ORIGINAL PAPER

Quantitative susceptibility mapping (QSM) and R_2^* in the human brain at 3 T Evaluation of intra-scanner repeatability

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Abstract

Quantitative susceptibility mapping (QSM) and the effective transverse relaxation rate (R_2) can be used to monitor iron and myelin content in brain tissue, which are both subject to changes in many neurological diseases but also during healthy aging. In this study, we quantitatively assessed the repeatability of QSM and R_2* by applying four independent scans in eight young healthy, female subjects on a 3 T MRI scanner. Since QSM does not yield absolute values for bulk magnetic susceptibilities, we additionally investigated the influence of the choice of a reference brain region for susceptibility by computing susceptibility differences with respect to five different brain structures (whole brain, frontal white matter (fWM), internal capsule (IC), cerebrospinal fluid (CSF) in the lateral ventricle, cortical gray matter (cGM)). The intra-class correlation coefficient (ICC), variance ratio (VR) and repeatability coefficient (RC) were used to evaluate the repeatability of the calculated susceptibility differences and the R_2* values in six different subcortical brain structures. Linear regression was used to analyze the correlation between susceptibility differences and R_2*. We found that the susceptibility differences with respect to each investigated reference region ($0.868 \leq$ mean ICC ≤ 0.914) and the R_2* values*

Quantitative Suszeptibilitätskartierung (QSM) und R_2^* im menschlichen Gehirn bei 3T Eine Intra-Scanner Reproduzierbarkeitsstudie

Zusammenfassung

Die Kartierung der magnetischen Suszeptibilität (quantitative susceptibility mapping, QSM) und der effektiven transversalen Relaxationsrate (R_2) ermöglicht die nicht-invasive Charakterisierung des Eisen- und Myelingehalts in Hirngewebe, die bei verschiedenen neurologischen Erkrankungen, aber auch während des gesunden Alterns, Veränderungen unterliegen. In der vorliegenden Studie wurde die Wiederholbarkeit der Suszeptibilitäts- und R_2*-Kartierung durch wiederholtes Scannen ($n = 4$) von acht jungen, gesunden, weiblichen Probandinnen mit einem 3T-Magnetresonanztomographen quantitativ beurteilt. Da die Suszeptibilitätskartierung keine absoluten magnetischen Suszeptibilitätswerte liefert, wurde zusätzlich der Einfluss verschiedener anatomischer Referenzstrukturen (komplettes Gehirn, frontale weiße Substanz, capsula interna, zerebrospinale Flüssigkeit im*

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(mean ICC = 0.923) were highly repeatable across the four times repeated scans. With consistently higher ICC, higher VR and lower RC, whole brain and cGM appeared to be the two most suitable reference regions for QSM with respect to repeatability.

Keywords: Repeatability, Quantitative susceptibility mapping, Effective transverse relaxation, Magnetic resonance imaging

lateralen Ventrikel, kortikale graue Substanz) auf die Ergebnisse der damit ermittelten Suszeptibilitätsdifferenzen untersucht. Die Wiederholbarkeit der berechneten Suszeptibilitätsdifferenzen und R_2-Werte wurde in sechs verschiedenen subkortikalen Hirnstrukturen mit Hilfe des Intraklassen-Korrelationskoeffizienten, des Varianzverhältnisses und des Reproduzierbarkeitskoeffizienten bewertet. Lineare Regressionen und Korrelationen zwischen den unterschiedlich referenzierten Suszeptibilitätsdifferenzen und den R_2*-Werten wurden durchgeführt. Die Suszeptibilitätsdifferenzen waren über die vierfachen Messungen bezüglich jeder untersuchten anatomischen Referenzstruktur (0,868 $\leq$ Mittelwert ICC $\leq$ 0,914) und R_2* (Mittelwert ICC = 0,923) hoch reproduzierbar. Mit durchweg höheren Intraklassen-Koeffizienten, höheren Varianzverhältnissen und niedrigeren Reproduzierbarkeitskoeffizienten ist eine Referenzierung mit dem Mittelwert der Suszeptibilität über das Gesamthirn oder über die kortikale graue Substanz im Hinblick auf die Wiederholbarkeit der Suszeptibilitätskartierung am besten geeignet.*

Schlüsselwörter: Wiederholbarkeit, quantitative Suszeptibilitätskartierung, effektive transversale Relaxation, Magnetresonanztomographie

Introduction

Quantitative susceptibility mapping (QSM) [1–6] is a recently developed MRI post-processing technique to non-invasively quantify the bulk magnetic susceptibility of tissue by exploiting the phase of the MR signal from T_2*-weighted gradient echo (GRE) sequences. To date, QSM has already been widely applied to assess magnetic susceptibility sources in brain tissue, including iron [7], myelin [8] and calcifications [9–11], metabolic oxygen consumption [12,13] and task-related blood oxygenation level variations [14,15] in normal subjects as well as in patients with intracranial hemorrhages [16,17], various neuro-degenerative diseases, such as multiple sclerosis [18], Parkinson's disease [19,20], Huntington's disease [21] and Alzheimer's disease [22]. Since multi-echo GRE pulse sequences are commonly employed for QSM data acquisition, the effective transverse relaxation rate, R_2*, can additionally be deduced from the magnitude data as a valuable by-product of [23]. R_2* represents an alternative measure to estimate the iron load in brain tissue and has been validated in both human and primate studies [24–26].

One significant problem of using QSM in cross-sectional and longitudinal studies is that the singularity at the origin of the *k*-space representation of the unit dipole response introduces an arbitrary, region-independent offset in the reconstructed susceptibility map [27]. Consequently, QSM is only capable to provide relative rather than absolute values of magnetic susceptibility. This significant obstacle is typically overcome by referencing the reconstructed susceptibility values to a specific region of the brain. The topic of choosing a suitable reference region has already been tackled in one previous cross-sectional [28] and longitudinal study [29]. The authors suggested to use frontal white matter (fWM) [28], the posterior limb of the internal capsule (IC) or cerebrospinal fluid (CSF) in the ventricle area as referencing structure [29]. It has also been suggested to employ the reconstructed susceptibility values directly after field-to-source inversion as these values are intrinsically referenced to the mean susceptibility of the whole tissue region used for susceptibility computation (e.g., the whole brain tissue in case of brain exams) and no obvious systematic bias was observed between the analysis of the susceptibility as a function of age with and without referencing to CSF [30]. However, so far no studies have been conducted to evaluate thoroughly the effect of different references to the magnetic susceptibility in cross-sectional or longitudinal studies.

Another important concern is that repeated independent MRI scans of the same subject will most likely result in different magnitude and phase images due to small variations of the subject's head position, imaging slab orientation, and/or MRI scanner calibration. These small differences may, in turn, lead to changes in the estimates of susceptibility and R_2* values in the different human brain structures. Thus, evaluation of scan–rescan repeatability (i.e., the same imaging