Assessment of Renal Function by ASL in Wilms Tumor Survivors

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Introduction: Wilms’ tumor is the most common pediatric renal malignancy and occurs in 1 in 10,000 children with 500 cases diagnosed in the United States annually (1). Although Wilms’ tumor was largely incurable before the development of systemic chemotherapy, over 85% of children treated in the current decade are expected to be long-term survivors. Despite the growing population of Wilms’ tumor survivors, little is known about the long-term consequences of the prescribed treatments which in unilateral Wilms’ tumor often includes nephrectomy of the affected kidney and whole abdominal radiation in the past. The prevalence of renal dysfunction in long-term survivors of unilateral Wilms’ tumor who have undergone nephrectomy is not known; neither is the role that abdominal radiotherapy (RT) plays in influencing renal function and neither the adaptive response to nephrectomy. Evidence of clinically significant renal impairment would suggest the need for further studies to identify underlying risk factors and design therapeutic interventions. Aim of this work was to assess renal function in 23 survivors of unilateral Wilms’ tumor by using functional renal MRI. As renal blood flow crucially affects kidney functions such as blood filtration and the regulation of the glomerular filtration rate (GFR), we focused on the measurement of renal blood flow (RBF) by arterial spin labeling (ASL), and the correlation of our results with GFR as measured by creatinine clearance (CrCl) tests (2).

Methods: Twenty-three long-term survivors of unilateral Wilms’ tumor (15 female, 8 male; age range: 30-48 years) were investigated in two study groups based upon therapy received: (A) no radiotherapy (N=11), and (B) whole abdominal radiotherapy (N=12). All patients underwent nephrectomy, and thus have only one kidney, and received no nephrotoxic chemotherapy. The study protocol was approved by our Institutional Review Board and written consent was obtained from all patients. GFR was estimated by using the 24 hour urine CrCl test (2): urine was collected for 24 hours to measure the amount of creatinine in the urine and the total urine volume; plasma creatinine was measured from a collected blood sample. Renal blood flow rates (RBF) were measured by Q2WISE (QUIPSS II with window-sliding saturation sequence) ASL (3) on a oblique sagittal slice through the long axis of the kidney using a clinical 1.5 MR scanner (Avanto, Siemens, Erlangen, Germany). Q2WISE was incorporated with a FAIR (Flow-sensitive alternating inversion recovery) True-FISP (fast imaging with steady-state precession) acquisition scheme. MRI measurement parameters were as follows: TE = 1.88ms; acquisition bandwidth = 606Hz/Pixel; flip angle = 70°; matrix=128 x 96; FOV = 320 – 350mm; imaging slice thickness/tagging slice thickness = 8/22mm; TR = 4 s, and measurements = 40 (20 pairs). A centric-reordered k-space acquisition scheme was applied. A variable flip angle preparation of 10 RF pulses was implemented to minimize transient signal oscillations. TTI = 1.3 s and T1 = 0.7 s. The acquired images were realigned using a robust estimation method on kidney masks (3-4). 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. Cortical T1 values of each survivor’s kidney were measured by using 1T weighted Snapshot FLASH imaging (5) with a flip angle of 5°, TE=1.33 ms, TR=10 s, and ΔTI=255 ms. Regions of interest were manually drawn on the cortex of kidneys.

Results: A renal perfusion map for a patient obtained with Q2WISE is shown in Fig. 1. The measured absolute GFR values were 105±32 ml/min for the non-radiotherapy group, and 88±26 ml/min for the radiotherapy group. No significant difference was found between the two groups by using a two-tailed Student’s t-test (df=21, t=1.39, P=0.17). The cortical RBF obtained with Q2WISE were 289±66 ml/100g/min for the non-radiotherapy group, and 285±89 ml/100g/min for the radiotherapy group. There was no significant difference between the two groups by using the two-tailed Student’s t-test (df=21, t=0.13, P=0.89). The correlation between absolute GFR (not normalized to human body area) and RBF*V (renal parenchyma volume, V, was included because GFR is proportional to V) was examined. Good correlation was observed in the radiation survivor group with a Pearson’s correlation coefficient r = 0.78 as shown in Fig. 2. The correlations were also examined by group: Fig. 3a and 3b show the correlations for the radiotherapy and non-radiotherapy groups, respectively. It can be seen that the correlation in the non-radiotherapy group (r=0.89) was better than that in the radiotherapy group (r=0.68).

Discussion: Renal function can be non-invasively examined by measuring perfusion values with the ASL method. Since no contrast agents are needed, ASL can be applied to all patients, including patients with known renal impairment. Another advantage of ASL is that the test is fast and repeatable. Our measured RBF in Wilms’ tumor survivors correlated well with GFR values, which may reflect the fact that the filtration depends on the renal blood flow. However, a weaker correlation between GFR and RBF was observed in the radiotherapy group. Due to radiation damage, these patients may have an increased probability for unstable renal function, which may cause the measured GFR values be less reliable as reported previously (2). A weaker correlation between GFR and RBF may result. We therefore conclude ASL may be an even better indicator for function/impairment in patients with unstable renal conditions.