Proton FLASH Ultra High Dose Rate Treatment Plans: Dosimetric Comparisons to Standard of Care

Anthony Magliari, MS, CMD
2023 AAMD National Meeting

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"

Previous AAMD national meeting talks:
2016 Role of the Dosimetrist in the Knowledge Based Planning Era
2017 IMRT and VMAT: current and future best practices
2019 FLASH Radiotherapy: A Look at Ultra-high Dose Rate Research and Treatment Plans
2022 Knowledge Sharing and the Power of Plan Challenge ScoreCards

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

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

1. FLASH Review
2. Defining Dose Rate
3. Dosimetric Comparisons
4. Future Possibilities

LET'S DO THIS

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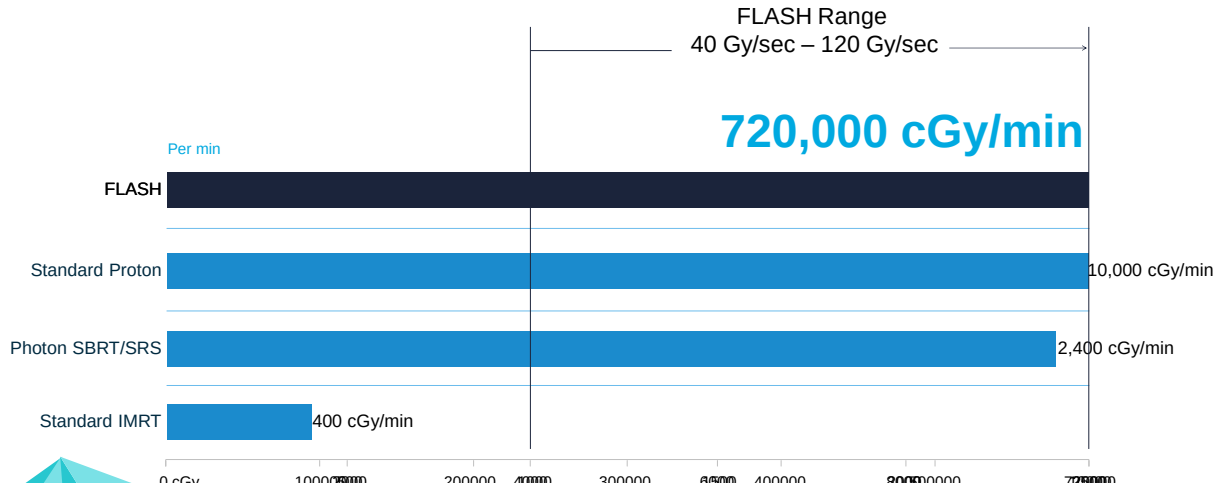
FLASH Review

Background slides to explain Flash Radiotherapy

1

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

Ultra High Dose Rates



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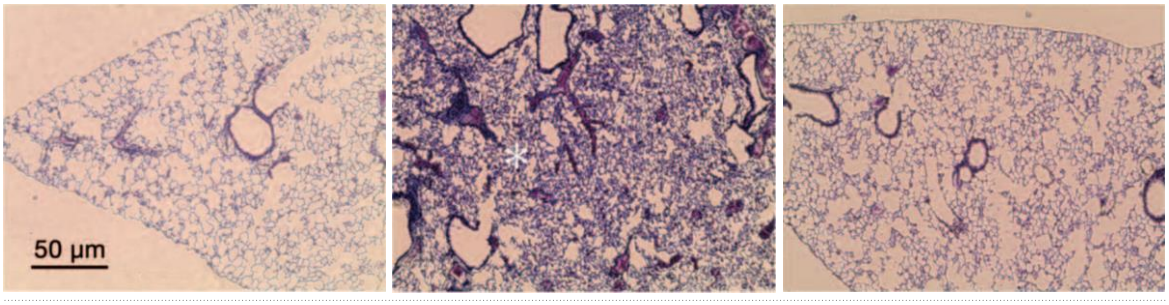
Electron Flash reduces lung fibrosis in mice compared to conventional electron therapy



Favaudon et al., Science Trans Med 2014

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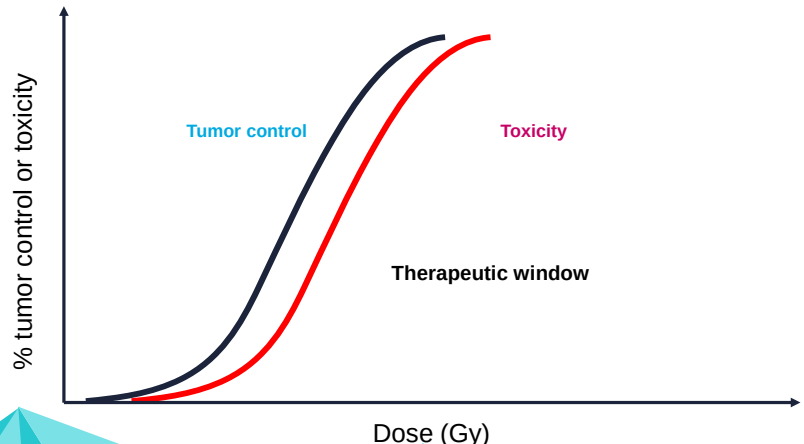
The promise of Flash



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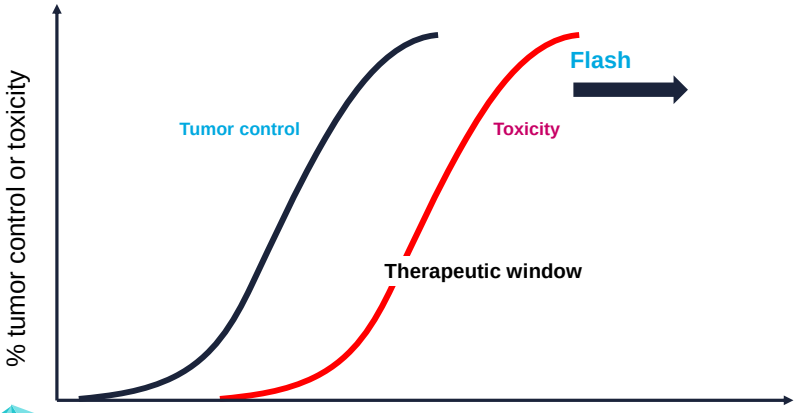
The promise of Flash



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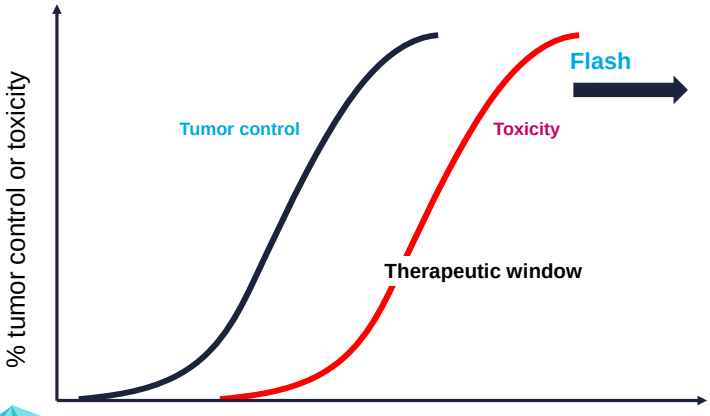
The promise of Flash



Significance

FLASH may allow dose escalation and/or tissue sparing at equivalent dose

The magnitude of the FLASH effect might be tissue specific: preclinical data are needed

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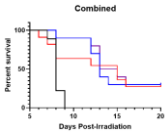
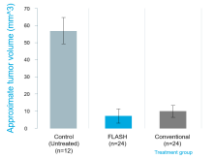
Consistent evidence of tumor control and reduction in toxicity—across anatomical sites

Tumor control studies

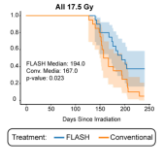


Same (or better) survival

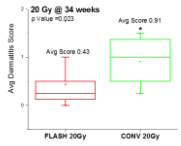


Same (or better) tumor control

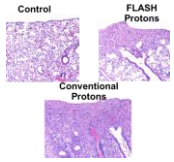
Toxicity reduction studies



20% improvement in survival



52% reduction in dermatitis



23% reduction in fibrosis

Pre-clinical studies in animal models demonstrate a different biological response to Flash therapy

Thorax, Leg, and Lung research conducted with mice. Brain research conducted with rats.

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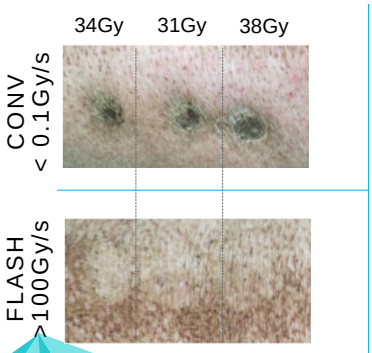
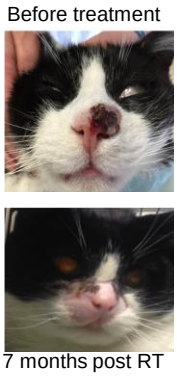
The FLASH effect is a biological effect

Healthy tissue sparing (mini-pig)



Maintained Tumor Control



Significance

- UHDR reduces toxicities in animal models
- UHDR remains efficient to control tumor in animal models
- The combination of these two outcomes is named the “FLASH effect”

Vozenin et al, Clinical cancer research, 2019

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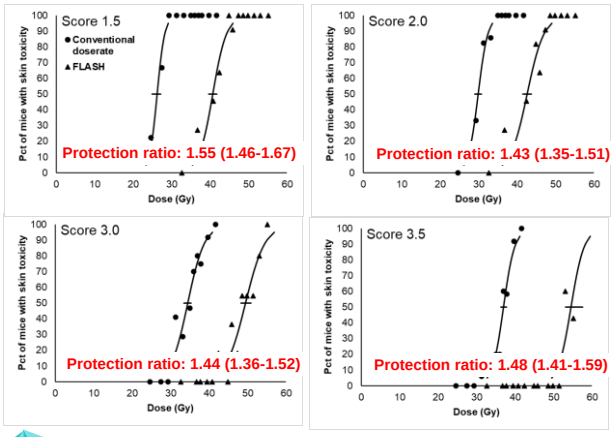
The first exhaustive dose escalation study comparing CONV and FLASH in mice



Significance

In mice, the calculated pFLASH sparing factor is around 40%.

Concretely and considering single dose regimen, the FLASH factor allowed a 10-15Gy dose escalation

Sorensen et al., Radiother & Oncol, 2022

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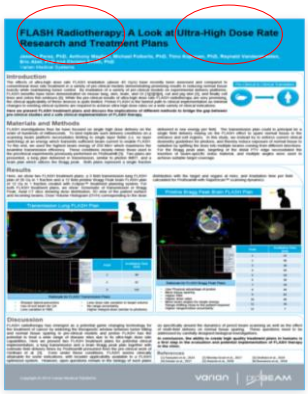
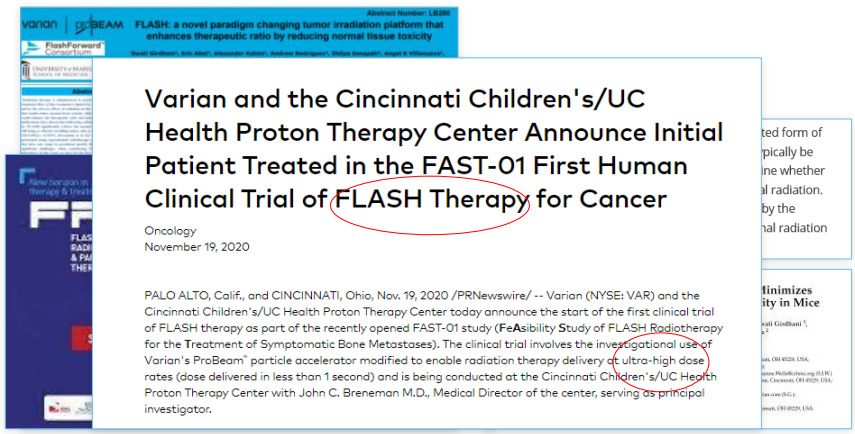
FLASH Therapy – a hot topic in cancer treatment

>200 peer-reviewed articles





The FLASH-enabled ProBeam® system is an investigational device and is limited by United States law for investigational use.

Defining Dose Rate

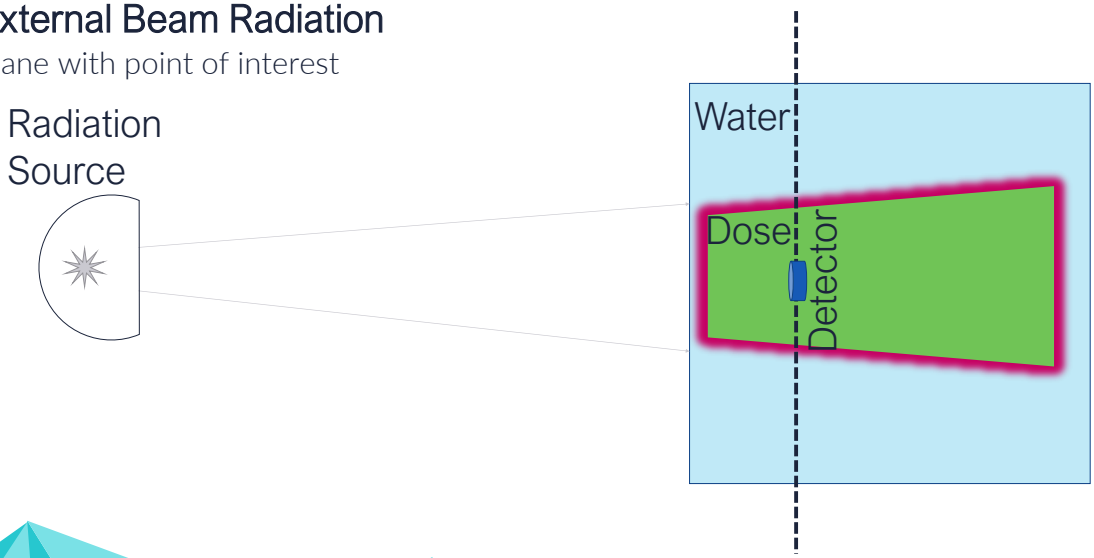
Pencil Beam Scanning Dose Rate

2

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

External Beam Radiation

Plane with point of interest



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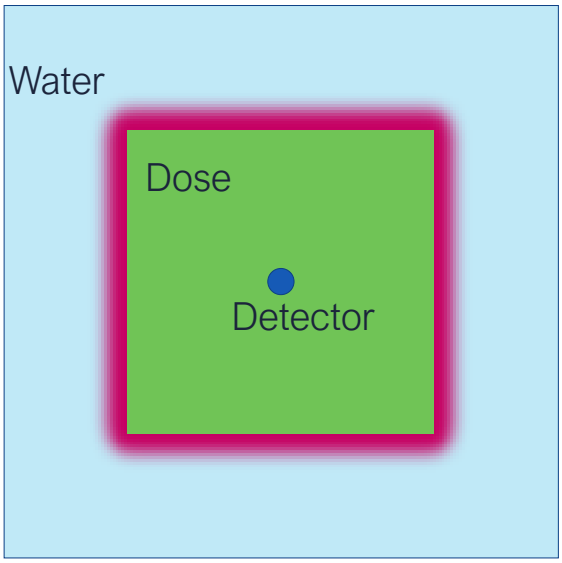
Beam's Eye View

Plane with point of interest



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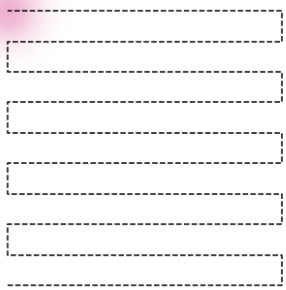
Conventional Delivery

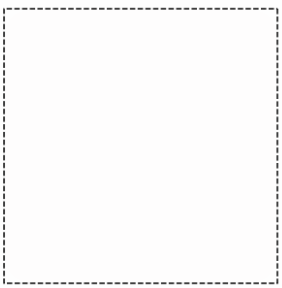
Proton

(Spot Scanning)



Photon/Electron

(Pulsed Broad Beam)



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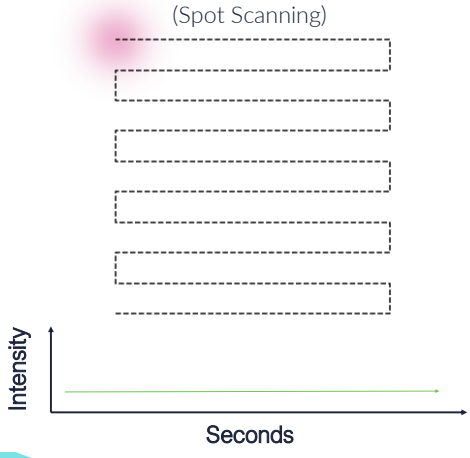
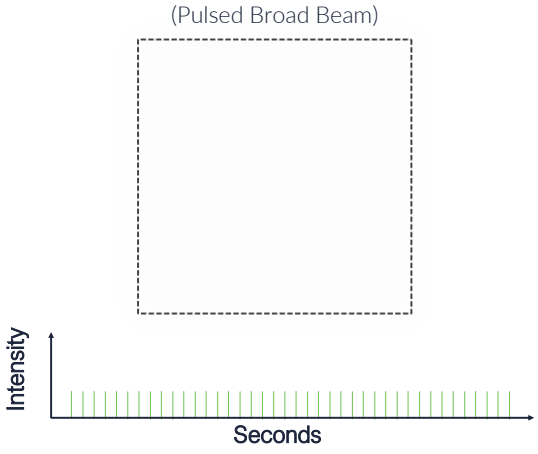
Conventional Dose Delivery

Proton
(Spot Scanning)



Photon/Electron
(Pulsed Broad Beam)



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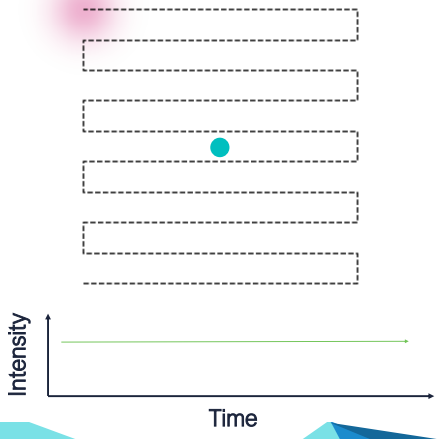
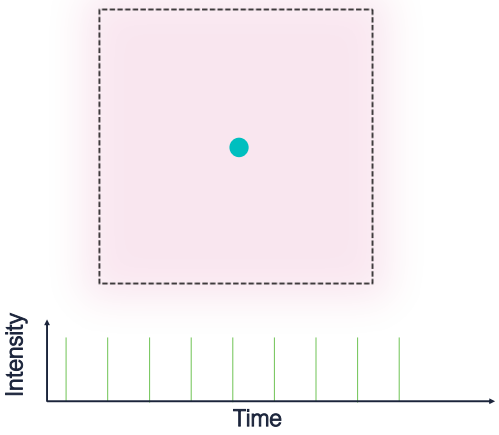
FLASH Dose Delivery (1/10th speed)

Proton
(Spot Scanning)



Photon/Electron
(Pulsed Broad Beam)



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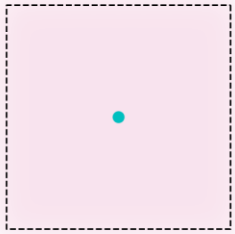
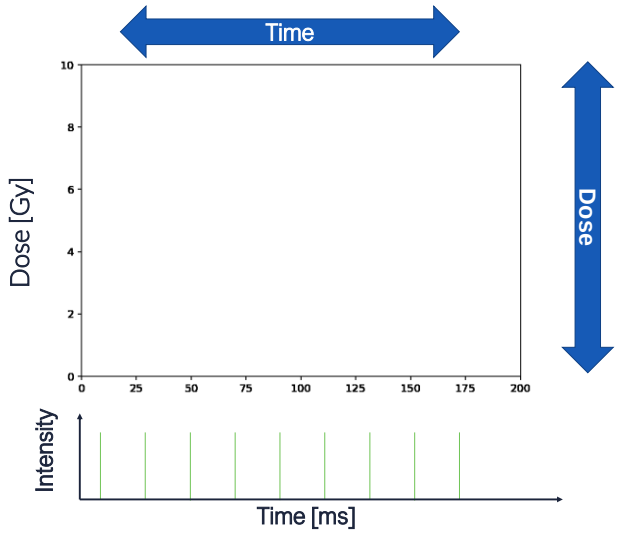
Average Dose Rate

Photon/Electron FLASH





- Dose Rate = $\frac{\Delta Dose}{\Delta Time}$ = 50 Gy/s
- "field" dose rate

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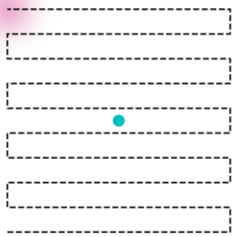
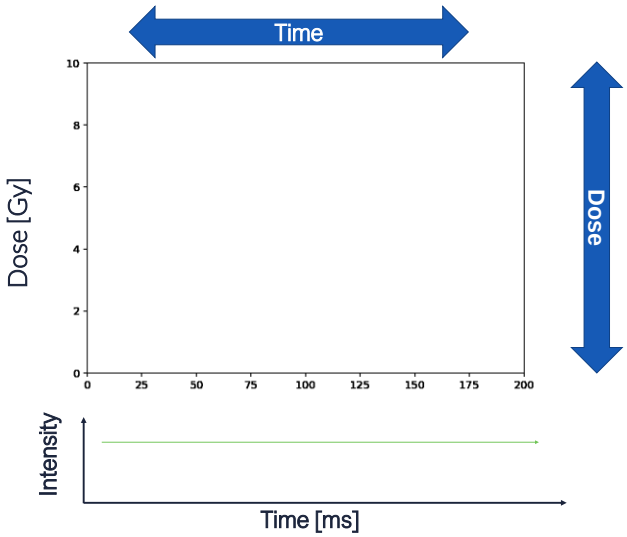
Average Dose Rate

Proton FLASH





- Field Dose Rate = $\frac{\Delta Dose}{\Delta Time}$ = 50 Gy/s
- Conventional

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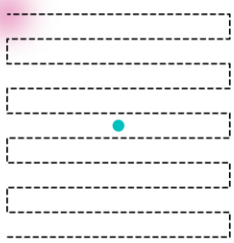
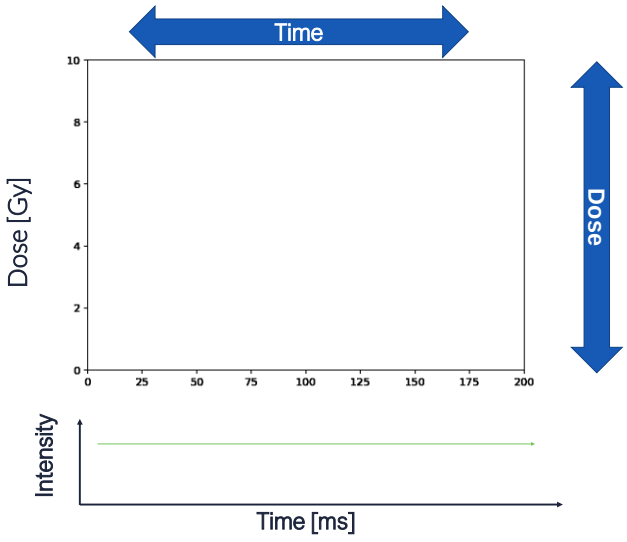
Pencil Beam Scanning Dose Rate

Proton FLASH





- "PBS" Dose Rate = $\frac{\Delta Dose}{\Delta Time}$ = 130 Gy/s

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Dose Rate Peer-Reviewed Article

Published September 2020

MEDICAL PHYSICS

The International Journal of Medical Physics Research and Practice

RESEARCH ARTICLE

A Framework for Defining FLASH Dose Rate for Pencil Beam Scanning

Michael Folkerts[*1], Eric Abel[†1], Simon Busold[1], Jessica Perez[1], Vidhya Krishnamurthi[1], C. Clifton Ling[‡1,2,3]

[1]Varian Medical Systems, Inc., Palo Alto, CA, USA

[2]Department of Radiation Oncology, Stanford University, Stanford, CA, USA

[3]Department of Radiation Oncology, Weill Cornell Medicine, New York, NY, USA

https://doi.org/10.1002/mp.14456

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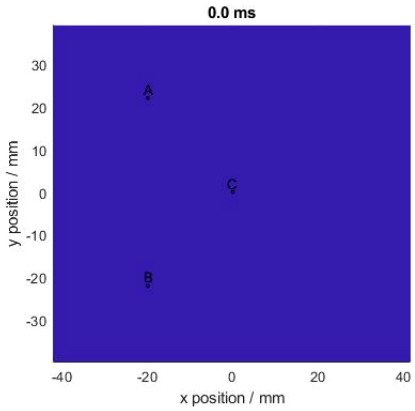
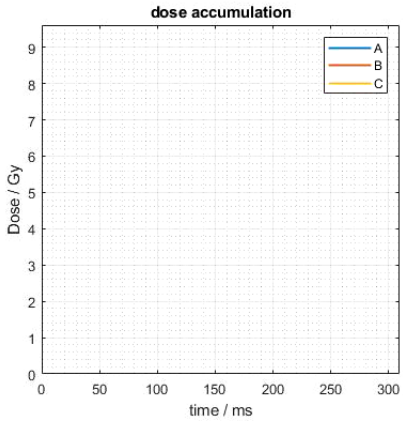
Dose rate and dose accumulation in PBS field

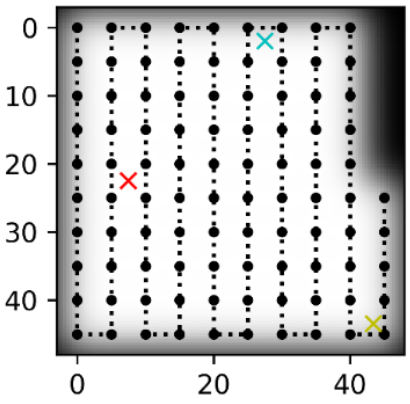
Dose accumulation over time depends on the location within the treatment field and the spot scanning pattern

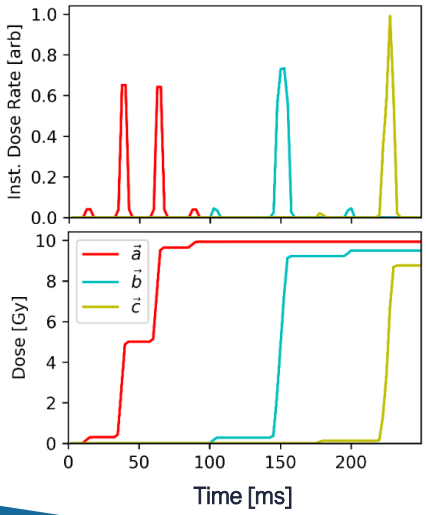




Dose rate and dose accumulation in PBS field

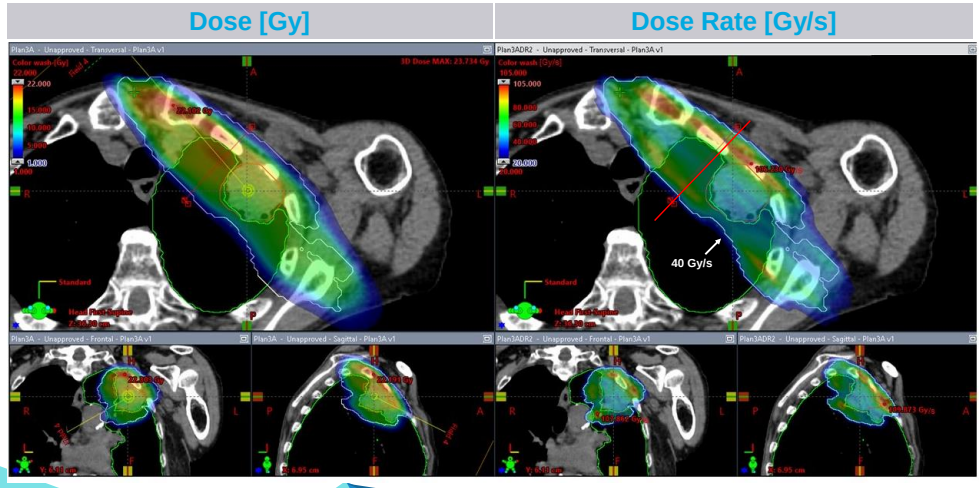
Dose accumulation over time depends on the location within the treatment field and the spot scanning pattern





Dose and Dose Rate Display

Single Field in a multi-field Flash Lung Treatment Plan



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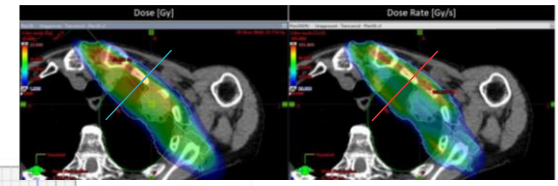
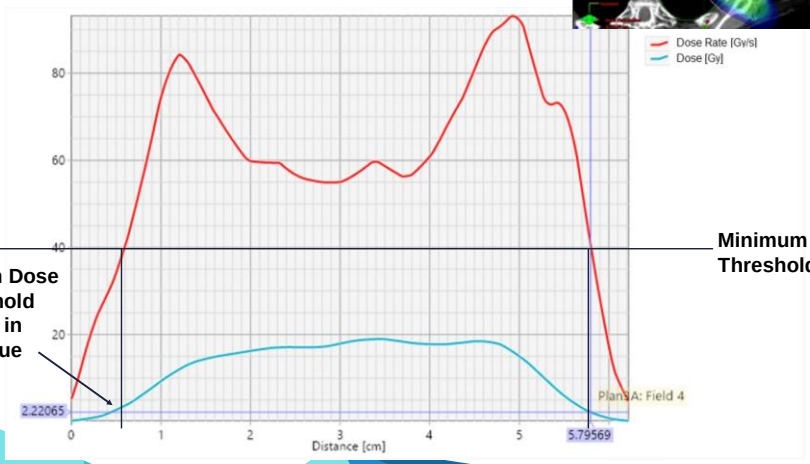
Dose and Dose Rate Line Profile

Through Normal Lung Tissue





Minimum Dose Rate Threshold (40Gy/s)

At Minimum Dose Rate Threshold Dose is low in healthy tissue

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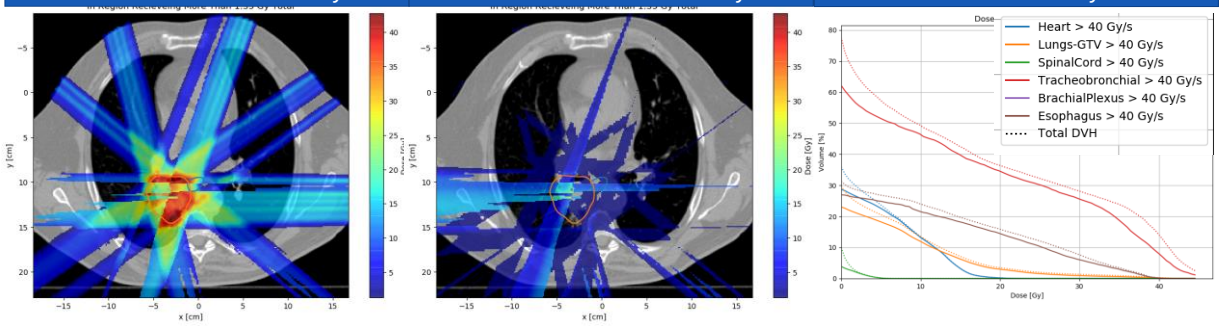
Rethinking Treatment Planning

How to Review a Flash Plan to ensure the Flash conditions are met?

Dose delivered above 40 Gy/s	Dose delivered below 40 Gy/s	DVH above 40 Gy/s



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Transmission planning

How to deliver at UHDR?

- Need

Ultra-High Dose Rate should be available for treatment to get in Flash range.

- Challenge

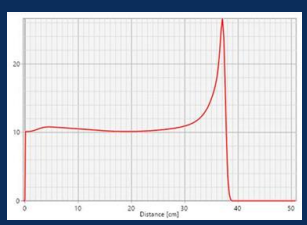
Dose rate drops significantly due to beam current loss.

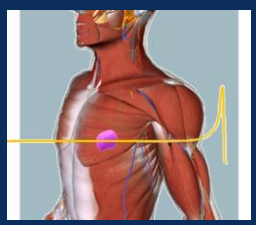
- Solution

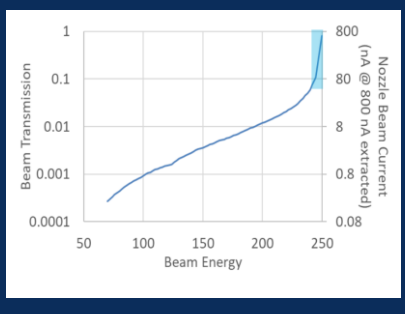
No use of upstream energy degrader.

Highest dose rate achieved at Maximum Beam Energy from cyclotron: 250 MeV

First approach: Bragg Peak is outside of Patient







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Optimization for Flash

How to optimize on both dose and dose rate?

- Need

Increase dose rate without compromising the dose distribution

- Challenge

Dose distribution suffers when dose rate (MUs) increase due

- Solution:
  - Optimize using the Min MU as a surrogate for dose rate (high min MU = high current = high dose rate)

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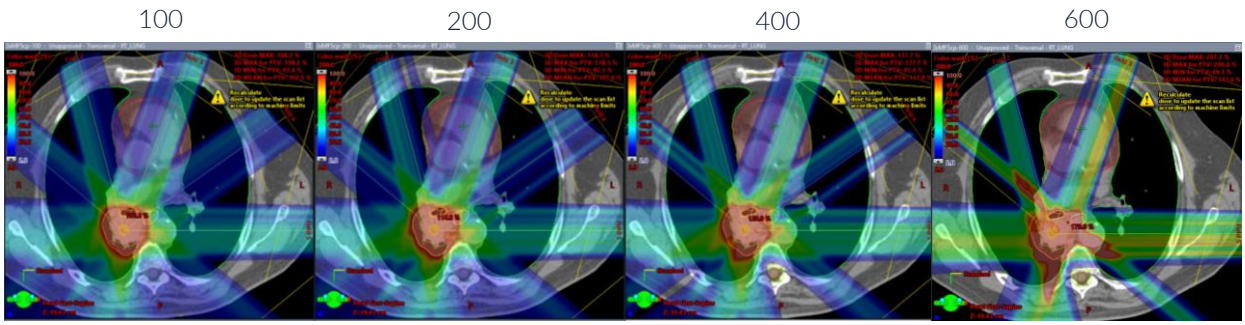
Increasing min MU to increase dose rate

Drastic degradation of plan dosimetry…if not done correctly



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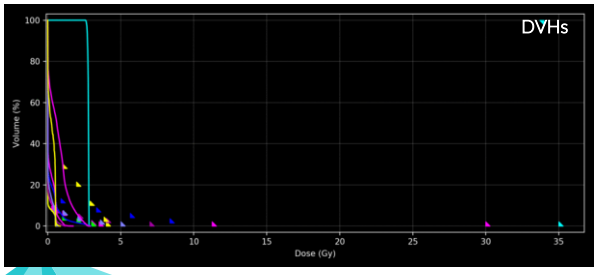
Dose Rate Optimization

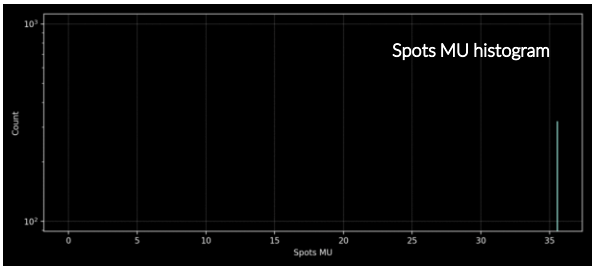
Standard Dose Volume Objectives:

minimum MU objective + priority

	Structure	Constraint	Type	Priority	Volume (%)	Value	
	Esophagus	DVC	max	50	0.59	3.00	Gy
	Esophagus	DVC	max	50	5.22	1.00	Gy
	Esophagus	DVC	max	50	2.83	2.09	Gy
	Esophagus	DVC	max	50	7.58	0.25	Gy
	Esophagus	DVC	max	75	0.00	3.50	Gy
	SpinalCord	DVC	max	75	0.00	3.00	Gy
	SpinalCord	DVC	max	75	1.49	2.00	Gy
	SpinalCord	DVC	max	75	2.89	1.00	Gy
	PTV	DVC	max	110	0.00	35.00	Gy
	PTV	DVC	min	250	100.00	34.00	Gy
	Lungs-GTV	DVC	max	50	1.59	8.37	Gy
	Lungs-GTV	DVC	max	50	6.81	3.33	Gy

minimum MU: 400 Priority: 400





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Optimization for Flash

How to optimize on both dose and dose rate?

- Need

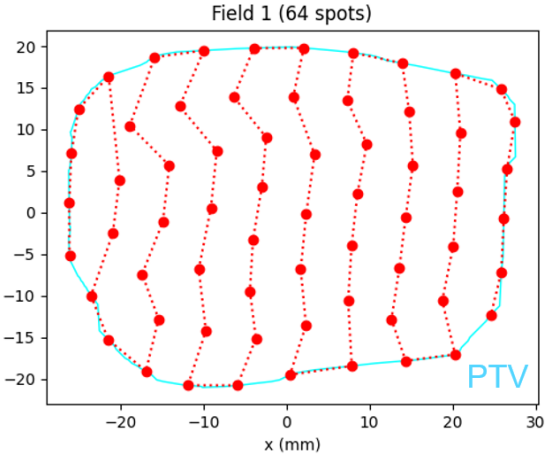
Maintain a homogenous dose distribution while increasing dose rate

- Challenge

Fewer spots with higher MUs per spot can lead to uneven dose distribution (hot or cold spots)

- Solution:

Place spots evenly to ensure homogenous dose distribution without hot spots



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Concept Review:

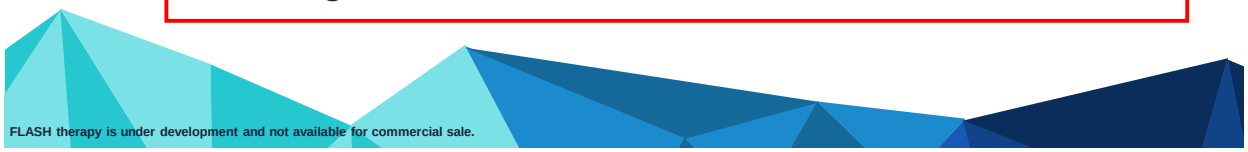
Best case scenario for achieving ultra-high dose rate Flash plans when utilizing the PBS dose rate definition:

a. Large targets with a low dose per fraction
b. Large targets with a high dose per fraction
c. Small targets with a low dose per fraction
d. Small targets with a high dose per fraction

Concept Review:

Proton spot spacing and layer spacing's effect on treatment quality is:

a. Inconsequential, using the defaults as defined in the treatment planning system is best
b. It matters and is best to have as many spots as possible with dense spot and layer spacing for the best dosimetric plan quality
c. Spending time finding an optimal sparse spacing of spots can lead to better dosimetry and larger minimum MU per field, also decreasing the treatment time



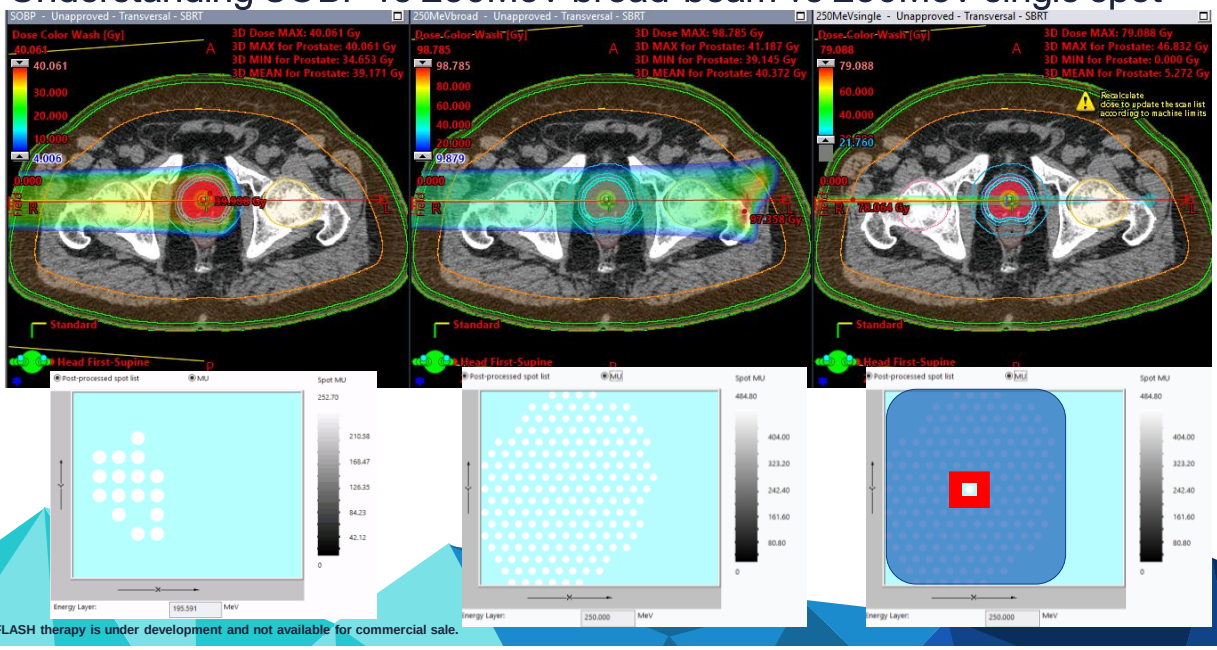
Dosimetric Comparison

FLASH plans compared to IMPT standard of care

3

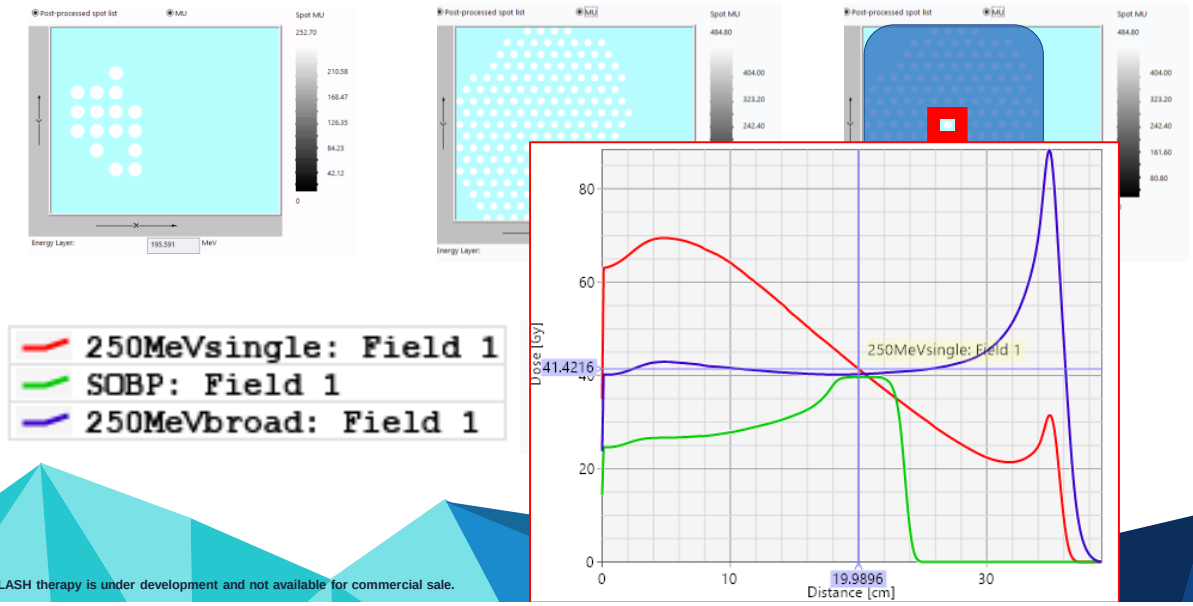
FLASH therapy is under development and not available for commercial sale.

Understanding SOBP vs 250MeV broad-beam vs 250MeV single spot



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

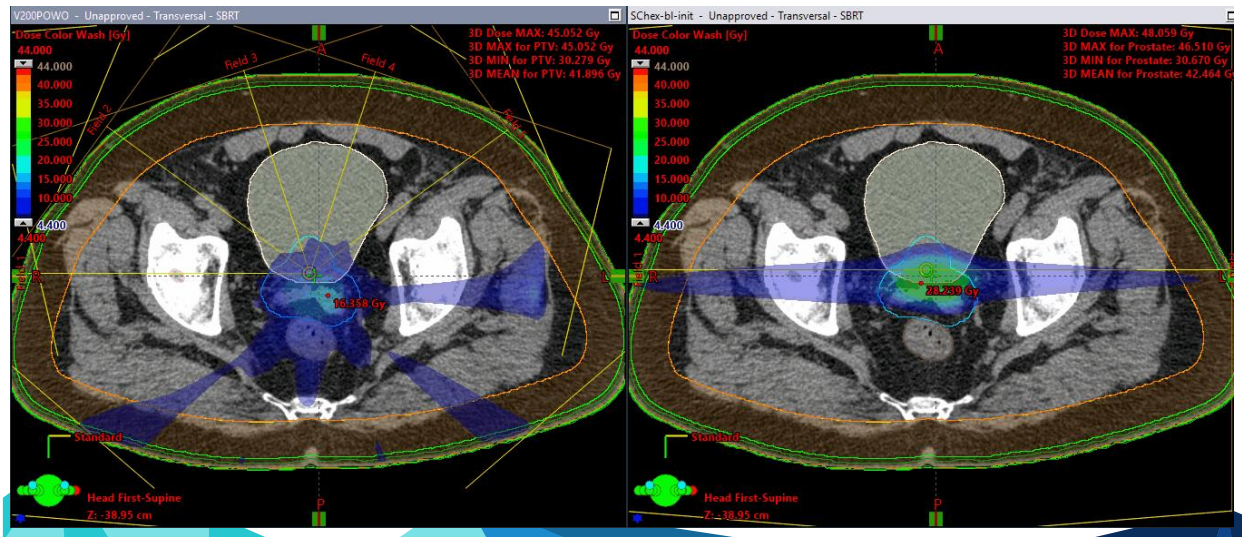
Understanding SOBP vs 250MeV broad-beam vs 250MeV single spot



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

Prostate SBRT with Urethral Sparing: 5 field 250MeV vs 2 field IMPT

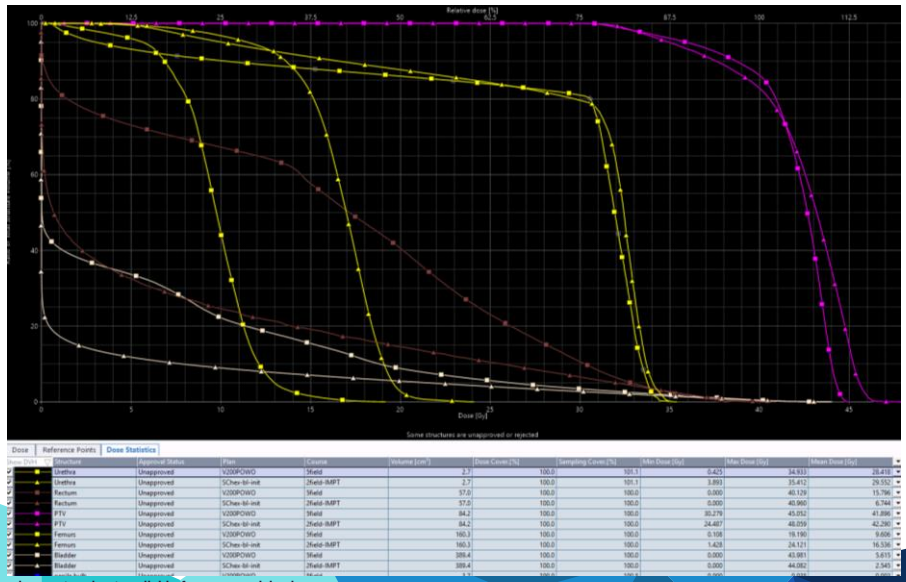
PTV37.5Gy SIB Prostate 40Gy, 5fx 10Gy/fx



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

Prostate SBRT with Urethral Sparing: 5 field 250MeV vs 2 field IMPT

PTV37.5Gy SIB Prostate 40Gy, 5fx 10Gy/fx



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

Prostate SBRT with Urethral Sparing: 5 field 250MeV vs 2 field IMPT

PTV37.5Gy SIB Prostate 40Gy, 5fx 10Gy/fx

StructureId	Metric Text	Max Score
PTV	Volume at 40Gy [%]	5
PTV	Volume at 36.25Gy [%]	5
PTV	Dose at 0.07% [Gy]	8
PTV-CTV	Dose at 0.15% [Gy]	3
PTV-UrethraPRV	Volume at 36.25Gy [%]	15
PTV-UrethraPRV	Volume at 40Gy [%]	20
PTV-UrethraPRV	Dose at 99.99% [Gy]	10
PTV+Urethra	Dose at 99.99% [Gy]	5
PTV+Urethra	Volume at 30Gy [%]	10
CTV-UrehtraPRV	Volume at 40Gy [%]	30
CTV-UrehtraPRV	Dose at 99.99% [Gy]	12
Rectum	Volume at 36.25Gy [%]	4
Rectum	Volume at 42Gy [%]	3
Rectum	Volume at 34.43Gy [%]	3
Rectum	Dose at 50% [Gy]	8
Rectum	Dose at 20% [Gy]	6
Rectum	Dose at 0.5% [Gy]	5
Bowel_Small	Volume at 35Gy [%]	6
Bowel_Small	Volume at 25Gy [%]	4
Bowel_Large	Volume at 35Gy [%]	3
Bowel_Large	Volume at 25Gy [%]	2
Bladder	Volume at 36.25Gy [%]	4
Bladder	Volume at 42Gy [%]	4
Bladder	Volume at 32.62Gy [%]	6
Bladder	Dose at 40% [Gy]	5
Urethra	Volume at 35Gy [%]	10
Urethra	Dose at 0.1% [Gy]	10
Femurs	Volume at 19.9Gy [%]	3
Fiducials	Dose at 1% [Gy]	1
PTV RING	Dose at 0.01% [Gy]	5
BODY RING	Dose at 0.01% [Gy]	5

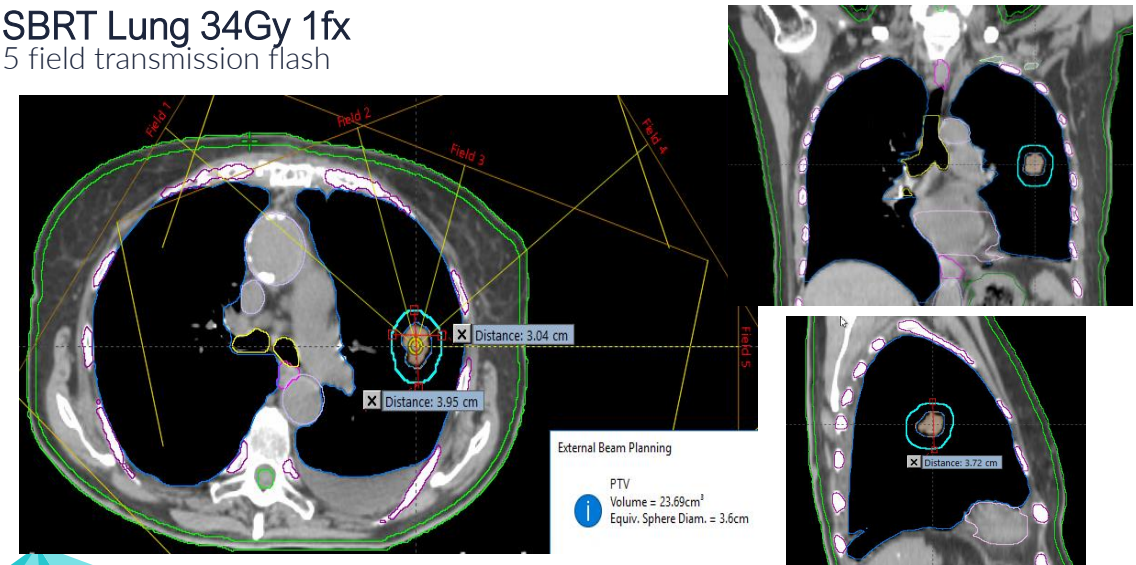
[N-Opt] V200POWO100.5: 150.74/220.00 (68.52%)
[2field-IMPT] SChex-bl-init: 104.57/220.00 (47.53%)

Plan Scores: RapidPlan: [N-Opt] V200POWO100.5: 150.74/220.00 (68.52%)
RapidPlan: [2field-IMPT] SChex-bl-init: 104.57/220.00 (47.53%)

Id	Structure	Score Metric	Plan Id	Value	Score	Max	Metric Plot
1	PTV	Volume at 40Gy [%]	V200POWO100.5	85.44 %	0.35	5.00	Score Stats Max=0.35 Mean=0.18 Min=0.00
			SChex-bl-init	82.85 %	0.00		Variation @ 90% 85.00 95.00
	VARIATION[0]	GOOD[4]	IDEAL[5]				
2	PTV	Volume at 36.25Gy [%]	V200POWO100.5	94.32 %	2.43	5.00	Score Stats Max=2.43 Mean=2.01 Min=1.58
			SChex-bl-init	92.81 %	1.58		Variation @ 98% 90.00 100.00
	VARIATION[0]	GOOD[4.5]	IDEAL[5]				
3	PTV	Dose at 0.07% [Gy]	V200POWO100.5	44.62 Gy	4.49	8.00	Score Stats Max=4.49 Mean=2.24 Min=0.00
			SChex-bl-init	46.92 Gy	0.00		Variation @ 44Gy 42.00 46.00
	IDEAL[8]	GOOD[6.5]	VARIATION[0]				
4	PTV-CTV	Dose at 0.15% [Gy]	V200POWO100.5	43.97 Gy	0.04	3.00	Score Stats Max=0.04 Mean=0.02 Min=0.00
			SChex-bl-init	45.25 Gy	0.00		Dose [Gy] 40.00 44.00
	IDEAL[3]	GOOD[2.5]	VARIATION[0]				
5	PTV-UrethraPRV	Volume at 36.25Gy [%]	V200POWO100.5	99.86 %	14.86	15.00	Score Stats Max=14.86 Mean=14.34 Min=13.82
			SChex-bl-init	98.82 %	13.82		Volume [%] 95.00 100.00
	VARIATION[0]	GOOD[13]	IDEAL[15]				

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

SBRT Lung 34Gy 1fx
5 field transmission flash



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

SBRT Lung 34Gy 1fx
RTOG 0915

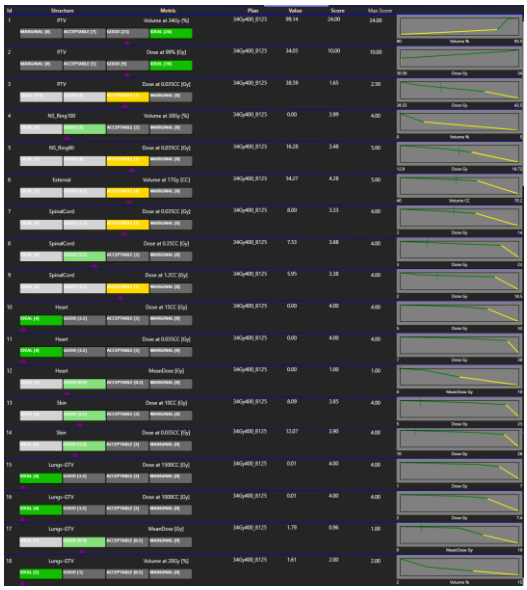
Table 1: Conformality of Prescribed Dose for Calculations Based on Deposition of Photon Beam Energy in Heterogeneous Tissue

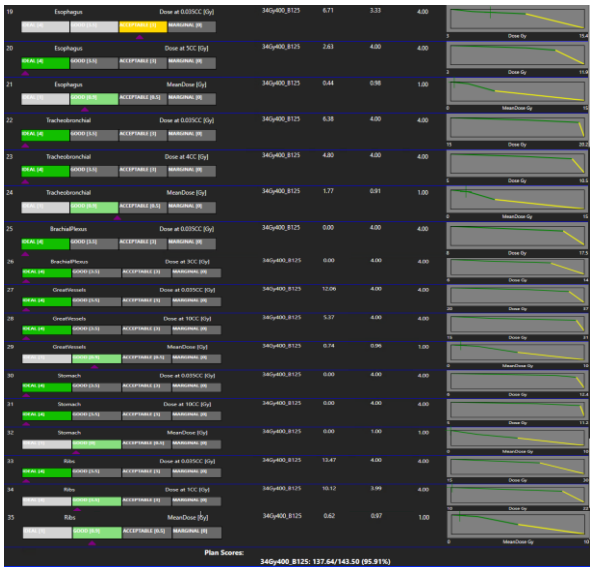
PTV Volume (cc)	Ratio of Prescription Isodose Volume to the PTV Volume		Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50\%}$		Maximum Dose (in % of dose prescribed) @ 2 cm from PTV in Any Direction, D_{2cm} (Gy)		Percent of Lung Receiving 20 Gy Total or More, V_{20} (%)	
	Deviation		Deviation		Deviation		Deviation	
	None	Minor	None	Minor	None	Minor	None	Minor
1.8	<1.2	<1.5	<5.9	<7.5	<50.0	<57.0	<10	<15
3.8	<1.2	.<1.5	<5.5	<6.5	<50.0	<57.0	<10	<15
7.4	<1.2	<1.5	<5.1	<6.0	<50.0	<58.0	<10	<15
13.2	<1.2	<1.5	<4.7	<5.8	<50.0	<58.0	<10	<15
22.0	<1.2	<1.5	<4.5	<5.5	<54.0	<63.0	<10	<15
34.0	<1.2	<1.5	<4.3	<5.3	<58.0	<68.0	<10	<15
50.0	<1.2	<1.5	<4.0	<5.0	<62.0	<77.0	<10	<15
70.0	<1.2	<1.5	<3.5	<4.8	<66.0	<86.0	<10	<15
95.0	<1.2	<1.5	<3.3	<4.4	<70.0	<89.0	<10	<15
126.0	<1.2	<1.5	<3.1	<4.0	<73.0	>91.0	<10	<15
163.0	<1.2	<1.5	<2.9	<3.7	<77.0	>94.0	<10	<15

Note 1: For values of PTV dimension or volume not specified, linear interpolation between table entries is required.
Note 2: Protocol deviations greater than listed here as "minor" will be classified as "major" for protocol compliance (see Section 6.7).

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

SBRT Lung 34Gy 1fx ScoreCard Example (143.5 total points)

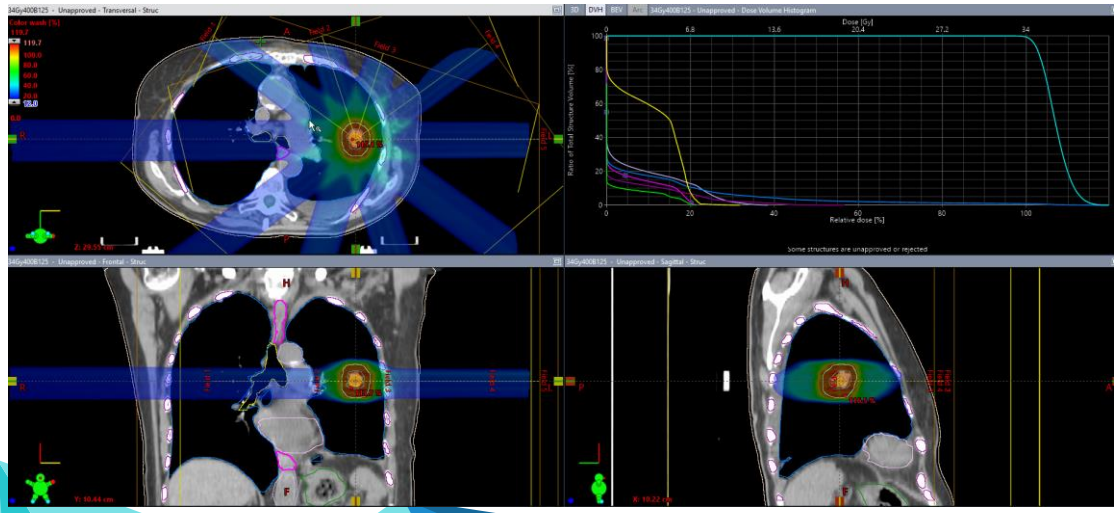




FLASH therapy is under development and not available for commercial sale.

SBRT Lung 34Gy 1fx

5 field transmission flash | CI: 1.33 | Plan Score: 136.46



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

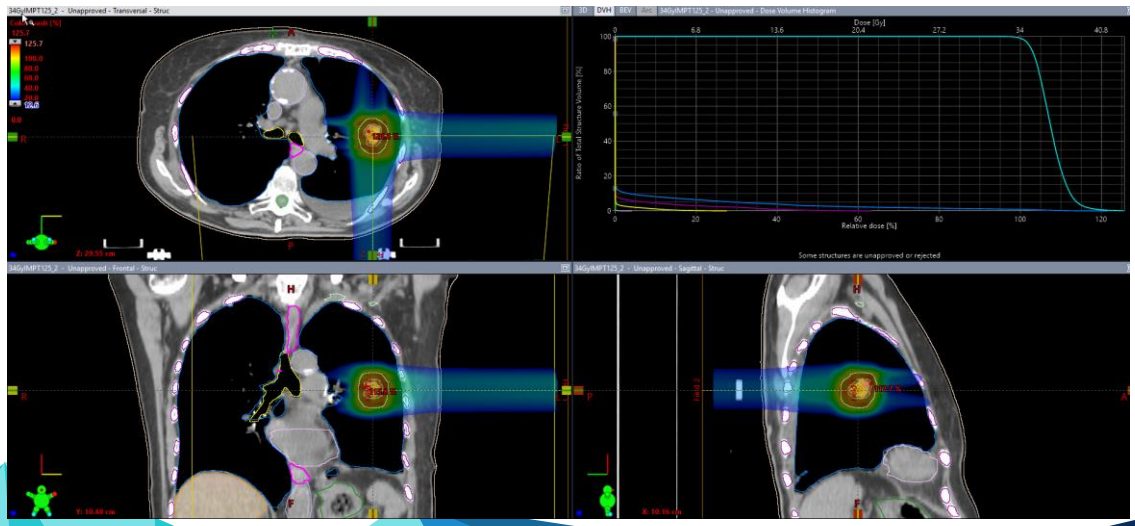
SBRT Lung 34Gy 1fx

5 field transmission flash MinMU=600 40Gy/sec Dose Rate Threshold DVH

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

SBRT Lung 34Gy 1fx

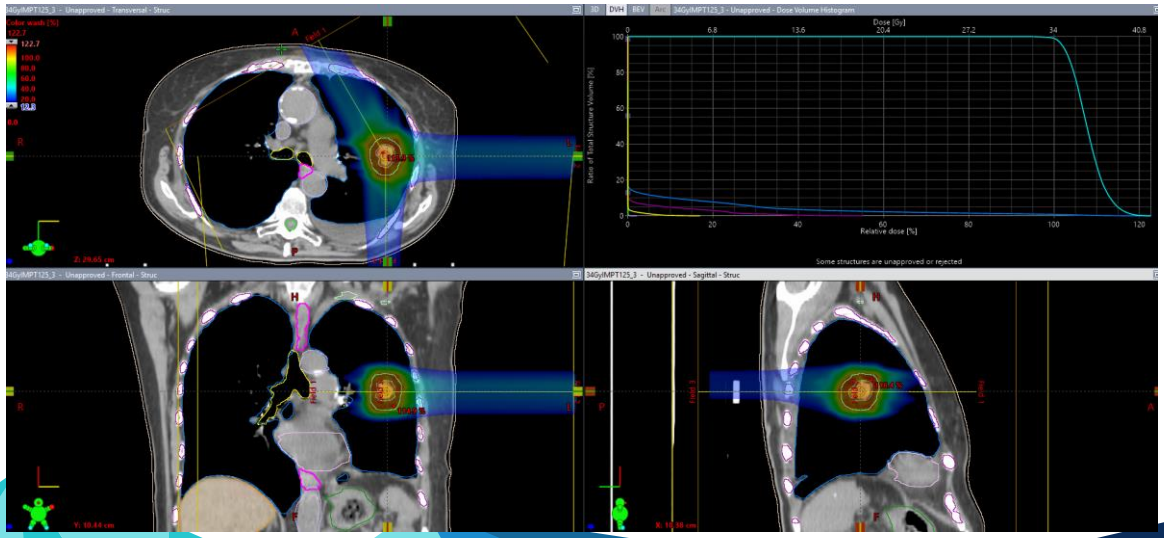
2 field IMPT | CI: 1.39 | Plan Score: 136.03



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

SBRT Lung 34Gy 1fx

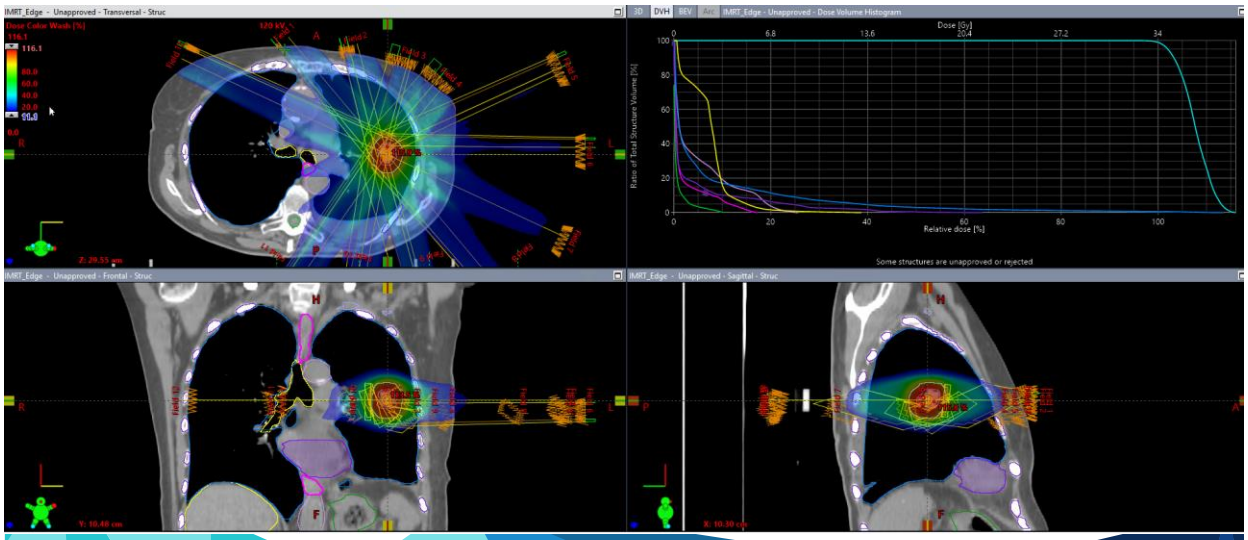
3 field IMPT | CI: 1.36 | Plan Score: 138.42



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

SBRT Lung 34Gy 1fx

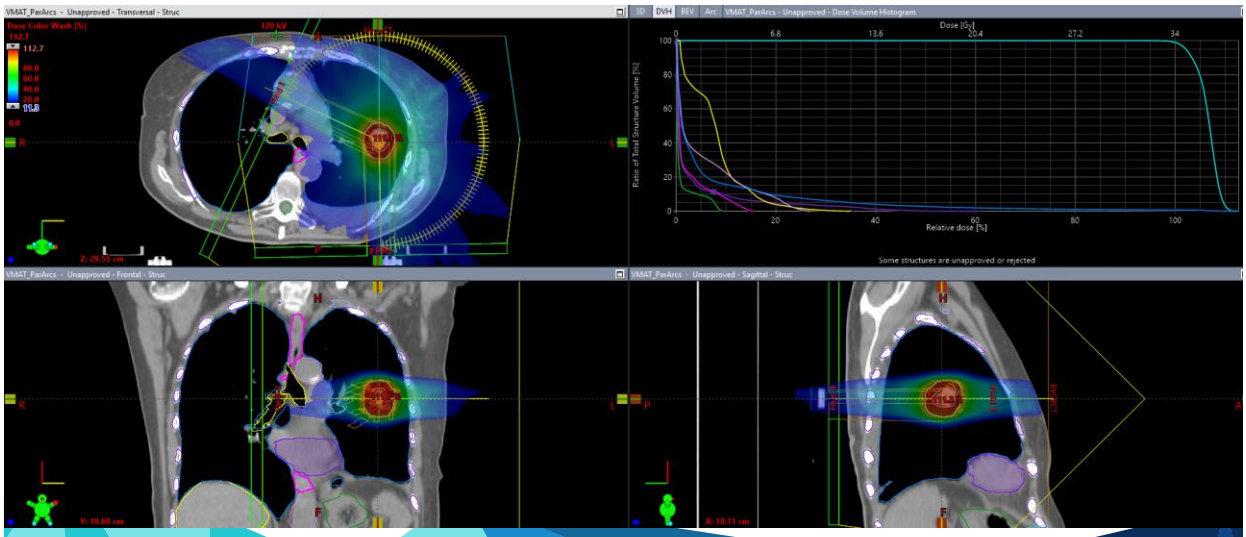
12 field IMRT (HD-120) | CI: 1.08 | Plan Score: 136.56



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

SBRT Lung 34Gy 1fx

Halcyon 4 partial arc | CI: 1.05 | Plan Score: 139.49



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

SBRT Lung 34Gy 1fx

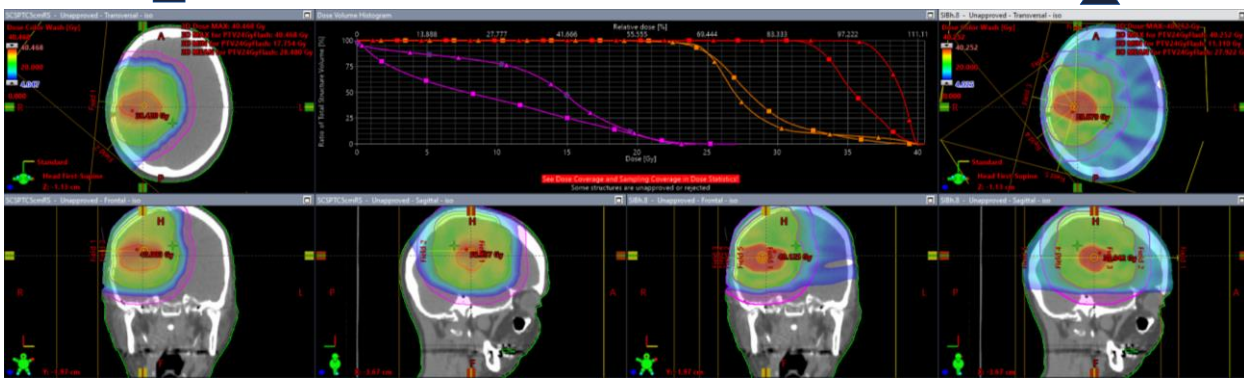
2 field IMPT, 3 field IMPT, 5 field FLASH comparison

Lung PTV=23.69cc	Score x/143.5	CI
FLASH 5 fields	136.46	1.33
IMPT 2 fields	136.03	1.39
IMPT 3 fields	138.42	1.36
IMRT 12 fields	136.56	1.08
VMAT 4 partial arcs	139.49	1.05

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

GBM 24Gy/36Gy SIB 6fx

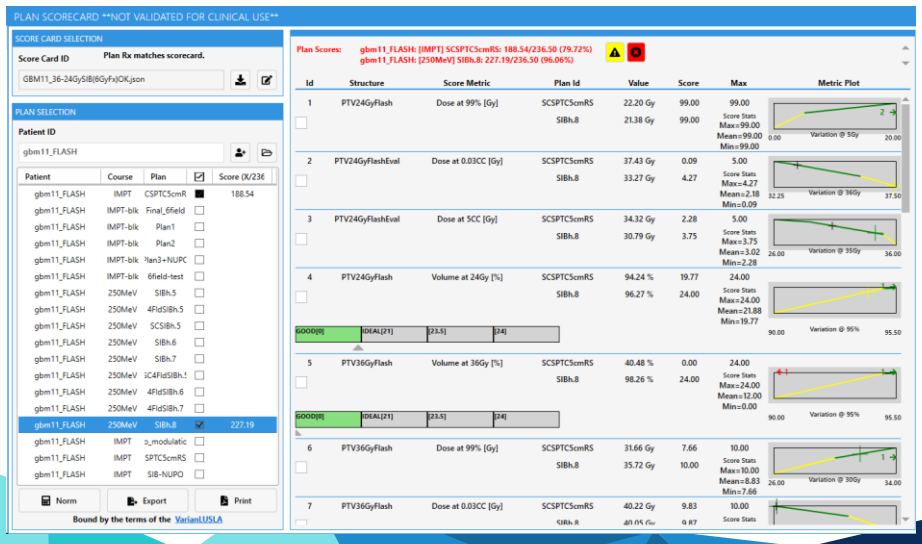
2 field IMPT vs 5 field transmission flash



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

GBM 24Gy/36Gy SIB 6fx

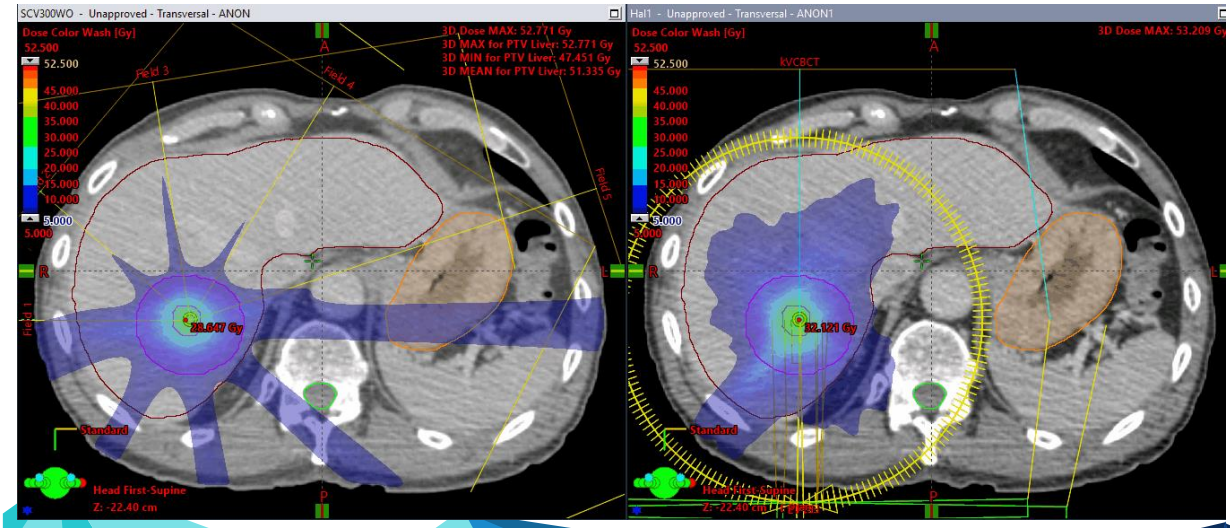
5 field transmission flash vs. 2 field IMPT



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

Liver 50Gy 5fx (10Gy fractions)

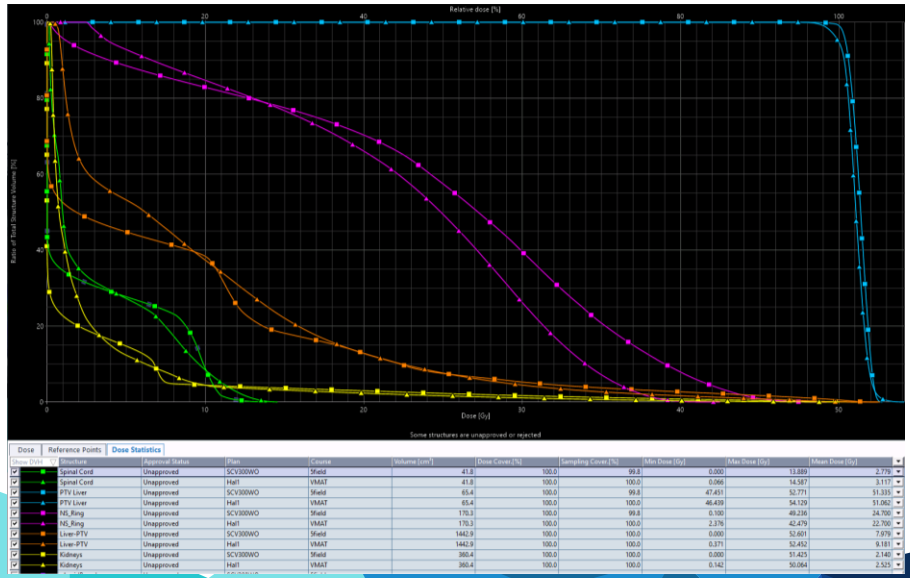
5 field transmission flash vs VMAT



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

Liver 50Gy 5fx (10Gy fractions)

5 field transmission flash vs VMAT

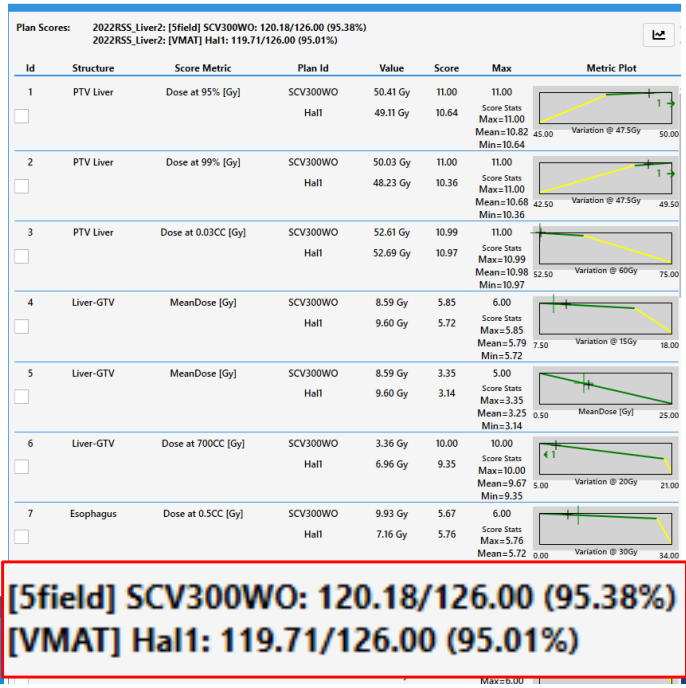


FLASH therapy is under development and not available for commercial sale.

Liver 50Gy 5fx (10Gy fractions)

5 field transmission flash vs VMAT

Metric Id	StructureId	Metric Text	Max Score
0	PTV Liver	Dose at 95% [Gy]	11
1	PTV Liver	Dose at 99% [Gy]	11
2	PTV Liver	Dose at 0.03CC [Gy]	11
3	Liver-GTV	MeanDose [Gy]	6
4	Liver-GTV	MeanDose [Gy]	5
5	Liver-GTV	Dose at 700CC [Gy]	10
6	Esophagus	Dose at 0.5CC [Gy]	6
7	Stomach	Dose at 0.5CC [Gy]	6
8	Duodenum	Dose at 0.5CC [Gy]	6
9	Bowel	Dose at 0.5CC [Gy]	6
10	Ring	Volume at 50Gy [%]	6
11	Ring	Dose at 0.05CC [Gy]	6
12	SpinalCordPRV	Dose at 0.5CC [Gy]	6
13	Kidneys	Dose at 33% [Gy]	6
14	Kidneys	MeanDose [Gy]	6
15	Kidneys	Dose at 10% [Gy]	6
16	Heart	Dose at 0.5CC [Gy]	6
17	Ribs	Dose at 2% [Gy]	6



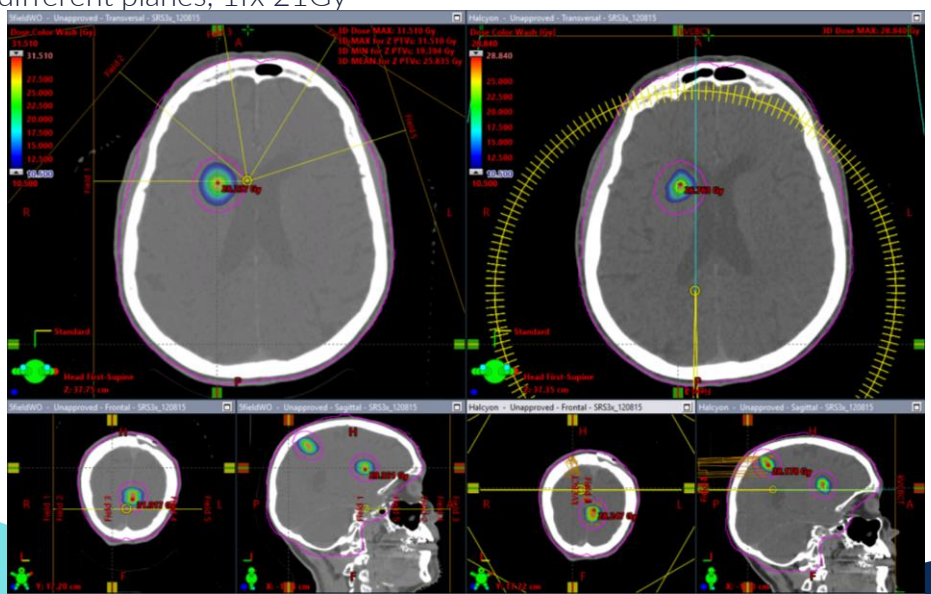
FLASH therapy is under development and not available for commercial sale.

MultiMet test

3 mets on different planes, 1fx 21Gy

50%

10.5Gy



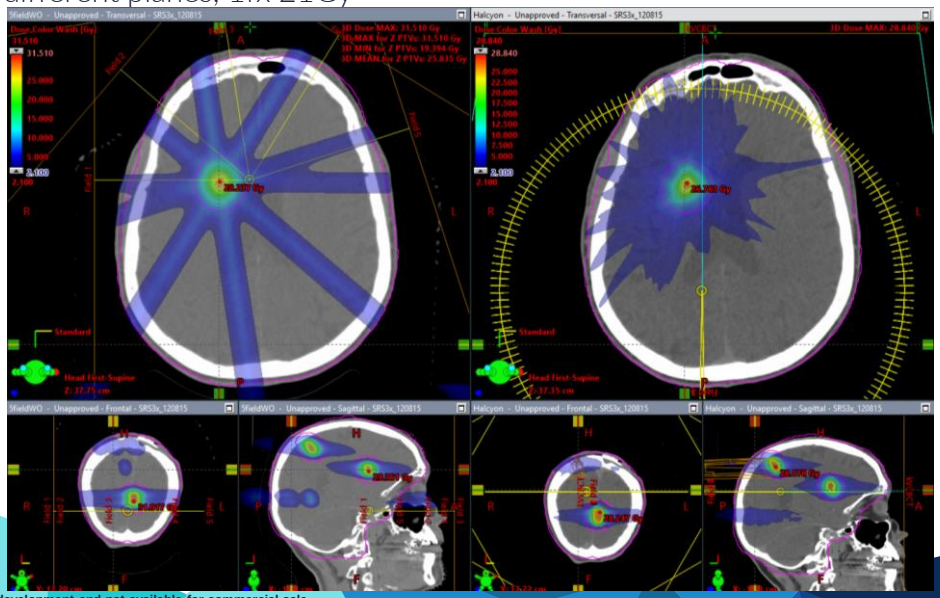
FLASH therapy is under development and not available for commercial sale.

MultiMet test

3 mets on different planes, 1fx 21Gy

10%

2.1Gy



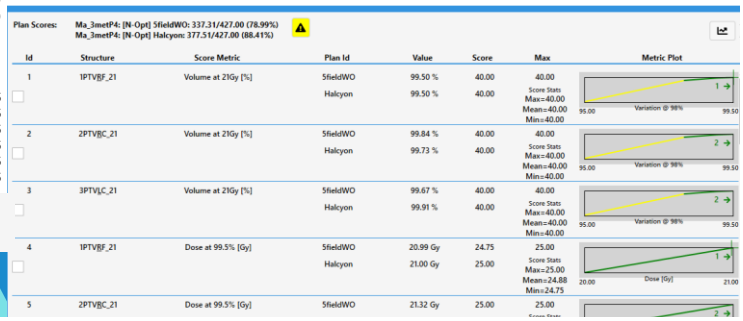
FLASH therapy is under development and not available for commercial sale.

MultiMet test

3 mets on different planes, 1fx 21Gy

Metric Id	StructureId	Metric Text	Max Score
0	1PTV_RF_21	Volume at 21Gy [%]	40
1	2PTV_RC_21	Volume at 21Gy [%]	40
2	3PTV_LC_21	Volume at 21Gy [%]	40
3	1PTV_RF_21	Dose at 99.5% [Gy]	25
4	2PTV_RC_21	Dose at 99.5% [Gy]	25
5	3PTV_LC_21	Dose at 99.5% [Gy]	25
6	1PTV_RF_21	Dose at 0.03CC [Gy]	18
7	2PTV_RC_21	Dose at 0.03CC [Gy]	18
8	3PTV_LC_21	Dose at 0.03CC [Gy]	18
9	RingRx.1-1_PTV1	Dose at 0.03CC [Gy]	10
10	RingRx.1-1_PTV2	Dose at 0.03CC [Gy]	10
11	RingRx.1-1_PTV3	Dose at 0.03CC [Gy]	10
12	RingMid.3-1.5_PTV1	Volume at 10.5Gy [%]	5
13	RingMid.3-1.5_PTV2	Volume at 10.5Gy [%]	5
14	RingMid.3-1.5_PTV3	Volume at 10.5Gy [%]	5
15	RingMid.3-1.5_PTV1	Dose at 0.01CC [Gy]	20
16	RingMid.3-1.5_PTV2	Dose at 0.01CC [Gy]	20
17	RingMid.3-1.5_PTV3	Dose at 0.01CC [Gy]	20
18	RingLow1.0_PTVs	Volume at 6Gy [%]	5
19	RingLow1.0_PTVs	Volume at 4Gy [%]	5
20	RingLow1.0_PTVs	Volume at 2Gy [%]	5
21	Brainstem	Dose at 1CC [Gy]	5
22	Brainstem	Dose at 0.03CC [Gy]	2.5
23	Brainstem	Dose at 0.1CC [Gy]	2.5
24	Cochl_L	Dose at 0.03CC [Gy]	2.5
25	Cochl_L	Dose at 0.1CC [Gy]	2.5
26	Cochl_R	Dose at 0.03CC [Gy]	2.5
27	Cochl_R	Dose at 0.1CC [Gy]	2.5
28	Chiasm	Dose at 1% [Gy]	5
29	Chiasm	Dose at 0.1CC [Gy]	2.5
30	Chiasm	Dose at 0.03CC [Gy]	2.5
31	OptNrv_L	Dose at 1% [Gy]	5
32	OptNrv_L	Dose at 0.1CC [Gy]	2.5
33	OptNrv_L	Dose at 0.03CC [Gy]	2.5
34	OptNrv_R	Dose at 1% [Gy]	5
35	OptNrv_R	Dose at 0.1CC [Gy]	2.5
36	OptNrv_R	Dose at 0.03CC [Gy]	2.5
37	Eye_L	Dose at 0.03CC [Gy]	1
38	Eye_L	Dose at 0.1CC [Gy]	1
39	Eye_R	Dose at 0.03CC [Gy]	1
40	Eye_R	Dose at 0.1CC [Gy]	1
41	Lens_L	Dose at 0.03CC [Gy]	1
42	Lens_L	Dose at 0.1CC [Gy]	1
43	Lens_R	Dose at 0.03CC [Gy]	1
44	Lens_R	Dose at 0.1CC [Gy]	1

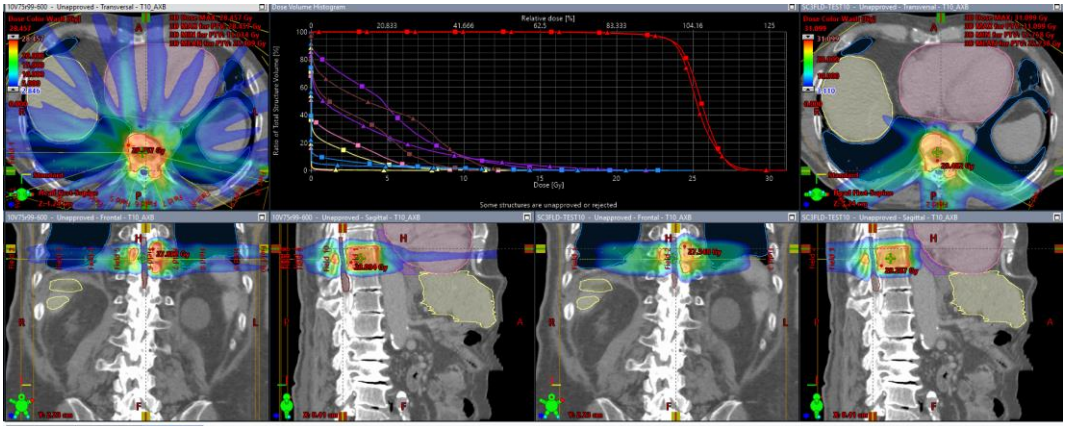
Ma_3metP4: [N-Opt] 5fieldWO: 337.31/427.00 (78.99%)
Ma_3metP4: [N-Opt] Halcyon: 377.51/427.00 (88.41%)



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

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

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

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

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%)

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	Score Stats Max=23.62 Mean=23.52 Min=23.42
			SC3FLD-TEST9	22.34 Gy	23.62		19.20 Dose [Gy] 24.00
2	PTVEVAL	Volume at 24Gy [%]	10V75r99-600p	88.58 %	12.86	20.00	Score Stats Max=14.98 Mean=13.92 Min=12.86
			SC3FLD-TEST9	89.99 %	14.98		80.00 Variation @ 90% 100.00
3	PTVEVAL	Volume at 22.8Gy [%]	10V75r99-600p	97.76 %	15.10	16.00	Score Stats Max=15.34 Mean=15.22 Min=15.10
			SC3FLD-TEST9	98.35 %	15.34		90.00 Variation @ 95% 100.00
4	PTVEVAL	Dose at 99.5% [Gy]	10V75r99-600p	21.09 Gy	13.43	15.00	Score Stats Max=13.49 Mean=13.46 Min=13.43
			SC3FLD-TEST9	21.14 Gy	13.49		14.40 Dose [Gy] 24.00
5	PTVEVAL	Dose at 0.035CC [Gy]	10V75r99-600p	28.80 Gy	13.00	15.00	Score Stats Max=13.00 Mean=9.07 Min=5.15
			SC3FLD-TEST9	30.25 Gy	5.15		27.12 Dose [Gy] 31.20
6	PTVEVAL	Volume at 28Gy [%]	10V75r99-600p	1.53 %	11.86	14.00	Score Stats Max=11.86 Mean=11.49 Min=11.12
			SC3FLD-TEST9	2.05 %	11.12		0.00 Volume [%] 10.00
7	PTVEVAL	Volume at 26.2Gy [%]	10V75r99-600p	27.32 %	7.26	10.00	Score Stats Max=8.37 Mean=7.82 Min=7.26
			SC3FLD-TEST9	22.20 %	8.37		10.00 Volume [%] 50.00
8	CTV	Dose at 99.9% [Gy]	10V75r99-600p	19.44 Gy	1.00	1.00	Score Stats Max=1.00 Mean=1.00 Min=1.00
			SC3FLD-TEST9	20.43 Gy	1.00		15.00 Variation @ 16Gy 16.00
9	PTV	Volume at 24Gy [%]	10V75r99-600p	86.80 %	0.68	1.00	

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**

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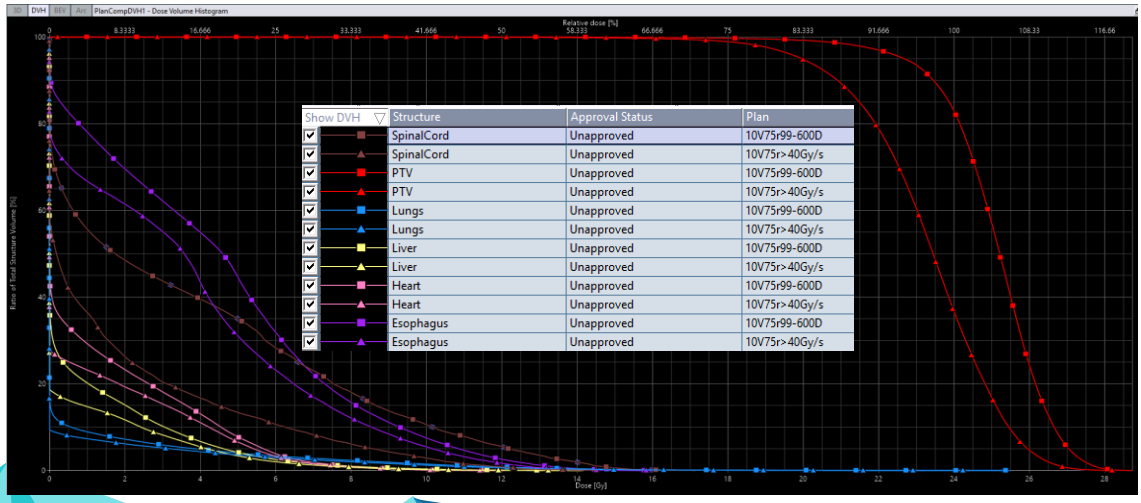
SBRT spine 24Gy 1fx

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



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Future Possibilities

Where FLASH proton planning could go next

4

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ScoreCard Based Optimization

Direct optimization on piecewise linear DVH based score function ranges

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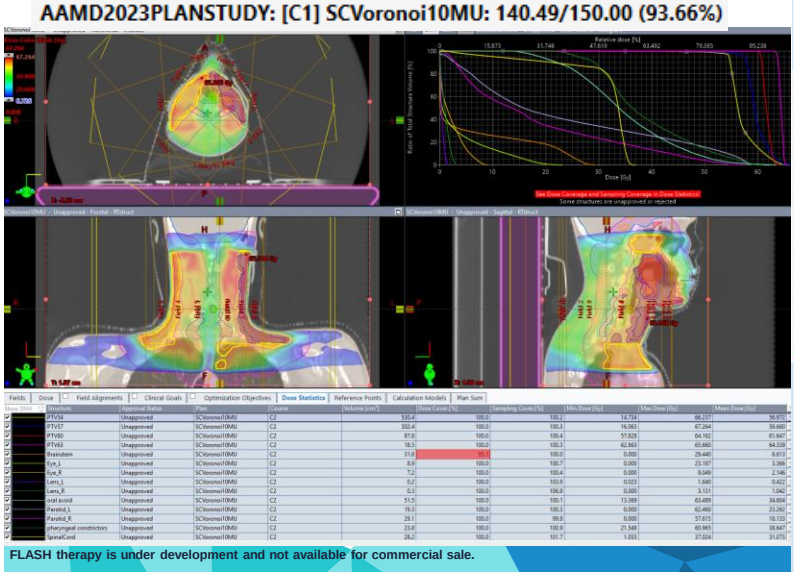
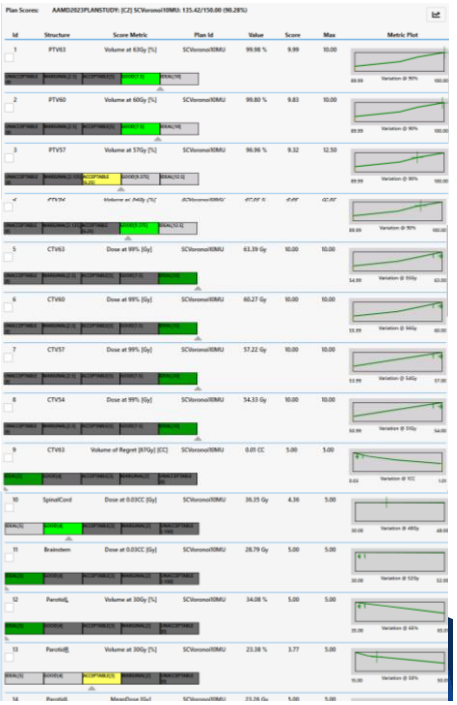
ScoreCard Based Optimization

250MeV (non Flash) AAMD 2023 Plan Study Phase 2

AAMD2023PLANSTUDY: [C2] SCVoronoi10MU: 135.42/150.00 (90.28%)
AAMD2023PLANSTUDY: [C1] SCVoronoi10MU: 140.49/150.00 (93.66%)





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Spot Weight And Position Optimization

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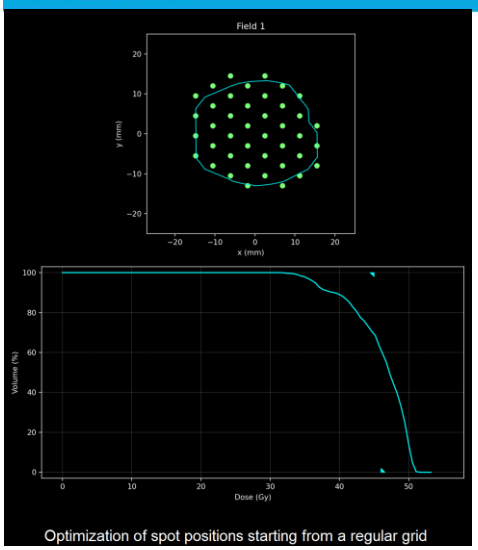
DIRECT MACHINE PARAMETER OPTIMIZATION FOR INTENSITY MODULATED PROTON THERAPY

P. Lansonneur*, A. Magliari, L. Rosa, J. Perez and M. Folkerts
Varian, a Siemens Healthineers Company



Optimization of spot positions starting from a regular grid

Results

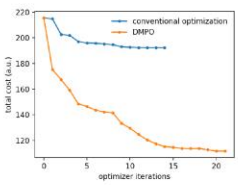


Fig. 2. Objective function evolution for conventional optimization and DMPO (case 1).

The evolution of the objective function during optimization is displayed in fig 2. The final cost reached with DMPO was two times lower than conventional optimization, with similar number of iterations. Unlike the conventional optimization scheme, all plans optimized with the DMPO algorithm passed the RTOG protocol inspired metrics (see table 2).

Metric	Goal	Conventional	DMPO
PTV, $V_{45\,Gy}$ (%)	> 90	99.0	99.0
PTV, D_{max} (Gy)	56.2	54.2	53.9
Ring80, D_{max} (Gy)	< 26.2	28.5	25.8
Ribs, D_{max} (Gy)	< 36.9	33.9	32.0
Ribs, D_{1cc} (Gy)	< 28.8	28.9	26.3
Spinal Cord, D_{max}	< 18	8.0	7.6
Esophagus, D_{max} (Gy)	< 25.2	15.4	13.7
Lungs, D_{mean} (Gy)	< 13.5	3.9	3.9

Table. 2. Several dose metrics and associated passing criteria evaluated for conventional optimization and DMPO. Failing metrics are indicated in red, marginal in orange and passing in green.

The dose distributions delivered above 40 Gy/s are displayed for each case in figure 3. For all fields, most of the dose is delivered at a dose rate above 40 Gy/s. Example field dose distributions are shown in figure 4.

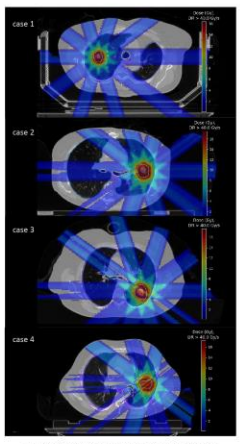


Fig. 3. Dose delivered at dose rate above 40 Gy/s.

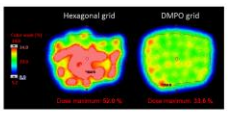


Fig. 4. Field dose distributions as seen from the BEV for a beam optimized from a hexagonal grid and with DMPO.

Compared to conventional optimization on a regular grid, DMPO resulted in smaller "hot" regions of lower magnitude in the final dose distributions. The fraction of irradiated volume receiving at least 40 Gy/s was above 91 % for lungs (excluding PTV) and above 92 % for esophagus (see table 3). Overall, DMPO resulted in significant plan quality improvement for all patients.

% FLASH	Esophagus	Lungs-PTV	Tracheobronchial
case 1	100 %	97 %	98 %
case 2	95 %	94 %	93 %
case 3	98 %	95 %	95 %
case 4	95 %	91 %	92 %

Table. 3. Fraction of irradiated volume (dose > 2 Gy) above 40 Gy/s several organs at risk.

Conclusion

We have proposed a new algorithm to optimize FLASH plans. Optimizing both the spot weights and positions leads to better plan quality than conventional (hex grid) optimization. This work will support the creation of fractionated IMPT plans for FLASH-RT. The authors tank M. Ropo and P. Niemela for their help. The DMPO algorithm is covered by a pending patent application.

References

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[2] P. Lansonneur et al. *PTCOG 60 poster* (2022).
[3] B. Nelms, *Practical Radiation Oncology* 2, 296–305 (2012).
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Bragg Peak Proton FLASH - AAPM 2023

End-to-end verification of multi-field-optimization FLASH-IMPT using a clinical GBM case

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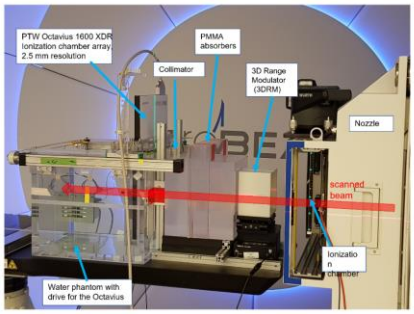

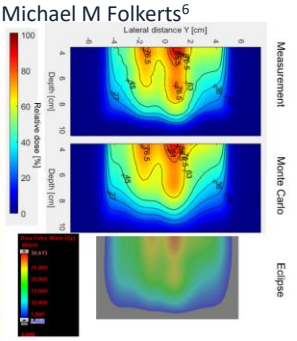

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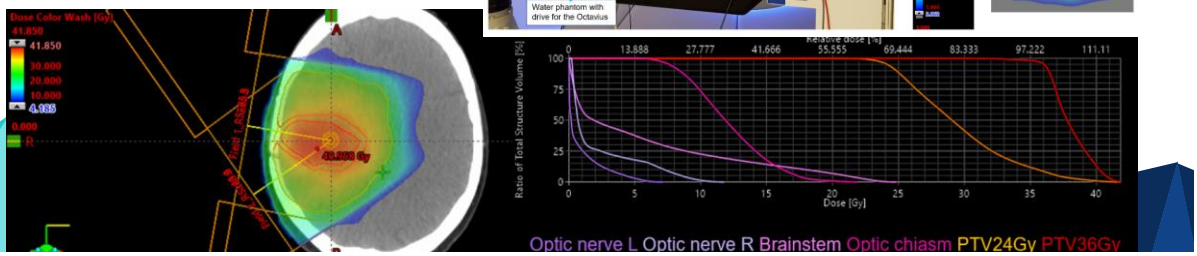

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- Jessica Perez
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- Miriam Krieger
- Lesley Rosa

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