# Aneurysm Wall Permeability as a Measure of Rupture Risk and Bleb Formation

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**Introduction:** Intracranial aneurysms affect 2-6% of the population with 30,000 Americans suffering an aneurysm rupture per year [1]. Because of the inherent risks associated with surgical clipping/coiling and the fact that only a small fraction of IAs rupture annually (<2%), treatment of unruptured IAs remains controversial. The purpose of this study was to quantify IA wall permeability ($k^{trans}$,$v_L$) to a contrast agent as a measure of aneurysm rupture risk and wall integrity utilizing a point-source diffusion based model. While, previous work has shown $k^{trans}$ to be associated with IA rupture risk, as defined by various anatomic, imaging and clinical risk factors [2], it employed a Tofts' based permeability model [3]. For aneurysmal modelling, a point-source diffusion model more accurately represents physiology and provides better resolution for determining wall thickness and potential bleb formation zones.

**Methods:** Twenty-seven unruptured IAs in 23 patients were imaged with DCE-MRI, and wall permeability parameters ($k^{trans}$, $v_L$) were calculated in regions adjacent to the aneurysm wall. $K^{trans}$ and $v_L$ were calculated using both a Tofts' permeability model as described in [2] and a finite-element point source diffusion model. For the FEM model we utilized the standard diffusion equation with a constant diffusion coefficient (Eq. 1) outside the walls of the aneurysm.

$$\frac{dC(x,y,t)}{dt} = D\nabla^2 C(x,y,t)$$

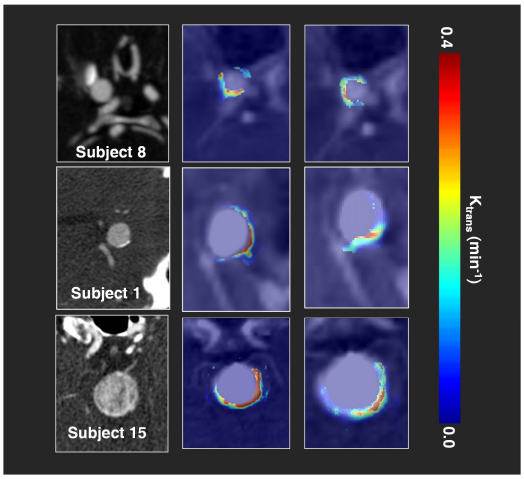


**Figure 1** Comparison between the two different models. Left shows $k^{trans}$ values calculated with Tofts whereas the right column is calculated using FEM point source diffusion. Both provide valuable information but the FEM data provides better resolution which is important when analyzing wall integrity.

The wall of the aneurysm was considered the source of contrast defined by an initial guess for $K^{trans}$ and $v_L$ provided by the Tofts model. For this study, diffusion was assumed to only occur in 2 dimensions. Concentrations were determined iteratively, by minimizing the square residual between the observed signal and the model estimate. For easy comparison, these fitted concentrations were then used to determine diffusion based $K^{trans}$ and $v_L$. In both cases, $K^{trans}$ and $v_L$ were evaluated as markers of rupture risk by comparing against established clinical (symptomatic lesions) and anatomic (size, location, morphology, multiplicity) risk metrics.

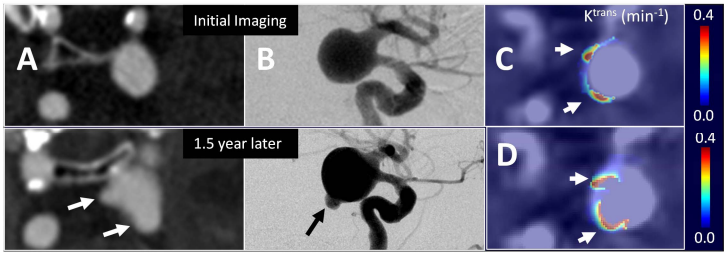


**Figure 2** The evolution of an untreated IA in a 61 year old male demonstrates that elevated $k^{trans}$ at baseline correlated with bleb formation. Morphological changes over 1.5 years are observed in CTA (A) and DSA (B); both techniques for calculating $k^{trans}$, demonstrated two regions with high $k^{trans}$ at the time of imaging initial imaging (C – Tofts) (D – FEM Diffusion). Notice the FEM method suggests extended wall compromise as opposed to a point compromise.

**Results:** All IAs had a pronounced increase in wall permeability compared to the paired healthy MCA ($p<0.001$). Regression analysis demonstrated a significant trend toward increased $k^{trans}$ with increasing aneurysm size ($p<0.001$). A comparison between the two different models is shown in Figure 1. Notice in subjects 1 and 8, the FEM model shows leakage from nearly a single point, whereas a large portion of the wall in subject 15 appears compromised. Of the 23 patients, one opted out of surgical intervention and was imaged 18 months after initial evaluation. It is clearly visible (Figure 2) that at initial imaging, $k^{trans}$ was elevated in both models. Furthermore, the FEM diffusion model suggests 2 regions of wall thinning (rather than a point, which may have suggested rupture). After 18 months, the regions with high $k^{trans}$ grew into new blebs off the aneurysm.

**Conclusions:** We found, regardless of modelling technique, contrast agent permeability across the aneurysm wall correlated significantly with both aneurysm size as well as size-independent anatomic risk factors. In addition, we show that a point source diffusion model for $k^{trans}$ provides additional information about the weakening of the aneurysmal wall.

**References:** [1] Weir, JNS 2002 [2] Vakil, AJNR 2014, [3] Tofts, JMRI, 1999
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