## DW-MRI analysis in BrainVoyager 2.0 and up

Version 1.2



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## **Before You Start**

BEFORE YOU START

The DTI module in BrainVoyager > 1.9 requires an additional license, which can be obtained free of charge by sending an e-mail to sales@brainvoyager.com. Please state your HASP dongle ID (in BrainVoyager: Help-->License Information-->HASP Dongle ID) your name, and your affiliation.

#### How to use this document

This document is a step-by-step manual for an analysis of a diffusion weighted MRI data set in BrainVoyager QX. It is assumed that the reader has basic understanding of the principles behind Diffusion-Weighted Imaging. It starts with data import and how to create a DMR: a *Diffusion weighted* **MR** dataset.

The next stage is co-registration of a DMR project to an anatomical data set (VMR). If you are familiar with BV, than you will immediately appreciate the similarity with FMR/VMR co-registration.

The manual will then show you how to calculate fractional anisotropy and mean diffusivity maps, and how to display them on the VMR.

We will then go into 3-D space and show how to display the tensor data. Fiber tracking, both ROI-based and interactively, will be treated next. Finally, some spatial transformations and fiber import/export are treated.

Menu/button commands etcetera are displayed in a typewriter font.

#### **Further support**

If you have any questions regarding DTI analysis in BrainVoyager after reading this manual, please contact support@brainvoyager.com.

#### BrainVoyagerQX version used for this manual



### Chapter 1

## Single subject DW-MRI Analysis

#### 1.1 Data

Data needed for doing a diffusion-weighted (DW) data analysis are the DW-MR images, the gradient direction information in a text file and an anatomical (T1-weighted) dataset, acquired in the same session. A few recommendations for data acquisition can be found at

http://support.brainvoyager.com/diffusion-weighted-imaging/61.

In this manual, we use a DWI scan measured with 31 diffusion directions: 1 b0 and 30 diffusion weighted directions. The gradient file for this measurement can be found in appendix 1.6.1. Furthermore, in the same session an ADNI (modified MPRAGE) anatomy was acquired. Details of the measurement are given below.

subject	healthy male 42yrs
scanner	3T Siemens Allegra
DWI	31dirs, b=800mm <sup>2</sup> /s, 75 slices, voxel size $2 \times 2 \times$
	2 mm
ADNI (T1)	192 slices, voxel size $1 \times 1 \times 1$ mm
Acquisition time	25mins

The sample data can be downloaded from the Brain Innovation ftp server on request, by emailing support@brainvoyager.com. Please put the data in \BVQXSampleData\DTI\Human31dir\ or equivalent folder.

#### 1.2 Creation of a Diffusion MR (DMR) Project

- 1. The create project wizard can be found in the menu File --> Create Project Wizard.... A welcome window will appear, click Continue.
- 2. Now it is time to specify the project type. Choose DMR Project.

00	Create Project Wizard
	Project Type
	Which project type do you want to create? Project type
	○ FMR project
	AMR project
	O VMR project O DMR project
	Description
	A DMR project ( <i>D</i> iffusion-weighted <i>M</i> agnetic <i>R</i> esonance) stores the data belonging to a series of recordings sensitive for the direction of water diffusion. A DMR project is the basis for Diffusion Tensor Imaging (DTI) analysis.
	Co Back Continu

3. Next step is to define the data type. In our case, this is Siemens DICOM, but Philips PAR/REC and ANALYZE are also supported. If you have Nifti data, please consult http://support.brainvoyager.com/available-tools/ 49/166.

) 😁	Create Project Wizard
	Raw Data Format
	What is the format of your data?
	Data format Description
	DICOM DICOM is a standard data ANALYZE format supported by most MRI PHILIPS_REC should use this format for project creation.
	If the above list does not contain the format of your data you may try creating your project using the "Create Project" dialog after quitting this wizard. For further assistance, contact "support@brainvoyager.com".
	Go Back Conti

4. Set the name of the DMR project to human31dir.dmr.

00	Create	Project Wizard	
	Select First So	urce File	
	Use the "Brows	e" button to navigate to th	e file
	Project name:	human31dir	.dmr
	Data directory:		Browse
		Go B	ack Continue

5. Click Browse to navigate to the directory containing the DICOM files. Note: in the browse window, the DICOM files will not be shown (the directory appears empty). So, you need to know where your DICOM files are, and select that specific directory.

◀ ▶ ः	Volumes/DATA/SampleDatman	31dir_BV20/raw/dicom 🗘 🔺
🏠 pim	Name	Size
Uolumes		
Desktop		
BVQXExtensions		
BVQXSampleData		
		4 Þ (
Directo	ry:	
Files of typ	e: Directories	\$
		Cancel Choose

6. In the next step, BrainVoyager will automatically show you the DICOM files belonging to several experiments you might have performed. Select the DI-COM file belonging to the DW-MRI experiment

pimpul_070907_	dti -	-0007-0	0001-	00001.	dcm.
----------------	-------	---------	-------	--------	------

	Projects So	ource Files		
Directory i	nspected for DICOM data			
Parks I		21.11.19.000.0	4 P	
Path: /	Volumes/DATA/SampleDataDTI/Humar	13 Idir_BV20/rav	v/dicom	
Select file	for project creation			
	First file of project	Number of files	Project type	
pimpul	_070907_dti =0007=0001=00001.dcm	2325	FMR (DMR)	
			Ca	ncel) Ok

00	Create Project Wizard
	Select First Source File
	Use the "Browse" button to navigate to the file
	Project name: human31dir .dmr
	Data directory: -0007-0001-00001.dcm Browse
	Detected image resolution
	Number of columns: 128 Number of rows: 128
	Go Back Continue

7. Enter the number of slices (75) and the number of volumes (31 = number of diffusion directions) in the next two windows.

0 0	Create Project Wizard
	Number of Slices
	How many different slices per volume have been scanned? For all MRI projects, the number of different slices comprising a volume has to be provided. Please enter the number of slices below. Number of slices: 75
	Co Back Continue
0 0	Create Project Wizard
	Number of Direction Volumes
	How many volumes have been scanned?
	For diffusion-weighted projects, the number of recorded brain volumes (directions) has to be provided. Please enter the number of volumes below.
	Number of volumes: 31
	It you have previously created a GRB hie describing the scanned gradient direction for each volume, you can specify it here in case that the current recording uses the same series of gradients. You can also leave this entry blank and specify directions and b values later in the "DMR
	Gradient direction file: Browse
	Go Back Continue

If you already have a gradient file, you can attach it during this stage of the project definition. Use the Browse button to locate the file mgh\_dti30.grb. See section 1.6.1 for details on the file format and contents. Otherwise, leave the field blank and continue by clicking Next.

8. BrainVoyager will now give you a summary of the project. Please take a moment to check whether everything is correct. Otherwise, you can use the Back button to redo a step.

00	Create Project Wizard
	Summary
	You have successfully specified all required information. If you would like to place created project files at another location than the orginal data, select a "Target folder" below. After clicking "Finish", BrainVoyager QX will create the following project:
	Data format: DICOM
	Number of slices: 75
	Number of volumes: 31
	Dimensions: 128 x 128
Y	Target folder: man31dir_BV20/raw/dicom Browse
	Go Back Done

9. Click Finish to start the DMR Project creation.

#### 1.2.1 DMR Properties

After the project is finished, the DMR Properties dialog pops up.

$\Theta \bigcirc \odot$	DMR Properties	
General information	on	
Nr of slices:	75	Nr of volumes: 31
Data type: 🛛	loat (4 bytes)	DWI storage format: 3
Voxel resolution d	definition	
Inplane X: 2	mm Slice thick.: 2	mm 🗹 Verified
Inplane Y: 2	mm Gap thick.: 0	mm Options
Temporal resoluti	on, slice timing amd TE definition [ms	1
TR: 3000	Inter slice time: 40	TE: 0 Verified
Referenced inplan	e (coplanar) AMR file	
File: human3	1dir_firstvol_as_anat.amr	Browse Detach
POS info	) Layout DWI Data.	Options Close

You can inspect here if BrainVoyager has taken the correct parameters of the data.

Gener	al information
Nr of slices	
Nr of volumes	should be identical to nr of diffusion direc-
	tions
DWI storage format	For internal use
Voxel Res	olution definition
X, Y, Z resolution	please check if correct ( $2 \times 2 \times 2$ mm)
Gap thickness	should be 0
Options	allows you to change in-plane resolution
Temporal Res	olution, slice timing
	Check for accuracy:
TR	8900
TE	78
	Check Verified
Refence inpla	ne (coplanar) AMR file
	should be automatically filled, otherwise use
	Browse to point to AMR.
DWI data	allows you to do calculations on the DMR.
	Will be discussed later in section 1.3.1
Options	opens the options dialog, allows you to
	change the DWI file prefix and nr of skipped
	volumes (should be 0 normally)

#### **1.3** Exploring a DMR project

The DMR project just created may look like this, where the first volume is displayed. In this case, it is the b0 volume. This volume contains 75 slices.

0	00	BrainVoyager QX									C					
Pre	ect Wizard	New Project	Open Save	Files Pane	Log Pane Info	Pane Prefe	rences Full	Screen Use	r's Guide							
100	D human31d	ir.dmr										Info	0.0	<b>a</b>		
<b>₽</b>		<i>.</i>	de.				- -				DICOM header: -0007-0001-000	pimpul_070907 01.dcm	_dti			
	. S.C.	6.0	1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 - 1997 -			and the second sec		1.10	- 891/-		Byte order: Little E	ndian				
	· <u>A</u>	- 65				· db.	1		• A	- A	Selected keys:					
	- S. C.S.	dial and	- AN & C	. T.S.	- A. C.S.	18 N.S.	12834	Ale.	- 19 Alexandre - 19 A	S. A.S.				dî 🕯		
	Ö		$\diamond$	$\bigcirc$	٢	٢	<u>```</u>	2.5	and the second s		ImageType	ORIGINAL\PRIMARY\ M\ND	(0008,0008)	-		
m	Å "	·	• · &	- (h	" a	•	* <u>A</u>	• <u>A</u>	· · · · ·		Modality	MR	(0008,0060)	+		
	1.442	1.		1000	100	SRip	्योदिङ	100	182		Manufacturer	SIEMENS	(0008,0070)			
8	17.1	103		.99	. 67.	(°9)-				(3)	ManufacturersModelNa me	Allegra	(0008,1090)			
125		1999	1992/	- 1992/ -			1997	- 39/			MagneticFieldStrength	3	(0018,0087)	l a		
LISTN .	2.2	2 2	212		ale.	1.	ale.	100	Sec.	Series.	InstitutionName	Maastricht Brain Imaging Center	(0008,0080)			
×	$\langle \mathfrak{H} \rangle$	( de	·	( <b>1</b> , <b>1</b> )						$( \sim )$	StudyDescription	Erik vd Bergh^basis set voor pim	(0008,1030)	1		
₽	1.20		1	-	1	• • • • • • • •		•	1	•	SeriesDescription	erivdber_ep2d_diff_m ddw	(0008,103e)	0.		
Ŗ	21212	120		124	633	133	13				PatientsName	pimpul_070907_dti	(0010,0010)			
	1		프	1. A 191							Rows	128	(0028,0010)			
	1999	1989	6304	405.5	1000	198		1900	1500	19:04	Columns	128	(0028,0011)			
	-	- dans	-								PixelSpacing	2.000000\2.000000	(0018,0030)			
	6 1	113		112							SpacingReturgesSlices	2.000	(0018,0050)			
	1.5.0	1.4.1	1.2.1	6.2.1	E.E.Y	Sec. 9	Pite 1	Per la	3.57	5.57	BitsAllocated	16	(0028.0100)	<b>1</b> A		
	1	- 19497 /		•		•	•	•	•	•	RepetitionTime	8900	(0018,0080)			
	-			- 112	1.1		1.1.1		1.1		SeriesNumber	7	(0020,0011)			
			63	63	633		1			A		1	AcquisitionNumber	1	(0020,0012)	
	1000	65	6.9	22	88	ଞ୍ଚ	ଞ୍ଚ	10			InstanceNumber	1	(0020,0013)			
	9 /	•	•	•	7						PatientPosition	HFS	(0018,5100)			
	10 Alexandre	100	0	~	~						ImagePositionPatient	-128\-135.99031496048 \-63.104114532471	(0020,0032)			
			- (H)	. 52	0						ImageOrientationPatien t	1\0\0\0\1\0	(0020,0037)	-		
0	4													_		

You can set the number of slices you want to see with the buttons on the left of the screen, see below. Play around with the different buttons to see their behaviour. With the Page up and Page down keys on your keyboard you can move through the slices.

You may explore the data via Options --> Time Course Movie. By clicking the play buttons >, BV will move through the volumes or diffusion directions of your measurement. The Recalibrate button in the Time Course Movie window automatically adapts brightness to the slice you are currently viewing. This feature is added because the intensities of a b0 images are far higher than those of a DW image.

00	Time Course Movie
Recalibrate	Close
Preload All	Time point: 1 + First <-> Last
<b>.</b>	
(  <	
Recalibrate	Recalibrate the intensities of the current volume
Preload all	Load all volumes in memory (on slower machines)
Time Point	Enter a value here to go directly to a specific vol
Loop	ume When checked, BV will loop the volumes Switch quickly between the first and the last vol
riist <-> Last	ume of the data set

The slice before and after recalibrating are shown below:





#### 1.3.1 Creation of FA and Mean Diffusivity maps

On the basis of the DMR data, it is possible to directly calculate tensors, FA and Mean Diffusivity maps. For background on tensor estimation, see [BJ02, Kin06c] among others. To recap, Mean Diffusivity is defined as

$$MD = (D_{xx} + D_{yy} + D_{zz})/3 \equiv \frac{Tr(D)}{3},$$
 (1.1)

and is in theory limited to the interval  $[0, \infty)$ . Fractional Anisotropy is defined as

$$FA = \sqrt{\frac{1}{2}} \frac{\sqrt{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_3 - \lambda_1)^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}.$$
 (1.2)

Fully isotropic voxels have FA = 0, while fully anisotropic voxels have FA = 1. This is illustrated in figure 1.1.



Figure 1.1: From left to right: isotropic tensor, where  $\lambda_1 = \lambda_2 = \lambda_3$  and FA close to 0. Oblate tensor where  $(\lambda_1 = \lambda_2) >> \lambda_3$  and prolate tensor where  $\lambda_1 >> (\lambda_2, \lambda_3)$ . FA of the oblate and prolate tensors might be similar.

Let's continue with the FA calculation procedure in BrainVoyager:

1. Tensor Calculation: Click File --> DMR Properties --> DWI data. A dialog pops up, which shows no gradient information, if you did not specify a gradient file during DMR creation:

	C I Y	Contra	6-17	1		Set b value(s) in table	
	Grad X	Grad Y	Grad Z	b value			
1	0	0	0	1000		b value: 1000 Set	
2	0	0	0	1000			
3	0	0	0	1000		From volume: 1	
4	0	0	0	1000		Ta	
5	0	0	0	1000		To volume: 31	
6	0	0	0	1000		Internet the of an direct second second	
7	0	0	0	1000		Interpretation of gradient components	
8	0	0	0	1000		X direction: Left to Right	
9	0	0	0	1000		-	V discriticaria ( A de la de De de la de
10	0	0	0	1000			Anterior to Posterior
11	0	0	0	1000		Z direction: Inferior to Superior 🛟	
12	0	0	0	1000			
13	0	0	0	1000		Volume (b0) for display	
14	0	0	0	1000	Ă	volume (bo) for display	
15	0	0	0	1000	Ŧ	Select Display volume: 1	
C	Load .C	GRB	Sa	ve .GRB.		Gradient directions and b value(s) verified	

2. Click Load GRB and load the appropriate gradient file mgh\_dti30.grb (see 1.6.1 for details). Accordingly, the data in the gradient table has changed. To set the right value for *b*, use the fiels in the top right of the dialog. Set volumes 2-31 to a *b*-value of 800, and set volume 1 to 0. You can do this by directly editing the table on the left of the dialog.

Set b value(s) in table					Set h value(s) in table
b value:	300 ( 2 🗘	Set			b value: 0 Set
To volume:	31				To volume: 1
Gradient dir	ections and b values tai	Desc ble Grad Z	DW ription b value	/I Data Calcu	lations Set b value(s) in table
1         0           2         1           3         0.770           4         0.256           5         0.797           6         -0.46           7         -0.22           8         -0.26           9         0.799           10         0.506           11         0.305           12         -0.79           13         -0.80           14         0.186           15         -0.38	0 319 -0.633448 145 -0.0249787 558 0.876173 322 0.853378 3079 -0.411305 245 0.585435 13 0.510329 433 -0.136436 -0.194962 254 -0.592602 254 -0.592602 255 -0.592602 255 -0.592602 255 -0.592602 255 -0.592602 256 -0.592	0 0.0731618 0.966316 0.593583 0.138872 -0.468193 -0.872707 0.135917 0.694843 -0.942388 -0.571265 -0.0446965 0.235566 0.915237	0 800 800 800 800 800 800 800 8	×	b value: 800 Set From volume: 2 To volume: 31 Interpretation of gradient components X direction: Left to Right Y direction: Anterior to Posterior Z direction: Inferior to Superior Volume (b0) for display Select Display volume: 1
Load .	JAD) (Jave				Cradient directions and b value(s) verified

3. Click OK and save the DMR (File > Save).

4. Now click on the Calculations tab.

00	DWI Data
	Description Calculations
Diffusion to	ensor data
DDT file	Load Save Estimate
🗹 Inten	sity-based masking using b0 volume Exclusion threshold: 100
Calculate n	naps
	Mean Diffusivity
	Fractional Anisotropy
	(Cancel) (OK)

You have the option here to mask out the background of the image. Please bear in mind that, by masking via a threshold, you always risk losing voxels in the brain itself. It is safer to use a mask based on the anatomical data, which is discussed in section 1.6.3. For now, because of the nice visualisation, check the mask box and click on Estimate to start the tensor estimation. After the calculations, BV will ask you to save the resulting DDT file, containing the tensor information. Save it as human31dir\_dmr.ddt. The ddt calculated from a dmr is different from the ddt calculated from a VDW file.

- 5. FA calculation: click the Fractional Anisotropy button, and the FA data will be overlayed onto the DMR. You may explore the resulting map similar to one of an FMR.
- 6. Mean Diffusivity: click the Mean Diffusivity button.



(a) FA map

(b) Mean Diffusivity map



In principle, one could start a complete analysis on these maps. For instance, to create a MD histogram of slice 39 (done in Matlab):



The disadvantage is that we stay in 2-D space. To do an analyis in 3-D, the DMR project has to be co-registered to a VMR, which is explained in the next sections.

#### 1.4 DMR-VMR coregistration

First, the VMR acquired in the same session needs to be created (see the BVQX Getting Started Guide for the procedure). If needed, the VMR can be brought into AC/PC or TAL space. For this demonstration it is not necessary, so we stay in native space. Close all open projects and open the VMR human.vmr.

#### 1.4.1 VMR Preparation

For BrainVoyager version 2.4.0 and up BrainVoyager can automatically improve the image quality of the VMR. To do this, go to Volumes --> Inhomogeneity correction, V16 tools. A dialog will pop up, click GO in the upper right corner.

U TOOIS
Intensity inhomogeneity correction (IIHC) No. of cycles: 2 2 Auto-IIHC: 60 Include mask generation (brain extraction) Map CM and WM peaks to standard VMR values Save resulting IIH corrected .V16 data to disk Tissue range threshold: 0.25 2 Detect WM Intensity threshold: 0.30 2 Multiplicative model Additive model Visualize fit (bias field) in secondary VMR Order of polynom for fit: 3 2 Presegmentation-based ("blue" WM): Correct IIH
Mirror data set along axis           Image: Wirror data set along axis         Flip X Axis           BV axes convention         Flip X Axis           Flip Y Axis         Flip Z Axis

BrainVoyager will create a number of new VMRs and other files. Close all the windows that have popped up, and close the open VMR. Load the file human\_IIHC.vmr.

**For BrainVoyager** < **2.4.0** Co-registration works better if the non-brain tissue is removed in the VMR. Go to Volumes --> Segregate Brain from Head Tissue. When BrainVoyager is finished, the result should look like this:



Save the VMR as human\_IIHC.vmr.

#### 1.4.2 Source Files

Make sure human\_IIHC.vmr is open. Go to DTI --> Coregister DMR/DWI to VMR. A menu appears with 4 tabs, Files, Source Options, Initial

Alignment and Fine-Tuning Alignment. Let's start with the first tab:

0 0			DMR-VMR	Coregistra	tion			
Files	Sourc	ce Options	Initial A	ignment	Fine-Tunin	ng Alignment		
Source and	target file	s						
DMR file:	human31dir.dmr Browse							
VMR file:	human_brain.vmr							
Resulting tra	ansformat	tion files						
Initial alig	inment:	human31d	ir-TO-hun	nan_brain_	IA.trf			
Fine-	Fine-tuning: human31dir-TO-human_brain_FA.trf							
			Œ	Run IA	Run FA	Close GO		

Use the Browse button to point to the DMR just created: human31dir.dmr. BV automatically creates file names for the transformation files, i.e.

<DMRname-TO-VMRname>\_IA.trf and <DMRname-TO-VMRname>\_FA.trf.
In principle, one could click on Run IA and Run FA now, but let's have a look

at the important other tabs first.

#### 1.4.3 Source Options



In this manual, we opt for the Use DMR data (DWI Slices), create edge display and invert intensities.

#### 1.4.4 Initial Alignment

Go to the Initial Aligment tab.

) 🔘	D	MR-VMR Coregistrati	on
Files	Source Options	Initial Alignment	Fine-Tuning Alignment
Alignment m	ethod		
🕒 Based (	on DMR and VMR he	ader information (sa	me session) Pos Info
0			
Matchi	ng of specified corr	esponding points	Points Info
🔿 Manual	alignment - use "T	oSAG" matrix	TRF Matrix.
-	-		
🔘 Initial a	lignment already p	erformed	TRF Matrix
		RunIA	Run FA Close
			Close

Based on DMR and VMR	This is the default and easiest option. POS
header information	info shows you the header information.
(Same session)	
Matching of specified	[Advanced] Do the co-registration based on
corresponding points	user-specified landmarks. Needed when no
	header information is available or when the
	co-registration based on the header informa-
	tion fails. Points info shows the defined
	points.
Manual alignment use	[Advanced] Manual alignment, only used
"To SAG" matrix	when automatic alignment fails. If in the
	Source Options a To SAG matrix was
	defined, it can be inspected via the TRF
	matrix button.
Initial Alignment	Trivial
already performed	

Now it's time to hit the Run IA button. A view similar to the one below



appears, and we can inspect the initial aligment using the F8 and F9 buttons on your keyboard. F9 defines the type of view and F8 toggles between the VMR and DMR. The green edges represent the DWI data.

#### 1.4.5 Fine-Tuning Alignment

After the initial alignment, the coregistration window has disappeared. Open it again via DTI --> Coregister DMR/DWI to VMR. Go to the Fine-Tuning Alignment tab:



```
NGF based affine
                             Default option
alignment (12
parameters)
                             Default option in BVQX < 2.0
Intensity Alignment
using multi-scale
approach
                             Not available
Edge alignment using
iterative closest point
(ICP) Method
Manual alignment - use
                             [Advanced], only recommended when auto-
current translation and
                             matic alignment fails.
rotation values
No fine-tuning
                             Use if initial alignment is satisfactory.
alignment
                             shows the current transformation matrix.
TRF matrix
```

Choose the default option using a NGF approach (you might want to try out different parameters, in the Options dialog), and click Run FA. A progress bar will appear and shortly afterwards BV has finished the alignment procedure. BV has saved the transformation parameters in separate files, which are used in the next step of the analysis.

## 1.5 Creation of a Volume Diffusion Weighted (VDW) data set

We will now create a VDW data set, using the files created during the co-registration phase. The procedure is quite similar to the VTC creation in fMRI data analysis.

Go to DTI --> Create 3D-Aligned Diffusion Weighted (VDW) Data. A window appears: Use the Browse button to locate the DMR file human31dir.dmr. Next, locate all necessary files for VDW creation. The window should now look similar to this:

0 0	VDW File	e Creation	
Spatial transformati	on of diffusion-weighted	data	
🖲 To Native	O To ACPC	O To TAL	Auto-Fill
Diffusion-weighted	slice-based data file (DM	IR)	
human31dir.dr	nr		Browse
FMR -> VMR coregi	stration file 1, i.e. header	-based ( _IA.TRF):	
human31dir-T	O-human_IIHC_IA.trf		Browse
FMR -> VMR coregi	stration file 2, i.e. intensi	ty-based fine-tuning	(_FA.TRF):
human31dir-T	O-human_IIHC_FA.trl	f	Browse
AC-PC translation/r	rotation file - Talairach, s	tep 1 ( _ACPC.TRF):	
			Browse
Cerebrum border fil	e for scaling – Talairach,	step 2 ( .TAL):	
			Browse
Resulting VDW file			
human31dir_N	ATIVE.vdw		
Clear Op	tions		Cancel GO

Be sure to select the option To Native.

Next, go to the Options window and check whether Sinc interpolation at Interpolation options is activated. DWI data is extremely sensitive to interpolation, so the best interpolation setting is required. However, sinc interpolation may easily take hours to compute, so if you don't have that time, take the next best option, which is Trilinear. The rest may be left as default. You may choose to turn on or change the Use intensity threshold to find brain voxels, but this is not recommended. Use masking, see section 1.6.3 instead.

0	00		Crea	te VDW O	ptions
	Target re	solution (in	VMR voxels]:		
	○ 1×1	×1	(	• 2x2x2	○ 3x3x3
	Target da	ita type			
	🕑 Floa	t (4 bytes)			O Integer (2 bytes)
	Interpola	tion options			
	🔘 Nea	rest neighl	bor 🔘	Trilinear	● Sinc R: 3 👘
	Talairach	bounding b	ox		
	💽 Stan	ıdard grid	space 🔘	Extended	space including cerebellum
	Bounding	box determ	nination (if tra	nsformation	not up to Tal space)
	🗌 Use	intensity t	hreshold to	find brair	n voxels: 100
	🗌 Use	fixed bou	nding box f	or target	Show TAL Box Values
		<b>X</b> :	Y:	<b>Z</b> :	
	From:	59	57	52	
	To:	197	231	172	
					Cancel Ok

 $Click \; \mbox{Ok} \; and \; \mbox{GO} \; in the \; \mbox{VDW} \; \mbox{File} \; \ \mbox{Creation} \; window.$ 

#### 1.6 Tensor, Diffusivity and FA calculation

First, close the VMR you may still have open, and reopen it (beware to use the \_ACPC.vmr or \_TAL.vmr if you went into standard space). Go to DTI->Diffusion Weighted Data Analysis. A VDW Analysis window appears. In the Linked 3-D aligned diffusion weighted data part, click the Browse button and point to the VDW file created in the previous part, which is human31dir.vdw.

Next, go to VDW Properties in the VDW Analysis window. You'll find the gradient table on the left and some other info on the right.

#### 1.6.1 The gradient table



The gradient table can be filled in two ways: manually, by entering the gradient direction and b-value directly into the table, and automatically by loading a so-called GRB *GRadient and B-value* file.

You might have a text file with gradient directions or otherwise you have to ask your MR technician for such a file.

For this particular experiment, we need a gradient table with 31 directions. If the gradients are not yet specified, do it by clicking "Load .GRB" and locate the file mgh\_dti30.grb. The gradient table can also be found in appendix **??**.

Now that the gradient table is filled, click the Gradient directions and b-values verified check box, and the VDW file can be saved by using Save As or Save. BV will remember the associated GRB file. The Set b-value(s) in table option on the top right may be used for changing the b-value as well, for bulk changes. You need to set correct b-values for your experiment, which in this case are: measurement 1: b=0, measurement 2-31: b=800. Typing directly in the table is also supported.

The interpretation of gradient components part of the VDW Properties window may be used if the data is flipped/reversed. The Spatial transformations of directions part may be used if BV makes a wrong interpretation of the scanner versus subject coordinate systems. Both options are explained in Appendix 3.1.1.

Press OK to leave the VDW Properties window. You will return to the VDW Analysis window.

#### 1.6.2 Tensor, Mean Diffusivity and FA Computation

Once the VDW file and gradient information are correct, click Estimate in the VDW Analysis window. Warning: BV may look irresponsive, but in fact it is busy calculating tensors. A DDT "Diffusion Tensor" file is created, and BV asks you to save this file. Save it as human3ldir\_vdw.dmr. A DDT file may also be saved in TVL format, by clicking the Export TVL, for use in the TrackMark software (information via support@brainvoyager.com).

#### 1.6.3 Recommended: masking the DDT data

In general you are not interested in data outside of the brain. Due to the nature of the acquisition however, there is noise present outside of the brain, which should be masked out. Besides the visual attractiveness, this also reduces the amount of voxels significantly, which increases processing speed in later steps.

**For BrainVoyager version 2.4.0 and up** In general you are not interested in data outside of the brain. Due to the nature of the acquisition however, there is noise present outside of the brain, which should be masked out. Besides the visual attractiveness, this also reduces the amount of voxels significantly, which increases processing speed in later steps.

In step 1.4.1 BrainVoyager has automatically created a mask vmr file. Close all open files and open human\_BrainMask.vmr. BrainVoyager requires the VDW file to determine the right dimensions of the mask. *If the VDW is not linked to the VMR, the mask will be incorrect.* Attach the VDW we've just created via DTI -> Diffusion Weighted Data Analysis. Browse for the VDW. The file name will be entered in the dialog:

00	VDW Analysis	
	Data Calculations	
Diffusion tensor data (eigenvect	tors and eigenvalues)	
DDT file:	Load Save Esti	mate
Use spatial masking	Mask file:	vse
Intensity-based maskin	ng using b0 volume Threshold: 100	.TVL
Linked 3D-aligned diffusion-we	lighted data	
VDW file: /DTI_Document	tation_BV20plus/Human31dir/human31dir_NATIVE.vdw	/se
○ Store reference to VDW	W file	nemory
VDW Properties		Quit

Close the dialog. Now we are ready to create the mask. Now, go to 3D Volume tools -> Segmentation -> Options -> Define VOI. A dialog pops up and give brain as the name of the VOI. Save the VOI using the Save button. The BrainVoyager window should look like this:



The VOI can now be converted to a mask file. Go to Analysis->Region Of Interest Analysis. A dialog will open with the VOI "brain" in it. Save the VOI as brain.voi. Select this VOI by clicking on it, and hit the Options button. In the VOI functions tab, set the options as follows, click Create MSK and save the mask file as brain.msk.

0 0	VOI Analysis Options	ł
	GLM Options VOI GLM ANCOVA VTC Data VOI Functions	
VOI -> Draw in VMR	Flip left / right VOI consistency Voxels with map values VOI Transparency	
Convert	Flip X axis         Verify VOI         VOI Details         Value: 0.6         1	
VOI -> Surface clusters	Overview table with VOIs center of gravity Map Peak Voxels	
Create	Individual VOIs     Across subjects     Table     Table	
Expand selected VOIs	Create MSK file from VOIs	
Dilate	Use selected VOIs Use all VOIs Resolution: 2 Create MSK	
Probability Maps	Multi-VOI event-related averaging plot VOIs with map values	
Create	AVC file: Browse Cenerate Plot Table	
	Close	

*If you forgot to link the VDW file, your mask will look like below, which is wrong. You have to start over and create a new mask.* 



**For BrainVoyager version** < **2.4.0** The pipeline for mask creation is as follows:

 $VMR \rightarrow Peel \ brain \rightarrow VOI \ containing the \ brain \rightarrow Mask \ file \rightarrow apply \ mask \ file to \ VDW$ 

We have already created a VMR containing only brain tissue. Open it and link the VDW file created in section 1.5 to the VMR: DTI -> Diffusion Weighted Data Analysis. In the Linked 3D-aligned diffusion-weighted data section, locate the VDW that was created earlier using the Browse button.

**WARNING** Do not forget to link the VDW file to the anatomy before proceeding! The VDW defines the "bounding box" of the mask

Now it's time to define a VOI containing all brain voxels. In order to get a smooth VOI without any holes in it, click the Gaussian button in the segmentation tab.

⊖ ○ \varTheta		3D Volume Tools
3D Coords	Coregistration	Spatial Transf Talairach Segmentation
Value range	Bounding box	
Min: 100	×: 0	(‡) 191 (‡) Options Autom. Segm.
Max: 255	y: 0	255 Clean Grow Region
New: 240	z: 0	255 Fill Box Expand
Filter, smoothing Gaussian Sigma Draw with mouse Enable	FWHM: 2 Range: 20 2D (in-plane)	Border Reload Dilate Marked Smooth Non-Marked Reconstruction Reload All Prepare
Size: 1	O 3D (cube)	Mini Dialog <<

Go to the 3D Volume tools -> Segmentation. Set Value range: Min to 1 and Value range: Max to 225, and hit the Range button. All brain voxels should be selected now and displayed as blue voxels. Now it's time to fill any holes which might still be present in the mask. Go to 3D Volume tools -> Segmentation -> Options -> Masking, and click the Fill Holes button, and then OK.

00	Volume	Tools Options	
	Main Masking	Operations Settings	
Masking functio	ns		
Mask file: B	rainTalMask.vmr		Browse
	Min mask value:	226	Merge
	Max mask value:	245	AND
Special function	s	Create VOI from segmer	tation border
Fill Holes		Segment color:	240
Thin Erode			Create VOI
			Cancel OK

At first, it seems like nothing has happened, but if you click inside a blue region, the screen will be updated and holes will have disappeared.

Now, go to 3D Volume tools -> Segmentation -> Options -> Define VOI. A dialog pops up and give brain as the name of the VOI. Save the VOI using the Save button. The BrainVoyager window should look like this:



The VOI can now be converted to a mask file. Go to Analysis->Region Of Interest Analysis. A dialog will open with the VOI "brain" in it. Save the VOI by clicking the Select this VOI by clicking on it, and hit the Options button. In the VOI functions tab, set the options as follows:

00	VOI Analysis Options	
(	GLM Options VOI GLM ANCOVA VTC Data VOI Functions	
VOI -> Draw in VMR	Flip left / right VOI consistency Voxels with map values	VOI Transparency
Convert	Flip X axis         Verify VOI         VOI Details	Value: 0.6
VOI -> Surface clusters	Overview table with VOIs center of gravity	Map Peak Voxels
Create	Individual VOIs     Across subjects     Table	Table
Expand selected VOIs	Create MSK file from VOIs	
Dilate	• Use selected VOIs O Use all VOIs Resolution: 2	Create MSK
Probability Maps	Multi-VOI event-related averaging plot	VOIs with map values
Create	AVC file: Browse Cenerate Plot	Table
		Close

and save the mask file as brain.msk.

#### 1.6.4 Tensor calculation

To apply the mask to tensor calculations creation, re-open the file human\_IIHC.vmr. Go to DTI -> Diffusion Weighted Data Analysis. Load the VDW created in section 1.5. Then, tick the use mask checkbox, and locate the mask file brain.msk with the Browse button:

● ○ ●	VDW Analysis	
	Data Calculations	
Diffusion tensor data (eigenvectors	and eigenvalues)	
DDT file:	Load	Save Estimate
☑ Use spatial masking	Mask file: _man31dir_BV20/raw/did	com/brain.msk Browse
Intensity-based masking	using b0 volume Threshold: 100	Export .TVL
Linked 3D-aligned diffusion-weigh	ted data	
VDW file: mpleDataDTI/Hum	1an31dir_BV20/raw/dicom/human31d	lir_NATIVE.vdw Browse
○ Store reference to VDW fi	le 💿 l	.oad VDW into working memory
VDW Properties		Quit

Hit the Estimate button to create a masked DDT file and save it accordingly as human31dir\_vdw\_masked.ddt. *If you get a warning like below, you need to go back and re-do step 1.6.3.* 



 $F\!A$  and mean diffusivity can be calculated in the <code>Calculations</code> tab in the <code>VDW</code> Analysis window.

00	VDW Analysis	
	Data Calculations	
Visualize basic diffusion properties		
Mean Diffusivity		Fractional Anisotropy
Visualize direction of primary eiger	ivector	
O Show only max color com	poonent	Veight with FA
• Show mix of two largest of	color components	
○ Show mix of all color com	nponents	Color Directions
VDW Properties		Quit

Mean Diffusivity is defined as

$$MD = (D_{xx} + D_{yy} + D_{zz})/3 \equiv \frac{Tr(D)}{3},$$
(1.3)

and is in theory limited to the interval  $[0, \infty)$ . Click the Mean Diffusivity button to produce a MD map, overlayed on the VMR. Upon clicking this button, a map, *interpolated* to VMR resolution is created. However, in most cases one would like to see the map in DWI resolution. This can be established via Analysis --> Overlay Volume Maps and un-checking the interpolate checkbox. Also in this window the value range can be set.



(a) MD in VMR resolution (interpolated)



Figure 1.3: Mean Diffusivities

Fractional Anisotropy is defined as

$$FA = \frac{\sqrt{3[(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_3 - \lambda_1)^2]}}{\sqrt{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}.$$
(1.4)

Fully isotropic voxels have FA = 0, while fully anisotropic voxels have FA = 1. Click the Fractional Anisotropy button to calculate a FA map overlayed on the VMR. Again this map is in VMR resolution.

For users of BrainVoyager 1.10 or lower: Be careful! For visualisation purposes, *FA is scaled up a factor 10 in BrainVoyagerQX* < 1.10!. So, *FA* = 2.0 in the map is in reality *FA* = 0.2.



(a) FA in VMR resolution (interpolated)

(b) FA in DWI resolution

In both MD and FA maps, values may be explored by moving the mouse pointer around. Values, reported as t=0.32781, are displayed in the Log tab of the Sidebar, or in the status bar in the lower left of the screen.

#### 1.6.5 Alternative Diffusion Measures

Of course we can extract the values of the eigenvectors and compute alternative diffusion measures such as shape measures, radial/axial diffusivities, trace(**D**) from the tensor file. This is implemented in a Matlab function available on http://support.brainvoyager.com/diffusion-weighted-imaging/66/349.

#### 1.6.6 Color coded maps

Color coded maps can be displayed by selecting one of the options in the Visualize direction of primary eigenvector part of the VDW analysis window. It is initially recommended to choose the Weight by FA option, see figure 1.4(d). The color options are:

option	impact on MD	impact on FA
Show only max	In a voxel, show	Based on eigenvector in-
color component	$\max(D_{xx}, D_{yy}, D_{zz}).$	formation; if the principal
	If max = $D_{xx}$ :=red,	eigenvector is largest in <i>x</i> -
	if max = $D_{yy}$ :=green,	direction, color=red; in <i>y</i> -
	$\max = D_{zz} := blue$	direction, color=green; z-
		direction, color=blue;
Show mix of two	Two largest component	ts are mixed: $x +$
largest components	<i>y</i> =red+green=yellow.	x + z = red + blue = purple.
	y + z=green+blue=cyan.	
Show mix of all	Colors similar to the mix	c of 2 components, but
color components	where 3 directions mix, the	map is colored white.

In figure 1.4 the different options are shown. The transparency of the colors may be changed using the Ctrl+Arrow up/down key combination.



(c) FA map based on 3 max components



(d) FA map based on a mix of 2 max components



(e) FA map based on a mix of 3 components



(f) FA map based on 2 components, but not weighted by FA, showing all data.



#### 1.7 Tensor visualization

After performing all steps until calculation of the tensors (DDT file creation), the tensors can be visualised in 3D space. Open human.vmr and load the DDT file human31dir\_vdw.dmr via DTI --> Diffusion Weighted Data Analysis --> Browse. Close this window and go to DTI --> Tensor Visualisation. A new main window opens and the tensor data is visualised as color coded lines. Color coding is identical to that of a FA/MD direction color coded map. The lines represent the major direction of the diffusion tensor. You may want to adjust the amount of visible tensors by de- or increasing the FA threshold.

	😝 🔿 🔿 Tensor Visualization
	Show tensors
	Show current mesh
	Perspective view
	Threshold
	Show if FA > 0.60 (*)
	Slice plane restriction
	Enable
	Distance: 3.00
Show Tensors	check/uncheck to show/hide tensors
Show current mesh	check/uncheck to show/hide a mesh
Perspective view	check/unchek to view data in perspective or
	not in perspective. Also activated by pressing
	P on your keyboard.
Threshold	FA threshold for tensor display. High thresh-
	old $\rightarrow$ few tensors and vice versa
Slice plane restrict	ion show only tensors limited to a slice plane, within a certain distance in mm from a slice.
	See text for instructions

You can navigate in 3-D space using the following gestures:

gesture	effect
hold left + move mouse	rotation
hold right + move mouse	translation
hold left + right + move mouse	zoom

The tensor view may also be limited to a slice instead of the whole volume. First, display one or more slices by clicking or (Shift)-clicking one of the "cut"buttons listed below. Brainvoyager will show you the selected slice, and by checking the Slice plane

restriction box, the tensors will be limited to the slice(s) selected. You can move the slices by the Alt+hold left click+move mouse key combination. In figure 1.5.b the view is shown.



Transversal slice cut Sagittal slice cut Coronal slice cut



(a) Tensors in the whole volume. FA > 0.6.



(b) Tensors limited to a sagittal and transversal plane. FA > 0.20



#### 1.8 Fiber Tracking

#### 1.8.1 Interactive Fiber Tracking

Interactive fiber tracking is meant for exploring the tracts. In real-time, you are able to "draw" fibers on a slice. BrainVoyager puts seedpoints on the location where you click. Using all that you know now about DTI analysis in BV, this is done as follows:

- 1. Open a VMR
- 2. Open a DDT file
- 3. (optional) calculate FA/MD maps
- 4. Go to DTI  $\rightarrow$  Fiber Tracking and Rendering
- 5. Display a slice by using the buttons from table ??
- 6. use Ctrl+Left mouse click to paint fibers on the slice

Since the method is interactive, it's very useful to test the various fiber tracking parameters. The table below shows the parameters and their meanings. Depending on your application, you are encouraged to play around with the parameters.

⊖ ○ ⊖	Fibe	r Tracking And Re	ndering	
Tracking options	5		Tracking terminatio	on options
Step size:	0.50 🗘 Inert	ia: 0.00 (*)	FA thre	shold: 0.20
Seed range:	1.00 🗘 Densi	ty: 3 ^3 🔹	Projection thre	shold: 0.25
🗌 Trilinear i	nterpolation		Angle thre	shold: 50 🗘
Rendering option	ns			
Fibers as	lines 🔘 Fibers as	tubes		🗹 Show fibers
<ul> <li>Show cold</li> <li>Show cold</li> </ul>	or of fiber groups or from fiber eleme	nts (direction co	oding)	
Fiber group				
Name: Inter	ractively Tracked			Start new group
Delete Al	D	Tube thickne	ss: 0.30 🔹	Color:

	Tracking Options	
Parameter	Meaning	Recommended
	-	value
Step size	integration step size in voxels	voxel size/4, e.g.
*	0 1	2mm/4=0.5
Inertia	Parameter that controls "smoothness" of	depending on the
	the fibers. Inertia close to 0 means very tor-	question
	tuous fibers, close to 1 very straight fibers.	1
Seed range	used in interactive tracking Places the	default <sup>.</sup> 1
Seea Lange	seeds at a distance range from the slice	
Seed density	amount of seed points per seed voxel	default $3^3 = 27$
Trilinear	use trilinear instead of linear interpolation	trilinear
internelation	use trifficar filstead of filtear filterpolation	timitear
Incerporación	Tracking termination options	
EN throchold	Provents fibers ponetrating isotronia re-	015.03 default at
FA UNTESNOID	rievents libers penetrating isotropic re-	0.15–0.5, default at
Ducientien	gions (FA< uneshou)	depending on the en
Projection	projection parameter, see [wwww-02]. De-	depending on the ap-
threshold	termines now much the shape of heigh-	plication.
	bouring tensors are used as a tracking	
	guideline in the current voxel.	1 1: .1
Angle treshold	angle threshold between integration steps,	depending on the ap-
	in degrees. Prevents sharp bends of the	plication, default 50-
	fibers.	60 deg.
	Rendering Options	
Fibers as lines	fastest option	
Fibers as tubes	nicely rendered tubes	
Show color of	color fibers according to seed VOI color	
fiber groups		
Show color from	RGB color coded fibers, indicating direc-	
fiber element	tionality	
(direction		
color coding)		
	Fiber group	
Name	name of last tracked fiber group	
Start new group	start new group for interactive fiber track-	
	ing	
Color	color of new group, may be changed by	
	clicking on the color	
Tube thickness	thickness of tubes in the Fibers as	
	tubes rendering mode (arbitrary units)	

In the end, you'll end up with an image like this:



#### 1.8.2 Fiber tracking from seed regions (VOI/ROI)

Fiber tracking can also be started from anatomically or functionally (fMRI) defined regions, usually termed regions of interest (ROI) or volumes of interest (VOI). We will use VOI here, since the VOIs can be defined in 3D.

**Anatomically defined VOIs** Anatomical VOIs are defined by drawing them on a VMR with or without an overlayed FA/MD map.

Open a VMR and the DDT file as explained before. Overlay a FA/MD colormap of your choice. For this demonstration, a FA map is overlayed, color coded according to the maximum values. Next, go to the VMR and open the 3-D Volume Tools dialog. Go to the Segmentation tab.



In the Draw with mouse section on the lower left of the tab, check the Enable box. We have now enabled a drawing pen, and the properties of this pen can be changed 1) by size and 2) 2D or 3D: in 2D, the pen draws a square ie  $2 \times 2$  voxels, in 3D a cube with dimensions set by Size, ie  $2 \times 2 \times 2$  or  $3 \times 3 \times 3$  voxels.

In the VMR window, you can now draw with Ctrl+Left mouse click. But beware! Since the VOIs you are drawing are seed regions for DTI fiber tracking, the borders of your VOIs need to be limited by the DTI data, and not by the VMR data. The DTI data (acquired with a DW-EPI sequence) is distorted relative to the T1 anatomical data. This is illustrated below. The red color shows high FA in left-right direction overlayed on T1 anatomy.



A VOI can be drawn now on the corpus callosum using Ctrl+left mouse click. With Shift+left mouse click, voxels may be removed from the VOI. When drawing is finished, click the Options button on the Segmentation tab. A new window pops op, click the Define VOI button. Then you'll be asked to enter a name for the VOI. Type a name, and click Ok. The VOI analysis window is now shown, displaying all currently defined VOIs.

When you would like to draw a second VOI afterwards, select all current VOIs and click Hide VOIs. Also, click the Reload All button in the segmentation tab. If you don't do this, the new VOI will be added to the visible VOI. A new color is automatically assigned to the VOI. Examples of VOIs in the corpus callosum and cortico-spinal tract are given in the figure below. The VOIs can be saved by clicking the Save button.



(a) VOI at the corpus callosum in orange.



(b) VOI at the brainstem for the corticospinal tract in blue.

#### Figure 1.6: VOIs

Next, set the parameters for fiber tracking in the DTI --> Fiber Tracking and Rendering window. Fibers from these VOIs can be tracked via DTI --> Track fibers from VOIs.

00	VOI Fiber Tracking
From VOIs CST CC	From VOIs to VOIs CST - CC
VOI inclusion mode	Seeding and selection mode
<ul> <li>Use all VOIs in list</li> <li>Use selected VOIs in list</li> </ul>	<ul> <li>○ Fibers from "From VOIs"</li> <li>○ Fibers from "From VOIs" to "To VOIs"</li> <li>● Fibers from "From VOIs" to "To VOIs" and vice versa</li> </ul>
Load VOIs	Cancel Track

The appearence of the fibers can be changed, to result in the following images:



(a) Fibers as lines, color according to seed VOI.



(b) Fibers rendered as tubes



(c) Fibers rendered as tubes and direction color coded.

Figure 1.7: Different visualizations of fibers.

**Using multiple VOIs** BrainVoyager can also track fibers from and to multiple VOIs. Suppose we have defined 3 VOIs: *A*, *B* and *C*. The following operations are permitted, when ticking the ``From VOIs to VOIs'' radio button in the VOI Fiber Tracking dialog:

00	VOI Fiber Tracking
From VOIs	From VOIs to VOIs A - B A - C B - C B - C
VOI inclusion mode	Seeding and selection mode
<ul> <li>Use all VOIs in list</li> <li>Use selected VOIs in list</li> </ul>	<ul> <li>○ Fibers from "From VOIs"</li> <li>○ Fibers from "From VOIs" to "To VOIs"</li> <li>● Fibers from "From VOIs" to "To VOIs" and vice versa</li> </ul>
Load VOIs	Cancel

$$\begin{array}{c} A \to B \\ A \to C \\ B \to C \end{array}$$

The ``From VOIs to VOIs and vice versa'' option allows for tracking in 2 directions:

$$A \rightleftharpoons B$$
$$A \rightleftharpoons C$$
$$B \rightleftharpoons C$$

The advantage of using the last option is that in potential more fibers are found. This is illustrated in the figure below. When tracking from A to B, only 3 fibers are found which go through A AND B. When tracking in the reverse direction, from B to A, 5 fibers are found. Combining the two results in 8 fibers.



#### 1.8.3 Loading and editing fibers

Once you have tracked fibers, you can save them into an fbr file. If you want to reload the fibers from scratch, you need to open a VMR, and load the DDT file in DTI->Diffusion Weighted Data Analysis. Afterwards, you can load the fibers via DTI->load fibers. In the fibers table dialog (DTI->Fibers Table there is the possibility to add an extra fbr file to the existing one.



#### **1.8.4** Spatial Transformations of fibers

**ACPC/TAL Transformation** Fibers may be transferred into ACPC or TAL space from native space. In this case, the only thing that is transformed, are the fiber bundles. There is no transformation of the original diffusion weighted data, as happens when you would transform the original DWI data into TAL or ACPC.

In order to do this, you need to bring the VMR into ACPC or TAL space. The transformation files that are created by BV during these steps are used now to transform the fiber bundles.

ACPC transformation In the DTI --> Spatial Transformations dialog, click Load .TRF, to load an <subject>\_ACPC.TRF. Click the Apply button to perform the transformation and OK to finish.

0	$\bigcirc$	Spatia	al Transf	ormation	of Fibers
,	Transformation				
		<b>X</b> :	Y:	Z:	(ACPC -> TAL)
	Translation:	0	0	0	TAL -> ACPC
	Rotation:	0	0	0	
	Scale:	1	1	1	
	Origin:	96	128	128	
	New origin:	128	128	128	
	Backward	Reset		pply	Fibers -> VMR
	Load .TRF		ave .TRF.		Cancel OK

Save the fibers as <subject>\_ACPC.fbr.

**TAL transformation** After the ACPC transformation, you can apply a Talairach transformation. To do this, load the <subject>.TAL file in the 3D Volume Tools > Talairach > Load .TAL dialog. The TAL file name will show up.

0 0			3D Volume Tools		
	3D Coords	Coregistration	Spatial Transf	Talairach	Segmentation
AC-PC	transformation				
1.	Find AC F	Point 2.	Find AC-PC Pla	ine 3.	Transform
Talaira	ch proportional g	rid reference points			
□ D ☑ D	iisplay full grid Iisplay partial g	AC Set	Point	Load .TAL ) Save .TAL	ACPC -> TAL TAL -> ACPC
) s O s	tandard TAL po ubject TAL poi	nts Show	Point File:	human_ACPC	tal
Max clu	uster spread rang	e		Avera	ge 3D data sets
Rang	ge: 10 🔹	Options			Combine Data Sets

Then, go to DTI --> Spatial Transformations and click the ACPC -> TAL button and OK to finish.

**Backprojection of fibers to the VMR** It is possible in BV to evaluate the fibers directly on the VMR, in 2-D space so to say. Again, be careful, the fibers may be distorted relative to the anatomy! In the DTI --> Spatial Transformations dialog, click the fibers -> VMR button and BV projects the fibers onto the VMR slices in the same colors as the fibers (that is, ROI colors). In the figure below, the result of such a backprojection for the corpus callosum fibers is shown. This backprojection leads to a new VOI, so it can also be used to get statistics from fibers, as explained in the next section.



#### 1.9 Statistical Analysis

#### 1.9.1 VOI Statistics

An example of using VOI statistics is given in this section. First, make sure you have a VMR and a FA or MD map loaded. Either create a VOI first, or point to Analysis --> Region of Interest Analysis to open the VOI dialog and load previously defined VOIs, either drawn or created by backprojection of fibers on a VMR.

Because a FA/MD map is loaded, BV can extract the FA/MD values at the VOIs. Open the VOI dialog if you haven't done this already. To show the data, select the VOI of your choice (here: corpus callosum) and click Options in the lower-right corner of the window. In the VOI Analysis Options dialog, go to the VOI functions tab.

0 0	VOI Analysis Options	
	GLM Options VOI GLM ANCOVA VTC Data VOI Functions	
VOI -> Draw in VMR	Flip left / right VOI consistency Voxels with map values	VOI Transparency
Convert	Flip X axis         Verify VOI         VOI Details	Value: 0.6
VOI -> Surface clusters	Overview table with VOIs center of gravity	Map Peak Voxels
Create	Individual VOIs     Across subjects     Table	Table
Expand selected VOIs	Create MSK file from VOIs	
Dilate	O Use selected VOIs 🕑 Use all VOIs Resolution: 3	Create MSK
Probability Maps	Multi-VOI event-related averaging plot	VOIs with map values
Create	AVC file: Browse Cenerate Plot	Table
		Close

Click the VOI details button and a window showing (in this example) the FA values of the VOI at all voxel locations is displayed, in column StatValue 1.

(

)	0 \varTheta	ROI Details	
	DETAILS FOR VO	I "В"	
	RandomEffectsAnalysis:	No	
	TypeOfStatistic:	FA	
	NrOfVoxels:	83	
	AbsStatMinValue:	0.279439	
	hosteria ver	0.5240/2	
	AvgPValue:	0.000000	
	StatWeightedMass: PWeightedMass:	47.713947 0.000000	
	ListOfVOIVoxels:		
	x y z StatValı	ue p	
	73 173 100 0.5644	80 0.000000	
	74 173 103 0.5630	66 0.000000	
	74 173 105 0.6531 75 173 101 0.6132	39 0.000000 97 0.000000	
	75 173 103 0.6156	86 0.000000	
	76 173 100 0.6326	80 0.000000	
	77 173 101 0.6063	60 0.000000 72 0.000000	
	77 173 106 0.6321	78 0.000000	
	78 173 98 0.7006	20 0.000000	
	78 173 100 0.6329	95 0.000000	
	78 173 101 0.5902	50 0.000000	
	78 173 103 0.5224	61 0.000000	-
	78 173 104 0.5256	79 0.000000	<b>‡</b>
	Save	Clo	se

The details can be saved as a textfile, and then processed outside of BV, for instance to show the FA profile of the corpus callosum in figure 1.9.



Figure 1.8: FA distribution of the corpus callosum in the anterior-posterior direction.



Figure 1.9: ADC distribution of the fibers of the corpus callosum.

## **Chapter 2**

## **DWI Group Analysis**

#### Before you begin

For DWI group analysis, you need BrainVoyagerQX 2.2 or higher.

#### Introduction

As more and more research is done on white matter morphology, the obvious question to ask is whether differences can be found between individuals or between groups, ie patients vs controls. Before we begin, I'd like to summarize some important acquisition issues.

#### **Data Acquisition**

- make sure you acquire data on each subject *exactly* the same. Be careful to use *exactly* the same TR/TE, b-value, voxel size and number of slices.
- *always* measure iso-voxel data. It's easy to understand why: when acquiring non-isovoxel data, and if a fiber structure would be aligned parallel to the long axis of a voxel, more contrast is added there due to the summation of diffusivity. Ergo, more artificial signal decay in that direction!
- try to *avoid* interpolating your data. This has a dramatic effect on derived measures such as *FA*. This is illustrated below, where the *FA* distribution for a native resolution VMP versus interpolated VMP is shown for a ROI in the corpus callosum.



- be very careful with interpretation of differences in *FA* or *ADC*. They might not be of anatomical nature but due to the acquisition, data processing etc.
- include a T1 weighted high-resolution anatomy in the session.

#### About native and Talairach space

We recommend computing the tensor and derived measures in native space (that is the space as the data was scanned in), and to do the group analysis in common space by converting the scalar FA/ADC maps to TAL space. This prevents introducing artefacts in the tensor data by interpolation. Interpolation of a tensor is not trivial and may introduce tensor deformation in the processing. For more information, see reference [AFPA06].

#### 2.1 Group analysis of FA/ADC maps

#### 2.1.1 Anatomical data Preparation

We will now start by preparing the anatomical data. The anatomy is used to transfer the data into a common space (Talairach space, abbreviated as TAL). The transformation files are later on used to transfer the DW-MRI data into TAL space as well.

It is assumed that you know how to put an anatomical data set into TAL space. If not, please go through the BVQX *Getting Started Guide*.

For each subject, create the <subject>\_TAL.vmr file. Make sure you do not delete <subject>\_ACPC.trf and <subject>.TAL.

#### 2.1.2 Diffusion Data Preparation

For each subject in your study, do the DW-MRI data analysis in native space, up to the point of creation of *FA* and *ADC* maps. Save each map as <subject>\_FA.vmp or <subject>\_ADC.vmp respectively.

## 2.1.3 Creation of talairach FA or ADC maps – starting in native space

The processing of *FA* maps is demonstrated here, but it is the same for *ADC* maps. It consists of two steps: 1) bringing the map to ACPC space and 2) going from ACPC to TAL space.

**Map to ACPC space** Open the native space VMR, <subject1>.vmr. Go to Analysis -> Overlay Volume Maps. Click Load VMP and load the file <subject1>\_FA.vmp you have created earlier. Close the dialog. You should see a *FA* map overlayed on anatomy.

Now, go to 3D Volume Tools -> Spatial Tranf. Load the <subject>\_ACPC.trf file created earlier and click Transform .VMP.

0 0		3D Volume	Tools		
3D Coords C	oregistration	Spatial Transf	Vol Rend	Talairach	Segmentation
Transformation files	Standardiz	e Ap	ply spatial trans	formation	
Load .TRF	) <b>T</b> o	Sag	Transform .	VMR	Export .AMR
Save .TRF	) Iso-'	Voxel 2	Transform .	VMP	Export .DCM
VMP display options	Com	pination of current ar	id loaded transi	formation	
🗹 Overlay 3D ma	ıp 💿	Replace current		O Appe	end after current
Show 3D map	Show	a volume of attached	d VTC data		
Two VMR display opt	ions 🔽	Trilinear internol.	G	how VTC Vo	
O Show primary	VMR	interpoli			
O Show seconda	ry VMR Inter	oolation method in se	cond row		
O Blend 1 O	Blend 2 💽	Trilinear 🔘	Nearest neig	hbor 💽	Mini Dialog << )

Save the result as <subject>\_FA\_ACPC.vmp:

Interpolation options	Framing cube dimension
<ul> <li>Nearest neighbor</li> <li>Trilinear interpolation</li> <li>Cubic spline interpolation</li> <li>Sinc interpolation R: 3 <sup>(*)</sup></li> </ul>	<ul> <li>256</li> <li>384</li> <li>512</li> <li>1024</li> </ul>
Transformation direction	
Apply forward	Apply backward
Resulting .VMP file	
<ul> <li>Standard, native resolution VMP</li> <li>Anatomical resolution VMP</li> </ul>	
Folder: ojects/company/multiSub	ojectDTI/cg Browse
File name: CG_FA_ACPC_NR.vmp	
	Cancel CO

The ACPC transformation is done. Close the VMR.

Map to TAL space from ACPC Now, open the file <subject>\_ACPC.vmr. Load the FA map: <subject>\_FA\_ACPC.vmp. Go to 3D Volume Tools -> Talairach. Load the TAL file <subject>\_ACPC.TAL by clicking the Load TAL button. Next, click ACPC -> TAL.

00	3D Volume Tools	
3D Coords Coregistration	Spatial Transf Vol Rend	Talairach Segmentation
AC-PC transformation		
1. Find AC Point	2. Find AC-PC Plane	3. Transform
Talairach proportional grid reference	points	0
<ul> <li>□ Display full grid</li> <li>✓ Display partial grid</li> </ul>	AC 1 Load .TA	ACPC -> TAL           AL           TAL -> ACPC
Standard TAL points	Show Point File: ca aco	or tal
<ul> <li>Subject TAL points</li> </ul>	The. cg_acp	(c.ta)
Max cluster spread range		Average 3D data sets
Range: 10 🗘 Option	15	Combine Data Sets
		11

Save the results as <subject>\_FA\_TAL.vmp (make sure the Apply to VMP checkbox is checked!):

nterpolation options	Select data set
O Nearest neighbor	
<ul> <li>Trilinear interpolation</li> </ul>	Apply to VMR
<ul> <li>Cubic spline interpolation</li> </ul>	
◯ Sinc interpolation R: 3 (*)	Apply to VMP
/MP type	
Anatomical resolution VMP	
Anatomical resolution VMP Talairach reference points (.TAL) file ojects/company/multiSubjectDTI/cg/cg_a	cpc.tal Browse
Anatomical resolution VMP Talairach reference points (.TAL) file ojects/company/multiSubjectDTI/cg/cg_a Resulting file(s) Folder:	cpc.tal Browse
Anatomical resolution VMP Talairach reference points (.TAL) file ojects/company/multiSubjectDTI/cg/cg_a Resulting file(s) Folder: File name: CG_FA_TAL_NR	cpc.tal Browse Browse .vmr/.vmp

Repeat the talairach process for each subject.

#### 2.1.4 Combining the maps

Now that we have created FA maps in TAL space, and have reframed them for each subject, it's time to do simple statistics. For analysis, first a TAL VMR needs to be opened. You may use the best VMR in your data set, but you can also create an average VMR from all data sets (Volumes > Combine 3D data sets).

Open the Analysis > Overlay Volume Maps dialog. This dialog can also be opened using the Ctrl+M shortcut. Now, load the FA map of each subject:

	Browse Statistics	Map Options	Advanced	
election Color Map Nan	ne			
1 CG_MD	_Reframed			
2 JR_MD_	Reframed			
verlay values	Hires VMP creation	Threshold		Browse maps
verlay values	Hires VMP creation	Threshold Min: 0.1	00 1	Browse maps

Browse all maps to see whether they correctly align with the VMR and inspect for other irregularities. Now we can use the Combine VMPs option in the Advanced tab. The dialog is divided into 4 parts. The top part shows the subjects maps, and gives you the opportunity to discriminate between 2 groups G1 and G2. A second part that can be used to analyze the maps without splitting them into groups. A third part that enables specific statistics on the basis of the maps separated into groups. Finally, an "exclusion" option that will help to shape specific maps according to their values and a value range selected by the user.

00	Combine VMPs
Group 1 VMP 1: CG, MD_Reframed VMP 2: JR, MD_Reframed	Group 2
Apply for selected VMPs in group 1 Add value: Multiply with: 1.0 Multiply V	MPs) (Sum VMPs) (Average VMPs) (T-Test <g1> 0&gt;)</g1>
Apply for selected VMPs in group 1 and group 2 VMP in C1 - VMP in C2 Corr <c1, c2=""> (T-Te</c1,>	Set range to value for selected VMPs in group 1
Exclusion options for selected VMPs in group 1 Value < 0.0 Value > 0.0	Exclusion options for selected VMPs in group 2           Value < 0.0         Value > 0.0
	Close

First, we try the statistics that are available for the single group (in the first field). We mark all subjects maps and use the Average VMPs option.

$\bigcirc \bigcirc \bigcirc$	Combine VMPs
Group 1 VWP 1: CC_MD_Reframed VMP 2: JR_MD_Reframed	Group 2
Apply for selected VMPs in group 1	
Add value: Multiply with: 1.0 Multipl	y VMPs Sum VMPs Average VMPs T-Test <g1> 0&gt;</g1>
Apply for selected VMPs in group 1 and group 2           VMP in C1 - VMP in C2         Corr <c1, c2="">         T</c1,>	Set range to value for selected VMPs in group 1 -Test <g1 g2="" vs=""> 0.0 - 0.0 Set to: 0.0</g1>
Exclusion options for selected VMPs in group 1	Exclusion options for selected VMPs in group 2
□ Value < 0.0 □ Value > 0.0	0 □ Value < 0.0 □ Value > 0.0
	Close

As the result, a new map will be created in the main dialog (at the end of the map list). We check the map to visualize the result of the average procedure.



#### 2.1.5 ANCOVA Analysis of FA/ADC maps

For this step, first create a map containing all maps (VMPs) of all subjects, and use the naming convention Subject <initials>: FA or the like:

5 😝	Volume Maps - [/	AllSubjects_FA_TAL.vmp]	
	Browse Statistics	Map Options Advanced	]
Selection Color Map Name           1         Subject S           2         Subject S           3         Subject S           4         Subject S	1: FA_TAL 2: FA_TAL 3: FA_TAL 4: FA_TAL 5: FA_TAL		
🙂 5 📕 Subject S	5: FA_TAL		
L			
Overlay values	Hires VMP creation	Threshold	Browse maps
Overlay values  Positive Negative	Hires VMP creation	Threshold Min: 0.010	Browse maps Map: 5

Then, go to the Advanced tab of the Volume Maps dialog. From there on, you can use the ANCOVA tool just as you would for an fMRI ANCOVA analysis. I'd like to refer you to the description in the User's Guide in the Basic Analysis, Random Effects Group Analysis section. You can also have a look at the description in http://web.mac.com/rainergoebel/RainersBVBlog/Rainers\_BV\_Blog/Entries/2007/9/25\_The\_'C'\_in\_ANCOVA.html.

As an example, I've divided 5 subjects into two groups (Dummy example, i.e. excellent readers in group 1 and poor readers in group 2), and I've added age as a covariate. The design table of the experiment looks like this:

					ANCOVA
_				nput	Design Table
	Subjects	FA_TAL	Between Factor 1	Age	
1	Subject S1		1	53	
2	Subject S2		1	46	
3	Subject S3		2	45	
4	Subject S4		2	62	
5	Subject S5		2	50	
					Load Table) (Save Table)
			Full Table M	1easur	Load Table         Save Table           rements         Groups         Covariates
)e:	sign type: S	ingle-Fa	Full Table M	1easur	Load Table     Save Table       rements     Groups     Covariates         Compute

Click GO to start the analysis.

#### 2.2 Group analysis of fiber tracts

Again, we will start with preparing the data in native space. Do the DTI preprocessing up to the tensor estimation, so you can start tracking fibers. The next step is to select the tract you are interested in, in the DTI > Fibers Table menu. Then, transform the fibers to ACPC or TAL space, as explained in 1.8.4.

Next, go to DTI > Spatial transformations and click the button Fibers -> VMR. This will project the 3-D fiber reconstruction onto the 2-D VMR slices. The result is a volume of interest (VOI) on the VMR. As explained earlier, if you add a VMP in Talairach space, you can extract the MD/ADC values from that VOI.



#### 2.2.1 Tract probability maps

Ofcourse we could overlay the tracts from all subjects on a TAL vmr, but a nicer option is to create probability maps of the tracts across subjects. To do this, convert the tracts from all subjects into TAL space, and use the naming convention <subject>\_tractname for each voi, eg CG\_CST. Add the vois of all subjects into one voi file, by using the Add function in the VOI analysis dialog.

$\Theta \cap \Theta$	Volume-Of-Interes	st Analysis
Volumes-Of-Interest list		Time course (VTC) files
<ul> <li>AK_CST</li> <li>GC_CST</li> </ul>	Show VOIs Hide VOIs Show time course In new window Significant voxels a AND b a OR b	Add Remove
Show "VOIs x Subjects" view	Delete Edit	
VOI file: \IISubjects_CST.voi	oad Add Sa	ave New Options Close

Then, click Options > VOI functions > Probability Maps, Create. Make sure you see only the tract name and not all subject names. You can use the Naming Convention radio buttons to change. Set the map resolution to  $1 \times 1 \times 1$  and click GO. The result is a VMP showing overlapping tracts. The colors indicate in what degree the tracts are overlapping. The percentage value is calculated according to 100 \* (number of times a tract overlaps)/(number of subjects).



### Chapter 3

## **Frequently Asked Questions**

#### WARNING

If your acquisition matrix is larger than 128x128, the automatic DMR-VMR co-registration feature in BrainVoyager QX will possibly fail. This means, you might need to do manual co-registration. We strongly recommend the acquisition matrix to be at maximum 128x128, since a larger matrix will be zero-filled in

k-space (=interpolated in image space), resulting in data redundancy. Please ask your MR technician to turn off interpolation for DW-MRI acquisition.

#### 3.1 General

#### 3.1.1 Incorrect color coding FA maps

*FA color coding is incorrect.* Why? Because co-ordinate system of scanner and Brain-Voyager is different. This is not a BV problem, since co-ordinate systems are not standardized.

Normal color coding:

**Red** Left-Right vv (= X direction)

**Green** Anterior-Posterior vv (= Y direction)

**Blue** Inferior-Superior vv (= Z direction)

An example of abnormal color coding:

Example: Original color
Ant-Post = blue
Inf-Sup = red
Left-Right = green

#### **Proposed change** X: direction = Inf-Sup Y: direction = Left-Right

Y: direction = Left-Right Z: direction = Ant-Post



#### Procedure to correct:

go to DTI -> Diffusion Weighted Data Analysis -> VDW Properties -> Gradients. Change x, y and z to what you think is correct. *This is a mathematical operation and has nothing to do with orientation in the brain*. Next, click the OK button.

	ni di setta di se		- Lable				h			LL.
rac	lient direction	is and b value	es cable		][	bet	D Va	alue(s	) in ta	
	Grad X	Grad Y	Grad Z	A			E	valu	e:	1000 Set
1	0	0	0			Fr	om ۱	/olum	e:	1 🚔
2	-0.500038	-0.707053	-0.500038				To y	olum	e. [	16
3	-0.500038	0.707053	-0.500038					orann		
4	-0.707107	0	0.707107		l c	Inte	erpre	etatio	n of g	gradient components
5	-0.706806	-0.698808	-0.10997	=				X di	rectio	n: Posterior to Anterior
6	-0.700024	-0.653023	0.28901					V di	ractio	Di Inforior to Superior
7	-0.331047	-0.7051	0.627089					T UI	reccio	
8	-0.273139	-0.702358	0.657335					Z di	rectio	n: Left to Right
9	-0.541808	-0.503821	-0.672762		1	бра	itial t	ransf	ormal	tions of directions
10	-0.491033	0.513034	0.704047			Van	ne:	hed 3	D Spa	ace (DICOM) Nr: 1 🚔
11	-0.253015	0.675039	-0.693041							
12	-0.70683	0.0279933	-0.70683				1	2	3	
e i	0.707057		0.00010			1	0	1	0	
• 1						2	0	0	-1	
Loa	ad .GRB	Save .GRB				3	-1	0	0	
	Gradient dire	ctions and b v	/alue(s) verifi	ed						1



Re-calculate the tensors by clicking the Estimate button. In the Calculations tab, create the color coded FA maps and check them for the right colors.

Then, Go to DTI -> Tensor visualisation and check for tensor directions. I always use the splenium of the corpus callosum to check for correct orientation.



Figure 3.1: Splenium of the corpus callosum, view from the top

#### 3.2 Project Creation related

## 3.2.1 I can't get my data into BrainVoyager, or the values are all wrong

Before calling BV support, please try to convert your data to Nifti, and try to import it using the Nifti plugin, which can be found in Plugins > Nifti Converter.

An excellent DICOM to Nifti convert is MRIcron by Chris Rorden, to download for free from http://www.sph.sc.edu/comd/rorden/mricron/.

#### 3.2.2 The create project wizard does not work or crashes Brain-Voyager

- BrainVoyager crashes while executing the create Project wizard
- My acquisition matrix is larger than  $128 \times 128$ . BrainVoyager incorrectly reads my data?
- I need byte swapping (can occur with PHILIPS PAR/RECdata), that is: from little Endian to big Endian or vice versa.
- the number of bytes per pixel of my raw data  $\neq 2$ ?
- the Siemens MOSAIC matrix is incorrectly read by BrainVoyager?

Please check out http://support.brainvoyager.com/
diffusion-weighted-imaging.html or contact the support team at
support@brainvoyager.com.

#### VDW related

#### 3.2.3 Fine-Tuning alignment does not work properly

By default, Fine-Tuning alignment uses the first volume in the data set. It might be, that this is a diffusion weighted image instead of a b0. The fine alignment fails at this point. The solution is to set the display volume to a b0 volume (see DMR Properties > DWI Data > Volume (b0) for display), and *save the DMR*. Then, in the alignment procedure, use the AMR as input.



#### 3.2.4 Optional: Manual Co-registration of DMR with VMR

In some cases the position information may be lost or incorrectly read by Brain-Voyager. The automatic co-registration will not work, and you are forced to use manual co-registration. In this section, the procedure is discussed step-by-step.

- 1. Open the VMR corresponding to the DTI data set, human.vmr.
- 2. Go to DTI-->Coregister DMR-DWI to VMR. Via the Browse button, locate the DMR human31dir.dmr.

00		[	OMR-VMR Coregistra	ation	
Files	Sourc	e Options	Initial Alignment	Fine-Tunir	ng Alignment
Source and	target file	s			
DMR file:	human	31dir.dmr			Browse
VMR file:	human	vmr			
Resulting tra	ansformat	ion files			
Initial alig	inment:	human31di	r-TO-human_IA.trf		
Fine-	tuning:	human31di	r-TO-human_FA.trf		
			Run IA	Run FA	Close GO

3. Go to the Source Options tab. In most cases, BrainVoyager has created an AMR file from the first volume, but if this did not happen, choose the use DMR data (DWI Slices), and check the invert intensities box. This has to be checked, since a DWI images has  $T_2$  contrast, while  $T_1$ contrast is needed for co-registration. Check the create edge display for DMR/AMR data box. Next, hit the Create Volume button. This will create a VMR from the first DMR volume.

Files	Source Options	Initial Alignment	Fine-Tuning Alignment
Options for D	MR/AMR source		
🖲 Use DM	R data (DWI slices)		🗹 Invert intensitie
🔾 Use link	ed AMR (coplanar	T1 or T2 weighted sl	ices)
Create e	edge display for DM	IR/AMR data	Create volume
Additional op	tions for manual (e.g.	corresponding points-ba	ased) alignment
🗌 Flip slice	e order		To SAG
Show sli	ce lines		

4. The window will look like this:



On the top row, we see the VMR, overlayed with the slice orientation of the DMR data set (light yellow lines) The bottom rows shows the VMR overlayed with the DMR data. The green lines represent the edges of the DMR data. As is immediately clear, the DMR is scanned in a transversal way, while the VMR is sagittally oriented. We will solve it in the next step, by converting the DMR to sagittal orientation.

5. Click the To SAG button in the co-registration dialog. A dialog pops up:

00	Transform To Standa	rd Orientation
Current SAG view	Rotation butto	ns Transformed SAG view
• • • •	X: -90 (4 Y: -90 (4 Z: -90 (4	90 90 90 90
Framing cube dimens	ion	
O 256 O 384	O 512 O 1024	O Keep original dimensions
Auto Clear	Ð	Cancel OK

By manipulating the data via the middle buttons, change the right view to a sagittal view. In this case, it means hitting the X: +90 button once, and Y: -90 button one, but in your data it may be different. Check the Framing cube dimension: 256 radio button, and click OK.

0 0	Transform To Standard Ori	entation
Current SAG view	Rotation buttons	Transformed SAG view
	X: -90 +90 Y: -90 +90 Z: -90 +90	s A
<ul> <li>● 256 ○ 384 (</li> </ul>	O 512 ○ 1024 C	) Keep original dimensions
Auto Clear	)	Cancel OK

6. Go to the Initial Alignment tab of the coregistration dialog and check the Manual Alignment -- use "To SAG" option. Click Run IA.



The result is the DMR in sagittal orientation overlayed on the VMR:



7. The result is a very crude alignment, so it needs to be adjusted. This is done by transformations and rotations. Go to the coregistration tab of the 3D Volume Tools:

			3D Volume Tools		
	3D Coords	Coregistration	Spatial Transf	Talairach	Segmentation
Transla	tion	Rotation	Scale	(FOV)	Mode
<b>x</b> : (	0.0	×: 0.0	* x:	256 🗘	Single VMR
<b>y</b> : (	0.0	y: 0.0	ф у:	256 🔹	FMR -> VMR
z: (	0.0	z: 0.0	↓ z:	256	VMR -> VMR
FMR-V Se VMR-V Se Corres	MR coregistration lect FMR MR coregistration lect VMR ponding points co fine Points	Align Align registration Align	Target display Show tran Show targ Blend: Tr Blend: Mo e Blend: Ed	options nsformed get ansparent osaic ges	Helper tools Center Set Translation Mini Dialog << Options

Using x, y, z translations and x, y, z rotations, try to align the DMR as good as possible to the VMR data set. In the bottom row of the data display, you can freely browse the data, and this is of course highly recommended. When aligning, concentrate on aligning gyri and sulci rather than the ventricles, since the tissue around ventricles suffers from (large) distortions in EPI data such as DMR. Try to be as precise as possible! For the current data set, the following parameters were found:

) 🔿 🔿	3D Volume Tools				
	3D Coords	Coregistration	Spatial Transf	Talairach	Segmentation
Transla	tion	Rotation	Scale	(FOV)	Mode
x: 2	2.5	×: -1.0	) x:	256 🗘	Single VMR
y: -	-11.0	y: 4.0	у:	256 🗘	FMR -> VMR
z: -	-9.5	z: 0.5	<b>z</b> :	256 🗘	VMR -> VMR
FMR-VMR coregistration     Align       Select FMR     Align       VMR-VMR coregistration     Select VMR       Select VMR     Align       Corresponding points coregistration     Define Points			Target display Show tran Show targ Blend: Tra Blend: Mo e Blend: Ed	options nsformed get ansparent osaic ges	Helper tools Center Set Translation Mini Dialog << Options

and the window looks like this:



8. Now, return to the DMR-VMR coregistration dialog, via DTI-->Coregister DMR/DWI to VMR. Go to the Fine Tuning Alignment tab, and check the Manual alignment -- use current translation and rotation values option:

Files       Source Options       Initial Alignment       Fine-Tuning Alignment         Alignment method       Ordions       Options       Options         Intensity alignment using multi-scale approach       Edge alignment using iterative closest point (ICP) method       Omtions         Manual alignment - use current translation and rotation values       No fine tuning alignment       TEE matrix
Alignment method O Gradient-based affine alignment (6-12 parameters) Options Intensity alignment using multi-scale approach Edge alignment using iterative closest point (ICP) method Manual alignment - use current translation and rotation values No fine tunion plicement TEE matrix
Cradient-based affine alignment (6-12 parameters) Coptions Intensity alignment using multi-scale approach Edge alignment using iterative closest point (ICP) method Manual alignment – use current translation and rotation values No fine tunion plicement TEE matrix
O Intensity alignment using multi-scale approach Edge alignment using iterative closest point (ICP) method O Manual alignment - use current translation and rotation values O No fine tuning a lignment (TEE matrix)
Edge alignment using iterative closest point (ICP) method     Manual alignment – use current translation and rotation values     No fine tuning alignment     TPE matrix
Manual alignment - use current translation and rotation values     No fine tuning alignment     TRE matrix
O No fine tuning alignment
O No me-tuning alignment

Hit the Run FA button.

9. Result of the manual alignment procedure:



BrainVoyager has saved the transformation values in the files human31dir-TO-human\_IA.trf and human31dir-TO-human\_FA.trf

## **Further Reading**

[AFPA06] Vincent Arsigny, Pierre Fillard, Xavier Pennec, and Nicholas Ayache. Log-Euclidean Metrics for Fast and Simple Calculus on Diffusion Tensors. Magnetic Resonance in Medicine, 421(April):411-421, 2006. [BJ02] PJ Basser and DK Jones. Diffusion-tensor MRI: theory, experimental design and data analysis - a technical review. NMR Biomed, 15:456-467, 2002. [CHPJ02] M Catani, RJ Howard, S Pajevic, and DK Jones. Virtual in vivo interactive dissection of white matter fasciculi in the human brain. NeuroImage, 17:77-94, 2002. [Jon04] DK Jones. The effect of gradient sampling schemes on measures derived from diffusion tensor MRI: A monte carlo study. Magnet Reson Med, 51:807-815, 2004. [Kin06a] PB Kingsley. Introduction to diffusion tensor imaging mathematics: Part i. tensors, rotations, and eigenvectors. Concept Magn Reson A, 28A(2):101–122, 2006. [Kin06b] PB Kingsley. Introduction to diffusion tensor imaging mathematics: Part ii. anisotropy, diffusion- weighting factors, and gradient encoding schemes. Concept Magn Reson A, 28A(2):123-154, 2006. [Kin06c] PB Kingsley. Introduction to diffusion tensor imaging mathematics: Part iii. tensor calculation, noise, simulations, and optimization. Concept Magn Reson A, 28A(2):155-179, 2006. [LBPAL06] D Le Bihan, C Poupon, A Amadon, and F Lethimonnier. Artifacts and pitfalls in diffusion mri. J Magn Reson Imaging, 24:478-488, 2006. [MB99] S Mori and PB Barker. Diffusion magnetic resonance imaging: Its principle and applications. Anat Rec, 257:102–109, 1999. [Mor07] S Mori. Introduction to Diffusion Tensor Imaging. Elsevier, 2007. [MWNPVZ05] S Mori, S Wakana, LM Nagae-Poetscher, and PCM Van Zijl. MRI atlas of human white matter. Elsevier, 2005. [WMM<sup>+</sup>02] CF Westin, SE Maier, H Mamata, A Nabavi, FA Jolesz, and R Kikinis. Processing and visualization for diffusion tensor MRI. Med Image Anal, 6:93–108, 2002.

## Appendix A Overview of DTI Procedures



## Appendix **B**

## **File types**

DMR	Diffusion MR project	text file, describing the project which data is in a DWI file (compare FMR $\leftrightarrow$ STC)
DWI	Diffusion Weighted Images	binary file containing raw diffusion weighted data
TRF	TRansformation File	text file, containing transformation parame- ters
VDW	Volume Diffusion Weighted file	binary file, 3-D diffusion weighted data set (compare to VTC)
GRB	Gradient directions and b- values	text file, containing gradient directions and b- values
DDT	Diagonalized Diffusion ten- sors file	
TVL	Tensor Volume file	binary tensor file for use in TrackMark
VMP	Volumetric Map	Binary file containing FA or mean diffusivity values for each voxel.
FBR	fiber file	text file containing the fiber points
VOI	Volume of Interest	text file, containing voxel positions for each voxel in the VOI/ROI

#### **B.1** BrainVoyager Fiber Coordinate system

This is the coordinate system in the OpenGL/Surface window.

Origin: [x, y, z] = 0.5\*VMR slice X-resolution, 0.5\*VMR slice Y-resolution, 0.5\*number of slices

*x*-axis: anterior to posterior 0 to X-resolution *y*-axis: superior to inferior 0 to Y-resolution *z*-axis: right to left 0 to Z-resolution

#### **B.2** Contents of the DDT file

DDT file format, for each voxel, with  $v_{ij}$  the eigenvector entries and eigenvalues  $\lambda_1 > \lambda_2 > \lambda_3$ , there are 12 values:

 $\begin{bmatrix} v_{1x} & v_{1y} & v_{1z} & v_{2x} & v_{2y} & v_{2z} & v_{3x} & v_{3y} & v_{3z} & \lambda_1 & \lambda_2 & \lambda_3 \end{bmatrix}$ 

If you want to reconstruct the tensor **D**, use the following:

$$\mathbf{DE} = \mathbf{EA}$$

$$\begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \begin{pmatrix} v_{1x} & v_{2x} & v_{3x} \\ v_{1y} & v_{2y} & v_{3y} \\ v_{1z} & v_{2z} & v_{3z} \end{pmatrix} = \begin{pmatrix} v_{1x} & v_{2x} & v_{3x} \\ v_{1y} & v_{2y} & v_{3y} \\ v_{1z} & v_{2z} & v_{3z} \end{pmatrix} \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$
and
$$\mathbf{DEE}^T = \mathbf{D} = \mathbf{EAE}^T$$

$$\mathbf{E}^T \mathbf{EA} = \mathbf{A} = \mathbf{E}^T \mathbf{DE}.$$

## Appendix C

## **GRB** file for the sample data set

#### C.1 Format of grb files

GRB files are plain text files. The format of a GRB file is as follows, demonstrated as an example here for a 6-direction + b0 scheme, each line having 3 entries X Y Z:

FileVersion: 1 IncludeBValues: no 7 NrOfEntries: Х Ү Ζ 0 0 0 0.577 0.577 0.577 -0.577 -0.577 0.577 0.577 -0.577 -0.577 -0.577-0.577 0.577 0.707 0.707 0 0.707 0 0.707

If the b-values (1000 in this case) are included, the file looks like this: Note that IncludeBValues is changed to "yes", and that each line now has 4 entries,  $X \neq Z$  b.

```
FileVersion:
               1
IncludeBValues: yes
NrOfEntries:
               7
       Ζb
Х
  Y
0
   0 0 0
0.577
       0.577
               0.577 1000
-0.577 -0.577 0.577 1000
0.577
       -0.577
               -0.577 1000
-0.577 0.577
               -0.577 1000
0.707
       0.707
               0 1000
       0 0.707 1000
0.707
\label{appendix:grb}
FileVersion:
                     1
```

NrOfEntries.	31	
X $Y$ $Z$	51	
0.0	0.0	0.0
1 000000000	0 0000000000	0 0000000000
0 7703189794	-0 6334477240	0.0731618129
0 2561448687	-0 0249786863	0.9663156169
0.2001440007	-0 1068670680	0.5935826751
-0 1615578229	0.2000070000	0.13887239/9
-0 229220/126	0.8533775040	-0 /681931632
-0 2630794898	-0 $1113017151$	-0.8727070603
0.2000794090	0 5854349684	0.1359171940
0.5067126566	0.5103287334	0.6948430524
0.3054330813	-0 1364364527	-0.9423883102
-0 7972741706	-0 1949622700	-0 5712649212
-0 8042542270	-0 5926021950	-0 0446964971
0.1865635668	0.9537832611	0.2355663949
-0 3881893823	0.1079319091	0.9152375137
-0.1339272628	0.6629447625	0.7365919699
-0.3384961835	-0.8809697404	0.3306246365
0.7673774759	0.3119018842	-0.5602222989
0.4065245350	-0.6656047592	0.6258658858
0.2871876223	-0.7612264361	-0.5814271946
-0.7661480348	0.4319864923	0.4758201964
-0.1793153505	-0.5264136055	0.8311045187
-0.7673768974	-0.3119020115	0.5602230203
0.2179780246	-0.9751760272	0.0389524925
0.4189866219	0.8397110024	-0.3454499142
0.1777380470	0.4786928124	-0.8598036857
-0.3397814897	-0.8554854208	-0.3907598163
-0.7844890989	0.5119797541	-0.3499336868
-0.4197498720	0.2604620840	-0.8694650929
0.7734515702	-0.3550403437	-0.5250895379
-0.9984481940	0.0477096943	0.0287226207

no

IncludeBValues:

## Appendix D

# Recommended DW-MRI scan protocols

Date: May 21, 2010

Disclaimer: this document contains recommendations for optimal DW-MRI acquisition. We (Brain Innovation BV) are not responsible for any damages caused in any way resulting from following these recommendations.

Sequence double-refocused single shot EPI reduces eddy current distortions.

**Field of View** minimal 240 mm (square)

k-space coverage symmetrical

- Number of Slices minimum needed to cover entire brain including cerebellum (usually > 55)
- Slice orientation axial

Voxel size Isotropic, 2.5 x 2.5 x 2.5 minimum recommended

Matrix size square 96x96, 128x128, etc

Slice gap 0 mm

Angulation none, could cause mis-calculation of tensors

TR shortest to accommodate all slices

TE minimum needed for full acquisition

Zero-filling No zero-filling or interpolation

Parallel imaging SENSE (factor 2) or GRAPPA

**Diffusion directions** > 6 directions for MD, > 20 directions for FA and fiber tracking, > 80 directions for HARDI applications

**b0** 1 b0 for every 6-10 diffusion weighted images

**b-value** 600-1200 s/mm<sup>2</sup> for DTI, > 2000 for HARDI/q-ball etc

- **Averages** As many as possible given the scan time. Do not average real-time on the scanner, but save each repetition as a seperate data set.
- Supported Raw data formats in BVQX DICOM, DICOM MOSAIC, PAR/REC, Nifti via Nifticonverter plugin

#### Sources:

- BIRN Imaging protocols <a href="http://nbirn.net/research/morphometry/imaging\_protocols.shtm">http://nbirn.net/research/morphometry/imaging\_protocols.shtm</a> May 21, 2010;
- S. Mori Introduction to Diffusion Tensor Imaging Elsevier 2007;
- ISMRM Diffusion and Perfusion study group mailing list