Renal Perfusion by ASL is Associated with GFR in Long-term Survivors of Wilms' Tumor

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TARGET AUDIENCE: MR scientists and clinicians who are interested in MRI-based assessment of renal function.

PURPOSE: Wilms' tumor is the most common pediatric renal malignancy with an incidence of 1 in 10,000 children in the United States.[1] Survival rates rose to 85% with advanced surgical techniques, radiation, and chemotherapy leading to a growing population of Wilms' tumor survivors. As part of a larger study that investigates the effects of radiation therapy on the renal function of long-term survivors of Wilms' tumor, this work investigates renal blood flow [i.e., cortical blood flow (CBF) and medullary blood flow (MBF)] assuming that crucial renal functions such as blood filtration and the regulation of the glomerular filtration rate (GFR) are linked to renal blood flow. Specifically, we investigated and compared CBF and MBF values measured by Arterial Spin Labeling (ASL) in Wilms' tumor survivors and healthy volunteers. We also tested the relationship between renal blood flow and GFR obtained by 24-hour urine creatinine clearance (CrCl) tests in these survivors.

METHODS: MRI and GFR data of 35 long-term survivors of unilateral Wilms' tumor [20 female/15 male; mean age 32 years (range 19-48 years); mean time after first diagnosis 28.6 years] were analyzed. All survivors underwent nephrectomy of the affected kidney and received chemotherapy as part of their initial treatment; a subset of 18 survivors also received radiation therapy. In addition, 4 healthy volunteers (3 female/1 male; ages 21, 21, 22, & 42 years) were examined as controls by MRI only. Both studies are IRB approved and written consent was obtained from all participants prior to the exam. Renal perfusion measurements were acquired in oblique sagittal slice position through the long axis of the kidney on a 1.5T Siemens Avanto using Q2WISE-ASL[2]. Q2WISE used a FAIR True-FISP acquisition scheme with the following parameters: TE 1.88ms, bandwidth 606Hz/Pixel, flip angle 70°, matrix 128x96, FOV (320–350mm)[2], imaging/tagging slice thickness 8/22mm, TR 4s, TI1 0.7s, TI2 1.3s, and number of measurements 40 (20 pairs). The acquired images were realigned on kidney masks. Quantitative perfusion maps were computed on a voxel-by-voxel basis from the magnetization ΔM using a tissue/blood partition coefficient λ of 0.9, and an inversion efficiency of 0.95, and blood T1 was set to 1.318s.[3] Renal cortex and medulla regions of interests (ROIs) were segmented on mean control images using ImageJ's (http://imagej.nih.gov/ij/) multi-threshold segmentation function. ROIs were finally reviewed and manually adjusted to ensure selections match respective locations on the perfusion map. Additionally, urine was collected for 24 hours and GFR was determined by the amount of creatinine in the total urine volume.[4] No GFR test was performed in the volunteers. For the correlation study, MBF and CBF were normalized to mean renal parenchymal volume $meanV_{paren}$ by $nCBF=CBF*V_{paren}/meanV_{paren}$ and $nMBF=MBF*V_{paren}/meanV_{paren}$, and absolute GFR was used. Parenchymal volume V_{paren} was measured by manual segmentation on multislice T1-weighted images using Amira (www.amira.com).

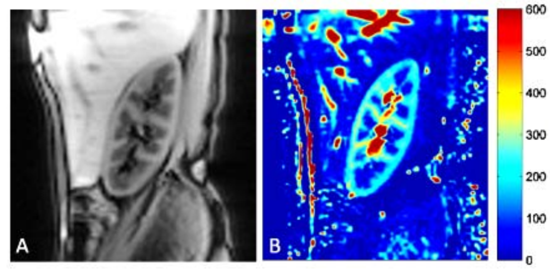

Figure 1. Mean ASL control image (A) and perfusion map (B) of a Wilms' survivor.

RESULTS: A mean ASL control image and renal perfusion map for a typical survivor is shown in Fig. 1. Renal cortex, medulla and pelvic structures are well delineated in these images. Fig. 2 shows the mean and standard deviation of CBF, MBF and GFR values for survivors with and without radiotherapy, and for the volunteers. There are no significant differences in CBF, MBF and GFR values ($P > 0.26$) between survivors who had received or had not received radiotherapy. However, the mean MBF value of the survivors is approximately 58% higher than that of the volunteers ($P < 0.0005$). No significant difference was observed for CBF in all cohorts. The measured mean parenchymal volume $meanV_{paren}$ was 245ml. Good correlation was observed between absolute GFR and nMBF or GFR and nCBF with R^2 of 0.66 and 0.52, respectively (see Fig. 3).

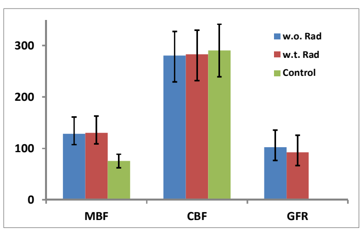

Figure 2. MBF, CBF (in ml/100g/min) and GFR (in ml/min/1.73m^2) values for the three cohorts.

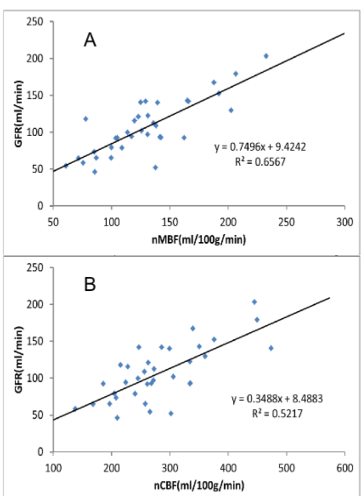

Figure 3. Correlations between GFR and nMBF (A) and between GFR and nMBF.

DISCUSSION: To our knowledge this is the first study to investigate renal perfusion by ASL in long-term survivors of Wilms' tumor. We found no significant difference between treatment groups in any tested functional parameter, i.e. CBF, MBF, and GFR. Previously, a significant difference in GFR was reported for irradiated and non-irradiated short term (1 year) survivors.[5] However, this difference was not observed in long term (8.8 years) survivors by other investigators,[6] which is in accordance with our findings in very long term (28.6 years) survivors. This may suggest that radiation treatment for Wilms' tumor has only a short-term effect on renal function. Our mean MBF obtained in healthy subjects is 75±13 ml/100g/min. This is well within the range of reported ASL values for healthy subjects (33-120 ml/100g/min).[7-9] CBF of our volunteers is 290±13ml/100g/min, which is also well within the range of reported values (190-378ml/100g/min).[2,9] This suggests that the applied ASL technique is robust and appropriate for renal perfusion quantification. When comparing CBF and MBF of healthy volunteers and Wilms' survivors, we found no significant difference in CBF, but a 58% higher MBF in the survivors. We suspect this high medullary blood flow may be associated with compensatory renal hypertrophy to maintain function with a single kidney. However, this observation needs to be confirmed and the hypothesis tested in a larger cohort with age matched healthy control subjects. In addition, our analysis shows that both normalized renal perfusion measures, nCBF and nMBF, are associated with absolute GFR. Hence, we believe that there may be a future role for ASL perfusion as surrogate marker of renal filtration and that ASL could therefore be used as a screening method for any population with impaired renal function.

CONCLUSION: ASL MRI provides a non-invasive way to assess renal function with the additional benefit of regional information. No significant differences were observed between irradiated and non-irradiated survivors in any measured renal function parameter. MBF values of the Wilms' tumor survivors are significantly higher than those of healthy volunteers. Normalized cortical and medullary blood flow is well correlated with absolute GFR.

REFERENCES: 1. Ehrlich PF, et al, Expert Rev. Anticancer Therapy 2001; 1:555-564. 2. Song R. et al, MRM 2012; 67:1127-32. 3. Guo J. et al. Med. Phys. 2005; 32:1083-93. 4. Waller DG, et al Postgraduate Med J. 1991;67:42-46. 5. de Graaf, S. et al, Eur J. Cancer 1996; 32:465-69. 6. Bailey S, et al. Br J Cancer 2002; 87:1092-8. 7. Marquez E, et al. J Nephrol 2012; 25:1075-80. 8. Artz N et al. MRI 2011; 29:74–82. 9. Martirosian P et al. MRM 2004;51:353-61.