Utilizing piecewise linear DVH based score functions to fully automate FLASH / IMPT dose optimization for objective treatment modality comparison

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Particle Therapy Co-Operative Group

FLASH therapy is under development and not available for commercial sale.

I am employed by Varian on the Medical Affairs team

My job currently includes testing new products and providing feedback including FLASH radiotherapy

I've been creating FLASH treatment plans since 2017

I used development builds of Eclipse and Non Clinical modes of the ProBeam delivery system for examples

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DISCLAIMER:

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"The views expressed in this presentation are mine, and mine alone. They do not represent those of Varian, A Siemens Healthineers Company"

Disclaimer 2: FLASH Intellectual Property

- Varian intends to leverage all intellectual property protections and is committed to protecting our innovations throughout the world.

- Varian has numerous pending and issued patents worldwide related to FLASH therapy and technology

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1. Dosimetric Scorecard Concepts
2. Direct Piecewise Linear Optimization
3. Dosimetric & Doserate Results

Dosimetric Scorecard Concepts

Piecewise linear DVH based score functions precisely capture clinical intent

1

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Dosimetric Scorecards: Basic Principles

- Between two different patients, scores should not be directly compared
- Designed to analyze multiple plan options for the same patient/case
- Scorecards can be created for a single patient, but better to be created per protocol or class of patients
- Max score should not be achievable
  - Scorecard total
  - Per metric
- Powerful tool for retrospective plan quality analysis
  - Create dosimetric wish list to document best achievable today to reexamine in the future

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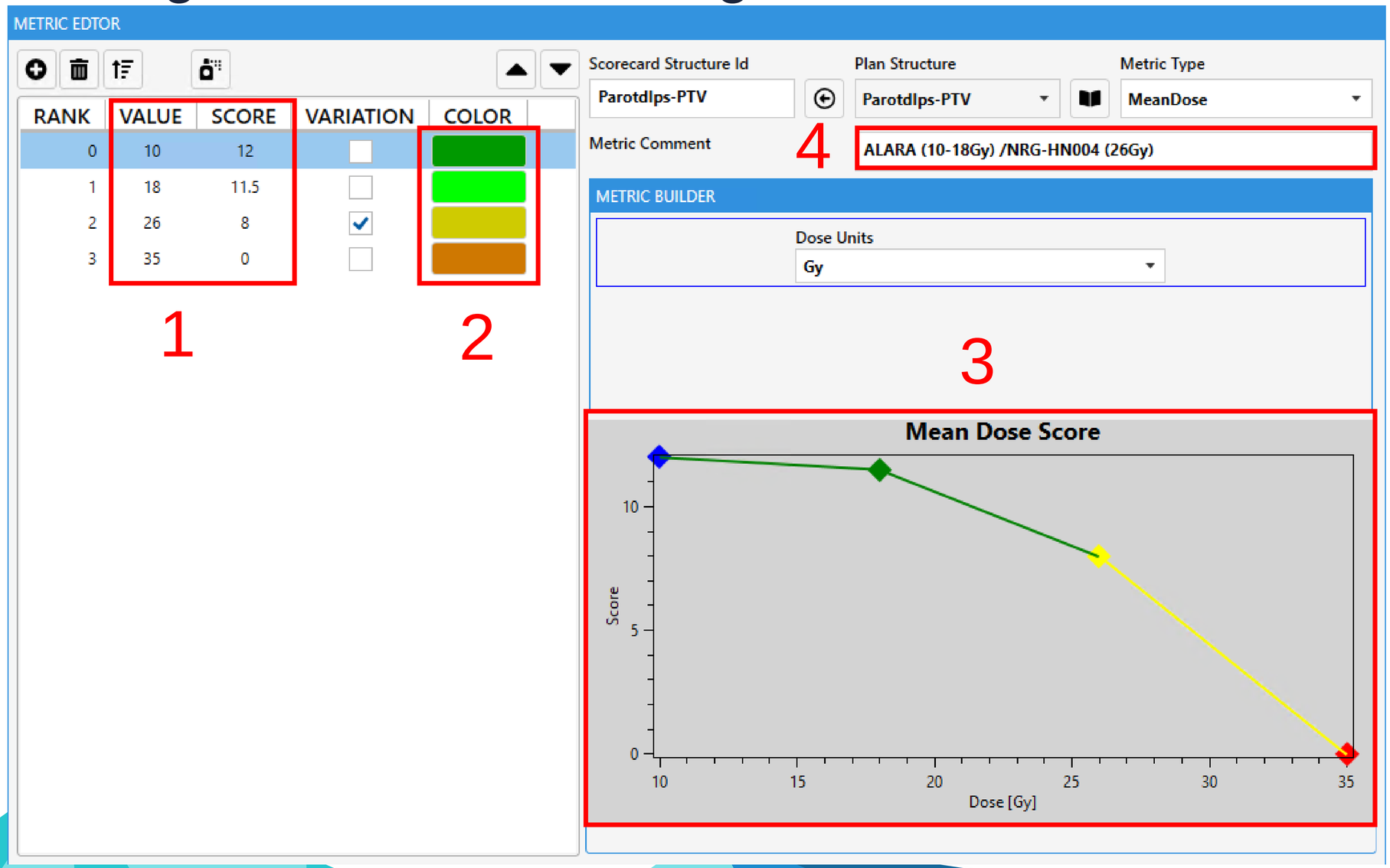
Building an individual scoring metric



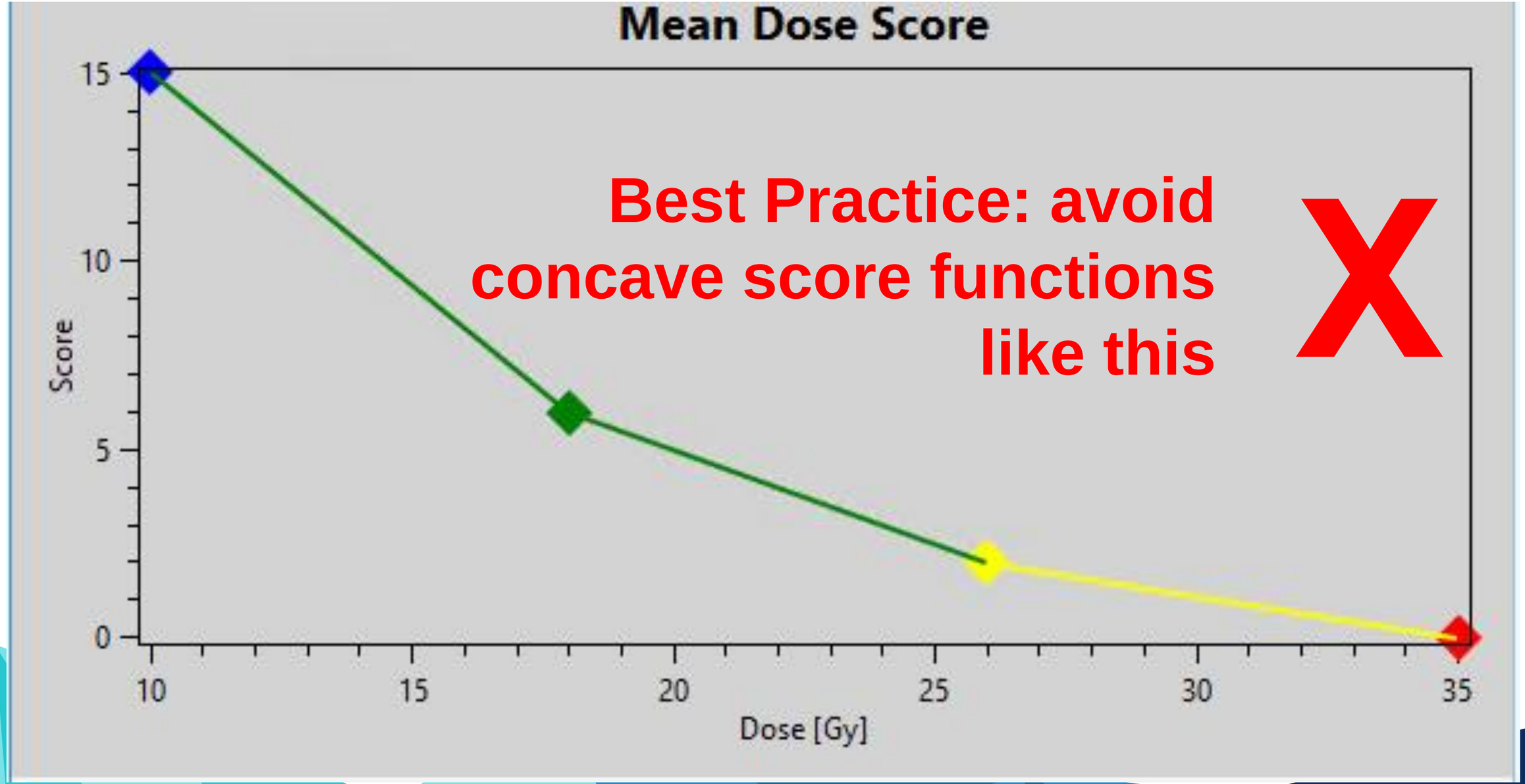
1. Points assigned for mean dose in Gy

2. Metric points scorecard expressed in qualitative colors
   - Orange = 0-8 points
   - Dark Green = Full points

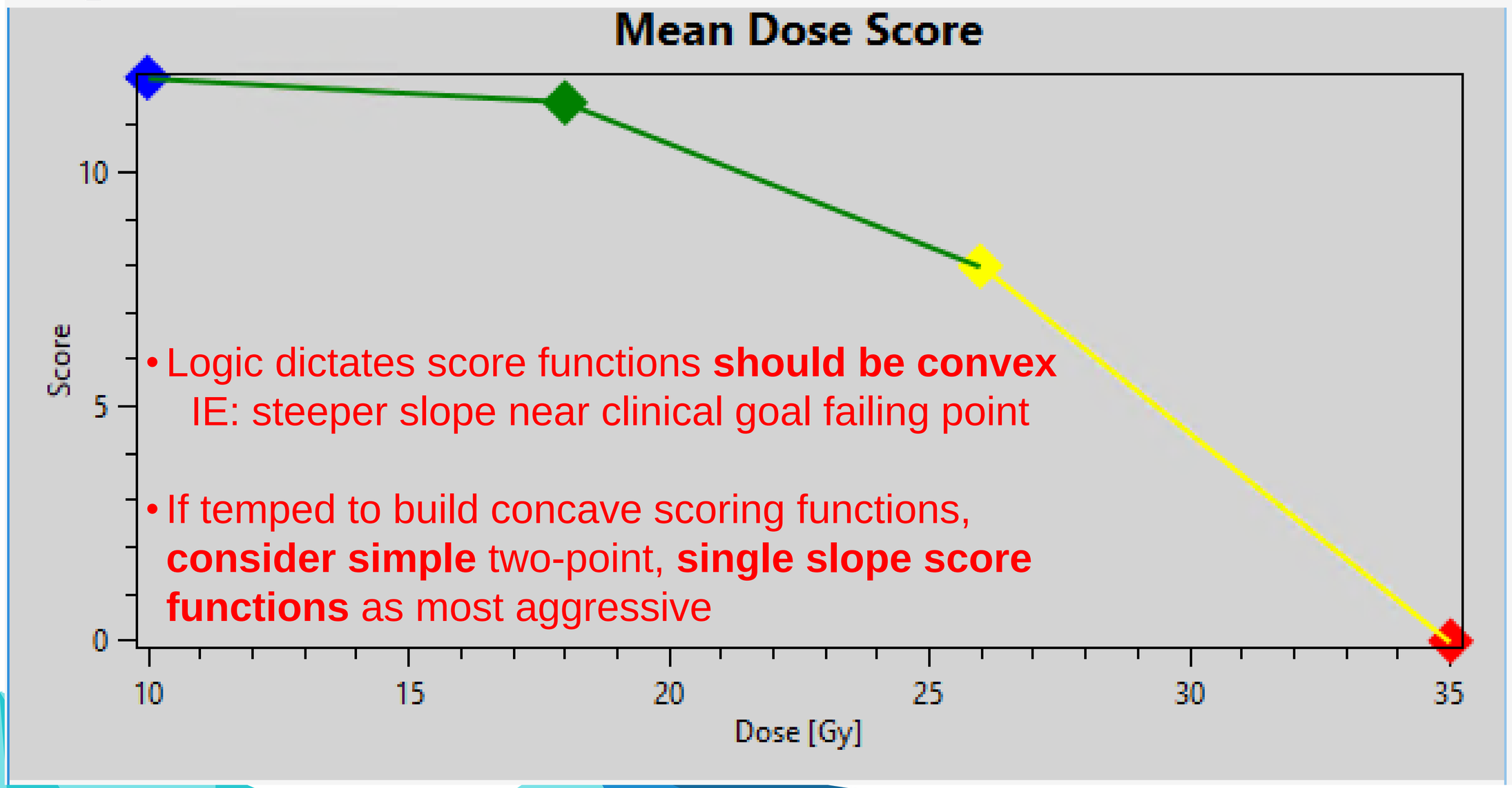
3. Points plotted as a piecewise linear function
   - Yellow symbolizes variation range

4. Comment box used for referencing protocol

Scoring metrics should not be concave



Scoring metrics should be convex



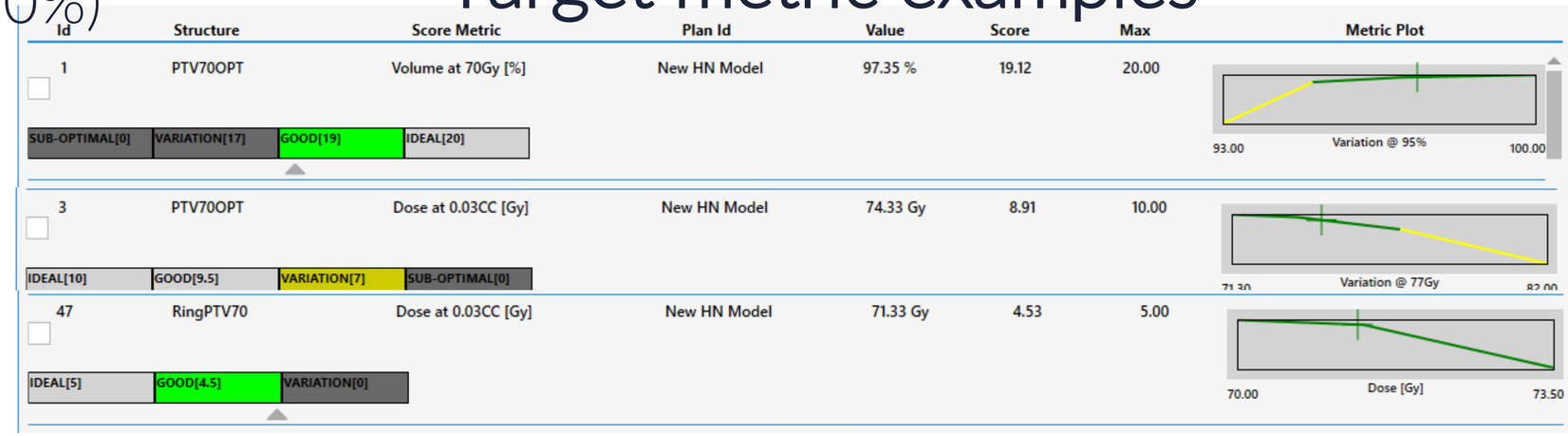
- Logic dictates score functions **should be convex**
  IE: steeper slope near clinical goal failing point

- If temped to build concave scoring functions, **consider simple** two-point, **single slope score functions** as most aggressive

Scorecard point distribution: Best Practices

- Balance Target metrics (up to 50%)
  - Max/min dose
  - % coverage
  - Homogeneity
  - Conformality
- OAR metrics
  - Volume at Dose
  - Mean dose
  - Dose at Volume (0.03cc)
- Highest points to PTV coverage
- Add multiple dose level rings
- Max is ideal (not achievable)

Target metric examples



OAR metric examples

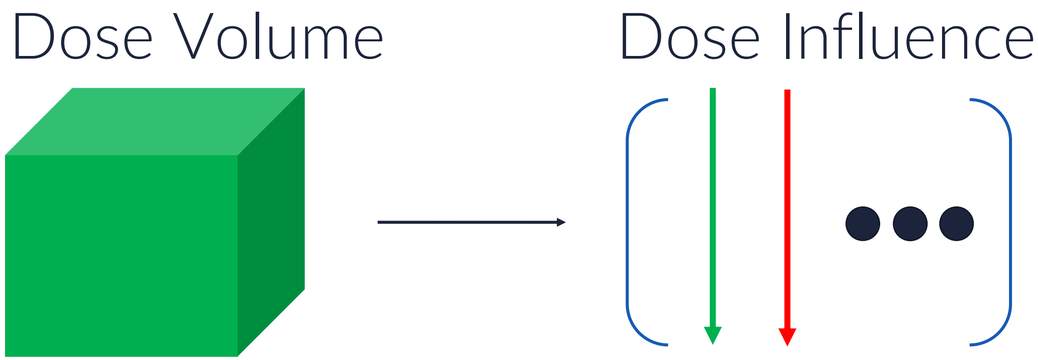
Direct Piecewise Linear Optimization

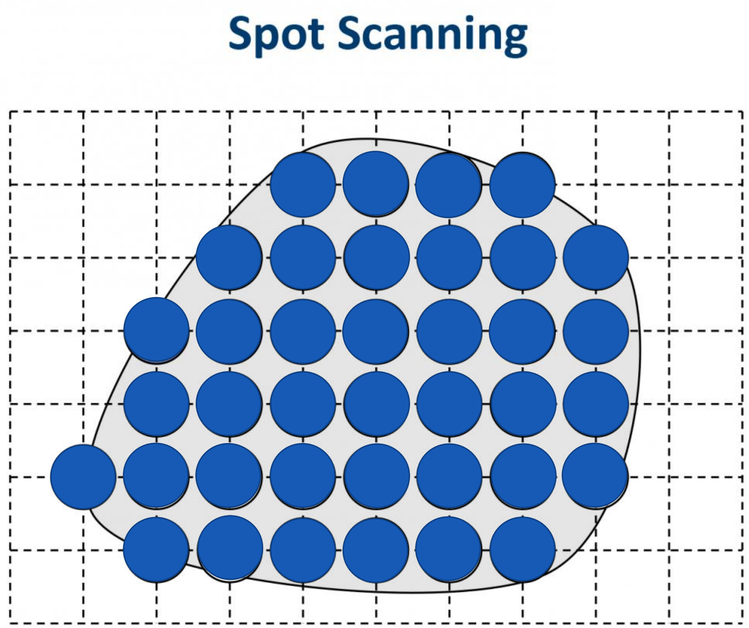
No stretchy quadradic functions: Higher Score = Better Plan

2

Calculate Dose Influence Matrix

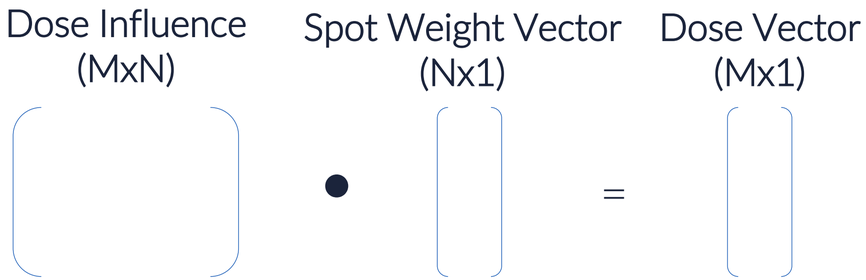
- Turn all but one spot completely off
  - Calculate the final dose
  - Flatten the dose to one dimension
  - Store as a column in 2D array
- Repeat for all spots
- End up with M x N dose influence matrix
  - M is number of pixels in patient volume, N is number of spots
  - Shows contribution of every spot to dose in every pixel



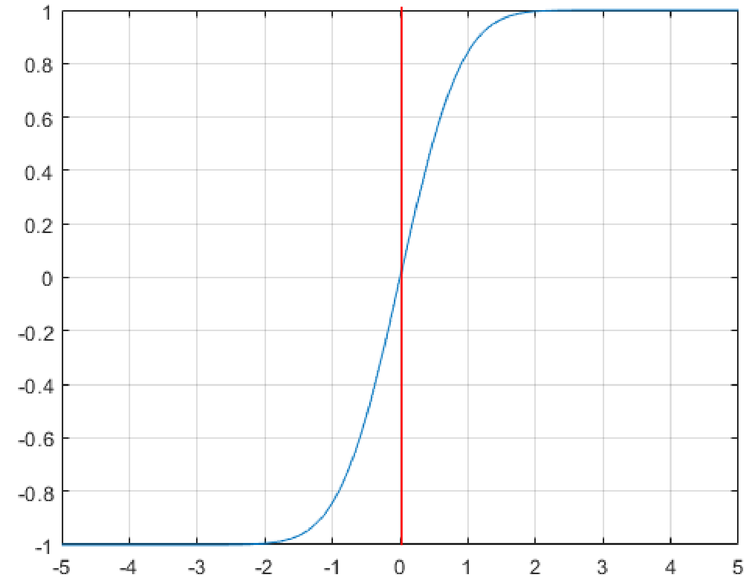


Dose Influence Matrix Optimization

- Simple matrix multiplication to optimize spot weights based on cost function of Dose Vector



- Optimizable VaD and DaV objectives
- Penalizes pixels with dose above threshold
  - Uses smoothed step function
- Essentially analyzes one point/area on DVH
  - Depends on inputs to the smoothing function



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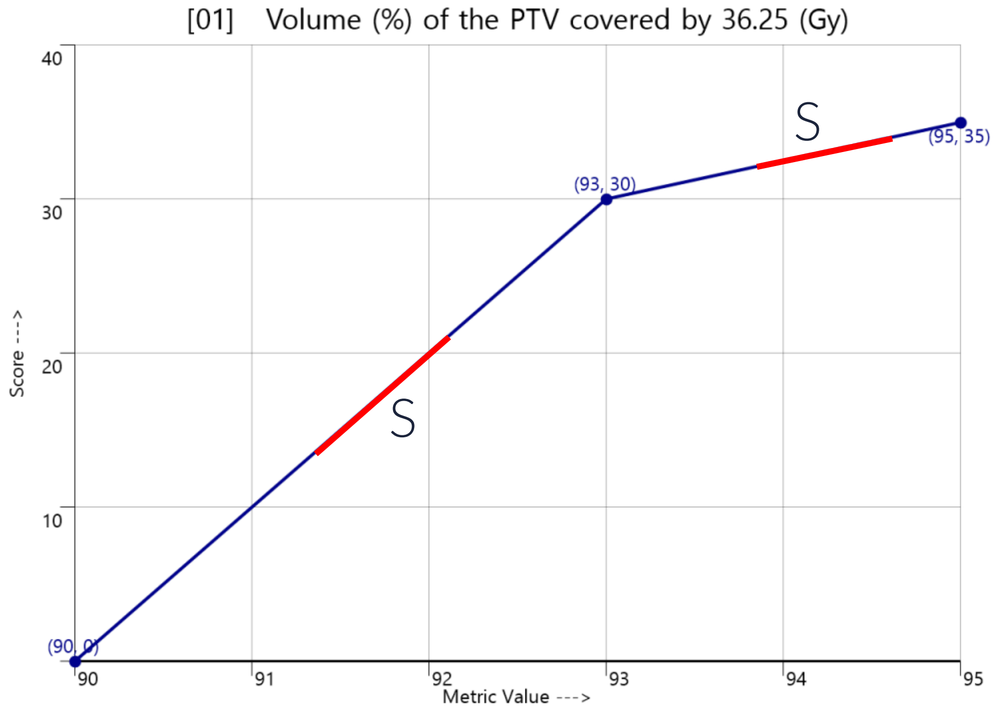
Piecewise linear slopes drive optimization

- Add up costs and gradients from all objectives and optimize
  - For each pixel: $\frac{\Delta VaD}{\Delta Dose}$
  - For each spot: $\frac{\Delta VaD}{\Delta Spot}$
  - For each spot: $\frac{\Delta Score}{\Delta Spot}$



[VaD Dose Gradient]^T (1xM) • Dose Influence (MxN) x Instantaneous Slope of Score Function S = Score Spot Gradient (Nx1)

ScoreCard Based Optimization

Direct optimization on piecewise linear DVH based score function ranges

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Spine Dosimetric & Doserate Result

FLASH compared to IMPT standard of care via Scorecard Optimization

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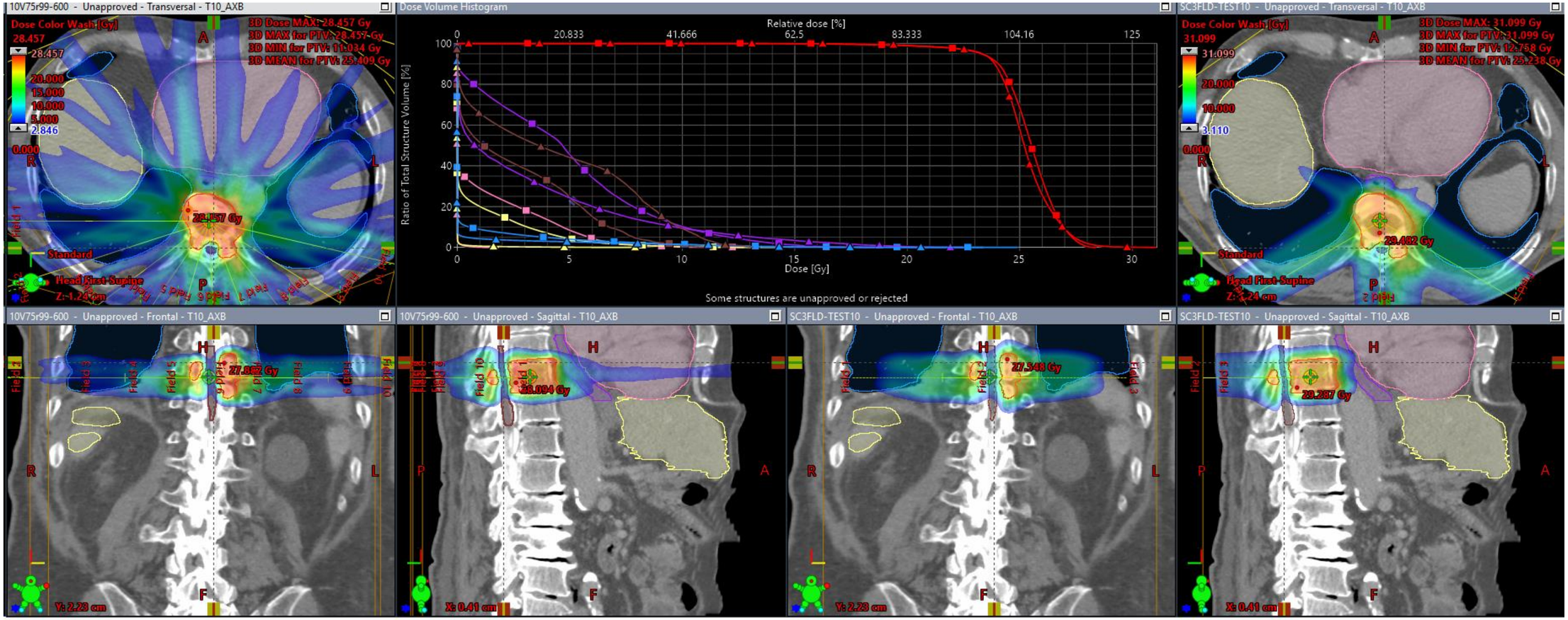
SBRT spine 24Gy 1fx

10 field transmission flash vs. 3 field IMPT



Fields | Dose | Reference Points | **Dose Statistics**

Show DVH	Structure	Approval Status	Plan	Course	Volume [cm³]	Dose Cover.[%]	Sampling Cover.[%]	Min Dose [Gy]	Max Dose [Gy]	Mean Dose [Gy]
☑	SpinalCord	Unapproved	10V75r99-600	FlashST-SCtest9	2.6	100.0	101.9	0.000	11.329	2.561
☑	SpinalCord	Unapproved	SC3FLD-TEST10	N-Opt	2.6	100.0	101.9	0.000	13.212	4.405
☑	PTV	Unapproved	10V75r99-600	FlashST-SCtest9	55.7	100.0	100.0	11.034	28.457	25.409
☑	PTV	Unapproved	SC3FLD-TEST10	N-Opt	55.7	100.0	100.0	12.758	31.099	25.238
☑	Lungs	Unapproved	10V75r99-600	FlashST-SCtest9	3045.2	100.0	100.0	0.000	24.948	0.521
☑	Lungs	Unapproved	SC3FLD-TEST10	N-Opt	3045.2	100.0	100.0	0.000	23.441	0.323
☑	Liver	Unapproved	10V75r99-600	FlashST-SCtest9	1914.6	100.0	100.0	0.000	14.312	0.773
☑	Liver	Unapproved	SC3FLD-TEST10	N-Opt	1914.6	100.0	100.0	0.000	8.037	0.024
☑	Heart	Unapproved	10V75r99-600	FlashST-SCtest9	947.0	100.0	100.0	0.000	12.768	1.196
☑	Heart	Unapproved	SC3FLD-TEST10	N-Opt	947.0	100.0	100.0	0.000	1.854	0.009
☑	Esophagus	Unapproved	10V75r99-600	FlashST-SCtest9	12.7	100.0	100.3	0.000	18.810	4.780
☑	Esophagus	Unapproved	SC3FLD-TEST10	N-Opt	12.7	100.0	100.3	0.000	22.466	3.126

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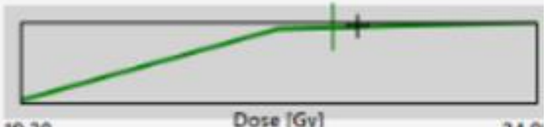
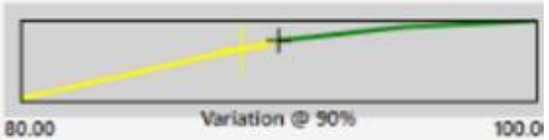
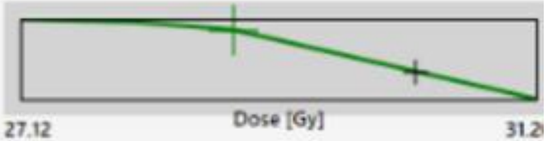
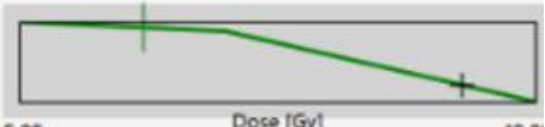
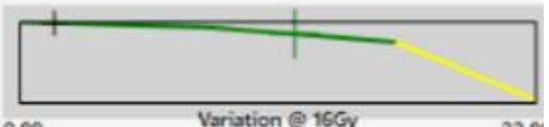
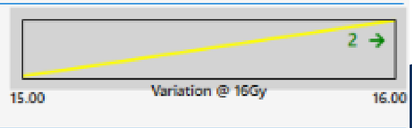
SBRT spine 24Gy 1fx

10 field transmission flash vs. 3 field IMPT

Plan Scores: [N-Opt] 10V75r99-600p: 277.31/310.00 (89.45%)
[N-Opt] SC3FLD-TEST9: 257.38/310.00 (83.02%)

Scorecard metrics (5 of 33 total)

Id	Structure	Score Metric	Plan Id	Value	Score	Max	Metric Plot
1	CTVEVAL	Dose at 99.9% [Gy]	10V75r99-600p	22.10 Gy	23.42	25.00	
			SC3FLD-TEST9	22.34 Gy	23.62	Score Stats Max=23.62 Mean=23.52 Min=23.42	19.20 Dose [Gy] 24.0
2	PTVEVAL	Volume at 24Gy [%]	10V75r99-600p	88.58 %	12.86	20.00	
			SC3FLD-TEST9	89.99 %	14.98	Score Stats Max=14.98 Mean=13.92 Min=12.86	80.00 Variation @ 90% 100.0
5	PTVEVAL	Dose at 0.035CC [Gy]	10V75r99-600p	28.80 Gy	13.00	15.00	
			SC3FLD-TEST9	30.25 Gy	5.15	Score Stats Max=13.00 Mean=9.07 Min=15.10	27.12 Dose [Gy] 31.2
18	SpinalCord	Dose at 0.35CC [Gy]	10V75r99-600p	6.19 Gy	15.81	17.00	
			SC3FLD-TEST9	9.29 Gy	3.55	Score Stats Max=15.81 Mean=9.68 Min=3.55	5.00 Dose [Gy] 10.0
24	Heart	Dose at 0.035CC [Gy]	10V75r99-600p	11.76 Gy	6.80	8.00	
			SC3FLD-TEST9	1.44 Gy	7.91	Score Stats Max=7.91 Mean=7.35	0.00 Variation @ 16Gy 22.0
						Min=7.26	10.00 50.00
8	CTV	Dose at 99.9% [Gy]	10V75r99-600p	19.44 Gy	1.00	1.00	
			SC3FLD-TEST9	20.43 Gy	1.00	Score Stats Max=1.00 Mean=1.00 Min=1.00	2 15.00 Variation @ 16Gy 16.00
			10V75r99-600p	86.80 %	0.68	1.00	

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SBRT spine 24Gy 1fx

10 field transmission flash vs. 3 field IMPT vs. failed options and non-FLASH

Number of fields	Min MU score assigned	Min MU target	Score /310
2 (ML-IMPT)	0	-	!
3 (ML-IMPT)	**0**	**-**	**257.38**
5 (250MeV)	0	-	!
10 (250MeV)	0	-	290.14
10 (250MeV)	40	150	287.82
10 (250MeV)	40	300	290.34
10 (250MeV)	40	450	290.28
10 (250MeV)	80	450	289.36
10 (250MeV)	r99	600	284.10
10 (250MeV)	**r99***	**600**	**277.31**

PTCOG 2022 Poster:

A novel IMPT optimization method enforcing a minimum spot MU per energy layer for FLASH

P. Lansonneur*, T. Leinonen, M. Ropo, L. Rosa, A. Magliari, M. Folkerts

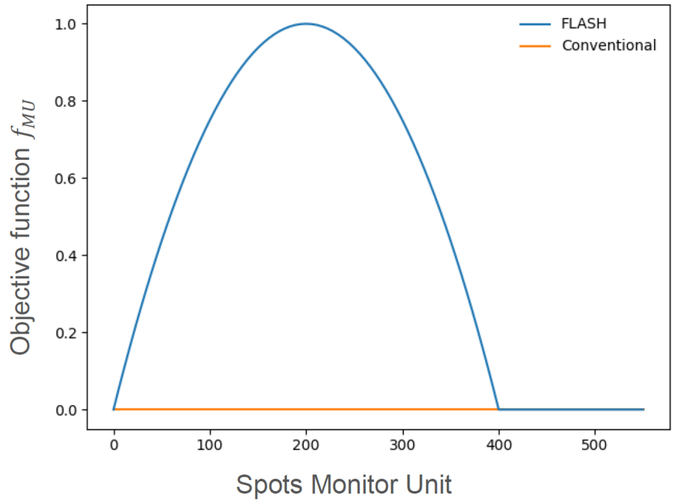

Fig. 1. Example of a minimum MU objective function, for a minimum MU $MU_{min} = 400$. Spots MUs above 200 tend to get increased to 400 while spots MUs below 200 tend to get reduced to zero and removed.

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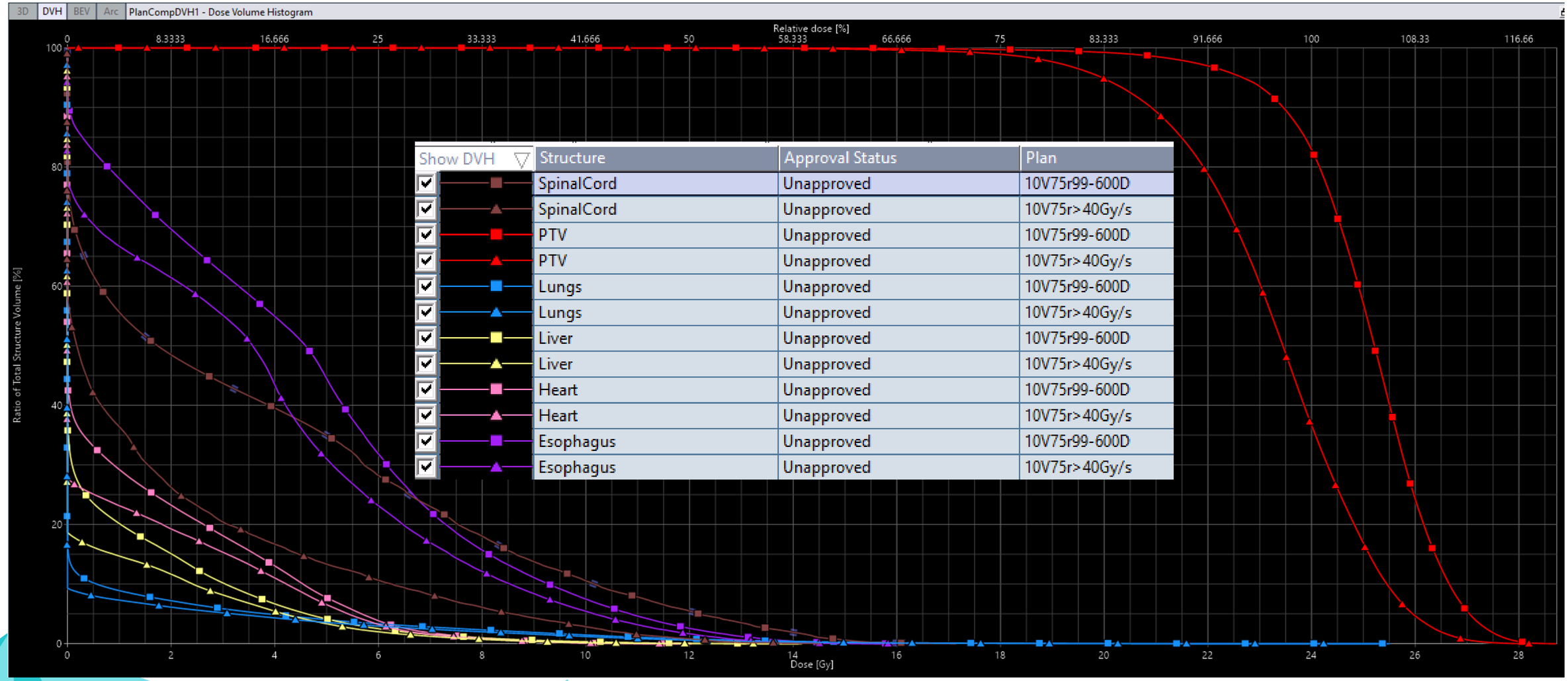
SBRT spine 24Gy 1fx

PBS Dose Rate analysis: Minimum MU=600 (Dose Rate Threshold DVH >40Gy/sec)



Show DVH	Structure	Approval Status	Plan
☑	SpinalCord	Unapproved	10V75r99-600D
☑	SpinalCord	Unapproved	10V75r>40Gy/s
☑	PTV	Unapproved	10V75r99-600D
☑	PTV	Unapproved	10V75r>40Gy/s
☑	Lungs	Unapproved	10V75r99-600D
☑	Lungs	Unapproved	10V75r>40Gy/s
☑	Liver	Unapproved	10V75r99-600D
☑	Liver	Unapproved	10V75r>40Gy/s
☑	Heart	Unapproved	10V75r99-600D
☑	Heart	Unapproved	10V75r>40Gy/s
☑	Esophagus	Unapproved	10V75r99-600D
☑	Esophagus	Unapproved	10V75r>40Gy/s

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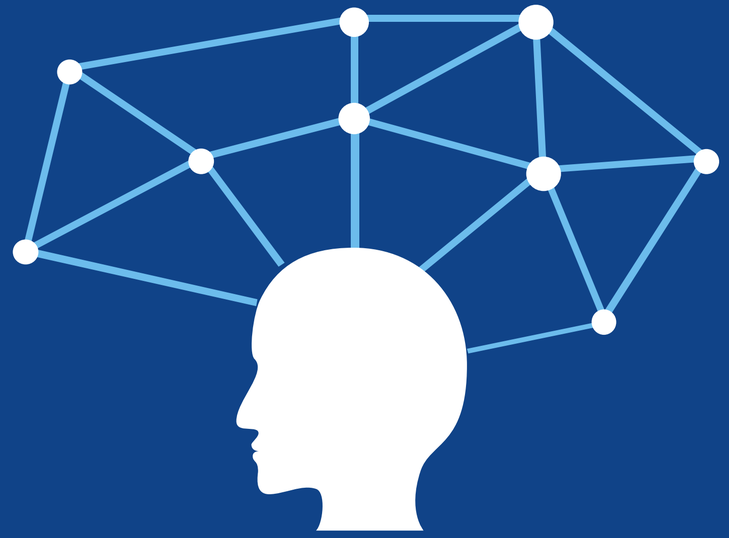
Scorecard Utility

Dosimetric Scorecards have great potential

- Current uses
  - Scoring treatment planning competitions
  - Quantifying dosimetric quality improvements of various techniques
    - energies, collimation devices, modalities, field arrangements
  - Tuning the inputs to common automated quadratic DVH point optimizers
    - RapidPlan and Ethos
  - Guiding manual treatment planning, even for novices
- Future uses
  - Published prospectively with popular trials to reduce variability for manual plans
  - Directly input to dose optimizers so only variability is technical limitation of hardware
- Dosimetric Scorecard evaluation tools have high availability
  - Varian MAAS GitHub, Elekta ProKnow, Sun Nuclear PlanIQ, etc

Thank you!

Special Thanks to:
- Michael Folkerts
- Pierre Lansonneur
- Jessica Perez
- Miriam Krieger
- Lesley Rosa
- Alexander Katsis



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