(Quantitative) Imaging for Adaptive Radiotherapy

Catherine Coolens, PhD CIPEM

Department of Medical Physics, 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
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- Modus Medical Devices Inc.
- Shelley Medical Imaging Technologies
Understanding Imaging: Overview

- Adaptive Imaging Specifications
- Functional Imaging Techniques
- Validation and Standardization
Imaging and Personalized Cancer Medicine

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

How interrogate the morphological and physiological status of the tumor before, during and after treatment?
1. Understanding Cancer: Target Definition

Reduced variation in delineation

Han et al. Radiotherapy and Oncology 120 (2016) 519–525
1. Understanding Cancer: Heterogeneity

1. Understanding Cancer: Microenvironment

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

Source: Nat Clin Pract Oncol
Only histogram moments analysis of parametric maps prognostic

2. Functional Imaging: Requirements

- High spatial resolution
- High temporal resolution
- Clinical convenience
- Non-invasive (single or no bolus)
- (Direct) Quantification
- Biologically relevant surrogate
- Meaningful parametric model
2. Functional Imaging: Overview

A. Size change: cytotoxicity
   Density: tissue enhancement
   Density: cystic or myxoid

B. Single voxel
   - $V_e$: plasma volume
   - $V_p$: vascular volume
   - Contrast-enhanced CT or MRI: proportion of enhancement
   - DCE-MRI or DCE-CT: blood flow, PS
   - Arterial spin labelling: blood flow
   - Diffusion-weighted imaging: tissue oedema, apoptosis

C. Single voxel
   - $V_o$: blood flow
   - $^{15}O-H_2O$: blood flow
   - $^{15}O-CO$: blood volume

D. Single voxel
   - FDG: glucose metabolism
   - FLT: cell proliferation
   - Growth factor expression
   - Growth factor inhibition
2. Frontiers: Multi-modal Imaging

Padhani & Miles, Radiology 2010
2. Functional Imaging: DCE Imaging
2. Functional Imaging: Kinetic modeling

\[ C_a(t) \rightarrow C_e(t) \rightarrow C_v(t) \]

2-Compartments

CT number

Time

Tofts et al 1999 JMRI

\[ C_{tiss}(t) = \frac{\rho F}{1 - Hct} \int_0^t C_a(t - \tau) R(\tau) d\tau, \]
2. DCE Imaging: Iodine vs Gd-DTPA

- Main Lesion has stayed roughly the same volume
- Contrast Bloom evident in MR but not CT

<table>
<thead>
<tr>
<th>Visipaque</th>
<th>Gadovist</th>
</tr>
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<tbody>
<tr>
<td>320 mgI/mL</td>
<td>1.0 mmol Gd/mL</td>
</tr>
<tr>
<td>MW 1550.2</td>
<td>MW 604.7</td>
</tr>
</tbody>
</table>
2. Functional Imaging: Transport Flow

Case Study (DCE-MRI) courtesy of T. Hompland
III. Robustness and Standardization

*Data preparation* accounts for about 80% of the work of data scientists.

Data scientists spend 60% of their time on cleaning and organizing data. Collecting data sets comes second at 19% of their time, meaning data scientists spend around 80% of their time on preparing and managing data for analysis.
Functional Imaging Validation Framework

- Standardization of image acquisition and analysis
- Correlation with outcome
- Correlation with pathology or tissue biomarkers
- Unified Transport modeling
MULT-SITE DCE CHALLENGE: A CLUSTER FAILURE
Parametric Sensitivity to Acquisition

Quantitative imaging biomarkers alliance (QIBA) recommendations for improved precision of DWI and DCE-MRI derived biomarkers in multicenter oncology trials

Amita Shukla-Dave PhD, Nancy A. Obuchowski PhD, Thomas L. Chenevert PhD, Sachin Jambawalikar PhD, Lawrence H. Schwartz MD, Dariya Malysarenko PhD, Wei Huang PhD... See all authors

First published: 9 November 2018  https://doi.org/10.1002/jmri.26518  Cited by: 5
QIPCM CLINICAL TRIAL IMAGING SUPPORT

- Image QC
- Extracted Imaging Features
- QIPCM PACS
- Virtual Desktop Infrastructure
- 2-Factor Authentication

CTP Anonymizer
Medical Images
90 TB Network Storage
EXTERNAI IMAGING INSTITUTION

EXTERNAL TRIAL INVESTIGATORS
Trial Clinicians and Analysts

https://technainstitute.com/qipcm/
**QIPCM: Standardized Tools**

**The DCE QA Tool**
- Using a validated dynamic flow phantom perform DCE QA for any CT scanner.

**4D TDA CT/MRI**
- A robust method for automatic 3D vasculature segmentation and unified parametric voxel-based analysis of DCE CT & DCE-MR, DWI scans without the need for manual tissue ROI delineation.

**Web Based RT Viewer**
- Browser-based RT-specific viewer for visualization, review and workflow (automated navigation and quality assurance tools)
Standards & Guidelines: RSNA

- Quantitative Imaging Biomarker Alliance (QIBA)

**QIBA organization**

QIBA has advanced through the generous commitment of volunteer committee members from academia, medical device, pharmaceutical and other business sectors and government.

There are four modality-based Coordinating Committees, including Q-CT, Q-MR, Q-NM and Q-US. Nineteen Biomarker Committees include:

- **CT**
  - CT Angiography
  - CT Volumetry
  - Lung Density
  - Small Lung Nodule
- **MR**
  - Arterial Spin Labeling (ASL)
  - Dynamic Contrast-Enhanced (DCE) MRI
  - Dynamic Susceptibility Contrast (DSC) MRI
  - Diffusion Weighted Imaging (DWI) MRI
  - Functional Magnetic Resonance Imaging (fMRI)
  - Magnetic Resonance Elastography (MRE)
  - Proton Density Fat Fraction (PDFF)
  - Musculoskeletal (MSK)
- **NM**
  - FDG-PET/CT
  - Quantifying Dopamine Transporters with 123Iodine Labeled Ioflupane in Neurdegenerative Diseases (I-123)
  - PET-Amyloid
  - Technetium-99m for body, oncology and immunology (TC99m)
- **US**
  - Contrast Enhanced Ultrasound (CEUS)
  - Ultrasound Shear Wave Speed (SWS)
  - Ultrasound Volume Blood Flow (VBF)

Each committee has specific responsibilities for its respective modalities or disease-based approach, and is open to interested persons.

View the QIBA organizational chart.
Standards & Guidelines: NCI

- Quantitative Imaging for Evaluation of Responses to Cancer Therapies (QIN)
Standards & Guidelines: AAPM

- MRI - Molecular Imaging in
  - TG 294: Magnetic Resonance Biomarkers in Radiation Oncology
  - TG 284: MRI Simulation in Radiotherapy: Considerations for Clinical Implementation, Optimization, and Quality Assurance
Summary

1. Importance of Functional Imaging in Simulation and Treatment Response Assessment

2. Multi-modality Imaging Approach to support complementary Response Assessment describing broader micro-environment

3. Further standardization and validation of functional image acquisition and analysis for clinical trials is needed
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Thank You

Questions?
catherine.coolens@uhn.ca
References