AAPM WGSBRT
NTCP
Optic Apparatus
(chiasm and nerve)

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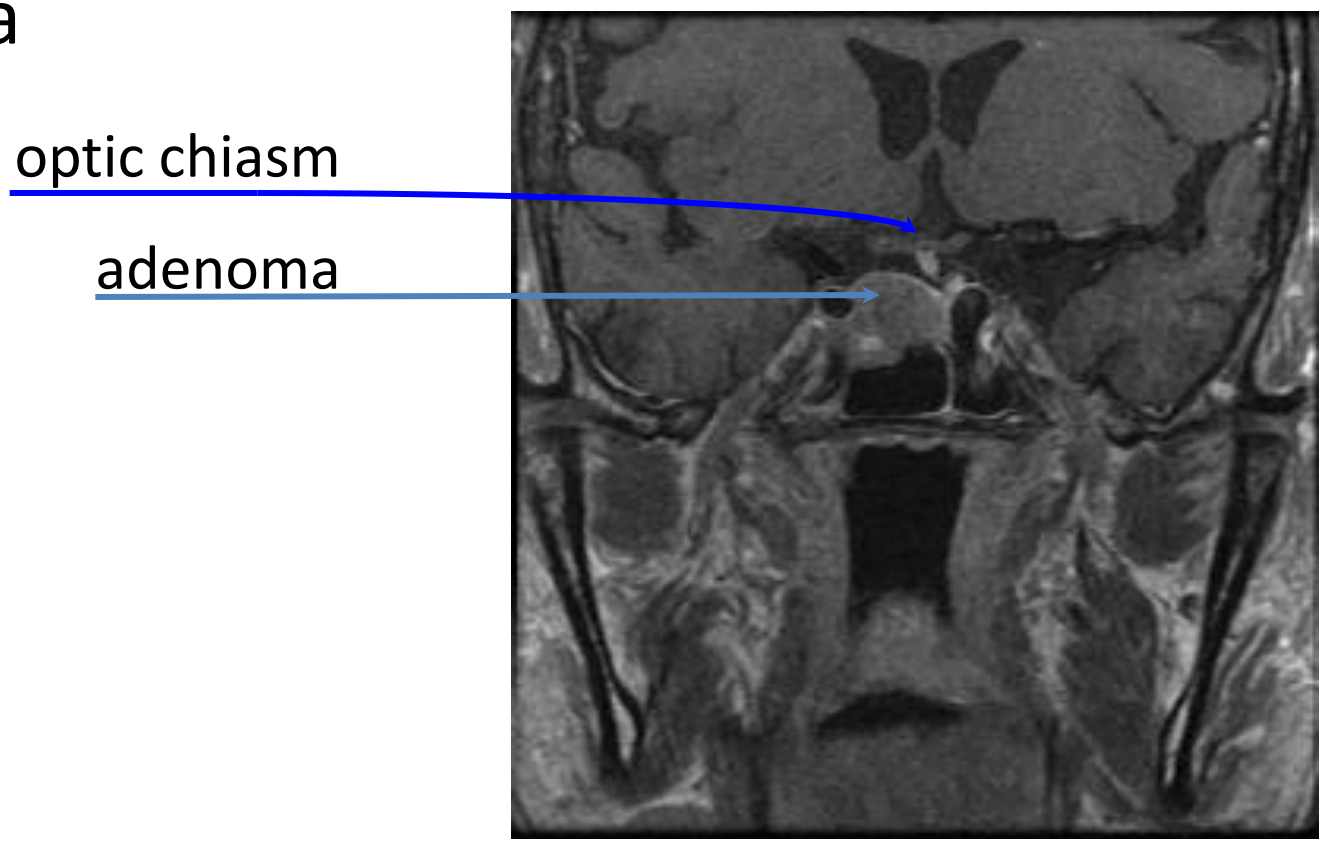
Optic nerves and chiasm

pituitary adenoma



Optic nerves and chiasm

- Toxicity: radiation-induced optic neuropathy (RION)
  - *decreased visual acuity*
  - *visual field deficits/vision loss*
    - generally occurs within 3 years after SRS

Scoring systems for optic nerve/chiasm toxicity

	RTOG/EORTC LENT SOMA	CTCAE version 3	CTCAE version 4
Grade 0	None	none	none
Grade 1	Afferent pupillary defect with normal appearing nerve	Asymptomatic, detected on exam/testing only	Asymptomatic; clinical or diagnostic observations only
Grade 2	< 1/4 pallor with asymptomatic visual field defect	Symptomatic, not interfering with ADL	Limiting vision of the affected eye (20/40 or better)
Grade 3	>1/4 pallor or central scotoma	Symptomatic, interfering with ADL	Limiting vision in the affected eye (worse than 20/40 but better than 20/200)
Grade 4	Profound optic atrophy, complete blindness	Life-threatening; disabling	Blindness (20/200 or worse) in the affected eye

RTOG: Radiation Therapy Oncology Group
EORTC: European Organisation for Research and Treatment of Cancer
LENT: Late Effects in Normal Tissue
SOMA: Subjective, Objective, Management, Analytic
CTCAE: Common Terminology Criteria for Adverse Events

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Definitions

- **Stereotactic Radiosurgery (SRS)**
  - 1 fraction
- **Fractionated SRS (fSRS)**
  - 2-5 *hypofractionated*

Methods

- Pooled analysis of studies reporting RION (or absence of RION) after SRS/fSRS
  - Summarize publish data
  - develop NTCP risk model

Methods

- PubMed search
  - *34 studies*
  - *1,578 patients*

Methods

- PubMed search
  - *34 studies*
    - *1990-Jun 2015*
    - *information on*
      - *optic apparatus maximal dose exposure*
      - *RION after SRS/fSRS*
  - *1,578 patients*

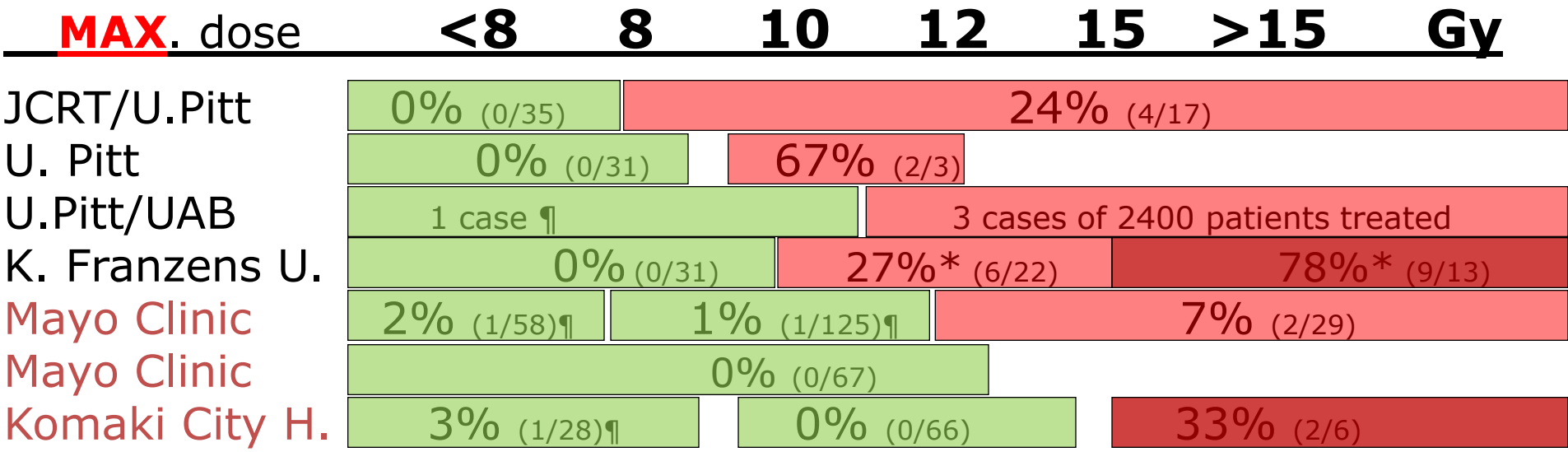
Methods

- PubMed search
  - *34 studies*
  - *1,578 patients*

- Maximum dose to optic nerve/chiasm

Optic nerves and chiasm

Risk of optic neuropathy



* Actuarial incidence @ 3-years

¶ SRS + fract. RT in case of optic neuropathy.
In Mayo series, all had preceding surgery as well

Tishler *IJROBP* **27**: 215-21 (1993)
Duma *Neurosurg*. **32**: 699-704 (1993)
Girkin *Opthamol*. **104**: 1634-43 (1997)
Leber *J Neurosurg*. **88**: 43-50 (1998)

Stafford *IJROBP* **55**: 1177-81 (2003)
Pollock *IJROBP* **70**: 1325-9 (2008)
Hasegawa *Neurosurg*. **66**: 688-95 (2010)

RION: Variables analyzed

- *no* patient treated after 1997 vs. *some/all* treated after 1997 — **p=0.023**; **p=0.019** *
- SRS delivery system
  LINAC, Gamma knife, Cyberknife — p=0.42; p=0.31 *
- Prior resection — p=0.66
- Prior radiotherapy — **p=0.004**

** For patients with no prior radiotherapy*

RION: Variables analyzed

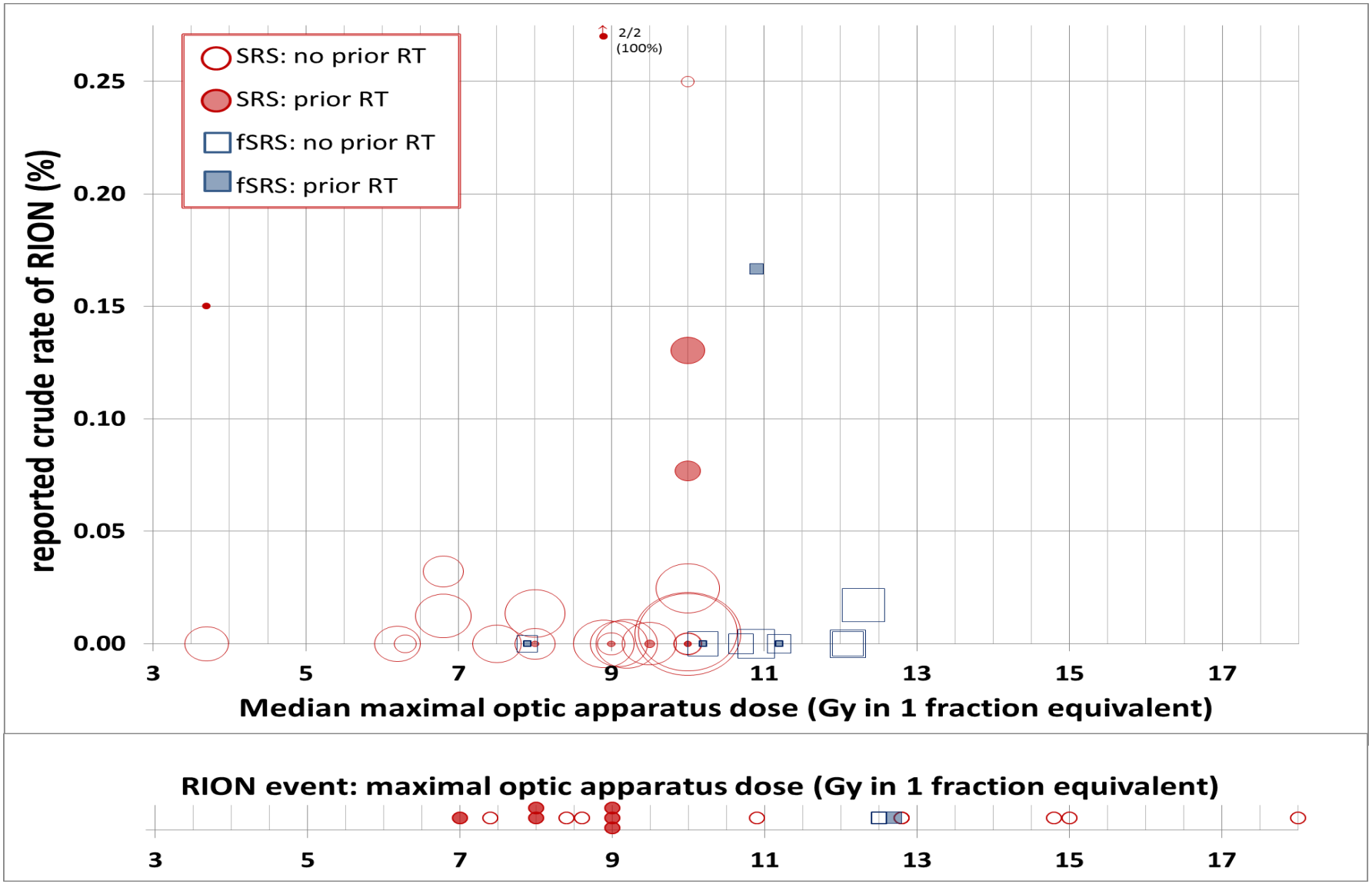
- *no* patient treated after 1997 vs. *some/all* treated after 1997 — **p=0.023**; **p=0.019** *
- SRS delivery system (LINAC, Gamma knife, Cyberknife) — p=0.42; p=0.31 *
- Prior resection — p=0.66
- Prior radiotherapy — **p=0.004**

10-fold increased risk

** For patients with no prior radiotherapy*

RION

Studies with *some or all* patients treated after 1997



Methods

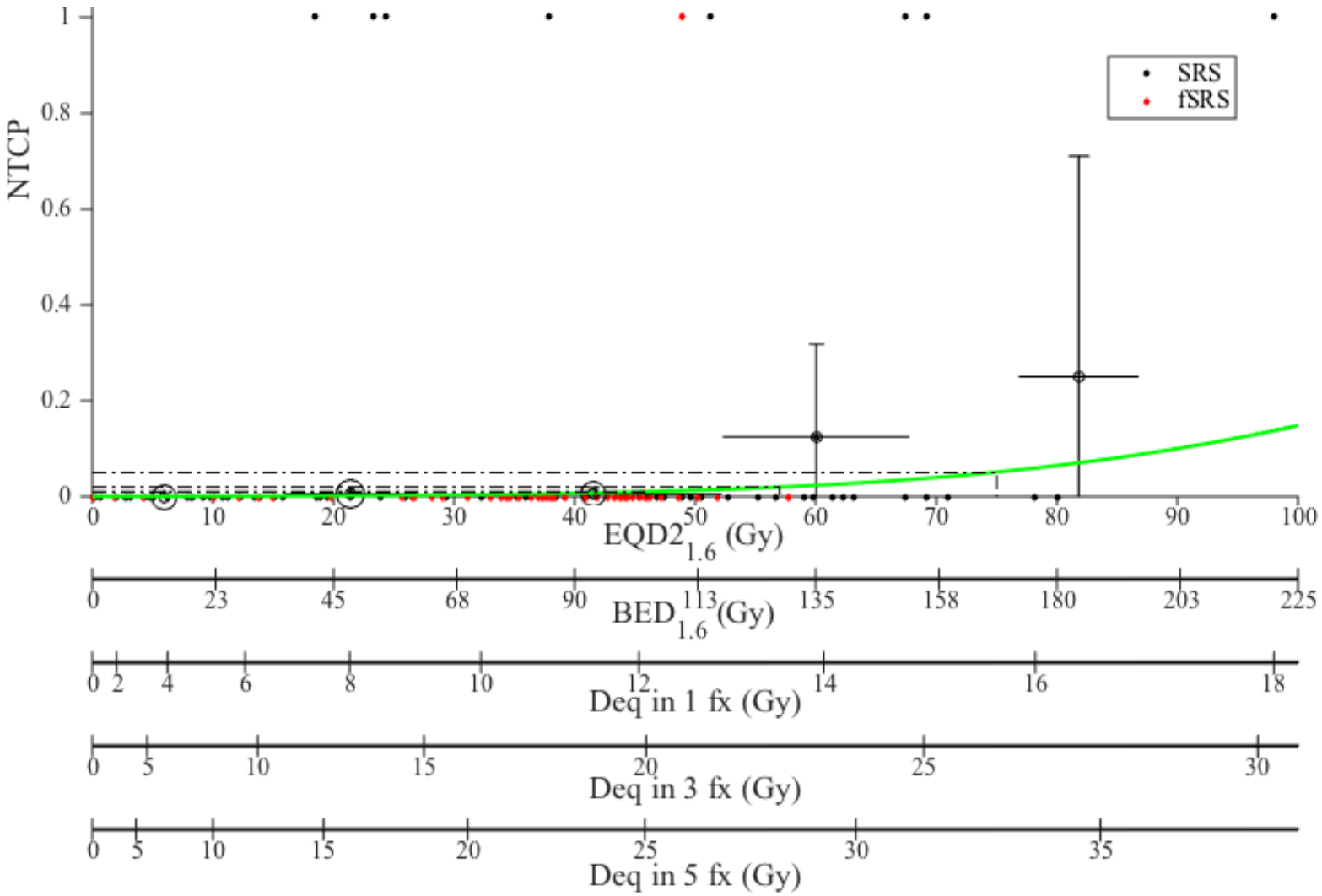
- NTCP modelling

$$NTCP = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{t} e^{\frac{-u^2}{2}} du$$

$$t = \frac{D - TD50}{m \cdot TD50}, \quad m = \frac{1}{\gamma_{50}\sqrt{2\pi}}$$

  - *α/β ratio = 1.6 Gy for dose conversions*

RION: NTCP Model



RION

	$EQD2_{1.6}$	1-fraction SRS	3-fraction fSRS	5-fraction fSRS
NTCP model including all studies				
1% risk	46.0 Gy	12.1 Gy	20.0 Gy	25.1 Gy
2% risk	59.1 Gy	13.8 Gy	23.0 Gy	28.9 Gy
5% risk	74.8 Gy	15.6 Gy	26.1 Gy	32.9 Gy
NTCP model including only single-fraction SRS studies				
1% risk	33.0 Gy	10.1 Gy	-	-
2% risk	41.0 Gy	11.4 Gy	-	-
5% risk	52.1 Gy	12.9 Gy	-	-

RION

	$EQD2_{1.6}$	1-fraction SRS	3-fraction fSRS	5-fraction fSRS
NTCP model including all studies				
1% risk	46.0 Gy	12.1 Gy	**20 Gy**	**25 Gy**
2% risk	59.1 Gy	13.8 Gy	23.0 Gy	28.9 Gy
5% risk	74.8 Gy	15.6 Gy	26.1 Gy	32.9 Gy
NTCP model including only single-fraction SRS studies				
1% risk	33.0 Gy	**10 Gy**	-	-
2% risk	41.0 Gy	11.4 Gy	-	-
5% risk	52.1 Gy	12.9 Gy	-	-

Limitations

- Limited data in high-dose range (P_{max}>13 Gy/1Fx)
- Uncertainties in a/b ratio
- Uncertainties in EQD2/BED calculations
- Error bars in NTCP curves
- NTCP calculations do not account for magnitude of toxicity (i.e. grade)
- Optic apparatus not uniformly defined/delineated

Future studies should …

- Detail prior therapy (surgery/RT)
- Clear define how OAR was defined
  - Image modalities/MRI sequences
  - Slice thickness
- Clearly describe planning algorithm and treatment system used

Future studies should …

- Define point ‘volume’ (i.e. 0.03 ml) for maximal dose
- Define small volume exposure (i.e. $D_{0.2ml}$)
- Describe mean dose

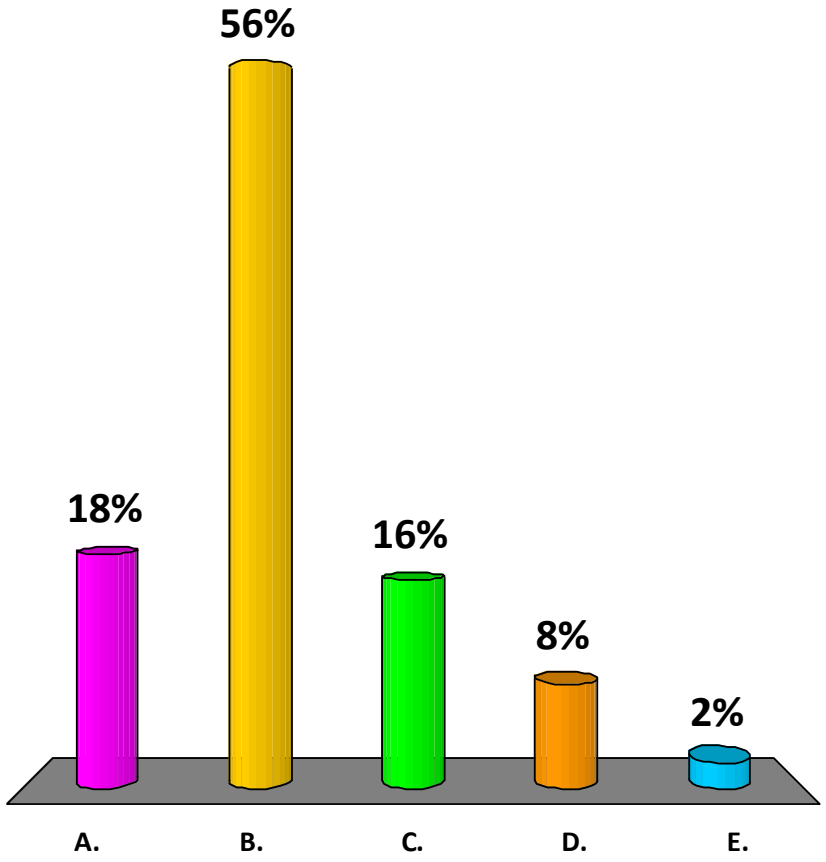
Future studies should …

- Describe patient follow-up
- Describe post-SRS visual assessment
- Standardize RION grade reporting

QUESTION 1

The incidence of grade 3+ radiation induced optic neuropathy (RION) for patients receiving modern cranial SRS is

A. Less than 0.1%
B. Less than 3%
C. More than 3%
D. More than 10%
E. More than 25%



ANSWER

a. Less than 0.1%
b. Less than 3%
c. More than 3%
d. More than 10%
e. More than 25%

EXPLANATION: Reported RION risks are on the order of <1-2% in modern series.

Provided Reference:

Milano MT et al. Stereotactic radiosurgery and hypofractionated stereotactic radiotherapy: normal tissue dose constraints of the central nervous system. Cancer Treat Rev. 2011 Nov;37(7):567-78.

QUESTION 2

The safest (with respect to vision preservation) dose-volume delivery to the optic nerve in a single fraction radiosurgery plan would be:

2%

A. Median dose of 7.8 Gy to optic nerve

56%

B. Maximal dose of 7.8 Gy to optic nerve

36%

C. Maximal dose of 13 Gy to optic nerve with 95% receiving 10 Gy or less

1%

D. Minimal dose of 7.8 Gy to optic nerve

5%

E. Average dose of 7.8 Gy to the optic nerve

ANSWERS

a. Median dose of 7.8 Gy to optic nerve

b. Maximal dose of 7.8 Gy to optic nerve

c. Maximal dose of 13 Gy to optic nerve with 95% receiving 10 Gy or less

d. Minimal dose of 7.8 Gy to optic nerve

e. Average dose of 7.8 Gy to the optic nerve

EXPLANATION: While maximal doses in excess of 10 Gy to the optic nerve are presumably safe, the plan delivering the lowest dose to the optic nerve is the safest.

Provided Reference:

Shrieve DC et al. Dose fractionation in stereotactic radiotherapy for parasellar meningiomas: radiobiological considerations of efficacy and optic nerve tolerance. J Neurosurg. 2004 Nov;101 Suppl 3:390-5.

THANK YOU FOR YOUR ATTENTION