

**Measurement of renal cortical thickness using non-contrast-enhanced steady-state  
free precession MRI with spatially selective IR pulse:  
Association with renal function**

## ABSTRACT

**Purpose:** To assess whether noncontrast-enhanced steady-state free precession (SSFP) magnetic resonance imaging (MRI) with a spatially selective inversion recovery (IR) pulse can improve the visibility of renal corticomedullary differentiation in patients showing renal dysfunction, and to investigate the correlation between renal cortical thickness and estimated glomerular filtration rate (eGFR).

**Materials and Methods:** Sixty five patients with and without chronic kidney diseases (CKD). Based on eGFR, patients were divided into 3 groups (Group1, eGFR<60; Group2, eGFR=60-90; and Group3, eGFR>90). All patients underwent non-contrast-enhanced SSFP MRI with spatially selective IR pulse, and minimal renal cortical thickness was measured.

**Result:** Mean corticomedullary contrast ratio was significantly higher in SSFP images with optimal TI than in in-phase images in all 3 groups ( $p \leq 0.001$ ). Positive correlation was seen between corticomedullary contrast ratio in SSFP images with optimal TI and eGFR ( $p=0.011$ ,  $r=0.314$ ). A significantly positive correlation was observed between minimal renal cortical thickness and eGFR ( $p < 0.01$ ,  $r=0.495$ ).

**Conclusion:** Noncontrast-enhanced SSFP MRI with a spatially selective IR pulse using optimal TI can improve the visibility of renal corticomedullary differentiation even in patients with renal insufficiency. The decrease in renal cortical thickness measured using this technique correlated significantly with eGFR.

**Key words:** corticomedullary differentiation; kidney; magnetic resonance imaging; cortical thickness; steady-state free precession (SSFP)

## INTRODUCTION

Chronic kidney disease (CKD) is divided into five stages, the last of which is called end-stage renal disease (ESRD), representing irreversible disease in which improvement of renal function is impossible [1]. . Patients with ESRD are at increased risk of developing complications, such as cardiovascular disease (CVD), anemia, renal osteodystrophy, metastatic calcification, tuberculosis and other respiratory infections [1].

In recent years, the number of ESRD patients has increased [2]. Early detection and diagnosis of CKD is particularly important because early treatment may not only prevent the progress to ESRD, but also lead to the possibility of the remission of CKD.. Renal volume and maximal renal length reportedly correlate with renal function, with atrophy of the renal cortex being particularly noted[3-8], however, few imaging studies have been conducted to evaluate this correlation. This is primarily because there is less than distinct corticomedullary differentiation in non-contrast-enhanced imaging studies including MRI in patients with renal insufficiency[9-13]. Evaluation of corticomedullary differentiation in the kidney is possible using contrast-enhanced MRI, but carries a risk of nephrogenic systemic fibrosis (NSF) [14].

Our preliminary study showed that distinct renal corticomedullary differentiation is possible using non-contrast-enhanced steady-state free precession (SSFP) MRI applying a spatially selective inversion recovery (IR) pulse with an optimal inversion time (TI) placed on the kidney of the patient with normal renal function[15, 16]. The purposes of this study were to assess whether noncontrast-enhanced SSFP MRI with a spatially selective IR pulse can improve the visibility of renal corticomedullary differentiation to measure renal cortical thickness in patients showing renal dysfunction,

and to investigate the correlation between renal cortical thickness and estimated glomerular filtration rate (eGFR) by depicting renal corticomedullary differentiation using SSFP MRI with a spatially selective IR pulse.

## **MATERIALS AND METHODS**

### **Subject**

The institutional review board of our hospital approved this retrospective study, and the requirement for patient informed consent was waived. This study included a total of 65 patients with or without CKD (39 men, 26 women; mean age, 61 $\pm$ 14 years; range, 28-85 years) who underwent abdominal MRI including non-contrast-enhanced SSFP sequences with spatially selective IR pulse between June 2010 and June 2013. Among these patients, 13 had been included in our previous study [15, 16]. No patients had any history of chronic liver disease, hypertension, or other vascular diseases, and had ipsilaterally atrophic kidney. Patients were referred for MRI examinations for further evaluation of CKD or the screening of benign abdominal diseases. Estimated glomerular filtration rate (eGFR) was measured in all patients. The eGFR was used to indicate renal function, but the specific diagnosis of the underlying kidney disease was not clearly known due to the unavailability of biopsy.

### **Image technique**

MR examinations were performed with a 1.5-T unit (Vantage Atlas MRT-2003; Toshiba, Tokyo, Japan) using an Atlas SPEEDER body coil. Non-contrast-enhanced SSFP MRI with spatially selective IR pulse was performed as part of our abdominal protocol. Coronal SSFP images with fat-suppression without applying spatially selective

IR pulse were first obtained at nearly the center of both kidney during a single breath-hold, and used as a localizer to determine the position for the placement of a spatially selective IR pulse to the kidney, using following parameters: repetition time (TR), 4.2 msec; echo time (TE), 2.1 msec; number of acquisitions, 1; parallel imaging factor, 2; flip angle, 90°; receiver bandwidth, 977 Hz/pixel; slice thickness, 7 mm; field-of-view, 400 × 400 mm; and acquisition matrix, 256 × 256. Then, non-contrast-enhanced SSFP MRI of the kidney with spatially selective IR pulse was performed using identical imaging parameters during a single breath-hold. A spatially selective IR pulse with a thickness of 130 mm to cover the entire kidney was set on the SSFP image (Fig. 1). A series of topographically identical SSFP sequences with spatially selective IR pulse using various inversion times (TIs), 700-1500 msec in increment of 100 msec (a total of 9 images) were obtained to determine the optimal TI to best visualize renal corticomedullary differentiation which showed serial signal changes according to TI (Fig. 2). Each of these images was obtained in a separate breath-hold. In addition, in-phase (IP) T1-weighted gradient-echo MR images were obtained during a respiratory suspension to compare the visibility of corticomedullary differentiation as well as the corticomedullary contrast ratio of SSFP MR images with spatially selective IR pulse. IP sequence used following imaging parameters : TR/TE =240/4.8 msec; number of acquisitions = 1; flip angle = 90°; receiver bandwidth = 488 Hz/pixel; slice thickness= 7 mm; field of view = 400×400 mm, and acquisition matrix= 320×192.

### **Data analysis**

All images were evaluated separately by two radiologists (A.K., Y.N) with 8 and

5 years of clinical experience in abdominal MRI, respectively, who were blinded to any clinical information of the patients. In cases with diagnostic discrepancies, images were reevaluated together by the same two radiologists, and any discrepancies were resolved by reaching a consensus. All images were reviewed on a clinical picture archiving and communication system workstation (Rapideye Core; Toshiba Medical Systems, Tokyo, Japan) with an adjustment of the optimal window setting in each case. Two radiologists measured the signal intensity (SIs) of the renal cortex and medulla using operator-defined region of interest (ROIs) by consensus. Circular or oval ROIs were positioned in the renal parenchyma of the cortex and medulla for the measurement of SI values in the right and left kidneys. Consequently, a total of four ROIs were placed in each subject. To keep the locations of ROIs consistent among each sequence obtained with variable TIs, images were displaced in a side-by-side manner, and the ROIs were positioned at the same location as accurately as possible over images using a copy-and-paste function. Additionally, ROI measurements were also performed on IP images. Since corticomedullary differentiation was sometimes poorly depicted on the IP image, ROI placement was performed by copy-and-paste function used on the SSFP image in such cases. The SI of the renal cortex and medulla in each subject was defined as a mean SI value of bilateral renal cortex and medulla. Corticomedullary contrast ratio was calculated from mean SI values of the renal cortex ( $SI_{\text{cortex}}$ ) and renal medulla ( $SI_{\text{medulla}}$ ) as:  $(SI_{\text{cortex}} / SI_{\text{medulla}})$ . The optimal TI value to best visualize corticomedullary differentiation was determined from a series of SSFP images with spatially selective IR pulse. Optimal TI was defined as the TI showing the highest corticomedullary contrast ratio among serial SSFP images with spatially selective IR pulse obtained with variable TIs. Consequently, optimal SSFP image was defined as SSFP image with spatially

selective IR pulse obtained with optimal TI in each patient, and used for additional measurements and data analysis. Mean corticomedullary contrast ratio was compared between SSFP images acquired with optimal TI and IP images. Additionally, the visibility of the corticomedullary differentiation was compared between optimal SSFP images and IP images as a qualitative analysis. The visibility of corticomedullary differentiation was visually categorized using a following 4-point scale (1 = poor; 2 = fair; 3 = good; 4 = excellent). Moreover, using optimal SSFP image with spatially selective IR pulse, maximal renal length and minimal renal cortical thickness were also measured and recorded in all patients. Minimal renal cortical thickness was measured at the mid portion of both kidneys and the averaged value of both kidneys was used for data analysis. Mean corticomedullary contrast ratio, maximal renal length and minimal renal cortical thickness were correlated with eGFR (mL/min/1.73 m<sup>2</sup>).

### **Statistical analysis**

Statistical analyses were performed using SPSS for Windows version 17.0 J software (Chicago, IL). All tests were two-sided and values of  $P < 0.05$  were considered statistically significant unless otherwise specified. Pearson product-moment correlation coefficient was used to investigate the correlation between eGFR and renal corticomedullary contrast ratio at optimal TI, eGFR and minimal renal cortical thickness, eGFR and maximal renal length. Corticomedullary contrast ratio and the visibility of corticomedullary differentiation in SSFP images with spatially selective IR pulse and IP images were compared using the Wilcoxon signed-ranks test and Paired t-test. The Kruskal-Wallis test and the single factor analysis of variance (ANOVA) were used to compare differences among the 3 groups based on eGFR. If a significant

difference was found, the two relevant groups were further compared using the Mann-Whitney test.

## RESULTS

Mean eGFR of all patients was 79.7 mL/min/1.73 m<sup>2</sup> (range, 36.1-125.9 mL/min/1.73 m<sup>2</sup>). Based on eGFR, patients were divided into 3 groups as follows: Group 1, eGFR <60 mL/min/1.73 m<sup>2</sup> (n=16); Group 2, eGFR = 60-90 mL/min/1.73 m<sup>2</sup> (n=35); and Group 3, eGFR >90 mL/min/1.73 m<sup>2</sup> (n= 14). Renal corticomedullary differentiation was clearly depicted in all patients on SSFP images with optimal TI. Mean corticomedullary contrast ratio was significantly higher in SSFP images with optimal TI than in IP images in all 3 groups (Group1, 4.51+/-1.34 versus 1.37+/-0.14; Group2, 5.06+/-1.43 versus 1.37+/-0.18; Group3, 6.01+/-1.84 versus 1.50+/-0.12) (p<0.001, p <0.001, p=0.001, respectively) (Fig.3). Additionally, the visibility of corticomedullary differentiation was significantly better in SSFP images with optimal TI than in IP images in all 3 groups (averaged grade in Group1, 4.0 versus 1.7; Group2, 4.0 versus 2.4; Group3, 4.0 versus 2.4) (p<0.001, p <0.001, p=0.001, respectively).

Regarding the relationship between corticomedullary contrast ratio and eGFR, positive correlation was seen between corticomedullary contrast ratio in SSFP images with optimal TI and eGFR (p=0.011, r= 0.314) (Fig.4). Additionally, there was a significant difference in corticomedullary contrast ratio in SSFP images among the 3 eGFR groups (p=0.028) (Fig.3). In the comparison between the groups, corticomedullary contrast ratio in Group1 was significantly lower than that in Group3 (p=0.025) (Fig.3) while there were no significant differences in corticomedullary contrast ratio in SSFP images between Group1 and Group2 (p= 0.688), and between

Group2 and Group3 ( $p= 0.151$ ).

Mean minimal renal cortical thickness measured on SSFP images with optimal TI was 4.68 mm (range, 1.90-7.75 mm). A significantly positive correlation was observed between minimal renal cortical thickness and eGFR ( $p<0.01$ ,  $r=0.495$ ) (Fig.5). Mean minimal renal cortical thickness was  $3.99\pm 1.55$ mm in Group 1,  $4.63\pm 1.00$ mm in Group 2, and  $5.59\pm 1.08$ mm in Group 3, respectively. Among the 3 eGFR groups, a significant difference was seen in minimal renal cortical thickness measured on SSFP images ( $p=0.02$ ) (Fig.6). In the comparison between the groups, significant differences were seen between Group 1 and Group 3 ( $p=0.001$ ) (Fig.7), and between Group 2 and Group 3 ( $p=0.036$ ).

Mean maximal renal length measured on SSFP images with optimal TI was 99.3 mm (range, 81-124 mm). There was a weak positive correlation between maximal renal length and eGFR ( $p<0.027$ ,  $r=0.274$ ) (Fig.8). However, in the comparison among the 3 groups, no significant difference was seen in maximal renal length measured by SSFP images ( $p=0.14$ ) (Fig.9).

## **DISCUSSION**

In this study, corticomedullary differentiation was significantly better in SSFP images with optimal TI than in IP images in all 3 groups, qualitatively and quantitatively. Especially, in Group1, visual corticomedullary differentiation in SSFP images was excellent in all patients while corticomedullary differentiation in IP images was poor in 7 of 16 patients, indicating that SSFP images with optimal TI can visualize corticomedullary junction even in patients with decreased eGFR. Regarding the relationship between corticomedullary contrast ratio and eGFR, a significantly positive

correlation was observed between corticomedullary contrast ratio in SSFP images with optimal TI and eGFR. Additionally, corticomedullary contrast ratio in Group1 was significantly lower than that in Group3, suggesting decreased renal corticomedullary differentiation according to the decline of eGFR. However, even in Group1, corticomedullary contrast ratio in SSFP images with optimal TI was approximately 3 times of that in IP images. In patients with renal insufficiency, an increased T1 relaxation time of the renal cortex probably due to increased water content (edematous changes) has been reported [5, 12, 17], causing the decreased difference in T1 values between the renal cortex and the medulla [18-25], resulting in diminished corticomedullary differentiation. However, the decreased difference in T1 values between the renal cortex and the medulla was accentuated by the use of SSFP images with spatially selective IR pulse using optimal TI, reflecting the difference of the recovery of protons longitudinal magnetization between the renal cortex and the medulla even in patients with renal insufficiency. These facts indicated that SSFP images with optimal TI can demonstrate corticomedullary junction even in patients with impaired renal function, and enables us to measure the cortical thickness or volumes without using contrast agents in CKD patients.

In this study, a positive correlation was observed between minimal renal cortical thickness measured on SSFP image and eGFR when using the optimal TI, showing decreased renal cortical thickness according to the decline of eGFR. In addition, significant differences in minimal renal cortical thickness measured on SSFP images were also observed in comparison of the three groups divided based on eGFR. Histopathological findings have shown that the main causes of volume reduction of the kidney in renal dysfunction with decreased eGFR were atrophy and fibrosis of nephrons

[26]. By volume, nephrons occupy a greater proportion of the cortex than the medulla; a relatively cortex-dominant atrophy was thus caused. These may be the reasons why the significant reduction of renal cortical thickness was observed along with a decline of eGFR in this study. Although mean maximal renal length on SSFP images was also positively correlated with eGFR in this study, renal cortical thickness has correlated more strongly with eGFR than maximal renal length. Additionally, no significant difference was seen in maximal renal length among the 3 groups. Therefore, we believe that measurement of minimal renal cortical thickness will be an important indicator for the more detailed assessment of renal function compared to measurement of the maximal renal length in accurately evaluating renal function. In addition, management based on renal cortical thickness may contribute to prevent the progress of the CKD stage early because renal cortical thickness in patients with minimally decreased eGFR (60-90) group 2 was significantly thinner than that in patients with normal renal function group 3.

There are several limitations to the present study. The retrospective design of our study did not allow for the measurement of T1 values directly, as specific imaging sequences needed for T1 calculations were not performed. Therefore, the exact mechanism of decreased renal corticomedullary differentiation according to the decline of eGFR remains unknown. In this study, we did not control for the type of underlying kidney disease in the subjects with an eGFR less than 90 mL/min/1.73m<sup>2</sup> due to the unavailability of biopsy. Therefore, we should note that our observations may not be generalizable to every etiology of renal insufficiency although there were significant differences between groups of our subjects simply based on the eGFR. Another limitation of this study is absence of a reference standard for precise renal cortical

thickness. This study, however, aimed at investigating the correlation between renal cortical thickness measured on SSFP images and eGFR, and it may not constitute a significant issue. Finally, the hydration level of the patients could not be controlled, and this potentially could affect the renal corticomedullary differentiation. Furthermore, instead of measuring GFR directly, eGFR values were calculated based on serum creatinine levels, and therefore may be imprecise estimations of renal function. Further study which evaluates the correlation with <sup>99m</sup>Tc-diethylene triamine pentaacetic acid renography will be needed. Despite these limitations, we believe that the validity of the basic conclusions from this study will not be reduced.

In conclusion, noncontrast-enhanced SSFP MRI with a spatially selective IR pulse using optimal TI can improve the visibility of renal corticomedullary differentiation to measure renal cortical thickness even in patients with renal insufficiency in comparison with conventional IP sequences. The decrease in minimal renal cortical thickness measured using this technique correlated significantly with eGFR as a marker of renal function.

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### Figure Legend

Figure1. Setting of a spatially selective IR pulse.

A spatially selective IR pulse with a thickness of 130 mm to cover the entire kidney was set on the SSFP image.

Figure2. A series of topographically identical SSFP sequences with spatially selective IR pulse using various inversion times (TIs), 700-1500 msec in increment of 100 msec (a total of 9 images) were obtained to determine the optimal TI to best visualize renal corticomedullary differentiation. Note serial signal changes of the renal cortex and the medulla according to TI. a) TI=700msec, b) TI=800msec, c) TI=900msec, d) TI=1000msec, e) TI=1100msec, f) TI=1200msec, g) TI=1300msec, h) TI=1400msec, i) TI=1500msec.

Figure3. Comparison of corticomedullary contrast ratio.

Mean corticomedullary contrast ratio was significantly higher in SSFP images with optimal TI than in IP images in all 3 groups. Comparison among the 3 eGFR groups, there was a significant difference in corticomedullary contrast ratio in SSFP images.

Figure4. Relationship between corticomedullary contrast ratio and eGFR.

Positive correlation was seen between corticomedullary contrast ratio in SSFP images with optimal TI and eGFR ( $p=0.011$ ,  $r=0.314$ ).

Figure5. Relationship between minimal renal cortical thickness and eGFR.

Positive correlation was observed between minimal renal cortical thickness and eGFR

( $p < 0.01$ ,  $r = 0.495$ ).

Figure6. Comparison of minimal renal cortical thickness among the 3 eGFR groups.

A significant difference was seen in minimal renal cortical thickness measured by SSFP images ( $p = 0.02$ ) among 3 groups.

Figure7. Comparison of renal cortical thickness between normal eGFR group and decreased eGFR group.

a) SSFP image and b) IP image in a patient in group1 (decreased eGFR group; eGFR value=48.2). c) SSFP image and d) IP image in a patient in group3 (normal eGFR group; eGFR value=109.8).

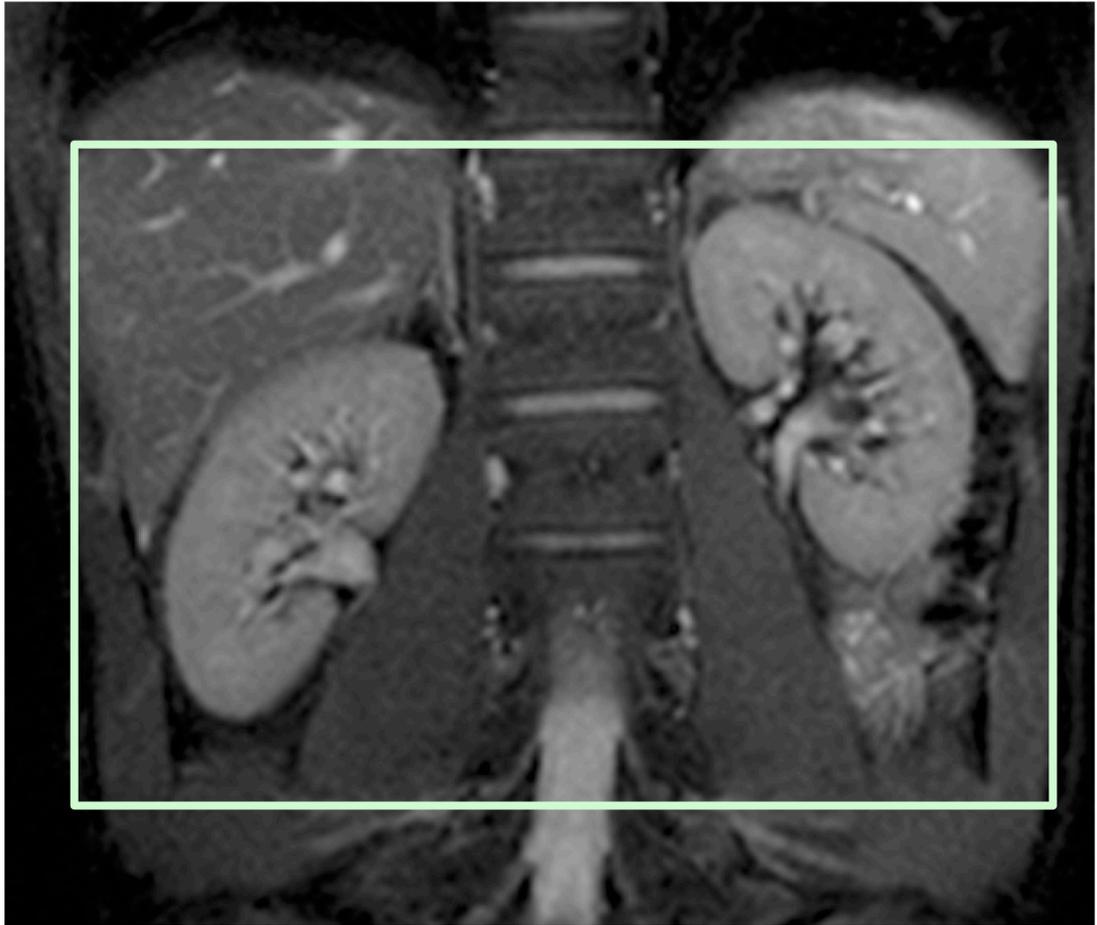
Minimal renal cortical thickness measured on SSFP image in a patient in group1 (4.5mm) was thinner than that in a patient in group3 (6.7mm). In a patient in group1, renal corticomedullary differentiation was unclear in IP image (b).

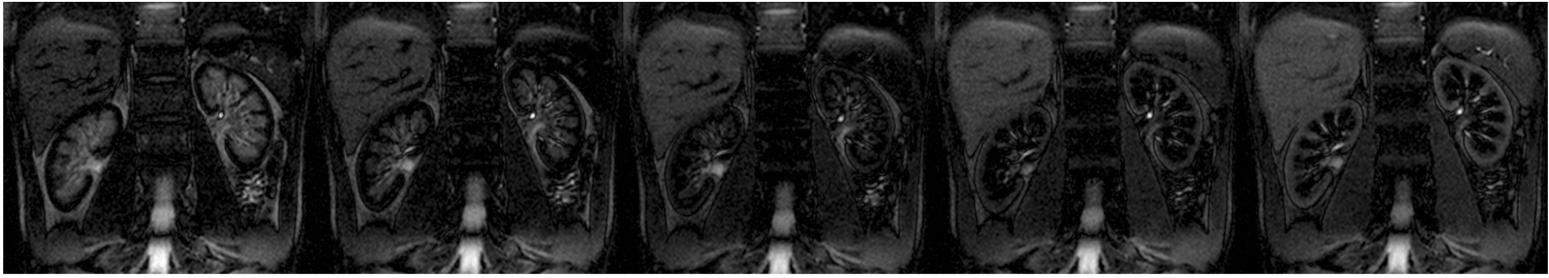
Figure8. Relationship between maximal renal length and eGFR.

There was a weak positive correlation between maximal renal length and eGFR ( $p < 0.027$ ,  $r = 0.274$ ).

Figure9. Comparison of maximal renal length among the 3 eGFR groups.

No significant difference was seen in maximal renal length measured by SSFP images ( $p = 0.14$ ) among 3 groups.





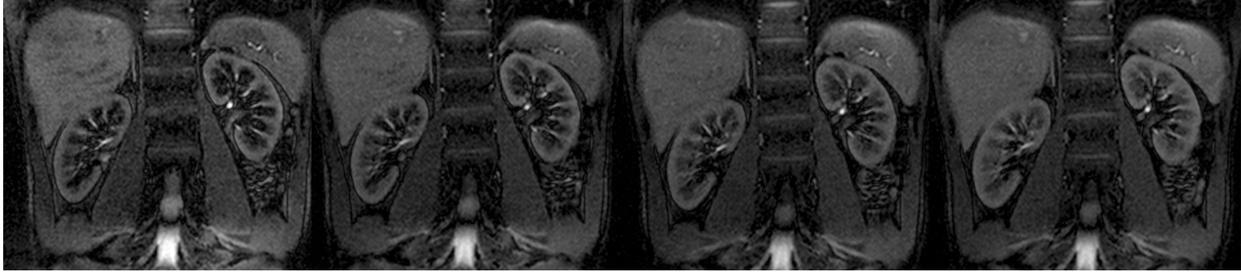
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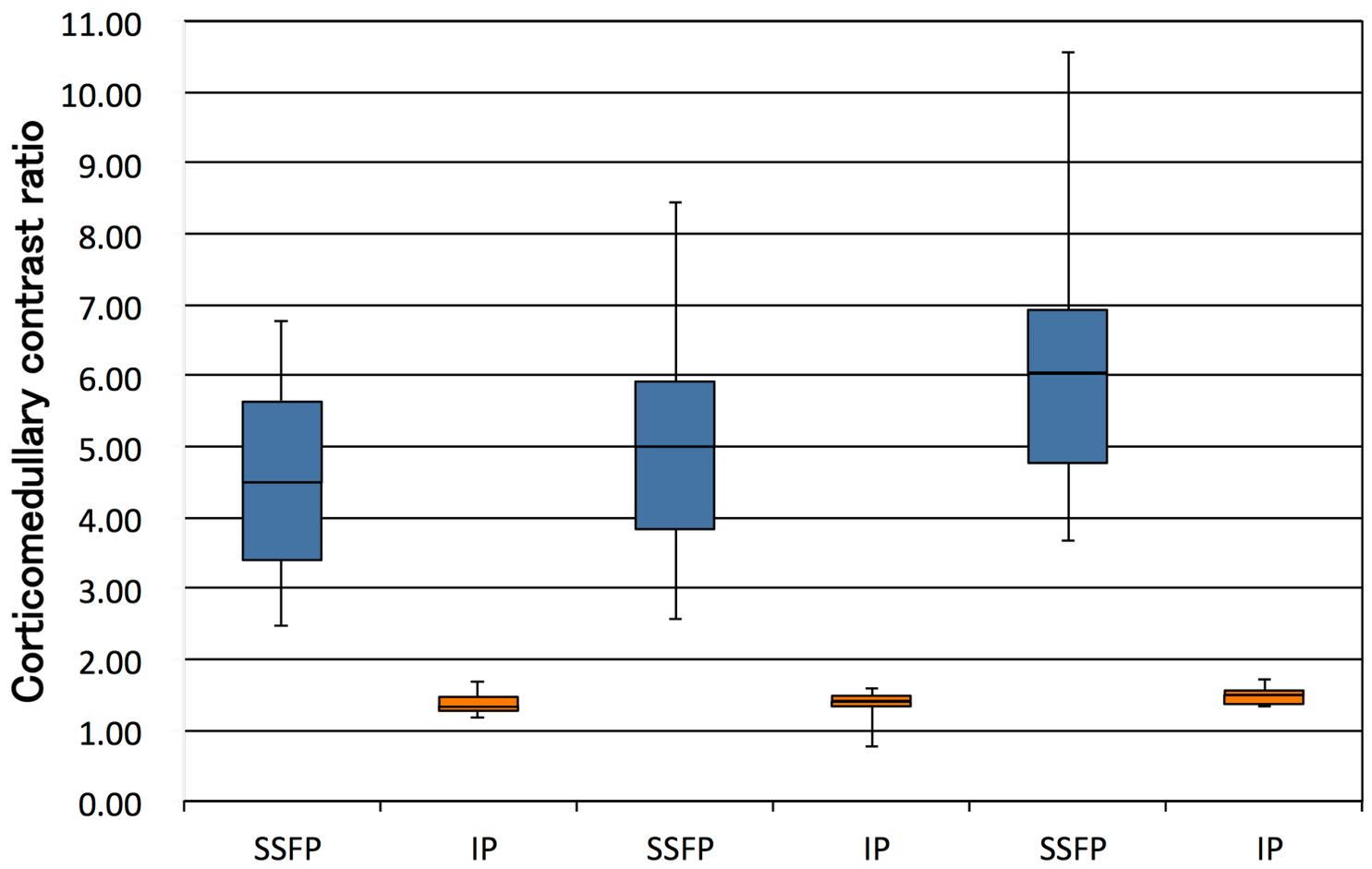


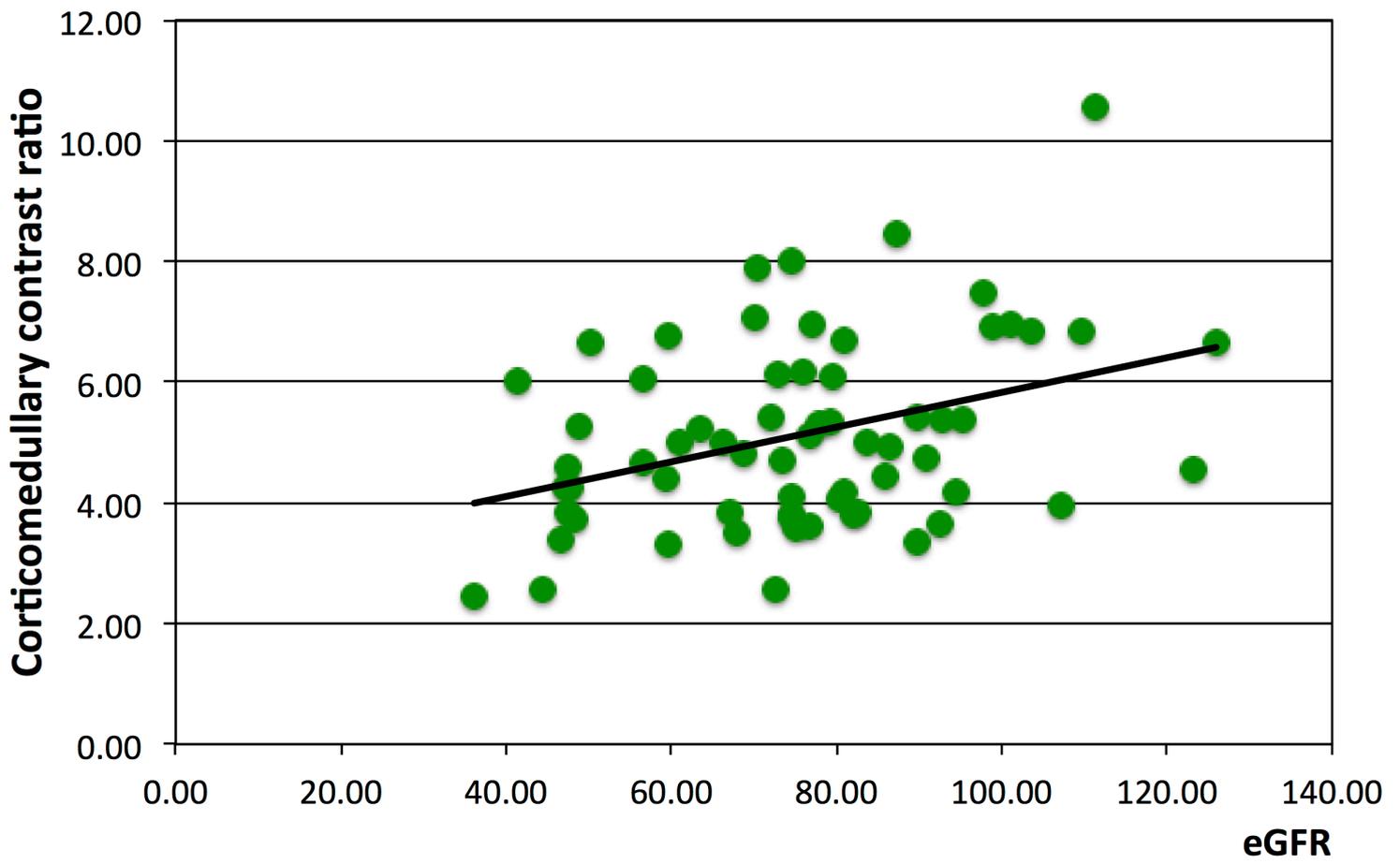
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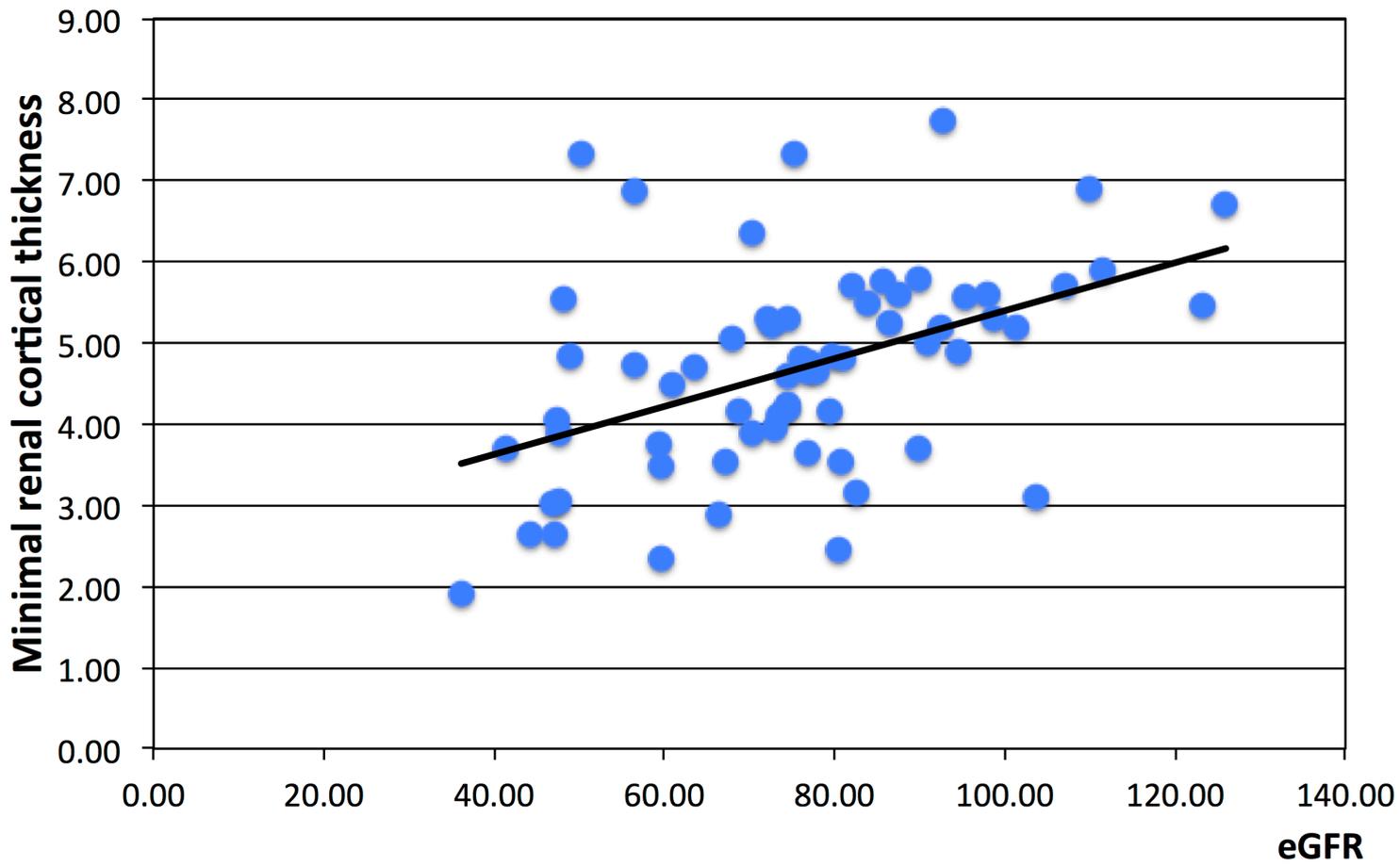
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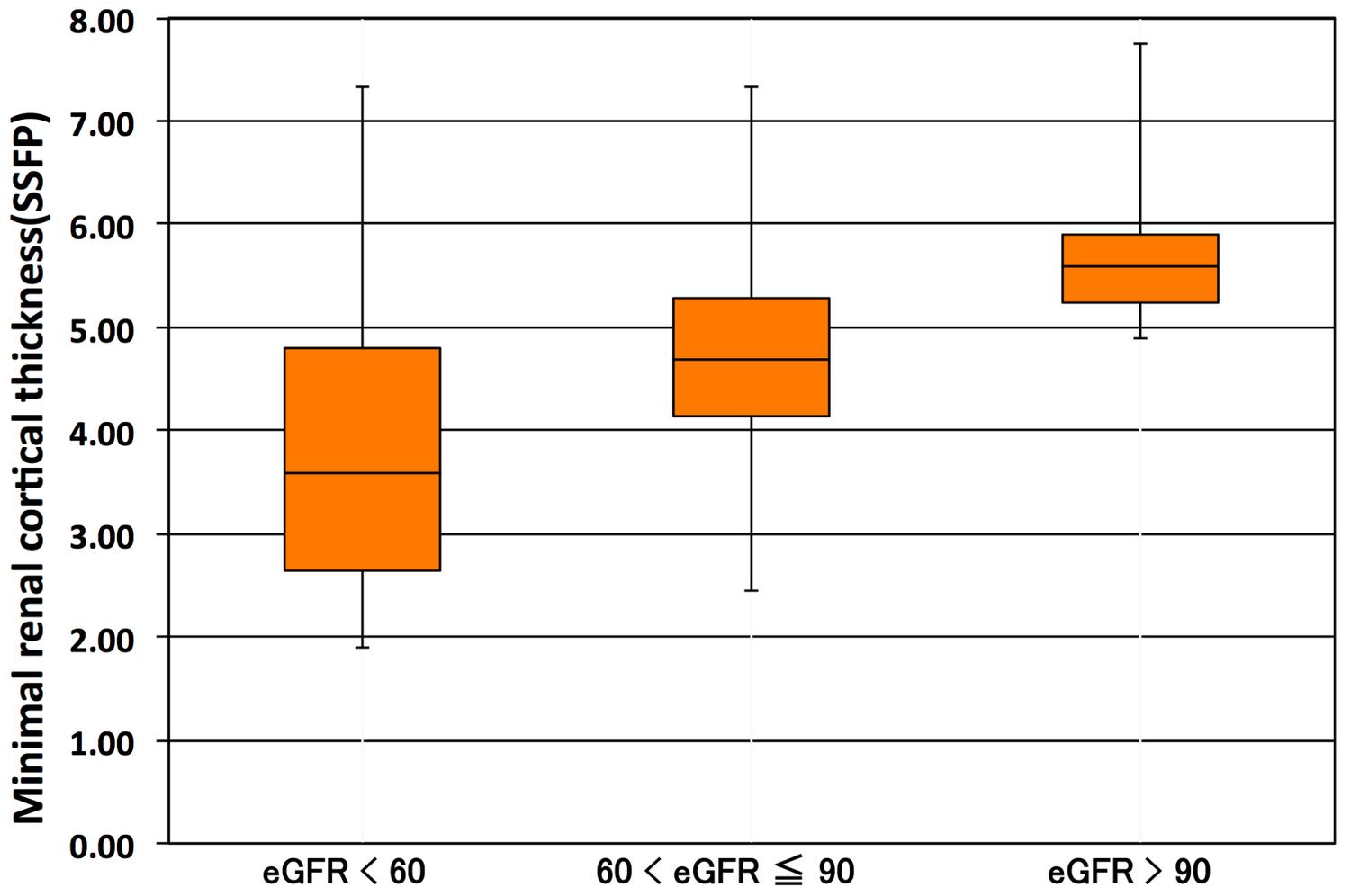
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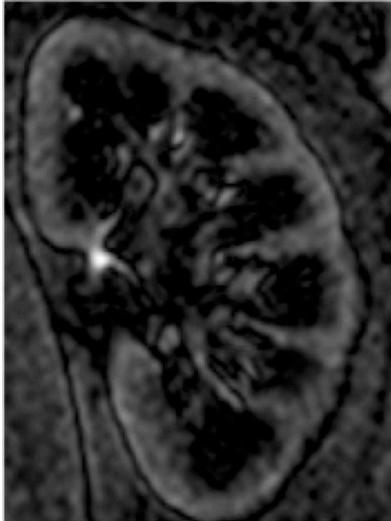
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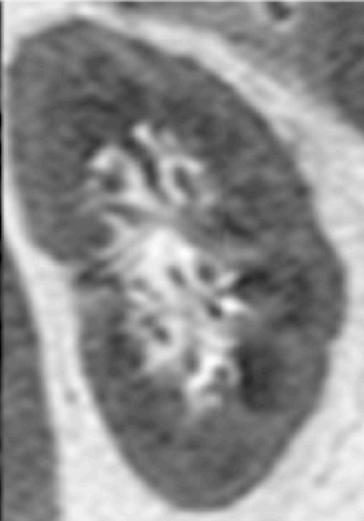








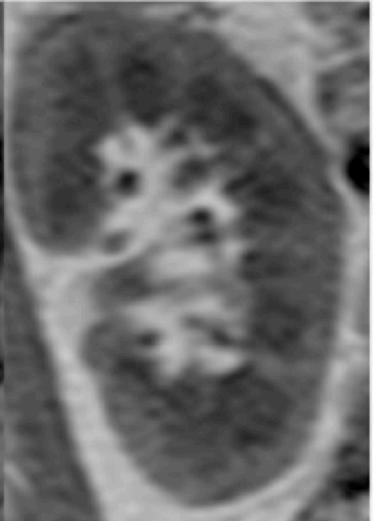
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