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Using 3D realistic blood vessel structures and machine learning for MR vascular Fingerprinting

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Synopsis

MR vascular fingerprinting aims at mapping cerebral vascular properties such as blood volume and blood oxygenation. We propose to improve the technique by generating dictionaries based on 3D vascular networks segmented from whole brain high-resolution (3 μm isotropic) microscopy datasets. In order to compensate for the limited number of available data and long computing times, we used a machine-learning reconstruction process to generalize our results and tested our approach in healthy, stroke and tumor animal models. Our results show high quality maps with expected contrast and baseline values in healthy animals as well as expected trends in pathological tissues.

Introduction

MR vascular Fingerprinting¹ (MRvF) proposes to use the Magnetic Resonance Fingerprinting² (MRF) framework to map cerebral microvascular properties; namely the blood oxygenation saturation (SO₂), blood volume fraction (BVf) and vessel averaged radius (R). Dictionaries are generated based on numerical voxels containing vascular structures and physiological parameters. The initial MRvF implementation used 2D synthetic vascular networks. In this study, we pursue previous work^{3,4} and use dictionaries based on 3D geometries, either created *in silico* (synthetic) or segmented from whole brain high resolution microscopy images. In order to compensate for the limited number of available data and long computing times, we use a machine-learning reconstruction process to generalize our results and test our approach in healthy, stroke and tumor animal models.

Materials & Methods

Animal data:

Data were acquired on a 4.7T Bruker system. The MRF acquisition pattern consists on the concatenation of two GESFIDE sequences acquired pre and post injection of USPIOs (P904, Guerbet, France, 200 μmol Fe/kg)¹. 26 animals were imaged:

- 8 healthy rats (Wistar)
- 9 rats (Fischer) implanted with 9L tumors, imaged 14 to 16 days after induction
- 9 rats (Sprague-Dawley) undergoing ischaemic stroke throughout acquisition

Dictionary generation:

3 Dictionaries were generated on Matlab (The MathWorks Inc., Natick, Ma, USA) with the MRVOX software⁵.

- Dictionary **3D micro.**: Around 28,000 MRI-size voxels containing realistic vascular structures were extracted from whole brain high-resolution (3 μm isotropic) microscopy datasets^{6,7} using ImageJ (Rasband, W.S., NIH, Maryland, USA), Fig. 1a. Erosion transformations were performed to obtain continuous BVf and R distributions (see histograms in Fig. 1c. After assigning to each MRI-size voxel one SO₂ and one T₂ value in the range [35,90]% and [45, 110]ms, respectively, MR simulations including magnetic field estimation and water diffusion were performed to create the "3D microscopy" dictionary.
- Dictionaries **2D synth.** and **3D synth.**: Based on the previous histograms, 2D circles or 3D cylinders with gaussian distribution of radii (Fig. 1b) were generated to create the "2D synthetic" and "3D synthetic" dictionaries respectively.

Reconstruction:

All data were processed with Matlab using the MP3 software⁸. MRvF maps were created either using a standard direct matching ("MRvF Matching") between dictionaries entries and *in vivo* data, or using a dictionary learning tool⁹ ("MRvF Learning"). On top of MRvF results, maps of BVf, Vessel Size Index (VSI) and SO₂ were also obtained with analytical models¹⁰. ROIs were manually defined in lesions and contralateral tissues. Paired Student's tests were used to assess the significance of distributions difference, with a p-value of 5%. The whole pipeline is presented on Fig. 1d.

Results

Fig 2 shows examples of maps obtained with the different approaches in one representative animal of each group. Fig 3, 4 and 5 present the numerical results obtained in all animals for BVf, R and SO₂, respectively. It can be seen that without any prior on the estimates, all the MRvF approaches provide high quality maps with expected contrast and baseline values in healthy animals (3% < BVf < 5% , 4 μm <R<6 μm , and 60% < SO₂ < 80% in healthy tissue).

Dictionary learning seems however necessary as it reveals lesions that are unseen with direct matching (see SO₂ maps in stroke animal with 3D micro approach). After learning, most trends between healthy and pathological tissue are in line with literature reports and similar between dictionaries (increase of BVf and R in tumors, decrease of BVf/SO₂ and increase of R in stroke). For all dictionaries, the T₂ measurements (not shown) are also in line with expectations and follow the same trend in all dictionaries (about 60ms in healthy tissue, 20ms increase in tumor, 5ms decrease in stroke). The dictionaries yielded different results in a few particular cases such as in the 9L tumors that appear hyperoxic with the 3D Micro dictionary, but normoxic with the synthetic geometries. These findings warrant further investigation with complimentary oxygenation measurements.

Conclusions

This study demonstrates the feasibility of using 3D realistic vascular structures in the MRvF framework and the possibility to obtain high quality maps after machine learning in both healthy and pathological brains. It is possible that adding realistic pathological vascular structures in the dictionaries will further improve the results in lesions. This work also opens the possibility to perform MRvF in voxels containing closed vascular networks, allowing for the simulation of blood flow and oxygen variations along the vessels.

Acknowledgements

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Figures

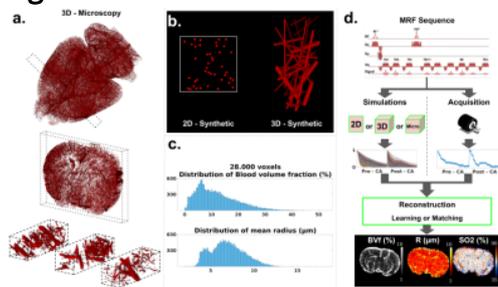


Figure 1: Methodological process. a. Eroded (for readability) versions of a real vascular network in a whole brain, a slice and single MRI-sized voxels. b. Examples of 2D and synthetic 3D voxels generated on MRVox. c. Vascular parameters distributions obtained after segmentation and characterisation of 28,000 realistic voxels. d. Acquisition and reconstruction protocol.

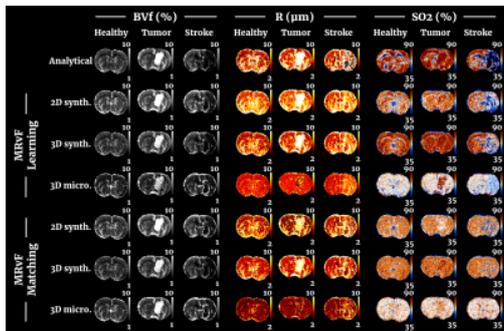


Figure 2: Results obtained with the analytical method and the different MRvF reconstructions in one slice of one animal in each group.

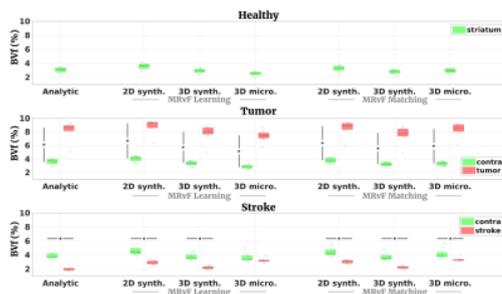


Figure 3: Statistical analysis of BVf values obtained in the animal groups, for analytical methods and MRvF with different dictionaries. Significance evaluated at 5% with paired t-test.

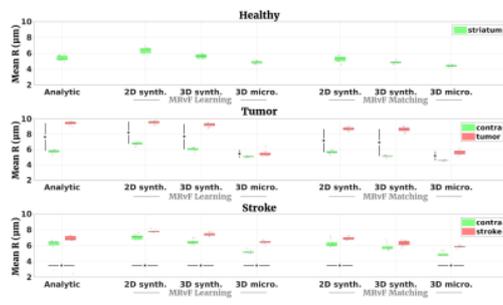


Figure 4: Statistical analysis of R values obtained in the animal groups, for analytical methods and MRvF with different dictionaries. Significance evaluated at 5% with paired t-test.

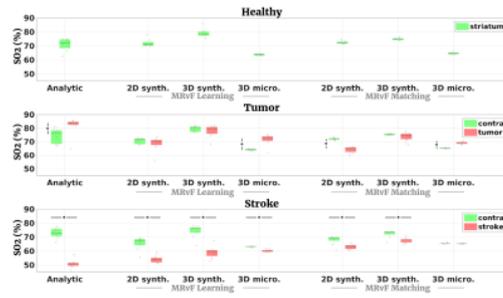


Figure 5: Statistical analysis of SO2 values obtained in the animal groups, for analytical methods and MRvF with different dictionaries. Significance evaluated at 5% with paired t-test.