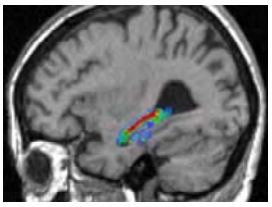
Dr. rer. nat. Klaus H. Fritzsche
German Cancer Research Center, Medical and Biological Informatics
Suedwestdeutscher Verlag fuer Hochschulschriften, ISBN 978-3838118765

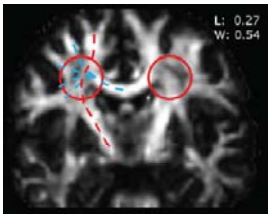
Quantification of structural changes in the brain using magnetic resonance imaging

MRI (Magnetic Resonance Imaging) and diffusion weighted MRI non-invasively deliver anatomical and even microstructural parameters of the living human brain with ever increasing resolution and detail. This work addresses the current main challenges in detecting early stage Alzheimer's Disease (AD) using MRI atrophy and diffusion measurements. The following contributions are presented:

1) An automated method for atlas-based, individual patient atrophy assessment on a macroscopic level is introduced. It avoids the time-consuming procedure of manual evaluations and the abstract, partly inexplicable decisions of automated classifiers.
2) A Diffusion Tensor Imaging (DTI) based approach to fiber integrity assessment on a microscopic level is proposed that circumvents ambiguities of DTI in Partial Volume (PV) situations.
3) Diffusion phantoms were designed that yield realistic properties and allow the controlled investigation of quantification methods under PV conditions.
4) A comprehensive set of in-vivo, in-vitro, and in-silico experiments was defined and applied to evaluate the Q-Ball Imaging (QBI) based Generalized Fractional Anisotropy (GFA). The Angularly defined Signal Ratio (ASR) for the directional quantification, the $GFA_{k,p}$ for superiorly adjusted quantification, and the GFA* for solid angle reconstruction based quantification of fiber integrity were newly defined and evaluated.



According to a retrospective study on a corpus of patients with memory impairment, both the newly proposed atrophic scores (1) and the proposed diffusion imaging based measures of fiber integrity (2) can deliver clear hallmarks of AD at stages of the disease that cannot be recognized by the use of conventional clinical tests. The atrophic scores correctly predicted a future conversion to AD in 70% of the subjects at 100% specificity. Using the diffusion measurements, an even perfect group separation was reached. Manual reference approaches were clearly outperformed.



Furthermore, the comprehensive evaluation (3+4) of QBI based fiber integrity indices showed that recent advances in diffusion imaging do not necessarily translate to improved quantification but may even perform worse than DTI. The GFA*, however, can overcome many of the ambiguities especially in crossing fibers and PV situations.

In conclusion, the presented methods and findings improve the understanding, applicability, and diagnostic use of very recently proposed diffusion imaging techniques and can be regarded as an essential step as well towards clinical application of quantitative diffusion imaging as towards computer assisted early AD diagnosis.

AD – Alzheimer's Disease
DTI – Diffusion Tensor Imaging
MRI – Magnetic Resonance Imaging
QBI – Q-Ball Imaging
ASR – Angularly defined Signal Ratio
GFA – Generalized Fractional Anisotropy
PV – Partial Volume