***Radiobiology in Radio surgery - F. Vernimmen***

## RADIOBIOLOGY IN RADIOSURGERY

F Vernimmen 2009

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## RADIOSURGERY

THE APPLICATION OF A SINGLE DOSE OF RADIATION

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## Years of clinical experience

1968
The first prototype of Leksell Gamma Knife® was installed in Stockholm, Sweden.

1999
Elekta refines the Art of radiosurgery by introducing Leksell Gamma Knife® C

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## Leksell GammaPlan®

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The reason why these treatments are tolerated is the very localized nature of the dose deposition and the very rapid dose fall off outside the target.

Based on a large body of clinical experience doses for radiosurgery are well established

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## Reasons for fractionation:

- **meningiomas growing around the optic apparatus**
- **hearing preservation in acoustic neuromas**
- **close proximity of critical structures**
- **non compact AVM nidus**
- **large target volume**
- **targets in eloquent areas of the brain**

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# I want to fractionate

But what is the total dose and the dose/fraction ?

# Biological Effective Dose (BED)

$$BED = \text{Total dose}\left(1 + \frac{\text{d / fraction}}{\alpha/ß}\right)$$

What is the α/ß ratio ?

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RADIOLOGICAL SLOW GROWING

RADIOBIOLOGICAL SLOWLY PROLIFERATING

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<u>How to determine these α/ß values?</u>

Cell culture techniques: “easy”, but are “in Vitro”

Animal models

Patient clinical data

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**α/ß ratio**

Meningiomas
Acoustic neuromas
Arteriovenous malformations
Optic chiasma

Using clinical data => FE plot
=> Tucker plot

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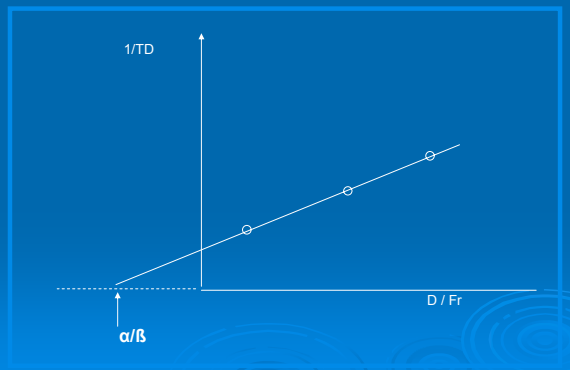
## The FE plot analysis is valid for a very specific observed end effect.

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**Tucker method**

Pairs of radiation doses that have an equal biological effect

Dn (given in dn) ⇔ Dm (given in dm)

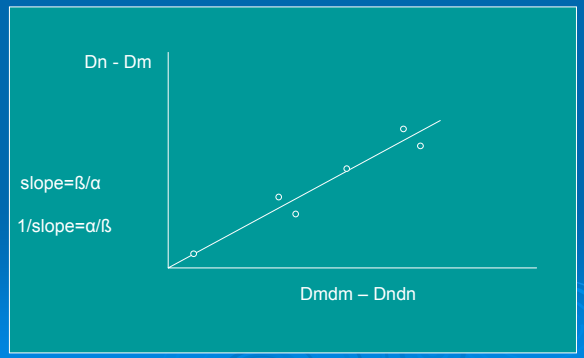


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**Table 1: Meningioma data**

| Author | Total dose in Gy | D/F in Gy | Radiological control | Complications |
|---|---|---|---|---|
| Flickinger[20] *et al* | 14 | 14 | 93% - 10y | 8.80% |
| Lo[21] *et al* | 14<br>54 | 14<br>2 | 92.7% - 3y<br>93.3% - 3y | 6%<br>5.50% |
| Roche[22] *et al* | 13 | 13 | 100% - 4y | 6% |
| Pollock[79] *et al* | 16 | 16 | 94% - 3y | 8% |
| Selch[24] *et al* | 50.4 | 1.8 | 97% - 3y | 0% |
| Villavicencio[23] *et al* | 15 | 15 | 95% - 5y | 9% |
| Vernimmen[16] *et al* | 24.8 | 8.26 | 88% - 3y | 5.50% |
| Debus[52] *et al* | 56.8 | 2 | 97% - 5y | 1.60% |
| Henzel[49] *et al* | 55.8<br>40<br>30<br>16.5 | 1.9<br>4<br>5<br>16.5 | 96.9% - 5y | 0% |

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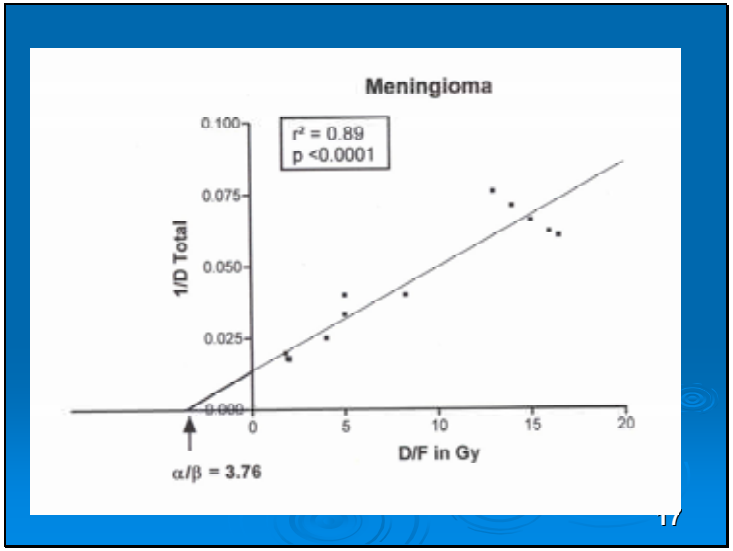


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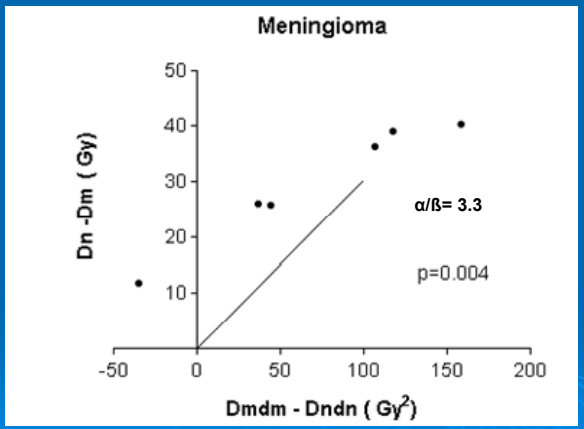


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**Table 2: Acoustic data**

| Author | Total dose in Gy | D/F in Gy | Radiological control | Complications | Hearing preservation |
|---|---|---|---|---|---|
| Combs[18] *et al* | 13 | 13 | 91% - 5y | 6% | 55% |
| Combs[7] *et al* | 57.6 | 1.8 | 93% - 5y | 5.70% | 94% |
| Huang[36] *et al* | 11.5 | 11.5 | 95.6% 2y | 2.20% | 76.90% |
| McClelland[22] *et al* | 54 | 1.8 | 100% 2y | 10 | 80 |
| Paek[34] *et al* | 12 | 12 | 92% - 4y | 5% | 88% |
| Chang[33] *et al* | 18<br>21 | 6<br>7 | 98% - 3y | 0% | 74% |
| Van Eck[32] *et al* | 13 | 13 | 87% - 2y | 2.50% | 83% |
| Lunsford[31] *et al* | 13 | 13 | 97% - 10y | 3% | 77% |
| Chung[30] *et al* | 11 | 11 | 93.6% - 3y | 1% | 60% |
| Hasegawa[29] *et al* | 14.6 | 14.6 | 87% - 11y | 7% | 68% |
| Ishihara[28] *et al* | 16.9 | 5.6 | 94% - 3y | 0% | 93% |
| Dhanachai[27] *et al* | 46.2<br>26.4<br>29.4 | 1.6<br>4.4<br>4.9 | 90% - 2y | 0% | 40% |
| Landy[26] *et al* | 11.1 | 11.1 | 98% - 4y | 0% | 85% |
| Chung[9] *et al* | 12<br>45 | 12<br>1.8 | 100% - 2y | 4% | 57% |
| Williams[6] *et al* | 25<br>30 | 5<br>3 | 100% - 2y | 0% | 62% |
| Andrews[37] *et al* | 12<br>50 | 12<br>2 | 98% - 2y<br>97% - 2y | 5%<br>7% | 33%<br>81% |

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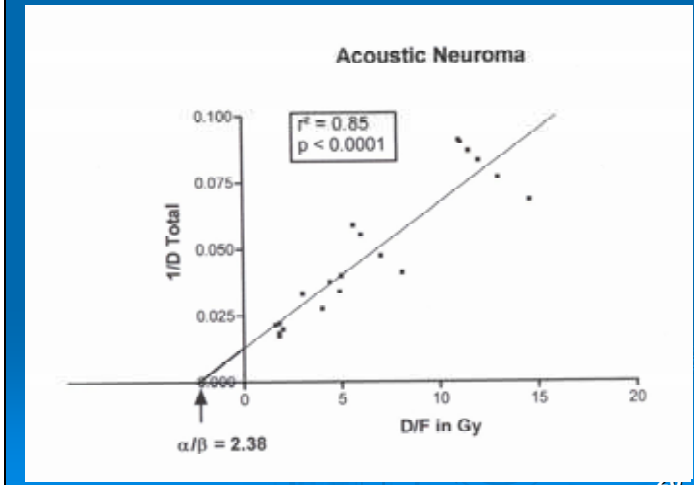


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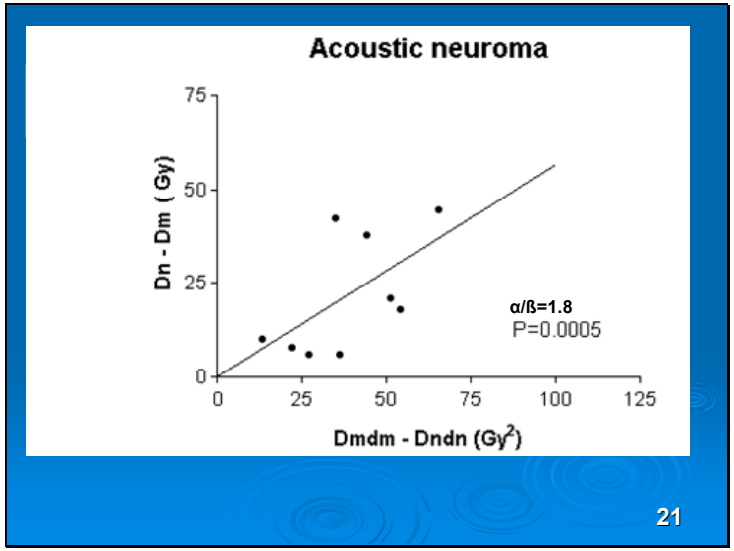
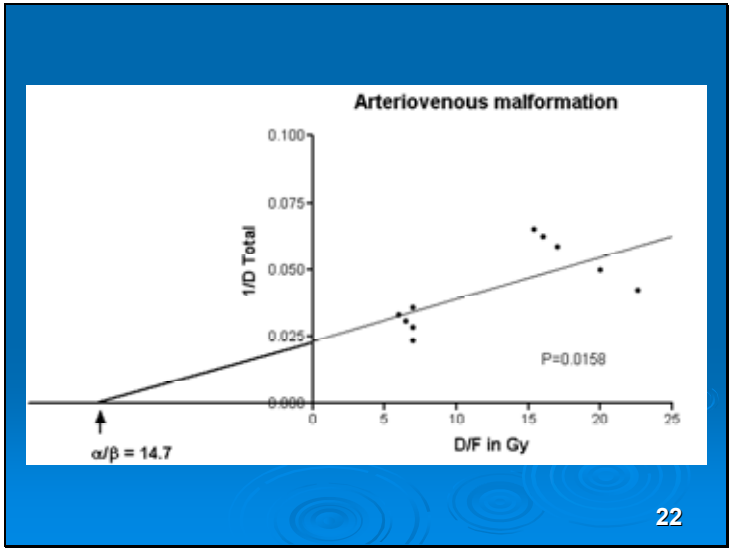


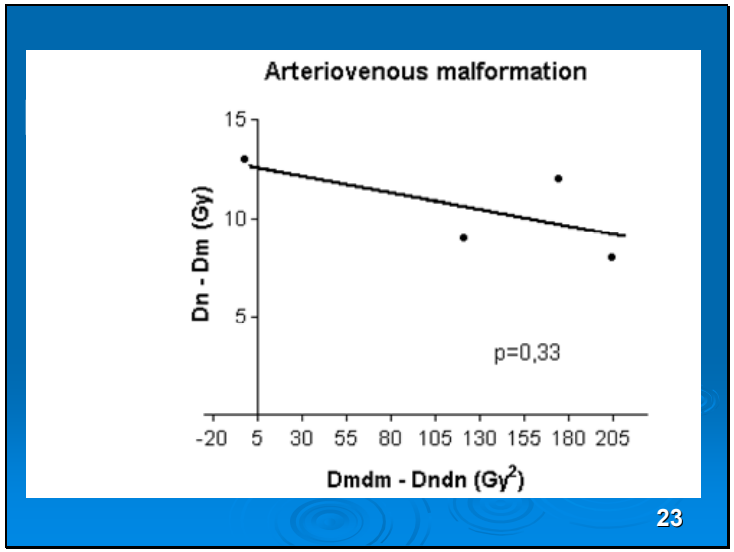
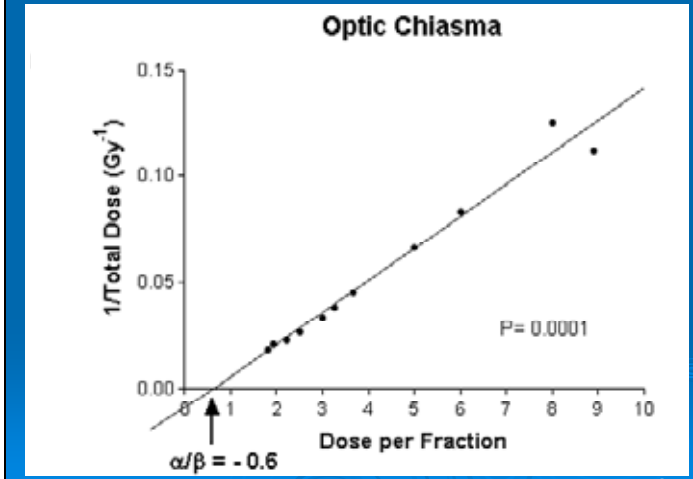




**Table 4: Optic chiasma radiation doses**

| Total dose | Dose / Fraction | Nr of Fractions | Optic Ret |
|---|---|---|---|
| 8.9* | 8.9 | 1 | 890 |
| 8* | 8 | 1 | 800 |
| 12* | 6 | 2 | 831 |
| 15** | 5 | 3 | 838 |
| 30*** | 3 | 10 | 885 |
| 37.5*** | 2.5 | 15 | 893 |
| 44* | 2.2 | 20 | 899 |
| 48*** | 2 | 24 | 891 |
| 54*** | 1.8 | 30 | 890 |
| 60.8*** | 1.6 | 38 | 884 |
| 66*** | 1.5 | 43 | 888 |
| 50* | 2 | 25 | 907 |

Total dose / fractionation schedules considered to be safe:
* Shrieve[65]
** Brenner[7]
*** Goldsmith[28]

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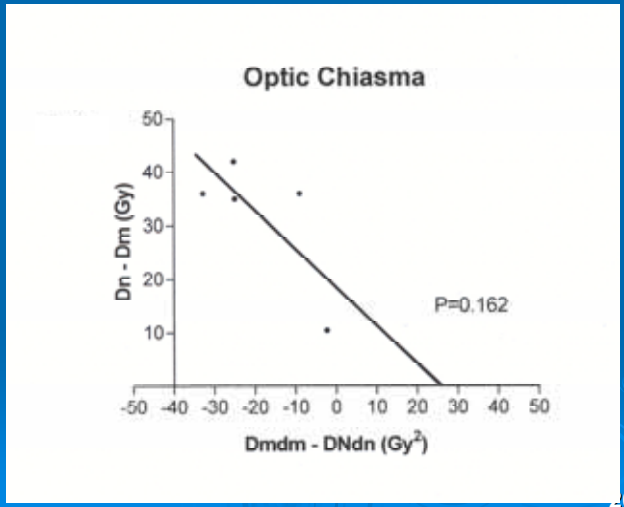


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**Table 5: Results**

| Author | AVM α/ß (Gy) | Author | Meningioma α/ß (Gy) | Author | Acoustic α/ß (Gy) |
|---|---|---|---|---|---|
| Kocher[40] *et al* | 3.5<br>4.6-6.4* | Vernimmen[73] *et al* | 3.7 | Linskey[45] *et al* | 2,5-4* |
| Wigg[75] *et al* | 10-14 | Shrieve[65] *et al* | 3.28 | Gross[27] *et al* | 1,6 |
| Hall & Brenner[28] *et al* | 0.2-5 | Henzel[24] *et al* | 2* | | |
| Vernimmen[74] *et al* | 9.4 | Gross[27] *et al* | 3.9 | | |
| Qi[60] *et al* | 2.1 | | | | |
| **This study**<br>FE plot<br>Tucker | 14.7<br>-5.7 | **This study**<br>FE plot<br>Tucker | 3.8<br>3.3 | **This study**<br>FE plot<br>Tucker | 2.4<br>1.8 |

* assumed not calculated
+ for small AVM volumes

**How valuable is the knowledge of these α/ß values?**

**The calculations of BED doses should be more clinically accurate**

**The α/ß value gives an indication of intrinsic value of fractionation**

**It allows to calculate tolerable dose/fractionation schedules for when the target is close to critical structures**

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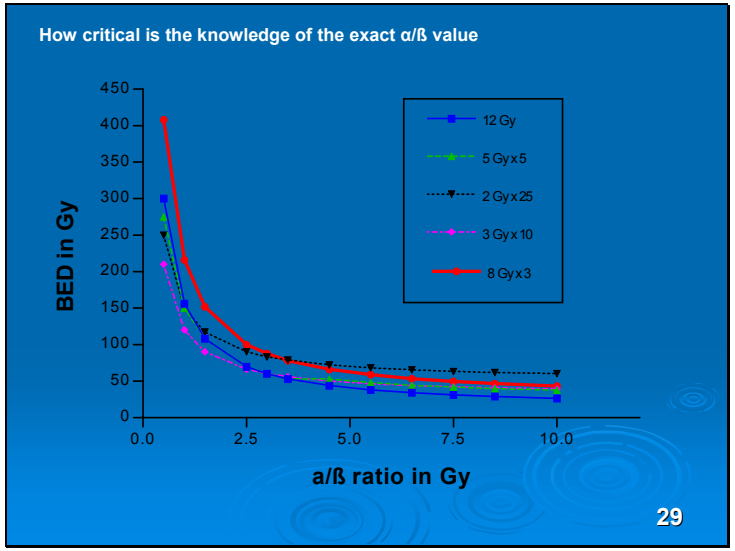
How critical is the knowledge of the exact α/ß value
BED in Gy
a/ß ratio in Gy
12 Gy
5 Gy x 5
2 Gy x 25
3 Gy x 10
8 Gy x 3
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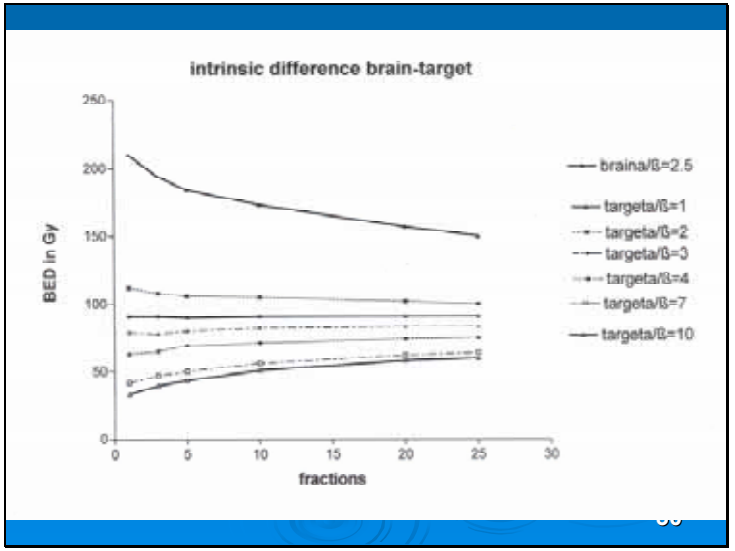
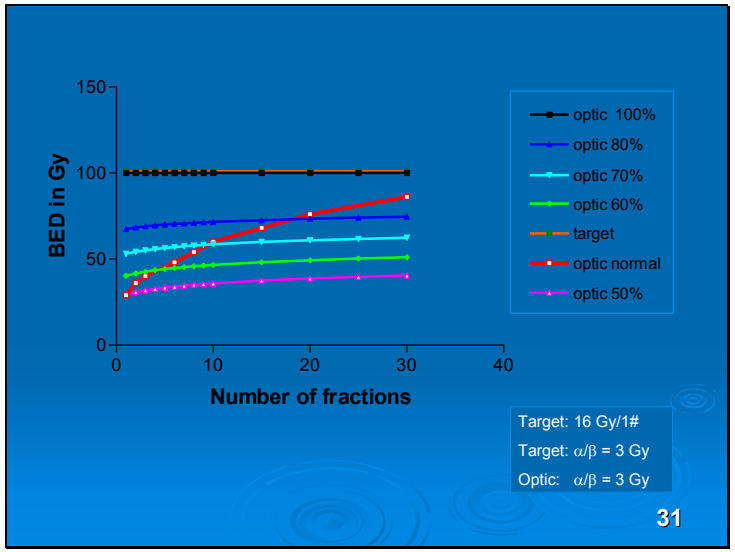

intrinsic difference brain-target
BED in Gy
fractions
braina/ß=2.5
targeta/ß=1
targeta/ß=2
targeta/ß=3
targeta/ß=4
targeta/ß=7
targeta/ß=10


BED in Gy
Number of fractions
optic 100%
optic 80%
optic 70%
optic 60%
target
optic normal
optic 50%
Target: 16 Gy/1#
Target: α/β = 3 Gy
Optic: α/β = 3 Gy
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THANK YOU