Universitätsklinikum Hamburg-Eppendorf

# Department of Radiotherapy and Radiation Oncology

## *Stereotactic treatment of brain and lung tumors.*

Maria Jäckel

UKE HAMBURG

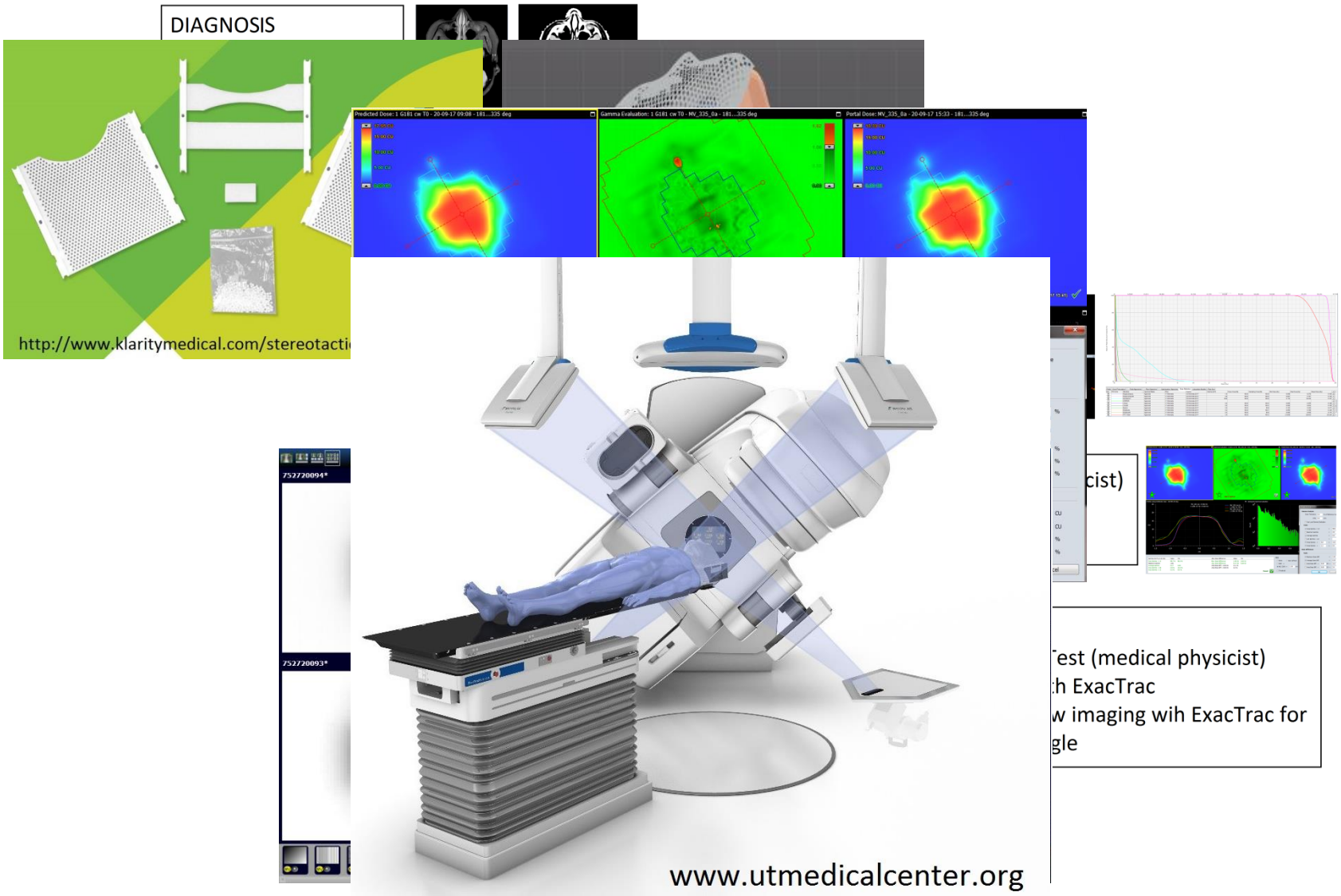
# What is stereotactic radiotherapy?



- Stereotactic (Greek στερεός stereós "hard, rigid" and τάξις táxis "arrangement") stands for coordinate-based.
- The concept of radiosurgery was introduced in 1951 by the Swedish neurosurgeon Lars Leksell. Today, this means that a tumor is irradiated in a small volume and highly precise manner.
- It is defined as a 1-5 time irradiation with ablative doses.

# SRS procedure

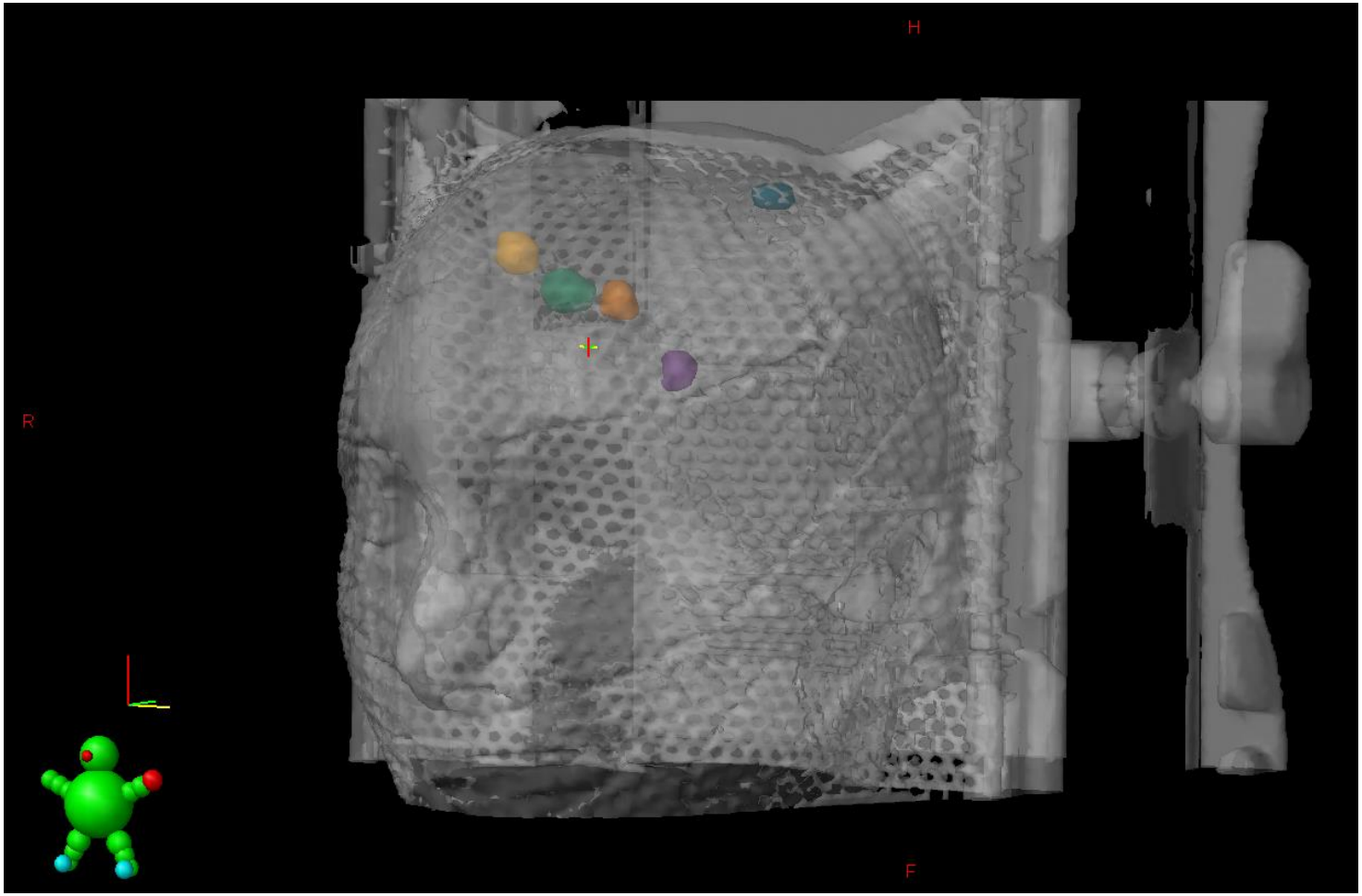




# Multiple brain metastases

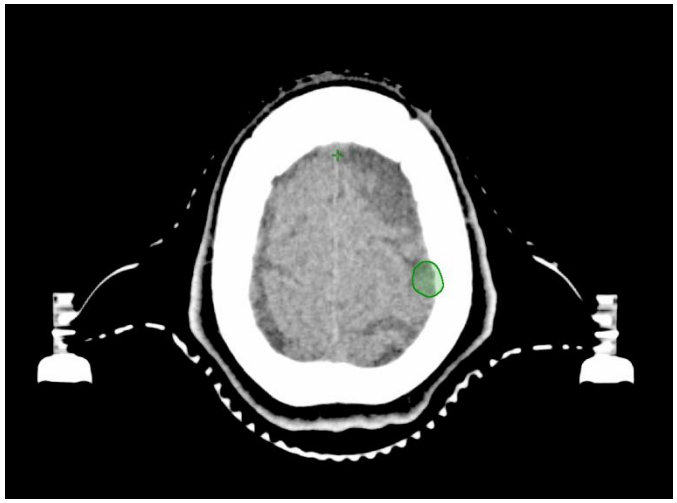


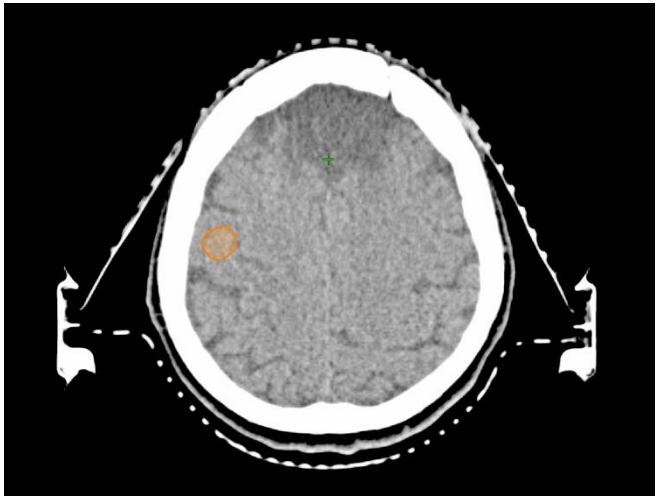
Dose prescription: PTVs 1-5 receive 24 Gy (ICRU)

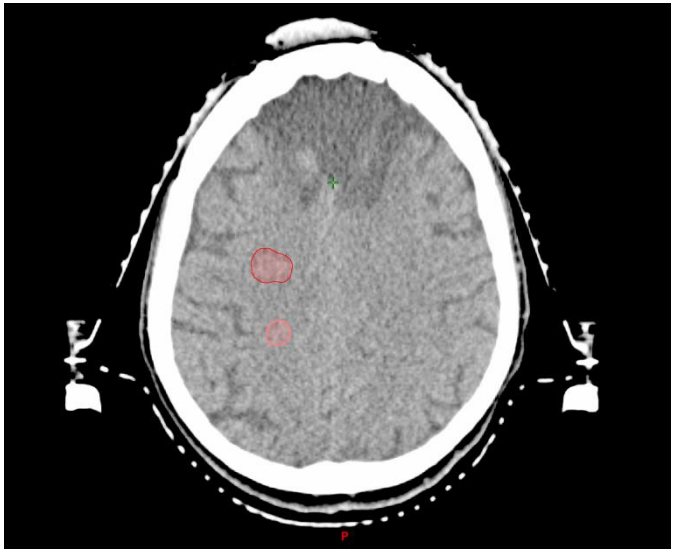


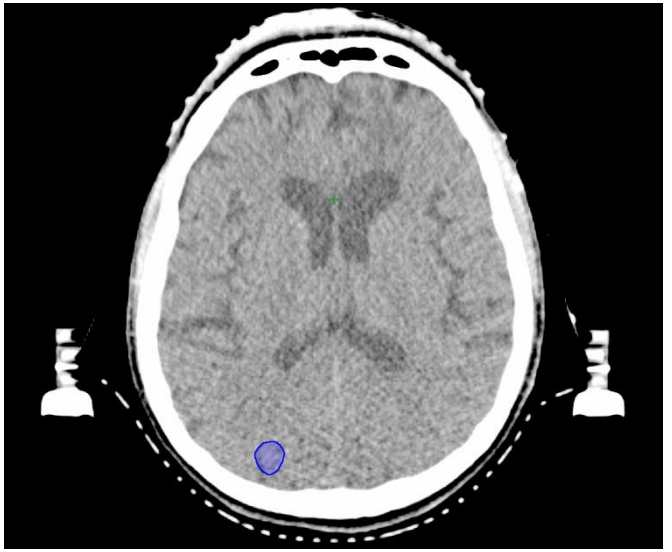
# Multiple brain metastases
# PTVs





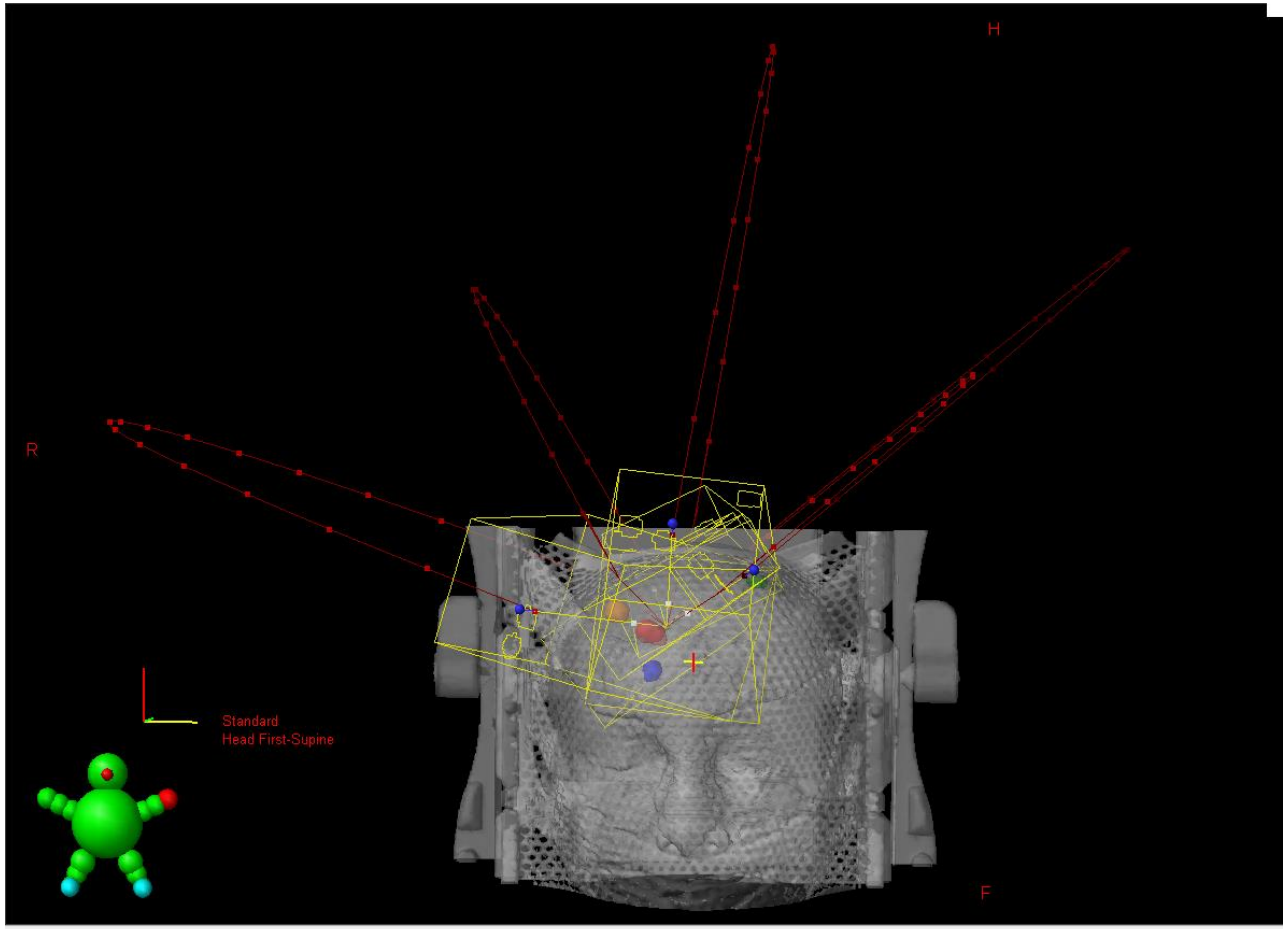






# Multiple brain metastases
# Treatment fields
# Elements Multiple Brain Mets SRS software

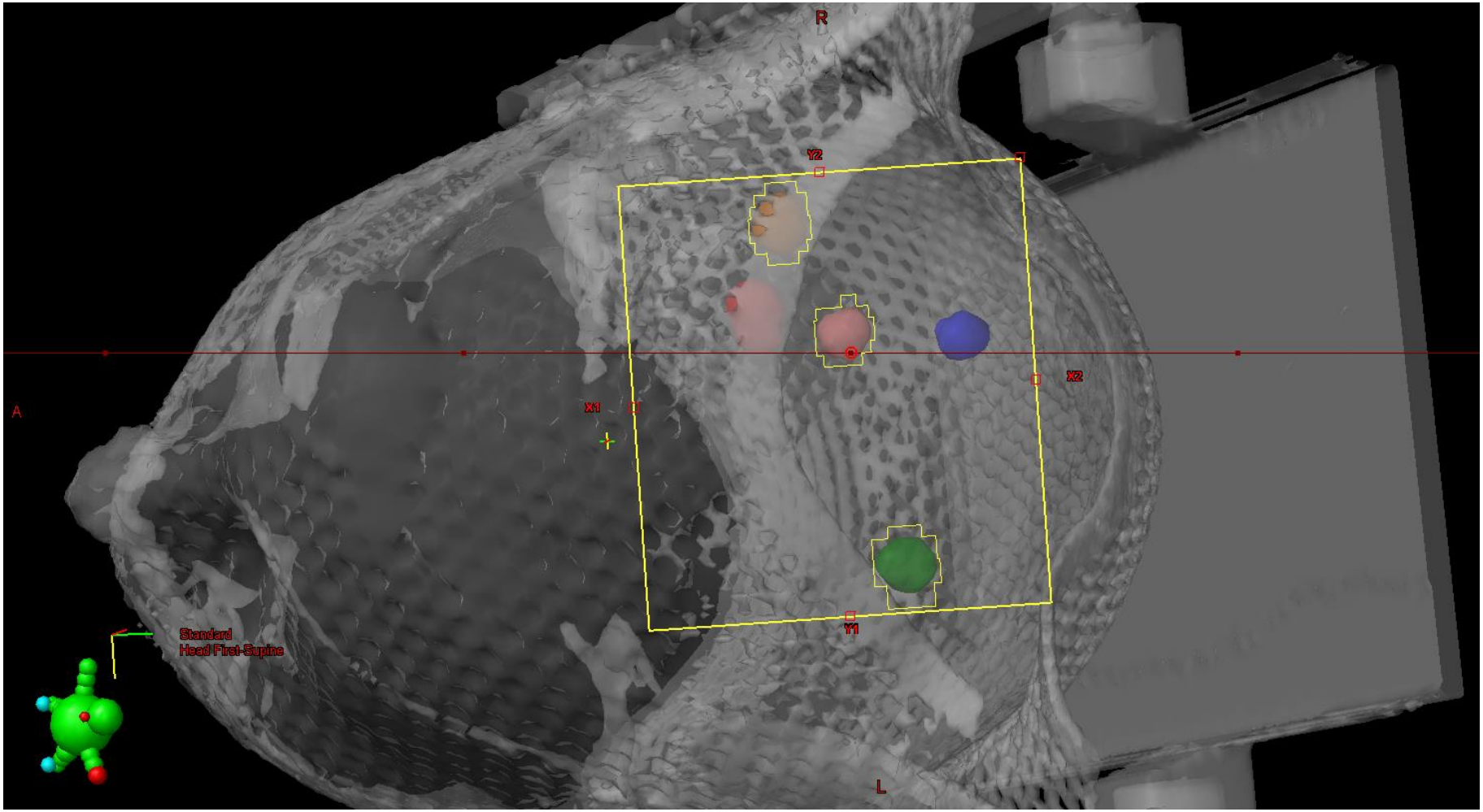





| Field ID | Gantry Rtn [deg] | Coll Rtn [deg] | Couch Rtn [deg] | Wedge | Field X [cm] | X1 [cm] | X2 [cm] | Field Y [cm] | Y1 [cm] | Y2 [cm] | X [cm] | Y [cm] | Z [cm] | SSD [cm] | MU |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 10.0 | 4.0 | 280.0 | None | 8.6 | -4.7 | +3.9 | 9.5 | -5.6 | +3.9 | -1.58 | 5.13 | 1.64 | 90.9 | 1294 |
| 2 | 170.0 | 4.0 | 320.0 | None | 9.6 | -3.5 | +6.1 | 6.0 | -2.6 | +3.4 | -1.58 | 5.13 | 1.64 | 88.5 | 1721 |
| 3 | 10.0 | 356.0 | 320.0 | None | 6.0 | -3.8 | +2.2 | 4.3 | -0.9 | +3.4 | -1.58 | 5.13 | 1.64 | 90.3 | 560 |
| 4 | 350.0 | 4.0 | 20.0 | None | 10.8 | -5.9 | +4.9 | 8.5 | -3.9 | +4.6 | -1.58 | 5.13 | 1.64 | 90.9 | 1960 |
| 5 | 190.0 | 4.0 | 60.0 | None | 4.2 | -0.9 | +3.3 | 8.7 | -2.1 | +6.6 | -1.58 | 5.13 | 1.64 | 88.5 | 999 |

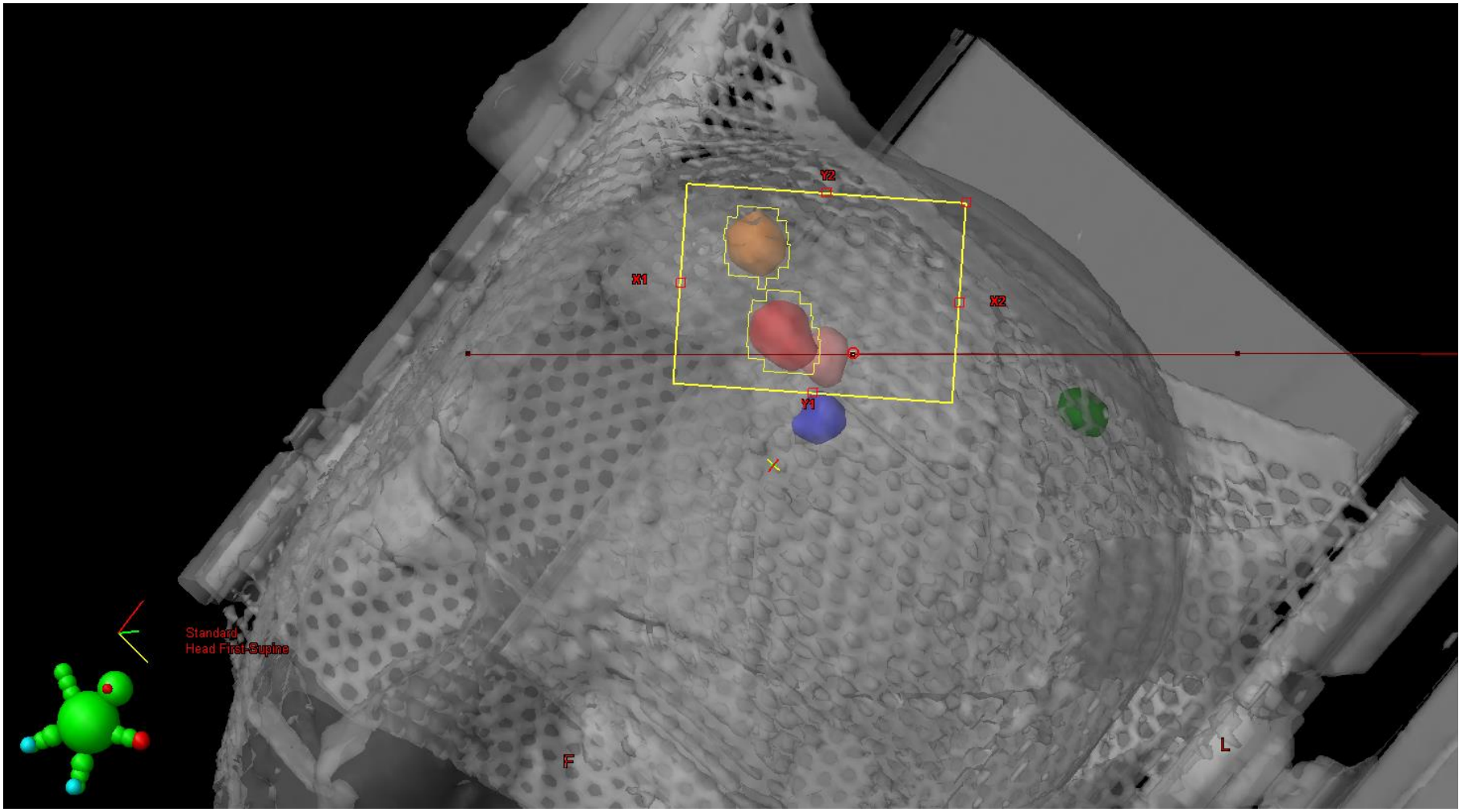
# Multiple brain metastases
# BEV Field 1





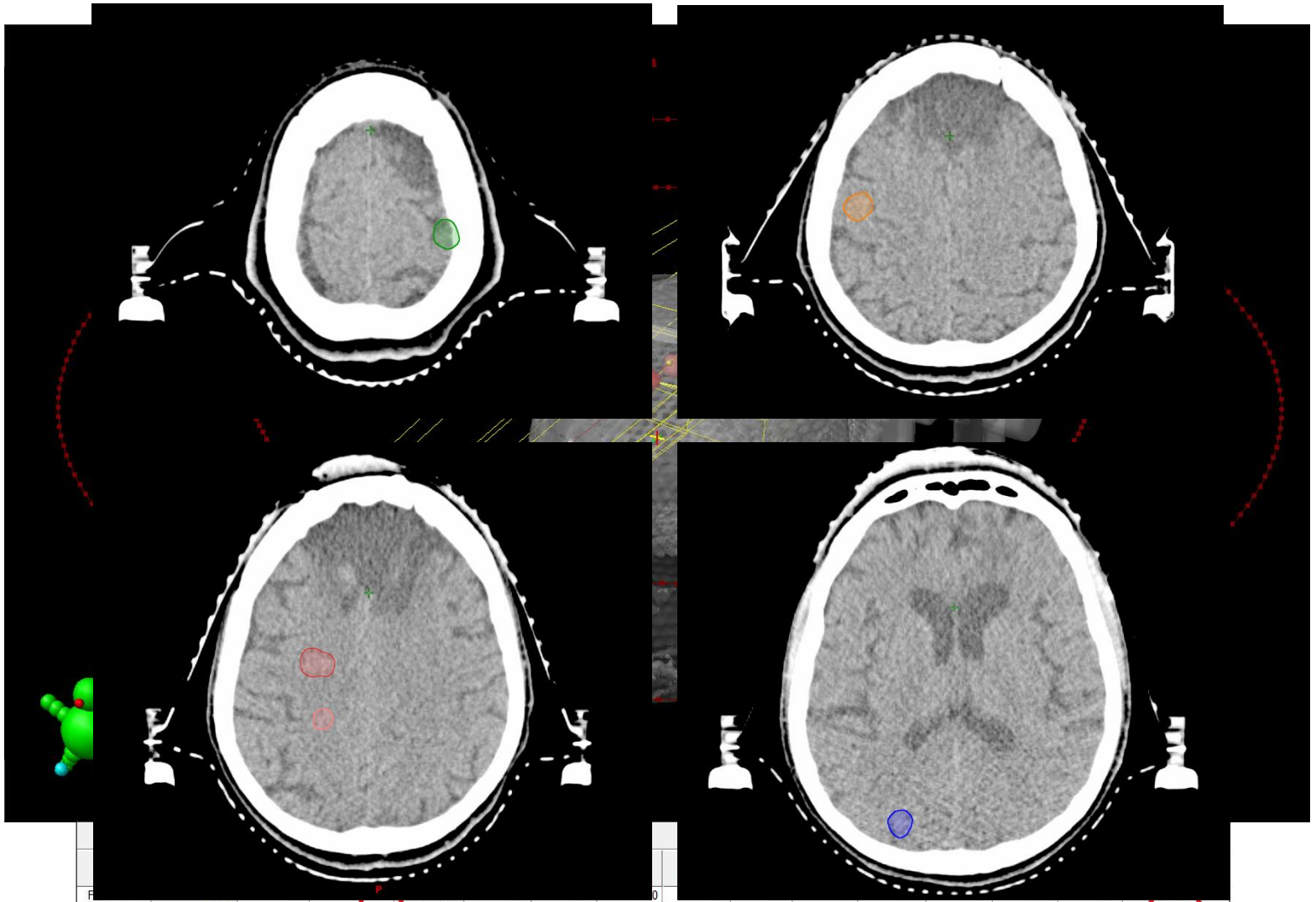
# Multiple brain metastases
# BEV Field 5





# Multiple brain metastases
# Treatment fields - VMAT

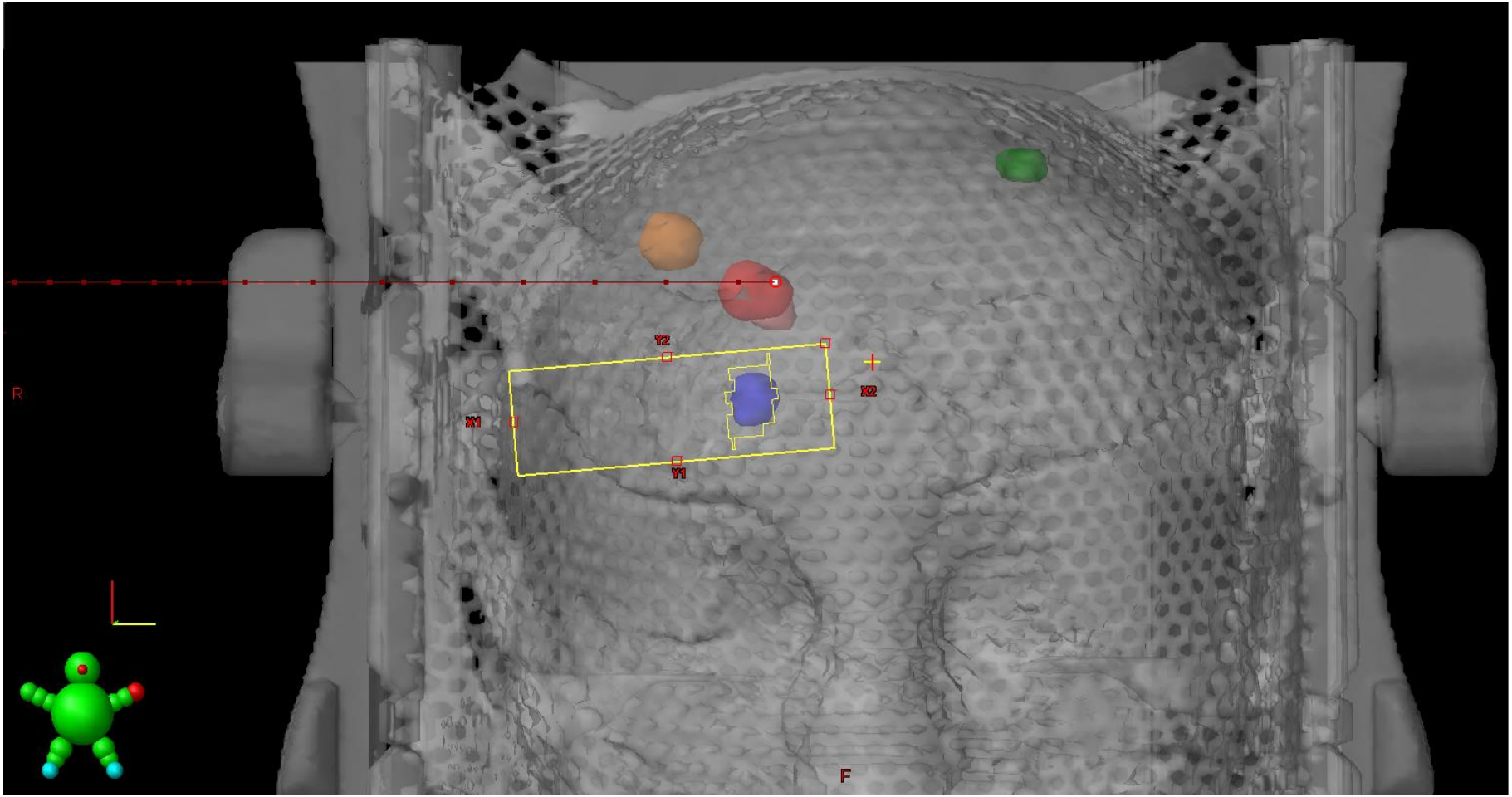




| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Field 1b | 0.0 | 355.0 | 0.0 | None | 6.9 | -5.4 | +1.4 | 2.1 | -3.8 | -1.8 | -1.99 | 4.75 | 1.63 | 89.9 | 2005 |
| Field 2a | 0.0 | 90.0 | 0.0 | None | 1.3 | +1.9 | +3.2 | 12.3 | -6.1 | +6.2 | -1.99 | 4.75 | 1.63 | 89.9 | 1975 |
| Field 2b | 179.0 | 90.0 | 0.0 | None | 1.3 | +1.9 | +3.2 | 12.3 | -6.1 | +6.2 | -1.99 | 4.75 | 1.63 | 88.3 | 2034 |
| Field 3a | 181.0 | 90.0 | 0.0 | None | 3.0 | -1.3 | +1.7 | 6.7 | -3.5 | +3.2 | -1.99 | 4.75 | 1.63 | 88.3 | 1958 |

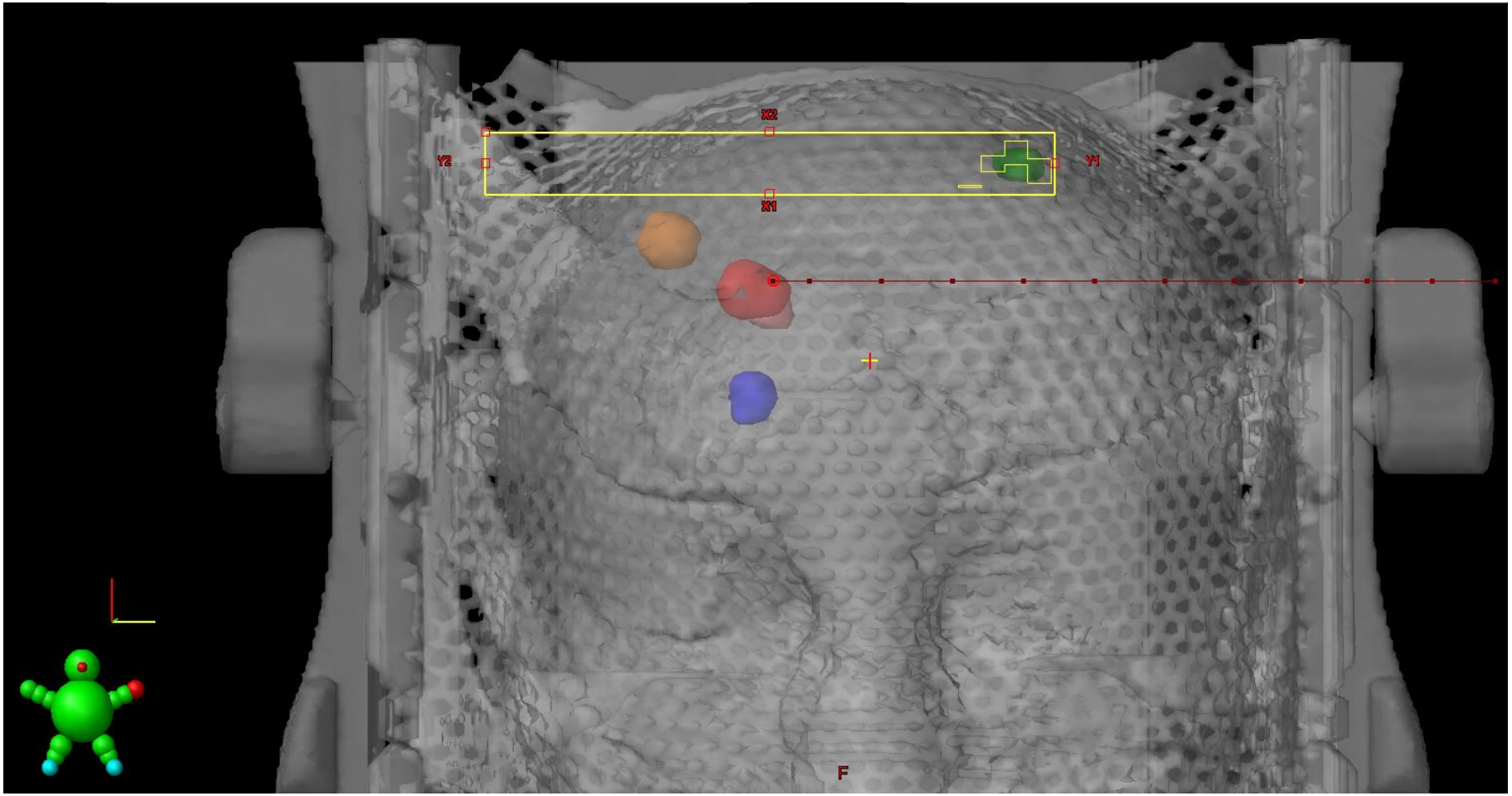
# Multiple brain metastases
# VMAT BEV Field1





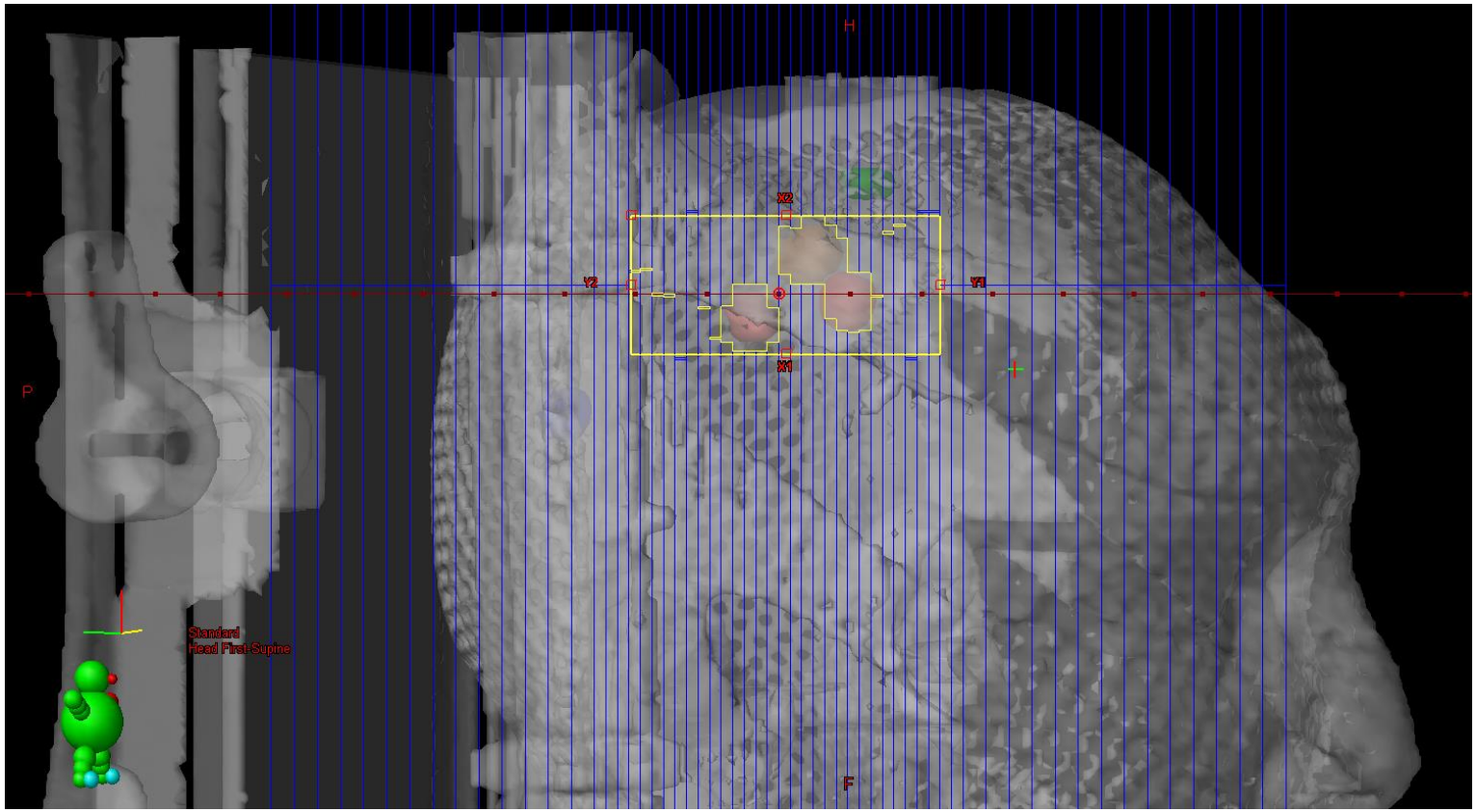
# Multiple brain metastases
# VMAT BEV Field2





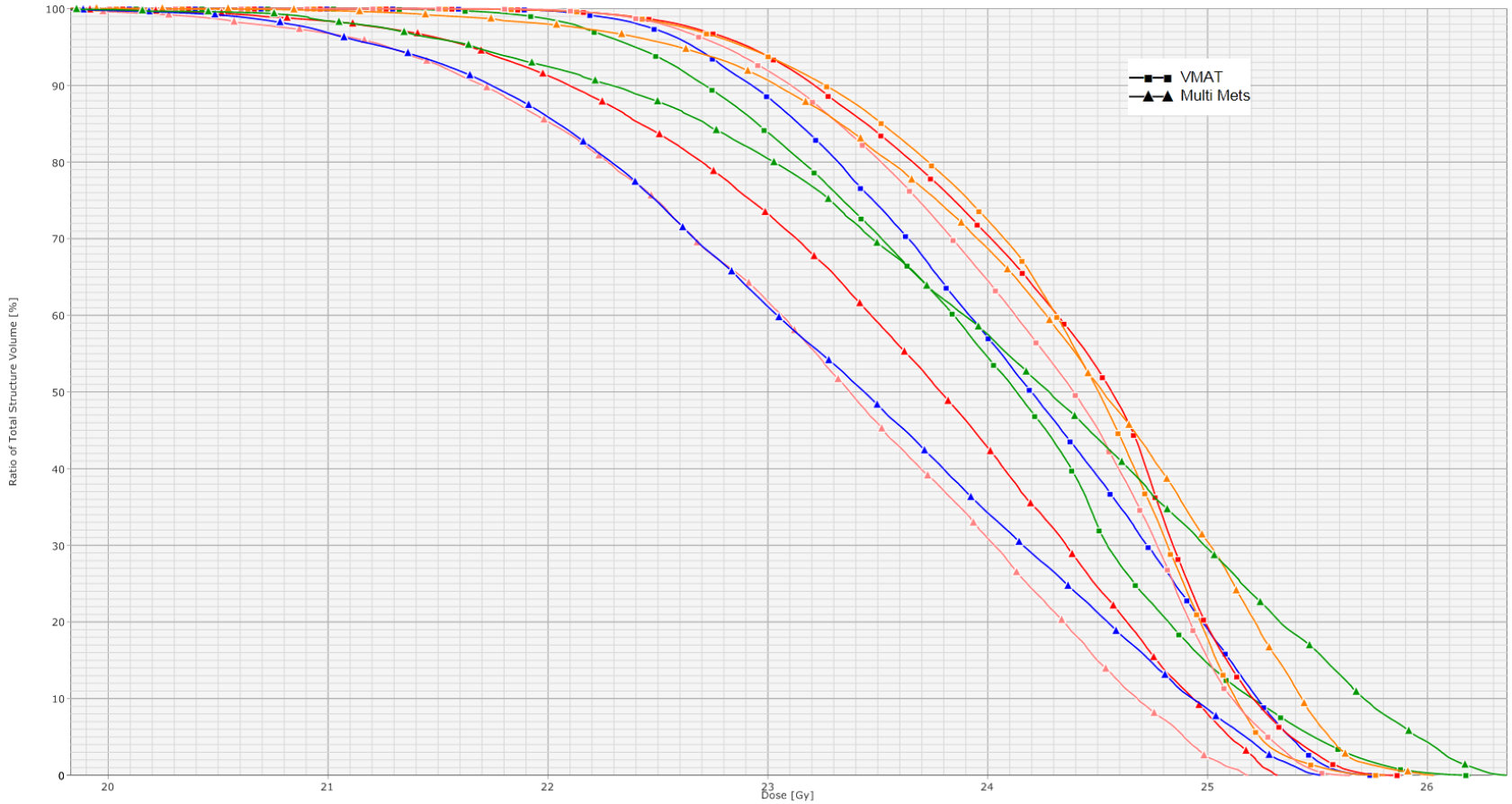
# Multiple brain metastases
# VMAT BEV Field3





# Multiple brain metastases
# VMAT vs Elements Multiple Mets

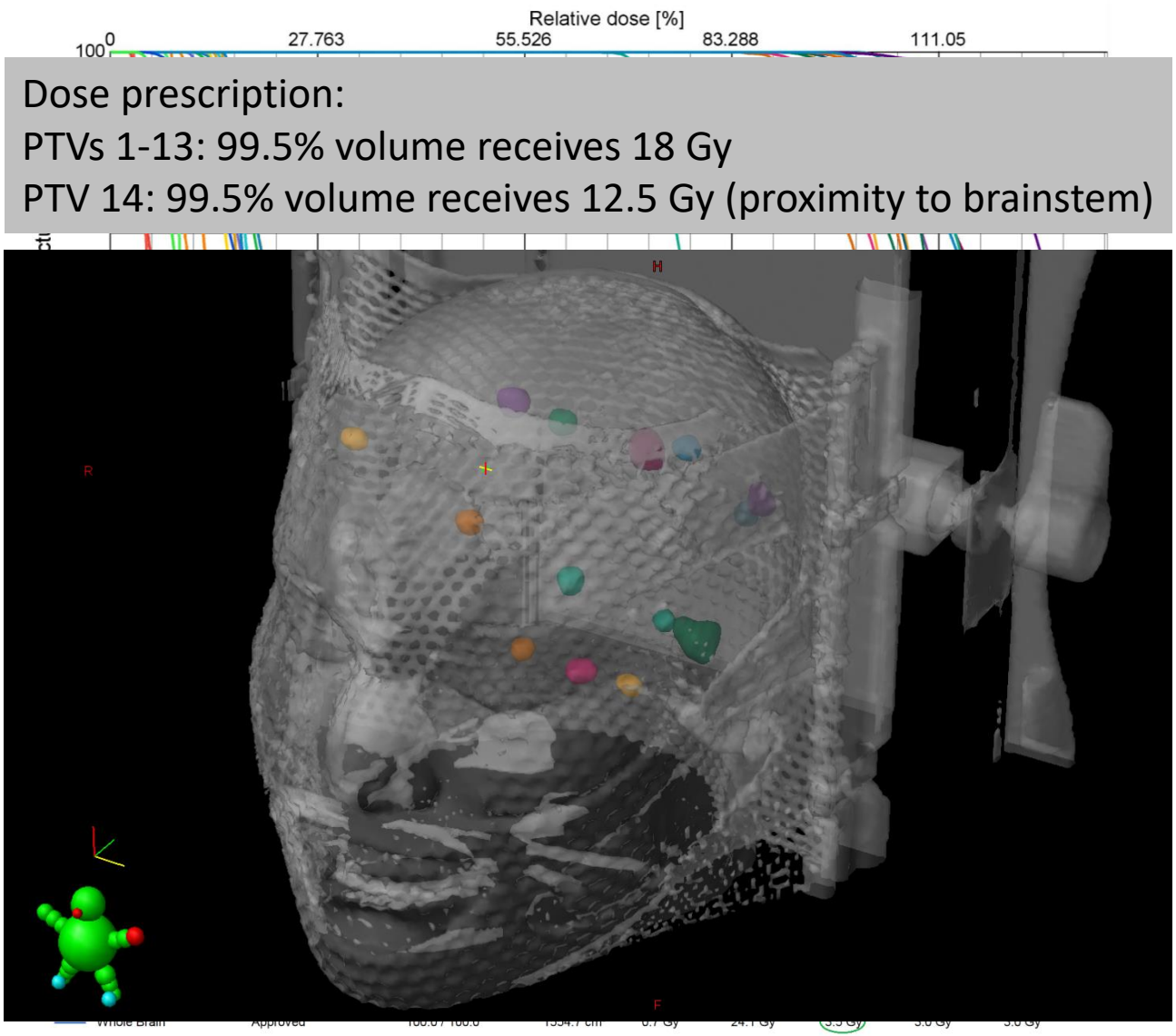





| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Whole Brain | Approved | 100.0 / 100.0 | 1539.8 cm³ | 0.0 Gy | 26.2 Gy | 1.9 Gy | 0.8 Gy | 3.0 Gy |
| PTV01R M periven | Approved | 100.0 / 100.6 | 0.7 cm³ | 18.6 Gy | 25.2 Gy | 23.3 Gy | 23.4 Gy | 1.1 Gy |
| PTV02R M zentral | Approved | 100.0 / 99.7 | 1.1 cm³ | 19.9 Gy | 26.0 Gy | 24.4 Gy | 24.5 Gy | 0.9 Gy |
| PTV03R M zentral | Approved | 100.0 / 100.2 | 1.3 cm³ | 19.3 Gy | 25.3 Gy | 23.6 Gy | 23.8 Gy | 1.1 Gy |
| PTV04R M occipit | Approved | 100.0 / 99.9 | 0.8 cm³ | 19.4 Gy | 25.5 Gy | 23.4 Gy | 23.4 Gy | 1.2 Gy |
| PTV05L M zentral | Approved | 100.0 / 100.0 | 0.7 cm³ | 19.6 Gy | 26.4 Gy | 24.1 Gy | 24.3 Gy | 1.3 Gy |
| Whole Brain | Approved | 100.0 / 100.0 | 1539.8 cm³ | 0.1 Gy | 26.4 Gy | 1.9 Gy | 1.0 Gy | 2.6 Gy |

# 14 brain metastases
# Elements Multiple Brain Mets SRS software






Dose prescription:
PTVs 1-13: 99.5% volume receives 18 Gy
PTV 14: 99.5% volume receives 12.5 Gy (proximity to brainstem)

# Multiple brain metastases
# VMAT vs Multiple Mets



*Original Article*

Technology in Cancer Research & Treatment
2017, Vol. 16(5) 639–644

DOI: 10.1177/1533034616666998
journals.sagepub.com/home/tct
SAGE

## A Systematic Analysis of 2 Monoisocentric Techniques for the Treatment of Multiple Brain Metastases

**Ganesh Narayanasamy, PhD[1,2], Sotirios Stathakis, PhD[1], Alonso N. Gutierrez, PhD[1], Evangelos Pappas, PhD[3], Richard Crownover, MD, PhD[1], John R. Floyd II, MD[4], and Niko Papanikolaou, PhD[1]**

**Abstract**

**Background:** In this treatment planning study, we compare the plan quality and delivery parameters for the treatment of multiple brain metastases using 2 monoisocentric techniques: the Multiple Metastases Element from Brainlab and the RapidArc volumetric-modulated arc therapy from Varian Medical Systems. **Methods:** Eight patients who were treated in our institution for multiple metastases (3-7 lesions) were replanned with Multiple Metastases Element using noncoplanar dynamic conformal arcs. The same patients were replanned with the RapidArc technique in Eclipse using 4 noncoplanar arcs. Both techniques were designed using a single isocenter. Plan quality metrics (conformity index, homogeneity index, gradient index, and $R_{50\%}$), monitor unit, and the planning time were recorded. Comparison of the Multiple Metastases Element and RapidArc plans was performed using Shapiro-Wilk test, paired Student *t* test, and Wilcoxon signed rank test. **Results:** A paired Wilcoxon signed rank test between Multiple Metastases Element and RapidArc showed comparable plan quality metrics and dose to brain. Mean ± standard deviation values of conformity index were 1.8 ± 0.7 and 1.7 ± 0.6, homogeneity index were 1.3 ± 0.1 and 1.3 ± 0.1, gradient index were 5.0 ± 1.8 and 5.1 ± 1.9, and $R_{50\%}$ were 4.9 ± 1.8 and 5.0 ± 1.9 for Multiple Metastases Element and RapidArc plans, respectively. Mean brain dose was 2.3 and 2.7 Gy for Multiple Metastases Element and RapidArc plans, respectively. The mean value of monitor units in Multiple Metastases Element plan was 7286 ± 1065, which is significantly lower than the RapidArc monitor units of 9966 ± 1533 ($P < .05$). **Conclusion:** For the planning of multiple brain lesions to be treated with stereotactic radiosurgery, Multiple Metastases Element planning software produced equivalent conformity, homogeneity, dose falloff, and brain $V_{12\ Gy}$ but required significantly lower monitor units, when compared to RapidArc plans.

# Multiple brain metastases
# VMAT



Practical Radiation Oncology (2012) 2, 306–313

practical radiation oncology
pro
www.practicalradonc.org

Original Report

## Plan quality and treatment planning technique for single isocenter cranial radiosurgery with volumetric modulated arc therapy

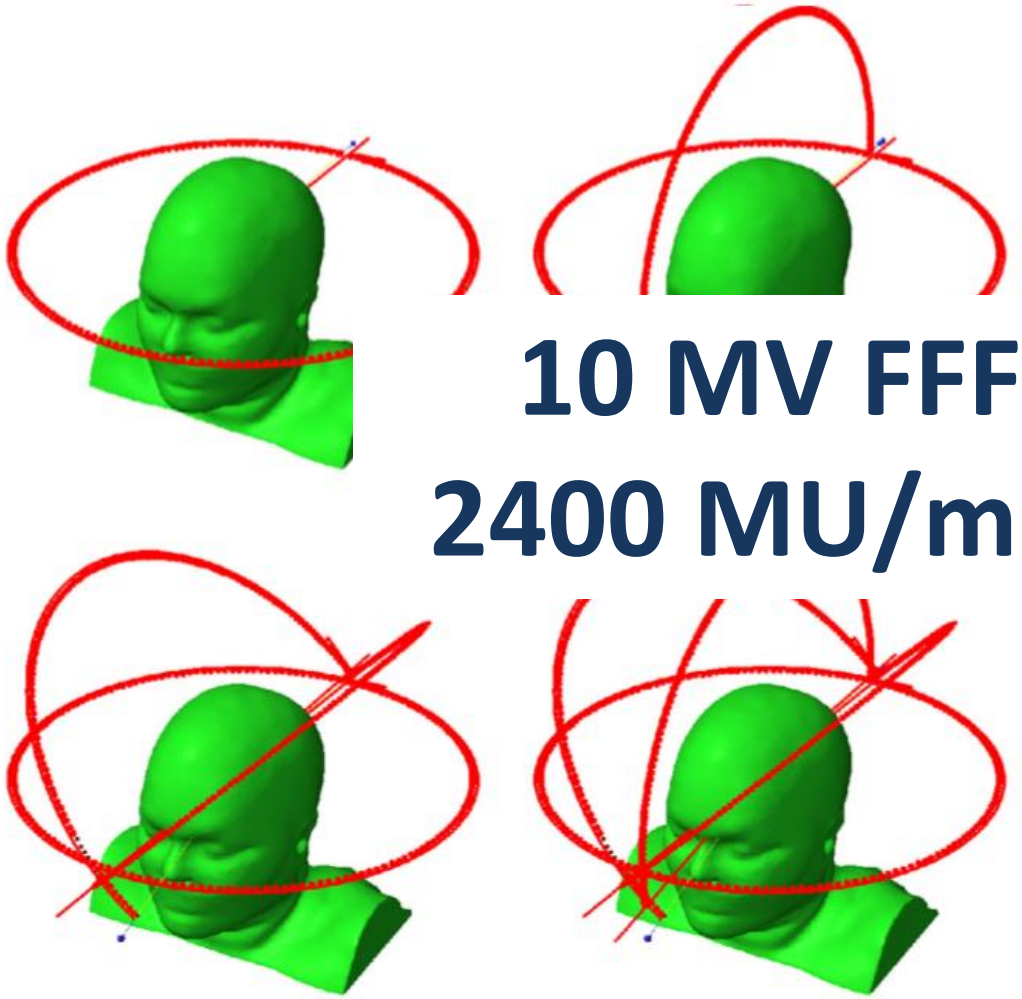
Grant M. Clark MD[a], Richard A. Popple PhD[a], Brendan M. Prendergast MD[a], Sharon A. Spencer MD[a], Evan M. Thomas MS[a], John G. Stewart MD[a], Barton L. Guthrie MD[b], James M. Markert MD[b], John B. Fiveash MD[a,*]

**Conclusions:** We have outlined a practical approach to cranial radiosurgery treatment planning using the single isocenter VMAT platform. One or 2 arc single isocenter plans are often adequate for treatment of single targets, while 2-4 arcs may be more advantageous for multiple targets. Given the high plan quality and extreme clinical efficiency, this single isocenter VMAT approach will continue to become more prevalent for linac-based radiosurgical treatment of 1 or more intracranial targets and will likely replace multiple isocenter techniques.

# Multiple brain metastases
# VMAT beam geometries







**10 MV FFF**
**2400 MU/min**

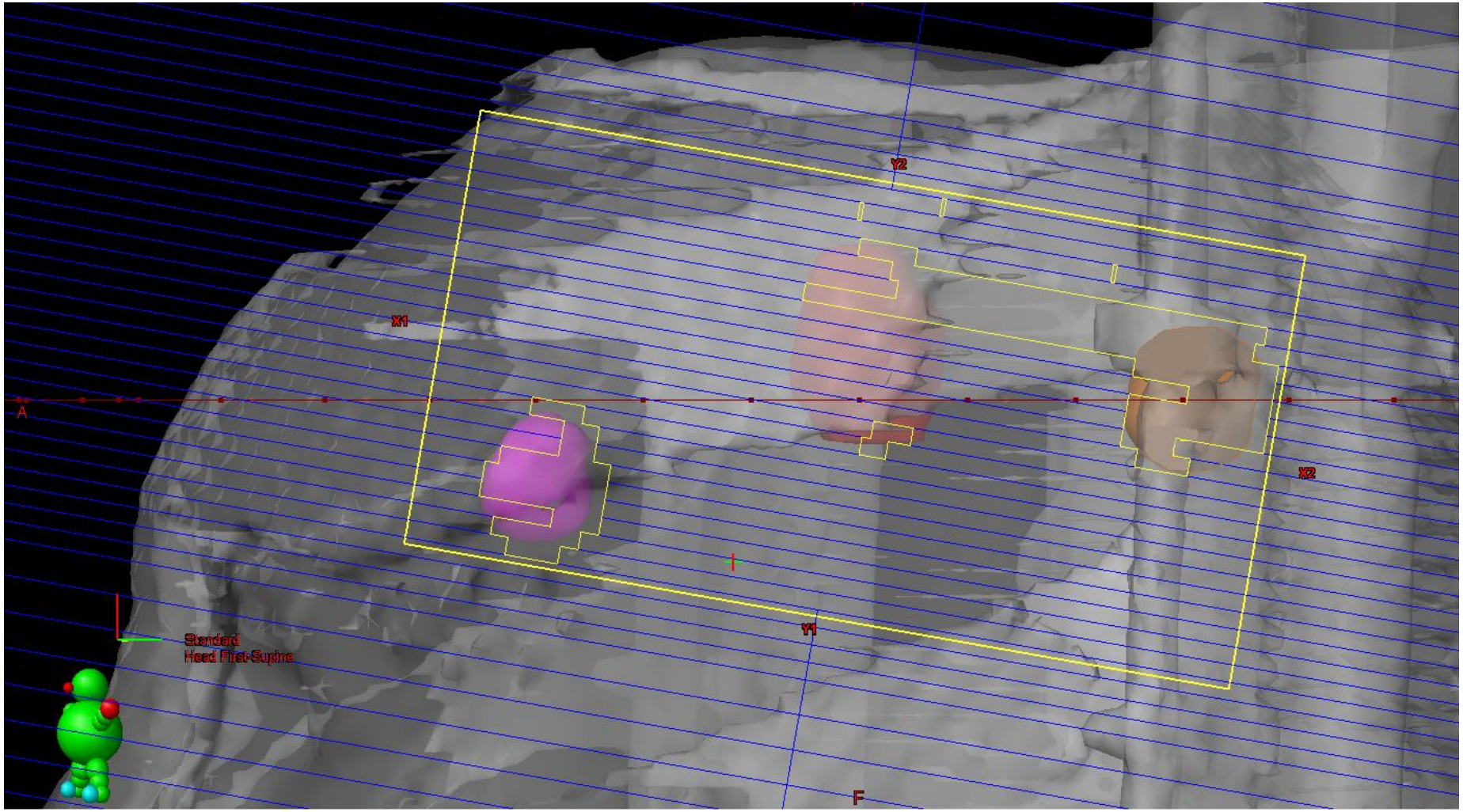
**Figure 2** Single- and multibeam geometries utilized for the single isocenter volumetric modulated arc therapy radiosurgery technique.

**Table 2** Targets, arc arrangements, and dose prescriptions

| Patient | No. of targets | No. of arcs | Prescription |
|---|---|---|---|
| 1 | 3 | 4 | 5 Gy × 5 |
| 2 | 3 | 4 | 6 Gy × 5 |
| [illegible] | 2 | 4 | 6 Gy × 5 |
| [illegible] | 3 | 4 | 16 Gy × 1 |
| [illegible] | 3 | 4 | 6 Gy × 5 |
| [illegible] | 3 | 4 | 6 Gy × 5 |
| [illegible] | 1 | 2 | 15 Gy × 1 |
| [illegible] | 1 | 2 | 15 Gy × 1 |
| [illegible] | 1 | 1 | 5 Gy × 5 |
| [illegible] | 1 | 2 | 12 Gy × 1 |
| [illegible] | 1 | 1 | 12 Gy × 1 |
| [illegible] | 3 | 3 | 5 Gy × 5 |
| 13 | 2 | 2 | 5 Gy × 5 |
| 14 | 5 | 2 | 6 Gy × 5 |
| 15 | 1 | 2 | 16 Gy × 1 |
| Mean | 2.2 | 2.7 | |
| Median | 2.0 | 2.0 | |
| Range | 1-5 | 1-4 | |

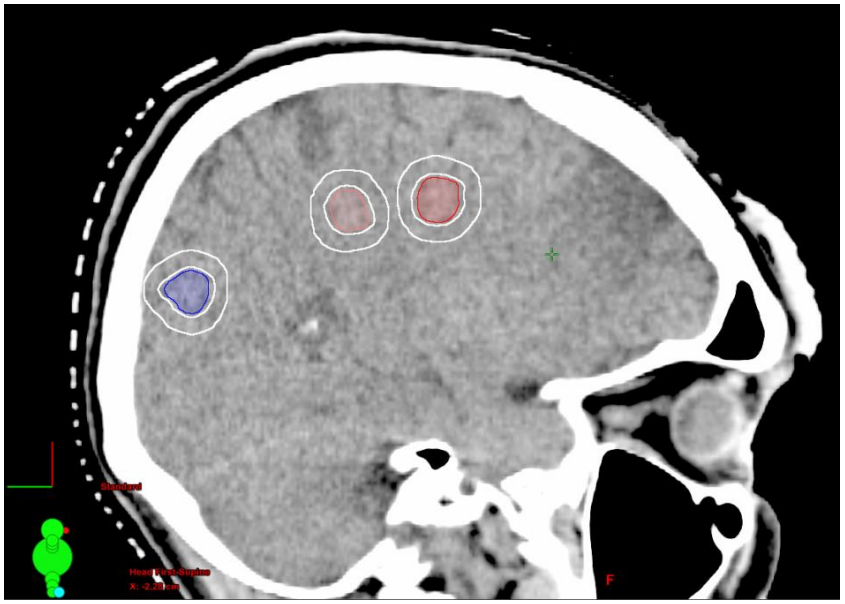
# Multiple brain metastases
# Leaf gap and dose spillage

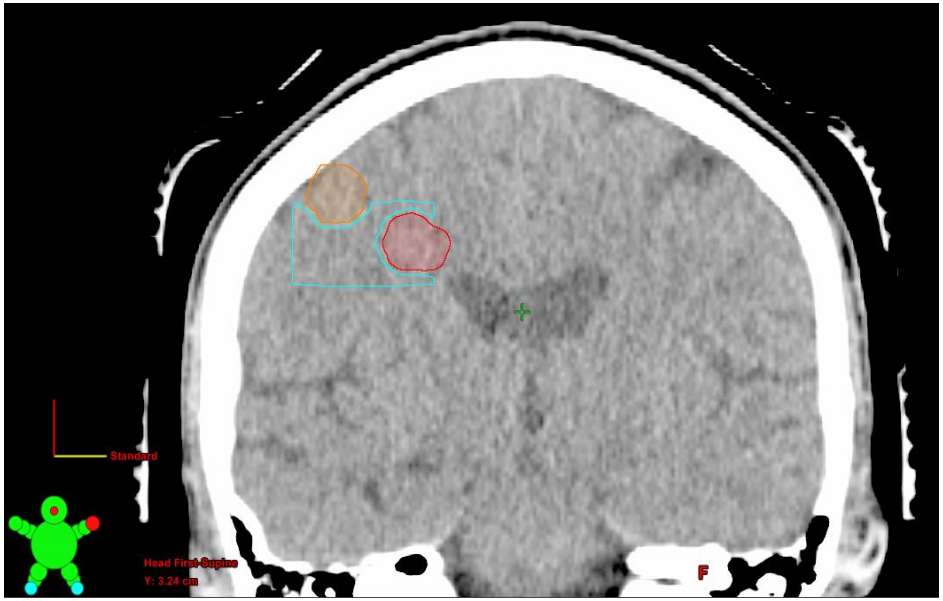


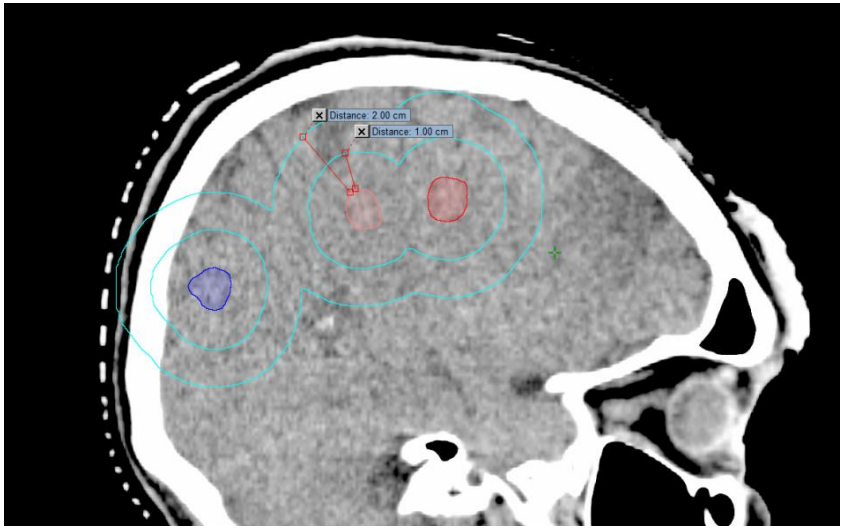


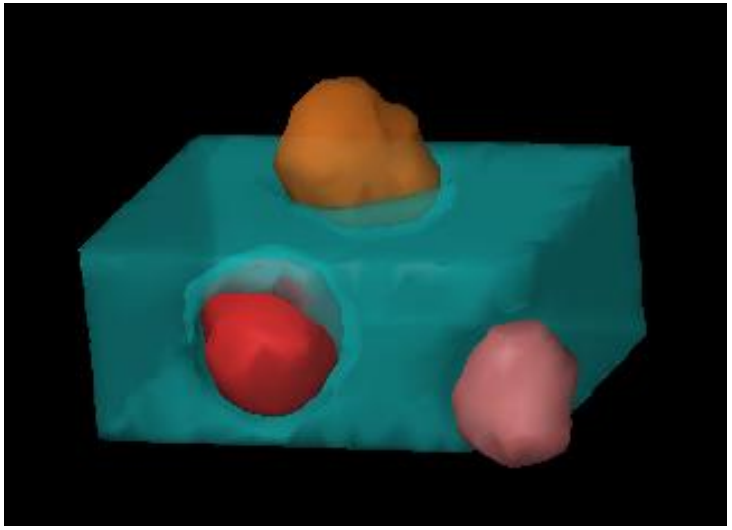
# Multiple brain metastases
# Help structures





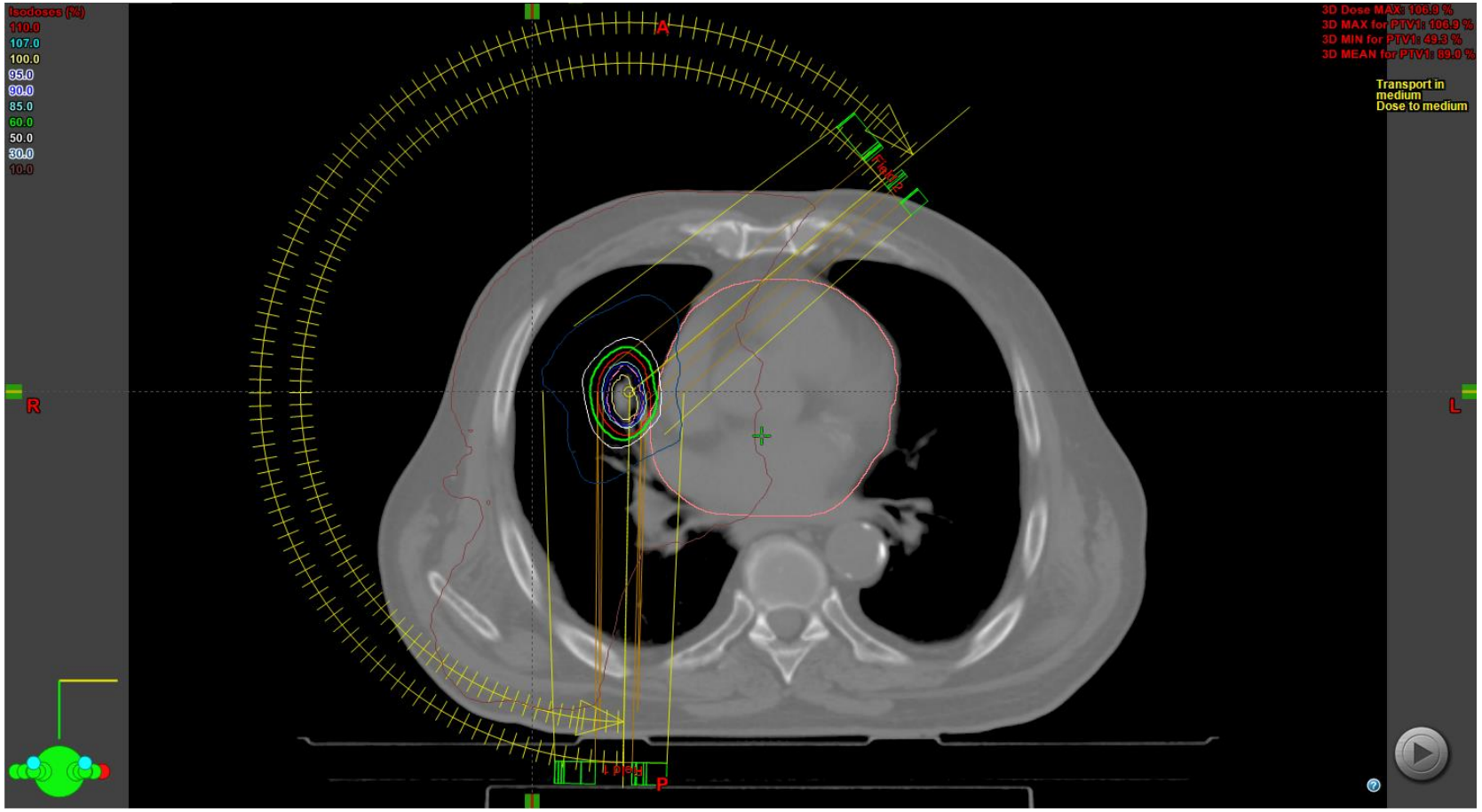


# SBRT Lung case





# Dose prescription



Systematic review

## Outcomes of stereotactic ablative radiotherapy for central lung tumours: A systematic review

Sashendra Senthi *, Cornelis J.A. Haasbeek, Ben J. Slotman, Suresh Senan

Radiotherapy and Oncology 106 (2013) 276–282

Results

Twenty publications met the inclusion criteria, reporting outcomes for 563 central lung tumours, including 315 patients with early-stage NSCLC. There was heterogeneity in the planning, prescribing and delivery of SABR and the common toxicity criteria used to define toxicities (versions 2.0–4.0). Tumour location (central versus peripheral) did not impact overall survival. Local control rates were ⩾85% when the prescribed biologically equivalent tumour dose was ⩾100 Gy. Treatment-related mortality was 2.7% overall, and 1.0%

**Table 1**
Baseline radiotherapy details.

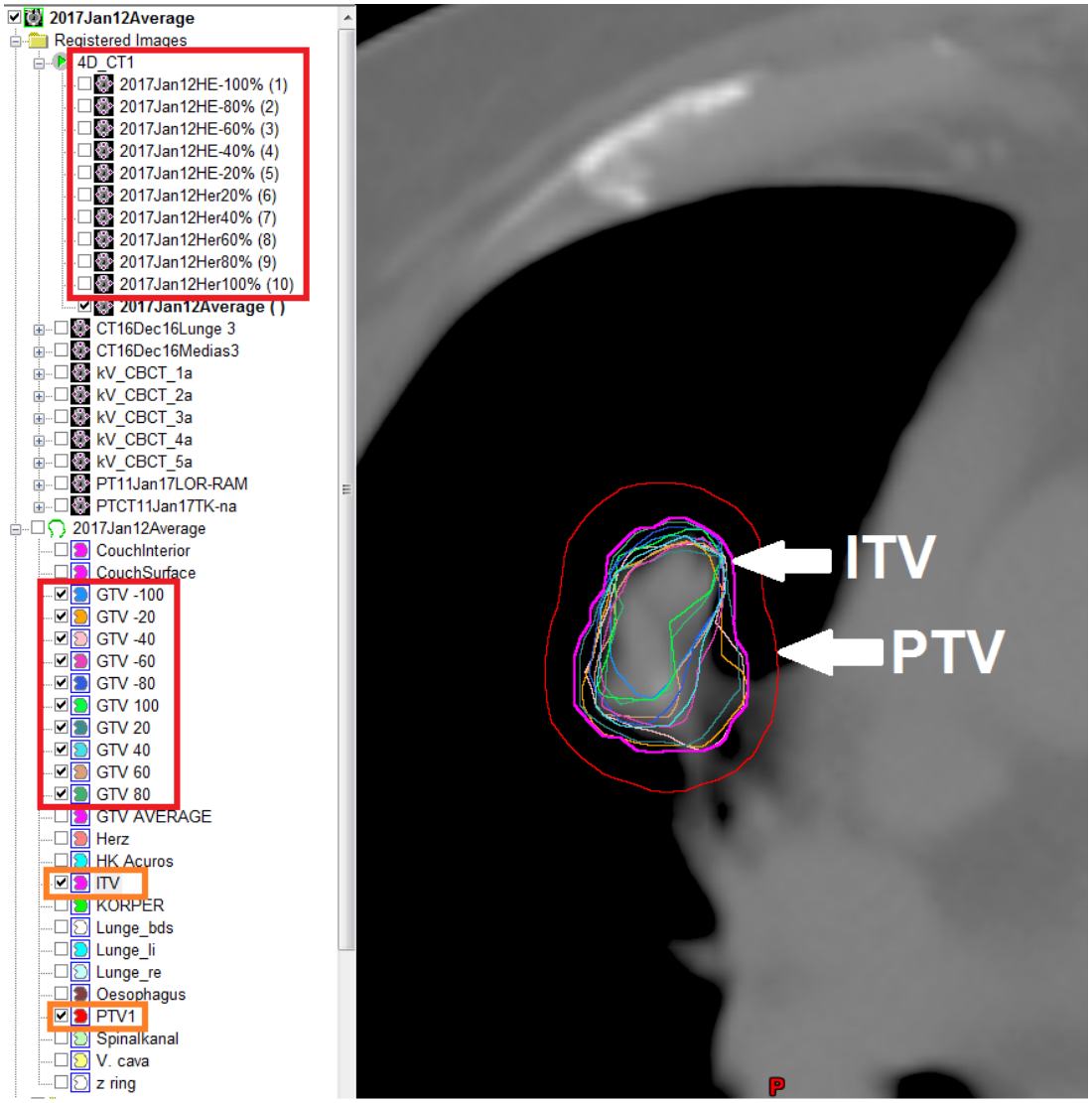
| Author (year) | Simulation | Target volumes | Image guidance | Prescription | Heterogeneity correction | Total dose gray/ fractions |
|---|---|---|---|---|---|---|
| Onimur | | | | Isocentre, PTV got 80% | No | 48/8 |
| Xia [22 | | | | 50% Isodose covering 95% PTV | No | 50/10 |
| Chang [ | | | | 75–90% Isodose covering PTV | Yes | 50/4 |
| Song [3 | | | | 85% Isodose covering 95% PTV | No | 48/4[a] |
| Milano | | | | Isocentre,PTV got 80% | No | 50/5[a] |
| Fakiris | | | | 80% Isodose covering 95% PTV | No | 60/3 |
| Gucken (200 | | | | 65% Isodose covering PTV | Yes | 48/8 |
| Unger [ | | | | 70–80% Isodose covering 95% PTV | Yes | 40/5 |
| Oshiro | | | | Not reported, likely to isocentre | No | 50/5[a] |
| Baba [3 | | | | Isocentre, 95% of PTV got 80% | Yes | 50/4 |
| Bradley | | | | 75–85% Isodose covering 95% PTV | Yes[b] | 45/5 |
| Andrats | | | | 60% Isodose covering 100% PTV | Yes | 35/5[a] |
| Haasbe | | | | 80% Isodose covering 99% PTV | No | 60/8 |
| Bral [23 | | | | 95% Isodose covering 95% PTV | No | 60/4 |
| Olsen [ | | | | 60–90% Isodose covering 95% PTV | Yes | 50/5[a] |
| Stauder [39] (2011) | 4-Dimentional CT | ITV + PBM = PTV | Conebeam CT | 100% Isodose covering 95% PTV | Yes[b] | 48/4 |
| Rowe [37] (2012) | 4-Dimentional CT | ITV + 7 mm = PTV | Conebeam CT | 100% Isodose covering 95% PTV | Yes | 50/4[a] |
| Nuyttens [30] (2012) | Standard CT | GTV + 5 mm = PTV | Respiratory tracking fiducial markers | 75–90% Isodose covering 95% PTV | Yes | 60/5[a] |
| Taremi [25] (2012) | 4-Dimentional CT | ITV + 5 mm = PTV | Conebeam CT | 100% Covered 95% of PTV | Yes[b] | 60/8 |
| Janssen [31] (2012) | 4-Dimentional CT | ITV + 3 mm = CTV + PBM = PTV | Conebeam CT | 80% Isodose covering PTV | No | 48/8 |

Population based margins (PBM) utilized to account for tumour motion were typically 5 mm radially and 8–10 mm longitudinally.
[a] Modal dose fractionation schedule shown when multiple schedules were utilized.
[b] Heterogeneity correction not utilized in all treatments.

# Internal Target Volume

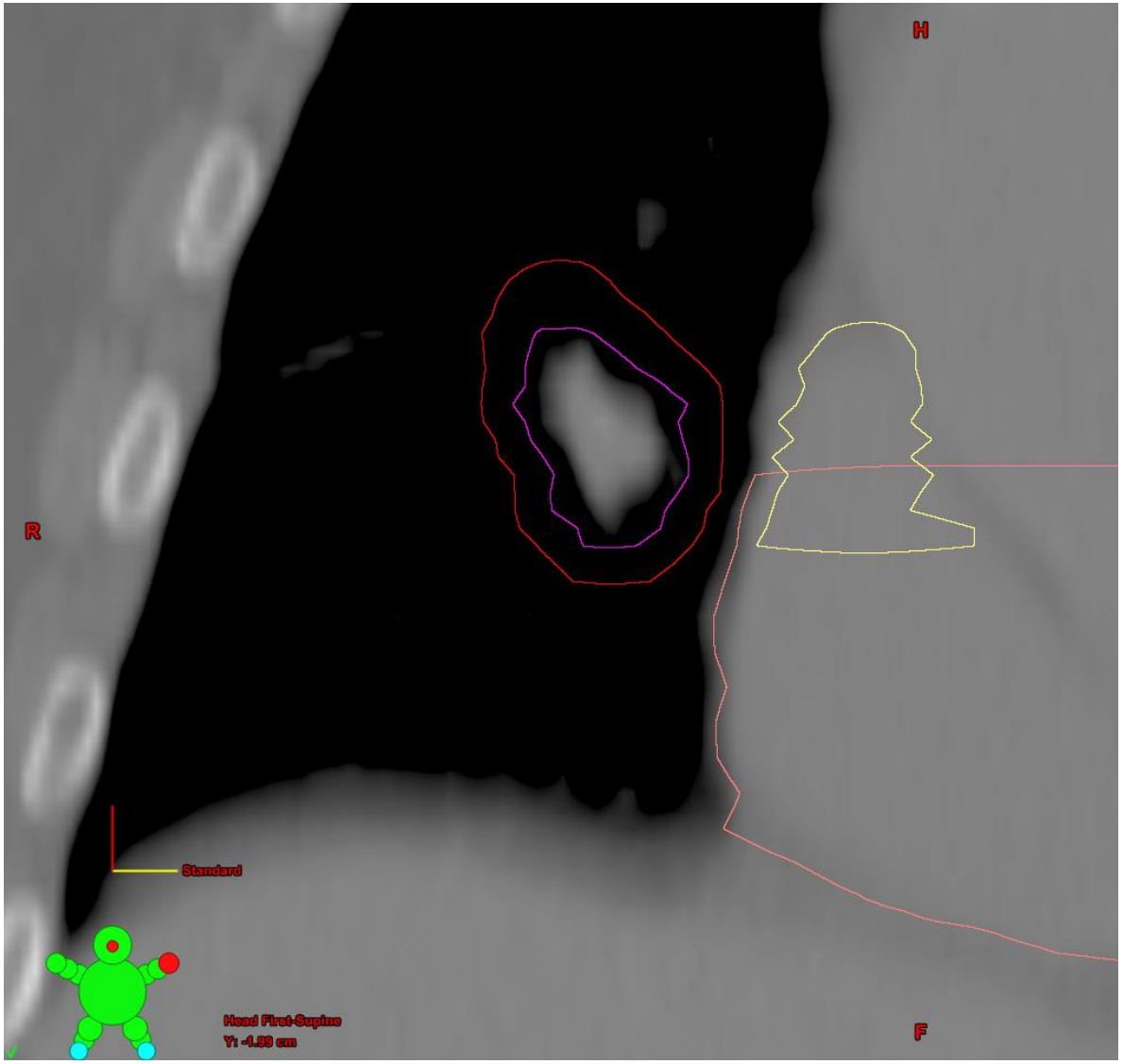


Internal Target Volume
(ITV)
ICRU 62
=
CTV
+
margin accounting for internal physiological movements as well as changes in CTV's shape and size



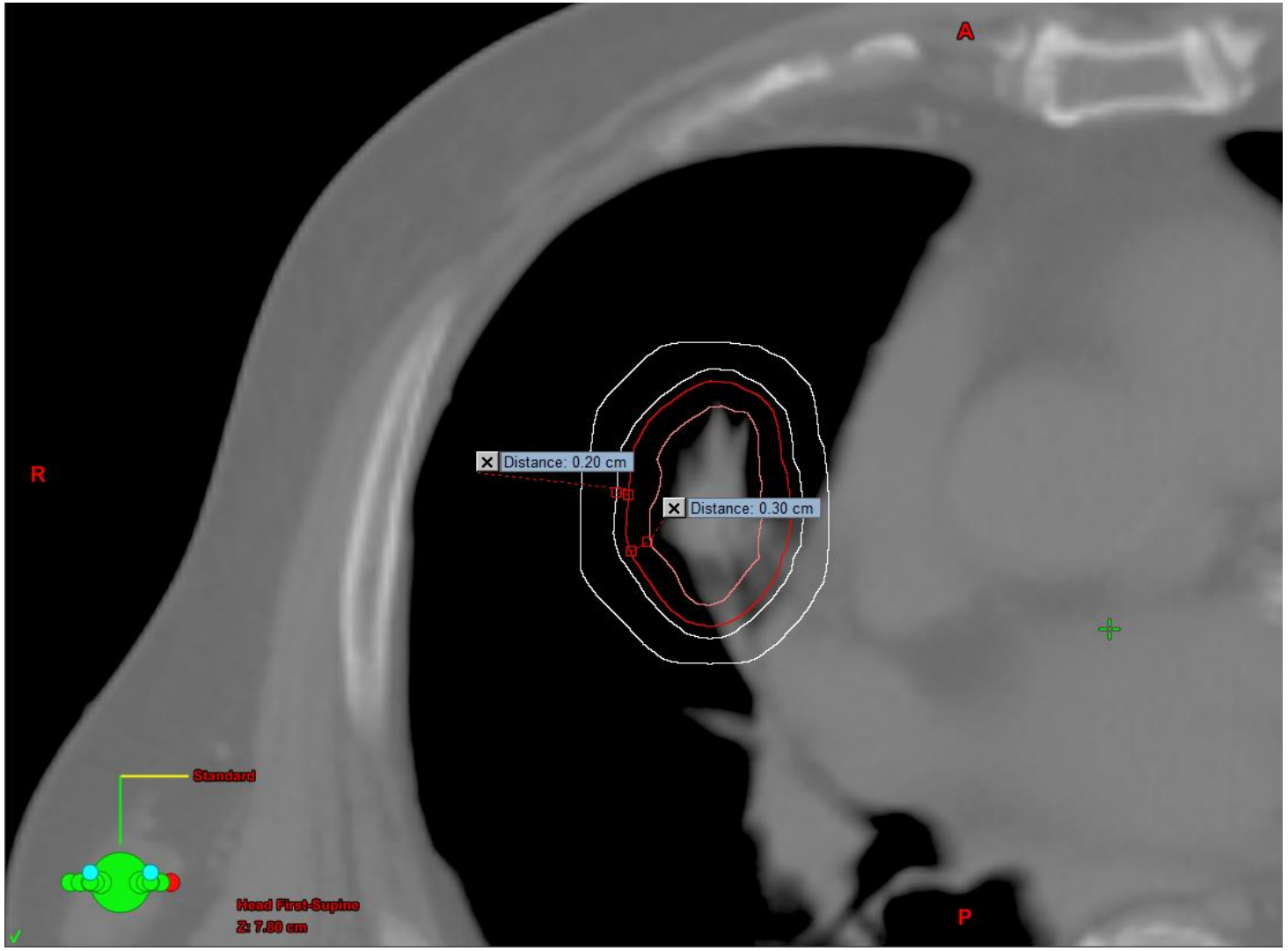
# Organs at risk





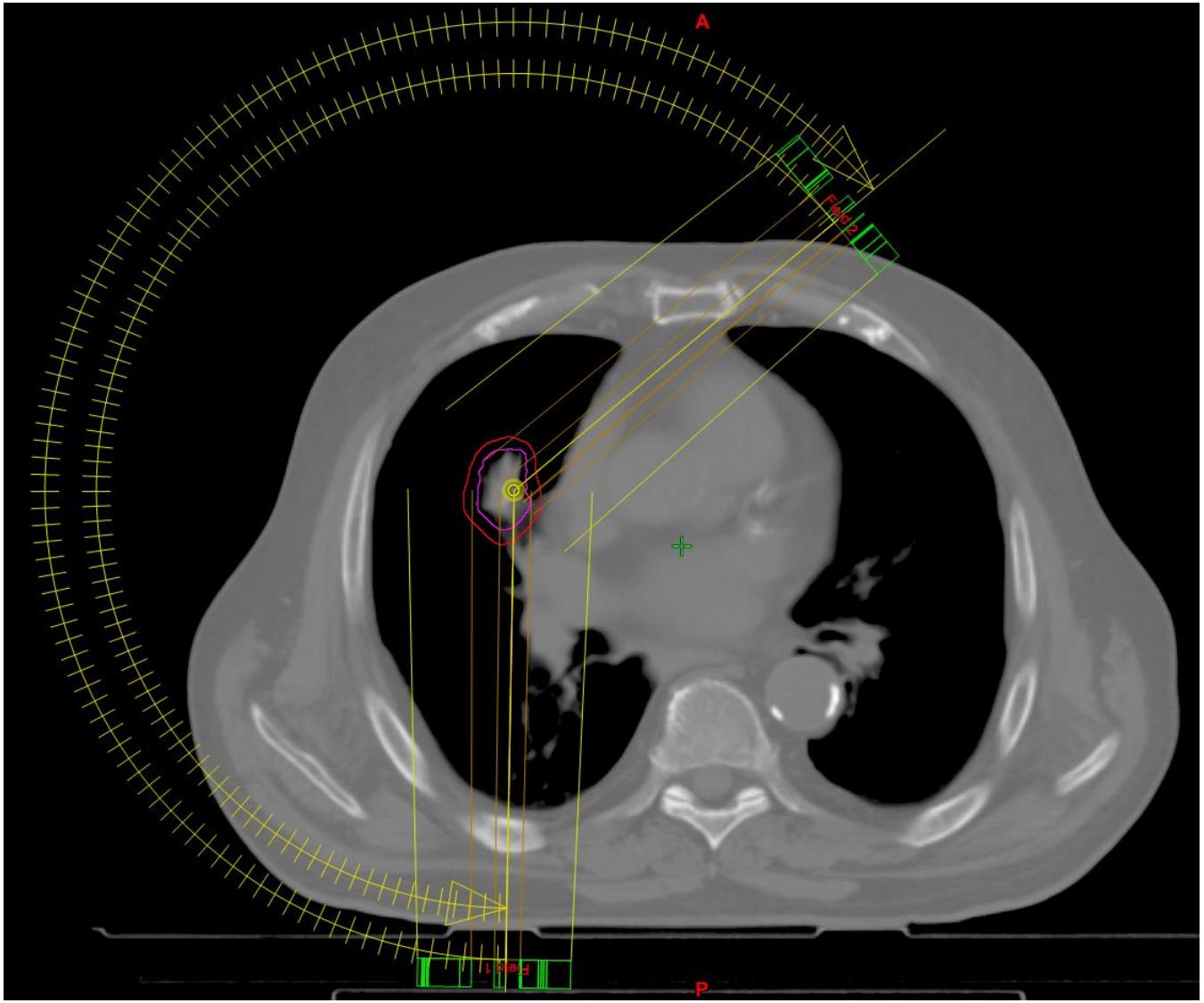
# Ring structure





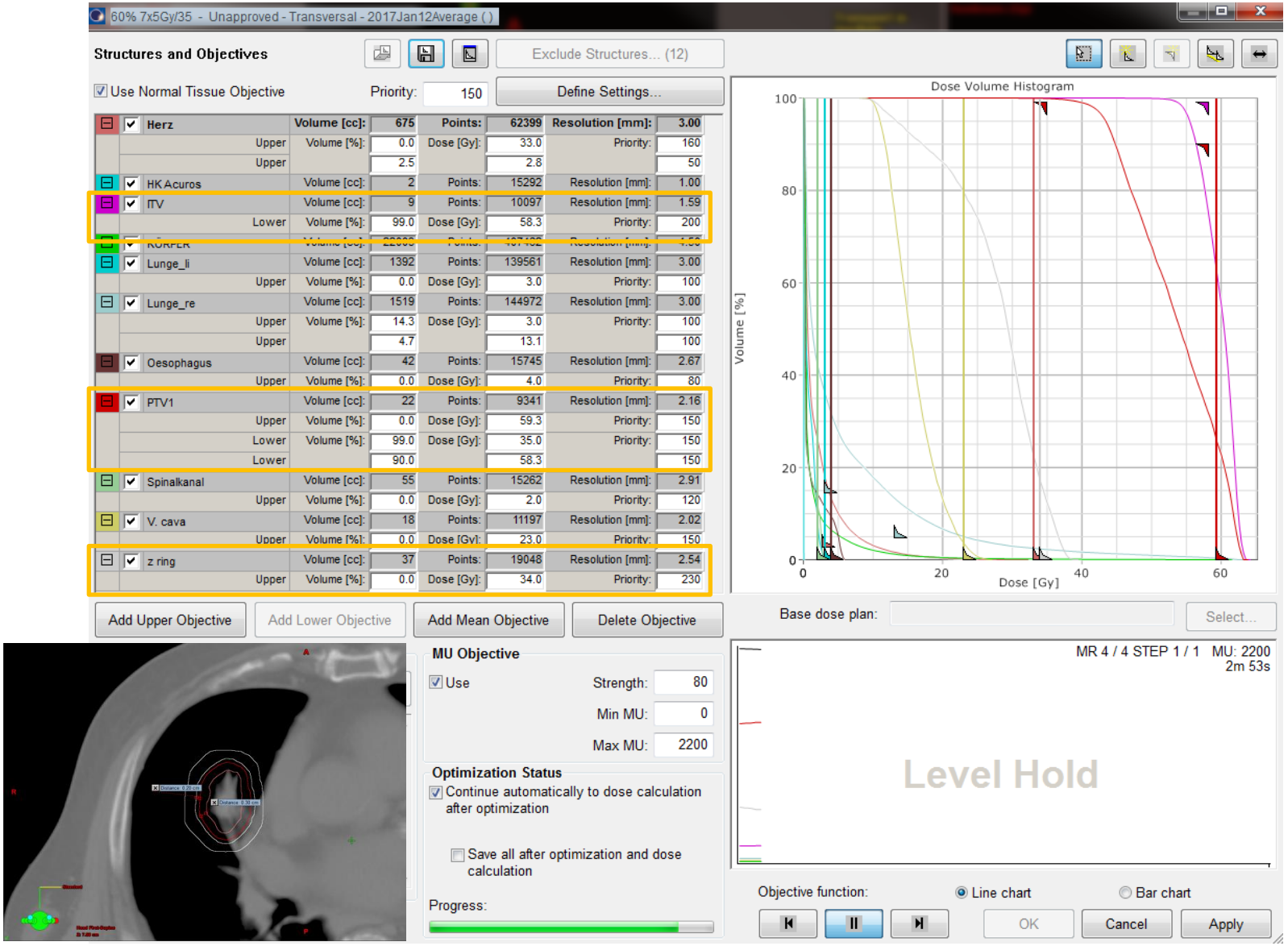
# Field geometry





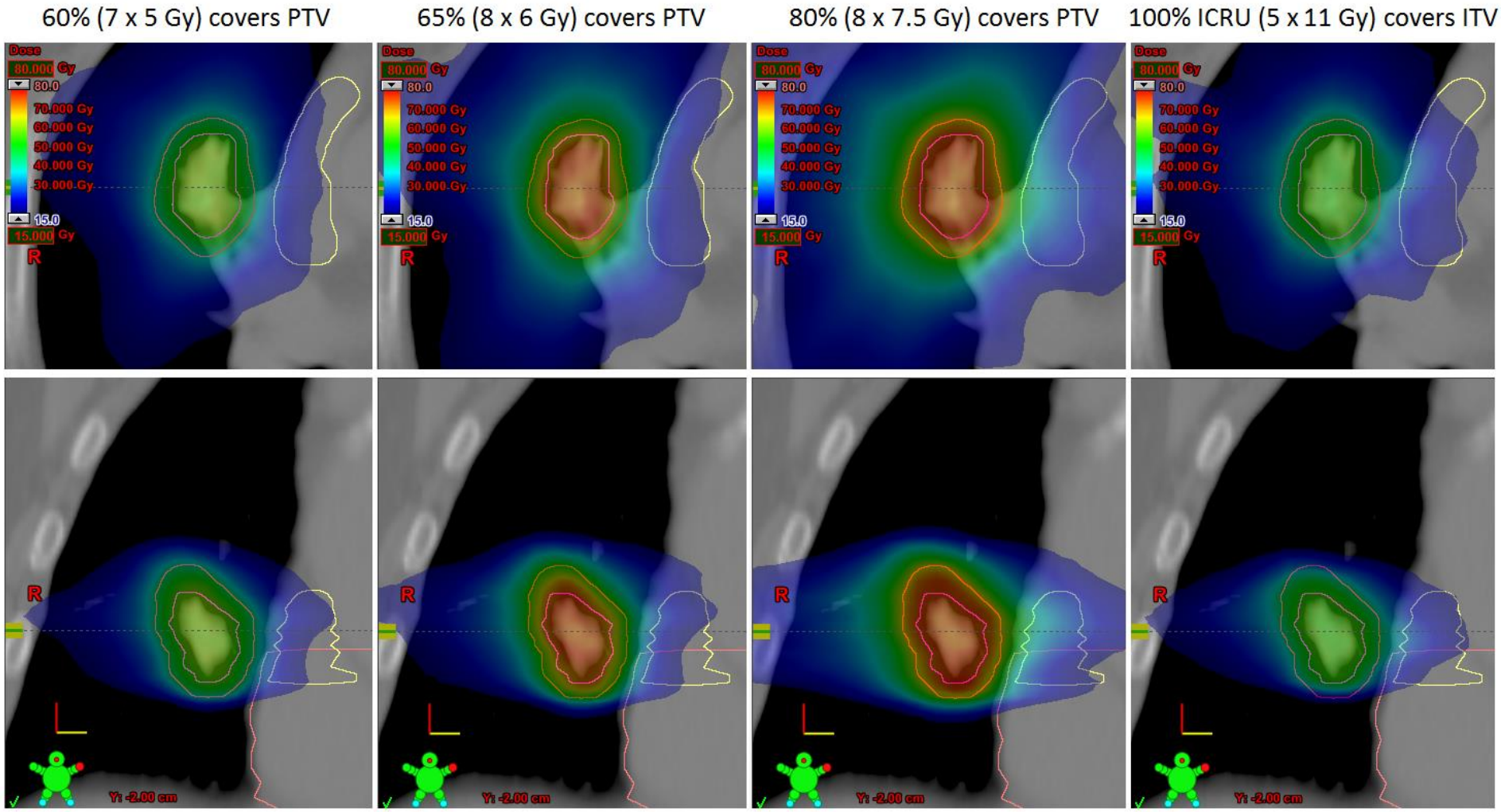
# Optimization objectives
# 60% isodose (7 x 5 Gy) covering PTV



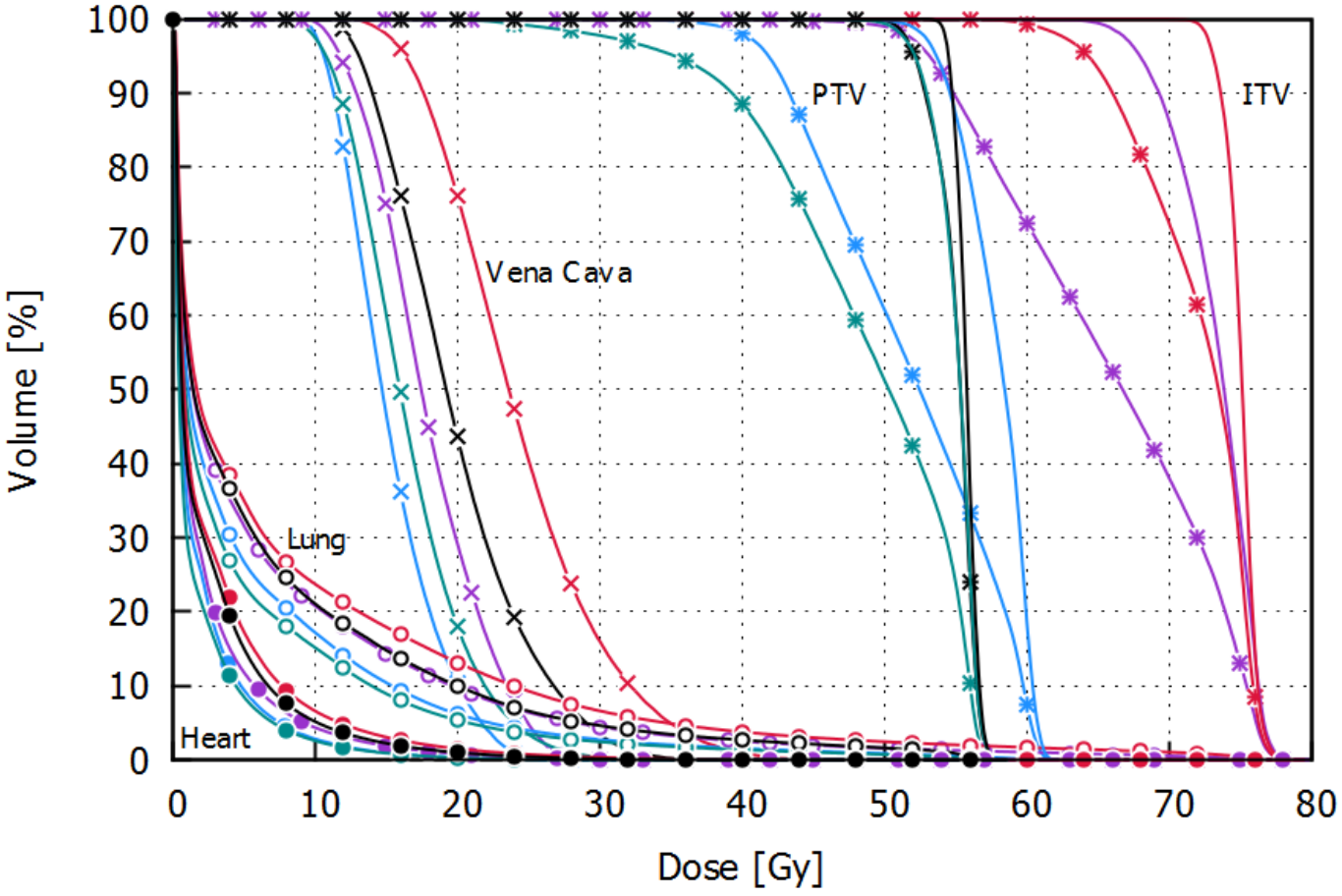


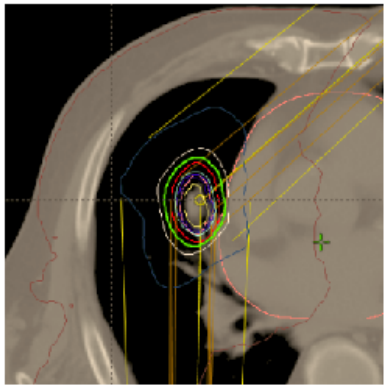
# Calculated dose
# 4 dose concepts





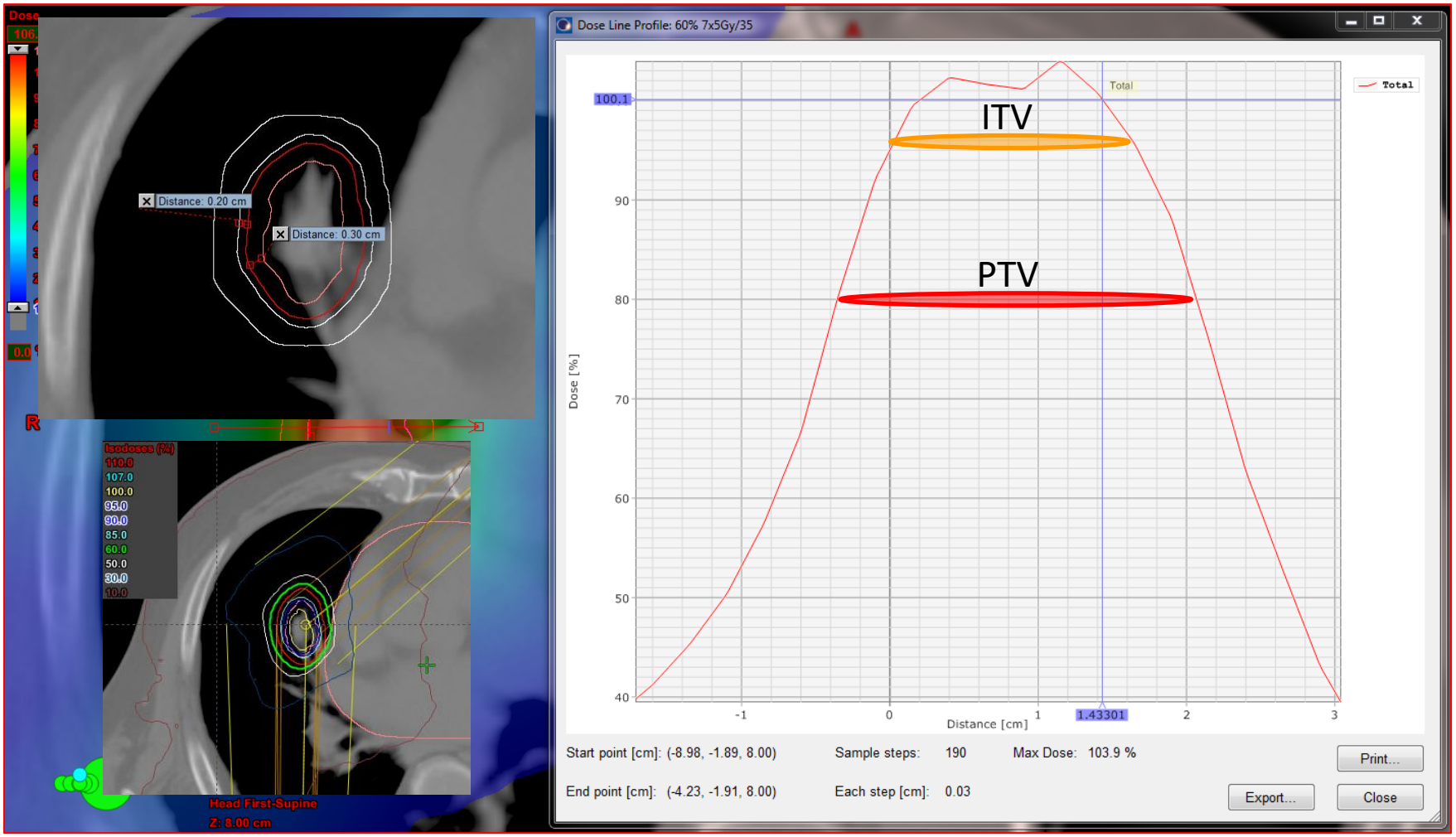
# DVH


Volume [%]
Dose [Gy]
PTV
ITV
Vena Cava
Lung
Heart
60% 35 Gy, 7x 5 Gy
65% 48 Gy, 8 x 6 Gy
80% 60 Gy, 8 x 7 Gy
ITV 55 Gy, 5 x 11 Gy
PTV 55 Gy, 5 x 11 Gy



# Dose profile

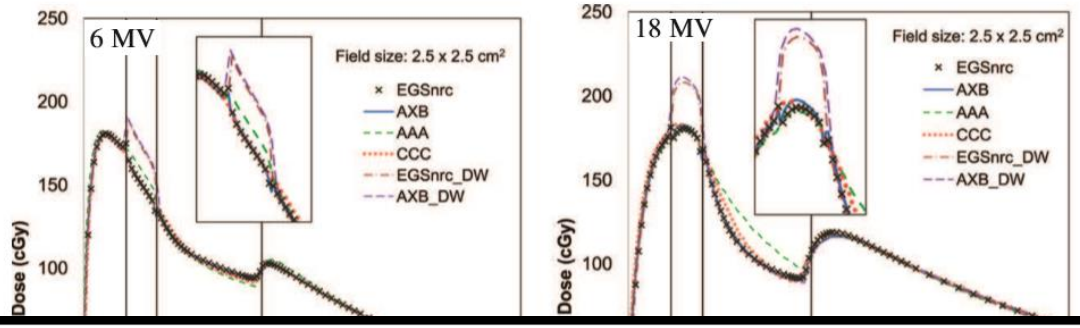




# Dose calculation algorithms
# Slab phantom



**Han *et al.*: Dosimetric evaluation of AXB in heterogeneities**
**Medical Physics, Vol. 38, No. 5, May 2011**




**Conclusions:** In heterogeneous media, AXB dose prediction ability appears to be comparable to MC and superior to current clinical convolution methods. The dose differences between AXB and AAA or CCC are mainly in the bone, lung, and interface regions.

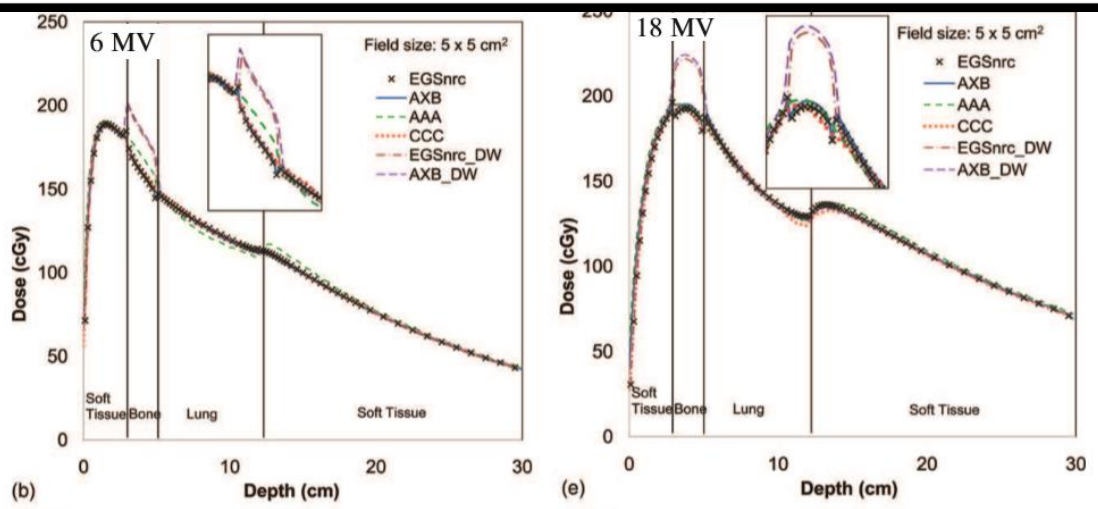
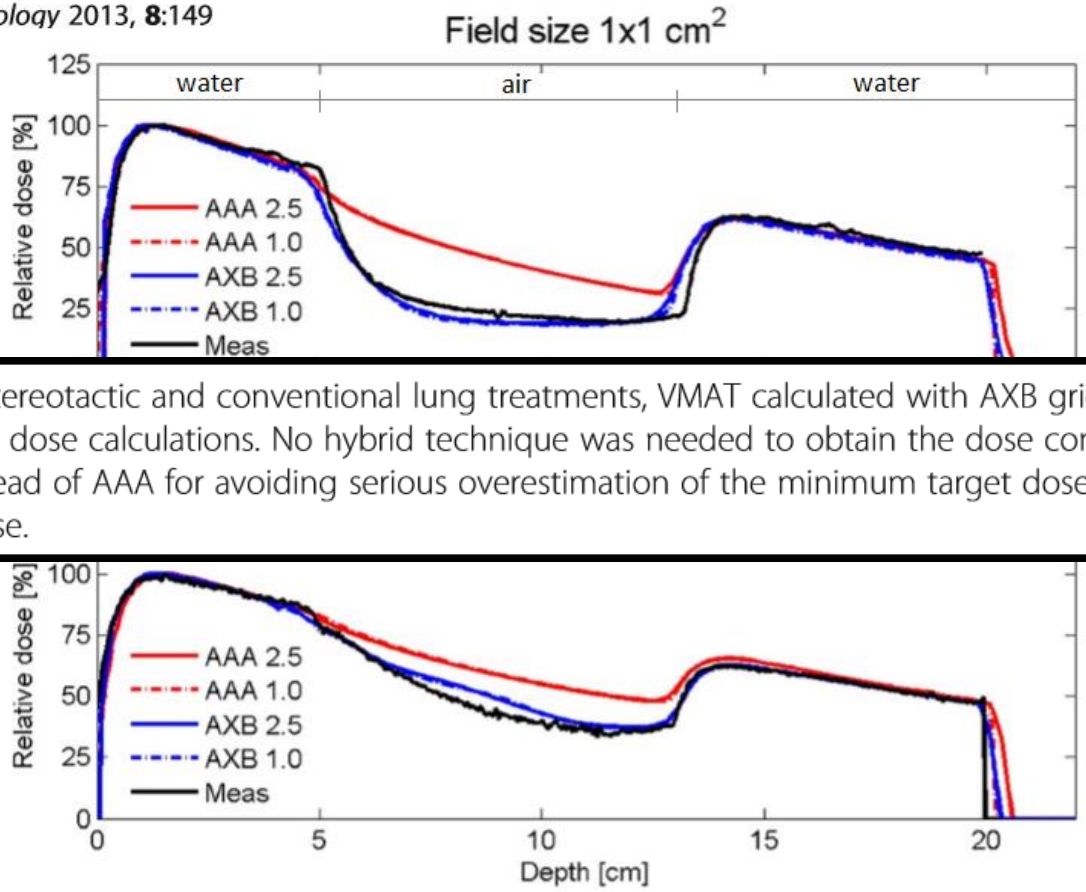



FIG. 5. Depth dose profiles in a heterogeneous slab phantom: 6 MV beams at field size of (a) 2.5 × 2.5, (b) 5 × 5; 18 MV beams at field size of (d) 2.5 × 2.5, (e) 5 × 5.

# Dose calculation algorithms
# Dose grid



Kroon *et al. Radiation Oncology* 2013, **8**:149




**Conclusions:** For stereotactic and conventional lung treatments, VMAT calculated with AXB grid size 2.5 mm resulted in accurate dose calculations. No hybrid technique was needed to obtain the dose constraints. AXB is recommended instead of AAA for avoiding serious overestimation of the minimum target doses compared to the actual delivered dose.

**Figure 1 Measured and calculated percentage depth dose curves in a slab-phantom.** Predicted percentage depth dose curves by AAA and Acuros XB grid sizes 2.5 and 1.0 mm compared to measured data using a slab-phantom with (top) 1.0x1.0 $cm^2$ and (bottom) 4.0x4.0 $cm^2$ 6 MV AP photon beams.

# Plan evaluation tools



https://en.wikibooks.org/wiki/Radiation_Oncology/Stereotactic_radiosurgery

## Treatment planning indices [edit]

- **Yomo; 2010** (PMID 19809786): Energy Index
  - EI = ID / (TV x PD)
  - ID = integral dose within target volume
  - PD = prescribed dose
  - Measure of dose homogeneity within target volume
- **Oliver; 2007** (PMID 17194494): Radical Dose Homogeneity Index
  - rDHI = $D_{min}$ / $D_{max}$
  - $D_{min}$ = minimum dose within target volume
  - $D_{max}$ = maximum dose within target volume
- **Oliver; 2007** (PMID 17194494): Moderate Dose Homogeneity Index
  - mDHI = $D_{95\%}$ / $D_{5\%}$
  - $D_{95\%}$ = dose to 95% of target volume
  - $D_{5\%}$ = dose to 5% of target volume
- **Paddick; 2006** (PMID 18503356): Dose Gradient Index
  - GI = $PIV_{half}$ / PIV
  - $PIV_{half}$ = Prescription isodose volume, at half the prescription isodose (e.g. at 25%)
  - PIV = Prescription isodose volume (e.g. at 50%)
  - Simplified UF Gradient Index
- **Wagner; 2003** (PMID 14575847): Conformity Gradient Index
  - CGI = (CGIc + CGIg) / 2
  - CGIc = TV / PIV * 100
  - CGIg = UF Gradient Index (see below)
- **Wagner; 2003** (PMID 14575847): UF Gradient Index
  - CGIg = 100 - (100 * ((REff,50%Rx - REff,Rx) - 0.3 cm))
  - REff,50%Rx = Effective radius of the isodose line that is equal to one-half of the prescription isodose volume
  - REff,Rx = Effective radius of the prescription volume
  - Evaluates the steepness of the gradient between prescription isodose line (e.g 50%) and half prescription isodose line (e.g. 25%)
- **Nakamura; 2001** (PMID 11728692): New Conformity Index
  - NCI = (TV x PIV) / $(TV_{PIV})^2$
  - Inverse Paddick Conformity Index
- **Paddick; 2000** (PMID 11143252): Paddick Conformity Index
  - Paddick CI = $(TV_{PIV})^2$ / (TV x PIV)
  - $TV_{PIV}$ = Target Volume covered by Prescription Isodose Volume
  - TV = Target Volume
  - PIV = Prescription Isodose Volume
  - This is two separate ratios multiplied together:
    - Undertreatment ratio: $TV_{PIV}$ / TV
    - Overtreatment ratio: $TV_{PIV}$ / PIV
- **ICRU; 1999** (ICRU Report): Conformity Index
  - CI = TV / PTV
  - [illegible] volume = volume eclosed by a given isodose surface (e.g. 50%, 95%)
  - PTV: Planning target volume = CTV + IM + SM
  - RTOG conformity index with ICRU terminology
- **Knoos; 1998** (PMID 9869245): Radiation Conformity Index
  - [illegible] / PIV
  - PTV: Planning target volume = CTV + IM + SM
  - PIV = Prescription Isodose Volume
  - Inverse of RTOG Conformity Index
- **RTOG; 1993** (PMID 8262852): Conformity Index
  - Conformity Index PITV = PIV / TV
  - PI = prescription isodose volume
  - TV = target volume
  - Normal 1.0-2.0, minor deviation if >2.0 or <1.0, major deviation if >2.5 or <0.9
- **RTOG; 1993** (PMID 8262852): Homogeneity
  - Homogeneity MDPD = MD / PD
  - MD = maximum dose within target volume
  - PD = prescribed dose
  - Minor deviation if >2.0, major deviation if >2.5
- **RTOG; 1993** (PMID 8262852): Coverage
  - Coverage = $D_{min}$ / PD
  - $D_{min}$ = minimum dose within target volume
  - PD = prescribed dose
  - Minor deviation if <0.9, major deviation if <0.8

- Homogeneity Index (HI) – Wu 2003
- Conformity Index – ICRU 1999
- Gradient Index (GI) – Paddick 2006

# Homogeneity Index (HI)



$$HI = [(D_2 - D_{98})/D_p] \times 100$$

$D_2$ - dose to 2% of the target volume
$D_{98}$ - dose to the 98% of the target volume
$D_p$ - prescribed dose

Example:
Prescription 24 Gy covers PTV (ICRU)
$D_2$ = 25 Gy (104%)
$D_{98}$ = 23 Gy (96%)

$HI = 25-23/24 \times 100 = 8,3$
*The ideal value is 0.*

# Conformity Index (CI)



$$CI = TV / PTV$$

TV - Treated Volume - volume enclosed by a prescribed isodose
PTV - Planning Target Volume

Example:
Prescription 20 Gy as 80% covers PTV
$TV_{20Gy} = 4{,}06\ cm^3$
$PTV = 3{,}37\ cm^3$

$CI = 4{,}06\ cm^3 / 3{,}37\ cm^3 = 1{,}2$
*The ideal value is 1.*

# Gradient Index (GI)



$$GI = PIV_{half} / PIV$$

$PIV_{half}$ - volume enclosed by a half of prescribed isodose
PIV - volume enclosed by a prescribed isodose

Example:
Prescription 20 Gy as 80% covers PTV
$PIV_{10Gy} = 18.54\ cm^3$
$PIV_{20Gy} = 4{,}06\ cm^3$

$GI = 18.54\ cm^3 / 4{,}06\ cm^3 = 4{,}6$
*The smaller the better.*
*50% isodose should be within 1 cm from PTV.*

# Small field dosimetry
# General aspects



Under which conditions can you consider a field as small?

- If the field is smaller than approximately 4 cm x 4 cm.
- If the focus is partially hidden by the collimators.
- If lateral electron equilibrium is not given in the center of the field.

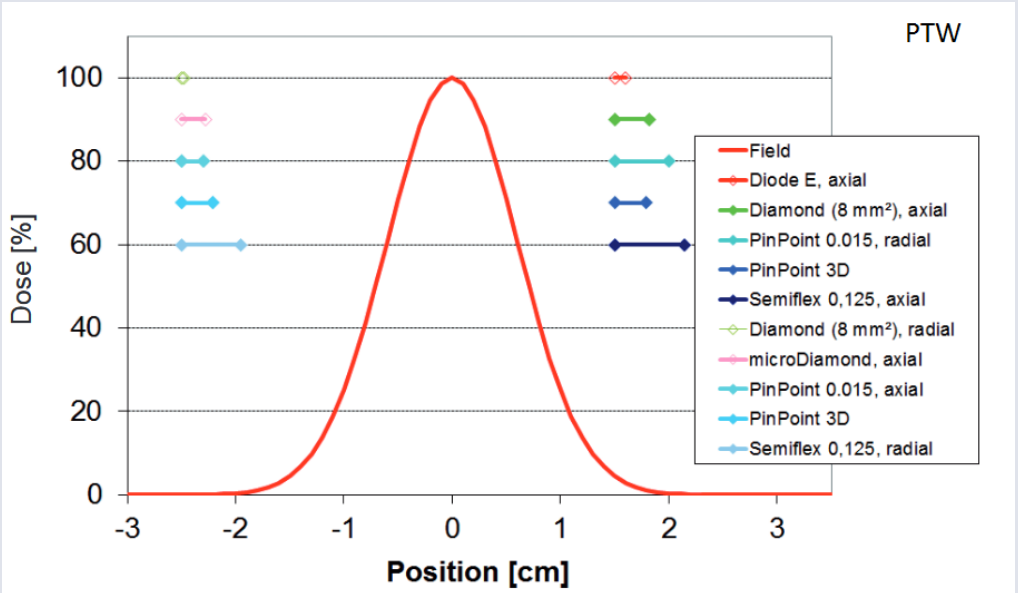
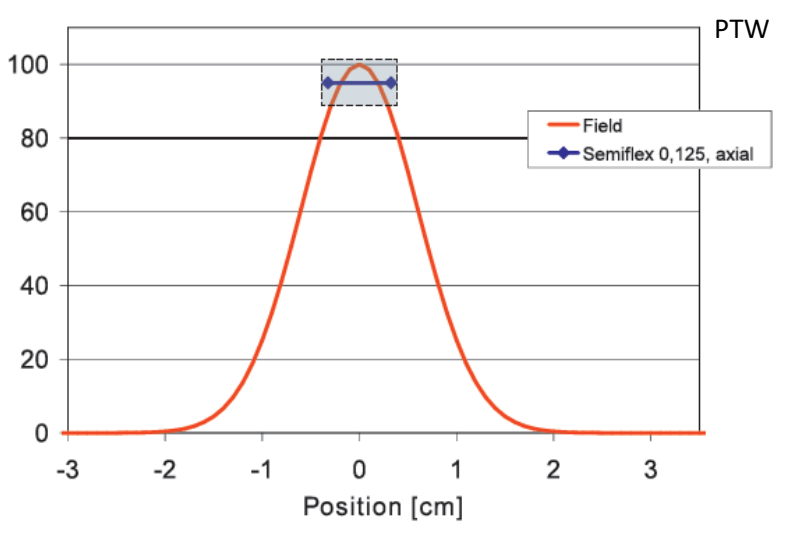


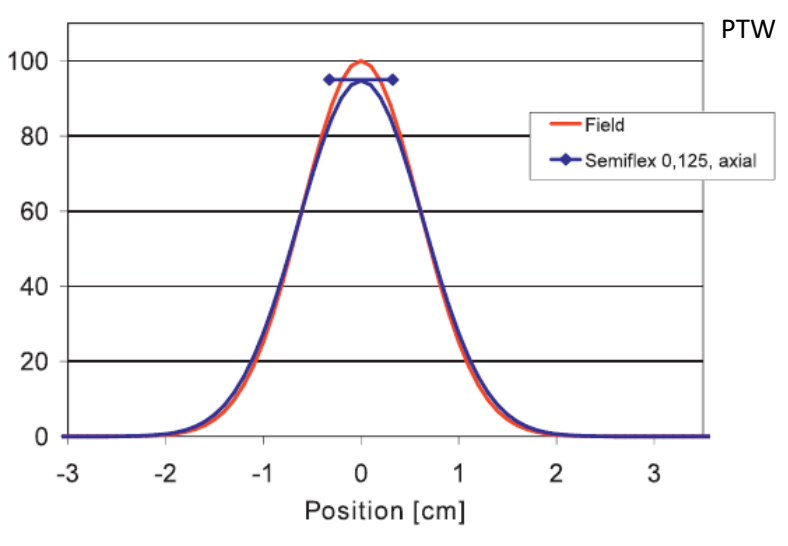

**Figure 1** Size comparison of a 1.4 cm x 1.4 cm FWHM Gaussian shaped field with some small field detectors.

# Small field dosimetry
# Dose volume effect



- Semiflex 0.125 cm³ chamber will average the dose across its sensitive volume, depicted as a blue box. When you move the chamber through the field, it will always average across its volume at every measurement position.
- The blue curve shows the signal after averaging. The CAX value of the dose is underestimated, and the penumbra is broadened.

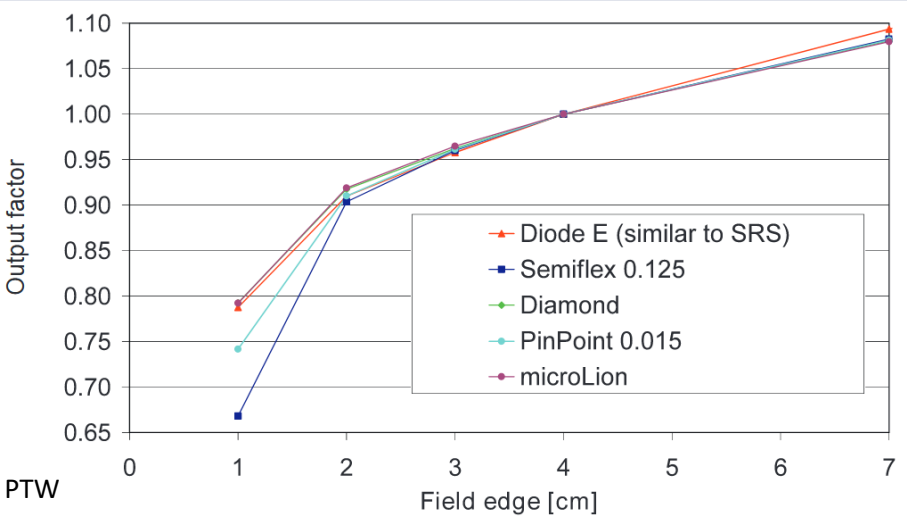


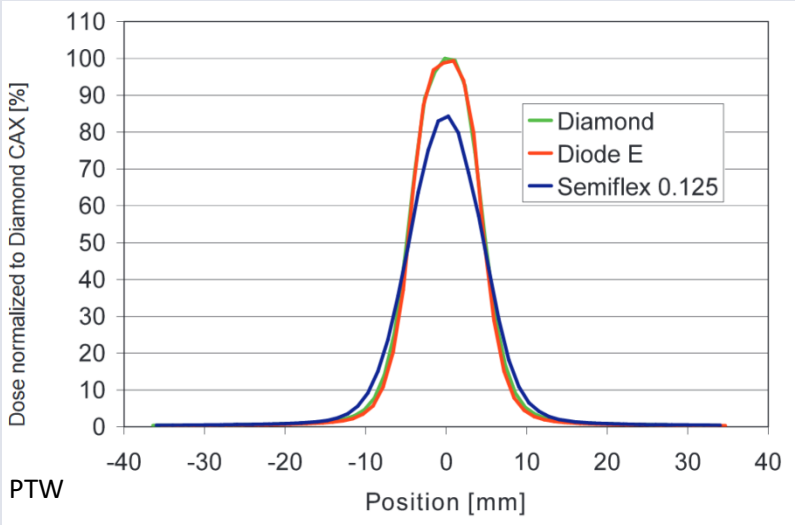



# Dose volume effect
# Output factors and profiles for 1 cm x 1 cm field



- The reduction of the measured dose for the Semiflex and the PinPoint chamber is clearly visible.
- Again, the dose reduction of the Semiflex chamber in the field center is apparent.



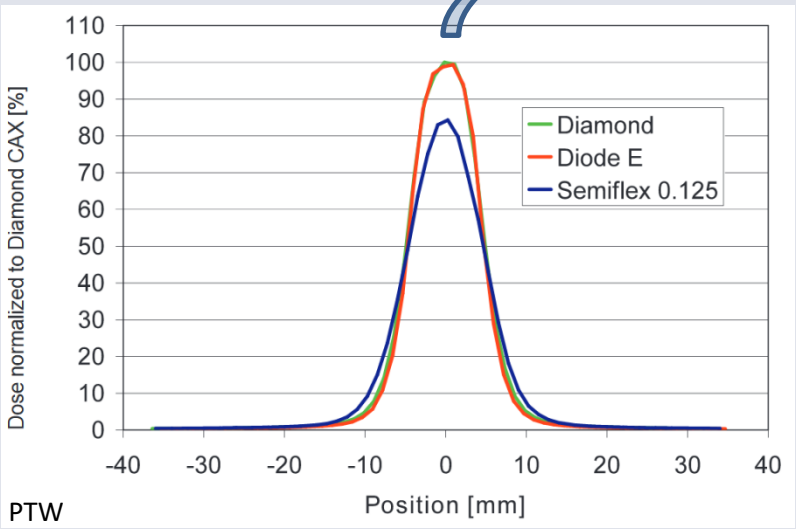



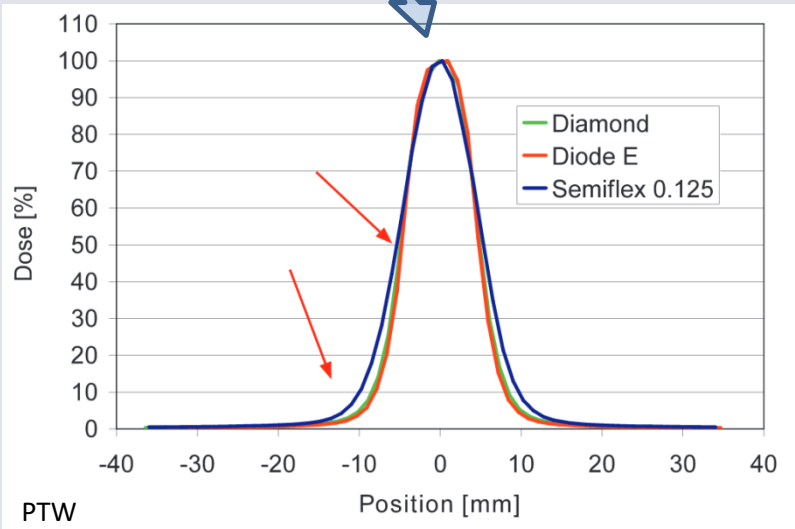
# Dose volume effect
# Profile of 1 cm x 1 cm field with CAX normilization.

In addition to penumbra broadening two more effects are visible (indicated by arrows):

- the FWHM of the Semiflex measurement seems larger than that of the other detectors. This is in contrast to the original measurement without CAX normalization,
- the dose in the out-of-field region is overestimated.

CAX normalization



# Small field dosimetry
# Summary



- If your detector is larger than roughly 1/4th of the lateral field dimension, you should watch out for a volume effect of several percent.
- If the volume effect is present,
  - the dose in the field center will be underestimated;
  - the penumbra appears wider than it is.
- If in addition to the volume effect you perform a CAX normalization in a small field,
  - the field (at half maximum) will appear wider than it is;
  - the dose in the out-of-field region will be overestimated;
  - the dose of PDDs at large depths can be overestimated.
- There exists no single detector that is suitable to perform high accuracy measurements in very small as well as very large fields. For absolute dose measurements, all small field detectors except air-filled ionization chambers must be **cross-calibrated** against a medium-size ionization chamber.

# Teşekkür ederim!

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