Measurement of reduced lymphatic flow velocity under conditions of obstructed lymphatic flow using spin labeling approach

Swati Rane1, Paula Donahue2,3, Theodoric Towe1, Sheila Ridner4, John C Gore1,4, Michael Chappell5, and Manus J Donahue6,8
1VUH, Radiology and Radiological Sciences, Vanderbilt University, Nashville, TN, United States, 2Vanderbilt Dayani Center for Health and Wellness, Vanderbilt University Med. Center, Nashville, TN, United States, 3Vanderbilt Physical Medicine and Rehabilitation, Vanderbilt University Med. Center, Nashville, TN, United States, 4School Of Nursing, Vanderbilt University, Nashville, TN, United States, 5Biomedical Engineering, Vanderbilt University, Nashville, TN, United States, 6Institute of Biomedical Engineering, University of Oxford, Oxford, OX, United Kingdom, 7John Radcliffe Hospital, Oxford Centre for Functional MRI of the Brain, Oxford, OX, United Kingdom, 8Psychiatry, Vanderbilt University, Nashville, TN, United States

TARGET AUDIENCE: Breast oncologists and imaging physicists with an interest in novel spin labeling methodology

PURPOSE: The purpose of this work is to (i) assess the sensitivity of a newly proposed lymphatic spin labeling approach for detecting variability in lymphatic flow to axillary lymph nodes, (ii) outline a quantitative framework for the interpretation of flow using this approach, and (iii) assess clinical potential in a cohort of advanced-stage lymphedema patients. Lymphedema is a chronic, debilitating disease caused by lymphatic flow obstruction and affects nearly 89% of breast cancer survivors undergoing mastectomy with axillary lymph node removal. However, there are currently no MRI procedures that can be used to stratify lymphedema risk or to evaluate changes in the lymphatic system in response to therapy. Very recently, it was shown that spin labeling approaches, commonly applied to measure blood flow,1 can be adapted to quantify lymphatic flow as well.2 However, significant gaps remain in our knowledge regarding (i) to what extent measurements are indicative of lymphatic flow, (ii) how measurements adjust in response to obstructed lymphatic flow labeling, and (iii) how models should be adapted to allow for lymphatic flow quantification. This work addresses these questions by extending the lymphatic spin labeling approach to measure lymphatic flow under manipulated flow obstruction using a pressure cuff, in Stage II lymphedema patients with unilateral lymph node removal, and results are interpreted in the context of an adapted kinetic model.

METHODS: Simulations. Simulations were performed to visualize how the shape and behavior of kinetic curves describing inflow of lymphatic fluid to axillary lymph nodes vary compared to more common perfusion kinetic curves obtained from arterial spin labeling experiments. Simulations were performed using measured lymphatic T2=3100 ms at 3T and assuming the difference magnetization (ΔM) is proportional to the product of the flow, equilibrium magnetization, and convolution of a transit time and T1-dependent input function and residue function describing flow into a simple, impermeable compartment with fixed residence time (Fig. 1). Experiment. All volunteers (n=6) provided informed consent in accordance with the local IRB and were scanned at 3T using a two channel parallel transmit body coil in conjunction with a 16-channel torso receive coil. Lymphatic spin labeling was assessed in three right-handed healthy volunteers and three Stage II lymphedema patients using (i) diffusion-weighted imaging with body signal suppression, DWIBS (TR/TE/TI=80/37/50 and b=800s/mm2), spatial resolution=3x3x5 mm3, (ii) adiabatic pulsed spin labeling scan (spatial resolution=3x3x5 mm3), SPIR fat suppression, inversion time, TI = 500, 1500, 2500, 3500, 4000–10,000 ms (500 ms intervals), averages=8, and single-shot gradient echo EPI readout. To simulate impaired flow conditions, lymphatic flow was obstructed in the left arm of healthy subjects, using a blood pressure cuff with pressure maintained at 60 mm Hg. Blood pressure was recorded prior to imaging to ensure that the diastolic blood pressure > 60 mmHg. Analysis: Lymphatic flow curves (ΔM) were compared in left and right axillary nodes. The DWIBS scan was used to locate the lymph nodes and distinguish them from blood vessels. This protocol was a free breathing protocol, so respiratory motion in the chest cavity caused significant displacement of the nodes and distortion of the node shape. Motion correction was therefore performed and measurements of lymph node displacement over the duration of the experiment were measured and accounted for in post-processing. Signal to noise ratio (SNR) was calculated across all acquisitions for each TI. Unlike blood flow, lymphatic flow over several mm may take several seconds. To account for this, SNR measurements were recorded at each TI and ΔM values where SNR<0 were set to 0.

RESULTS AND DISCUSSION: Fig. 1 shows simulated kinetic curves for lymph flow into axilla; note the steep rise and fall of (ΔM) in lymph nodes for varying arrival time and long node residence time=1.6s. Note that the kinetic curves rise and fall quickly, analogous to the macrovascular component of signal in blood water spin labeling models.

CONCLUSION: We extended preliminary lymphedema spin labeling studies to demonstrate sensitivity of this approach for measuring lymphatic kinetics under conditions of known lymphatic flow obstruction using both a pressure cuff to manipulate lymph flow in healthy volunteers and knowledge of physiological impairment in patients with Stage II lymphedema. Furthermore, algorithms have been developed that account for lymph node motion and flow quantification. Further development of this approach may expand abilities to assess lymphedema risk and patient response to therapy in this highly prevalent yet understudied condition.