Implementing in vivo perfusion measurements using DCE MRI

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Learning objectives

- To understand practical issues to extract quantitative imaging metrics
- To understand how to increase robustness and objectiveness in the analysis
- To understand limitations of derived quantitative imaging metrics

Quantitative imaging as a biomarker

- Various physiological, metabolic and molecular parameters of tissue may serve as both prognostic as well as evaluative methods for disease and therapeutic response/outcome
- Imaging systems have significant power to aid in vivo estimation of these parameters

What is the relevance of perfusion analysis?

- Blood supply is critical to the sustainability of tissue
  - Nutrients and oxygen are supplied by vessels
- Vasculature and blood supply to tissue may be a highly relevant biomarker in cancer therapy
  - Neovascularization $\rightarrow$ Tumor aggressiveness
  - Changes in neovascualture $\rightarrow$ Tumor response
  - Changes in normal vasculature $\rightarrow$ Normal tissue damage
Quantitative metrics related to perfusion

- Metrics include blood flow, transit time, transfer rates to tissue, blood volume
- These metrics are estimated using parametric and/or compartmental models
- The proper model selection depends upon the organ of interest as well as the physiological condition
- There is no single model that can be applied to all systems and physiological conditions
- It is important to understand
  - What problem is to be addressed
  - What assumptions are used in the models
  - What physiological parameters are derived from the model
  - How parameters are related to each other

Examples of perfusion related models

- Brain perfusion model
  - Brain perfusion (Ostergaard MRM 1999)
  - Transfer constant to tissue and blood volume
- Kety model (Toft JMRI 1999)
- Dual-input and single compartment liver perfusion model
  - Arterial and portal venous perfusion

Comments

- Models approximate problems and have their limitations
- Different physiological parameters can be estimated from different models
- Interpretation of extracted parameters depends upon the model, organ, image acquisition, and biological conditions
- Models will be discussed in detail in CE-Imaging: MRI III (WE-A-303A-1 7:30 AM)
Choose acquisition sequence, parameters and models

- What is targeted in the clinical trial
  - Anti-VEGF therapy in recurrent GBM

- What is targeted in the clinical trial
  - Chemotherapy + RT in HN Cancer

- What is targeted in the clinical trial
  - Radiation effect on liver function

Choose acquisition sequence, parameters and models

- Choose right acquisition, parameters and a model
  - $K_{trans}$ and blood volume
    - $T_1$-weighted images during a bolus of Gd-DTPA injection
  - $TR/TE$ (ms) and $flip$ angle
  - $plane$ and $resolution$

DCE MRI acquisition paradigm

- Imaging sequence and parameters
  - $2D$ or $3D$ flash or SPGR sequence to acquire dynamic $T_1$-weighted images
  - $TR/TE$ (ms) and $flip$ angle
  - $plane$ and $segmentation$

- Dynamic acquisition
  - Long enough to be sensitive to contrast uptake in tissue

- Temporal resolution
  - Blood flow $\rightarrow$ high temporal resolution
Example: liver DCE protocol

- 3D gradient-echo pulse sequence on Philips 3T scanner
  - FOV of 330 mm
  - 75% of FOV in the phase encoding direction
  - ~60 slices in the oblique sagittal coronal orientation
  - voxel size of 1.3x2x2 mm³
  - TFE of 200, T1/TR of 2.1/4.5 ms
  - flip angle of 20 degrees
  - sense factor of 2 in 2 directions
  - Temporal 2.5 s per volume

Example: DCE Data for HN cancer

Image Acquisition:
- Sagittal Plane → reduce the in-flow effect
- 3D Volumetric → cover the primary tumor and involved node
- Voxel size 2x2x2 mm → reformat images as axial

Extraction of perfusion parameters from DCE MRI via post-processing

- General paradigm for data analysis
  - Re-align dynamic image volumes within series
  - Correct baseline signal intensities
  - Determine artery input function
  - Choose a physiological model
- Process dynamic images

Realignment of dynamic volumes within series

- Before registration
- After registration
Extraction of perfusion parameters from DCE MRI via post-processing

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Baseline correction

- T1 weighted signal intensity
  \[ S = S_o \frac{1 - e^{-t/T1}}{1 - \cos \alpha e^{-t/T1}} \]

- If \( TR \times T1 \ll T1 \),
  \[ S = S_o \frac{\sin \alpha}{1 - \cos \alpha} TR \times R \{1 + O(10^{-3})\} \]

- Signal intensity difference after and before contrast
  \[ \Delta S = S_o - S_o = S_o \frac{\sin \alpha}{1 - \cos \alpha} TR \times \Delta R \]

Determine artery input function

- Artery input function
  - Threshold intensities to find the most rapid contrast uptake voxels in artery
- Large artery vs small artery
  - Small artery
    - Close to tissue of interest
    - Suffers from partial volume averaging
  - Large artery
    - Less partial volume effect
    - Distant from tissue of interest
    - Time delay
  \[ C(t) = K \cdot \int e^{-t/(t_1)} C(t) \cdot (t-I) \cdot t + v \cdot C(t-I) \]
Extraction of perfusion parameters from DCE MRI via post-processing

- General paradigm for data analysis
  - Re-align dynamic image volumes within series
  - Correct baseline signal intensities
  - Determine artery input function
  - Choose a method of analysis
  - Process dynamic images

Choose a method for analysis

- Most people use available (commercial) software
  - This may or may not be adequate for the problem being addressed
- Understand the underlying model
- Test the software (model) with a set of simulated dynamic data (with known truth)
- Understand performance of tested software

Process dynamic Images

- FIAT: General Toft model
  - NLLS, TLS, GLS, LLS
Potential sources of error

- Performance of the scanner and coil
  - T1 Phantom → QA
  - Homogeneity of B0 and B1 fields, artifacts, noise, R1 vs C, stability
- Flow phantom → QA of flow assessment
- Human study
  - Image quality
  - Noise, distortion, motion artifacts
  - Temporal resolution
  - Length of dynamic acquisition
  - T1 change over time interval of assessment
    - Quantify native T1
    - Allow us to correct T1 effect if there is any change
  - Artery input function
    - Errors and inconsistency

Other concerns

- Quantitative image consistency – need for test-retest to determine a minimum change that can be detected reliably
- OVER-ANALYSIS – extracting information that exceeds the limits of the measurement method
  - How many parameters can be fitted in a model given SNR of dynamic DCE MRI
  - A balance between complexity and reliability

Develop and test Software tools

- Implementation of perfusion-related measurement and model application is not standard for all image acquisition methods or applications
- Robust and flexible software tools are needed to ensure proper data management
- Test performance of software tools
  - Simulated phantom data sets with known “truth”

A Concern!

- Toft models

\[
C_i(t) = K^{\text{trans}} \int_0^t e^{-\kappa_p(t-\tau)} C_p(\tau) d\tau + v_p C_p(t)
\]

\[
C_i(t) = K^{\text{trans}} \int_0^t e^{-\kappa_p(t-\tau)} C_p(\tau) d\tau
\]

extravascular contribution

intravascular contribution

Values of the two \(K^{\text{trans}}\)s are not comparable!
We have developed a simulated DCE phantom for testing the standard DCE model (general Toft model)

- Parameters have been considered:
  - CNR, temporal resolution, dynamic acquisition time, \( k_{tr} \), \( V_p \), \( k_{ep} \), input function temporal jitter, …
  - >1 million simulations to cover a large range of variations of parameters
  - 2500 simulations for each combination of the parameters → statistics

\( K^{trans} \) and \( V_p \) do not have same sensitivity to noise!

Stability of large \( K^{trans} \) values depends upon the sample interval

We form a TG to evaluate software tools for quantification of DCE MRI

- Validate data, test tools, report results
- Make data available for public via CaBIG, QIN, QIBA and possible professional society, e.g., AAPM
- Publish the test results
- This test will provide:
  - a common ground to communicate between investigators
  - Guidance for image acquisition design
  - QA for multi-center clinical tools
- We call for participants to test their software tools using the same data sets
- Please send email to yuecao@umich.edu
Resources are still needed to aid in DCE-based perfusion as a biomarker

- Standards for acquisition, models, and terminologies
- Criteria for reproducible imaging
- Validation methodologies
  - Phantoms: T1, flow, and simulated phantoms
  - "Gold standard", "standard" or validated data
- Multiple efforts are underway to provide such resources
  - QIBA
  - NIH PAR 08-225 – Quantitative Imaging Network

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- Open positions for Post-Doctoral fellows
  - Send CV to yuecao@umich.edu