Quantitative assessment of renal obstruction in multi-phase CTU using automatic 3D segmentation of the renal parenchyma and renal pelvis: A proof of concept

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HIGHLIGHTS
- The algorithm enables accurate segmentation of the renal parenchyma and renal pelvis.
- The algorithm estimates the amount of contrast media in the various CTU phases.
- Objective indicators were developed to alert the presence of renal obstruction.
- In hydronephrotic kidneys the total amount of contrast media did not decrease.
- In hydronephrotic kidneys the drainage time, $T_{1/2}$, was longer than 20 min.

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Keywords: CT urography, 3D kidney segmentation, Renal obstruction, Urine drainage rate

ABSTRACT

Purpose: Quantitative evaluation of renal obstruction is crucial for preventing renal atrophy. This study presents a novel method for diagnosing renal obstruction by automatically extracting objective indicators from routine multi-phase CT Urogramy (CTU).

Material and methods: The study included multi-phase CTU examinations of 6 hydronephrotic kidneys and 24 non-hydronephrotic kidneys (23,164 slices). The developed algorithm segmented the renal parenchyma and the renal pelvis of each kidney in each CTU slice. Following a 3D reconstruction of the parenchyma and renal pelvis, the algorithm evaluated the amount of contrast media in both components in each phase. Finally, the algorithm evaluated two indicators for assessing renal obstruction: the change in the total amount of contrast media during the CTU phases, and the drainage time, $T_{1/2}$, from the renal parenchyma.

Results: The algorithm segmented the parenchyma and renal pelvis with an average dice coefficient of 0.97 and 0.92 respectively. In all the hydronephrotic kidneys the total amount of contrast media did not decrease during the CTU examination and the $T_{1/2}$ value was longer than 20 min. Both indicators yielded a statistically significant difference ($p < 0.001$) between hydronephrotic and normal kidneys, and combining both indicators yielded 100% accuracy.

Conclusions: The novel algorithm enables accurate 3D segmentation of the renal parenchyma and pelvis and estimates the amount of contrast media in multi-phase CTU examinations. This serves as a proof-of-concept for the ability to extract from routine CTU indicators that alert to the presence of renal obstruction and estimate its severity.
1. Introduction

Obstruction of the upper urinary tract is a common medical condition, which, if not diagnosed in the early stages, can lead to various complications, including hydronephrosis, renal dysfunction, inflammation, and renal atrophy [1]. In order to characterize the severity of obstruction, an evaluation of the urine drainage rate is typically performed by diuretic renal scintigraphy, in which both a diuretic and a radiopharmaceutical are injected, and dynamic images of the kidneys are obtained with a gamma camera [2]. However, renal scintigraphy does not provide anatomical information regarding the renal tissue [3], which is usually required. Some studies predict kidney function using ultrasound imaging [4,5], which provides anatomical information, but usually does not provide quantitative information regarding kidney function. Moreover, ultrasound is an operator dependent modality and the imaging may be incomplete due to overlying bowel gas. Magnetic Resonance Urography (MRU) provides anatomical and quantitative information regarding renal disorders [6,7]. However, in addition to the prohibitive economic costs, MRU is relatively insensitive for detecting kidney stones [8]. Recently, fluoroscopic images of the renal pelvis during a nephrostogram have also been used to estimate the drainage rate of the urine from the kidney, but this method is invasive and requires a catheter insertion into the renal pelvis [9].

Computed Tomographic Urography (CTU) is a contrast enhanced examination for imaging the urinary tract (kidneys, ureters, and bladder) during a series of phases in relation to the time of contrast agent administration [10]. In CTU, two-dimensional slices are reconstructed, and the attenuation coefficient of the tissue within each voxel is calculated in Hounsfield units (HU) [11]. CTU is a highly accurate method for diagnosing and characterizing urinary obstructions due to the ability to follow the flow of contrast media through the different phases and for comparing the tissue attenuation of the contrast media during the various phases [12,13]. However, these measurements are not feasible in routine clinical practice, since the contour of each kidney must be manually defined on each slice in each phase of the CTU. Therefore, in a routine clinical environment, renal obstruction estimation is observational and largely subjective.

This study aims to develop an algorithm for diagnosing renal obstruction by extracting quantitative information from routine CTU imaging. In the first stage, an algorithm for 3D segmentation of the renal parenchyma and the renal pelvis in all the CTU phases was developed, without the need for an enormous training dataset. Then, the automatic segmentation was used to diagnose renal obstruction and assess its severity by comparing the amount of contrast media within the various components of the kidney in the different CTU phases. The indicators provided by the algorithm may alert to the presence of a renal obstruction in the early stage and improve patient management.

2. Materials and methods

2.1. Dataset

This retrospective study is based on image processing of CTU anonymized examinations obtained using a Philips Brilliance 256-slice helical CT scanner. Thirty kidneys were analyzed, from 15 patients which were randomly selected from examinations performed between June 2017 and November 2019. Ten (66.7%) patients were males and five (33.3%) were females with a mean age of 59.4 ± 15.2 years. Based on the CTU examinations, 6 kidneys were classified as hydronephrotic and 24 kidneys as non-hydronephrotic by an experienced radiologist and an experienced urologist in consensus. Two of the patients with hydronephrotic kidneys had transitional cell carcinoma involving the ureter. One patient had a congenital uretero-pelvic junction stenosis and another patient had a ureteral narrowing due to previous surgery. In the case of bilateral hydronephrosis, there was benign prostatic hypertrophy as the underlying cause.

Each CTU examination included four phases. Phase 1 images were taken before the injection of contrast media (Fig. 1a). Phase 2 images, i.e. nephrographic phase images [14], were taken 90 s after the injection of 90–120 cc of iodinated contrast media (Iomeron 300, Bracco, Italy), as shown in Fig. 1b. Phase 3 images, i.e. excretory phase images [15], were taken 9.5 – 11.5 min after the injection of contrast media (Fig. 1c). Phase 4 images were taken 14 – 17 min after the injection of contrast media (Fig. 1d). Although the images in phases 1 – 3 were taken in a supine position while the images in phase 4 were taken in a prone position, in all the axial slices, the right kidney is on the left side of the image. In each of Figs. 1a – 1d, the renal parenchyma is marked by arrows, and the renal pelvis by circles. It should be noted that while the use
of a diuretic has been incorporated into the CTU protocol in some institutions, it is not part of the CTU protocol in the facility in which the study was undertaken.

Processing of the images in all the phases was performed on the axial slices. In phase 1 images, the attenuation of the renal parenchyma is similar to that of the surrounding organs [16]. In phase 2 images the renal parenchyma is filled with contrast media and its attenuation is therefore higher [17]. In phase 3 and phase 4 images the renal pelvis is filled with a high concentration of contrast media [18] and less contrast media remains in the renal parenchyma. The database is composed of 30 kidneys, while each CTU examination consists of hundreds of slices, in the various phases of the examination. The mean number of slices was $313 \pm 50$ in phase 1, $479 \pm 90$ in phase 2, $367 \pm 165$ in phase 3, and $226 \pm 98$ in phase 4. The slice thickness, slice increment, and voxel spacing varied between examinations, and between phases, and each slice in each phase can be considered a unique data point for developing and testing the algorithm. The slice thickness varied from 1 to 3 mm, the slice overlap ranged between 0% and 50% and the pixel size ranged between 0.7 mm and 0.9 mm.

2.2. The image processing algorithm

The developed algorithm used the DICOM® images of CTU and was implemented using MATLAB®, version R2018a [19]. Three CTU examinations (6 kidneys), including all the slices in all the CTU phases (3998 slices), were used for the algorithm development. Fig. 2 illustrates an overview of the algorithm used to accurately detect the 3D contour of the renal parenchyma and the renal pelvis, and assess the kidney function. The algorithm is complex since it must correctly segment the renal parenchyma even though, in many slices, the renal parenchyma appears inseparable from adjacent organs with similar HU values.

2.3. Selecting an initial slice, in which the kidney appears isolated

The first step of the algorithm is to automatically select an initial slice for starting the kidney segmentation. In the initial slice, the kidney must be isolated from all adjacent organs since, the segmentation of the renal parenchyma in subsequent slices is based on the segmented kidney in the preceding slice, as a reference.

The algorithm for selecting the optimal initial slice is different in each CTU phase. In phase 1, the selection of the optimal initial slice is challenging, since the attenuation of the renal parenchyma is similar to that of the surrounding organs [16]. In phase 2 images the renal parenchyma is filled with contrast media and its attenuation is therefore higher [17]. In phase 3 and phase 4 images the renal pelvis is filled with a high concentration of contrast media [18] and less contrast media remains in the renal parenchyma. The database is composed of 30 kidneys, while each CTU examination consists of hundreds of slices, in the various phases of the examination. The mean number of slices was $313 \pm 50$ in phase 1, $479 \pm 90$ in phase 2, $367 \pm 165$ in phase 3, and $226 \pm 98$ in phase 4. The slice thickness, slice increment, and voxel spacing varied between examinations, and between phases, and each slice in each phase can be considered a unique data point for developing and testing the algorithm. The slice thickness varied from 1 to 3 mm, the slice overlap ranged between 0% and 50% and the pixel size ranged between 0.7 mm and 0.9 mm.

![Fig. 2. A flow chart overview of the algorithm for defining 3D borders of the kidney in each CTU phase and diagnosing renal obstruction.](image)

![Fig. 3. Identifying an isolated kidney in phase 2 for selecting an optimal initial slice: (a) An axial slice of CTU in Phase 2. (b) A Binary image of the slice using a low threshold of $-35$ HU. (c) The binary image following object filtration by size. This stage removed also the renal parenchyma in the left side of the image which was adjacent to another organ. (d) The isolated kidney on the right side of the image after applying a threshold range of $75 - 275$ HU and filtering the remaining objects by shape and location. Therefore, this slice can serve as the initial slice for the kidney on the right side of the image.](image)
other tissues [20]. Therefore, the process of selecting an optimal initial slice is first performed in phase 2 images, in which the renal parenchyma is more easily identified as it contains contrast media, with a significantly higher attenuation (Fig. 1b).

This process includes several steps. First, for each slice in phase 2 (Fig. 3a), a binary image was generated by applying a low threshold value of -35 HU in order to include all the abdominal organs and muscles in the image [21] (Fig. 3b) and filtering all objects with an area larger than 4500 mm$^2$ or smaller than 960 mm$^2$ which are not likely to be isolated renal parenchyma [22] (Fig. 3c). Then, all organs with average attenuations outside the range of 75 and 275 HU, which is the expected attenuation of the parenchyma in phase 2 [16,17], were removed. Additional filters were applied to remove objects not fitting the spatial location of the renal parenchyma, which should be within the perirenal space [23], and objects with an eccentricity greater than 0.8, since the renal parenchyma shape should be approximately circular [24]. If the resulting image contains an appropriate object (Fig. 3d), this slice can serve as the initial slice.

Following the selection of the initial slice in phase 2, the initial slice in phase 1 was selected using the identified renal parenchyma in phase 2 as a reference. In this phase, a binary image was generated in all the slices by applying a threshold between -35 to 275 HU, and the relevant objects in each image were compared to the identified renal parenchyma in phase 2. The initial slice was selected as the slice containing the object with the most similar location and area to the renal parenchyma in phase

Table 1  
Performance of the algorithm for kidney segmentation, in each CTU phase.

|                        | Phase 1 | Phase 2 | Phase 3 | Phase 4 |
|------------------------|---------|---------|---------|---------|
| Success rate of initial slice identification | 86.7%   | 93.3%   | 73.3%   | 83.3%   |
| Accuracy of identification of kidney poles    | 0.92    | 0.95    | 0.94    | 0.92    |
| DC of renal parenchyma segmentation   | 0.96    | 0.98    | 0.95    | 0.97    |
| DC of renal pelvis segmentation  | N/A     | N/A     | 0.92    | 0.91    |

Fig. 4. Cropping and generating binary images by attenuation thresholding: (a) ROI in the original image, defined based on the spatial position of the kidney in the previous slice. Arrows pointing to renal parenchyma and pelvis. (b) BinaryLow image generated by applying a low threshold for identifying renal parenchyma. (c) BinaryHigh image generated by applying a high threshold for identifying renal pelvis.

Fig. 5. (In color) Segmentation results in the various CTU phases. The contours of renal parenchyma and the renal pelvis are marked in blue and green, respectively: (a) Non-contrast phase (phase 1). (b) Nephrographic phase (phase 2). (c) First excretory phase (phase 3). (d) Second excretory phase (phase 4).

Fig. 6. 3D reconstruction results: (a) The renal parenchyma of both kidneys. (b) The renal pelvis of both kidneys. (c) The generated MIP image of both kidneys.
2. In phases 3 and 4, the renal parenchyma is not as radio-opaque as in phase 2, and therefore it is more difficult to identify. However, in these phases, it is easier to identify the renal pelvis since it is filled with a high concentration of contrast media as shown in Figs. 1 c and 1 d. The identification of the renal pelvis serves as a reference point for defining a group of slices that also contain the renal parenchyma. Within this group of slices, the optimal initial slice for the renal parenchyma of each kidney was selected as described for the slices in phase 2.

For each kidney, in each CTU phase, the algorithm displays to the user the selected initial slice and asks for confirmation that the kidney is indeed isolated from adjacent tissues. If in the automatically selected slice the kidney is in contact with adjacent tissues, the algorithm enables the user to select manually another initial slice and then the algorithm continues the segmentation process automatically using the initial slices selected manually.

2.4. Defining ROI of the kidney in subsequent slices

For each CTU phase, the kidney was segmented separately in each slice, starting from the selected optimal initial slice and advancing sequentially toward the superior and inferior poles. In the first stage, a Region of Interest (ROI) containing the kidney is automatically cropped in each subsequent slice by expanding the bounding box of the identified kidney in the preceding slice by 25 mm in each direction, assuming that the spatial coordinates of the kidney should not change significantly between adjacent slices [25]. After the ROI of the kidney is defined, a BinaryLow image of the ROI, containing the renal parenchyma and other soft tissues, was generated in all the phases by applying a threshold.

Table 2
A detailed list of the indicators evaluated by the algorithm for each kidney in the dataset compared to the clinical assessment of hydronephrosis.

| Kidney (Patient, Side) | Hydronephrosis | Decrease in Total Contrast Media | Drainage Time of Parenchyma T_{1/2} (min) | Drainage Curve Correlation with exp. function | Kidney (Patient, Side) | Hydronephrosis | Decrease in Total Contrast Media | Drainage Time of Parenchyma T_{1/2} (min) | Drainage Curve Correlation with exp. function |
|------------------------|----------------|----------------------------------|-----------------------------------------|----------------------------------|------------------------|----------------|----------------------------------|-----------------------------------------|----------------------------------|
| 1,R NO YES             | 11.4           | 0.99                             |                                         | 8,L NO NO                       | 14.4                   | 1  | 10,L NO YES                       | 14.4 | 0.99                             |                                         | 8,L NO NO                       | 14.4                   | 1  | 10,L NO YES                       | 14.4 | 0.99                             |                                         |
| 1,L NO YES             | 12.8           | 0.95                             |                                         | 9,R NO YES                       | 18.2                   | 0.96 | 9,L NO YES                       | 18.2 | 0.96                             |                                         | 9,L NO YES                       | 18.2                   | 0.96 | 9,L NO YES                       | 18.2 | 0.96                             |                                         |
| 2,R NO YES             | 17.3           | 0.99                             |                                         | 10,R NO NO                       | 8.6                    | 0.97 | 10,L NO YES                       | 8.6  | 0.97                             |                                         | 10,L NO YES                       | 8.6  | 0.97 | 10,L NO YES                       | 8.6  | 0.97                             |                                         |
| 2,L NO YES             | 18.2           | 0.99                             |                                         | 11,R NO YES                       | 40.8                   | 1   | 11,L NO YES                       | 40.8 | 1                                |                                         | 11,L NO YES                       | 40.8 | 1   | 11,L NO YES                       | 40.8 | 1                                |                                         |
| 3,R NO YES             | 14.4           | 0.99                             |                                         | 12,R NO YES                       | 26.7                   | 0.97 | 12,L NO YES                       | 26.7 | 0.97                             |                                         | 12,L NO YES                       | 26.7 | 0.97 | 12,L NO YES                       | 26.7 | 0.97                             |                                         |
| 3,L NO YES             | 13.3           | 0.98                             |                                         | 13,R NO YES                       | >100                   | 0.59 | 13,L NO YES                       | >100 | 0.59                             |                                         | 13,L NO YES                       | >100 | 0.59 | 13,L NO YES                       | >100 | 0.59                             |                                         |
| 4,R NO YES             | 15.4           | 0.95                             |                                         | 13,L NO YES                       | 31.5                   | 0.95 | 14,R YES NO                       | 25.7 | 0.99                             |                                         | 14,R YES NO                       | 25.7 | 0.99 | 14,R YES NO                       | 25.7 | 0.99                             |                                         |
| 4,L NO YES             | 14.1           | 0.96                             |                                         | 14,L NO YES                       | 10.3                   | 0.99 | 15,R NO YES                       | 27.7 | 0.88                             |                                         | 15,R NO YES                       | 27.7 | 0.88 | 15,R NO YES                       | 27.7 | 0.88                             |                                         |
| 5,R NO YES             | 13.9           | 0.98                             |                                         | 15,L NO YES                       | 23.1                   | 0.85 | 15,L NO YES                       | 23.1 | 0.85                             |                                         | 15,L NO YES                       | 23.1 | 0.85 | 15,L NO YES                       | 23.1 | 0.85                             |                                         |
| 5,L NO YES             | 14.7           | 0.96                             |                                         | 16,R NO YES                       | 13.9                   | 0.96 | 16,R NO YES                       | 13.9 | 0.96                             |                                         | 16,R NO YES                       | 13.9 | 0.96 | 16,R NO YES                       | 13.9 | 0.96                             |                                         |
| 6,R NO YES             | 16.5           | 0.97                             |                                         | 16,L NO YES                       | 19.9                   | 0.95 | 17,R YES NO                       | 29.4 | 0.95                             |                                         | 17,R YES NO                       | 29.4 | 0.95 | 17,R YES NO                       | 29.4 | 0.95                             |                                         |
| 6,L NO YES             | 16.1           | 0.99                             |                                         | 17,L NO YES                       | 26.4                   | 0.99 | 18,R YES NO                       | 33.1 | 0.99                             |                                         | 18,R YES NO                       | 33.1 | 0.99 | 18,R YES NO                       | 33.1 | 0.99                             |                                         |
| 7,R NO YES             | 18.7           | 0.93                             |                                         | 18,L NO YES                       | 31.5                   | 0.95 | 19,R YES NO                       | 31.5 | 0.95                             |                                         | 19,R YES NO                       | 31.5 | 0.95 | 19,R YES NO                       | 31.5 | 0.95                             |                                         |
| 7,L NO YES             | 14.7           | 0.93                             |                                         | 19,L NO YES                       | 27.7                   | 0.88 | 20,R YES NO                       | 37.7 | 0.88                             |                                         | 20,R YES NO                       | 37.7 | 0.88 | 20,R YES NO                       | 37.7 | 0.88                             |                                         |
| 8,R NO YES             | 13.3           | 0.99                             |                                         | 20,L NO YES                       | 33.1                   | 0.95 | 21,R YES NO                       | 42.3 | 0.88                             |                                         | 21,R YES NO                       | 42.3 | 0.88 | 21,R YES NO                       | 42.3 | 0.88                             |                                         |

Fig. 7. ROC analysis for discriminating between hydronephrotic and non-hydronephrotic kidneys by the drainage time of the contrast media from the renal parenchyma. The AUC is 0.97.

Fig. 8. Indicators for assessing renal function: (a-b) The automatic MIP of a non-hydronephrotic kidney (a) and a hydronephrotic kidney (b). (c-d) The exponential drainage curve of the contrast media from the parenchyma and the corresponding T_{1/2} of both kidneys. (e-f) The changes in the total HU value during phases 2-4 in both kidneys.
between – 1 to 375 HU (Fig. 4b). Since the parenchyma may include some pixels with a higher concentration of contrast media, especially in the border with the renal pelvis, the upper threshold was set to be higher than that used for finding the isolated parenchyma in the initial slice, to include all the pixels in the parenchyma. In phases 3 and 4, a BinaryHigh image was also generated by applying a bottom threshold value of 375 HU in order to include the renal pelvis (Fig. 4c). However, this BinaryHigh image may also include the ureter and some bony tissues.

2.5. Segmentation of the renal parenchyma and renal pelvis

In each slice, the renal parenchyma was segmented within the cropped ROI. In subsequent slices, the renal parenchyma might appear attached to other organs, with similar HU values, and should be separated from the adjacent tissues. To determine whether this process is required, the BinaryLow image of the ROI in the present slice is analyzed. First, the object that contains the renal parenchyma in this ROI is identified as the object with the largest spatial overlap with the isolated renal parenchyma in the ROI of the preceding slice. An overlap area which is less than 70% of the total area of the identified object in the present slice, indicates that the renal parenchyma in this slice is attached to other tissues and needs to be separated. In such cases, four different segmentation techniques, which are described in the appendix, are applied to find the technique that optimally separates the kidney from adjacent organs. This was performed to increase the probability that at least one of the techniques would be successful and provide the most accurate segmentation of the renal parenchyma for that particular slice. The developed algorithm automatically selected the technique which identified the renal parenchyma with the largest overlapping with that in the preceding slice. Renal cysts were filtered automatically based on their different attenuation [26] and shape [27] and were not included in the final segmentation of the parenchyma (For more details see the attached code).

For segmenting the renal pelvis, the BinaryHigh images of the ROI in phases 3 and 4 were analyzed. These images may include the renal pelvis, bony tissues, and sometimes the ureter. Since the renal pelvis can extend only anteriorly or medially to the renal parenchyma, objects which were located posteriorly or laterally to the bounding box of the identified parenchyma were removed. Remaining objects with an area smaller than 40 mm$^2$ or with a distance greater than 15 mm from the renal parenchyma were also removed.

2.6. Identifying the superior and inferior poles of the kidney and 3D reconstruction

The superior and inferior poles of the kidney were identified based on the fact that the area of the renal parenchyma decreases as it approaches the superior and inferior poles. Starting from the initial slice and advancing sequentially toward the superior and inferior poles, the area of the renal parenchyma in each slice was calculated. First, the slice with the maximal area of the renal parenchyma was identified. Then, the slices containing the superior and inferior poles were identified when the parenchymal area progressively decreased in preceding slices and the area of the renal parenchyma in these slices was smaller than 15% of the maximal area.

Following the segmentation of the renal parenchyma and the renal pelvis in all the relevant slices, the RadiAnt™ DICOM viewer was used to generate 3D reconstructions of these renal components, and demonstrate a volume rendering of each component separately. In addition, Maximum Intensity Projections (MIP) [28] renderings of the renal parenchyma, the renal pelvis, and their combination were generated.
2.7. Assessing the accuracy of the segmentation stages

The success rate of identifying automatically the initial slice was defined as the percentage of kidneys in which the selected initial slice included an isolated renal parenchyma.

The accuracy of identifying the slices containing the superior and inferior poles of the renal parenchyma was determined by comparing the slices selected automatically for each kidney to those identified manually. First, the error in identifying the poles, \( error_{poles} \), was defined as:

\[
error_{poles} = error_{sup} + error_{inf}
\]

where \( error_{sup} \) is the absolute distance between the automatically identified superior pole and the actual superior pole, and \( error_{inf} \) is the distance obtained for the inferior pole. The accuracy of the automatic identification of the poles, \( acc_{poles} \), was defined as:

\[
acc_{poles} = 1 - \frac{error_{poles}}{distance_{poles}}
\]

where \( distance_{poles} \) is the distance between the manually identified superior and inferior poles.

The accuracy of segmenting the renal parenchyma and the renal pelvis in each phase was evaluated in two challenging cases, where the renal parenchyma appeared attached to adjacent organs in many slices. For these cases, the accurate contours of the renal parenchyma and renal pelvis, in all the slices of the 4 CTU phases (approximately 400 slices for each phase) were manually drawn and approved by an experienced radiologist. Then, the segmentation accuracy was assessed by calculating the Dice Coefficient (DC) [29] of the manually drawn and the automatically identified contours for each kidney component in each phase.

2.8. Setting indicators for assessing partial obstruction

The first indicator is the “drainage time”, \( T_{1/2} \), in which half of the contrast media has been drained from the parenchyma [9]. \( T_{1/2} \) was calculated by evaluating the amount of contrast media in the renal parenchyma in each of phases 2–4. For this purpose, the average HU values of all the voxels within the identified 3D borders of the renal parenchyma was calculated in each phase. To estimate only the amount of the contrast media, the average HU value of phase 1, reflecting the intrinsic HU value of the parenchyma itself, was subtracted from the average HU values of phases 2–4.

Then, an exponential regression function that best fits the average HU value of the contrast media in phases 2–4 as a function of the imaging time was generated. This function yielded the drainage curve of the contrast media with a decay time \( \tau \). The “drainage time” of the contrast media from the renal parenchyma was calculated by:

\[
T_{1/2} = \tau \cdot \ln(2)
\]

The second indicator was the variation in the total amount of contrast media in the kidney, which in a normal kidney should decrease over time during phases 2–4. The amount of contrast media in the renal parenchyma and the pelvis was estimated by multiplying their average HU value by their volume (in mm\(^3\)). The total amount of contrast material in the kidney was estimated by summing the amount of contrast material in both components.

3. Results

3.1. Evaluation of the segmentation algorithm

The algorithm was tested on the slices of all the CTU phases of the 30...
The kidneys in the dataset, altogether 23,164 slices. As shown in Table 1, the highest success rate for selecting automatically the initial slice (93.3%) was obtained in phase 2 images, in which the renal parenchyma can be more easily identified as it contains the highest amount of contrast media. In this phase, the optimal initial slice was successfully identified for 28 of the 30 kidneys (93.3%). As mentioned above, in cases where the selected initial slice was not confirmed by the user, the algorithm continues the segmentation process using a manually selected slice.

The accuracy of identifying the renal parenchyma poles in the various CTU phases was calculated by (3) and found to be between 0.92 and 0.95 and it was slightly higher in phases 2 and 3, where the poles appeared brighter. The DC of the renal parenchyma segmentation in the four CTU phases ranged between 0.95 and 0.98 and for the renal pelvis segmentation, the DC in phases 3 and 4 were 0.92 and 0.91, respectively.

Fig. 5 illustrates the ROI containing the kidney, as defined by the algorithm, as well as the identified contours of the renal parenchyma and the renal pelvis in the various CTU phases. The figure demonstrates that the algorithm successfully identified the kidney although in the non-contrast phase it appears attached to adjacent organs.

The accurate segmentation of the kidney, provided by the algorithm, in all the relevant slices, enables automatic and reliable reconstruction of the 3D surfaces of the renal parenchyma and the renal pelvis. Fig. 6a and b show examples of the 3D reconstruction of the renal parenchyma and the renal pelvis of both kidneys in a coronal orientation. Fig. 6c shows the generated MIP image of the kidneys for the same case.

3.2. Assessing the renal function

Accurate segmentation of the renal parenchyma and the renal pelvis in the various phases enables the algorithm to calculate the indicators for assessing the renal function, specifically, the drainage time of parenchyma (T1/2) and the decrease of the total amount of contrast media during the CTU phases.

To calculate the drainage time T1/2, a significant correlation between the drainage curve and the exponential function is required. As shown in Table 2 the Pearson correlation coefficient between the drainage curve and the exponential function was high (0.97 ± 0.03), except for one kidney with a severe obstruction (13,R) where the drainage was extremely low. In this case, the resulting T1/2 was higher than 100 min and therefore it was not included in the following statistics.

As shown in Table 2, the T1/2 values of the 24 non-hydronephrotic kidneys ranged between 7.97 and 18.73 min, except for one extreme T1/2 value of 31.5 min, with an average of 15.14 ± 4.48 min. The table also shows that for the 5 hydronephrotic kidneys cases, the T1/2 values ranged between 23.1 and 40.77 min with an average of 27.48 ± 7.39 min. The difference between the T1/2 values in the two groups, calculated by the Mann-Whitney U test, was found to be highly significant (p < 0.001).
The Area Under the Curve (AUC) of the Receiver Operating Characteristic (ROC) analysis for $T_{1/2}$ was found to be 0.97 (Fig. 7). A threshold of the $T_{1/2}$ value between 19 and 23 min, for discriminating between kidneys with and without hydronephrosis, resulted in a sensitivity of 100%, specificity of 95.8% and accuracy of 96.7%. It should be noted that the exceptional non-hydronephrotic kidney with the high $T_{1/2}$ value of 31.5 min (13,L) was the contralateral kidney to the kidney with the extremely severe obstruction (13,R).

The total amount of contrast media in phases 2–4 of the CTU examination, which serves as the second indicator, was also calculated and in all 6 hydronephrotic kidneys it did not decrease as shown in Table 2. In 21 of the non-hydronephrotic kidneys, the total amount of the contrast media decreased markedly during these phases, except for 3 non-hydronephrotic kidneys in which this trend was not observed. However, each of the 3 kidneys, in which the amount of contrast media did not decrease, exhibited a large extrarenal pelvis. These results indicate that the second indicator yielded a sensitivity of 100%, specificity of 87%, and accuracy of 89.7%.

It should be emphasized, that in all hydronephrotic kidneys both indicators showed improper kidney drainage and in all non-hydronephrotic kidneys at least one indicator indicated normal drainage. Therefore, a combination of both indicators yielded 100% accuracy for distinguishing between cases with and without hydronephrosis.

Fig. 8 shows examples of the information which was provided by the algorithm for a non-hydronephrotic kidney (9,L) and a hydronephrotic kidney (11,R). The automatically reconstructed MIP images of the kidneys are shown (Fig. 8a,b) as well as the two indicators: the $T_{1/2}$ value based on the drainage curve of the contrast media from the parenchyma (Fig. 8c,d) and the changes in the total amount of contrast media during phases 2–4 (Fig. 8e,f). The figure shows that although in phase 2 the average HU value of the contrast media in the parenchyma, as well as the total HU of the contrast media, are very similar in both kidneys, in phases 3 and 4 these values are substantially different as a result of partial urinary obstruction in the hydronephrotic kidney.

4. Discussion

The algorithm designed in this study enables an accurate 3D segmentation of the renal parenchyma and the renal pelvis in the various phases of CTU. The segmentation algorithm analyzed each of the 23,164 CTU slices separately. Although in each slice the kidney contour was significantly different and in each slice the nature of adjacent tissues also varied, in all the phases, the algorithm accurately segmented the renal parenchyma and the renal pelvis with average DC of 0.97 and 0.92 respectively. Following this segmentation, the amount of contrast material in each phase was automatically assessed, and based on this assessment the algorithm evaluated two indicators for detecting the presence of renal obstruction. For both indicators, there was a statistically significant difference ($p < 0.001$) between non-hydronephrotic kidneys and hydronephrotic kidneys diagnosed with inhibited drainage.

The results showed that a drainage time from the parenchyma ($T_{1/2}$), greater than 20 min, can serve as a non-invasive indicator of improper kidney drainage. The association between hydronephrotic kidneys and
long $T_{\text{1/2}}$ was high, with a sensitivity of 100%, specificity of 95.8%, and accuracy of 96.7%. The second indicator was the lack of a reduction in the total amount of contrast media through the different imaging phases. As shown, the association between hydronephrotic kidneys and the second indicator yielded a sensitivity of 100%, specificity of 87%, and accuracy of 89.7%. A combination of both indicators yielded 100% accuracy since in all hydronephrotic kidneys both indicators showed improper kidney drainage, and in all non-hydronephrotic kidneys, at least one indicator was consistent with normal drainage. The small number of cases in which only one indicator reveals normal kidney drainage should be examined in detail by the physician before dismissing them as normal.

To segment the kidney, the ROI containing the kidney in each slice was automatically defined. In the algorithm described in this study, the ROI was defined based on the kidney identification in the preceding slice, while in previous studies the ROI had to be manually selected [30, 31]. Our approach significantly reduces the computational burden since filtering or morphological operations for defining the ROI in each slice are not required. Secondly, the probability of defining a correct ROI around the kidney by this approach is higher, as the chance that the ROI will be defined around a different organ with a size, shape, and location similar to that of the kidney is negligible.

Automatic segmentation of the kidneys in CTU has been a long-standing problem that remains unresolved despite intensive efforts [30, 32]. The most challenging aspect of kidney segmentation is separating the renal parenchyma from other organs and large blood vessels with similar attenuation [33,34], since the shape of the kidney and the manner in which it appears attached to the adjacent organ is different in each slice. In recent years the use of Convolutional Neural Networks (CNNs) has shown promising results for kidney segmentation in various datasets of CT images [35-39]. However, training CNN for 3D kidney segmentation in multi-phase CTU images requires a dataset of hundreds of CTU examinations with manual markings of the kidney contour in all the phases, and to the best of our knowledge such a free dataset is not available. The algorithm described in this study attempts for each slice multiple segmentation techniques and by comparing them to the kidney segmentation in the preceding slice, the optimal technique is automatically utilized. This novel approach which optimized segmentation by automatically combining four different techniques yielded a successful segmentation of the renal parenchyma in multiple CTU phases with DC varying between 0.95 and 0.98.

The accurate segmentation of the renal parenchyma and the renal pelvis in the various phases enabled the calculation of two indicators for assessing renal obstruction, the drainage time of parenchyma ($T_{\text{1/2}}$) and the decrease of the total amount of contrast media during the CTU phases. Although hydronephrosis is related to renal obstruction [40], its diagnosis can only be performed visually and the diagnostic accuracy is highly dependent on the skill of the physician [41]. In contrast, the indicators developed in this study which are objective and calculated automatically, make the use of an additional examination such as renal scintigraphy redundant. Interestingly, the threshold value for $T_{\text{1/2}}$ (19–23 min), which differentiates between kidneys with or without renal obstruction in our study, is similar to the threshold values used in renal scintigraphy (20 min). It should be noted that in renal scintigraphy the $T_{\text{1/2}}$ values are expected to be shorter, and $T_{\text{1/2}}$ values of 10–20 min are considered to be equivocal [42] since in renal scintigraphy diuretics are administered to the patient [2], while in CTU it is not a conventional approach. In situations using a diuretic as part of the CTU protocol, the cut-off values optimally separating hydronephrosis from non-hydronephrotic kidneys would probably be different, and the developed algorithm would need to be run on another dataset in which a diuretic was used to determine the correct cut-off values for such cases.

The discrepancies found in some cases between the values of the objective indicators obtained in this study and the visual appearance of hydronephrosis can be due to several causes. In one case, the prolonged $T_{\text{1/2}}$ value in the non-hydronephrotic kidney may be due to the fact that the contralateral kidney exhibited extremely severe hydronephrosis and therefore the non-hydronephrotic kidney takes longer to filter the contrast media since it is not being filtered by the contralateral kidney. In three non-hydronephrotic kidneys, the total amount of contrast media did not decrease. However, all the three kidneys exhibited an extrarenal pelvis, which is naturally enlarged [44]. The enlarged renal pelvis, which retains a larger amount of contrast media, may explain why no reduction was observed between the nephrographic phase and the excretory phases. While the total amount of contrast did not decrease in the patients with an extrarenal pelvis, the $T_{\text{1/2}}$ was not prolonged, since there is no functional obstruction in a kidney with an extrarenal pelvis.

The main limitation of the study is that our dataset includes only 6 hydronephrotic kidneys and 24 non-hydronephrotic kidneys. For both indicators provided by the developed algorithm, a significant difference was found between non-hydronephrotic kidneys and hydronephrotic kidneys. However, in a future study, a larger dataset will need to be used for analyzing the accuracy of the identified indicators in a clinical environment. The second limitation of our study is that it was done only in one institution, where diuretic is not used in the CTU protocol. For establishing the proper cut-off value for separating hydronephrosis from non-hydronephrotic kidneys for CTU protocols in which a diuretic is used, a dataset from an institution that uses such a protocol should be evaluated by the developed algorithm.

5. Conclusions

In this proof-of-concept study, a novel algorithm was developed for kidney segmentation in CTU imaging by selecting an optimal segmentation technique separately for each CT slice based on an inter-slice comparison. Using this algorithm, fully automatic 3D reconstructions of the renal parenchyma and renal pelvis in multiple CTU phases were obtained for all the cases in the dataset and the amount of contrast material in each phase was automatically evaluated. Using this information, two newly defined objective indicators were extracted from routine multi-phase CTU examinations for identifying renal obstruction. These indicators may provide an important non-invasive diagnostic tool in the clinical setting assessing the excretory function of the kidney and further improve the efficacy of routine CTU in the field of unilateral kidney disorders.

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Ethical approval

All procedures performed in this anonymized and retrospective study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

CRediT authorship contribution statement

Chanoch Kahn: Methodology, Software, Formal analysis, Writing - original draft, Visualization. Isaac Leichter: Conceptualization, Methodology, Supervision, Writing - original draft, Writing - review & editing. Richard Lederman: Validation, Data curation, Writing - review & Editing. Jacob Sosna: Conceptualization, Resources, Writing - review & editing. Mordechai Duvdevani: Conceptualization, Data curation, Writing - review & editing. Talia Yeshua: Conceptualization, Methodology, Supervision, Writing - original draft, Visualization, Writing - review & editing.
Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix

See appendix Fig. A.1,A.2,A.3,A.4.

As described in the manuscript, in each slice four segmentation methods were applied for separating the renal parenchyma from adjacent organs. Then, the technique that resulted in the most accurate segmentation was selected for the specific slice.

1. Canny edge technique

The first segmentation technique was based on the Canny edge detector [45] and removed the detected edges from the BinaryLow image. Fig. A.1 displays an example of a slice in which this technique yielded successful segmentation. Fig. A.1a shows the ROI defined by the algorithm and Fig. A.1b shows the respective BinaryLow where the renal parenchyma appears attached to the liver. Then, the edges detected by the Canny technique (Fig. A.1c) were removed from BinaryLow and as a result, the renal parenchyma was separated from the liver (Fig. A.1d).

After removing objects in contact with the border of the ROI, the overlap between each remaining object and the identified renal parenchyma in the preceding slice was calculated. The object with the largest overlap was selected and then the previously removed edge pixels were returned to this object. Fig. A.1e shows the final segmentation result of the renal parenchyma.

2. Canny edge technique with morphological erosion

The second segmentation technique adds additional steps to the Canny segmentation technique since in certain cases the edge detection was not completely successful. Fig. A.2a shows the ROI defined in a different slice of the same case where after removing the detected edges from the BinaryLow image, the renal parenchyma was still connected to a loop of bowel anterior to it (Fig. A.2d). Therefore, in order to separate the connected objects, after filling the holes in the objects, a morphological erosion was performed, with a disk-shaped structuring element, exhibiting a diameter of 7 mm (Fig. A.2e). After identifying the object which optimally represents the renal parenchyma, all the other objects were deleted with the same structuring element used for the erosion. Then, the diluted objects were removed from the original BinaryLow and as a result, the remaining mask of the original renal parenchyma was not distorted by the morphological operators (Fig. A.2f).

3. Distance transform watershed technique

In the third segmentation technique, the objects were separated using a distance transform watershed algorithm [46], which is performed on a binary image and takes into account the distance of each segmented pixel to the background pixels. Fig. A.3a shows the ROI defined by the algorithm in a slice where the renal parenchyma, marked by an arrow, appears attached to the liver. The distance transform watershed algorithm is applied on the BinaryLow (Fig. A.3b) and yields a segmented binary image with many connected components (Fig. A.3c). Connected components in contact with the borders of the ROI were then removed from the original BinaryLow (Fig. A.3d). Finally, the object exhibiting the highest overlap with the segmented renal parenchyma in the preceding slice was identified (Fig. A.3e).

4. Superpixels technique

In the fourth segmentation technique, the objects in the ROI were segmented using Superpixels, which are regions of pixels defined by the distance between the pixels and the similarity in their grey level values [47]. Fig. A.4a shows an ROI defined by the algorithm in a slice where the renal parenchyma (marked by an arrow) appears attached to a loop of the bowel. The resulting superpixels are shown in Fig. A.4b, overlaying the image of Fig. A.4a. Superpixels that were in contact with the ROI borders were then removed from BinaryLow (Fig. A.4c), and the object exhibiting the highest overlap with the renal parenchyma in the preceding slice was selected (Fig. A.4d).

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