Normal Brain Analytical Dose Calculation Derived From Quality Metrics for Metastasis for Avoiding Necrosis

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INTRODUCTION

The outcome of Metastasis is function of TCD50, Prescription dose, 12Gy Normal Brain Volume. Less than 15Gy is not allowed since controlling probability is very low. Mets from melanoma, sarocoma, renal are resistive and others are sensitive. There should be necessity of preserving cognitive(hippocampal area, Broca's and Wernicke's), nearby OARs and parenchyma of brain is more important and is achievable through Stereotactic Radio Surgery(SRS) through prescribing proper dose according to volume.

AIM

Hence there should be simple practical applicability in order to achieve better results by calculating normal brain dose from knowing the quality metrics and analytical formulas.

METHOD

Analytical formulation is deduced from the quality metrics. The required isovolumes can be calculated from planning using algorithm tmr10. The margins are analysed and treatment problem discussed.

For better results from surgical dose
Less necrosis+better tumor vasucular damage+ proper gap among fractionation.

1. Diameter should be less than 4cm.
2. Solitary volume should be less than 12cc.
3. 12 Gy<10cc, 14Gy < 7cc, 10Gy <15cc.
4. For multiple mets, total volume should be less than 20cc.(check calculation)
5. In the model Sujitha et al. for LC at 2 years, k was 35 and TCD50 was 30 Gy. BED10 values of 40, 50 and 60 Gy10 yield predicted LC rates at 2 years of 62%, 69% and 81%, respectively (1).
6. Tumor--20Gy SF(single fraction)= BED 60 (a/b=10Gy)
7. Tumor—22Gy SF= BED 70.4
8. Normal Brain---12Gy SF = BED 60 Gy(a/b=3 Gy).
9. 12Gy is 40Gy/20 equivalent for white matter destruction.
10. 5.5 Gy is 10Gy/5f equivalent for NSR--neurogenic stem cell reduction, especially these stem cells are found in two zones of the dentate gyrus (part of the hippocampus) in the brain, as well as in the striatum (part of the basal ganglia located deep within the cerebral hemispheres).

RESULTS AND DISCUSSION

How fractionation is effective:

There was no difference in local control or radiation necrosis between HF-SRS and SF-SRS. For HF-SRS, a $BED_{10} \geq 50$ may improve local control(1). So in considering benefit of critical organs, much more advantageous in delivering hypofractions, most of the time 3 fractions are optimum.

The effect is discussed as follows.

Organ fractional dose(OFD) with respect to tumor is ratio of organ admitted max dose to the tumor dose for the same fractionation.

The fractionation advantage(FA) for the organ is defined as the ratio of OFD for the multifraction to single fraction. FA= (OFD_mf/OFD_sf). Almost constant for any tumor dose.

Advantage Index is defined as FA_organ/FA_brain. This is the indication of dose reduction for Risk organ due to fractions for constant allowed 12 Gy volume. If the normal brain volume allows the dose can be increased to have better tcp.

The fractionation advantage is clearly shown in figure. The fitting formulas for FA are x^0.28, x^0.22, x^0.10, x^0.07

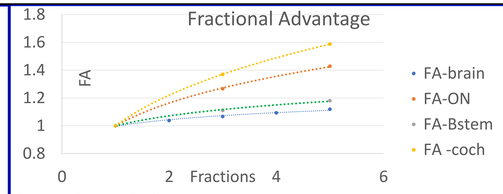

Figure 1. Fractional Advantage.

Fractions	dose	brain a/b=3	OFD-brain	FA-brain	ON -0.036cc	OFD-ON	FA-ON	RAI-ON
1.0	20.0	12.0	0.600	1.000	10.0	0.500	1.000	1.000
2.0	26.0	16.2	0.623	1.038				
3.0	30.0	19.2	0.640	1.067	19.0	0.633	1.267	1.188
4.0	32.9	21.6	0.656	1.094				
5.0	35.0	23.5	0.671	1.119	25.0	0.714	1.429	1.277
	Bstem 0.036	OFD-Bstem	FA-Bstem	RAI-Bstem	cochlea 0.036	OFD-Coch	FA -coch	RAI-coch
	15.0	0.750	1.000	1.000	9.0	0.450	1.000	1.000
	25.0	0.833	1.111	1.042	18.5	0.617	1.370	1.285
	31.0	0.886	1.181	1.055	25.0	0.714	1.587	1.418

fractions. Advantage Index(AI) is defined as (organ FA/ brain FA) is
x^(0.28-0.07), x^(0.22-0.07), x^(0.1-0.07)
where x is fractions

Fractionation.

Many references available for fractionation schedule.Fractionation has to be considered according to volume and nearby OAR. It can be number of fractions
(1+quotient(Vol(cc)/4)).
But considering Vascular surgical effectiveness of SRS, mostly 3 fractions are effective as 3*9=27Gy which is 18 Gy single dose equivalent. If 12 Gy volume less than 10cc then the dose can be increased in order to have better tcp.

Gamma knife planning is done with different set of cone arrangement in a five ring pattern arranged through sectors. The planning uses optimization engine where different set of filling can be done in required ratio of smaller to bigger cones. The importance of input parameters are coverage, selectivity, gradient index, beam on time will provide for the better optimization. Once if we achieve
TV~=TTV, that is coverage is almost 1, other parameters can be checked.

Iso dose fall off with different fillings.

As the cone size for tumor volume filling decreases initial value decreases, that means the lower iso volume decreases. This is very effective after 12 cc.
At the beginning initial high dose volume is higher for the larger cones. This is obvious in fig1 and fig 2.
The Deduced formula for calculating the Intended iso volume(IIV) is with std error of 6%, provided GI should be <3.
$IIV=300*(TV/S)^{1.07}*((RD/PD)*PP)^{-1.5}$.

Where TV-Tumor volume, S-selectivity, RD-Required Dose(say 12 Gy), PD-Prescribed Dose, PP-Prescribed Percentage. IIV—Intended Isodose volume
The extra correction need to be applied for effective volume more than 12cc if smaller cones are used. Above formula should be multiplied with
(1-0.0003*TV^2).
Normal Brain volume=12Gy volume(required dose volume(RDV))-Tumor volume.

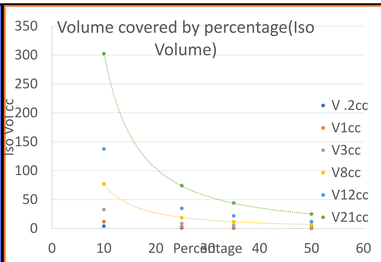

Figure 2. Isodose volumes for different tumor volumes

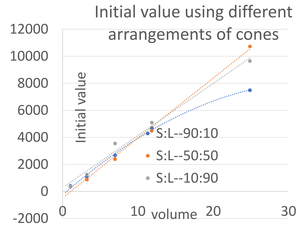

Figure 3. Initial value using different arrangements of cones

TV	S	GI	RD	PD	RPD	cal Iso volume	Measured 12Gy
6.78	0.85	2.86	19.2	23.4	41.02564	10.53115	11.172
4.6355	0.67	2.91	19.2	23.4	41.02564	9.04402	9.7
1.595	0.62	2.61	19.2	26.7	35.95506	3.788545	4.067

P(necrosis)	Flickiger et al. e^B(1+e^B), where B=const(-7.8713)+0.7506*(SPIE)+0.0734*(V12)
SPIE	significant post radiosurgery injury expression.
PIE	post radiosurgery injury expression.

Down shows the table created from data using the flickinger et al. formula, still as per the many literatures still keeping the 12 Gy brain volume under the 10cc, 10Gy under 15cc.

Site name	Symbol	SPIE	Allowed (cc)	B value	5% P
Frontal	A	1	20	-5.6527	0.0034392
Temporal	B	1.89	15	-5.351666	0.0046215
Intraventricular	C	3.72	12	-4.198268	0.0141035
Parietal	D	4.83	12	-3.365102	0.0307645
Cerebellar	E	4.87	12	-3.335078	0.0316238
Corpus Collasum	F	5.99	8	-2.788006	0.0518401
Occipital	G	6.04	8	-2.750476	0.053599
Medulla	H	6.96	2	-2.500324	0.0668371
Thalamus	I	7.71	0.5	-2.047474	0.0990905
Basal Ganglia	J	8.01	0.5	-1.822294	0.1204072
Pons midbrain	K	10	0.2	-0.35062	0.5501608

Ref.(3).

	Single Fraction				
size	<20mm	21-30	31-40	21-40	BED
Gy	%Local control				
22	93				81.6
20					60
18	85				50
18		75			50
15			69		37.5
	Fractionation				
27/3	(18Gy equivalent)			80	50
35/5	(20 Gy equivalent)				60

Problem:

The patient came up with 4 mets totally 30cc, after 6 months of wbrt . How to avoid necrosis.

After a single exposure to moderately high doses of radiation, e.g. 5–10 Gy, tumor blood flow initially increases, returning to preirradiation levels or slightly below the preirradiation levels in 2–3 days(5).
We have treated with full stipulated dose with proper reduction of dose (5-10%) for 3 mets and keeping 12 Gy volume around 12cc.
Another one treated with two fractions of 5Gy , totally 10 Gy and given time for further followup and treatment.

CONCLUSIONS

1. **The Required iso volume can be calculated above mentioned way. Since 12Gy equivalent brain volume is indication of necrosis, should not exceed 10cc, and at inevitable maximum of 15cc. So calculating iso volume is more important. The Dose can be considerably reduced for the Organ at risk while doing fractionation.**
2. **These calculations can be used in treatment planning system in order to have better prognostic decisions.**
3. **Three surgical fractions given in alternative days may provide better results than continuously three days since vascular damage is maximum after two days, if dose is more than 8 Gy per fraction**
4. **Monitoring and Margins for tumor.**
   Since tumor motion is monitored by IR camera system, Nose marker as surrogate for tumor, there should be margin necessary to deliver the dose properly.
   The mean Movement of 1mm is common.
   1. **If less than 1cc if OAR permits, then 1mm**
   2. **For others 0.5mm if 12cc Volume permits.**
   3. **0.5mm all around except at OAR.**
5. **System Requirement**
1. **Current system does not give any information about online directional movement. 3D Information is necessary to take the decisions for doing CBCT or continuation. Directional Information is imperative.**

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CONTACT INFORMATION

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