Fully Automated Longitudinal Assessment of Renal Stone Burden on Serial CT Imaging Using Deep Learning

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Abstract

Purpose

Use deep learning (DL) to automate the measurement and tracking of kidney stone burden over serial computed tomography (CT) scans.

Materials and Methods

This retrospective study included 259 scans from 113 symptomatic patients being treated for urolithiasis at a single medical center between 2006 and 2019. These patients underwent a standard low-dose (SLD) non-contrast CT scan followed by ultra-low dose (ULD) CT scans limited to the level of the kidneys. A DL model was used to detect, segment, and measure the volume of all stones in both initial and follow-up scans. The stone burden was characterized by the total volume of all stones in a scan ($SV$). The absolute and relative change of $SV$, ($SVA$ and $SVR$, respectively) over serial scans were computed. The automated assessments were compared with manual assessments using Concordance Correlation Coefficient (CCC), and their agreement was visualized using Bland-Altman and scatter plots.

Results

228/233 scans with stones were identified by the automated pipeline; per-scan sensitivity was 97.8% (95% CI: [96.0 – 99.7]). The per-scan positive predictive value was 96.6% (95% CI: [94.4 - 98.8]). The median $SV$, $SVA$ and $SVR$ were 476.5 mm$^3$, $-10$ mm$^3$ and 0.89, respectively. After removing outliers outside were 0.995 (0.992 – 0.996), 0.980 (0.972 – 0.986), and 0.915 (0.881 – 0.939), respectively

Conclusions

The automated DL-based measurements showed good agreement with the manual assessments of the stone burden and its interval change on serial CT scans.
Introduction

The prevalence of kidney stones in the United States is said to be 10.6% in men and 7.1% in women.\textsuperscript{1} Recurrent stones are also common, exceeding 30\% to 40\% at 5 years.\textsuperscript{2} A key component in the management of symptomatic urolithiasis is serial assessment of the patient’s stone burden. The AUA guidelines suggest using renal imaging for periodic follow-up and assessment.

Non-enhanced CT can be used to accurately diagnose and quantify kidney stones.\textsuperscript{3} Though other imaging modalities such as kidney, ureter and bladder (KUB) radiography and ultrasound (US) are often employed due to cost or availability constraints, they suffer from much lower sensitivity and/or specificity.\textsuperscript{4,6} Furthermore, these modalities also fail to assess stone size accurately.\textsuperscript{7-9} Therefore, noncontrast CT is the best modality for detecting stones and assessing their size.

Despite its accuracy, CT imaging incurs high cost and carries a radiation risk. To mitigate both cost and radiation risks, an ultra-low dose (ULD) limited kidney protocol has been developed and validated for the follow-up of kidney stones.\textsuperscript{10} Compared to a standard low dose (SLD) CT, the ULD scan reduces radiation dosage significantly (target \textasciitilde 90\%) by adjusting tube current range, slice thickness, and noise index, and costs less due to the limited scan area.

The CT based follow-up allows the accurate assessment of stone sizes. However, linear measurements, either in 1D (axial or coronal plane), or 2D (reported as length \times width) typically used in the clinic may have substantial interobserver variability and may be sensitive to window/level settings.\textsuperscript{11} Automated computer-aided volumetric measurements mitigate this issue and are reproducible.\textsuperscript{12,13} High interobserver variability (\textasciitilde 15-20\%)\textsuperscript{13} can make it difficult to assess changes in stone size over time. Additionally, volumetric measurements are more sensitive to interval change than linear measurements (for a \Delta r change in radius, the change in volume \Delta V \propto r^2 \times \Delta r) and can enable better assessment of stone size change in follow-up.

The total stone burden, defined as the sum of the volumes of all stones in the kidneys, is a key metric of interest in evaluating kidney stones and assessing interval change between
the initial and follow-up scans. Indeed, in predicting future symptomatic stone events, the total volume of all stones in a scan was found to be the most predictive, more so than other features such as the largest stone diameter or the number of stones.\textsuperscript{14}

In this paper, we modify and use the deep-learning based model proposed and validated in previous work to assess and track kidney stone burden between initial SLD scans and subsequent follow-up ULD CT scans.\textsuperscript{15} While deep learning models have been developed and used for various applications including detecting or segmenting kidney stones, inferring stone types, or predicting outcomes, to the best of our knowledge, the current work is the first that evaluates their usage in assessing stone burden and its interval change in serial CT scans.\textsuperscript{16-19}

**Materials and Methods**

**Patient population and CT protocol**

This was a retrospective study from a single medical center, was HIPAA-compliant and was approved by the Institutional Review Board. The need for additional signed informed consent was waived.

A summary of the study plan is illustrated in Figure 1. The cohort comprised 113 patients evaluated for urolithiasis between 2006 and 2019 and followed up with an ultra-low-dose CT (ULD) scan between 2017 and 2019 (259 total CT scans). Every patient in the cohort had an initial standard low dose (SLD) noncontrast CT scan. The median follow-up interval was 770 days, (IQR: [294, 1768] days). 15, 7 and 1 patients had two, three and four follow-up scans, respectively. The ULD follow-up scan coverage was limited to the level of the kidneys. Aggressive dose reduction of the ULD series was achieved by adjusting tube current range and noise index. All ULD CT scans were performed without intravenous contrast on a 64-detector-row Discover CT750 HD scanner (GE Healthcare) at 120 kV with variable tube current modulation (Smart mA). The mean effective dose was 4.1 mSv for the ULD compared to 13.4 mSv for the SLD (p<0.01).
CT Reconstruction and Preprocessing

All images were reconstructed in 2.5 mm slice thickness at 1.25 mm intervals in the transverse (axial) plane. The SLD series was reconstructed using filtered back-projection (FBP), and the ULD series was reconstructed using model-based iterative reconstruction (MBIR). One axial supine scan that included the entire kidney was selected from each study and resampled to 1 mm slice spacing.

Kidney stone detector algorithm

The stone detection and segmentation pipeline is a slightly modified version of the one presented in previous work. The pipeline segments the kidneys using a 3D U-Net, and then candidate stones are identified within the kidney using thresholding at 130 HU, followed by connected components analysis on the thresholded binary mask. Finally, a convolutional neural network (CNN) based classifier then predicts if the “candidate” is a stone. In this work, we trained a new kidney segmenter using the nnU-Net framework, using several publicly available datasets which contain segmentations of the kidney: Beyond the Cranial Vault (BTCV), Multi-Modality Abdominal Multi-Organ Segmentation Challenge 2022 (AMOS), the 2021 Kidney and Kidney Tumor Segmentation Challenge, and Fast and Low-resource semi-supervised Abdominal oRgan sEGmentation challenge (FLARE) 2021 and 2022. For each dataset, we only used the kidney segmentations from the labeled examples in the respective training sets to use as ground truth for training the kidney segmenter. After training the nnU-Net model, the kidney segmenter was quantitatively validated on 20 validation cases from the FLARE 2022 dataset for which the ground truth was available. Since the stone detection and segmentation pipeline was primarily trained and used for small stones, it rejected large stones as false positives using a volume threshold criterion; however we removed the volume threshold to account for the large stones in our cohort. The CNN classifier, being trained on primarily small stones also tended to reject large stones as false positives – to mitigate that, the CNN was not used on stone candidates with volume greater than or equal to 250 mm$^3$. We also impose a minimum stone size criterion since the high noise in the ULD scans causes single voxel false positive detections. We reject all stone candidates with volume < 3mm$^3$ (equivalent spherical diameter of 1.8 mm) since smaller stones are often not considered to be clinically
significant, and it helps us reduce the false positive rate in the noisy ULD scans.\textsuperscript{24,25} The software outputs the volumetric size (mm\textsuperscript{3}), location (XYZ coordinates, upper/lower pole, left/right kidney), and attenuation (mean, median, standard deviation, maximum Hounsfield unit, HU) of kidney stones.\textsuperscript{15}

**Manual screening of the automatically detected stones**

A board-certified radiologist (13 years of experience) manually reviewed the results of the kidney stone detector to identify false-positive detections and missed stones. Ground truth segmentations were obtained by correcting the automated segmentations: missed stones were segmented using a 130 HU threshold paint brush module and false positive stone segmentations were removed using 3D Slicer (version 4.10.2) software. The stone burden per scan was assessed based on the ground truth segmentation, as described below.

**Assessing stone burden**

We consider the total volume of all stones ($SV$) as the primary measure of stone burden. An individual stone in the initial scan may remain stable, grow or disappear in the follow-up scan, or new stones can appear on the follow-up scan. For assessing the change in stone burden, we considered two statistics: the absolute and relative change in total stone volume. Given a pair of consecutive scans (initial and follow-up) of the same patient, we computed the (signed) absolute difference $SV_A = SV_{FU} - SV_{initial}$ and the relative change $SVR = SV_A / SV_{initial}$ for the manual and the automated measurements. If $SV_{initial}$ was zero, $SVR$ was set to ‘undefined’ and dropped in subsequent statistical analysis.

**Evaluating agreement between manual and automated measurements**

First, we evaluate the agreement between the manual and automated measurements of $SV$ considering every scan in a cohort as an individual sample. For $SV_A$ and $SVR$, every pair of consecutive scans from each patient is considered as a sample. We use Lin’s Concordance Correlation Coefficient (CCC) to evaluate the agreement between manual and automated measurements of $SV$, $SV_A$ and $SVR$. We also trim our data to remove outliers beyond the 5\textsuperscript{th} and 95\textsuperscript{th} percentiles while calculating the $SV$, $SV_A$ and $SVR$, since
CCC is sensitive to outliers and non-normality of data due to its reliance on the squared distance function.

We also created Bland-Altman and scatter plots to visualize the agreement between manual and automated measurements for $SV$, $SVA$ and $SVR$.

**Statistics**

All statistics were done with R version 4.2. For computing CCC, we used the “DescTools” (v. 0.99.46) libraries in R. The “BlandAltmanLeh” (0.3.1) and “ggplot” (v. 3.3.6) libraries were used to construct the Bland-Altman plots.

**Results**

Table 1 summarizes key characteristics of the cohort. The median number of stones per scan was 2 (IQR: [2,5]) and the median $SV$ was 476.5 mm$^3$ (IQR: [196.5, 2043] mm$^3$) per scan.

The kidney segmenter achieved a mean Dice coefficient of 0.968 (std: 0.030) on the 20 test cases obtained from the FLARE validation set. Qualitative evaluation also showed adequate performance even in the presence of large stones, compared to the previously validated method.

Manual assessment identified 233 (out of 259) scans with at least one stone, of which 228 were identified by the DL pipeline (per scan sensitivity 97.8% (95% CI: [96.0 - 99.7])). 228 out of 236 scans identified by the DL pipeline had a true stone (positive predictive value per scan was 96.6% (95% CI: [94.4 - 98.8])). 51/233 scans had numerous stones, nephrocalcinosis, or had stones that were confluent with adjacent stones, making it difficult to discern individual stones. Barring these cases, 726/830 stones greater than or equal to 3 mm$^3$ in volume were detected by the DL with a per stone sensitivity of 87.5% (95% CI: [85.2 – 89.7]); the median number of false positives per scan was 0 (IQR: [0,1], mean: 0.72). False positive stone detections were due to dense renal calcification (in 23 scans), cyst related calcification (15), coarse noise (14), metal artifacts (6), foreign bodies such as metal or catheter (6), atherosclerotic plaque (4), adjoining vertebra, rib or other extraneous features outside the kidney caused by over-segmentation of the kidneys (3).
Figure 2 shows a few examples of stone segmentation, while Figure 3 and Figure 4 show some examples of missed stones and false positive stone detections, respectively.

Figure 5 shows the trajectory of $SV$ over multiple scans for three selected patients. The median $SVA$ was -10 mm$^3$ (IQR: [-521, 99]) at an annualized rate of -5.2 mm$^3$ / yr. The median SVR was 0.89 (IQR: [0.33, 1.28]) with an annualized rate of 0.95 (IQR: [0.62, 1.15]). The CCC between the manual and automated measurements for $SV$ was 0.995 (95% CI: 0.993 – 0.996). For $SVA$ and $SVR$, the CCC was 0.980 (0.972 – 0.986) and 0.914 (0.881 – 0.939), respectively. The median (signed) difference between the manual and the automated measurement of $SV$ was 0 mm$^3$ (IQR: [-1, 36.75] mm$^3$). For $SVA$ and $SVR$, the median differences were 0 mm$^3$ (IQR: [-59, 19] mm$^3$) and 0 (IQR: [-0.04, 0.01]), respectively. Figure 6 shows Bland-Altman and scatter plots showing the agreement between manual and automated measurements for $SV$, $SVA$ and $SVR$. The extreme outliers on Figure 6 (a) were due to mis-segmentation of the kidneys and subsequent false positive stone detections outside the kidneys. Despite the presence of a few outliers, Figure 6 shows the strong agreement between the manual and automated measurements for $SV$, $SVA$ and $SV$.

**Discussion**

We used fully automated DL software to detect and measure kidney stones, assess the stone burden and track its change between initial and follow-up scans. We considered a cohort of patients who underwent a noncontrast SLD scan and were followed up by one or more noncontrast ULD scans limited to the level of the kidneys, targeted to reduce radiation dose by about 90%. While we focused on the total stone volume across both kidneys ($SV$) as the measure of stone burden in this paper, our method can be used to measure and track stone burden for individual kidneys as well.

Requiring no human intervention, our method can be very cheap and fast. Such automated tracking of stone burden can be very useful for following up individual patients with kidney stones, making treatment decisions, and for assessing the efficacy of stone related interventions in individuals as well as large cohorts; stones are often prone to recurring – even after interventions such as extracorporeal shock wave lithotripsy or percutaneous
nephrolithotomy – and follow-up with ULD scans and the proposed automated assessment method may improve outcomes in the clinic.\textsuperscript{19,25}

We found that the agreement of the automated measurements with manual measurements in terms of $SV$ is very high. The disagreement between manual and automated measurements mainly stemmed from either missed stones or from false positive detections. In the presence of large stones or artifacts in the imaging, the kidney segmenter sometimes undersegmented the kidneys, resulting in missed stones in the undersegmented kidney regions (see Figure 3). False positive detections were typically bright spots in the kidney caused by dense renal calcifications (which may be considered pre-stones and not true false positives), cyst related calcification, CT imaging artifacts caused by noise, atherosclerotic plaque in renal vessels, or foreign bodies such as catheter or metal. (Figure 4).

While detecting, measuring, and tracking kidney stones can be a tedious task with significant intra-reader and inter-reader variability, the automated method presents a viable alternative. Normally, the size of a kidney stone is measured by the maximal transverse diameter. However, this diameter is a poor indicator of the stone’s volume because stones are rarely spheres\textsuperscript{27} and because the linear measurement varies between readers\textsuperscript{12} and window settings,\textsuperscript{11} especially when the stones have complex 3D shapes. The automated DL-based method provides accurate volumetric measurements (validated in a prior study\textsuperscript{15}) that can be more informative in the clinical setting. Further, small size changes over time are easier to assess with 3D volumetric measurements compared to linear size measurement. Focusing on the total stone volume has additional benefits when tracking stone burden change. An individual stone in an initial scan can move, grow, split into two, or be passed, and new stones may form during the follow-up interval. Thus, tracking individual stones can be difficult and error-prone. Obtaining corresponding ground truth may be tedious, time consuming and even impossible to ascertain, except for relatively small cohorts. Furthermore, tracking individual stones may have limited value in clinical practice. Besides providing prognostic and clinical value, focusing on the total stone volume, and using the automated method allows us to examine large cohorts that would have been otherwise out of reach.
Some limitations should be noted. The cohort was obtained from a single institution in the United States, and the robustness of results to variations in CT acquisition or patient characteristics across different institutions could not be assessed. We plan to validate our method on external cohorts in the future. Secondly, although we used thin slice spacing CT scans (1.25mm), partial volume averaging can affect the stone volume measurements—we have not considered its effect here since the ground truth assessments performed by the radiologist did not consider it either. Thirdly, we have also not considered stone composition when computing the stone burden. Finally, in computing $SVA$ and $SVR$, we have assumed that $SV$ measurements on SLD and ULD scans are directly comparable. While we do not expect any significant discrepancies between $SV$ measurements made on SLD and ULD scans, this has not been validated in this study.

In summary, we used fully automated DL software to detect and measure kidney stones and track stone burden over multiple ULD follow-up scans. The automated measurements of stone burden and its change over follow-up scans shows good agreement with their manual counterparts.

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**Author Contribution Statement**

PM: conceptualization, data curation, formal analysis, methodology, software, writing – original draft, writing – review and editing
SL: conceptualization, data curation, formal analysis, methodology, software, writing – original draft, writing – review and editing

DE: conceptualization, data curation, methodology, software, writing – review and editing

SN: data curation, writing – review and editing

PJP: conceptualization, data curation, writing – review and editing, supervision, project administration

RMS: conceptualization, data curation, supervision, resources, project administration, writing – review and editing
References


Abbreviations:

CT: Computed Tomography
DL: Deep Learning
SLD: standard low dose scan
ULD: ultra-low dose scan
SV: total stone burden, sum of volumes of all stones in a scan
SVA: stone burden change (absolute)
SVR: stone burden change (relative)
CCC: Concordance correlation coefficient
KUB: Kidney, ureter and bladder
US: ultrasound
IQR: intra-quartile range
FBP: filtered back-projection
MBIR: model based iterative reconstruction
BTCV: Beyond the Cranial Vault
AMOS: Multi-Modality Multi-Organ Segmentation Challenge
FLARE: Fast and Low-resource semi-supervised Abdominal oRgan sEgmentation
CNN: Convolutional Neural Network
HU: Hounsfield Units
CI: confidence interval
### Table 1: Cohort characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Cohort</th>
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<tr>
<td>Number of subjects (n)</td>
<td>113</td>
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<tr>
<td>Number of scans per patient (median, IQR)</td>
<td>2, (2, 2)</td>
</tr>
<tr>
<td>Time interval between scans (days) (median, IQR)</td>
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</tr>
<tr>
<td>Number of kidney stones per scan (median, IQR)</td>
<td>2, (2, 5)</td>
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<tr>
<td>Total stone burden per scan SV (mm$^3$) (median, IQR)</td>
<td>476.5, (196.5, 2043)</td>
</tr>
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<td>Volume of individual stones (mm$^3$) (median, IQR)</td>
<td>40, (13, 160)*</td>
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<tr>
<td>Maximum diameter of individual stones (mm) (median, IQR)</td>
<td>6, (3.3, 10.2)*</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Male</td>
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<tr>
<td>Female</td>
<td>70 (61.9%)</td>
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<tr>
<td>Unknown</td>
<td>0</td>
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<tr>
<td>Age at initial scan (yrs) (median, IQR)</td>
<td>59.5, (48.25, 68)**</td>
</tr>
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</table>

*Scans with numerous stones, nephrocalcinosis, or with stones confluent with adjacent stones were excluded*

**Age information was unavailable for 4 patients**
**Figures**

![Diagram of study outline](Image)

Figure 1: Outline of the study.
Figure 2: Examples of stone detection and segmentation by the automated pipeline. The left column shows the original CT (windowed) while the right column shows the stone segmentations overlaid on the CTs. The yellow arrows mark the position of the stones.
Figure 3: Examples of stones missed by the automated pipeline. The left column shows the original CT (windowed) while the right column shows the kidney segmentations overlaid on the CTs. The yellow arrows mark the position of the missed stones. In (a) and (b), the kidneys are under-segmented resulting in missed stones. In (c), the left kidney is missed completely, possibly due to severe imaging artifacts, resulting in missed stones in the left kidney.
Figure 4: Examples of false positive stone detection by the automated pipeline. The left column shows the original CT (windowed) while the right column shows the stone segmentations overlaid on the CTs. The yellow arrows mark the position of the stones. In (a) and (b), the detections are likely due to calcification in the wall of a cyst and a proximal ureteral calculus (not truly a false positive), respectively. In (c), the false positive is caused due to severe artifacts in the image.
Figure 5: Total stone burden (SV) trajectories over time for three selected patients. Patient (a) is male, age 79 yrs on the initial scan date, (b) is female, age 46 yrs on the initial scan date, and (c) is female, age 79 on the initial scan date. The SV decreases steadily for (a), fluctuates for (b) and increases steadily for (c).
Figure 6: Agreement between the automated and the manual measurements for SV, SVA and SVR. The left column shows the Bland-Altman plots while the right column shows scatter plots with automated and manual measurements. The upper and lower horizontal lines in the Bland-Altman plots represent the 95% CI. The grey bands in the scatter plots represent the 95% CI for the best fit regression line (the solid black line). The red dashed line denotes perfect agreement. Please note that outliers were removed for the scatter plots on the right.