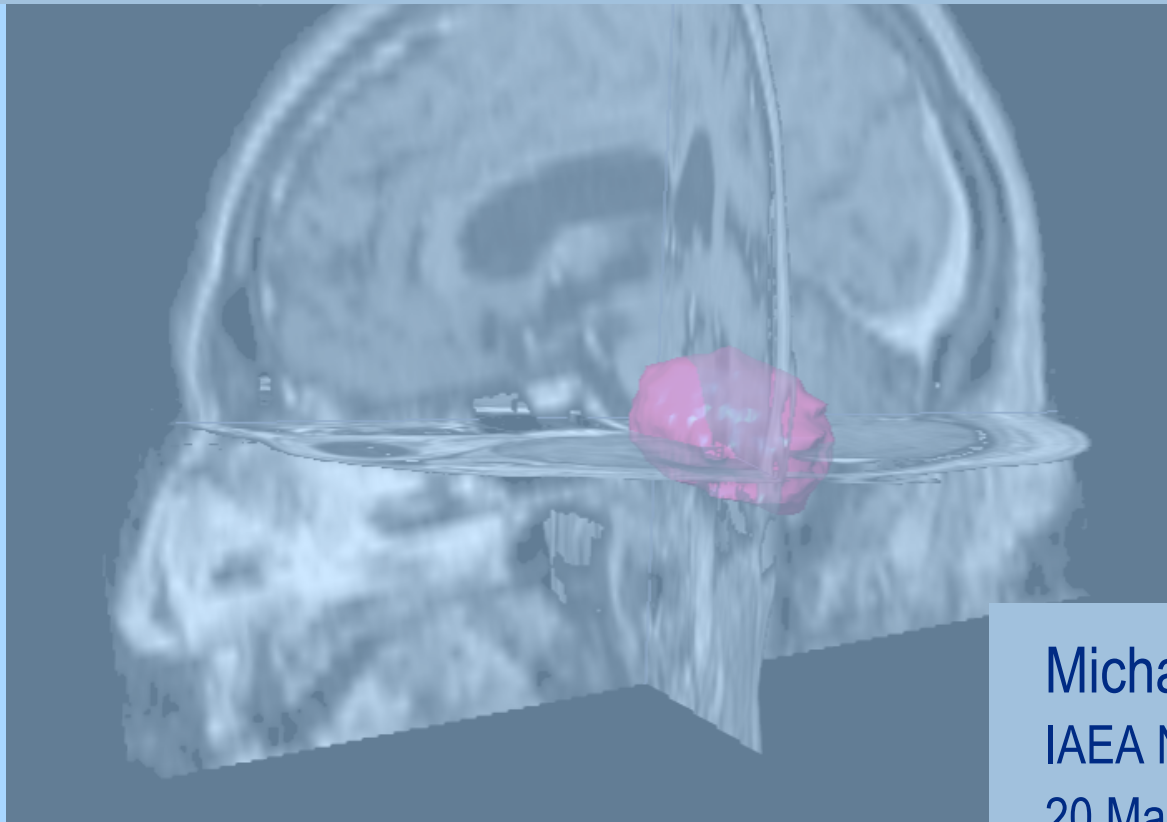
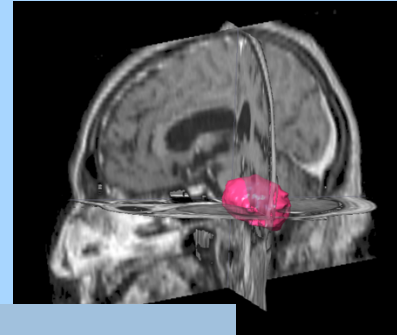


Evaluating outcome of fSRT/SRS for benign brain tumours



Michael Brada
IAEA NTC Bratislava
20 March 2018

Principles



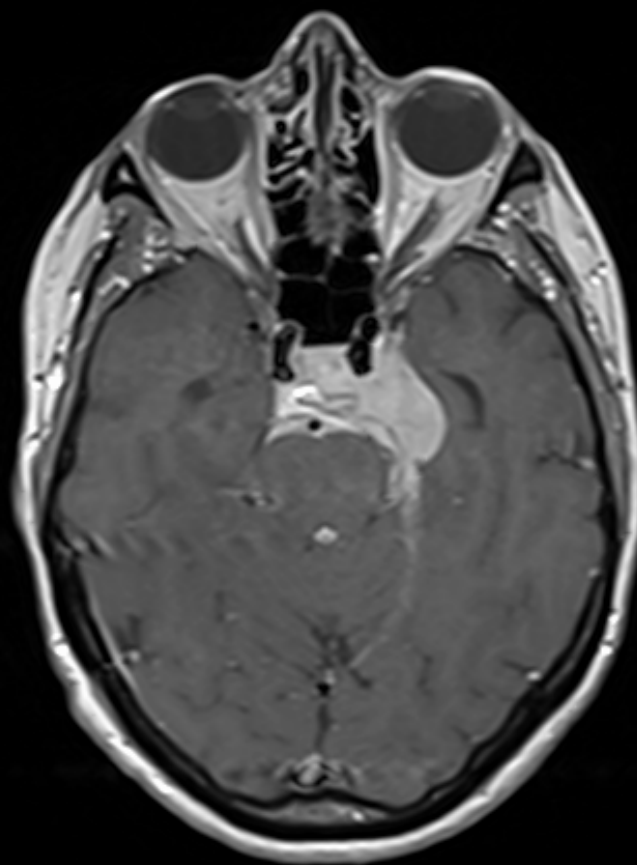
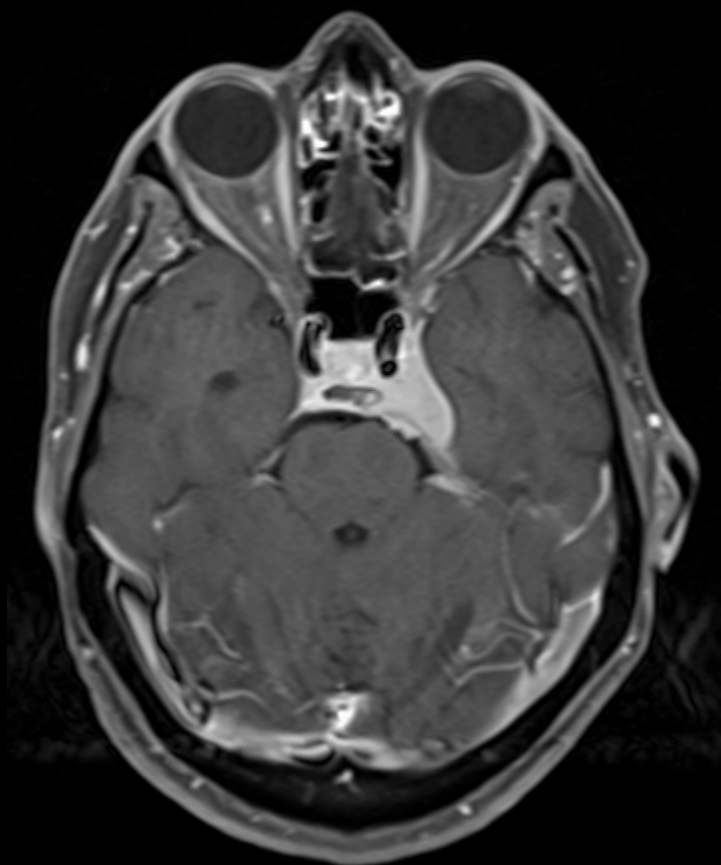
indolent tumours

long natural history

rarely life threatening

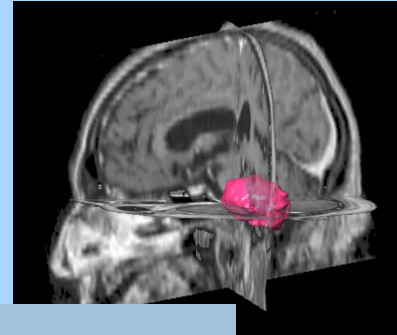
radiotherapy - one of available options

Management of benign brain tumours



no treatment for 3.5 years

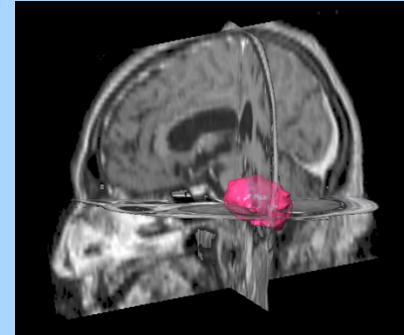
Radiotherapy prerequisites



need to understand:
natural history
imaging
other treatment options

balance of risks

Management of benign brain tumours



Surveillance	Surgery
Radiotherapy	Medical therapy

Management options in benign brain tumours

Benign brain tumours

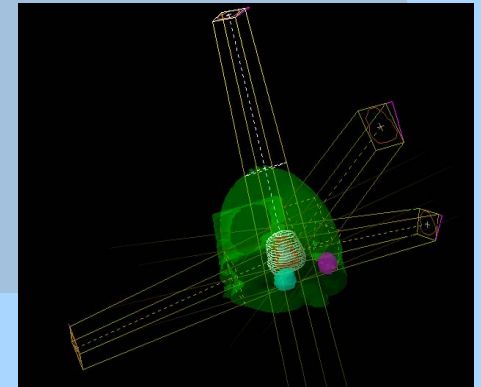
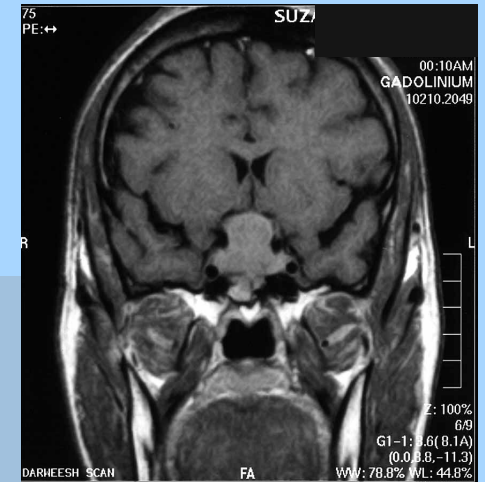
pituitary adenoma

craniopharyngioma

acoustic neuroma

skull base meningioma

childhood low grade glioma



Management of benign brain tumours

Benign brain tumours

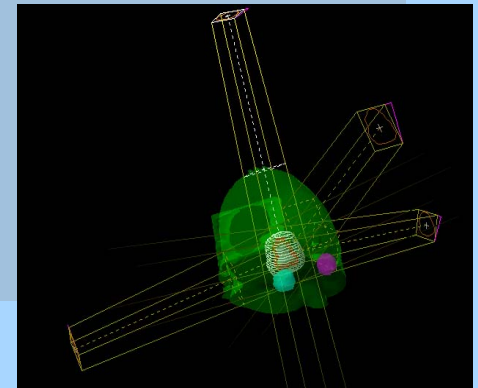
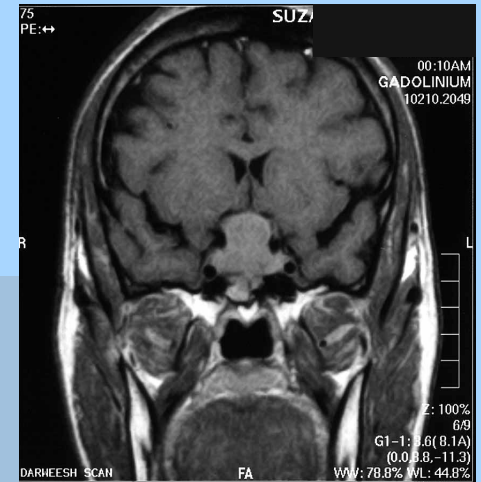
pituitary adenoma

craniopharyngioma

acoustic neuroma

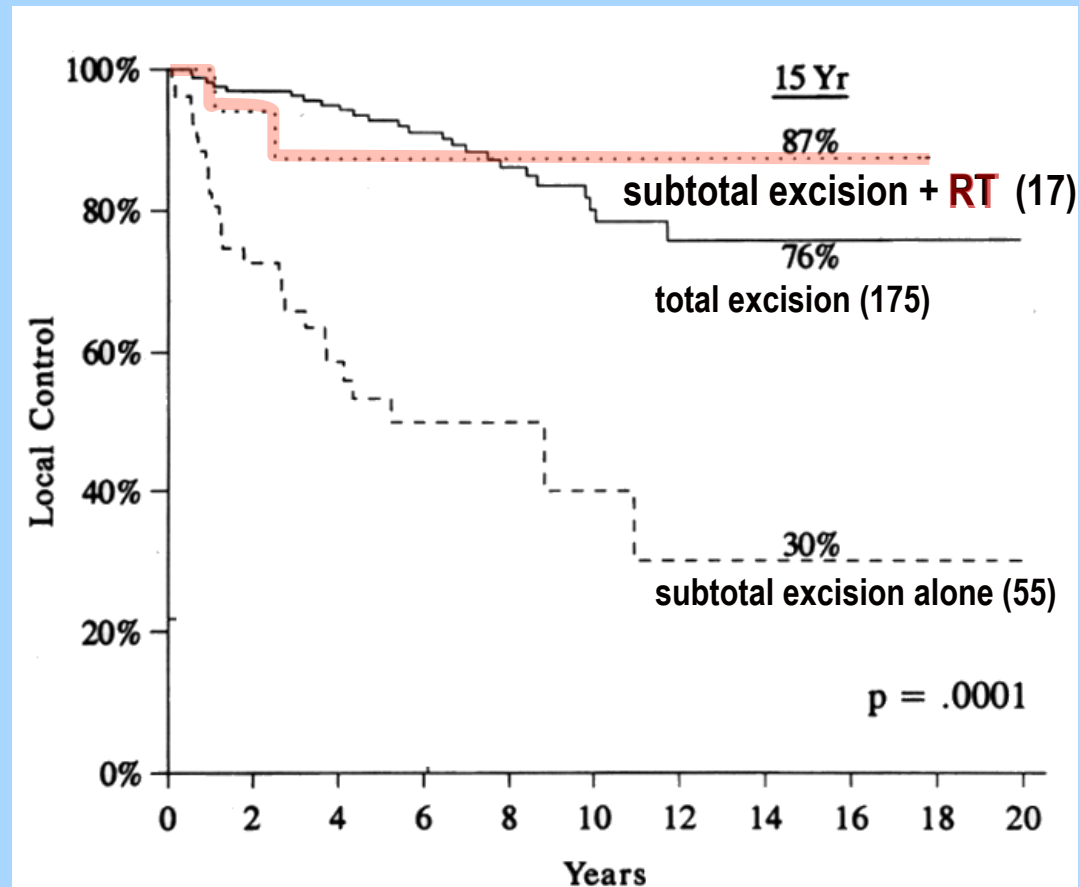
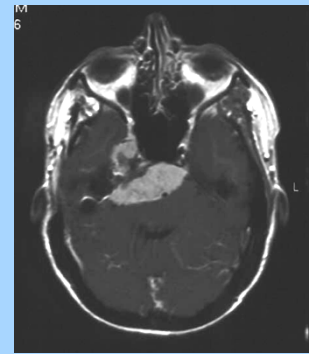
skull base meningioma

childhood low grade glioma



Management of benign brain tumours

Tumour control - surgery and radiotherapy



Radiotherapy in meningioma

Stereotactic radiotherapy for WHO grade I skull base meningioma

is best treated while asymptomatic

single fraction radiosurgery is the best radiation technique

fractionated stereotactic is the best radiation technique

tumour control rate is the same for conventional and fractionated stereotactic RT

tumour debulking is important prior to radiotherapy

Endpoints

Efficacy

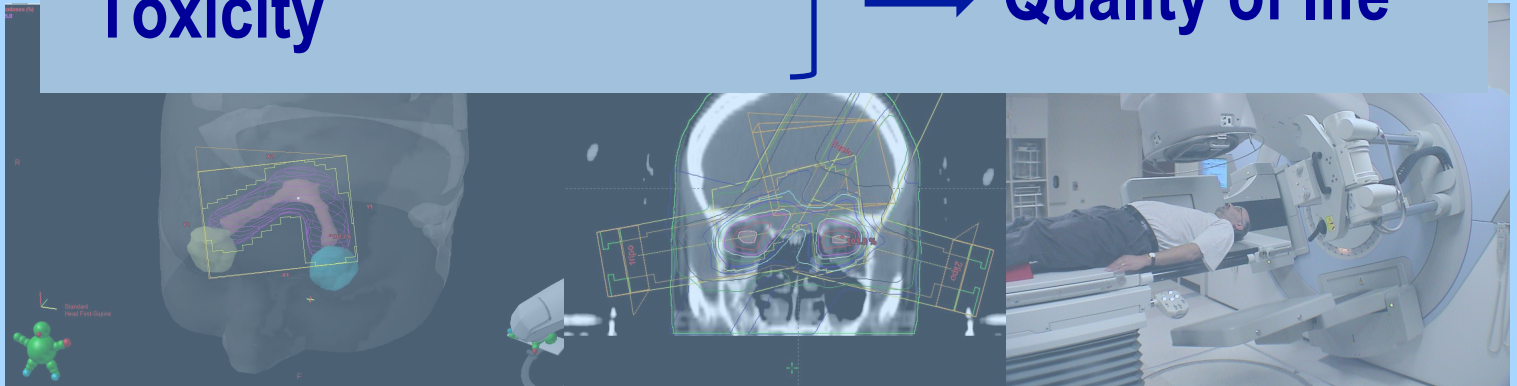
Actuarial tumour control

→ Survival

Functional benefit

Toxicity

} → Quality of life



Radiotherapy in meningioma

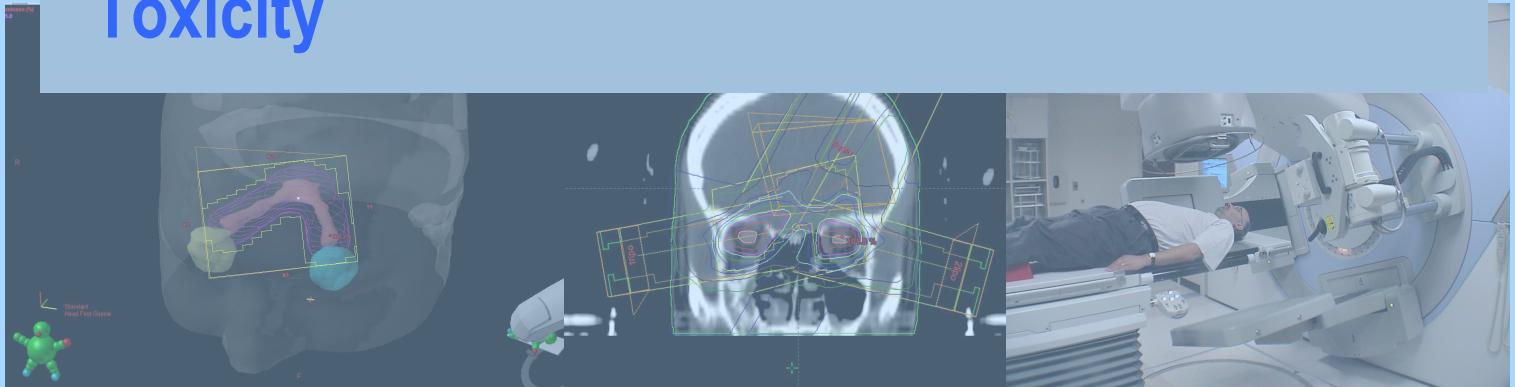
Endpoints

Efficacy

Actuarial tumour control

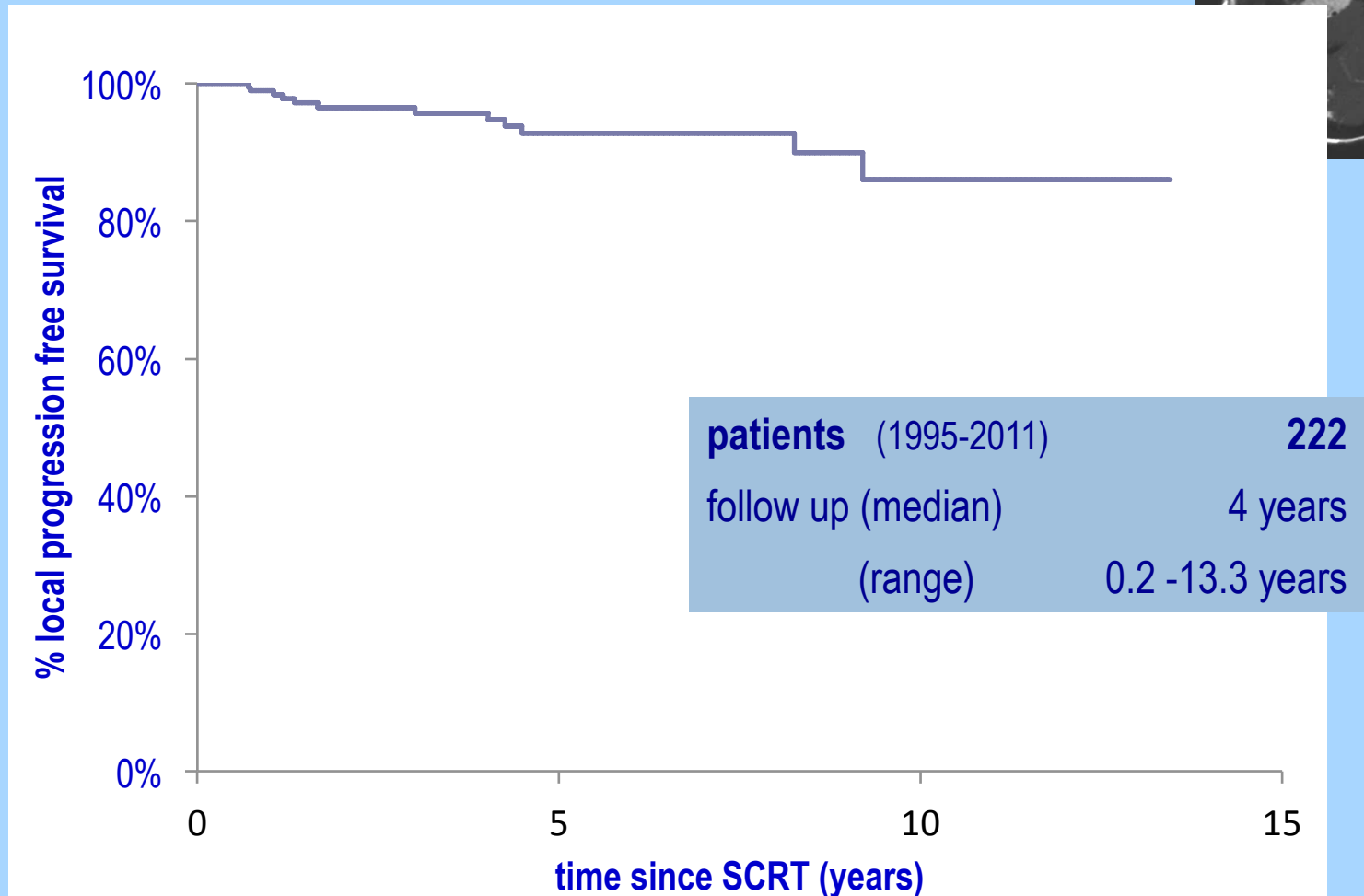
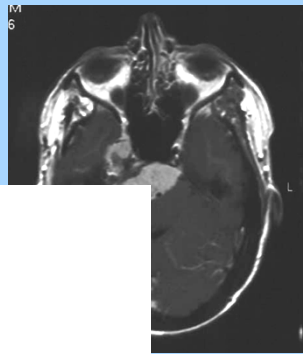
Functional benefit

Toxicity



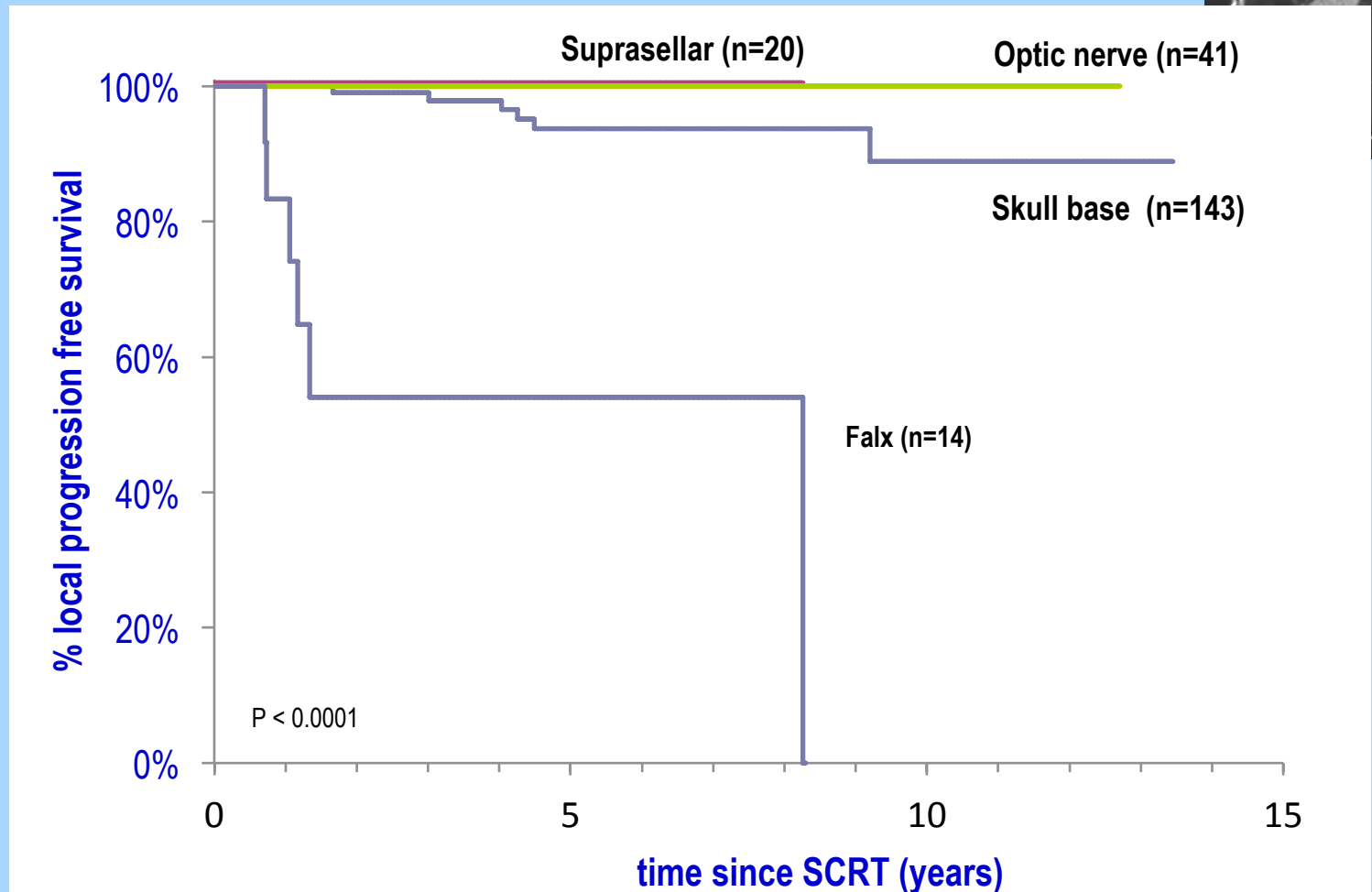
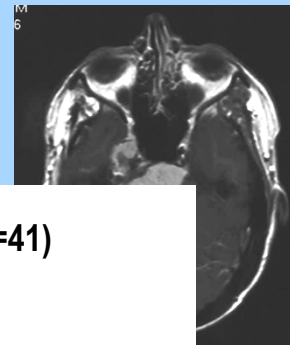
Radiotherapy in meningioma

Tumour control (benign meningioma)



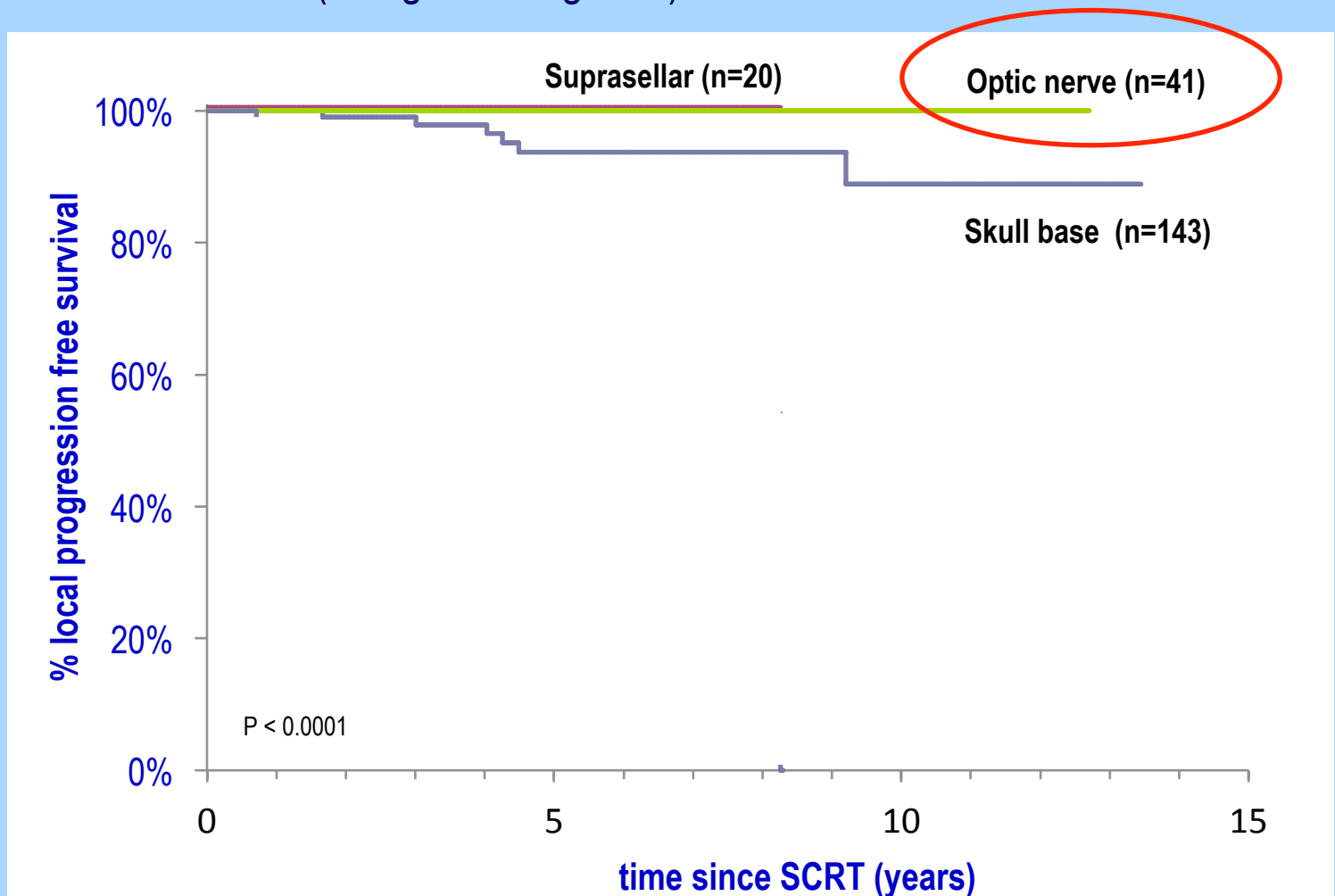
Fractionated stereotactic radiotherapy

Tumour control (benign meningioma)

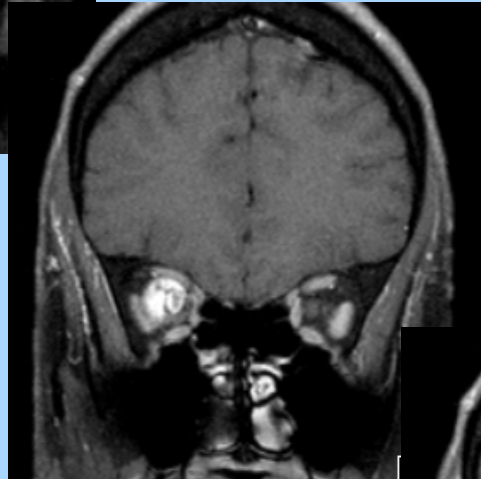
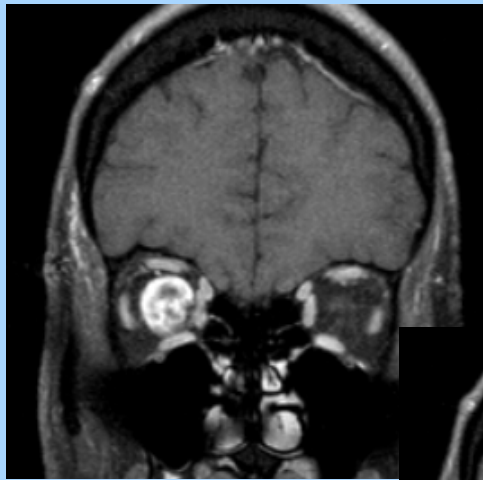


Fractionated stereotactic radiotherapy

Tumour control (benign meningioma)

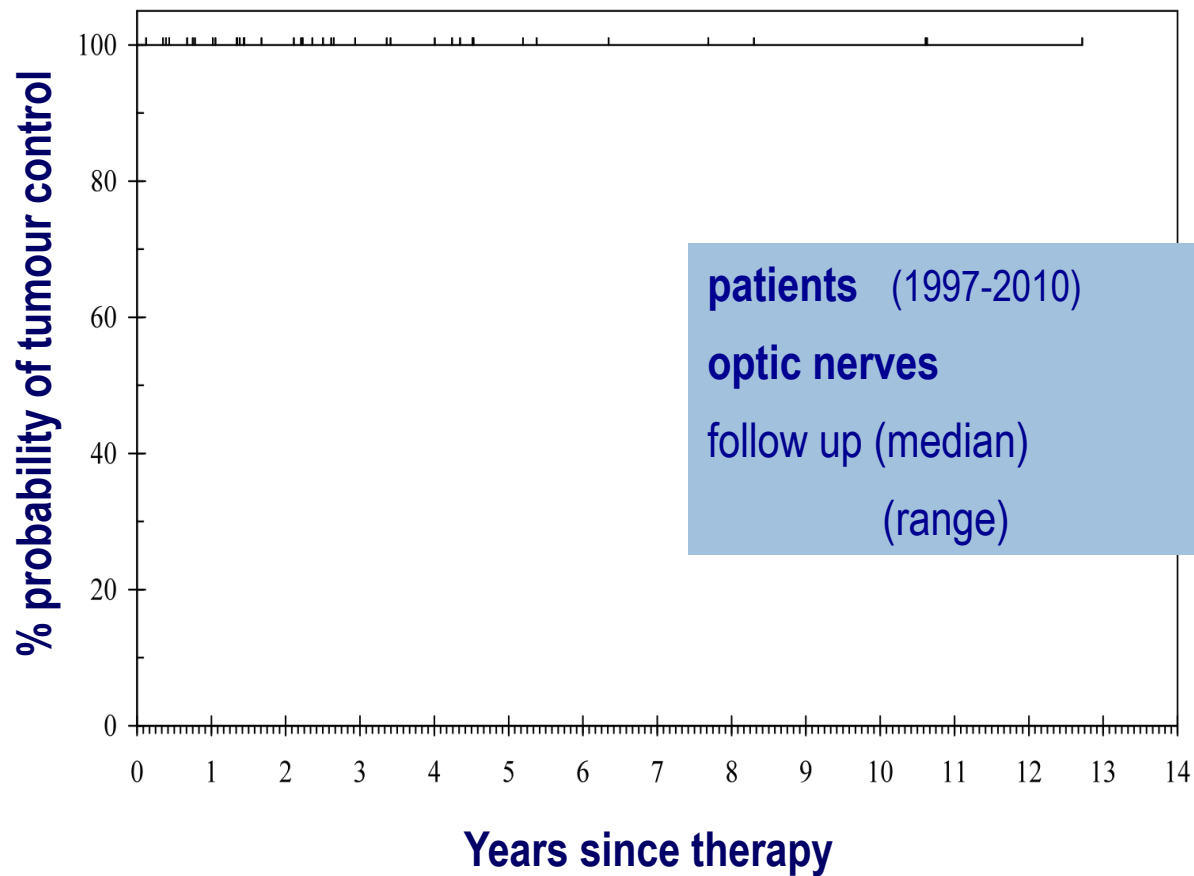
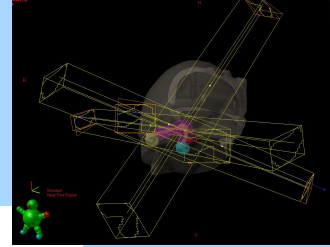


Fractionated stereotactic radiotherapy



Optic nerve sheath meningioma

Tumour control (optic nerve sheath meningioma)



Optic nerve sheath meningioma

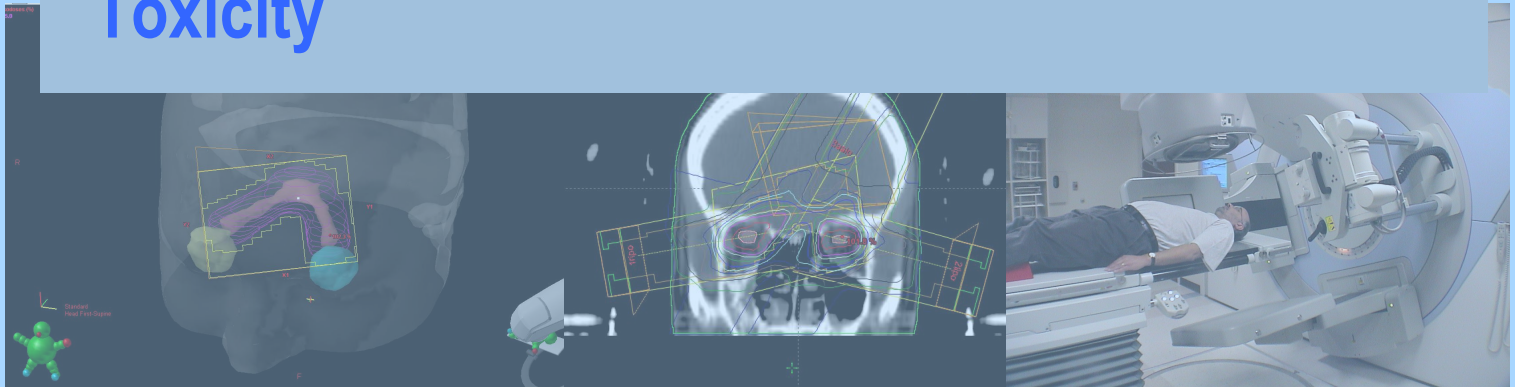
Endpoints

Efficacy

Actuarial tumour control

Functional benefit

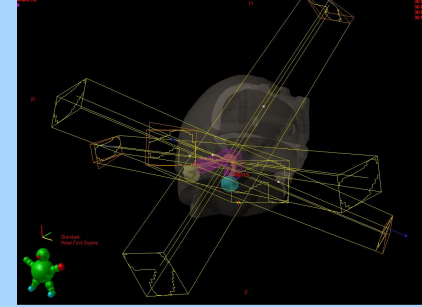
Toxicity



Meningioma radiotherapy

Visual status

51 (46 evaluable) optic nerves



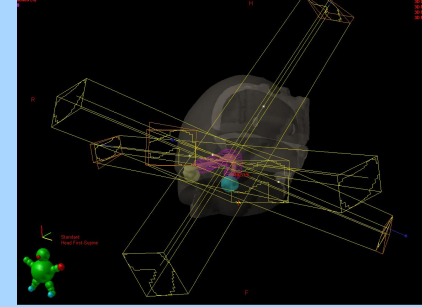
<i>vision at presentation</i>	<i>vision at follow up</i>			<i>Total</i>
	<i>improved</i>	<i>stable</i>	<i>deteriorated</i>	
normal	-	3	0	3
impaired	13	21	4	38
blind	0	5	-	5

Optic nerve sheath meningioma & vision

Solda, Wharram, Gunapala, Brada 2012, Clin Oncol. 24 (8):e106-12

Visual status

51 (46 evaluable) optic nerves



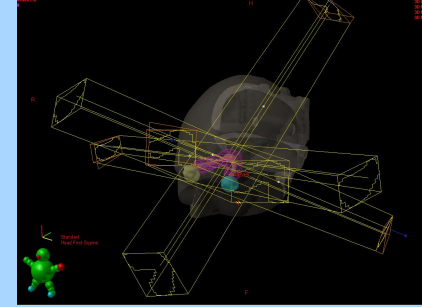
<i>vision at presentation</i>	<i>vision at follow up</i>			<i>Total</i>
	<i>improved</i>	<i>stable</i>	<i>deteriorated</i>	
normal	-	3	0	3
impaired	13	21	4	38
overall	34%	55%	18%	
	89%			

Optic nerve sheath meningioma & vision

Solda, Wharram, Gunapala, Brada 2012, Clin Oncol. 24 (8):e106-12

Visual status

Review of published literature to 2011

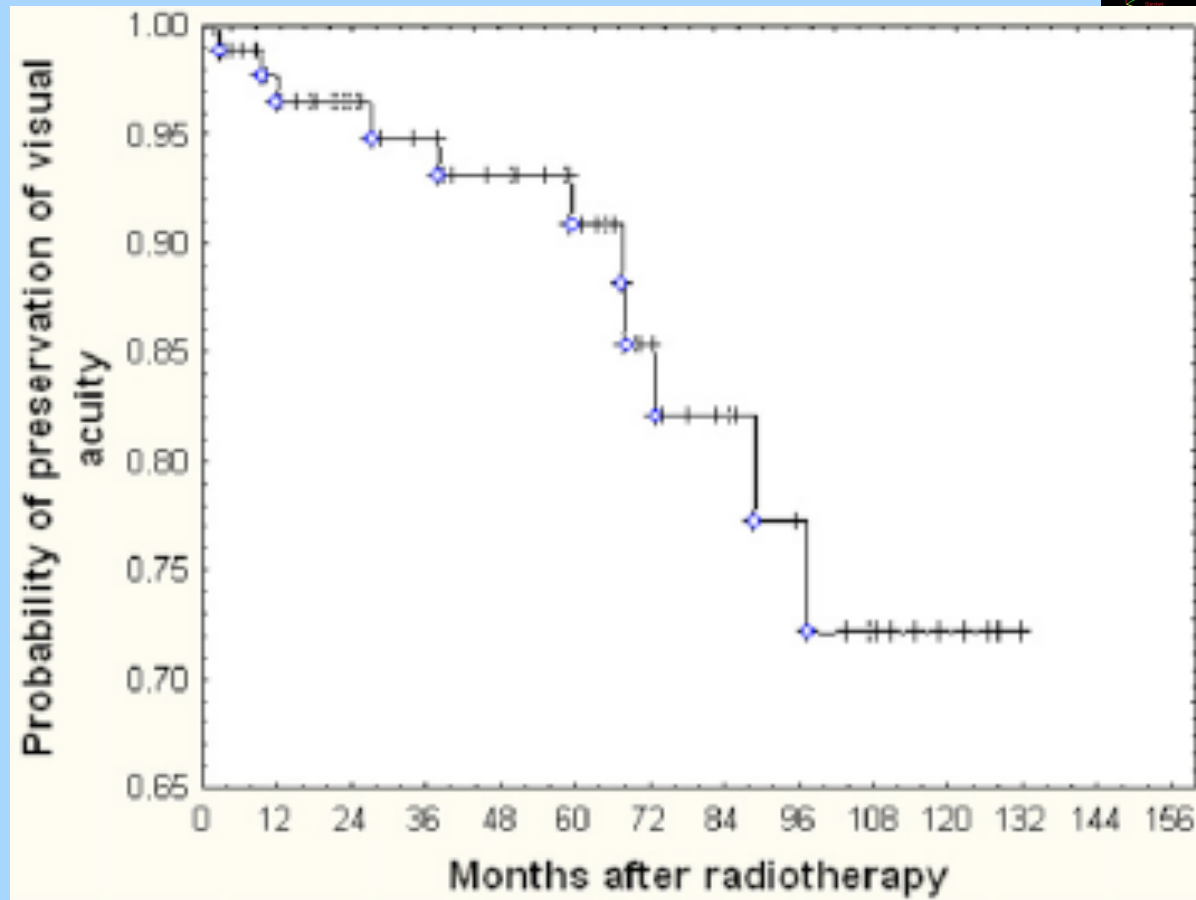


<i>vision at presentation</i>	<i>vision at follow up</i>			<i>Total</i>
	<i>improved</i>	<i>stable</i>	<i>deteriorated</i>	
not defined	82%		18%	290

Optic nerve sheath meningioma & vision

Solda, Wharram, Gunapala, Brada 2012, Clin Oncol. 24 (8):e106-12

Visual status



Optic nerve sheath meningioma & vision

Endpoints

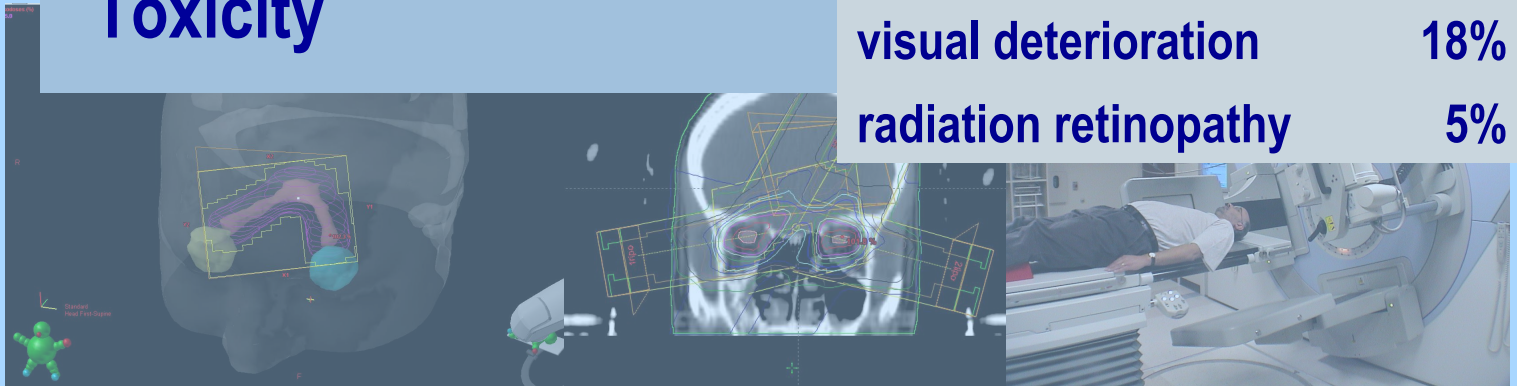
Efficacy

Actuarial tumour control

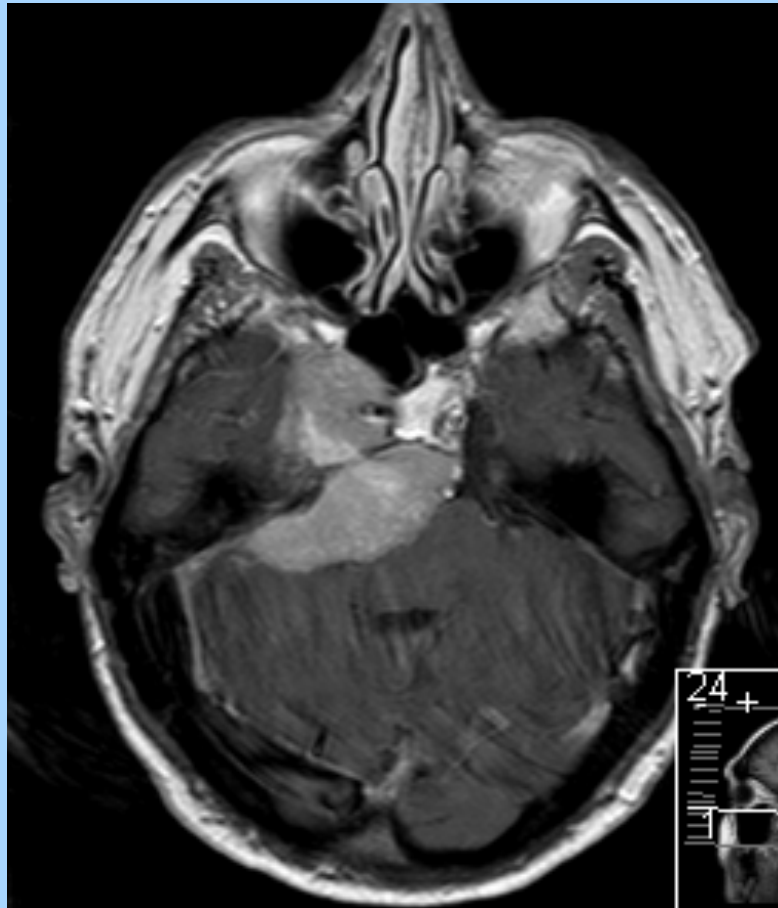
Functional benefit

Toxicity

visual deterioration	18%
radiation retinopathy	5%

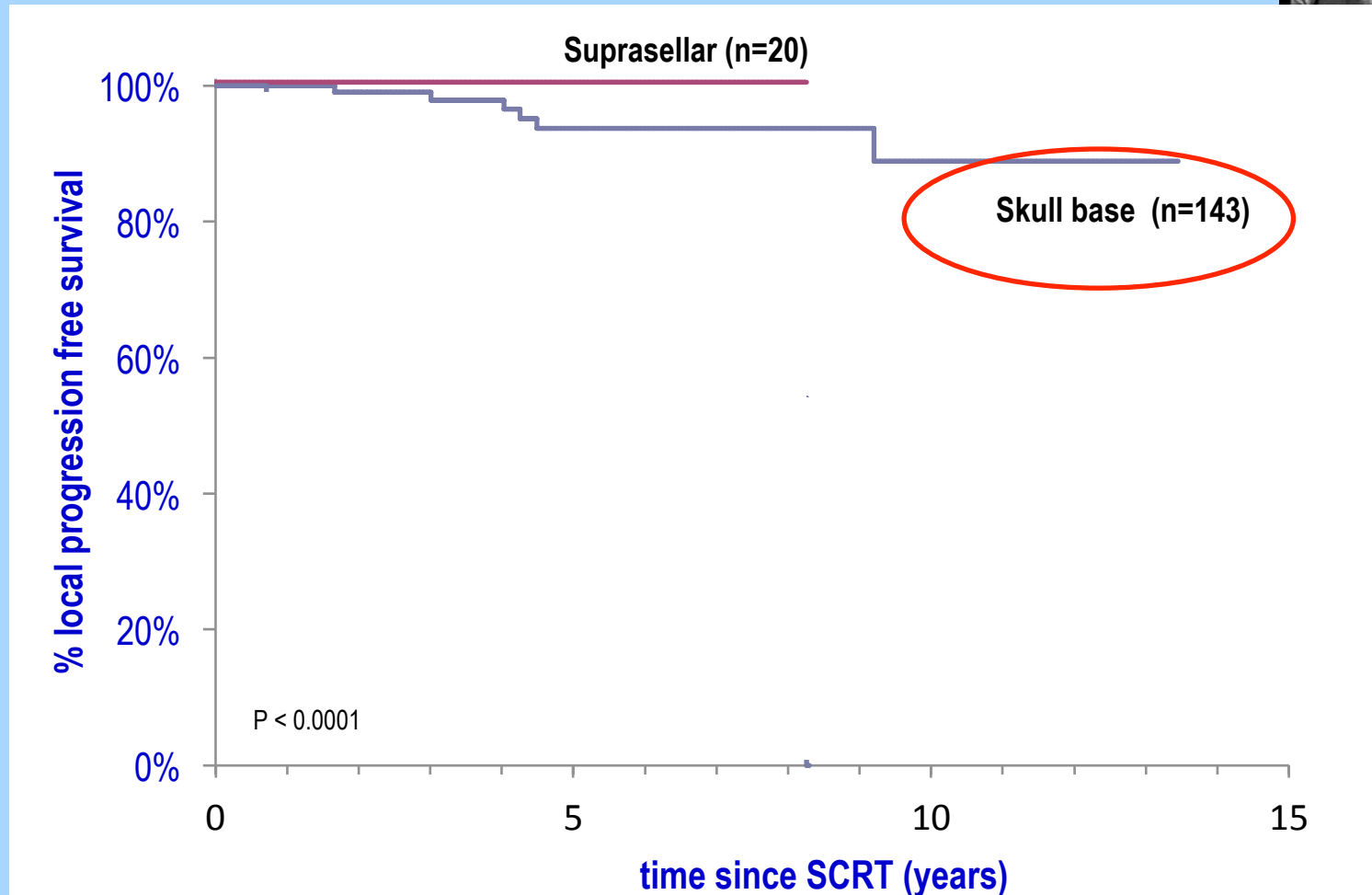


Optic nerve sheath meningioma



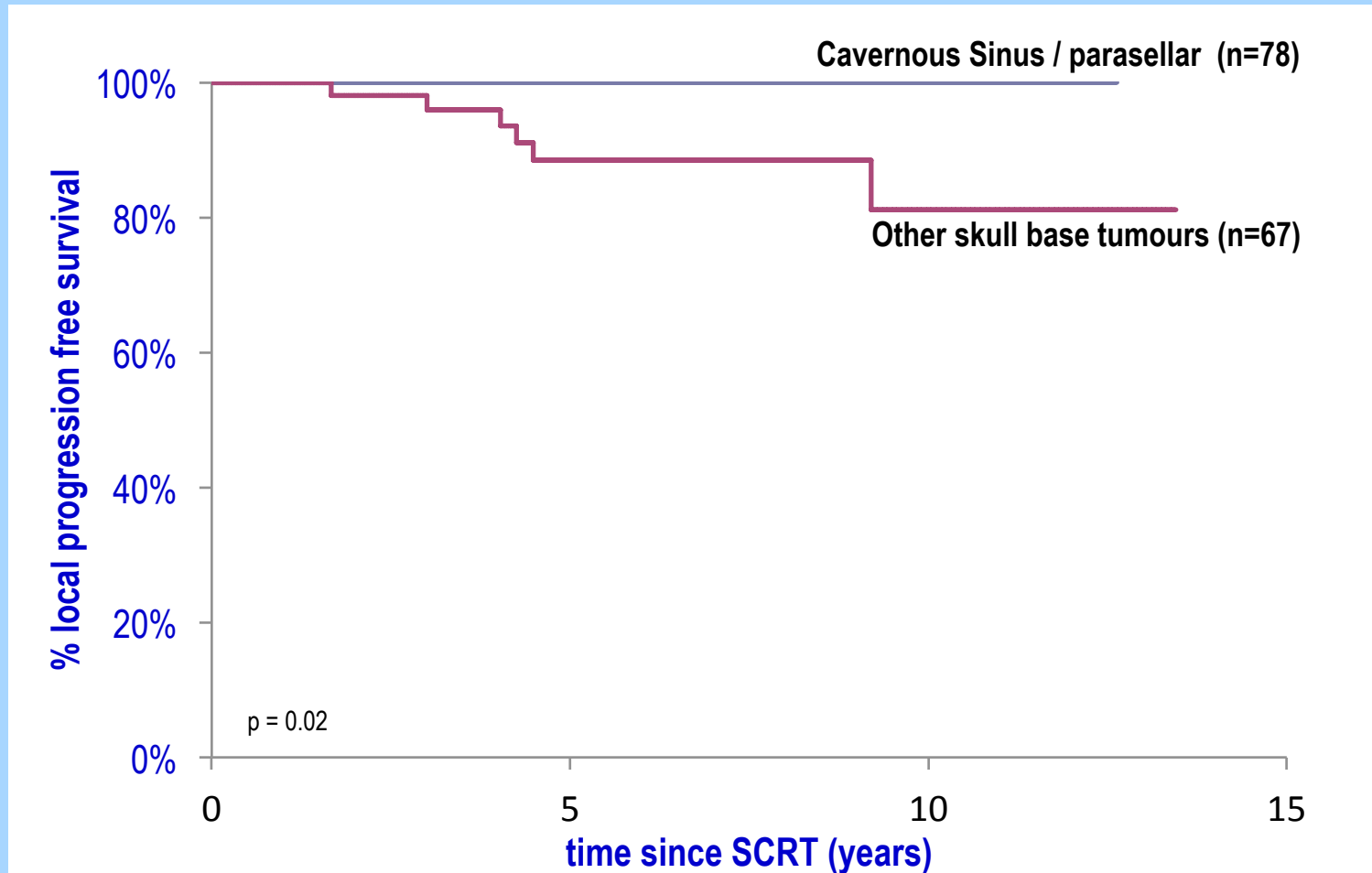
Radiotherapy in meningioma

Tumour control



Fractionated stereotactic radiotherapy

Tumour control (skull base meningioma)



Fractionated stereotactic radiotherapy

Comparison of results in grade I meningioma

Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy		
single fraction radiosurgery (GK)		
fractionated stereotactic RT		

GK - gamma knife

RT - radiotherapy

PFS - progression free survival

Radiotherapy in meningioma

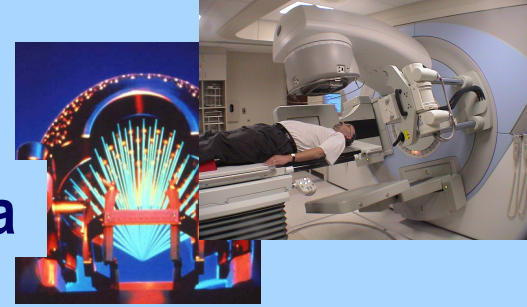
Systematic review - methodology



Meningioma ref.	Number of patients	follow up (months)	5 year PFS (%)	mean dose (Gy)	% late toxicity
Jalali '02	41	21	100	57	1.6
Lo '02	18	30.5	n/a	55	12.1
Torres '03	77	24	n/a	54	5
Selch '04	45	36	n/a	49	5.2
Milker-Zabel '05	317	67	91	56	0
Henzel '06	84	30	97	58	8.2
Brell '06	30	50	93 at 4 years	56	n/a
Hamm '08	183	36	97	52	6.6
Litre '09	100	33	94 at 3 years	56	8.2
Metellus '10	47	82.8	98	45	0
Tanzler '10	144*	96	n/a	53	2.6
Minniti '11	52	42	93	53	7
Onodera '11	27	63	100	50	5.5
Mean (weighted)	1169	50	94%	54	5%

Fractionated stereotactic radiotherapy

Comparison of results in grade I meningioma



Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy		
single fraction radiosurgery (GK)		
fractionated stereotactic RT		

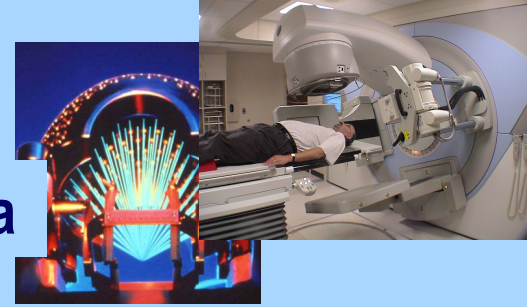
GK - gamma knife

RT - radiotherapy

PFS - progression free survival

Radiotherapy in meningioma

Comparison of results in grade I meningioma



Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy	91%	8%
single fraction radiosurgery (GK)		
fractionated stereotactic RT		

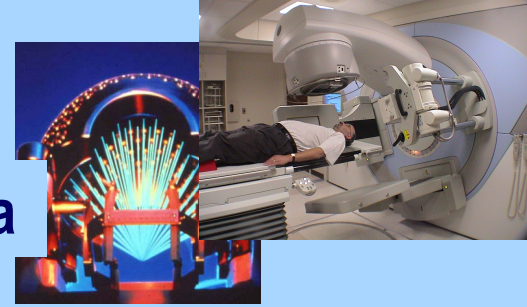
GK - gamma knife

RT - radiotherapy

PFS - progression free survival

Radiotherapy in meningioma

Comparison of results in grade I meningioma



Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy	91%	8%
single fraction radiosurgery (GK)		
fractionated stereotactic RT		

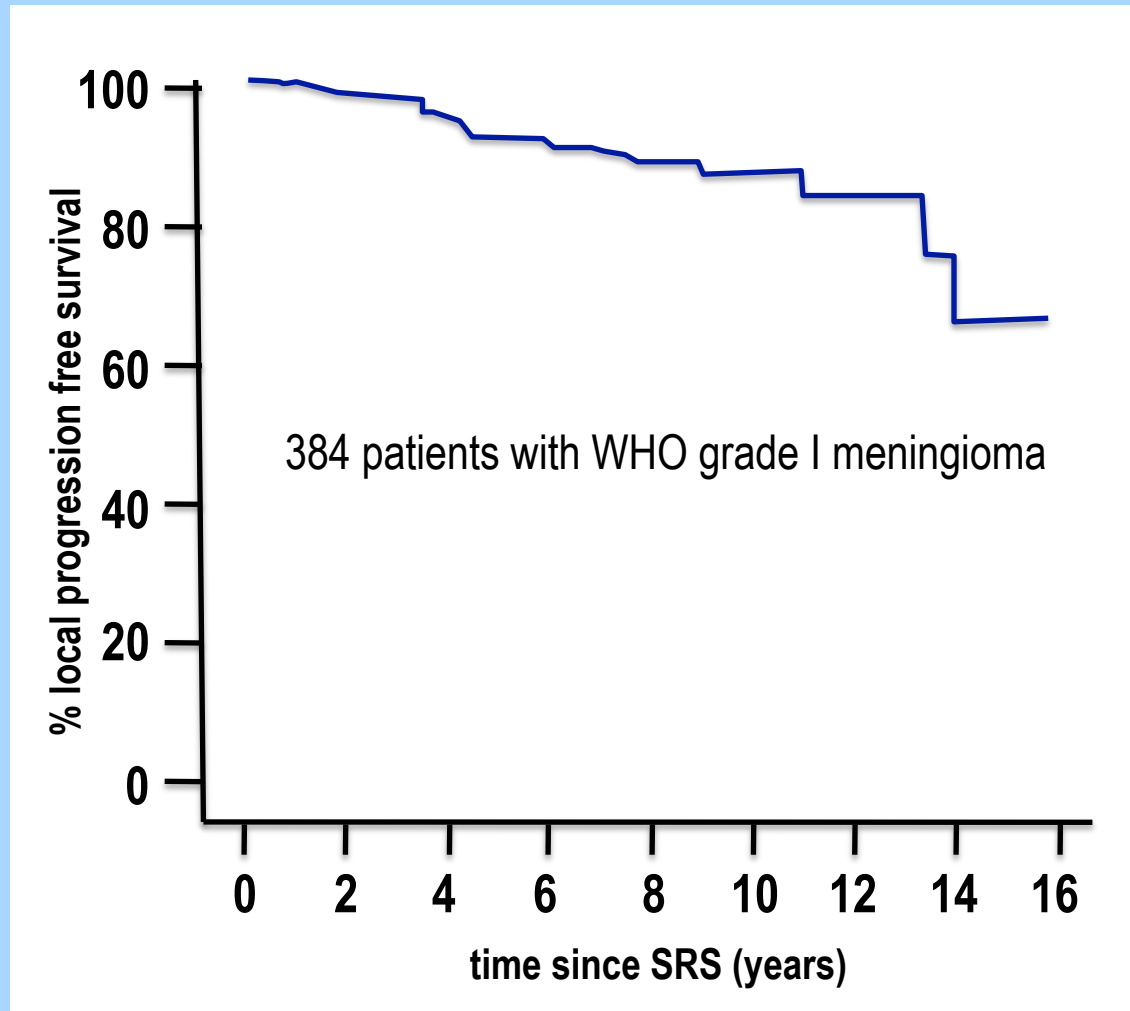
GK - gamma knife

RT - radiotherapy

PFS - progression free survival

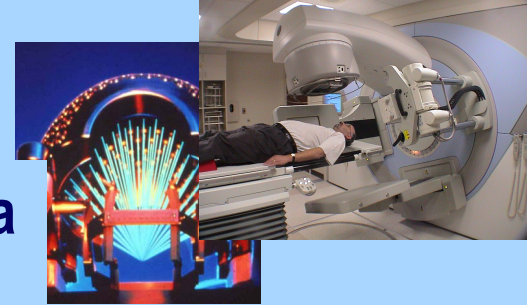
Radiotherapy in meningioma

Tumour control



Single fraction radiosurgery – gamma knife

Comparison of results in grade I meningioma systematic review of published literature up to 2011



Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy	91%	8%
single fraction radiosurgery (GK)	94%	8%
fractionated stereotactic RT		

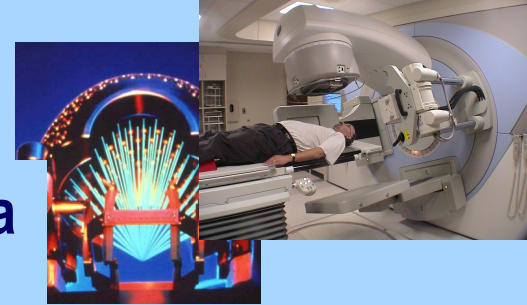
GK - gamma knife

RT - radiotherapy

PFS - progression free survival

Radiotherapy in meningioma

Comparison of results in grade I meningioma systematic review of published literature up to 2011



Treatment technique	5 year PFS (%)	late toxicity (%)
conventional radiotherapy	91%	8%
single fraction radiosurgery (GK)	94%	8%
fractionated stereotactic RT	94%	5%

GK - gamma knife

RT - radiotherapy

PFS - progression free survival

Radiotherapy in meningioma

Benign brain tumours

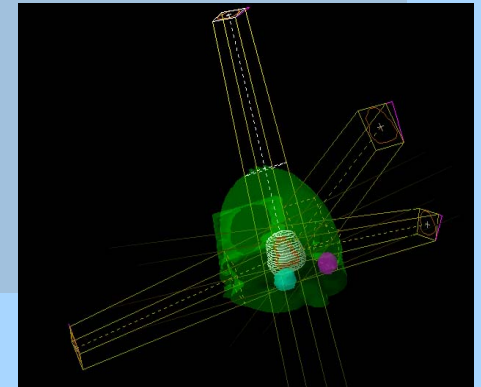
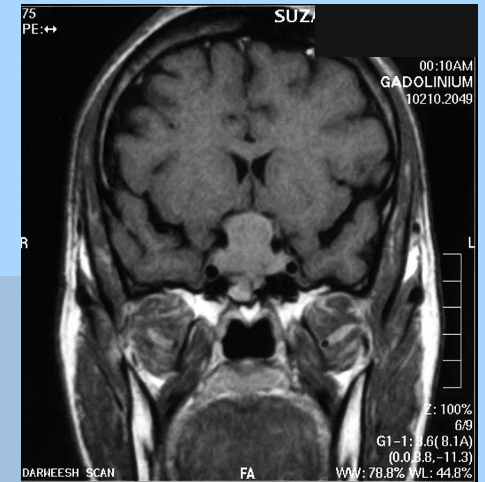
pituitary adenoma

craniopharyngioma

acoustic neuroma

skull base meningioma

childhood low grade glioma



Management of benign brain tumours

Fractionated radiotherapy in pituitary adenoma

prolongs survival

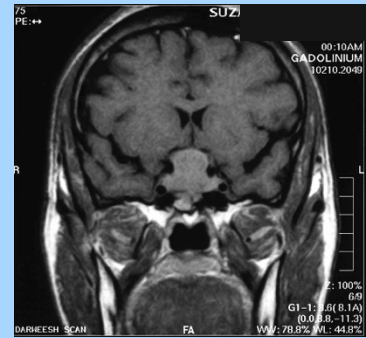
should be given soon after
incomplete resection

should avoid
hypothalamus

all of these

none of these

Pituitary adenoma



Efficacy

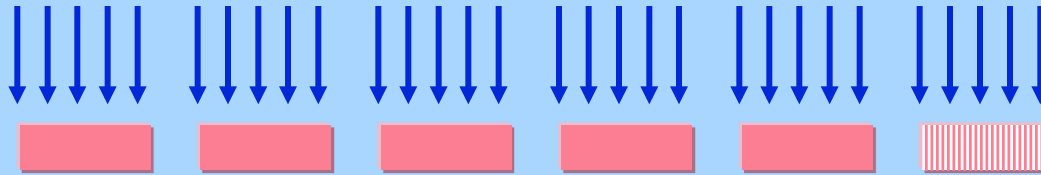
Actuarial tumour control

Endocrine control

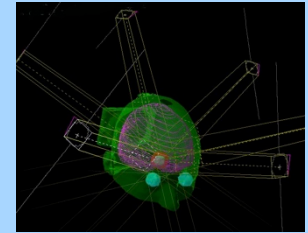
Toxicity

Endpoints in the evaluation of irradiation

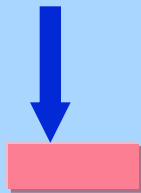
Fractionated high precision conformal radiotherapy



45 – 50 Gy in 25 - 30 fractions



Single fraction radiosurgery

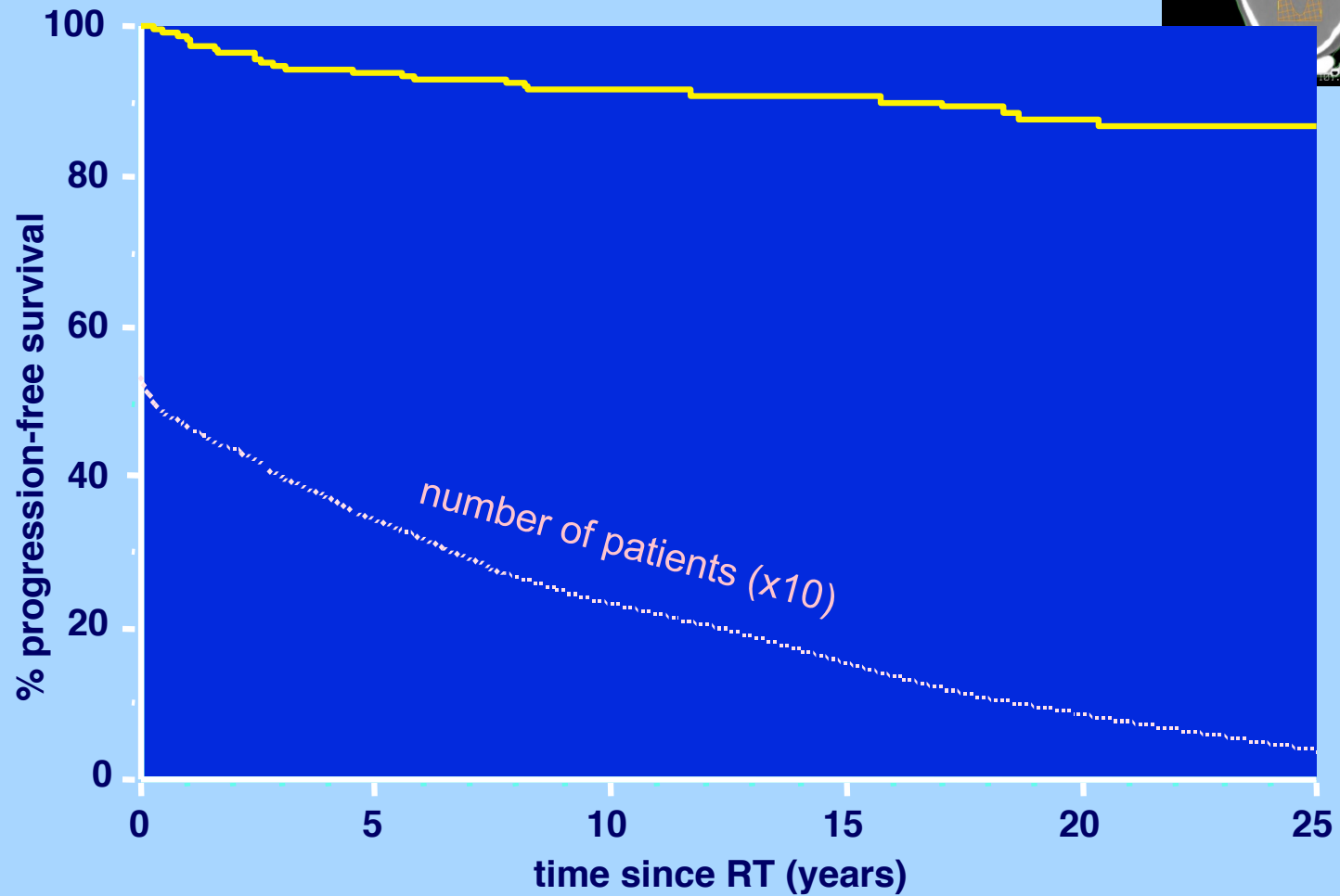
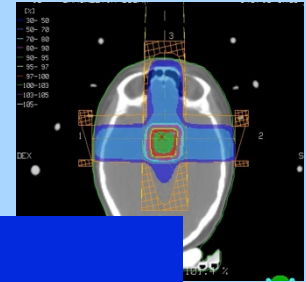


10 – 25 Gy in 1 fraction



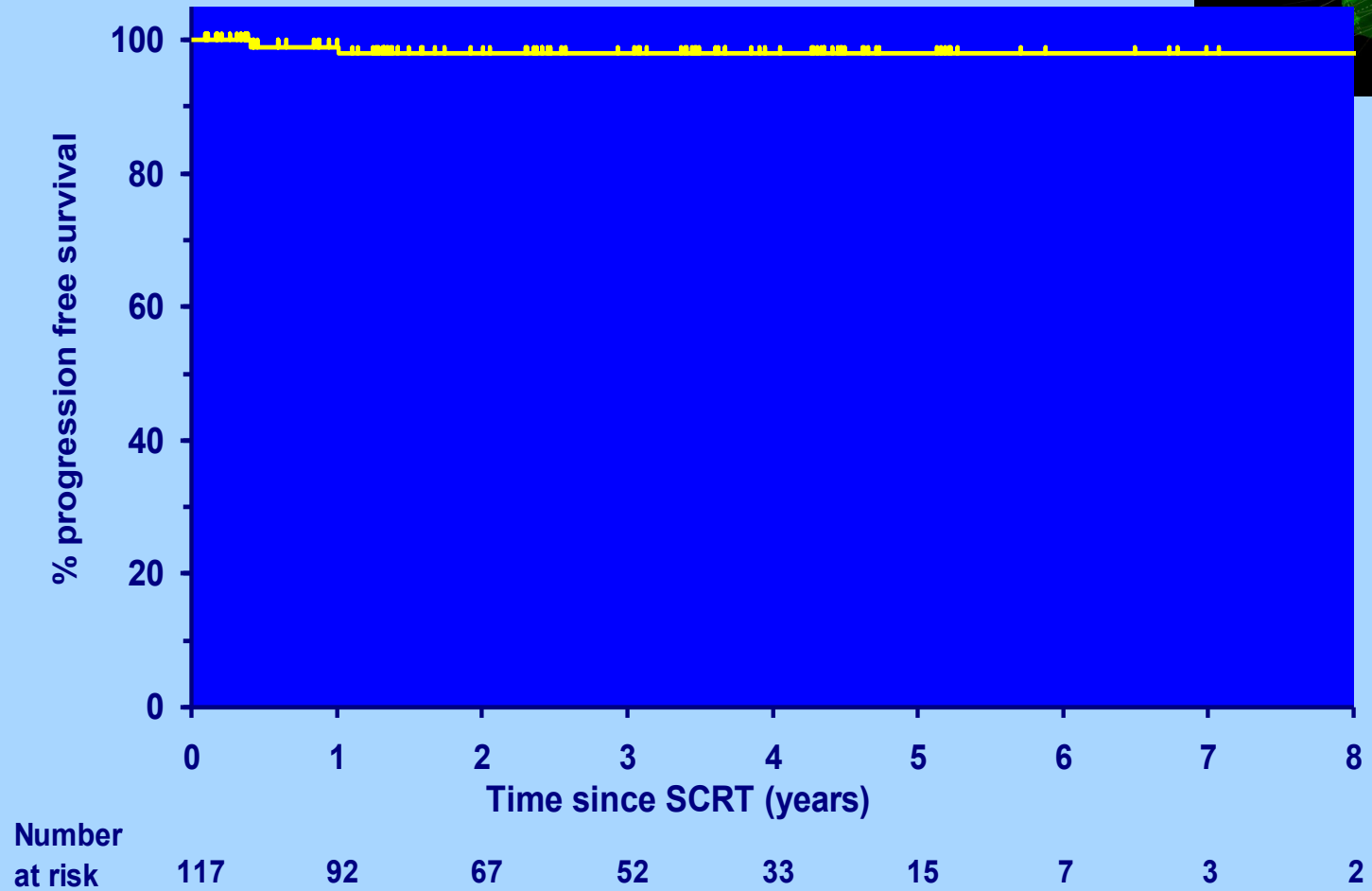
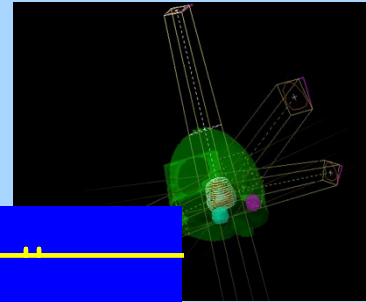
Comparison of high precision techniques

Tumour control



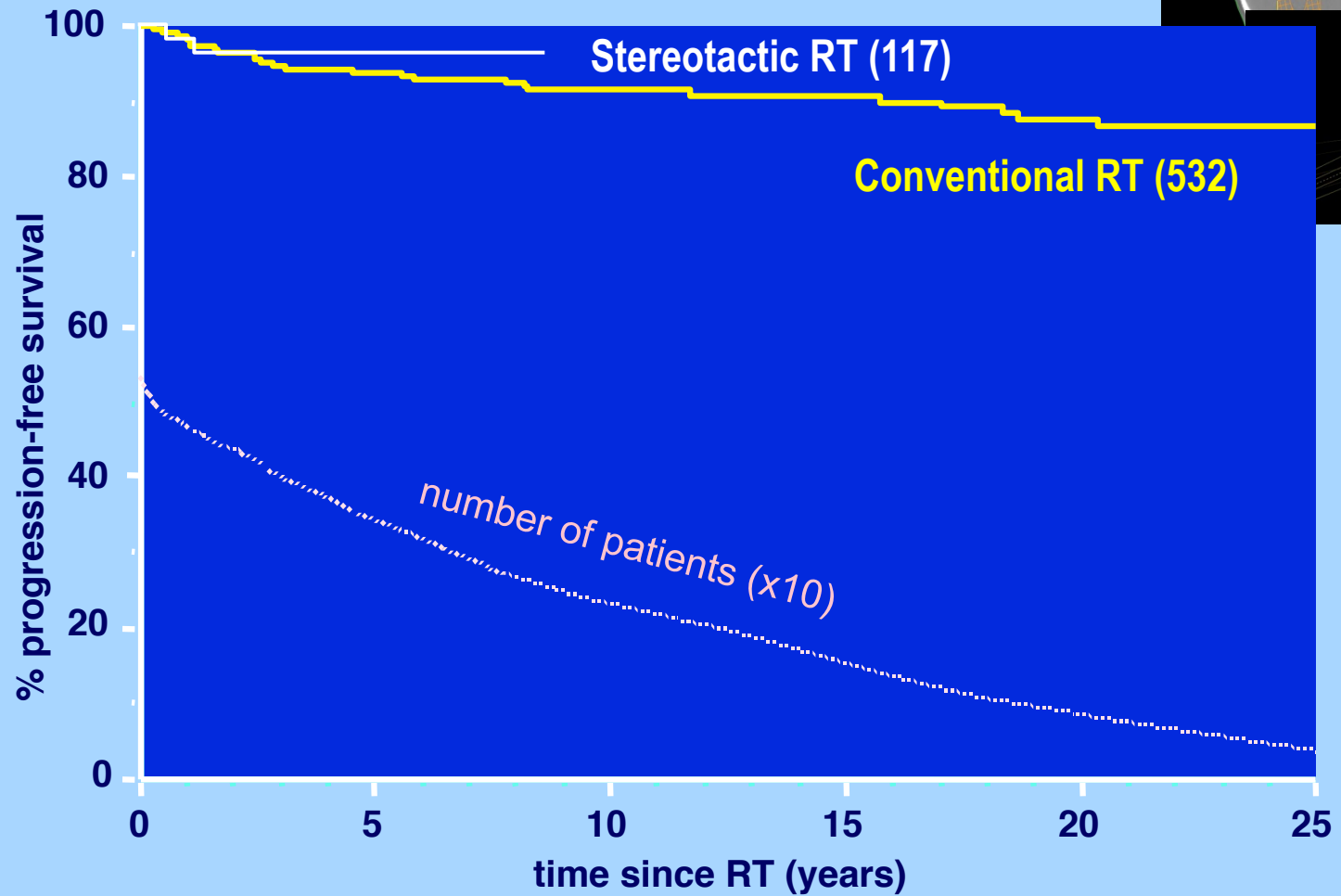
Conventional radiotherapy

Tumour control



Fractionated stereotactic radiotherapy (SCRT)

Tumour control



Conventional & stereotactic radiotherapy



Systematic review of published literature

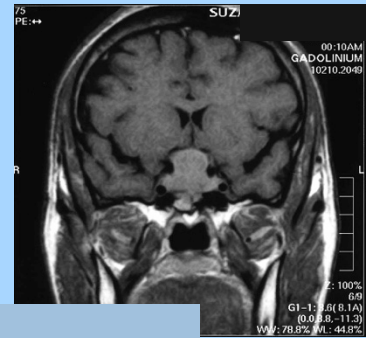
Nonfunctioning pit. adenoma	Number of patients	5 year PFS
Weighted mean	393	92%

Brada & Jankowska

Endocrinol Metab Clin N Am 37 (2008) 263–275

Gamma knife radiosurgery in nonfunctioning p.a.

Pituitary adenoma



Efficacy

Actuarial tumour control

Endocrine control

Toxicity

Stereotactic radiotherapy similar to conventional RT
GK radiosurgery worse than fractionated RT

Endpoints in the evaluation of irradiation

Pituitary adenoma

Efficacy

Actuarial tumour control

Endocrine control

Toxicity

Endpoints in the evaluation of irradiation

Radiotherapy in hormone secreting pituitary adenoma

is the primary treatment for persistent elevation of GH after surgery for acromegaly

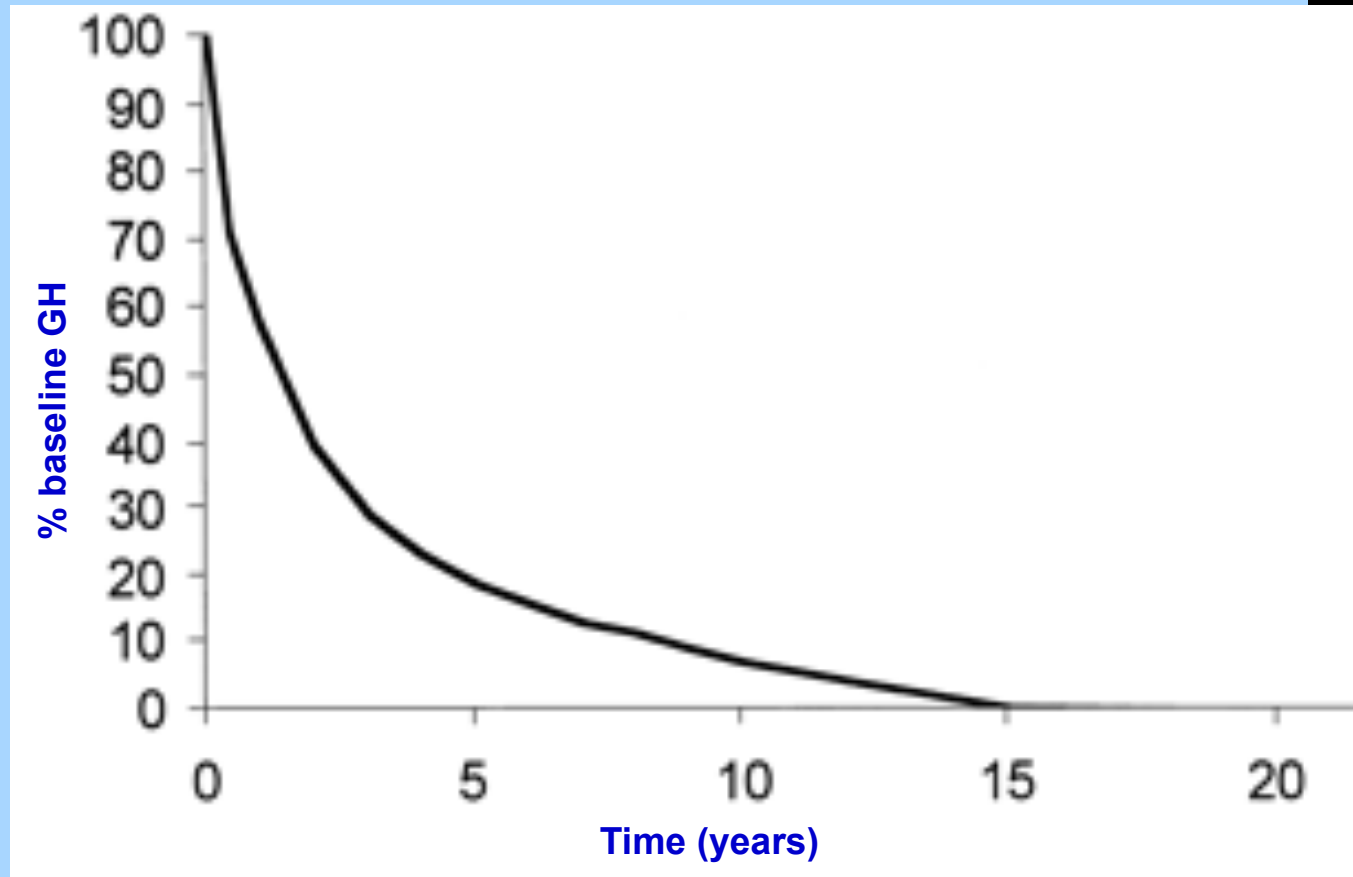
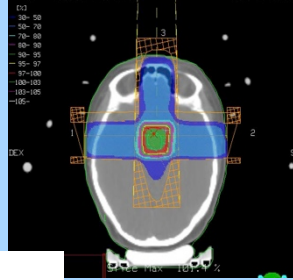
higher total dose leads to faster hormone decline

radiosurgery compared to fractionated treatment leads to faster hormone decline

all of these

none of these

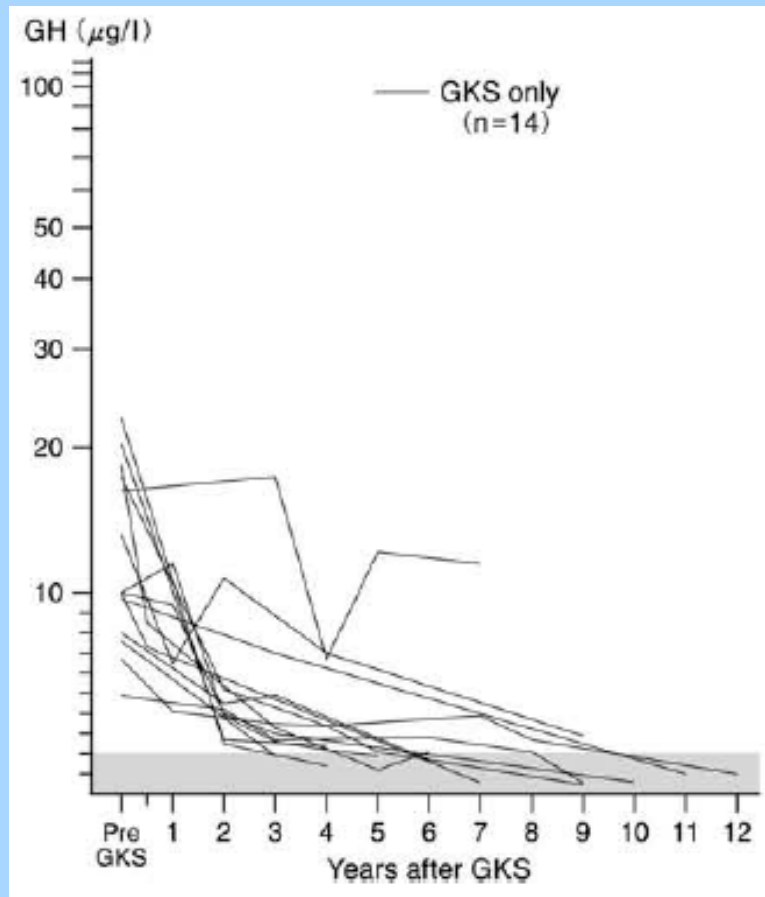
GH control in acromegaly



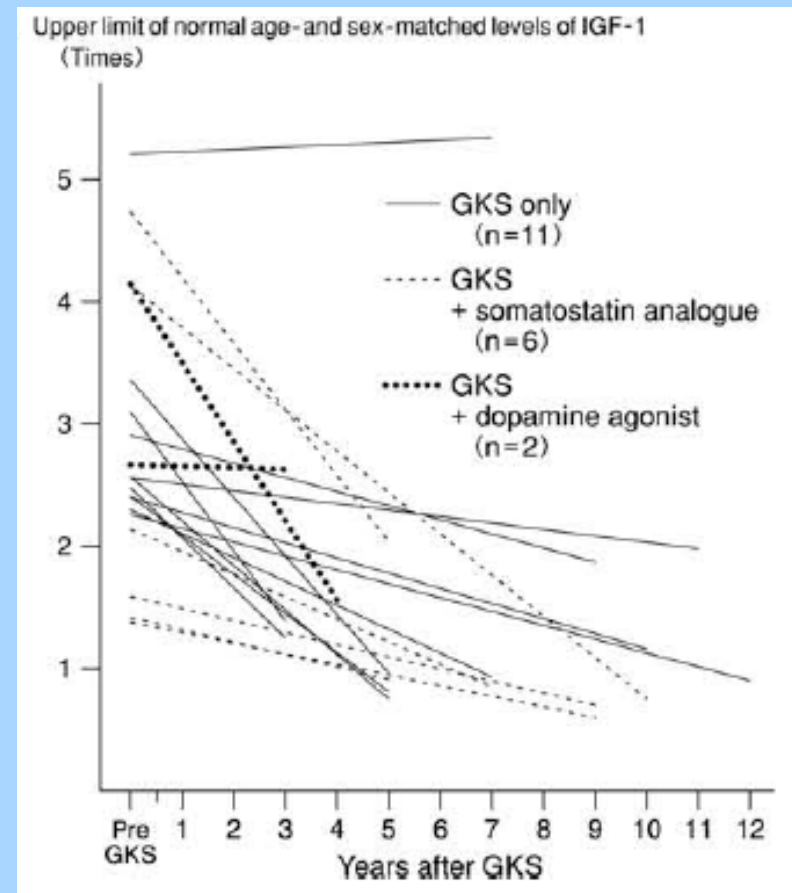
128 patients
mean FU 11 yrs

Conventional radiotherapy for acromegaly

GH & IGF1 control in acromegaly



GH



IGF-1

GK radiosurgery for acromegaly

Pituitary adenoma

Efficacy

Actuarial tumour control

Endocrine control

Toxicity

Stereotactic radiotherapy similar to conventional RT
GK radiosurgery no better than fractionated RT

Endpoints in the evaluation of irradiation

Pituitary adenoma

Efficacy

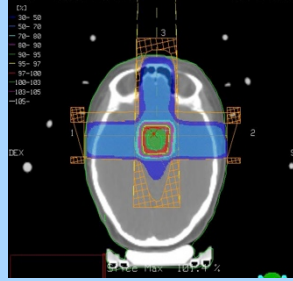
Actuarial tumour control

Endocrine control

Toxicity

Endpoints in the evaluation of irradiation

Toxicity



Neurological damage

Vision

Temporal lobe damage

Cognitive function

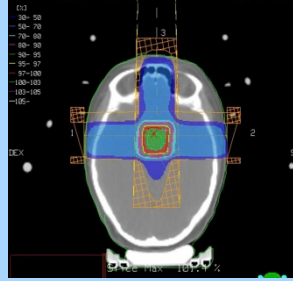
Endocrine failure

Second malignancy

Cerebrovascular accident (CVA)

Radiotherapy for pituitary adenoma

Toxicity



Neurological damage

Vision

Temporal lobe damage

Cognitive function

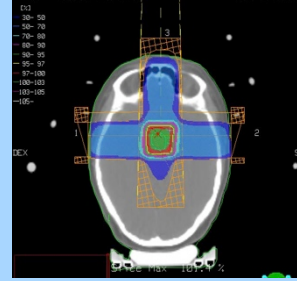
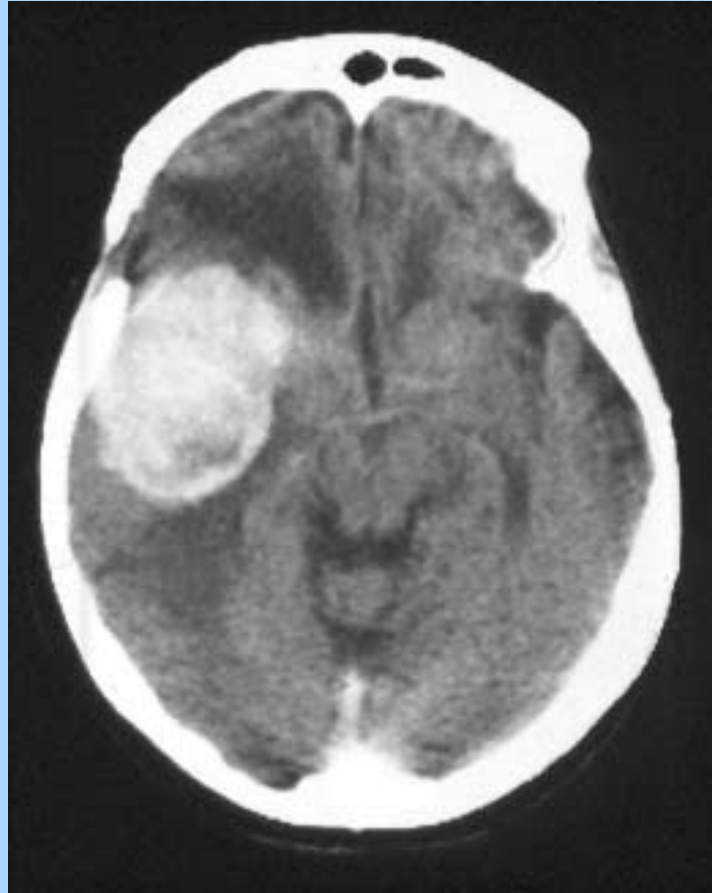
Endocrine failure

Second malignancy

Cerebrovascular accident (CVA)

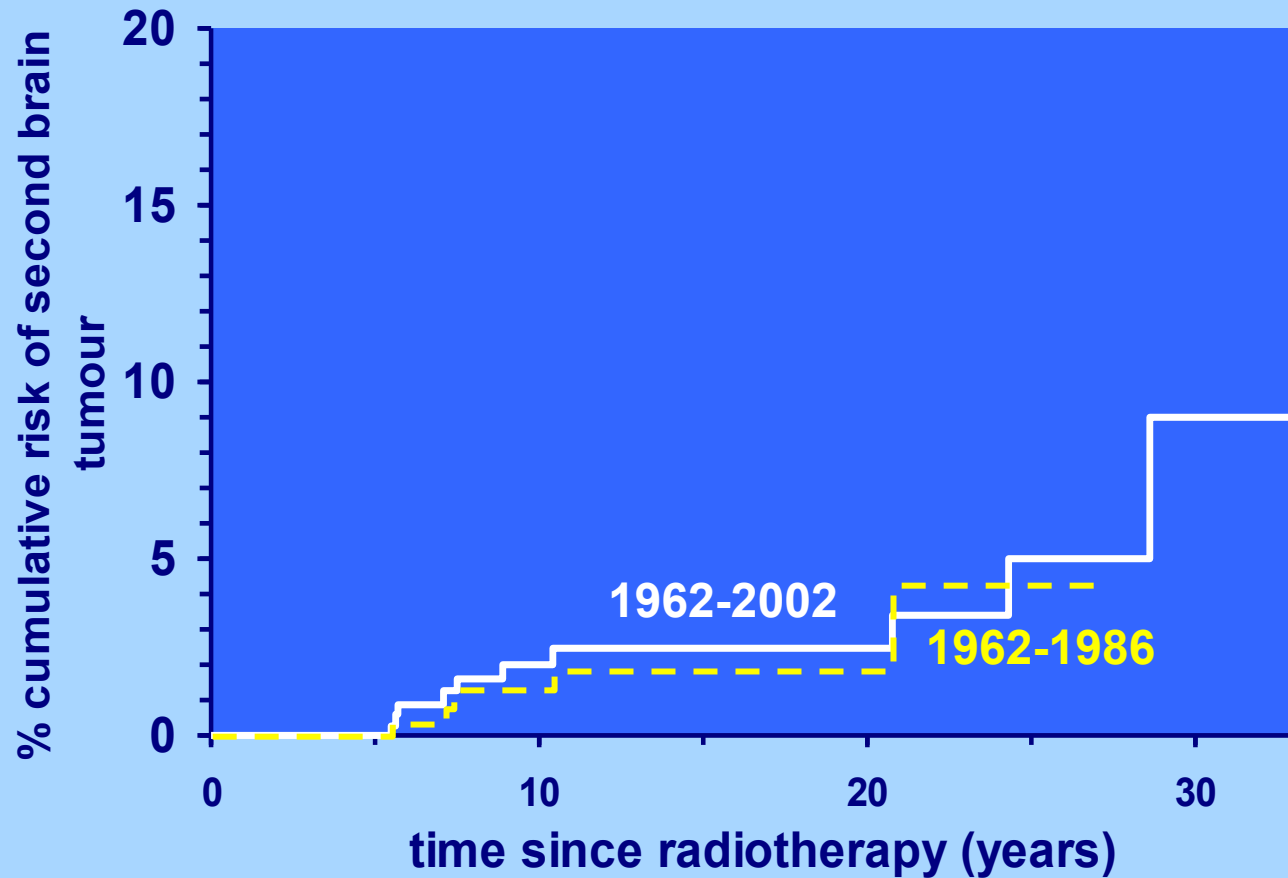
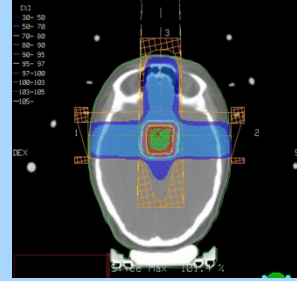
Radiotherapy for pituitary adenoma

Radiation induced second malignancy



Radiotherapy for pituitary adenoma

Radiation induced second malignancy

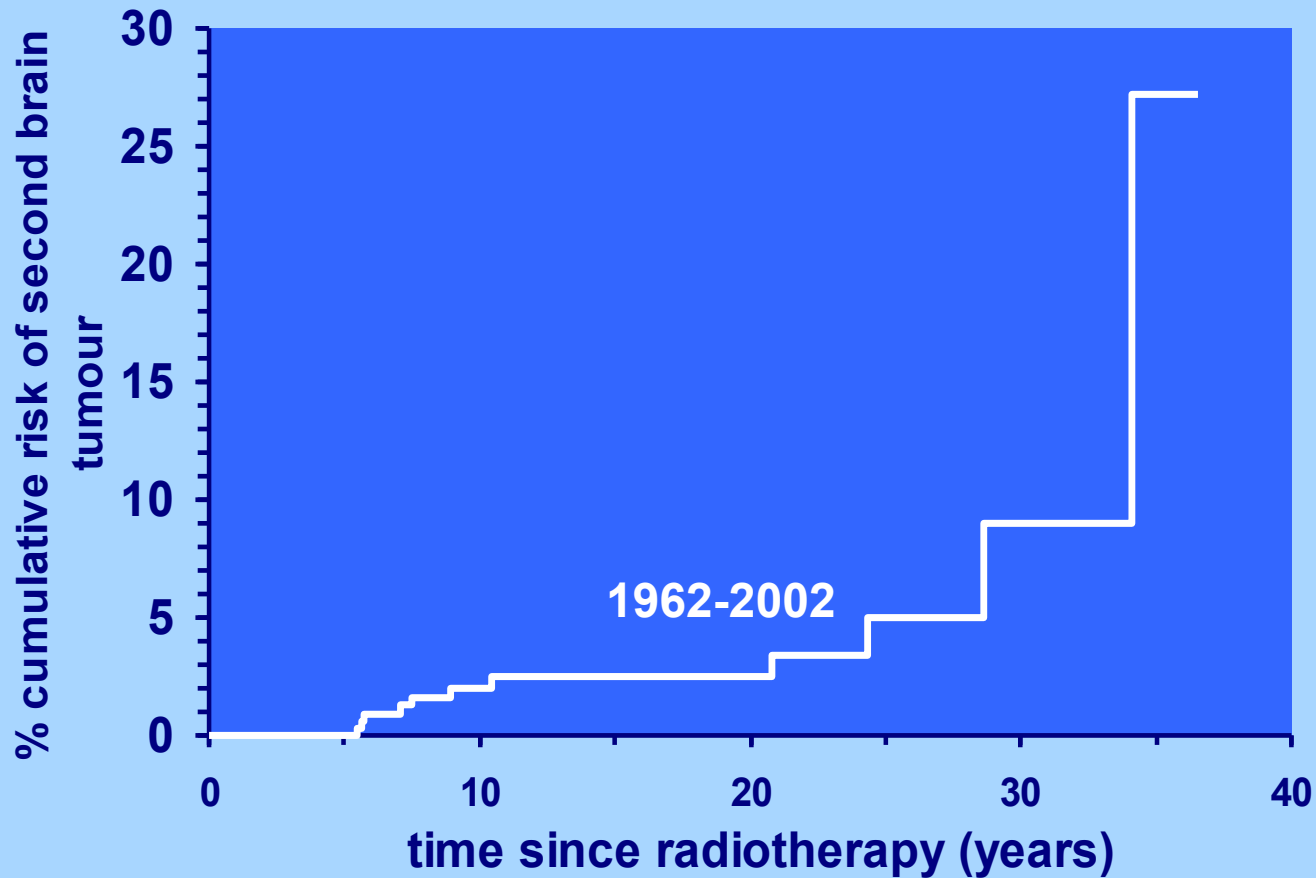
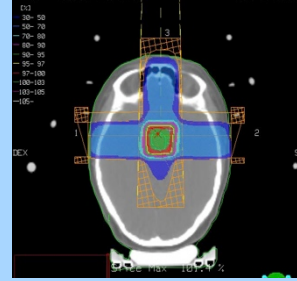


Radiotherapy for pituitary adenoma

Brada, Ford, Ashley et al 1992, BMJ, 304:1343-1346

Minniti, Traish, Ashley, Gonzalves, Brada 2005 J Clin Endocrin Metab, 90(2):800-804

Radiation induced second malignancy



Radiotherapy for pituitary adenoma

Brada, Ford, Ashley et al 1992, BMJ, 304:1343-1346

Minniti, Traish, Ashley, Gonzalves, Brada 2005 J Clin Endocrin Metab, 90(2):800–804

Efficacy

Actuarial tumour control

Endocrine control

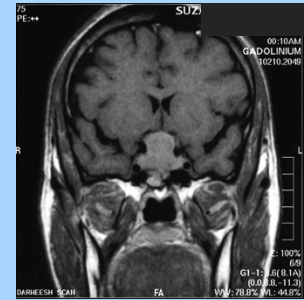
Toxicity

Stereotactic radiotherapy – potential reduction in toxicity requires long term follow up

Single fraction radiosurgery more toxic for larger tumours

Endpoints in the evaluation of irradiation

Pituitary adenoma



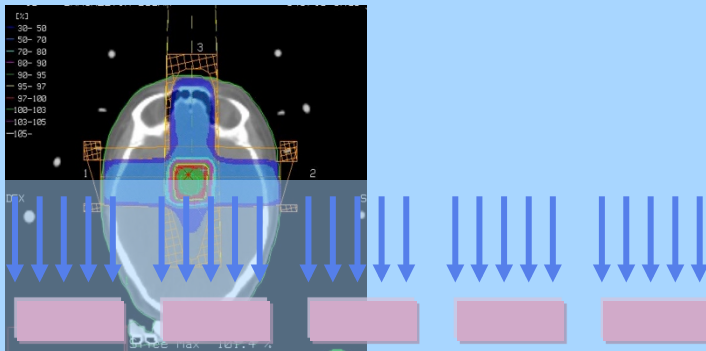
Efficacy

Actuarial tumour control

Endocrine control

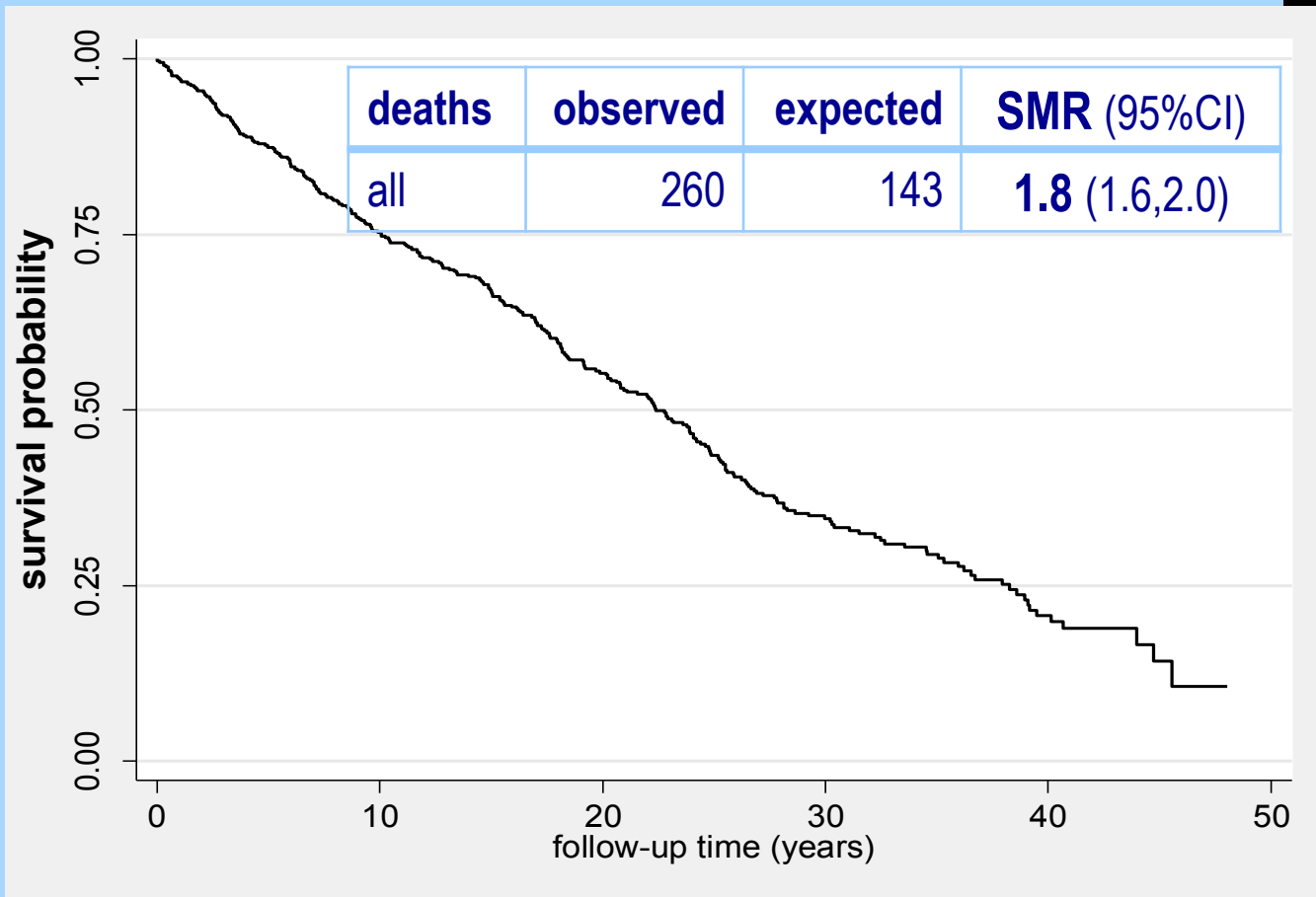
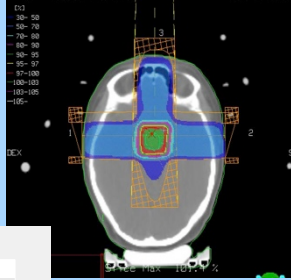
Toxicity

survival



Endpoints of efficacy

Risk of death as standardised mortality ratio (SMR)



426 patients
treated 1962 - 1994

Survival following conventional radiotherapy

Benign brain tumours

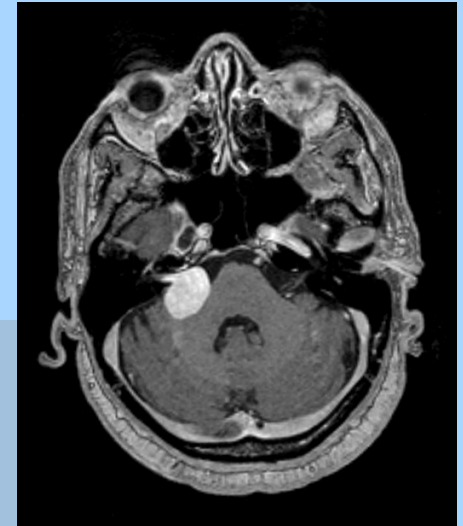
pituitary adenoma

craniopharyngioma

acoustic neuroma

skull base meningioma

childhood low grade glioma



Management of benign brain tumours

Acoustic neuroma and radiotherapy

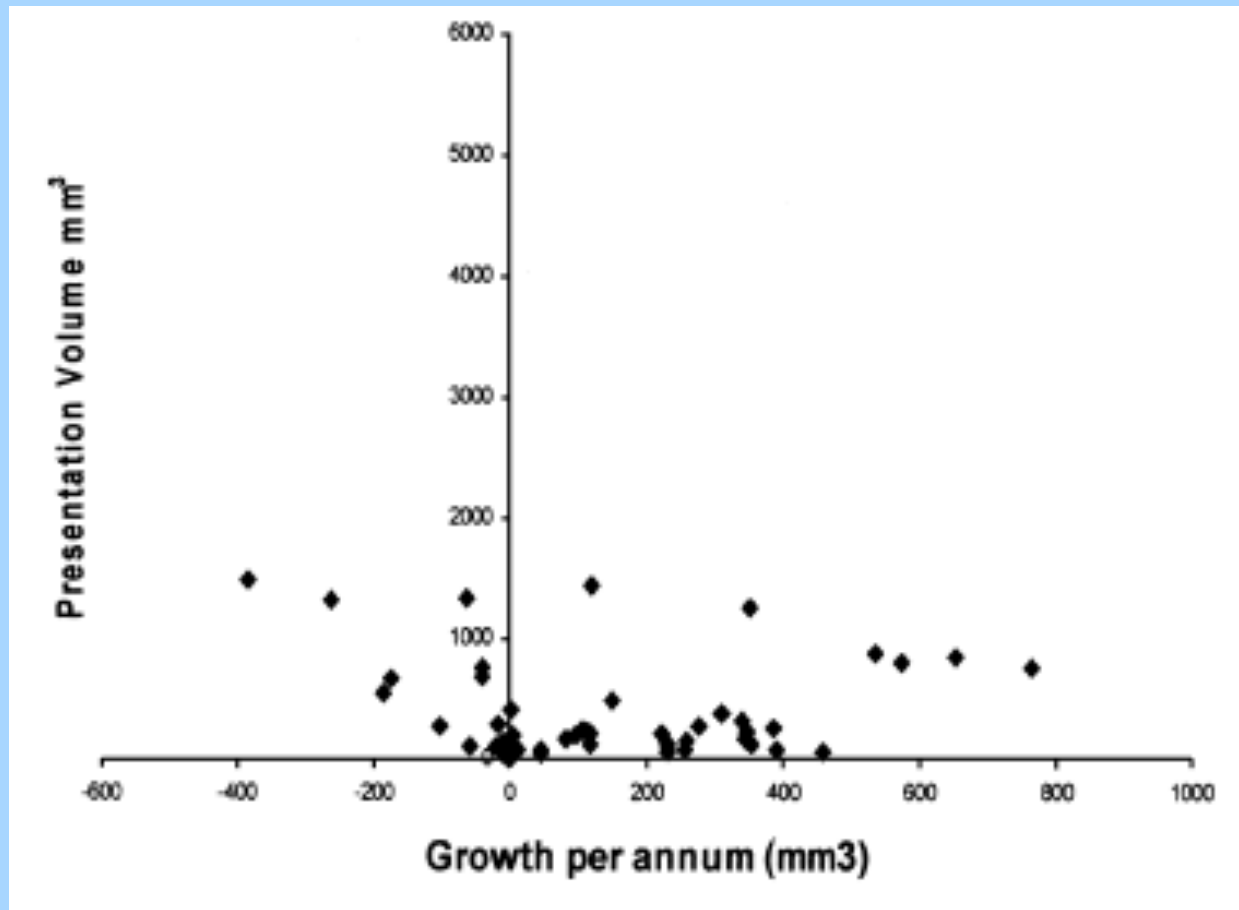
- 1. tumour control is dose dependent (dose/response)**
- 2. radiotherapy can be associated with life threatening complications**
- 3. surveillance prior to RT is associated with risk of facial palsy**
- 4. early radiotherapy preserves hearing**
- 5. all of these**
- 6. none of these**

surveillance	surgery
radiotherapy	medical therapy

Management options in vestibular schwannoma

surveillance	surgery
radiotherapy	medical therapy

Management options in vestibular schwannoma



Herwadker et al 2005
Manchester

Surveillance

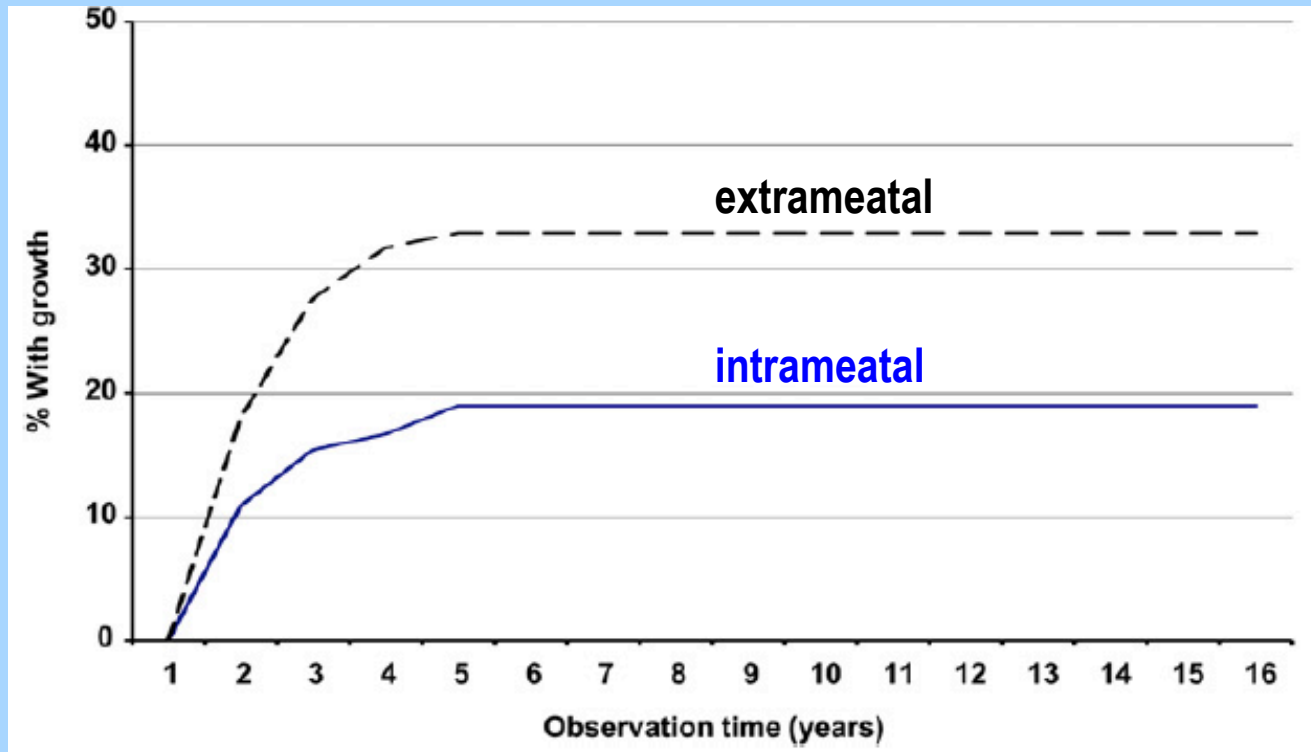
patients with AN (1977 –2005)
≤ 2cm max diameter (sporadic)

	number of patients
total	1989
observation	729
at least 2 scans	552
intrameatal	230
extrameatal	322

growth on surveillance

Danish cohort

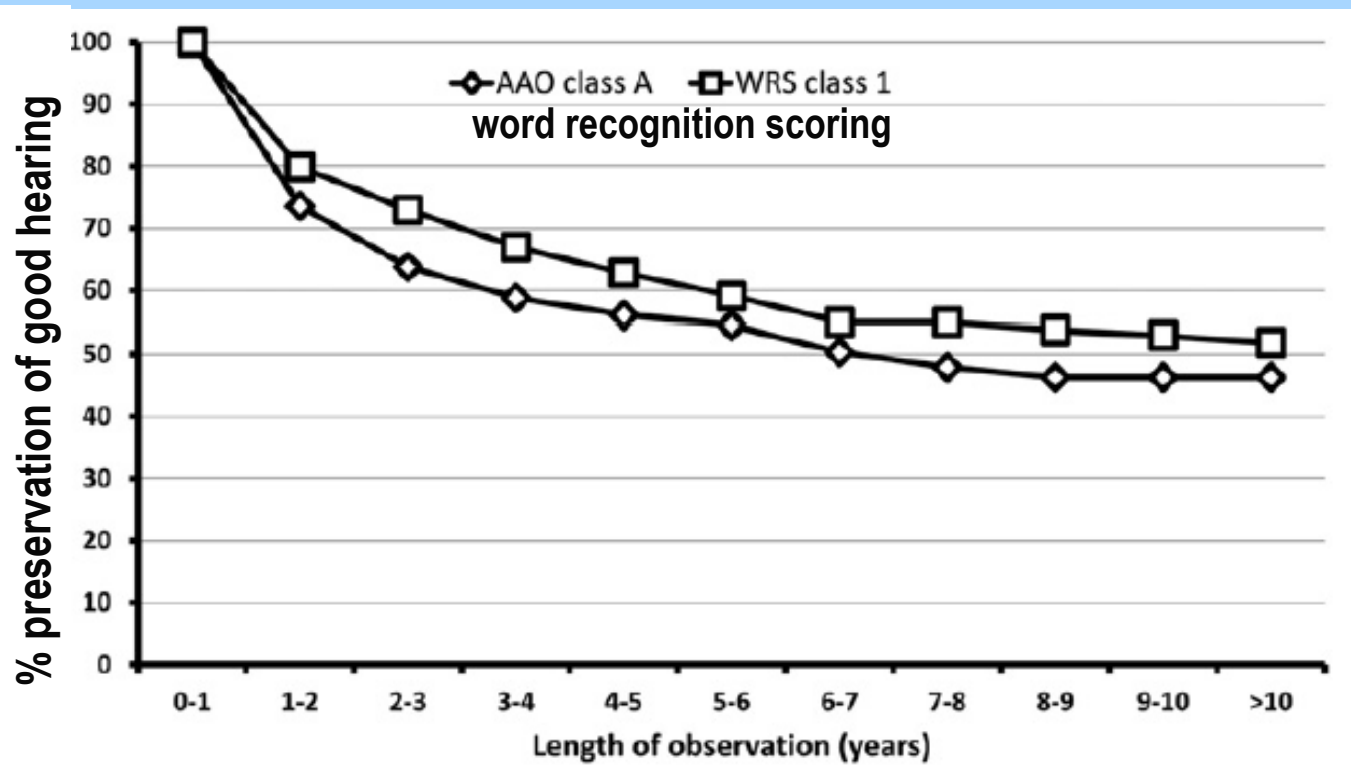
AN \leq 2cm max diameter (sporadic)



hearing loss on surveillance

Danish cohort

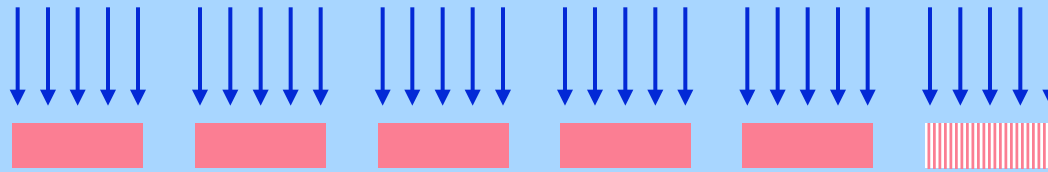
AN ≤ 2 cm max diameter (sporadic)



surveillance	surgery
radiotherapy	medical therapy

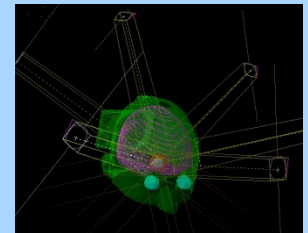
Management options in vestibular schwannoma

Fractionated “stereotactic” radiotherapy

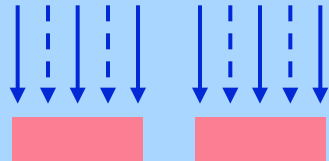


45 - 50Gy in 25 - 30 fractions

fractions
weeks

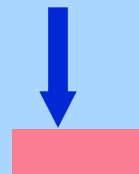


Hypofractionated “stereotactic” radiotherapy

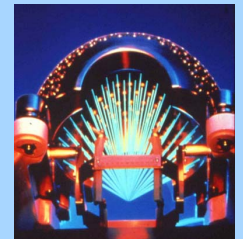


20 - 30Gy in 6 - 10 fractions

Single fraction radiosurgery

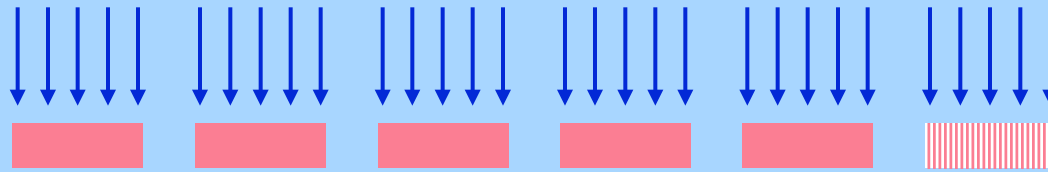


10 - 25Gy in 1 fraction



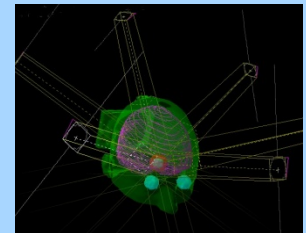
Fractionation in high precision radiotherapy

Fractionated “stereotactic” radiotherapy

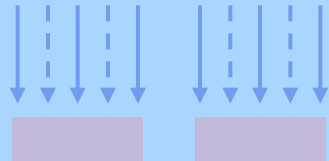


45 - 50Gy in 25 - 30 fractions

**fractions
weeks**

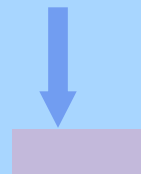


Hypofractionated “stereotactic” radiotherapy

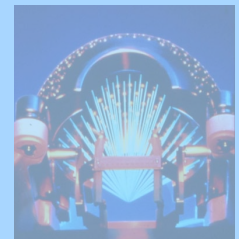


20 - 30Gy in 6 - 10 fractions

Single fraction radiosurgery

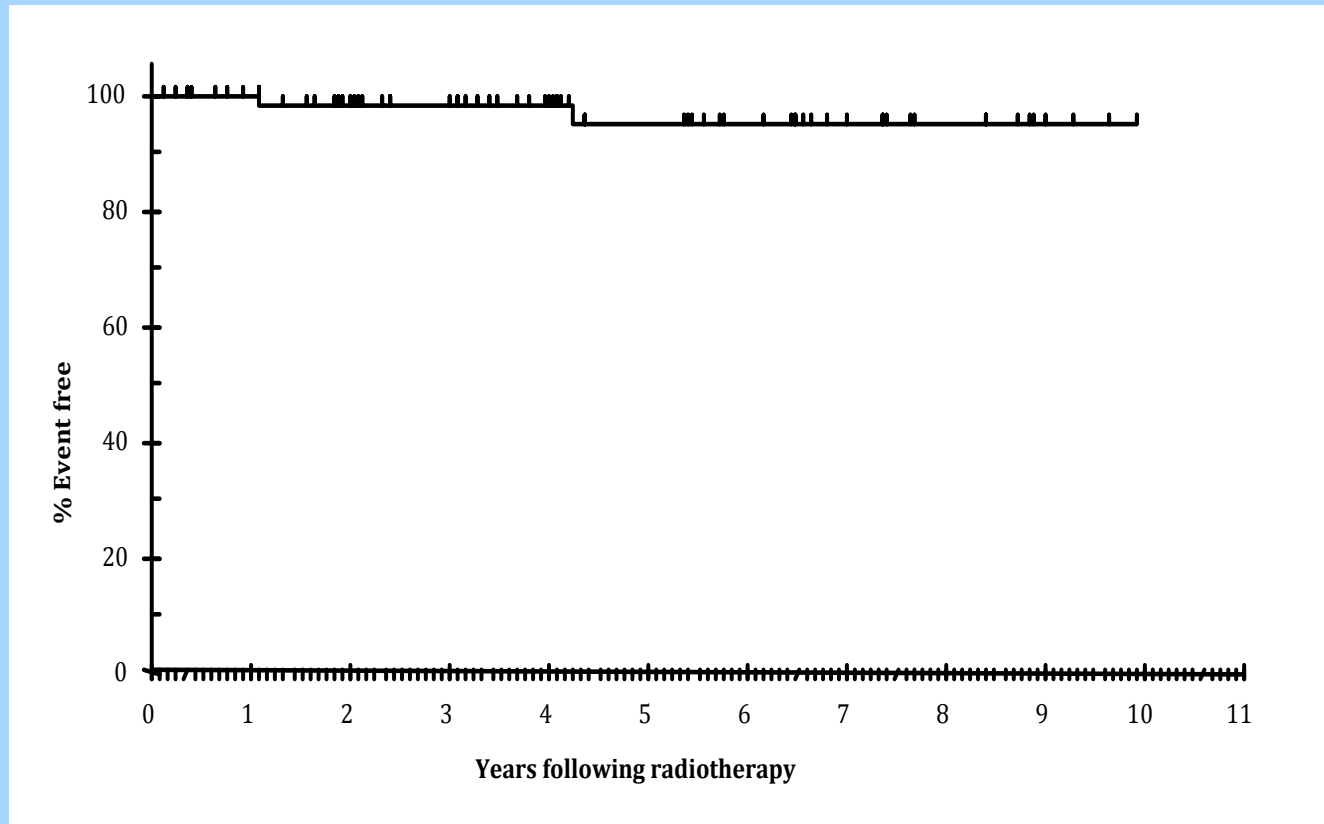


10 - 25Gy in 1 fraction



Fractionation in high precision radiotherapy

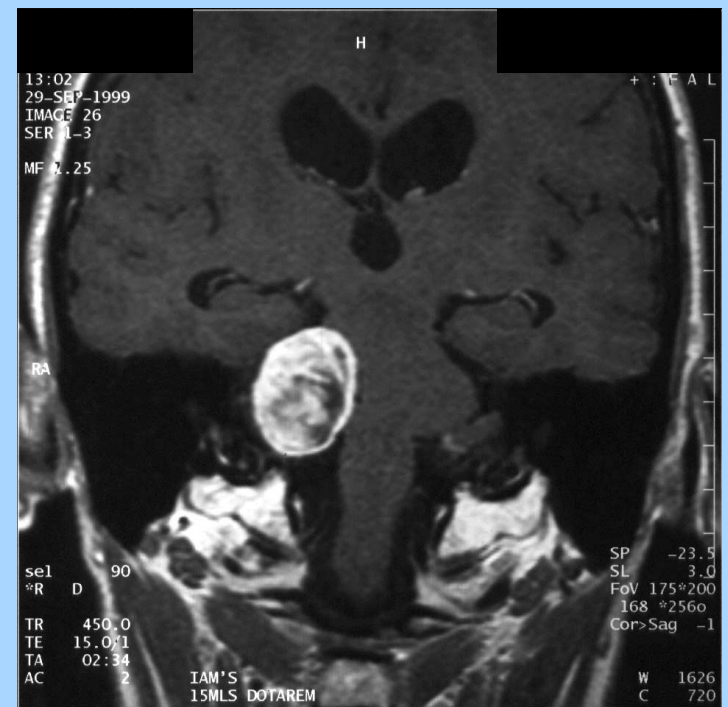
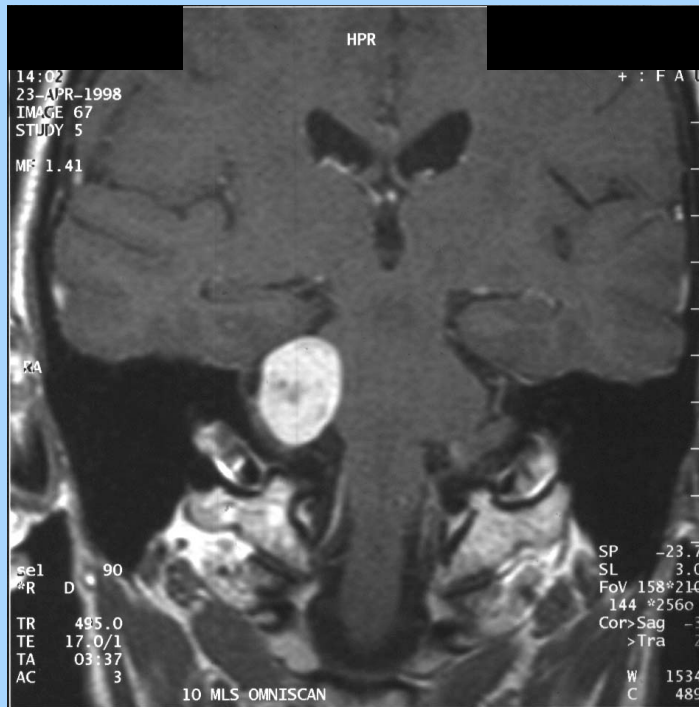
Tumour control



72 patients with acoustic neuroma, fSRT, Royal Marsden Hospital

Stereotactic RT for acoustic neuroma

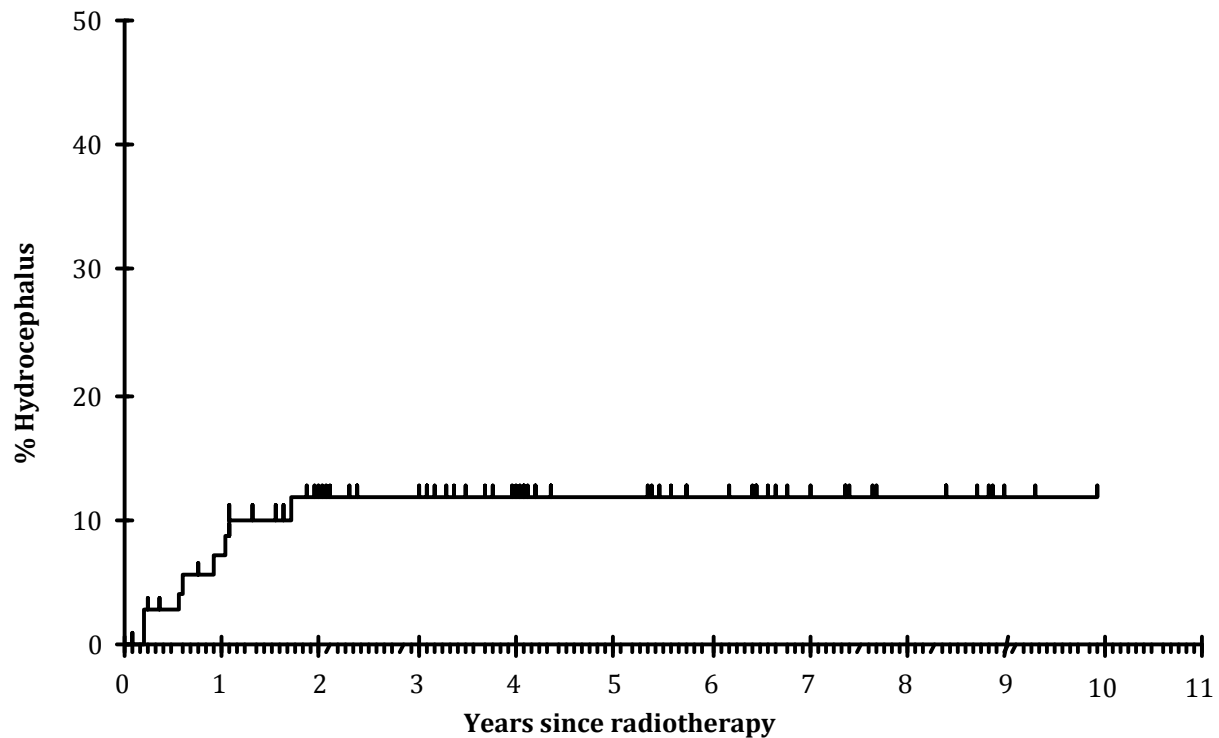
Transient enlargement & hydrocephalus



17 months later

Stereotactic RT for acoustic neuroma

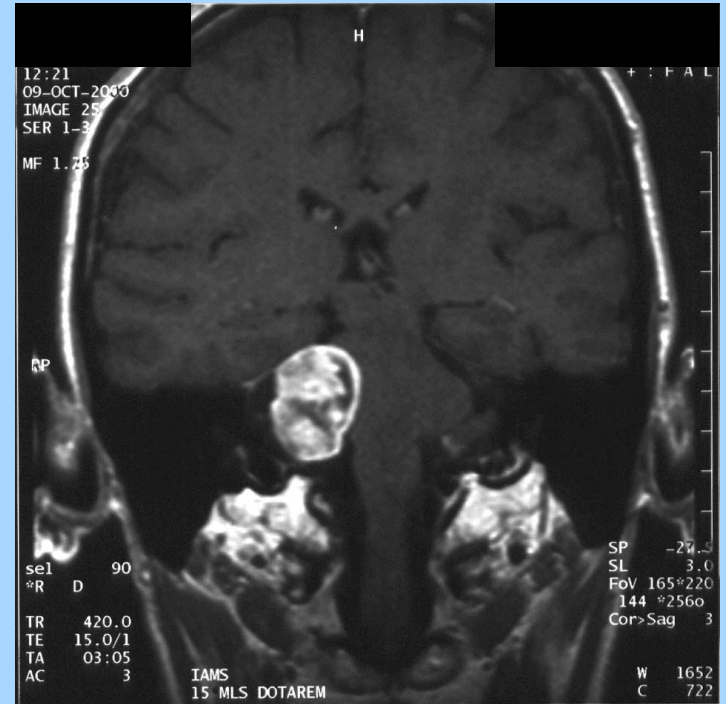
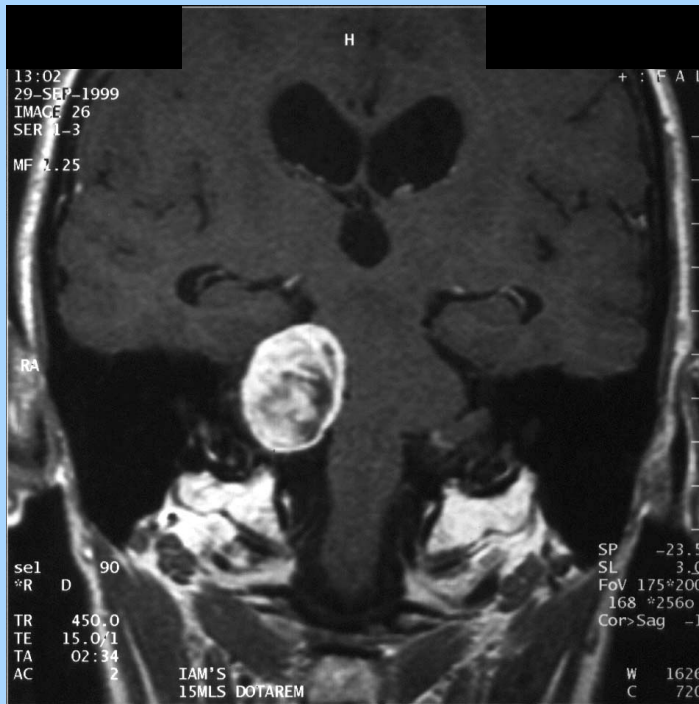
Incidence of hydrocephalus



72 patients with acoustic neuroma, fSRT, Royal Marsden Hospital

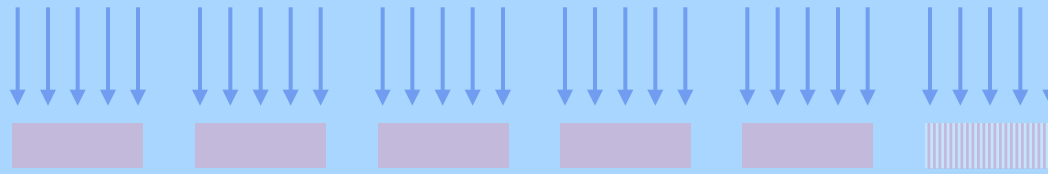
Stereotactic RT for acoustic neuroma

Transient enlargement resolution



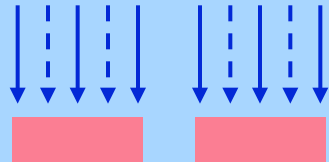
Stereotactic RT for acoustic neuroma

Fractionated “stereotactic” radiotherapy



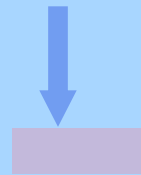
45 - 50Gy in 25 - 30 fractions

Hypofractionated “stereotactic” radiotherapy



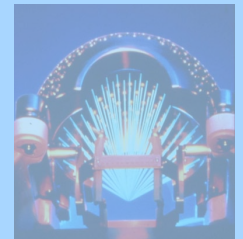
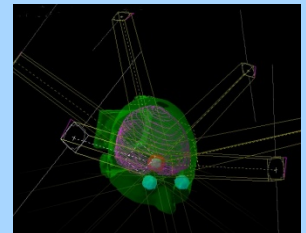
20 - 30Gy in 6 - 10 fractions

Single fraction radiosurgery



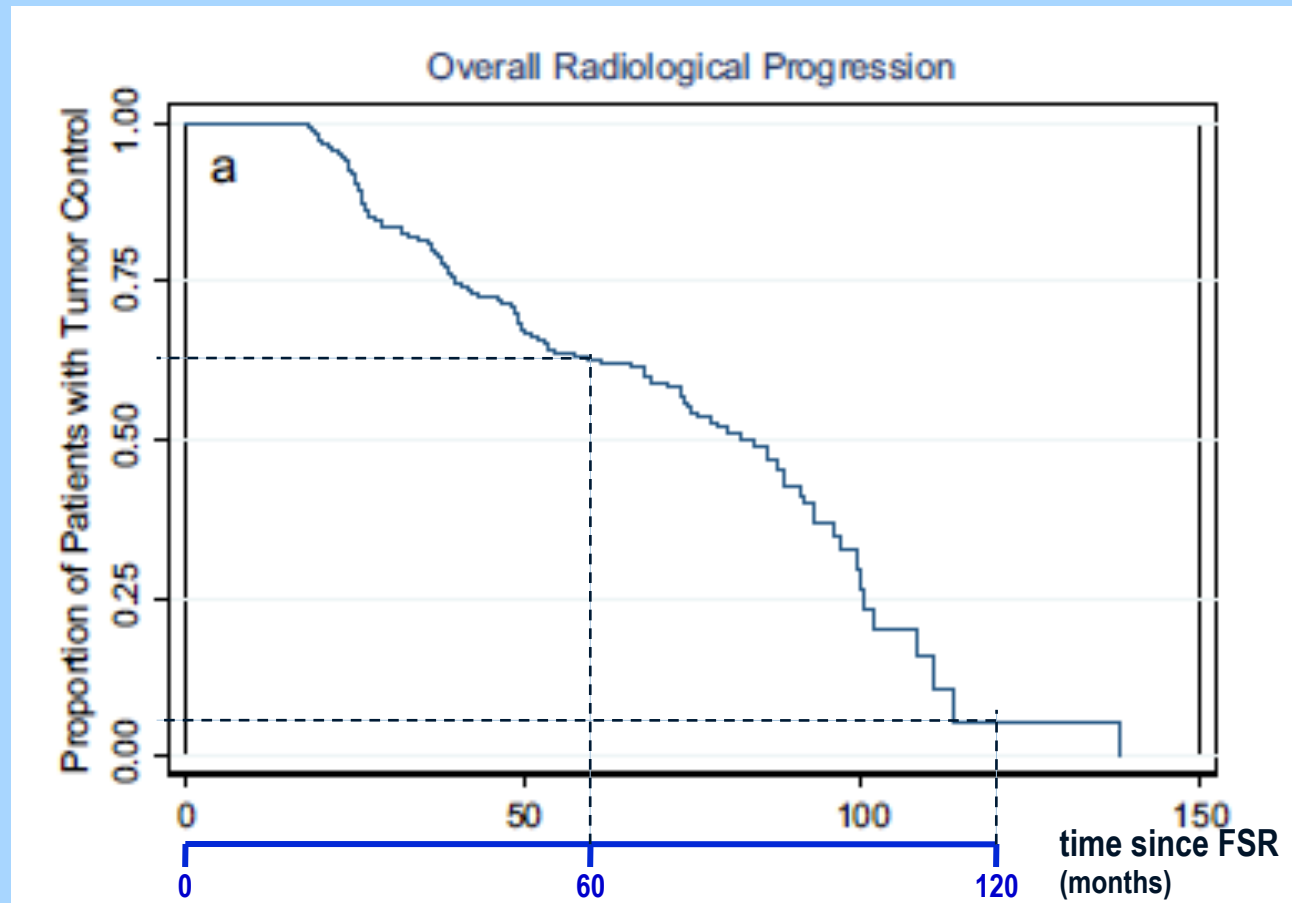
10 - 25Gy in 1 fraction

fractions
weeks



Fractionation in high precision radiotherapy

Tumour control



Hypofractionated stereotactic RT for acoustic neuroma

Evaluating outcome of fSRT/SRS for benign brain tumours



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Bebington, Wirral, CH63 4JY

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Benign brain tumours

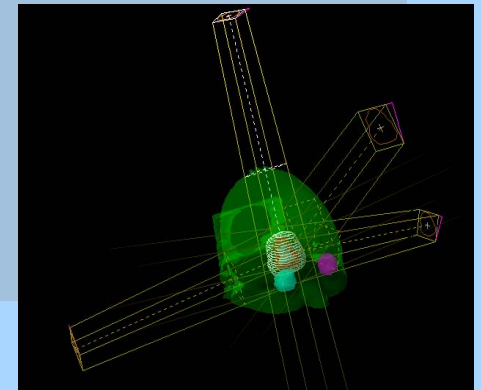
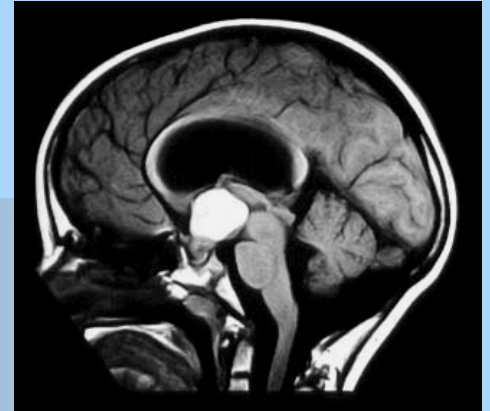
pituitary adenoma

craniopharyngioma

acoustic neuroma

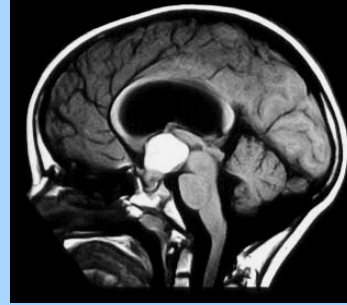
skull base meningioma

childhood low grade glioma



Management of benign brain tumours

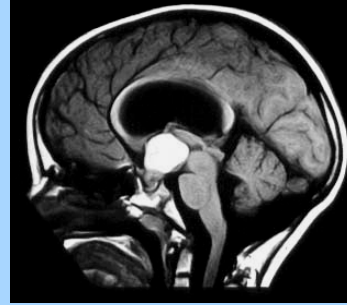
Primary therapy



Surveillance	Surgery
Radiotherapy	Medical therapy

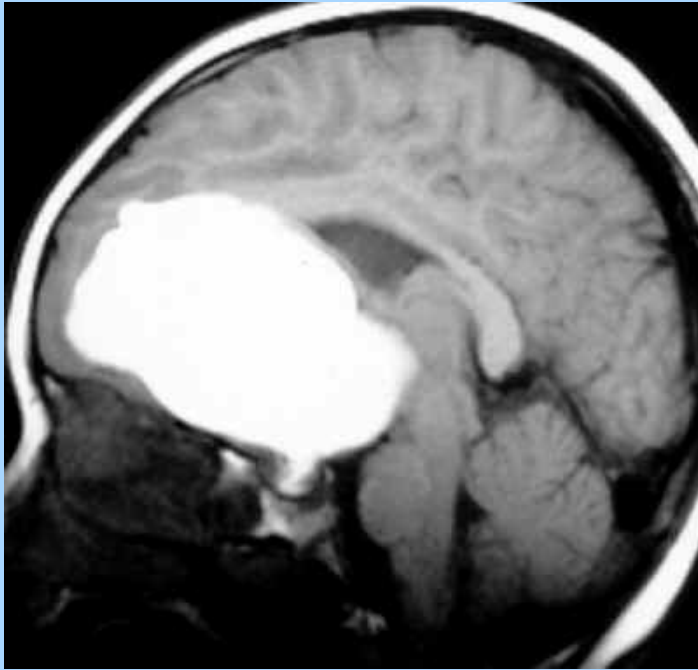
Management options in craniopharyngioma

Primary therapy



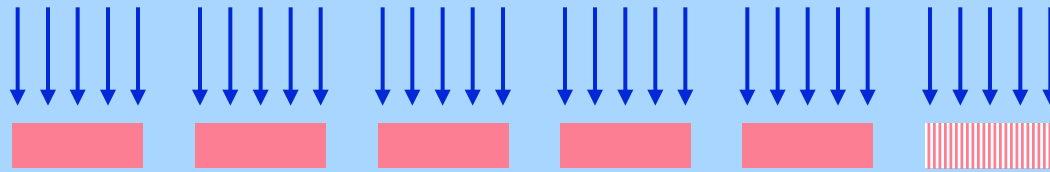
Surveillance	Surgery
Radiotherapy	Medical therapy

Management options in craniopharyngioma



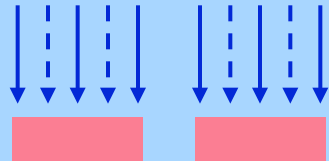
Surgery for craniopharyngioma

Fractionated “stereotactic” radiotherapy



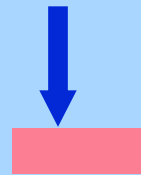
45 - 50Gy in 25 - 30 fractions

Hypofractionated “stereotactic” radiotherapy

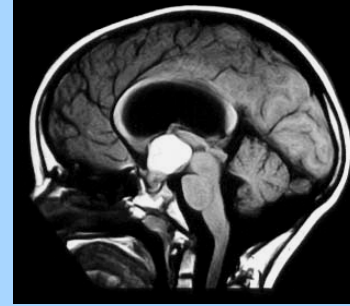


20 - 30Gy in 6 - 10 fractions

Single fraction radiosurgery

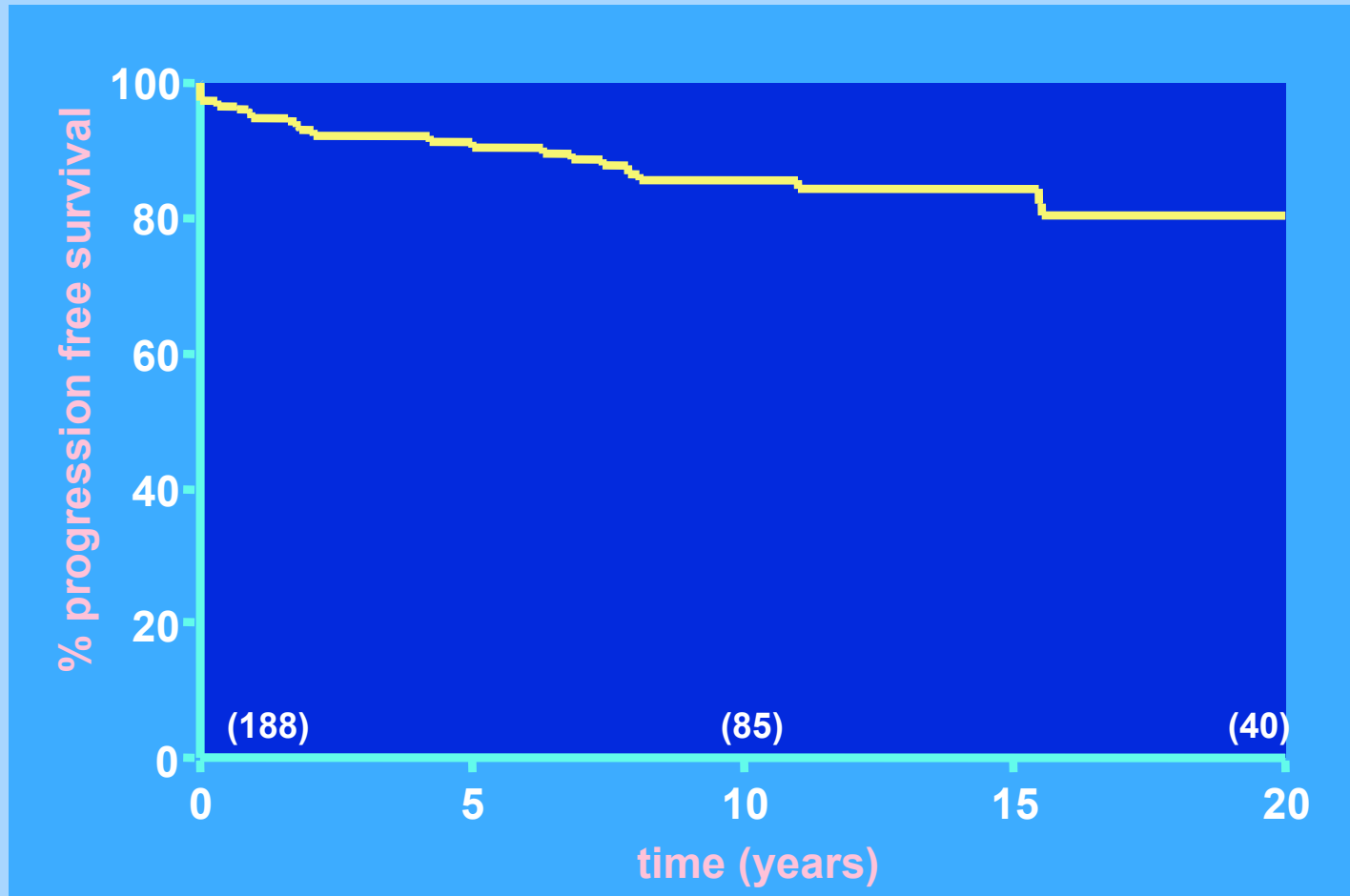


10 - 25Gy in 1 fraction



Radiotherapy for craniopharyngioma

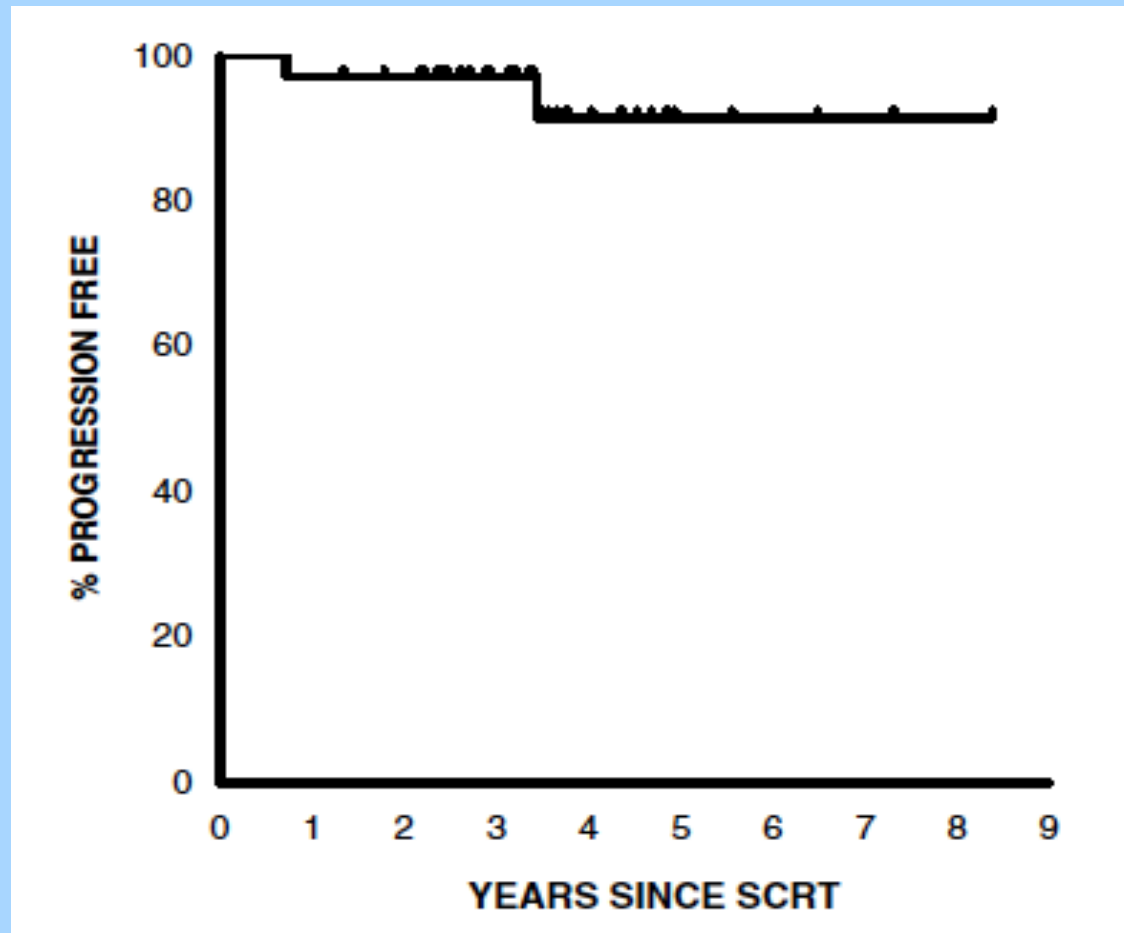
Tumour control



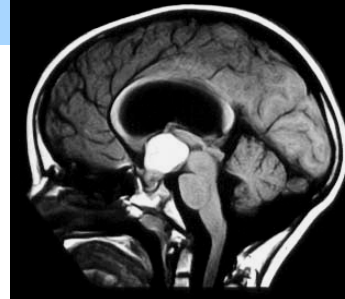
188 patients conservative surgery and radiotherapy

Conventional radiotherapy for craniopharyngioma

Tumour control



High precision radiotherapy for craniopharyngioma



Author	Patients (n)	Dose (Gy)	Mean Tumour size (cm ³)	Control (%)
Gamma knife				
Xu et al ⁴¹	37	14.5	1.6	67% at 5 yrs
Niranjan et al ⁴²	46	13	1	68% at 5 yrs
Kobayashi et al ³⁴	98	11.6	3.5	61% at 5 yrs 54% at 10 yrs
Yomo et al ⁴³	18	11.5	1.8	(94%)
Amendola et al ³⁶	14	14	3.7	(86%)
Ulfarsson et al ²¹	21	3-25	7.8	(36%)
Chiou et al ³⁷	10	16.4	1.7	(58%)
Chung et al ³⁵	31	9.5-16	9	(87%)
Mokry ⁴⁴	23	8-9.7	7	(74%)
Prasad et al ⁴⁵	9	13	10	(63%)
Cyberknife				
Iwata et al ³⁹	40	13-25	2	85% at 3 yrs
Miyazaki et al ⁴⁶	13	22.7	NA	(84%)
Lee et al ³⁸	11	21.6	6	(91%)
fSRT				
Kaneska et al ⁴⁸	16	30	1.8	82% at 3 yrs
Combs et al ¹⁶	40	52.2	13.3	100% at 10yrs
Minniti et al ¹⁵	39	50	10.2	92% at 5 yrs
Schulz-Ertner et al ³³	26	52.2	5.2	100% 10 yrs
Selch et al ⁴⁹	16	55	7.7	75% at 3 yrs

Tumour control following radiotherapy