Gamma Knife Radiosurgery

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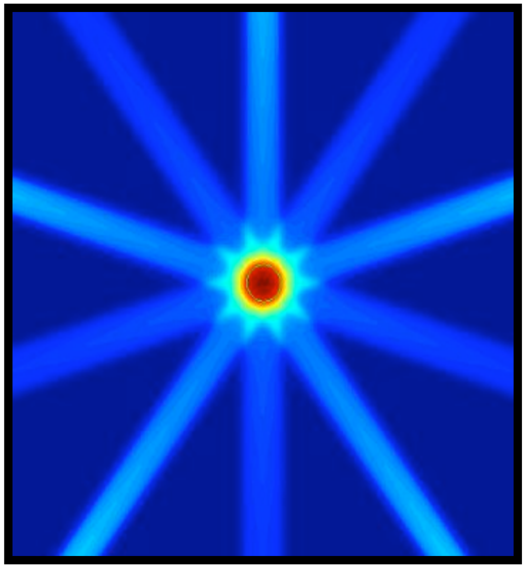
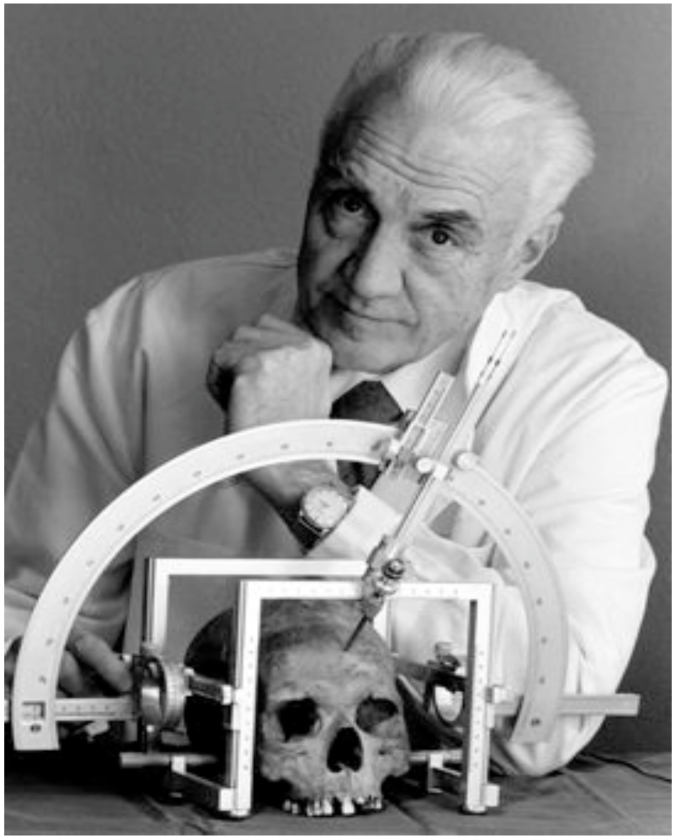
Disclosure: P. Petti is a PFX system-start consultant for Elekta Instrument AB

Lars Leksell, neurosurgeon, introduces idea of stereotactic radiosurgery in 1951

"The stereotactic technique enables the accurate insertion of a needle electrode into any given structure of the brain…



It would therefore be feasible to replace the needle by narrow beams of radiant energy directed at the target in the brain and thereby produce a local destruction of the tissue…"

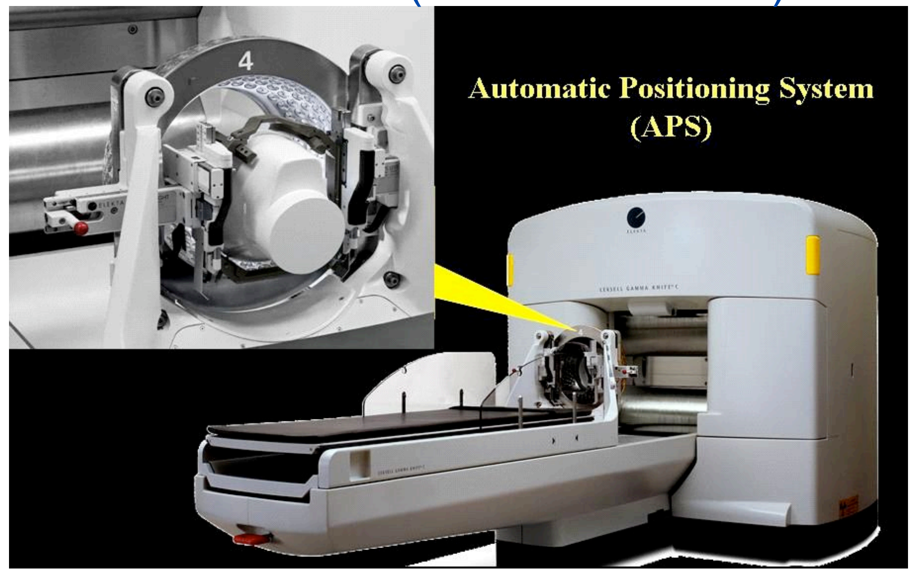


L. Leksell, Acta Chir Scand 102:316-319, 1951

Leksell Gamma Knife

Model U: (Introduced 1986)

Model C: (Introduced 1999)



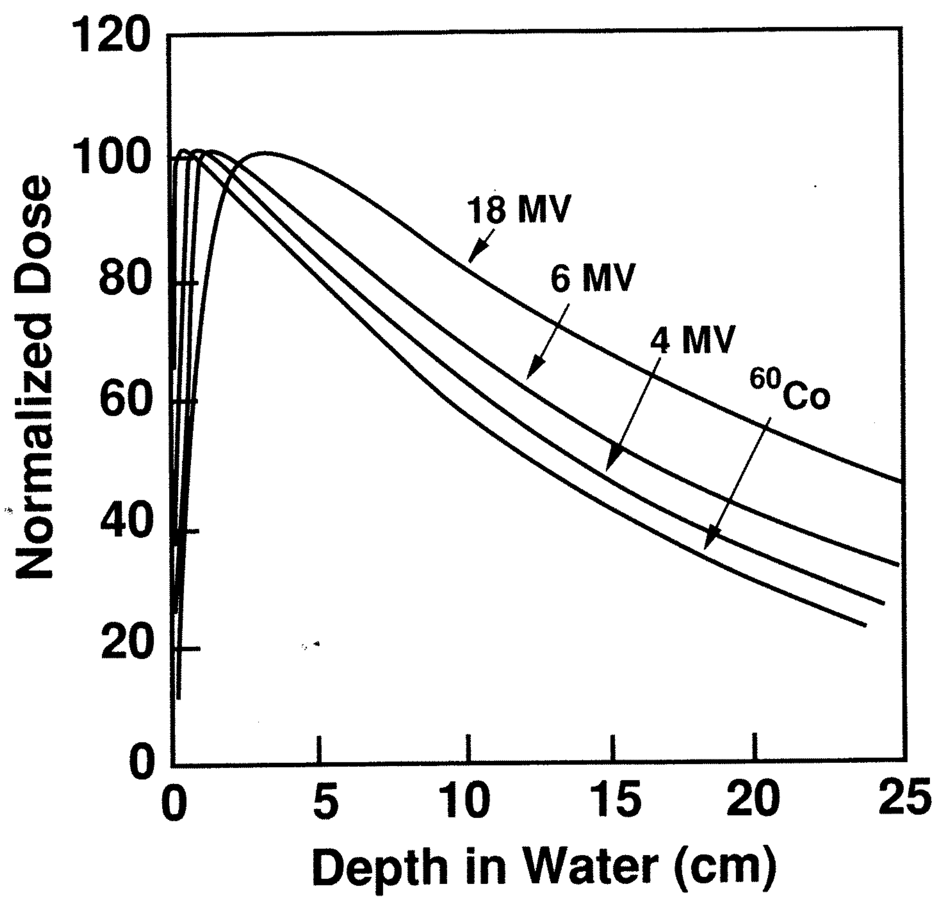
Perfexion: (Introduced 2006)

Properties of Leksell Gamma Knife® Radiosurgery

- ~200 ^{60}Co sources (6000 Ci total initial activity)
- Sources positioned and collimated to focus radiation precisely at isocenter
- Prescription volume shaped to match the target volume by:
  - translating the patient in 3 orthogonal directions between “shot” settings
  - using appropriately sized collimators for each shot

Properties of ^{60}Co

^{60}Co isotope produced by bombarding ^{59}Co with neutrons in a nuclear reactor $\Rightarrow$ The U.S. Nuclear Regulatory Commission (NRC) oversees its use

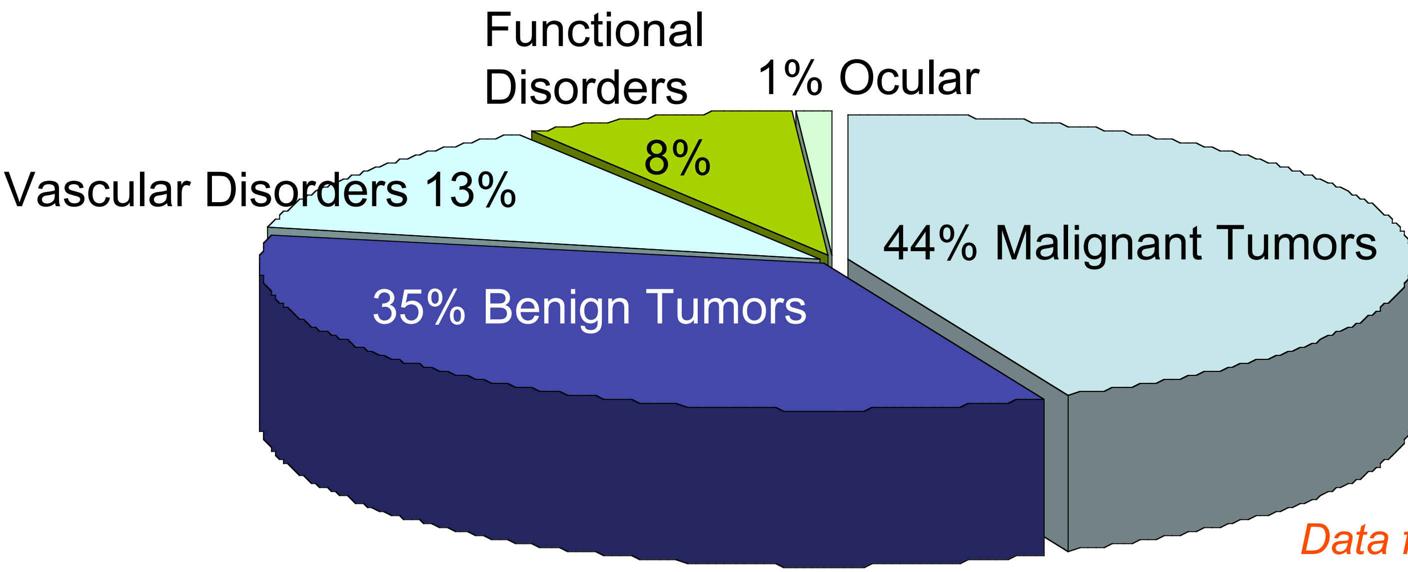


^{60}Co decays via beta decay, producing 2 mono-energetic γ-rays, 1.17 and 1.33 MeV in the process

The half life of ^{60}Co is 5.27 yrs.

Depth dose distribution similar to 4 MV photons

Indications for Gamma Knife Radiosurgery



Data from Leksell Gamma Knife Society, worldwide 2009 statistics

Examples:

Malignant tumors: Brain metastases, glial tumors

Benign tumors: Meningioma, vestibular schwannoma, pituitary adenoma

Vascular disorders: Arteriovenous malformation

Functional disorders: Trigeminal neuralgia

Criteria for Gamma Knife Radiosurgery

Single-fraction GK SRS

- Largest tumor dimension ≤ 3 to 4 cm
- Minimum distance to optic apparatus ≥ 2 mm
- Max number of lesions that can reasonably be treated in a single session ~ 30
- Can treat very small tumors (e.g. small brain metastases with dimension of the order 2 mm)

Multiple-fraction GK SRS (Extend system)

- Largest tumor dimension > 4 cm
- Tumor “too close” to optic apparatus
- Occasionally, patient preference

Localization Systems for GK

Leksell Stereotactic Frame: attached to patient via 4 pins

Single-fraction radiosurgery

Leksell Extend re-locatable frame system: vacuum bite block

Fractionated radiosurgery

Images from Elekta brochures

GK Model Comparison

Models U, C and 4C	Perfexion™
Secondary collimators are external, must be manually changed	All collimation is internal
Source position fixed	Sources move
Patient position changed manually or semi-automatically	Patient position changed automatically
	Treatment couch = the patient positioning system

Perfexion™ Collimator

- 3 collimator sizes (4-, 8- and 16-mm)
- 576 collimating channels
- Material is tungsten

Material	Density (kg/m^3)	^{60}Co approx. HVL(mm)
Tungsten	19300	7.9
Steel	7800	21

(Images courtesy of Elekta)

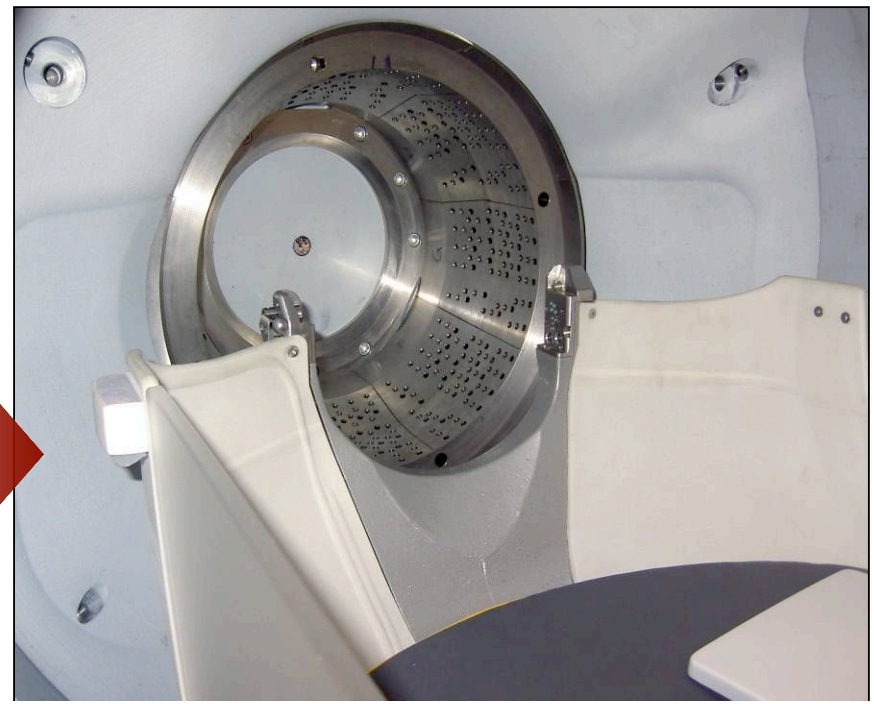
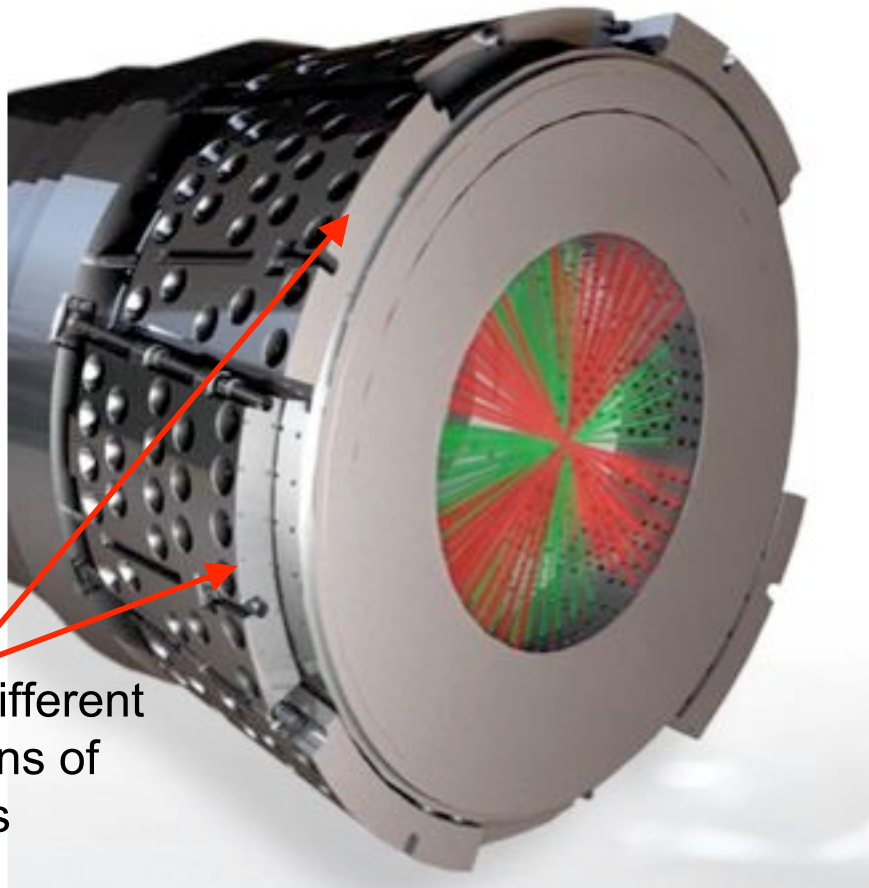


Illustration of Sector Positions



Note different positions of sectors

Sectors alternating 16-mm (red) and 8-mm (green) collimators

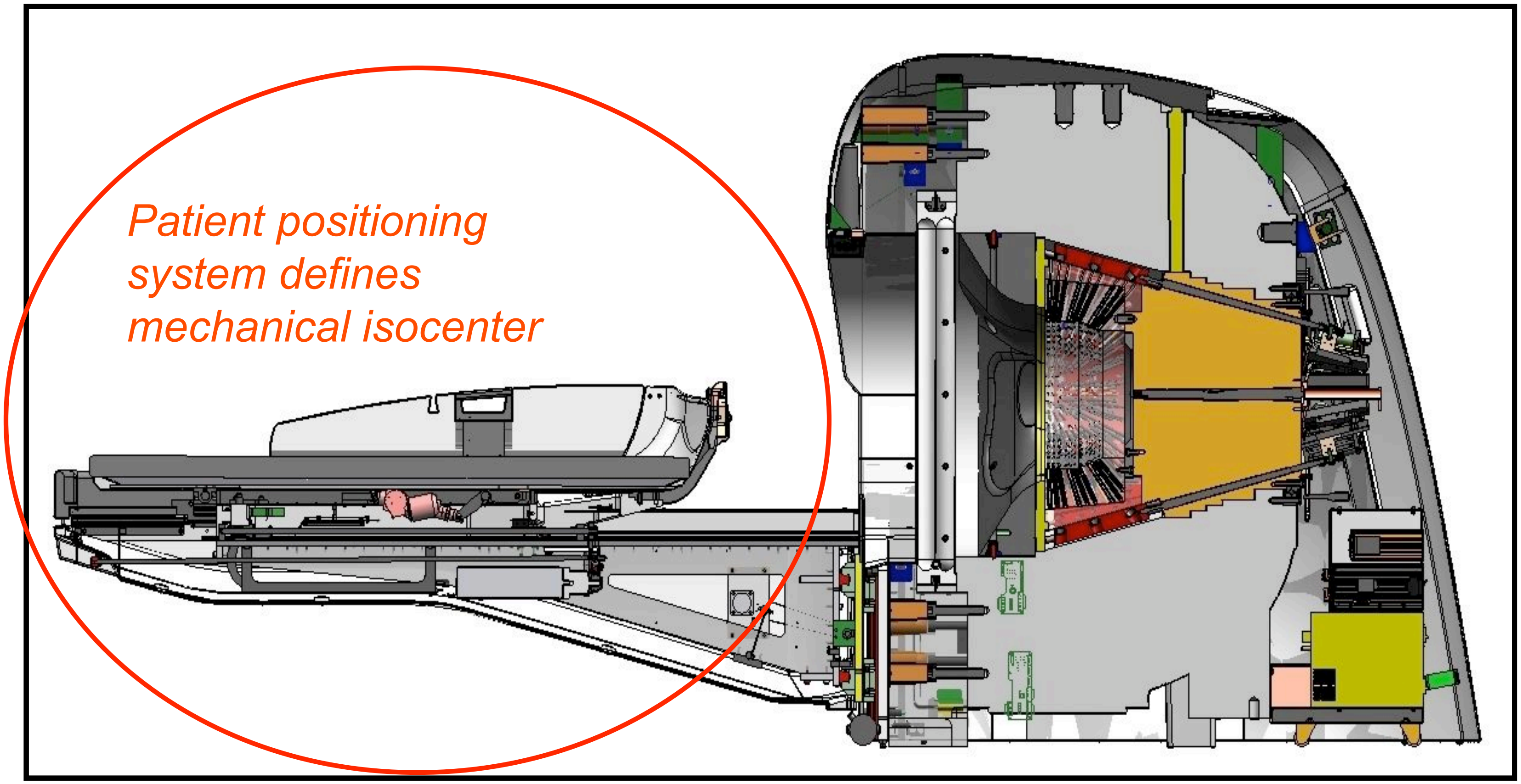
5 sector Positions:

Home
8-mm
Blocked
4-mm
16-mm

Radiological Accuracy

- Alignment of the radiation focus and the mechanical isocenter

Sources and collimating system defines radiation focus

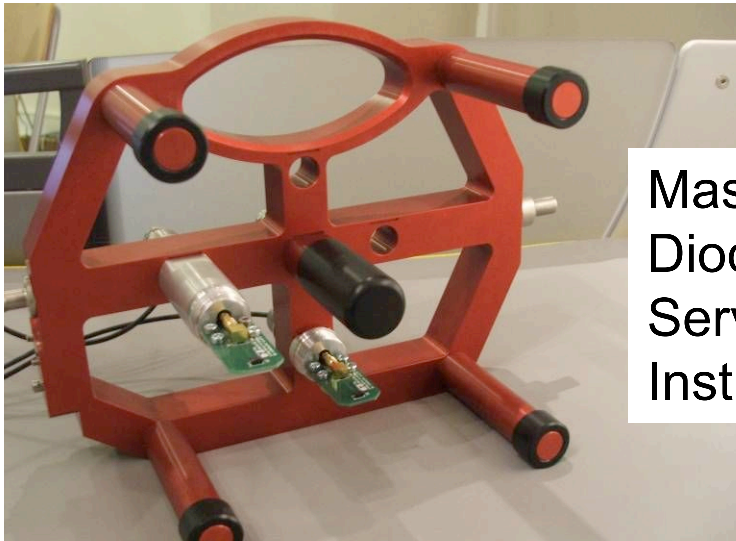


Critically important since the hallmark of radiosurgery is the ability to deliver focal radiation with sub-millimeter precision

GK Perfexion™: Selected Technical Specifications

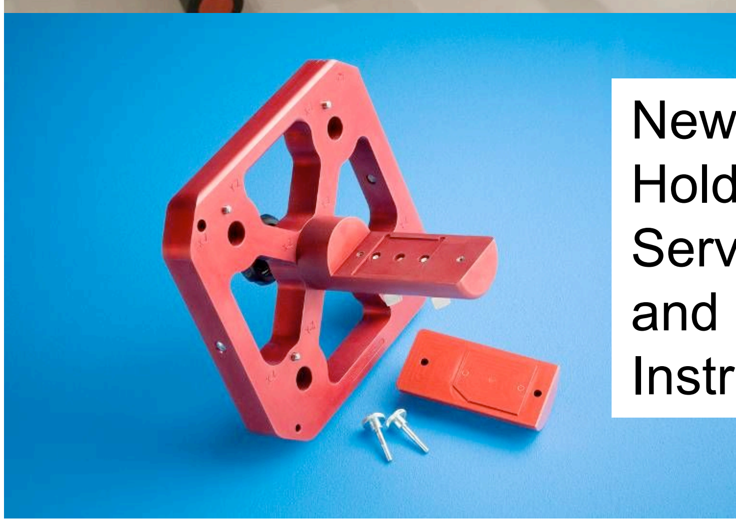
Typical couch repositioning time	< 3 s
Couch positioning repeatability	< 0.05 mm
Maximum patient weight	210 kg (460 lbs)
Typical collimator size setup time	< 3 s
Radiological accuracy	<0.5 mm

Instruments used to check the alignment of patient positioning system with radiation focus for LGK Perfexion:

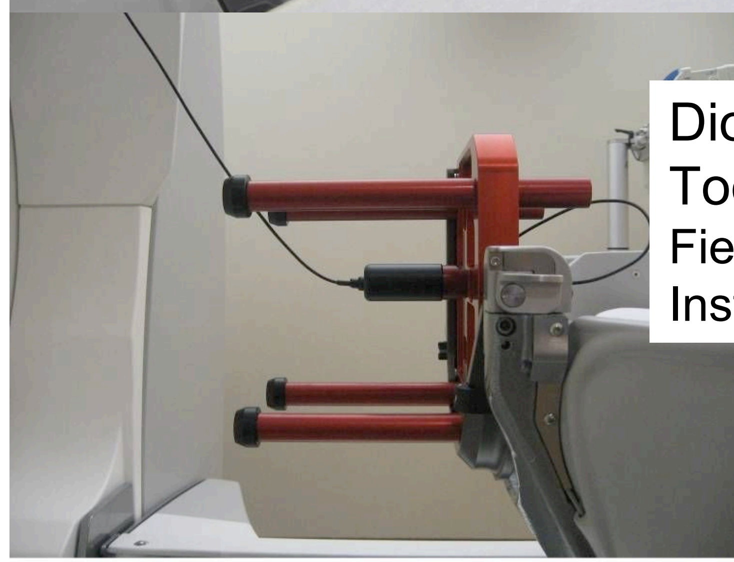


Master Diode Tool: Service Instrument

Old-Style Film Holder: Field Instrument



New Film Holder: Service and Field Instrument

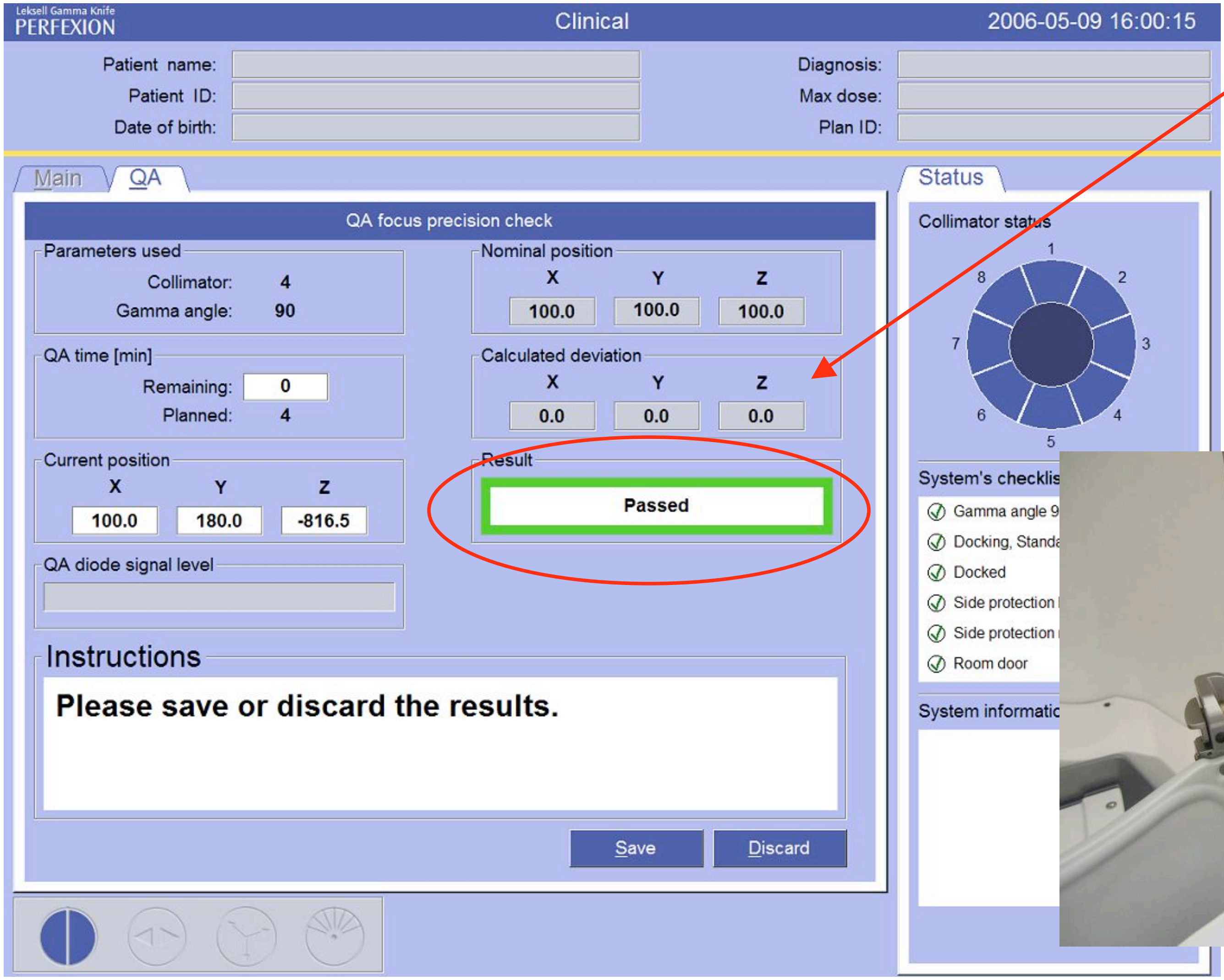


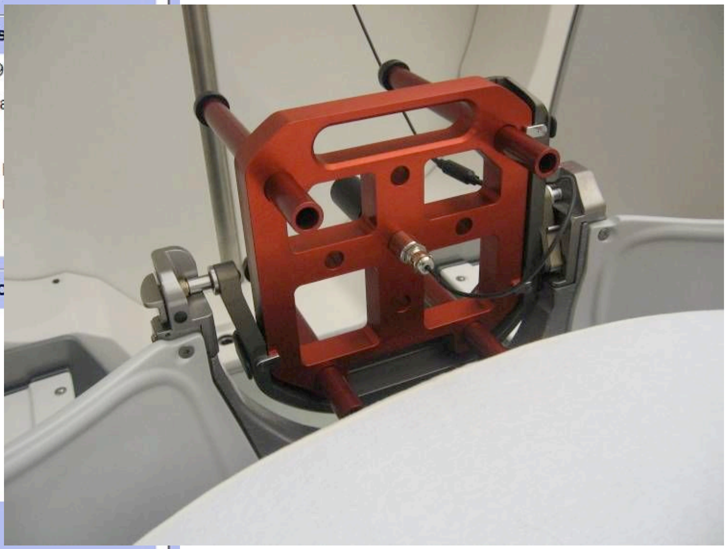
Diode Tool: Field Instrument

Diode QA Test

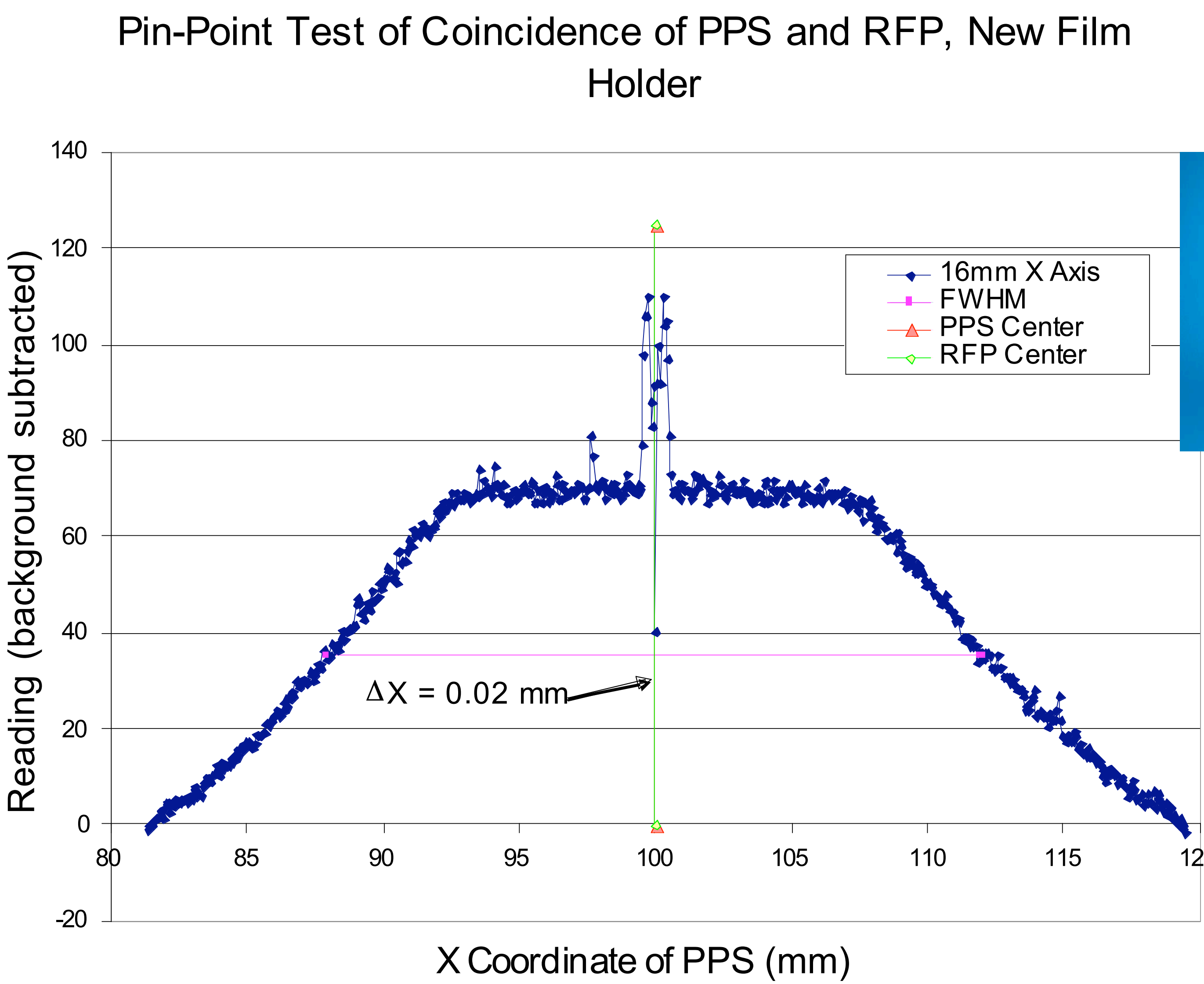
- The diode is scanned through the irradiated field in X, Y and Z for the 4-mm collimator. Average deviations are reported.

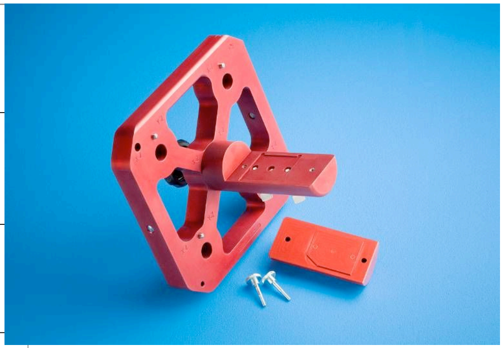
Calculated Deviation

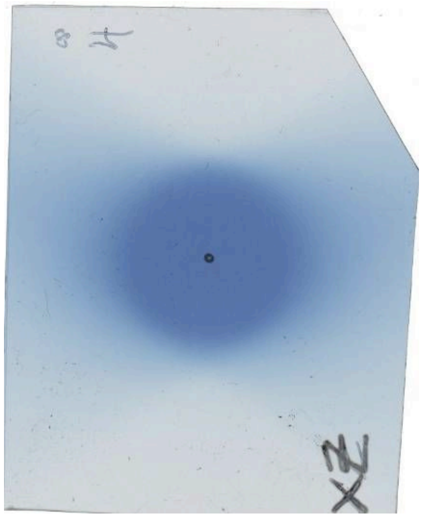




Example of Results:







Results of Pin-Point Test at WHHS Averaged over 4 years from 2007 to 2011

Collimator	Averaged Δr* over 4-year time period (mm)	Standard Deviation (mm)
4-mm	0.16	0.07
8-mm	0.23	0.07
16-mm	0.27	0.08

$$^*\Delta r = \sqrt{\Delta x^2 + \Delta y^2 + \Delta z^2}$$

= deviation of radiation focal point from center of patient positioning system

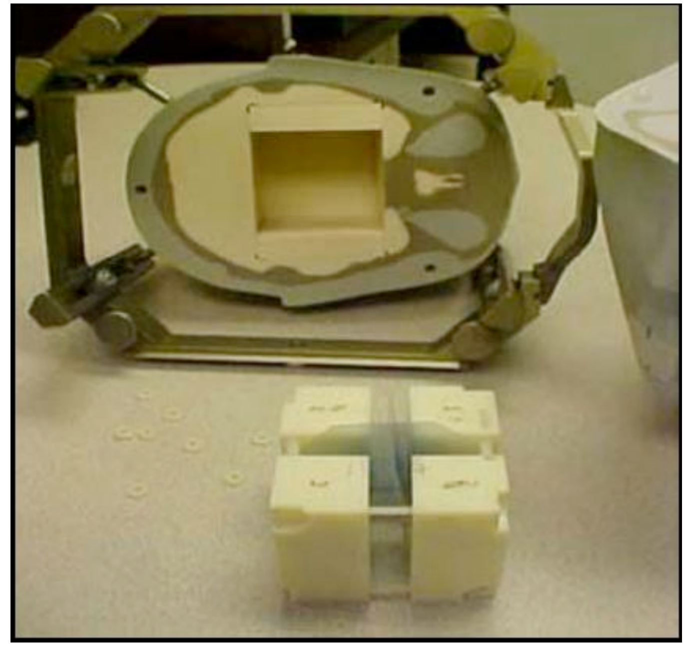
Results within the specified 0.5 mm radiological accuracy of the Perfexion positioning system

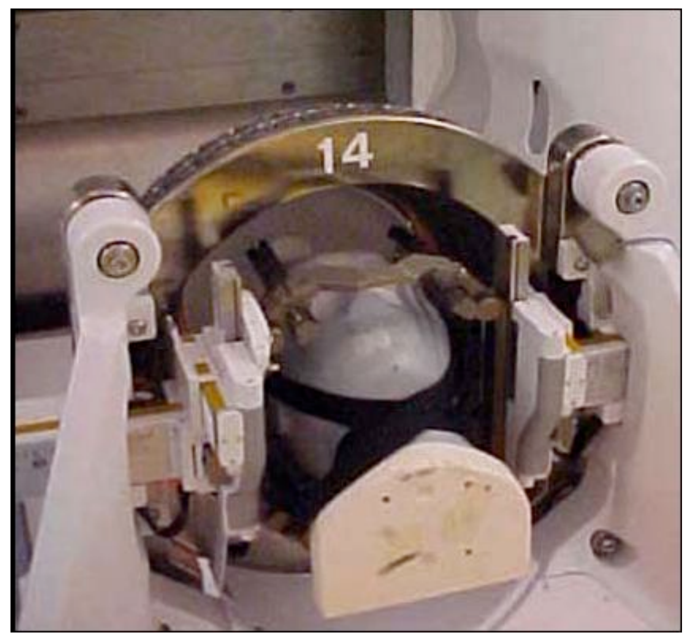
End-to-End Tests

- Tests described on previous slides assess the precision with which the radiation focal point is aligned to the mechanical isocenter
- They do not test the accuracy of the entire GK procedure
- End-to-end tests are not done routinely for GK
- A few studies have been reported

End-to-End Experiments

- L. Ma et al., Med Phys. 35, 5110-14 (2008).
  - Attached LGK SRS frame to phantom
  - Obtained CT scan
  - Inserted film in phantom
  - Irradiated film for 6 representative treatment plans



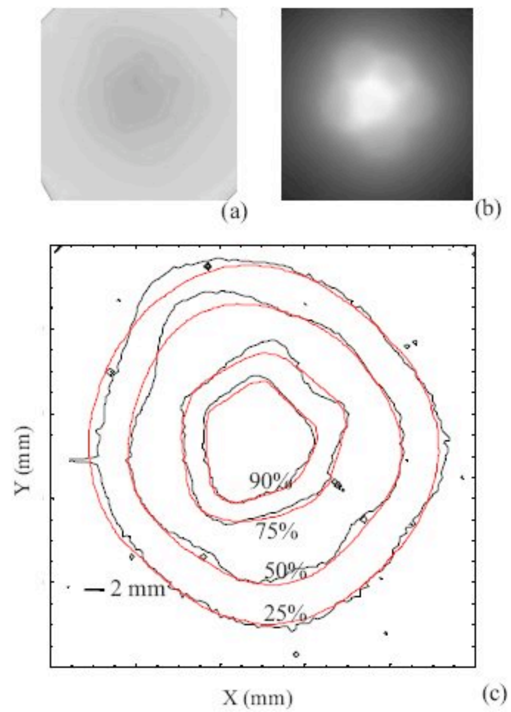


Results from L. Ma Study

TABLE I. Summary of film measurement results as compared with the Leksell Gamma Plan dose calculations at different levels of the isodose lines, i.e., 25%, 50%, and 75% and 90% in distance-to-agreement (Δ): the maximum, the average and the standard devidation (Std) values are given.

Case No.	No. of shots	Max $\Delta_{25\%}$ (mm)	Mean ± Std $\Delta_{25\%}$ (mm)	Max $\Delta_{50\%}$ (mm)	Mean ± Std $\Delta_{50\%}$ (mm)	Max $\Delta_{75\%}$ (mm)	Mean ± Std $\Delta_{75\%}$ (mm)	Max $\Delta_{90\%}$ (mm)	Mean ± Std $\Delta_{90\%}$ (mm)
1	1	0.8	0.4 ± 0.28	0.5	0.2 ± 0.15	0.3	0.1 ± 0.12	2.0	1.2 ± 0.76
2	2	1.0	0.6 ± 0.31	0.5	0.3 ± 0.16	1.0	0.6 ± 0.32	0.8	0.6 ± 0.19
3	9	2.0	1.2 ± 0.50	1.8	1.1 ± 0.49	1.8	1.2 ± 0.39	2.0	1.0 ± 0.65
4	12	2.1	1.5 ± 0.49	1.5	0.9 ± 0.36	1.8	1.1 ± 0.49	2.0	1.3 ± 0.58
5	12	2.0	1.6 ± 0.35	1.0	0.5 ± 0.46	1.7	1.2 ± 0.46	1.5	0.8 ± 0.48
6	16	2.0	1.4 ± 0.59	2.1	1.2 ± 0.71	1.6	0.9 ± 0.58	0.8	0.4 ± 0.37

- E.g., for 50% isodose line, average DTA was 1.02 ± 0.18 mm
- Considering all isodose levels, no statistically significant difference in uncertainty with increasing number of shots



Uncertainties in Extend System

- Data reported at AAPM 2012 meeting:
  - SU-E-T-405: *UCSF*
  - SU-C-BRCD-2: D. Schlesinger et al. *UVA*
  - SU-E-T-398: N. Gopishankar et al., *All India Inst. of Med. Sciences*
  - SU-E-T-55: M. White et al., *U. Missouri-Columbia, Washington U., St. Louis*

For the Leksell Gamma Knife, measurements of the alignment between patient-positioning system (PPS) and the radiation focal point (RFP) are typically ≤ ___ mm, and the manufacturer’s specification is that the alignment be ≤ ____ mm

0%	1.	0.1,	0.3
0%	2.	0.3,	0.5
0%	3.	0.6,	1.0
0%	4.	1.0,	1.5
0%	5.	1.5,	2.0

10

For the Leksell Gamma Knife, measurements of the alignment between patient-positioning system (PPS) and the radiation focal point (RFP) are typically ≤ ___ mm, and the manufacturer's specification is that the alignment be ≤ ____ mm

Answer: 2: M. Schell et al., AAPM Report No. 54, "Stereotactic Radiosurgery," p. 65 (1999). Also, note that the values listed on slide 18 are ≤ 0.3 mm. Specifications for the radiological accuracy of the Perfexion system are stated in Elekta's documentation, "LGK Perfexion, System Description."

Collimator	Averaged Δr^* over 4-year time period (mm)	Standard Deviation (mm)
4-mm	0.16	0.07
8-mm	0.23	0.07
16-mm	0.27	0.08

Typical measurement results

Based on reports in the literature, the distance-to-agreement (DTA) for the 50% isodose level in a multi-shot GK treatment is approx. ____ mm

0% 1. 0.1

0% 2. 0.5

0% 3. 1.0

0% 4. 1.8

0% 5. 2.5

10

Based on reports in the literature, the distance-to-agreement (DTA) for the 50% isodose level in a multi-shot GK treatment is approx. ___ mm

Answer: 3: L. Ma et al., “Whole-procedure clinical accuracy of Gamma Knife treatments of large lesions,” Med. Phys. 35: 5110-5114, (2008)

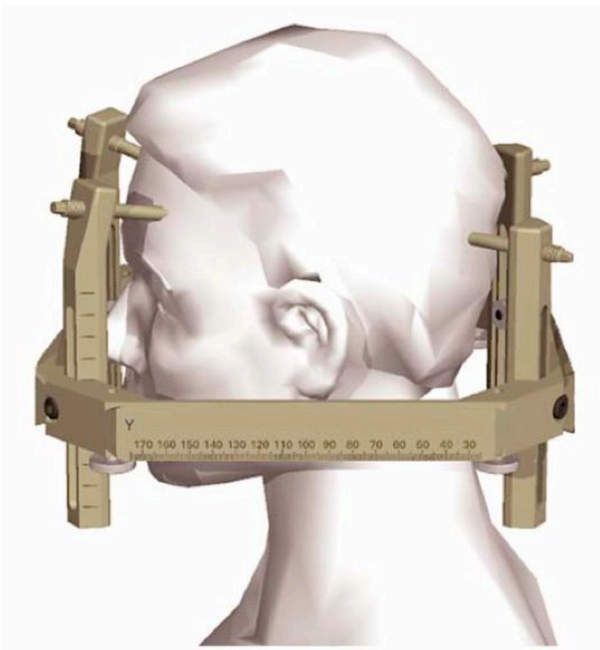
Workflow for Frame-Based GK SRS

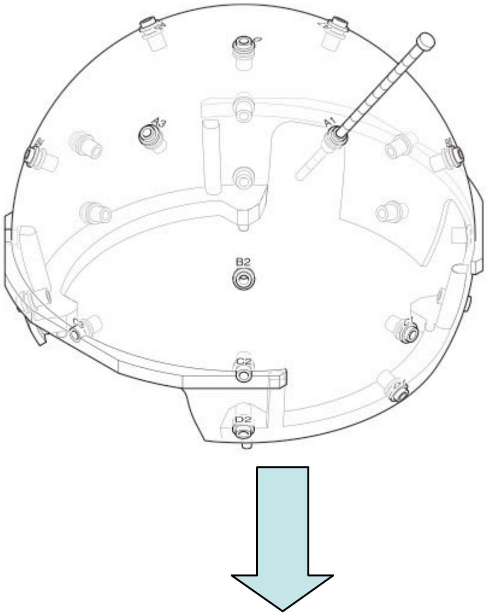
- Neurosurgeon attaches stereotactic frame
- Skull and frame measurements obtained
- MR and/or CT images acquired
- Treatment planning performed (*by either physicists or MDs)*
- Treatment plan approved
- Treatment delivered

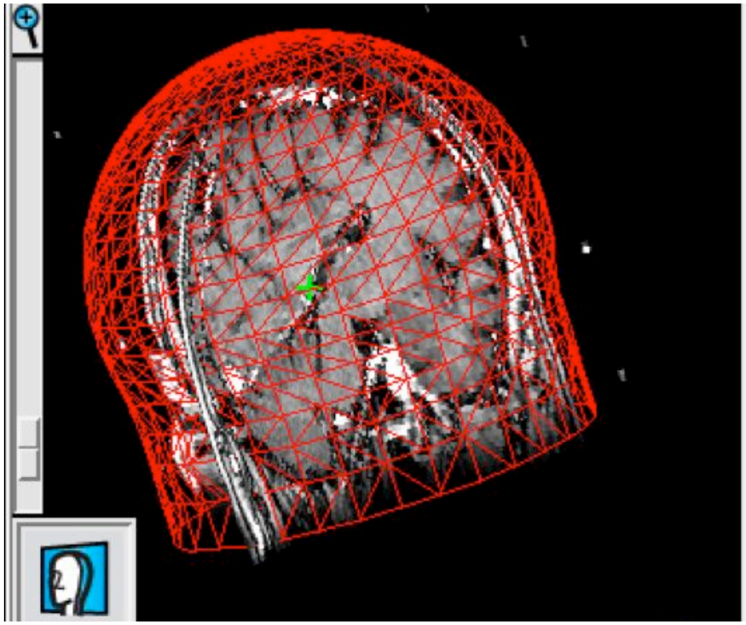
All steps completed in one day

Several patients can be treated per day depending on complexity of cases and staffing

Frame attachment, Skull Measurements





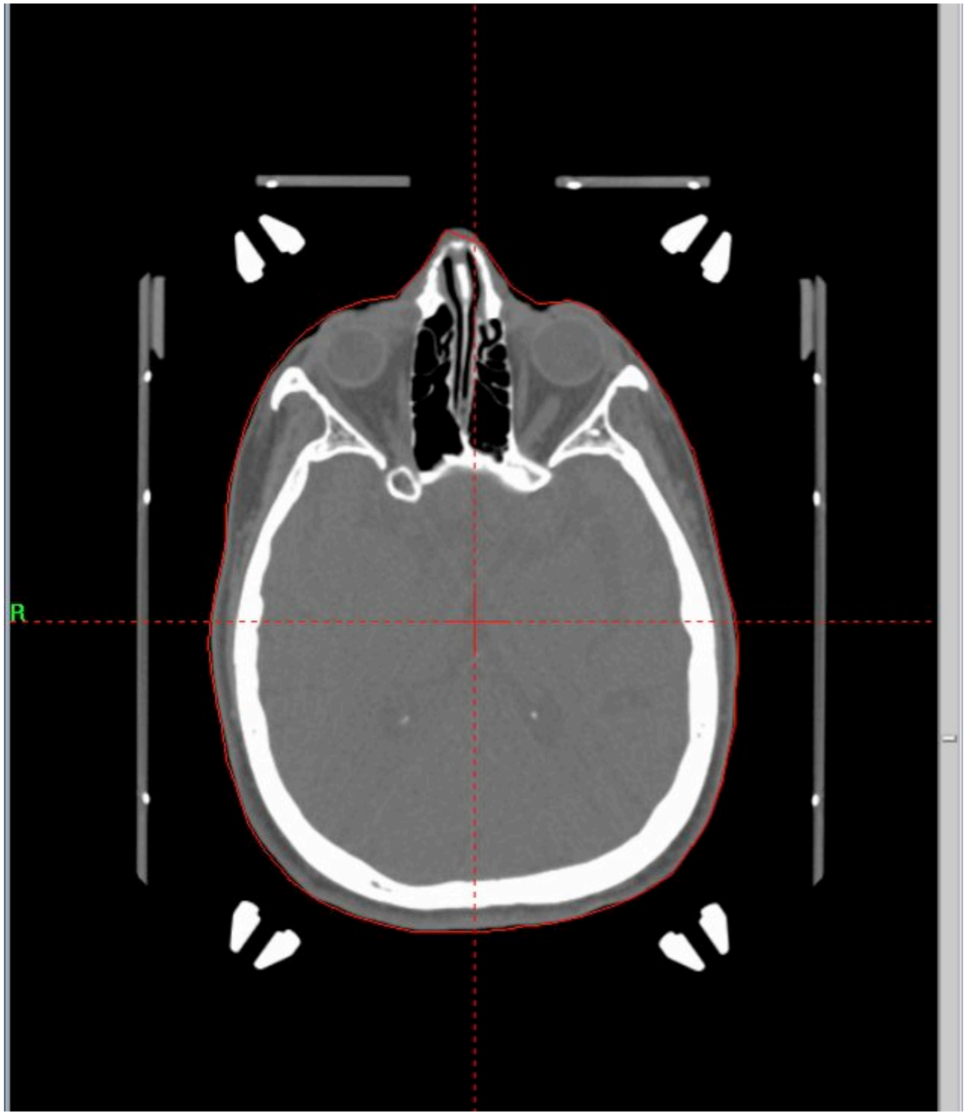


Stereotactic Frame defines LGK coordinate system

Surface of the head determined by skull scaling instrument ("bubble")

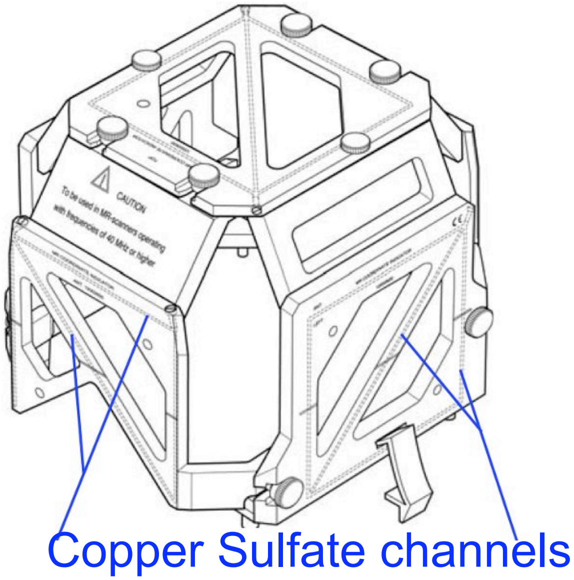
Everything inside skull, as determined by bubble, is assumed to be unit density

Skull Definition from CT



- Relatively new feature:
  - Determine skull outline from CT scan
  - Use CT to make tissue heterogeneity correction via convolution dose calculation algorithm
  - Pros: More accurate dose calc
  - Cons:
    - Requires CT as well as MR for treatment planning
    - Existing data for dose prescriptions based on unit-density approximation

MRI Fiducial Boxes



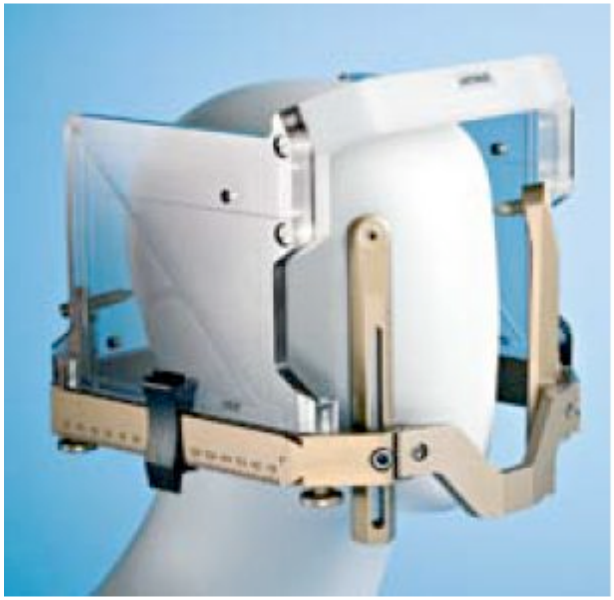
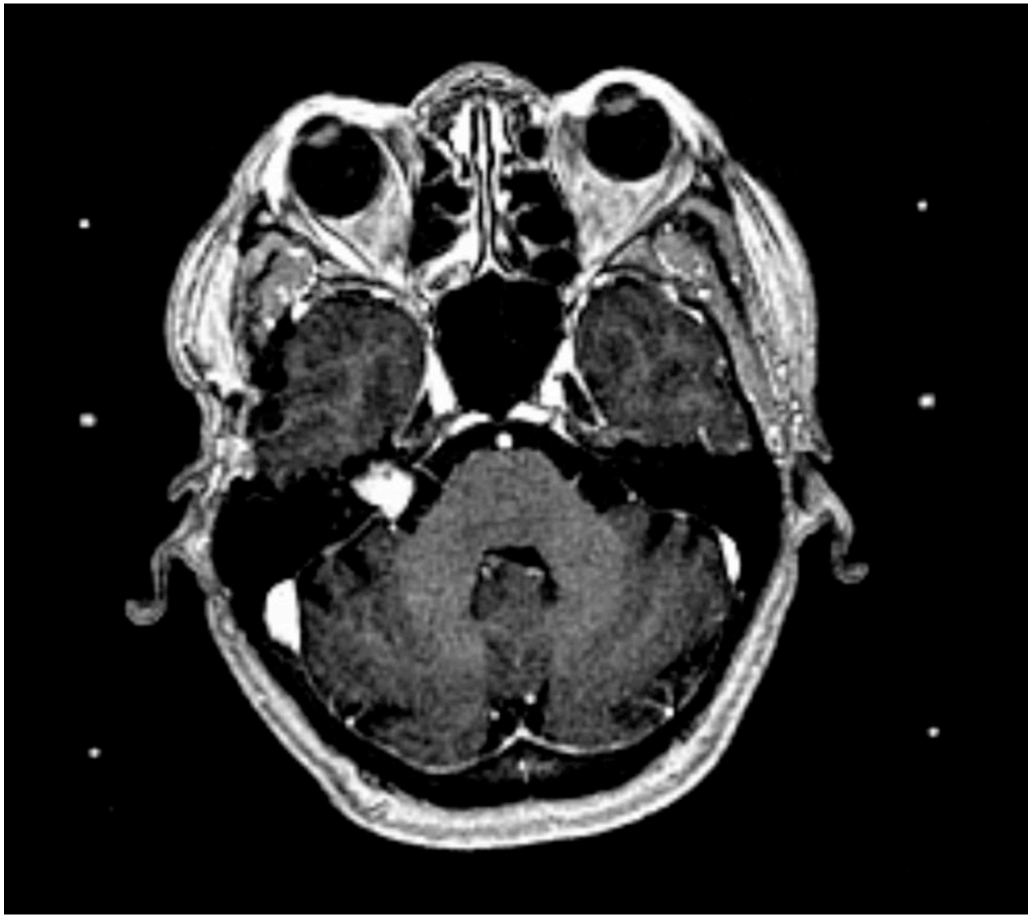


Image Definition



Distortions in MRI Images

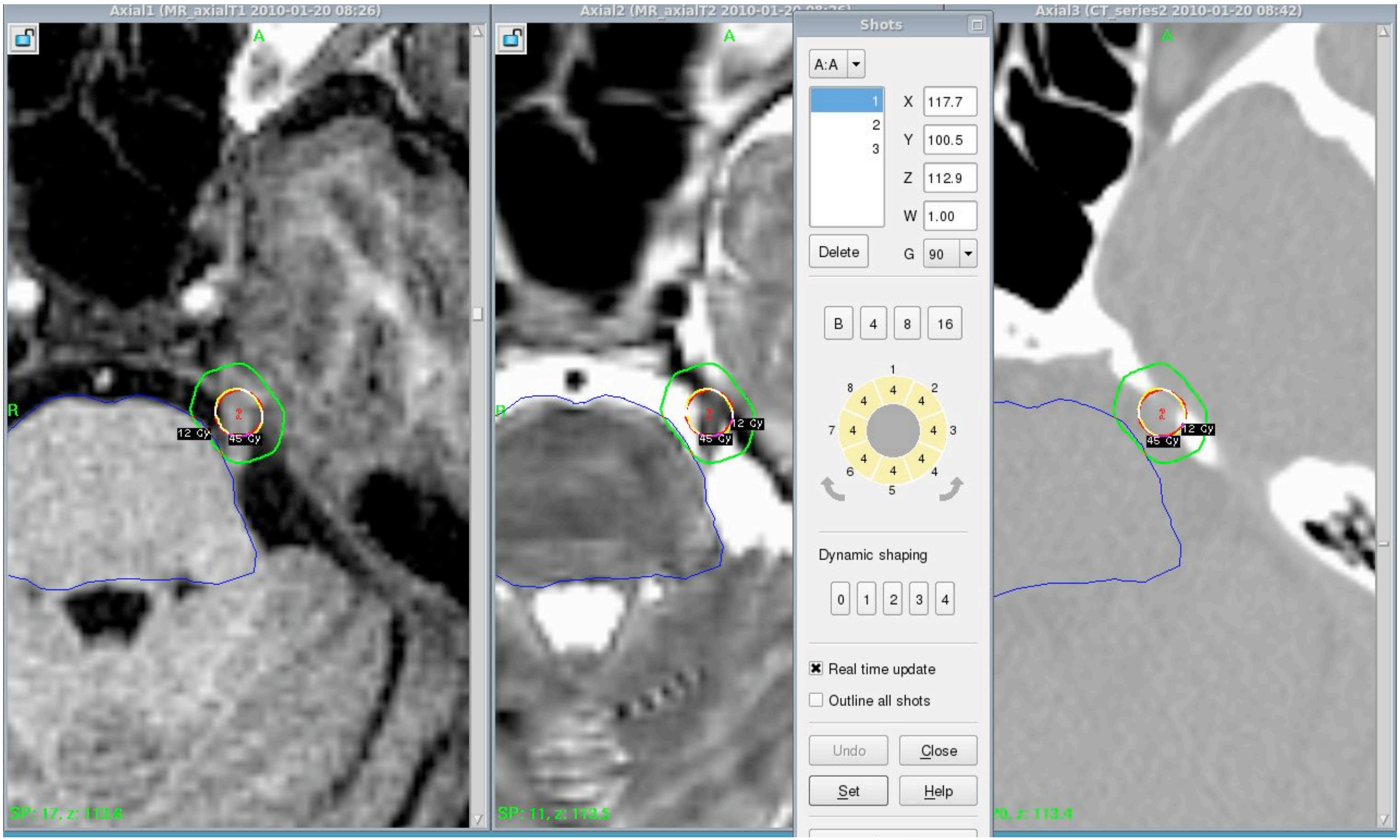
- Sources of distortion in MR images:
  - Different pulse sequences
  - Different magnetic susceptibilities of individual patients
  - The presence of magnetic objects such as surgical clips
- Investigators* have documented distortions in MRI images used for GK SRS to be of the order of 1 mm or less

*e.g., A. Ertl et al., Med Phys. **28**, 166-170, (1999)

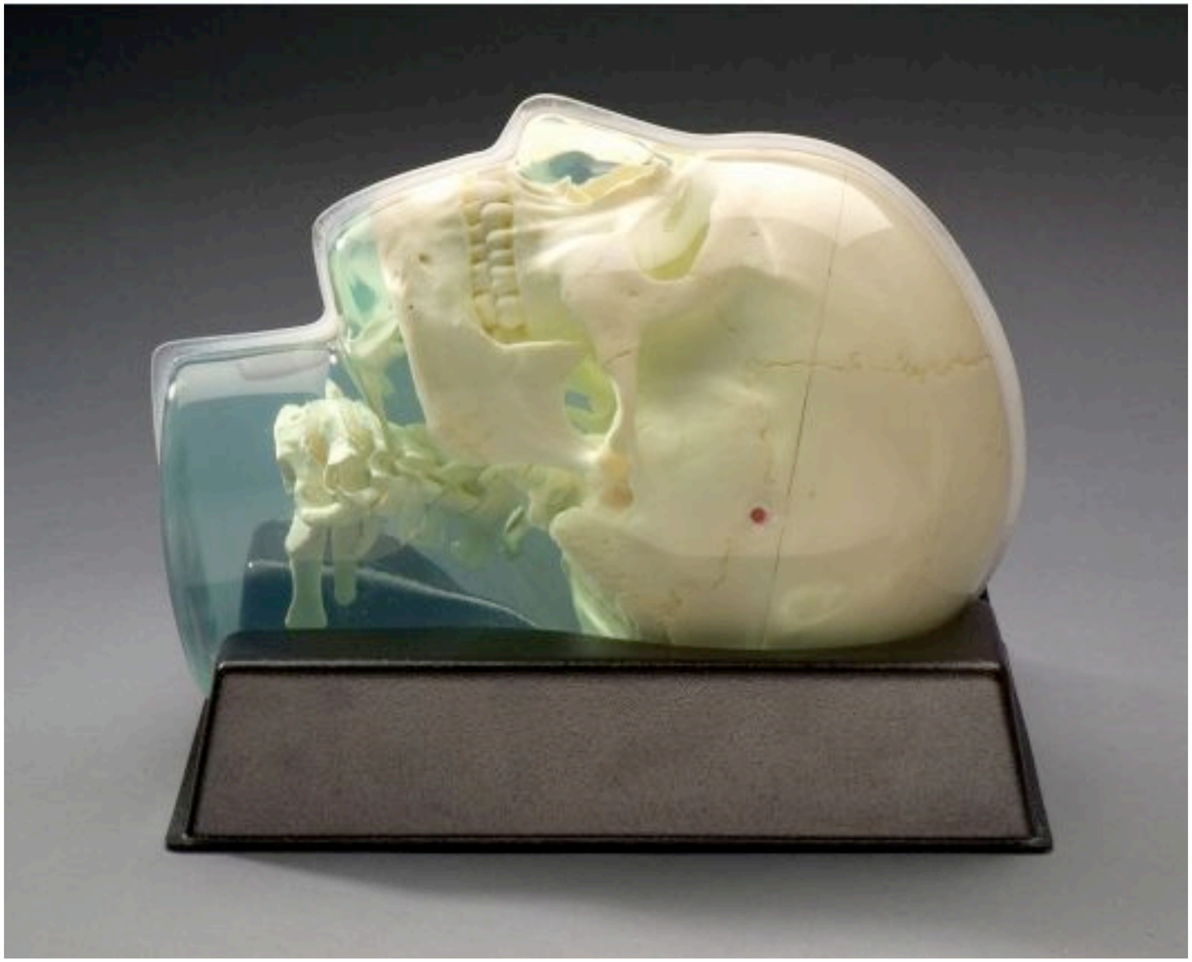
Assessing Distortion in MR Images

- Consider obtaining CT scans in patients for whom a 1 mm shift in targeting could be critical
  - Fuse the CT with the MR (i.e., overlay corresponding pixels of defined images)
  - Or, simply assess targeted area on CT scan
- Perform phantom measurements to assess distortions on MR as part of regular QA

To reduce geometric uncertainty for cases where shot placement is critical (e.g., single-shot treatment for TN), consider acquiring CT as well as MR



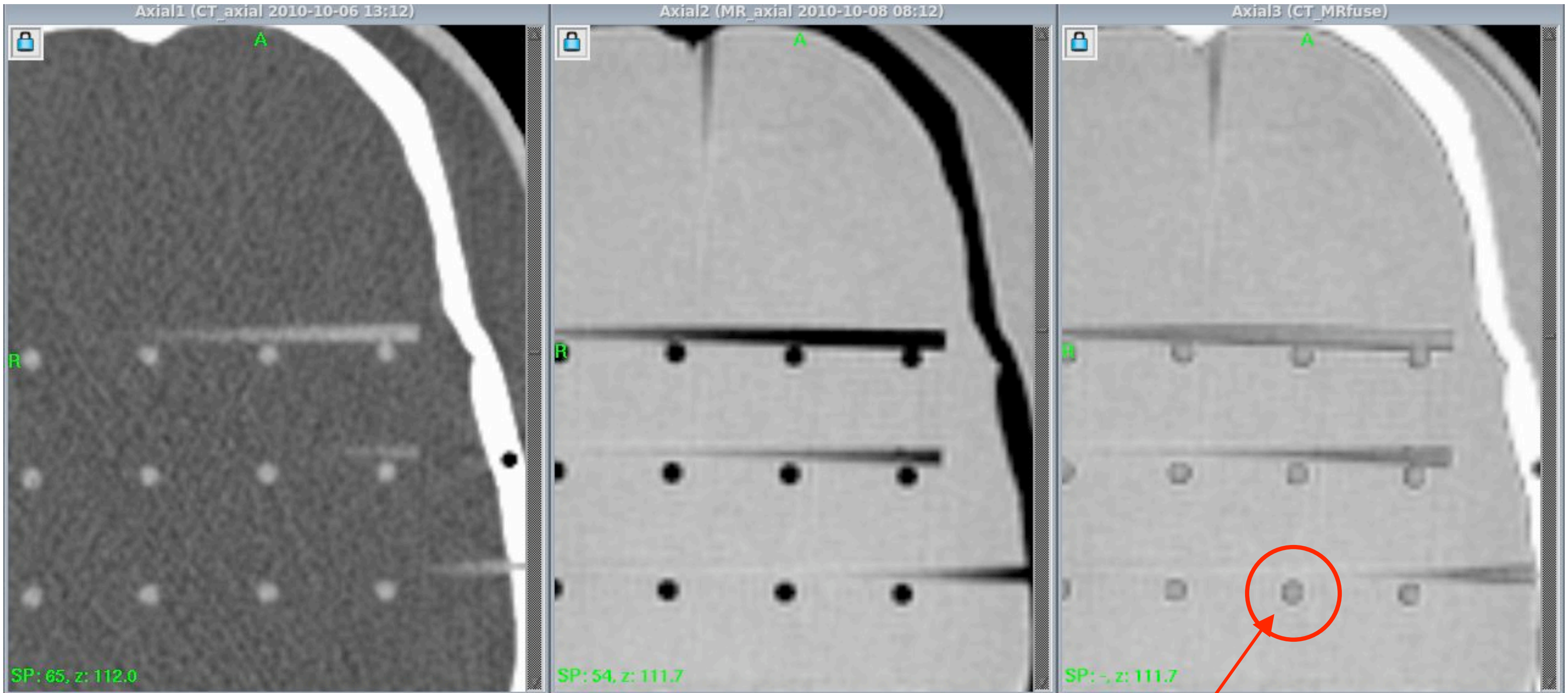
An Example of a QA Phantom from CIRS



- Phantom filled with a proprietary water-based polymer that images well on MR and CT. The skull is made from an epoxy-based tissue substitute
- Rods running in orthogonal directions inside the phantom are used to assess distortions
- Can attach the Leksell frame to phantom

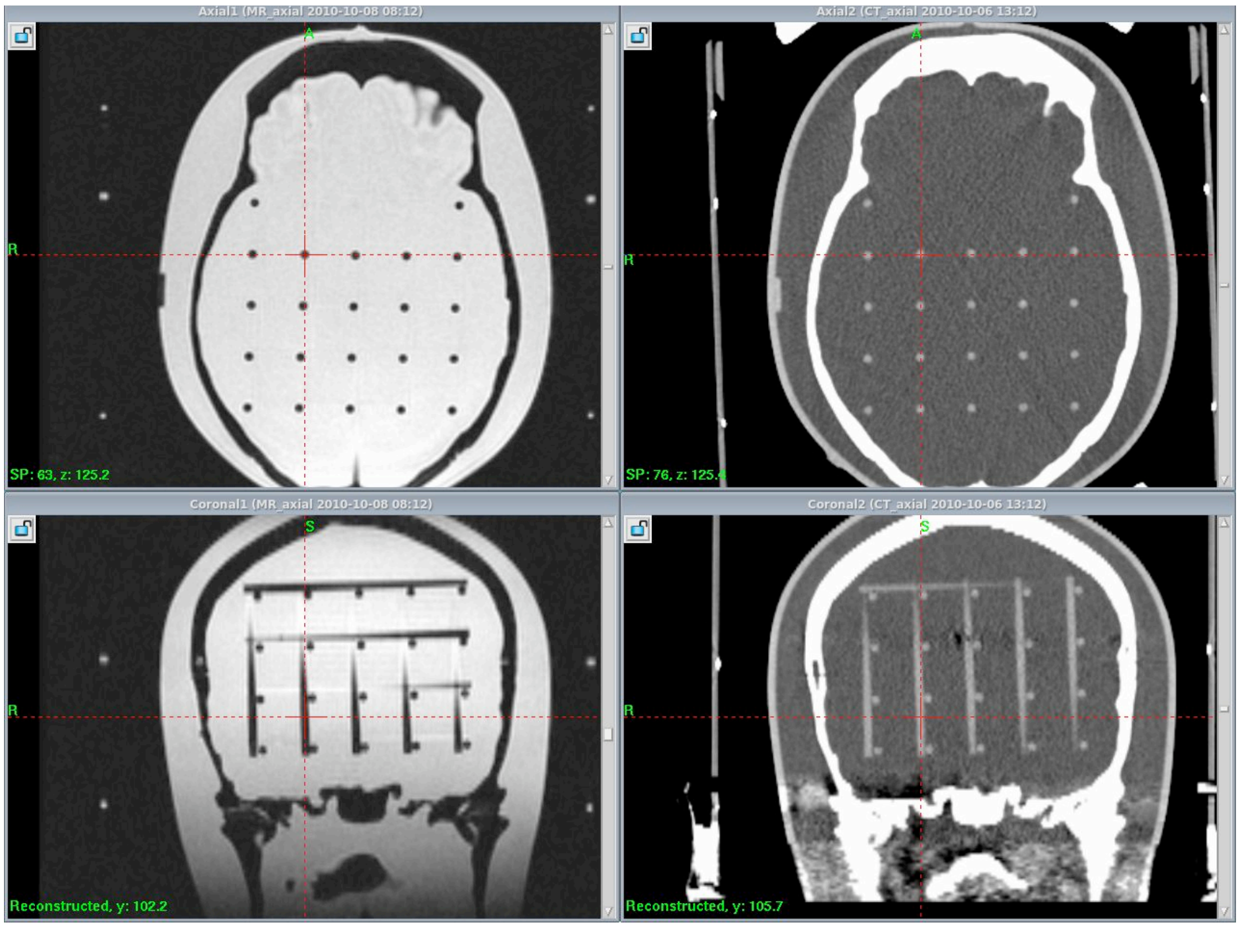
Qualitative Assessment of Distortions in MR Images

CT	MR T1	Fused MR/CT



Can visually assess spatial agreement between images by examining overlap of fiducials

Quantitative Assessment of Distortions in MR Images



- Identify corresponding points on CT and MR
- Use measuring tool in LGP to assess differences

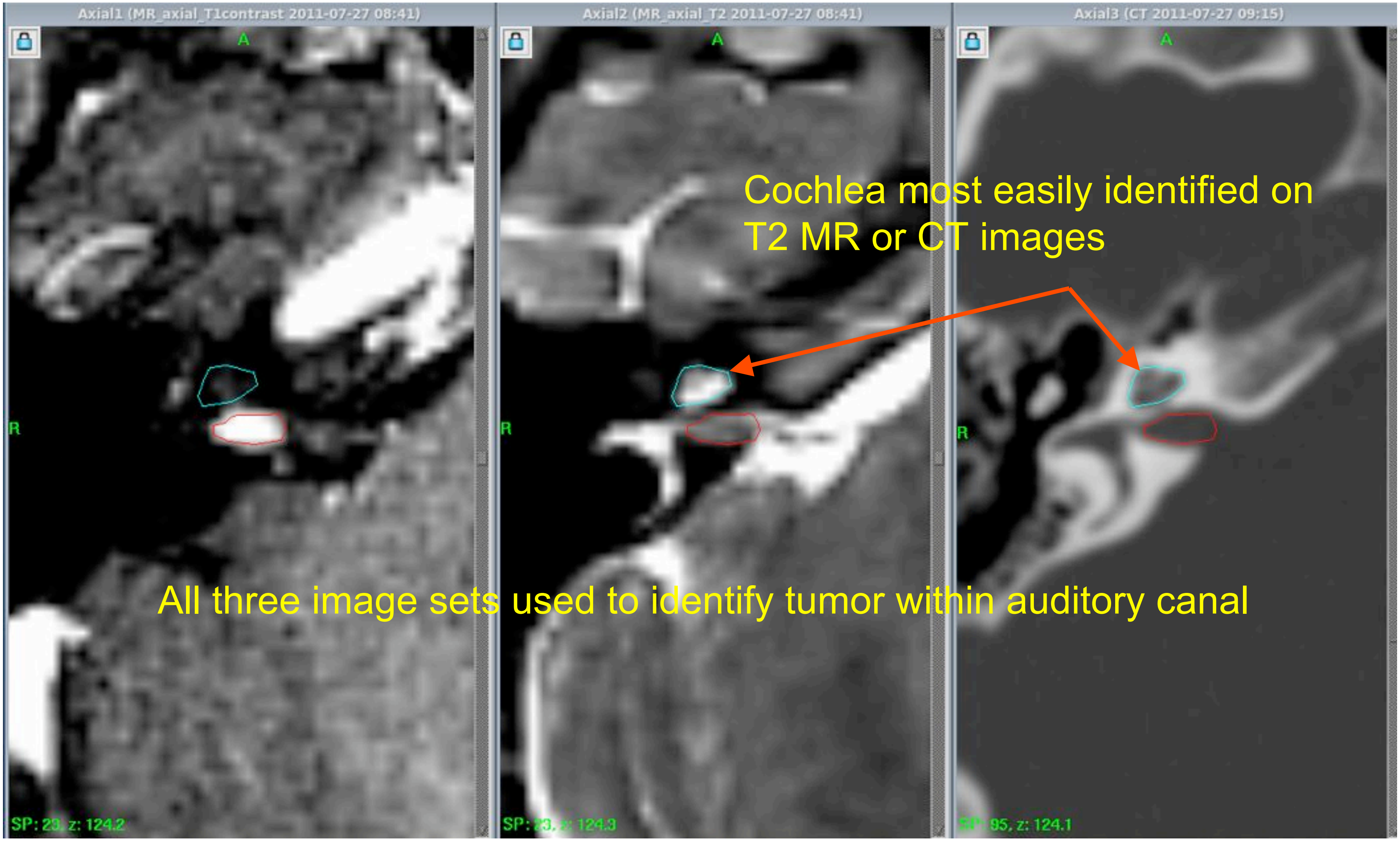
Typically, I have found RMS differences of about 0.5 mm

Tumor Definition for GK

- T1 MR sequences
- T2 MR useful for benign lesions (e.g. meningioma and vestibular schwannoma)
- CT useful for skull-base lesions
- Margins are generally <u>not</u> added to the Gross Tumor Volume

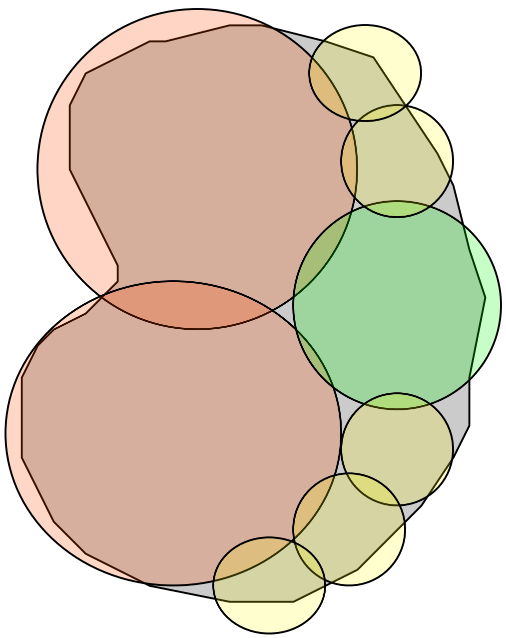
Tumor and Critical Structure Definition

T1-, T2- MR and CT to Visualize Acoustic Tumor and Cochlea



Treatment Planning Basics

Different size "shots" of radiation delivered to target

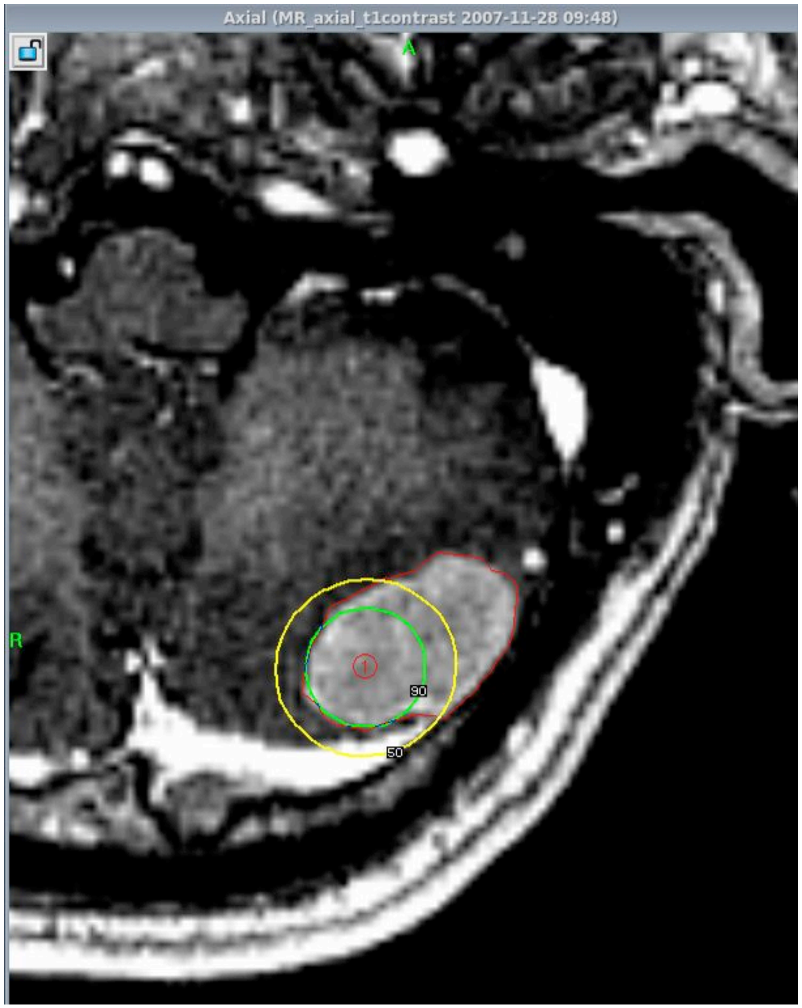


Target is shaded gray

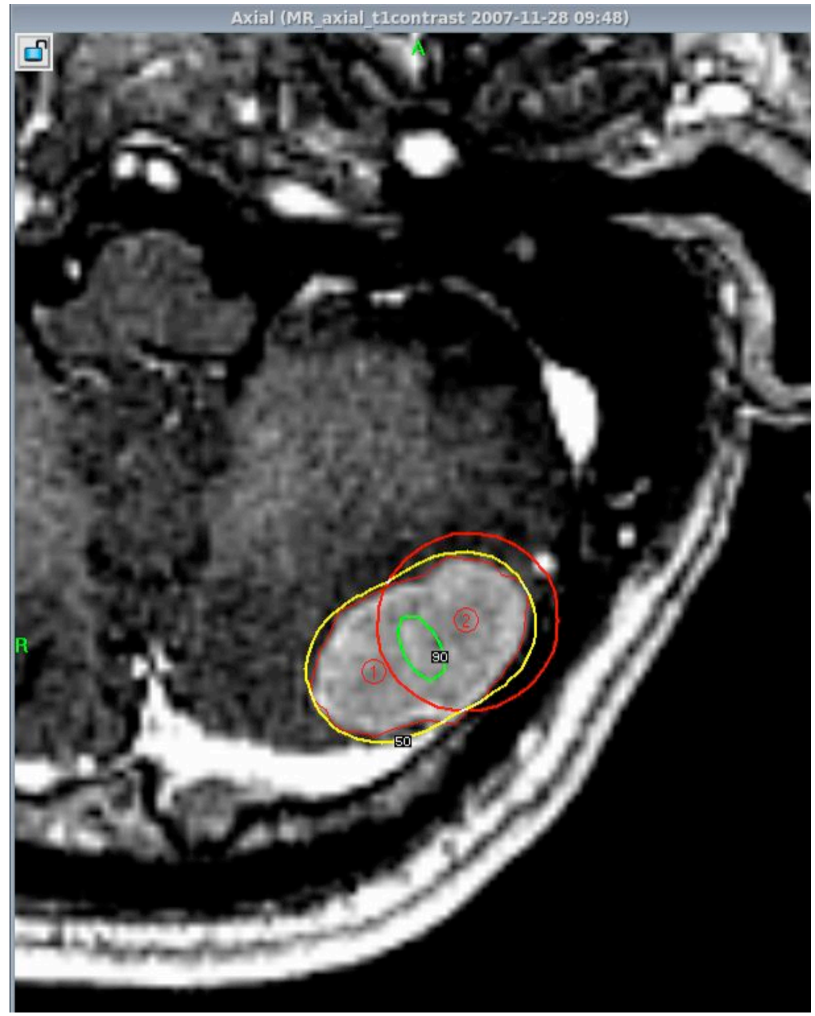
- Treatment planning consists of determining:
  - the positions for each focus of radiation
  - the collimator size for each focus
  - the tilt of the patients head (gamma angle) for each focus

Until recently, all GK was forward planned, inverse planning is now an option

GK Treatment Planning Basics

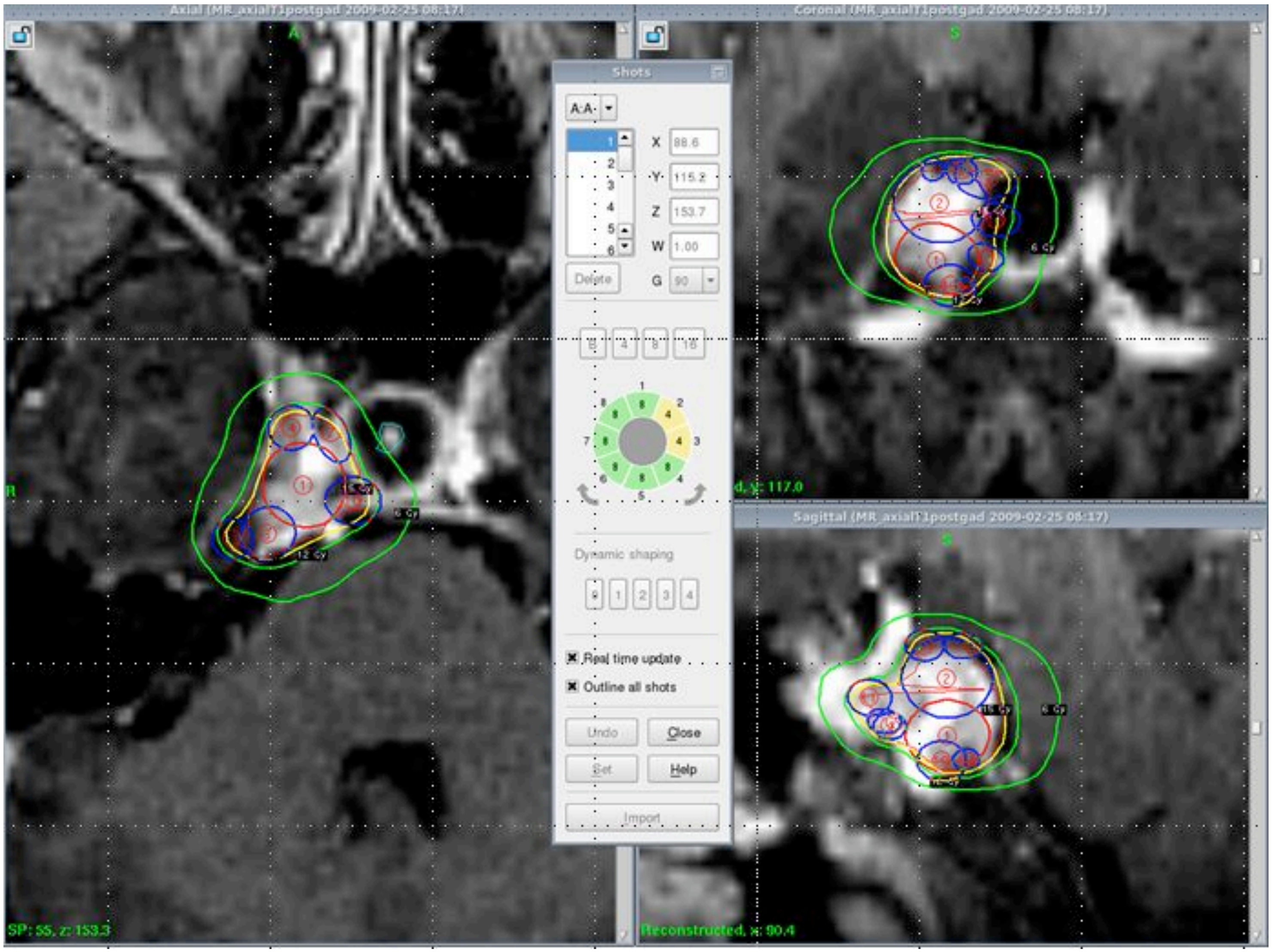


Placement of first shot



Placement of second shot

A GK shot-placing strategy for GK: large shots placed centrally, smaller shots used to “fill in” with smaller collimators “near” the critical structures



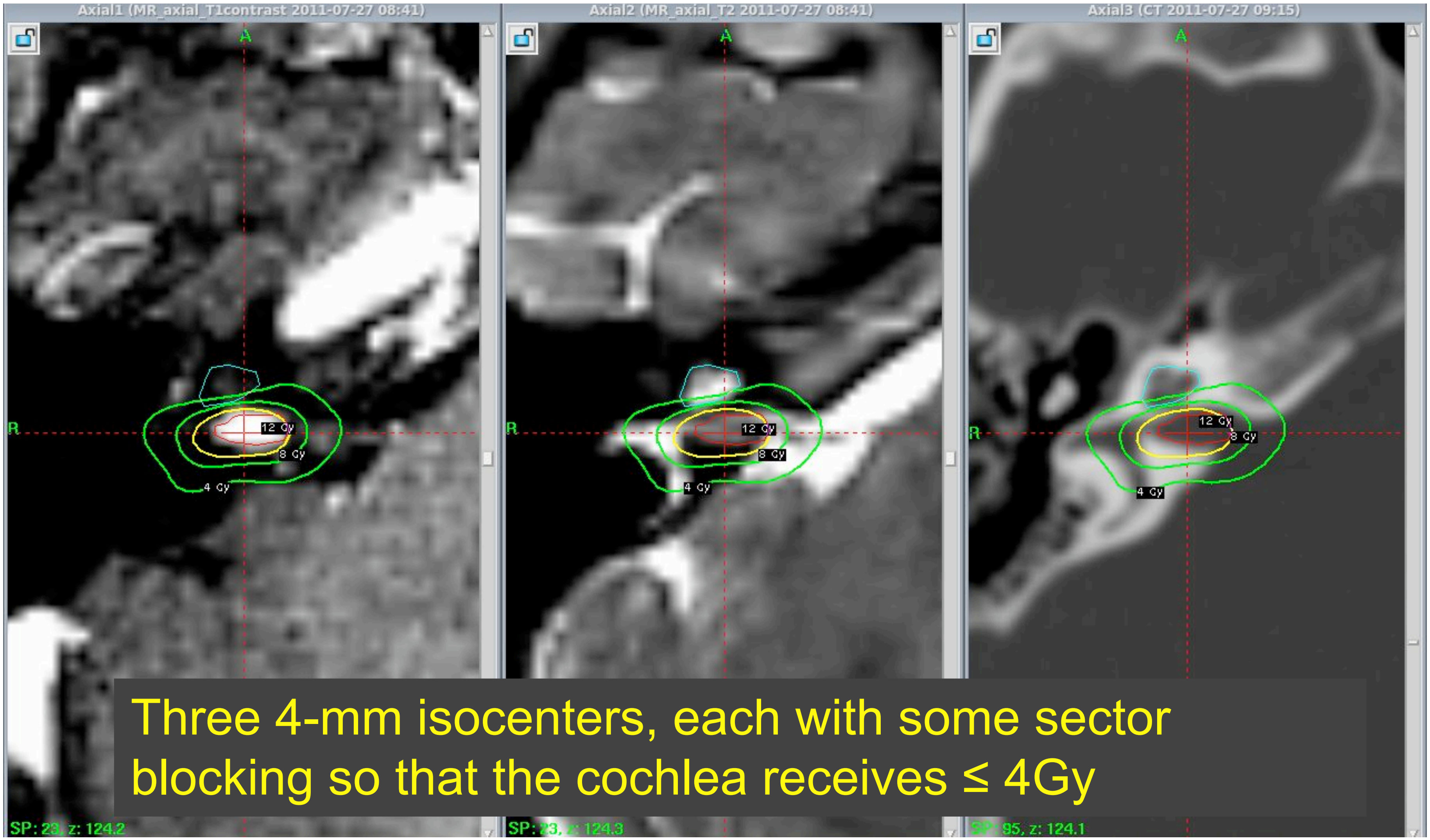
Cavernous sinus meningioma, V_P = 15 Gy

Max dose to pituitary stalk is 6.5 Gy

Max dose to optic structures is 4 Gy

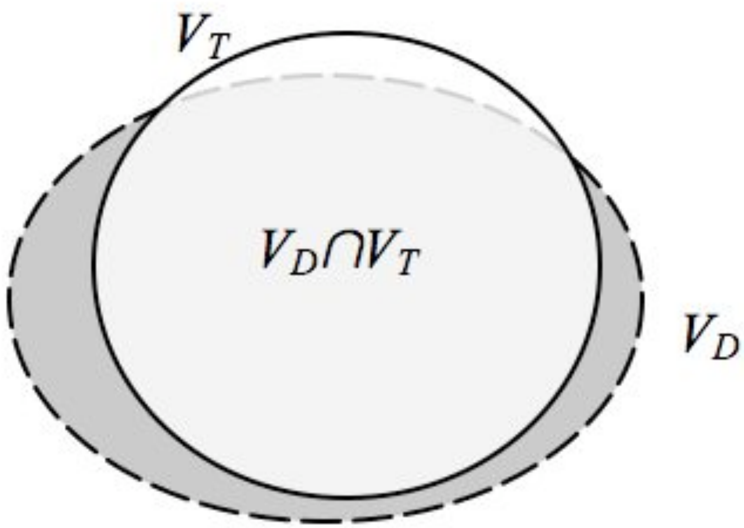
16mm^3 of brainstem receives > 12 Gy

Plan for Small Vestibular Schwannoma



Three 4-mm isocenters, each with some sector blocking so that the cochlea receives ≤ 4Gy

Treatment Plan Evaluation: Some Definitions:



V_T = Target Volume

D = Prescription dose

V_D = Volume receiving dose D (i.e., the prescription volume)

Target Coverage

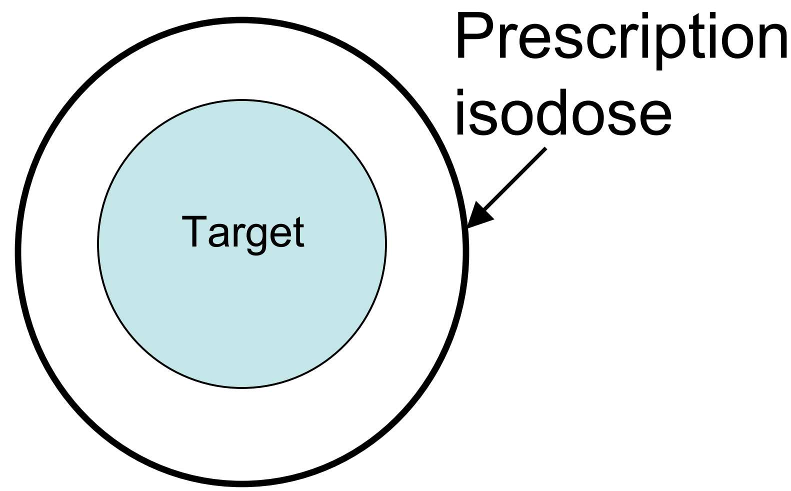
$$c = \frac{V_D \cap V_T}{V_T}$$

Plan Selectivity

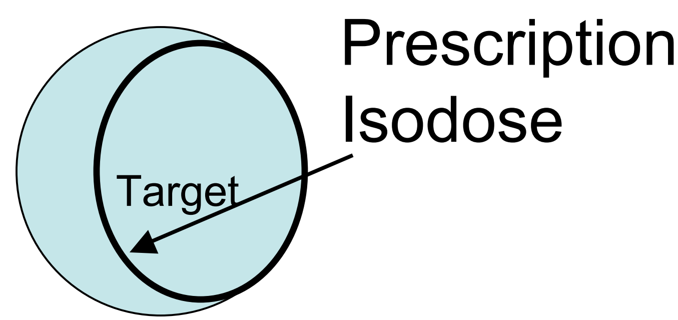
$$s = \frac{V_D \cap V_T}{V_D}$$

Coverage versus Selectivity

- Excellent target coverage, poor selectivity



- Excellent selectivity, poor target coverage



Conformity Indices

RTOG conformity index*:

$$C_S = \frac{V_D}{V_T} = \frac{c}{s}$$

Usually ≥ *1, but can be < 1 if coverage is sub-optimal.*

Paddick conformity index**:

$$C_P = c \times s$$

Always ≤ 1

C_P *= 1 represents perfect conformity*

*E. Shaw et al., Int. J. Radiat. Oncol. Biol. Phys. **27**, 1231-1239 (1993).

I. Paddick, J. Neurosurg. (Suppl) **93, 219-222 (2000).

Relationship between Shaw (RTOG) and Paddick Conformity Indices

$$C_P = \frac{c^2}{C_S}$$

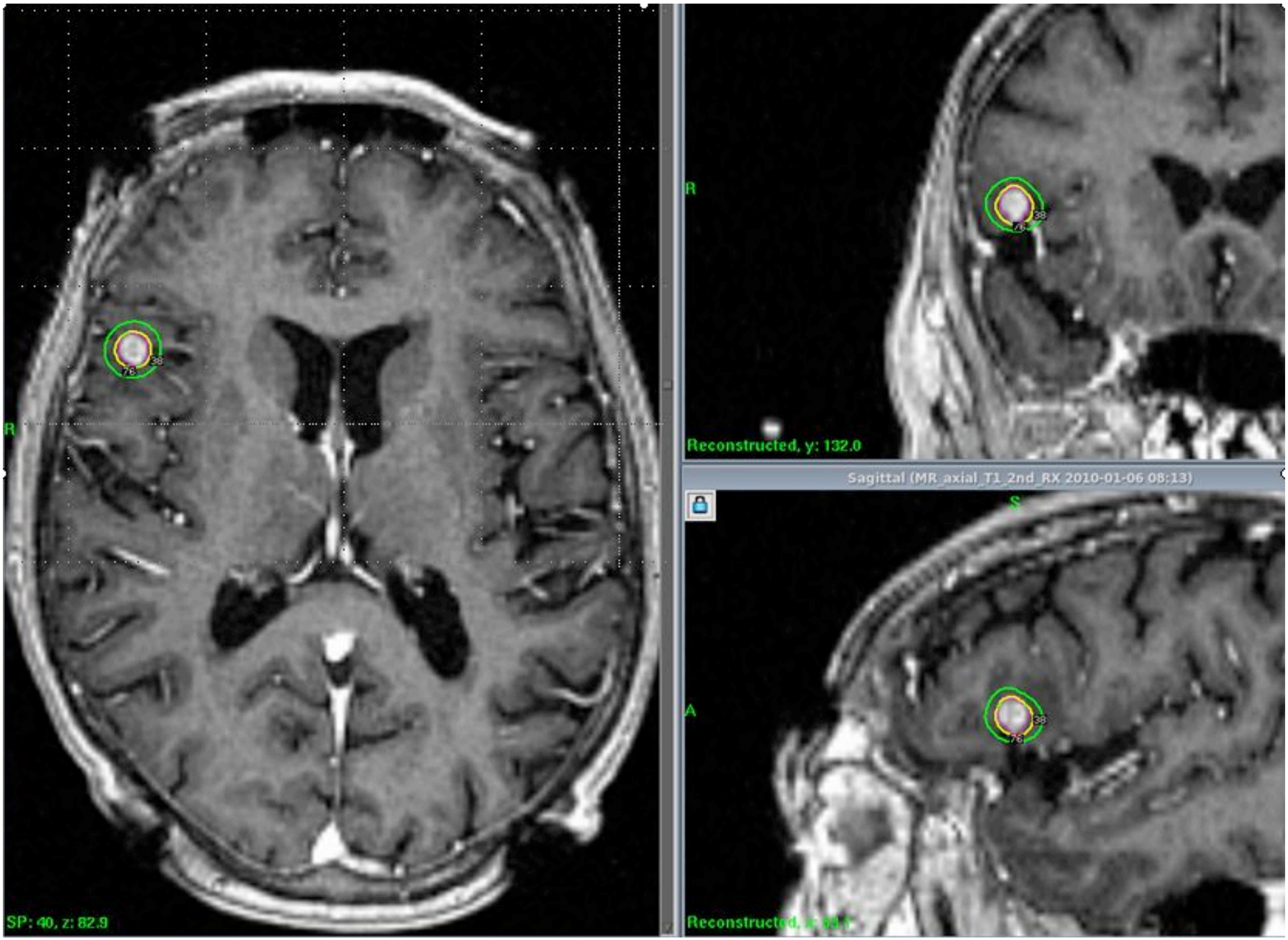
- C_P is inversely proportional to C_S, with proportionality constant equal to the square of the target coverage

- $C_P = 1/C_S$ if the target coverage is 100% (i.e., $c = 1$)

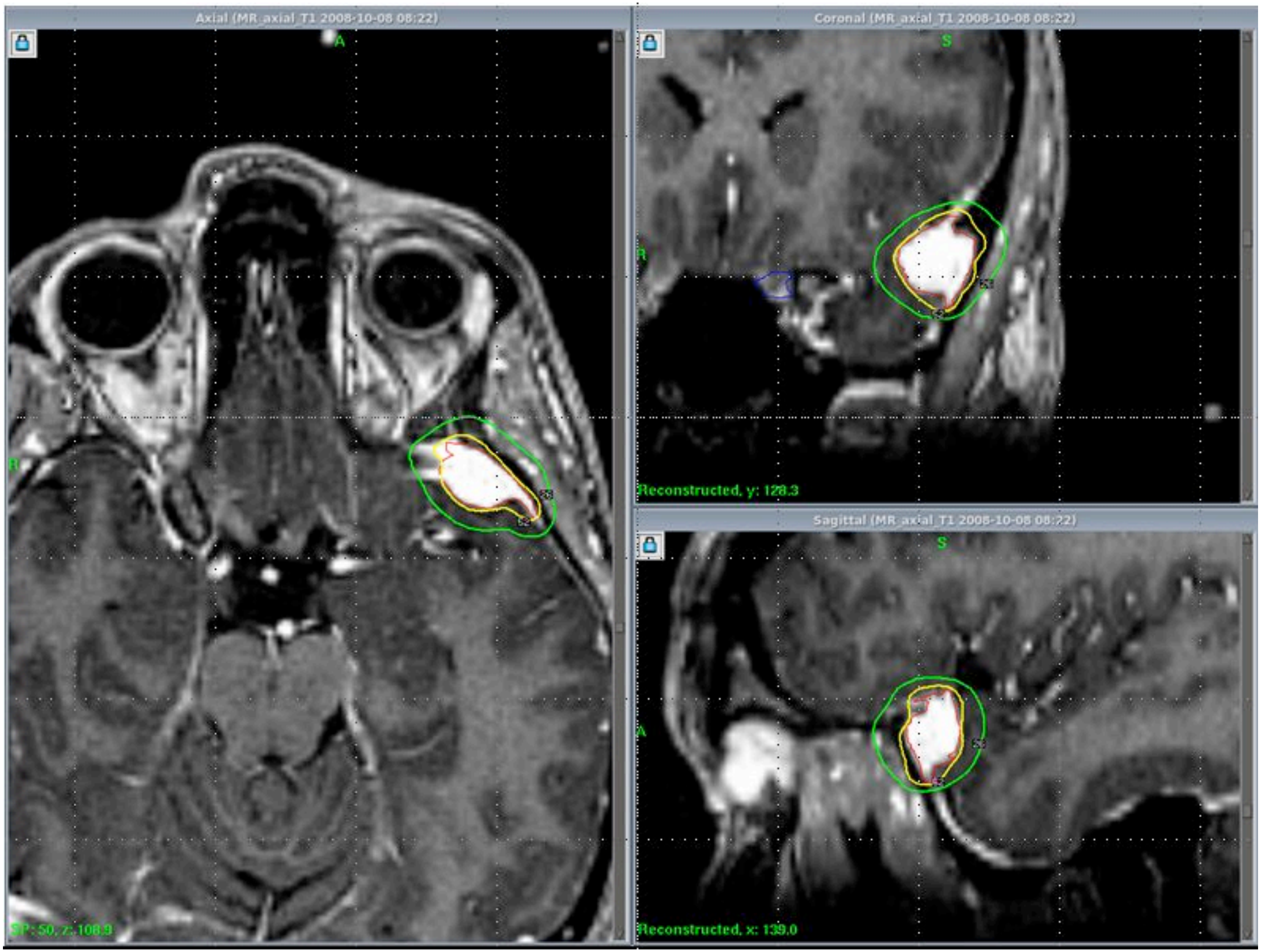
- In GK SRS we seem to be moving towards using C_P

To understand the meaning and implication of conformity index, consider the dose plans shown on the next three slides…..

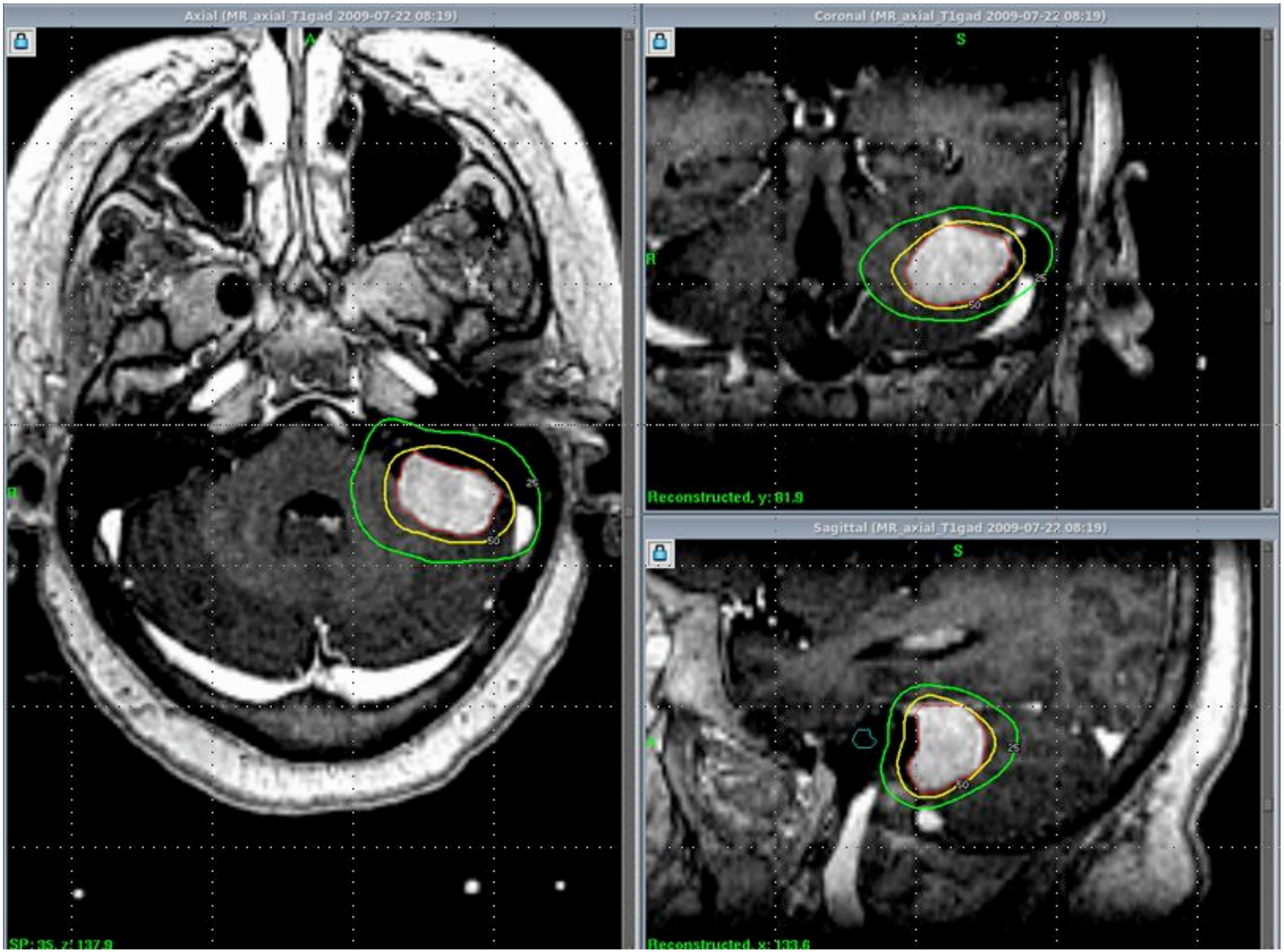
Brain Met: $V_T = 0.15$ cc



Meningioma: V_T = 1.2 cc



Meningioma: VT = 5.5 cc



Considering the 3 plans shown on the preceding slides, which of the following statements regarding their Paddick conformity indices is true?

0%	1.	C_P *(sm met)* $>$ C_P *(sm meningioma)* $>$ C_P *(lg mening)*
0%	2.	C_P *(sm met)* $<$ C_P *(sm meningioma)* $<$ C_P *(lg mening)*
0%	3.	C_P *(sm met)* $=$ C_P *(sm meningioma)* $>$ C_P *(lg mening)*
0%	4.	C_P *(sm met)* $>$ C_P *(sm meningioma)* $=$ C_P *(lg mening)*
0%	5.	C_P *(sm met)* $=$ C_P *(sm meningioma)* $=$ C_P *(lg mening)*

10

Considering the 3 plans shown on the preceding slides, which of the following statements regarding their Paddick conformity indices is true?

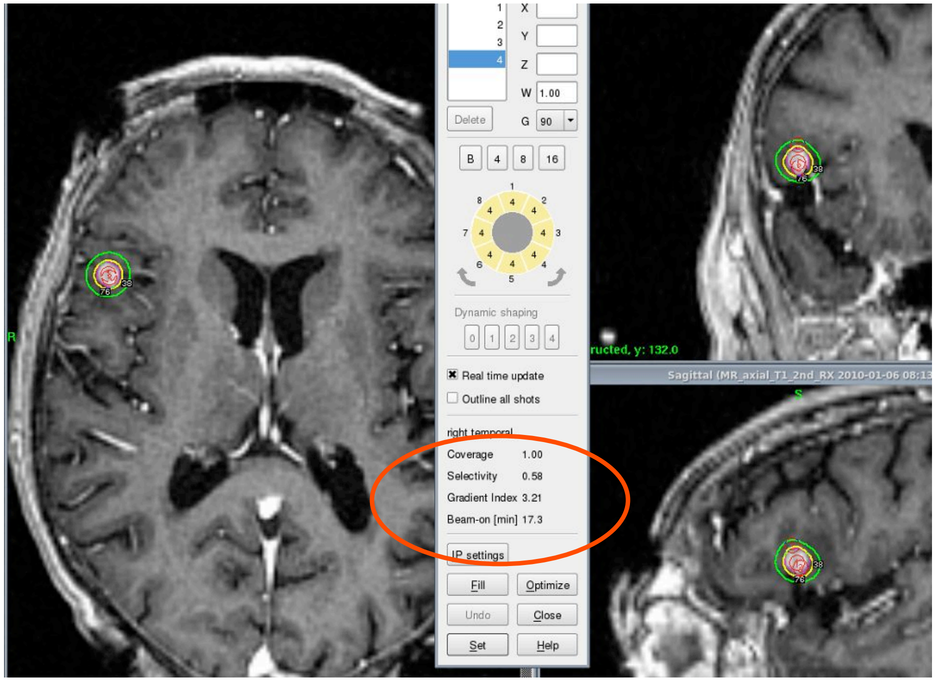
Answer: 5:

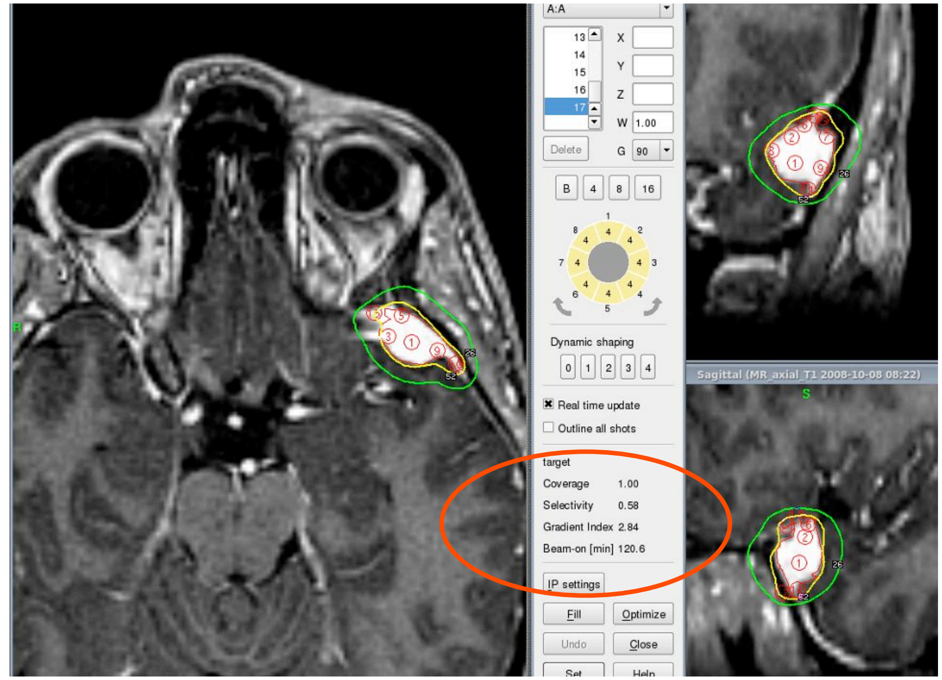
C_P *(small met)* = C_P *(small meningioma)* = C_P *(large meningioma)*

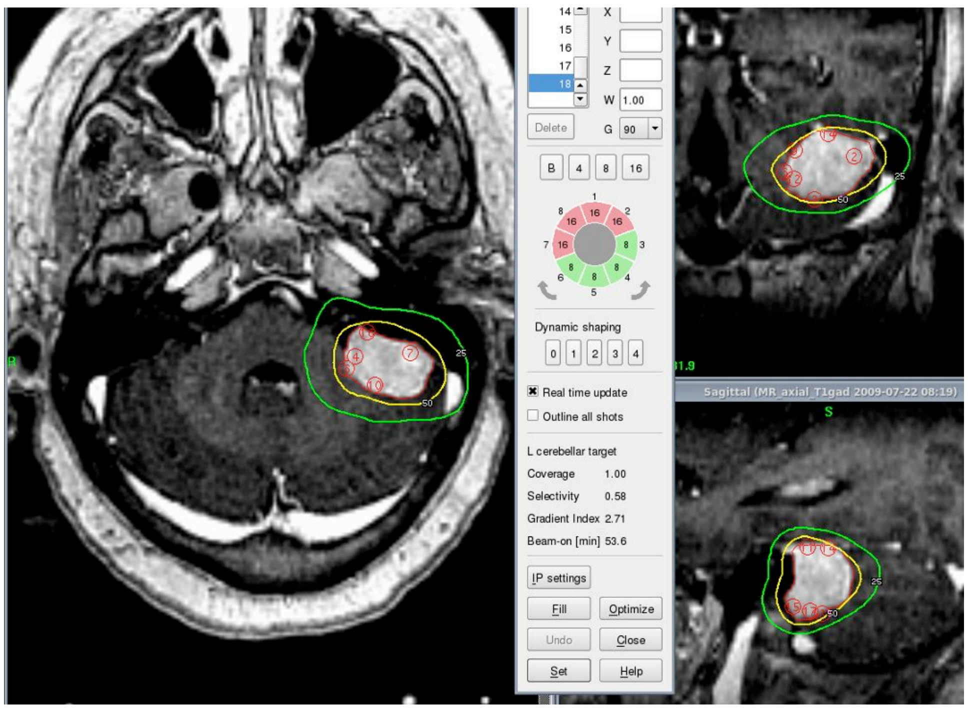
All 3 plans have the same Paddick conformity index.

(Recall that larger values of C_P correspond to better conformity and that $C_P = 1.0$ represents "perfect" conformity.)

References: E. Shaw et al., "RTOG: Radiosurgery quality assurance guidelines," Rad. Oncol. Biol. Phys. 27, 1231-39 (1993), and I. Paddick, "A simple scoring ratio to index the conformity of radiosurgical treatment plans," J. Neurosurg. (Suppl) 93, 219-22 (2000).







For all 3 plans:

Target Coverage = 1.0

Plan selectivity = 0.58

$\therefore\ C_P = 0.58, \quad C_S = 1.72$

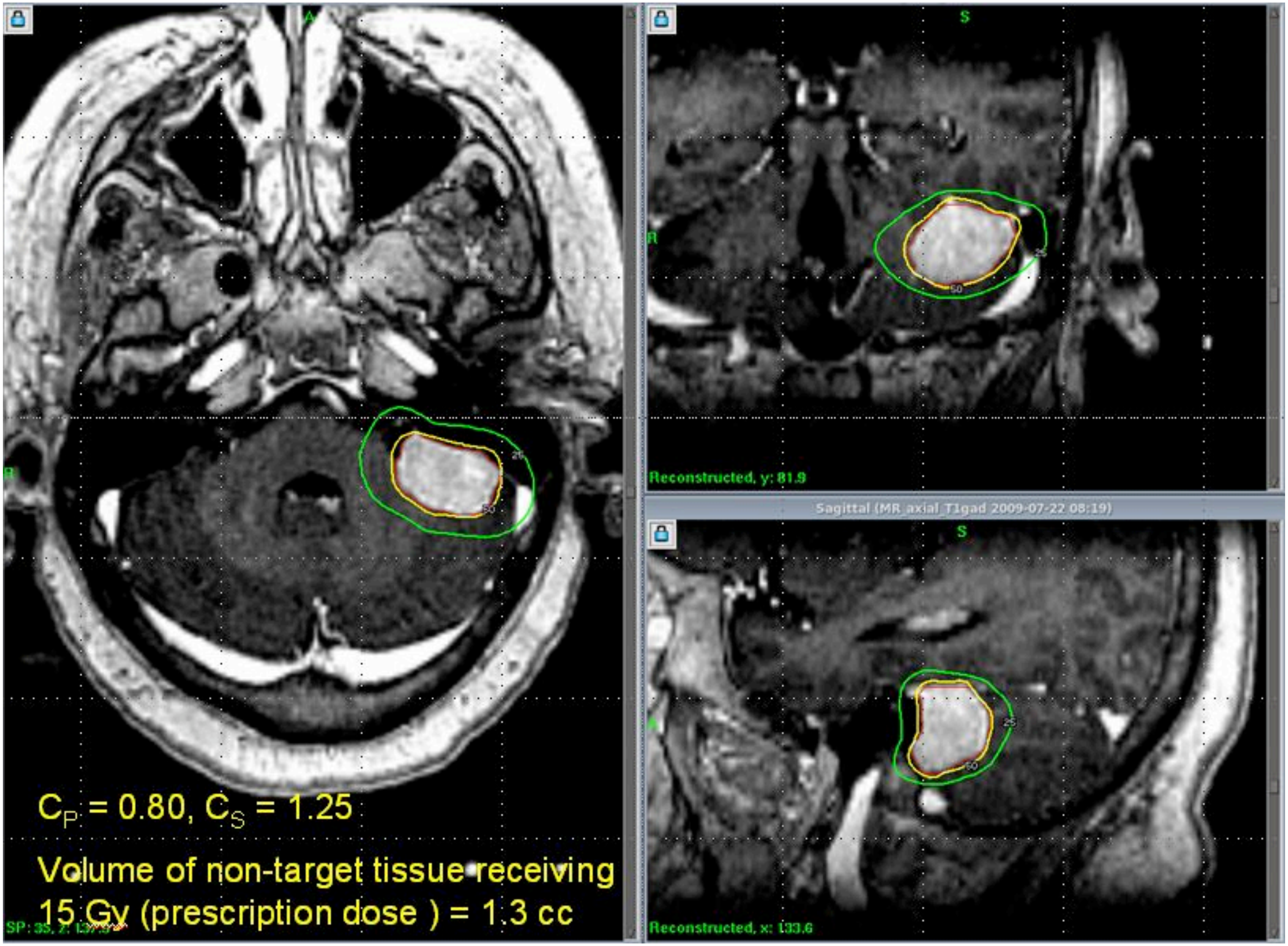
However, the volume of non-target tissue receiving the prescription dose is:

Small met: 0.1 cc

Small Meningioma: 0.9 cc

Large Meningioma: 3.9 cc

Actual Plan for Large Meningioma



J.L. Nakamura et al., "*Dose conformity of Gamma Knife radiosurgery and risk factors for complications*," Int. J. Radiat. Oncol. Biol. Phys. 51, 1313 – 19, (2001).

- 1181 evaluable lesions treated between 1993 and 1998
- Symptomatic radiation toxicity associated with larger:
  - Target volume (V_T)
  - Prescription volumes (V_P)
  - Larger volume of non-target tissue receiving the prescription dose
- But <u>not</u> with:
  - Worsening conformity index (V_P/V_T)

The moral of the story…

- Conformity index is simply a ratio of volumes
- Does not tell us the absolute volume of normal tissue irradiated
- Larger targets are likely to require better conformity
  - (probably > 0.75 for $V_T > 3\ cm^3$)*

*Petti et al., Med Phys., **38**, 2812-2819, (2011).

QA and Radiation Safety for Gamma Knife

- Large doses delivered in a single fraction
- Imaging, planning and treatment performed in a single day
- Often, multiple patients treated in a single day

⇓

- GK team members are often under stress to compete steps involved for GK treatment

  + distractions including the occasional necessity to "multi-task"

Potential for Human Error

- Types of errors that have occurred
  - Left/Right inversion errors
  - Delivering the wrong treatment plan to a patient
  - Entering incorrect prescription dose
  - For older model GKs, setting coordinates incorrectly

Gamma Knife users must adhere to recommendations put forth by the

0%	1. U.S. Food and Drug Administration
0%	2. U.S. Environmental Protection Agency
0%	3. National Institute of Health
0%	4. U.S. Nuclear Regulatory Commission
0%	5. National Institute of Standards and Technology

10

Gamma Knife users must adhere to recommendations put forth by the…

Answer: 4: The US Nuclear Regulatory Commission*

Unlike other forms of radiosurgery, GK SRS falls under the jurisdiction of the NRC (because Co-60 is reactor bi-product material)

*NRC10 CFR Part 35.600 Subpart H, "Photon Emitting Remote Afterloader Units, Teletherapy Units and Gamma Stereotactic Radiosurgery Units" and http://www.nrc.gov/materials/miau/med-use-toolkit/perfexion-guidance.pdf

NRC Requirements for PFX

- Training of AUs and AMPs, and documentation of training
- Preparation and use of “written directive”
- Routine QA

Purpose of both the NRC requirements and of many of the technological developments in hardware and software for the Gamma Knife over the years has been to reduce the likelihood of human error

Thank you for your attention!