Does Low B-value can Handle Q-ball and DTI Reconstructions?
Diffusion MRI Experiment of Ex-vivo Pigs Spinal Cord Phantom

Aleksandra Klimas[2], Kamil Gorczewski[1], Przemysław Pencak[3], Zofia Drzazga[2] and Uwe Klose[1]
[1]*Section for Experimental Methods for MR in the CNS, University of Tuebingen, Germany*
[2]*Department of Medical Physics, University of Silesia, Katowice, Poland,*
[3]*Radiology Department, Mielecki University Hospital of Silesian Medical University, Katowice, Poland*

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Abstract The direction of axons in white matter can be estimated using a deterministic fibre tracking algorithms and diffusion weighted imaging. The aim of this work was to evaluate the data, obtained from pig spines phantom measurements with relatively low b-value, using two types of reconstructions: diffusion tensor imaging (DTI) and q-ball approach. Pigs spines submerged in agar gel were used to prepare a phantom with two crossing populations of fibres. The phantoms were measured in 3T MR scanned for b-value of 1000 and 2000 s/mm^2 for q-ball and 200-2000s/mm^2 for DTI reconstruction. Analysis of crossing and single fibre population regions in the scanners showed that the median dispersions from the reference directions in case of single fibre population were c.a. 4° and for crossing area c.a. 12° and 6.5° for b-value of 1000 s/mm^2 and 2000 s/mm^2 respectively. The q-ball approach was able to resolve crossing problem for both low b-values. It was shown here that coherent results can be achieved even with lower b-values than proposed by the theory.

1 INTRODUCTION

The clinical applications of MR diffusion measurement were suggested in 90s by LeBihan and Basser when the development of echo planar imaging (EPI) technique made MR imaging faster. The diffusion measurement relays on MR signal attenuation from water molecules. Those molecules can move inside and in-between axons in the presence of field gradient. The change in the spin position results in phase shift in precession and a signal loss. The obstacles, like cell membranes, keep the phases coherent. The attenuation level is proportional to the free path that molecules can travel so the signal is attenuated along axons. The anisotropic diffusion behaviour can be coupled to the orientation of fibers what gives the possibility to brain connectivity.

One can choose how strong images depend on the diffusion using the diffusion-sensitizing factor, called b-value, which can be calculated as follows:

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

where: γ - gyromagnetic coefficient, δ - duration of diffusion gradients, G - gradient strength, Δ - time from the beginning of the first gradient to the beginning of the second one.

There are several ways to evaluate the main direction of diffusion from measured data. The most common is diffusion tensor imaging (DTI) described in details by Bammer (2003) and Jones in (2004), which requires at least 7 measurements with gradient applied in different directions. A diffusion tensor is fitted to data to obtain only one direction of diffusion. The degree of diffusion anisotropy, enabling biological information about the integrity and orientation of white matter tracts in the brain can be determined by fractional anisotropy (FA) which is independent of the orientation of the diffusion in the voxel (FA = 0 – isotropic diffusion, FA = 1 – infinite anisotropy). Some regions of brain white matter such as the corpus callosum and the splenium show very high FA (c.a. 0.8) while others have considerably lower FA (Jellison et al. 2004); (Masutani et al. 2003.). If the direction of diffusion is known in each point of the brain it is possible to follow those directions in order to reconstruct pathway of connection. DTI provides just an approximation of direction of diffusion, since the real diffusion is more complex. The idea of using excised animal nerve tissue to MR diffusion measurements has already been introduced in literature, in example by Madi et al. (2005).for the

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testing of diffusion sequences, to develop new fibre tracking algorithms proposed by Campbell et al. in 2005, for the validation of diffusion models such as the composite hindered and restricted model of diffusion (CHARMED) described in details in 2004 by Y. Assaf et al. Another application of mentioned nerve tissue was the method validation on phantom showed by M. Perrin et al. in 2005, spherical harmonics presented in 2007 by Descoteaux et al. and tissue classification (Freidlin, et al., 2007). These different MR diffusion methods were also successfully applied in neuroimaging applications and described by P. C. Sundgren et al. (2004). However, some parts of the brain remained untraceable. Disagreement between complex diffusion situation and rather simple approximation by one direction of diffusion leads to errors in tracking.

Recently introduced methods of diffusion measurements with high-angular-resolution diffusion imaging (HARDI) allow to retrieve more complex shape of diffusion than in case of DTI showing more than one direction of diffusion. A couple of reconstruction algorithms were proposed. The first one was the q-ball evaluation by D. Tuch, 2004. Afterwards, other techniques were shown, like a diffusion orientation transform (DOT) shown in 2006 by Ozarslan, et al., a spherical deconvolution (Tournier et al. 2004) or PAS-MRI presented by Parker and Alexander in 2005. In its original proposed form, the q-ball methodology requires high diffusion weighting (b-values > 3000 s/mm^2) in respect to those used in DTI. The spherical deconvolution technique depends on the used b-value (Tuch, 2004). For low b-values the angular dependency of the signal (from layer which contains both fibre directions) is relatively small and the reconstruction of the fibre orientation distribution function (ODF) is very sensitive to noise. When using high b-values, the angular dependency is better defined, but the noise is too big and it begins to dominate. It was suggested that optimal value is between 3000 and 4000 s/mm^2 because the strong angular dependence is necessary to resolve the fibre orientations without attenuating the signal down to the noise level. However, the use of high b-value causes the decrease of SNR. Therefore to obtain a good quality images one has to increase averaging.

Diffusion tensor imaging calculations and q-ball method require a quality control of the reconstructed directions, but it is very difficult to produce an artificial phantom, that could simulate anisotropy levels found in a human brain. In case of q-ball methods it is even more difficult because the phantom should not only have high anisotropic properties but also would simulate areas of crossing fibre bundles. We examined the possibilities to design a phantom using ex-vivo spinal cord from slaughtered pigs.

The motivation for this work was the validation of q-ball and diffusion tensor imaging reconstruction accuracy of direction extraction using chosen acquisition parameters. The aim was also to show the comparison of both techniques presenting their possibilities and limitations.

2 METHODS

2.1 Phantom Construction

Fresh samples of spinal cord from pigs were obtained from the local slaughterhouse. The phantom productions were performed within 6 hours post mortem.

The pig spinal cords of 12 mm in diameter were fixed in 2% agar-agar solution in a rectangular container (suitable to insert into the head-coil of the MR scanner) in order to create a cross. The crossing spines were put in two layers – one above the other. Only one spine went through the crossing area on each layer, spines in second direction were just approaching crossing region (which were cut in a half) what is presented in detail in Figure 1.

Several phantoms were performed, in example by A. Klimas et al. in 2008, with fibers crossing at different angles but phantoms with 90° crossing seem to be the best for studies due to minimization of the influence of interaction between sampling angle density and the fibres crossing angle (the 90° can fulfill the Nyquist condition). The representative model analyzed in this work showed the deviation about 5,5° in Z and about 3,5° in X direction of the MR system (see Figure 1).

2.2 Data Acquisition

The prepared phantom was inserted into head-coil of 3T MR system (Trio–Siemens, Erlangen, Germany). Diffusion data were obtained in 252 directions, equally distributed over the sphere. Gradient directions were obtained by tessellation of an icosahedron. A double refocusing spin echo MR sequence was used as it was proposed in 2003 by Reese, T. G et al. One unweighted image and 252 diffusion weighted images were acquired with following parameters: TE=126ms, TR=2000ms, b-values: 1000 and 2000 s/mm^2.

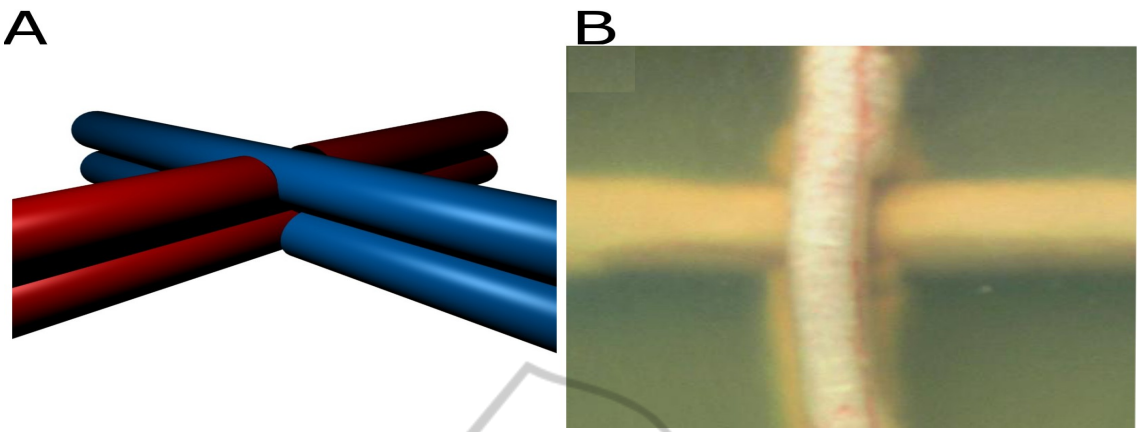

Figure 1: Pigs spinal 90 crossing phantom. This way of construction was minimizing the partial volume effects and it was assuring no fibres had to be bent during preparation. A) model of construction, B) photo of pigs spines submerged in agar gel used in measurement.

Field of view (FoV) was 256mm with pixel size of 2mm. The slice thickness was set to 10mm in order to cover fibres from both layers of phantom.

The diffusion measurement returns an average signal over the full volume of the voxel. Phase-read plane was aligned to XZ plane of the MR system. Eight averages were taken for each image, resulting in total acquisition time of c.a. 70min.

DTI data acquisition was made at wide range of parameters: b-value 200–2000 s/mm^2, TE 70–110ms, TR 1300–1600ms. The orientation of acquired slices was parallel to the direction of the spinal cords. A high in-plane resolution of 2x2mm was used, while a large slice thickness of 10mm was chosen to obtain signals from both layers in the crossing area. Twelve gradient directions were derived from the vertices of an icosahedron as it was shown in 2003 by T. G Reese et al.

2.3 Direction Estimation in Linear and Crossing Region

Data were analyzed with MATLAB software (MathWorks, MA, USA). The q-ball reconstruction algorithm was implemented basing on the work shown by Tuch (2004) with smoothing kernel $\sigma = 0.009$ rad (0.5°). More details about used algorithm and the smoothing kernel can be found in the PhD thesis presented in 2010 by Gorczewski.

The directions of diffusion were obtained from the orientation distribution function (ODF). The maxima in ODF shapes were extracted using following algorithm: starting from a random seed point, it was advancing towards the direction of the maximal gradient of ODF function. The procedure was repeated for a hundred times starting from a different seed point each time. In this way, the algorithm was independent of starting point position. The resulting directions were grouped into distinct directions of diffusion present in the ODF shape. Each maximum was treated as direction of diffusion. The principal diffusion direction in q-ball shape was the direction of the maximum with the highest value of orientation distribution function.

The phantoms crossing area was in XZ plane. The directions of diffusion were divided into two groups: voxels with single fibre population pointing X direction (group A) and voxels with single fibre population pointing Z direction (group B).

An average direction from all voxels was calculated in both groups. Dispersion of the diffusion directions was estimated by a median value.

The average directions of diffusion found in the arms of the cross served as references in analysis of reconstruction stability. The angles between reference direction and directions of diffusion found in each voxel belonging to the crossing area were calculated. To estimate the angle dispersion in a given diffusion direction a median from all angles was calculated. The standard deviation cannot be used since the distribution of angles is not a Gaussian one. A median angle draws a cone containing half of the reconstructed diffusion directions. In this article, it is referred to as dispersion cone angle (DCA). The more stable direction, the narrower the cone is. Averaged directions of diffusion were calculated in each group and those directions were used to estimate the dispersion. The results from the arms (single fibre population) were compared with the corresponding diffusion directions found in the crossing area (two

fibre populations).

3 RESULTS

3.1 Visualization of Diffusion in DTI and Q-Ball

Q-ball reconstruction was able to identify regions of higher anisotropy properly. Figure 2B and C shows the q-ball reconstruction of the selected areas of interest. Both low b-values visually reveal the directional structure of the phantom. The ODF in arms of the phantom have a peanut-shape which represents the single fibre population as assumed. However the directions of diffusion in each arm are parallel.

Diffusion tensor imaging measurements reveal high FA index of 0.7 in arm-regions proving validity of constructed spine phantom for a clinical scanner. DTI shapes within the voxel presented in Figure 2A confirm that the detected orientations are coherent with the underlying fibre directions.

3.2 Estimation of Diffusion Direction in Single Fibre Population and Crossing Area

A comparison between Figure 2A, B, and C demonstrates how both methods deal with the

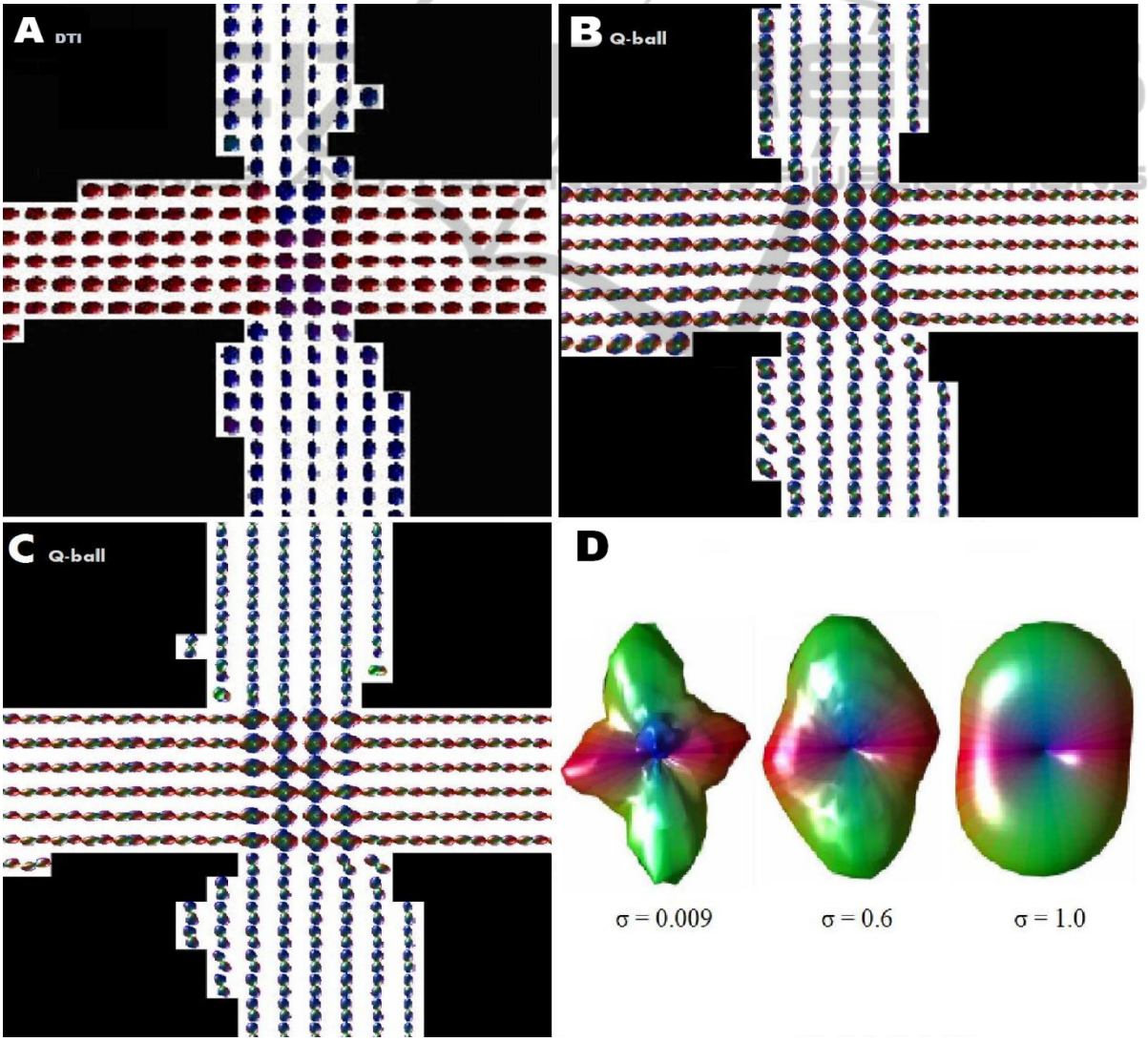

Figure 2: Visualization of phantom obtained by A) DTI with b-value of 800s/mm^2, B) Q-ball shapes obtained with b-value of 1000 s/mm^2, C) Q-ball shapes obtained with b-value of 2000 s/mm^2. D) Examples of reconstructed ODFs as a function of smoothing kernels σ (2009 Gorczewski et al., modified).

multiple fibre populations. One can see that the main direction of diffusion in arms in DTI reconstruction can be clearly visible unlike in the crossing area where obtained diffusion tensors have a plate-shape. Q-ball technique gives better results in the crossing area because the first diffusion direction is separated from the second one.

In the q-ball approach the analysis of the directions acquired with b-value 1000 s/mm^2 in arm-regions shows that the median is equal to 4.0° for X (group A) and 4.4° for Z direction (group B). In case of b-value 2000 s/mm^2 both medians are equal to 3.8°. Stability of diffusion direction estimation for double fibre population resulted in a DCA of 12.7° in X, 10.8° in Z for 1000 s/mm^2 and 6.6° in X, 5.5° in Z direction for 2000 s/mm^2.

The influence of the reconstruction stability was examined by calculating DCA in the crossing area against the smoothing kernel σ from reconstruction algorithm like in the work of D. Tuch, 2004. The example of the blurring influence is shown in Figure 2D. Two initially distinct directions of diffusion in q-ball shape disappear when the σ is increased. As we can observe, the two directions are replaced by one, averaged diffusion direction. Reasonably low smoothing kernels should be used to maintain good directional data quality.

4 DISCUSSION

Fibre tracking becomes an effective tool in clinical practice as well as in research combined with functional imaging. Recent development of methods for multiple diffusion direction extraction prepares even better data for connectivity exploration. New methods of water molecules diffusion measurement with HARDI methods provide more detailed information about the structure of the white matter. The tensor model for single fibre populations works very well. The error estimation and its propagation in relation to acquisition factors such as sampling directions, b-value or SNR was shown earlier in 2004 by Jones D.K. The tensor approach was successfully used in clinical routine (the sequence duration was acceptable) but it cannot fulfill all of the assumptions of the theoretical model. In case of multiple fibre population the tensor model shows a decrease of FA and two eigenvalues of similar amplitude manifesting in a plate-shape of diffusion tensors. In this way only a plane of crossing was determined, but it was impossible to retrieve information about the directions of the crossing fibres. In our study the diffusion directions provided by tensor model were successfully applied in single fibre population unlike to in crossing area. The q-ball algorithm has an assumption about high b-value, which cannot be fulfilled in clinical due to the long measurement time - a clinical routine always have to consider a trade between quality of measurement and time. The building time of the b-value is dependent on the integral over the gradients amplitudes. Using short gradient time implies TE shorting, so stronger signal is acquired and less averages is needed.

It was shown here, that even not being strict with the assumptions of the q-ball measurement theory gives coherent results. When acquiring patients, it is important to reduce time of acquisition as much as it is reasonably possible.

Moreover it should be noted that the decrease of b-value, which has a major impact on the acquisition time, still provides data that can be used to resolve fibre crossing problem.

Another possibility to shorten the time of the measurements is the reduction of diffusion direction number. According to the Nyquist condition sampling frequency should be at least 2n+1, where n is the highest expected frequency in data. Decreasing the angular resolution double the minimal angle that can be distinguished. It is better to speed up acquisition by other means, than by losing the angular resolution. That is the reason why the reduction of the diffusion directions is unwanted. However, recently the Nyquist theorem has been improved as was shown in 2011 by McEwen and Wiaux an successfully applied in the same year by A. Daducci et al.

Half of the diffusion directions felt into 5 degree wide cone for a single fibre bundle case. The fibre crossing area was successfully resolved. Two pairs of maxima were present in all voxels.

This work deals with the reconstruction of data from phantom measurements whereas a comparison between diffusion tensor imaging and q-ball results obtained from in-vivo measurements can be found in the work shown by Gorczewski et al. in 2009.

5 CONCLUSIONS

To conclude, we show that even if the condition of high b-value is not met q-ball reconstruction can successfully retrieve proper directions of diffusion in single as well as in multi fibre population cases. The stability of this evaluation is still in ranges of degrees. The data measured in lower b-values ranges can be properly processed by fibre tracking

algorithms.

REFERENCES

Le Bihan D., Turner R., Douek P., Patronas N. (1992). Diffusion MR imaging: clinical applications. *American Journal of Roentgenology,*159(3), 591-599.

Basser P. J., Mattiello J., LeBihan D. (1994). Estimation of the effective self-diffusion tensor from the NMR spin echo. *Journal of Magnetic Resonance - Series B*, 103(3), 247-254.

Bammer R. (2003). Basic principles of diffusion-weighted imaging. *European Journal of Radiology,* 45(3), 169-184.

Jones D.K. (2004). The Effect of Gradient Sampling Schemes on Measures Derived From Diffusion Tensor MRI: A Monte Carlo Study. *Magnetic Resonance in Medicine.* 51(4), 807-815.

Jellison B. J., Field A. S., Medow J., Lazar M., M. Shariar Salamat and Alexander A. L. (2004). Diffusion Tensor Imaging of Cerebral White Matter: A Pictorial Review of Physics, Fiber Tract Anatomy, and Tumor Imaging Patterns. *American Journal of Neuroradiology*. 25, 356–369.

Masutani Y., Aoki S., Abe O., Hayashi N., Otomo K. (2003). MR diffusion tensor imaging: recent advance and new techniques for diffusion tensor visualization. *European Journal of Radiology*, 46, 53-/66.

Madi, S., Hasan, K. M., Narayana, P. A. (2005). Diffusion tensor imaging of in vivo and excised rat spinal cord at 7 T with an icosahedral encoding scheme. *Magnetic Resonance in Medicine,* 53, 118-125.

Campbell, J. S., Siddiqi, K., Rymar, V. (2005). Flow-based fiber tracking with diffusion tensor and q-ball data: validation and comparison to principal diffusion direction techniques. *Neuroimage*; 27(4) 725-736.

Assaf, Y., Freidlin, R. Z., Rohde, G. K., Basser, P. J. (2004). New Modeling and Experimental Framework to Characterize Hindered and Restricted Water Diffusion in Brain White Matter. *Magnetic Resonance in Medicine*, 52, 965–978.

Perrin, M., Poupon, C., Rieul, B., Leroux, P. (2005). Validation of q-ball imaging with a diffusion fibre-crossing phantom on a clinical scanner. *Philosophical Transactions of the Royal Society B: Biological Sciences,* 360, 881-891.

Descoteaux, M., Angelino, E., Fitzgibbons, S., Deriche, R. (2007). Regularized, Fast, and Robust Analytical Q-Ball Imaging. *Magnetic Resonance in Medicine,* 58, 497–510.

Freidlin, R. Z., Ozarslan, E., Komlosh, M. E., Chang, L. (2007). Parsimonious Model Selection for DTI Tissue Segmentation and Classification: Study on Simulated and Experimental Data. *IEEE Transactions on Medical Imaging,*26(11), 1576-1584.

Sundgren, P. C., Dong, Q., Gómez-Hassan, D., Mukherji (2004). Diffusion tensor imaging of the brain: review of clinical applications. *Neuroradiology,* 46, 339-350.

Tuch D. S. (2004). Q-ball imaging. *Magnetic Resonance in Medicine***,** 52(6), 1358-1372.

Ozarslan, E., Shepherd, T. M., Vemuri, B. C., Blackband, S. J. (2006). Resolution of complex tissue microarchitecture using the diffusion orientation transform (DOT). *Neuroimage,* 31(3), 1086-1103.

Tournier, J. D., Calamante, F., Gadian, D. G., Connelly, A. (2004). Direct estimation of the fiber orientation density function from diffusion-weighted MRI data using spherical deconvolution. *Neuroimage,* 23(3), 1176-1185.

Parker, G. J., Alexander, D. C. (2005). Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue. *Philosophical Transactions of the Royal Society B: Biological Sciences,* 360, 893-902.

Klimas, A., Gorczewski, K., Klose, U., Drzazga, Z. (2008). Preparation and validation of an easy-to-make organic DTI phantom. *41st Polish Seminar on Nuclear Magnetic Resonance and Its Applications*.

Reese, T. G., Heid, O., Weisskoff, R. M., Wedeen, V. J. (2003). Reduction of eddy-current-induced distortion in diffusion MRI using a twice-refocused spin echo. *Magnetic Resonance in Medicine***,** 49(1), 177-182.

Gorczewski K. (2010). Multi-directional diffusion weighted imaging: Implementation, verification and clinical application, PhD thesis.

McEwen J. D., Wiaux Y. (2011). A novel sampling theorem on the sphere. *IEEE Transactions on Signal Processing,* 59, 5876–5887.

Daducci A., McEwen J., Van De Ville D., Thiran J. P., Wiaux Y. (2011). Harmonic analysis of spherical sampling in diffusion MRI. *Proceedings* of *the International Society for Magnetic Resonance in Medicine,* 3929.

Gorczewski, K., Mang, S, Klose, U. (2009). Reproducibility and consistency of evaluation techniques for HARDI data**.** *Magnetic Resonance Materials in Physics Biology and Medicine*, 22(1), 63-70.