Neurovascular uncoupling

The mechanism and effects of hemodynamic insufficiency can only be appreciated through assessment of neurovascular coupling. During the last 20 years, the field of functional brain mapping has shown that MRI can view neural activity by measuring signal changes caused by activity-induced modulation in local blood flow. Blood flow secondary to neuronal activation can increase significantly. In one study, a 45% increase above resting levels was observed during visual stimulation, but oxygen consumption increased by only 16%,5 indicating that far more oxygen is being delivered than is consumed. This has been termed neurovascular uncoupling by many; however, from a medical perspective, this is a misnomer because this difference between blood flow and oxygen consumption during neuronal activation in healthy individuals is a normal observation. Uncoupling infers disease. It would make more sense to refer to the normal condition as functional hyperemia [1)]

The coupling mechanism between neuronal firing and cerebrovascular dilatation can be significantly compromised in cerebral diseases, making it difficult to identify eloquent cortical areas near or within resectable lesions by using Blood Oxygen Level Dependent (BOLD) fMRI. Several metabolic and vascular factors have been considered to account for this lesion-induced neurovascular uncoupling (NVU), but no imaging gold standard exists currently for the detection of NVU. However, it is critical in clinical fMRI studies to evaluate the risk of NVU because the presence of NVU may result in false negative activation that may result in inadvertent resection of eloquent cortex, resulting in permanent postoperative neurologic deficits. Although NVU results from a disruption of one or more components of a complex cellular and chemical neurovascular coupling cascade (NCC) MR imaging is only able to evaluate the final step in this NCC involving the ultimate cerebrovascular response. Since anything that impairs cerebrovascular reactivity (CVR) will necessarily result in NVU, regardless of its effect more proximally along the NCC, we can consider mapping of CVR as a surrogate marker of NVU potential. We hypothesized that BOLD breath-hold (BH) CVR mapping can serve as a better marker of NVU potential than T2* Dynamic Susceptibility Contrast gadolinium perfusion MR imaging, because the latter is known to only reflect NVU risk associated with high grade gliomas by determining elevated relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) related to tumor angiogenesis. However, since low and intermediate grade gliomas are not associated with such tumoral hyperperfusion, BOLD BH CVR mapping may be able to detect such NVU potential even in lower grade gliomas without angiogenesis, which is the hallmark of glioblastomas. However, it is also known that glioblastomas are associated with variable NVU, since angiogenesis may not always result in NVU. Perfusion metrics obtained by T2* gadolinium perfusion MR imaging were compared to BOLD percentage signal change on BH CVR maps in a group of 19 patients with intracranial brain tumors of different nature and grade. Single pixel maximum rCBV and rCBF within holotumoral regions of interest (i.e., “ipsilesional” ROIs) were normalized to contralateral hemispheric homologous (i.e., “contralesional”) normal tissue. Furthermore, percentage signal change on BH CVR maps within ipsilesional ROIs were normalized to the percentage signal change within contralesional homologous ROIs. Inverse linear correlation was found between normalized rCBF (r(flow)) or rCBV (r(vol)) and normalized CVR percentage signal change (r(CVR)) in grade IV lesions. In the grade III lesions a less steep inverse linear trend was seen that did not reach statistical significance, whereas no correlation at all was seen in the grade II group. Statistically significant difference was present for r(flow) and r(vol) between the grade II and IV groups and between the grade III and IV groups but not for r(CVR). The r(CVR) was significantly lower than 1 in every group. Our results demonstrate that while T2*MR perfusion maps and CVR maps are both adequate to map tumoral regions at risk of NVU in high grade gliomas, CVR maps can detect areas of decreased CVR also in low and intermediate grade gliomas where NVU may be caused by factors other than tumor neovascularity alone. Comparison of areas of abnormally decreased regional CVR with areas of absent BOLD task-based activation in expected eloquent cortical regions infiltrated by or adjacent to the tumors revealed overall 95% concordance,

thus confirming the capability of BH CVR mapping to effectively demonstrate areas of NVU. ed by factors other than tumor neovascularity alone. Comparison of areas of abnormally decreased regional CVR with areas of absent BOLD task-based activation in expected eloquent cortical regions infiltrated by or adjacent to the tumors revealed overall 95% concordance, thus confirming the capability of BH CVR mapping to effectively demonstrate areas of NVU [2].

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http://stroke.ahajournals.org/content/44/6_suppl_1/S55.long

2)

Pillai JJ, Zacà D. Comparison of BOLD cerebrovascular reactivity mapping and DSC MR perfusion imaging for prediction of neurovascular uncoupling potential in brain tumors. Technol Cancer Res Treat. 2012 Aug;11(4):361-74. Epub 2012 Mar 1. PubMed PMID: 22376130.