Trattamento dei tumori benigni extra-assiali: la RADIOCHIRURGIA

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S.C. di Radioterapia Oncologica & * Neurochirurgia, Azienda Ospedaliera “S. Maria”, Terni
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
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
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.
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 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
Patients with these tumors are candidates for surgery, radiosurgery (SRS), surgery + post-op SRS, or observation. So, it is necessary to perform a proper patient selection.

A PROPER PATIENT SELECTION

on the basis of:

- Presence or absence of symptoms
- Tumor diameter ($< 3$ cm vs. $\geq 3$ 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-multileaf collimator
- High Conformity and Homogeneity
- No-coplanar dynamic arcs
- Multimodal imaging for target identification

CT & MRI image fusion
**Period: from 12.9.01 to 18.10.12 (11 years)**

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WHO grade 1: benign
WHO grade 2: atypical
WHO grade 3: malignant (anaplastic)
Post-op RT in incomplete resection or if WHO grade 3
Symptomatic

Small (< 30 mm)

Surgery if accessible, followed by RT if WHO Grade 3\(^c\) or RT\(^e\)

Large (≥ 30 mm)

Surgery if accessible, followed by RT if WHO Grade 3\(^c\); consider RT if incomplete resection and WHO Grade 1/2\(^c\) or RT\(^e\)

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

<table>
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<tr>
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<th>Total N° of Patients</th>
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Period: from 12.9.01 to 18.10.12 (11 years)
35 pts (74% with neurologic symptoms)
- hFSRT 42/45 Gy, 3 Gy/fr, 5 fr/wk
  \((\alpha/\beta \text{ ratio for meningioma } = 3 \rightarrow \text{EQD2 } = 50.4/54\text{Gy})\)

- 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, 10-51 months)
Table I.—Localization of 35 treated meningiomas.

<table>
<thead>
<tr>
<th>Tumor sites</th>
<th>Patient number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavernous sinus</td>
<td>9</td>
<td>26</td>
</tr>
<tr>
<td>Tubercle of sella</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Sphenoidal/petroclival</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Cerebello-pontine angle</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Spheno-orbital</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Tentorium</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Temporal</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Occipital</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Clivus</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Parasagittal</td>
<td>1</td>
<td>3</td>
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Hypofractionated stereotactic radiotherapy for intracranial meningiomas: preliminary results of a feasible trial

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

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

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

- 6 pts (23%): complete deficit resolution
- 16 pts (61%): improvement
- 4 pts (16%): no improvement
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)
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 Ø ≥3cm? Which dose/s? ).
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)
ACOUSTIC NEUROMA:

Topics

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STEREOTACTIC RADIOSURGERY FOR ACOUSTIC NEUROMAS: WHAT HAPPENS LONG TERM?


*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.
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.),* Bev Warden, F.R.C.R.P.*†

*Neuro-oncology, Queen Elizabeth Hospital, University of Birmingham, U.K.
†NHS Midlands, University Hospitals Birmingham, U.K.

Fig. 1. Example of no effacement of the fourth ventricle (A) and partial effacement (B).
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.
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.
Period: from 12.9.01 to 18.10.12 (11 years)

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<tr>
<td>Radiotherapy:</td>
<td>N. of patients</td>
<td></td>
<td></td>
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<td>--------------------------------------------------</td>
<td>----------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Radiosurgery</td>
<td>53 (95%)</td>
<td></td>
<td></td>
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<tr>
<td>- Stereotactic fractionated radiotherapy</td>
<td>3 (5%)</td>
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<tr>
<th>Neurological deficits:</th>
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<tr>
<td>- No</td>
<td>3 (5%)</td>
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<tr>
<td>- <strong>Yes</strong></td>
<td>53 (95%)</td>
</tr>
<tr>
<td>Acoustic nerve deficit</td>
<td>42 (79%)</td>
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<tr>
<td>Mixed deficit (VIII, VII and/or V)</td>
<td>11 (21%)</td>
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<tbody>
<tr>
<td>- Radical</td>
<td>5</td>
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<tr>
<td>- No radical</td>
<td>10</td>
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### Stereotactic RT of Acoustic Neuroma: Our Experience

<table>
<thead>
<tr>
<th></th>
<th>Patient n.</th>
<th>Median dose (range)</th>
<th>Minimal dose (range)</th>
<th>Target volume</th>
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<tbody>
<tr>
<td><strong>SRS</strong></td>
<td>53 (95%)</td>
<td>17 Gy (13-20)</td>
<td>14 Gy (9-16.5)</td>
<td>(Ø cm 0.5-2.5)</td>
</tr>
<tr>
<td><strong>FSRT</strong></td>
<td>3 (5%)</td>
<td>42-45 Gy 3 Gy/fr</td>
<td>(37-40) (Ø cm 2.6-3.5)</td>
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### Stereotactic RT of Acoustic Neuroma: Our Experience

#### Follow up ≥ 2 years

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<tbody>
<tr>
<td><strong>31/56</strong></td>
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#### Late toxicity

- **deficit V**
- **deficit VII**
- **deficit V & VII**

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<tr>
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<tr>
<td>9</td>
<td>29%</td>
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<tr>
<td>5</td>
<td></td>
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<tr>
<td>2</td>
<td></td>
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#### Clinical response

- **Stability**
- **Improvement**
- **Progression**

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<tr>
<td><strong>20/6</strong></td>
<td>84%</td>
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<td></td>
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#### MRI response

- **Stability**
- **Partial remission**
- **Complete remission**
- **Progression**

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<tr>
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<tr>
<td><strong>21/7</strong></td>
<td>94%</td>
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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.
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