



## Complete Summary

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### GUIDELINE TITLE

Stereotactic radiosurgery for patients with pituitary adenomas.

### BIBLIOGRAPHIC SOURCE(S)

IRSA. Stereotactic radiosurgery for patients with pituitary adenomas. Harrisburg (PA): IRSA; 2004 Apr. 12 p. (Practice Guideline Report; no. 3-04). [70 references]

## COMPLETE SUMMARY CONTENT

SCOPE  
METHODOLOGY - including Rating Scheme and Cost Analysis  
RECOMMENDATIONS  
EVIDENCE SUPPORTING THE RECOMMENDATIONS  
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS  
QUALIFYING STATEMENTS  
IMPLEMENTATION OF THE GUIDELINE  
INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT  
CATEGORIES  
IDENTIFYING INFORMATION AND AVAILABILITY

## SCOPE

### DISEASE/CONDITION(S)

Pituitary adenomas, acromegaly, Cushing's disease, Nelson's syndrome, prolactinoma

### GUIDELINE CATEGORY

Management  
Treatment

### CLINICAL SPECIALTY

Endocrinology  
Neurological Surgery  
Neurology  
Radiation Oncology

### INTENDED USERS

Health Care Providers  
Hospitals  
Managed Care Organizations  
Nurses  
Physicians  
Utilization Management

#### GUIDELINE OBJECTIVE(S)

To provide guidelines about the use of stereotactic radiosurgery in symptomatic patients with imaging identified pituitary adenomas with treatment recommendations to be used by medical and public health professionals

#### TARGET POPULATION

Men and women >2 years old with imaging identified functional or nonfunctional pituitary adenomas

Note: Patients may or may not be candidates for alternative management strategies that include observation, medical management, surgical resection via transsphenoidal approach or craniotomy, and fractionated radiation therapy.

#### INTERVENTIONS AND PRACTICES CONSIDERED

Stereotactic Radiosurgery

1. Single procedure or occasionally staged procedure (volume staging) techniques
2. Intraoperative stereotactic guidance
3. Digitally acquired images (computed tomography [CT] or magnetic resonance imaging [MRI])
4. Doses ranging from 11 to 16 Gy for non-functional (nonsecretory) adenomas and from 25 to 35 Gy for hormone normalization in cases of functional (secretory) pituitary adenomas

#### MAJOR OUTCOMES CONSIDERED

Long-term growth control (stabilization or regression) of non-functional pituitary adenomas and pituitary hormone normalization in cases of functional pituitary adenomas are the primary end points of interest. Maintenance of quality of life, employability, and prevention of adverse radiation effects are also considered.

## METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

MEDLINE and PUBMED searches were completed for the years 1971 to April 2004. Search terms included pituitary adenomas, acromegaly, Cushing's disease, prolactinoma, stereotactic radiosurgery, Gamma Knife, irradiation, Linac radiosurgery, proton beam radiosurgery, Bragg peak proton therapy, clinical trials, research design, practice guidelines, and meta-analysis. Bibliographies from recently published reviews were reviewed and relevant articles were retrieved.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)  
Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

This classification is based on the Bandolier system (<http://www.jr2.ox.ac.uk/bandoiler/band6/b6-5.html>) adapted for a systematic review.

#### Type & Strength of Evidence in Medical Literature

Type I: Evidence from a systematic review (which includes at least one randomized controlled trial and a summary of all included studies).

Type II: Evidence from a well designed randomized controlled trial of appropriate size.

Type III: Evidence from a well designed intervention study without randomization. A common research design is the before-and-after study.

Type IV: Evidence from a well designed non-experimental study, e.g., cohort, case-control or cross-sectional studies. (Also includes studies using purely qualitative methods. Economic analyses [cost-effectiveness studies] are also classified as Type IV evidence.)

Type V: Opinions of respected authorities, based on clinical evidence, descriptive studies or reports of expert consensus committees.

#### METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review with Evidence Tables

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The recommendations were originally suggested by a core group of two members. These recommendations were electronically mailed to all committee members. Feedback was obtained in order to revise the proposed guidelines. Committee members were asked whether the recommendations should serve as a practice guideline. No significant disagreements existed.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

External Peer Review  
Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The final statement incorporates all relevant evidence obtained by the literature search in conjunction with the final consensus recommendations supported by all working group members. The guideline was approved by the IRSA (International RadioSurgery Association) Board of Directors and issued in April 2004.

# RECOMMENDATIONS

## MAJOR RECOMMENDATIONS

Stereotactic radiosurgery is defined as a relatively high dose of focused radiation delivered precisely to the pituitary adenoma, under the direct supervision of a medical team (neurosurgeon, radiation oncologist, registered nurse, and medical physicist), in one surgical treatment session.

### Patient Selection

- Patients with pituitary adenomas, defined by modern neurodiagnostic imaging (computed tomography [CT], magnetic resonance imaging [MRI] scan) constitute the study group. Such patients typically present with symptoms related to pituitary hormone imbalance (acromegaly, Cushing's disease, prolactinoma, etc.) in cases of functional adenomas, and symptoms of mass

effect (headache, visual changes, and progressive neurological deficits) in cases of non-functional adenomas. Pituitary adenomas are considered suitable for multimodal management, including observation, surgical excision, fractionated radiation therapy, and stereotactic radiosurgery. Stereotactic radiosurgery is typically employed in combination with prior surgery but may be employed alone in particular circumstances. The selection of patients suitable for radiosurgery is dependent on the prior treatment history, the age of the patient, existing comorbidities, anatomic location of the tumor, and clinical history. Single session radiosurgery, a minimally invasive, single high-dose, closed skull treatment strategy, may be especially suitable for patients in advanced age groups, those with excessive medical comorbidity risk factors for surgical excision, and those with adenoma involving the cavernous sinus.

## Treatment/Management

- The optimal dose range for volumetric conformal stereotactic pituitary radiosurgery has been largely established based on tumor anatomy (proximity to visual apparatus), hormonal secretory status, volume, estimated adverse radiation risks, pre-existing neurological conditions, and prior history of radiation therapy. Minimum doses to the margin of the non-functional pituitary adenomas typically range from 12 to 16 Gy in a single fraction. For secretory adenomas, minimal margin doses as high as 30 to 35 Gy are optimal if they can be administered safely given the anatomic relationship of the tumor edge to surrounding radiosensitive structures. Stereotactic volumetric imaging (high resolution) is usually necessary for precise conformal dose planning. MRI target imaging is preferred. Depending upon the technology used, the margin of the radiosurgery dose is usually 50 to 90% of the central target dose within the tumor. Sharp fall-off of the radiation dose outside of the target volume is required. Current radiation delivery technologies for volumetric stereotactic conformal single session radiosurgery include Gamma Knife®, proton beam using Bragg peak effect, and specially modified linear accelerators.
- Patients may receive a single stress dose of corticosteroids at the conclusion of the radiosurgery procedure. It is recommended that hormone suppression therapy (dopaminergic drugs for prolactinomas and octreotide for acromegaly) be discontinued at least 1 to 2 months prior to radiosurgery. Currently used long acting drugs (e.g., slow release octreotide) should be discontinued 3 to 4 months prior to radiosurgery. These medications can be restarted one week after the radiosurgery procedure. Patients can continue to take other medications as recommended by their physicians.
- Postradiosurgical clinical examinations and magnetic resonance (MR) studies are requested by referring physicians at six-month intervals for the first year and then annually to assess the effect of radiosurgery for 4 to 5 years. Visual field and acuity testing along with serum and urinary hormone screening are recommended at intervals coinciding with clinical and neuroimaging reevaluations. Tumors proven to be stable over five years can then be subsequently reassessed at 2 to 4 year intervals.
- For non-functional adenomas, estimated tumor control rates vary from 90 to 100%. Stereotactic radiosurgery should not be considered as the panacea for large volume pituitary adenomas, which are better managed initially by surgery. This is particularly true for patients who present with sudden symptomatic mass effect from pituitary apoplexy.

- Causes for failure of stereotactic radiosurgery include inadequate visualization of the tumor, lack of intraoperative stereotactic three-dimensional (3-D) (volumetric) imaging, and insufficient dose (due to proximity with optic apparatus) to achieve the growth control response.

#### CLINICAL ALGORITHM(S)

The original guideline contains clinical algorithms for management choices for pituitary adenomas and pituitary adenoma surgical management.

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Type I, II, and III evidence exists in support of stereotactic radiosurgery for pituitary adenomas. Refer to the "Rating Scheme for the Strength of the Evidence" field.

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- All the published studies have shown a significant tumor control response of stereotactic radiosurgery for non-functioning pituitary adenomas with a low (satisfactory) rate of adverse radiation effect. For functional adenomas, normalization of hormone levels is considered necessary in order to define success. Successful outcomes include complete tumor control (stabilization or regression), symptomatic relief, no new neurological deficits, no long-term complications, and normalization of pituitary hormone levels.
- Literature has documented the cost savings benefit of stereotactic radiosurgery versus invasive surgical procedures and the lower risk potential of bleeding, anesthesia problems, infections, and side effects which may result in transient or permanent disabilities from open surgery.

#### Subgroups Most Likely to Benefit

- Patients with residual or recurrent pituitary adenoma after resection
- Patients with small pituitary adenoma without any previous surgery

#### POTENTIAL HARMS

Major adverse effects of radiosurgery are based on location, volume, and dose, and these risks can be estimated based on published data and experience. Individual risks are related to the anatomic proximity of pituitary adenoma with the optic apparatus and structures of cavernous sinus. Risk of delayed hypopituitarism after single session radiosurgery is low.

#### Subgroups Most Likely to be Harmed:

- Patients with large volume adenomas causing symptomatic mass effect on optic apparatus who are treated with large doses in a single session radiosurgery as primary management
- Patients with functional adenomas treated with low dose will benefit least from the surgery.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

This guideline is not intended as a substitute for professional medical advice and does not address specific treatments or conditions for any patient. Those consulting this guideline are to seek qualified consultation utilizing information specific to their medical situation. Further, the International RadioSurgery Association (IRSA) does not warrant any instrument or equipment nor make any representations concerning its fitness for use in any particular instance nor any other warranties whatsoever.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Living with Illness

### IOM DOMAIN

Effectiveness  
Patient-centeredness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

IRSA. Stereotactic radiosurgery for patients with pituitary adenomas. Harrisburg (PA): IRSA; 2004 Apr. 12 p. (Practice Guideline Report; no. 3-04). [70 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Apr

GUIDELINE DEVELOPER(S)

IRSA - Professional Association

GUIDELINE DEVELOPER COMMENT

IRSA (International RadioSurgery Association) is a non-profit entity dedicated to promoting the development of scientifically relevant practice guidelines for stereotactic radiosurgery. IRSA works to educate and provide support for physicians, hospitals, insurers, and patients.

SOURCE(S) OF FUNDING

IRSA (International RadioSurgery Association)

GUIDELINE COMMITTEE

IRSA (International RadioSurgery Association) Physician Advisory Board Guidelines Committee and other professionals who provide radiosurgery

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Committee Members: L. Dade Lunsford, MD, Neurosurgeon, (Chair); Ajay Niranjana, MBBS, MCh, Neurosurgeon; Tatsuya Kobayashi, MD, PhD, Neurosurgeon; Mark Linskey, MD, Neurosurgeon; Thomas Witt, MD, Neurosurgeon; Alex Landolt, MD, Neurosurgeon; Roman Liscak, MD, Neurosurgeon; Edward R. Laws, Jr., MD, Neurosurgeon; Mary Lee Vance, MD, Endocrinologist; John Buatti, MD, Radiation Oncologist; Jonathan Knisely, MD, Radiation Oncologist; Paul Sperduto, MD, Radiation Oncologist; Sammie Coy, PhD, Medical Physicist; Tonya K. Ledbetter, MS, MFS, Editor; Rebecca L. Emerick, MS, MBA, CPA, ex officio

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).

Print copies: Available from the IRSA (International RadioSurgery Association), 3005 Hoffman Street, Harrisburg, PA 17110.

#### AVAILABILITY OF COMPANION DOCUMENTS

None available

#### PATIENT RESOURCES

The following are available:

- Pituitary tumors. Brain Talk 2003;8(3):1-8. Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).
- Radiosurgery & radiation therapy overview. Another Perspective 1999;4(2):1-12. Electronic copies: Available in Portable Document Format (PDF) from the [IRSA Web site](#).
- Proper treatment of pituitary tumor may restore patient's eyesight. Another Perspective 1997; 2(4):1-12.
- Pituitary tumors and stereotactic radiosurgery (brochure). Harrisburg (PA): IRSA; 2004.

Print copies: Available from the IRSA, 3005 Hoffman Street, Harrisburg, PA 17110.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

#### NGC STATUS

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