Diffusion Tensor Imaging
Overview

Assia JAILLARD
MATICE - Pôle recherche
Unité IRM 3 T Recherche
IRMaGe: Inserm US 37 / CNRS UMS 3552
CHU Grenoble - France

Introduction
Diffusion Weighted Imaging
Diffusion tensor matrix
Diffusion coefficients
Tractography
Applications

OUTLINE

- Introduction
- Diffusion Weighted Imaging
- Diffusion tensor matrix
- Diffusion coefficients
- Tractography
- Applications

- Cyril Poupon slides
Introduction

- Many brain functions are mediated by parallel distributed networks. For instance, language relies on efficient information transmission along long range fiber pathways connecting distant cortical areas. See Catani’s work.
- Diffusion tensor imaging (DTI) provides information on white matter tract orientation. => tractography to examine brain structural connectivity
- DTI is a non invasive way of understanding brain structural connectivity
- White matter ultrastructural integrity
- Diffusion Imaging has been first developed to measure anisotropic diffusion=>ADC. Clinical applications = Stroke and tumors
- DTI derived measurements: Fractional anisotropy (FA) altered in disease with motor control impairment
- Research applications in healthy brain, ageing, neurologic and psychiatric disorders


Aims

- basic principles of Diffusion Weighted Imaging (DWI)
- Diffusion Tensor Imaging (DTI)
- Diffusion coefficients
- Tractography approaches
**Introduction**

**Diffusion**

Diffusion is based on Brownian water molecule motions
Random thermal motion (thermal shocks)

Free diffusion (ventricles) versus restricted diffusion (cell wall)

- WATER protons = signal
- Diffusion property of water molecules (D)
- Diffusion (D)
- Apparent Diffusion coefficient (ADC)

Poupon JIRFNI 2009
Anisotropy

A. Isotropic Diffusion

B. Anisotropic Diffusion

Introduction
Diffusion
DTI
DTI Coefficients
Tractography
Applications

DWI sequence - Pulsed Gradient Spin-echo (EPI)

“Imagerie de diffusion par RMN”, C. Poupen
Basic DWI Calculation: b

- The b-value gives the **degree of diffusion weighting** and is related to the strength and duration of the pulse gradient as well as the interval between the gradients.
- Areas where diffusion occurs most rapidly will exhibit a greater decrease in MR signal as the b-value increases.
- Collect multiple images each with a different b-value. Typically just 2 b-values (0 and 1000).

\[
\ln(S) = \ln(S_0) - b \cdot ADC
\]

---

What is b?

- b-value gives the **degree of diffusion weighting** and is related to the strength and duration of the pulse gradient as well as the interval between the gradients.
- b changes by lengthening the separation of the 2 gradient pulses => more time for water molecules to move around => more signal loss (imperfect rephasing).

\[
b = G^2 \delta^2 \left( \Delta - \frac{\delta}{3} \right)
\]

- G = gradient amplitude
- \(\delta\) = duration
- \(\Delta\) = trailing to leading edge separation
Diffusion Weighted Imaging (DWI) Sequence

- This loss of signal creates darker voxels (volumetric pixels).
- Diffusion is measured by repeating the process of diffusion weighting in multiple directions to model the DTI.
- In clinical imaging, ADC maps may be measured using only 3 diffusion gradients + a b0 map are required to compute an ADC map.

Apparent Diffusion Coefficient (ADC)

- The simplest and possibly most useful scalar for clinical applications is the apparent diffusion coefficient (ADC).
- In clinical imaging ADC maps may be measured using only 3 diffusion gradients.
- ADC map:
  - high ADC = less barriers
  - low ADC = more barriers
  - Areas with higher rate of diffusion are brighter
  - Little contrast between gray and white matter
• ADC map = Dark regions = water diffusing slower = more obstacles to movement/increased viscosity
• Diffusion Weighted Imaging (DWI): Bright regions = decreased water diffusion in case of cytotoxic edema
• Intensity of pixels proportional to extent of diffusion
• DWI is useful clinically: diagnosis of acute stroke => thrombolysis <3h

Water diffusion in brain tissue

Depends upon the environment:
- Proportion of intracellular vs extracellular water: cytotoxic oedema in stroke vs vasogenic edema in tumor
  => ADC
- Physical orientation of tissue e.g. nerve fibre direction
  => DTI
### DIFFUSION TENSOR IMAGING

**Diffusion Tensor Imaging (DTI)**

- DTI is a technique in which contrast is based on both rate and direction in the diffusion of water molecules: the areas with restricted diffusion will have a directional bias which is used to determine the direction of diffusion.
Types of Isotropy

Anisotropic

In gray matter, diffusion is isotropic (similar in all directions) = A
In white matter, diffusion is anisotropic (prefers motion along fibers) = B

O’Donnell and Westin, 2011

Diffusion Tensor Imaging (DTI)

- Because the cellular diffusion of water in the brain is limited by cell geometry, in particular axons, DTI can be used to examine the structure of white matter
DTI can measure
- the direction of motion
- both the velocity and preferred direction of diffusion
Diffusion Tensor Imaging

- Technique: Repeat the DWI sequence with gradients applied in a number of different directions. From the contribution of all the different directions we can calculate the direction of diffusion as well as the relative rate of diffusion.
- To create a tensor, we need to collect multiple directions.
- At least 6 directions.
- More directions offer a better estimate of optimal tensor.

The diffusion tensor

The diffusion tensor (DT) describes the displacements of the water molecules using the covariance matrix of a 3 dimensional Gaussian distribution model.
The Tensor Matrix

\[
D_{\text{prin}} = \begin{bmatrix}
\lambda_1 & 0 & 0 \\
0 & \lambda_2 & 0 \\
0 & 0 & \lambda_3
\end{bmatrix}
\]

- Direction of the principles axes = Eigenvector
- Size of the principles axes = Eigenvalue = \( \lambda_1, \lambda_2 \) and \( \lambda_3 \)

\( \lambda_1 \) indicates the value of maximum diffusivity or primary eigenvalue. \( \lambda_1 \) is termed axial diffusivity.

\( \lambda_2 \) and \( \lambda_3 \), termed radial diffusivity, represent the magnitude of diffusion in a plane transverse to the primary one.

DTI

- Eigenvalues of the diffusion tensor (\( \lambda_x, \lambda_y \) and \( \lambda_z \)) provides length of the ellipsoid in the three principal directions of diffusivity
- Eigenvectors provide information about the direction of diffusion
- The eigenvector corresponding to the largest eigenvalue is used as the main direction of diffusion
- Several measures of anisotropy can be computed from the eigenvalues and eigenvectors
**Measures of Diffusion anisotropy**

Axial diffusivity (AD), radial diffusivity (RD), mean diffusivity (MD) and fractional anisotropy (FA) can be computed from the 3 eigenvalues.

\[
AD = \lambda_1; \quad RD = \frac{\lambda_1 + \lambda_3}{2}; \quad MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3};
\]

\[
FA = \sqrt{\frac{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}{\lambda_1 + \lambda_2 + \lambda_3}}
\]

Indices of Anisotropic Diffusion

- **Fractional anisotropy (FA)** is a difference between eigenvalues and reflects directional diffusion

\[
FA = \frac{1}{2} \sqrt{\frac{(\lambda_1 - D)^2 + (\lambda_2 - D)^2 + (\lambda_3 - D)^2}{\lambda_1 + \lambda_2 + \lambda_3}}
\]

FA is the most reliable scalar

- **Mean diffusivity (MD)** is an addition of eigenvalues reflecting overall diffusion

\[
MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}
\]
**FA** Measure of degree of anisotropy regardless of direction

- A = MD
- B = FA
- C = Principle Tensor Vector

**Colour FA map**

- Colour coding of the diffusion data according to the principal direction of diffusion:
  - red - transverse axis (x-axis)
  - blue – superior-inferior (z-axis)
  - green – anterior-posterior axis (y-axis)

- Brightness of the colour is proportional to the FA: Brighter areas correspond to areas with higher degree of anisotropic diffusion

- Ranges from 0 – 1 where FA=1 corresponds to completely anisotropic
Introduction
Diffusion
DTI
DTI Coefficients
Tractography
Applications

Axial and Radial Diffusivity

Tractography

[Virtual Hospital, 1998]
Cingulum (1) arching over the corpus callosum (2)

**Anatomy**

**Gross dissection**

**DTI**

**Introduction**

**Diffusion**

**DTI**

**DTI Coefficients**

**Tractography**

**Applications**

3- Corticospinal tract (CST)
4- The arcuate fasciculus/
Superior longitudinal tract
5- Inferior longitudinal tract
6- Uncinate fasciculus

language & aphasia

Tractography reconstruction of the white matter
pathways involved in the most frequent
neurodegenerative disorders, some of which
affect
language function


Introduction
Diffusion
DTI
DTI Coefficients
Tractography
Applications

Tractography - Overview

Voxels are connected based upon similarities in the maximum
diffusion direction
Not a measure of individual axons, rather the data extracted
from the imaging data is used to infer where fibre tracts are.

Johansen-Berg et al.
Tractography – 2 approaches

Degree of anisotropy | Deterministic tractography | Probabilistic tractography
---|---|---

| 10% | 5% | 3% |
| 15% | 10% | 5% |
| 20% | 10% | 5% |
| 50% | 30% | 10% |
| 90% | 50% | 30% |
| 99% | 90% | 50% |

Degree of anisotropy | Streamline tractography | Tract density = voxel probability

Corticospinal Tract - Deterministic

Corticospinal Tract - Probabilistic

Deterministic tractography

- Connects neighbouring voxels from user defined voxels (SEED REGIONS) e.g. M1 for the CST
- User can define regions to restrict the output of a tract e.g. internal capsule for the CST
- Tracts are traced until termination criteria are met (e.g. anisotropy drops below a certain level or there is an abrupt angulation)

Internal capsule, axial view. A and B, Illustration (A) and directional map (B).

The major eigenvector may not be aligned with a fiber tract in the case of crossing fibers.

O’Donnell and Westin, 2011

Crossing - kissing fibres

Crossing fibres ?
Kissing fibres ?

Low FA within the voxels of intersection (the eigenvalue of the principal vector is reduced)
Crossing fibres  Kissing fibres

Low FA within the voxels of intersection (the eigenvalue of the principal vector is reduced)

Crossing or kissing fibers?

Assaf et al
J Mol Neurosci 34(1) 51-61 (2008)
O’Donnell and Westin, 2011

False negative

O’Donnell and Westin, 2011
Probabilistic tractography

- Value of each voxel in the map = the probability the voxel is included in the diffusion path between the ROIs
- Run streamlines for each voxel in the seed ROI
- Provides quantitative probability of connection at each voxel
Probabilistic tractography

Robust to noise and partial volume effect => allows tracking into regions where there is low anisotropy e.g. crossing or kissing fibres

[Perin, 2006]
[Chao, 2007]
[Descoteaux, 2008]
Probabilistic tractography limitations

- Time consuming
- Crossing fiber problem remains an issue
- False positive
- Low reliability for the main tracts compared to deterministic approach
- Needs a minimum of 30 directions
  => More directions (256), higher resolution (1 mm³), more time
  => Multiband
  => Other algorithms

Evolution of the DWI glyph
High order models to solve the crossing fiber issue using more than one direction at the voxel level

a–d: (Kindlmann et al., 2004), e: (Tuch et al., 2002), f: (Tuch, 2004), g: (Prčkovska et al., 2011).
HARDI fiber-tracking

DTI

HARDI

O’Donnell and Westin, 2011
Fig. 3  Diffusion imaging of neuronal fiber track display accelerated with simultaneous image acquisition. The 3D images show neuronalaxon fiber tracks in the human brain, in vivo, using simultaneous image refocused (SIR) EPI with either 2 or 3 images per...

David A. Feinberg, Kawin Setsompop

Ultra-fast MRI of the human brain with simultaneous multi-slice imaging

Journal of Magnetic Resonance, Volume 229, 2013, 90-100

http://dx.doi.org/10.1016/j.jmr.2013.02.002

Introduction

Diffusion

DTI

DTI Coefficients

Tractography

Applications

The dataset was reconstructed using least squares tensor estimation (DTI). Anatomical descriptions of the brainstem were based on a single postmortem examination. MR imaging was performed on a 7T system using a 65 mm internal diameter quadrature RF coil. Diffusion data were acquired at 200 μm isotropic resolution using a 3D spin echo pulse sequence (TR/TE = 100/24 ms) with 120 diffusion directions (b = 4000 s/mm²) and 12 non-diffusion weighted images (b0) distributed over a ~227 hr acquisition. Bore temperature was controlled with a water circulation system and monitored using a fiberoptic probe. The dataset was reconstructed using three different models: 1) least squares tensor estimation (DTI), 2) spherical harmonic orientation distribution function (ODF) deconvolution (q-ball), and 3) BEDPOSTX. Deterministic tractography and tract segmentations were performed on q-ball ODF data using DSI Studio. Probabilistic tractography was carried out using FSL's PROBTRACKX.
Both the microstructural and macrostructural organization of white matter pathways differentially contributes to understand brain network organization.

Sponsors
- SFR1 (MRI - A. Krainik)
- SFR3 (Stendhal University)
- FLI: France Life Imaging
- GrenobleAlpes Metropole
- GIN: Grenoble Institute Neuroscience

Second Brain Connectivity Course Grenoble 2015

http://brain-connect.sciencesconf.org