Perfusion Imaging for Personalised Response Assessment

Catherine Coolens, PhD CIPEM

Radiation Medicine Program, Princess Margaret Cancer Centre, Toronto
Department of Radiation Oncology, University of Toronto
Institute of Biomaterials and Biomedical Engineering, University of Toronto
Joint Department of Medical Imaging, University of Toronto
Adjunct Faculty, Techna Institute, Toronto

UHN Toronto General Toronto Western Princess Margaret Toronto Rehab

UNIVERSITY OF TORONTO

TECHNA

Acknowledgements

Caroline Chung
Laura Dawson
Cynthia Menard
David Jaffray
Ivan Yeung
Harry Keller
Brandon Driscoll
Tina Shek
Stephen Breen
Warren Foltz
Ana Simeonov
Andrew Hope
Anthony Brade
Kristy Brock
Joanne Moseley
Mike Velec
CT staff

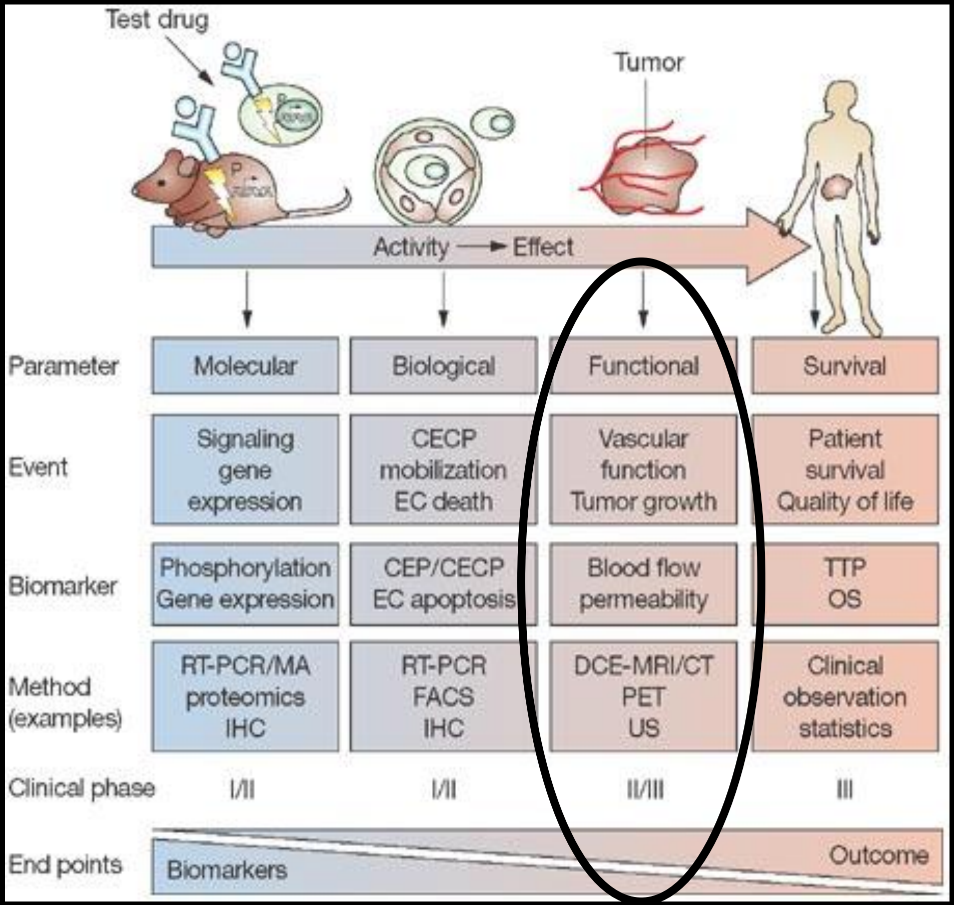
NSERC CRSNG
OICR Ontario Institute for Cancer Research
braintumour foundation OF CANADA
UNIVERSITY OF TORONTO
TOSHIBA

Disclosures

- Patented technology
- Modus Medical Devices Inc.
  - Commercialization License Contrast CT QA
- Shelley Medical Imaging Technologies
  - Commercialization License DCE Phantom

Understanding Cancer: Imaging

Macroscopic Imaging Biomarkers: Tissue Perfusion



Source: Nat Clin Pract Oncol

- Angiogenesis
- Interstitial Fluid Pressure
- Oxygenation/Hypoxia
- Cell density
- Vessel Permeability

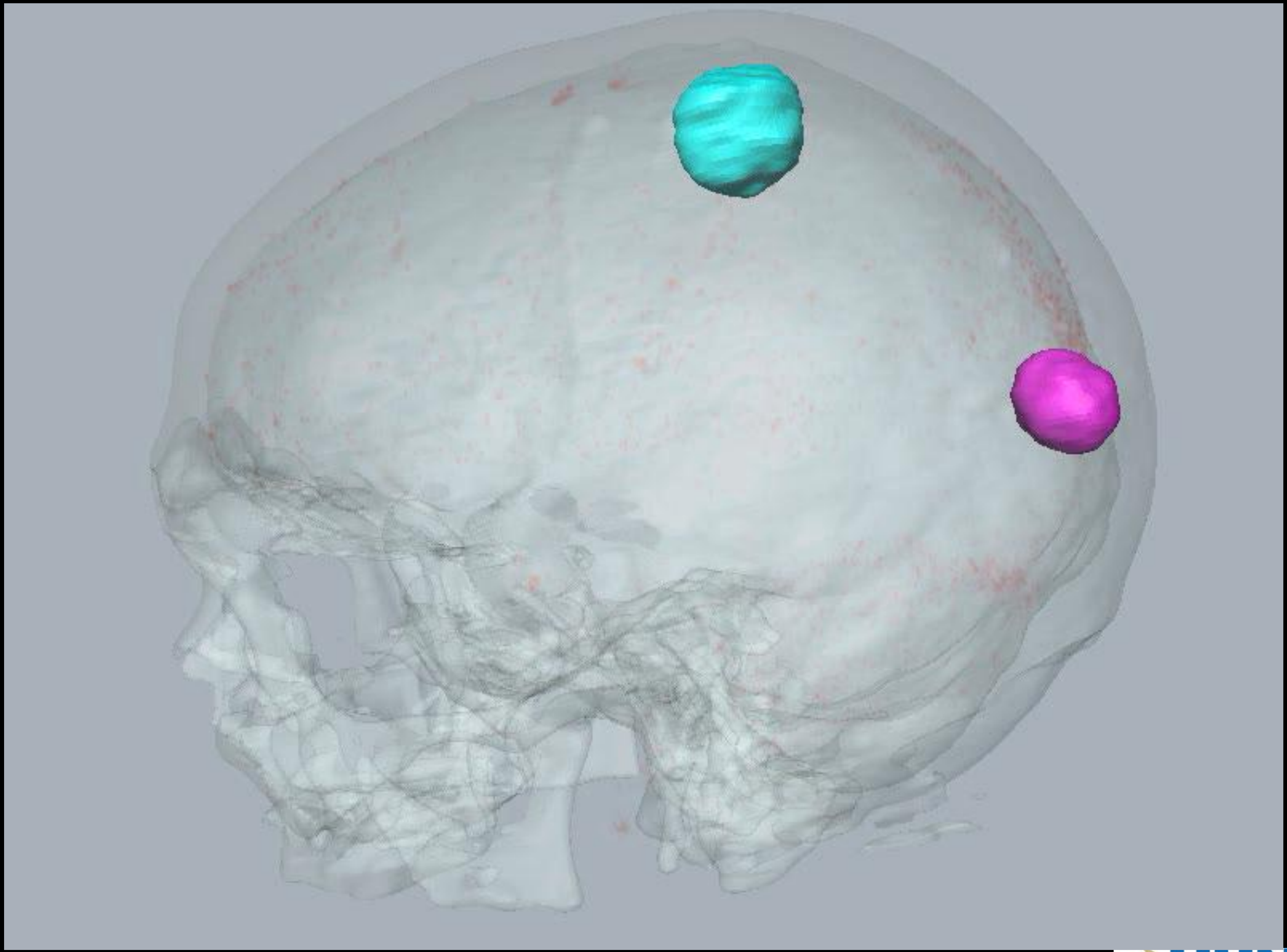
Imaging and Personalized Cancer Medicine

- Quantify individual tumor microenvironment
- Earlier physiological effect than volume change
- Response Assessment to adapt treatment where needed

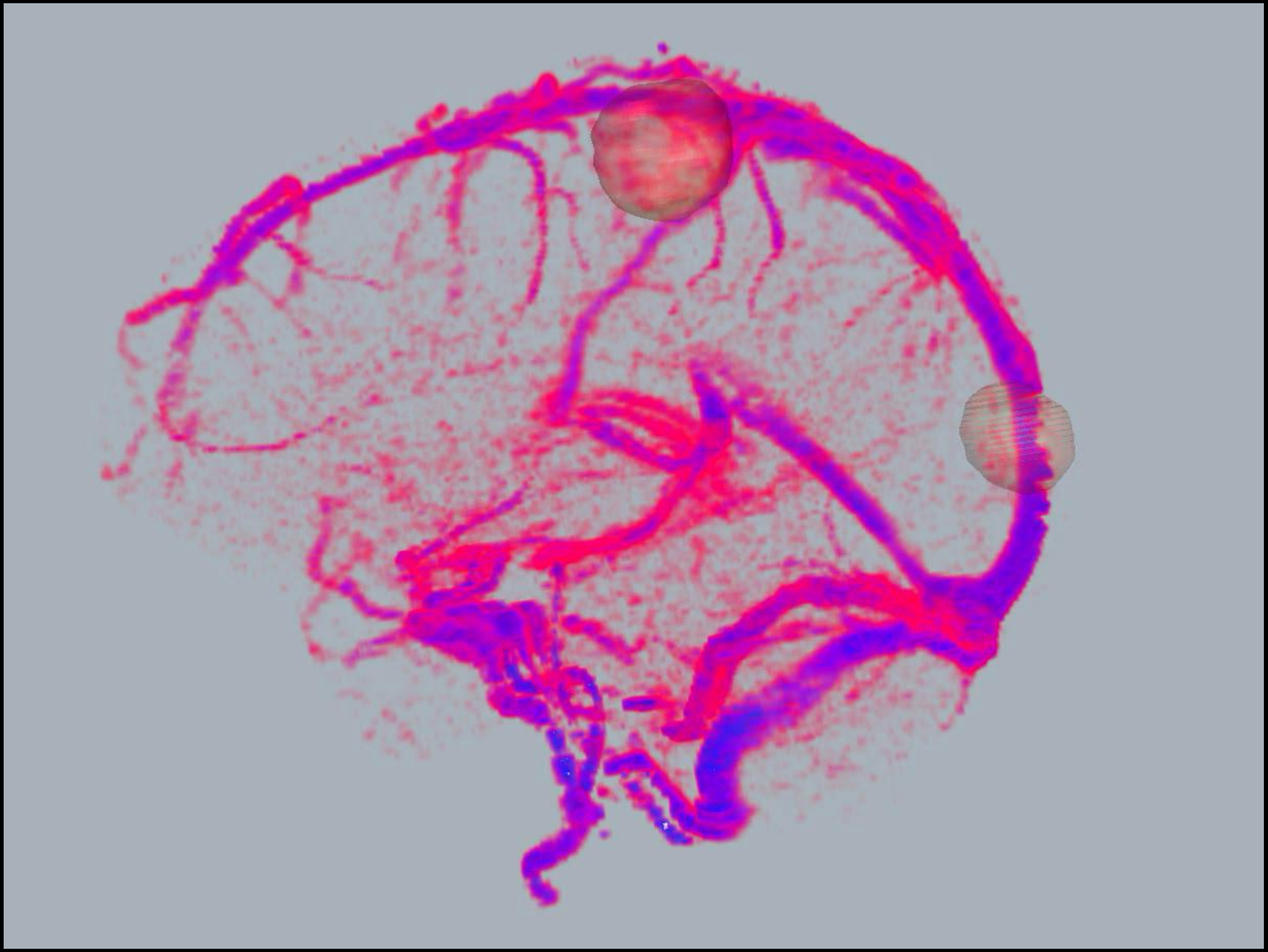
↓

How to interrogate the morphological and physiological status of the tumor before, during and after treatment?

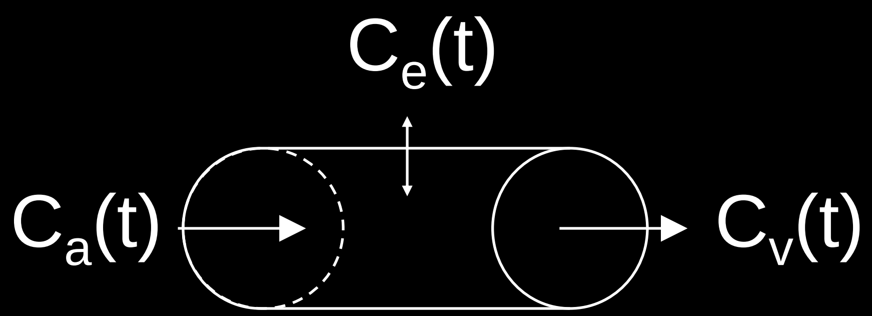
Dynamic Contrast Enhanced (DCE) Imaging

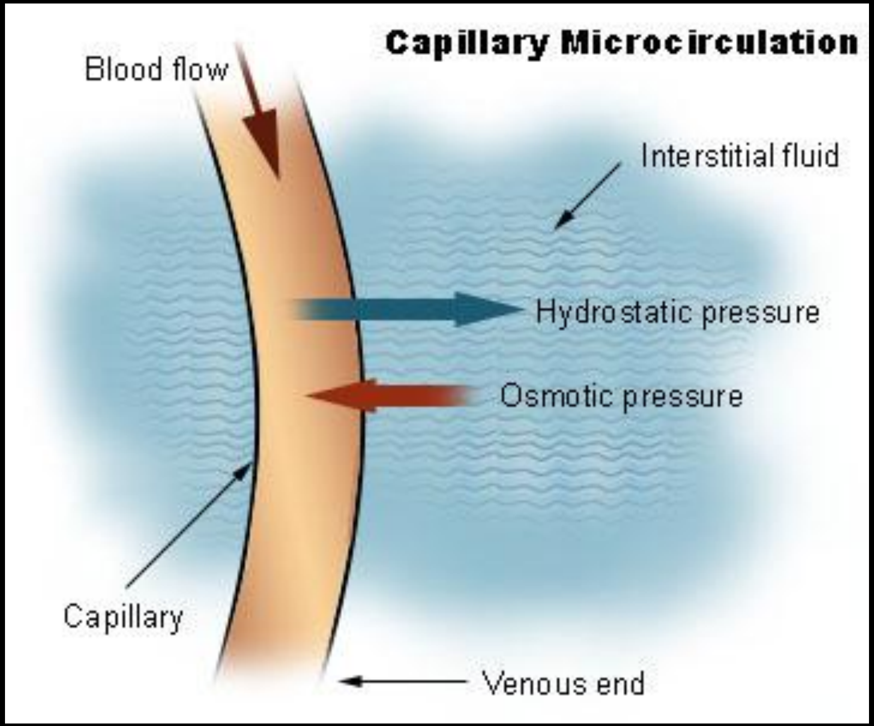


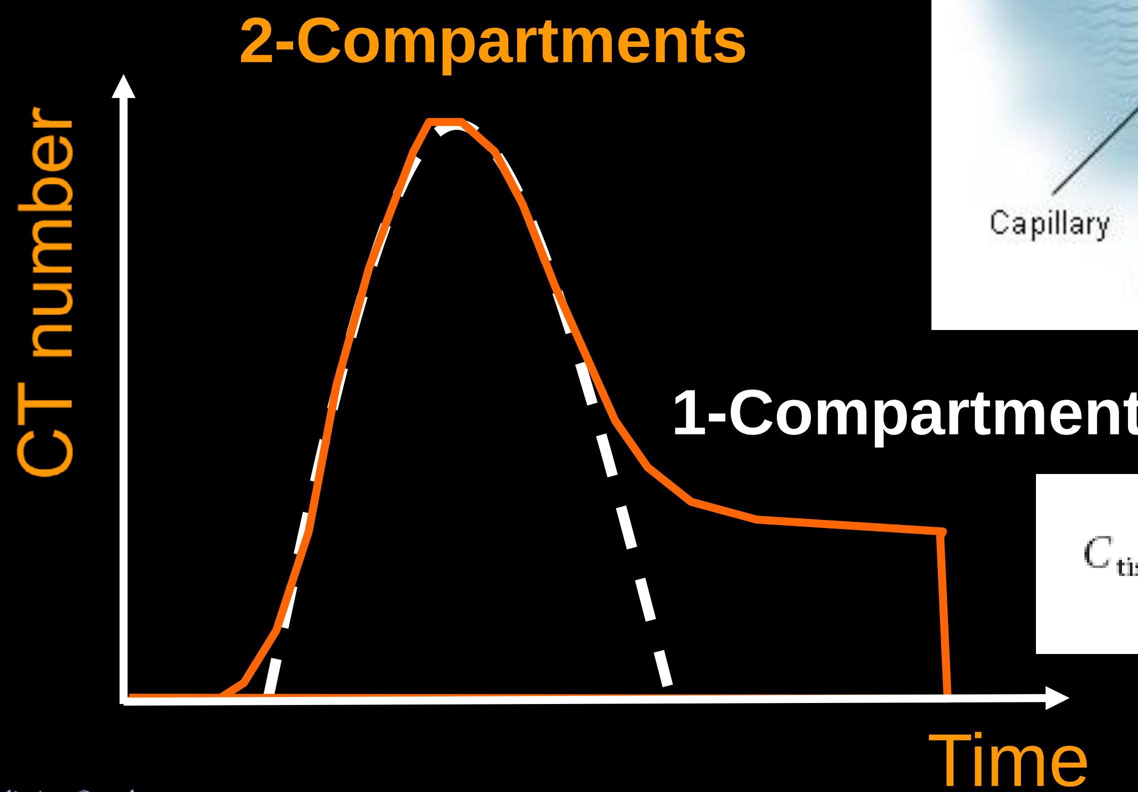
Dynamic Contrast Enhanced (DCE) Imaging



DCE-CT: Kinetic modeling (Perfusion)







$$C_{\text{tiss}}(t) = \frac{\rho F}{1 - Hct} \int_0^t C_a(t - \tau) R(\tau) d\tau,$$

Radiation Oncology
UNIVERSITY OF TORONTO

UHN Princess Margaret Cancer Centre

Perfusion Imaging: Tumor Physiology

hrough

- Bloo
- Bloo
- Mea
- Cap

- Imagin

Eur Radiol (2007) 17: 2441–2457
DOI 10.1007/s00330-007-0619-9

MOLECULAR IMAGING

Markus Rudin

Imaging readouts as biomarkers or surrogate parameters for the assessment of therapeutic interventions

lo. 2, pp. 502–508, 2010

CLINICAL INVESTIGATION — Cervix

LONGITUDINAL CHANGES IN TUMOR PERFUSION PATTERN DURING THE RADIATION THERAPY COURSE AND ITS CLINICAL IMPACT IN CERVICAL CANCER

Nina A. Mayr, M.D.,* Jian Z. Wang, Ph.D.,* Dongqing Zhang, Ph.D.,* John C. Grecula, M.D.,* Simon S. Lo, M.D.,* David Jaroura, Ph.D.,[†] Joseph Montebello, M.D.,* Hualin Zhang, Ph.D.,*
...[‡]
E.E.[¶]

Imaging of Angiogenesis: Clinical Techniques and Novel Imaging Methods

James M. Provenzale[1]

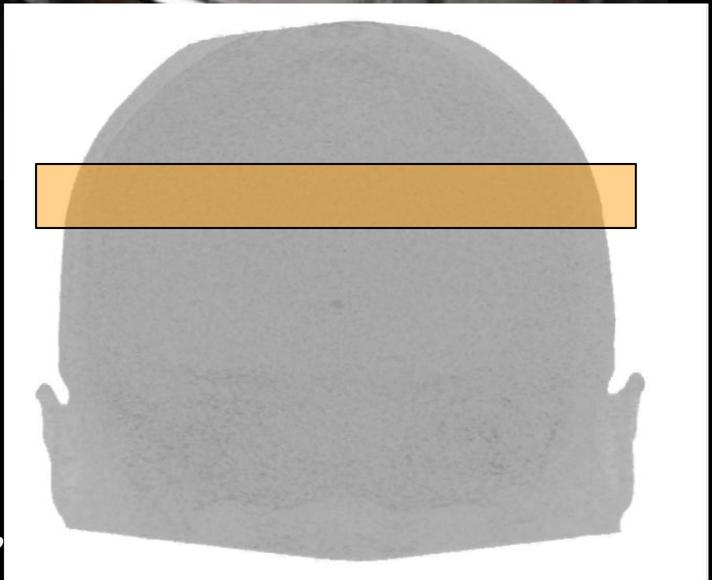
OBJECTIVE. A wide variety of antiangiogenic agents have been developed for the treatment of neoplasms. Imaging studies play an important role in assessing the effects of these treatments.
CONCLUSION. This review article introduces radiologists to features of these therapies and the most important clinical and preclinical imaging techniques for evaluating antiangiogenic agents.

DCE Imaging: Challenges and Progress

- Measurement:
  - Desire for Single Bolus
  - Coverage and Scan Range
  - Motion
  - Temporal Sampling Rates
  - Spatial Resolution (MR-PET)
  - CT dose / Noise
  - MR signal linearity
- Analysis:
  - ROI
  - Manual Segmentation / Bias / Workload
  - Averaging/Filtering of Vessels
  - Observer Variability
- Modeling:
  - Kinetic Model
  - Arterial Input Function
  - Optimization Method

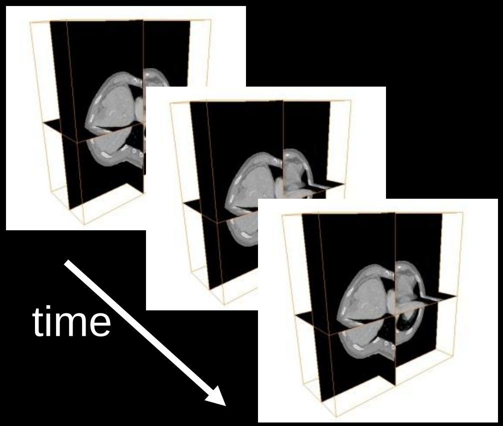
Frontiers: Advances in 4D CT

- 320 Slice CT Scanner
  - FOV (160mm at isocentre)
  - High acquisition speed (0.35 sec)
  - High isotropic spatial resolution (0.5mm)
  - Linearity (HU vs contrast concentration)
  - Motion
  - Moderate AIF Effects
- Physiological relevance
- Clinical convenience



Coolens *et al*. (2009), Med. Phys., vol. 36 (11),

Frontiers: Temporal Dynamic Analysis

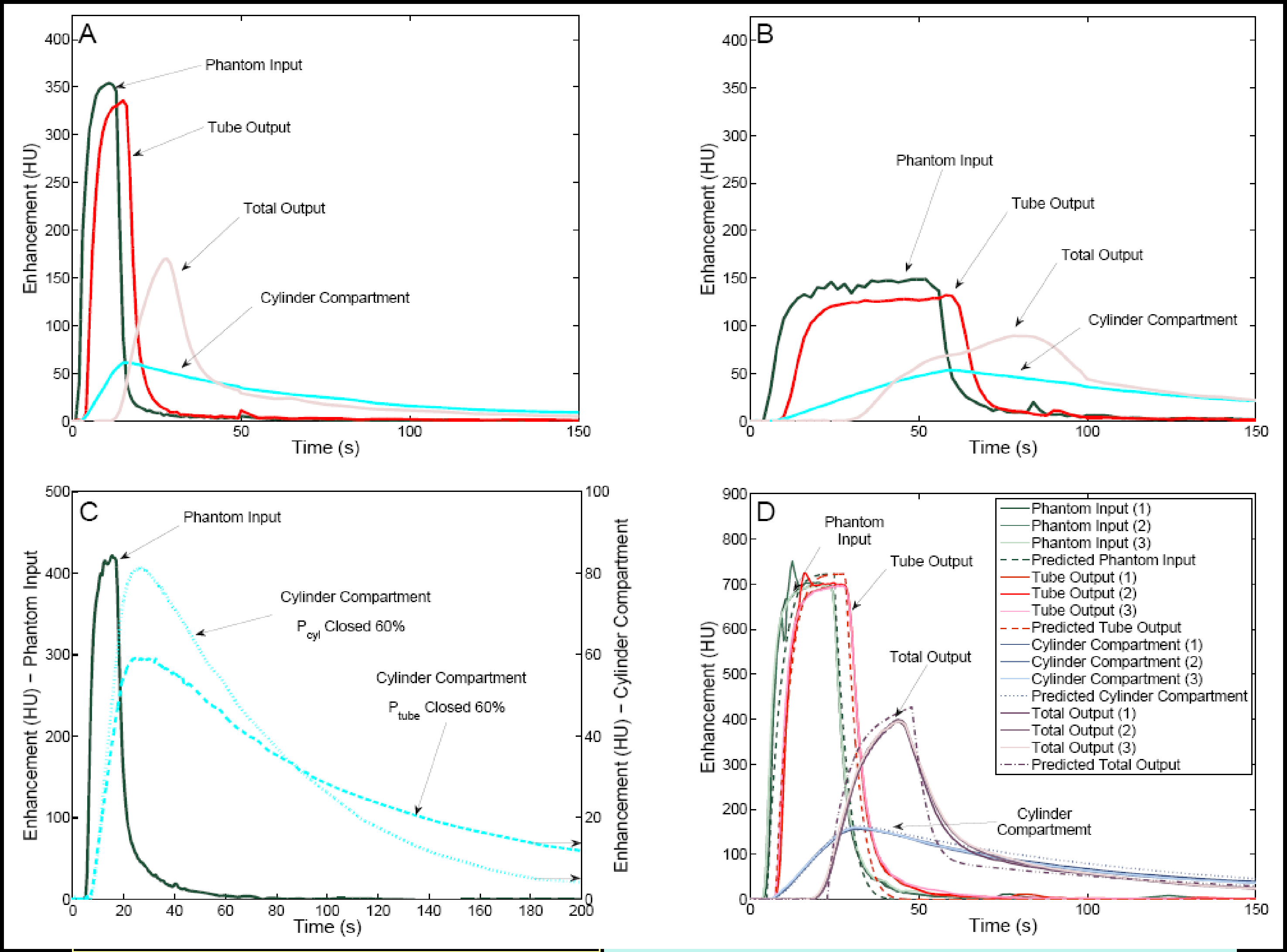


4D DCE CT

voxel

Automated Voxel-based Analysis of 4D DCE CT data improves the measurement of serial changes in tumor vascular biomarkers - Coolens *et al* 2014 – IJROBP. 91(1) pp. 48-57

Frontiers: Quantification of DCE



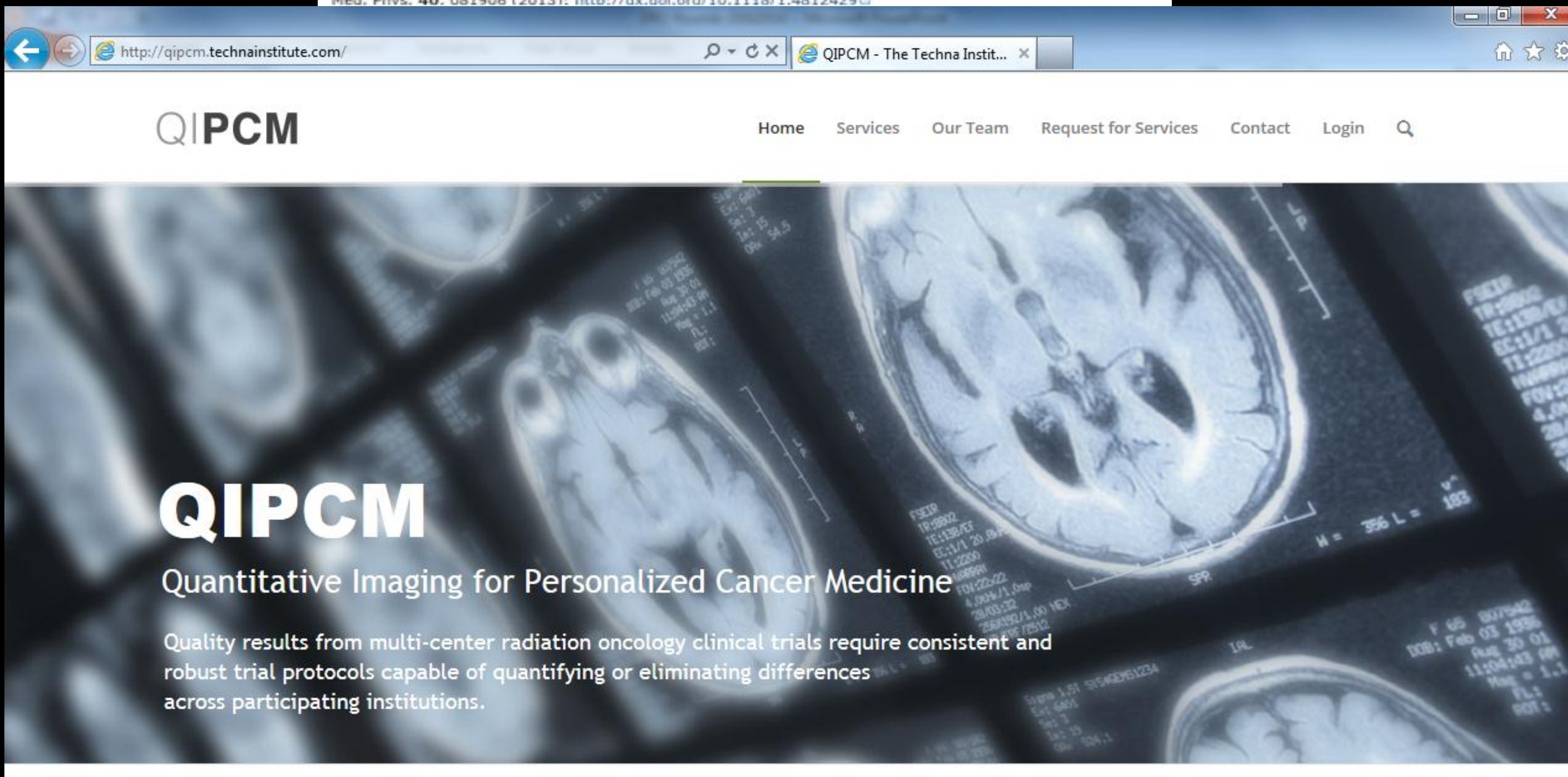
Development of a dynamic flow imaging phantom for DCE CT. Med. Phys. 38, p.4866 (2011)

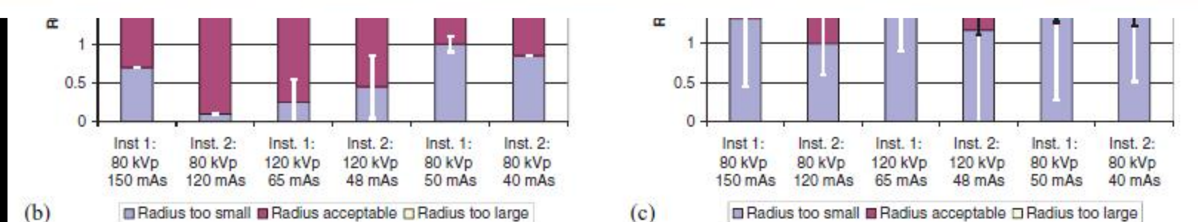
Frontiers: Multi-institutional Testing

Development of a dynamic quality assurance testing protocol for multisite clinical trial DCE-CT accreditation CrossMark

B. Driscoll[1,a)], H. Keller[2], D. Jaffray[3] and C. Coolens[3]

Med. Phys. 40, 081906 (2013); http://dx.doi.org/10.1118/1.4812429





Radiation Oncology
UNIVERSITY OF TORONTO

UHN Princess Margaret Cancer Centre

Clinical Research using DCE-CT

1. Brain Cancer – RT Treatments
2. Liver Cancer Normal – RT + Sorafenib

Brain Stereotactic Radiosurgery (SRS)

- Changes in the brain following radiotherapy can be difficult to distinguish from recurrent disease, and can have variable appearance.
- The proximity to original tumor site, presence of contrast enhancement, growth over time, surrounding edema, and positive mass effect can all closely mimic malignancy.
- Radiation necrosis is frequently seen following standard irradiation

Question: Can we use DCE methods to provide earlier measures of response?

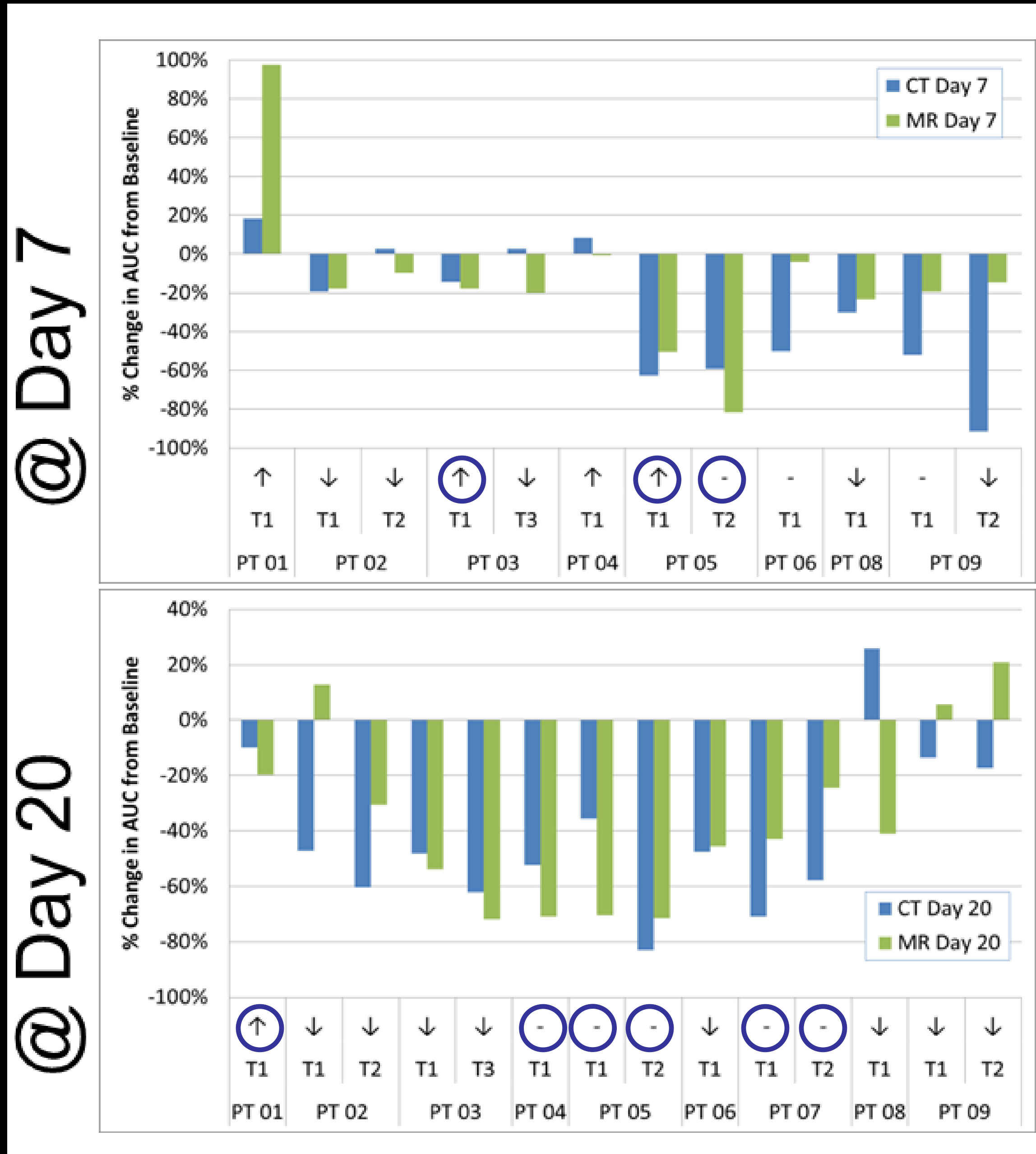
Trial Design: SRS Biomarker Study

SRS dose between 18-21 Gy in single fraction

Day	-7	0	7	9	1 Mth	3Mths	6 Mths	9Mths	12 Mths
Sunitinib (DL 1-2)		────────	────────	────────	──→				
SRS			X						
DCE-CT	←X→		X		X				
MRI(research)	←X→		X[ab]	X	X				
MRI(diagnostic)						X	X	X	X
Neuropsych.	←X→					X	X		X
Biomarker Collection (Serum/plasma, Urine)	←X→		X[a]	X	X				

- DCE MRI at same time points with additional Day 3 scan

Results: Perfusion Imaging vs. Response



$\Delta V \neq$
ΔPerfusion

Radiation Oncology
UNIVERSITY OF TORONTO

UHN Princess Margaret Cancer Centre

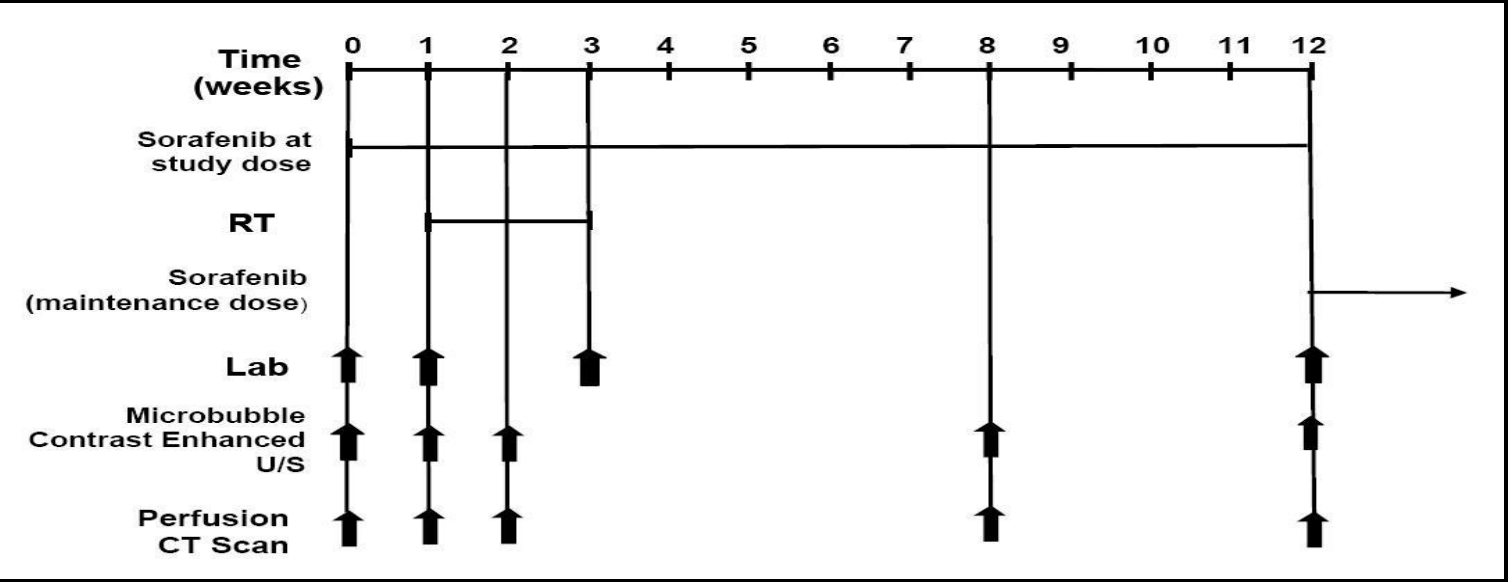
HCC treated with Radiation and Sorafenib

- Hepatocellular carcinoma (HCC) patients treated with Radiation and Sorafenib
- SBRT dose of 30-54Gy in 6 fractions over 2 weeks
- Sorafenib is an anti-angiogenic tyrosine kinase inhibitor administered for 12 weeks following completion RT, followed by standard of care maintenance dose

Question: Can we use DCE methods to provide earlier measures of response?

Trial Design : Biomarker Imaging Study

- Companion DCE Imaging + Serum/urine/tissue Biomarker to evaluate early response as well as long term outcome

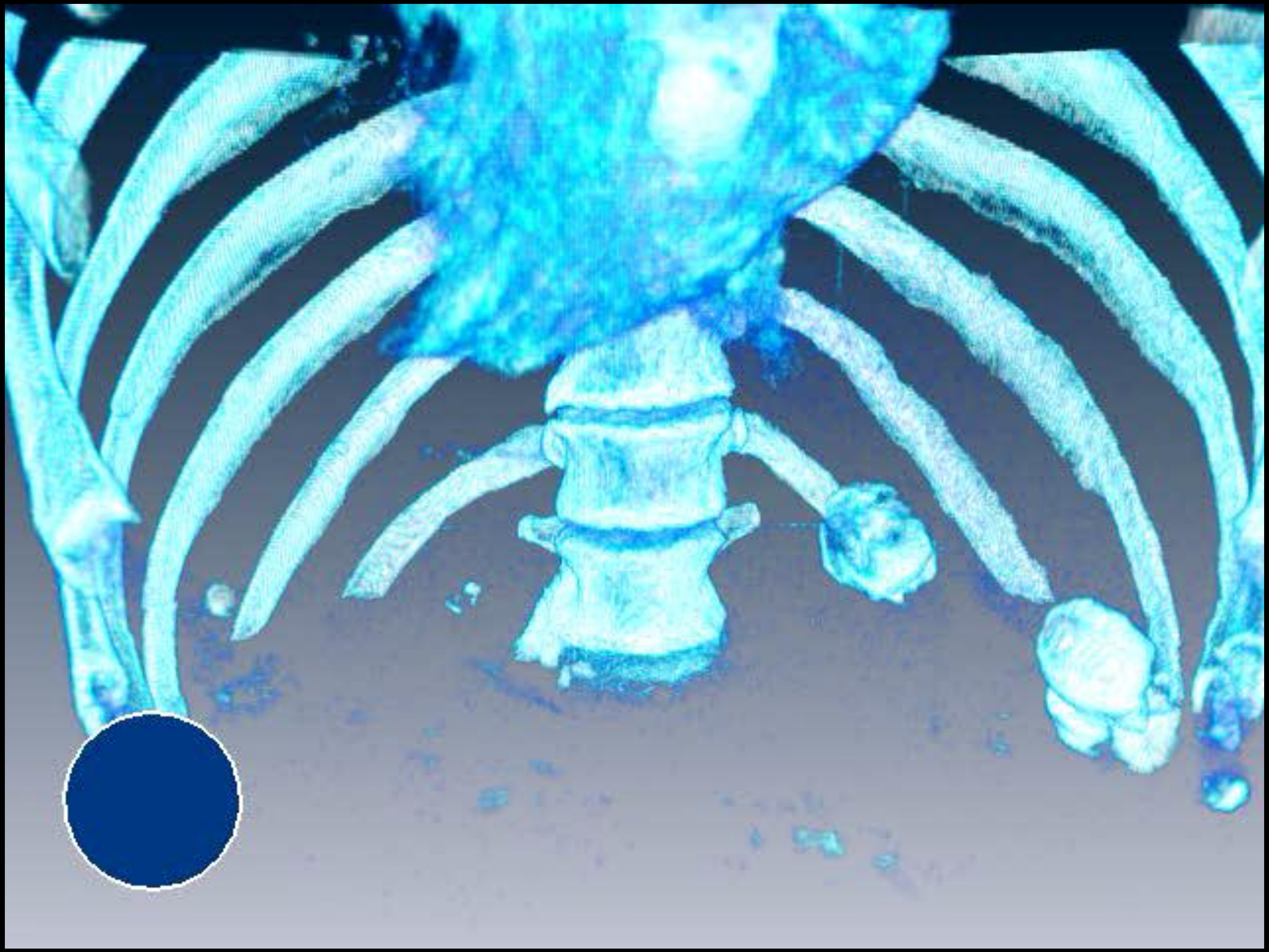


Perfusion CT at different times during treatment

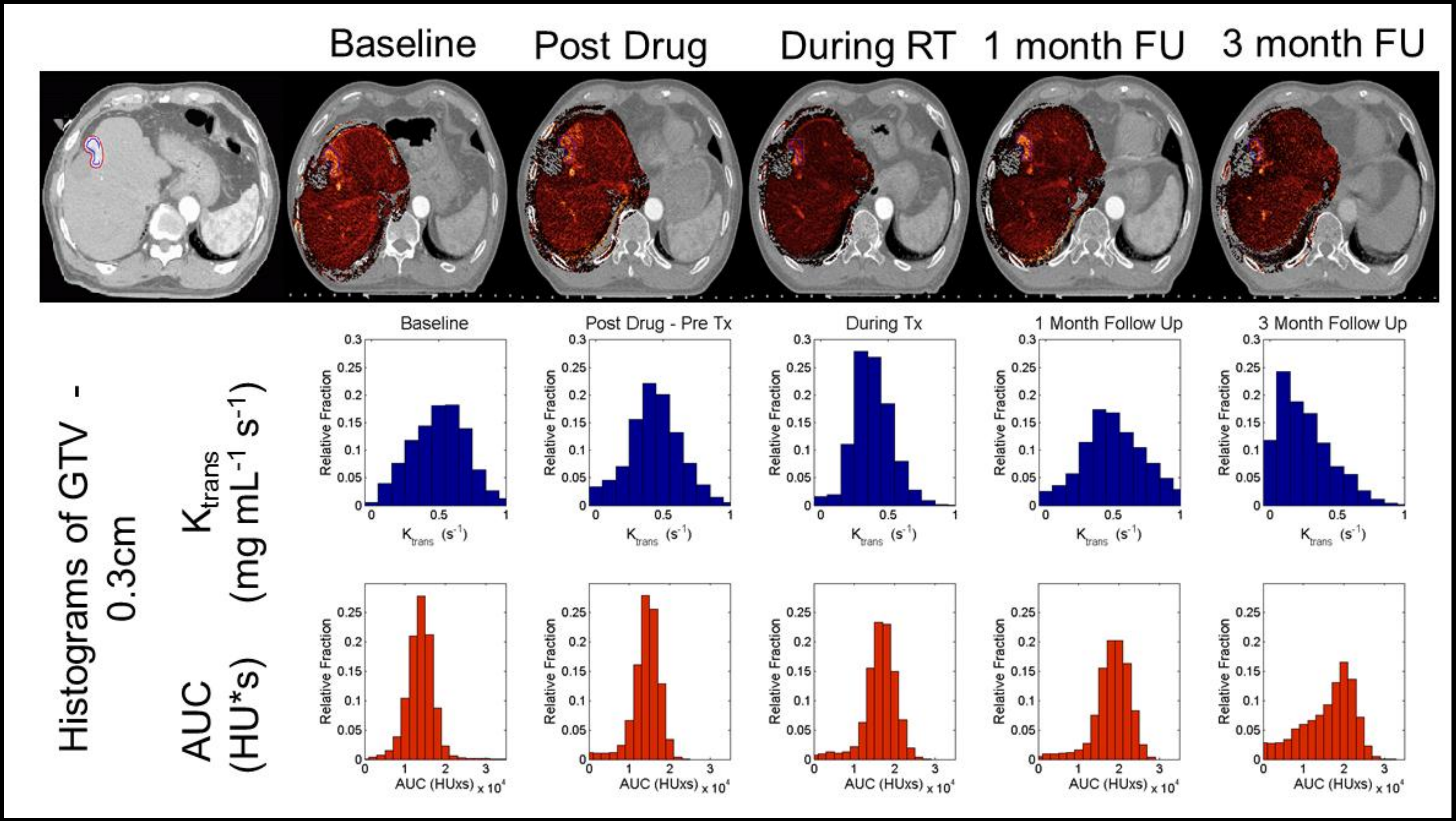
- Baseline
- Post Drug – Pre RT
- During RT
- 1 month FU
- 3 month FU

Methods – 4D DCE CT

Visualization of Perfusion @ 4.5 x

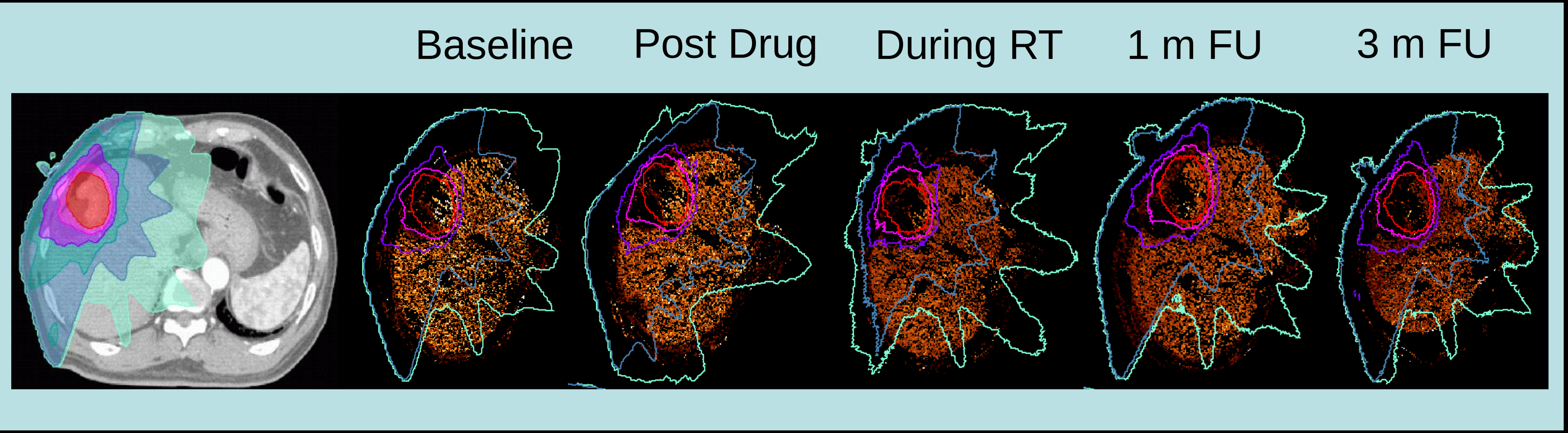


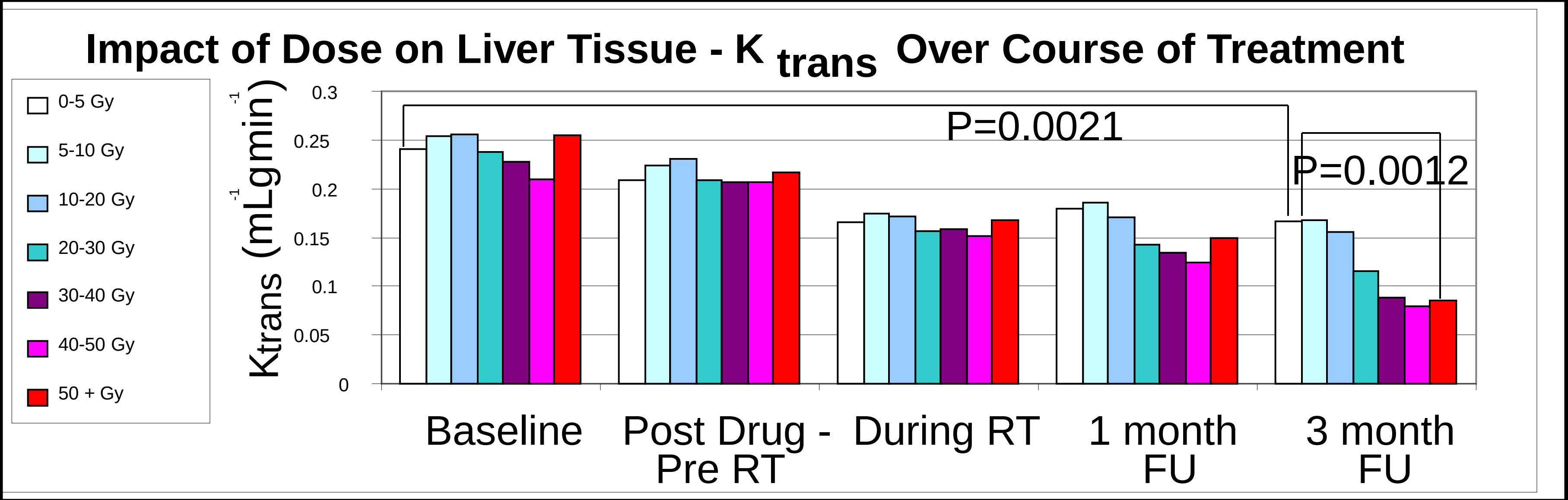
Results: Gross Tumor Volume (GTV) Effects



- Voxel-based analysis provides tumor heterogeneity information
- Interplay with Sorafenib

Results: Normal Liver Radiation Effects





Summary

- Advances in Perfusion Imaging as a Quantitative Biomarker in a validated and multi-institutional framework

- Early Response assessment in application of SRS brain metastases

- Response and normal tissue complication characterisation in liver cancer patients in presence of breathing-induced organ motion