Treatment Assessment of Radiotherapy using MR Functional Quantitative Imaging: Promises and Challenges

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Outline

➢ Introduction of MR quantitative imaging for treatment assessment
➢ Review of diffusion imaging, DCE/DSC imaging…
➢ Treatment assessment using diffusion MRI
➢ Treatment assessment using DCE-MRI
➢ Developments of MR quantitative imaging for treatment assessment
➢ Challenges and future directions
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Introduction

Recent developments in MRI have substantially improved its performance. Anatomic ➔ Angiographic ➔ Physiologic ➔ Interventions

Making it a potentially powerful tool for not only diagnosis but also therapy.
Various MR quantitative functional techniques including, but not limited to, DWI, DTI, MRS and DCE/DSC imaging, have been investigated to assess therapeutic outcome in radiotherapy.
Treatment Simulation

Treatment Planning

Image-Guided Treatment

?
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Diffusion imaging techniques are used to determine the rate and principle direction of thermal (Brownian) motion of protons.

Diffusion affected by intra-cellular and extra-cellular architecture

Hamstra, et al, JCO 2007
Diffusion-Weighting Gradients

Tissue A
Restricted Diffusion
Bright Contrast

Tissue B
Freely Diffusion
Dark Contrast
**Diffusion-Weighting Gradients**

Diffusion-weighting gradient is often referred to as bipolar gradient (or Stejskal-Tanner gradient)

Spin Echo: $90^\circ$ RF, first gradient lobe, $180^\circ$ RF, second gradient lobe

Stejskal, Tanner. J Chem Physics, 1965
Diffusion-Weighting Gradients

90°  180°

\[ b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3) \]

\[ \frac{S}{S_0} = \exp(-bD) \]

b-factor for rectangular pulse of spin echo
High $b$-Value Diffusion

Zhou, et al. MRM, 2010
Diffusion is truly a three-dimensional process. Hence, molecular mobility in tissues may not be the same in all directions.

- Diffusion can be described by a tensor, with min. 7 acquisitions.
- The diffusion tensor can be an ellipsoidal approximation

\[ \bar{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} \]

\[ \bar{D} = \bar{E}^{-1} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \bar{E} \]
Diffusion Tensor Imaging

Diffusion is truly a three-dimensional process. Hence, molecular mobility in tissues may not be the same in all directions.

➢ Diffusion can be described by a tensor, with min. 7 acquisitions.

D Le Bihan, et al. JMRI, 2001
Y. Masutani et al. EJR, 2003
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Angiogenesis

- Angiogenesis is a complex process critical to the growth and metastasis of malignant tumors.
- Tumor growth beyond 1–2 mm in solid tissues cannot occur without vascular support.
- Early detection of such changes would allow assessment of the therapeutic outcome of anti-vascular agents and aid in diagnosis.

J. Folkman  Eur J Cancer 1996
Detection of Angiogenesis

Current methods of assessing angiogenesis can be considered as either direct or indirect.

➢ direct method: microvascular density counting with immunostaining (most frequently used)
  - invasive and no functional information

➢ indirect method: indirect biomarkers of angiogenesis detected by imaging such as MRI using contrast agent (e.g. Gd)
  - Non-invasive and provide functional information
### DCE and DSC MRI

#### Table 1
Comparison of the T2*- and T1-weighted Dynamic Contrast-enhanced MR Imaging Techniques

| Parameter                              | T2*-weighted Imaging | T1-weighted Imaging |
|----------------------------------------|-----------------------|---------------------|
| Change in tissue signal intensity      | Darkening             | Enhancement         |
| Duration of effect                     | Seconds               | Minutes             |
| Period of optimal data acquisition     | Subsecond             | 2–25 sec            |
| Magnitude of effect                    | Small                 | Larger              |
| Optimal dose of contrast medium        | ≥0.2 mmol/kg          | 0.1–0.2 mmol/kg     |
| Quantification methods used            | Relative more than absolute | Relative and absolute |
| Physiologic properties measured        | Perfusion, blood volume | Transendothelial permeability, capillary surface area, lesion leakage space |
| Kinetic parameters derived             | Blood volume and flow, transit time | Transfer and rate constants, leakage space |
| Pathologic correlates                  | Tumor grade, microvessel density | Microvessel density, vascular endothelial growth factor |
| Clinical MR imaging applications       | Characterization of breast, liver, and brain lesions; noninvasive grading of brain tumors; directing biopsy of brain tumors; determination of prognosis for brain tumors; monitoring treatment (eg, radiation therapy) | Lesion detection and characterization; improving accuracy of tumor staging; prediction of response to treatment; monitoring response to treatment; allowing novel therapies, including antiangiogenic drugs; detection of tumor relapse |

J.A. d’Arcy  RadioGraphics 2006
DCE-MRI

M.V. Knopp, et al. MCT, 2003
DCE-MRI: Pharmacokinetic Model

Plasma Flow

Plasma \( C_p, \nu_p \)

Endothelium

\( K_{in}^{\text{trans}} \)

\( K_{out}^{\text{trans}} \)

EES \( C_{EES}, \nu_e \)

P.S. Tofts, et al. JMRI, 1997
Pharmacokinetic Model

\[ C(t) = C_{EE_S}(t) + \nu_p C_p(t) \]

\[ C(t) = \int_0^t C_p(t')e^{-\frac{K_{out}^{an}}{\nu_e}(t-t')}dt' + \nu_p C_p(t) \]

\( C(t) = \text{[Gd]} \) in tissue measured

P.S. Tofts, et al. JMRI, 1997
Pharmacokinetic Model

\[ C(t) = \text{Kin}^{\text{trans}} \int_0^t C_p(t') e^{-Ko_{\text{atr}} / \nu_e (t-t')} \, dt' + \nu_p C_p(t) \]

Assume small plasma volume \( \nu_p = 0 \) and \( K_{in}^{\text{trans}} = K_{out}^{\text{trans}} \)

\[ C(t) = Kt^{\text{trans}} \int_0^t C_p(t') e^{-k_{ep} (t-t')} \, dt' \]
**DCE-MRI Analysis**

- **Qualitative**
  - Uptake curves

- **Semi-quantitative**
  - Area under the curve (AUC)

- **Quantitative**
  - Tracer-kinetic modeling ($K_{\text{trans}}, V_B, F_B$, etc)

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M.V. Knopp, et al. MCT, 2003

A.D. King, et al, PLOS, 2015

Wang, et al, TCRT 2016
Introduction of MR quantitative imaging for treatment assessment

Review of diffusion imaging, DCE/DSC imaging…

Treatment assessment using diffusion MRI
  - Assessment of tumor response
  - Assessment of radiation-induced normal tissue damage

Treatment assessment using DCE-MRI

Developments of MR quantitative imaging for treatment assessment

Challenges and future directions
Assessment using Diffusion MRI – Brain tumors

- For malignant glioma, the radiologic response (RR) method using 3D measurements of tumor volume - association with survival.
- One disadvantage of volume measures is the time for changes to occur, with 8 to 10 weeks necessary to assess response.
- Diffusion imaging (DTI) could be used to investigate the feasibility of detection of early response…
- A brain study of 60 patients with high-grade glioma, with gross tumor treated to a final median dose of 70 Gy in 6-7 weeks. Diffusion imaging with a single-shot, spin-echo, echo-planar imaging (EPI) sequence. Scanned 1 week before and 1, 3, and 10 weeks after the start of radiation.

D. A. Hamstra, JCO, 2008
Assessment using Diffusion

Functional diffusion map (fDM): Red – ADC Increased

Early Assessed; Better OS

D. A. Hamstra, JCO, 2008
For malignant glioma, the radiologic response (RR) method using 3D measurements of tumor volume - association with survival.

One disadvantage of volume measures is the time for changes to occur, with 8 to 10 weeks necessary to assess response.

Increased diffusion of water molecules (measured as an increase in the apparent diffusion coefficient (ADC)) occurs shortly after a successful treatment, and correlates with the breakdown of cellular membranes and reduction in cell density that both precede changes in tumor size.

D. A. Hamstra, JCO, 2008
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Assessment using Diffusion MRI – White Matter Damage

- Stereotactic radiosurgery (SRS) has been an effective treatment for the management of brain metastases, acoustic neuromas and other brain diseases.

- Few data are available regarding radiation induced white matter (WM) damage by SRS.

- Diffusion tensor imaging (DTI) was used to investigate WM changes following SRS ...

- A study of 15 patients with recurrent unifocal malignant gliomas, treated with concurrent SRS/BVZ treatment, with radiation dose of from 18Gy to 25Gy. Scanned 1-4 days prior to SRS and 7 days and two months after SRS treatment

Chang Z, et al., Technol Cancer Res Treat, 2014.
Assessment using Diffusion MRI – White Matter Damage

Chang Z, et al., Technol Cancer Res Treat, 2014.
Assessment using Diffusion MRI – White Matter Damage

FA decreased significantly by 6.8% (p<0.01) with nearly 40% (p = 0.02) decline of NF after two months of SRS in the VOIs of white matter receiving ≥ 5Gy.

Chang Z, et al., Technol Cancer Res Treat, 2014.
Assessment using Diffusion MRI – White Matter Damage

- Stereotactic radiosurgery (SRS) has been an effective treatment for the management of brain metastases, acoustic neuromas and other brain diseases.

- Few data are available regarding radiation induced white matter (WM) damage by SRS.

- As compared with non-irradiated contralateral area, considerable decrease in fractional anisotropy (FA) and tracked neural fibers in the irradiated white matter volumes after 1-week of SRS, with further decrease after 2-month after SRS.

Chang Z, et al., Technol Cancer Res Treat, 2014.
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Assessment using DCE-MRI – Brian SRS

➢ Stereotactic radiosurgery (SRS) has been an effective treatment for the management of brain metastases, acoustic neuromas and other brain diseases.

➢ A study of 12 patients with recurrent unifocal malignant gliomas, each up to 5 cm in maximum dimension.

➢ Patients were treated with concurrent SRS/BVZ treatment, with radiation dose of from 18Gy to 25Gy. Scanned 1-4 days prior to SRS and 7 days and two months after SRS treatment.

➢ Diffusion imaging and DCE-MRI were used to investigate for possible OS prediction.

Wang, et al., J. Radiosurgery and SBRT, 2018.
Results: Tumor Response

White arrows indicate the PTV location

Functional MR Parametric Maps from a selected patient.

Wang, et al., J. Radiosurgery and SBRT, 2018.
### Results: Tumor Response

Summary of functional parameter statistics.

| Para | ROI       | Pre scan      | Post 1 scan   | Post 2 scan          |
|------|-----------|---------------|---------------|----------------------|
| $K_{\text{trans}}$ | PTV       | 0.0183 ± 0.0115 | 0.0104 ± 0.0084 | 0.0030 ± 0.0054* (p=0.035) |
|       | GTV       | 0.0196 ± 0.0155 | 0.0147 ± 0.0195 | 0.0064 ± 0.0033* (p=0.035) |
|       | V12Gy – PTV | 0.0100 ± 0.0068 | 0.0080 ± 0.0065 | 0.0058 ± 0.0091* (p=0.035) |
|       |           | 0.0084 ± 0.0055 | 0.0075 ± 0.0073 | 0.0065 ± 0.0080 |
| $F_B$ | PTV       | 0.0992 ± 0.0721 | 0.0687 ± 0.0581* (p=0.017) | 0.0368 ± 0.0214* (p=0.017) |
|       | GTV       | 0.0921 ± 0.0622 | 0.0680 ± 0.0565* (p=0.017) | 0.0392 ± 0.0247* (p=0.035) |
|       | V12Gy     | 0.0800 ± 0.0441 | 0.0682 ± 0.0481 | 0.0498 ± 0.0349 |
|       | V12Gy – PTV | 0.0766 ± 0.0399 | 0.0685 ± 0.0456 | 0.0530 ± 0.0388 |
| $V_B$ | PTV       | 0.0127 ± 0.0093 | 0.0069 ± 0.0067 | 0.0034 ± 0.0022* (p=0.017) |
|       | GTV       | 0.0117 ± 0.0087 | 0.0066 ± 0.0061 | 0.0037 ± 0.0028* (p=0.035) |
|       | V12Gy – PTV | 0.0100 ± 0.0072 | 0.0066 ± 0.0047 | 0.0056 ± 0.0052* (p=0.035) |
|       |           | 0.0095 ± 0.0070 | 0.0067 ± 0.0044 | 0.0062 ± 0.0060 |
| ADC  | PTV       | 2664.4 ± 579.1  | 2704.8 ± 870.3 | 2609.3 ± 543.7 |
|       | GTV       | 2664.8 ± 514.8  | 2755.4 ± 752.5 | 2621.6 ± 558.0 |
|       | V12Gy – PTV | 2749.1 ± 517.1  | 2794.4 ± 623.6 | 2744.1 ± 477.2 |
|       |           | 2766.3 ± 550.0  | 2792.5 ± 603.4 | 2765.7 ± 463.0 |

Wang, et al., J. Radiosurgery and SBRT, 2018.
# Radiomics

Wang, et al., J. Radiosurgery and SBRT, 2018.

## Intensity

| #  | Short | Feature Name   |
|----|-------|----------------|
| 1  | I-1   | Energy         |
| 2  | I-2   | Entropy        |
| 3  | I-3   | Skewness       |
| 4  | I-4   | Kurtosis       |

## Morphological

| #  | Short | Feature Name   |
|----|-------|----------------|
| 5  | M-1   | Volume         |
| 6  | M-2   | Surface Area   |
| 7  | M-3   | Sphericity     |
| 8  | M-4   | Spherical Disproportion |
| 9  | M-5   | Compactness 1  |
| 10 | M-6   | Compactness 2  |

## Coarse Texture

| #  | Short | Feature Name                             |
|----|-------|------------------------------------------|
| 11 | C-1   | Short Run Emphasis                       |
| 12 | C-2   | Long Run Emphasis                        |
| 13 | C-3   | Gray Level Non-Uniformity                |
| 14 | C-4   | Run Length Non-Uniformity                |
| 15 | C-5   | Run Percentage                           |
| 16 | C-6   | Low Gray Level Run Emphasis              |
| 17 | C-7   | High Gray Level Run Emphasis             |
| 18 | C-8   | Short Run Low Gray Level Emphasis        |
| 19 | C-9   | Short Run High Gray Level Emphasis       |
| 20 | C-10  | Long Run Low Gray Level Emphasis         |
| 21 | C-11  | Long Run High Gray Level Emphasis        |

## Fine Texture

| #  | Short | Feature Name                  |
|----|-------|------------------------------|
| 22 | F-1   | Autocorrelation              |
| 23 | F-2   | Cluster Prominence           |
| 24 | F-3   | Cluster Shade                |
| 25 | F-4   | Cluster Tendency             |
| 26 | F-5   | Contrast                     |
| 27 | F-6   | Correlation                  |
| 28 | F-7   | Difference Entropy           |
| 29 | F-8   | Dissimilarity                |
| 30 | F-9   | GLCM Energy                  |
| 31 | F-10  | GLCM Entropy                 |
| 32 | F-11  | Homogeneity 1                |
| 33 | F-12  | Homogeneity 2                |
| 34 | F-13  | Informational Measure of Correlation 1 |
| 35 | F-14  | Informational Measure of Correlation 2 |
| 36 | F-15  | Inverse Difference Moment Normalized |
| 37 | F-16  | Inverse Difference Normalized  |
| 38 | F-17  | Inverse Variance             |
| 39 | F-18  | Maximum Probability          |
| 40 | F-19  | Sum Average                  |
| 41 | F-20  | Sum Entropy                  |
| 42 | F-21  | Sum Variance                 |
| 43 | F-22  | Variance                     |
Results: Radiomics

Normalized changes of radiomics features in different ROIs

6 different image modalities in 4 different ROIs

Wang, et al., J. Radiosurgery and SBRT, 2018.
**OS Prediction**

- Selected radiomics features with high coefficient $r$ values in correlation tests were investigated with support vector regression (SVR) to predict OS with leave-one-out cross validation.

- When using a selected group of 5 features’ normalized changes (Ktrans: C-6 in PTV; ADC: C-7 in PTV; T1w: F-2 and C-7 in PTV; C-7 in GTV) in the 2nd post-treatment scan for outcome prediction, 9 out of 12 patients’ OS time were accurately predicted (Mean absolute error = 1.47 mo, RMSE = 2.10 mo).

Wang, et al., J. Radiosurgery and SBRT, 2018.
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Assessment using DCE-MRI—Neurocognitive Dysfunction

- Radiation therapy (RT) is a major treatment modality for malignant and benign brain tumors.
- The major limiting factor in its use is neurotoxicity, often as late neurocognitive dysfunctions.
- Important to identify biomarkers (e.g. cerebral vascular injury) for early assessment and prediction of late neurotoxicity…
- A study of 10 patients with low-grade glioma or benign tumor, treated with 3D conformal RT, with radiation dose of 50.4–59.4 Gy in 1.8 Gy fractions. 1–2 weeks prior to RT, at weeks 2–3 and weeks 5–6 during the course of RT, and at 1 month and 6 months following the completion of RT.

Cao, et al., Clin Cancer Res. 2009
Assessment using DCE-MRI–Neurocognitive Dysfunction

Changes in vascular volumes (Vp) & blood-brain permeability (Ktrans) versus doses

Cao, et al., Clin Cancer Res. 2009
Learning scores decline as changes in Ktnasn and Vp

Cao, et al., Clin Cancer Res. 2009
Challenges and Limitations

Various technical challenges and limits encountered:

➢ Artifacts: distortions, motion artifacts ....
➢ Long data processing for PK analysis in DCE-MRI
➢ Relatively low temporal resolution in DCE-MRI
➢ .......
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Challenges and Limitations

Various technical challenges and limits encountered:

- Artifacts: distortions, motion artifacts, ...
- Long data processing for PK analysis in DCE-MRI
- Relatively low temporal resolution in DCE-MRI
- ....
Distortion Correction for Diffusion MRI using EPI

- Spatial and intensity distortion in EPI images due to inhomogeneous static magnetic fields is a well-known phenomenon

  - Spatial distortion in SE and GRE EPI, and additionally signal loss in the latter, have restricted its use

  - Distortion is most pronounced in PE direction in EPI

  - Depends on applied magnetic field, magnetic susceptibilities within the subject, geometry of the subject, and its orientation

Holland et al., Neuroimage. 2010
Distortion Correction for Diffusion MRI using EPI

- Distortions in EPI-based Diffusion MRI: Eddy-currents and EPI distortions affect DWIs, including the $b = 0 \text{ s/mm}^2$.
Distortion Correction for Diffusion MRI using EPI

- FA increase by 113% due to distortion
- TR (trace) increase by 69% due to distortion
Distortion Correction for Diffusion MRI using EPI

- Spatial and intensity distortion in EPI images due to inhomogeneous static magnetic fields is a well-known phenomenon
  - Spatial distortion in SE and GRE EPI, and additionally signal loss in the latter
  - Distortion is most pronounced in PE direction in EPI
  - Depends on applied magnetic field, magnetic susceptibilities within the subject, geometry of the subject, and its orientation

- Various distortion correction methods have been proposed: the unwarping methods, PLACE, the reversed gradient methods

Holland et al., Neuroimage. 2010
Distortion Correction for Diffusion MRI using EPI

- The reversed gradient method makes use of the fact that the distortion behaves “symmetrically” when reversing the phase encoding direction.

Teruel et al., MRM. 2015
Distortion Correction for Diffusion MRI using EPI

➢ Evaluating the correction strategies is challenging
  ➢ Computer simulation,
  ➢ Hardware phantoms,
  ➢ Undistorted image (e.g. T1W image)
  ➢ Framework based on the reversed PE and gradient methods

A perfect distortion correction method to the two datasets with opposite diffusion encoding directions or PE directions would produce identical images.

Irfanoglu et al., MRM. 2019
Distortion Correction for Diffusion MRI using EPI

- Evaluating the correction strategies is challenging
- Framework based on the reversed gradient methods

Calculating the variability map as a measure of difference of images

Prior to Correction

Post Correction

variability maps, considered as “residue” after correction

Irfanoglu et al., MRM. 2019
Froeling et al., MRM. 2017
Challenges and Limitations

Various technical challenges and limits encountered:

- Artifacts: distortions, motion artifacts ….
- Long data processing for PK analysis in DCE-MRI
- Relatively low temporal resolution in DCE-MRI
- ……
PK parameters in DCE-MRI analysis are commonly calculated with nonlinear least-squares (NLSQ) methods or linear least-squares method using the integral form of the PK model (ILLSQ).

- NLSQ methods require intensive computation and may lead to erroneous results at the local optima.
- The computation time required for ILLSQ rapidly increases as temporal resolution of image acquisition increases.

Another efficient method for calculating pharmacokinetic (PK) parameters developed for DCE-MRI studies.
To improve the computational efficiency, a new method for calculating PK parameters for DCE-MRI analysis was proposed.

In this method, curve fitting based on linear least-squares method was applied to the derivative expression of the PK model with a KZ low-pass filter (abbreviated as the DLLSQ method).

\[
\frac{dC_t(t)}{dt} = (K_{trans} + v_p \cdot k_{ep}) \cdot C_p(t) - k_{ep} \cdot C_t(t) + v_p \cdot \frac{dC_p(t)}{dt}
\]

\[
C_t(t) = K_{trans} \int_0^t C_p(u) \cdot e^{-k_{ep}(t-u)} \, du + v_p \cdot C_p(t)
\]
2D simulation

(a) True values;
(b) DLLSQ results;
(c) ILLSQ results;
(d) NLSQ results;
(e) difference map of DLLSQ results;
(f) difference map of ILLSQ results;
(g) difference map of NLSQ results.
In vivo study

- $K_{\text{trans}}$
- $k_{ep}$
- $v_p$

Comparison of DLLSQ, ILLSQ, and NLSQ methods.
Efficient Calc. for DCE-MRI

| Δt(s) | 0.1 | 0.5 | 1   | 2   | 3   | 4   | 5   | 10  | 15  | 20  |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| DLLSQ | 15.46 | 2.21 | 1.28 | 0.98 | 0.92 | 0.87 | 0.84 | 0.77 | 0.76 | 0.76 |
| ILLSQ | 7.6x10² | 32.90 | 9.31 | 3.21 | 2.06 | 1.63 | 1.41 | 1.09 | 1.02 | 1.00 |
| NLSQ  | 2.86x10⁴ | 1.89x10³ | 5.86x10² | 1.52x10² | 82.53 | 52.17 | 31.96 | 13.04 | 13.86 | 12.40 |

In the simulation and in vivo studies, the calculated parameters using the proposed method were comparable to those using the existing methods with improved efficiency.

When analyzed within certain parameter intensity ranges at Δt=1s, the proposed method was more accurate than the current methods with improved efficiency by a factor up to 478.

C.Wang, FF. Yin, Z.Chang, MRM, 2015
Efficient Calc. for DCE-MRI using Deep Learning

- Machine learning (ML) based approach to directly estimate the PK parameters from the acquired DCE-MRI image-time series

Ulas, et al., Front Neurol. 2019
Efficient Calc. for DCE-MRI using Deep Learning

➢ Machine learning (ML) based approach to directly estimate the PK parameters from the acquired DCE-MRI image time series.

Over 160 million training samples, i.e., number of total voxels, out of 15 patients

Deep Learning Architecture: Ulas, et al., Front Neurol. 2019
Efficient Calc. for DCE-MRI using Deep Learning

➢ More robust and faster than conventional model fitting

SSIM: 0.998
SSIM: 0.961

A few seconds on a GPU machine

Ulas, et al., Front Neurol. 2019
Challenges and Limitations

Various technical challenges and limits encountered:

- Artifacts: distortions, motion artifacts ….
- Long data processing for PK analysis in DCE-MRI
- Relatively low temporal resolution in DCE-MRI
- ……
Fast Imaging for DCE-MRI

High temporal resolution is desirable in DCE-MRI

➢ To ensure the accuracy of pharmacokinetics (PK) analysis

    Reliable AIF information derivation demands 1 s or faster

➢ To achieve feasible perfusion measurement

    Requires high temporal resolution to capture vascular phase of contrast medium delivery
Fast Imaging for DCE-MRI

To accelerate MRI acquisition, various fast imaging methods have been proposed:

- Physically manipulate spin dynamics to use available magnetization more efficiently
  - EPI, Spiral, RARE, GRASE, …

- Sparsely sample k-space and reconstruct a complete image through a non-standard reconstruction
  - keyhole, SENSE, GRAPA, BLAST, SPEED, CS, TV, …
Fast Imaging for DCE-MRI

- Sparse radial sampled data can be reconstructed by using total variation (TV)/total generalized variation (TGV)

- The concept is based on the first order/second order derivative calculation was commonly adopted in the constrained image reconstruction as to minimize the gradient of the reconstructed image

- To explore the feasibility of fast DCE-MRI with TGV for tracer-kinetic (TK) studies
Fast Imaging for DCE-MRI

Original post-injection image (a) and reconstructed image with 32 radial k-space lines (b). The red contour indicates ROI that contains the tumor.
Fast Imaging for DCE-MRI

$K_{\text{trans}}$  
$F_B$  
$V_B$

Permeability  
Perfusion  
Perfusion

Original  Reconstructed (x4)  Difference

Wang CH, et al., TCRT, 2016
Fast TK Mapping

- These techniques as “indirect” methods, because the anatomical image series are reconstructed first, followed by a separate step for TK parameter fitting
  - 1) Spatial TK parameter maps have much lower dimensionality than those of dynamic image series (two to four parameters, compared to 50–100 time points, per voxel), and
  - 2) TK model-based reconstruction directly exploits what is known about contrast agent kinetics
- “Direct” estimation of TK parameters from undersampled (k,t)-space data or undersampled DCE-MRI data
Fast TK Mapping

➢ These techniques as “indirect” methods, because the anatomical image series are reconstructed first, followed by a separate step for TK parameter fitting

➢ “Direct” estimation of TK parameters from undersampled (k,t)-space data or undersampled DCE-MRI data
Fast TK Mapping

DCE-MRI forward model flow chart:
Conversion from TK parameter maps to undersampled (k,t)-space.
Patlak model is used to convert TK parameter maps to contrast concentration
Fast TK Mapping

Retrospective evaluation of direct and indirect reconstruction of Ktrans and $v_p$ maps.

Y Guo, et al., MRM, 2017

Ktrans map by Direct Method with the sparsity constraint

Undersampling rate: $R = 100$

Only Patlak model used; Use of more-sophisticated models (e.g., extended Tofts model) possibly nonconvex, to be further investigated.

- Long computation time
Fast TK Mapping

- These techniques are "indirect" methods, because the anatomical image series are reconstructed first, followed by a separate step for TK parameter fitting.

- "Direct" estimation of TK parameters from undersampled (k,t)-space data or undersampled DCE-MRI data.
Fast TK Mapping using Deep Learning

Deep Learning Architecture

Ulas, et al., MICCAI 2018
Fast TK Mapping using Deep Learning

Undersampling rate:
R = 10

3D volume takes ~ 1.5 s for DL while the model-based direct method requires ~95 min

Ulas, et al., MICCAI 2018
Y Guo, et al., MRM, 2017
Outline

- Introduction of MR quantitative imaging for treatment assessment
- Review of diffusion imaging, DCE/DSC imaging...
- Treatment assessment using diffusion MRI
- Treatment assessment using DCE-MRI
- Developments of MR quantitative imaging for treatment assessment
- Challenges and future directions
Challenges and future directions

➢ Reproducibility of quantitative data

To achieve this goal, standardized acquisition protocols, data analysis and assessment shall be promoted.

➢ Interpretation of biomarker

Physiologic meanings need to be fully examined towards the future clinical application.

➢ Image quality improvement

Potentially affect the quantitative assessment outcome.

➢ Novel image analysis methodology

Morphological information image texture features, deep machine learning.

Z.Chang, et al. WJR, 2015
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