Purpose
Both cerebral tumor and cardiovascular disease may compromise cerebrovascular reactivity due to abnormal angiogenesis or blood supply. Functional MRI during hypercapnia stress, such as breath-holding (BH), has been used to assess the cerebrovascular reactivity. However, in clinical settings, patients may not be able to hold their breath well, which can reduce the sensitivity for detection when an fMRI model-based analysis is applied. In view of the global effect induced by breath-holding, this study proposed a model-independent analysis, using the whole-brain-averaged time curve as a reference function (WBRF), and compared with the results using the canonical hrf (CHRF).

Methods
T2*-weighted images were acquired using a single-shot GE EPI sequence on 1.5T MR scanner, with TR/TE= 3000ms/60ms. Four experiments were performed on two normal volunteers: (1) BH after deep inspiration, (2) after an instruction, BH after the end of the natural expiration, (3) self-paced BH by button pressing and (4) take in a short breath during the BH duration. For model-independent analysis, the WBRF was the averaged time curve over the whole brain tissue. For model-dependent analysis, the CHRF was adopted from the SPM2. Voxels with statistically increased signals were determined (p<0.001), and then the fractional activation volume (activated volume/whole volume) was calculated.

Results
In all cases, the WBRF was able to show the real breath-holding paradigm performed by the subjects. From the four experiments, the fractional activation volumes by model-independent analysis were 62, 53, 57, 54 % and 58, 4, 5, 12 % by model-dependent analysis, respectively.

Conclusion
The results illustrated model-independent analysis is a more reliable approach. This is caused by the fact that WBRF better reflects the true breath-holding situation than CHRF. Due to the impaired patient performance in clinical applications, the method proposed by this study can help increasing the sensitivity of cerebrovascular reactivity MRI.