Operatively defined ischemic core, penumbra and oligemia in human acute stroke using sequential MR perfusion images


Introduction
Depending on the severity of injury and final fate, cerebral ischemic tissues have been operatively categorized into ischemic core, penumbra, and oligemia. Ischemic core dies regardless of subsequent reperfusion status. Penumbra may survive if effective reperfusion occurs in time, or otherwise it may evolve to infarction. On the other hand, oligemia represents brain regions showing abnormal perfusion but will survive independent of whether or not receiving treatment, i.e. effective reperfusion in the context of this study. In this study, we developed an operator-defined approach in an attempt to categorize ischemic tissues into ischemic core, penumbra and oligemia based on how perfusion improvements alter tissue survival rates.

Methods
Twenty one acute ischemic stroke patients were studied with informed consent. All patients were serially scanned with MRI (3T Trio, Siemens) at 2.7 ± 0.7 hours (tp1), 6.4± 0.4 hours (tp2) and 1 month (tp3) after stroke onset. Dynamic susceptibility contrast (DSC) scans were performed to assess tissue perfusion at both tp1 and tp2. Mean transit time (MTT) maps were computed as a ratio between cerebral blood volume (CBV) and cerebral blood flow (CBF) using a singular value decomposition (SVD) method. FLAIR images acquired at tp3 were used to manually delineate the final lesion. Image registration was performed to align all images acquired at different time points. MTT prolongation was defined as MTT- median MTT of the contralateral hemisphere. Tissue survival rate (1-infarction rate) was computed for all voxels from ipsilateral hemisphere at given tp1 and tp2 MTT prolongation time ranging from 0 second to 25 seconds. Moreover, the survival rate maps were grouped and represented using four quartiles of survival rate ranges: >=75%, 50-75%, 25-50% and 0-25%. To minimize the effects of variation induced by noise, small isolated volume (<1 ml) at each bin were excluded from this analysis.

Results
Figure 1 shows tissue survival rates as a function of tp1 and tp2 MTT prolongation. The blue diagonal line indicated regions with unchanged MTT, while all the bins above this line represent perfusion improvement and all the bins below this line represent perfusion deterioration from tp1 to tp2. Figure 1 indicated that tissue perfusion might either improve or deteriorate during the first few hours after stroke. Following a general trend, tissue survival rate might be low if the initial MTT abnormality was more severe and/or perfusion tissue worsened from tp1 and tp2. After grouping survival rates into four quartiles as shown in Figure 1b, distinct patterns have emerged. In this study, we primarily focus on voxels with unchanged or improved MTT from tp1 to tp2 (bins at or above the diagonal line) to evaluate whether perfusion improvement may alter tissue survival rate. For all regions with tp1 MTT prolongation <=4 seconds, tissue had a very high chance to survive (>75%) regardless whether MTT improved or remained unchanged. On the other hand, perfusion improvement represented as shortened MTT from tp1 to tp2 (above the blue diagonal line) increased tissue survival rate to >50% (at least) in regions with MTT prolongation ranging from 5-14 seconds. For example, regions with a MTT prolongation of 10 seconds had a low chance to survive (25-50%) if MTT remained unchanged from tp1 to tp2, while the survival rate might increase to 50-75% or even >75% depending on how much MTT might decrease from 10 seconds from tp1 to tp2. Our results shows that tissues with abnormal MTT within the range of 5-14 seconds have an undetermined fate and perfusion improvement can improve their tissue outcome. In regions with MTT prolongation >=15 seconds, the chance of tissue survival is always below 50% regardless of subsequent tissue perfusion improvements. Based on the definition of three tissue types, our findings suggested that three MTT ranges: (1) 0-4 seconds; (2) 5-14 seconds; and (3) >15 second may correspond to the operatively categorized oligemia, penumbra and, ischemic core. Among these three regions, the penumbra region is of the most clinical relevance since its fate can be altered by an effective treatment.

Discussion and Conclusions
Tissue survival rate as a function of both tp1 and tp2 MTT prolongation revealed that distinct patterns of perfusion and subsequent perfusion changes can be utilized to operatively define ischemic core, penumbra and oligemia. This operator defined approach is developed based on whether perfusion improvement may or may not increase tissue survival rate. Regions survived or died regardless of perfusion improvement are considered as oligemia and ischemia core, respectively, while regions may either survive or die depending on reperfusion is considered as penumbra. Our findings suggested that tissues with MTT prolongation >=15 seconds, 5-14 seconds and 0-4 seconds may represents ischemic core, penumbra and oligemia, respectively.

References
2. Siesjo et al, JCBFM 1999;19:19