PET for HN Cancer ART: Dose Response Feedback and Adaptive DPbN

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Disclosures

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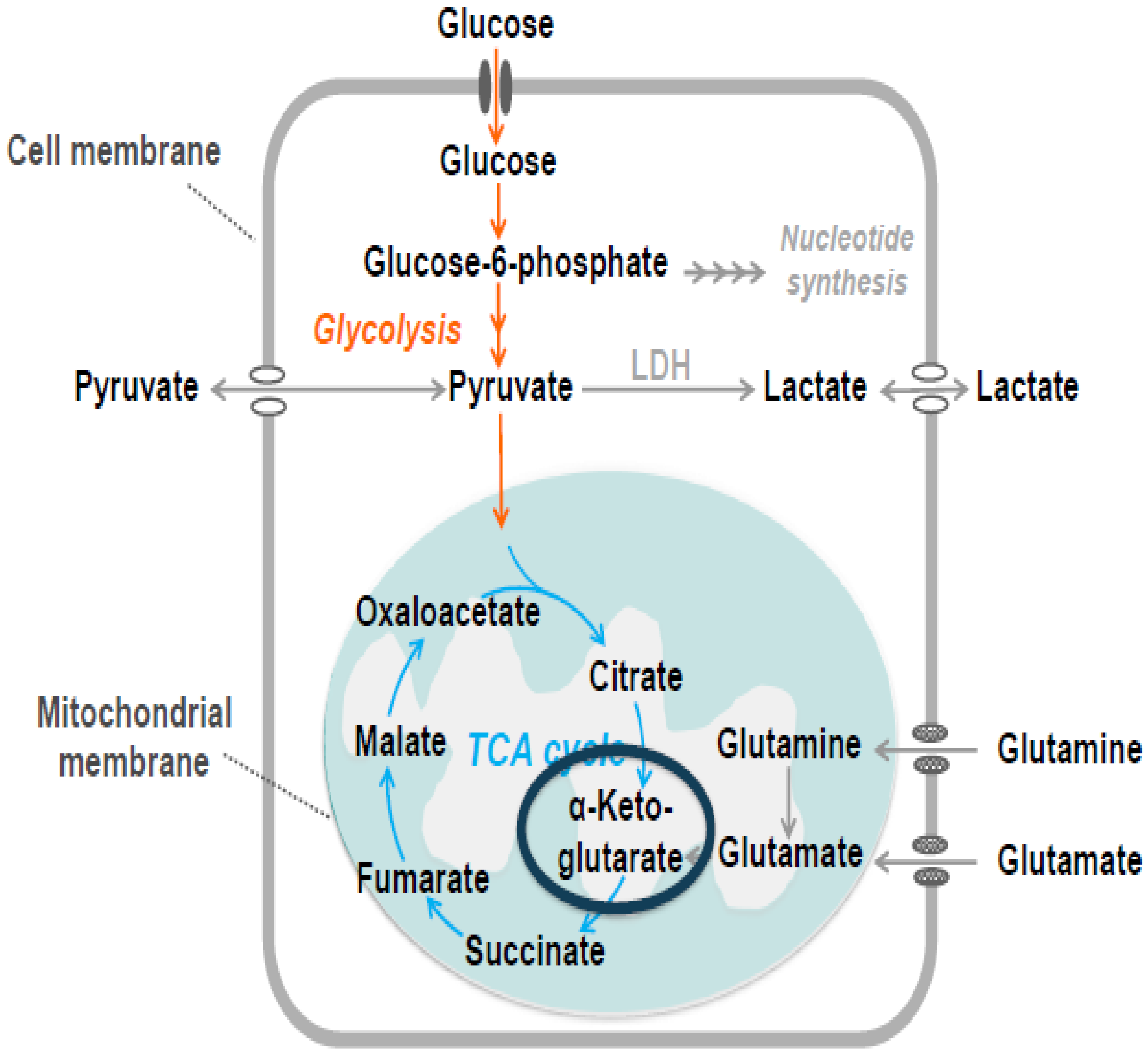
Learning Objectives

- Metabolic imaging and dose response feedback for adaptive tumor dose painting
- Optimization of dose painting by number in target
- Clinical feasibility & workflow for adaptive DPbN

Metabolic Imaging

- **PET**: [^{18}F, ^{11}C] Glucose, Glutamine, Glutamate, Lactate, Acetate, Choline
- **MRI**: Glu-CEST, Hyperpolarized [1-^{13}C] Pyruvate, Lactate, Glucose



Metabolic Imaging: Application in RT

- Tumor has enhanced metabolic activity, which promotes the clinical use of metabolic imaging for target identification/delineation and post treatment response monitoring
- Metabolic image may not be a specific bio-marker to guide a targeting drug, but could be very useful for radiation treatment due to its link to all cancer hallmarks*

*D Hanahan & R Weinberg, Hallmarks of Cancer: the Next Generation. Cell 144, 2011

- Radioresistant tumor cells should maintain unaltered metabolic activity as measured using a metabolic image following fractionated radiation treatment
  - *Therefore, it is possible to use Tumor Voxel Dose Response derived from **temporal changes** of metabolic image voxel intensity as the feedback for treatment adaptation*

FDG-PET Imaging/Dose Response Feedback

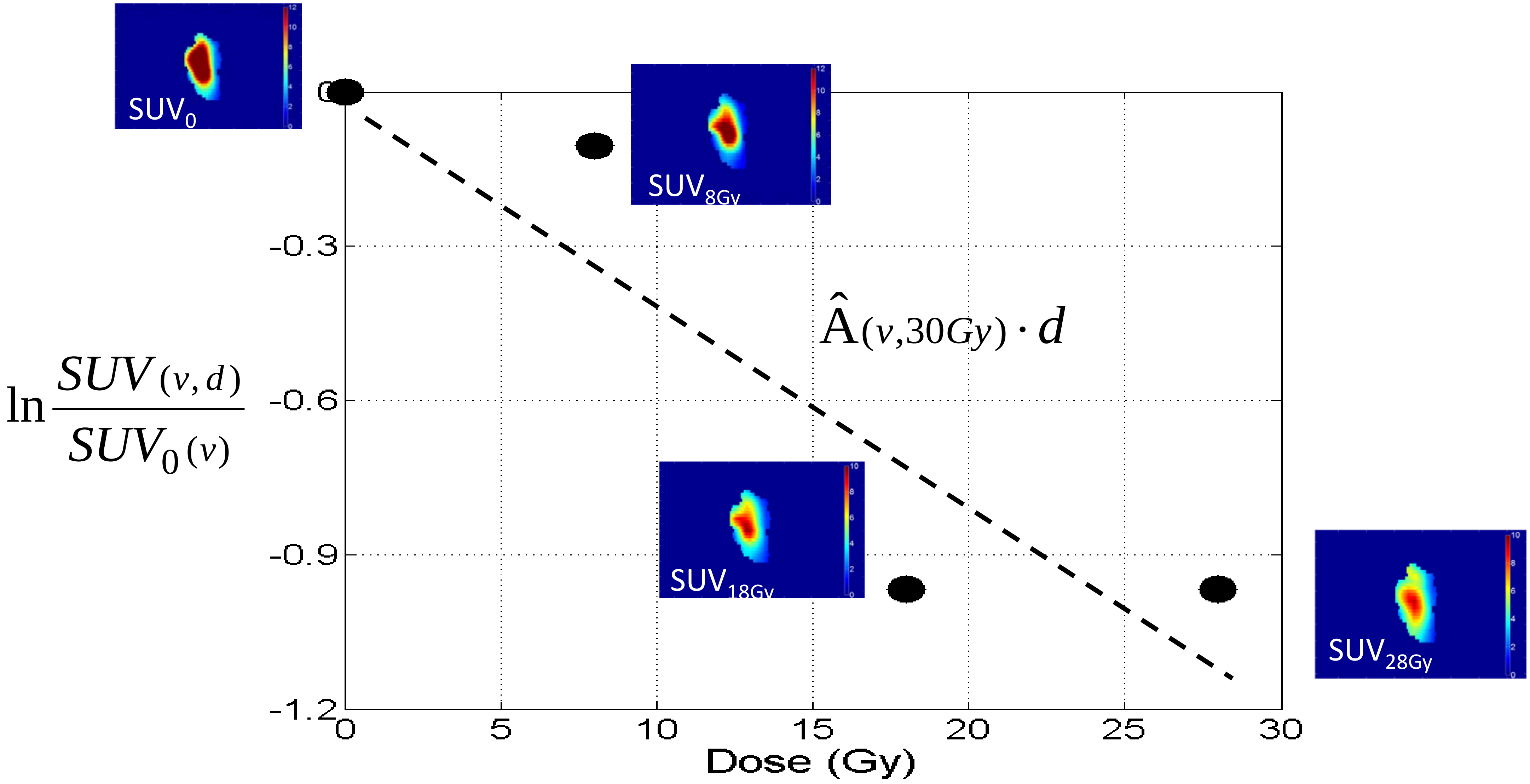
FDG PET/CT image is a metabolic image, *not the best*, but very practical in clinics with relatively low cost,

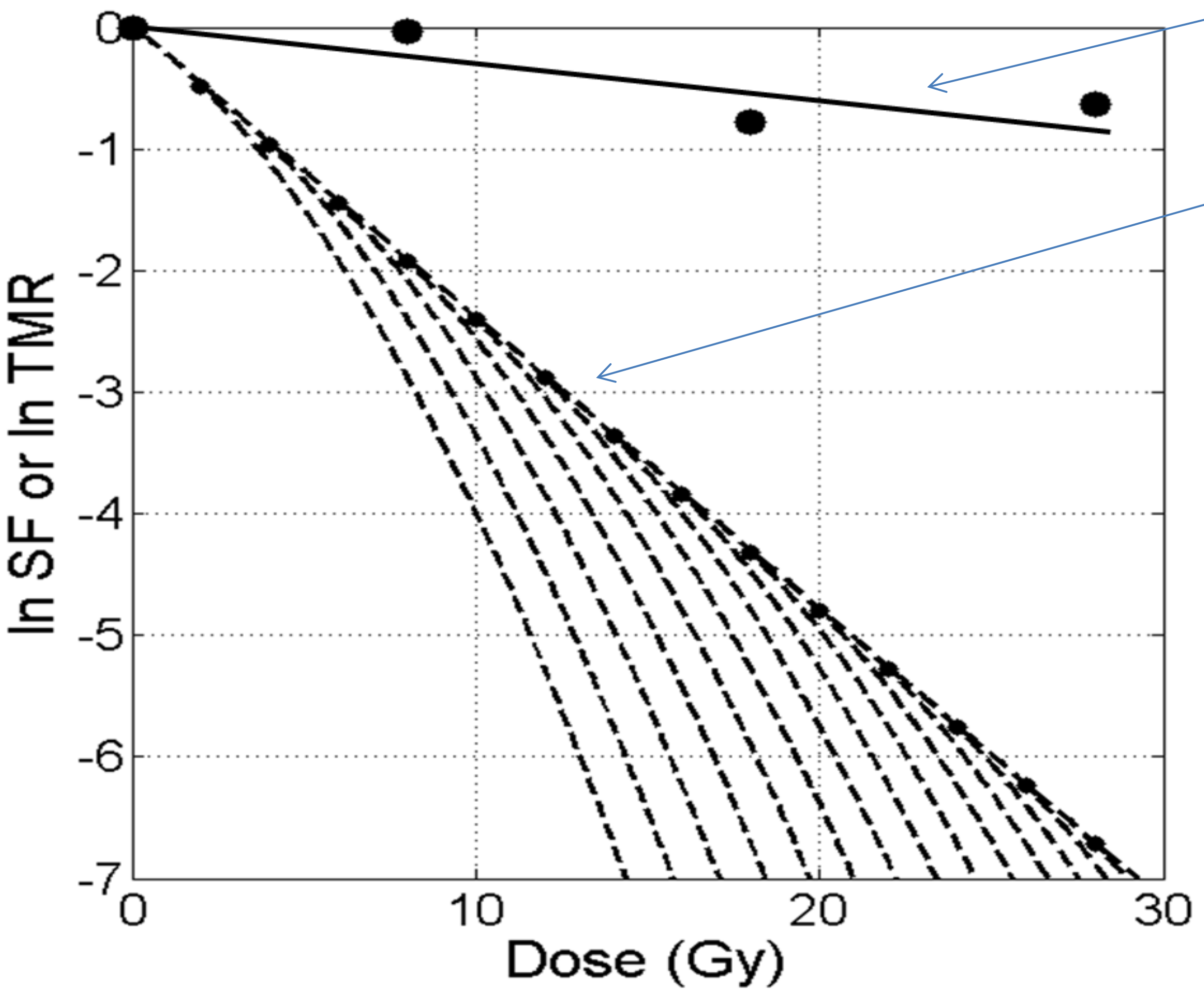
I. Tumor Voxel Dose Response Matrix (**DRM**) from the temporal changes of image intensity obtained during the treatment course (PET/CT deformable image registration)

II. Tumor voxel Dose Prescription Function (**DPF**) with using the **DRM** and its baseline **SUV**$_0$

III. **DPF** is used to be the objective function for tumor **DPbN** planning optimization

FDG-PET Imaging: Estimate Tumor Dose Response Matrix





$$\hat{A}(v,\bar{d}) \cdot d$$

$$\frac{\ln SF_2(v)}{2} \cdot d$$

SF_2 - tumor voxel survival fraction in 2Gy

A linearly proportional to ***SF$_2$***, i.e.

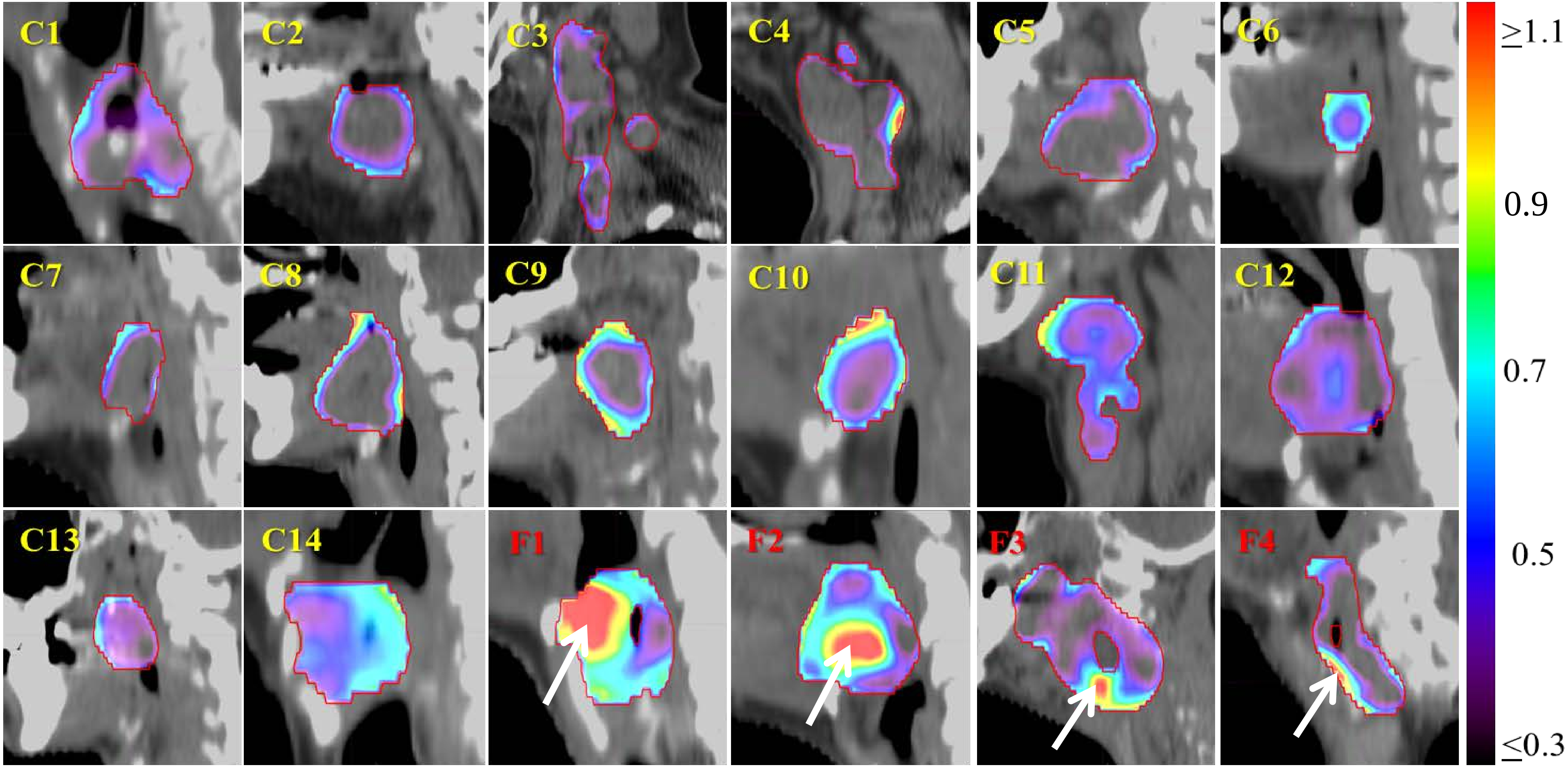
$$\hat{A}(v,\bar{d}) = k \cdot \frac{\ln SF_2(v)}{2};$$

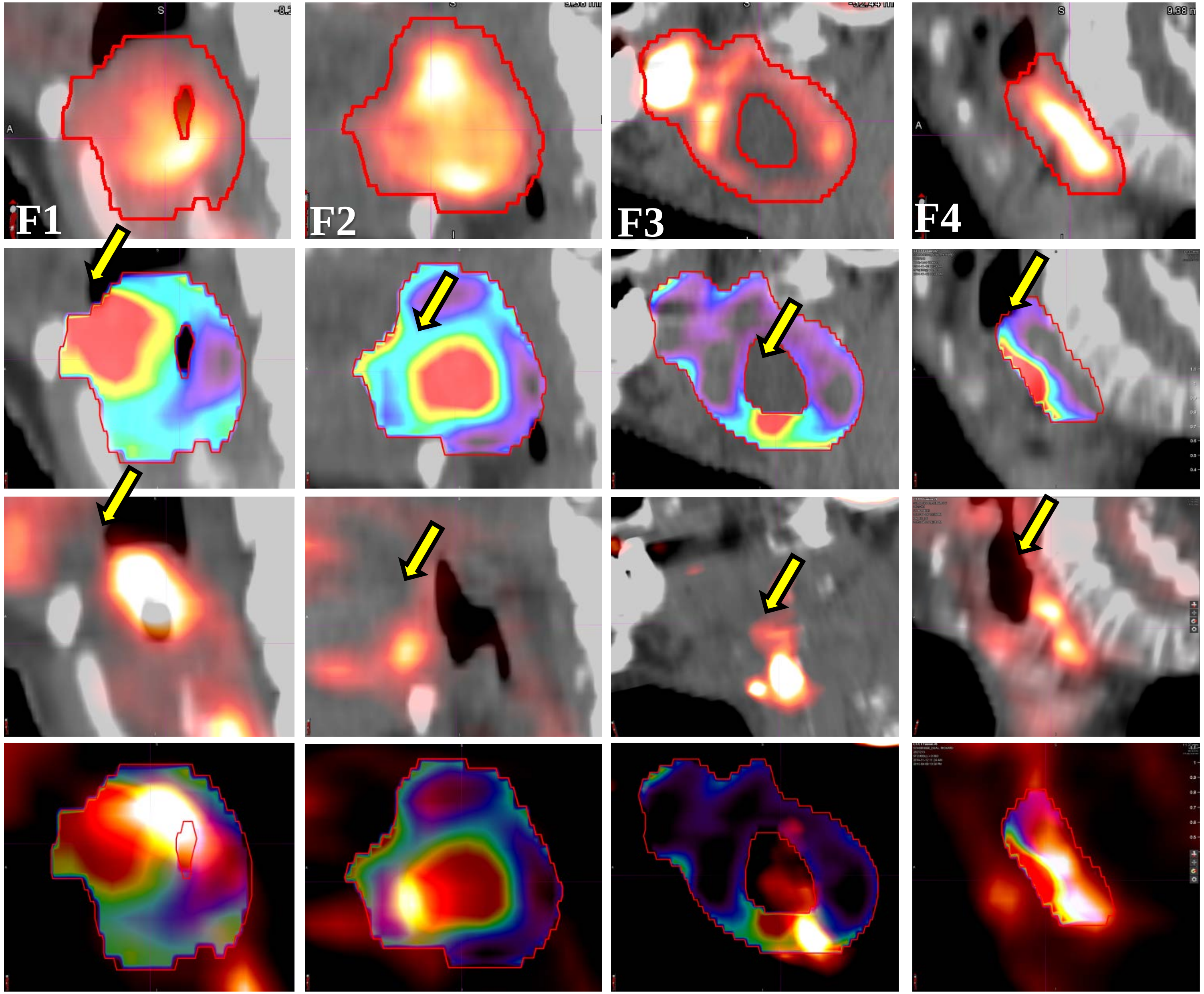
$$SF_2(v) \sim \exp\left(\frac{2 \cdot \hat{A}(v,\bar{d})}{k}\right) = DRM(v,\bar{d})$$

$DRM(v,30Gy) = \exp\left(31.75 \times \hat{A}(v,30Gy)\right)$ Calibrated to have the numerical range of SF_2.

Bjork-Eriksson T, West C, etc. The in vitro radiosensitivity of human HN cancer. British J of Cancer. 1998;72:2371-5. **Mean-*SF$_2$* = 0.48**

Tumor Voxel Dose Response Matrix (DRM)





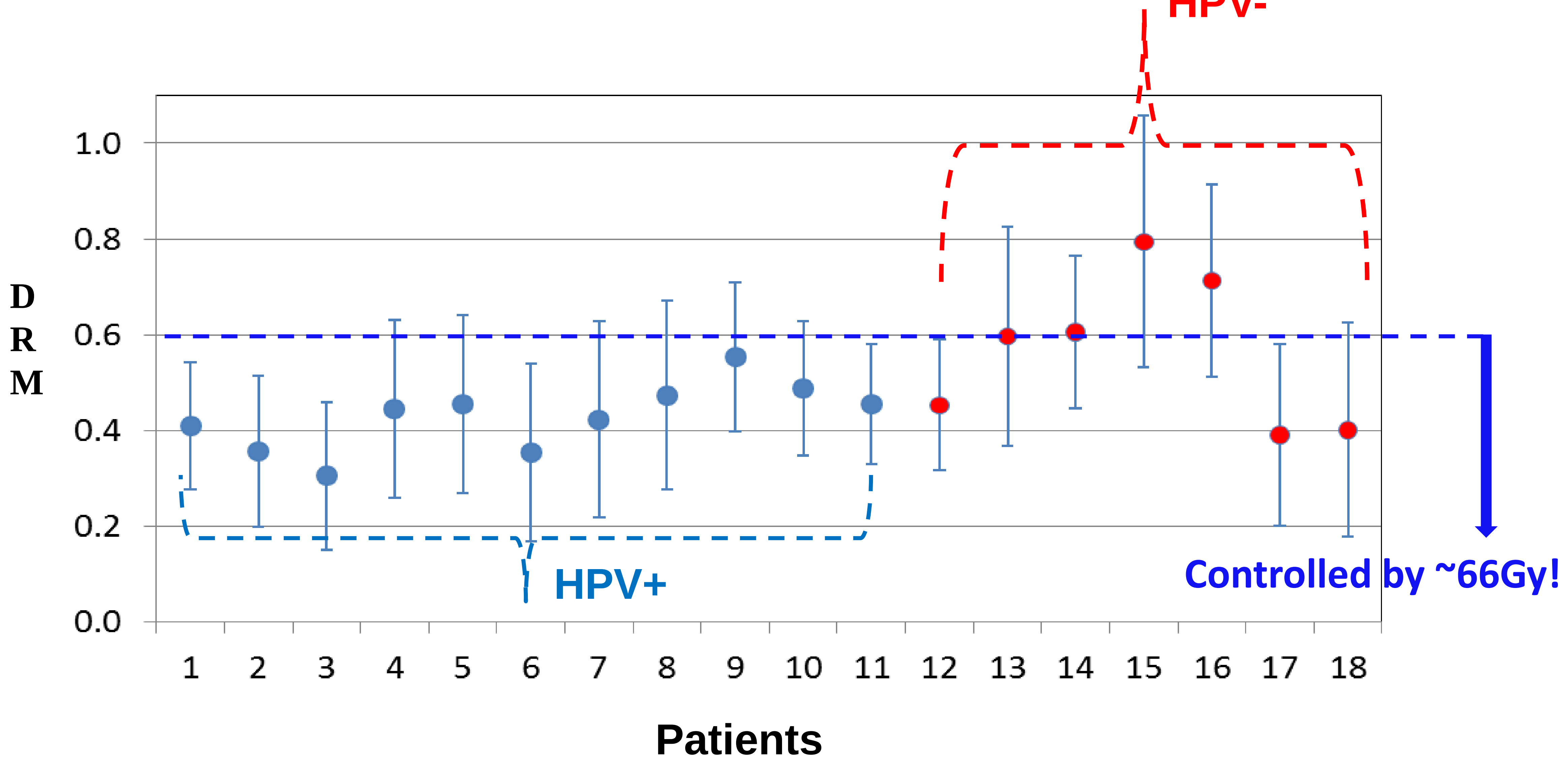
Pre-tx SUV

DRM
(Created in the week 4)

Local failure
(3/6 months Post-Tx PET)

Overlap

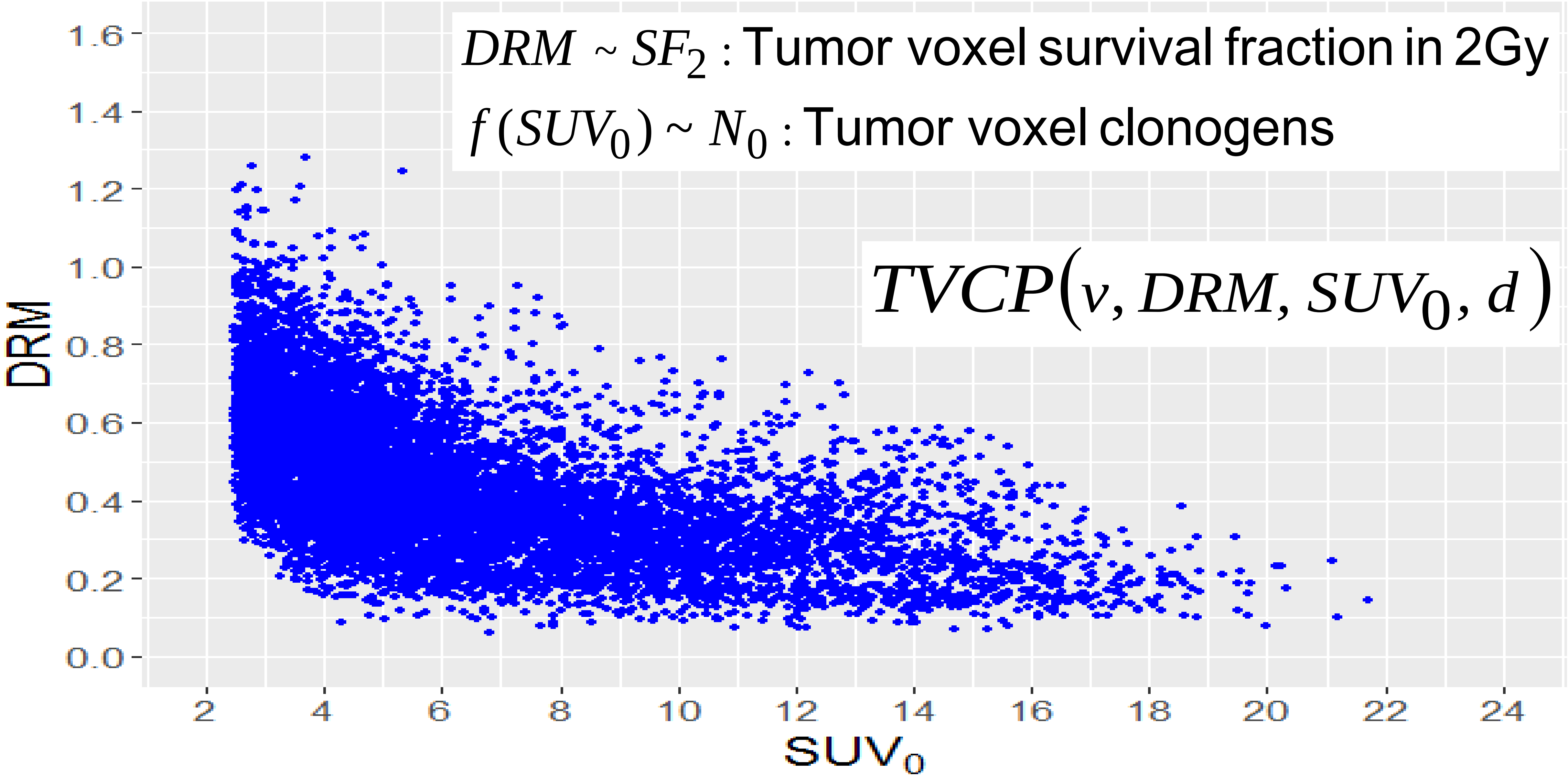
Inter- & Intra-tumoral Variation in Dose Response

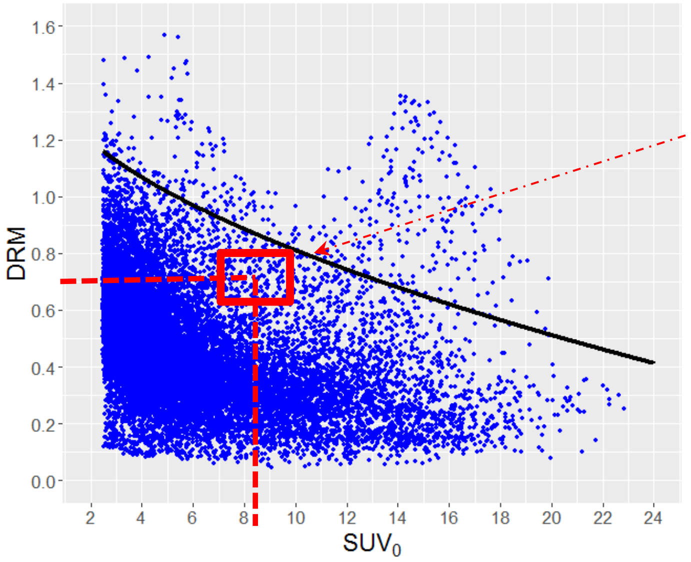


Tumor Voxel Dose Prescription Function (DPF)

- Mathematic link between specific values of imaging intensity and the optimum clinical dose to be prescribed to the corresponding tumor voxel
- DPF can be designed to achieve a desired tumor control, while maintains the minimized integral dose
  - *Is this necessary? Can we safely increase the uniform dose in target as high as needed?*

Locally Controlled Tumors (35x2Gy)

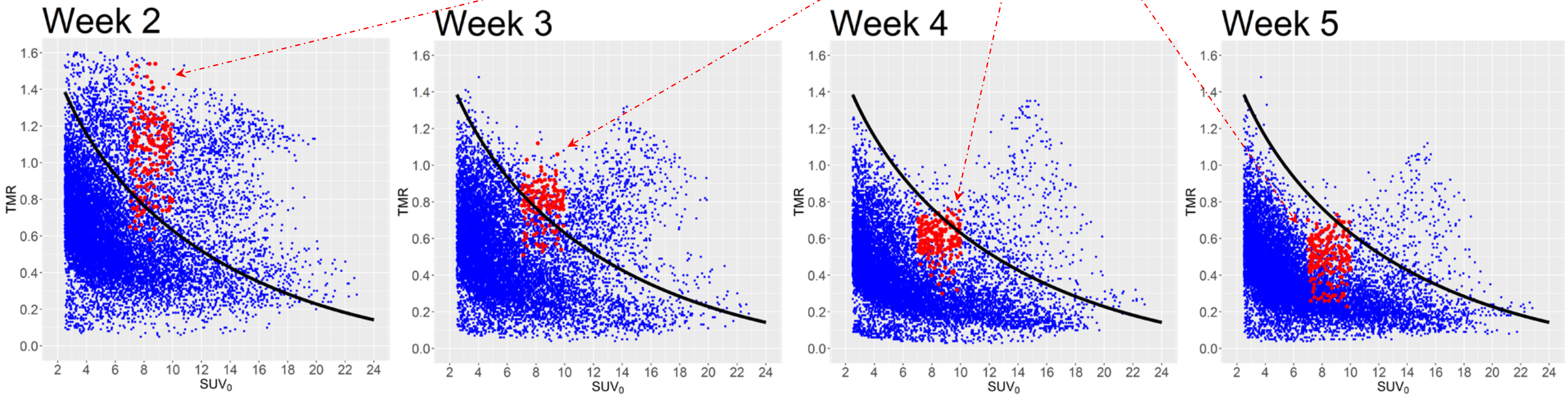




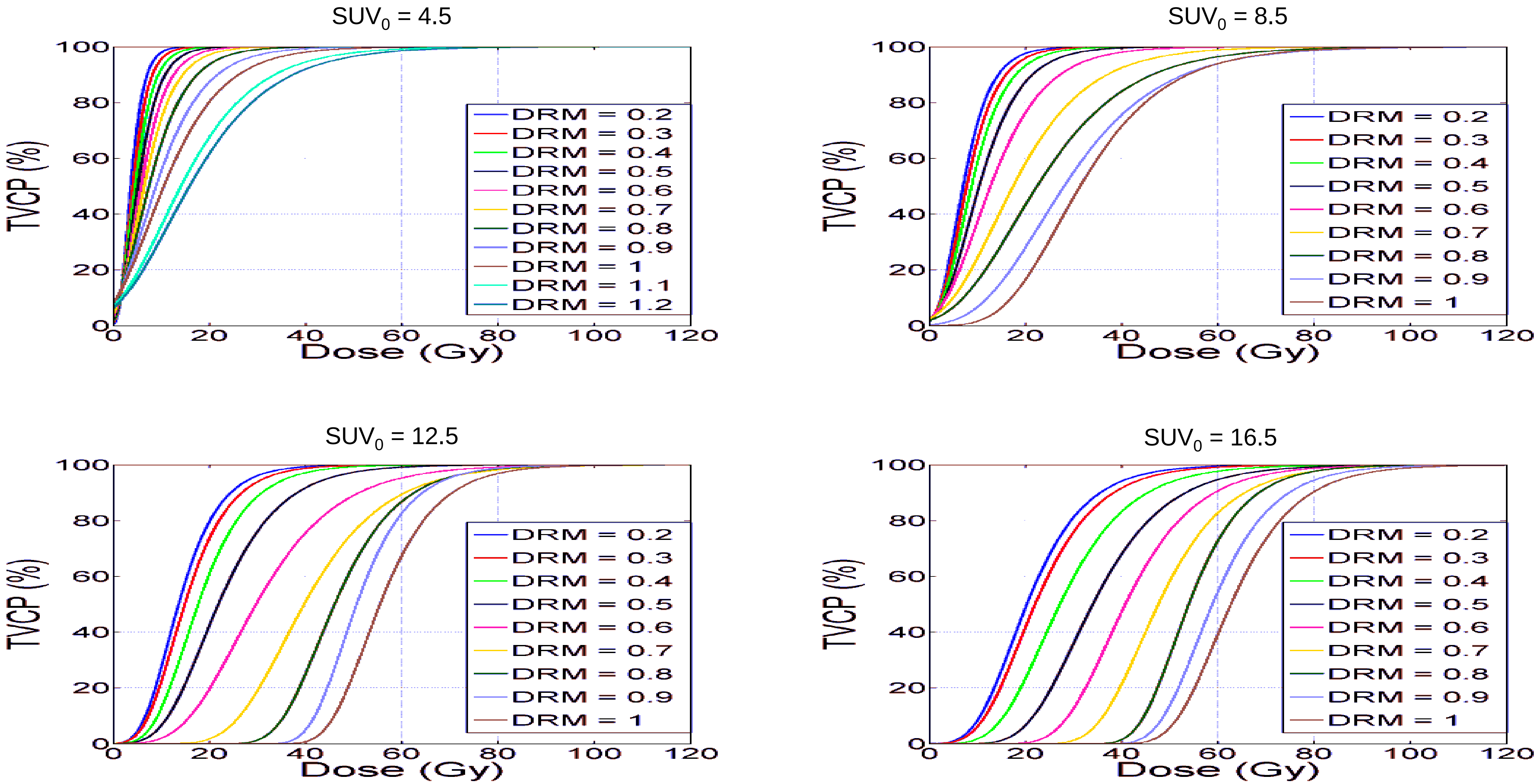
$$TVCP(SUV_0, DRM, TCD_{50}, \gamma_{50}, d)$$

determined using a likelihood of potential control and failure of tumor voxel on each weekly (SUV_0 , TMR) plot

$$Max\, L(TCD_{50}, \gamma_{50} \mid TVCP(d_i); i = 1, 2, ..., 7)$$



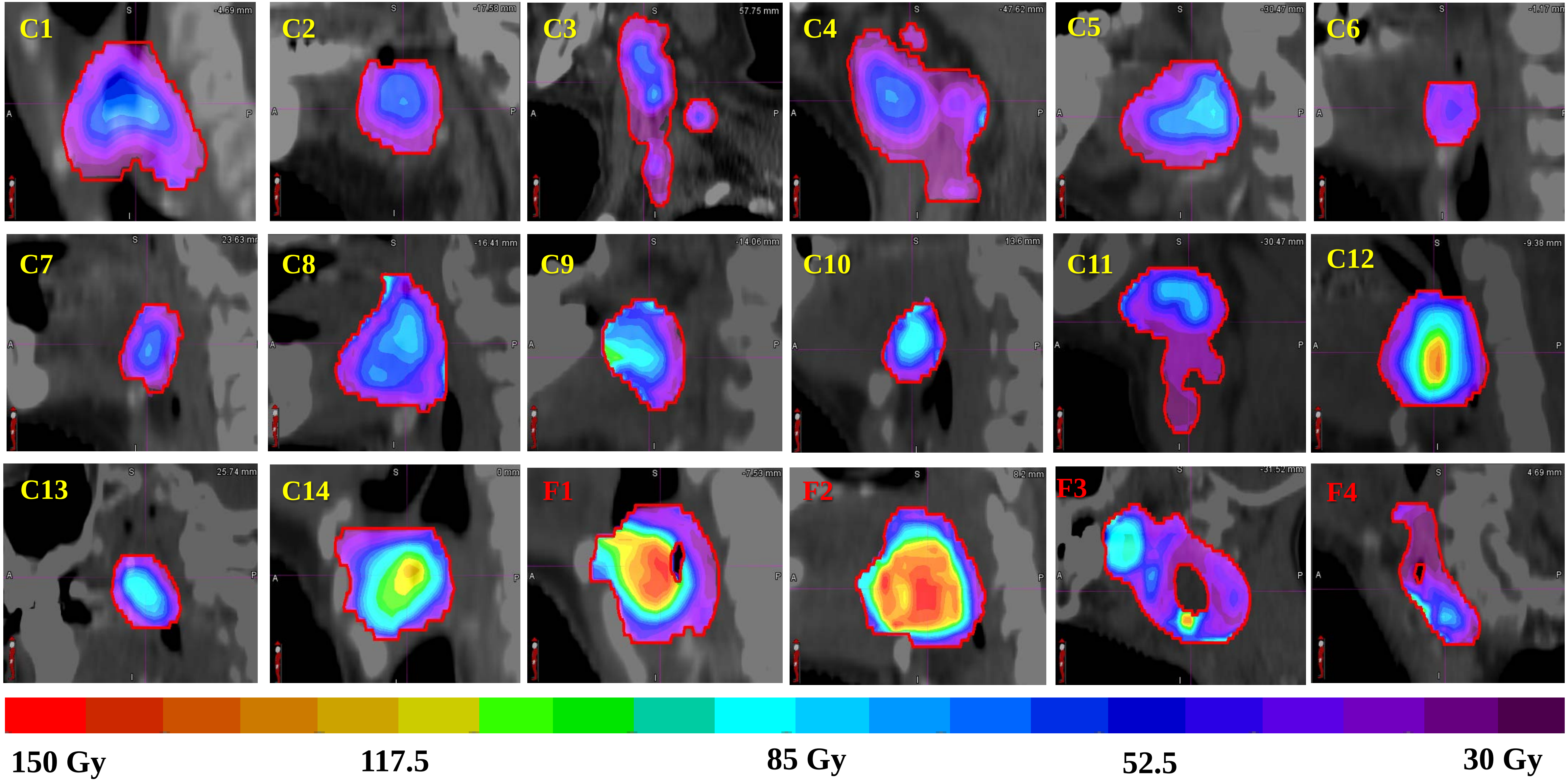
Dose Prescription Function (DPF): TVCP Lookup Table



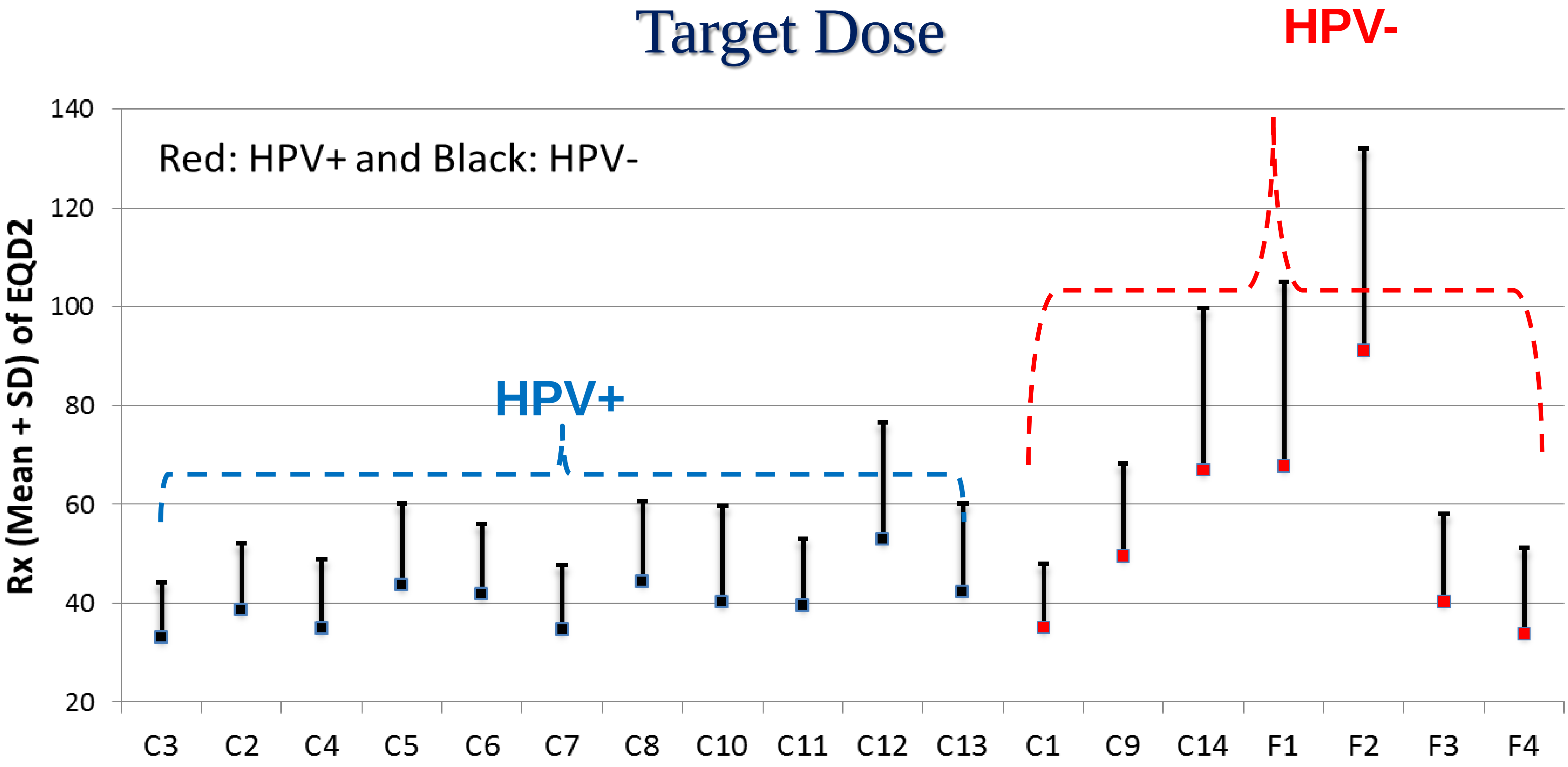
Dose Prescription Function: TVCP Lookup Table

(TCD_{50}, γ_{50})	$SUV_0 = 4.5$	$SUV_0 = 8.5$	$SUV_0 = 12.5$	$SUV_0 = 16.5$
DRM = 0.2	(3.72, 0.72)	(7.07, 0.63)	(13.62, 0.82)	(20.34, 0.87)
DRM = 0.3	(4.11, 0.66)	(7.79, 0.62)	(14.9, 0.82)	(22.05, 0.88)
DRM = 0.4	(4.6, 0.62)	(8.8, 0.62)	(17.69, 0.87)	(27.18, 0.97)
DRM = 0.5	(5.16, 0.59)	(10.41, 0.62)	(21.91, 0.87)	(34.01, 1.15)
DRM = 0.6	(5.81, 0.56)	(12.77, 0.58)	(29.71, 0.91)	(40.78, 1.44)
DRM = 0.7	(6.45, 0.52)	(17.44, 0.58)	(39.7, 1.24)	(47.65, 1.73)
DRM = 0.8	(7.46, 0.49)	(22.4, 0.61)	(46.08, 1.83)	(53.99, 2.42)
DRM = 0.9	(8.93, 0.46)	(28.03, 0.73)	(50.65, 2.42)	(58.92, 2.42)
DRM = 1.0	(10.58, 0.45)	(31.38, 0.91)	(55.51, 2.42)	(62.74, 2.42)
DRM = 1.1	(14.08, 0.47)	NA	NA	NA
DRM = 1.2	(15.87, 0.48)	NA	NA	NA

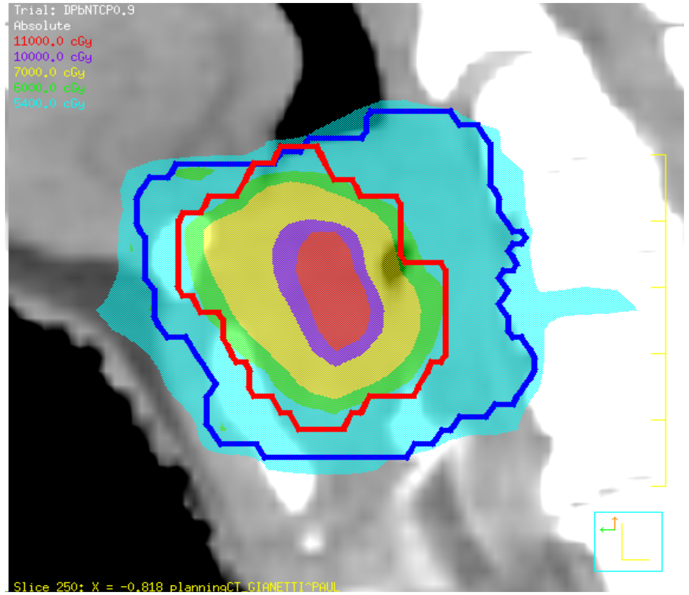
Tumor Voxel DPF (TCP = 0.9) design based on (SUV_0, DRM)



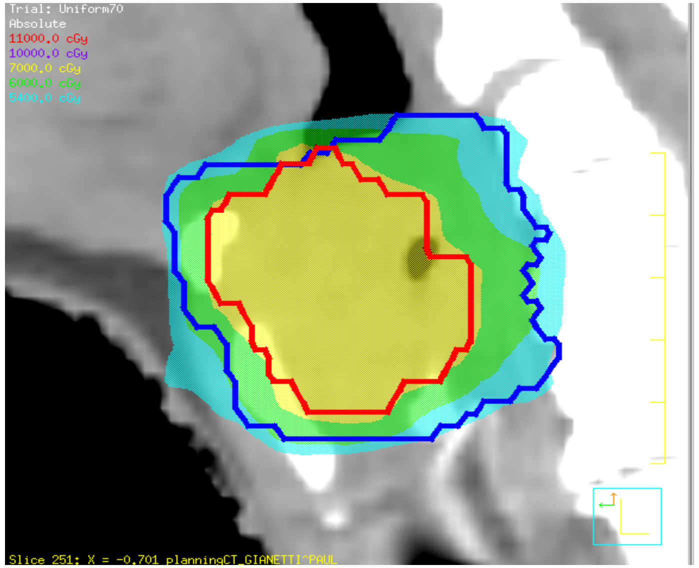
Target Dose



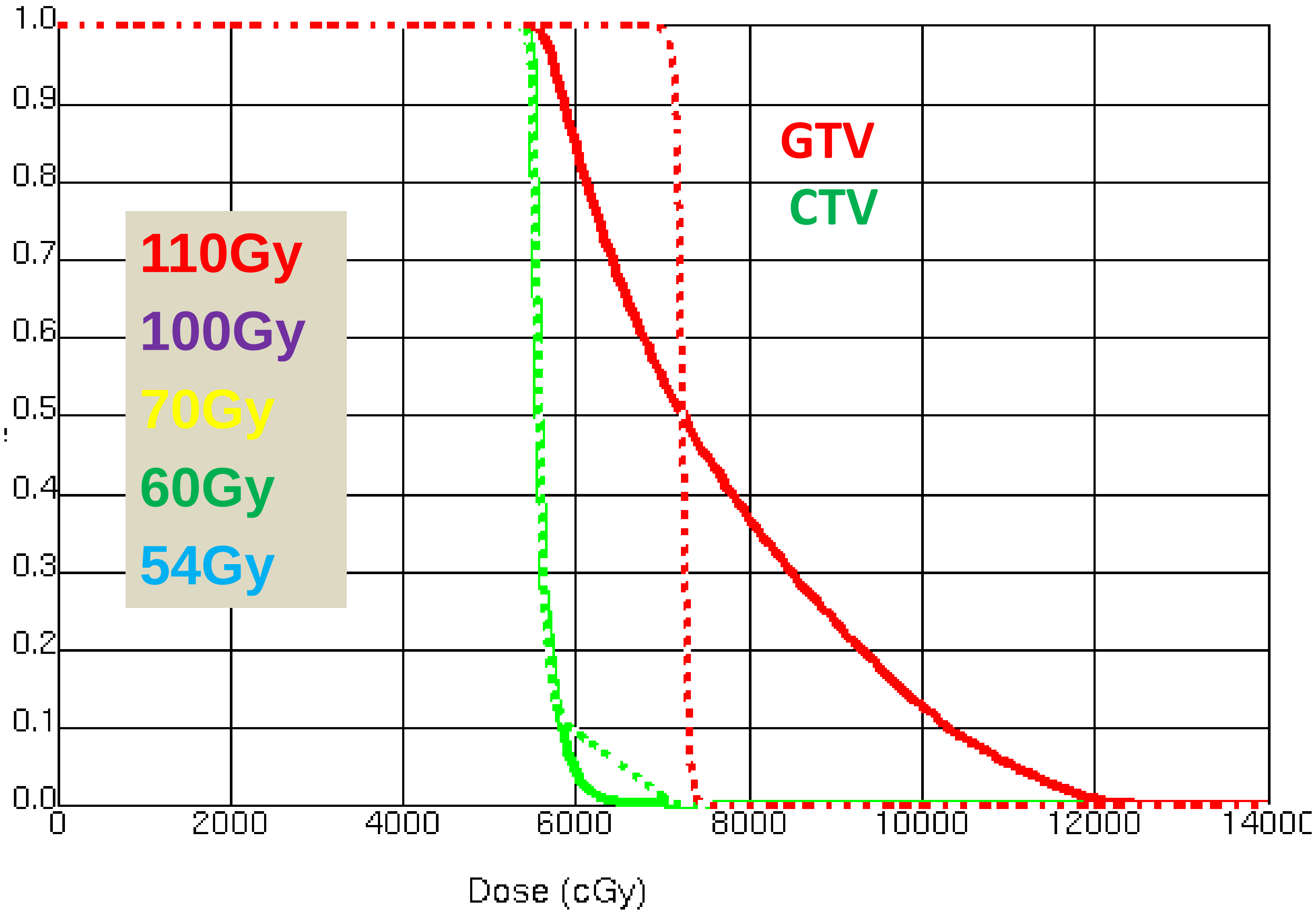
Can it be managed safely by using the uniform prescription dose up to 150Gy?



DPbN (Solid Line; TCP = 0.9)



Convent (Dash Line; TCP=0.17)

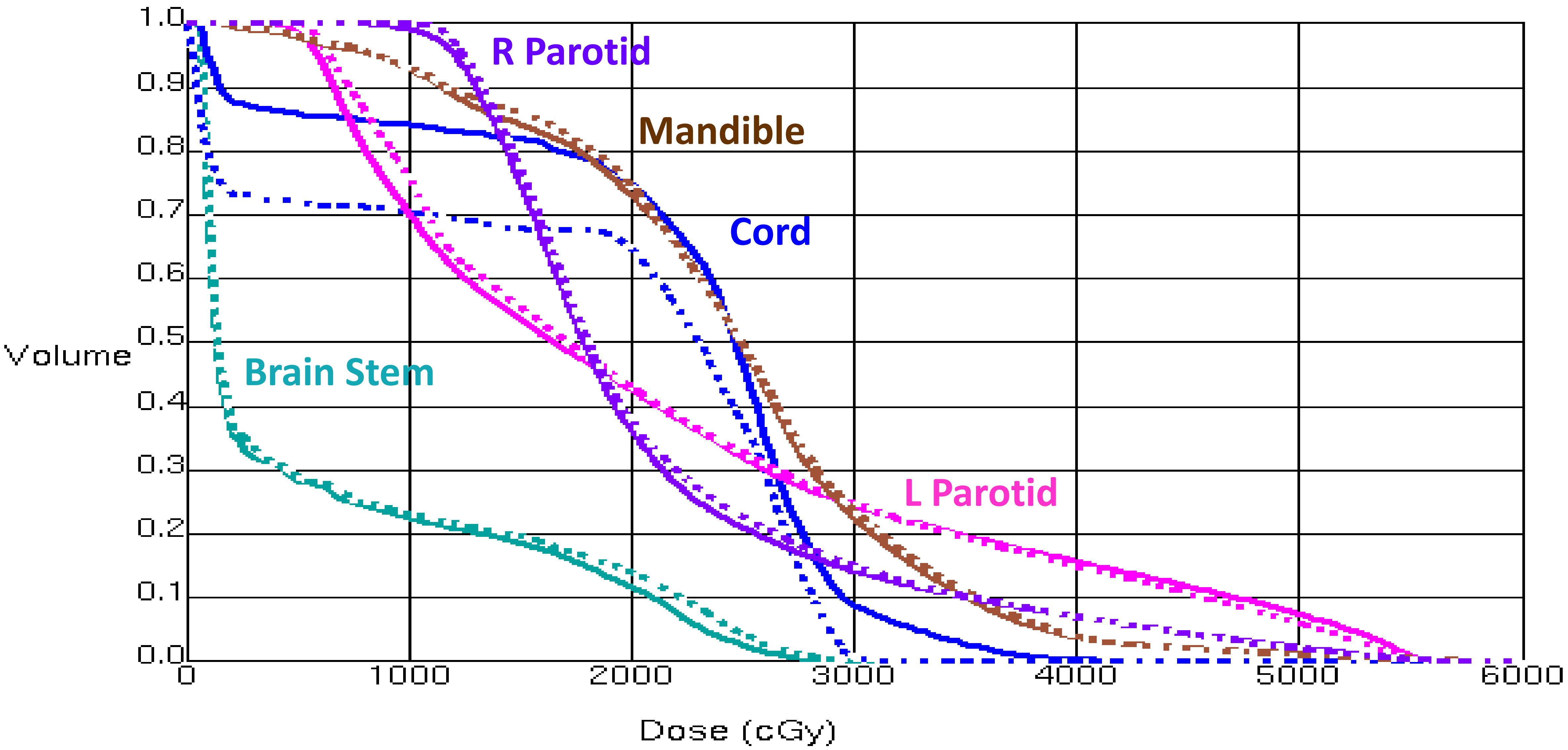


9 beams IMRT:

Conventional Plan: 54Gy to CTV & 70Gy to GTV

DPbN Plan: 54Gy to CTV & Dose Painting to GTV

DPbN (solid-line) *vs* Standard IMRT (dash-line)



Summary

- Dose response matrix can be constructed using FDG-PET/CT images
- Tumor *DRM* with its baseline SUV_0 provide very useful, maybe unique, information to design the optimal dose for each tumor voxel
- DPbN is necessary and could be safely applied
- How many images needed to implement the adaptive DPbN?