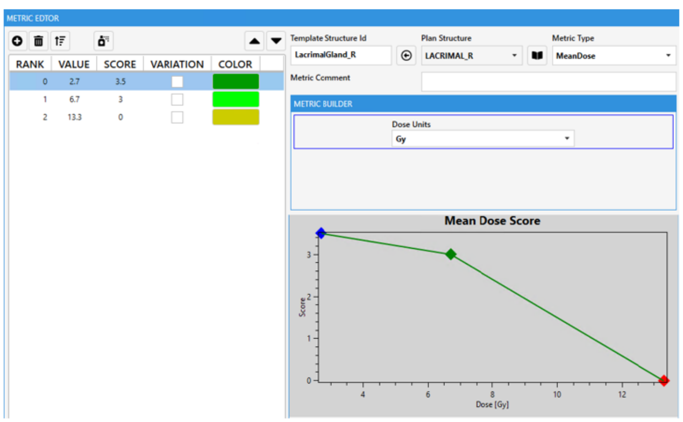


HSWBv2

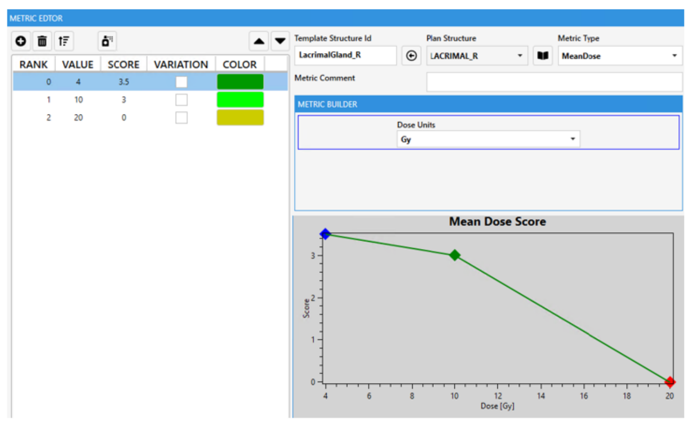


Lacrimal Glands – **Mean Dose (scaled)**

HLS-EC-WB

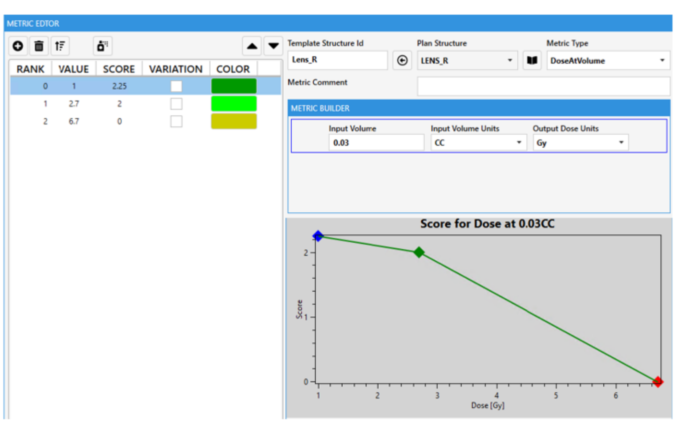


HSWBv2

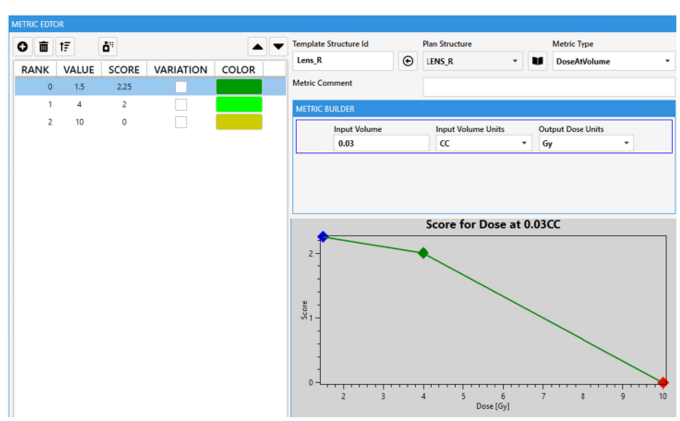


Lens– **Dose at 0.03cc (scaled)**

HLS-EC-WB



HSWBv2

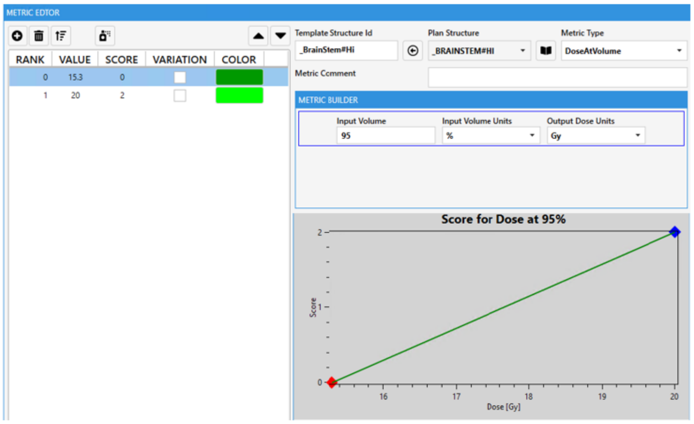


Annex B: Dosimetric scorecard and PlansScoreCard ESAPI tool

B4 Scorecard modifications HLS-EC-WB from HSWBv2

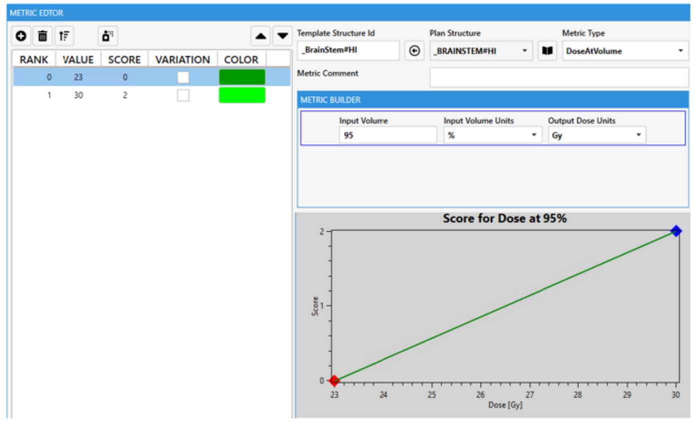
Brainstem Sub Hippocampi + 5mm – **Dose at 95% (scaled)**

HLS-EC-WB



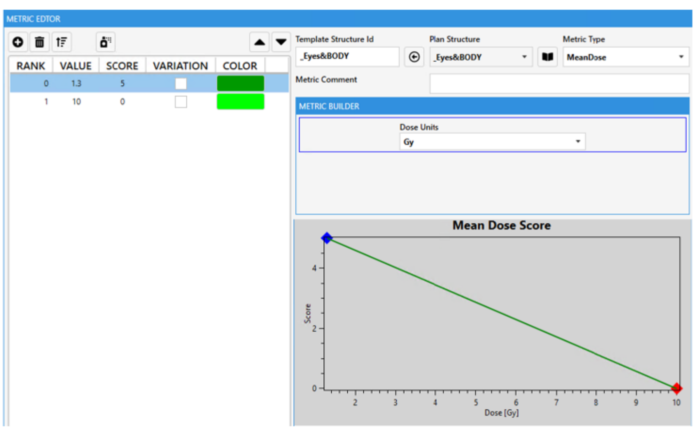
Brainstem Sub Hippocampi + 8mm – **Dose at 95%**

HSWBv2

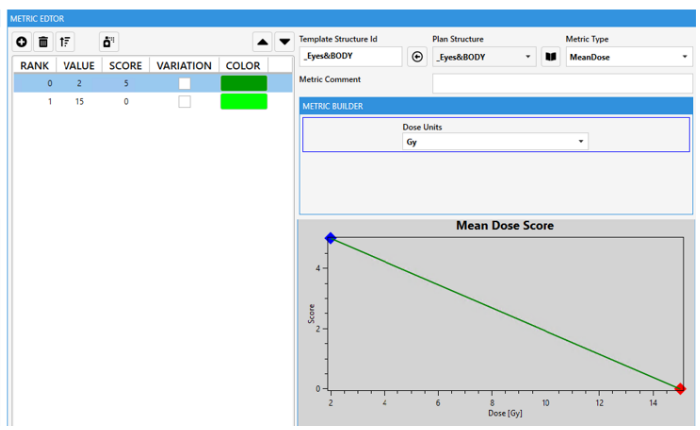


Face– **Mean Dose (scaled)**

HLS-EC-WB

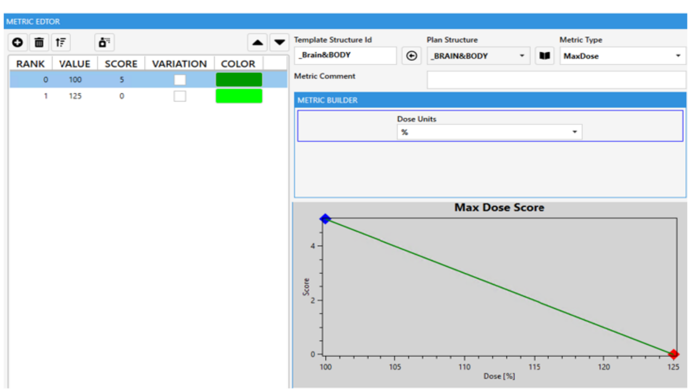


HSWBv2

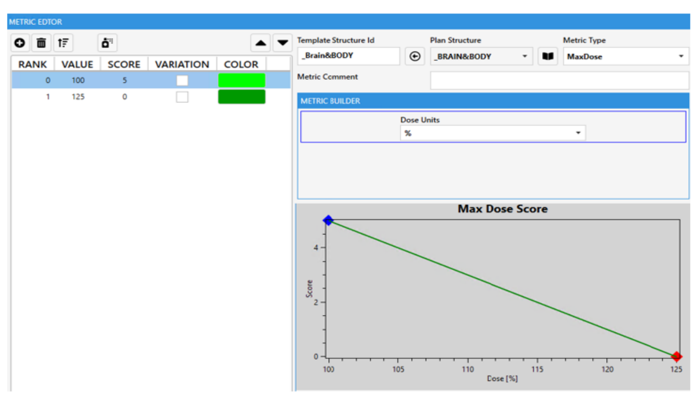


Ring– **Max Dose**

HLS-EC-WB



HSWBv2

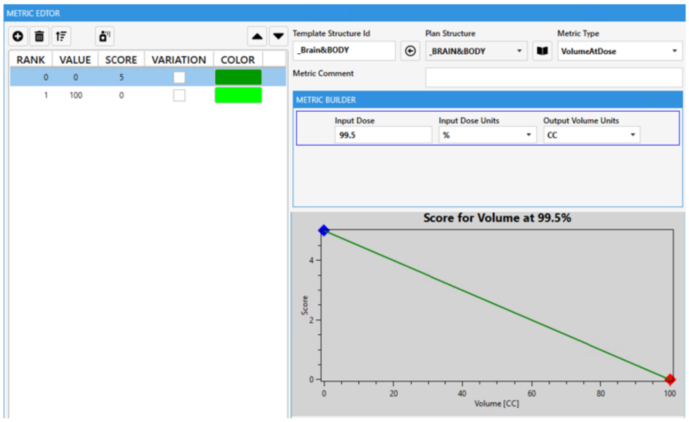


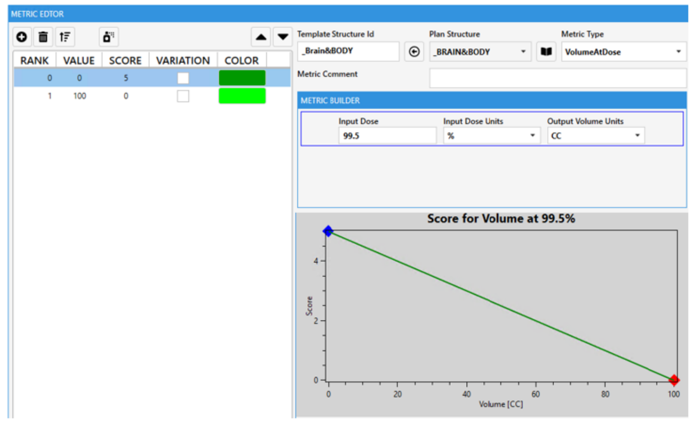
Annex B: **Dosimetric scorecard** and **PlansScoreCard** ESAPI tool

B4 Scorecard modifications HLS-EC-WB from HSWBv2

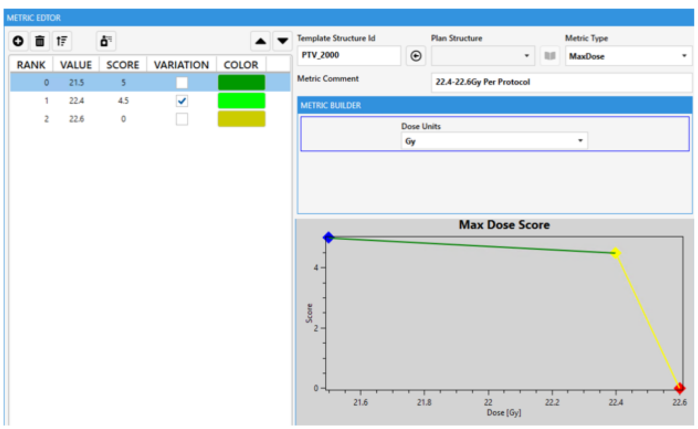
Ring– **Volume at 99.5%**

HLS-EC-WB **HSWBv2**

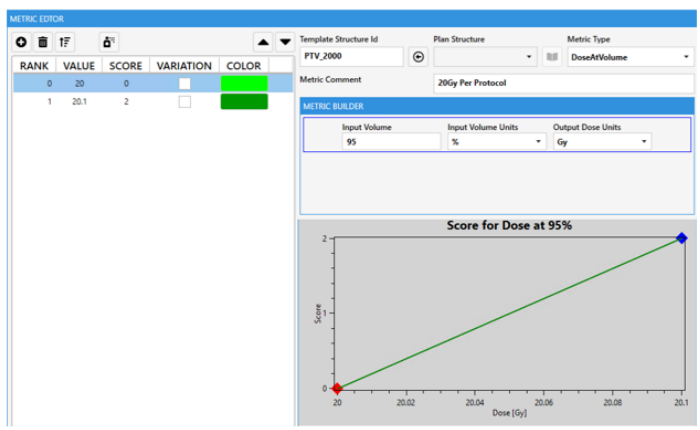




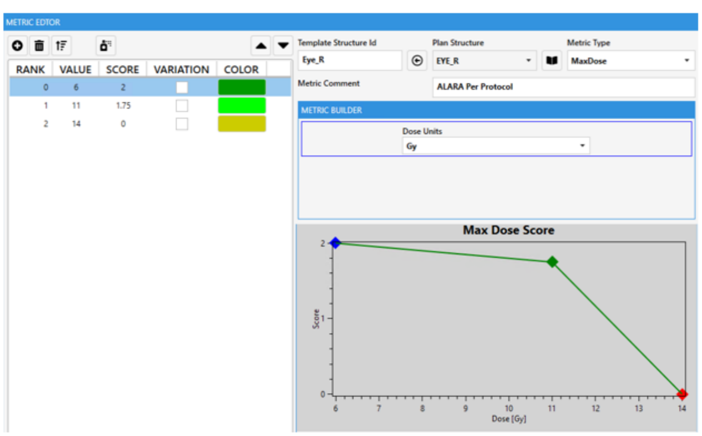
PTV Brain – Max Dose **(NEW HLS-EC-WB)**



PTV Brain – Dose at 95% **(NEW HLS-EC-WB)**

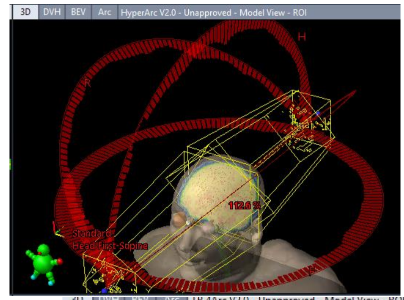


Eyes – Max Dose **(NEW HLS-EC-WB)**



Annex C: Validation Results

C1: Beam Arrangements (6X-FFF, AcurosXB v17, extended convergence mode, MR3 return, 2x Intermediate dose)



HLS-EC-WB additional 5 case validation on Halcyon and TrueBeam (M120 MLC)

Halcyon SX2MLC: *coplanar collimator: 315°, 0°, 45°, 90°.*

Truebeam M120MLC

HyperArc: *full 4 arc arrangement*

4 Arcs Non-Coplanar: *2 full arcs 0° couch* 315°/45°

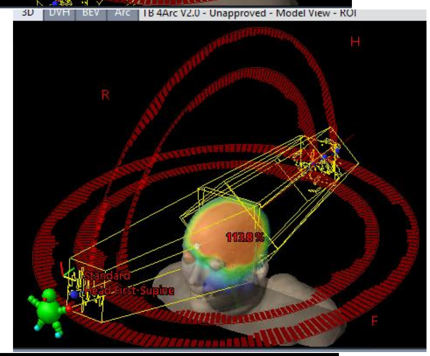
collimators and two vertex 180° (PA) -> 5° (from AP)

90° couch CW/CCW paired arcs with 315°/45° collimator

3 Arcs Coplanar: *collimator: 315°, 45°, 90°*

4 Arcs Coplanar: *collimator same as 3 Arcs except*

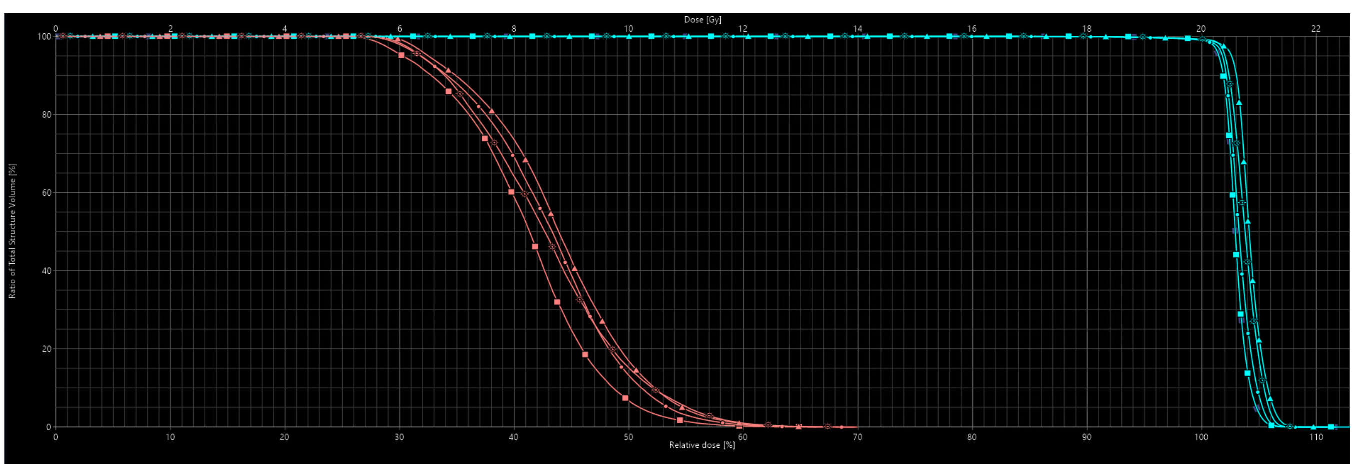
90° split X jaw superior/inferior to hippocampus



	Halcyon	TrueBeam			
Patient	**4 Arcs (Coplanar)**	**4 Arcs (Non-Coplanar)**	**3 Arcs (Coplanar)**	**4 Arcs (Coplanar)**	**HyperArc (Non-Coplanar)**
36	141.32	137.2	128.01	137	137.88
37	143.93	141.02	140	142.28	138.16
39	143.31	137.32	127.29*	138.12	137.01
40	137.3	131.18*	117.89**	125.68*	131.36
41	141.54	131.07	132.13	135.85	133.11
Average	**141.48**	**136.65**	**133.38**	**138.31**	**135.50**

* For each metric failing (0 points received)

Patient 36 selected DVH:



Dose | Reference Points | Dose Statistics

Show DVH	Show DVHE	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [%]	Max Dose [%]	Mean Dose [%]
☑		PTV_3000	Unapproved	V2.01	20Gy	1228.7	100.0	100.0	76.6	111.9	103.0
☑		PTV_3000	Unapproved	V2.01-3FTB	20Gy	1228.7	100.0	100.0	75.2	112.9	104.2
☑		PTV_3000	Unapproved	V2.01-4FTB	20Gy	1228.7	100.0	100.0	75.3	111.7	103.3
☑		PTV_3000	Unapproved	V2.01HyperArc	20Gy	1228.7	100.0	100.0	73.9	111.0	103.8
☑	☐	Hippocampi	Unapproved	V2.01	20Gy	3.2	100.0	100.2	25.1	66.4	41.1
☑	☐	Hippocampi	Unapproved	V2.01-3FTB	20Gy	3.2	100.0	100.2	28.3	69.7	43.9
☑	☐	Hippocampi	Unapproved	V2.01-4FTB	20Gy	3.2	100.0	100.2	27.2	68.8	43.0
☑		Hippocampi	Unapproved	V2.01HyperArc	20Gy	3.2	100.0	100.2	26.4	70.0	42.8

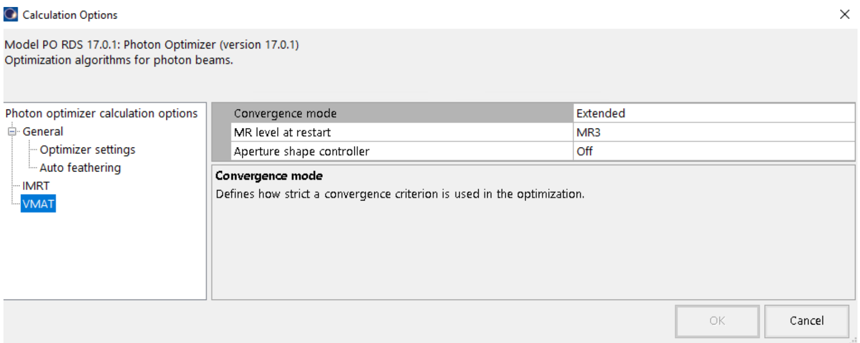
Annex C: Validation Results

C2: 1xMR3, 2xMR3, 3xMR3 (Convergence Mode: Extended)

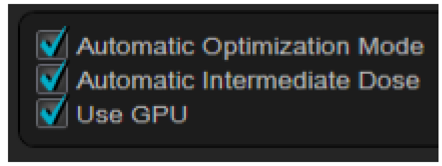
(v17 algorithms, extended convergence mode, MR3 return)

HLS-EC-WB additional 5 case validation on Halcyon

Always use extended convergence mode and MR3 return:

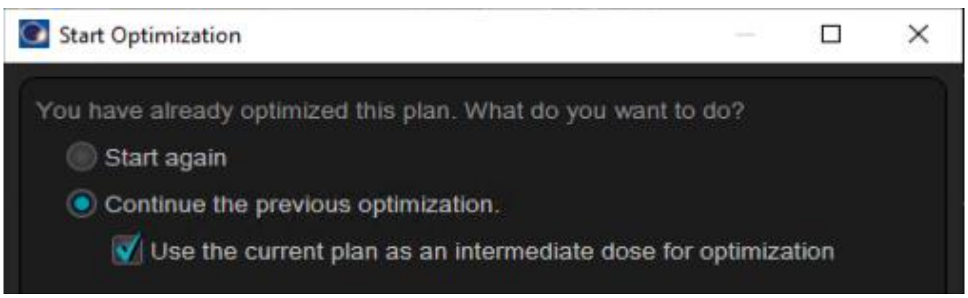


1XMR3= "Automatic Intermediate dose"



*GPU not required

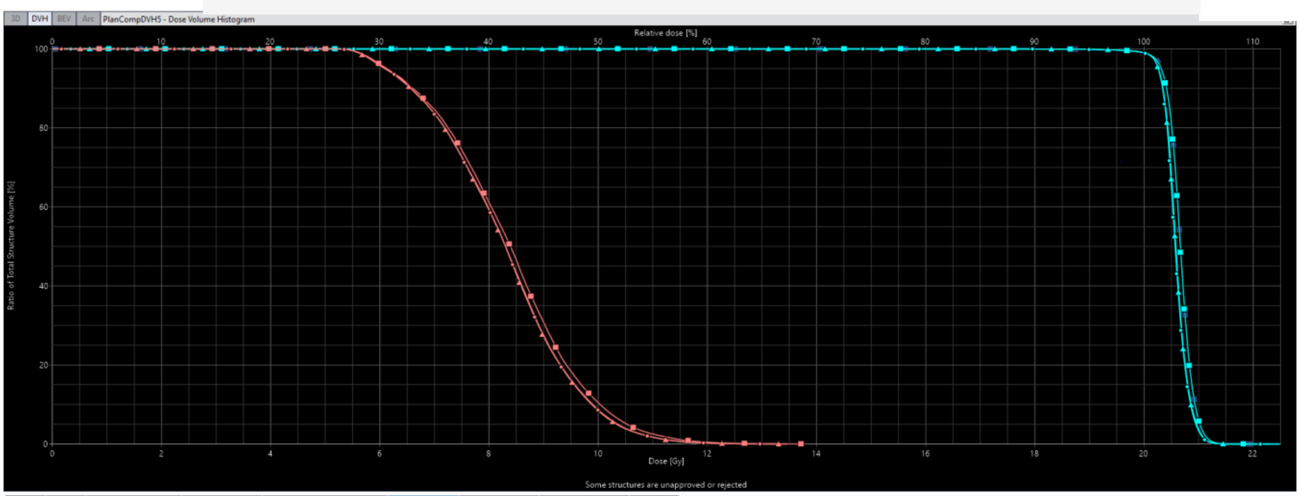
2XMR3 and 3XMR3: multiple Intermediate dose optimizations, "current plan as an intermediate dose for optimization"



Patient 36

Scores / DVH:

036: [20Gy]	HLS-EC-WB	1xMR3*: 137.49/158.50 (86.74%)	**2516.2 MU**
036: [20Gy]	HLS-EC-WB	2xMR3*: 139.58/158.50 (88.06%)	**2602.0 MU**
036: [20Gy]	HLS-EC-WB	3xMR3*: 142.88/158.50 (90.14%)	**2677.4 MU**



Fields | Dose | Field Alignments | Clinical Goals | Optimization Objectives | Dose Statistics | Reference Points | Calculation Models | Plan Sum

Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
PTV_2000	Unapproved	_V2.01_1xMR3*	20Gy	1369.3	100.0	100.0	15.914	22.503	20.662
PTV_2000	Unapproved	_V2.01_2xMR3*	20Gy	1369.3	100.0	100.0	15.817	22.485	20.590
PTV_2000	Unapproved	_V2.01_3xMR3*	20Gy	1369.3	100.0	100.0	15.498	22.321	20.578
Hippocampi	Unapproved	_V2.01_1xMR3*	20Gy	3.2	100.0	100.2	5.163	13.798	8.364
Hippocampi	Unapproved	_V2.01_2xMR3*	20Gy	3.2	100.0	100.2	5.173	13.338	8.265
Hippocampi	Unapproved	_V2.01_3xMR3*	20Gy	3.2	100.0	100.2	5.164	13.468	8.276

Annex C: Validation Results

C3: Rapidplan v15.6 and v17 model versions (Halcyon 4 arc, 6X-FFF, AcurosXB v17)

This model was created on a V17 Eclipse system. For backwards compatibility, all training set cases were exported and imported into a V15.6 system. The V15.6 model was trained and the optimization objectives from the V17 model were replicated. Finally, the V15.6 model was exported from the V15.6 system back into the V17 system and plans were reoptimized with scores compared with the results of the V17 native model.

	Halcyon	
	4 Arcs (Coplanar)	
Patient	**V15.6**	**V17**
36	141.27	141.32
37	144.45	143.93
39	144.03	143.31
40	137.58	137.3
41	142.45	141.54
Average	**141.956**	**141.48**

C4: HLS-EC-WB model **evolution process** (scores) on validation set

	HLS-EC-WB Scorecard (158.5 points)			
Patient	**V2.0 Model (Manual Scaling)**	**HLS-EC-WB Initial Model**	**HLS-EC-WB Initial Model (New Priorities)**	**Final HLS-EC-WB Recursive Model**
36	138.9	140	139.81	141.32
37	143.32	144.66	145.24	143.93
39	140.32	138.07	139.24	143.31
40	133.21	127.92	132.74	137.3
41	140.88	140.12	141.21	141.54
Average	**139.326**	**138.154**	**139.648**	**141.48**

Annex D: Examples applying this model for Simultaneous Integrated Boost

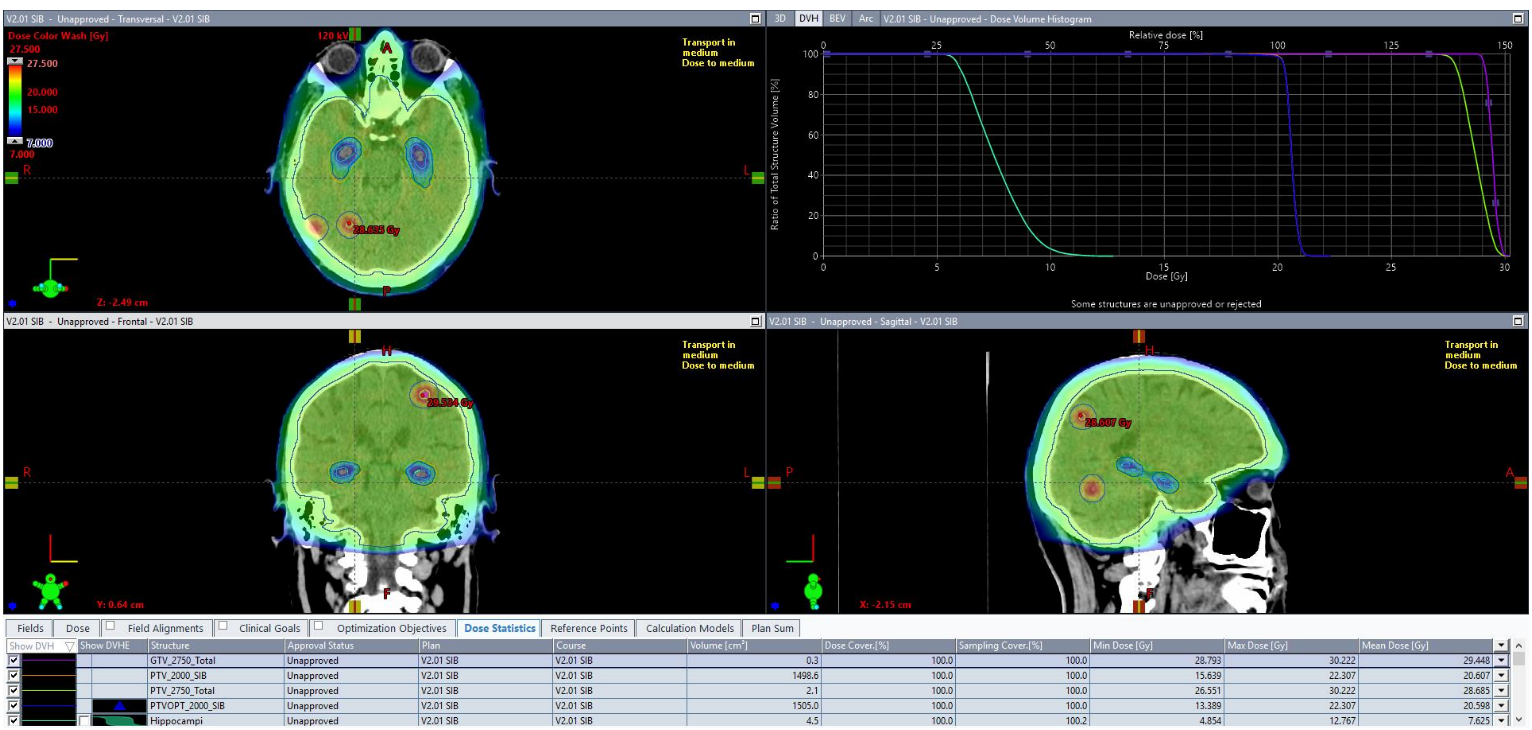
This model was trained for only the PTV whole brain target. However, it could be used to create SIB plans by cropping the PTV_WBopt, with some additional margin, from the PTVBoost target(s). The PTV whole brain should also be removed from the high risk PTV + 7mm to evaluate heterogeneity within the target. In the below examples, an additional 7mm margin was also used between the WB_PTVopt (20Gy) and the PTV_Boost (27.5Gy) target.

After cropping additional margins out of the PTV whole brain and PTV_WBopt, use HLS-EC-WB to automatically populate the optimizer as intended. Manually add upper and lower dose constraints for the PTVBoost, per prescription. Ensure that the margin removed from the WB_PTVopt, to accommodate the PTVBoost, is not too conservative or aggressive. Consider increasing the MU objective Maximum MU to >2500 if utilizing this RapidPlan model for SIB treatment plans.

When using this method, the HLS-EC-WB model has no knowledge of the higher dose level target when generating the DVH prediction bands and relative optimization objectives. This situation could cause the model to create objectives that are no longer relevant for your patient and could, as a result, create undesirable plans. The degree to which the objectives are off relates directly to the distance that the higher dose target is from the OARs. This is especially important for the hippocampus DHV bands being predicted and the increased dose the high risk PTV is prescribed relative to the PTV whole brain. In scenarios where the PTVboost is near the hippocampi, it is advised to copy the hippocampi into an evaluation structure and that is cropped with an additional margin away from the PTVboost. This hippocampi evaluation structure is to then be matched to the hippocampi in the HLS-EC-WB model for DVH estimation and optimization. Due to these various clinical scenarios, the usage of SIB cannot be endorsed by the creators of this model. However, what each user does with this model is at the discretion of the user and their associated clinical, physics, and medical staff.

D1: Example SIB Plan 27.5Gy in 5Fx

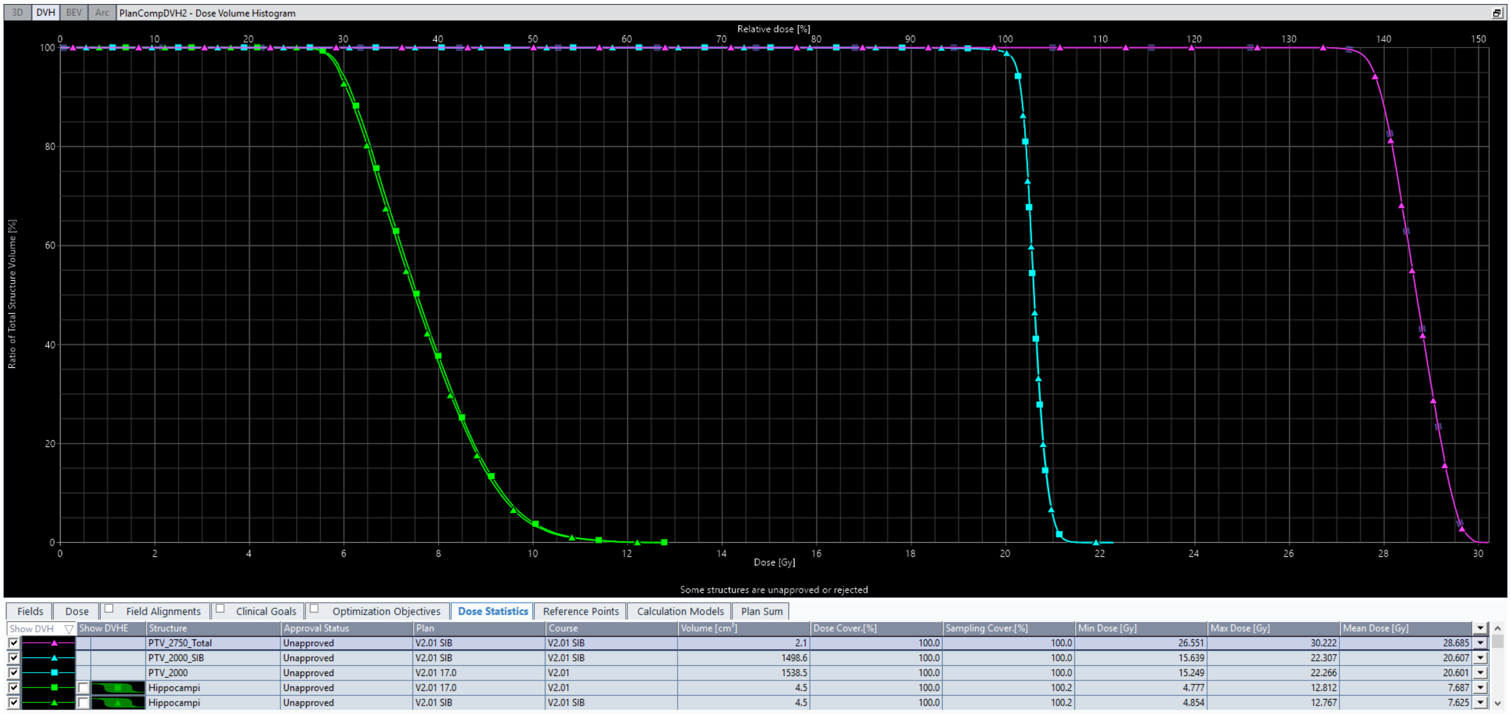
PTV_2750_Total boost to 27.5Gy and PTV_2000_SIB to 20Gy (Halcyon 4 arc, 6X-FFF, AcurosXB v17).



Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
GTV_2750_Total	Unapproved	V2.01 SIB	V2.01 SIB	0.3	100.0	100.0	28.793	30.222	29.448
PTV_2000_SIB	Unapproved	V2.01 SIB	V2.01 SIB	1498.6	100.0	100.0	15.639	22.307	20.607
PTV_2750_Total	Unapproved	V2.01 SIB	V2.01 SIB	2.1	100.0	100.0	26.551	30.222	28.685
PTVOPT_2000_SIB	Unapproved	V2.01 SIB	V2.01 SIB	1505.0	100.0	100.0	13.389	22.307	20.598
Hippocampi	Unapproved	V2.01 SIB	V2.01 SIB	4.5	100.0	100.2	4.854	12.767	7.625

D2: SIB DVH Comparison

DVH comparison: SIB (HCSWB_SIB) vs Non-SIB (HCSWB HLS-EC-WB) plans

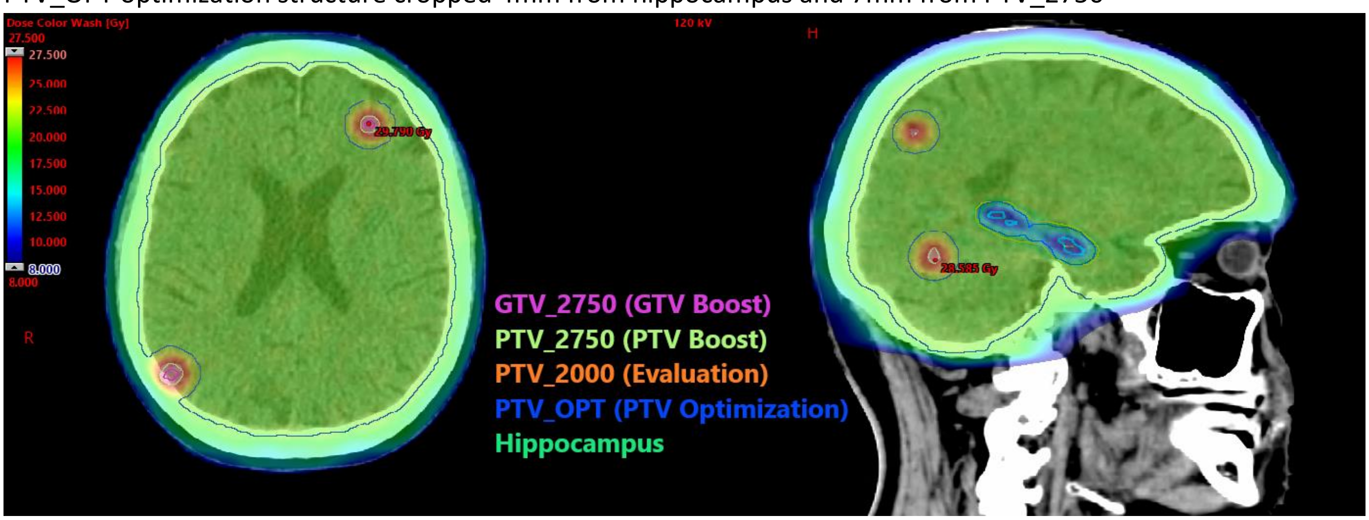


Show DVH	Show DVHE	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
		PTV_2750_Total	Unapproved	V2.01 SIB	V2.01 SIB	2.1	100.0	100.0	26.551	30.222	28.685
		PTV_2000_SIB	Unapproved	V2.01 SIB	V2.01 SIB	1498.6	100.0	100.0	15.639	22.307	20.607
		PTV_2000	Unapproved	V2.01 17.0	V2.01	1538.5	100.0	100.0	15.249	22.266	20.601
		Hippocampi	Unapproved	V2.01 17.0	V2.01	4.5	100.0	100.2	4.777	12.812	7.687
		Hippocampi	Unapproved	V2.01 SIB	V2.01 SIB	4.5	100.0	100.2	4.854	12.767	7.625

D3: SIB planning structures

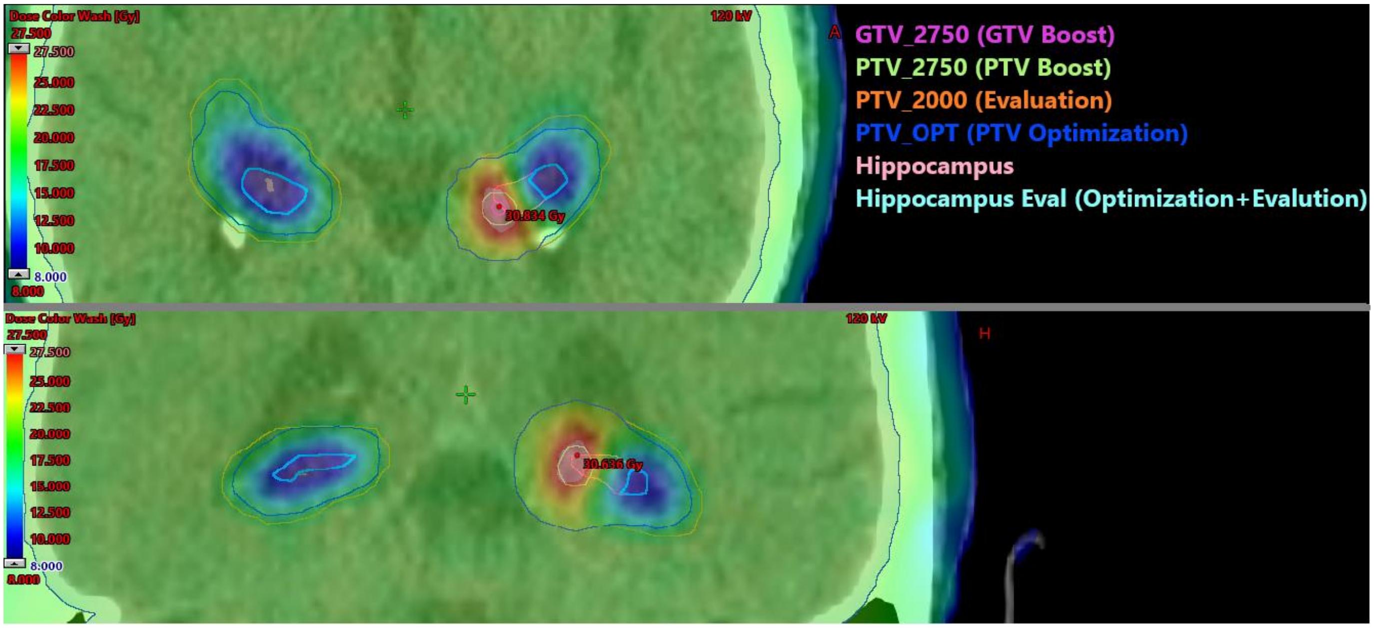
PTV_2000 structure cropped 5mm from hippocampus and 7mm from PTV_2750

PTV_OPT optimization structure cropped 4mm from hippocampus and 7mm from PTV_2750



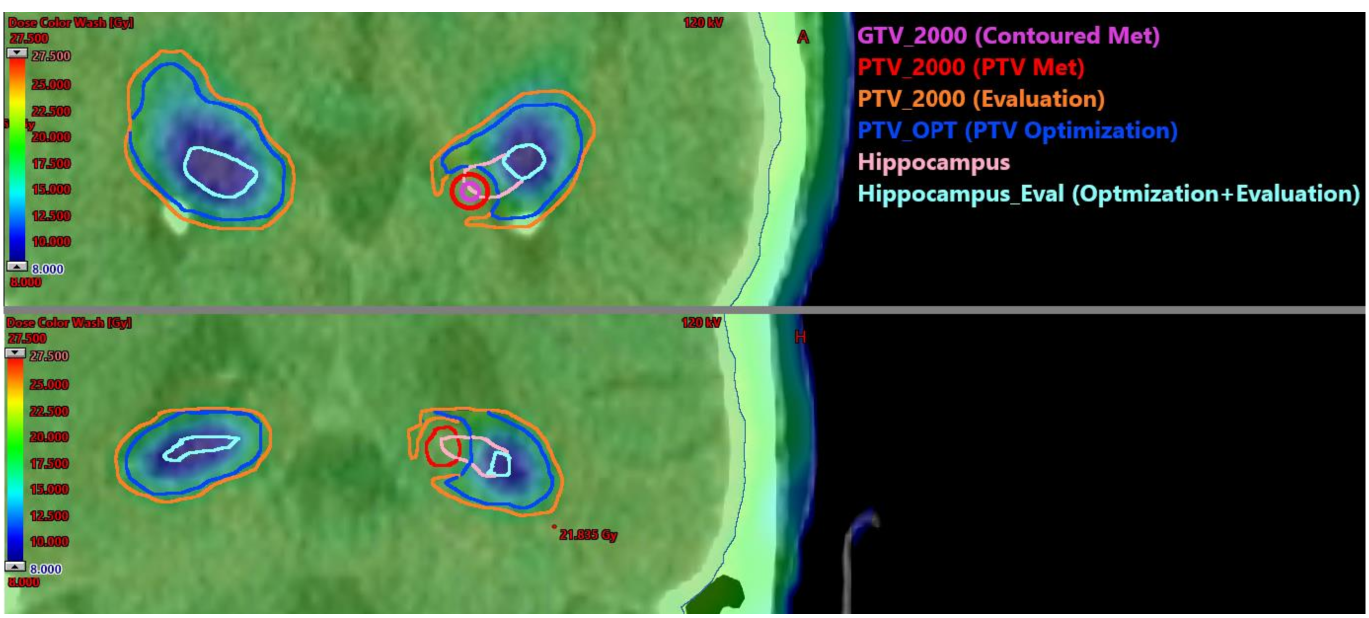
D4: PTV boost proximity to hippocampi

CCTG CE. 7 allows for hippocampal sparing wherever possible, even with metastasis close to or overlapping. In the below example, to achieve desired hippocampal sparing with this proximity to the boost volume, the Hippocampus is copied and cropped by 5mm from the PTV boost. This hippocampus_Eval structure is then matched to the hippocampus structure in the HLS-EC-WB model for optimization and evaluation.



D5: Metastases proximity to hippocampi (sequential boost)

The following workflow can be used in the occurrence for when contoured brain metastases are in proximity of the hippocampus and sequential boosting is implemented. To maintain prescription dose (20Gy) to the contoured GTV and PTV brain metastases, the hippocampus is copied and cropped by 5mm from the "PTV met". This hippocampus_Eval structure is then later matched to the hippocampus structure in the HLS-EC-WB model for optimization and evaluation. After the PTV_2000 structure and PTV_OPT structures are cropped 5mm and 4mm from the hippocampus respectively, the PTV Met with an additional 2mm margin can be added back to the both the PTV_2000 and PTV_OPT. This allows the model to account for the desired gradient to achieve coverage of the PTV met and reduce dose to the hippocampus_Eval.



Annex E: Acknowledgements

Manually optimized plans created by Ryan Clark, MS CMD

All data generated and complied by Ryan Clark, MS CMD and Anthony Magliari, MS CMD

Dosimetric Scorecard HLS-EC-WB and derived structures designed by Anthony Magliari, MS CMD and Ryan Clark, MS CMD

Model generated plans created by Lesley Rosa, CMD, Ryan Clark, MS CMD and Anthony Magliari, MS CMD

Clinical Description document created by Anthony Magliari, MS CMD, Ryan Clark, MS CMD and Lesley Rosa, CMD

Please reference future publication:

Dosimetric Scorecards express clinical intent with precision: alternate hippocampal sparing whole brain RapidPlan models with enhanced target coverage, homogeneity and less aggressive hippocampal sparing

Kareem Rayn, Anthony Magliari, Ryan Clark, Lesley Rosa, Robert Doucet, Line Comeau, Alan Nichol, Russel Ruo, David Roberge

Annex F: Distribution and compatibility

This RapidPlan model is to be distributed exclusively via the links found on Varian Medical Affairs:

https://medicalaffairs.varian.com/wholebrain-limited-hippocampalsparing-20gy-vmat2

Please do not re-distribute this model as number of downloads will be tracked (strictly to judge the success of this project).

This RapidPlan model was created, tested, and rebuilt with both Eclipse v17.0 and v15.6. For older versions of Eclipse (v13.x), please find the older HSWBv1.