Trattamento dei tumori benigni extra-assiali: la RADIOCHIRURGIA

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S.C. di Radioterapia Oncologica & * Neurochirurgia,
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Extra-axial benign brain tumors

Extra-axial tumors are the **extracerebral** located central nervous system tumors:

- **meningioma**
- **acoustic neuroma/vestibular schwannoma**
- pituitary adenoma
- neurofibroma
- mesenchymal tumors of the skull & dura mater

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- pituitary adenoma
- neurofibroma
- mesenchymal tumors of the skull & dura mater

Extra-axial benign brain tumors

Surgical resection is considered the first line treatment

but

- some of these tumors ***cannot be resected*** and others **may recur** despite resection,
- several of these tumors ***remain quiescent*** and do not require intervention,
- whereas others ***may grow and become refractory*** to standard therapy.

Extra-axial benign brain tumors

Patients with these tumors are **ideal candidates for radiosurgery (SRS)** for the following reasons:

- **these tumors rarely invade the adjacent tissue**
- **are typically well visualized with MRI**
- **SRS makes radiobiologic sense:**

> ***target and adjacent nervous system act as a late responding tissues due to their slow rate of proliferation; so, precise high-single fraction SRS results theoretically better than fractionated conformal RT***

Extra-axial benign brain tumors

So, patients with these tumors are **ideal candidates for surgery** and/or **radiosurgery (SRS)**

but

- **Available literature data are of poor quality** ***(class I and few class II evidence).***
- **RCTs are difficult to perform:**
  - ***relatively low incidence and necessity of a long FU;***
  - ***some physician is polarized in his thinking and convince patient of his thinking***

Extra-axial benign brain tumors

Patients with these tumors are candidates for **surgery, radiosurgery (SRS), surgery + post-op SRS, or observation**

So, it is necessary

A PROPER PATIENT SELECTION

on the basis of:

- ***Presence or absence of symptoms***
- ***Tumor diameter*** ***(< 3 cm vs. ≥ 3 cm)***
- ***Tumor site*** ***(e.g., tumor contacting optic apparatus, supra-tentorial vs. skull-base tumors, cavernous sinus meningiomas)***
- ***Tumor type*** ***(e.g., anaplastic meningioma that is not a benign tumor)***

Radiosurgery *in extra-axial benign brain tumors*

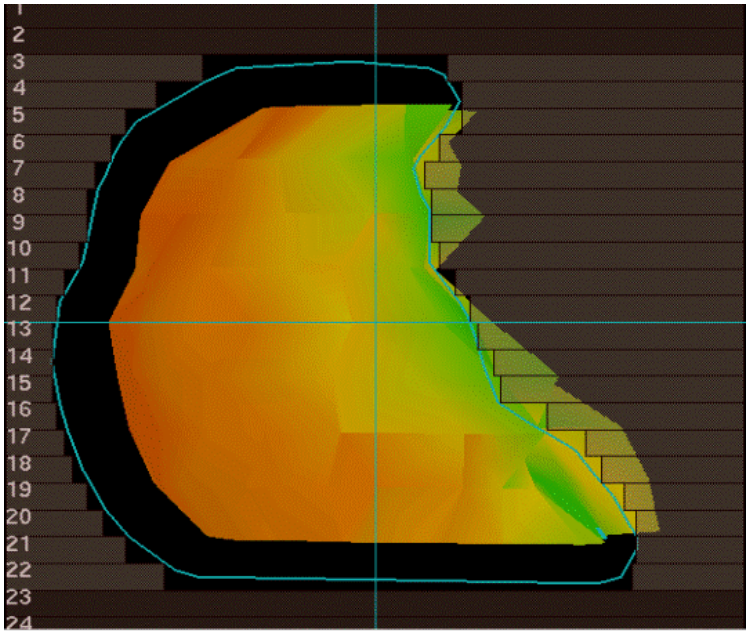
- Stereotactic radiosurgery (**SRS**) treats brain disorders with a precise delivery of a single high dose of radiation in a one-day session.

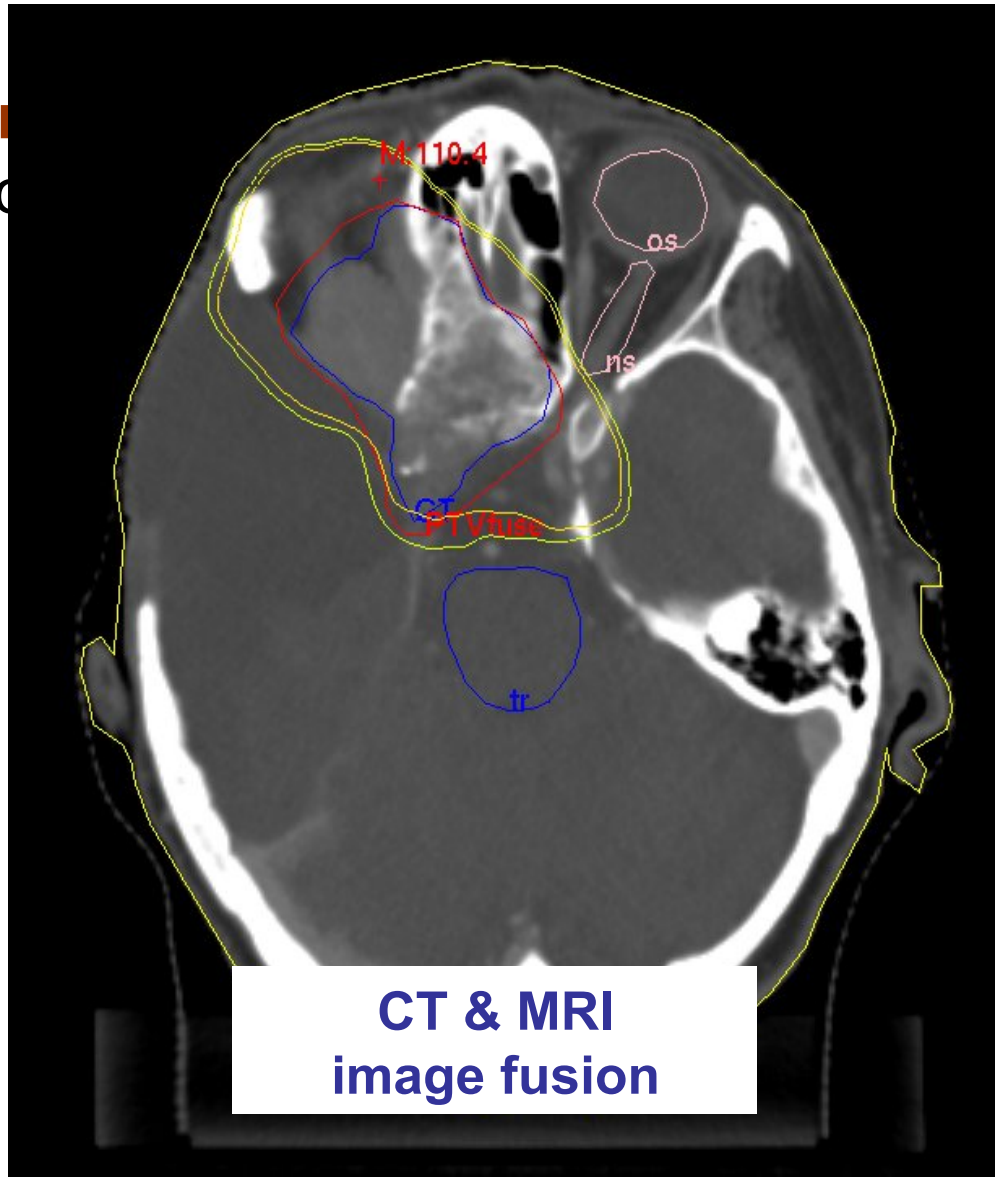
- Fractionated stereotactic radiotherapy (**FSRT**) combines precision of the stereotactic approach with the radiobiological advantage of fractionation, and can be ***an alternative to SRS*** when

  - a ***large volume of tumor*** must be covered and/or
  - when dose prescription is limited by the ***tolerance of critical structures*** (**e.g., pituitary gland and optical pathways**)

Modified LINAC Radiosurgery for *extra-axial benign brain tumors*

- Beam shaping with micro-
- High Conformity and Homo
- No-coplanar dynamic arcs
- Multimodal imaging for target identification





CT & MRI image fusion

OUR EXPERIENCE on meningioma & neuroma

Period: from 12.9.01 to 18.10.12 (11 years)

	N° of patients	SRS	FSRT
MENINGIOMA	378	221 (58%)	157 (42%)
ACOUSTIC NEUROMA	140	124 (89%)	16 (11%)
Total	**518**	**345**	**173**

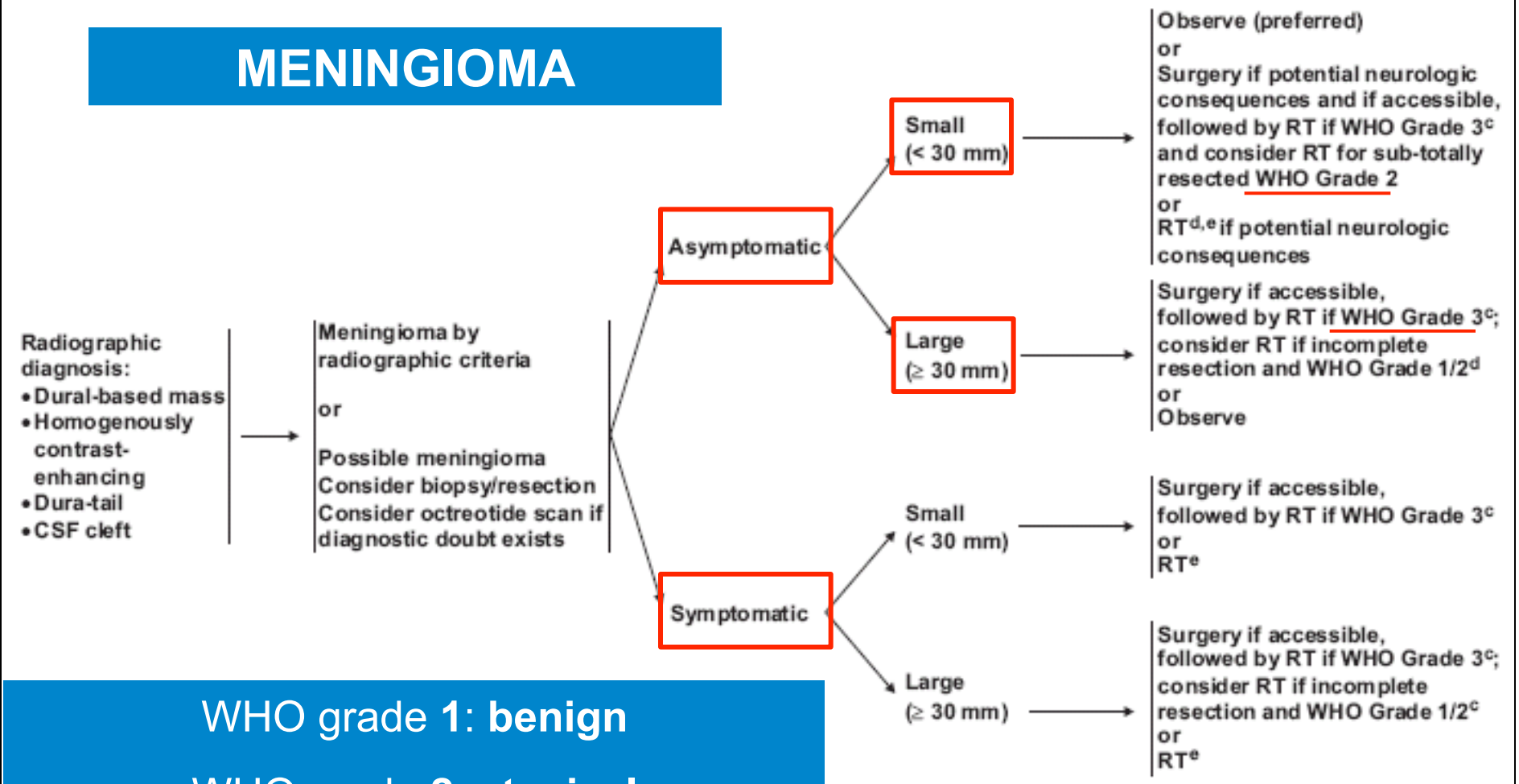

XXII CONGRESSO
AIRO
ROMA 2012
17-20 novembre
Ergife Palace Hotel
Associazione
Italiana
Radioterapia
Oncologica

MENINGIOMA

NCCN Guidelines Version 2.2012
Meningiomas

NCCN Guidelines Index
CNS Table of Contents
Discussion

MENINGIOMA

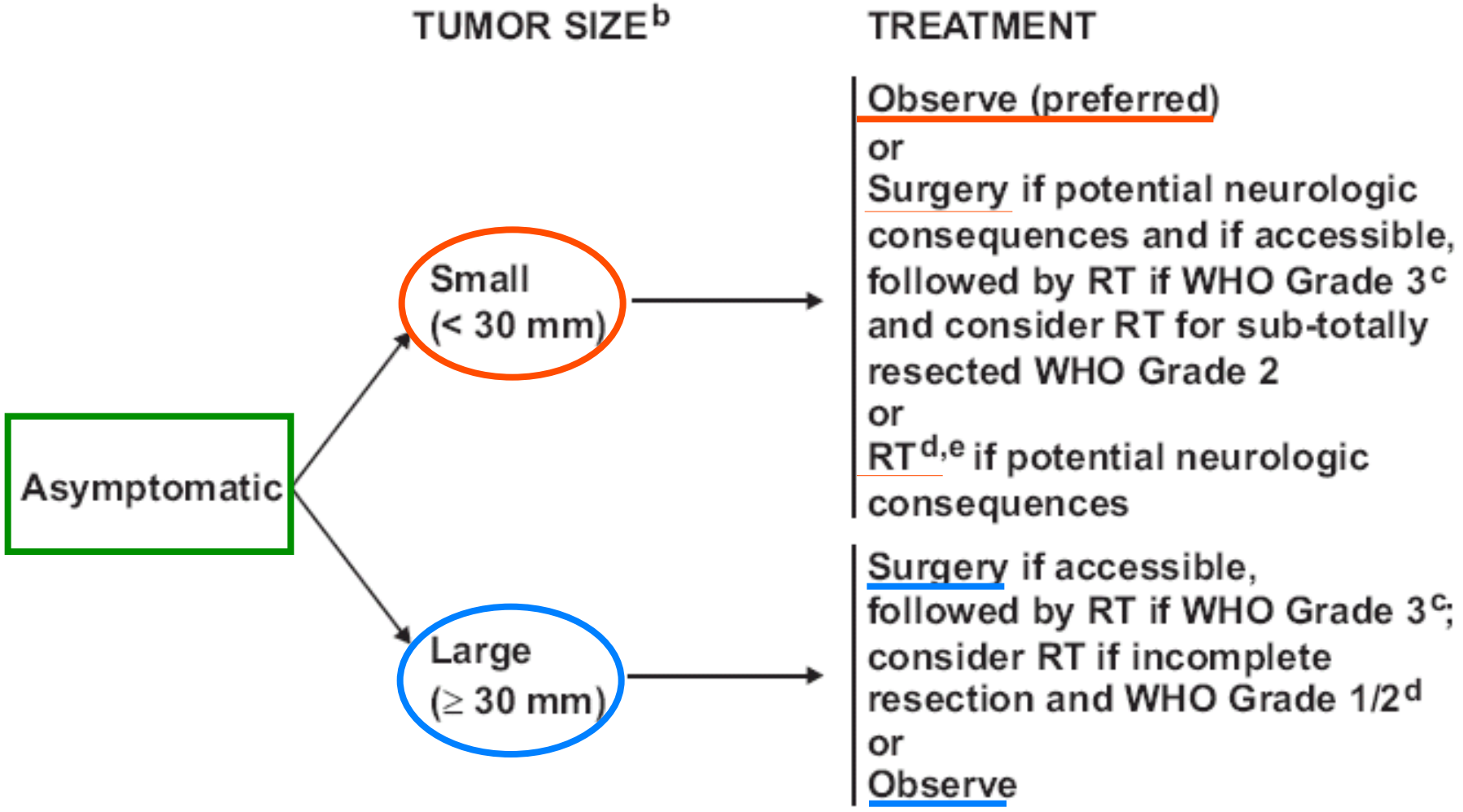


WHO grade **1**: **benign**

WHO grade **2**: **atypical**

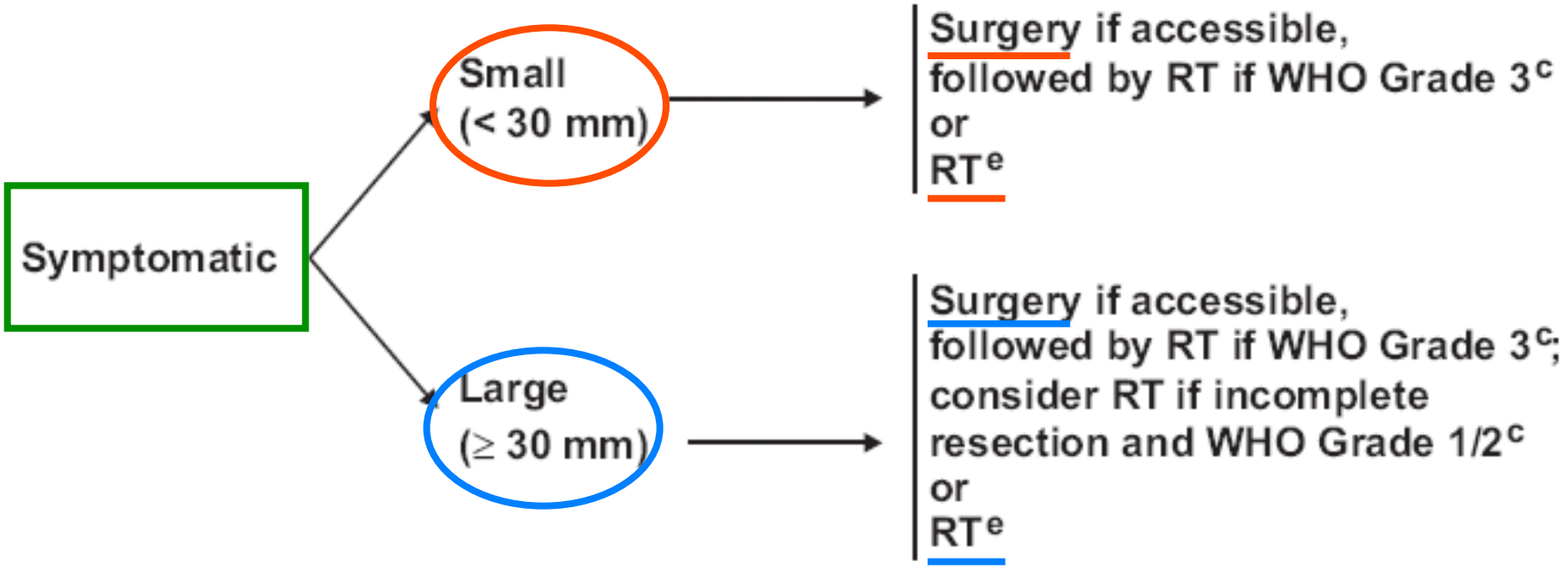
WHO grade **3**: **malignant** (anaplastic)

NCCN Guidelines Version 2.2012
Meningiomas



Post-op RT in incomplete resection or if WHO grade 3

NCCN Guidelines Version 2.2012
Meningiomas



Post-op RT in incomplete resection or if WHO grade 3

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2012 Meningiomas

PRINCIPLES OF BRAIN TUMOR RADIATION THERAPY

- WHO **grade 1 & 2** may be treated by **3D-CRT** with doses of **45-54 Gy**
- WHO **grade 3** should be treated **as malignant tumors** with tumor bed and ***GTV + a margin*** (2-3 cm) receiving **54-60 Gy**
- WHO **grade 1** may also be treated with stereotactic **radiosurgery** doses of **12-14 Gy** in a single fraction when appropriate

STEREOTACTIC RADIOSUGERY OF BENIGN INTRACRANIAL TUMORS. Pollack BE. *J Neurooncol 2009;92:337-343*

Surgery and **Radiosurgery (SRS)** give same results in term of local control and survival (PFS)

- No difference in 3- and 7-year actuarial PFS for patients having Simpson Grade 1 resection (100% and 96%) or SRS (100% and 95%).
- SRS better than subtotal resection
- Planned subtotal resection **+** SRS can be performed to achieve tumor control with acceptable toxicity for **large tumor involving major sinus**

IJROBP 2011

Single-fraction Radiosurgery for Presumed Intracranial Meningiomas: Efficacy and Complications From a 22-Year Experience

Bruce E. Pollock, M.D.,*,† Scott L. Stafford, M.D.,† Michael J. Link, M.D.,* Yolanda I. Garces, M.D.,† and Robert L. Foote, M.D.†

*Departments of *Neurological Surgery and †Radiation Oncology, Mayo Clinic College of Medicine, Rochester, MN*

- **Radiosurgery** (**12-14 Gy**) provides a **high rate of tumor control** and **PFS** for patients with intracranial meningiomas.
- Patients with small- to medium-sized tumors involving the **skull base** had **lowest risk of RT-related complications**
- **Cavernous sinus meningiomas** can be adequately treated with **SRS**
- **Surgery** should remain the primary treatment for patients with **symptomatic or enlarging dural-based masses** and/or **supratentorial located** meningiomas

OUR EXPERIENCE on MENINGIOMA

Period: from 12.9.01 to 18.10.12 (11 years)

	Total N° of patients	SRS	FSRT (2-50Gy; 3-42/45Gy)
MENINGIOMA	378	221 (58%)	157 (42%)
ACOUSTIC NEUROMA	140	124 (89%)	16 (11%)

Hypofractionated stereotactic radiotherapy for intracranial meningiomas: preliminary results of a feasible trial

F. TRIPPA, E. MARANZANO, S. COSTANTINI, C. GIORGI

ORIGINAL ARTICLES

J NEUROSURG SCI 2009;53:7-11

2009

- **35 pts (74% with neurologic symptoms)**
  - **hFSRT 42/45 Gy, 3 Gy/fr, 5 fr/wk**
    (α/β ratio for meningioma = 3 → EQD2 = 50.4/54Gy)
- **Median treatment volume 23 cc** (range, 4-58 cc; 66% > 20cc)
- **Median follow-up 29 months** (range, 10-51 months);
- **Median progression free survival 30 months** (range, 10-51months)

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TABLE I.—*Localization of 35 treated meningiomas.*

Tumor sites	Patient number	Percent
Cavernous sinus	9	26
Tubercle of sella	6	17
Sphenoidal/petroclival	5	14
Cerebello-pontine angle	5	14
Spheno-orbital	3	8
Tentorium	2	6
Temporal	2	6
Occipital	1	3
Clivus	1	3
Parasagittal	1	3

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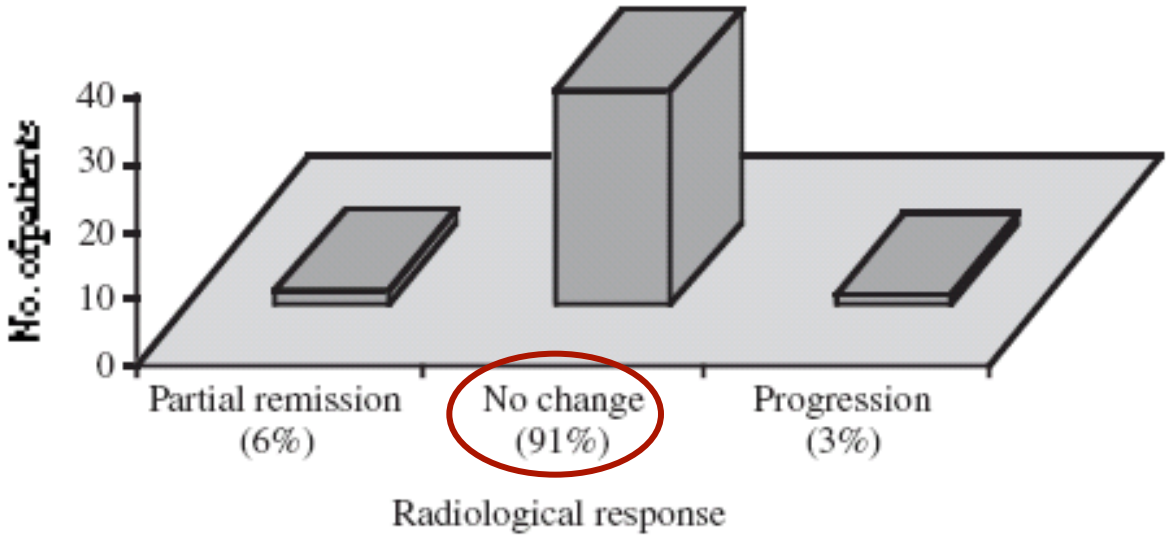

Figure 1.—Radiological response of 35 patients treated with hypofractionated stereotactic radiotherapy.

Hypofractionated stereotactic radiotherapy for intracranial meningiomas: preliminary results of a feasible trial

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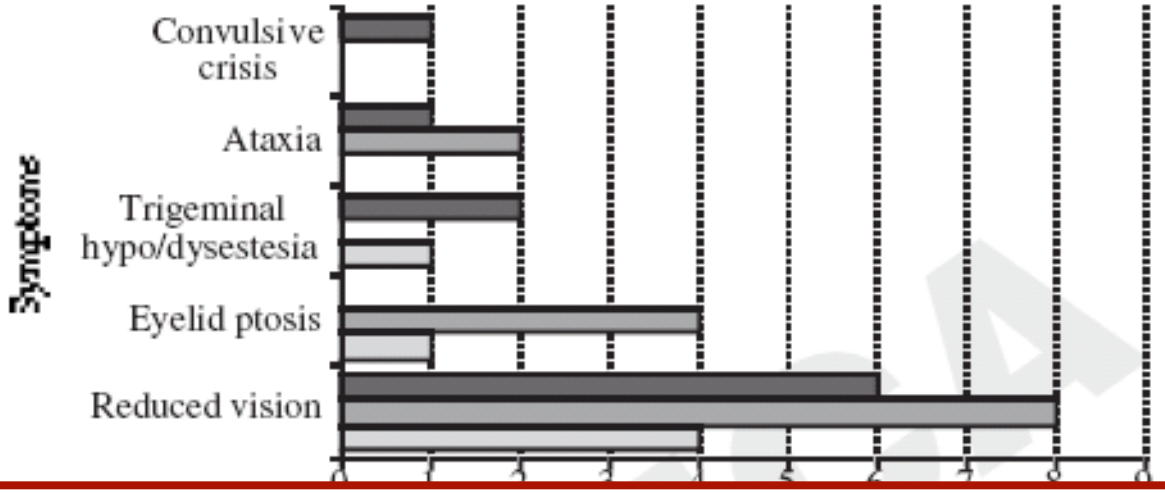
Clinical response



- 6 pts (23%): complete deficit resolution
- 16 pts (61%): improvement
- 4 pts (16%): no improvement

Hypofractionated stereotactic radiotherapy for intracranial meningiomas: preliminary results of a feasible trial

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Toxicity

- During hFSRT, a subjective intermittent headache secondary to RT-induced edema (acute grade 2 toxicity) was found in 2 pts (6%), and controlled with low doses of steroids.

- No other clinically significant acute or late toxicity was observed after hFSRT. In particular, no necrosis was seen during MRI follow-up.

ACOUSTIC NEUROMA
(VESTIBULAR SCHWANNOMA)

ACOUSTIC NEUROMA:

Topics

- The best management of patients with small- to medium sized neuromas is one of the most controversial topics in neurooncology (i.e., **surgery or radiosurgery?**).

- Several retrospective case-control series have been performed comparing surgical resection with SRS and, SRS had improved facial nerve outcomes and hearing preservation rates (i.e.,**less toxicity with SRS?**)

- It remains to be proven that the low SRS doses provides the same high rate of tumor control respect to higher SRS doses (i.e., **12–13Gy or 14–16Gy?**)

- Recently, many centres are using fractionated stereotactic RT (FSRT) to treat patients with bigger lesions. The dose and fractionation schemes adopted vary widely in published studies (i.e., **FSRT for lesions with ∅ ≥3cm? Which dose/s?**)

STEREOTACTIC RADIOSUGERY OF BENIGN INTRACRANIAL TUMORS. Pollack BE. *J Neurooncol 2009;92:337-343*

…..the number of neuroma patients having SRS continues to increase

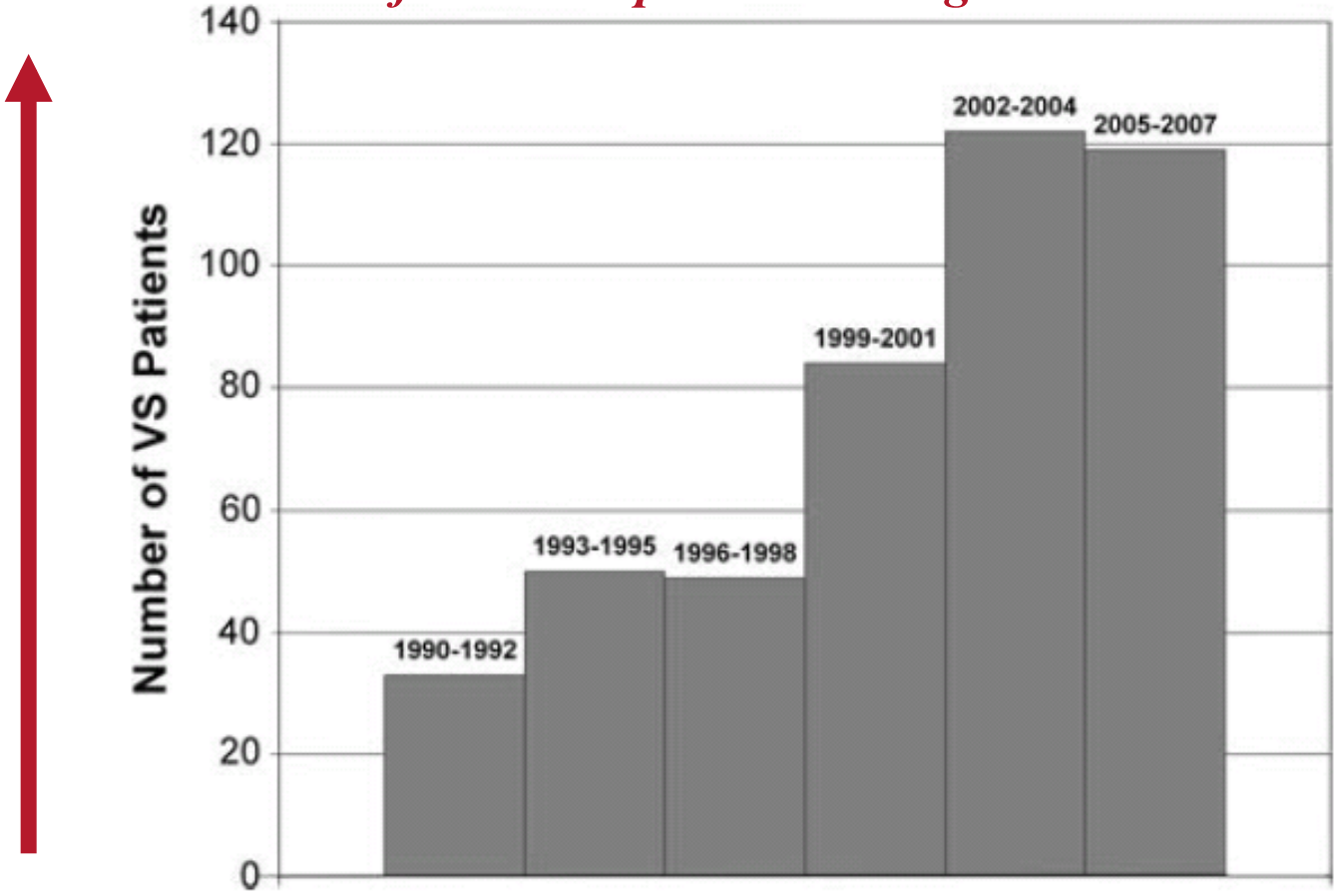

Fig. 2 Graph showing number of vestibular schwannoma patients having radiosurgery at the Mayo Clinic from 1990 to 2007 ***(Rochester,USA)***

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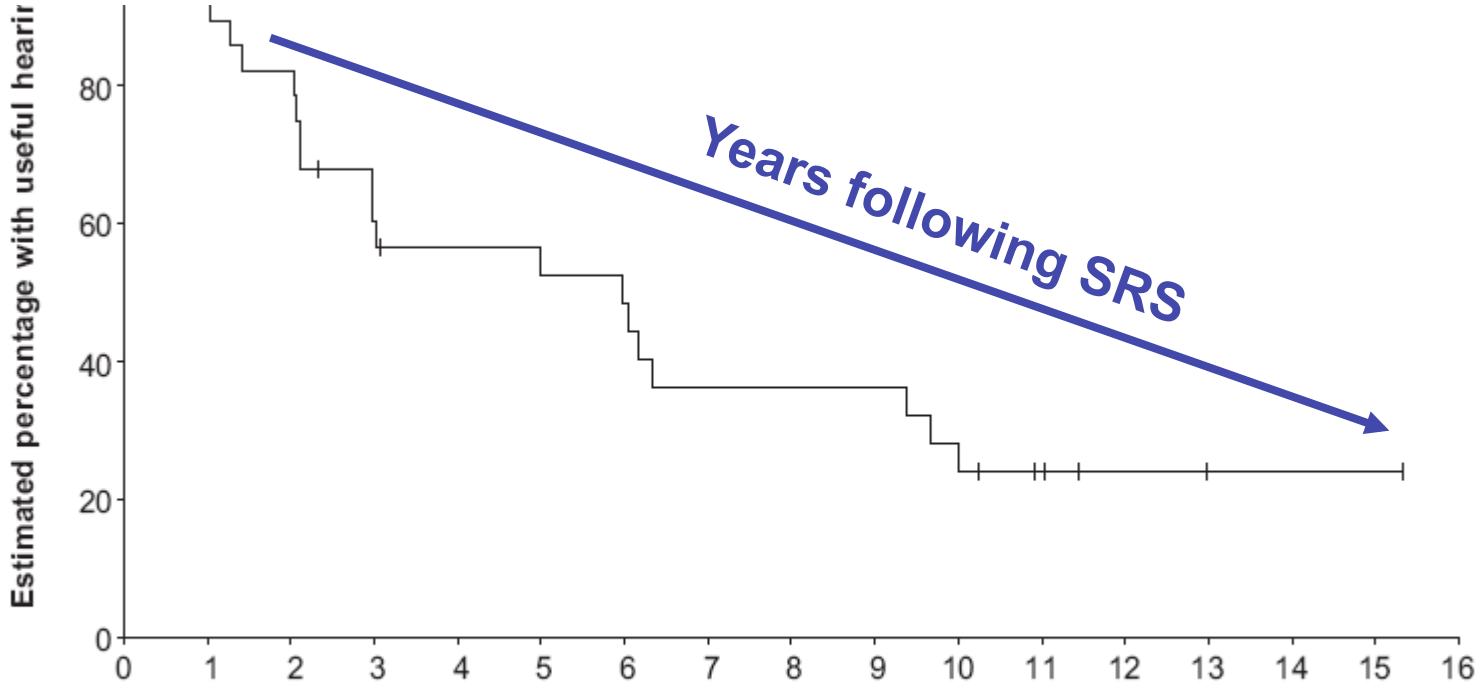
STEREOTACTIC RADIOSURGERY FOR ACOUSTIC NEUROMAS: WHAT HAPPENS LONG TERM?

DANIEL E. ROOS, B.SC.(HONS.), M.D., F.R.A.N.Z.C.R.,*‡ ANDREW E. POTTER, B.MED.SC., F.R.A.N.Z.C.R.,* AND BRIAN P. BROPHY, F.R.A.C.S.†‡

*Departments of Radiation Oncology and †Neurosurgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia; and ‡University of Adelaide School of Medicine, Adelaide, South Australia, Australia



Kaplan-Meier hearing preservation curve for 28 patients with initially useful hearing.

Red J 2012

CLINICAL INVESTIGATION Central Nervous System

STEREOTACTIC RADIOSURGERY FOR ACOUSTIC NEUROMAS: WHAT HAPPENS LONG TERM?

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*Departments of Radiation Oncology and †Neurosurgery, Royal Adelaide Hospital, Adelaide, South Australia, Australia; and ‡University of Adelaide School of Medicine, Adelaide, South Australia, Australia

CONCLUSIONS

The present analysis of Acoustic Neuromas patients undergoing SRS and treated ≥10 years earlier has confirmed

- **the excellent long-term tumor control and**
- **absence of late side effects, apart from**
  - **a low rate of hydrocephalus and**
  - **a continuing decline in useful hearing**

ACOUSTIC NEUROMA:

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ACOUSTIC NEUROMAS:
Dose/fractionation of SRS and FSRT

SRS:

- 12-13 Gy

vs.

- 14-17 Gy

FSRT:

- Standard fractionation: 2 → 50/54 Gy

vs.

- hFSRT: 3Gy→30 Gy, 3Gy→45Gy, 5-6Gy → 25-42Gy

FRACTIONATED STEREOTACTIC RADIOTHERAPY IN THE TREATMENT OF VESTIBULAR SCHWANNOMA (ACOUSTIC NEUROMA): PREDICTING THE RISK OF HYDROCEPHALUS

CERI POWELL, F.R.C.R.,* CAROLINE MICALLEF, F.R.C.R.,† ADAM GONSALVES, B.Sc. (HONS.),*
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*Neuro-oncolo gy and

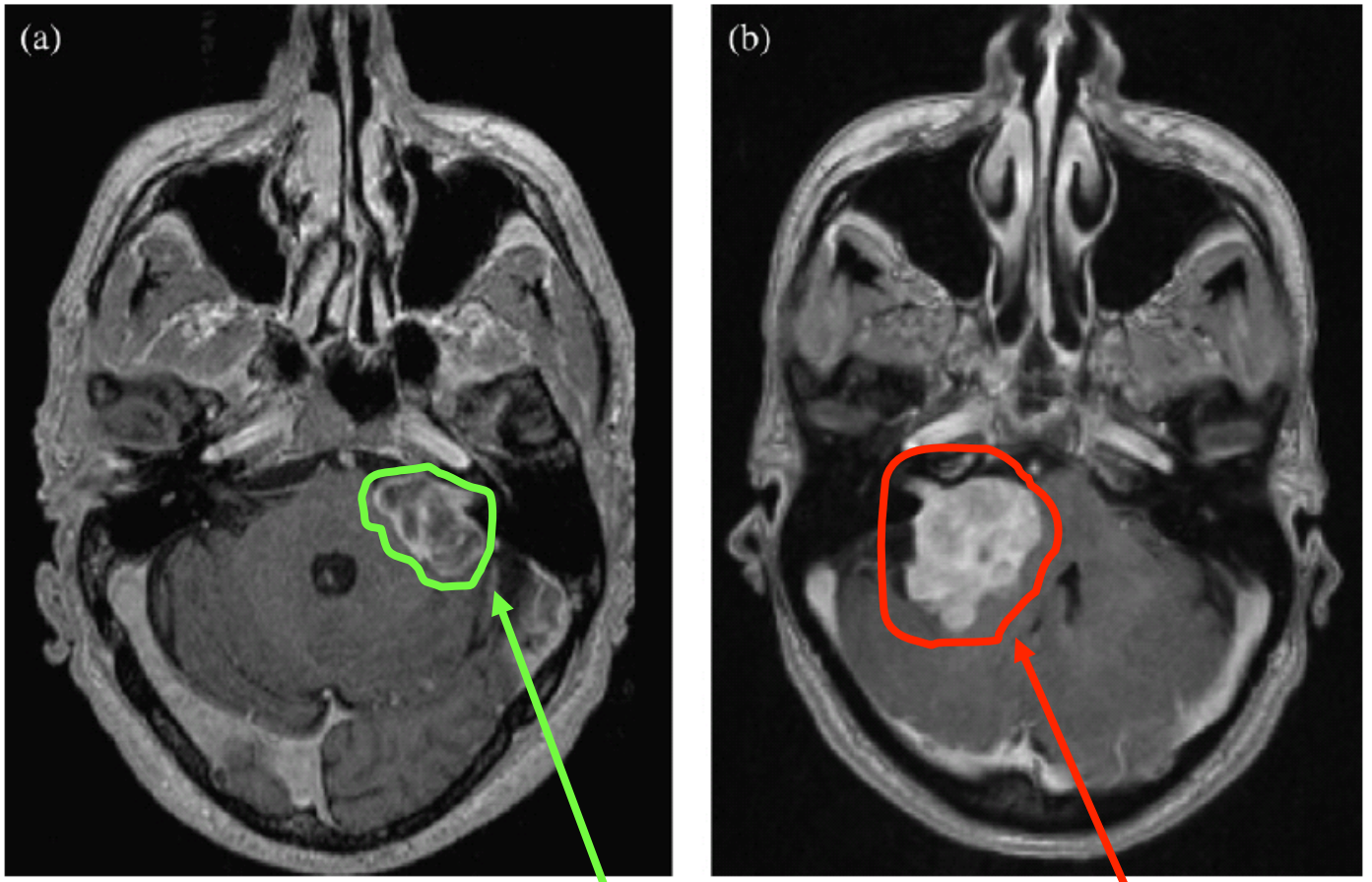

Fig. 1. Example o no effacement of the fourth ventricle (A) and partial effacement (B).

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*Neuro-oncology Unit, Royal Marsden NHS Foundation Trust, London, United Kingdom; †National Hospital for Neurology and

Conclusions:

- **Fractionated stereotactic radiotherapy (45–50 Gy in 25–30 fractions over 5 to 6 weeks) results in excellent tumor control of neuroma, though with a risk of developing hydrocephalus.**

- **Patients at high risk, identified as those with larger tumors with partial effacement of the fourth ventricle before treatment, should be monitored more closely during follow-up.**

- **It would be preferable to offer treatment to pts with progressive neuroma while the risk of hydrocephalus is low, before the development of marked distortion of fourth ventricle before tumor diameter significantly exceeds 2 cm**

IRSA® -International RadioSurgery Association guideline

Radiosurgery Practice Guideline Initiative

Stereotactic Radiosurgery for Patients with

Vestibular Schwannomas

Delayed Oncogenesis

- After radiosurgery, delayed malignant transformation of a histologically "benign" vestibular schwannoma to a more aggressive neoplasm is potentially possible.
- The observed incidence of secondary tumors after radiosurgery is unclear
- The estimated risk of such oncogenesis over a 5–30 year period (fitting the description of a radiation related cancer) is estimated to be less than 1:1000.
- This can be compared to the surgical mortality at Centers of Excellence of 0.5% of patients (1/ 200) in the first post-operative month after microsurgery.

OUR EXPERIENCE on NEUROMA

Period: from 12.9.01 to 18.10.12 (11 years)

	Total N° of patients	SRS	FSRT
MENINGIOMA	378	221 (58%)	157 (42%)
ACUSTIC NEUROMA	**140**	**124 (89%)**	**16 (11%)**

Stereotactic RT of Acoustic Neuroma: OUR EXPERIENCE

Patients and methods

	N. of patients
Radiotherapy:	**56**
- Radiosurgery	53 (95%)
- Stereotactic fractionated radiotherapy	3 (5%)
Neurological deficits:	
- No	3 (5%)
- **Yes**	53 (**95%**)
Acoustic nerve deficit	42 (79%)
Mixed deficit (VIII, VII and/or V)	11 (21%)
Previous surgery:	**15** (27%)
- Radical	5
- No radical	10

Stereotactic RT of Acoustic Neuroma: OUR EXPERIENCE

Doses

	Patient n.	Median dose (range)	Minimal dose (range)	Target volume
SRS	**53** **(95%)**	**17 Gy** **(13-20)**	**14 G** **(9-16.5)**	**(Ø cm 0.5-2.5)**
FSRT	**3** **(5%)**	42-45 Gy 3 Gy/fr	(37-40	**(Ø cm 2.6-3.5)**

Stereotactic RT of Acoustic Neuroma: OUR EXPERIENCE

Results

	Patients	
Follow up ≥ 2 years	31/56	
Late toxicity	9	29%
•*deficit V*	5	
•*deficit VII*	2	
•*deficit V & VII*	2	
Clinical response		84%
•*Stability*	20	
•*Improvement*	6	
•*Progression*	5	
MRI response		94%
•*Stability*	21	
•*Partial remission*	7	
•*Complete remission*	1	
•*Progression*	2	

Stereotactic RT of Acoustic Neuroma: OUR EXPERIENCE
Conclusions

In our experience, SRS of acoustic neuroma with no dedicated linac results in

- **a good local control rate**
- **a risk of cranial nerve toxicity slightly superior to that reported in literature.**
- **To reduce late toxicity, a more accurate pts selection has recently done reserving SRS to**
  - → **small lesions (≤ 2cm of ∅)**
  - → **prescribing doses not exceeding 15 Gy.**
- **Inoperable patients with large acoustic neuromas receive FSRT**

Extra-axial benign brain tumors: CONCLUSIONS

Patients with these tumors are **ideal candidates for surgery** and/or **radiosurgery**

but

- **Available literature data are of poor quality** *(class I & few class II evidence).*
- **RCTs are difficult to perform:**
  - *relatively low incidence and necessity of a long FU;*
  - ***some physician is polarized in his thinking and convince patient of his thinking***

Giotto - Scrovegni - Christ among the Doctors