A new method for computer-assisted differentiation of the urinary opacities: calculi and mimickers

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Aims and objectives

Stones in the urinary tract are common and can be diagnosed by current technology (1). However, computed tomography (CT) scans, especially obtained in emergent conditions can lead to difficulties in differential diagnosis of urinary tract stones and calcifications that develop along the urinary tract or within its close proximity (2). In this study, we aimed to specify the turbidity characteristics of ureteric stone, renal stone, and non-calcular turbidities by using an image analysis program that detects micro-structural characteristics of urinary stones. In this way, we aimed to analyze the automatically differentiation of abnormal turbidities that may cause a diagnostic dilemma near or within the urinary tract, via the integration of this program to the urinary tract CT software.

Methods and materials

CT technique and Patients

This study was approved by the Institutional Review Board and Ethics Committee. Informed consent was obtained from all the cases. Concurrently, this research was conducted with another study which aims at a chemical analysis of calculi, to determine the chemical characteristics of stones with CT, the urinary tract images (n=38, 27 male, 11 female, mean age: 41 years) obtained from dual energy CT system (Somatom Definition Flash, Dual Source CT, Siemens, Erlangen, Germany) in our clinic. Dual energy CT (DE-CT) examinations were obtained using a two-acquisition protocol. First, a lower-dose and then higher-dose unenhanced acquisition from the upper kidney lobe to the pubic symphysis was performed with tube potentials, 80 and 140 kV, tube current, 340 and 90 mAs, collimation, 2×64×0.6 mm; pitch, 1.2; rotation time, 0.5 second; image reconstruction thickness, 1 mm; reconstruction interval, 0.8 mm). This protocol is routinely used at our institution to diagnose patients with acute flank pain suspected to have renal colic.

The calculi that were detected at DE-CT images were grouped as renal (n=40) and ureteric (n=45). These urinary calculi in 38 cases were also confirmed with another modality [ultrasonography (n=13), IVP (n=18), CT-urography (n=7)]. Other radio-opaque structures at CT sections that were identified outside but within close proximity of the urinary tract, such as atherosclerotic calcifications in iliac arteries, phleboliths in pelvis, and calcifications inside or around the prostate or cervix, were all recorded as "other turbidities" (n=43).

Image processing technique
DECT images were created automatically as 80kV+140kV hybrid images and DICOM formats of images were transferred into an image processing program named as ImageJ. ImageJ is a java based, open source code "multithreaded" image processing and analyzing program developed by National Institute of Health (NIH), USA (3). ImageJ plugin is code particles written in Java language that can be run on ImageJ platform and it was developed to add a new function to ImageJ platform (4).

The images used in this study had a 1268x1936 resolution and 8 bit color depth. The demarked calcification zone to be analyzed was cut and detached from the picture, and then the cut segments were converted into black-white (binary) image using the threshold command of ImageJ program (Fig. 1).

When this command is run it turns to black above a threshold level and to white below. Finally, morphological analysis was done using ImageJ plugins on the created black-white image. Area value represents the occupied place by the object in pixel². Perimeter value represents the circumference of the object in pixel. Major, minor and angle are the values related to "best fitting ellipse" to that object. Major and minor represents the length of primary and secondary axis of the ellipse whereas angle value represents the angle between primary axis and x axis of image. Circularity, aspect ratio, round and solidity values gives the roundness of the object in numerical value. Circularity value is only 1 for a complete circle. When the value comes close to zero the object gets an elongated shape. The last calculated values were Feret measurements of the object. The straight line drawn between the farthest two points on the border of the selected object using callipers was called Feret angle. Feret value represents the length of this line. FeretX and FeretY values give the initial coordinate values of Feret diameter. MinFeret value represents the distance between the nearest two points on the border of the object. Feret Angle represents the angle between Feret diameter and horizontal axis. The morphological terminology was summarized in Table 1.

**Table 1.** The morphological characteristics of calculi or calcification evaluated by ImageJ.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Explanations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Area</td>
<td>Area of selection in square pixels</td>
</tr>
<tr>
<td>Area Fraction</td>
<td>The percentage of pixels in the image or selection</td>
</tr>
<tr>
<td>Perimeter</td>
<td>The length of the outside boundary of the selection</td>
</tr>
<tr>
<td>Major</td>
<td>primary axis of the best fitting ellipse.</td>
</tr>
<tr>
<td>Minor</td>
<td>secondary axis of the best fitting ellipse.</td>
</tr>
<tr>
<td>Angle</td>
<td>the angle between the primary axis and a line parallel to the X-axis of the image.</td>
</tr>
<tr>
<td>Circularity</td>
<td>$4\pi \times \frac{\text{area}}{\text{perimeter}^2}$</td>
</tr>
</tbody>
</table>
More circular when approaching 1.0, more elliptical when approaching to “0”

**Solidity**

\[ 4 \times \frac{\text{Area}}{\text{major_axis}^2} \]

Shows how granular the object is

**Feret**

The longest distance between any two points along the selection boundary, also known as maximum caliper

**FeretX**

Feret diameter on X The starting coordinate.

**FeretY**

Feret diameter on Y The starting coordinate.

**FeretAngle**

Angle between two coordinates

**MinFeret**

do indicate normal distribution.

After the evaluation of turbidities for each of the three groups using ImageJ, the provided data were transferred into excel tables and recorded.

**Statistical Analysis**

All of the statistical analyses were performed by using the SPSS v15 (SPSS Inc., Chicago, IL) package for Windows. Homogeneity of Variance test analysis was performed to test the distribution of groups. For Gaussian-distributed variables, the data are expressed as arithmetic mean±standard deviation (SD). For those variables that were not Gaussian distributed, the data are indicated as median (25th-75th interquartile range). Comparisons among the three groups were undertaken by using the One-Way Anova analysis or Kruskal-Wallis variance analysis for Gaussian and non-Gaussian-distributed variables, respectively. If the differences were significant, pairwise comparisons would be based on the Student t-test or Mann-Whitney U-test with adjustment for Bonferroni correction to reveal which subgroups were different, respectively. All of the reported P-values were two-tailed, and those less than 0.005 were considered to be statistically significant. Because total area, minor, angle, feretangle and minferet did not indicate normal distribution, non-parametric tests were applied. For the rest of the morphological characteristics parametric tests were used. The diagnostic accuracy of the biochemical variables were assessed by calculating the areas under the receiver operating characteristic (ROC) curves, sensitivity, specificity and odds ratio. ROC curves were used to determine the best cutoff points to identify the presence of renal opacity or ureteral turbidity. The odds ratio values for each variable were assessed by using multivariate logistic regression analysis.

**Images for this section:**
**Fig. 1:** Figure 1.a-h. Especially, a calculus that shows the stages in processing some of the parameters that are statistically significant in the ImageJ programme a) Original axial CT Image. b) The cut zone from the image, c) The black-white image after running threshold command, d) Determination of the border of object, e) Drawing of an ellipse best fit to the border of object, f) Feret diameter of object, g) Measuring the Angle, h) Measuring the Feret angle.
Results

The mean value (±2 SD) of data for each variable calculated for turbidities at ureteric, renal and other groups detected via ImageJ program was shown in Table 2.

Table 2. The mean value (±2 SD) for all variables at groups of renal, ureter and other turbidities.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Renal (n=40)</th>
<th>Ureter (n=45)</th>
<th>Others (n=43)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total area</td>
<td>600(263-1626)</td>
<td>527(245-864)</td>
<td>392(204-898)</td>
<td>0.247</td>
</tr>
<tr>
<td>Area fraction</td>
<td>7.2±3.9</td>
<td>5.9±3.5</td>
<td>6.1±4.7</td>
<td>0.326</td>
</tr>
<tr>
<td>Perimeter</td>
<td>99.5±58.1</td>
<td>88.5±41.6</td>
<td>77.3±35.2</td>
<td>0.088</td>
</tr>
<tr>
<td>Major</td>
<td>33.4±18.7</td>
<td>31.0±14.7</td>
<td>27.2±12.9</td>
<td>0.188</td>
</tr>
<tr>
<td>Minor</td>
<td>21.5(15.5-32.2)</td>
<td>20.0(14.2-27.6)</td>
<td>18.5(13.3-26.5)</td>
<td>0.177</td>
</tr>
<tr>
<td>Angle</td>
<td>76.3(41.5-116.5)</td>
<td>69.2(47.6-92.2)</td>
<td>99.1(84.2-121.9)</td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Circularity</td>
<td>0.86±0.08</td>
<td>0.88±0.07</td>
<td>0.88±0.088</td>
<td>0.395</td>
</tr>
<tr>
<td>Solidity</td>
<td>0.93±0.04</td>
<td>0.94±0.02</td>
<td>0.94±0.03</td>
<td>0.188</td>
</tr>
<tr>
<td>Feret</td>
<td>35.1±19.4</td>
<td>32.0±14.9</td>
<td>28.1±12.8</td>
<td>0.127</td>
</tr>
<tr>
<td>Feret X</td>
<td>58.5±49.1</td>
<td>58.8±50.7</td>
<td>68.7±71.7</td>
<td>0.651</td>
</tr>
<tr>
<td>Feret Y</td>
<td>44.7±26.7</td>
<td>50.1±21.9</td>
<td>40.8±26.0</td>
<td>0.219</td>
</tr>
<tr>
<td>Feret angle</td>
<td>88.5(50.6-128.0)</td>
<td>66.9(49.3-91.5)</td>
<td>102.2(69.0-120.7)</td>
<td><strong>0.004</strong></td>
</tr>
<tr>
<td>Min Feret</td>
<td>22.5(16.6-32.4)</td>
<td>20.9(14.8-28.5)</td>
<td>18.3(14.0-26.0)</td>
<td>0.130</td>
</tr>
</tbody>
</table>

aP <0.01 versus ureteral opacity group and P= 0.027 versus renal group; There is statistically significant difference between ureteral turbidity group and others, renal stone group and others for angle parameter.

bP <0.01 versus ureteral opacity group. Statistically significant difference exists between ureteral turbidity group and others for Feretangle parameter.

Furthermore, the values related to calculous turbidity and non-calculous turbidity were summarized to make a general comparison. The ROC curves constituted after the evaluation of ROC analysis of variables (Fig. 2) and the AUC and P values related to these data were shown in Table 3.

Table 3. The comparison of mean parametric values of calculous and non-calculous turbidities.
Calcular opacities (n=85) Non-calcular opacities(n=43) $p$ value

total area 561(248-1174) 392(204-898) 0.147
area fraction 6.5±3.7 6.1±4.7 0.637
perimeter 93.7±50.0 77.3±35.2 0.034
major 32.2±16.7 27.2±12.9 0.067
minor 20.8(15.0-29.6) 18.5(13.3-26.5) 0.094
angle 75.0(43.9-105.4) 99.1(84.2-121.9) 0.001

circularity 0.87±0.077 0.88±0.088 0.496
solidity 0.94±0,03 0.94±0.03 0.875
feret 33.5±17.1 28.1±12.8 0.046
feret X 50.0(31.0-64.5) 44.0(28.0-65.0) 0.565
feret Y 47.5±24.3 40.8±26.0 0.162
feret angle 70.9(50.7-112.2) 102.2(69.0-120.7) 0.006
min feret 21.2(15.8-31.4) 18.3(14.0-26.0) 0.070

As for values obtained frm Table 3 and the constituted ROC curves; no statistical significant difference was found between three groups for all variables except those for angle and Feretangle. There was statistically significant difference between calculi group and non-calculous turbidities for these two parameters ($p<0.001$; $p=0.006$, respectively).

The mean values for angle parameter at renal, ureter and other turbidities were 80.598±7.692 (4.20-169.32), 69.341 ± 5.278 (2.50 - 133.62) and 1.023 ± 4.983 (41.70 - 172.90) respectively.

The mean values for Feret angle at renal, ureter and other turbidities were 88.275 ± 7.511 (6.01 - 168.02), 68.959 ± 4.976 (12.53 - 128.66) and 97.886 ± 5.204 (16.93 - 167.74) respectively.

The data for angle and Feret angle were shown in separate information with ROC curve graphs (Figs. 3, 4).

According to the statistical data, sensitivity and specificity rates obtained at different threshold values were constituted. These threshold values for angle and Feretangle
parameters that can be used in differentiating the calculi and control group. For example, considering the cut-off value of 83 for Angle; it is possible to differentiate the opacity with 79% sensitivity, 61% specificity. For Feret Angle, considering the cut-off value of 68.6; it is possible to differentiate the opacity with 82% sensitivity, 48% specificity.

The analysis performed for calculous and non-calculous group showed that Angle and Feretangle are most effective parameters for differentiation. The multivariate logistic regression analysis of renal and ureteric calculi group showed that these two groups have discriminative statistically significant differences for Feretangle and Minor parameters (Table 4).

Table 4. The difference between Renal and Ureteric calculi

<table>
<thead>
<tr>
<th>Variables in the Equation</th>
<th>Parameter</th>
<th>Wald</th>
<th>Odds ratio (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Feretangle</td>
<td>10.372</td>
<td>5.477(1.946-15.418)</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>Minor</td>
<td>8.721</td>
<td>8.060(2.018-32.201)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Multivariate logistic regression analysis showed that, high minor (OR 8.060, 95%CI 2.018-32.201, P = 0.003) and high feretangle (OR 5.477, 95%CI 1.946-15.418, P = 0.001) were statistically significant parameters to distinguish the renal calcules from ureteral stones.

The odds ratio for feretangle was 5.477. This demonstrates the probability of renal stone formation is 5.477 fold increases as the feretangle value exceeds 80.45 compared to below 80.45. The odds ratio for Minor variable was 8.060. This means that the probability of renal stone formation is 8.060 fold increases as the minor value exceeds 19.89 compared to below 19.89.

Images for this section:
**Fig. 1:** Figure 1.a-h. Especially, a calculus that shows the stages in processing some of the parameters that are statistically significant in the ImageJ programme a) Original axial CT Image. b) The cut zone from the image, c) The black-white image after running threshold command, d) Determination of the border of object, e) Drawing of an ellipse best fit to the border of object, f) Feret diameter of object, g) Measuring the Angle, h) Measuring the Feret angle.
**Fig. 2:** Figure 2. Combined ROC curve graphs of parameters that have statistically significant characteristics.
Fig. 3: Figure 3. ROC curve and the statistical data related to angle (a Under the nonparametric assumption, b Null hypothesis: valid area = 0.5).
Fig. 4: Figure 4. ROC curve and the statistical data related to Feret Angle. There is a correlation between the positive actual state group and the negative actual state group at feret angle. Statistics may be biased. (a Under the nonparametric assumption, b Null hypothesis: valid area = 0.5).
Conclusion

Morphologic parameters that are computed based on binary morphological analysis can help us to distinguish the calculi along the urinary tract from other radio-opaque structures. The same approach can also be used to automatically differentiate between renal and ureteric stones. We believe that computer-aided diagnosis tools can be developed based on the findings presented in this study to identify urinary opacities in CT images.

Personal information

References