Quantitative Imaging: Techniques, Applications and Challenges -- MR

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QI: MRI Techniques

- Dynamic susceptibility contrast (DSC) imaging
- Dynamic contrast enhanced (DCE) imaging
- Diffusion weighted (DWI), diffusion tensor (DTI), intravoxel diffusion kurtosis imaging
- Spectroscopy (e.g., 1H, 31P)
- Quantitative susceptibility and tensor imaging (QSI, QSTI)
- Hyperpolarized nuclei imaging and spectroscopy (e.g., 13C, 3He, 129Xe)

MR QIB

- MR image acquisition protocols
  - Optimized, harmonized, following QIBA profiles
  - QA/QC
- Physiological parameter quantification from raw image data
- Application in clinical problems
  - Algorithms to extract meaningful "features"/metrics
  - Models in relating quantitative image metrics with clinical endpoints

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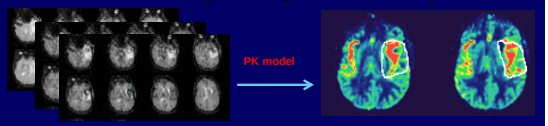
MR QIB: DSC imaging (brain)

- Dynamic T2*/T2-w images during a bolus of Gd injection



- Physiological parameters, CBV, CBF, MTT, K^{trans} (vascular leakage), v_e(extravascular extracellular space)
  - standard models
    - CBV Rosen MRM 1991
    - CBF Ostergaard MRM 1999
    - …

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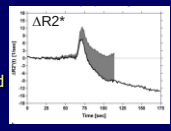
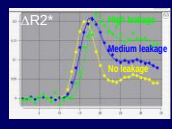
Challenges: CBV in GB

- Challenges in quantitative CBV
  - Contrast effect on T1 (long T1)
  - Vascular leakage effect on CBV estimation
  - Bias and variation from different scanners, field strengths (1.5 T vs 3 T), and sequences



Paulson and Schmainda 2008

- Possible solutions
  - Minimizing T1 weighting by acquisition parameters, pre-loading contrast
  - Correction for contrast leakage (Weisskoff 1994, Johnson 2003, Cao 2006, Bjornerud 2011)
  - Standardized CBV (Bedekar MRM 2010)



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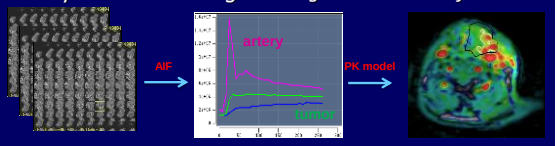
MR QIB: DCE imaging

- Dynamic T1W images during a bolus of Gd injection



- Physiological parameters: K^{trans}, V_p, V_e, BF
  - Standard models
    - 2 or 3 parameter Toft model
    - dual-input single-compartment model in the liver

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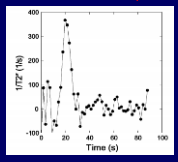
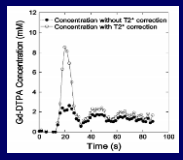
Challenges: DCE quantification

- Challenges in DCE quantification
  - Reliable and reproducible arterial input function
    - T2* effect, B1 field variation, inflow effect, temporal and spatial resolution, water spin exchange between intra- and extra-cellular molecules …
- Possible solutions
  - Dual-echo to estimate and correct T2* effect (Bazelaire, Eur Radiol 2006)

T2* effect at the 1st pass



AIF from aorta at 3T



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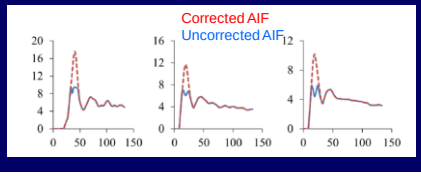

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  - Contrast agent Phase-effect (Akbudak MRM 1997)

$$\Delta\phi = \gamma \frac{\Delta \mathbf{B} \cdot \mathbf{H}_o}{\|\mathbf{H}_o\|} TE = 4\pi\omega_o \chi_M \mathcal{F}C \cdot TE$$

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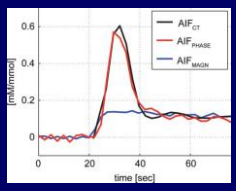
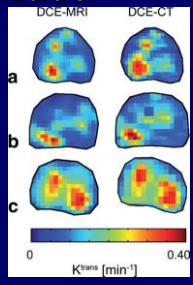
AIF_{phase} from MRI vs AIF from CT

- 12 patients with prostate DCE MRI and CT





Korporaal and van der Heide, MRM 2011

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Challenges: DCE quantification

- Challenges in DCE quantification
  - Reliable and reproducible arterial input function
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- Possible solutions
  - Dual-echo to estimate and correct T2* effect
  - Post-processing (Wang, JMRI 2012)
  - Contrast agent Phase-effect (Akbudak MRM 1997)
  - Slow contrast injection rate to reduce T2* effect
  - Universal AIF

Trade-off!
Simple and practical
vs fundamentally sound, accurate

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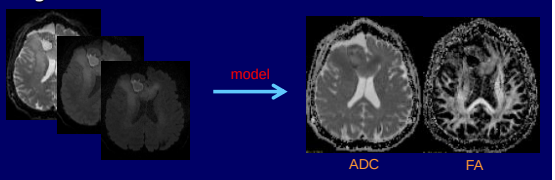
MR QIB: DW Imaging

- DW images acquired with multiple b values and gradient directions



- Physiological parameters: ADC, Anisotropy diffusion indices (FA, AD, RD), IDK indices

Challenges: ADC quantification

- Challenges
  - Non-monoexponential -> what b values should be?
  - Separation of diffusion from perfusion
  - High noise
  - Geometric distortion and artifact from EPI acquisition
- Possible solutions
  - Intravoxel incohent motion model (Le Bihan 1988)
    - $S(b) = (1 - f_v)e^{-bADC} + f_v\emptyset(b)$
  - Using low b (100-500) values instead b=0 for two-point fitting

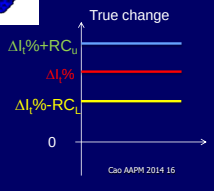
QIB for Therapy Assessment

- To develop a QIB for predicting tumor tx failure/progression or response/outcome
- Sensitivity and specificity
  - Clinical end points
  - Specific for tumor and therapy types
- Repeatability and Reproducibility
  - Separation of a true change from variation
  - Barnhart, Barboriak, Trans Oncol 2009, & *Stat Methods Med Res*

Repeatability of DT indices

- Assess true changes in WM structures of individual patients after receiving brain RT and their associations with late neurocognitive dysfunctions (Nazem-Zadeh,PMB 2013)
  - Algorithms segmented corpus callosum, cingulum, fornix from DTI

- Repeatability coefficient (RC) estimated from test and retest DTI data (NBIA) of 12 patients
- A true longitudinal change $\Delta I_t\%$ in an individual patient with 95% confidence



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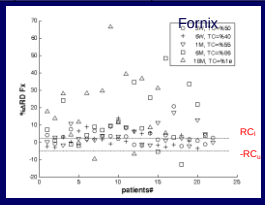
Is a RD increase a true change?

Radial Diffusivity	Cingulum	Fornix	CC
RC%(RC_L,RC_U)	3.4(2.4,5.6)	3.0(2.1,4.9)	5.9(4.3,9.8)



86% and 100% of the patients had RD changes in the fornix beyond the uncertainty range 6 and 18 months after RT, respectively.

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QIB for Tumor Therapy Assessment

- Complexity
  - Tumor biology
  - Imaging techniques
  - Tumor response to therapy

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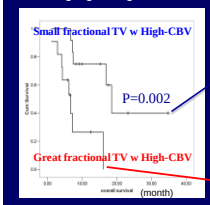
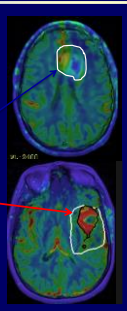
High CBV: Prognostic Indicator in Gliomas

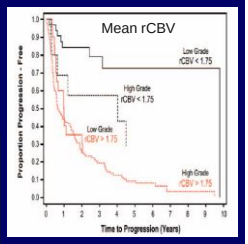
High-grade gliomas





Cao, IJROPB, 2006

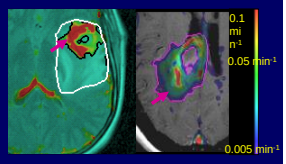
Gliomas



Law, Radiology 2008

Vascular Permeability: Prognostic indicator for high-grade gliomas

- Large vascular leakage volume, reflecting angiogenesis, was associated with worse OS.

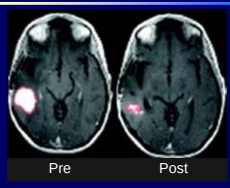


Vascular leakage volume

Cao, Cancer Research, 2006

Vascular Normalization Index

- Patients: recurrent GB
- Therapy: cediranib, anti-VEGF agent
- VNI
  - Changes in K^{trans}, CBV, and plasma collagen IV 1 d after the first treatment



$$VNI = -[a\Delta \log K^{trans} + b\Delta \log CBV + c\Delta \log collIV]$$

- Predictors for OS and TPS

Sorensen, Cancer Research 2009

Non-enhanced Hypercellularity Component in Glioblastoma

- The non-enhanced, hypercellularity component of GB could be treated inadequately
  - Surgical resection and radiation therapy could be limited to the enhanced gross tumor volume, due to the ill-differentiation of non-enhanced tumor, edema and normal tissue, and concerns of complications.
  - The undisrupted blood-brain-barrier can result in a low concentration of TZM in the non-enhanced tumor region.
- Incapable to detect non-enhanced hypercellularity components might cause mis-diagnosis of response and progression

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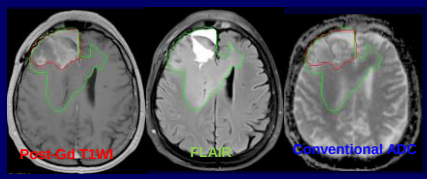
Challenges

- To differentiate hypercellularity components of GB from high-vascular components, edema, and normal tissue using conventional MRI and ADC (b= or < 1000 s/mm^2)



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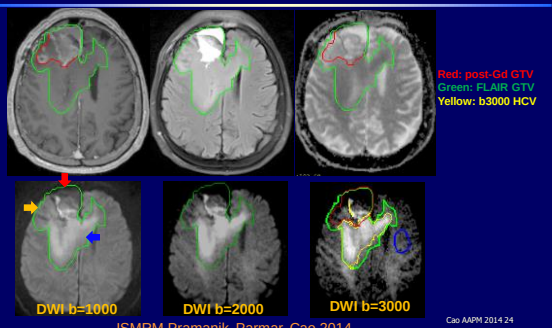
Hypercellularity by high b DWI



ISMRM Pramanik, Parmar, Cao 2014

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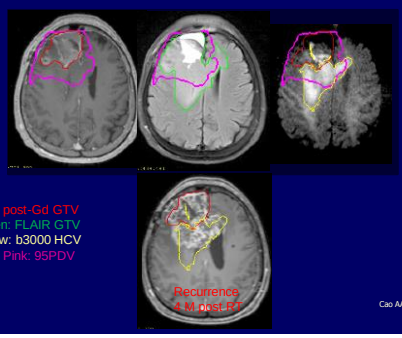
Radiation Coverage & Recurrence



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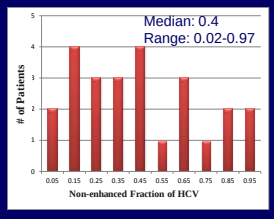
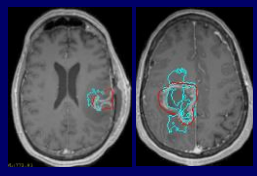
Enhanced and non-enhanced HCV





Red; post-Gd GTV
Cyan: b3000 HCV

The HCVs extended beyond the FLAIR GTVs in 6 patients

Pramanik, Parmar, Cao, ISMRM 2014

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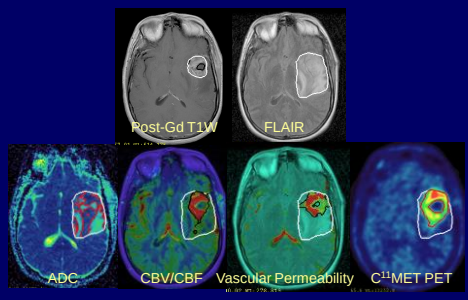
Heterogeneity in Glioblastomas



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What we have learned

- Tumor heterogeneity
  - The mean value of a physiological image parameter in the tumor is not very useful for treatment assessment
- Correlations between multiple physiological and metabolic image parameters (eg, BV vs BF)
  - The biological processes involved may be different
  - Additive value ?
- Predictive of physiological image parameters
  - Not all image parameters have predictive values for therapy assessment or are useful to define a boost target

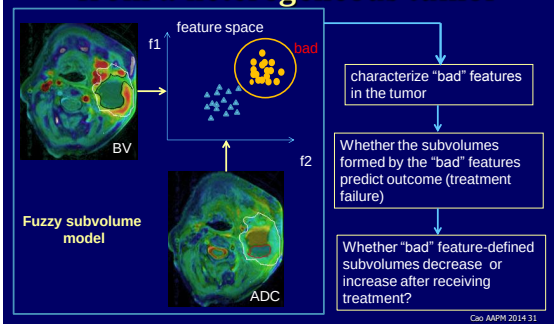
Hypotheses

- 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 outcome of the whole tumor

What we need

- Quantitative Image Tools
  - Characterize tumor heterogeneity
  - Determine complementary or redundant physiological image parameters
  - Create quantitative image metrics
    - Predictive for treatment failure
    - Highly reproducible
    - Candidate to be a radiation boost target

How to extract sub-volumes from a heterogeneous tumor



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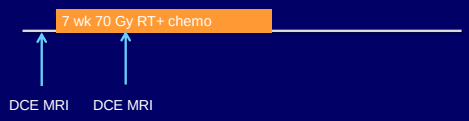
HNC: ChemoRT



The aim is to test whether the poorly perfused subvolume of the tumor and persisting during the early course of RT is associated with LR failure.

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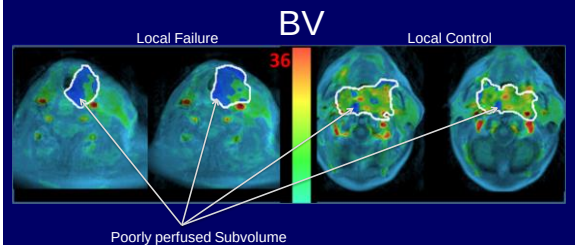
Poorly Perfused Sub-Volumes in Advanced HN Cancers



Wang, et al Med Phys 2012

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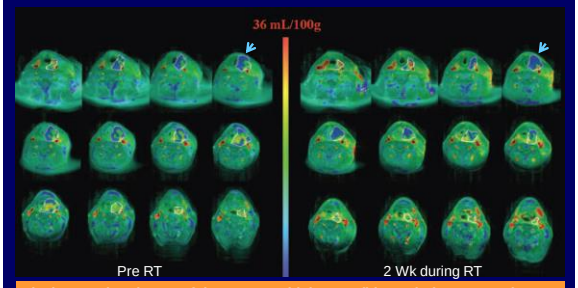
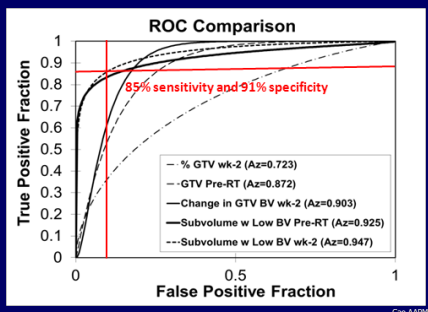
Persisted Poorly Perfused Subvolume in HNC



The large sub-volumes of the tumors with low BV (blue color) pre-Tx and 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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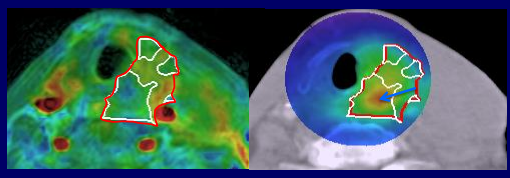
Association with Pattern Failure



Poorly-perfused Subvolume pre RT

FDG 3 mon post RT

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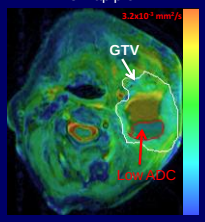
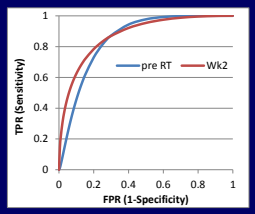
Subvolume of the Tumor with High Cellularity

ADC map pre-RT



Prediction for local and regional failure



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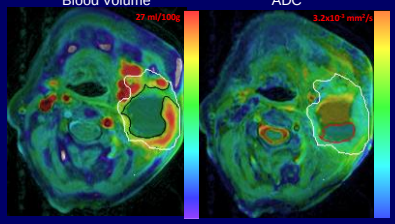
Additive Value of Diffusion Imaging in HNC

Blood Volume

ADC



Hypoperfused and high cellularity (low ADC) subvolume -> high risk for failure?

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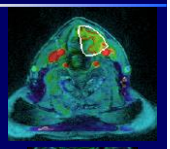
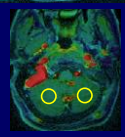
Bias and Variation Between Imaging Systems

- Scanners, sequences, acquisition parameters…
- DCE study in HN cancers
  - Initiate on a 3T Philips and continue on a 3T Siemens
  - Recalibration using histograms
    - Cerebellum as a control region
    - N=9,M_{phi}, SD_{phi} and N=11,M_{sie}, Sd_{sie}
      - $\frac{S_{sie}-M_{sie}}{SD_{sie}} = \frac{S_{phi}-M_{phi}}{SD_{phi}}$





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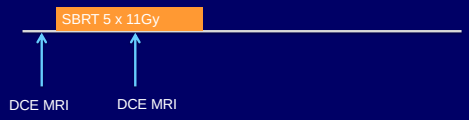
Intrahepatic Cancer: SBRT



Aim: test whether an increase in the subvoluem of the tumor with elevated arterial perfusion after 60% of treatment of SBRT is associated progression.

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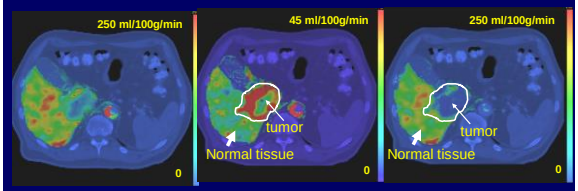
Perfusion in Hepatic Cancer



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

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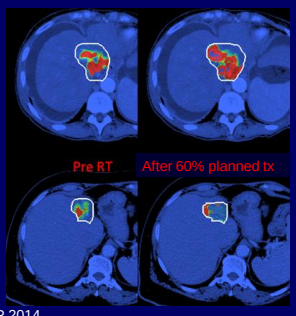
Hepatic cancer: high arterial perfusion subvolume

progressive

responsive



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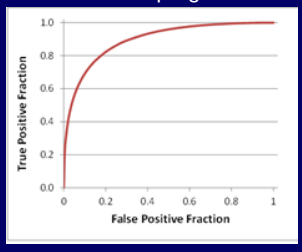
Sensitivity and Specificity

Prediction of progression



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Summary

- Optimize, harmonize and standardize MR image acquisition protocols
  - High quality images
- Quantify physiological parameters
  - high repeatability
  - high sensitivity and specificity
- Apply to clinical problems
  - Algorithms to extract meaningful "features"/metrics
  - Statistical and ML models in relating quantitative metrics with clinical endpoints

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