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学位論文内容の要旨

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Spectral Analysis of Fluctuation in Time Series Spin-echo MR Signal of Human Brain and its

Application: Evaluation of Vasomotor Function of Arterioles

(MRI における Spin-echo 時系列信号揺らぎの周波数解析と

その応用：大脳細動脈機能の評価)

Purpose: Cerebral arteriolar vasomotor function (AVF) plays an important role in brain health and its deterioration may be an early marker of dementia. Since CO_2 in blood vasodilates arterioles, respiratory oscillation in the partial arterial pressure of CO_2 (PaCO_2) changes volume of arterioles at respiratory frequencies. This resting-state arteriolar vasomotion results in the respiratory fluctuation of cerebral blood flow (CBF) and hence venous blood oxygenation, which can be monitored by magnetic resonance (MR) signals of venous blood. We developed a method to elucidate the respiratory fluctuation of cerebral venous oxygenation in the superior sagittal sinus that is the largest vein in brain. And we also developed a method to map the AVF by analyzing the time series of MR images of brain. Applying these methods to young and middle aged volunteers, deterioration of AVF with aging was clarified quantitatively and spatially.

Methods: A slice perpendicular to the superior sagittal sinus of each young volunteer was imaged successively every 0.25 s with a rapid MR imaging (SE-EPI). The time series of the signal intensity of the superior sagittal sinus was Fourier-transformed and the spectral fluctuation intensity (SFI) at respiratory frequencies was obtained. The proportional relation between the SFI and the average signal intensity was derived by varying slice thickness from 5 to 15 mm. Using this proportionality and the relationship between oxygenation and MR signal intensity of blood, the amplitude of the respiratory fluctuation in the cerebral venous oxygenation (ΔY_T) was calculated. To validate the influence of the magnetic field strength of an MR equipment, this experiment was performed at 1.5 and 3.0 T. Time series imaging of a single slice of brain was performed in a 3-T MR system by using the same pulse sequence mentioned above with a fixed slice thickness (5 mm). Young adult (YA: 23 ± 2 , $n = 9$) and middle aged (MA: 45 ± 3 , $n = 5$) volunteers were participated. SFI at each pixel was obtained and the amplitudes of the respiratory (R) and cardiac (C) frequency fluctuation in brain parenchyma were mapped. The respiratory fluctuation in ROI at the skull edge was also obtained to evaluate the slice

shift induced by chest motion. The end-tidal partial pressure of CO₂ (PetCO₂) and the mean arterial blood pressure (MAP) were measured before and after the scan. Measurements of ΔY_r mentioned in the above experimental methods were also performed.

Results and discussion: The amplitude of respiratory fluctuation in the cerebral venous oxygenation was quantified as 1.2% at 1.5 T and 1.1% at 3 T showing that there is no influence of the magnetic field on the ΔY_r measurement. There was no correlation between ΔY_r and the mean value of R map averaged in brain parenchyma ($\langle R \rangle$), indicating a large influence of slice shift on R map; $\langle R \rangle$ of YA group showed a significant correlation ($r = 0.75$ $p < 0.05$) with respiratory fluctuation in ROI at the skull edge which reflects the fluctuation induced by slice shift. On the other hand, the mean value of C map ($\langle C \rangle$) correlated strongly with ΔY_r (YA: $r = 0.92$, MA: $r = 0.99$) in spite of the different observation frequencies. Since $\langle C \rangle$ reflects the passive volume changes in arteries caused by cardiac pulsatile blood pressure, the result of this strong correlation implies the correspondence between the pulsatile arterial volume changeability and the degree of AVF. The ΔY_r decreases with an increase in CBF following the Fick's law and CBF increases proportionally with an increase in $MAP^{0.73}$ from the literature. Removing the influence of MAP, the plot of $\langle C \rangle / MAP^{0.73}$ versus ΔY_r showed a significant proportionality from the origin respectively for YA ($r = 0.84$) and MA ($r = 0.99$). The proportionality of this plot decreased from YA to MA by 0.69 times. As this proportionality is calculated from $(\Delta Y_r \cdot MAP^{0.73}) / \langle C \rangle$ indicating the ratio of volume changes in arterioles and arteries, this result implies that arterioles deteriorate more rapidly with aging. As the C map is representing the degree of AVF, this map was normalized by its mean value to obtain the distribution of the degree of AVF and the value of ΔY_r was multiplied to show the AVF quantitatively. Decreases in AVF with aging in frontal, occipital lobe and thalamus were clearly observed.

Conclusions: We firstly revealed that cerebral venous oxygenation fluctuates by 1% at respiratory frequencies in the resting state reflecting the globally-averaged AVF of a healthy human brain. The AVF in brain parenchyma was mapped and its deterioration with aging was demonstrated. The spectral analysis of MR signal fluctuations may provide a new MR imaging technique to map AVF.