Introduction
Renal cell carcinoma (RCC) is the most common solid tumor of the kidney, and it is often detected incidentally owing to the increased use of diagnostic imaging devices (1). Nephrectomy is a surgical procedure that removes a kidney infected with renal malignancy, and it has been considered the standard treatment for localized non-metastatic RCC (2). However, the progression of renal insufficiency may become aggravated after nephrectomy. When a patient is scheduled for nephrectomy, the maintenance of renal function should be highly prioritized to avoid the risk of renal insufficiency after surgery. Serial assessment of the contralateral kidney could provide information regarding disease progression or renal outcomes. Therefore, we performed a longitudinal study with MRI to investigate the adaptive responses of the contralateral kidney in patients with RCC after radical nephrectomy (RN).

Materials and Methods
A total of 11 patients who were scheduled to receive laparoscopic RN of a functioning kidney with RCC were included as the RN group. Fifteen patients with unilateral adrenal tumors who were scheduled to receive laparoscopic adrenalectomy were recruited as the control group. T2-weighted (T2W) imaging and dynamic contrast-enhanced (DCE) imaging were performed to estimate the renal volume and renal blood flow (RBF) of the contralateral kidney on a 3T MR system (Siemens, Erlangen, Germany). After scout imaging, multiple coronal slices were acquired using a T2W half Fourier single-shot turbo spin-echo pulse sequence (TR/TE/FA=2s/91ms/150°, matrix=320x256, echo-train length=256, slice thickness=6mm, spatial resolution=1.12mm). After the bolus injection of 0.0125mmole/kg of Gd-DTPA, DCE images were acquired using a non-selective saturation-recovery turbo fast low-angle shot pulse sequence (TR/TE/FA=1.08ms/0.98ms/10°, matrix=192x172, slice thickness=8mm, spatial resolution=1.98mm, GRAPPA=2) at two coronal slices, placed at middle section of the contralateral kidney, and one axial slice located at the level of aortic orifice of the renal artery to the contralateral kidney. For each slice, a time series of 80 images was acquired with a temporal resolution of 834ms. All the patients underwent serial MRI studies; the first study was performed before the surgery, and the subsequent 3 studies were performed at 1 week, 1 month and 3 months after the surgery. At the time of the MRI studies, the patients’ serum creatinine levels were examined to determine the estimated glomerular filtration rate (eGFR) using a Cockcroft-Gault calculator (3). From the coronal T2W images, the renal contours were manually traced to outline a region of interest (ROI) of the contralateral kidney. The area enclosed by each ROI of the kidney was computed for each level. The renal volume was measured by Simpson’s rule, which computes the sum of the areas of the corresponding levels multiplied by the slice thickness. With DCE data, RBF was computed by [C(t) - deconv. Ca(t)]/eGFR, where C(t) and Ca(t) were the concentration-time curves of tissue and the abdominal aorta, respectively, and C(t) = log(S(t)/S0)/TE, where S0 was the signal before the arrival of contrast agent. Block-circulant deconvolution (4) was adopted for its insensitivity to the arrival timing of bolus. Continuous variables were expressed as the means and 95% confidential interval (CI), and categorical variables were expressed as percentages. Group differences in clinical characteristics, pre-surgical eGFR, RBF and renal volume were tested for significance by the Mann-Whitney non-parametric U test for comparison of the medians between the groups. The paired comparisons of the changes in eGFR, RBF and renal volume were tested using Wilcoxon’s non-parametric signed-rank test. Linear regression analysis was used to evaluate the correlation between changes in RBF and changes in renal volume before and after surgery. A value of p < 0.05 was considered significant.

Results
In the RN group, eGFR was significantly decreased at 1 week and 1 month after surgery by 14.9% (p = 0.049) and 21.0% (p = 0.027), respectively. eGFR then decreased to the pre-surgical level at 3 months. The RBF of the contralateral kidney showed a significant increase at 1 week (2.78 ml/min/g, 95%CI 2.16-3.40, p = 0.002) and 1 month (2.65 ml/min/g, 95%CI 2.08-3.22, p = 0.002) after surgery, compared to the pre-surgical values (1.94 ml/min/g, 95%CI 1.53-2.35), and it returned to pre-surgical levels at 3 months (2.11 ml/min/g, 95%CI 1.62-2.60, p = 0.432). Comparing the renal volume before and after surgery at 3 months, the volume of the contralateral kidney increased significantly in the RN group (198 ml, 95%CI 137-253 vs. 329 ml, 95%CI 211-447, p < 0.001). The change in renal volume at 3 months was significantly correlated with the change in RBF at 1 week versus baseline (r = 0.609, p = 0.047) and the change in RBF at 1 week versus 3 months (r = -0.706, p = 0.015)(Fig 1). In the Control group, there were no significant interval changes in eGFR, RBF or renal volume, nor any significant correlations between the changes in RBF and renal volume.

Conclusion
Adaptive responses of the contralateral kidney after radical nephrectomy are essential to compensate for the loss of renal function. In this study we used MRI-derived RBF and renal volume to evaluate the adaptive responses. Our results indicate that radical nephrectomy in patients with RCC results in an early increase in RBF of the contralateral kidney. At 3 months, the patients showed normalization of the RBF, accompanied by compensatory renal hypertrophy. In patients with reduced renal mass, an early increase in RBF is associated with late renal hypertrophy. Therefore, given healthy conditions of the kidneys at baseline, we might be able to predict the late renal function of the contralateral kidney based on its early response to RBF.

References

Fig 1. Scatter plots of the change in renal blood flow (RBF) and the change in renal volume obtained from patients with radical nephrectomy (BS, baseline; 1-WK, 1 week; 3-MO, 3 months).