Challenges on Assessment of Treatment Response for Physiologically Adaptive Radiation Therapy

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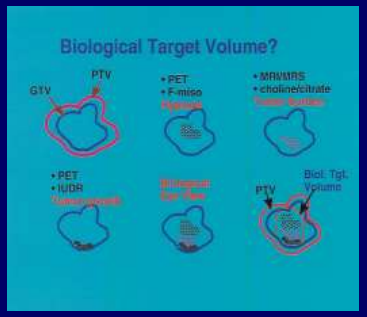
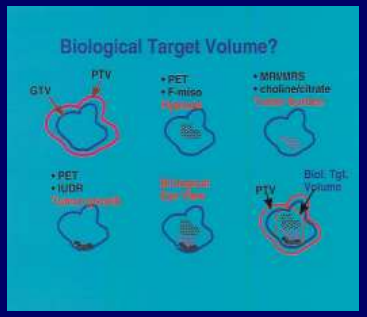
Biological Target Volume, Tx Predictor, Dose Adaption



Ling, IJROPB, 2000

A tumor target volume could be defined and segmented as multiple biological target subvolumes.

Biological Target Volume, Tx Predictor, Dose Adaption

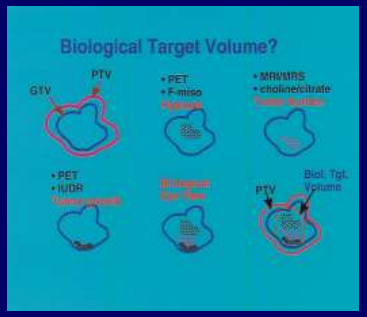


Ling, IJROPB, 2000

The subvolumes defined by multiple physiological imaging studies should be prognostic or predictive indicators

Imaging for Tx Assessment

Biological Target Volume, Tx Predictor, Dose Adaption



Ling, IJROPB, 2000

Dose sculpting of multiple biological target subvolumes and adaptation based upon early response could lead to better outcome.

Imaging for Tx Assessment

Physiological adaptation

Dose sculpting & adaption

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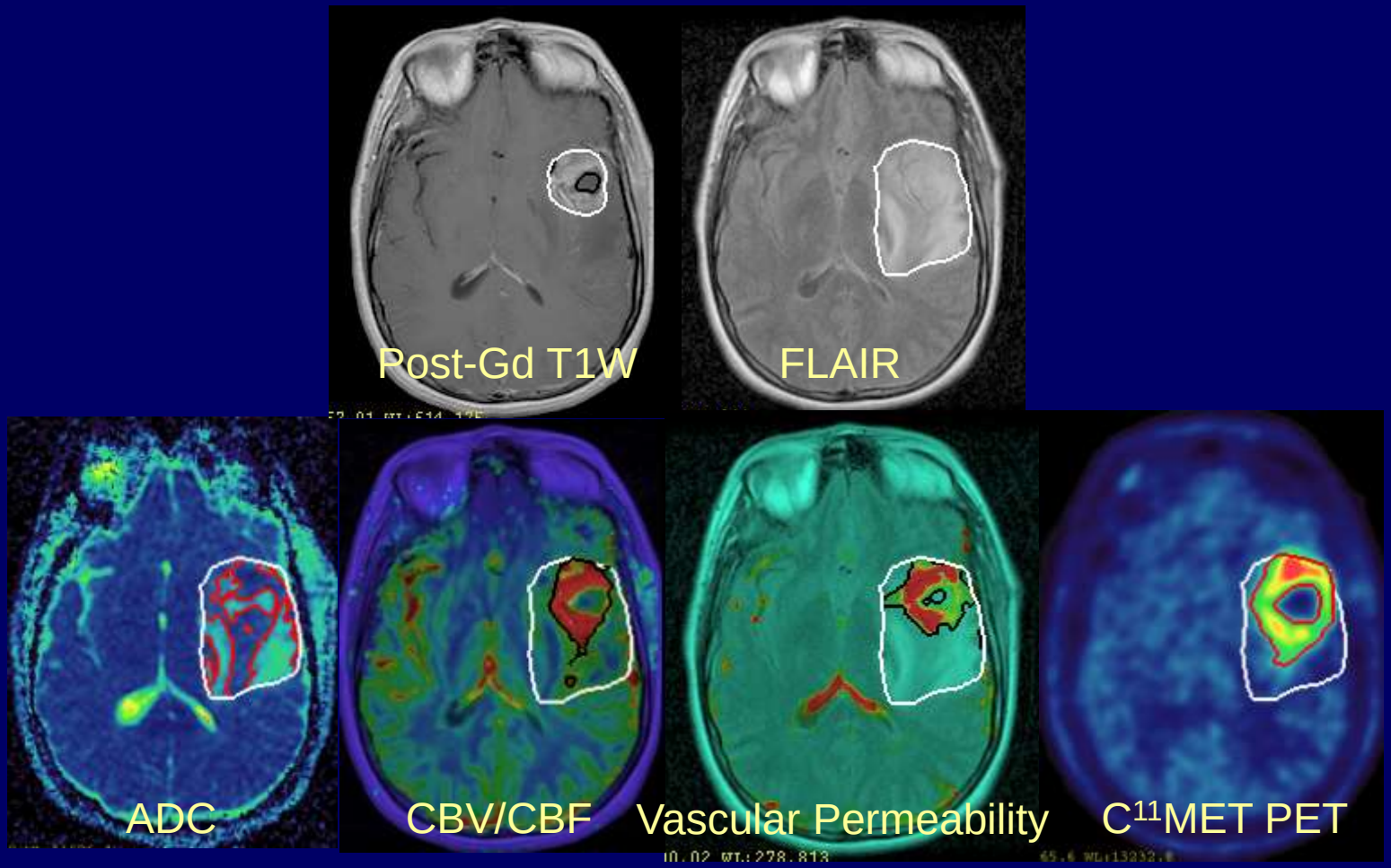
How to Establish an Imaging Biomarker for Therapy Assessment

- Reproducibility
  - Separation of a true change from variation
- Sensitivity and specificity
  - Clinical end points, specific for tumor and therapy types
- Utility
  - biomarker associated w failure/progression
  - adaptive therapy for intensification or toxicity reduction

Heterogeneous Subvolumes in GBM



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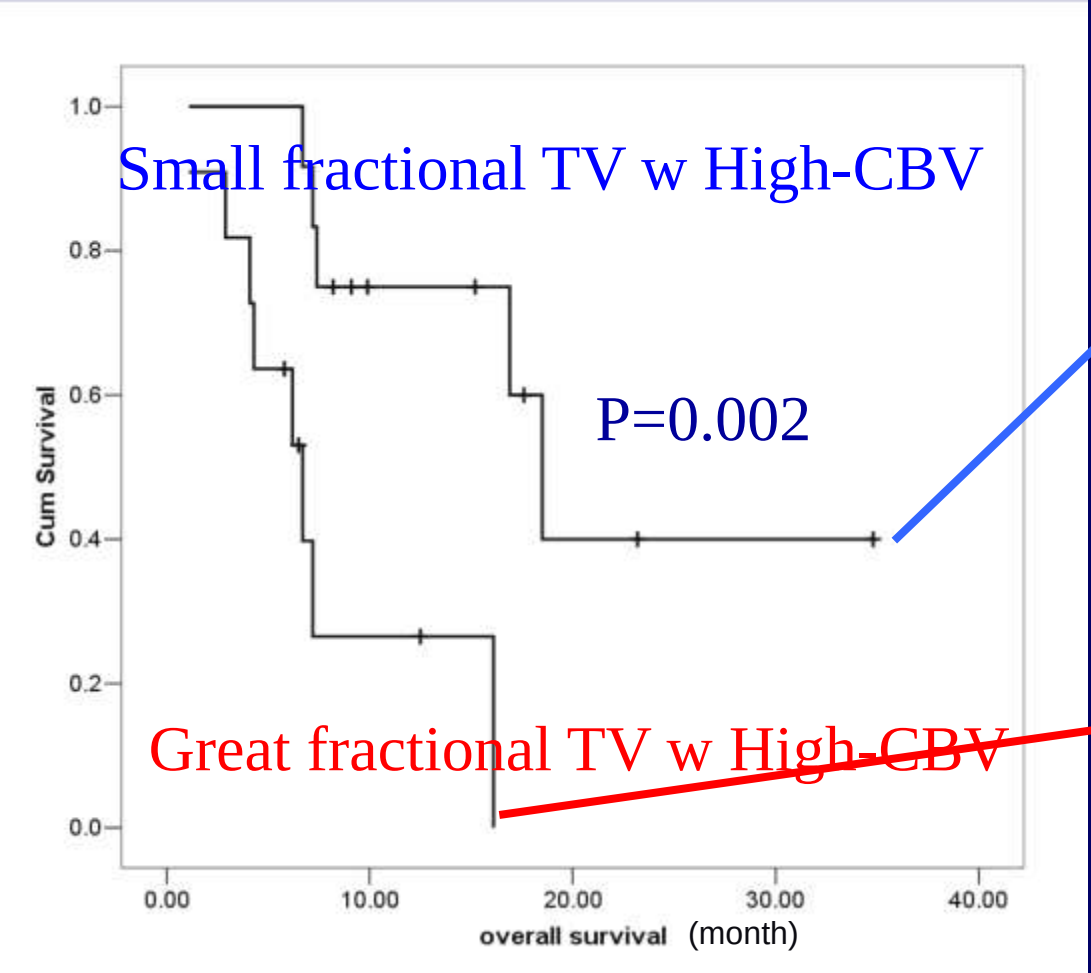
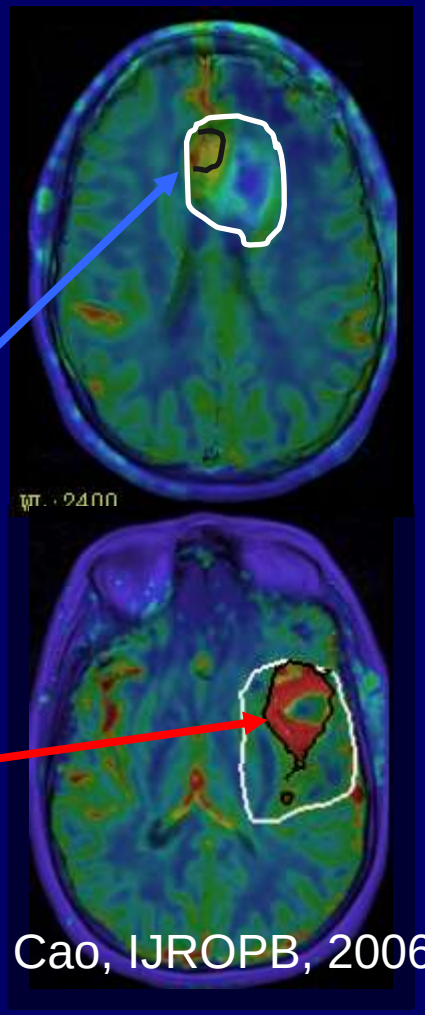
Imaging-driven Response-Induced Subvolume of a Tumor

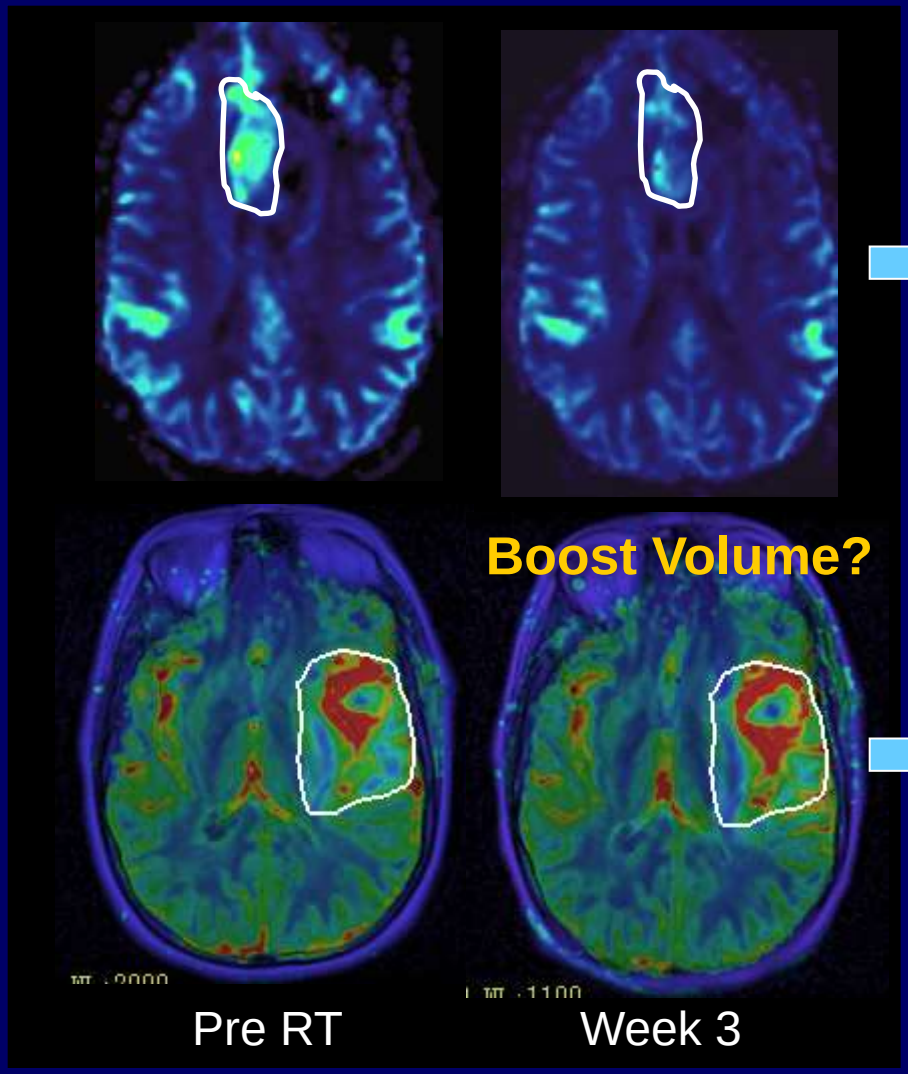
- Heterogeneous therapy response of a tumor could be primarily due to biological heterogeneity in the tumor
- The most aggressive or resistant sub-volume in a tumor could predominantly determine therapy response or outcome of a treatment to the whole tumor
- Aims: Extract the physiological imaging–defined tumor subvolume that is:
  - Predictive for treatment response
  - Highly reproducible
  - A candidate to be a boost target

High CBV: Prognostic Indicator in High-grade Gliomas





Change in high-CBV During RT



Decrease

Better OS

Little Change

Worse OS

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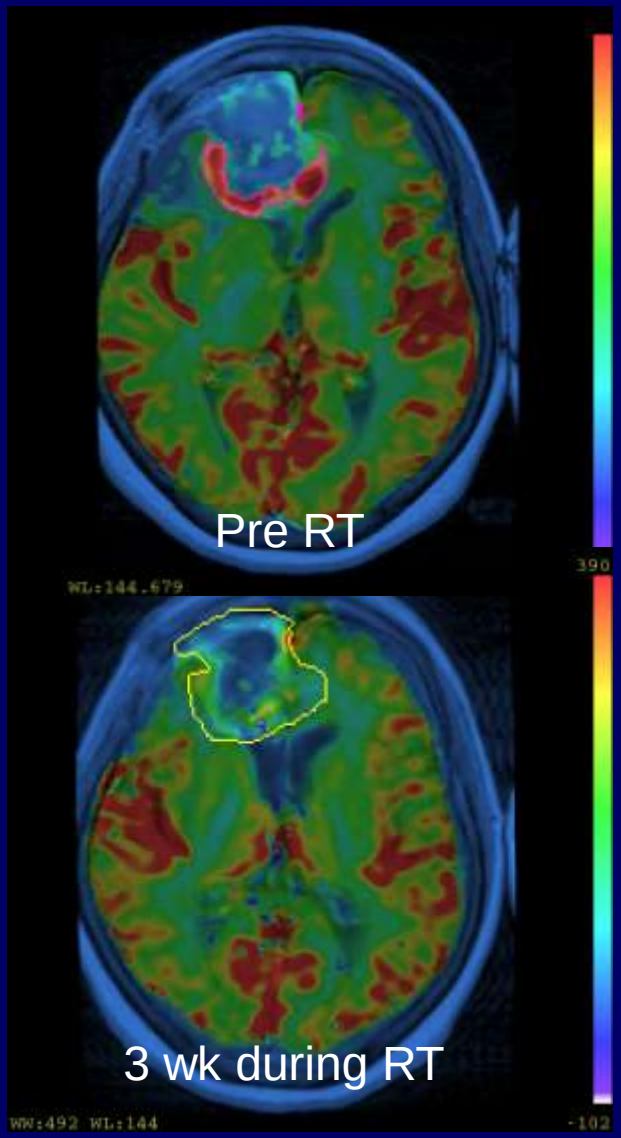
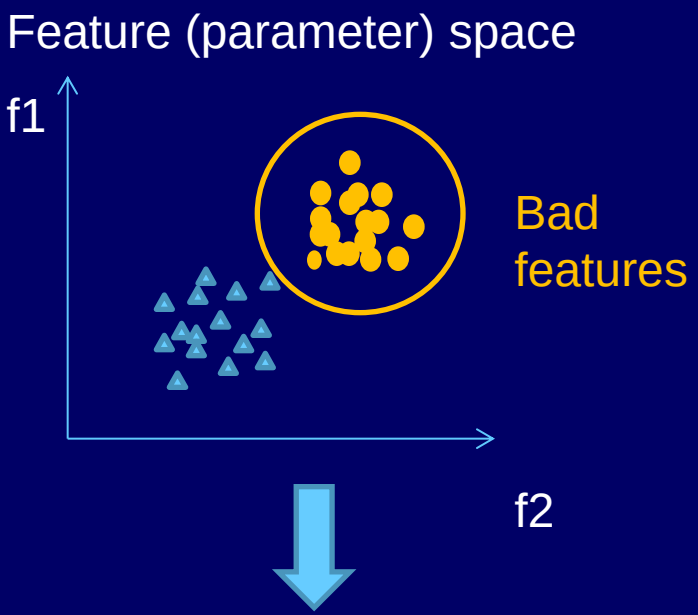
Summary

- These early studies show that certain features of a tumor, and their changes during RT, which are identified by physiological imaging, are associated with outcome, or failure, and thereby can be candidates for radiation boosting or adaptation.

How to extract sub-volumes from a heterogeneous tumor





Quantitative metric:
Subvolumes of the tumor with the “bad” features

Whether “bad” features decrease after receiving treatment?

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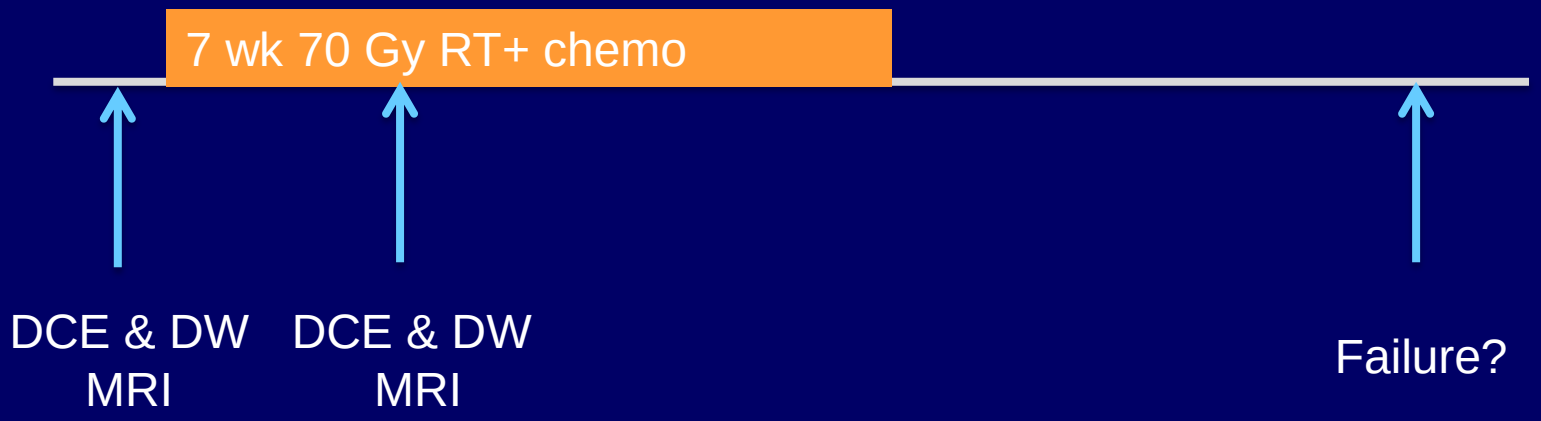
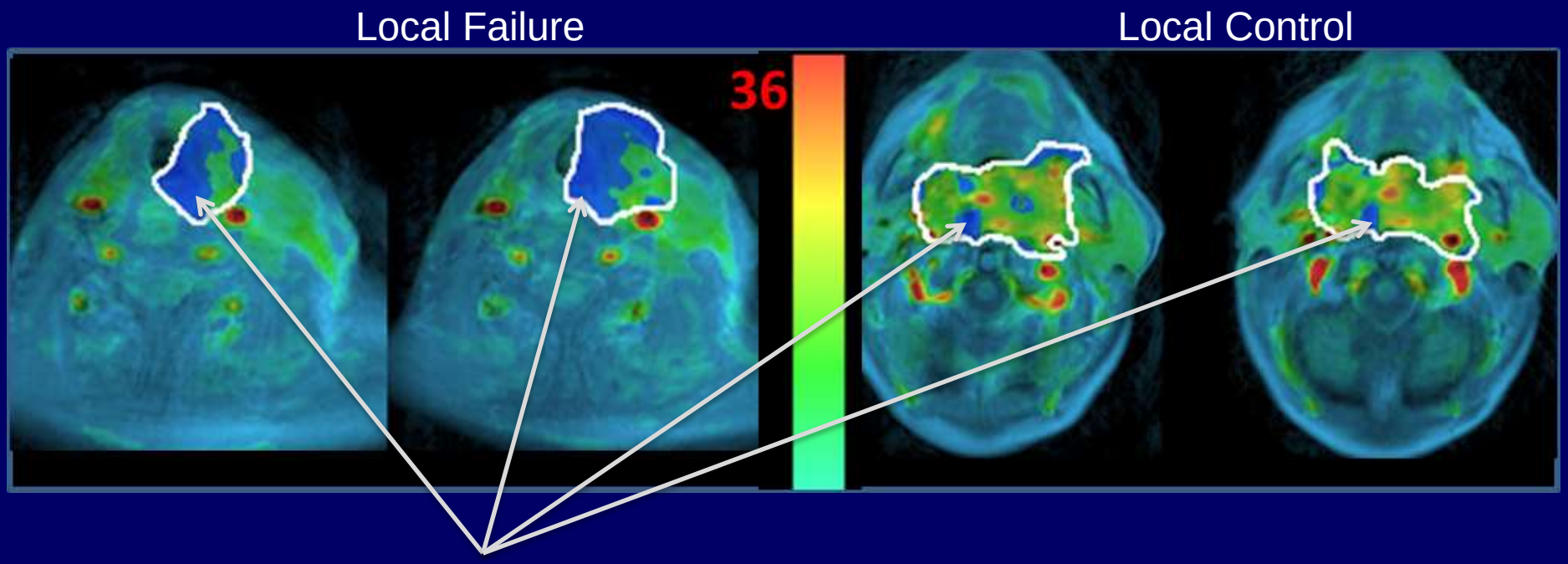
Advanced HNC: ChemoRT



Study aim: To test whether the poorly perfused subvolume of the tumor that persists during the early course of RT is associated with LR failure.

Poorly Perfused Sub-Volumes in Advanced HN Cancers

Blood Volume (BV)



The large sub-volumes of the tumors with low BV (blue color) pre-Tx is significantly associated with LF.
Wang, et al Med Phys 2012

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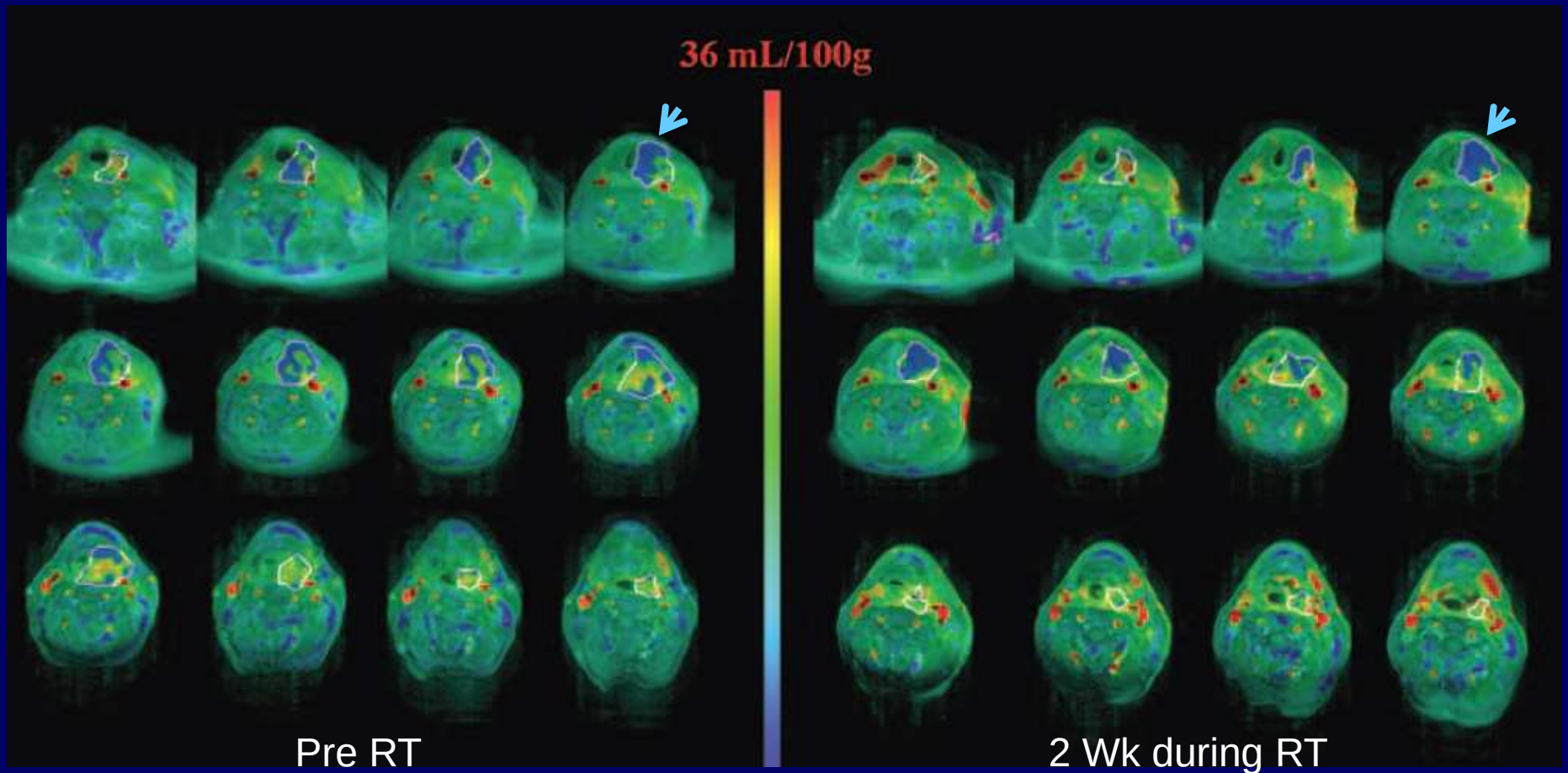
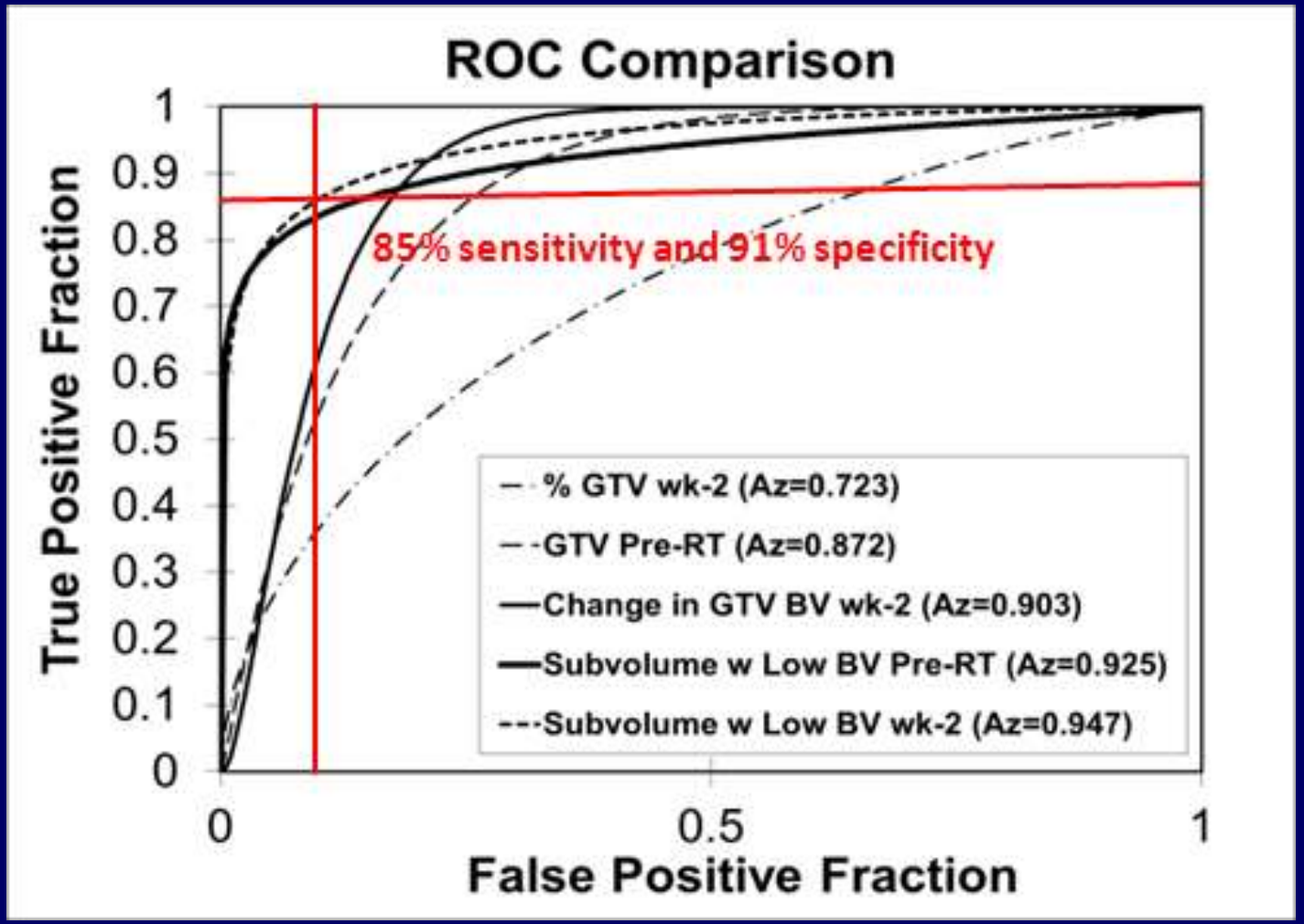
Persistent Poorly Perfused Subvolumes in HNC



The large sub-volumes of the tumors with low BV (blue color) pre-Tx and persisting during the early course of CRT (2 weeks) are significantly associated with LF

Prediction of Local Failure



Wang, et al Med Phys 2012

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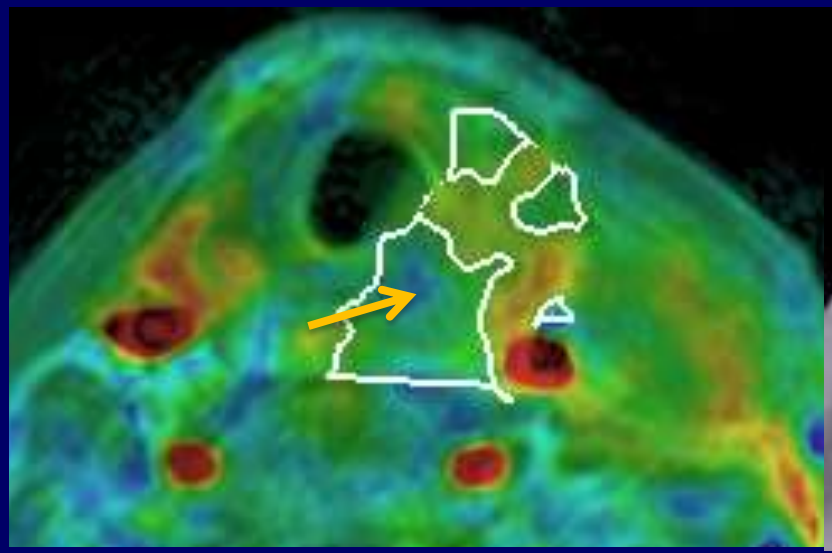
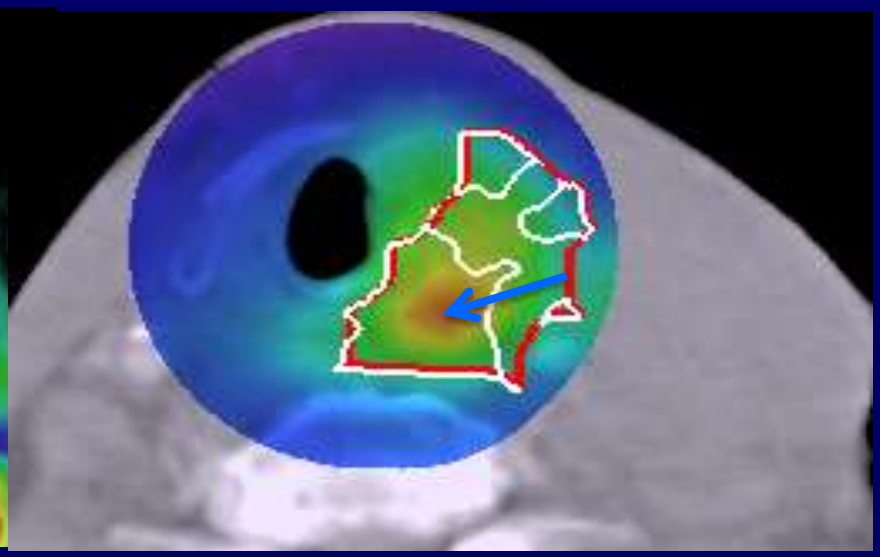
Association with Pattern Failure



Poorly-perfused Subvolume of the Tumor pre RT



FDG 3 moths post RT

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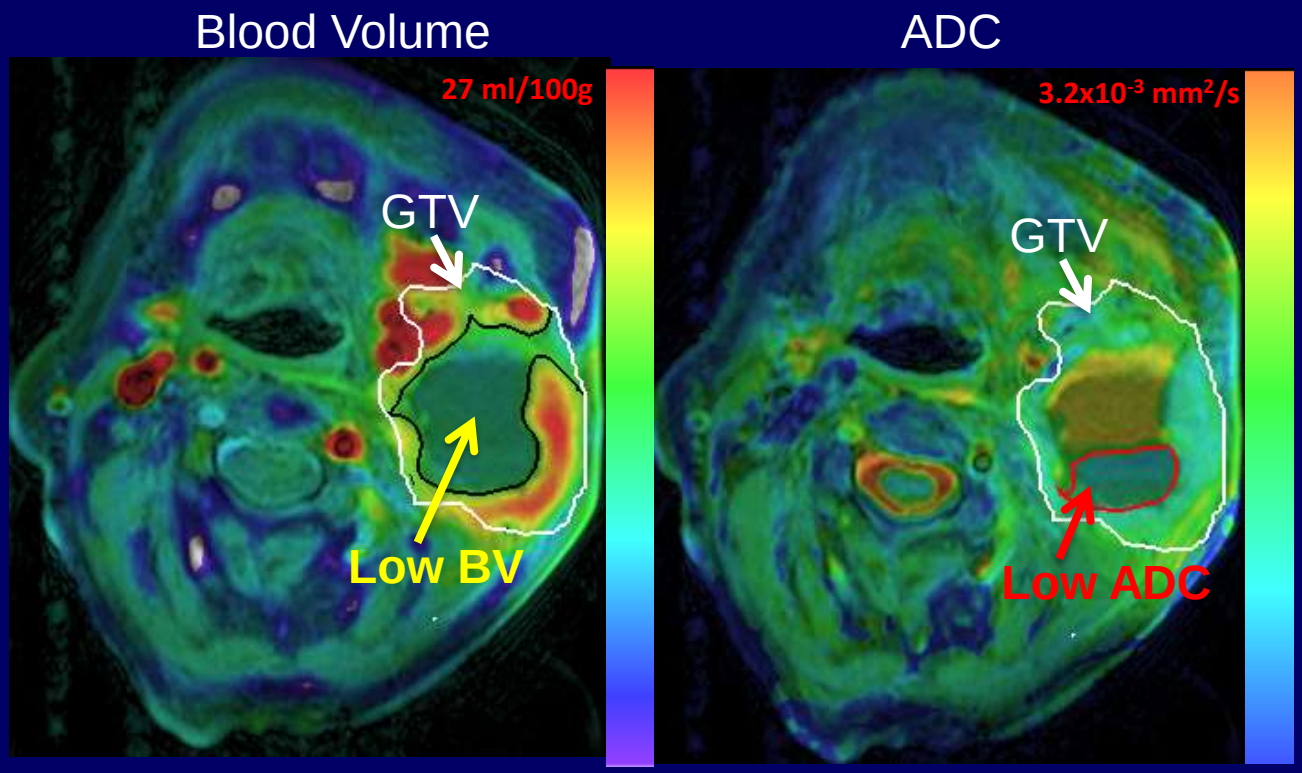
Subvolumes of a Tumor

- A physiological imaging defined response-induced subvolume of a tumor is a better predictor for outcome and could be a candidate for an intensified therapy target
- Our approach can be applied to other physiological/metabolic imaging parameters
- Our method does not depend upon voxel-level accuracy of registration of a pair of images acquired over a period of therapy
- Our method produces metrics robust to image noise and other random factors

Additive Value of Diffusion Imaging in HNC



Subvolume with low BV (poor perfusion) and low ADC (high cellularity) -> Outcome?

Subvolume of the tumor with high Cellularity

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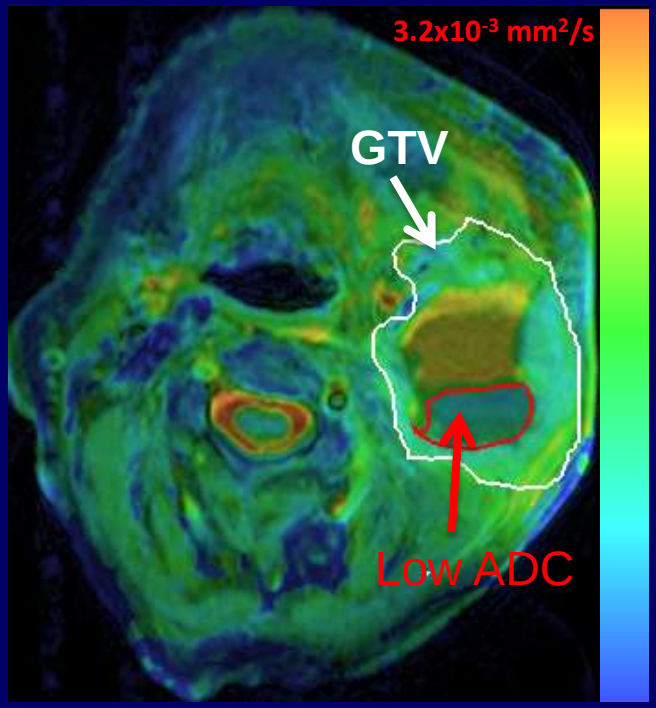
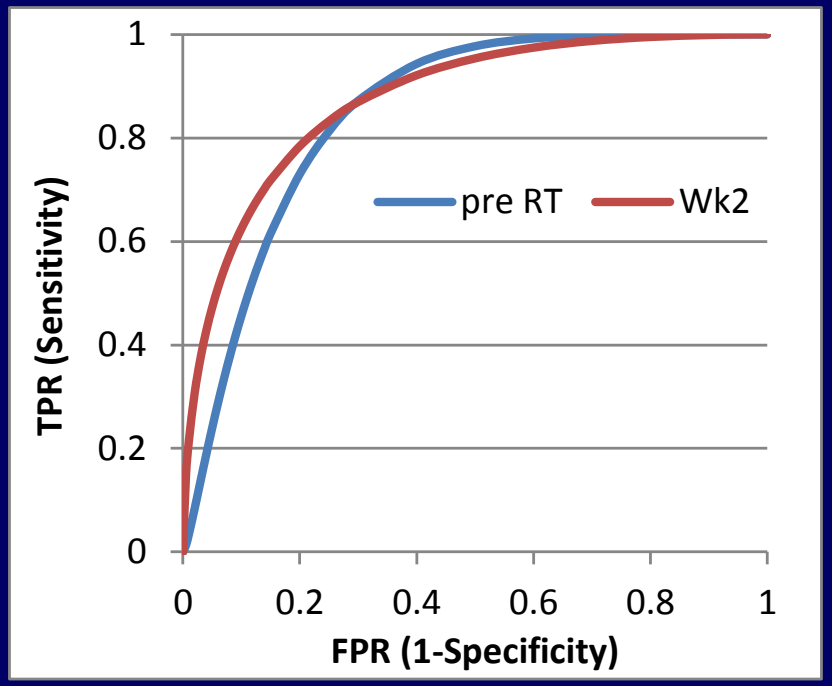
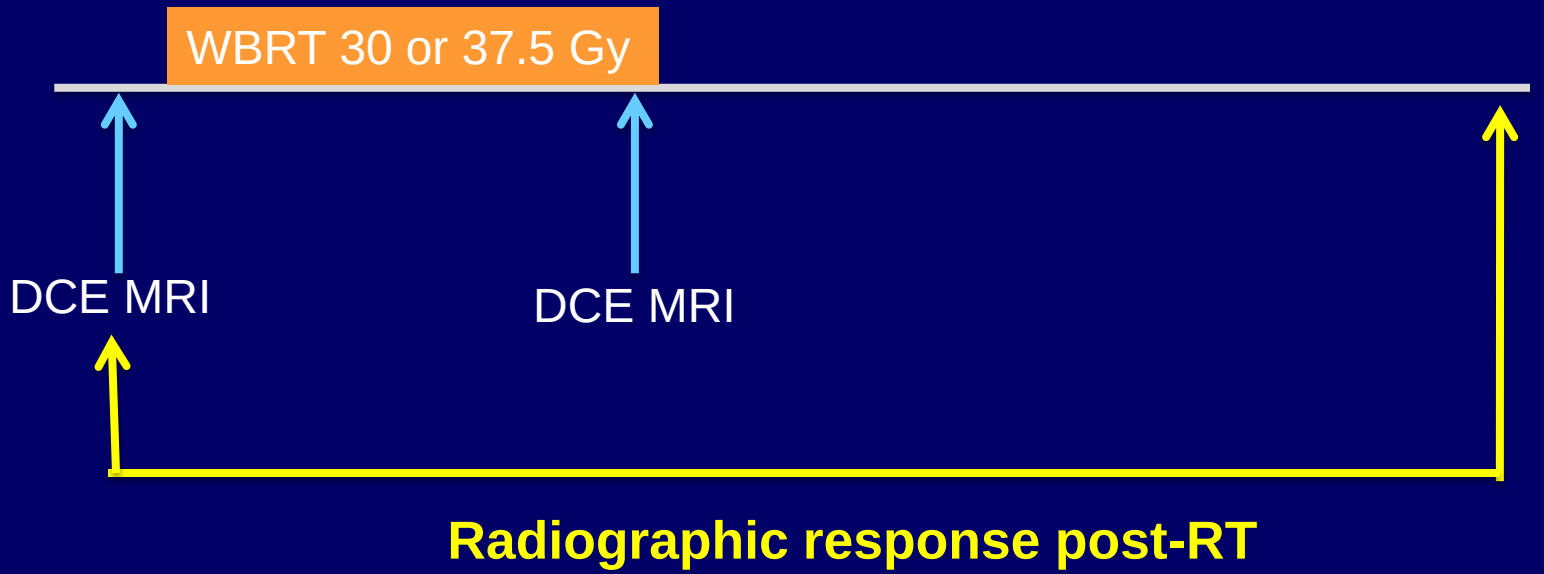
ADC map pre-RT



Prediction for local and regional failure



Brain metastases: WBRT



Aim: Test whether a decrease in the subvolume of the tumor with elevated CBV and high vascular permeability at the end of RT is associated with post-RT response.

Brain metastases (Farjam 2013)

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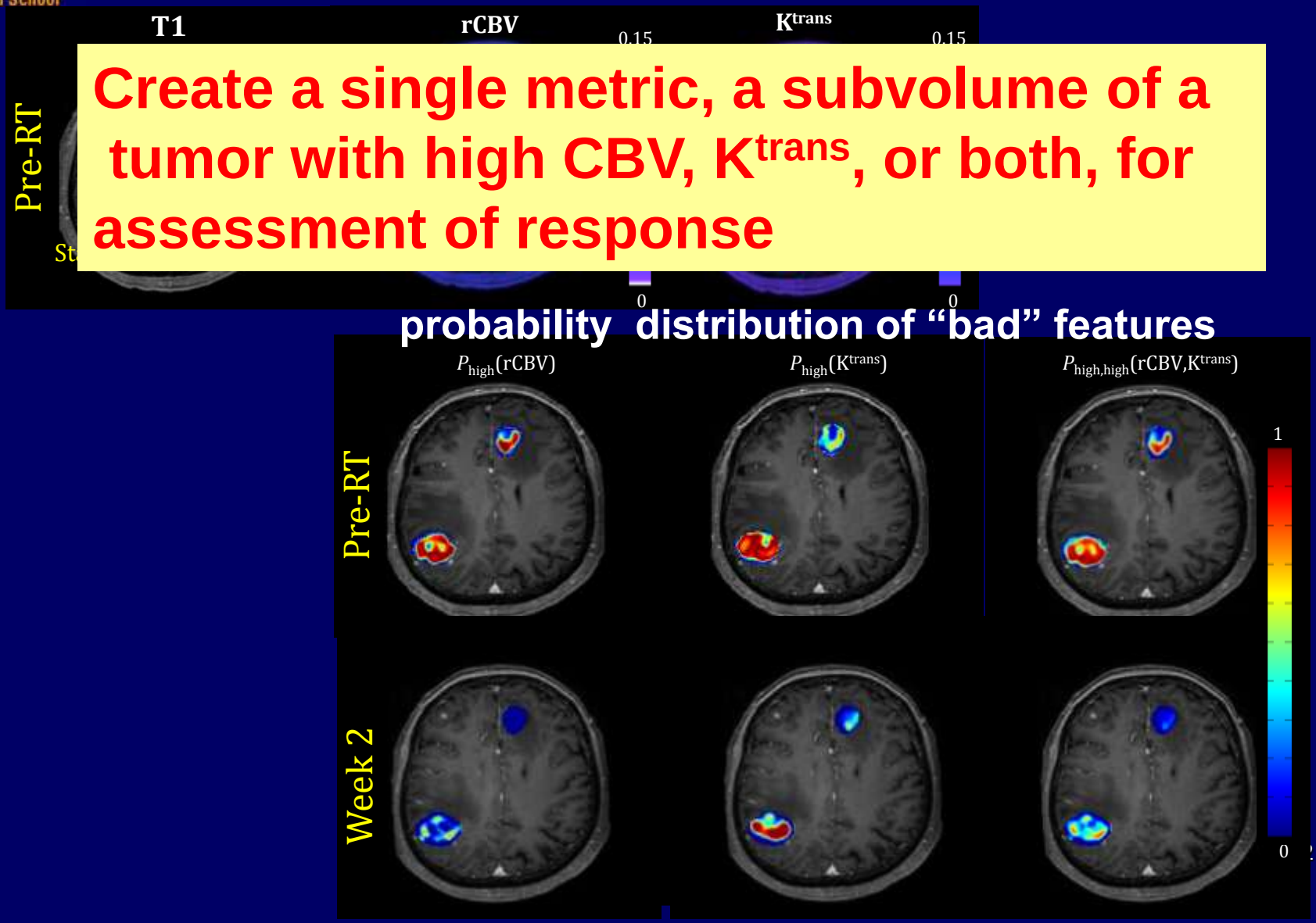
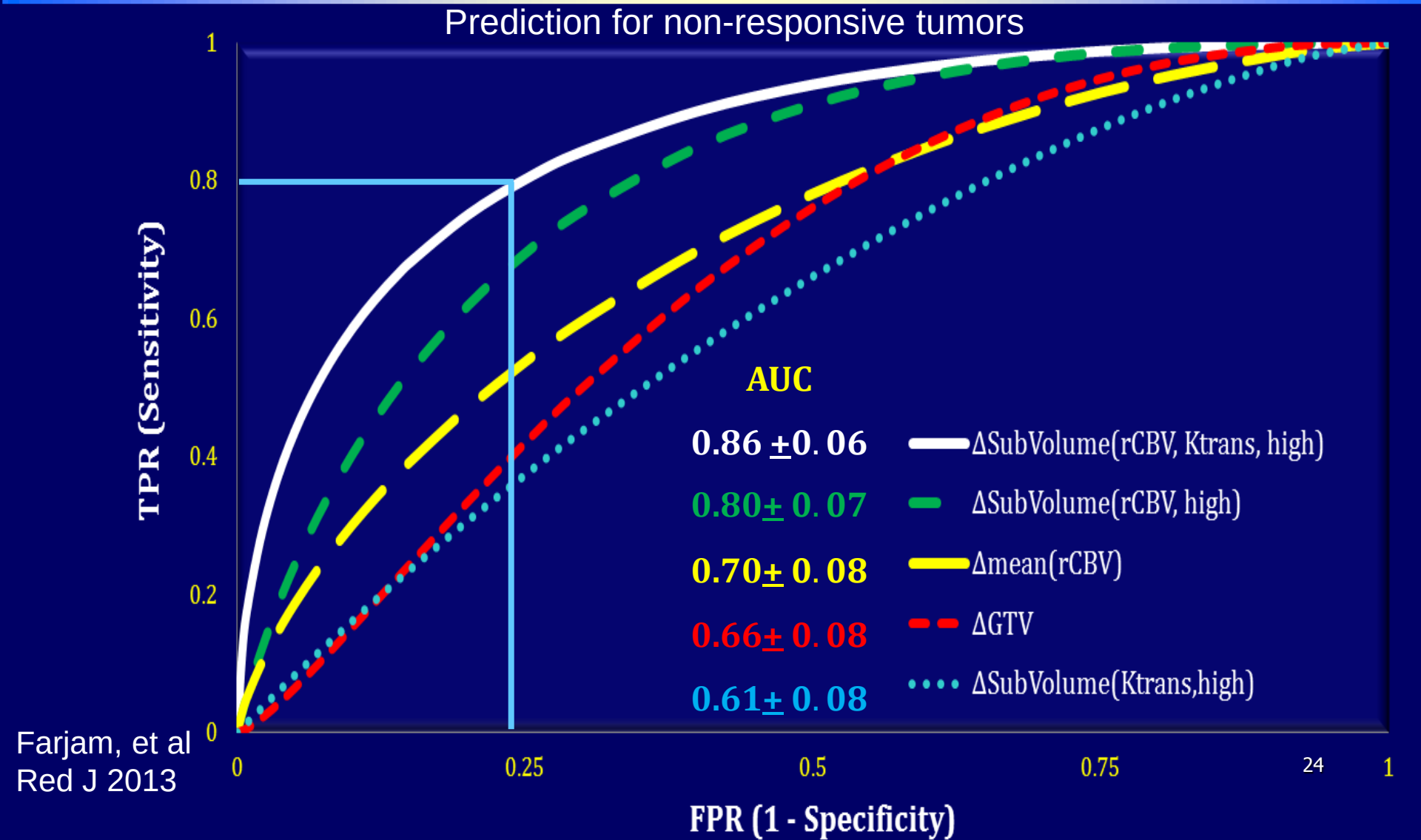
Create a single metric, a subvolume of a tumor with high CBV, K^{trans}, or both, for assessment of response



Does the tumor subvolume with high CBV predict response?

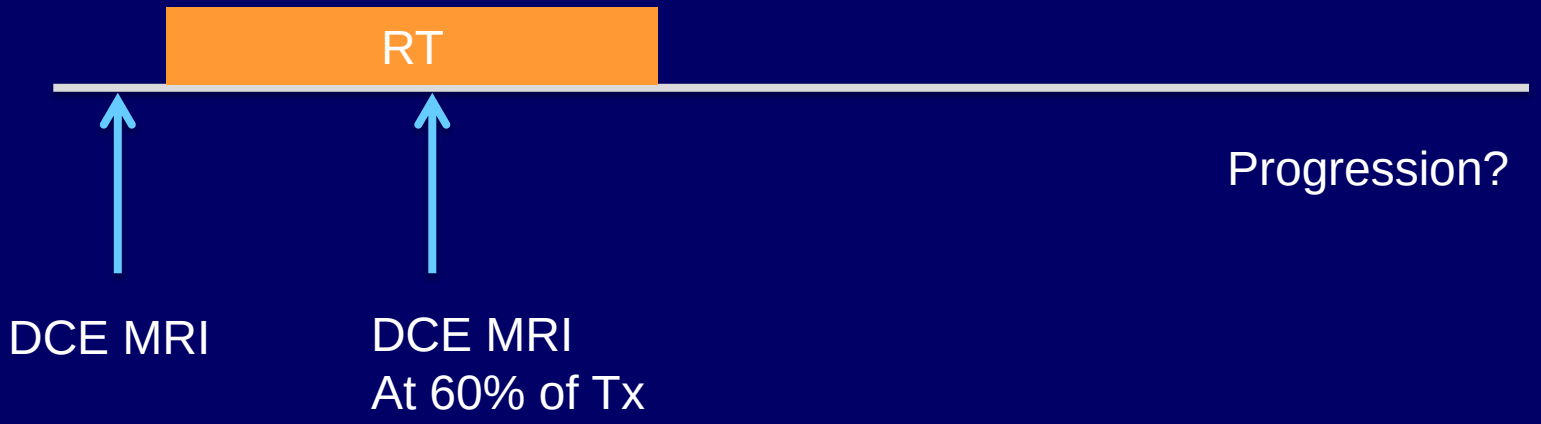
- End point
  - Post-RT radiographic response
    - $\Delta GTV_{post} = GTV_{1mpost} - GTV_{preRT}$
    - Non-responsive: ΔGTV_{post} <-25 %
- Early prediction for non-responsive tumors
  - A change in the subvolume with high CBV, high K^{trans}, or both at the end of WBRT

Sensitivity and Specificity



Farjam, et al
Red J 2013

Intrahepatic Cancer: RT



Aim: Test whether an increase in the subvolume of the tumor with elevated hepatic arterial perfusion after receiving 60% of treatment of RT is associated with progression.

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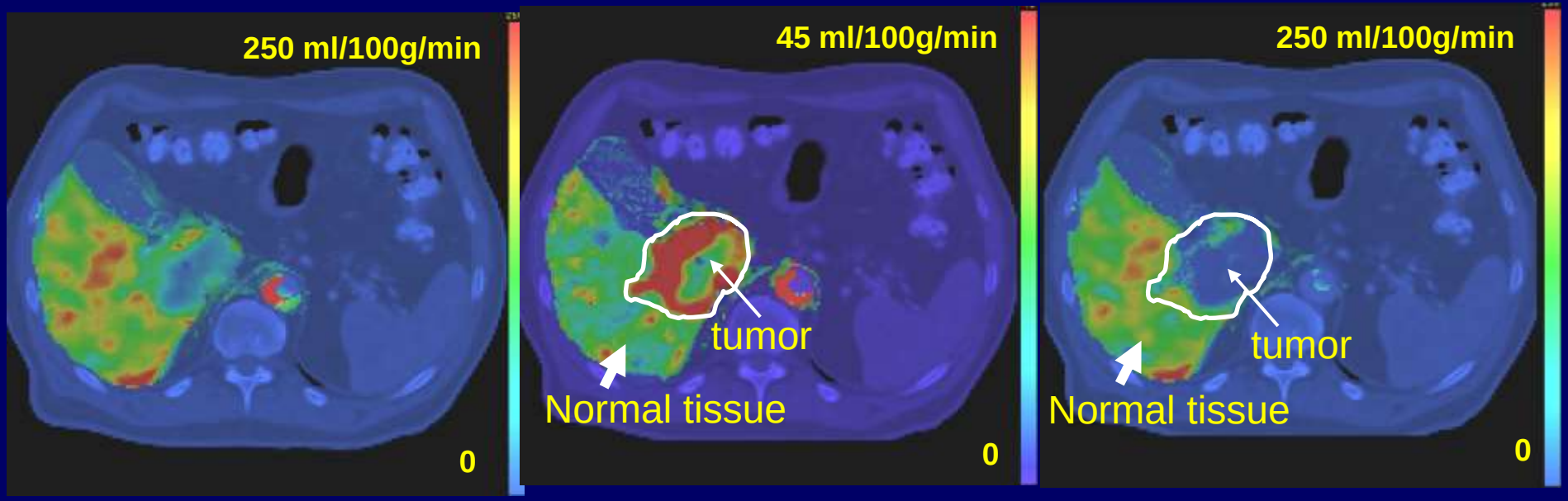
Perfusion in Hepatic Cancer



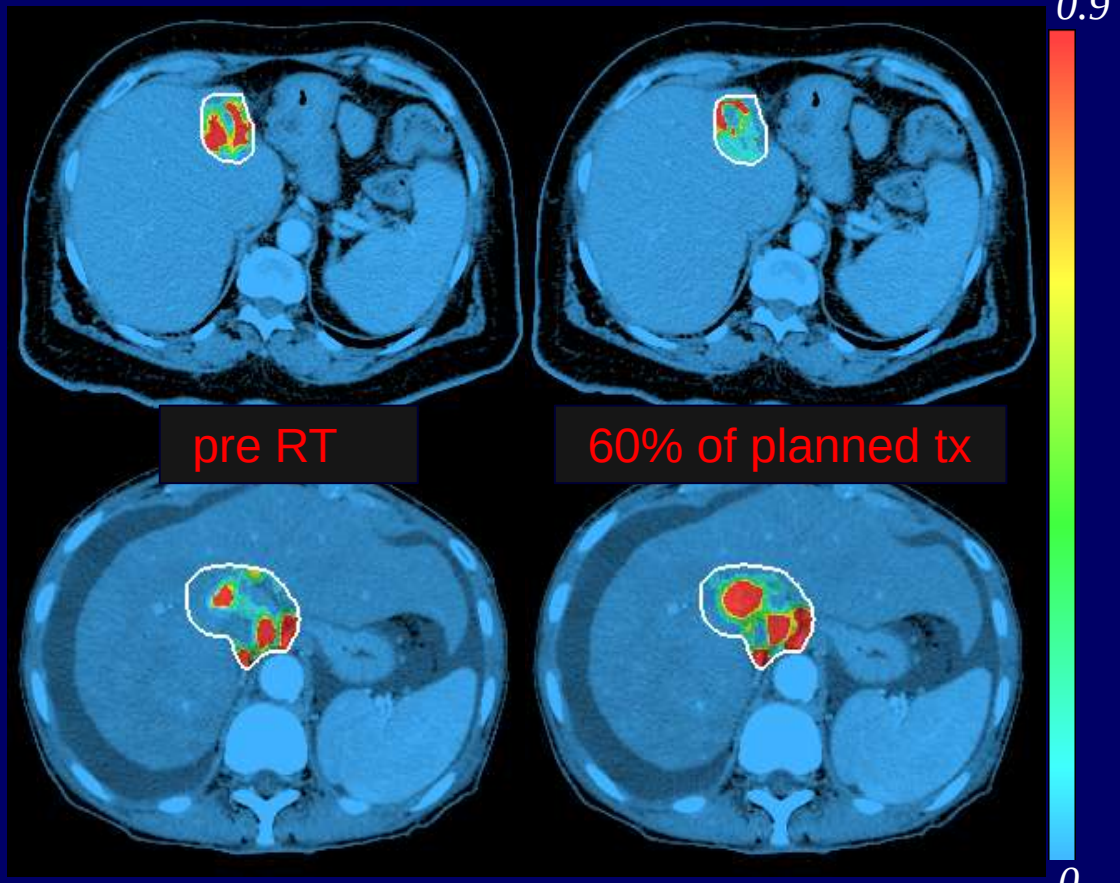
Total perfusion **Hepatic arterial perfusion** **Portal venous perfusion**

Normal liver: ~20% arterial perfusion and ~80% portal venous perfusion
Intrahepatic cancer: elevated arterial perfusion and decreased portal venous perfusion

Hepatic cancer: high arterial perfusion subvolume

responsive

progressive



Wang, AAPM 2013

Cao AAPM 2013 27

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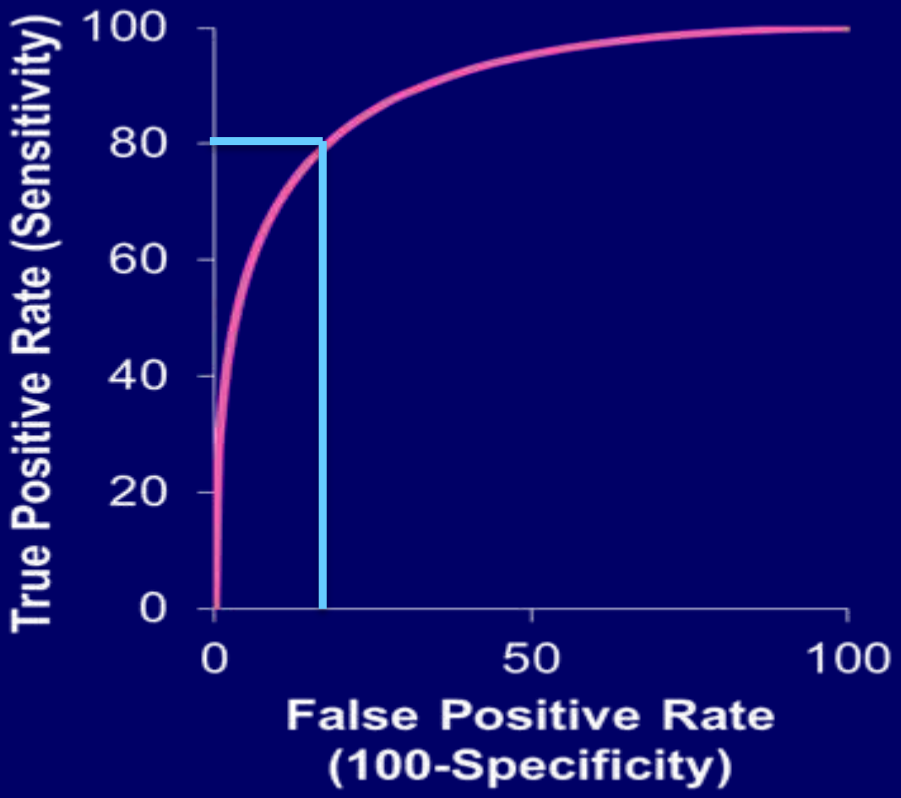
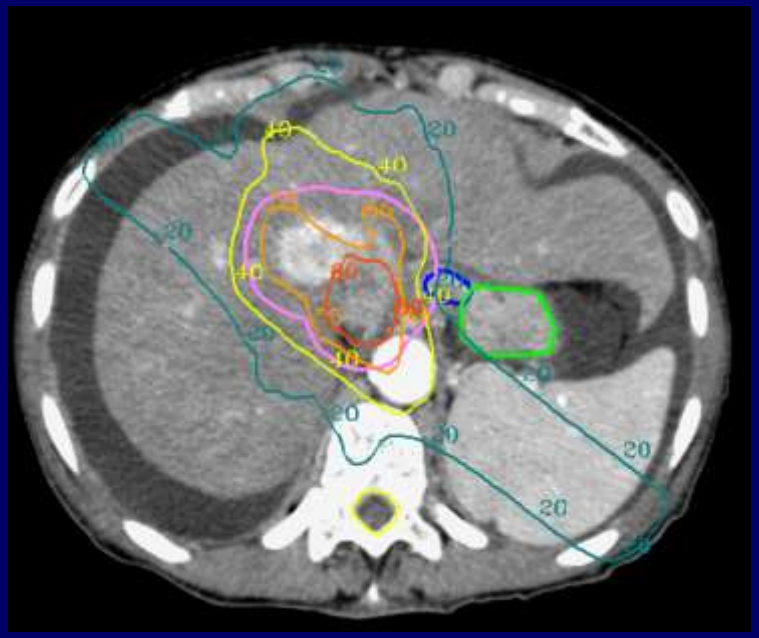
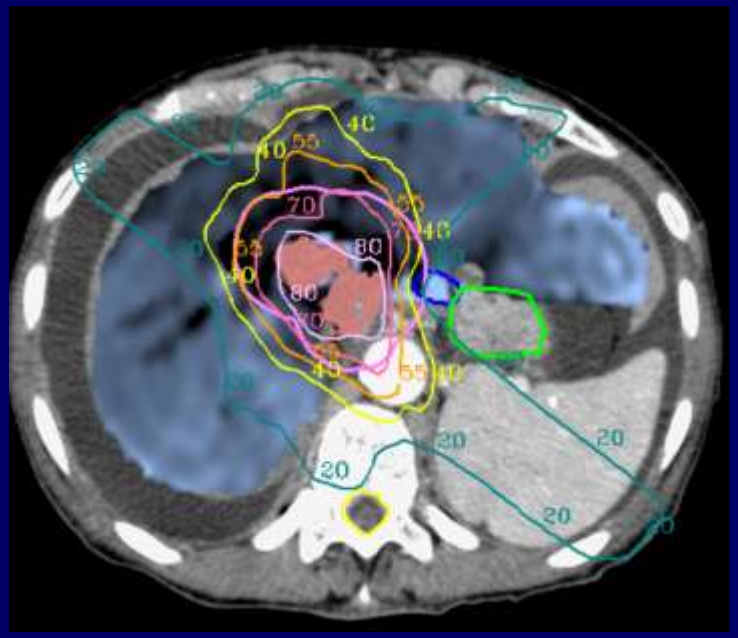
Sensitivity and Specificity

Prediction of progression



Adaptation: targeting the active residual tumor





SBRT Standard course
55 Gy (5 Fx)
NTCP:10%

SBRT Adaptive course
80 Gy (5 Fx)
NTCP: 10%

M. Matuszak, M. Feng, 2013

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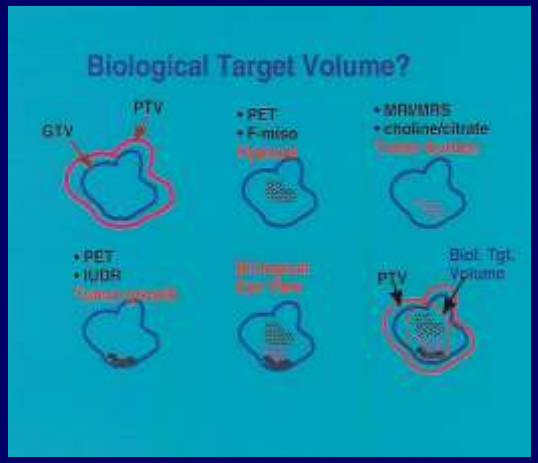
Summary



Imaging-defined response-derived subvolume

Dose adaption & boosting

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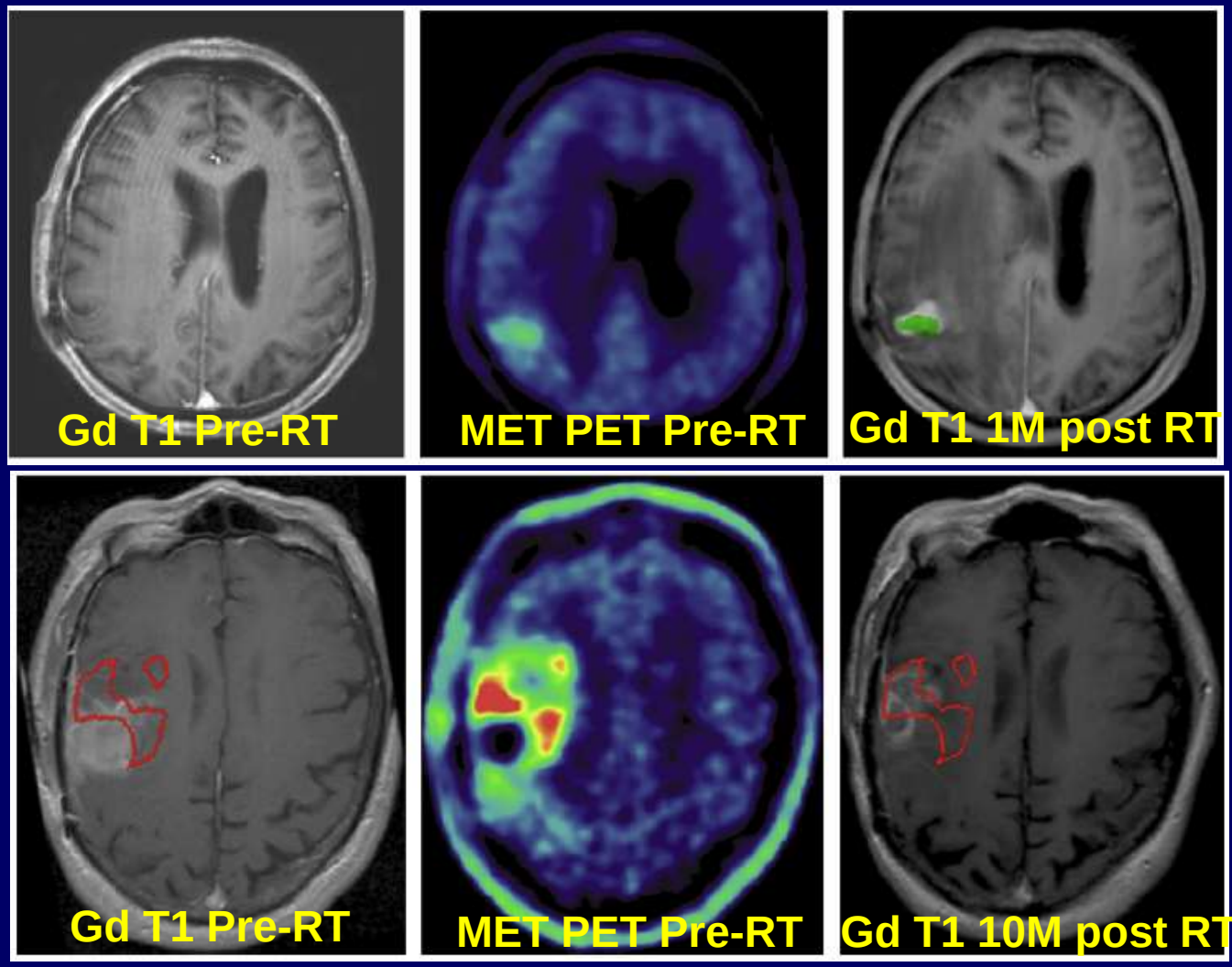
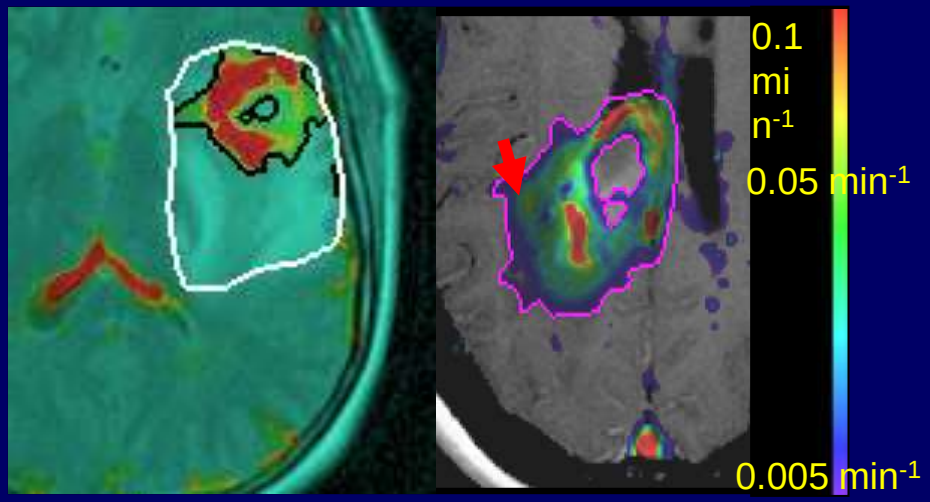
MET Uptake is associated with Patterns of Failure (Lee & Tsien, 2009)



Permeability: Prognostic indicator for high-grade gliomas

- Large vascular leakage volume, reflecting angiogenesis, was associated with worse OS
- Post-Gd T1 or FLAIR GTV failed to predict OS



Cao, Cancer Research, 2006

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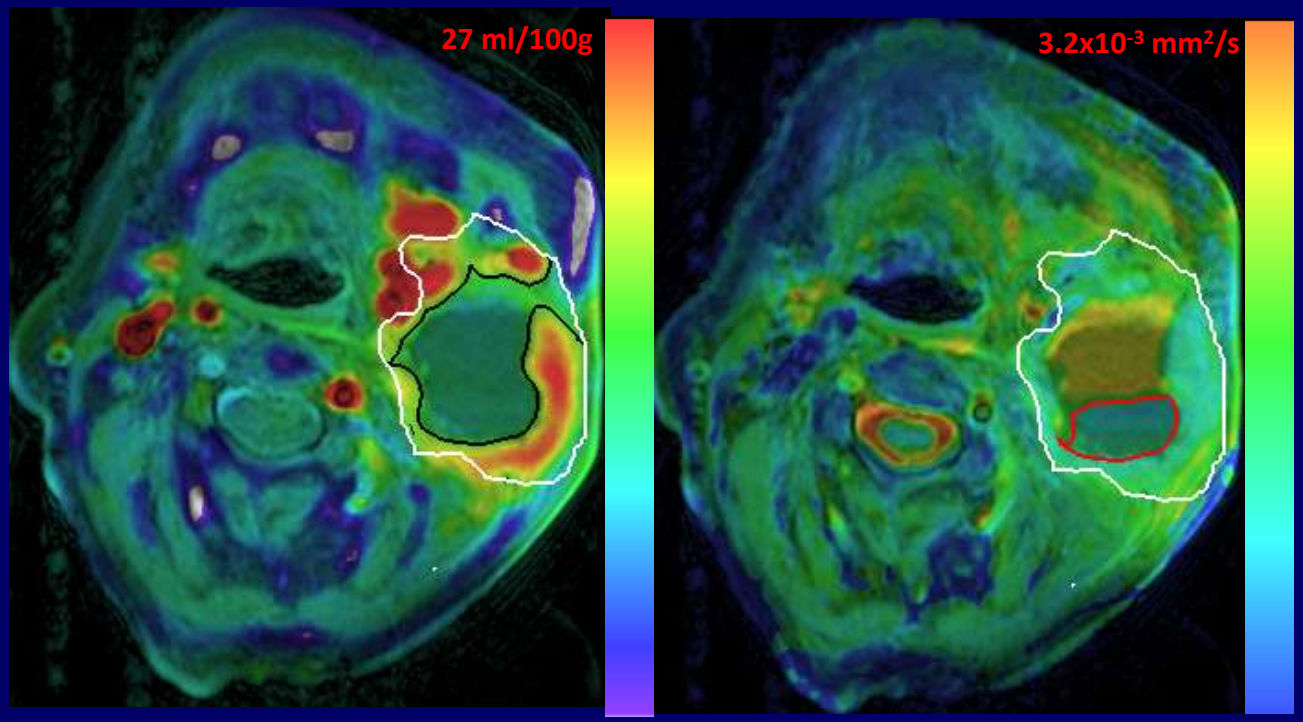

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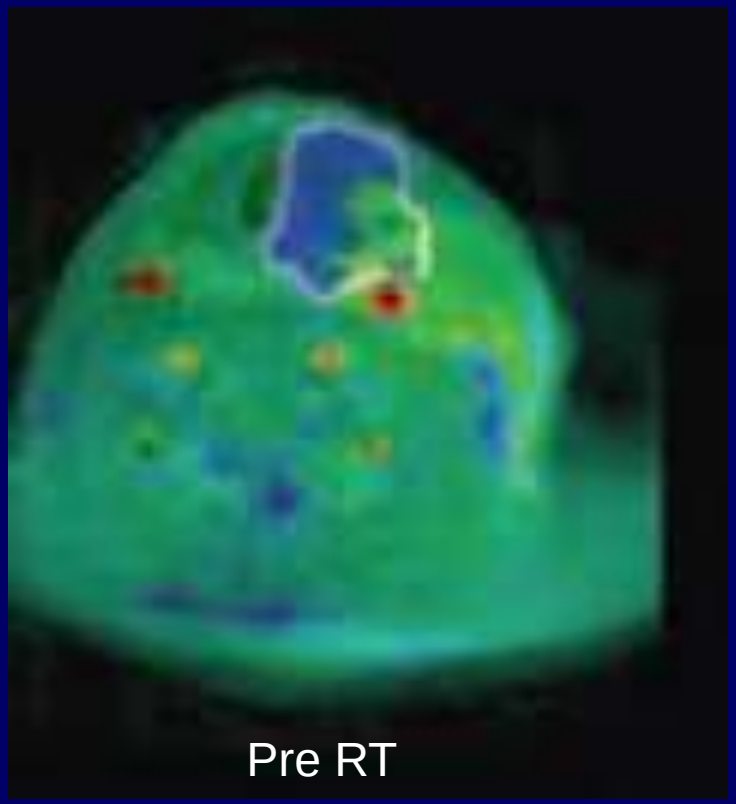
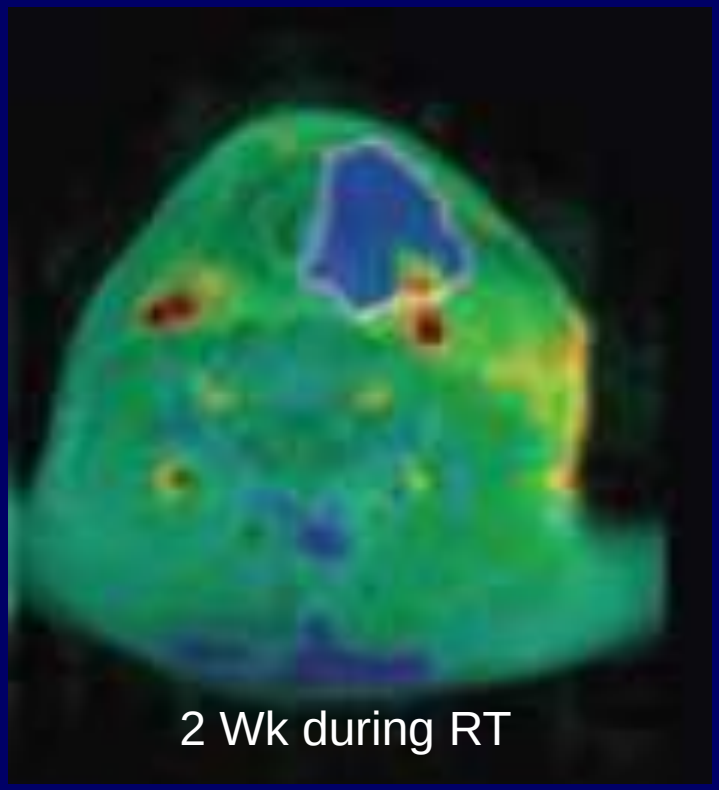
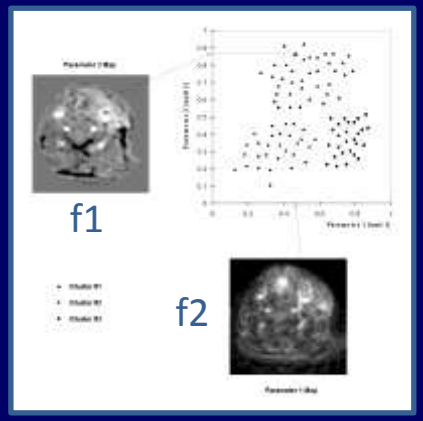
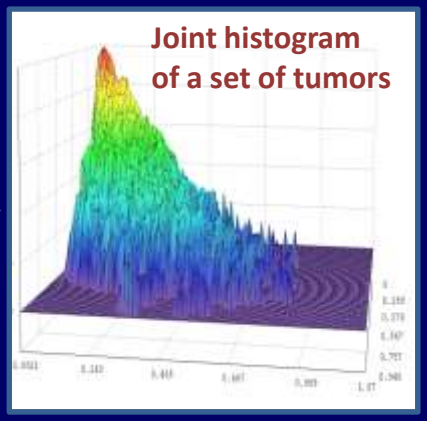
Poorly Perfused Subvolumes in HNC





Fuzzy-Subvolume Model





Cluster analysis:

PMF({f}, class$_1$)

…

PMF({f}, class$_j$)

…

{f}: a set of parameters

PMF({f}, {class})

New tumor