Treatment of Brain Metastases with Cyberknife Robotic Radiosurgery

Alfredo Conti
University of Messina, ITALY

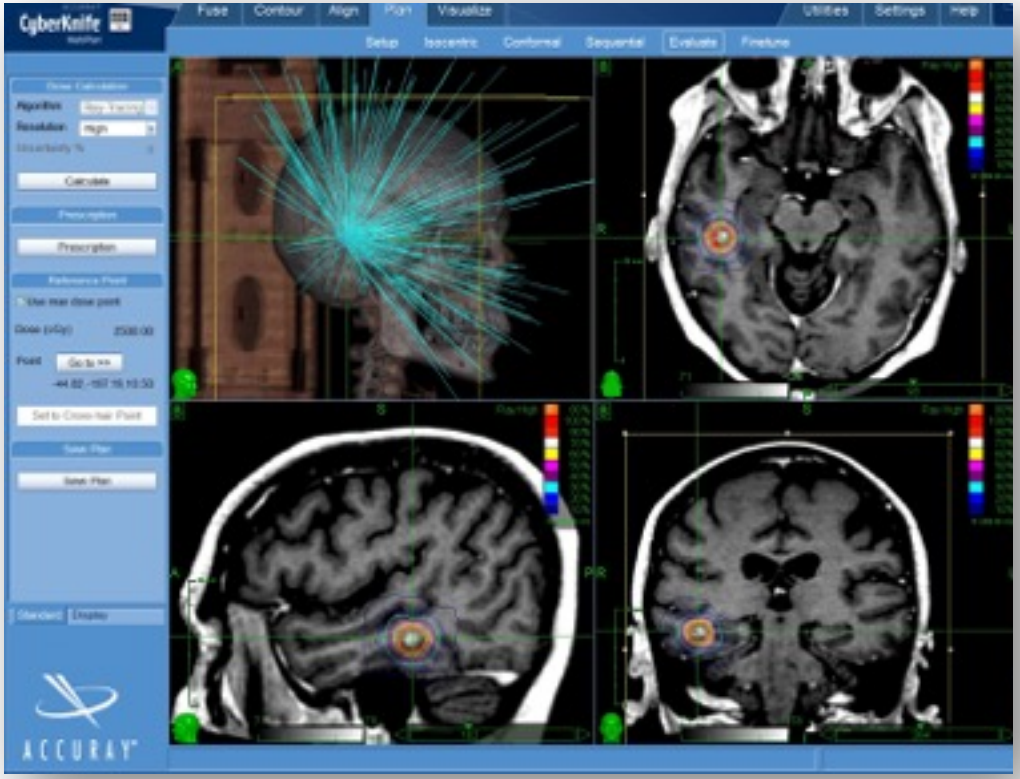
ACCURAY®

Precise, innovative tumor treatments™

Is there any benefit (or limitation) in frameless radiosurgery for brain metastases?

Brain Metastases July 2007-Sept. 2015

Cyberknife Centre University of Messina - Italy



Characteristics of Patients	
431 Patients	848 Lesions
mean age 60 years (range 35-77 years)	

Tumor Histologies	
Non small cells lung cancer	48%
Breast cancer	33%
Melanoma	5%
GI Cancer	5%
Kidney Carcinoma	4%
Prostate adenocarcinoma	2%
Bladder urethelioma	2%
Ovarian cancer	1%

Treatment Planning Algorithms

5%

Isocentric Technique

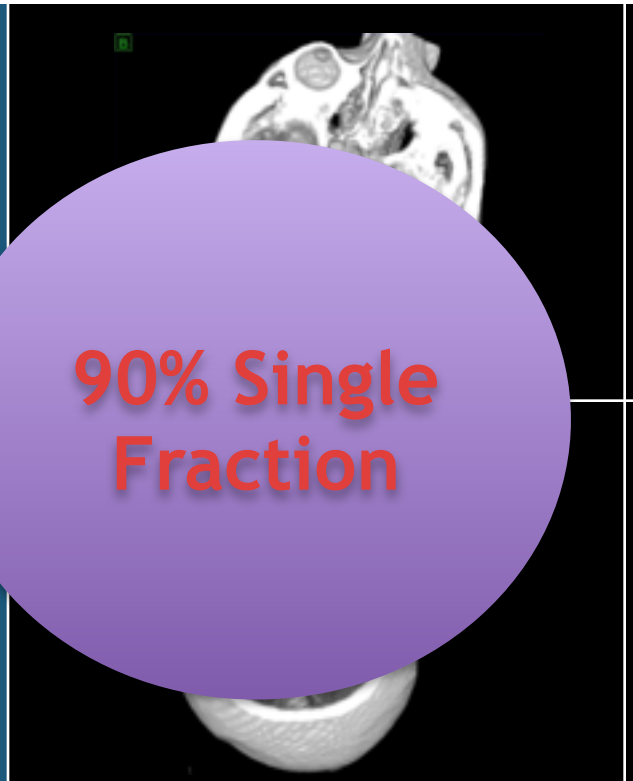
2%

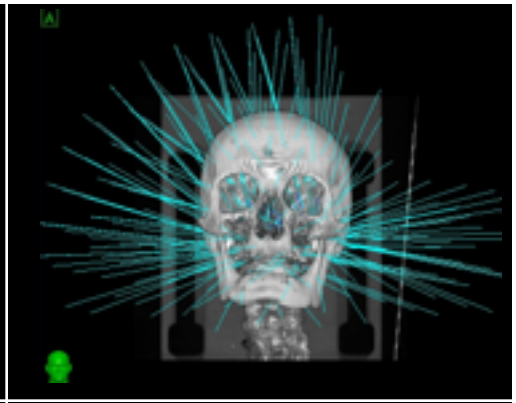
Conformal Isocentric Technique

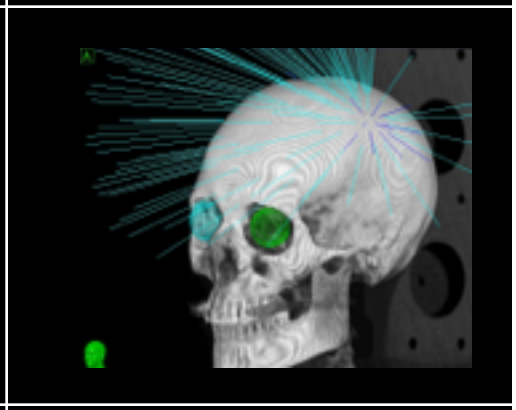
93%

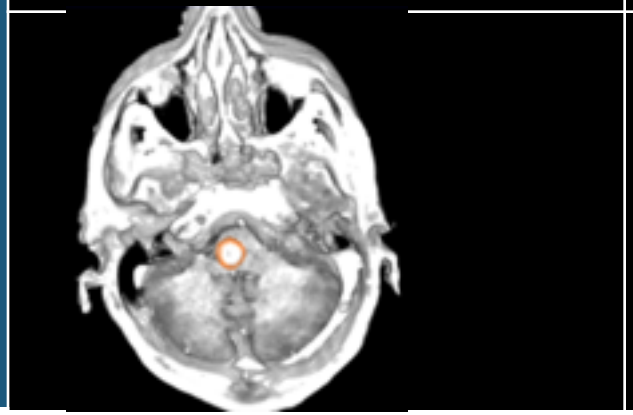
Conformal Non-Isocentric Technique

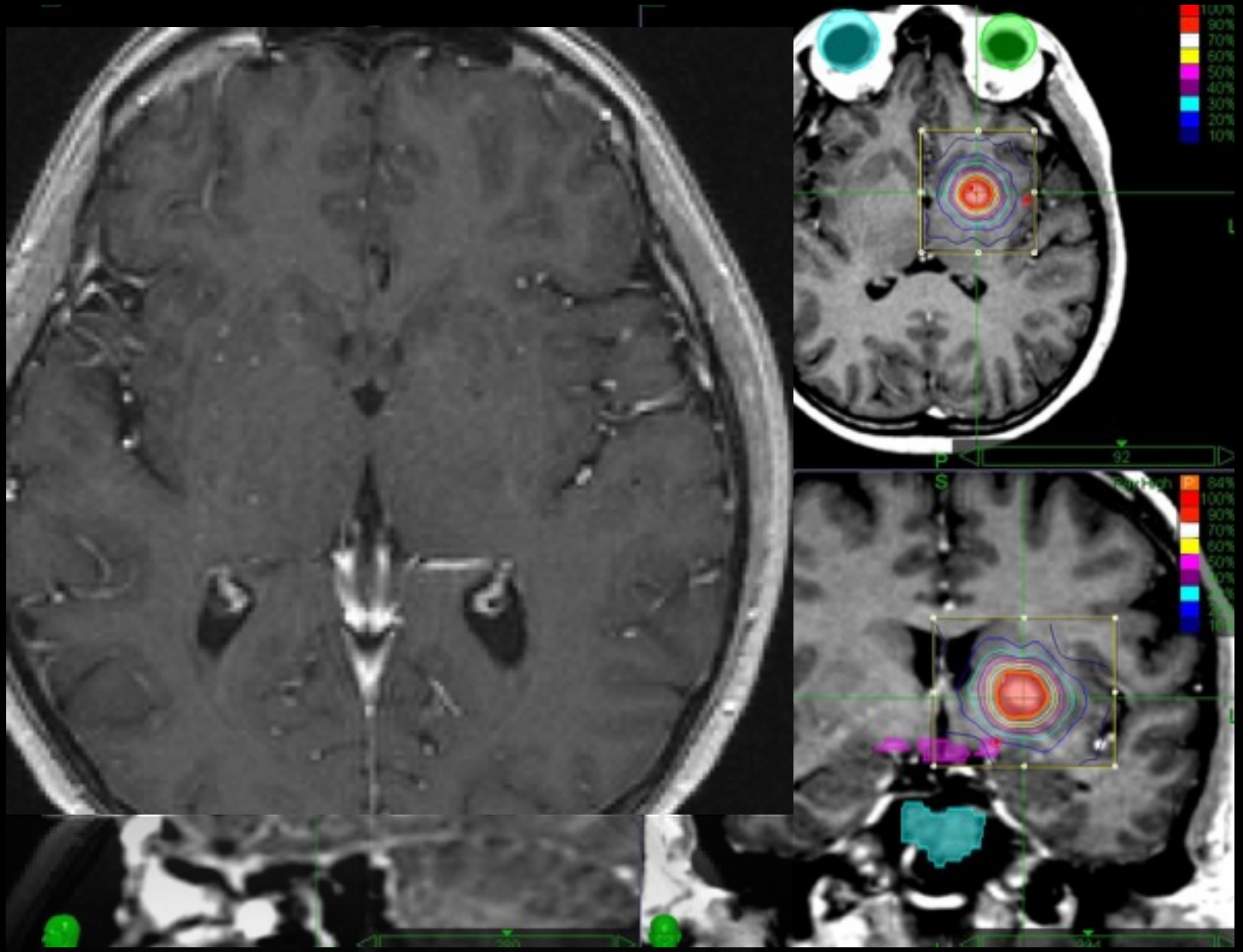
90% Single Fraction

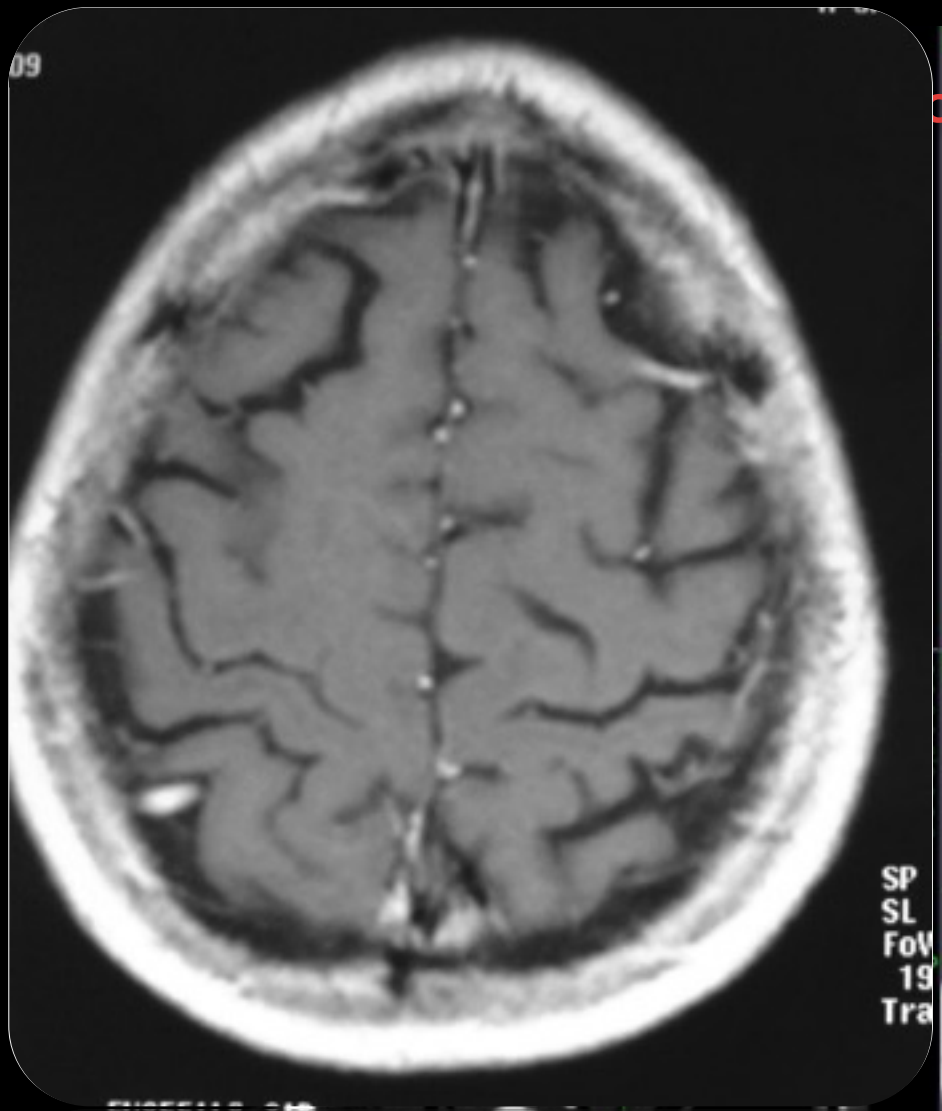


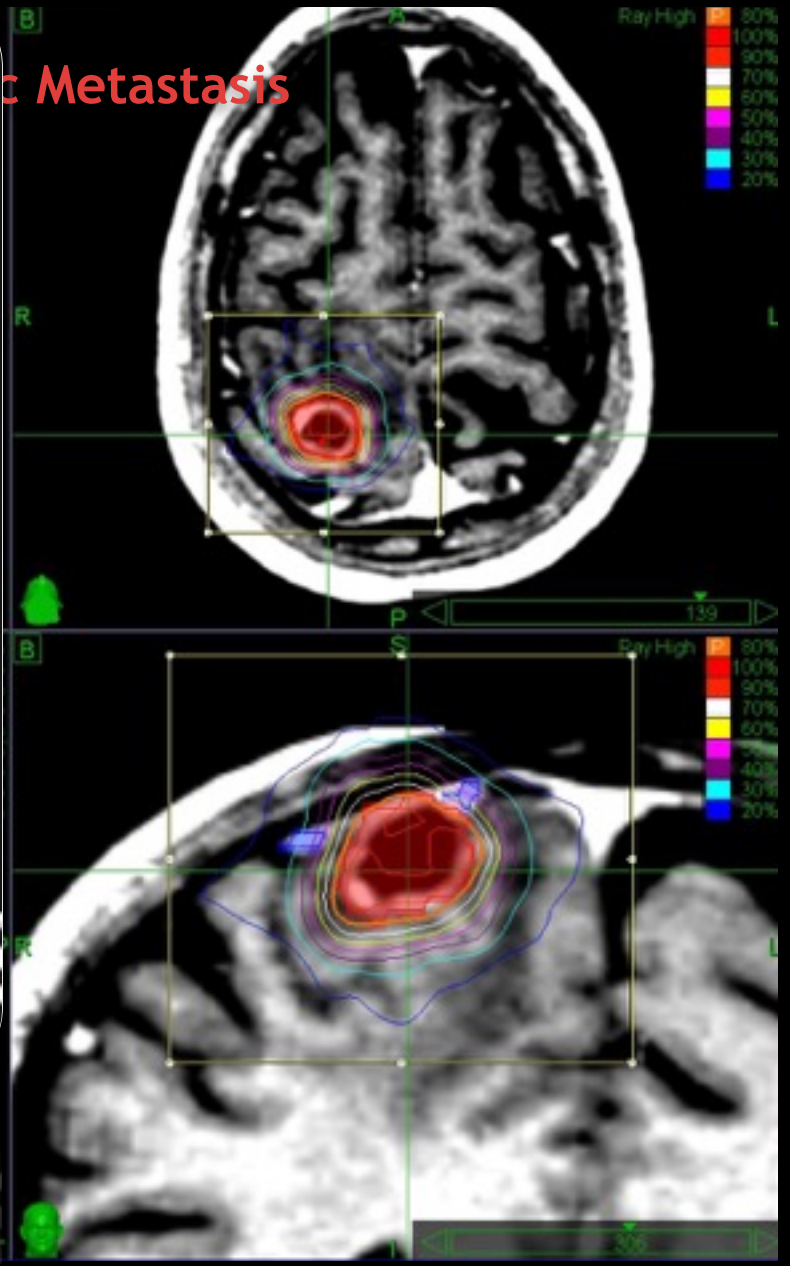


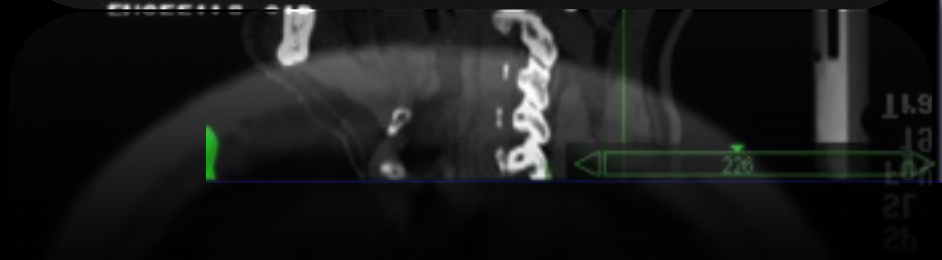




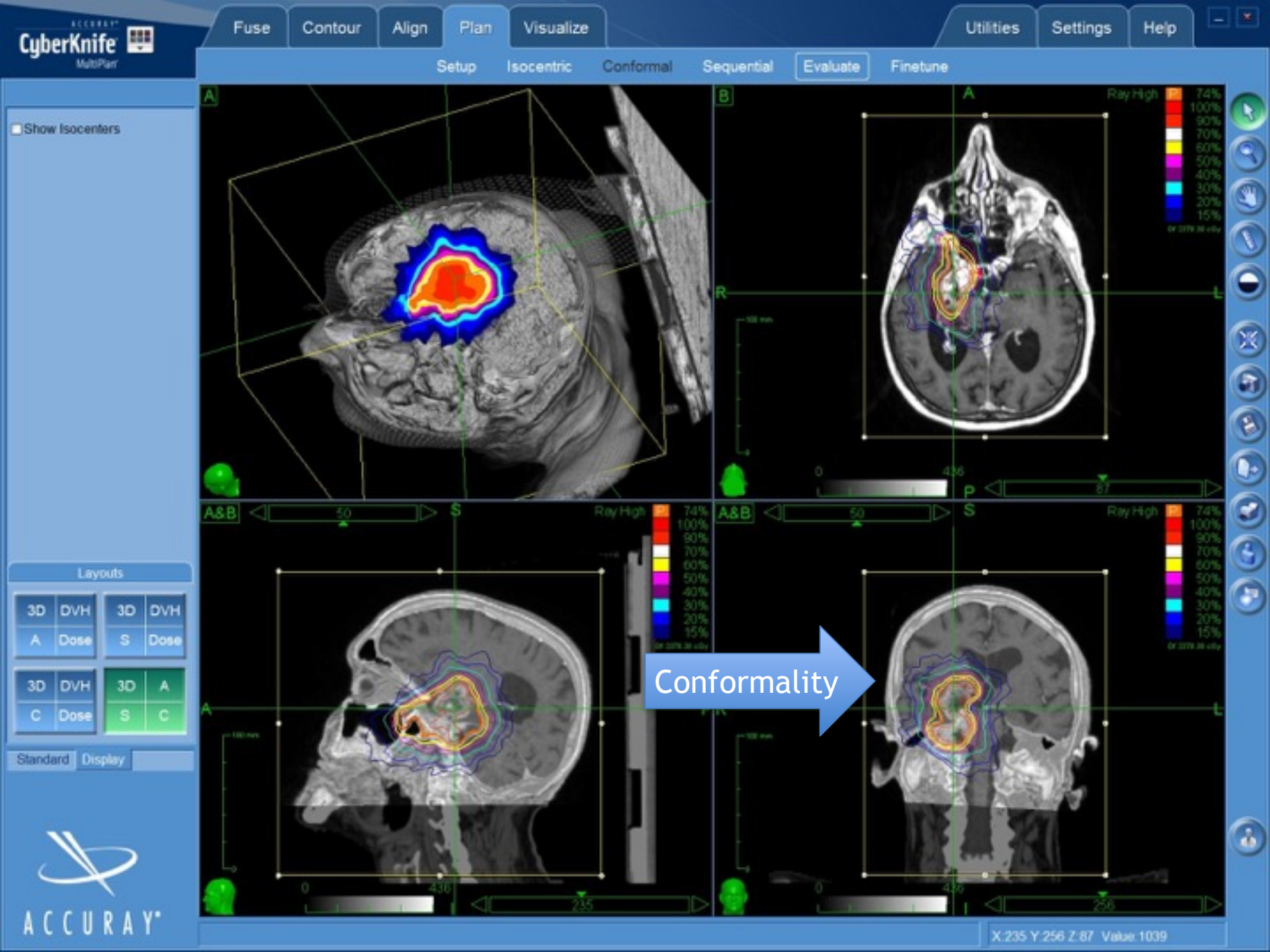

100%
90%
70%
60%
50%
40%
30%
20%
10%
L
92
P
S
84%
100%
90%
70%
60%
50%







c Metastasis


CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Show Isocenters
Layouts
3D
DVH
A
Dose
S
C
Standard
Display
Ray High
Conformality
ACCURAY
X:235 Y:256 Z:87 Value:1039

Precision: can we rely on frameless technology?

Summary of E2E Results
(AUGUST 2009 - AUGUST 2014)

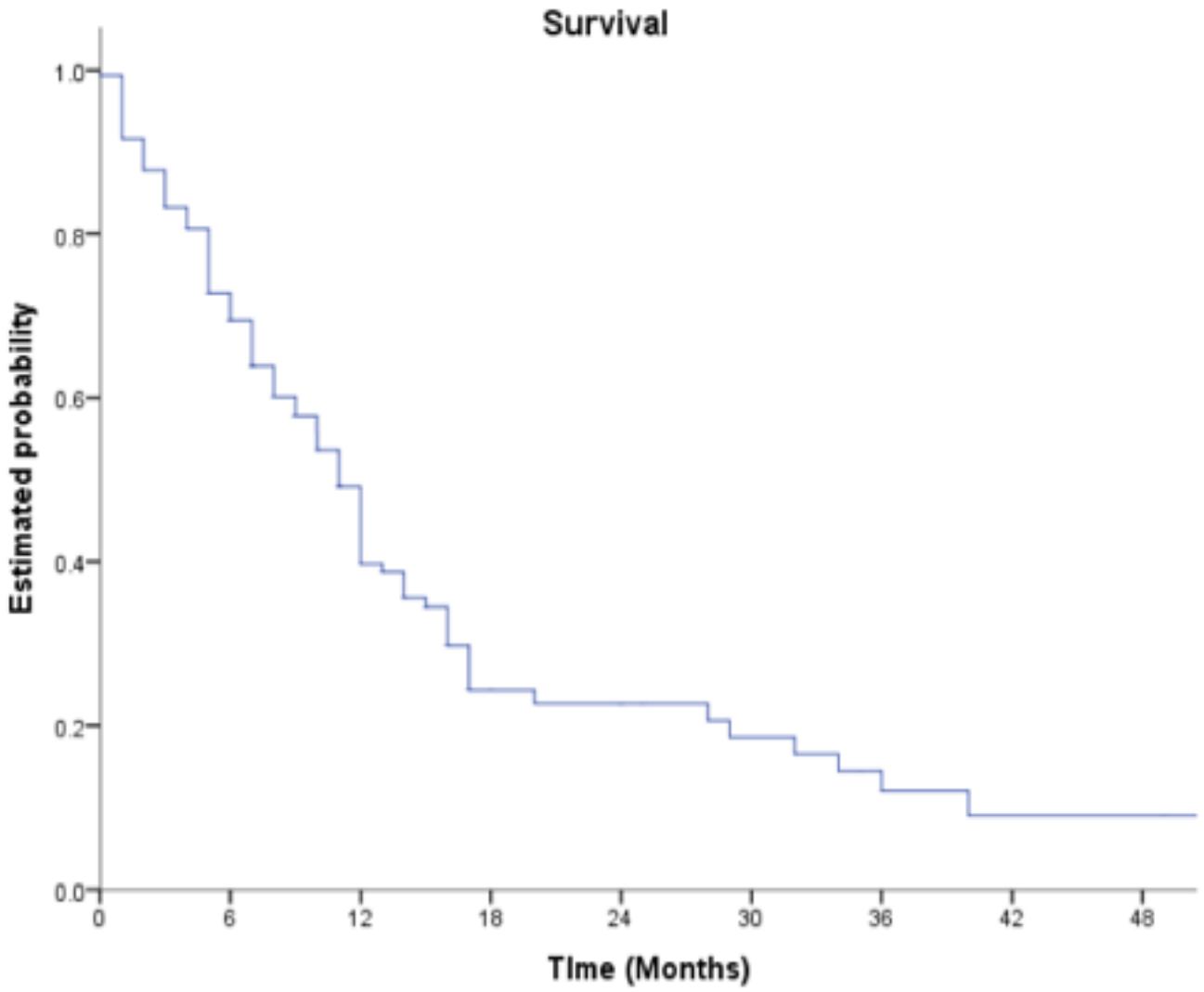
Tracking (Fixed Collimator)	**6D-Skull**
(Total targeting error ± 1 σ) mm	0.57±0.16
Max allowed error (mm):	*0.95*
Tracking (IRIS Collimator)	**6D-Skull**
(Total targeting error ± 1 σ) mm	0.56±0.17
Max allowed error (mm):	*0.95*

No need for target volume expansion to a PTV

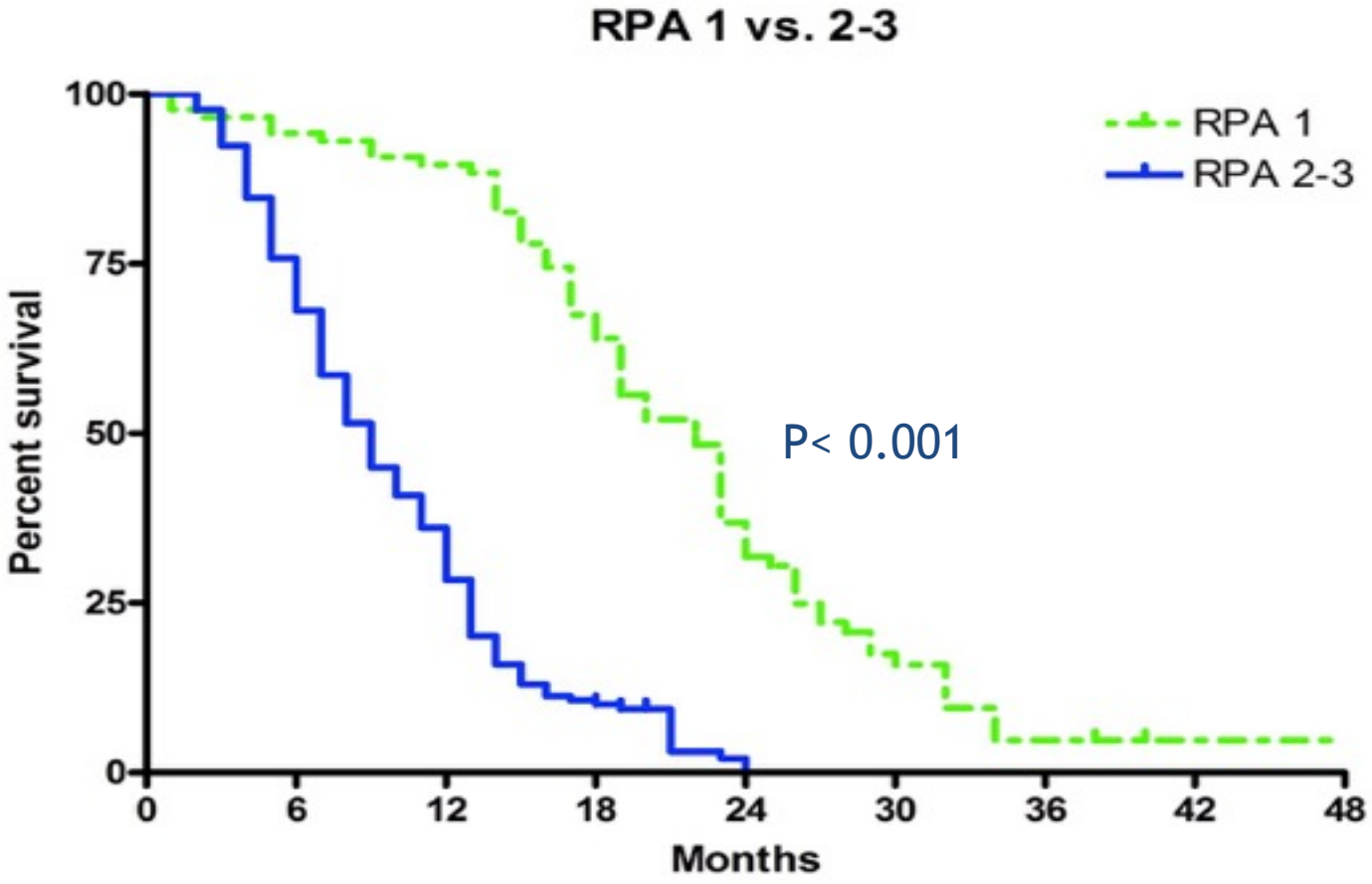
Results of the Whole Series

- 848 Lesions
- 431 Patients
- Median No. of lesions 2 (1-18)
- Median dose SRS 20 Gy (17-22 Gy)
- Median dose hSRT 27.5 Gy in 5 fractions (24-30 Gy)
- Median isodose 75%

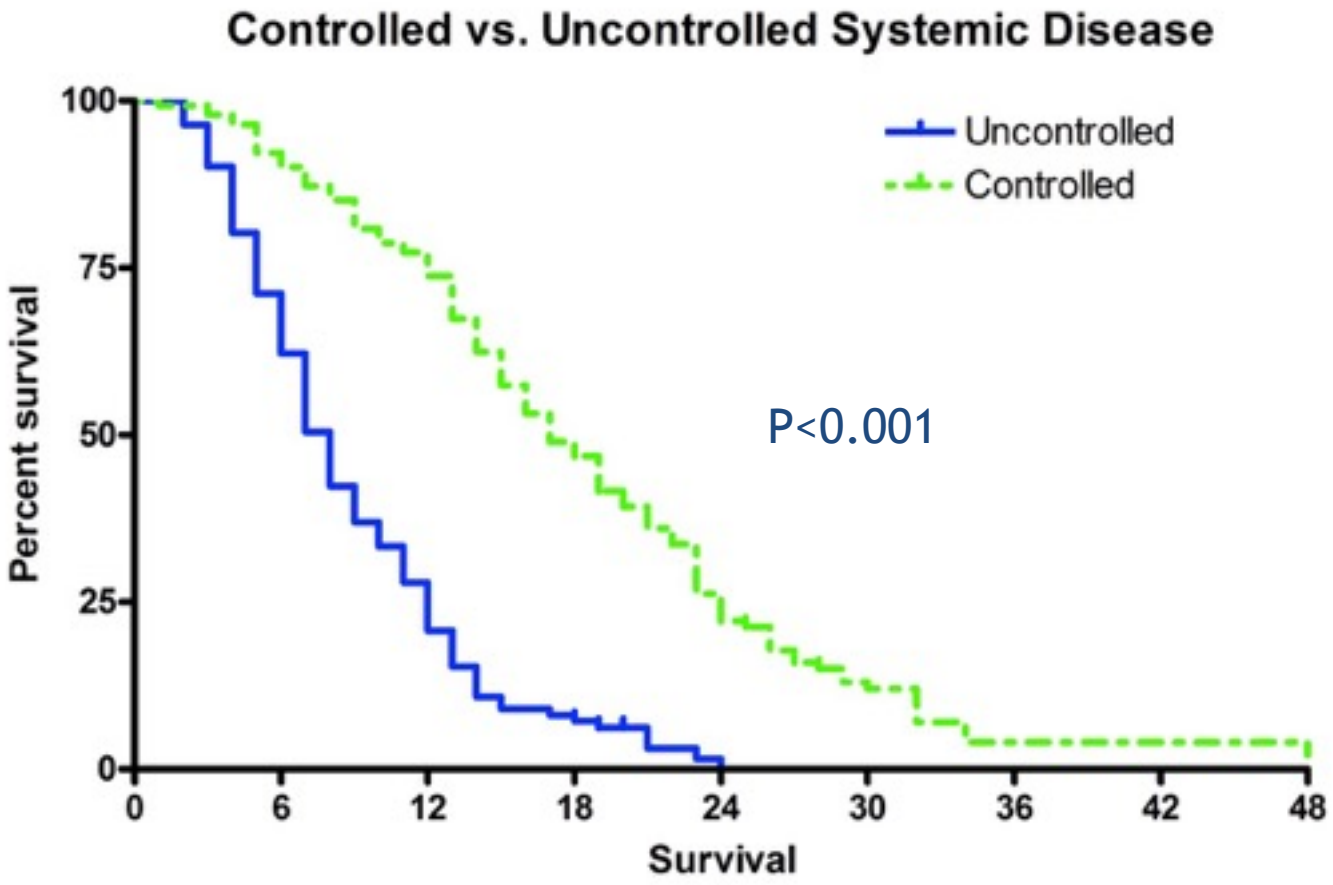
Median Survival: 11 months

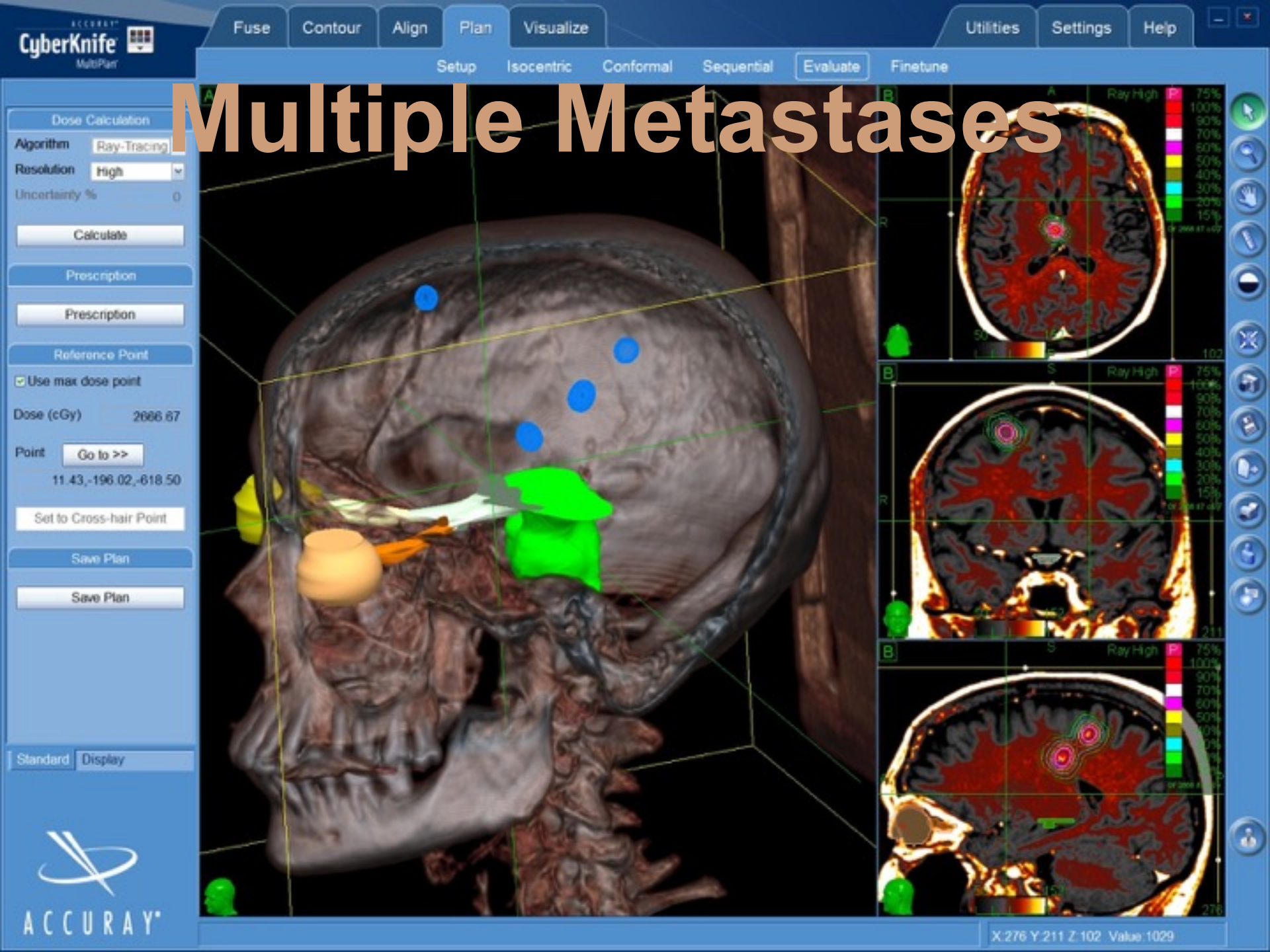


Median Survival according to RPA Classes



Survival according to Extracranial Disease Control




CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Multiple Metastases
Dose Calculation
Algorithm
Ray-Tracing
Resolution
High
Uncertainty %
Calculate
Prescription
Prescription
Reference Point
Use max dose point
Dose (cGy)
2686.67
Point
Go to >>
11.43,-196.02,-618.50
Set to Cross-hair Point
Save Plan
Save Plan
Standard
Display
ACCURAY
X:276 Y:211 Z:102 Value:1029

International Journal of
Radiation Oncology
biology • physics
Official Journal of the American Society for Radiation Oncology
ASTRO

Repeat Courses of Stereotactic Radiosurgery (SRS), Deferring Whole-Brain Irradiation, for New Brain Metastases After Initial SRS

David B. Shultz, MD, PhD, Leslie A. Modlin, BA, Priya Jayachandran, MD, Rie Von Eyben, MS, Iris C. Gibbs, MD, Clara Y.H. Choi, MD, PhD, Steven D. Chang, MD, Griffith R. Harsh IV, MD, Gordon Li, MD, John R. Adler, MD, Steven L. Hancock, MD, Scott G. Soltys, MD

Received: December 11, 2014; Received in revised form: March 3, 2015; Accepted: April 15, 2015; Published Online: April 27, 2015

J Neurosurg (Suppl 2) 121:16–25, 2014

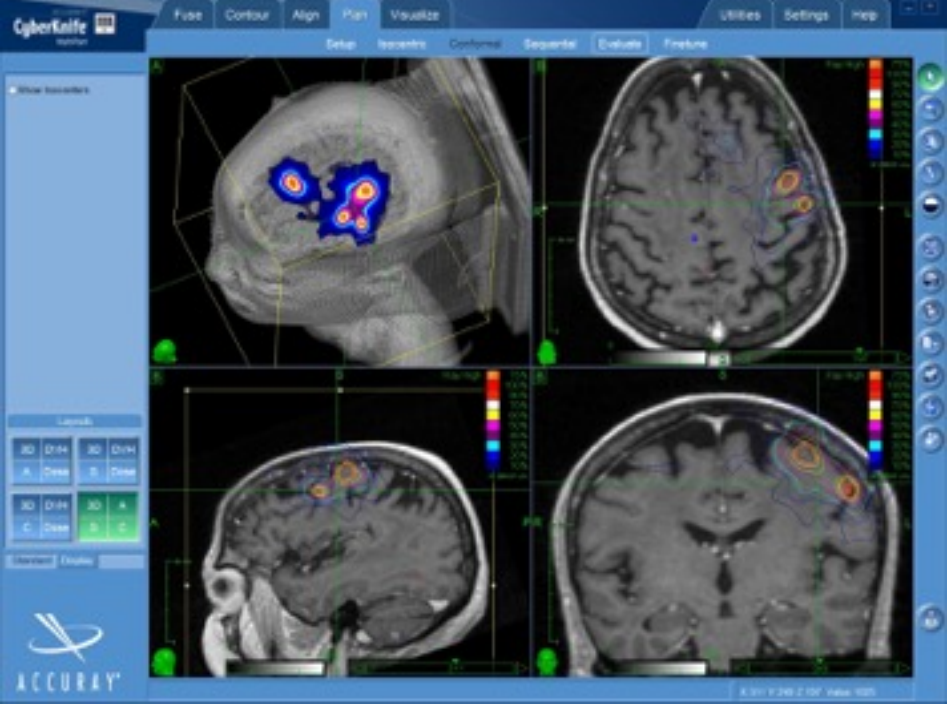
Stereotactic radiosurgery for patients with multiple brain metastases: a case-matched study comparing treatment results for patients with 2–9 versus 10 or more tumors

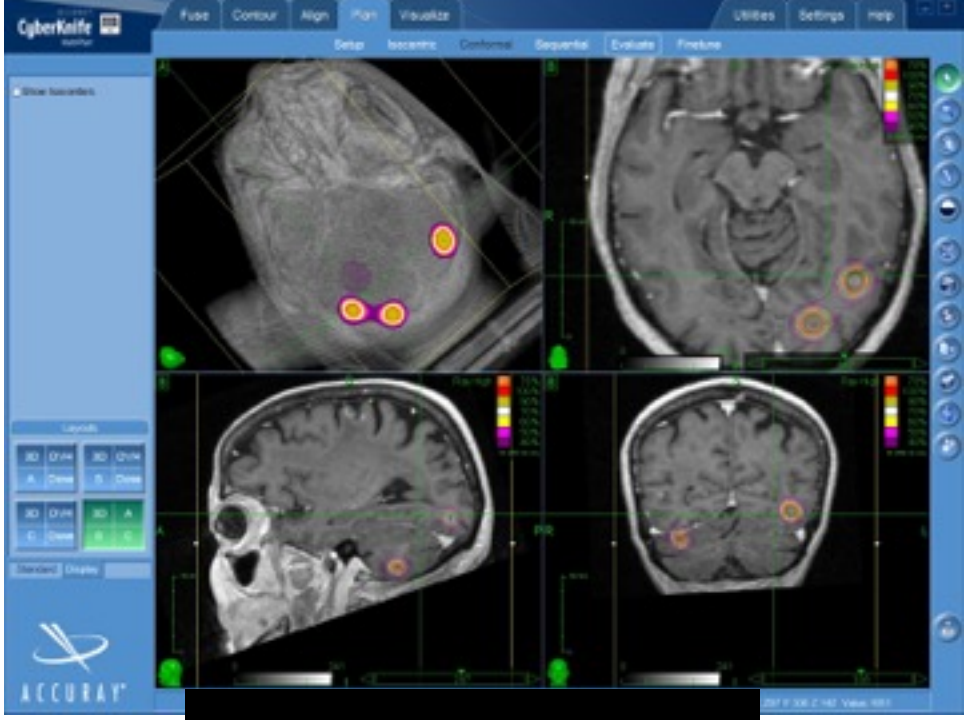
Clinical article

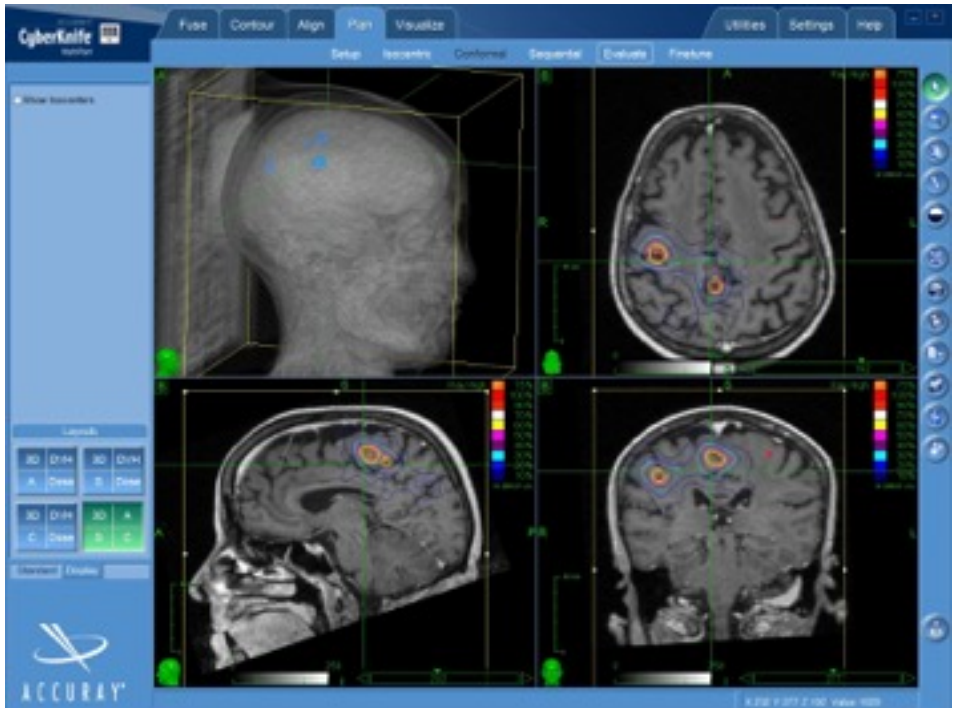
Masaaki Yamamoto, M.D.,[1,2] Takuya Kawabe, M.D.,[1,3] Yasunori Sato, Ph.D.,[4] Yoshinori Higuchi, M.D.,[5] Tadashi Nariai, M.D., Ph.D.,[6] Shinya Watanabe, M.D.,[1,7] and Hidetoshi Kasuya, M.D.[2]

Possible Advantages in Frameless SRS

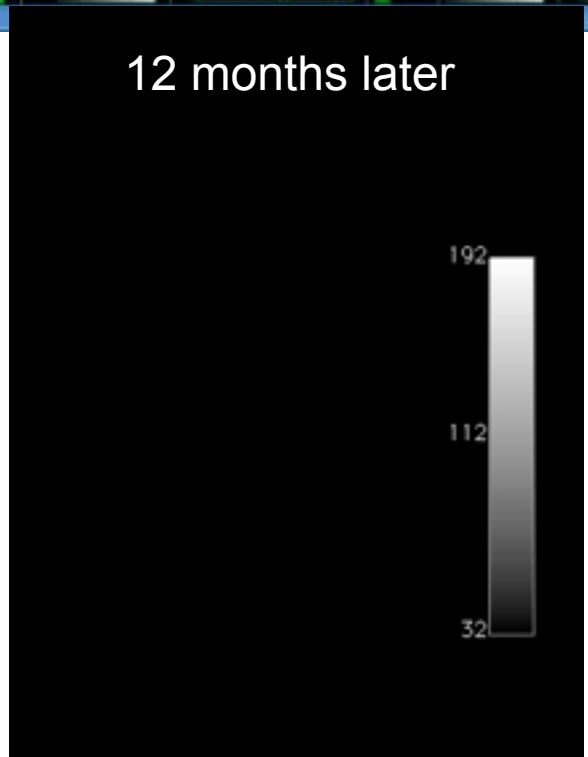
- Treatment of multiple lesions in several days to allow a certain degree of normal brain recovery
- Multisession (brainstem)
- Time for planning and treatment delivery

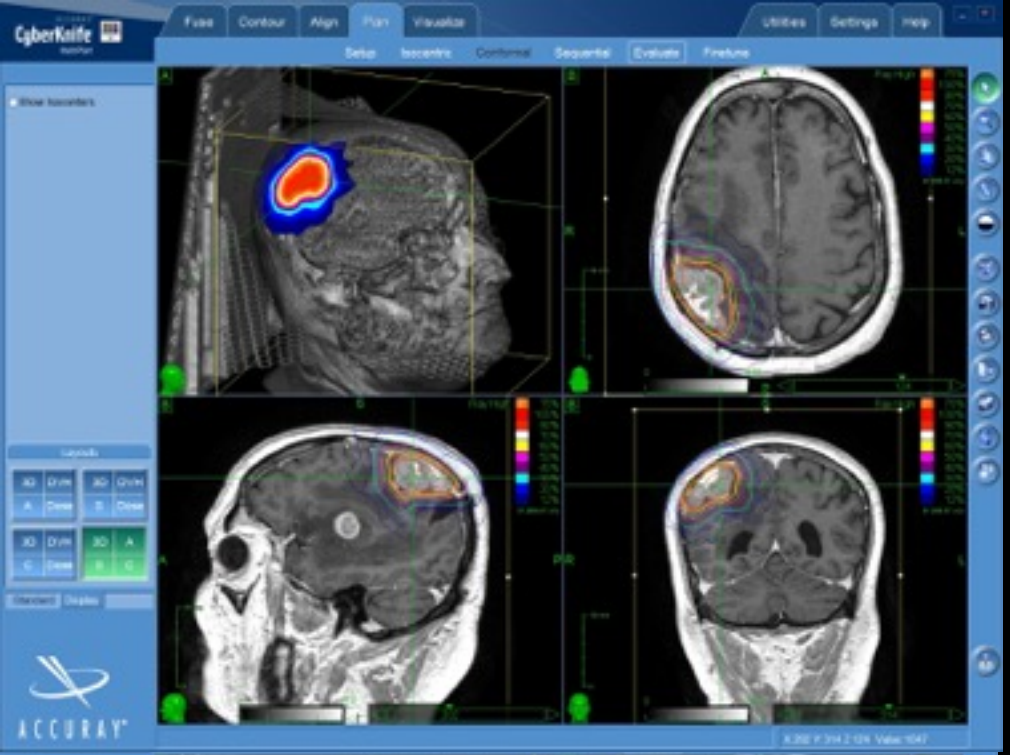


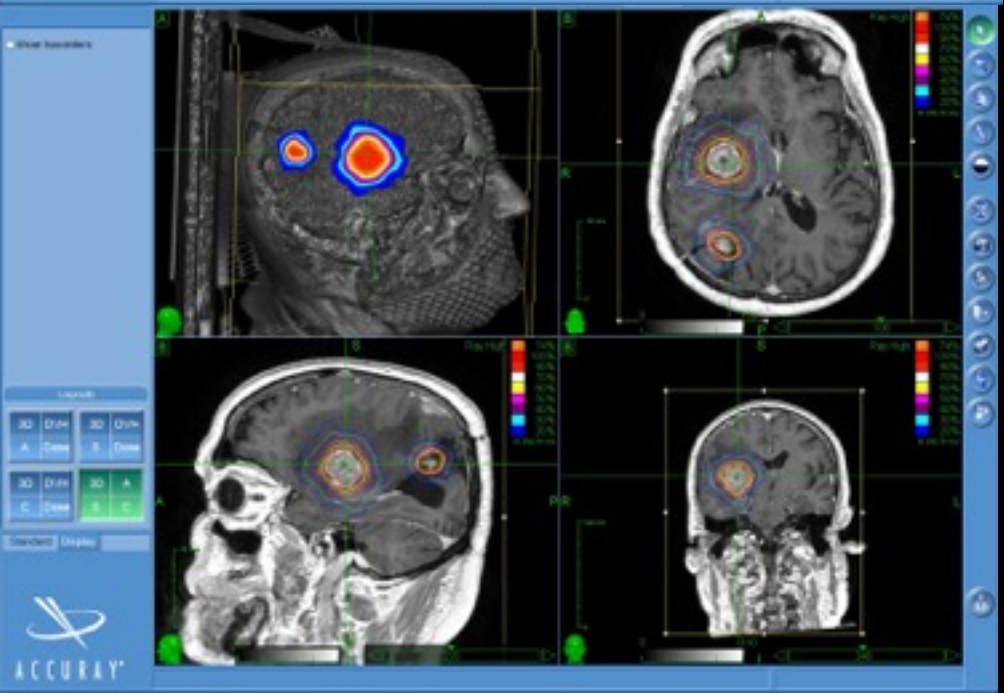


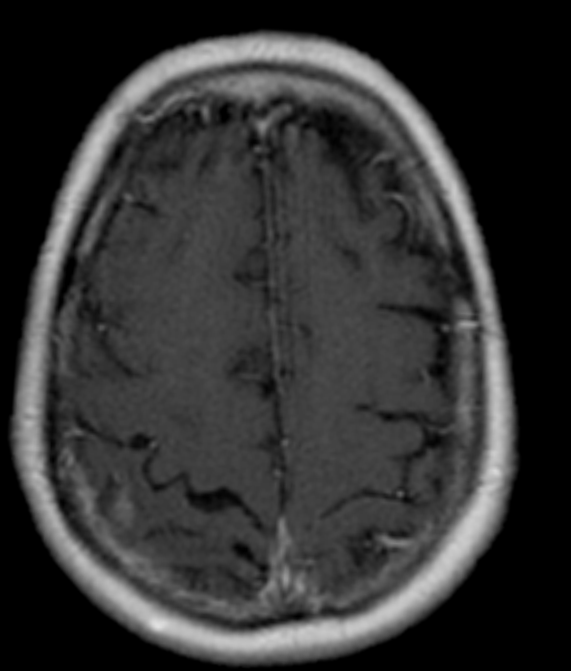


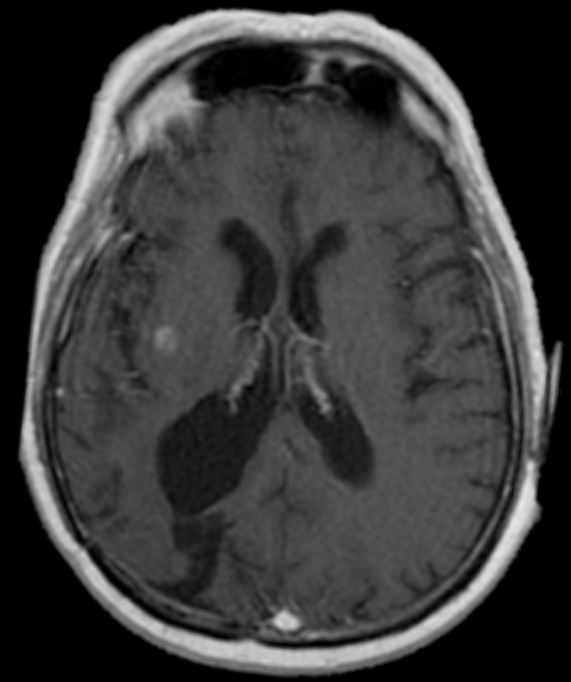
12 months later

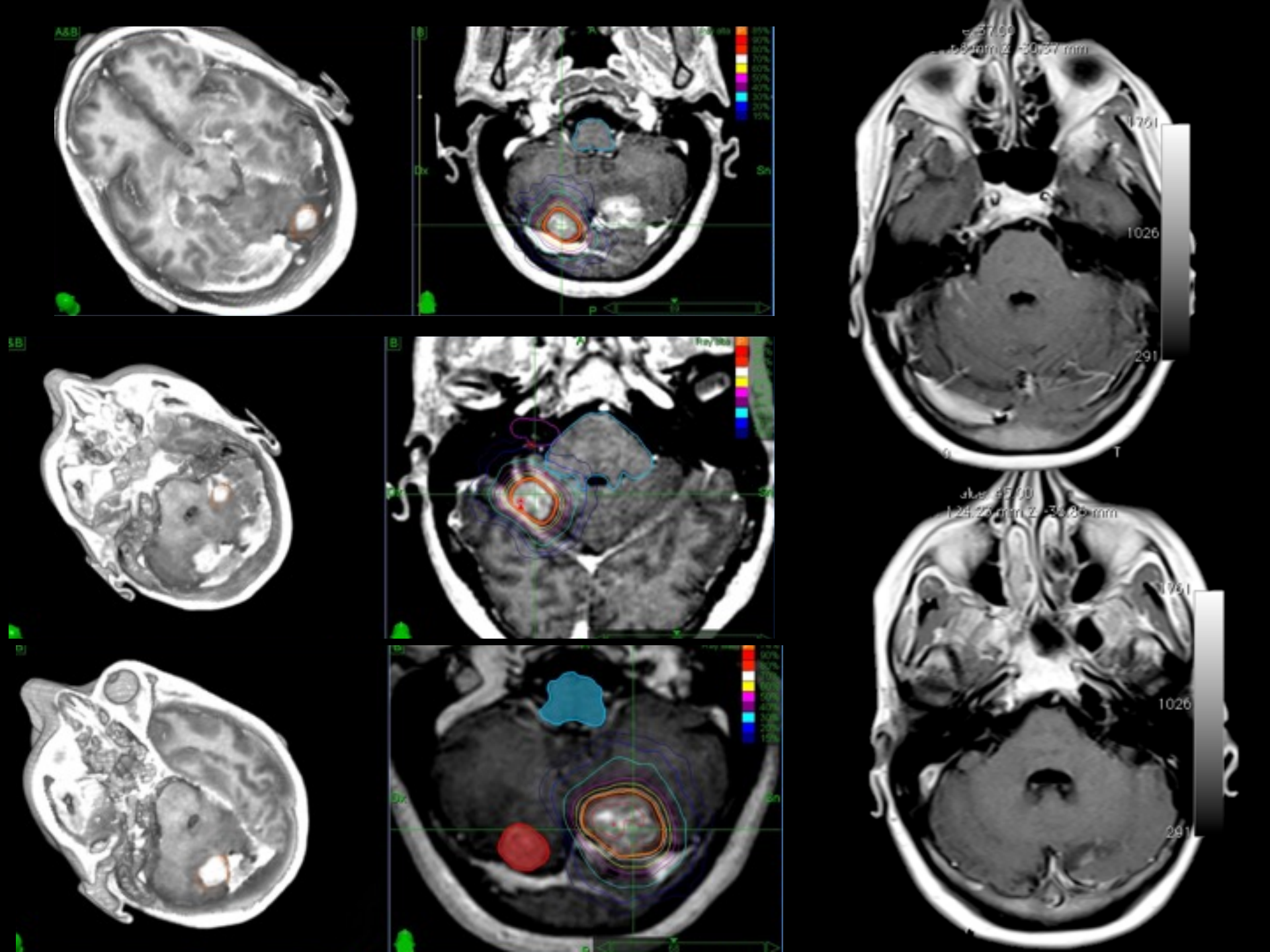



CyberKnife
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentre
Conformal
Sequential
Evaluate
Fineluna
ACCURAY

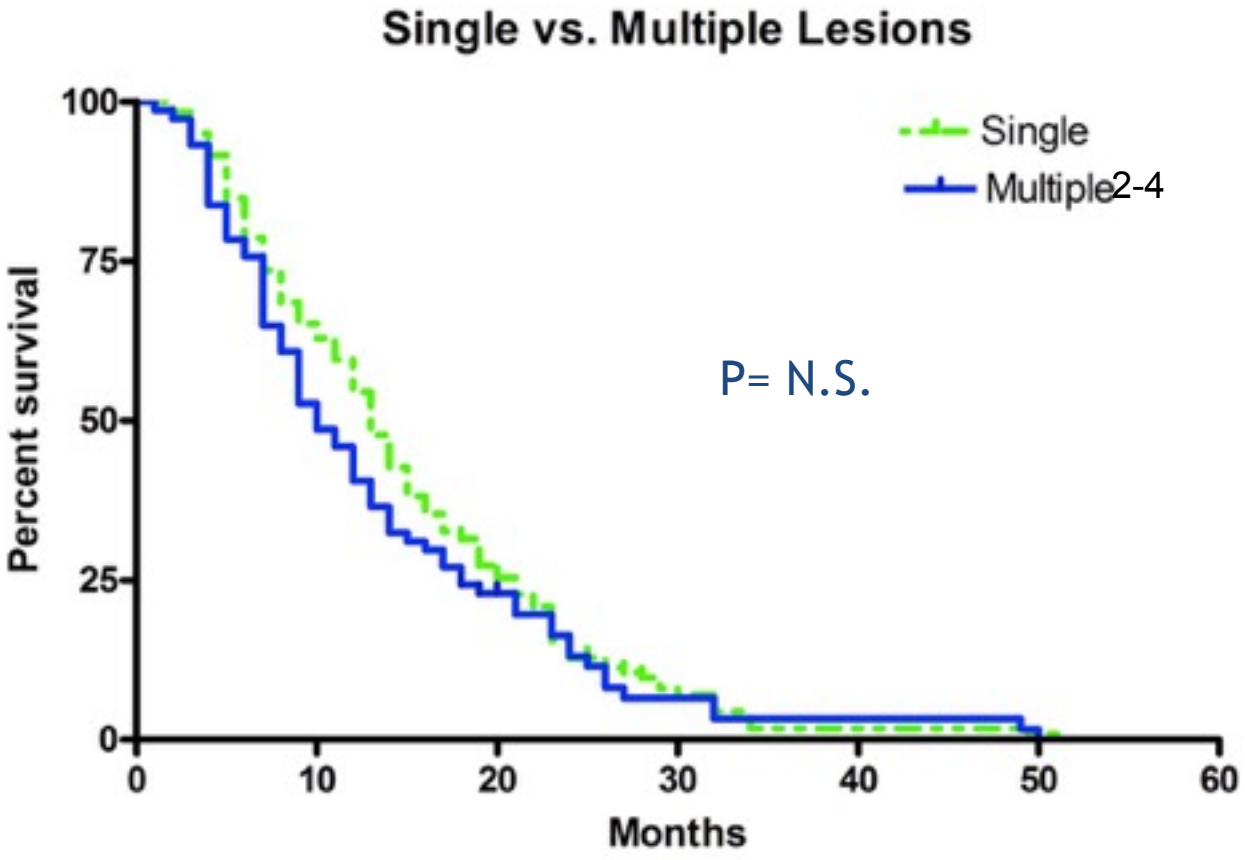

ACCURAY






1761
1026
291
1761
1026
291

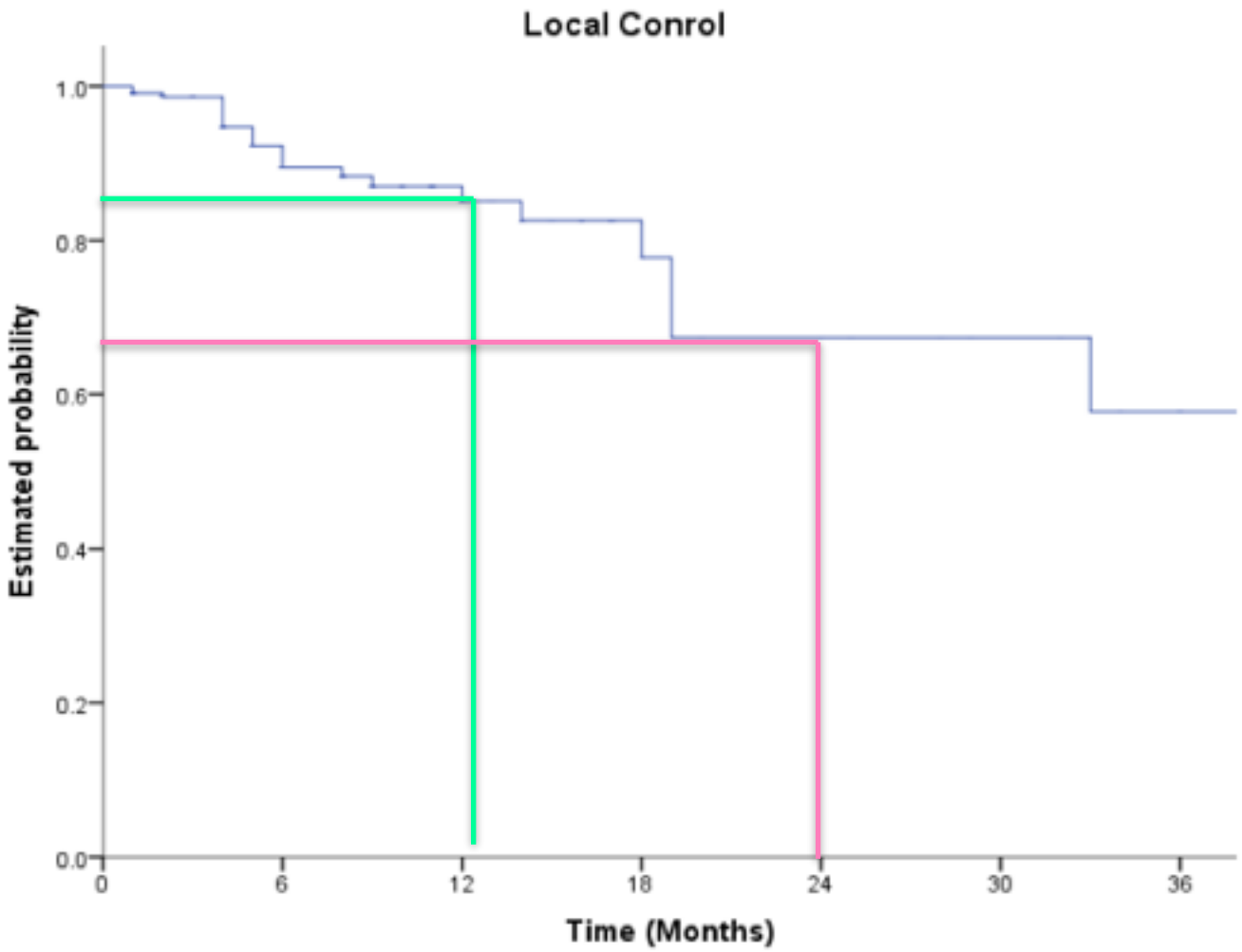
Survival according to Number of Brain Metastases



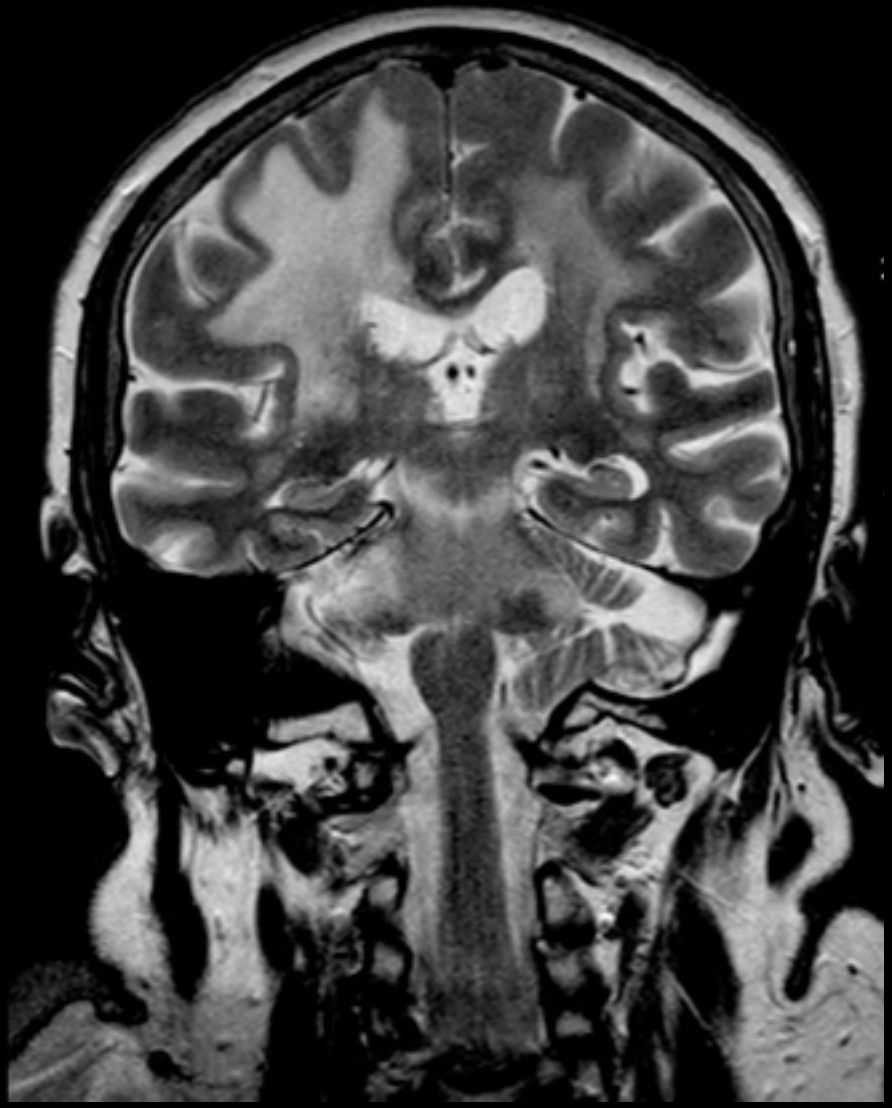
P= N.S.

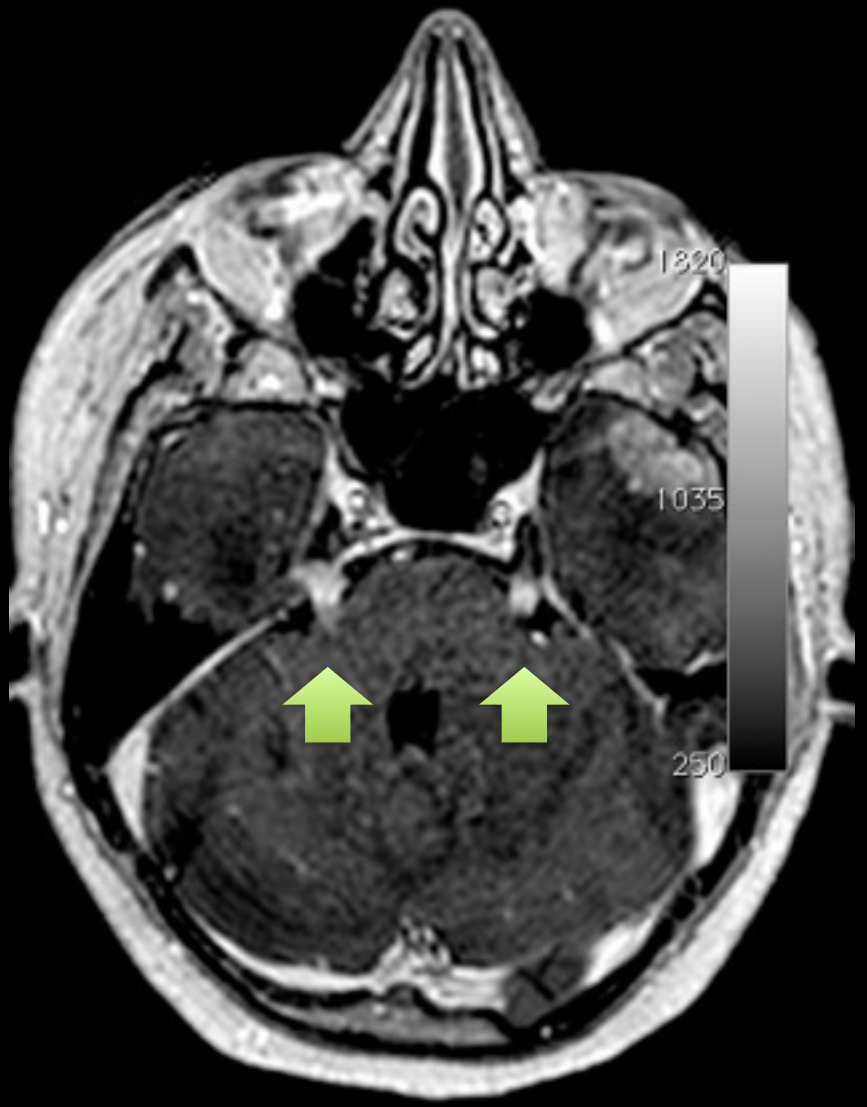
2-4

Median PFS: 38 months

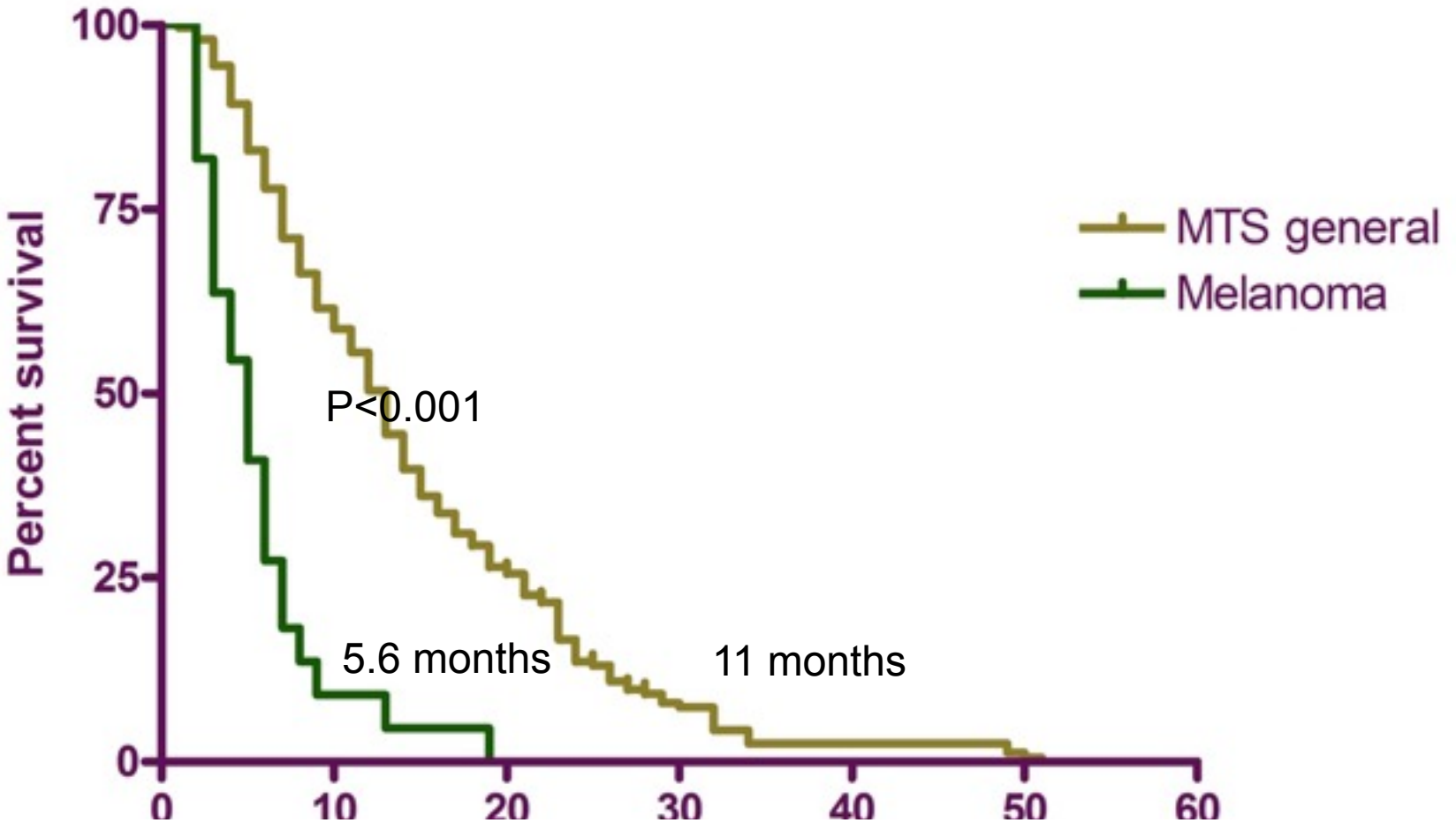


RT-induced side effects and widespread neoplastic diffusion in long-term survivors

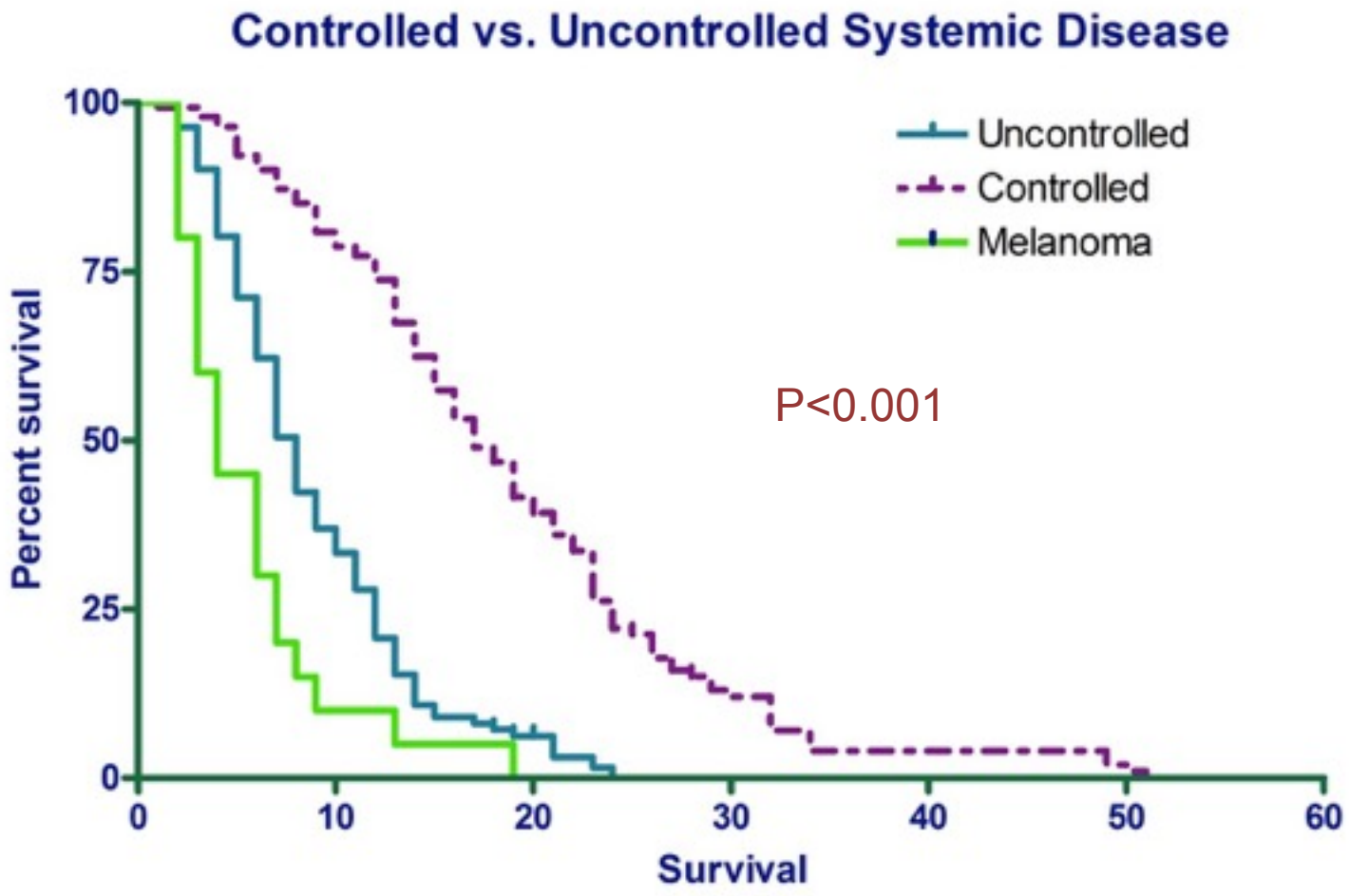




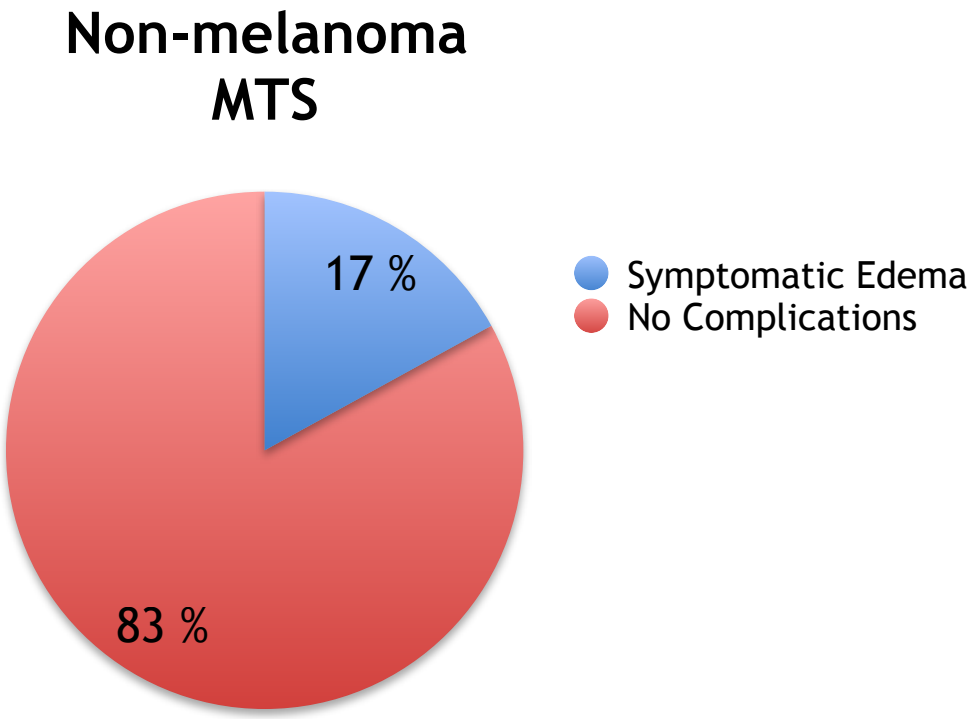
Radioresistant Histotypes

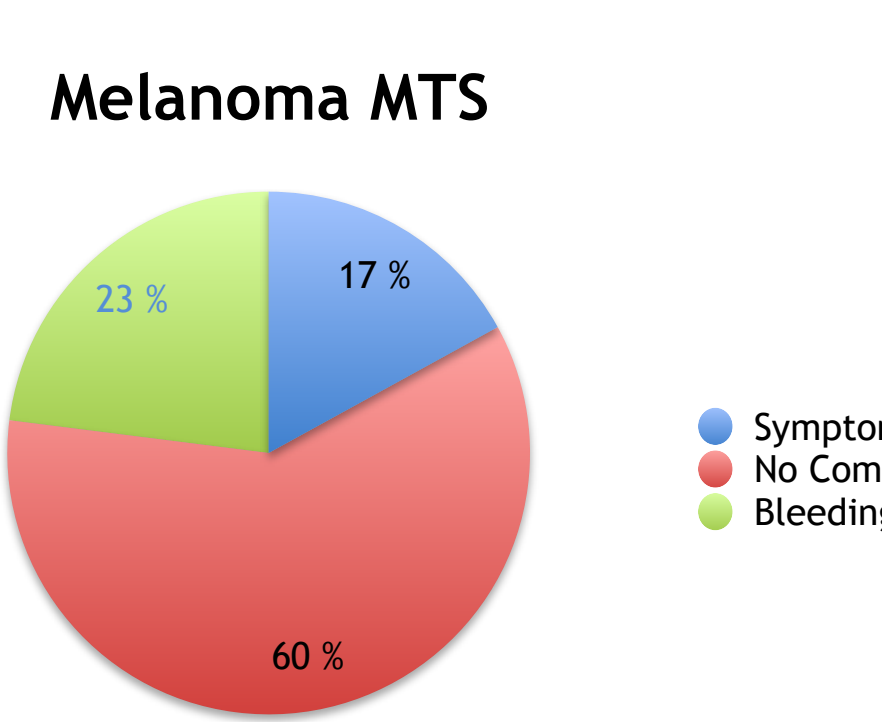


Survival according to Extracranial Disease Control



Complication Rate



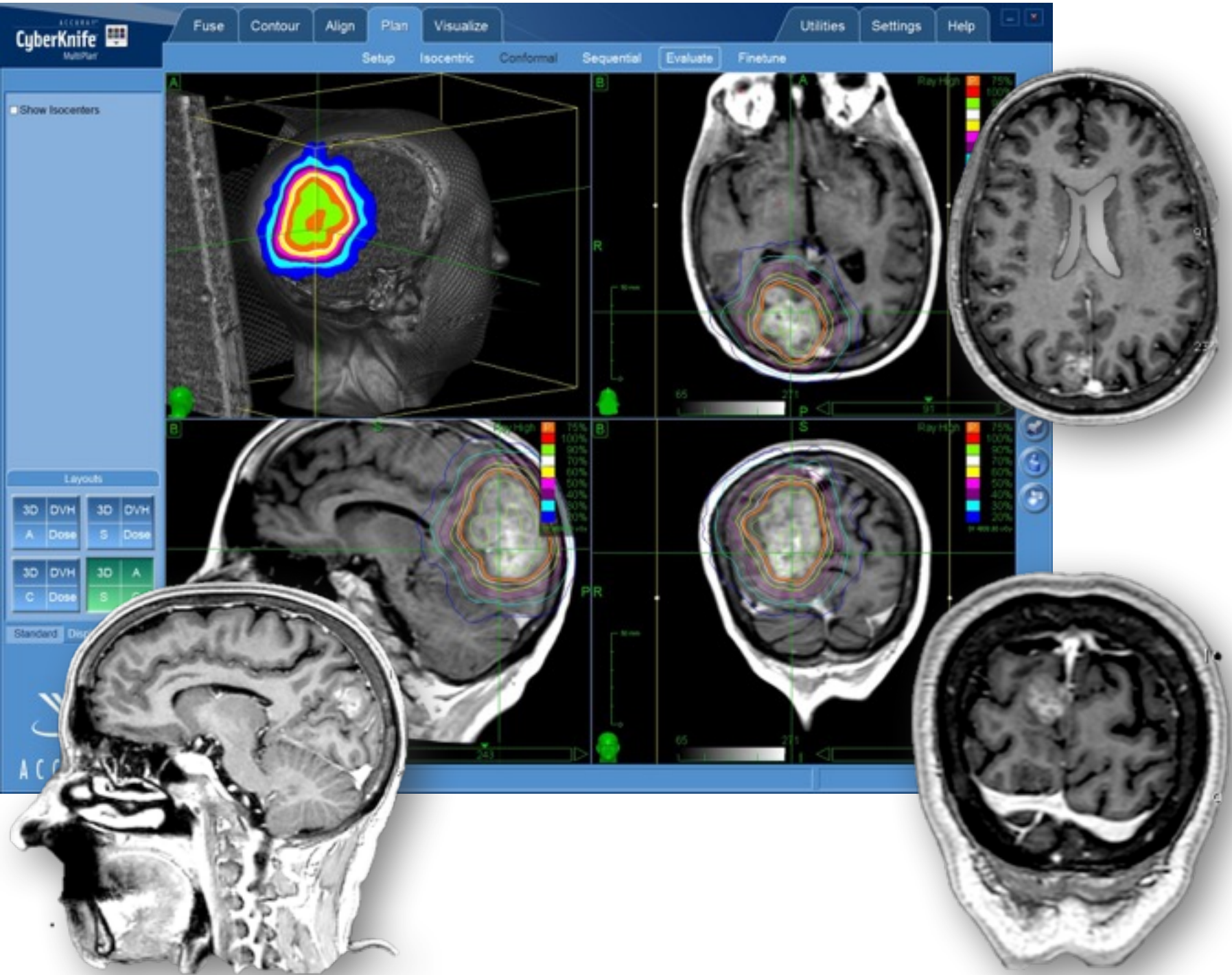


Multisession Radiosurgery

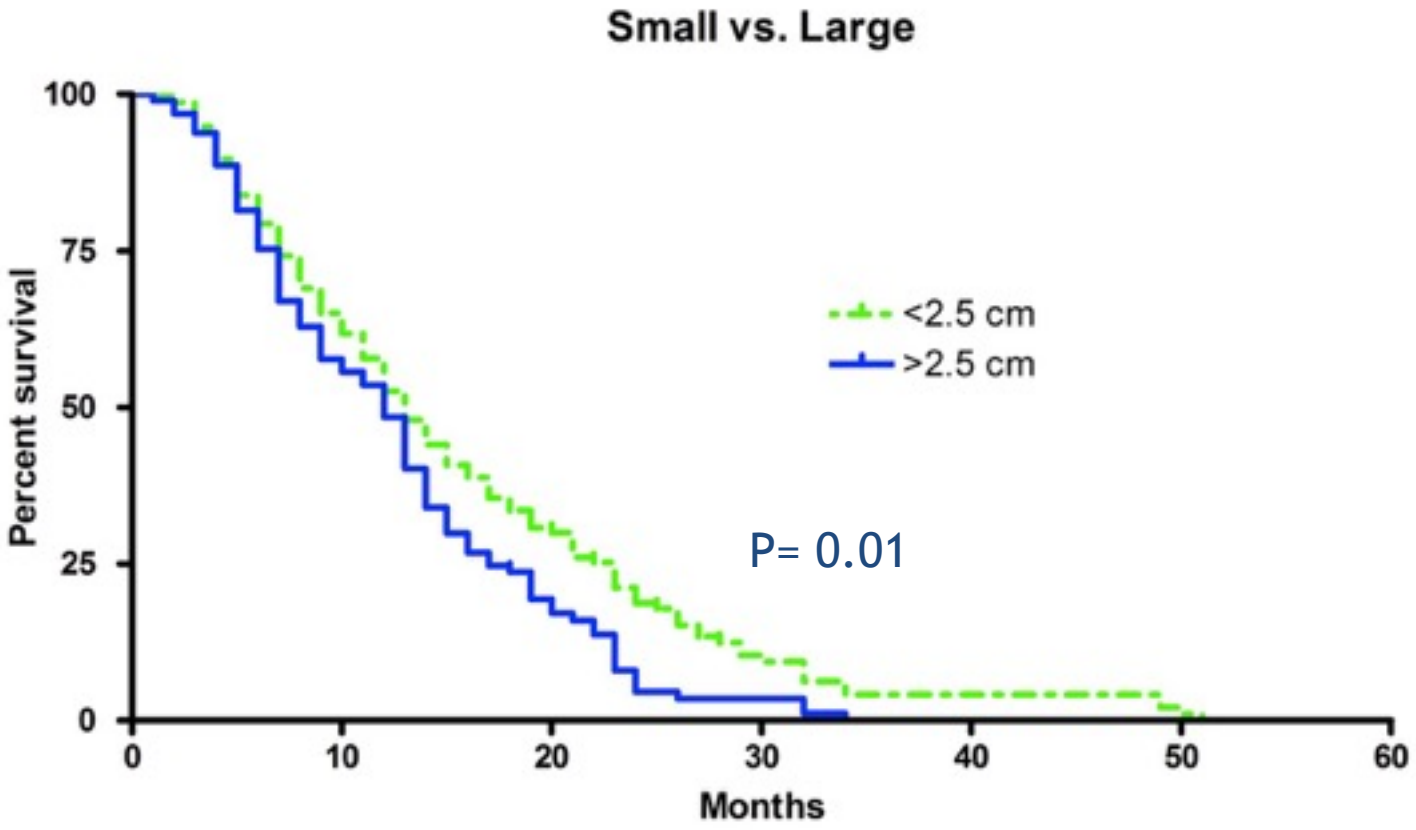
- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts

Multisession Radiosurgery

- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts

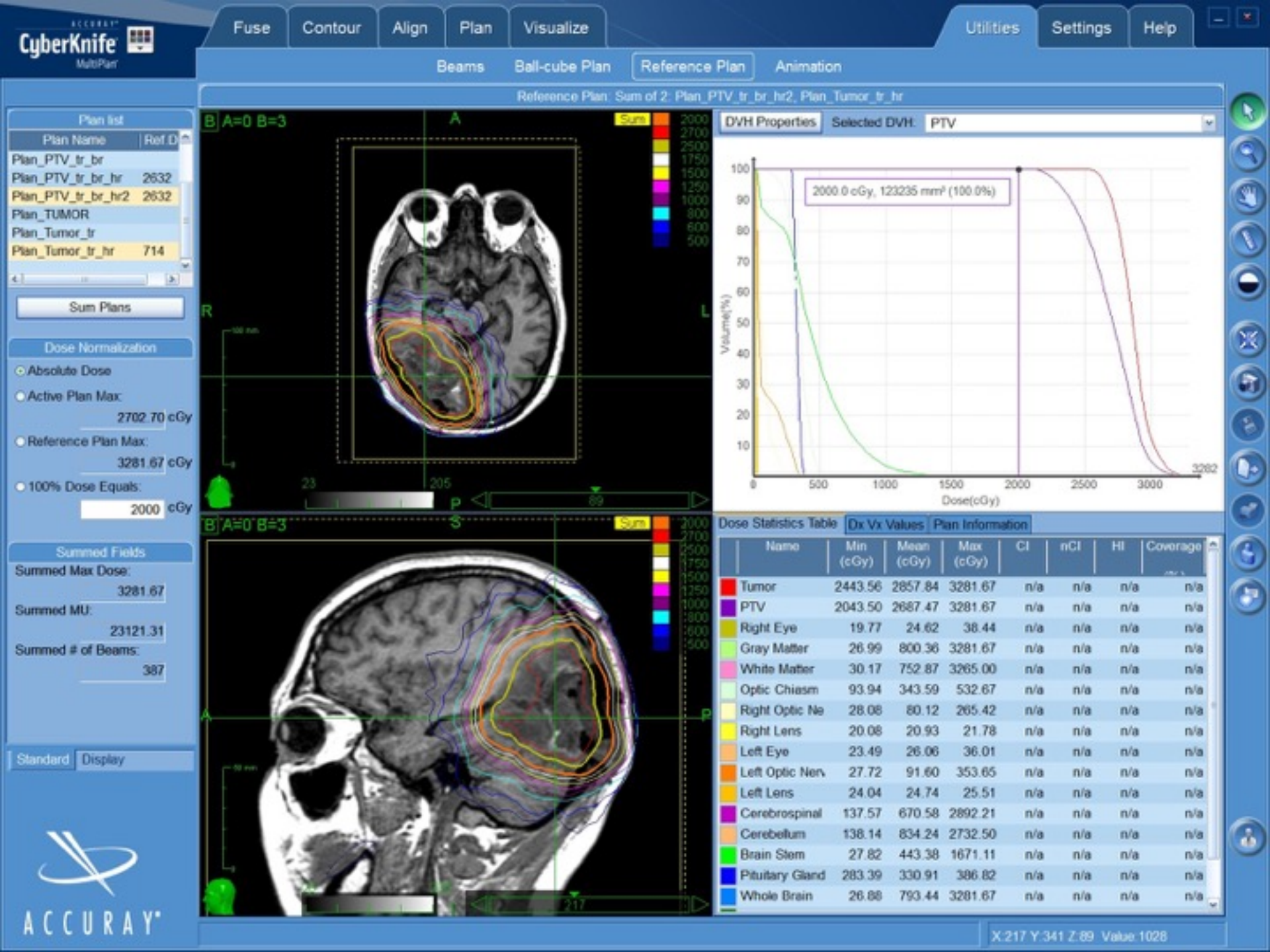

CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Show Isocenters
Layouts
3D
DVH
A
Dose
S
C

Survival according to Lesions Volume



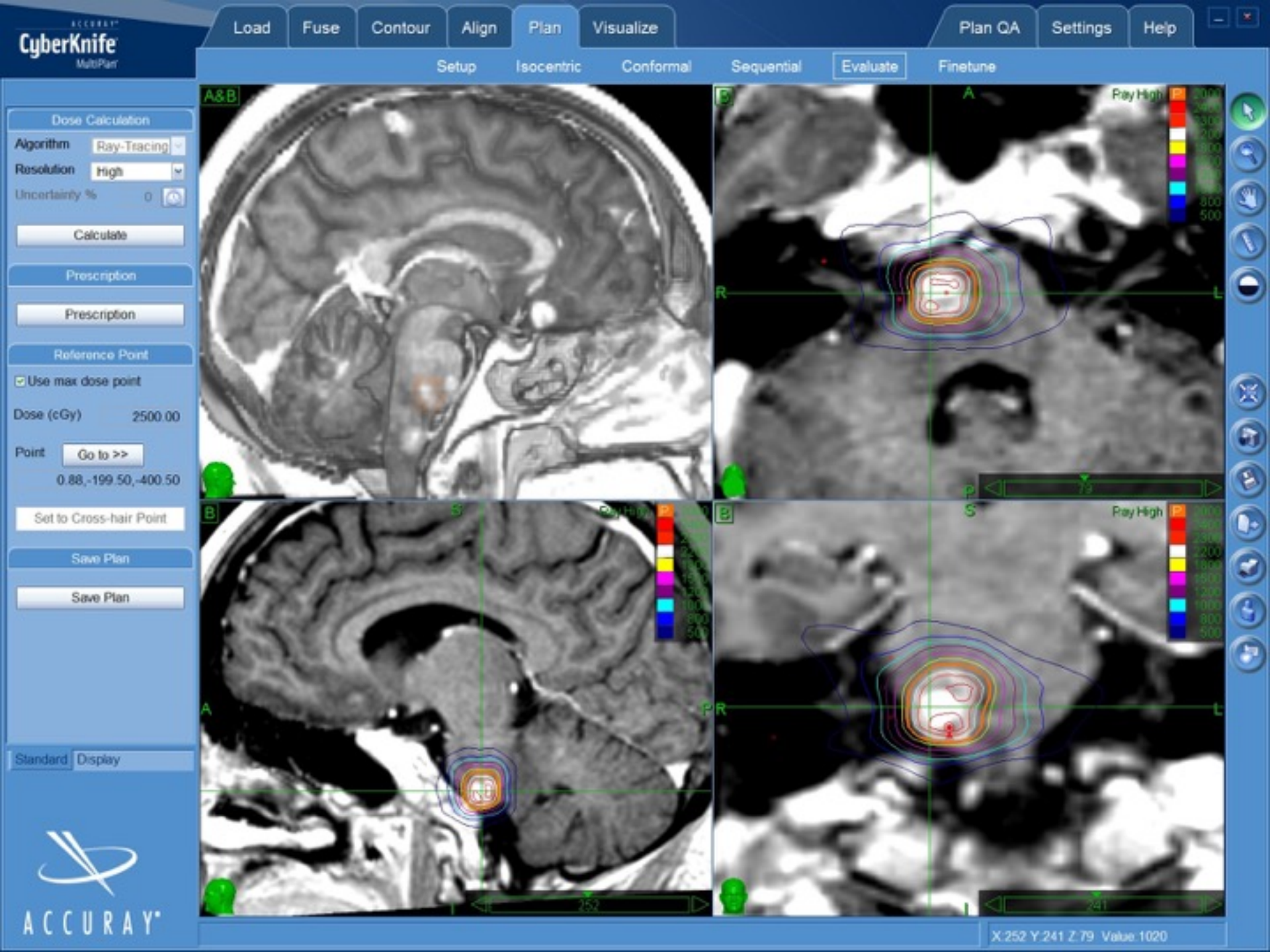
Multisession Radiosurgery

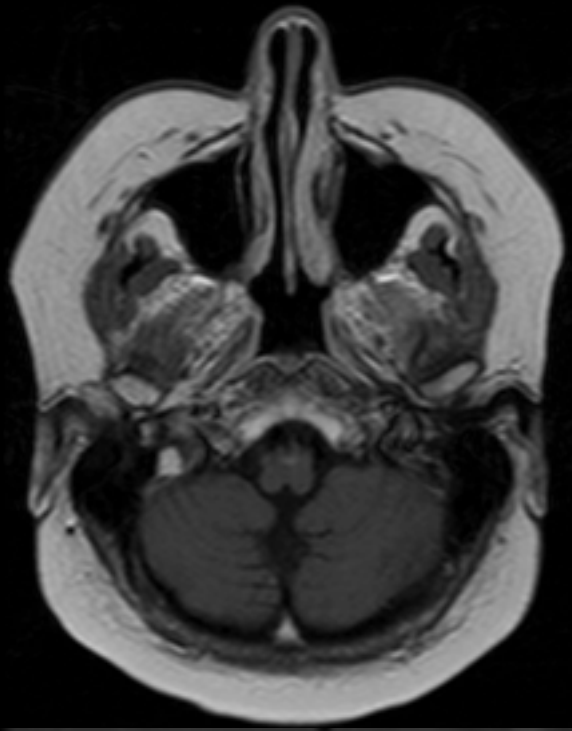
- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts

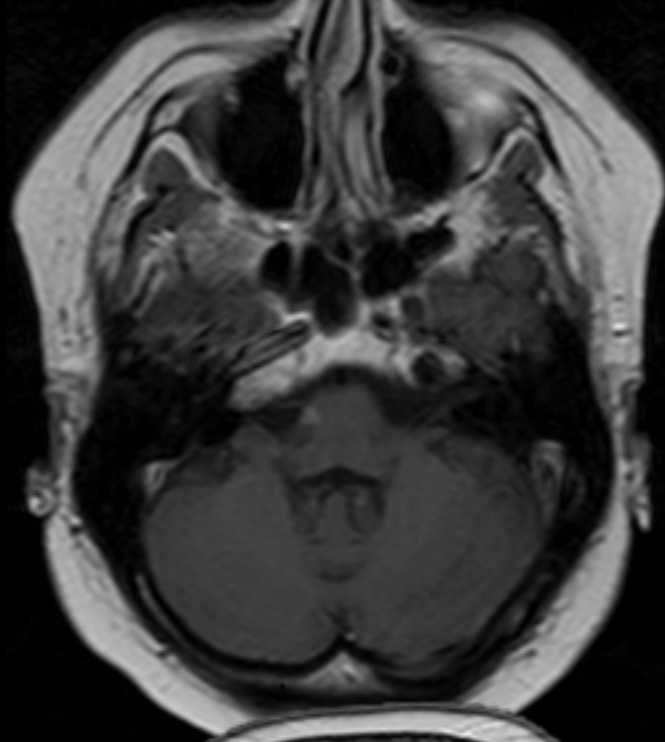

CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Beams
Ball-cube Plan
Reference Plan
Animation
Reference Plan: Sum of 2: Plan_PTV_tr_br_hr2, Plan_Tumor_tr_hr
Plan list
Plan Name
Ref D
Plan_PTV_tr_br
Plan_PTV_tr_br_hr 2632
Plan_PTV_tr_br_hr2 2632
Plan_TUMOR
Plan_Tumor_tr
Plan_Tumor_tr_hr 714
Sum Plans
Dose Normalization
Absolute Dose
Active Plan Max:
2702.70 cGy
Reference Plan Max:
3281.67 cGy
100% Dose Equals:
2000 cGy
Summed Fields
Summed Max Dose:
3281.67
Summed MU:
23121.31
Summed # of Beams:
387
Standard
Display
B A=0 B=3
Sum
DVH Properties
Selected DVH:
PTV
2000.0 cGy, 123235 mm³ (100.0%)
Volume(%)
Dose(cGy)
Dose Statistics Table
Dx Vx Values
Plan Information
Name
Min (cGy)
Mean (cGy)
Max (cGy)
CI
nCI
HI
Coverage
Tumor 2443.56 2857.84 3281.67 n/a n/a n/a n/a
PTV 2043.50 2687.47 3281.67 n/a n/a n/a n/a
Right Eye 19.77 24.62 38.44 n/a n/a n/a n/a
Gray Matter 26.99 800.36 3281.67 n/a n/a n/a n/a
White Matter 30.17 752.87 3265.00 n/a n/a n/a n/a
Optic Chiasm 93.94 343.59 532.67 n/a n/a n/a n/a
Right Optic Ne 28.08 80.12 265.42 n/a n/a n/a n/a
Right Lens 20.08 20.93 21.78 n/a n/a n/a n/a
Left Eye 23.49 26.06 36.01 n/a n/a n/a n/a
Left Optic Nerv 27.72 91.60 353.65 n/a n/a n/a n/a
Left Lens 24.04 24.74 25.51 n/a n/a n/a n/a
Cerebrospinal 137.57 670.58 2892.21 n/a n/a n/a n/a
Cerebellum 138.14 834.24 2732.50 n/a n/a n/a n/a
Brain Stem 27.82 443.38 1671.11 n/a n/a n/a n/a
Pituitary Gland 283.39 330.91 386.82 n/a n/a n/a n/a
Whole Brain 26.88 793.44 3281.67 n/a n/a n/a n/a
X:217 Y:341 Z:89 Value:1028
ACCURAY

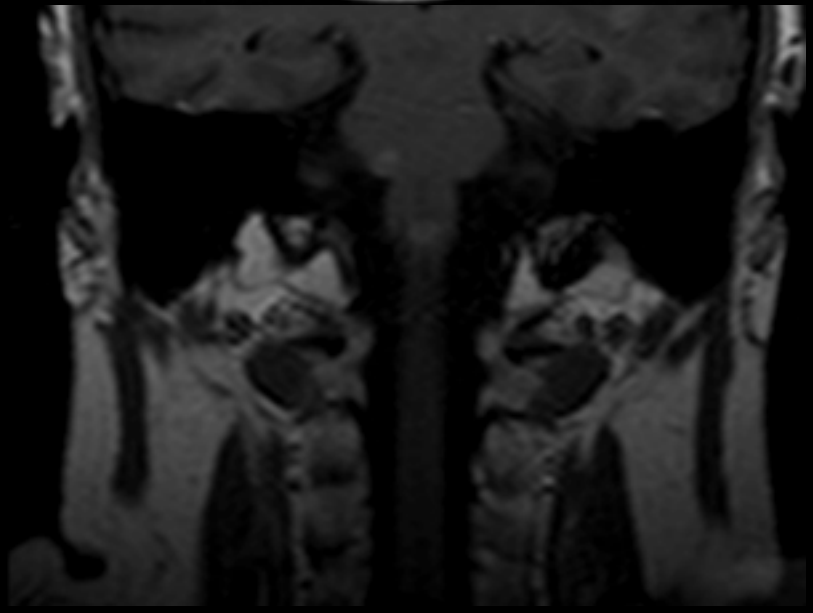
Multisession Radiosurgery

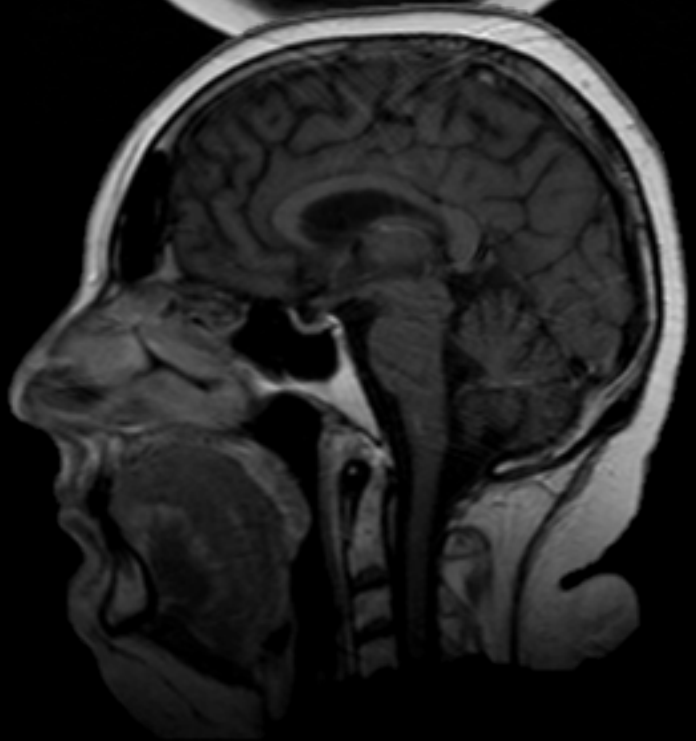
- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts


CyberKnife
MultiPlan
Load
Fuse
Contour
Align
Plan
Visualize
Plan QA
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Dose Calculation
Algorithm
Ray-Tracing
Resolution
High
Uncertainty %
0
Calculate
Prescription
Prescription
Reference Point
Use max dose point
Dose (cGy)
2500.00
Point
Go to >>
0.88,-199.50,-400.50
Set to Cross-hair Point
Save Plan
Save Plan
Standard
Display
A&B
Ray High
X:252 Y:241 Z:79 Value:1020
ACCURAY



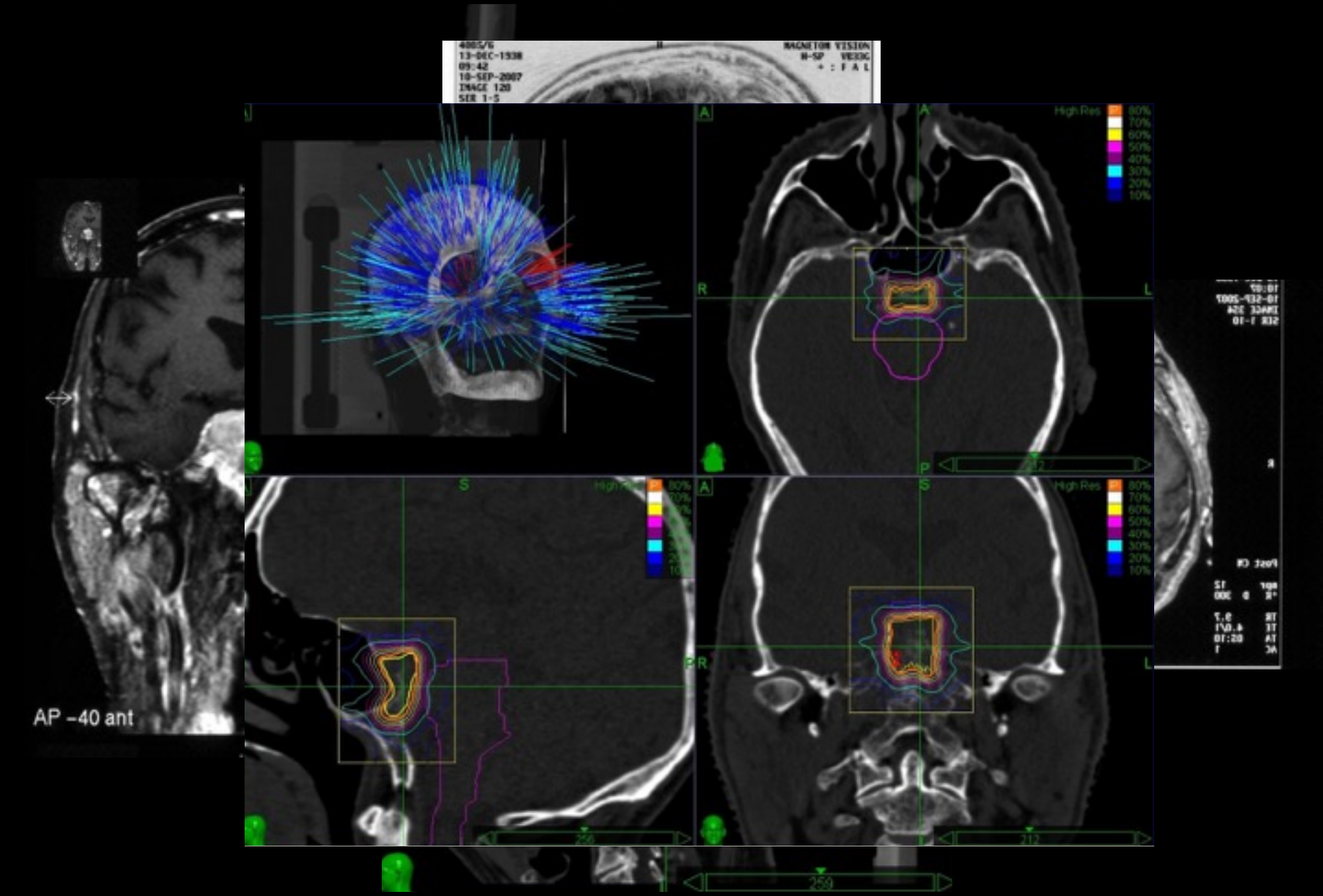


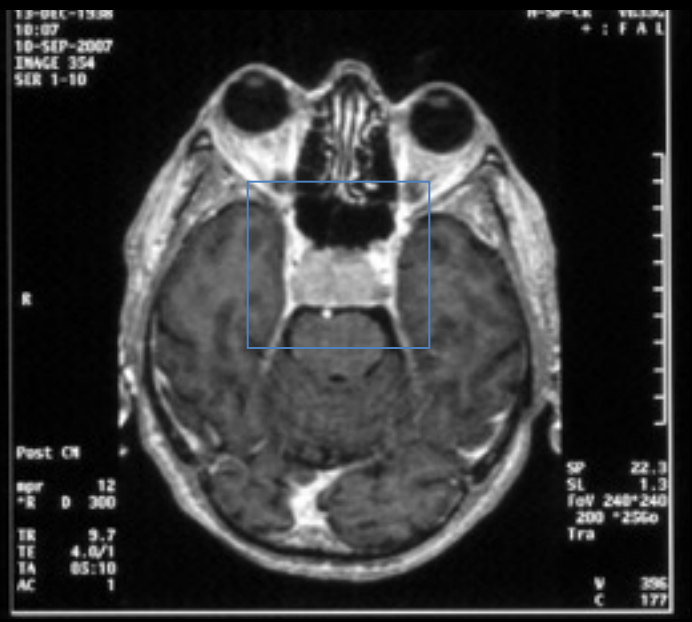




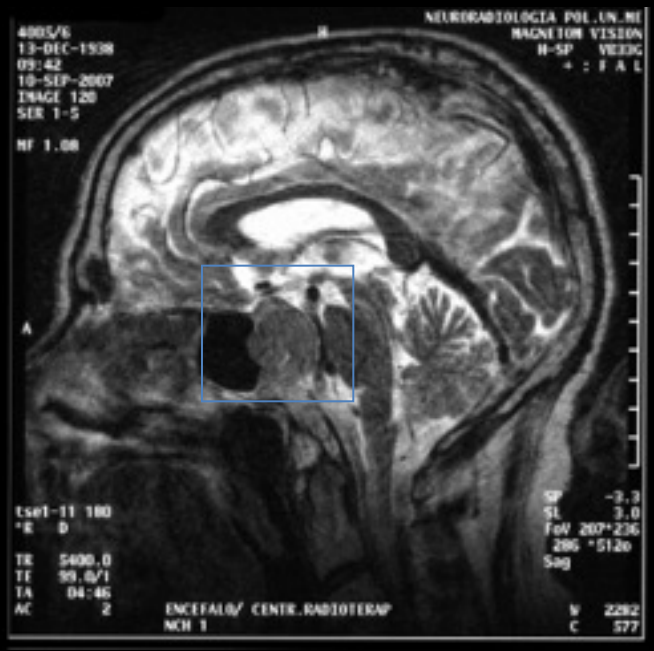
Multisession Radiosurgery

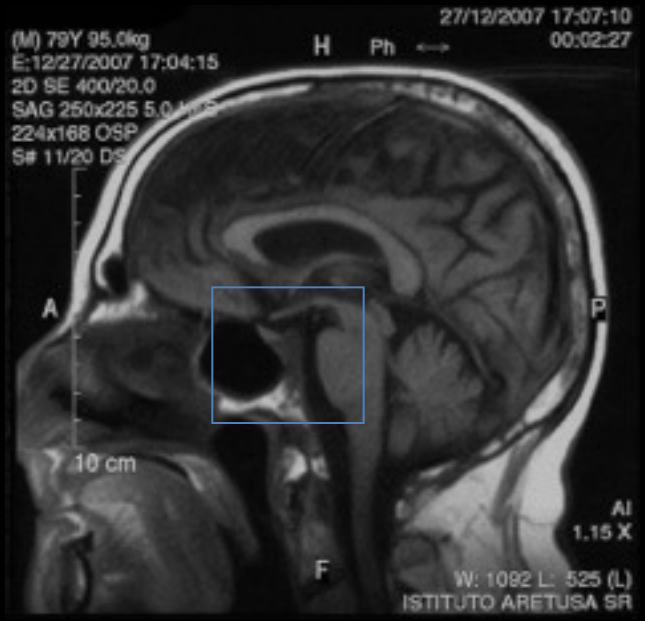
- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts

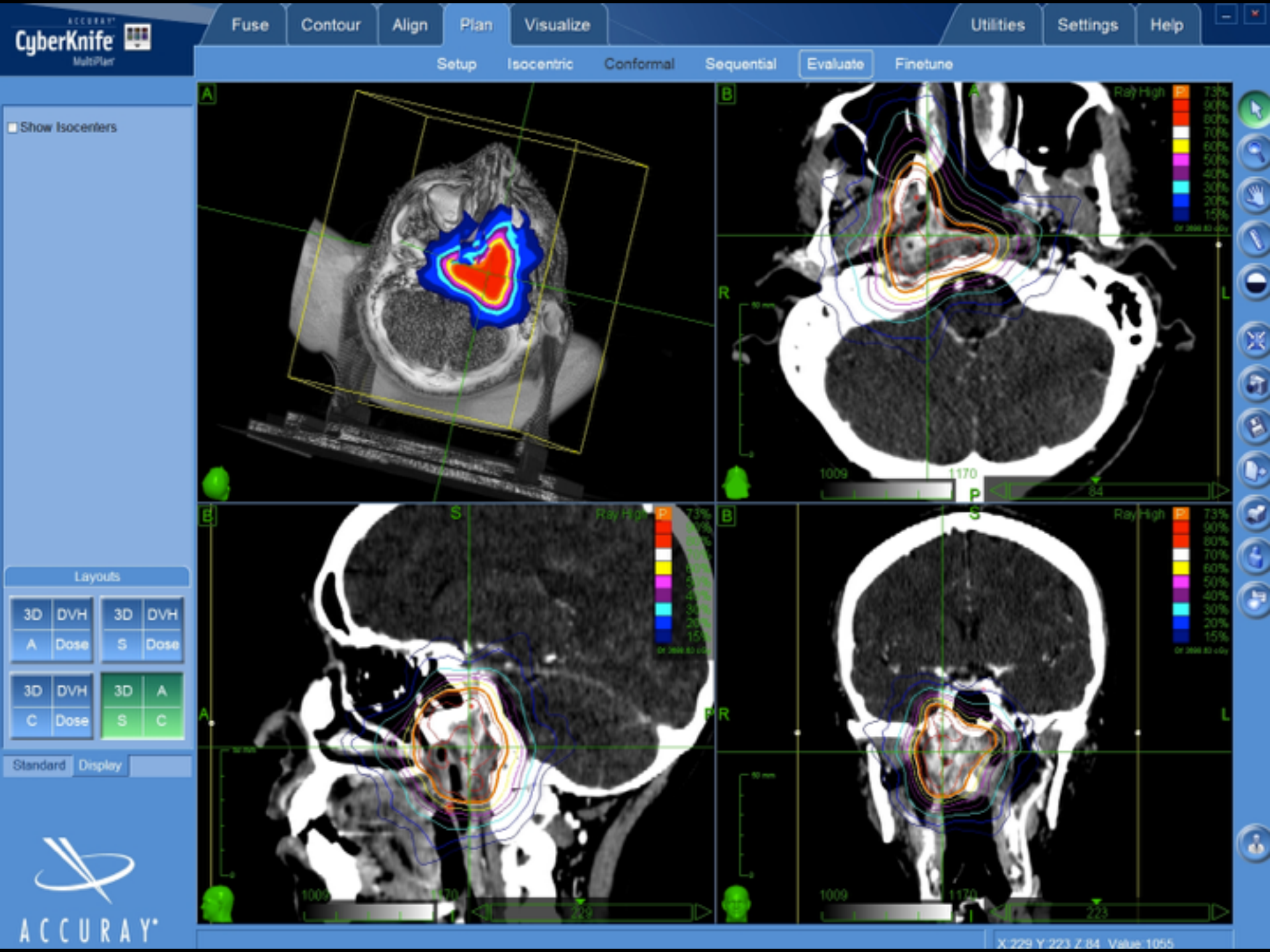

13-DEC-1538
09:42
10-SEP-2007
IMAGE 120
High Res
AP -40 ant

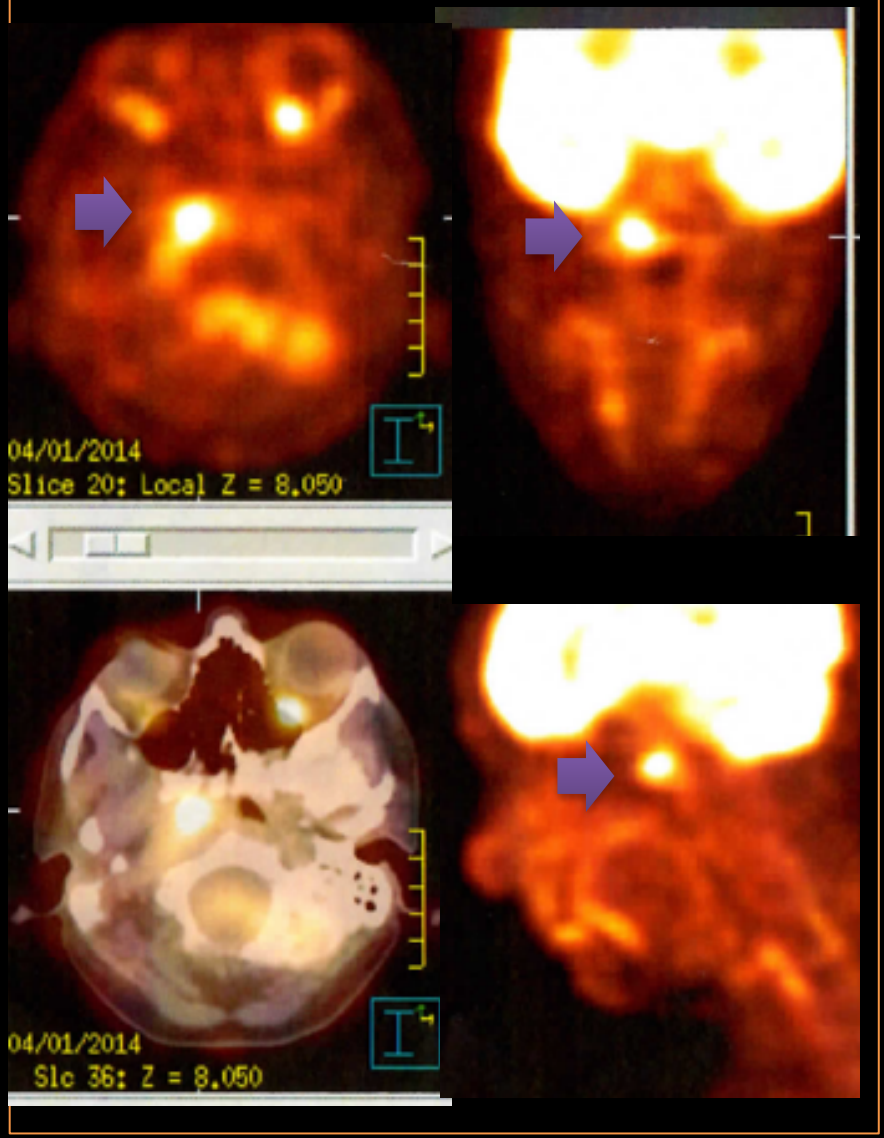

10:07
10-SEP-2007
IMAGE 354
SER 1-10
R
Post CN
TR 9.7
TE 4.0/1
TA 05:10
AC 1
SP 22.3
SL 1.3
FoV 240*240
Tra

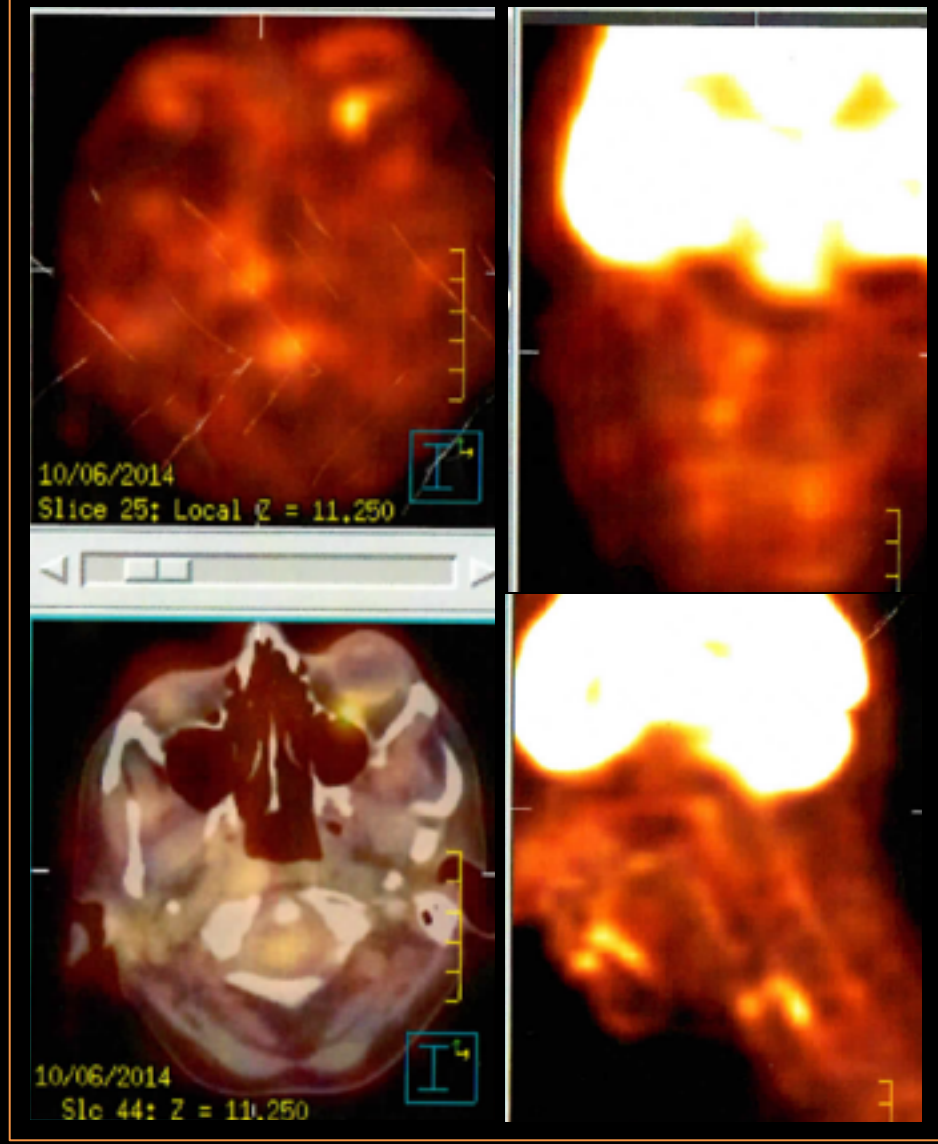

27/12/2007 17:23:08
00:02:52
(M) 79Y 95.0kg
E:12/27/2007 17:04:15
2D SE 500/20.0
224x158 OSP
S# 7/20 DS
A
Ph
R
L
10 cm
P
AI
1.15 X
W: 877 L: 475 (L)
ISTITUTO ARETUSA SR


NEURORADIOLOGIA POL.UN.MI
MAGNETOM VISION
4005/6
13-DEC-1938
09:42
10-SEP-2007
IMAGE 120
SER 1-5
A
Esel-11 180
TR 5400.0
TE 99.0/1
TA 04:46
AC 2
SP -3.3
SL 3.0
FoV 207*236
Sag
ENCEFALO/ CENTR.RADIOTERAP


27/12/2007 17:07:10
00:02:27
(M) 79Y 95.0kg
E:12/27/2007 17:04:15
2D SE 400/20.0
224x168 OSP
S# 11/20 DS
H
Ph
A
P
10 cm
F
AI
1.15 X
W: 1092 L: 525 (L)
ISTITUTO ARETUSA SR

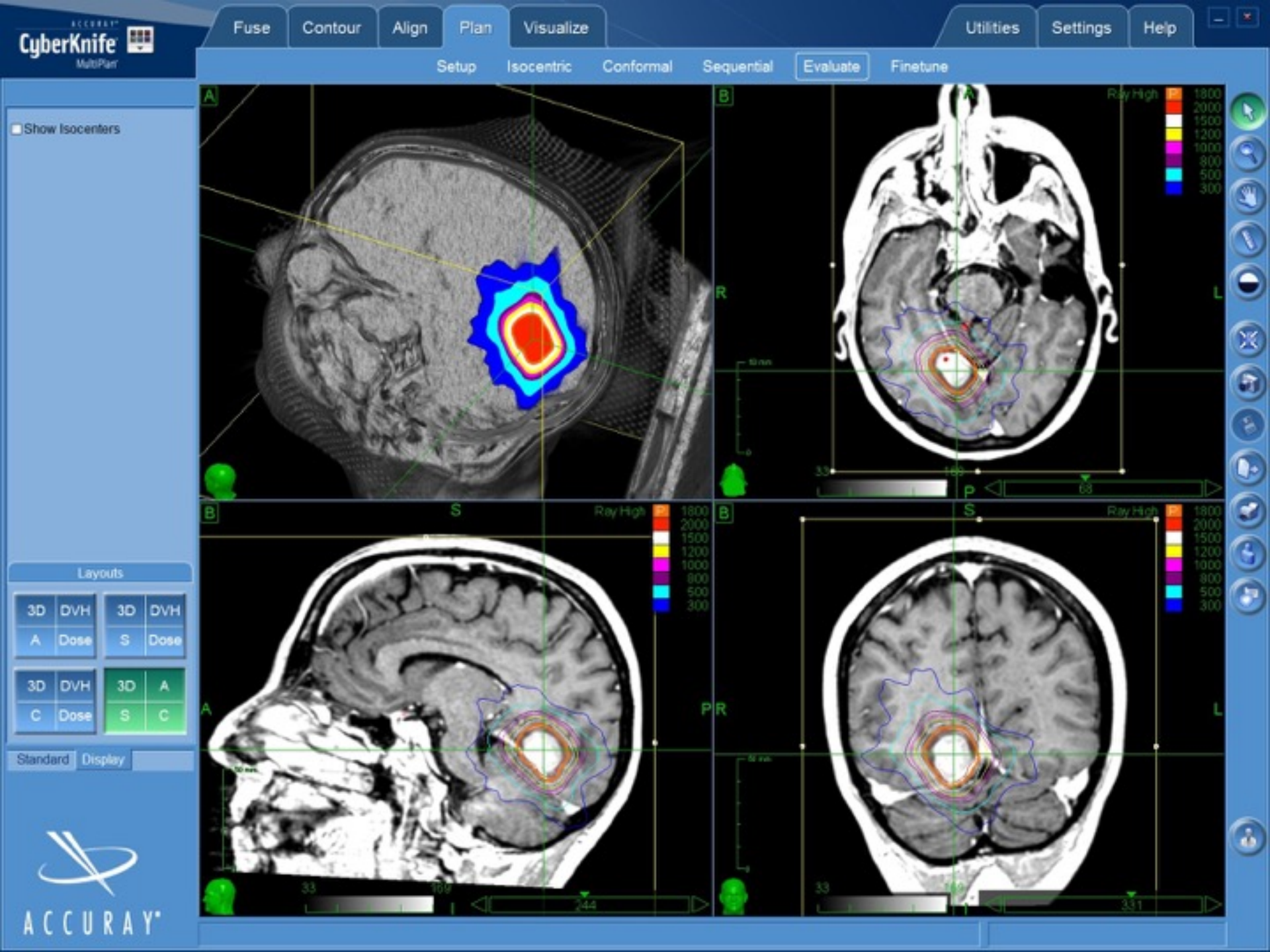

CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Show Isocenters
Layouts
3D DVH A Dose
3D DVH S Dose
3D DVH C Dose
3D A S C
Standard
Display
ACCURAY
Ray High
1009
1170
84
229
223


04/01/2014
Slice 20: Local Z = 8.050
04/01/2014
Slc 36: Z = 8.050

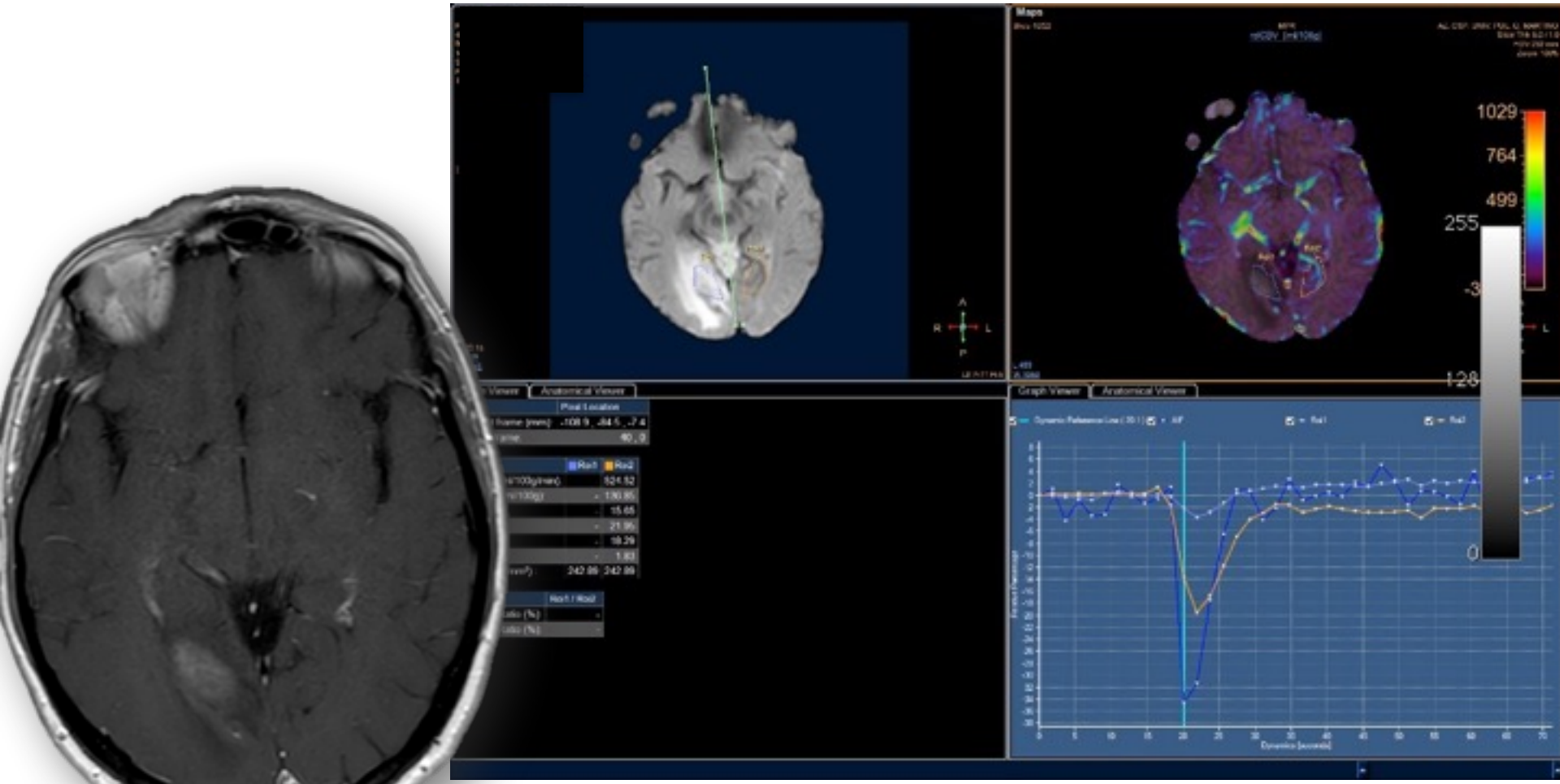

10/06/2014
Slice 25: Local Z = 11.250
10/06/2014
Slc 44: Z = 11.250

Multisession Radiosurgery

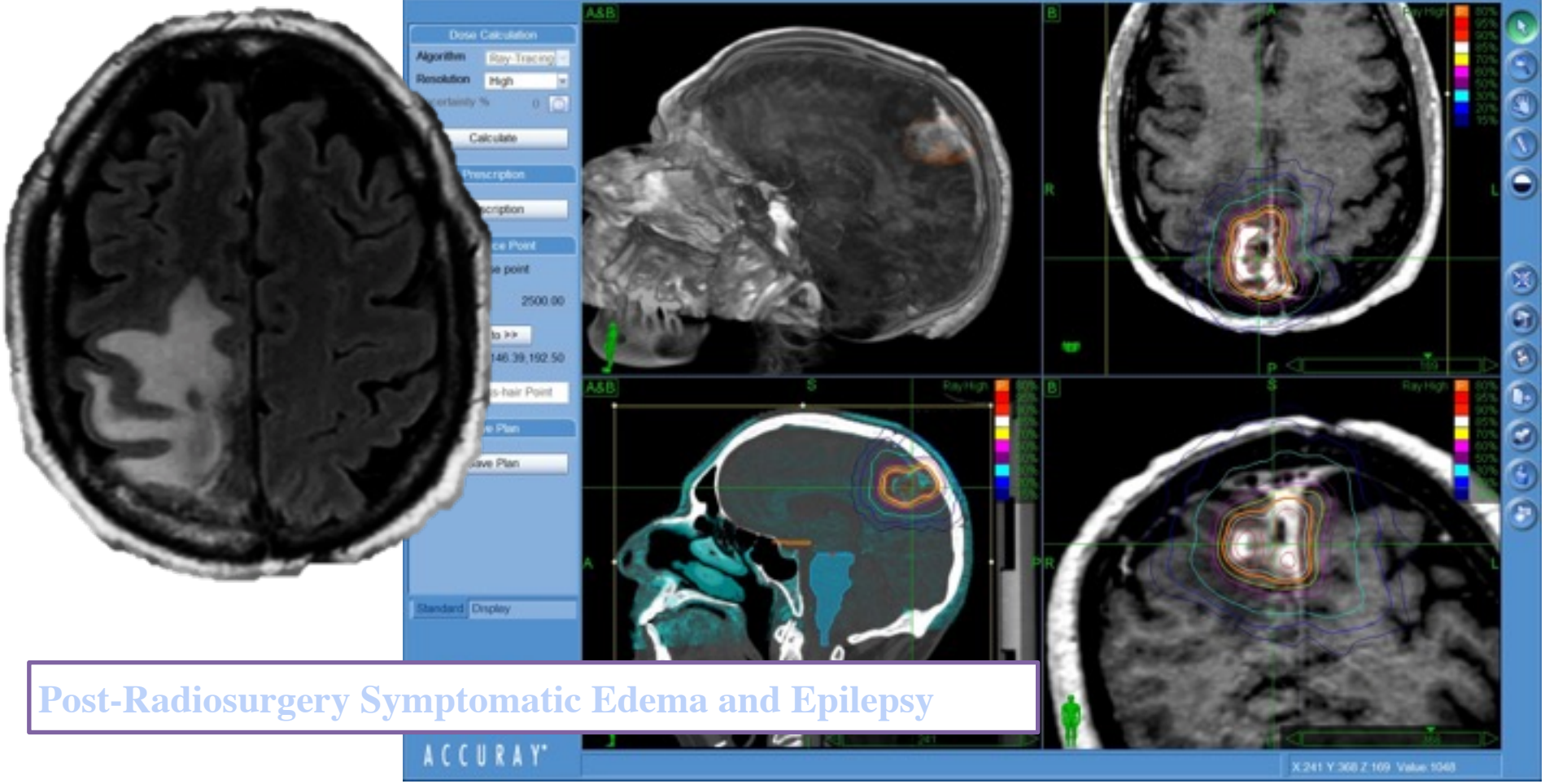
- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts


CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Show Isocenters
Layouts
3D DVH A Dose
3D DVH S Dose
3D DVH C Dose
3D A S C
Standard
Display
Ray High
1800
2000
1500
1200
1000
800
500
300
ACCURAY

Recurrence vs. Radionecrosis



Re-Treatment



Post-Radiosurgery Symptomatic Edema and Epilepsy

Biological heterogeneity of Surviving Cells

J Neurosurg (Suppl 2) 121:110–115, 2014

To fractionate or not to fractionate? That is the question for the radiosurgery of hypoxic tumors

Laboratory investigation

IULIANA TOMA-DASU, PH.D.,[1] HELENA SANDSTRÖM, M.SC.,[1] PIERRE BARSOUM, M.SC.,[2] AND ALEXANDRU DASU, PH.D.[3]

[1]Medical Radiation Physics, Stockholm University and Karolinska Institutet; [2]Department of Medical Physics, Karolinska University Hospital, Stockholm; and [3]Departments of Radiation Physics and Medical and Health Sciences, Linköping University, Linköping, Sweden

Object. This study aimed to investigate the impact of tumor hypoxia on treatment outcome for metastases commonly treated with radiosurgery using 1 fraction of radiation and the potential gain from reoxygenation if the treatment is delivered in a few radiation fractions.

Methods. In silico metastasis-like radiosurgery targets were modeled with respect to size, density of clonogenic cells, and oxygenation. Treatment plans were produced for the targets using Leksell GammaPlan, delivering clinically relevant doses and evaluating the tumor control probability (TCP) that could be expected in each case. Fractionated schedules with 3, 4, and 5 fractions resulting in similar biological effective doses were also considered for the larger target, and TCP was determined under the assumption that local reoxygenation takes place between fractions.

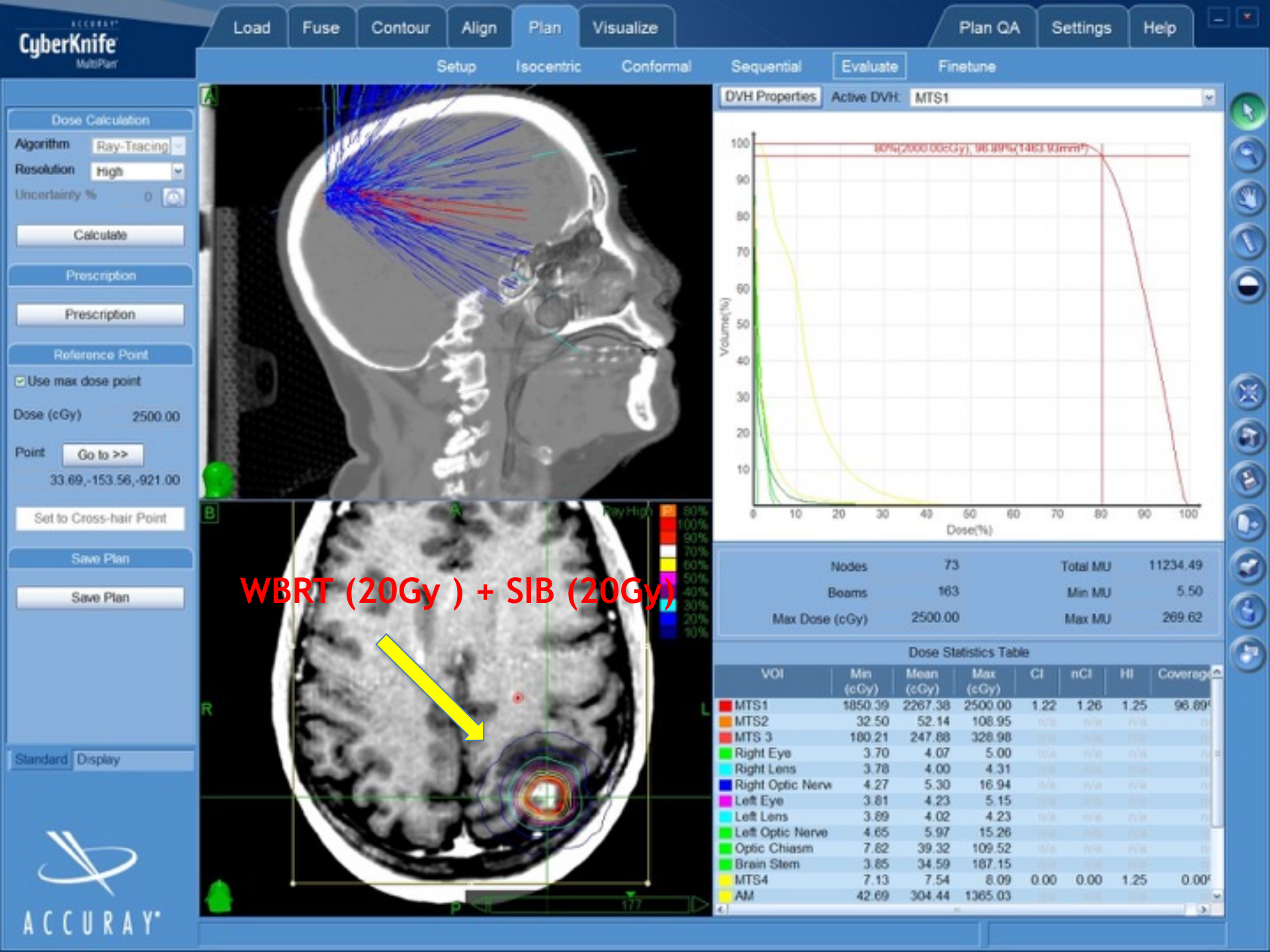
Results. The results showed that well-oxygenated small- and medium-size metastases are well controlled by radiosurgery treatments delivering 20 or 22 Gy at the periphery, with TCPs ranging from 90% to 100%. If they are moderately hypoxic, the TCP could decrease to 60%. For large metastases, the TCPs from single-fraction treatments ranged from 0% to 19%, depending on tumor oxygenation. However, for fractionated treatments, the TCP for hypoxic tumors could significantly increase up to 51%, if reoxygenation occurs between fractions.

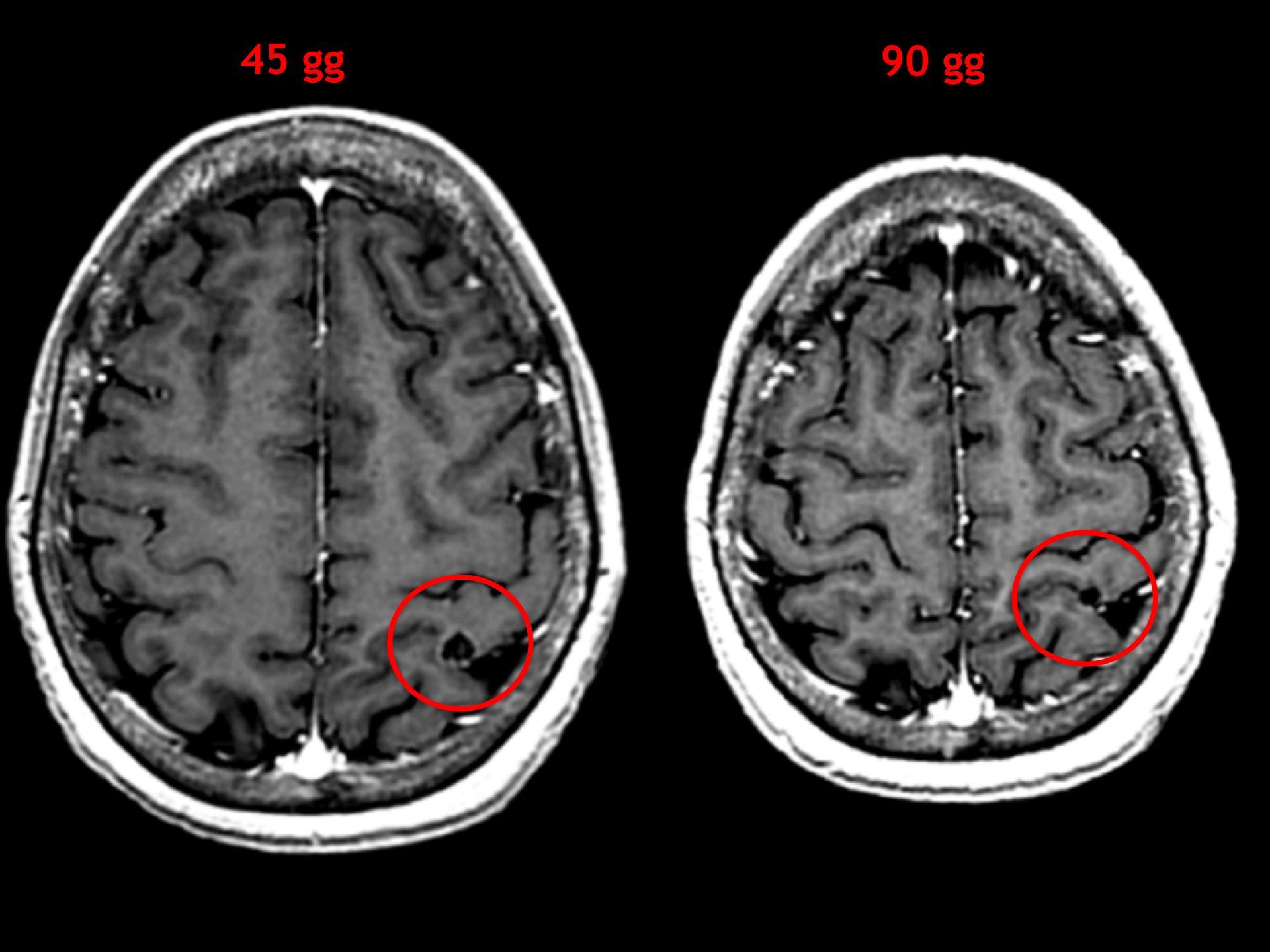
Conclusions. This study shows that hypoxia worsens the response to single-fraction radiosurgery, especially for large tumors. However, fractionated therapy for large hypoxic tumors might considerably improve the TCP and might constitute a simple way to improve the outcome of radiosurgery for patients with hypoxic tumors.
(http://thejns.org/doi/abs/10.3171/2014.8.GKS141461)

KEY WORDS • **radiosurgery** • **metastases** • **tumor hypoxia** • **fractionation** • **stereotactic radiosurgery**

Multisession Radiosurgery

- Large or Very Large Tumors
- Treatment of Tumor Bed
- Brain Stem Metastases
- Complex Skull Base Lesions
- Re-treatment
- SIB in WBRT for Radioresistant Mts


CyberKnife
MultiPlan
Load
Fuse
Contour
Align
Plan
Visualize
Plan QA
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
Dose Calculation
Algorithm
Ray-Tracing
Resolution
High
Uncertainty %
0
Calculate
Prescription
Prescription
Reference Point
Use max dose point
Dose (cGy)
2500.00
Point
Go to >>
33.69,-153.56,-921.00
Set to Cross-hair Point
Save Plan
Save Plan
Standard
Display
ACCURAY
DVH Properties
Active DVH:
MTS1
Volume(%)
Dose(%)
Nodes
73
Beams
163
Max Dose (cGy)
2500.00
Total MU
11234.49
Min MU
5.50
Max MU
269.62
WBRT (20Gy) + SIB (20Gy)
Dose Statistics Table
VOI
Min (cGy)
Mean (cGy)
Max (cGy)
CI
nCI
HI
Coverage
MTS1 1850.39 2267.38 2500.00 1.22 1.26 1.25 96.89
MTS2 32.50 52.14 108.95
MTS 3 180.21 247.88 328.98
Right Eye 3.70 4.07 5.00
Right Lens 3.78 4.00 4.31
Right Optic Nerve 4.27 5.30 16.94
Left Eye 3.81 4.23 5.15
Left Lens 3.89 4.02 4.23
Left Optic Nerve 4.65 5.97 15.26
Optic Chiasm 7.82 39.32 109.52
Brain Stem 3.85 34.59 187.15
MTS4 7.13 7.54 8.09 0.00 0.00 1.25 0.00
AM 42.69 304.44 1365.03

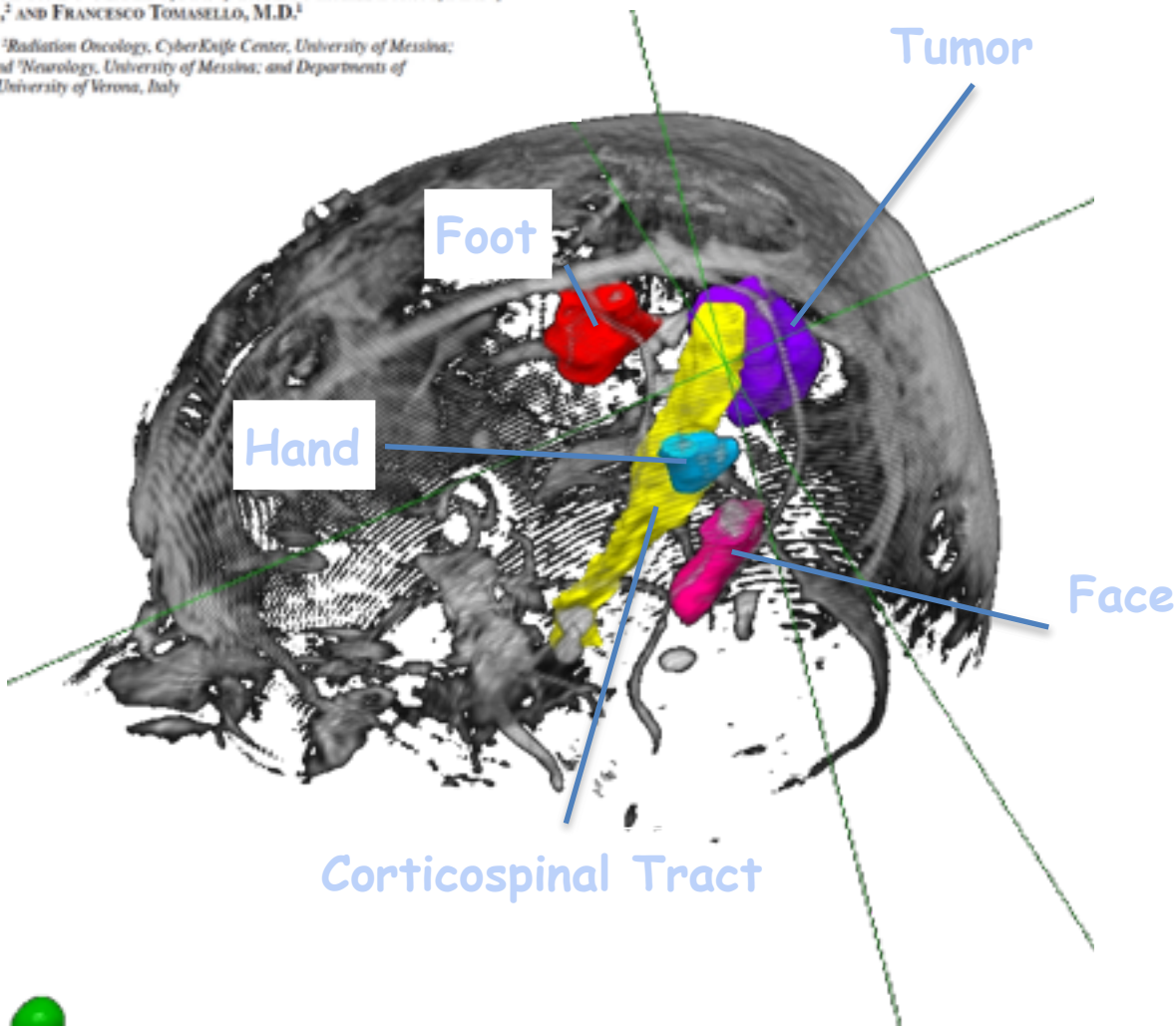

45 gg
90 gg

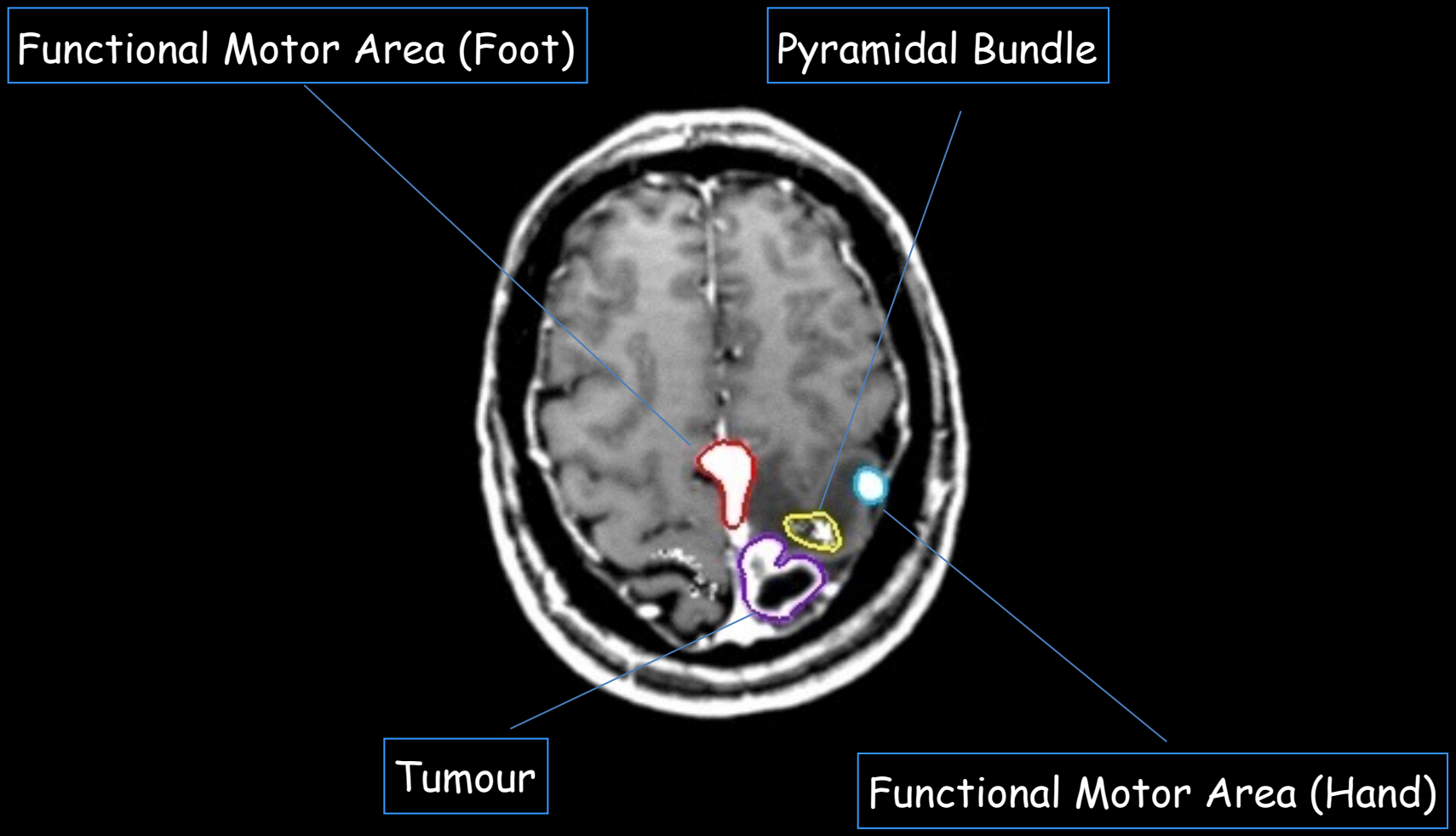
Neurosurg Focus 34 (4):E5, 2013

Integration of functional neuroimaging in CyberKnife radiosurgery: feasibility and dosimetric results

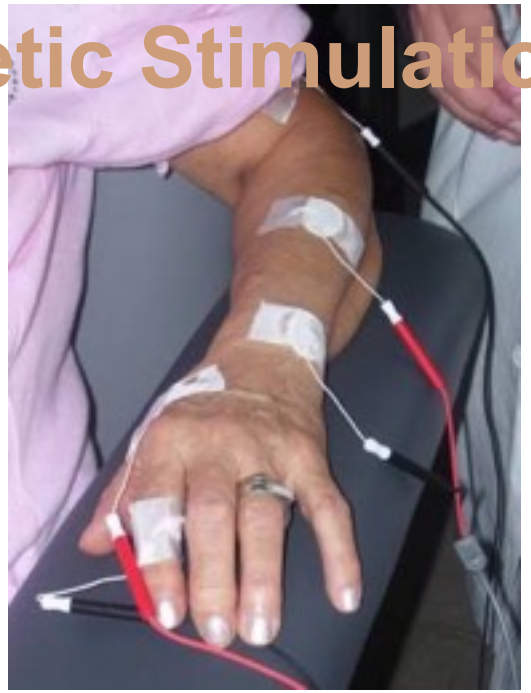
Alfredo Conti, M.D., Ph.D.,[1] Antonio Pontoriero, M.D.,[2] Giuseppe K. Ricciardi, M.D.,[3] Francesca Granata, M.D.,[4] Sergio Vinci, M.D.,[4] Filippo F. Angileri, M.D., Ph.D.,[3] Stefano Pergolizzi, M.D.,[5] Concetta Alafaci, M.D.,[3] Vincenzo Rizzo, M.D.,[5] Angelo Quartarone, M.D.,[5] Antonino Germanò, M.D.,[3] Roberto Israel Foroni, Ph.D.,[5] Costantino De Renzis, M.D.,[2] and Francesco Tomasello, M.D.[1]

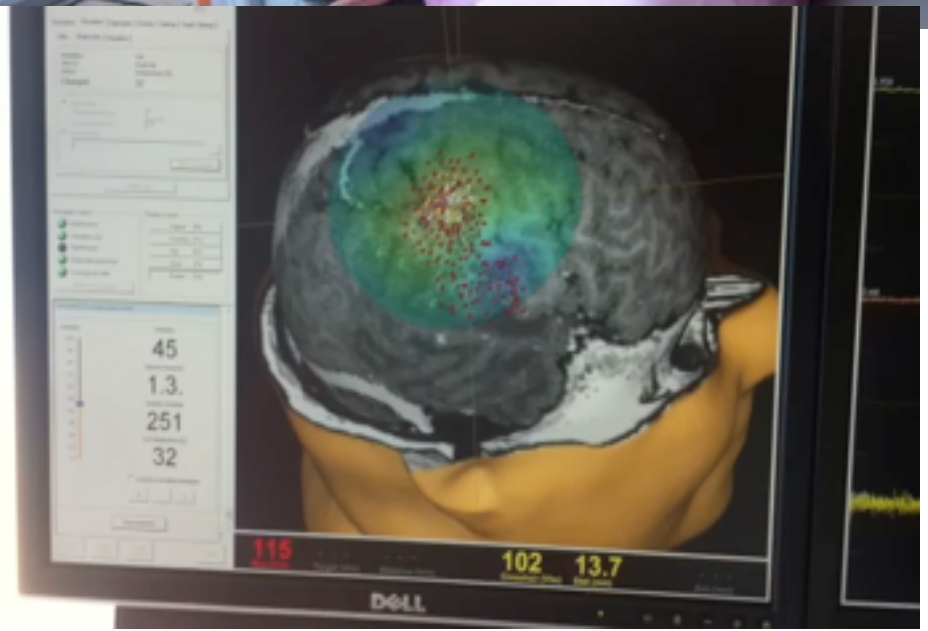
Departments of [1]Neurosurgery and [2]Radiation Oncology, CyberKnife Center, University of Messina; Departments of [3]Neuroradiology and [4]Neurology, University of Messina; and Departments of [5]Neuroradiology and [6]Stereotaxis, University of Verona, Italy

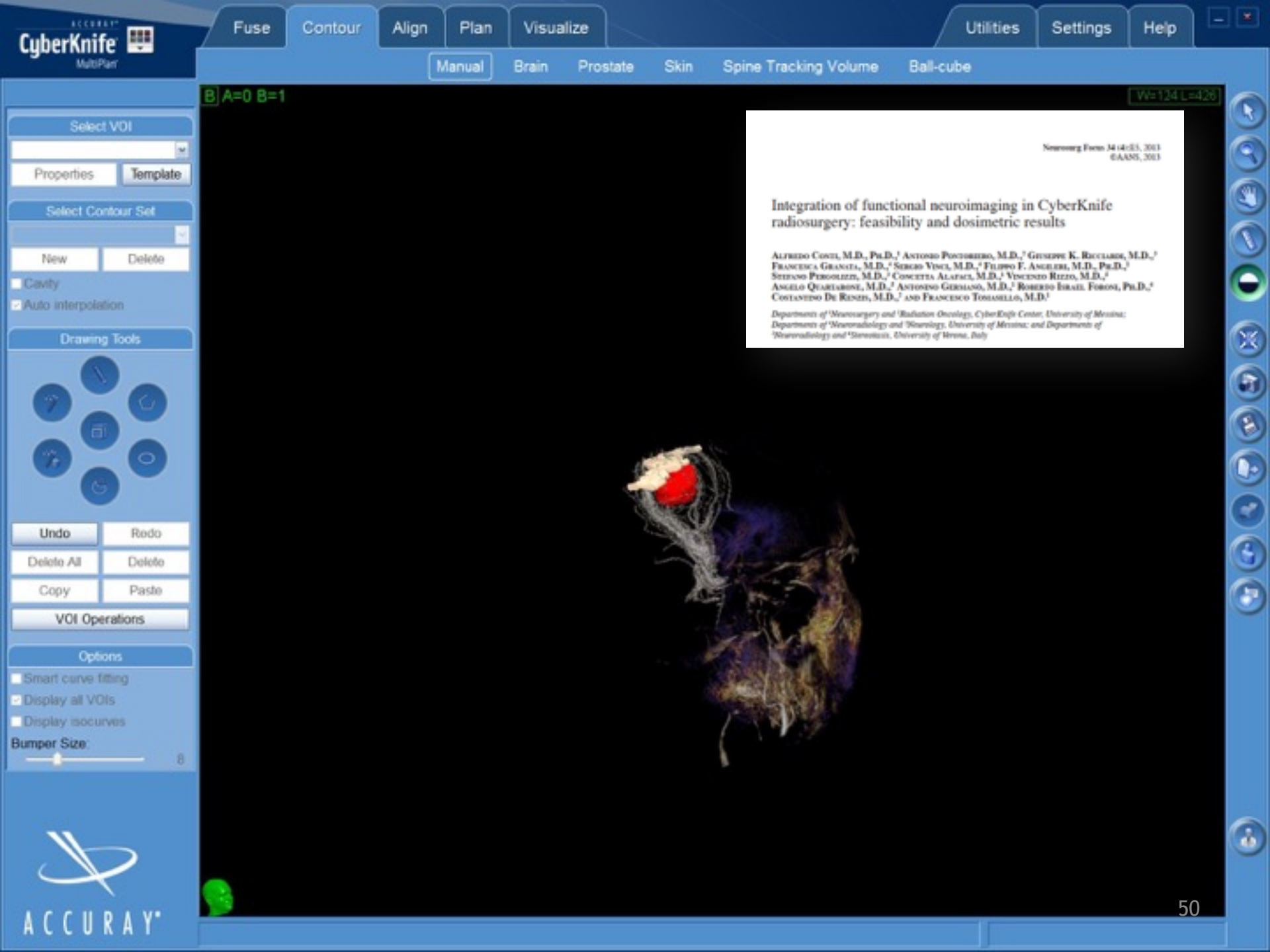


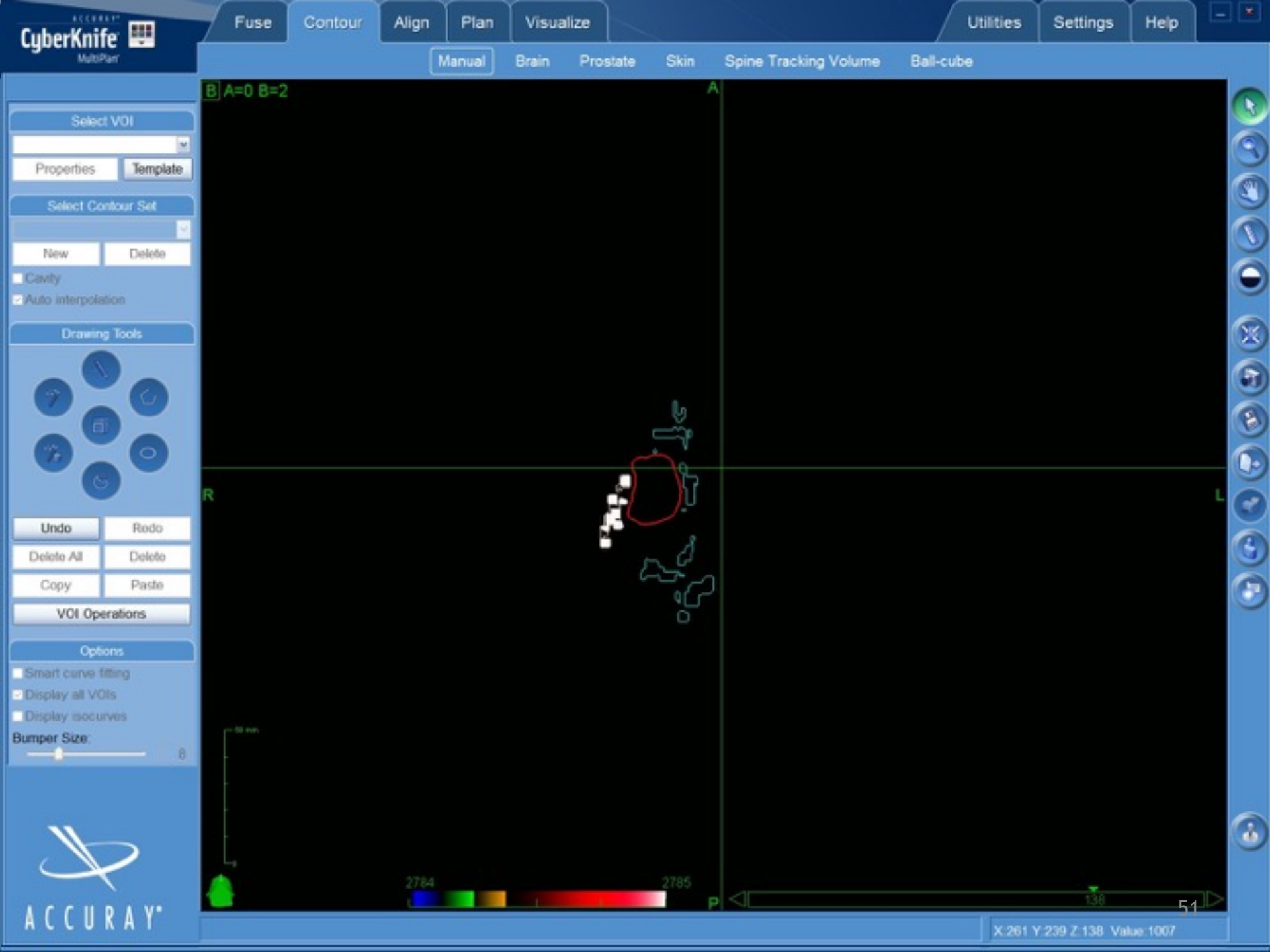

Functional Motor Area (Foot)
Pyramidal Bundle
Tumour
Functional Motor Area (Hand)

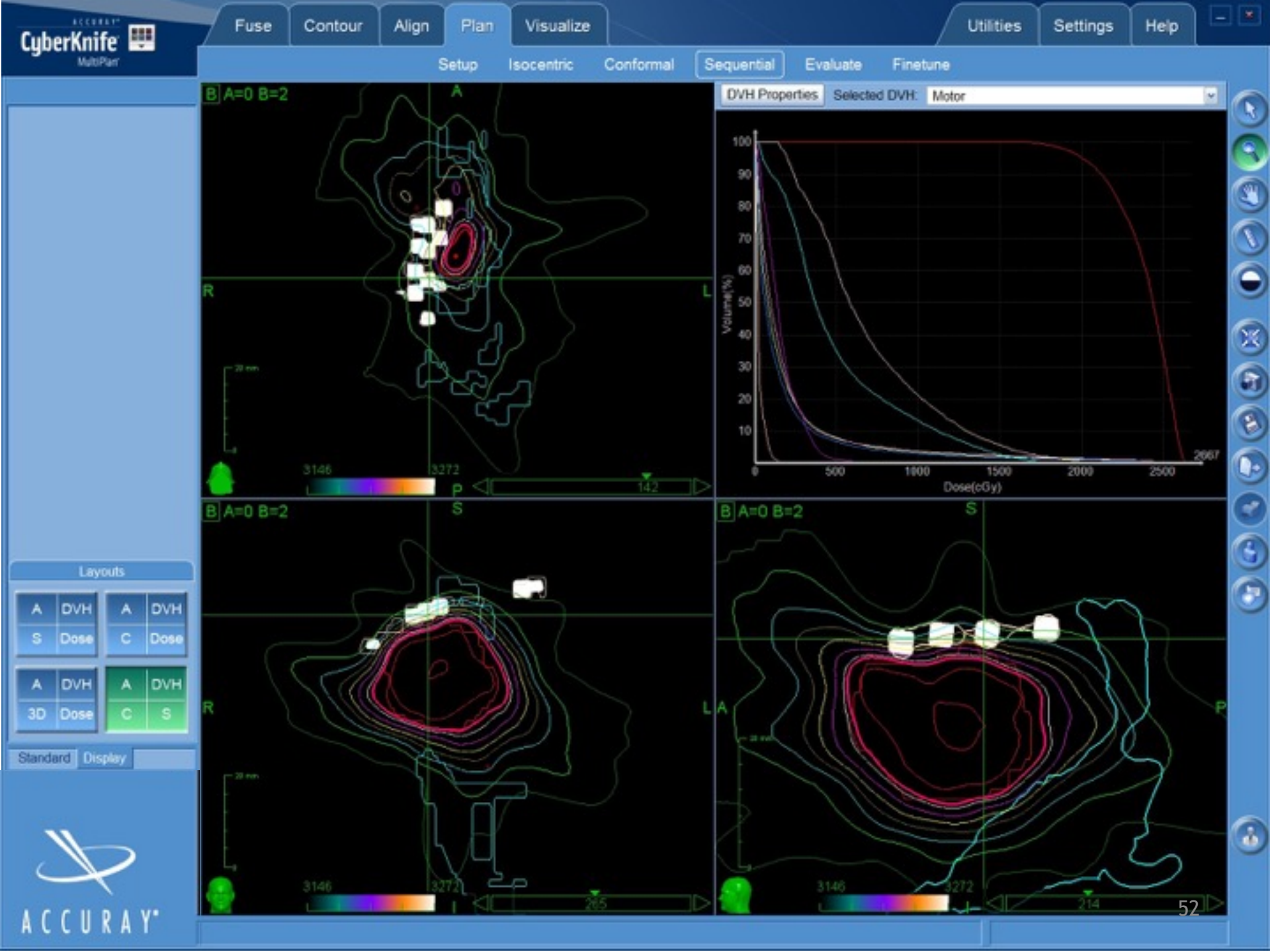
Navigated Transcranial Magnetic Stimulation

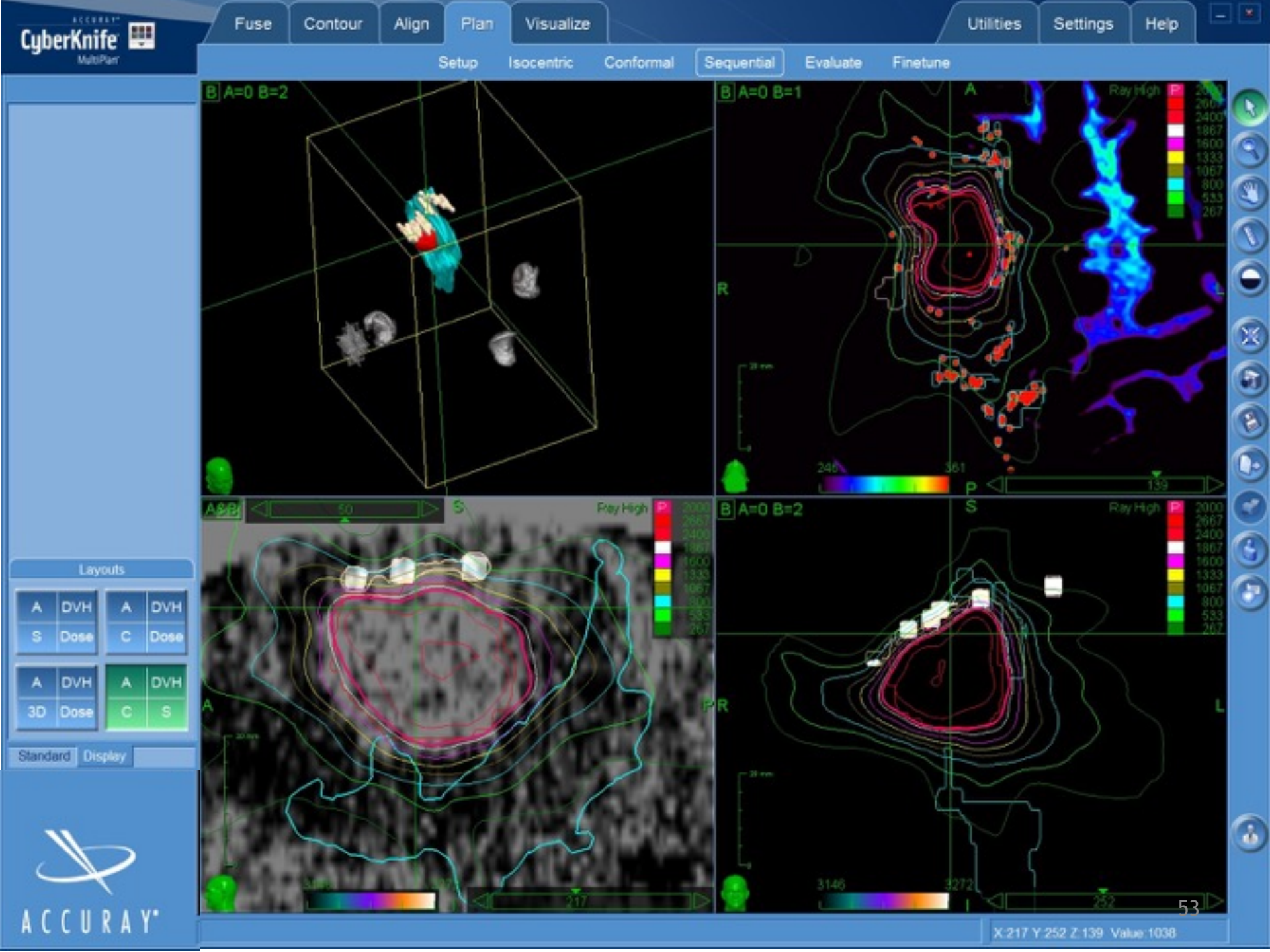





CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Manual
Brain
Prostate
Skin
Spine Tracking Volume
Ball-cube
B A=0 B=1
W=124 L=426
Select VOI
Properties
Template
Select Contour Set
New
Delete
Cavity
Auto interpolation
Drawing Tools
Undo
Redo
Delete All
Delete
Copy
Paste
VOI Operations
Options
Smart curve fitting
Display all VOIs
Display isocurves
Bumper Size
8
ACCURAY
Integration of functional neuroimaging in CyberKnife radiosurgery: feasibility and dosimetric results
Alfredo Conti, M.D., Ph.D.,[1] Antonio Pontoriero, M.D.,[2] Giuseppe K. Ricciardi, M.D.,[3] Francesca Granata, M.D.,[4] Sergio Vinci, M.D.,[4] Filippo F. Angilieri, M.D., Ph.D.,[3] Stefano Pergolizzi, M.D.,[2] Concetta Alafaci, M.D.,[1] Vincenzo Rizzo, M.D.,[2] Angelo Quartarone, M.D.,[2] Antonino Germanò, M.D.,[1] Roberto Israel Foroni, Ph.D.,[4] Costantino De Renzis, M.D.,[1] and Francesco Tomasello, M.D.[1]
Departments of [1]Neurosurgery and [2]Radiation Oncology, CyberKnife Center, University of Messina; Departments of [3]Neuroradiology and [4]Neurology, University of Messina; and Departments of [5]Neuroradiology and [6]Stereotaxis, University of Verona, Italy


CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Manual
Brain
Prostate
Skin
Spine Tracking Volume
Ball-cube
B A=0 B=2
A
R
L
P
Select VOI
Properties
Template
Select Contour Set
New
Delete
Cavity
Auto interpolation
Drawing Tools
Undo
Redo
Delete All
Delete
Copy
Paste
VOI Operations
Options
Smart curve fitting
Display all VOIs
Display isocurves
Bumper Size
8
2784
2785
138
X:261 Y:239 Z:138 Value:1007
ACCURAY
51


CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
B A=0 B=2
A
R
L
P
3146
3272
142
DVH Properties
Selected DVH:
Motor
Volume(%)
Dose(cGy)
2067
B A=0 B=2
S
R
L
I
265
B A=0 B=2
S
A
P
I
214
Layouts
A DVH
S Dose
A DVH
C Dose
A DVH
3D Dose
A DVH
C S
Standard
Display
ACCURAY


CyberKnife
MultiPlan
Fuse
Contour
Align
Plan
Visualize
Utilities
Settings
Help
Setup
Isocentric
Conformal
Sequential
Evaluate
Finetune
B A=0 B=2
B A=0 B=1
A&B A=0 B=2
Ray High
Layouts
A DVH
S Dose
A DVH
C Dose
A DVH
3D Dose
A DVH
C S
Standard
Display
ACCURAY
X:217 Y:252 Z:139 Value:1038
53

CONCLUSIONS

- CyberKnife Radiosurgery is an effective strategy to treat metastatic brain disease
- Local control is satisfactory (at least at mid-term), whereas survival is dismal
- Best results in patients in RPA class 1, with lesions < 2.5 cm and controlled extracranial disease
- Multisession radiosurgery a reasonable option in case of large lesions, lesions within or close to critical structures, retreatment