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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

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

Source: Nat Clin Pract Oncol
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)

\[ C_{e}(t) \]

\[ C_{a}(t) \quad \rightarrow \quad C_{v}(t) \]

2-Compartments

CT number

1-Compartment

Time

\[ C_{tiss}(t) = \frac{\rho F}{1 - Hct} \int_{0}^{t} C_{a}(t - \tau) R(\tau) d\tau, \]
Molecular Imaging

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

Clinical Investigation

Longitudinal changes in tumor perfusion pattern during the radiation therapy course and its clinical impact in cervical cancer

Imaging of Angiogenesis: Clinical Techniques and Novel Imaging Methods

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), pp. 5120-5127
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
Development of a dynamic flow imaging phantom for DCE CT.
Frontiers: Multi-institutional Testing

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

B. Driscoll, H. Keller, D. Jaffray and C. Coeens
Med. Phys. 40, 081906 (2013); http://dx.doi.org/10.1118/1.4812429

QIPCM
Quantitative Imaging for Personalized Cancer Medicine

Quality results from multi-center radiation oncology clinical trials require consistent and robust trial protocols capable of quantifying or eliminating differences across participating institutions.
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

- DCE MRI at same time points with additional Day 3 scan
Results: Perfusion Imaging vs. Response

\[ \Delta V \neq \Delta \text{Perfusion} \]
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

Impact of Dose on Liver Tissue - $K_{\text{trans}}$ Over Course of Treatment

- **Baseline**
- **Post Drug**
- **During RT**
- **1 m FU**
- **3 m FU**

**Baseline**

- Post Drug
- During RT
- 1 month FU
- 3 month FU

- 0-5 Gy
- 5-10 Gy
- 10-20 Gy
- 20-30 Gy
- 30-40 Gy
- 40-50 Gy
- 50+ Gy

$K_{\text{trans}}$ (mLg$^{-1}$min$^{-1}$)

- $P=0.0021$
- $P=0.0012$

Radiation Oncology
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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