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Original contribution

The influence of spatial patterns of capillary networks on transverse relaxation

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ABSTRACT

Tissue-inherent relaxation parameters offer valuable information about the arrangement of capillaries: in an external field, capillaries act as magnetic perturbers to generate local inhomogeneous fields due to the susceptibility difference of deoxygenated blood and the surrounding tissue. These field inhomogeneities influence the free induction decay in a characteristic way, and, conversely, the above tissue parameters can be recovered by multi-parametric fits of adequate theoretical models to experimentally sampled free induction decays. In this work we study the influence of different spatial patterns of capillary positions on the free induction decay. Starting from the standard single capillary approximation (Krogh cylinder) for a symmetric array of capillaries, the free induction decay is analyzed for increasingly random capillary positions, using a previously described Gibbs point field model. The effects of diffusion are implemented with a flexible and fast random walk simulation. We find that the asymmetric form of the obtained frequency distribution is more robust against variations of capillary radii than against shifts of capillary positions, and further that, for an inclusion of diffusion effects, the single capillary approximation models the uniform alignment of capillaries in the hexagonal lattice to great accuracy. An increase in randomization of capillary positions then leads to a significant change in relaxation times. This effect, however, is found less pronounced than that of changes in the off-resonance field strengths which are controlled by the oxygen extraction fraction, thus indicating that observed changes in BOLD imaging are more likely to be attributed to changes in oxygenation than to capillary alignment.

1. Introduction

The quantitative evaluation of subtle tissue changes that involve microscopically small structures such as capillaries and cells is useful in assessing the form, extent and dynamic change of pathophysiological processes that are usually well below the resolution of MR scanning devices in clinical routine. For example, Karch et al. demonstrated a relationship between the degree of irregularity of capillary arrangements in cardiac tissue and some cardiac pathologies [1]. Likewise, techniques that are based on the BOLD (blood oxygen level-dependent) effect [2] can be used to evaluate microstructural changes that are associated with hemodynamic and metabolic pathology-related alterations in brain tissue (see [3] for a review of some theoretical models). The range of applications is large and stretches from diagnostic to monitoring and even therapeutic purposes [4,5]. With regard to magnetic resonance imaging it is therefore important to know how much information about microstructural patterns in a voxel can actually be extracted from the corresponding MR signal.

On a microscopic scale, two intrinsic tissue properties dominate the MR signal decay: the spatial pattern of magnetic susceptibility inclusions in the tissue (e.g. the arrangement of capillaries in muscle tissue that contain blood with paramagnetic properties [2]), and the mobility of spins that surround these susceptibility inclusions. The first effect can be described in terms of a local Larmor frequency $\omega(\mathbf{r})$ that encodes information about the shape of the microscopically small

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magnetic perturbers (which generate local magnetic field inhomogeneities in an external field). The second effect is usually modeled as a diffusion process that is characterized by the diffusion coefficient D and boundary conditions that are imposed by the spatial arrangement of the perturbers. The time evolution of the local transverse magnetization is then determined by the solution of the Bloch-Torrey equation (see below) that takes into account both susceptibility and diffusion effects [6]. For capillary networks, several deterministic analytical models about MR signal behavior were brought forward recently [7–13], see also [14] and references therein. Most approaches accurately describe the limiting regimes of static dephasing, where diffusion effects are negligible, and the regime of strong diffusion effects: the motional narrowing limit (see also [15,16]). They either rely on assumptions on the spin phase distribution [8], an approximation of the NMR signal in weak fields [9], second order perturbation theory for low diffusion effects [10], or stochastic approximations of diffusion-mediated field fluctuations [17]. One recent approach provides a solution of the Bloch-Torrey equation for the specific spatial pattern of symmetrically positioned capillaries [12,13] that is based on a single capillary approximation in analogy to Krogh's cylinder model [18]: in this geometrical model, it suffices to study (restricted) diffusion in the Krogh cylinder around one capillary. The Krogh model divides the biological tissue into independent parallel cylindrical unit cells that each host one capillary in their center. This necessarily leads to a loss of structural information, see also Fig. 1. It was shown recently, however, that the signal evolution of the magnetization inside a unit cell differs for quadratic and circular shapes [19]. In addition, the single capillary approximation may be adequate for some tissues (e.g. muscle tissue [20–22]), but most tissues do not display a uniform regular capillary position arrangement (e.g. the heterogeneous construction of a capillary supply network for pathological tumor growth [23], brain capillaries [14] or pathology-related capillary arrangements in cardiac tissue [1]).

In this work, we numerically evaluate and compare the influence of simplified model geometries on the frequency distribution in one MR voxel for square lattices, hexagonal lattices, the Krogh model and, eventually, the transition towards irregularly arranged capillaries (termed plasma) with the help of an entropy point field model that was proposed recently [24]. The effects of diffusion of spin-carrying particles are implemented with a random walk simulation. We show that irregular patterns of capillaries have a substantial influence on transverse relaxation times.

2. Methods

In this work, capillary arrangement patterns that cover the whole tissue space are assumed as being either based on a square lattice, a hexagonal lattice or a random positioning of capillaries (multi-capillary models; Fig. 1b–d), whereas the Krogh model represents the single capillary approximation where the study of the whole capillary network is reduced to the study of axial spin diffusion inside the concentric Krogh cylinder around one capillary (see also Table 1 for a comparison of capillary-tissue volume fractions and capillary densities in the different geometries). The volume elements in which dephasing processes of spin-carrying particles occur are then aligned as either quadratic prisms or hexagonal prisms (as in the cross-section of a face-centered cubic Bravais lattice), see Fig. 1c,d. This prevents remaining residual space between volume elements. Here, we only consider the two-dimensional planes of capillary cross-sections (see Fig. 1a–b); however, the results can easily be generalized to three dimensions and are the same as long as the capillaries remain parallel. This assumption may be reasonable for muscle tissue [22], yet, in the Krogh model, a (spatially equally distributed) randomization of vessel orientations can be achieved by considering the integration of the local frequency over the distribution function of the tilt angle β for randomly oriented cylinders, i.e. $\sin(\beta)/2$ (see also Section 3.5 below). In the following we will briefly introduce the Krogh model and its implications on the frequency distributions for static and dynamic dephasing processes. We will then evaluate the frequency distributions for square and hexagonal lattices to compare them with that of the Krogh model for different volume fractions.

2.1. Single capillary approximation: the Krogh model

The transition to the Krogh model or single capillary approximation consists in replacing the quadratic and hexagonal prisms with cylinders of equal volume, see Fig. 1e–g. In this process, neighboring

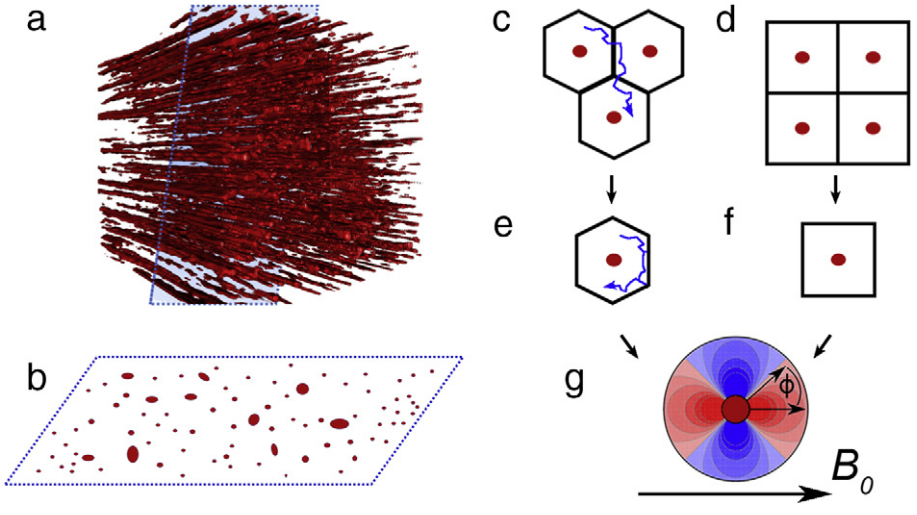

Fig. 1. Capillary arrangement patterns for biological tissue. (a) Microscopic blood vessels in the brain cortex, provided courtesy of B. Tews, National Center for Tumor Diseases, Heidelberg, Germany. (b) Schematic view of the cross section area (dotted blue line in (a)) with a random arrangement of capillary positions with variable radii. (c–d) Simplified spatial pattern of the capillaries in (b) in a hexagonal lattice (c) and a square lattice (d): the underlying assumption is that bulk tissue can be divided into simple, uniform and independent unit cells that each contain a single capillary. (e–f) Simplification steps for the transition of the hexagonal and the square lattice to the Krogh model: diffusion of magnetization between the unit cells is modeled by reflective boundaries of the unit cells (exemplified in the blue trajectory for the hexagonal lattice). (g) The unit cell in the Krogh model is simplified as a cylinder that co-axially surrounds a cylindriform capillary with radius R_C. The two-dimensional dipolar off-resonance field, as given in Eq. (1) with polar coordinates (r, ϕ), is portrayed in the Krogh cylinder with red (positive) and blue (negative) field portions. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)