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Estimation of microvascular capillary physical parameters using MRI assuming a pseudo liquid drop as model of fluid exchange on the cellular level

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ABSTRACT

Aim: One of the most important microvasculatures' geometrical variables is number of pores per capillary length that can be evaluated using MRI. The transportation of blood from inner to outer parts of the capillary is studied by the pores and the relationship among capillary wall thickness, size and the number of pores is examined.

Background: Characterization of capillary space may obtain much valuable information on the performance of tissues as well as the angiogenesis.

Methods: To estimate the number of pores, a new pseudo-liquid drop model along with appropriate quantitative physiological purposes has been investigated toward indicating a package of data on the capillary space. This model has utilized the MRI perfusion, diffusion and relaxivity parameters such as cerebral blood volume (CBV), apparent diffusion coefficient (ADC), ΔR_2 and ΔR_2^* values. To verify the model, a special protocol was designed and tested on various regions of eight male Wistar rats.

Results: The maximum number of pores per capillary length in the various conditions such as recovery, core, normal-recovery, and normal-core were found to be 183 ± 146, 176 ± 160, 275 ± 166, and 283 ± 143, respectively. This ratio in the normal regions was more than that of the damaged ones. The number of pores increased with increasing mean radius of the capillary and decreasing the thickness of the wall in the capillary space.

Conclusion: Determination of the number of capillary pore may most likely help to evaluate angiogenesis in the tissues and treatment planning of abnormal ones.

Abbreviations: ADC, apparent diffusion coefficient; CBF, cerebral blood flow; CBV, cerebral blood volume; VSI, vessel size index; TCL, total capillary length; MTT, mean transit time; ROI, region of interest; MCA, middle cerebral artery; RF, radio frequency; FLASH, fast low angle shot; DWI, diffusion weighted imaging; PWI, perfusion weighted imaging; 2DFT, two-dimensional Fourier transform; FOV, field of view.

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1. Background

Some theories have been proposed to recognize the performance of tissues via estimating some microvascular capillary physical parameters. Those may be developed to evaluate tissue metabolism in MRI. Capillaries are a part of cardiovascular system, consisting of single layer endothelial cells, permit rapid exchange of water and solutes with interstitial fluid via the pores created dynamically as ding-dong in the capillary wall, and form an interconnecting network of tubes of different lengths. Capillary density distribution and its geometrical specifications vary from tissue to tissue. In metabolically active tissues the capillaries are numerous, whereas in less active tissues the capillary density is low. Therefore, geometry evaluation of capillaries may be useful in medicine.

The MRI perfusion, diffusion and relaxivity parameters such as cerebral blood volume (CBV), apparent diffusion coefficient (ADC), the differences between relaxation rates pre-contrast and post-contrast agent injection ($\Delta R_2 = R_2 - R'_2$ and $\Delta R^*_2 = R_2 - R'^*_2$ without and with considering magnetic field impurity correspondingly) were using to characterize the microvasculature space. For instance, an approach suggested by Dennie et al.[1] which measures changes in the spin–spin suggested relaxation rates $1/T'_2 = R'_2$ and $1/T'^*_2 = R'^*_2$ caused by the injection of a blood pool restricted contrast agent, are proposed to be sensitive to microvessel density. Van Rijswijk et al.[2] have reported that apparent diffusion coefficient (ADC) values of all tumors, subcutaneous fat, and muscle were significantly higher than true diffusion coefficients, indicating a contribution of perfusion to the ADC. Also, true diffusion measurements, which are corrected for the perfusion effect, have potential to be used as a noninvasive parameter in the characterization of soft-tissue masses. Therefore, in theory, diffusion and perfusion information in MRI maps are combined to obtain morphological information such as mean radius, volume and possibly capillary plasma velocity. Also, the appropriate practical investigations on measuring mean radius of capillary in the various regions of rat brain are presented.

Gambarota et al.,[3] an enhanced contrast method in measuring blood volume have utilized for brain tumors via Gadolinium-DTPA/USPIO agents to distinguish vascular leakage and ultra-small iron oxide particles. Although the defined index in micro- and macro-vasculatures has been characterized, it hast been not estimated by different weighted and b-values. On the other hand, some researchers[4–7] recently have reported the diffusion-weighted imaging (DWI) of soft tissue and musculoskeletal lesions to estimate perfusion fractions to compare with the ADC values. Pekcevik et al.,[4] have determined the mean ADC amounts by single-shot echo-planar imaging technique using a 1.5 T MRI device that some overlap have reported between benign and malignant tumors. In this study, combination of diffusion and perfusion maps including capillary density, volume, capillary plasma velocity, CBV, ADC and the differences between relaxation rates before and after contrast-agent injection is utilized to determine the relation among mean radius, number of pores and wall thickness of capillary in four different regions. To differentiate normal from abnormal domains, the corrected perfusion effect can be scrutinized by a new method called pseudo-liquid drop model.

2. Aim

A combined model is suggest to confirm a package of data on geometrical parameters and an essential way in transportation of blood from inner to outer parts of the capillary. It is utilized from CBV, ADC, ΔR_2 and ΔR^*_2 values to calculate the number of pores per capillary length. The aim is to estimate mean radius, length and capillary density in normal and abnormal regions by introducing pseudo-diffusion coefficient.

3. Materials and methods

3.1. *Theory*

One may estimate the mean capillary radius (r_c) by using the CBV, ADC, ΔR_2 and ΔR^*_2 values as follows,[8,9]

$$r_{c(\mu m)=}\left(7.57\times10^{3}\frac{D.CBV}{Vol_{(voxel)}}.\frac{\Delta R^{*2}_{2}}{\Delta R^{3}_{2}}\right)^{0.5} \quad (1)$$

where D is diffusion constant of water.[10,11] The residence time of blood in a capillary is also only on the order of 1–2 s. Therefore, each capillary may only support a very small volume of tissue in which the blood pass from the capillary thickness as pseudo-liquid drops based on twofold permeable process. The capillary lumen lies within a circumferential ring of several endothelial cells, as shown in Fig. 1. The endothelium is perforated by numerous small holes called fenestrae which are considered for passing blood as pseudo-liquid drop. The fenestrae are sometimes covered by a thin membrane that provides selectivity with regard to the size of solutes that are allowed to pass through. The flow of charged molecules through channels in the cell membrane is responsible for the creation of the membrane potential. Solute transport occurs both through bulk fluid motion and by solute diffusion due to the presence of solute concentration gradients. The diffusion of a solute will also be affected by the presence of a variety of heterogeneous structures. Solutes will need to diffuse through porous structures such as the capillary wall, around or through cells within the extravascular space, and through the interstitial fluid containing a variety of macromolecules.[12] In general, the transport of essential water soluble molecules across the cell membrane is achieved through the use of special transmembrane proteins that have a high specificity for a

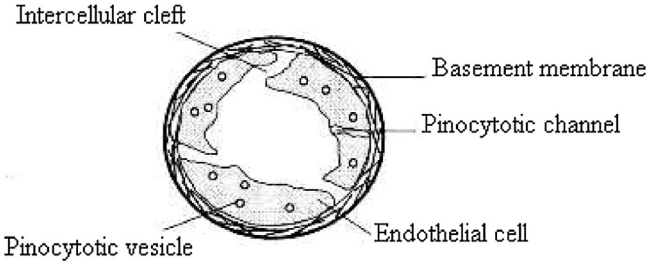

Fig. 1 – Cross section diagram of a capillary[12] [p. 104].