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Automated assessment of renal cortical surface roughness from computerized tomography images and its association with age

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Abstract

Rationale and Objectives—Nephrosclerosis occurs with aging and is characterized by increased kidney sub-capsular surface irregularities at autopsy. Assessments of cortical roughness in-vivo could provide an important measure of nephrosclerosis. The purpose of this study was to develop and validate an image-processing algorithm for quantifying renal cortical surface roughness in-vivo and determine its association with age.

Materials and methods—Renal cortical surface roughness was measured on contrast-enhanced abdominal CT images of potential living kidney donors. A roughness index was calculated based on geometric curvature of each kidney from 3D images, and compared with visual observation scores. Cortical roughness was compared between the oldest and youngest donors, and its interaction with cortical volume and age assessed.

Results—The developed quantitative roughness index identified significant differences in kidneys with visual surface roughness scores of 0 (minimal), 1 (mild), and 2 (moderate) ($p<0.001$) in a random sample of 200 potential kidney donors. Cortical roughness was significantly higher in the 94 oldest (64–75y) versus 91 youngest (18–25y) potential kidney donors ($p<0.001$). Lower cortical volume was associated with older age but not with roughness ($r=-0.03$, $p=0.75$). The association of oldest age group with roughness (OR=1.8 per SD of roughness index) remained significant after adjustment for total cortex volume (OR=2.0 per SD of roughness index).

Conclusion—A new algorithm to measure renal cortical surface roughness from CT scans detected rougher surface in older compared to younger kidneys, independent of cortical volume

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loss. This novel index may allow quantitative evaluation of nephrosclerosis in vivo using contrast-enhanced CT.

Keywords

Nephrosclerosis; surface roughness; computerized tomography; kidney aging

Introduction

Nephrosclerosis (glomerulosclerosis, tubular atrophy, interstitial fibrosis, and arteriosclerosis) occurs with normal aging, hypertension, and chronic kidney disease (CKD) (1–4). Detection of nephrosclerosis in vivo requires a renal biopsy. Autopsy studies have characterized nephrosclerosis by a rough, irregular cortical surface (5). The detection of these morphological surface changes in the kidney may help clinicians identify nephrosclerosis. However, the ability to assess cortical surface roughness in vivo has not been previously demonstrated.

Volume CT imaging with contrast agent enhancement provides sub-millimeter spatial resolution and good image contrast for kidney anatomy. Kidney volume, decreases with older age, while kidney function and other CKD risk factors can be associated with either increased or decreased volume (6–8). The decline in cortical volume that occur with older age has been attributed to underlying atrophy and sclerosis of nephrons (nephrosclerosis). However, it is not known whether changes in cortical surface morphology are detectable with CT imaging or whether such changes, if observed, relate to clinical characteristics.

The purpose of this study was to develop an image analysis algorithm to quantify renal cortical surface roughness and validate it against visual observations. Additionally, for proof of concept, the algorithm was used to demonstrate in vivo the association between cortical surface roughness and older age.

Methods

Study Population

Subject data used in this study were obtained under local institutional review board-approved protocols involving potential living kidney donors. We studied subsets from potential donors seen at our institution between 2000 and 2008 for whom renal CT angiograms were obtained using clinical protocols for donor evaluations (6). There were 1192 potential kidney donors with CT scans available for study that had a mean age of 44 years, were 60% women, and 89% white race.

Four sets of data drawn from our potential kidney donor cohort were evaluated as part of this study:

- **Development data (Set-1):** 40 kidneys from 29 subjects, including 20 with the roughest and 20 with the smoothest appearing cortical surfaces, were identified from among 100 randomly selected subjects. The image data from this cohort were used to develop our algorithm for surface roughness assessment.

- **Validation data (Set-2):** 200 other kidneys (both kidneys from 100 subjects) were randomly selected from the donor database. The effectiveness of the developed algorithm was determined with this cohort using the viewer's visual assessment as the reference standard.
- **Reproducibility data (Set-3):** Occasionally, potential kidney donors undergo a second clinic visit and CT scan for a re-evaluation as a donor. This occurred in 23 potential donors in our data set. We evaluated these 46 kidneys scanned within a mean of 2.4 years to evaluate algorithm reproducibility.
- **Age difference data (Set-4):** We targeted the 100 oldest and 100 youngest donors. However, due to inadequate image quality (e.g. one kidney was partially outside the imaging window or the cortex could not be segmented due to poor timing of the angiogram phase images) 374 kidneys (both kidneys from the 96 oldest and 91 youngest potential donors) were analyzed to detect differences in roughness between kidneys from old and young subjects using the algorithm.

Image acquisition

The scans performed between 2000 and 2004 used a four-channel multi-detector row CT scanner (LightSpeed QXi, GE Healthcare, Milwaukee, WI), and between 2004 and 2008 used a 64-channel multi-detector CT scanner (SOMATOM Sensation 64; Siemens Healthcare, Erlangen, Germany). On the GE scanner, images were acquired using a collimation of 4*1.25 mm with 1.25 mm image thickness and 0.75 mm increments. On the Siemens scanner, 64*0.6 mm collimation, 1.5 mm image thickness and 1.5 mm increments were used.

Kidney segmentation

As detailed elsewhere (6), archived CT image data (DICOM files) were analyzed to generate kidney cortex image maps from the angiographic (arterial) phase images. The kidney cortex was segmented using an automated algorithm (ITK SNAP, version 2.2, University of Pennsylvania, Philadelphia, PA, www.itksnap.org), which uses an active contour evolution technique and an energy-minimizing spline algorithm (9). From the DICOM images, regions of interest that included the kidney cortex but excluded other anatomical features were created. Using appropriate intensity threshold values, feature images were created. The automated segmentation was initiated by placing spherical bubbles on the feature image to segment the kidney cortex. Cortical volume was directly calculated for each kidney from the segmented the left and right kidney cortex, and summed to yield total cortical volume.

Renal cortical surface roughness algorithm

The segmented surface of the contrast-enhanced renal cortex was displayed using 3D surface rendering techniques (Figures 1 and 2). One viewer trained by an experienced radiologist examined the roughness of the cortical surface for each kidney in Set-1 and Set-2. For Set-2, each kidney was scored as having a smooth surface (score=0), mild surface roughness (score=1), and moderate surface roughness (score=2).

Cortical surface morphology was quantified using a roughness index derived from the segmented images in Set-1. A triangular mesh of the surface was generated using kidney cortical segmentation, which provides a mathematical representative of cortical surface, and then the mesh was smoothed for noise suppression. The mean curvature of each vertex on the mesh was calculated based on a previously reported algorithm (10–12). A histogram of the vertex curvatures was plotted. The roughness index was calculated from the full width at half maximum of the histogram, which was used to describe the overall surface morphology of the kidney cortex. Data processing was done using Matlab software (Mathworks Inc., Natick, MA).

Statistical Analysis

The calculated roughness index for each score group was analyzed using chi-square, ANOVA, and Wilcoxon /Kruskal-Wallis tests as appropriate. Correlation was calculated between repeated scan (Set-3) and between left and right kidneys (Set-2). For Set-4, correlation was also calculated between cortical volume and the roughness index. The association of age group with roughness index was calculated as odds ratio using logistic regression with and without adjusting for cortical volume. Roughness index per cortical volume was also compared between age groups. Analyses were performed using JMP (SAS Institute Inc., NC).

Results

Characteristics of the groups studies are shown in Table 1. The roughness index was derived using Set-1. The value ranged from 0.81 to 1.54 with higher values indicating a rougher renal cortical surface. For the Set-1 cohort, roughness index was 1.21±0.15 (mean ± standard deviation) for the 20 roughest kidneys and 0.96±0.09 for the 20 smoothest kidneys. Using the roughness index to discriminate the roughest from the smoothest kidneys, the area under the receiver operator characteristic curve was 0.93.

In the Set-2 cohort, 119 kidneys were subjectively scored as 0 for minimal surface roughness, 68 were scored as 1 for mild surface roughness and 13 were scored as 2 for moderate roughness. Figure 2 shows representative 3D rendering of kidneys scored as 0, 1 and 2. There were significant differences in roughness index between the kidneys manually scored as 0, 1 and 2 (1.02±0.13, 1.18±0.14, 1.37±0.22, $p<0.0001$)(Figure 3). Figure 4 shows the scatter plot of roughness index for left and right kidney in the same subject, which showed a good correlation (r=0.70, 95% CL 0.58–0.79).

For Set-3 cohort of 23 subjects (46 kidneys) undergoing two separate CT scans, there was a good correlation between the calculated roughness index of each kidney between the two scans (r=0.63, 95% CL 0.42–0.78) with a mean coefficient of variation of 6.3%.

In Set-4, the 96 oldest subjects (ages 64 to 75 years) were compared to the 91 youngest subjects (ages 18 to 25 years) (Figure 5). Using the mean roughness index of the left and right kidneys, the oldest subjects had rougher renal cortical surfaces than the youngest subjects (mean 1.14 vs 1.06, p=0.0005). A roughness index >1.30 occurred in 14% of the oldest subjects and 2% of the youngest subjects (p=0.002).

While the oldest subjects had lower total cortical volume than youngest subjects (mean 181 cc vs 223 cc, $p<0.0001$), total cortical volume was not correlated with roughness index in these same subjects ($r=-0.03$, $p=0.75$). The oldest age group associated with smaller total cortical volume (OR=3.0 per −SD of cortical volume, $p<0.0001$), yet its association with roughness (OR=1.8 per SD of roughness, $p=0.0004$) was not attenuated with adjustment for total cortical volume in a logistic regression model (OR=2.0 per SD of roughness, $p<0.001$). Roughness per cortical volume associated more strongly with the oldest donors (OR=4.0 per SD of roughness per total cortical volume, $p<0.0001$) than either cortical volume alone (OR=3.0 per −SD) or roughness alone (OR=1.8 per SD). These findings were similar when analysis was performed separately for each of the two scanners (data not shown).

Discussion

In this work, we developed and validated a method to quantify in vivo the surface roughness of kidney cortex. We found this method to be reproducible between separate CT image scans. We found that our formula detected rougher kidneys in older compared to younger subjects, as would be expected given the strong association of nephrosclerosis with aging. Finally we found that age-related cortical roughness was fully independent of age-related cortical volume loss, so that accounting for both by indexing cortical roughness to cortical volume may be a useful clinical parameter for assessing nephrosclerosis from kidney CT images.

Granular cortical surface caused by nephrosclerosis has been previously observed (13), but its implication and association with other risk factors has not been established for living subjects. One reason is the lack of a quantitative technique to measure such information in vivo. Although CT imaging provides excellent spatial and contrast resolution, a technique to quantify surface morphology has not been previously available, in part due to the complexity of the task compared with volume estimation. Curvature-based descriptors can be used to quantify surface shape (14) and texture, as previously described in colonic polyp detection at CT colonography (15, 16) and lung nodule detection in thoracic CT (17, 18). However, these studies focused on the overall geometric shape of the object surface, rather than its fine details. However, renal roughness can start with subtle granularity, which is more difficult to detect and quantify objectively. Therefore, we developed a method that combines a curvature descriptor with statistical methods to provide a single value that represents the roughness of the cortical surface in a manner relatively robust to image noise.

The validation against observer study (Set 2) indicated that the proposed roughness index is consistent with subjective human visual observation and offers an automated, efficient, and objective method for quantifying renal surface roughness with good repeatability (Set-3). The oldest versus youngest subject study (Set-4) demonstrated that the developed roughness index was able to detect surface changes that occur with aging, even within a healthy population of potential kidney donors. Indeed, our method may have a greater power to discern sign of nephrosclerosis in patients with renal dysfunction (though contrast nephropathy is a concern with CT angiograms in this population). Importantly, increased kidney surface roughness was additive to rather than redundant with cortical volume decline for discriminating kidney structural changes with aging.

There were limitations of the study. We selected for specific tasks, subsets of subjects in our database, rather than test them all. This study focused on algorithm development, validation, and demonstration of feasibility to detect surface changes in vivo. Evaluation of a larger subject cohort will be needed to be included in future epidemiological studies to determine the potential utility of the developed surface roughness index. Unlike visual scoring by a human observer, the algorithm does ignore any contribution of congenital lobulation of the kidney to the roughness index, yet congenital lobulation is not common (19). Finally, we only compared the roughness index against subject age, a reasonable surrogate for underlying nephrosclerosis in kidney donors (1), but direct comparison to renal biopsy pathology is required for definitive validation. This is needed to determine the sensitivity and specificity of roughness index for biopsy proven nephrosclerosis.

Whether or not roughness index scores have a role in clinical medicine requires further research. Kidney surface roughness may help inform the selection process of living kidney donors and in determining which kidney should be donated. There may also be a role of kidney surface roughness for improving the evaluation and staging of chronic kidney disease, though safer contrast agents in patients with chronic kidney disease are needed that do not cause contrast nephropathy (20). Further, it is unknown whether the roughness index score is informative of renal outcomes independent of more easily obtained renal biomarkers (e.g., serum creatinine and urine albumin)

Conclusion

An algorithm was developed and validated to quantify renal cortex surface roughness using contrast-enhanced CT images. We found that our algorithm was highly consistent with human visual scoring and in a feasibility data analysis; the calculated roughness index was able to improve the differentiation of older kidneys from younger kidneys from that based on cortical volume decline alone. This indicates that age-related structural changes in the surface of the renal cortex can be detected in vivo using contrast-enhanced CT scanning, and may play a potential role in identification and monitoring of nephrosclerosis.

Acknowledgments

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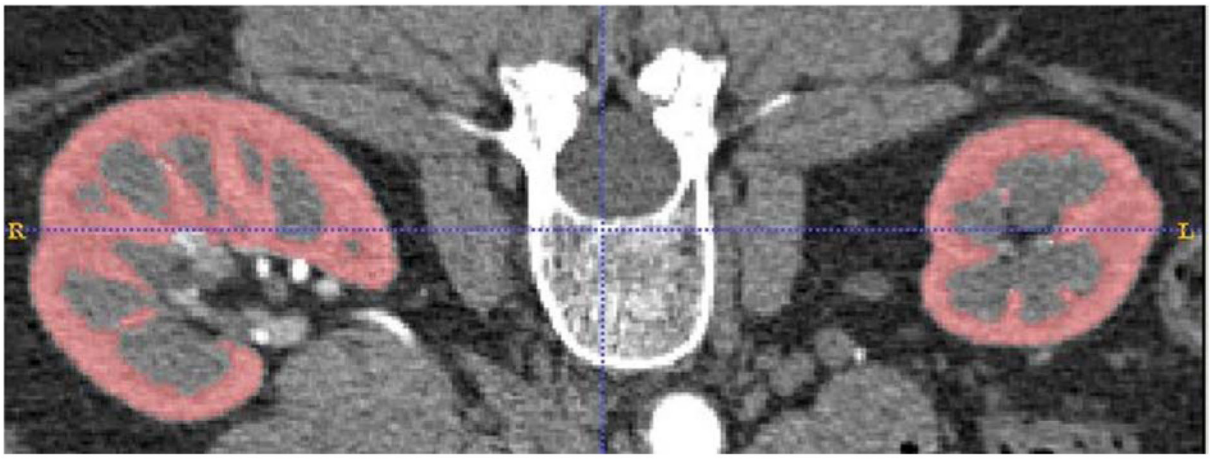
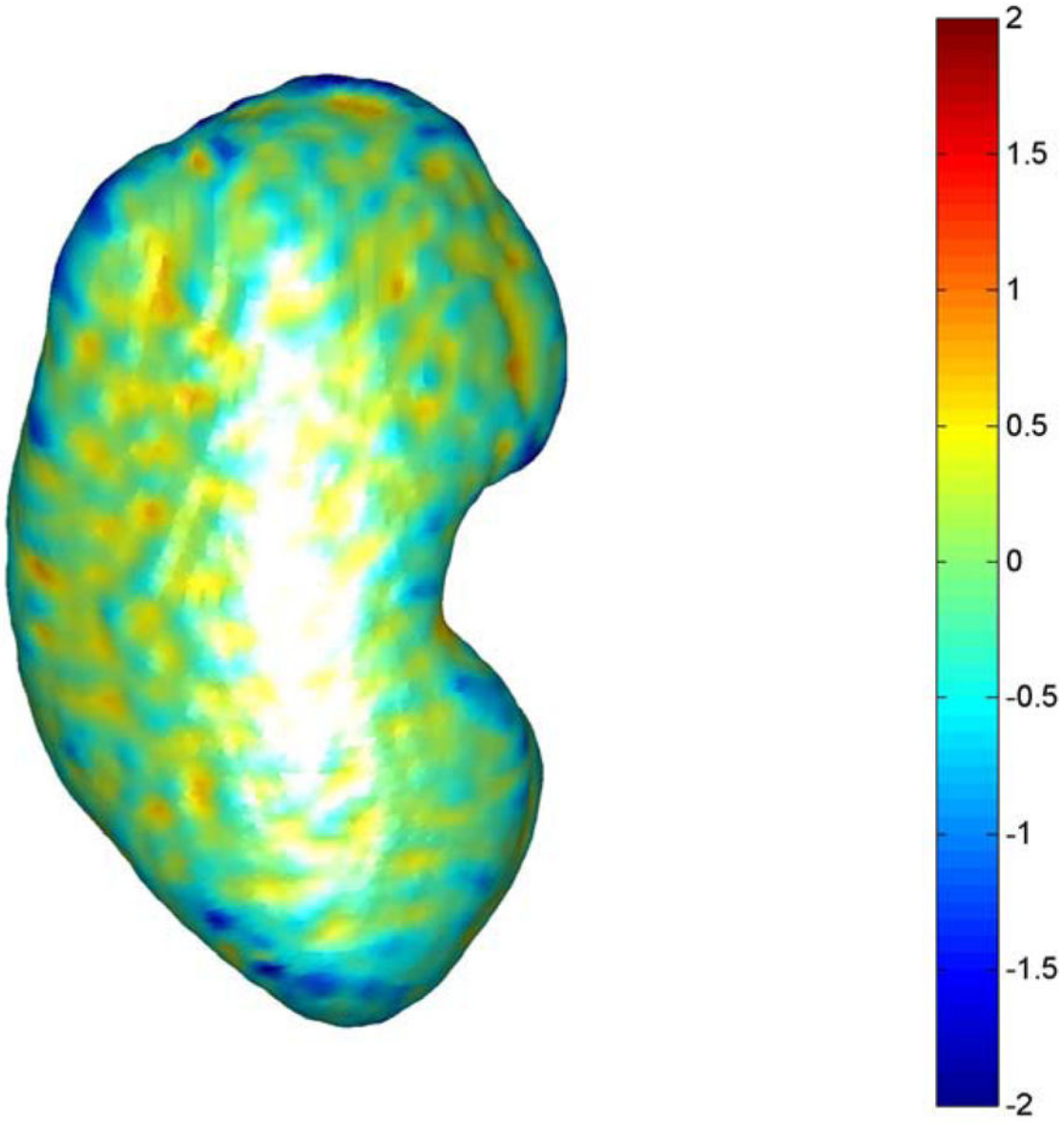
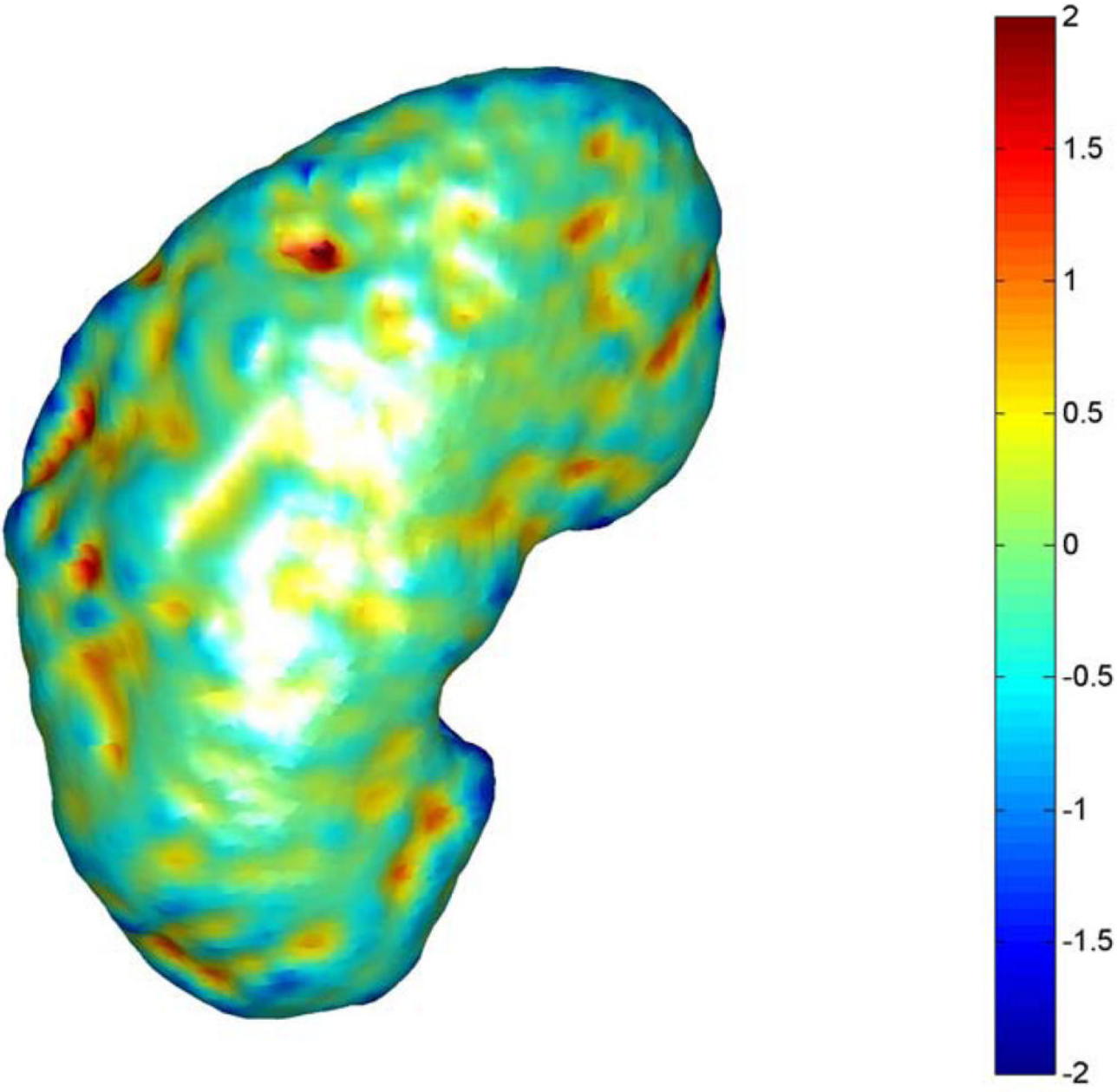


Figure 1.
Segmented renal cortex. The cortical surface roughness and volume were calculated from the segmented image map.





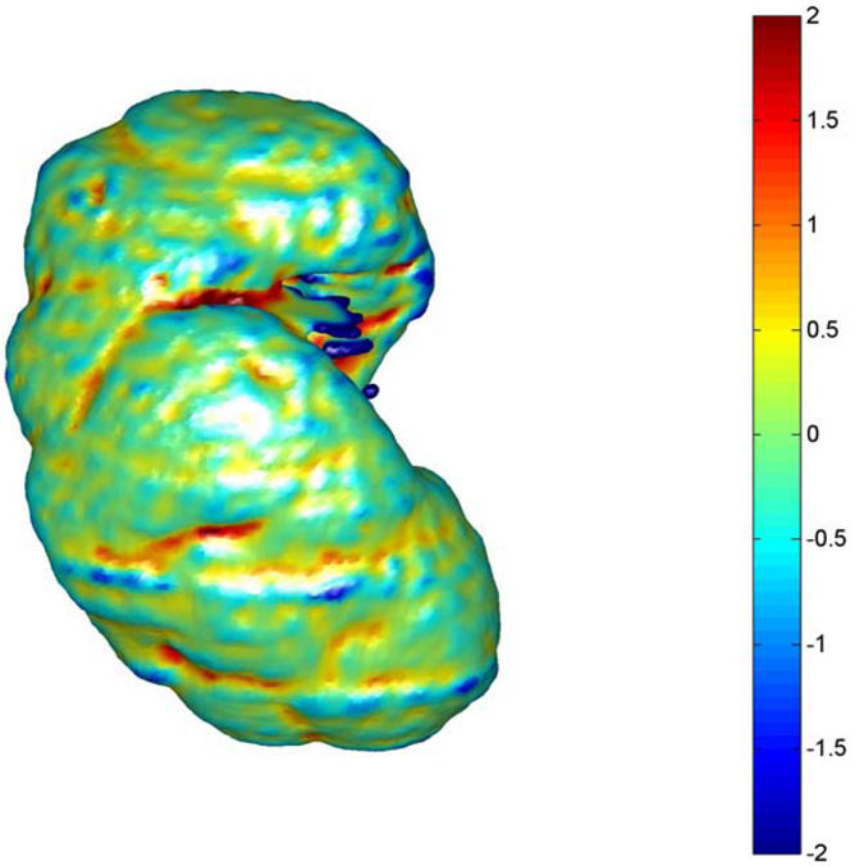


Figure 2.

Three-dimensionally rendered images for kidney visually scored to have (a) negligible (score 0), (b) mild (score 1), and (c) moderate (score 2) renal cortex surface roughness. The color map corresponds to the calculated roughness index and was scaled for display purpose.

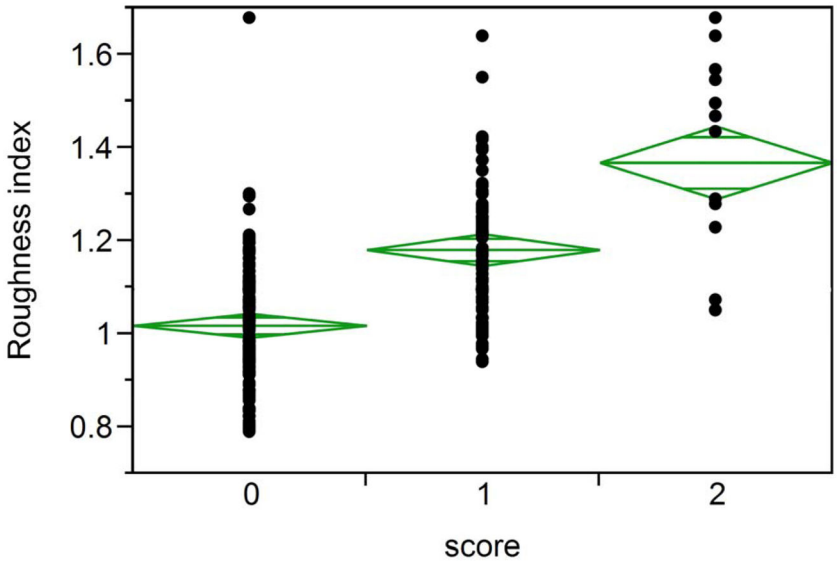


Figure 3.

Roughness index for Set-2 200 kidneys scored as 0 (smooth surface), 1 (mild roughness) and 2 (moderate roughness). The line through the center of each diamond is the group mean. The top and bottom diamond vertices are the respective upper and lower 95% confidence limits (CI) about the group mean.

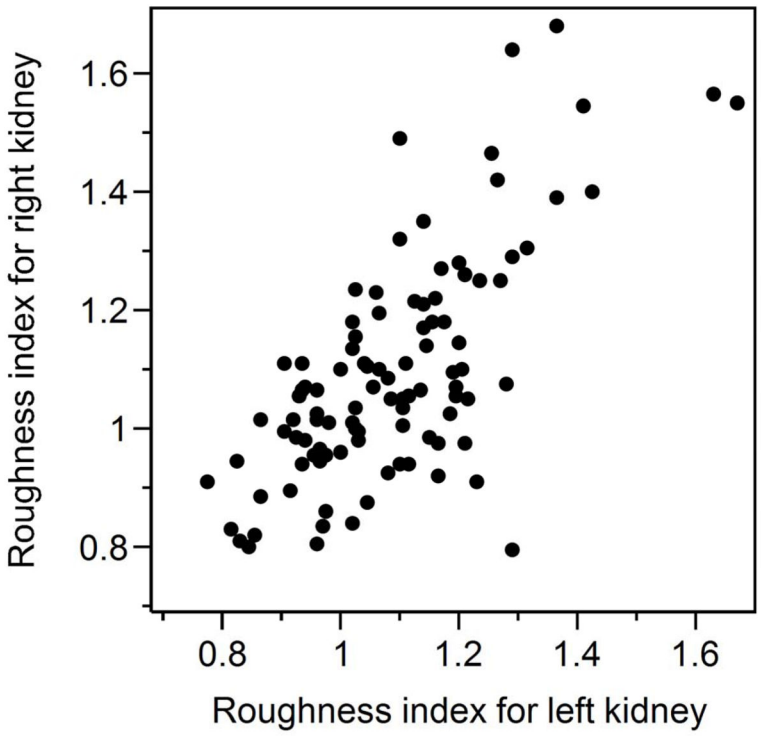


Figure 4.
Scatter plots of roughness index of left (L) and right (R) kidneys for Set-2 (n=200 kidneys from 100 subjects) (r=0.70, 95% CL 0.58–0.79).

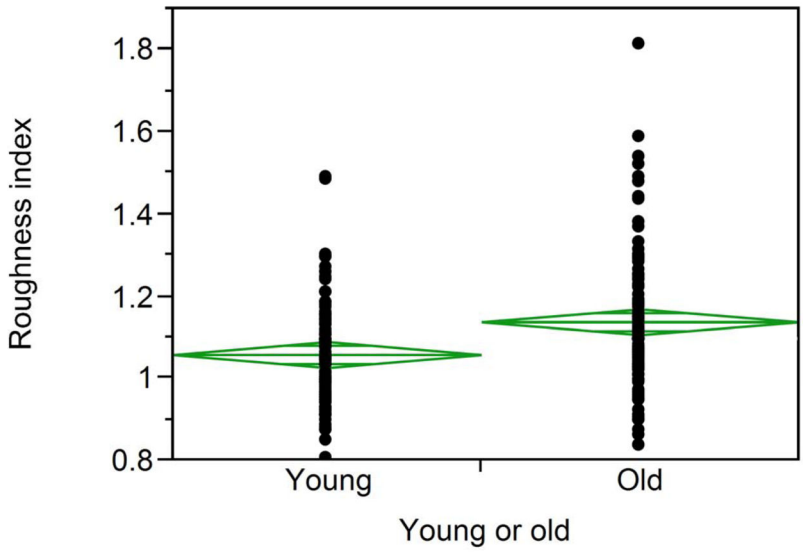


Figure 5.

The roughness index (average of left and right kidneys) of young subjects was significantly lower than in old subjects (p=0.0005).

Table 1

Demographic characteristics for each date set analyzed

	Age, years (Mean ± SD)	Female	White
Set-1	44 ± 12	53%	100%
Set-2	44 ± 13	61%	97%
Set-3	48 ± 11	57%	100%
Set-4	Old group: 67 ± 3 Young group: 22 ± 2	Old group: 57% Young group: 40%	Old group: 100% Young group: 93%