SRS Using Multiple Isocenters

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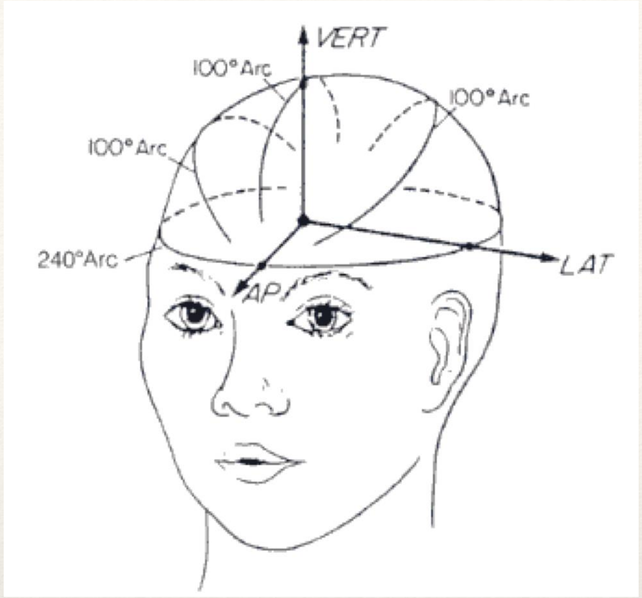
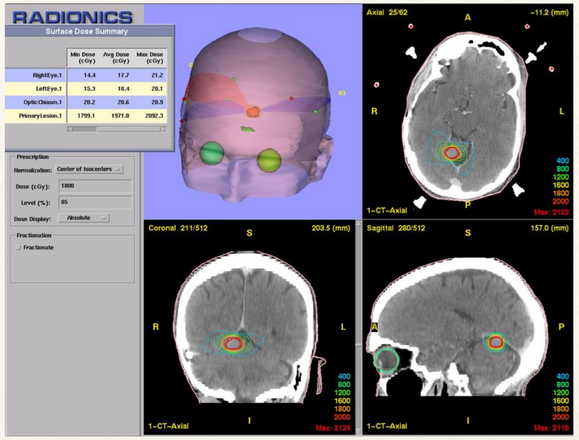
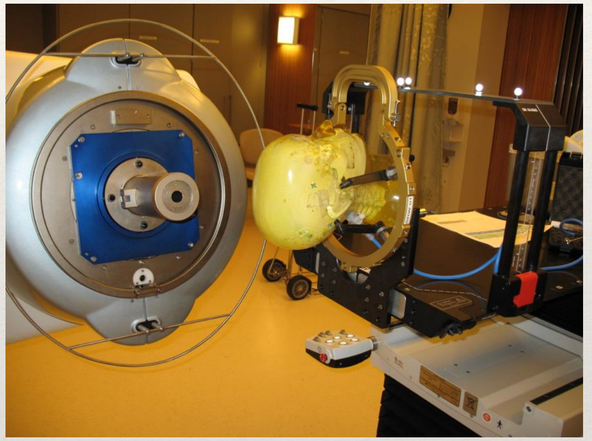
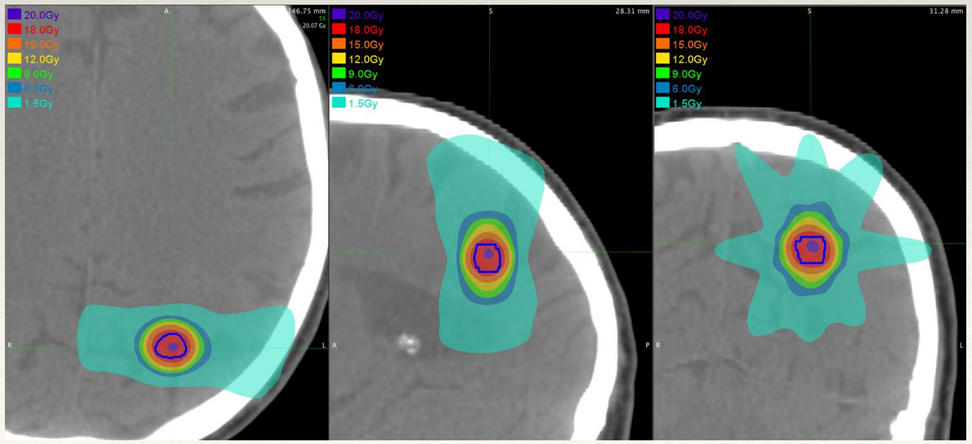
Outline

1. Clinical Goals
2. Treatment planning
3. Conformality
4. Setup uncertainties
5. Conclusions



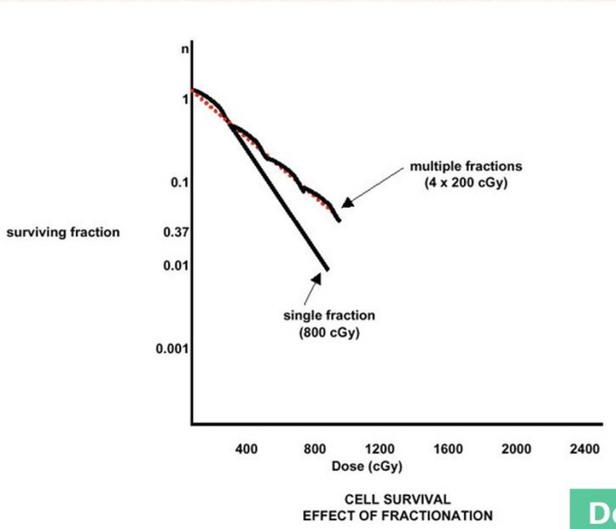


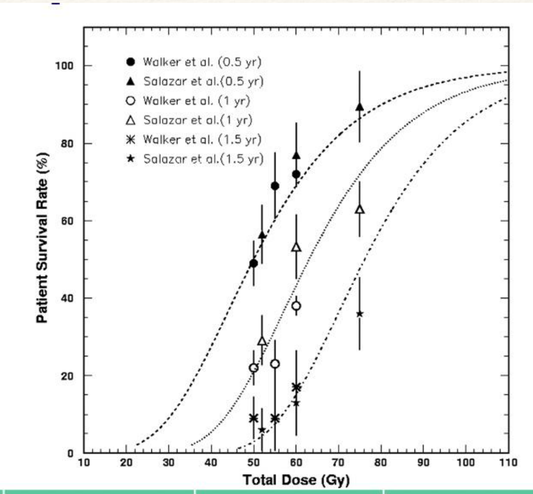




Clinical Goals

- SRS: Primary goal is geometric localization of the dose
  - Single, ablative dose delivered to a highly localized area
  - No (or limited) fractionation affects
- Minimize dose to normal brain and particularly to the optics, brainstem, and other regions determined by the physicians. Eg. Motor strip or hippocampus
- Avoid radionecrosis





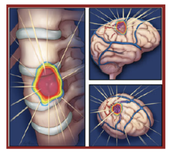
Biologically:

(8 Gy x 1) > (2 Gy x 4)

Dose	α/β = 1 Gy (2GyEq)	α/β = 5 Gy (2GyEq)	α/β = 10 Gy (2GyEq)
15 Gy	80 Gy	42.9 Gy	31.3 Gy
18 Gy	114 Gy	59.1 Gy	42.0 Gy
24 Gy	200 Gy	99.4 Gy	68.0 Gy

Biologically: equivalent dose calc fails at high single fraction doses!

Radionecrosis



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Does Stereotactic Radiosurgery Have a Role in the Management of Patients Presenting With 4 or More Brain Metastases?

Stereotactic radiosurgery (SRS) and whole brain radiation therapy (WBRT) are effective treatments for management of brain metastases. Prospective trials comparing the 2 modalities in patients with fewer than 4 brain metastases demonstrate that overall survival (OS) is similar. Intracranial failure is more common after SRS, while WBRT is associated with neurocognitive decline. As technology has advanced, fewer technical obstacles remain for treating patients with 4 or more brain metastases with SRS, but level I data supporting its use are lacking.

Observational prospective studies and retrospective series indicate that in patients with 4 or more brain metastases, performance status, total volume of intracranial disease, histology, and rate of development of new brain metastases predict outcomes more accurately than the number of brain metastases. It may be reasonable to initially offer SRS to some patients with 4 or more brain metastases. Initiating therapy with SRS avoids th acute and late sequelae of WBRT. Multiple phase III trials of SRS vs WBRT, both currentl open or under development, are directly comparing quality of life and OS for patients wit 4 or more brain metastases to help answer the question of SRS appropriateness for thes patients.

KEY WORDS: Brain metastases, Stereotactic radiosurgery, Whole brain radiation

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TABLE 2. Series Reporting Rates of Radiation Necrosis Based on V12

Series	Treated with SRS	Symptomatic vs asymptomatic	V12 RT necrosis threshold	% radiati necrosi
Flickinger[23] n = 85; 45 mo	AVM	Symptomatic	10 cc	30
Ohtakara[59] n = 131; 18 mo	Brain metastases	8.4% symptomatic, 6.9% asymptomatic	8.4 cc	15
Korytko[21] n = 129	Non-AVM brain tumors	Symptomatic	10 cc	25
Blonigen[60] n = 173; 14 mo	Brain metastases	Symptomatic	7.9 cc	10
Minniti[22] n = 310	Brain metastases	Symptomatic and asymptomatic	8.5 cc	>10

AVM, arteriovenous malformation; RT, Radiation therapy.
[a]N = number of lesions treated, follow up in months.

CLINICAL INVESTIGATION **Brain**

IRRADIATED VOLUME AS A PREDICTOR OF BRAIN RADIONECROSIS AFTER LINEAR ACCELERATOR STEREOTACTIC RADIOSURGERY

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Results: Sixty-three patients were reviewed, with a total of 173 lesions. Most patients (63%) had received previous whole-brain irradiation. Mean prescribed SRS dose was 18 Gy. Symptomatic RN was observed in 10% and asymptomatic RN in 4% of lesions treated. Multivariate regression analysis showed V8 Gy–V16 Gy to be most predictive of symptomatic RN ($p < 0.0001$). Threshold volumes for significant rise in RN rates occurred between the 75th and 90th percentiles, with a midpoint volume of 10.45 cm^3 for V10 Gy and 7.85 cm^3 for V12 Gy.
Conclusions: Analysis of patient and treatment variables revealed V8 Gy–V16 Gy to be the best predictors for RN using linear accelerator–based single-fraction SRS for brain metastases. We propose that patients with V10 Gy >10.5 cm^3 or V12 Gy >7.9 cm^3 be considered for hypofractionated rather than single-fraction treatment, to minimize the risk of symptomatic RN. © 2010 Elsevier Inc.

The cumulative volume of brain receiving 12 Gy (V12) is consistently used as a predictor of radiation necrosis after SRS (Table 2). The type of lesions treated across multiple series included patients with arteriovenous malformations, brain metastases, benign brain tumors, and patients who had received previous WBRT. Radiation necrosis occurs at a median of 10 to 12 mo after initial SRS.[21-23] Most of the data in these series were generated from patients with a small number of brain metastases, in whom a dominant metastasis represented the largest portion of the V12. Solitary metastases with a V12 of less than 8 to 10 cc have low rates of radiation necrosis (<10%). Beyond this threshold, rates of radiation necrosis increase, approaching 20% to 50%. In the setting of multiple small metastases that sum to a volume of >10 cc, the rate of radiation necrosis may be significantly less, compared to a dominant lesion that occupies the majority of the treated volume. The upcoming CE.7 randomized trial limits any contiguous V12 to less than 8.5 cc, but constrains the cumulative brain V12 to 30 cc.[24]

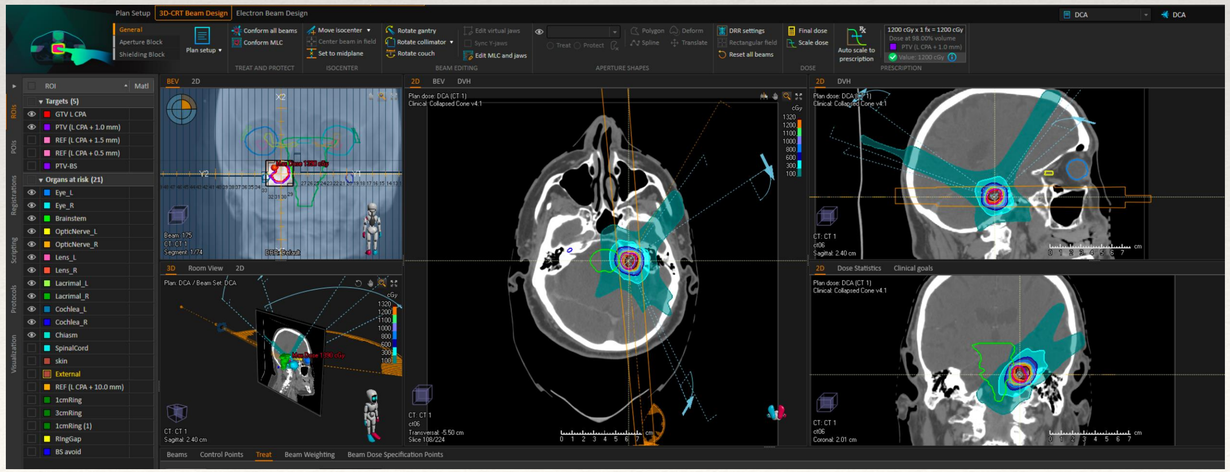
Table 3. Rate of radionecrosis for V10 Gy and V12 Gy volumes

Volume (cm^3)	Radionecrosis (%)
V10 Gy	
<2.2	4.7
2.2–6.3	11.9
6.4–14.5	34.6
>14.5	68.8
V12 Gy	
<1.6	4.7
1.6–4.7	11.9
4.8–10.8	34.6
>10.8	68.8

Abbreviations: V10 Gy, V12 Gy = volume of brain receiving 10 Gy and 12 Gy, respectively.

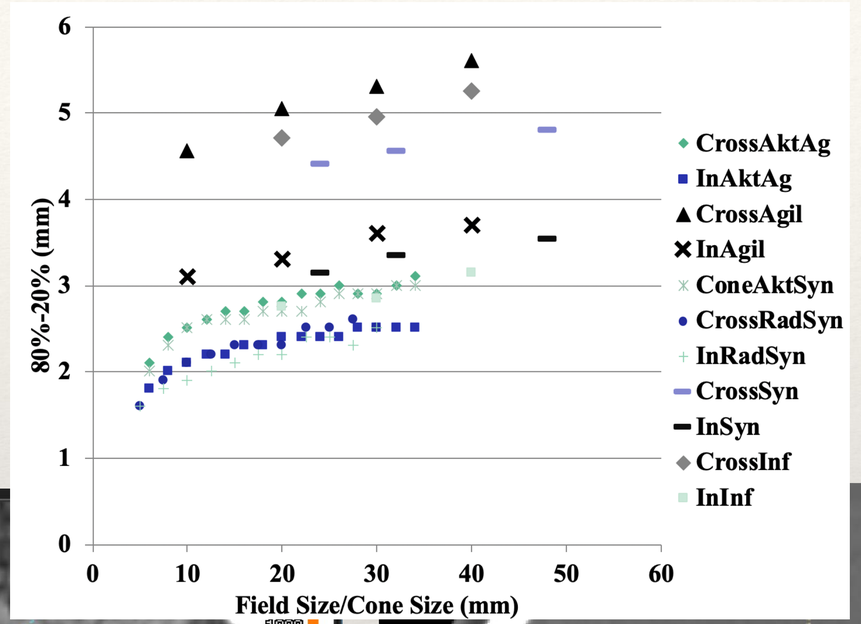
Treatment planning

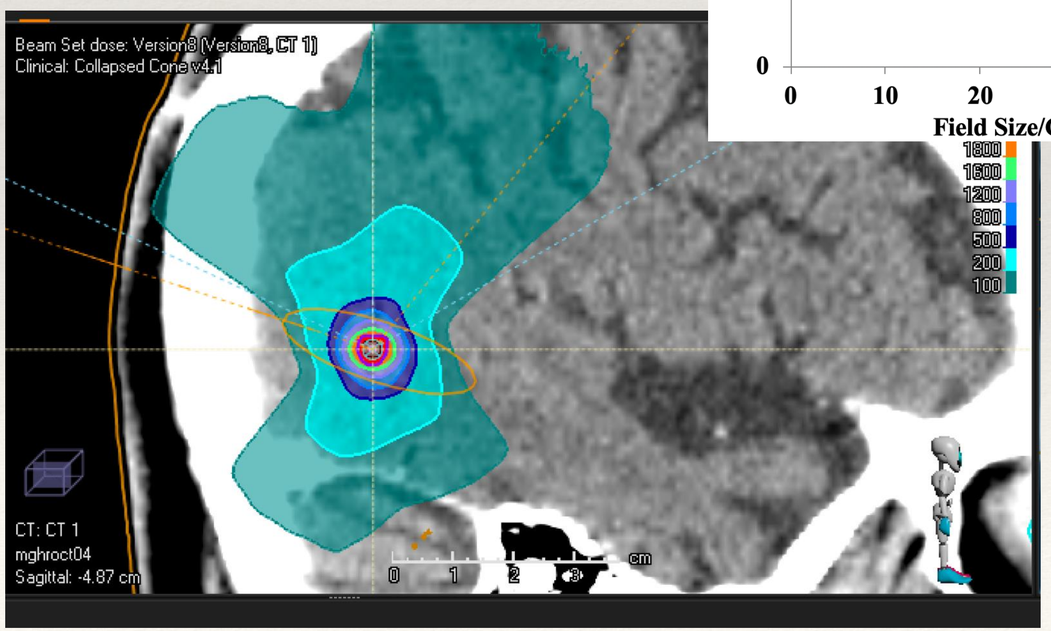
- Treatment planning can be performed with:
  - Cones
  - MLC
    - DCA
    - IMRT
    - VMAT
- For n = 1:num lesions
  - treatment planning
  - paperwork/documentation
- End

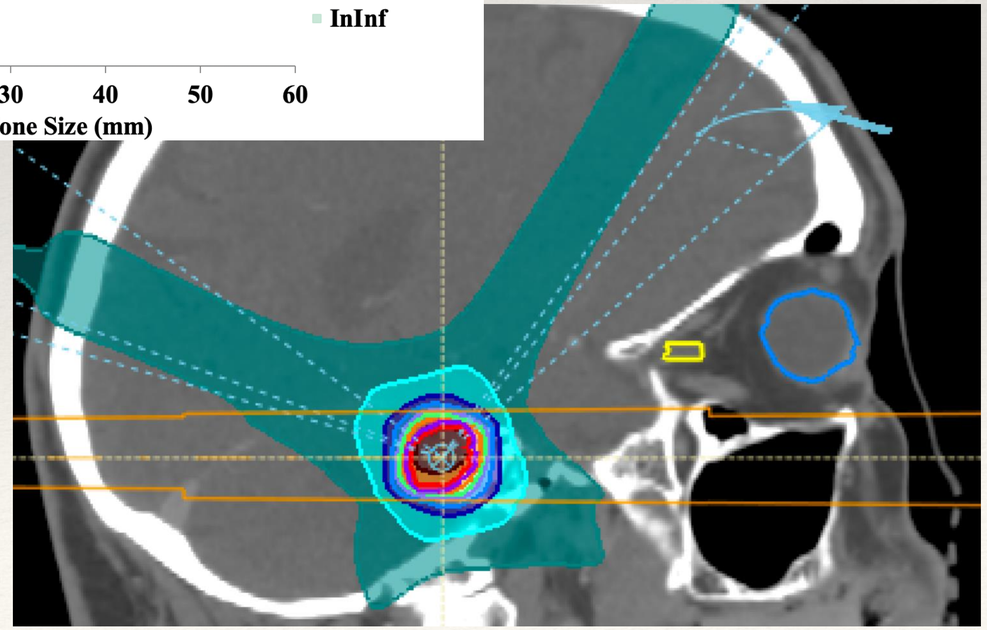


How to select modality

- Size and shape of lesions
- Planning constraints
  - OARs in close proximity
  - Dose uniformity
  - SIB

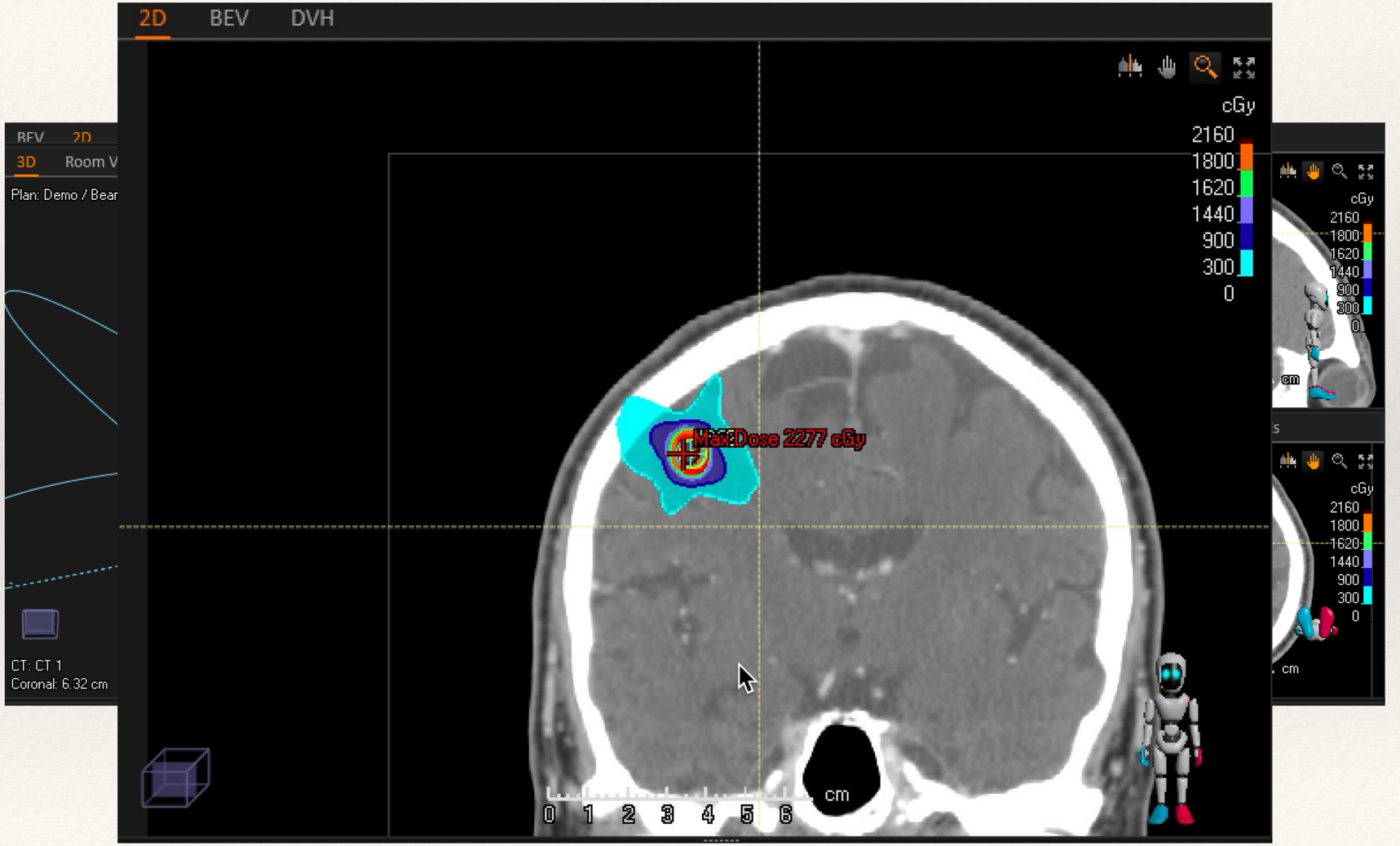




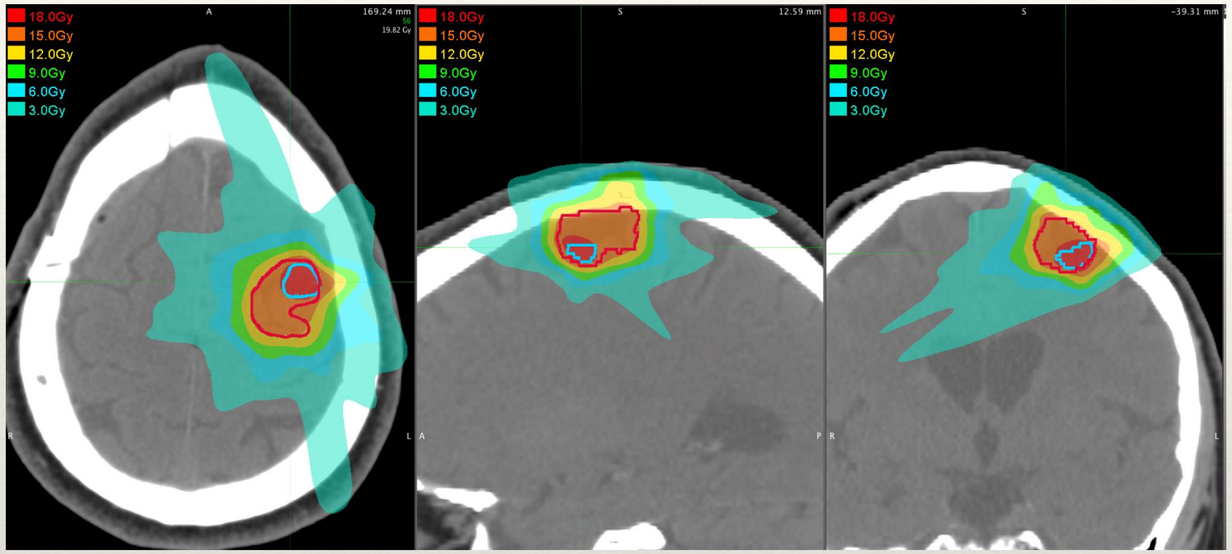


Cones

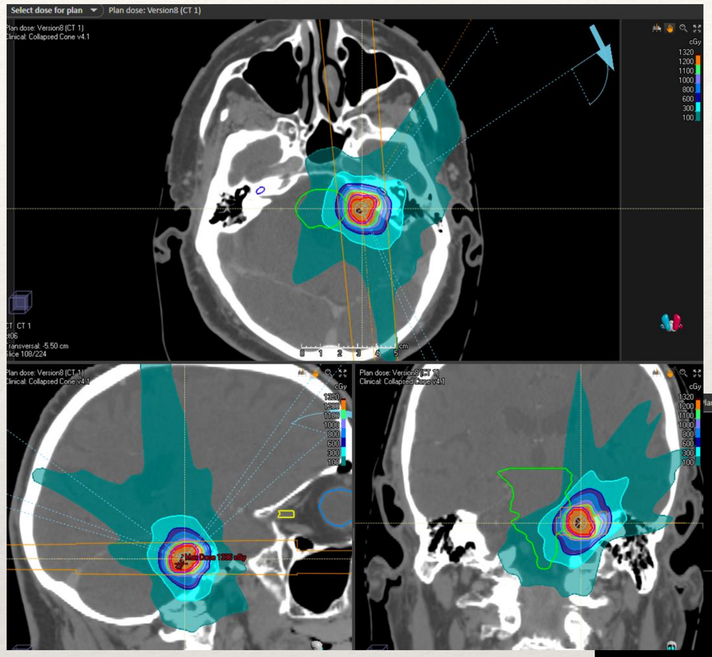
- Classic forward (manual) optimization
  - Cone size
  - Arc angles
  - Couch angles
  - Beam weights
  - Templates/scripting
- Planning times can be fast for simple spheres, longer for multiple isocenters or regions of avoidance



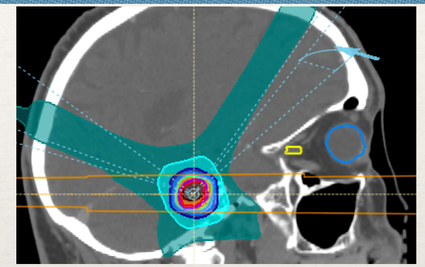
Linac IMRT and VMAT

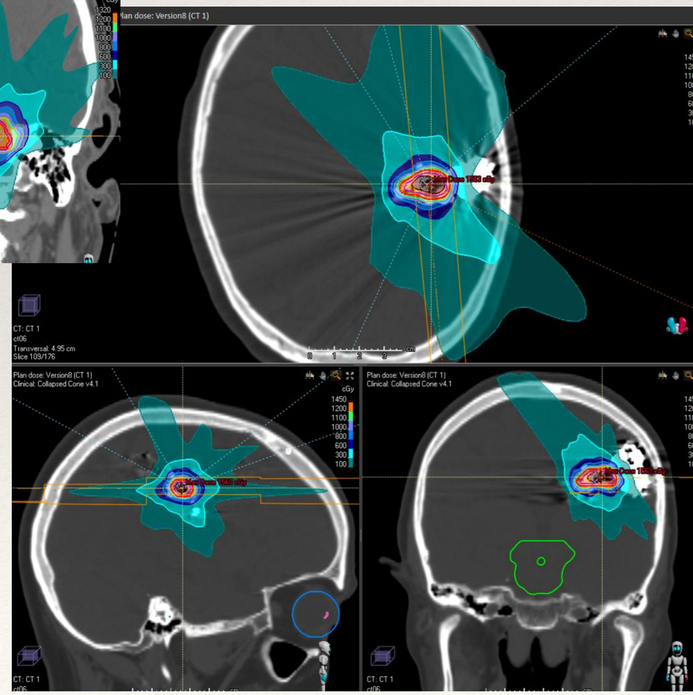


IMRT to Cavity with SIB



DCA: less homogeneous dose





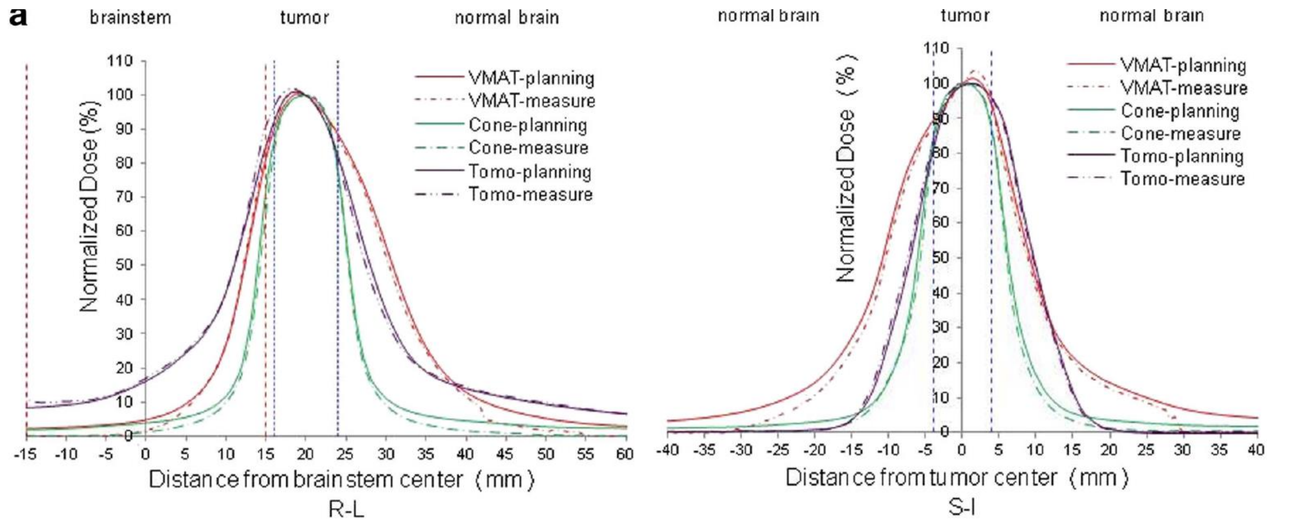
VMAT

Cones vs VMAT

- Hsu et al *Rad Onc* 2017
- Single lesion comparison

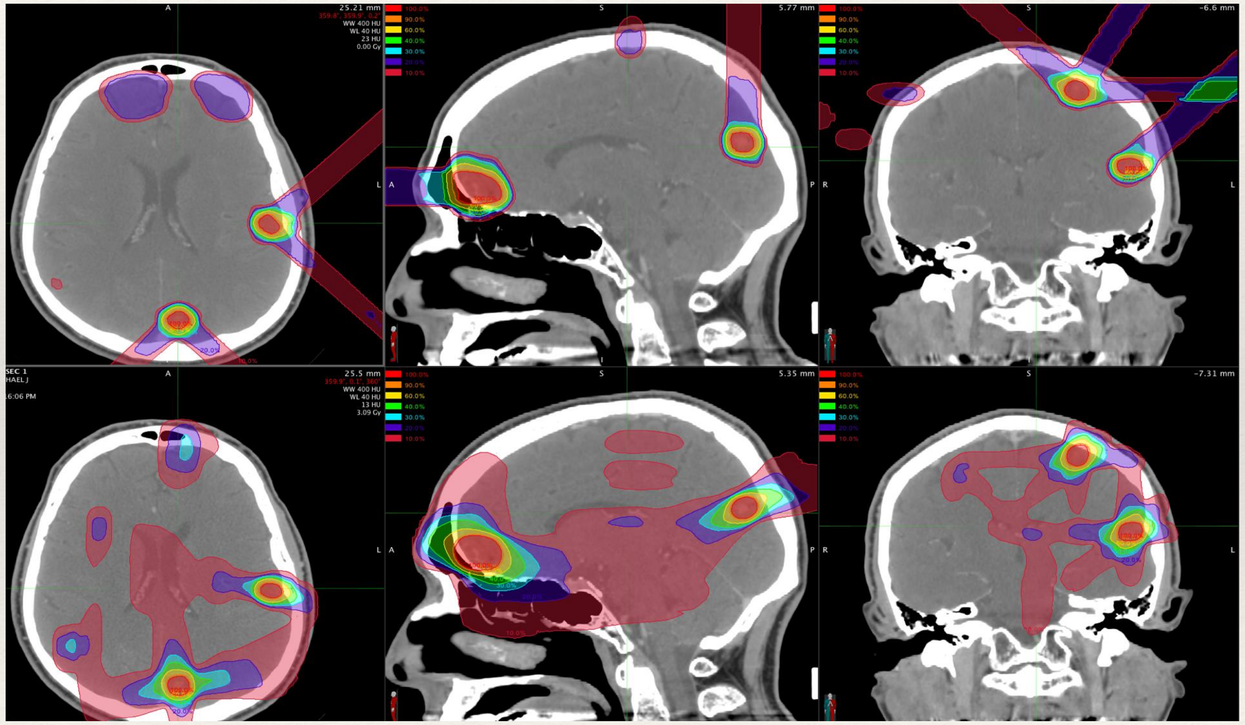
Table 1 HI, CGI, and Paddick indices calculated by the treatment planning system using the cone-based linac, FFF-VMAT linac, and tomotherapy treatment modalities

Tumor Diameter	8 mm						18 mm						28 mm					
Distance from brainstem	1 mm			6 mm			1 mm			6 mm			1 mm			6 mm		
Modality	Cone-based	FFF-VMAT	Tomo	Cone-based	FFF-VMAT	Tomo	Cone-based	FFF-VMAT	Tomo	Cone-based	FFF-VMAT	Tomo	Cone-based	FFF-VMAT	Tomo	Cone-based	FFF-VMAT	Tomo
HI	1.24	1.25	1.20	1.23	1.25	1.23	1.20	1.19	1.25	1.20	1.17	1.24	1.17	1.23	1.21	1.16	1.19	1.23
CGI_c	84.59	48.89	47.96	86.25	67.93	46.79	92.02	75.66	69.75	95.35	73.99	67.76	98.99	95.44	86.04	99.84	92.27	86.68
CGI_g	103.25	66.45	74.39	103.15	74.30	75.96	88.43	60.53	60.61	89.33	59.71	62.68	74.02	52.79	48.02	75.26	61.62	50.49
CGI	93.92	57.67	61.18	94.71	71.11	61.38	90.23	68.10	65.18	92.34	66.85	62.22	86.50	74.11	67.03	87.55	76.95	68.58
$CI_{Paddick}$	0.82	0.48	0.47	0.84	0.66	0.45	0.90	0.73	0.68	0.92	0.72	0.66	0.94	0.92	0.84	0.95	0.88	0.81
$GI_{Paddick}$	4.23	10.97	9.07	4.28	10.58	8.57	3.02	4.90	4.83	3.00	4.93	4.62	2.73	3.67	4.14	2.69	3.21	3.90



Multiple Targets and Isocenters

- Repeat the planning process for each target
- Small, spherical mets are most common for 3+ lesions —> Cones most common
- Planning is incremental
- Scripting and templates can help with the more general planning steps
- Proton SRS is outside the scope of this talk…

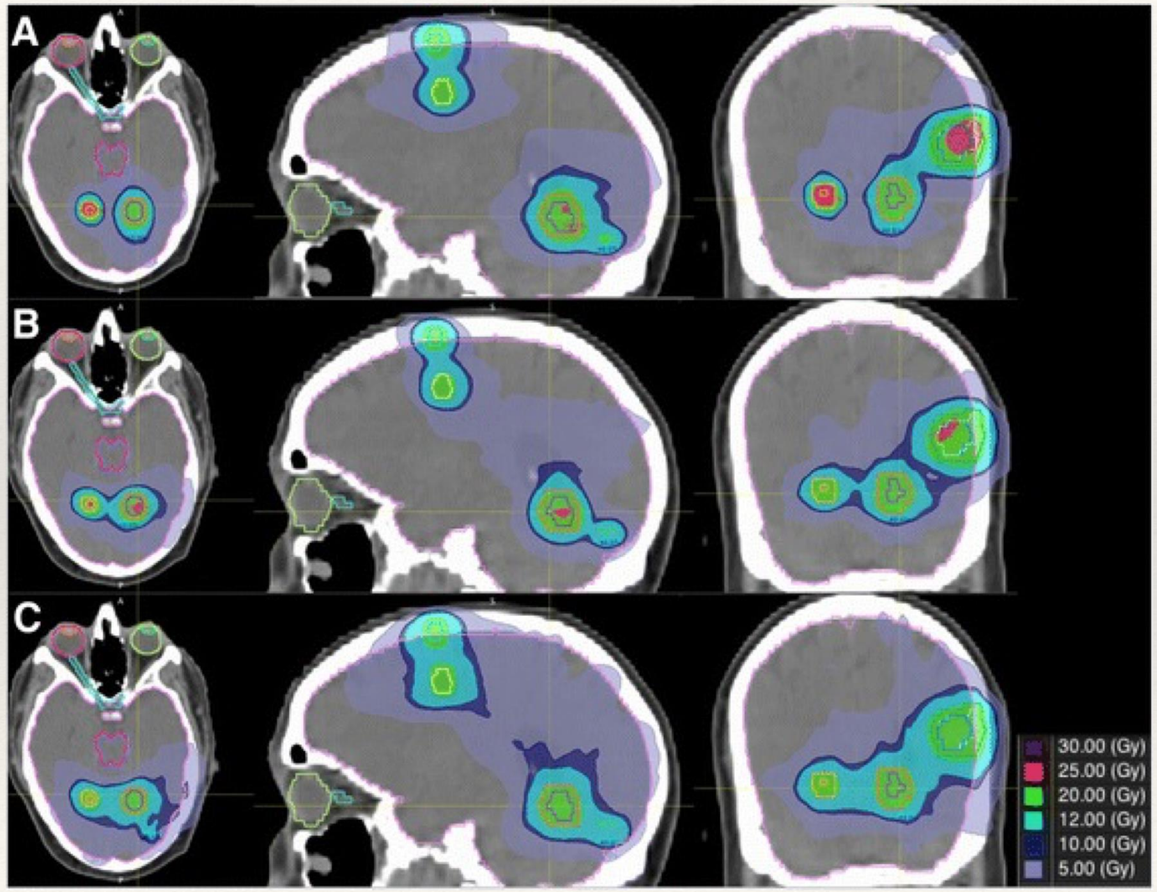


Comparisons: DCA vs VMAT

DCA
Multi Iso

VMAT
Multi Iso

VMAT
Single Iso



Gavaert, et al 2016 *Rad Onc*

Comparisons: GK vs VMAT/HA

Multi-Institutional Dosimetric Evaluation of Modern Day Stereotactic Radiosurgery (SRS) Treatment Options for Multiple Brain Metastases

- Vergalasova *et al Front Onc* 2019

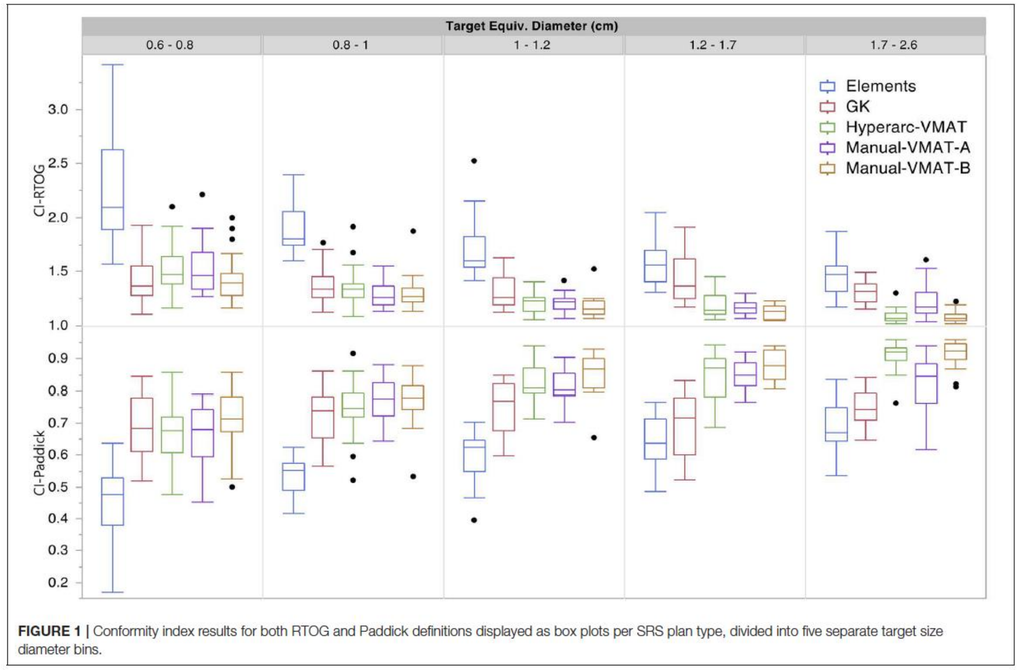


FIGURE 1 | Conformity index results for both RTOG and Paddick definitions displayed as box plots per SRS plan type, divided into five separate target size diameter bins.

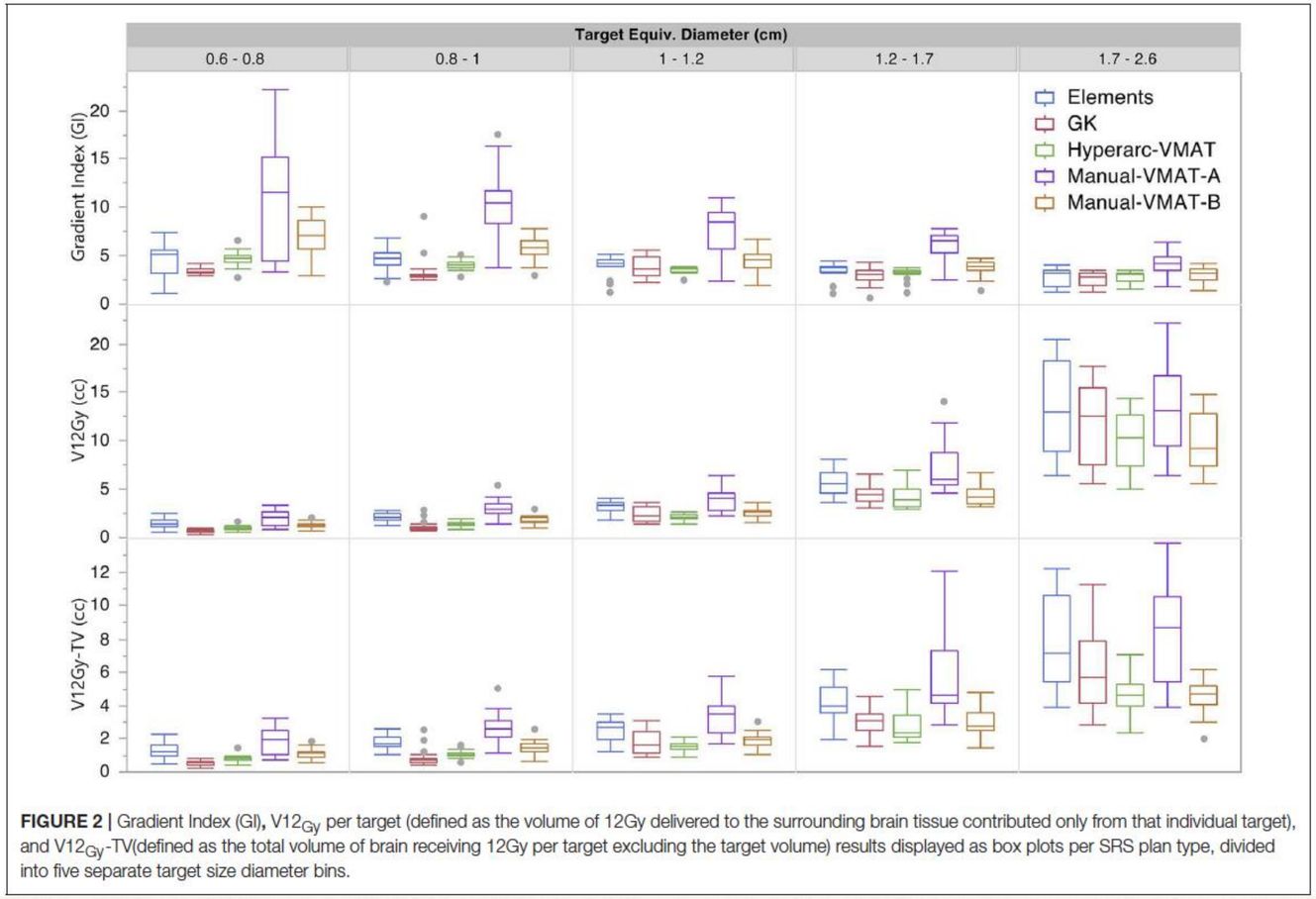
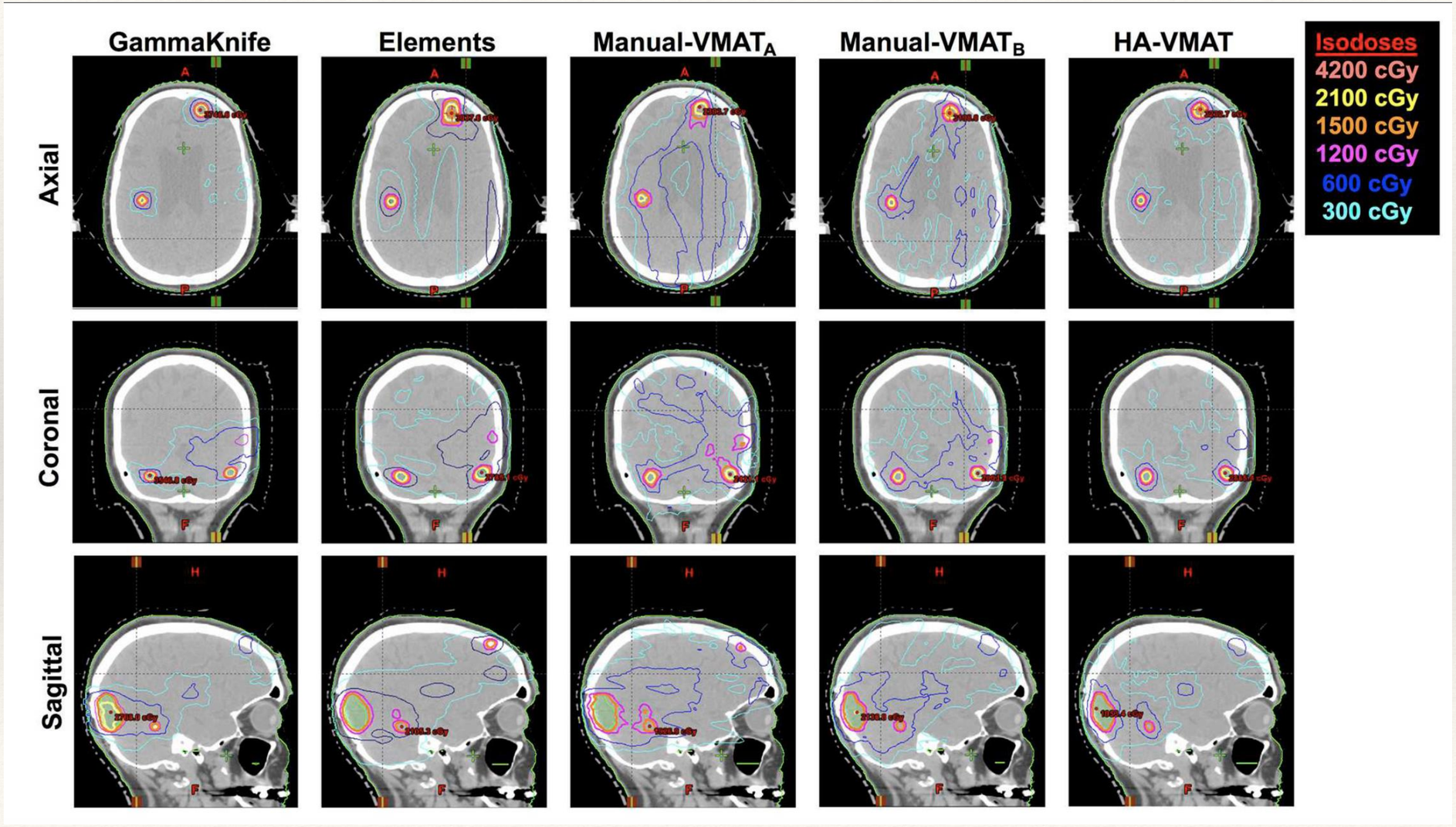


FIGURE 2 | Gradient Index (GI), $V12_{Gy}$ per target (defined as the volume of 12Gy delivered to the surrounding brain tissue contributed only from that individual target), and $V12_{Gy}$-TV(defined as the total volume of brain receiving 12Gy per target excluding the target volume) results displayed as box plots per SRS plan type, divided into five separate target size diameter bins.

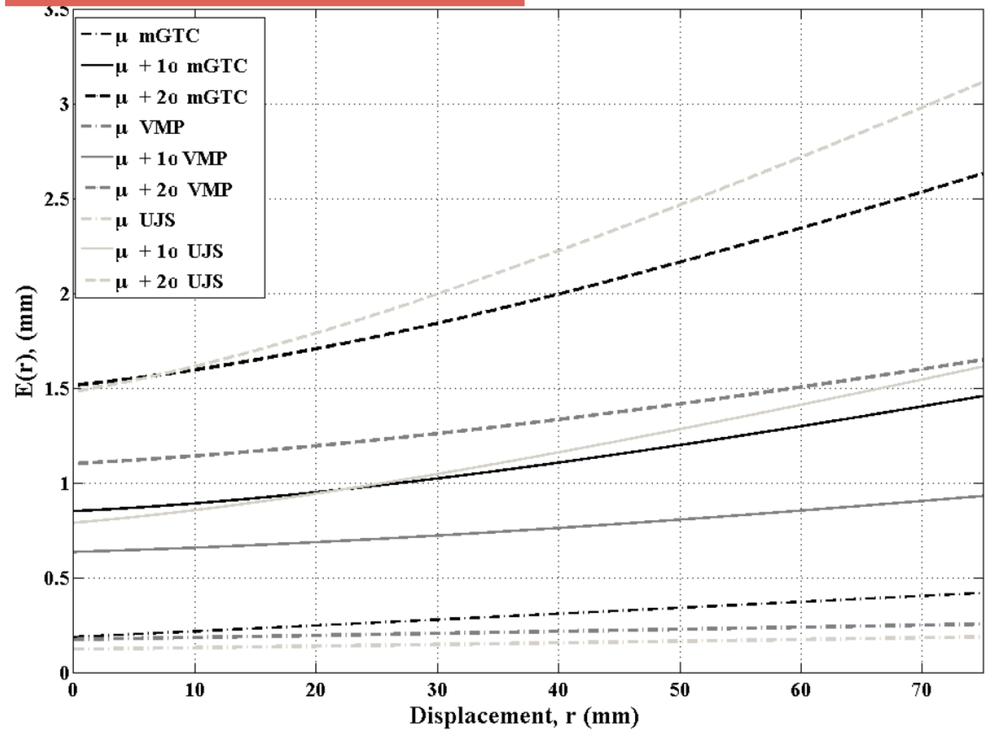
Comparisons: GK vs VMAT/HA



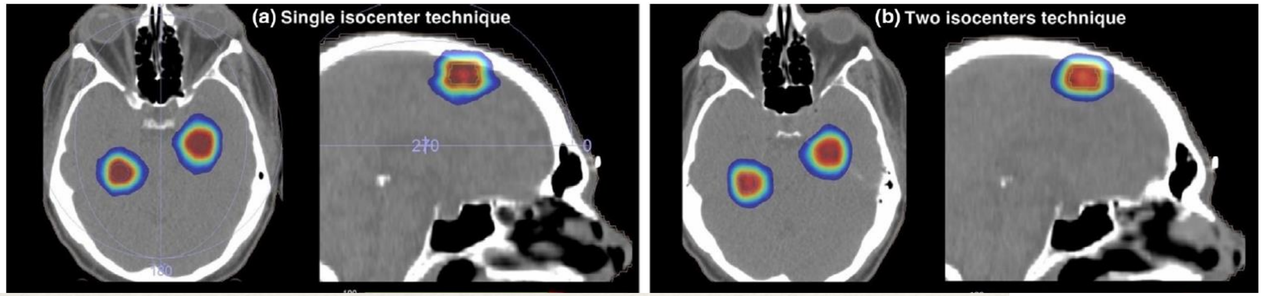
Uncertainties

- All data so far has assumed equal dose uncertainties for multiple isocenters versus a single
  - Uncertainties that change little between single and multi-isocenter:
    - Planning, CT, Segmentation
  - Setup uncertainties can vary due to rotational uncertainties
  - Immobilizations have a limit of uncertainties
- Dose model commissioning?
  - Winey *et al JACMP* 2015

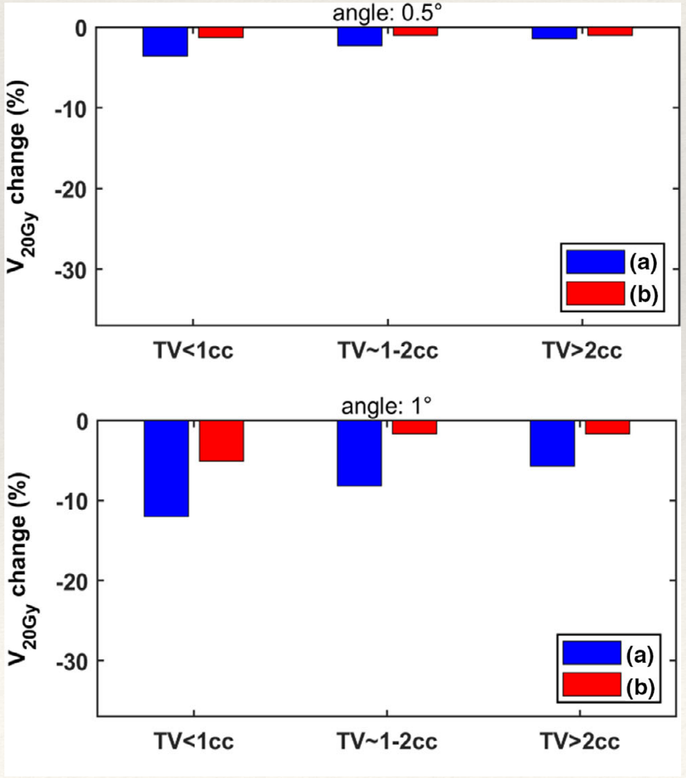
Dimension	*Intrafraction*			*Interfraction*		
	mGTC	*VMP*	*UJS*	*mGTC*	*VMP*	*UJS*
Lateral (LAT), mm	-0.12±0.37	-0.11±0.29	-0.11±0.28	-0.04±0.55	0.58±0.61	0.69±0.78
Ant/Post (AP), mm	-0.09±0.37	-0.03±0.21	0.01±0.26	0.09±1.29	0.40±0.48	0.46±0.78
Cran/Caudal (CC), mm	0.11±0.41	0.13±0.30	0.05±0.58	0.09±1.13	-0.47±0.95	-0.01±1.47
Pitch (about LAT), °	0.14±0.20	-0.02±0.14	-0.05±0.48	0.07±1.07	-0.42±0.38	-0.41±0.95
Yaw (about AP), °	0.10±0.50	0.06±0.27	0.02±0.46	-0.08±0.51	0.06±0.38	0.18±0.80
Roll (about CC), °	0.06±0.25	-0.02±0.15	0.02±0.49	0.05±0.59	-0.03±0.40	0.21±0.70

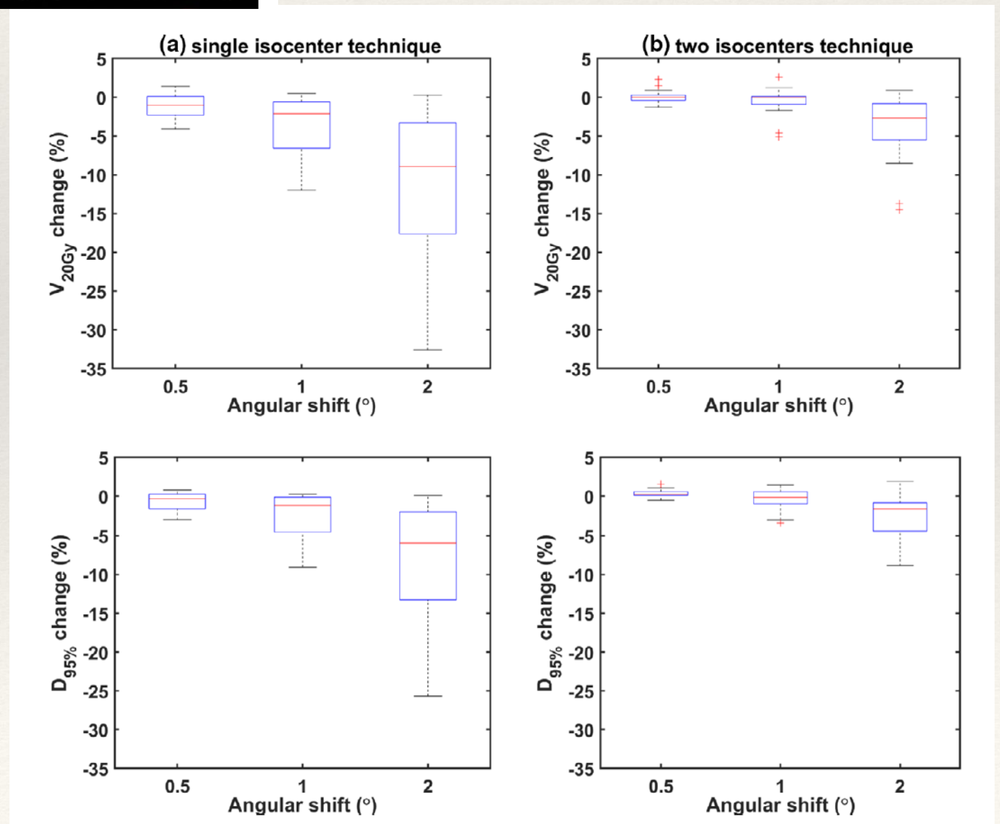


Single vs Multiple Isocenters: VMAT



- Prentou *et al JACMP* 2020
- 10 patients, 36 lesions





Conclusions: multiple isocenters

- Can be more conformal
- No PTV
- Less integral dose
- Cones have less QA (no moving parts)
- Repeat QA for each isocenter (likely same for both techniques)

- Patient time on the treatment table can be long—> increased discomfort and potential for motion
- Treatment planning time can be longer, particularly when running multiple optimizations
- Repeated paperwork and plan checks

- Machines are more accurate with the ability to check intrafraction position
- And! newer algorithms, machines, and delivery techniques