Cerebral Aneurysm Wall Permeability, A New Parameter for Assessing Ruptue Risk

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Introduction: Cerebral aneurysms pose a significant risk to the public with incidence estimates of up to 6%.[1] Aneurysm size is one of the most commonly used metrics for assessing rupture risk. Aneurysms larger than 10mm are generally considered dangerous and referred for surgical or endovascular intervention.[3] However, many aneurysms smaller than 10mm are also known to rupture, highlighting the need for more comprehensive, quantifiable, and non-invasive metrics that may distinguish progressing aneurysms from stable ones. We studied the permeability of the aneurysm wall to an intravascular contrast agent using DCE-MRI as a new metric for assessing aneurysm rupture risk.

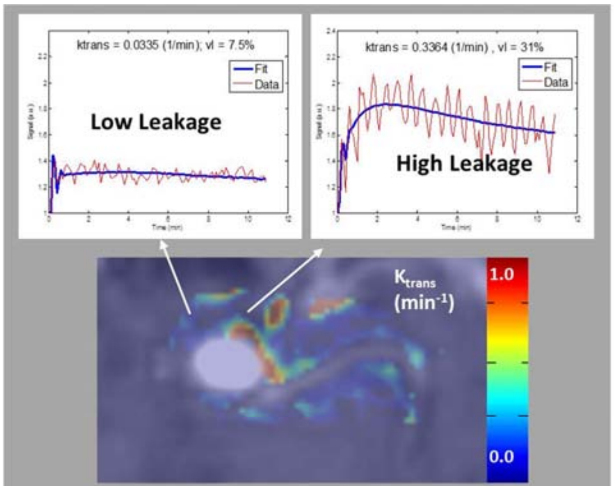

Figure 1: Permeability modeling of a 1.4 cm L ICA aneurysm showing regions of high and low contrast agent leakage rates

Materials/Methods: With IRB approval we conducted a prospective study on 12 patients with angiographically-confirmed saccular cerebral aneurysms. Using a standard dynamic contrast enhanced MRI protocol[3] we modeled cerebral aneurysm wall permeability using Tofts's Model[3] in order to quantify contrast agent leakage rate (k_{trans}) and the leakage space volume (v_l), and compared these parameters against aneurysm size, a well-established marker for aneurysm rupture risk, using linear regression analysis. To address partial volume contamination of vascular signal from the initial pass of the bolus, we modified Tofts's classic model to incorporate a vascular term given by the arterial input function (AIF), $C(t) = \alpha \cdot AIF(t) + (1-\alpha) \cdot c_{Tofts}(t)$ where α is the proportion of vascular signal in each voxel ($\alpha \leq 1$) and c_{Tofts} is Tofts's classic model[4] given by $C_{tofts} = Dk_{trans}\sum_{i=1}^{2} a_i \, (e^{-m_3 t} - e^{-m_i t})/(m_i - m_3)$ with dose D, $m_3=k_{12}/v_l$, and $m_1 = 0.144\ min^{-1}$ and $m_2=0.0111\ min^{-1}$.[3] Regions of interest were drawn adjacent to the aneurysm wall to calculate mean k_{trans} and v_l for each patient. Aneurysm size was assessed using CT angiography.

Results/Discussion: In total, we scanned 12 patients (8W, 4M; mean age = 67.5 years ± 10.2 ; range, 56-76 years). The mean contrast leakage rate, k_{trans}, through the aneurysm wall was significantly larger compared to healthy parent vessels ($0.20\pm0.17\ min^{-1}$ vs $0.04\pm0.03\ min^{-1}$, p=0.0030 student t-test). Similarly the leakage volume, v_l, adjacent to the aneurysm was significantly larger compared to the healthy parent (46±28% vs. 12±11%, p<0.001). Figure 1, shows k_{trans} parametric map superimposed on the same slice of a T1-weighted contrast enhanced anatomic image of a 56 year old woman with a 1.4cm aneurysm on the left internal carotid artery. Furthermore, we found that both k_{trans} (R=0.597,p=0.040) and v_l (R=0.712,p=0.0093) correlated strongly with aneurysm size (Figure 2, vl not shown), indicating that wall permeability modeling may be a useful metric for clinicians in assessing aneurysm rupture risk.

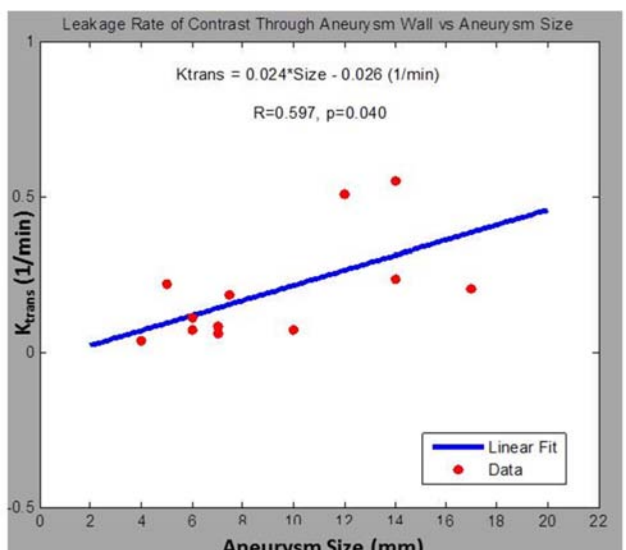

Figure 2: K_{trans} and v_l(not shown) was found to correlate strongly with aneurysm size.

Conclusion: Our preliminary studies in patients with unruptured cerebral aneurysms indicate that DCE-MRI kinetic modeling of aneurysm leakage provides quantitative metrics which correlate with classical rupture risk criteria. Such measurements may be combined with other quantitative metrics such as wall shear stress, blood velocity, and aneurysm shape indices to provide a more comprehensive picture of aneurysm natural history.

References: 1) Wiebers et al, Lancet 2003; 2) Carandang et al, JAMA 2006; 3) Tofts et al, MRM 1995 4) Tofts et al MRM 1989