How the spatial distribution of the vessels affects T2*? A 2D simulation study.

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Introduction:

For several years, various techniques based on susceptibility contrast originating from vessels have proven relevant to estimate perfusion estimates such as blood volume fraction (BVf), blood flow, vessel size index (VSI), vessel density, SO2, etc. In these approaches the underlying model relies on the idea that the vessels can be modeled as a random distribution of straight cylinders in a voxel. In this case, under certain assumptions, an analytical model can be designed [1,2] thereby establishing a link between perfusion parameters and MR signals [1,3,4]. This models stands for the statistical limit when the number of vessels, N, tends to infinity, i.e. in an infinite voxel volume. This analytical model is in good agreement with corresponding simulation works [5]. In the latter case, authors deal with the infinite assumption by averaging the MR signal from different sets of cylinders randomly arranged into a finite volume. In vivo, the MR signal results from a voxel containing a finite number of vessels whose spatial arrangement may not be locally uniform. In this study, we investigated how the spatial distribution of the vessels impacts the relaxation rate of the MR signal.

Materials and Methods:

Calculations were performed in the Matlab (Mathworks Inc. Natick, MA, USA) environment using homemade software. Various sets of vessels with different constraints were generated in 2D. The constraint is expressed as a specific area surrounding each vessel where non-other vessel can be located. The radius Rext defines this 'vessel free' area. The 2D approach was favored to ease the constraint implementation. Two different vessel arrangements were generated: 'Norm' (BVf=3%, R=3µm, Rext=[3-21]µm, (N=1061)), 'Tumor' (BVf=5%, R=6µm, Rext=[3-33]µm, (N=442)). For each set of parameters, 10 different arrangements were randomly created for statistical purposes. All other parameters remain constant (Δχ between blood and tissue was set to Δχ0.Hct.(1-S02) with SO2=60%, Hct=40% and Δχ0=0.264ppm, water diffusion was set to ADC=1000µm^2.s^{-1}). Simulations were conducted at 7T on a 1 mm^2 2D plan. The magnetic field perturbations were computed using a Fourier based approach [6] and 3 orthogonal directions of B_0 to mimic an isotropic orientation of the vessels. Relaxation and water diffusion effects were taken into account using the approach proposed by Klassen et *al.*[7] and based on Bloch equations and diffusion kernel. MR signal was then computed and T_2* eventually obtained using an exponential fit of the signal.

To characterize the vessel distribution, the distance map to the closest vessel, D(x,y), was calculated and analyzed with the power-spectrum, P(kx,ky) = (TF{D})^2 [8]. Then P was expressed as a function of kxy=(kx^2+ky^2)$^{1/2}$ and fitted using an affine function with an initial plateau (Fig. B). It is known that below a characteristic cutoff the power spectrum saturates. It leads to a characteristic spatial frequency, F_D. This frequency is related to the corresponding wavelength (L_D) above which the vascular distance or the vascular density may be considered as homogeneous [8].

Results:

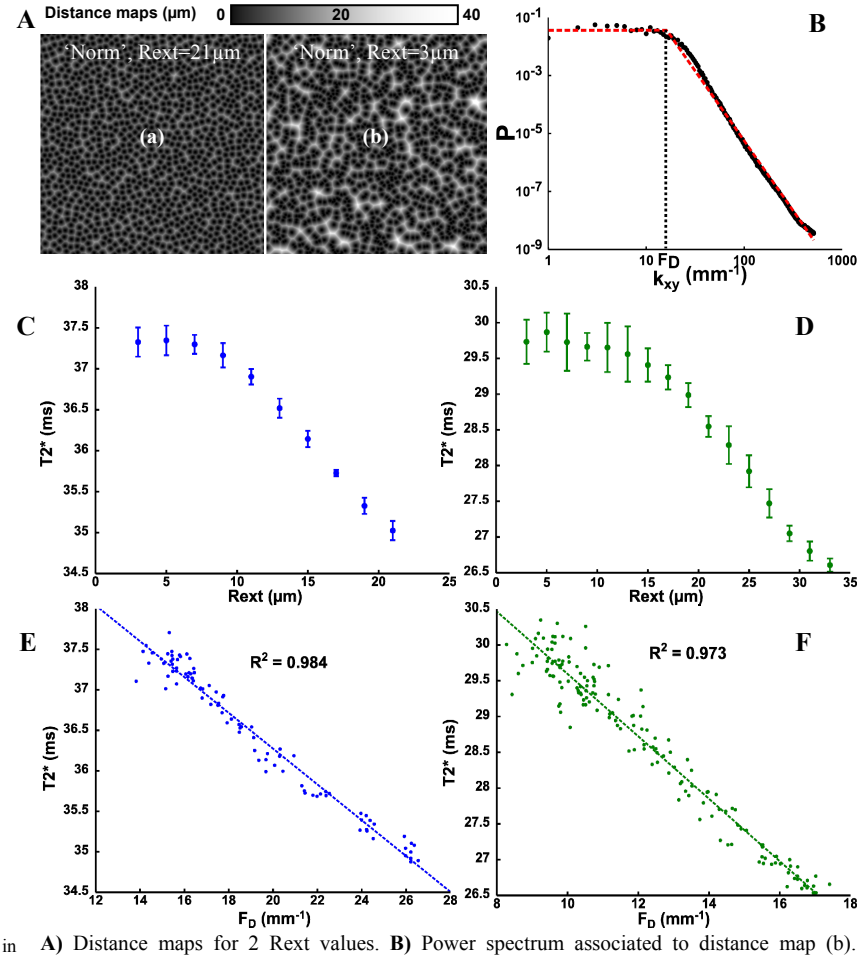
Figure A presents two distance maps with the "Norm" parameters with Rext = 21µm ((a), constrained, F_D=16.2mm^{-1}) and Rext = 3µm ((b), unconstrained, F_D=26.5mm^{-1}). Arrangement (a) is locally less heterogeneous than (b) and leads to a shorter T2*. At 7T, the variations observed for T2* values are about 2.5ms for the 'Norm' case (Fig. C) and about 3.5ms for the 'Tumor' case (Fig. D). As shown in ***Figures C and D***, these fluctuations do not appear to be linearly related to the parameter Rext. Above a given Rext value, T2* estimate starts to shorten. As already shown in [7], the deviation in the 'Tumor' case is larger than in the 'Norm' case since the number of vessels is smaller.

Figure B presents the power-spectrum P vs kxy corresponding to the distance map shown in A(b). The regression line in red provided an automatic way to determine the cutoff at F_D. The connection between T_2* and F_D is presented on ***Figures E*** and ***F***, for the 'Norm' and 'Tumor' cases respectively. The high coefficients of correlation suggest that a linear relation may exist between these two parameters.

Discussion:

In this study, we push a step forward the understanding of the susceptibility contrast mechanisms originated from vessel arrangements. At 7T, we quantified the T_2* fluctuations due to the spatial distribution of the vessels. The observed range of variations may lead, for instance, to an error of about 8% on SO_2 estimate using models that do not currently take into account this variability [4]. Moreover, the linear relation found between T2* and F_D might be of interest to further develop a mean to measure the spatial distribution of the vessels. Other parameters, for instance the standard deviation of D or the characteristic length provided by a box counting approach [9], do not lead to such a straightforward relationship (data not shown).Finally, added to BVf and VSI, a parameter that could estimate the spatial distribution of the vessels might be of interest to achieve a better characterization of the microvascular structure. Such a parameter would provide information regarding how far from a vessel the cells are. This may be particularly useful for drug delivery and to investigate various pathologies with microvasculature changes.

Reference: [1] Yablonskiy et *al.*, MRM, 1994. [2] Kiselev et *al.*, Phys. Rev. Lett. 1998. [3] Troprès et *al.*, MRM, 2001. [4] Christen et *al.*, NMR in Biomedicine, 2010. [5] Boxerman et *al.*, MRM, 1995. [6] K. M. Koch et *al.* Phys Med Biol, 2006. [7] Klassen et *al.*, Biophys J, 2007. [8] Risser et *al.*, JCBFM, 2007. [9] Gazit et *al.*, Microcirculation, 1995.



A) Distance maps for 2 Rext values. **B)** Power spectrum associated to distance map (b). regression curve in red. **C and D)** Mean± standard-deviation of T2* estimate as a function of Rext for the 'Norm' case (C, blue) and the 'Tumor' case (D, green). **E and F)** T2* estimate as a function of F_D for the 'Norm' case (E, blue) and the 'Tumor' case (F, green).