Towards multi-scale personalized modeling of brain vasculature based on magnetic resonance image processing

Marek Kociński [1], Andrzej Materka [1], Andreas Deistung [2], Jürgen Reichenbach [2], Arvid Lundervold[3]
[1] Lodz University of Technology, Institute of Electronics, 90-924 Lodz, Poland
[2] Friedrich-Schiller University Jena, Institute for Diagnostic and Interventional Radiology, 07-747 Jena, Germany
[3] University of Bergen, The Department of Biomedicine, N-5020 Bergen, Norway
marek.kocinski@p.lodz.pl

Abstract - **A technique is proposed for personalized modeling of cerebral brain vasculature based on three-dimensional magnetic resonance images**. **High resolution ToF, QSM MR images were used to build 3D geometric models of arteries and veins. To make a next step towards modeling of the whole vascular system, a surface of gray matter was extracted from T1 weighted image. Then, within selected part of the cortex, a computer-synthesized blood vessels originating from nearby artery were built as mesoscopic part of the cerebral blood system. Limitations of the ToF and QSM-based approach to development of such a comprehensive model are pointed out and discussed.**

Keywords - **Multi-scale modeling; cerebral vasculature; blood vessel segmentation; subpixel accuracy**

I. INTRODUCTION

An accurate modeling of blood-vessel structures depicted in 3D raster images is a crucial issue in vascular disease diagnosis and treatment. Magnetic resonance imaging (MRI) include several modalities allowing one to acquire 3D raster images in which blood vessels are visualized. From many of related measurement sequences one can point out: phase contrast (PC), time-of-flight (ToF) [1], susceptibility weighted imaging (SWI) [2, 3], simultaneous ToF-SWI [4] for co-registered arterial and venous trees, and a relatively new quantitative susceptibility mapping (QSM) [5]. Using the image information about vasculature offers a possibility to create an accurate and comprehensive 3D geometrical model of arteries and veins for each individual patient, with personalized geometry and structure of blood vessels [6]. Computational modeling has also a great potential to simulate behaviors of cancers, elucidate regulatory mechanisms [7], and is usually less expensive than real-world experiments. A computer model to quantify oxygen advection in the microcirculation, tissue oxygen perfusion, and consumption in the human cortex was proposed by Linninger [8]. Personalized modeling and computer simulation can provide medical professionals a secure environment for investigation of the subject organism condition and trying different scenarios of treatment before the actual intervention. Using MRI as the input for modeling is an attractive option, as the images can be acquired without application of contrast agents.

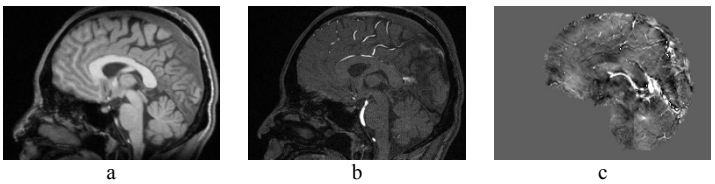
This work was supported by the Polish National Research Centre under Grant No. 2013/08/M/ST7/00943.

Various models of blood systems are reported in literature, but few of them deal with multi-scale ones [6, 9]. Some are intended to mimic behavior of thick vessels, and other account for phenomena that take place in capillary bed. This project is an attempt to building a personalized model, that consists of macro- and mesoscopic scale blood vessels. The ToF and QSM image data were used to reconstruct thick branches of, respectively, arterial and venous side of circulatory system. Based on T1 weighted image, the surface of gray matter was extracted. Finally, computer synthesized vascular trees to provide local blood supply to the neighboring cortex were appended a selected brain artery. Some of the inherent characteristics of the ToF and QSM techniques appeared to have a significant influence on modeling results. The actual vessel tree structure, as seen in these images, needs to be interpreted cautiously. This will be discussed later.

II. MATERIALAS AND METHODS

A. The Reference Images

A Time-of-Fligth (ToF), Quantitative susceptibility mapping (QSM) and T1 weighted 3D brain images were used in this study. Based on ToF and QSM data, 3D models of arterial and venous side of vascular system were build. T1 weighted MR data serve as basis for extraction of brain gray matter surface. The images were acquired for a healthy volunteer (approved by ethical committee of Friedrich Schiller University in Jena, Germany), using a 3T experimental MRI system. Three orthogonal cross-sections of these images are shown in Fig. 1.



a b c

Figure 1. Orthogonal cross-sections of a (a) T1 weighted (structural), (b) Time-of-Flight (artery), and (c) Quantitative Susceptibility Mapping (veins) images

The elongated bright regions represent blood vessels both in ToF (blood in motion) and QSM (voxel intensity is linearly proportional to the underlying tissue apparent magnetic susceptibility) data. T1 data depicts anatomical structure of the

brain. All image data consist of 346x448x319 cubical voxels (0.49x0.49x0.49 mm^3). The high resolution was obtained at the expense of long acquisition time (16 min.). The images were co-registered using a rigid body (affine) intra- and inter-modal brain image registration with FLIRT (FMRIB's Linear Image Registration Tool) [10, 11], Fig. 2.

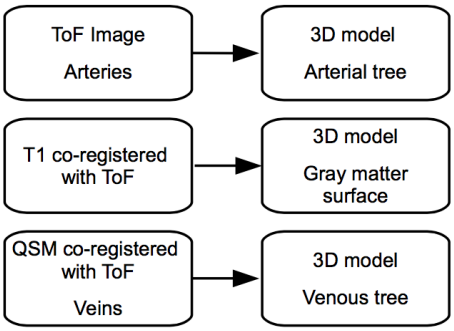


Figure 2.MR images processed in this study for geometric modeling of brain structures.

B. Building 3D geometrical models

A detailed image processing methodology and geometric modeling of vessel branches is described in [12, 13, 14]. In this Section, a general description will be provided, illustrated in Fig. 3.

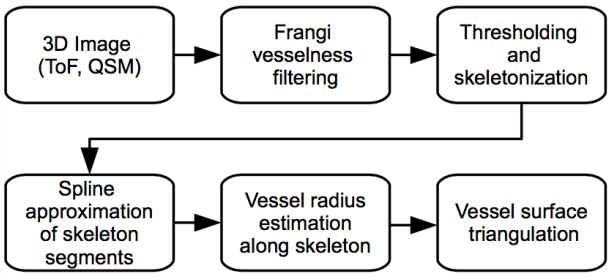
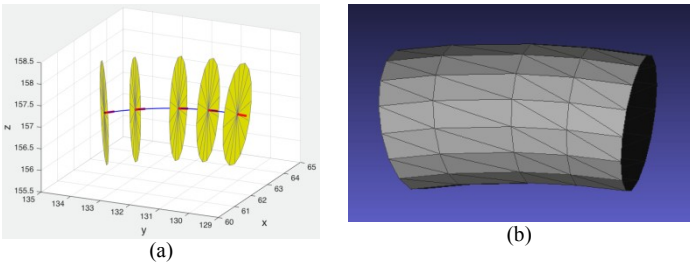


Figure 3. Image processing and modeling pipeline.

To segment arteries and veins, the ToF and QSM image intensities were scaled to range [0,1] and filtered with the use of Frangi vesselness filter [15]. Accounting for varying radius of the arteries along their length, the filtering was done for various widths of the Gaussian filtering kernel. The maximum over these responses was assigned to vesselness filter output. Next, the resulting image was thresholded and skeletons of the binary objects were extracted with the use of ITK library [16]. Each continuous skeleton segment (between blood vessels bifurcations), was approximated by a smooth spline functions. For each skeleton point, a circle was defined on the plane perpendicular to the tangent vector at this point. The circle circumference was then divided into a number of segments (e.g. 16) The segments of neighboring skeleton points are joined by rectangular, triangulated patches and stored to STL file. The final step of this process is presented in Fig. 4.



(a) (b)

Figure 4. Branch sidewall triangulation (a) centerline in blue, tangent vectors in red, circles in yellow, (b) wireframe model (Meshlab®).

To segment anatomical brain structure and obtain surface of brain gray matter, the ITK-SNAP software [17] was used. The presegmentation mode was set as thresholding with both lower and upper thresholds. After segmentation, a surface of gray matter was stored in STL file.

C. Simulation of vascular tree growth

In this study, we adopted vascular tree growth algorithm proposed by Karch [18,8]. This approach is based on some physical laws such as mass preservation principle (1), Poiseuille law (2) and split law (3) [19].

$$Q = Q_l + Q_r \quad (1)$$

$$\Delta P = Q\frac{8\eta L}{\pi R^4} \quad (2)$$

$$R_p^\gamma = R_l^\gamma + R_p^\gamma \quad (3)$$

where:

- Q- blood flow,
- ΔP - pressure drop in a vessel segment,
- η - blood viscosity,
- L, R - length and radius of the vessel segment, respectively,
- p, l, r – indexes denoting parent, left and right child branch,
- γ - bifurcation coefficient, equal to 3 in this study.

The algorithm relies on successive addition of output branches of the tree inside a given 3D volume which represents the region of blood delivery. The newly chosen point is connected to a midpoint of the nearest branch within the whole tree. The simulation is stopped when a specified number of branches is added. Initially, all simulation parameters were set as in [18], except for the shape of the tree-growth regions (ellipsoidal instead of spherical).

III. RESULTS

The above described methods designed to extract blood vessels and build their geometric triangulated surface was implemented in Matlab®. They were applied to 3D ToF and QSM images, Fig. 5a. For visualization of 3D models stored in STL files a Paraview ® software was used [20]. In Fig. 5b, the geometrically modeled artery and vein trees are displayed over the surface of gray matter cortex segmented out of the T1 weighted image of the same subject.

978-1-5090-6344-4/17/$31.00 ©2017 IEEE

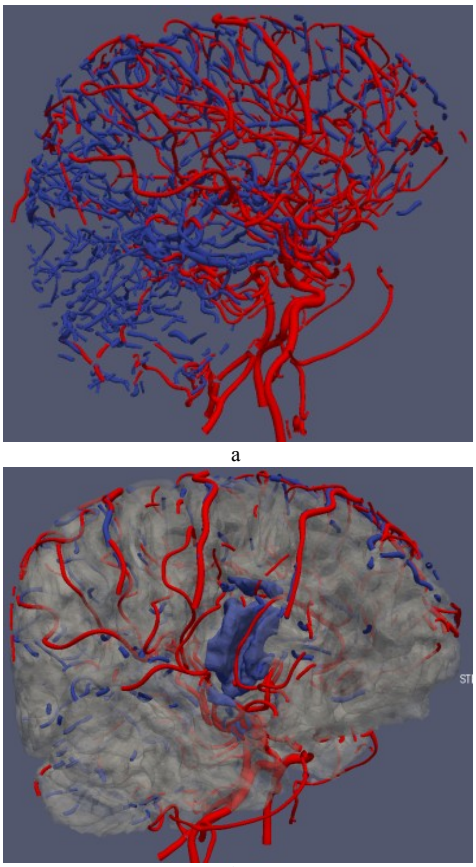


Figure 5. Visualization of (a) geometric models of tubular sections of the arterial (red) and venous (blue) trees, extracted respectively from ToF and QSM images, (b) the models of arterial and venous trees superimposed over the surface of gray matter (right hemisphere).

A closer view (Fig. 6) on the two vessel trees shows – in quantity and in quality – that the vessel information contained in ToF and QSM of a subject is the same, to a significant degree. Namely, segments of alleged arteries and veins overlap over part of their lumen. This effect is especially prominent in the top region of the head. Then the assumption of having independent sources of information about the structure of artery and vein trees had to be abandoned. Apparently, the ToF predominantly displays arteries and QSM predominantly represents the veins.

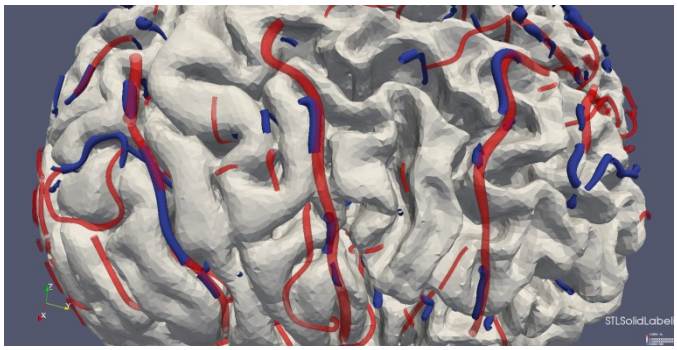


Figure 6. Models of tubular objects found in ToF (red) and QSM (blue) images (right hemisphere)

In the next step, a cortex fissure located at the temporal region (marked in light-blue in Fig. 5b), with an artery passing between its walls, was chosen to simulate the growth of mesoscale vessel trees, from this single artery to capillaries embedded in gray and white matter. There is little information about the draining veins in the QSM data; the tubular segments are generally much shorter than the segments of arteries. Therefore, the growth of the mesoscale draining tree of venules was not simulated out in this project.

An example of simulated trees is shown in Fig. 7. The mesoscopic scale vessel growth simulation was done several times using different parameters [8, 21, 22]. In all cases, plausible synthesized trees were obtained, illustrating feasibility of this approach.

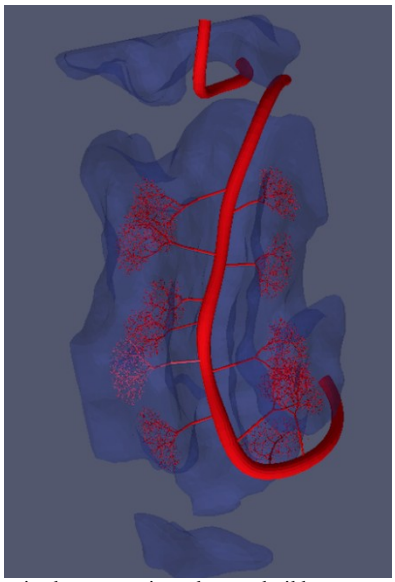


Figure 7. Synthesized mesoscopic scale trees build upon cortex penetrating arterioles which bifurcate from the segmented selected brain artery.

IV. Discussion

In Fig. 8, a maximum intensity projection of the ToF image is presented. Regular image intensity variation along the vertical direction is visible. The most popular sequence used for ToF image acquisition is MOTSA (multiple overlapping thin slab acquisition) [23]. The MOTSA-originated effect of signal intensity variation in the direction perpendicular to the slabs, is a characteristic artefact in ToF images.

The ToF MR imaging uses a short echo time and flow compensation to make regions of flowing blood much brighter than stationary tissue. As flowing blood enters the area being imaged, it has "seen" a limited number of excitation pulses so it is not saturated. This gives it a much higher signal than the saturated stationary tissue. In short, to obtain an artefact-free image for a given slab, spin saturation in the slab above it is needed. There is no slab above the top one in the head, thus

978-1-5090-6344-4/17/$31.00 ©2017 IEEE

the flow of blood in top veins produces bright response in the ToF image. In Fig. 8, as indicated by arrows in the top part of the head, at least two veins can be seen in this ToF image, the superior sagittal sinus and superior cerebral sinus. What is more, an arrow at the lower right part of the image in Fig. 8 shows a sudden disappearance of the vessel depicted above the arrows' head, presumably at a slab boundary.

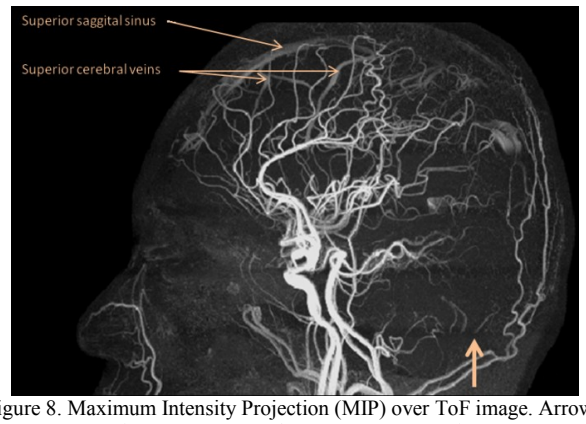


Figure 8. Maximum Intensity Projection (MIP) over ToF image. Arrows points on structures that can represents veins.

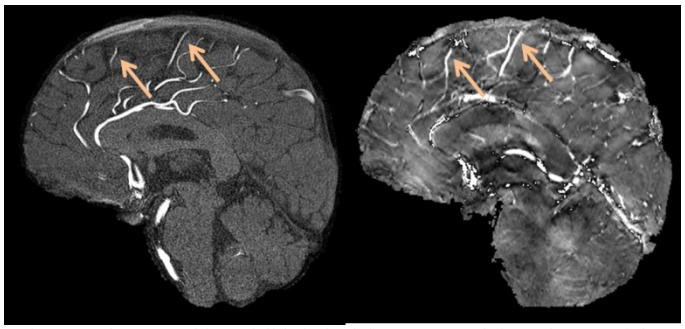


Figure 9 The same object visible in both images ToF (left) and QSM (right)

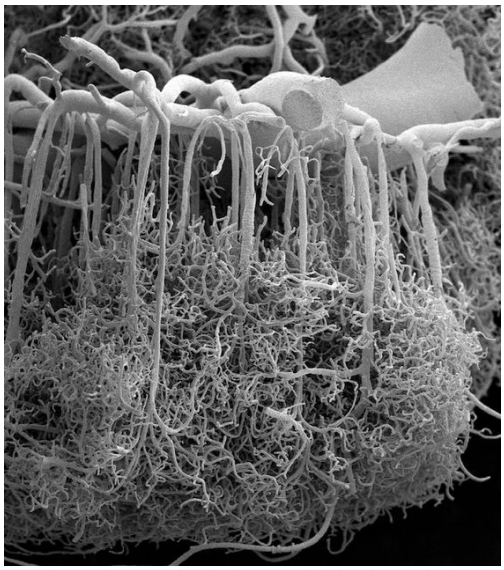


Figure 10. A photomicrograph of microscopic blood vessels from "Portrets of the Mind", 2010, pp. 216-217. Reproduced with a kind permission of the authors: Alfonso Rodríguez-Baeza and Marisa Ortega-Sánchez from Department of Morphological Sciences, Medicine Faculty at the Universitat Autònoma de Barcelona, Spain.

In Fig. 9, the arrows apparently indicate the same objects present in both, ToF and QSM images. This further supports the observation about the overlap of the content of this two MR image types.

A microphotograph of mezoscopic scale vessels taken from a real brain, Fig. 10, show some similarities and some differences to the synthesized one presented in Fig. 7. Both structures feature a thick feeding artery and straight cortex penetrating branches. The thinner simulated branches in Fig. 7 are simplified versions of highly curved real-life ones. In final implementations of the holistic model, however, the space between the straight simulated branches will be filled with a small-eyelet mesh of highly connected capillary branches [8, 24]. Such a network structure will then regain its resemblance to natural capillary bed fed and drained by, respectively, arterioles and venules [25].

V. CONCLUSIONS

Apparently, the ToF and QSM images can not be interpreted as representing only arteries and veins, respectively, at least for the aim of geometric modeling of macroscopic blood vessel trees. Further careful analysis is needed to resolve the issue of classifying the voxels as belonging to artery or to vein region. Another cause of misinterpretation of arteries and veins might be in co-registration of the images. This needs further investigation. Regardless of this ambiguity, the mutual localization between the segmented gray matter and tubular vessel branches both show very good accuracy

Independent information about brain blood perfusion and microscopic structure (mean vessel density and radius) is needed to fully characterize the spatial distribution of the blood flow in the cortex tissue. This will provide quantitative data about the physical environment to which the blood is distributed by the synthesized branches, and help simulate a plausible equivalent personalized vessels' model. It seems that for an MRI-based holistic modeling of the brain blood vessel system, one will need T1, ToF, PC, QSM/SWI and ASL imaging.

REFERENCES

[1] G. Laub, M. Drobnitzky, "Magnetic Resonance Angiography Techniques", electromedica 66,vol 2, pp. 68-75, 1998,

[2] E.M. Haacke, J. Tang, J. Neelavalli, and Y.C.N. Cheng, "Susceptibility mapping as a means to visualize veins and quantify oxygen saturation", Journal of Magnetic Resonance Imaging, vol. 32, pp. 663-676, 2010.

[3] E.M. Haacke and J.R. Reichenbach, Susceptibility Weighted Imaging in MRI, Wiley, 2011

[4] A. Deistung, E. Dittrich, J. Sedlacik, A. Rauscher, and J.R. Reichenbach, "ToF-SWI: Simultaneous Time of Flight and Fully Flow Compensated Susceptibility Weighted Imaging", Journal of Magnetic Resonance Imaging, vol. 29, pp. 1478-1484, 2009.

[5] J. R. Reichenbach, F. Schweser, B. Serres, A. Deistung, "Quantitative Susceptibility Mapping: Concepts and Applications", Clinical Neuroradiology, vol. 25, supplement 2, pp. 225-230, 2015

[6] A. Quarterioni, "Modeling the Cardiovascular System – A Mathematical Adventure: Part I", SIAM News, vol. 34(5), pp. 1-3, 2001.

978-1-5090-6344-4/17/$31.00 ©2017 IEEE

[7] Z. Wang, P. K. Maini, "Editorial Special Section on Multiscale Cancer Modeling", IEEE Transactions on Biomedical Engineering, vol. 64, no. 3, 2017

[8] A. A. Linninger, I. G. Gould, T. Marrinan, C.-Y. Hsu, M. Chojecki, A. Alaraj, "Cerebral Microcirculation and Oxygen Tension in the Human Secondary Cortex", Annals of Biomedican Engineeing, vol. 41, no. 11, 2013.

[9] L. Grinberg, T. Anor, J. R. Madsen, A. Yakhot, G. E. Karniadakis, "Large-Scale Simulation of the Human Arterial Tree", Clicical and Experimental Pharmacology and Physiology, vol. 36, pp. 194-205, 2009.

[10] M. Jenkinson, P. Bannister, J. M. Brady, S. M. Smith, "Improved Optimisation for the Robust and Accurate Linear Registration and Motion Correction of Brain Images", NeuroImage, 17(2), pp. 825-841, 2002

[11] D. N. Greve, B. Fischl, "Accurate and robust brain image alignment using boundary-based registration", NeuroImage, 48(1), pp.63-72, 2009

[12] J. Blumenfeld, M. Kociński, and A. Materka, "A centerline-based algorithm for estimation of blood vessels radii from 3D raster images", IEEE SPA 2015, Poznań, Sept. 2015, pp. 38-43.

[13] A. Materka, M. Kociński, J. Blumenfeld, A. Klepaczko, A. Deistung, J. Reichenbach, "Automated Modeling of Tubular Blood Vessels in 3D MR Angiography Images", IEEE 9th Int. Symp. On Image and Signal Processing and Analysis, Sept. 2015, Zagreb, Croatia, pp. 56-61.

[14] M. Kociński, A. Materka, A. Deistung, J. Reichenbach, "Centerline-based surface modeling of blood-vessel trees in cerebral 3D MRA", IEEE SPA 2016, Poznań, Poland, pp. 85-90.

[15] A.F. Frangi, W.J. Niessen, P.J. Nederkoorn, J. Bakker, W.P.T.M. Mali, and M. Viergever, "Quantitative analysis of vascular morphology from 3D MR angiograms: in vitro and in vivo results", Magnetic Resonance in Medicine, vol. 45, pp. 311-322, 2001.

[16] http://itk.org, accessed on March. 5, 2017.

[17] P. A. Yushkevich, J. Piven, H. C. Hazlett, R. G. Smith, S. Ho, J. C. Gee, G. Gerig, "User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability", Neuroimage, 31(3), pp. 1116-288, 2006.

[18] R. Karch, F. Neumann, M. Neumann, W. Schreinger, "A three-dimensional model for arterial tree representation, generated by constrainded constructive optimization", Computers in Biology and Medicine, vol. 29, pp. 19-38, 1999.

[19] M. Kociński, A. Klepaczko, A. Materka, M. Chekenya, A. Lundervold, „3D image texture analysis of simulated and real-world vascular trees", Computer methods and programs in biomedicine, vol. 107, pp.140-154, 2012.

[20] www.paraview.org, accessed on March 5, 2017

[21] K. B. Chandran, S. E. Rittgers, A. P. Yoganathan, Biofluid Mechanics, The Human Circulation, 2nd Ed., CRC Press, Boca Raton, 2012.

[22] Y. C. Fung, Biodynamics. Circulation, Springer, New York, 1984.

[23] D. L. Parker, C. Yuan, D. D. Bladder, "MR angiography by multiple thin slab 3D acquisition", Megnetic Resonance in Medicine, vol. 17, pp. 434-451, 1991.

[24] J. A. Grogan, B. Markelc, A. J. Connor, R. J. Muschel, J. M. Pitt-Francis, P. K. Maini, H. M. Byrne, "Predicting the Influence of Microvscular Structure on Tumor Response to Radiography", IEEE Transactions on Biomedical Engineering, vol. 64, No. 3, pp. 504-511, 2017.

[25] R. Turner, "How Much Cortex Can a Vein Drain? Downstream Dilution of Activation-Related Cerebral Blood Oxygenation Changes", NeuroImage vol. 16, pp. 1062-1067, 2002.

978-1-5090-6344-4/17/$31.00 ©2017 IEEE