Tractography

PRESENTATION
SOFTWARE PACKAGES
CONTACTS
Medtronic2
VCU
SYNAPTIVE
SIEMENS RESOLVE – COPING WITH SHIFTS
DTI PARAMETERS
DURATION OF SCAN
NEX5
DIRECTIONS (GRADIENTS)
ADC, FA, DEC
TRACTOGRAPHY OF CRANIAL NERVES
DTI SHIFTS
Summary of strategies
BLIP UP/BLIP DOWN (TOPUP)
Mike Lennon10
DR-BUDDI11
RESOLVE (SIEMENS)
CSD (CONSTRAINED SPHERICAL DECONVOLUTION)
DKI
ARTICLES
DTI basics
DTI in DBS12
EMAILS
MEDTRONIC12
Synaptive16
Jersey Boy aka Matt16
Wes17
MA18
1
219
3
4

5	23
DTI protocol for DBS – see >>	

PRESENTATION

>>

SOFTWARE PACKAGES

Medtronic StealthViz

My notes – see p. D99 >> User Manual >>

Synaptive BrightMatter

User Reference (full) >> Brief Starting Guide >> Validation study instruction video >>

FSL (Oxford) – gold standard; probabilistic algorithm
MedINRIA (http://med.inria.fr/) – deterministic algorithm
DSI-studio
Camino
MRIcron (module DCM2NII) – converts DICOM to NIFF format for FSL
VOLUME-ONE version 1.72 - developed by VOLUME-ONE Developers Group. It is software free to download, free to use, and free to redistribute (all for noncommercial use). The diffusion TENSOR Visualizer II (dTV.II) (University of Tokyo Hospital, Tokyo, Japan) is the integrated MR DTI analysis plug-in software of VOLUME-ONE.

CONTACTS

MEDTRONIC

See here >>

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Siemens RESOLVE – coping with shifts

Siemens proprietary software that alters the filling of k space called RESOLVE (see https://usa.healthcare.siemens.com/magnetic-resonance-imaging/options-and-upgrades/clinical-applications/syngo-resolve).

DTI PARAMETERS

2.0 mm /3NEX/12 directions (HDH) - worst 2.5 mm/3NEX/30 directions (VCU) - best 2.0 mm/1NEX/30 directions (VA) - mediocre

DURATION OF SCAN

<u>GE 3T:</u> NEX of 2 - 8 min, 17 sec NEX to 3 - 12 min, 22 sec

NEX

↑ improves accuracy

• trouble with NEX/# of averages is time (and patient motion between acquisitions). As a rule of thumb to double the signal you need a NEX of 4. In other words, (as far as signal goes) a 7 minute DTI scan on a 3T unit would take about 28 minutes on a 1.5T.

<u>Vorona</u>

As you probably know, the trouble with NEX/# of averages is time (and patient motion between acquisitions). As a rule of thumb to double the signal you need a NEX of 4. In other words, (as far as signal goes) a 7 minute DTI scan on a 3T unit would take about 28 minutes on a 1.5T.

DIRECTIONS (GRADIENTS)

- ↑ improves variability (precision)
- only 6 directions are required to compute tractography
- more directions would provide more directional fidelity at the cost of some planar fidelity (e.g. more opportunity for tracks to "disappear" within a slice).

Ben Ewing

In theory, more directions would provide more directional fidelity at the cost of some planar fidelity (e.g. more opportunity for tracks to "disappear" within a slice). Also, although only 6 directions are required to compute tractography, the vast majority of Siemens datasets that I've worked with are 30 direction.

ADC, FA, DEC

Apparent Diffusion Coefficient (ADC) - voxel-by-voxel measure of the magnitude of diffusion.

<u>Fractional Anisotropy (FA)</u> - measures preferential directionality of diffusion and expressed as a numerical value between 0 to 1. A high FA indicates a great degree of preferential directionality (anisotropy) such as in the highly organized WM tracts, and low FA indicates less preferential directionality such as in the gray matter and CSF where FA is 0 (isotropy).

Directionally Encoded Color-coded map (DEC).

• by convention the blue color is used to highlight the tracts traveling in the inferior-superior direction, green in the anteroposterior direction, and red in the left-right direction.

TRACTOGRAPHY OF CRANIAL NERVES

			Tracking parameters			
Group	Nerve	ROI placement	FA threshold	Number of fibers	Maximal curvature angle (°)	Maximal length (mm)
1	Optic nerve ll	Whole optic chiasma	0.3	1000	45	10
2	Oculomotor nerve III	Cisternal segment before cavernous sinus	0.3	500	45	10
3	Trigeminal nerve V	Mid-cisternal point	0.3	700	45	10
4	Abducens nerve VI	Dorello canal entrance	0.2	100	45	10
5	Acoutic facial bundle VII-VIII	Whole Internal Acoustic Canal	0.3	300	45	10
6	Lower nerves IX, X, XI	Cisternal segment at the flocculus level	0.2	200	45	10

The limits of the acquisition box - the optic tracts superiorly and the foramen magnum inferiorly.

The olfactory and hypoglossal nerves are most often outside of the acquisition box.

The trochlear nerve is too thin to be seen in the anatomical T2 sequence and tracked

Strategy of the ROI placement. A-B, To overcome the residual distortion between anatomical and diffusion images at the skull base, the ODF map was superimposed onto anatomical T2 sequence. For example, to track the right oculomotor nerve (orange arrow, A), a single ROI (in yellow) was used here with a volumic (cubic) shape. Its position was adjusted at the 'best aspect' of the cranial nerve cisternal segment in the 3 dimensions: axial, sagittal, and coronal (orange arrows, C). D, The final reconstructed tracts show the cranial nerve trajectory from the brainstem to the skull base foramen:



DTI SHIFTS

Lennon

My best guess is that along with increase in the signal that we want (DTI info), there is an increase in artifacts at 3T. Interface with air at the skull bases is a challenge in DTI, and our patients may have more pneumatization of the mastoids and sphenoids? I'd love to be able to see the whole scans of these patients to see if that's the case.

To reduce artifacts, we are using parallel imaging (GEs version is called ASSET), over sampling our B0 (5 acquisitions), using the dedicated head coil and performing the DTI immediately after shimming. There's not much more I know of to do

Steinberg

Dr. Ma is proposing to use Parallel Imaging (Multiband SENSE) in order to achieve whole brain diffusion acquisition with many diffusion directions (High Angular Direction Diffusion Imaging: "HARDI") and also multi-shell for kurtosis imaging (multiple b values) with reasonable total scan duration (less than ten minutes). For parallel imaging (test set 2), the Irfanoglu et al. (2014) paper showed that the differences between the DR-BUDDI and TOPUP correction methods were minor in general and that the differences in FA values between the two methods were not statistically significant.

SUMMARY OF STRATEGIES

- 1. blip up/blip down technique called TOPUP
- 2. Parallel imaging (GEs version is called ASSET)
- 3. Over sampling of B0 (5 acquisitions)
- 4. Dedicated head coil
- 5. Performing the DTI immediately after shimming.
- 6. CSD (constrained spherical deconvolution)
- 7. RESOLVE (Siemens)
- 8. DSI
- 9. DR-BUDDI technique
- 10. EDDY

BLIP UP/BLIP DOWN (TOPUP)

blip up/blip down technique called TOPUP for the past several months. These blip up and blip down scans for TOPUP are two very brief scans that precede the actual DTI, and they do not change the actual DTI protocol or its duration. The TOPUP blip up and blip down scans combined add less than two minutes to the total acquisition time.

TOPUP distortion correction is a widely accepted blip-up/blip-down correction methodology that is implemented in FSL and has been the tool of choice for the NIH Human Connectome project

https://www.ncbi.nlm.nih.gov/pubmed/25433212

MIKE LENNON

I've attached a recent article regarding one of the techniques proposed for blip up/blip down. I would draw your attention to the schematic on page 5, and the accompanying description of the post-processing involved:

We integrated the proposed blip-up blip-down correction algorithm into the TORTOISE diffusion image processing software package (Pierpaoli et al., 2010). An illustration of the complete pipeline is depicted in Fig. 2. Processing starts with dependent motion and eddy current distortion corrections for both the blip-up and down data sets in the DIFFPREP tool of TORTOISE. After this step, all DWI volumes in both data sets are aligned to their corresponding b = 0 s/mm2 images and the B-matrices for all volumes are properly reoriented (Rohde et al., 2004). DIFFPREP also outputs two transformation files, one for each data set, describing the entire motion and eddy current distortions for all volumes. These transformation files are fed into the DR-BUDDI tool. The b = 0 s/mm2 images for both blip-up and down data are then quadratically registered to the structural image within DR-BUDDI to correct for concomitant field distortions and align both images to the structural image's space, where blip-up blip-down correction is then performed using both the b = 0 and diffusion-weighted images. The resulting deformation fields are subsequently combined with each DWI'smotion and eddy current transformations to generate the overall displacement fields, which are used along with the original DWIs to generate the corrected blip-up and down diffusion data sets with one interpolation step. Lastly, these two data sets are combined using geometric averaging to generate the final corrected data set. Because of the B-matrix rotation process during motion correction in DIFFPREP, the two B-matrices of the corrected blip-up and down data sets will most likely not be identical. As a heuristic solution, the arithmetic average of these two B-matrices is output as the B-matrix of the final corrected data, which are ready for tensor operations in DIFFCALC

The software reference here is available as open source at http://www.tortoisedti.org but likely not able to be installed on the VA computers. At the moment, I can't even open the webpage here! In my experience, these packages lack easy interface and require a large ramp up time to learn how to use. I guess what I am saying is I am enthusiastic that this may help correct the issue of geometric distortion, but it won't be easy. Acquiring the data is one issue, and I am working on that end with calls to GE and a colleague who has some tangential experience. I'll let you know if I make any headway. Processing and applying the data will be another challenge that we may want to work on simultaneously, as I am pretty certain that StealthViz would not be able to process the raw out put from the MRI scanner

There is more than one method to applying blip up/blip down, but I think the processing issue would apply to all methods. (Dr Pierpaoli who proposed the initial method of Blip up/Down claimed on a recent conference call that I was on that you need to acquire the whole data set and not just B=0 as BU/BD for processing through the deeper fibers of the midbrain)

DR-BUDDI

To implement the DR-BUDDI technique would double the DTI scan duration. The DR-BUDDI authors (Irfanoglu et al., 2014) in the Discussion section of their paper suggest that the DR-BUDDI scan time could be reduced by decreasing the number of diffusion directions. However, decreasing the number of diffusion directions would compromise the quality of the probabilistic fiber tracking methodology.

RESOLVE (SIEMENS)

Vorona

The CHOP study employs another technique to minimize distortion/susceptibility artifact - optional (i.e. more \$) proprietary software that alters the filling of k space called RESOLVE (see https://usa.healthcare.siemens.com/magnetic-resonance-imaging/options-and-upgrades/clinical-applications/syngo-resolve). My understanding is that we currently do not have this option installed on our scanners.

CSD (CONSTRAINED SPHERICAL DECONVOLUTION)

J Neurosurg 118:1367–1377, 2013 White matter fiber tractography: why we need to move beyond DTI Shawna FarquharSon, M.Sc., 1–3 J.-DonalD Tournier, Ph.D., 1,2 FernanDo calaManTe, Ph.D., 1,2 Gavin Fabinyi, M.b.b.S., F.r.a.c.S., 4 Michal SchneiDer-KolSKy, Ph.D., 3 GraeMe D. JacKSon, M.D., F.r.a.c.P., 1,2 anD alan connelly, Ph.D



Fig. 7. Dorsal views of the right pyramidal tract. A: Coronal plane [sketch] depicting the pyramidal tract of the right hemisphere (dorsal view) and its landmarks (1 = wall of the lateral ventricle, 2 = upper circular [periinsular] sulcus, 3 = the cingular sulcus). B: Specimen of the right pyramidal tract (dorsal view) and its landmarks (lateral wall of the lateral ventricle, superior circular sulcus). C: Tractography results using CSD and a probabilistic algorithm. D: Tractography results using DTI and a deterministic algorithm. Panels A and B are reprinted from Ebeling U, Reulen HJ: Subcortical topography and proportions of the pyramidal tract. *Acta Neurochir (Wien)* 118:164–171, 1992 (Figs. 1 and 5), with kind permission from Springer Science and Business Media.

TRACTOGRAPHY



DKI

http://academicdepartments.musc.edu/cbi/dki/

<u>Dr. Ma</u>

DKI data can be considered as combined two set of DTI data with different b values.

DKI extends DTI model to account for non-Gaussian diffusion effects. Previous studies have applied DKI to investigate different neuronal disorders; An empirical study (Glenn et al., 2016) has shown it superiority over DTI; Its some features (small maximum b values and relatively shorter scanning time) make it attractive for clinical settings. These are the motivations that I am planning to conduct this pilot study. The objective of this pilot study is to select the best one from the candidate tractography methods (such as DKI based fiber tracking, DTI based probabilistic fiber tracking and or deterministic fiber tracking).

ARTICLES

DTI BASICS

Brian J. Jellison "Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns" AJNR Am J Neuroradiol 25:356–369, March 2004

DTI IN DBS

J Neurosurg. 2014 Oct; 121(4):929-35. doi: 10.3171/2014.6.JNS131673. Epub 2014 Jul 25. Correlation of diffusion tensor tractography and intraoperative macrostimulation during deep brain stimulation for Parkinson disease. Said N1, Elias WJ, Raghavan P, Cupino A, Tustison N, Frysinger R, Patrie J, Xin W, Wintermark M.

Critique:

- 1. DTI is too crude use 4 mm, 20 directions only
- 2. No sedation with VIM but Precedex with GPi
- 3. Motor side effects symptom vs. sign unclear in article
- 4. Even if software is probabilistic fibers go only to leg area.
- 5. Automatic measurement from lead surface (MRI blooming artefact lead looks thicker) we use center of lead.
- 6. Use intraop stim testing crude voltage jumps, patient is unreliable, busy environment) we use postop mapping with slow voltage advancements.
- 7. When MRI is done immediate (brain shift due to pneumo?) vs. 2 week.
- 8. Seeding density is low only few fibers in Fig. 2

EMAILS

MEDTRONIC



TRACTOGRAPHY

D80 (16)



SYNAPTIVE

JERSEY BOY AKA MATT

I did work at Medtronic Navigation for quite a while before coming to Synaptive and am familiar with StealthViz so I would be remiss if I didn't respond to your question. That software was licensed from a company called Visage and received approval in 2008 (http://www.accessdata.fda.gov/cdrh_docs/pdf8/K081512.pdf). While it is a capable software package, I firmly believe that Brightmatter Plan is far more sophisticated in its capabilities and reflects the current advancements in the field since that time.

We offer whole brain, automatically rendered DTI that is highly geometrically accurate and robust. We have the ability to plan surgical trajectories looking at tracts that intersect with your plan in a far more interactive way than Stealthviz can provide. In addition, as Brad has given you an early glimpse at, we will be releasing a feature to automatically segment these tracts by major fiber bundle. You might be able to draw and label all of these tracts with StealthViz, but each particular data set would take hours of manual input and interpretation by Neuroradiologist or Neurosurgeon- whereas ours are done on the backend by our advanced algorithms and you have comprehensive tractography in about 10 minutes which you can then verify and adjust. This also allows for DTI to be easily incorporated into other uses, such as monitoring of neurodegenerative diseases or tract recovery/reaction post-operatively as a follow up modality without creating hours of manual tract drawing.

As you mentioned, we do have a very capable team of engineers, mathematicians and MR physicists in-house that are dedicated to the continued advancement of this software (taking the important feedback from clinicians like yourself into consideration for every release). Finally, we also have the ability to bring all of your pre-operatively planning data into the OR with Servo- our robotically assisted surgical optics and guidance platform.

Jersey Boy aka Matt

WES

Thanks for taking the time to review the screenshots we sent, Dr. Holloway. My name's Wes Hodges - we spoke at AANS. I'm a cofounder, and our Director of External Collaborations.

I agree that DTI is limited when it comes to crossing fibres, most notably where the CST and arcuate cross. Without a doubt, there are other acquisition techniques that can provide sub-voxel directional resolution to address this problem.

DSI is one of them, however, the challenge with that is scan time, file size, and availability. There's also a long regulatory pathway regarding its use in a commercial product. That being said, we're certainly interested in investigating it.

An intermediate acquisition technique en route to DSI may be DKI (Diffusion Kurtosis Imaging), which is a multi-shell acquisition that appears to show promise in addressing several crossing issues, while still keep scan time low. I'm new to it though; need to dig in more.

Regardless, white matter tract imaging has three main components for us: the acquisition technique, the tractography generation algorithm, and the tract classification algorithm. Currently, those sit at DTI, FACT, and a patient-registered atlas for us, respectively. Our next steps are to look at HARDI (for tract gen), and edema and pathology correction for the classification. We have partnerships with multiple academic institutions to help us with those initiatives.

It would certainly be worth discussing what is possible (and practical) on the acquisition front. I'd welcome a phone call at any time to dig in deeper here.

Thanks again for taking the time to review our work so far!

Wes



Hi Viktor,

Answers to your specific questions:

1. I would suggest to use the most caudal part of the posterior limb of the internal capsule as the seed ROI, and the subcortical white matter in the ipsilateral precentral gyrus as the target ROI. Please see Yoshiura et al. (2008) for the details of the methods regarding these seed/target ROIs.

2. You can use any DTI parameters. However, the parameters you choose should be consistent with your research objectives/interest. For example, we are more interested in impaired white matter integrity in subjects with drug dependence, so we choose to use FA. In addition, you should also consider previous studies, choose appropriate parameters based on previous findings. Make sure to use the parameters commonly used in the literature, in addition to those specific to your studies.

I am not familiar with the Medtronic StealthViz software. Is it a probabilistic or deterministic DTI tractography method? If it is a deterministic method, this may account for your problems. The pyramidal tract has cross fiber with other major white matter fibers (e.g., superior longitudinal fasciculus, fibers emerging from corpus collosum). It is well know that deterministic tractography methods can not effectively deal with cross-fiber problems. In a recent study, Bucci et al. (2013) reported that probabilistic methods are more sensitive in tracing the pyramidal tract fibers than the deterministic methods.

I strongly suggest you to follow the ROI methods described in Yoshiura et al. (2008). In addition, you may also consider to use way point ROIs (masks you think that your fibers of interest pass through), and exclusion ROIs (masks you think that your fibers of interest should not pass through). Furthermore, please make sure that your ROIs really connect to the nearby major white matter tract, for all the subjects. If not, you can extend your ROI so that it connects to the nearby white matter tracts.

I hope that these can help. Please let me know if you need to meet me.

Best, Liangsuo

2

Dear Dr. Ma,

I am working on tractography of pyramidal tract using your recommendations – cerebral peduncle as the seed ROI, and the subcortical white matter in the ipsilateral precentral gyrus as the target ROI. I cannot make fibers go to the face and hand area in the motor cortex. All fibers go to the leg area only. I am using angles of up to 110 degrees – does not help at all. Then I used fMRI cortical activation regions for lip pursing and finger tapping as sole seed ROI to see what fibers originate there – fibers from there do not go to internal capsule!

By the way, our software package (Medtronic StealthWiz) is using deterministic method. Is that the reason? Here are examples:









3

Good morning Viktor,

I am sorry for the delayed response as I was busy in different things in the past week. Among several potential reasons of your issue, the software, which uses deterministic method, may be the most possible causal factor. As I pointed out in my previous email, the pyramidal tract has cross fibers with other major white matter fibers (e.g., superior longitudinal fasciculus, fibers emerging from corpus callosum). In principle, deterministic tractography methods are incapable in doing this kind of jobs. The Medtronic StealthWiz software (using deterministic method) has found fibers from cerebral peduncle to the leg area in the motor cortex, but failed to find the face and hand area. This may be due to that the face and hand area are relatively more

lateral (thus more cross fibers are involved), and that the leg area is relatively more medial (thus less affected by the cross fibers). I consulted Dr. Steinberg, who is the director of our neuroimaging lab. Dr. Stienberg shares similar feeling.

Thus, a possible way to solve your problem is to use probabilistic tractography methods. FSL is an excellent candidate. It is free for non-profit organization. You can start to learn it, and get the software from http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/ . Please let me know if you have further questions.

Best, Liangsuo

4

Good afternoon, Dr. Ma

Is there any chance I could watch you working on tractography for 1 or 2 of your patients? Any day, any time. I have never seen the expert doing tractography and everything I have learned so far is only from reading. I promise not to distract you much from your work. We are using my prepared tractography for actual DBS surgeries for Dr. Holloway's movement disorder patients and I feel responsibility that I am doing it in the right way. Thank you in advance,

Viktor

5

I agree with Dr. Moeller. For your purpose, it would be better to have directions more than 30. Yes, we do have 42 and 64 directions DTI running on our scanner.

Some researchers (e.g., Wang et al., 2012, please see below for the detailed information about this publication) have conducted empirical studies to evaluate the effects of number of directions and number of repetitions on the quality of DTI tractography. Wang et al. (2012) found that increasing the number of gradient directions with equivalent scan time reduced variability whereas increasing repetition for 30-direction DTI improved the accuracy of tractography measurements. Based on Wang et al. (2012) and my own experience, I would answer your questions as following:

1.Q Which scanning parameters would be "the best" and which ones "the worst" for pyramidal and rubrothalamic tracts or even for general DTI tractography?

1.A: "The best" one would be b) 2.5 mm/3NEX/30 directions, and "the worst" one would be a) 2.0 mm/3NEX/12 directions.

2.Q If we are using 12 directions, must we decrease the FA starting value lower than default 0.20?

2.A: The 12 directions one should be "the worst" one. But if you really want to use it, I do not see any rationales that you should decrease FA starting value.

3.Q Would 2.0 mm/3NEX/30 directions be the super protocol that would make a difference? **3.A: Yes. According to Wang et al. (2012), this protocol will reduce the variability and increase the accuracy.**

Neuroimage. 2012 Apr 2;60(2):1127-38. doi: 10.1016/j.neuroimage.2011.12.062. Epub 2011 Dec 29.

A comprehensive reliability assessment of quantitative diffusion tensor tractography.

Wang JY 1, Abdi H, Bakhadirov K, Diaz-Arrastia R, Devous MD Sr.

Author information

Abstract

Diffusion tensor tractography is increasingly used to examine structural connectivity in the brain in various conditions, but its test-retest reliability is understudied. The main purposes of this study were to evaluate 1) the reliability of quantitative measurements of diffusion tensor tractography and 2) the effect on reliability of the number of gradient sampling directions and scan repetition. Images were acquired from ten healthy participants. Ten fiber regions of nine major fiber tracts were reconstructed and quantified using six fiber variables. Intra- and inter-session reliabilities were estimated using intraclass correlation coefficient (ICC) and coefficient of variation (CV), and were compared to pinpoint major error sources. Additional pairwise comparisons were made between the reliability of images with 30 directions and NEX 2 (DTI30-2), 30 directions and NEX 1 (DTI30-1), and 15 directions and NEX 2 (DTI15-2) to determine whether increasing gradient directions and scan repetition improved reliability. Of the 60 tractography measurements, 43 showed intersession CV ≤ 10%, ICC ≥ .70, or both for DTI30-2, 40 measurements for DTI30-1, and 37 for DTI15-2. Most of the reliable measurements were associated with the tracts corpus callosum, cingulum, cerebral peduncular fibers, uncinate fasciculus, and arcuate fasciculus. These reliable measurements included factional anisotropy (FA) and mean diffusivity of all 10 fiber regions. Intersession reliability was significantly worse than intra-session reliability for FA, mean length, and tract volume measurements from DTI15-2, indicating that the combination of MRI signal variation and physiological noise/change over time was the major error source for this sequence. Increasing the number of gradient directions from 15 to 30 while controlling the scan time, significantly affected values for all six variables and reduced intersession variability for mean length and tract volume measurements. Additionally, while increasing scan repetition from 1 to 2 had no significant effect on the reliability for DTI with 30 directions, this significantly reduced the upward bias in FA values from all 10 fiber regions and fiber count, mean length, and tract volume measurements from 5 to 7 fiber regions. In conclusion, diffusion tensor tractography provided many measurements with high test-retest reliability across different fiber variables and various fiber tracts even for images with 15 directions (NEX 2). Increasing the number of gradient directions from 15 to 30 with equivalent scan time reduced variability whereas increasing repetition from 1 to 2 for 30-direction DTI improved the accuracy of tractography measurements.

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TRACTOGRAPHY

D80 (25)

Best, Liangsuo