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Renal Volume Loss During Partial Nephrectomy Due to Resected Healthy Parenchyma: A Tool for Quick Estimation

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Key words: carcinoma, renal cell; partial nephrectomy; kidney function test; robotics

Abstract

Purpose: Our objective is to evaluate a technique for estimating the amount of healthy margin resected during partial nephrectomy.

Materials and Methods: The resected healthy margin volume was determined by planimetry (gold standard), which was performed in a prospective manner on 30 freshly resected renal masses by cross-sectional slicing every ~5mm. A single cross-sectional slice containing the largest tumor diameter (bivalved tumor) was chosen to build a model for estimating the amount of healthy kidney removed. This single-slice technique was then applied to a second series of patients (n=39) status post partial nephrectomy. Three-dimensional models were created using pre and postoperative CT scans to determine the overall volume loss following partial nephrectomy.

Results: The median (range) for tumor diameter and tumor volume was 3.2cm (1-6.1) and 10.7cm^3 (0.5-101.9), respectively for the 30 partial nephrectomy specimens used to build the single-slice estimation equation. The median (range) healthy margin volume calculated by planimetry and single slice technique was 9.0cm^3 (1.0-22.1) and 7.8cm^3 (1.0-31.0), respectively (p=0.37). The Pearson correlation was 0.84, and the median (range) percent difference between the planimetry and single slice techniques was -0.5% (-39% to 57%). For the 39 partial nephrectomy patients, the median (range) total renal volume loss, 25.8cm^3 (3-79), was significantly greater than the volume of healthy margin removed during resection, 5.7cm^3 (1-22), p<0.001.

Conclusions: The healthy margin resected during partial nephrectomy varies widely and can be estimated from a single cross-section. The healthy margin resected accounted for <50% of the total volume loss seen during partial nephrectomy.

Introduction

With the increase in availability and use of robotic assistance, partial nephrectomy (PN) is used regularly to treat small renal masses.[1] Many studies have shown that the use of PN in order to spare parenchymal volume has been correlated to the preservation of renal function.[2] Nevertheless, not all renal function is spared during PN and this functional loss is generally thought to be due to the resection of healthy renal tissue, reconstruction injury, or ischemic injury.[3-5] Long-term renal damage, however, is not thought to result from ischemic injury by hilar clamping when ischemia times are less than 30 minutes. Methods for minimizing resected renal tissue include enucleation and smaller healthy resection margins (1-10 mm).[6]

Enucleation has been proposed as a method to eliminate parenchymal loss by staying on the capsule of the tumor during resection. There is concern, however, that this increases the risk for microscopic positive margins as up to 38% of capsules show at least partial invasion by tumor.[7-9] Therefore, many surgeons still include a small healthy margin during resection. Despite numerous studies evaluating renal function loss after partial nephrectomy, few have attempted to quantify the amount of healthy kidney removed during resection. Our objective was to construct a user-friendly technique for quantifying the volume of the healthy margin resected and then use this technique to compare healthy margin loss to overall renal volume loss.

Materials and Methods

Between September of 2014 and July of 2015, 30 renal masses were obtained in a prospective manner immediately following robotic-assisted partial nephrectomy performed by a single surgeon. They were available for immediate postoperative planimetry in which the tumor with the healthy margin was sectioned at approximately 5 mm intervals along the long axis in the frozen section room by a pathology technician under the direction of the staff pathologist. The samples were then photographed alongside a ruler for scaling purposes (Figure 1). The photographs were uploaded on OsiriX Lite and each sample slice area was calculated and multiplied with the thickness to evaluate the volume of the slice. Each slice was then summed to determine the volume loss for planimetry. This was used as the gold standard for analyzing the amount of resected tissue. A single-slice equation[10] was built using the contact angle between the tumor and healthy margin and assuming two concentric circles (Figure 2). The volume calculated by the single-slice method was then compared against the planimetry analysis.

A second group of 39 patients undergoing robotic PN between the years of 2010 and 2014 were found to have both single-slice gross pathology images and the necessary pre- and postoperative CT scans for volume loss analysis. The images were used via the single-slice equation to estimate the amount of healthy kidney removed during PN. The total volume loss was then calculated using the preoperative and postoperative CT scans. CT based volumes were calculated using a semi-automatic segmentation algorithm where perfused renal parenchyma was selected in each axial slice to build a three-dimensional model as described previously.[10,11] The study received IRB approval.

A priori significance was set at $p<0.05$ for two-sided statistical tests. A table was prepared using the single-slice estimation (Figure 3) as a quick reference for the resected healthy margin based on three variables: exophytic/endophytic, tumor diameter, and resection margin length. The median contact angle (163°) was used to represent the "typical" exophytic tumor and the 90th percentile contact angle (247°) was used to represent the endophytic tumor. The Mann-Whitney test was used to compare means and the Pearson coefficient was used to compare correlation between the single-slice estimation and whole-mount. Stata 13.1 was used for all statistical analyses (StataCorp LP, College Station, TX).

Results

Thirty whole mount partial nephrectomy specimens were evaluated with median (range) tumor diameter and volume of 3.2cm (1-6.1) and 10.7cm^3 (0.5-101.9), respectively. The median healthy margin length was 5.6mm. The median (range) healthy margin volume calculated by the whole mount and single-slice technique was 9.0cm^3 (1.0-22.1) and 7.8cm^3 (1.0-31.0), respectively ($p=0.37$). The Pearson correlation was 0.84 (Figure 3), and the median (range) percent difference between the whole mount and single slice techniques was -0.5% (-39% to 57%). Using the single-slice technique with common healthy margin lengths and tumor diameters, the volume of resected healthy renal parenchyma was calculated for both typical exophytic and endophytic tumors. This data was compiled in figure 4 for easy reference.

Thirty-nine robotic partial nephrectomies performed between 2010 and 2014 were found to have both whole mount images and the necessary pre- and postoperative CT scans for analysis. A two-layer suture closure was used in 27 (69%) while base-layer only renorrhaphy was used in 12 (31%). See Table 1 for demographic data. The median (IQR) age and diameter were 64.8 years (54-69) and 2.9 cm (2.4-4.5). The median (IQR) nephrometry score was 7 (6-8). The median (IQR) BMI and Charlson comorbidity index were 31 kg/m^2 (27-36) and 2 cm (2-3). See table 2 for preoperative and pathologic data. The median (range) warm ischemia time was 15 minutes (0-28). See table 3 for volume measurements. The median (range) healthy margin length was 6mm (2-11). The median (range) total renal volume loss and healthy margin volume loss were 25.8cm^3 (3-79) and 5.7cm^3 (1-22), respectively ($p<0.001$). The two-layer renorrhaphy cases had a larger total volume loss than base-layer only (31.4 vs. 21.6, $p=0.03$) by Mann-Whitney U-test. The healthy margin length was not different between renorrhaphy types ($p=0.58$).

Discussion

Understanding renal volume loss during partial nephrectomy is important both for patients at risk of renal failure (solitary kidneys, chronic kidney disease, etc.) and for the research community as surgical techniques are evaluated.[3,12] In this paper, a tool is presented for predicting or estimating renal volume loss due to resected healthy renal margin and demonstrates (figure 4) a wide range of volume losses based on 3 inputs: resection margin, tumor size, and endophytic/exophytic. We also demonstrate that the resected volume loss makes up less than 25% of the overall volume loss in a contemporary partial nephrectomy cohort. Risk of cancer recurrence after partial nephrectomy (PN) is a driving force in maintaining a healthy resection margin. Historically, a surgical margin of 1-2 cm was maintained.[13] Some also advocate that the margin can be reduced entirely (enucleation) in tumors with a homogenous smooth outer pseudocapsule (e.g. clear-cell renal cell carcinoma) 16, 9.[14,15] Few studies have attempted to quantify the renal volume lost due to contemporary resection margins (<10mm).

Usability is important for any system assessing volume loss. The "inputs" used in the presented equation can be quickly taken from preoperative imaging or a single cross-sectional slice of the extirpated tumor. This technique can be utilized for both quick clinical predictions (Figures 2C and 4) and more exacting research efforts, which requires software-based area measurements (Figure 2.D.).

Figure 4 demonstrates wide variability in the amount of healthy renal margin resected. For example, a 5mm margin on a 3cm exophytic tumor results in 8.8cm^3 lost while a 10mm margin with an endophytic tumor results in a 35.2cm^3 lost. In the present validation cohort, we found a median (range) resected healthy margin of 5.7cm^3 (1-22), which is due to small exophytic tumors (median diameter = 2.9cm) and a small margin length of 6mm.[2,12] When considering the average kidney volume in our study was 160cm^3, the resection margin makes up a small percentage (5.7/160=3.5%).

Few methods for quantitatively/numerically describing resection techniques have been described, but methods of qualitative description exist. For example, Minervini, et al. report a scoring system to describe resection techniques based on the surface, intermediate, and base of the tumor resection [6] Visual assessment scores lead to the resection being categorized as pure enucleation, enucleoresection, or resection. In validation[16] and external validation[17] papers, the healthy renal margin ranged from 0mm (enucleation) to 3mm (resection). We would estimate a healthy renal margin volume of only 2.9cm^3 assuming an average 2mm margin, their tumor diameter of 3cm, and a typical exophytic tumor.

Most systems focus on tumor complexity, but not on surgeon factors (e.g. resection and renorrhaphy technique). For example, the contact surface area (CSA) between tumor and kidney has been used for predicting surgical outcomes and renal function loss after partial nephrectomy.[18] A simplified equation for calculating CSA (2 inputs) has been described and improves usability.[19] Recently, CSA was externally validated and demonstrated a ROC of 0.93 for predicting a 20% renal function loss at a single institution.[20] This is an impressive ROC for this institution, but is very specific to the surgeons involved. We advocate for systems that also control for surgeon factors such as resection and renorrhaphy techniques.

The current project does not attempt to describe tumor complexity, but rather to understand the nature of renal volume loss after partial nephrectomy. Specifically, what is the contribution of resected healthy renal margin to overall renal volume loss. In our validation cohort, we found the estimated resected margin (5.7cm^3) was much smaller (p<0.001) than the overall volume loss as calculated on CT-based three-dimensional models (25.8 cm^3). Aside from resected margin (enucleation vs healthy margin), renorrhaphy technique and ischemia (hilar clamping) time have been studied as causes of renal volume loss. As contemporary warm ischemia times are <25minutes, we advocate for further study of renorrhaphy techniques and volume loss.

This project is limited in nature as it is validated only at a single institution. Also, the formulas described are based on theoretical spheres while tumors and resection margins contain considerable variability in shape. We adjusted for this variability through exact area calculations using a software program (Figure 2A, 2D), and we were able to show reasonable correlation (0.84, Figure 3) with the gold-standard (planimetry).

Conclusions

In conclusion, resected healthy renal margin during partial nephrectomy varies considerably depending on tumor diameter, resection margin, and endophytic/exophytic nature. However, in a contemporary series with a resection margin <10mm, resection related renal volume loss is small when compared to overall volume loss. Surgeon related factors such as resection margin and renorrhaphy technique should be controlled for in studies evaluating renal volume loss.

Disclosures

Haley S Plattner	None
Liang Cheng	None
Chandru P Sundaram	None
Clinton D Bahler	None

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Abbreviations:

PN- Partial Nephrectomy

CSA- Contact Surface Area

CT- Computed Tomography

Table 1: Demographics, testing the estimation formula

	Total
Number	39
Age (years), median (IQR)	64.8 (54-69)
Male, no. (%)	20 (51)
DM, no. (%)	6 (15)
HTN, no. (%)	19 (49)
Charlson Index >2, no. (%)	16 (41)
Preoperative creatinine, median (IQR)	0.96 (0.84-1.1)
Preoperative GFR (mL/min/1.73 m^2), median (IQR)	75.7 (62-87)
Diameter (cm), median (range)	2.9 (1.1-7.4)
Nephrometry, mean (range)	6.9 (4-10)

Table 2: Perioperative details and pathology

	Total
Number	39
O.R. duration (min.), median (IQR)	199 (178-229)
Warm ischemia time (min.), median (IQR)	15 (12-20)
Est. blood loss (mL), median (range)	100 (50-200)
Transfusions, no. (%)	0 (0)
Intraoperative complications, no. (%)	0 (0)
Length of stay (days), median (range)	2 (2-3)
Complications	
Bleed, no. (%)	1 (3)
Urine leak, no. (%)	0 (0)
RCC, no. (%)	37 (95)
Fuhrman >2, no. (%)	11 (28)
Margin positive, no. (%)	0 (0)

Table 3: Margin and volume measurements

	Total	p-value*
Number	39	
Healthy margin length (mm), median (range), n=39	6 (2-11)	0.59
Base layer only renorrhaphy (n=12)	6 (3-10)	
Base + cortical renorrhaphy (n=27)	6 (2-11)	
Volume loss estimated from healthy margin (cm^3), median (range)	5.7 (1-22)	
Volume loss seen from CT (preop. minus postop., cm^3), median (range)	25.8 (3-79)	
Renal volume (cm^3) preoperative, median (range)	159.6 (96-302)	
Renal volume (cm^3) postoperative, median (range)	135.5 (56-261)	
%volume loss affected kidney, median (range), n=39	15.7% (2-59)	0.002
Base layer only renorrhaphy (n=12)	11.7% (2-22)	
Base + cortical renorrhaphy (n=27)	19.4% (3-59)	
Months between surgery and follow CT, median (range)	4.3 (3-10)	

*Mann-Whitney test

**All volumes represent affected side only

Figure Legends:

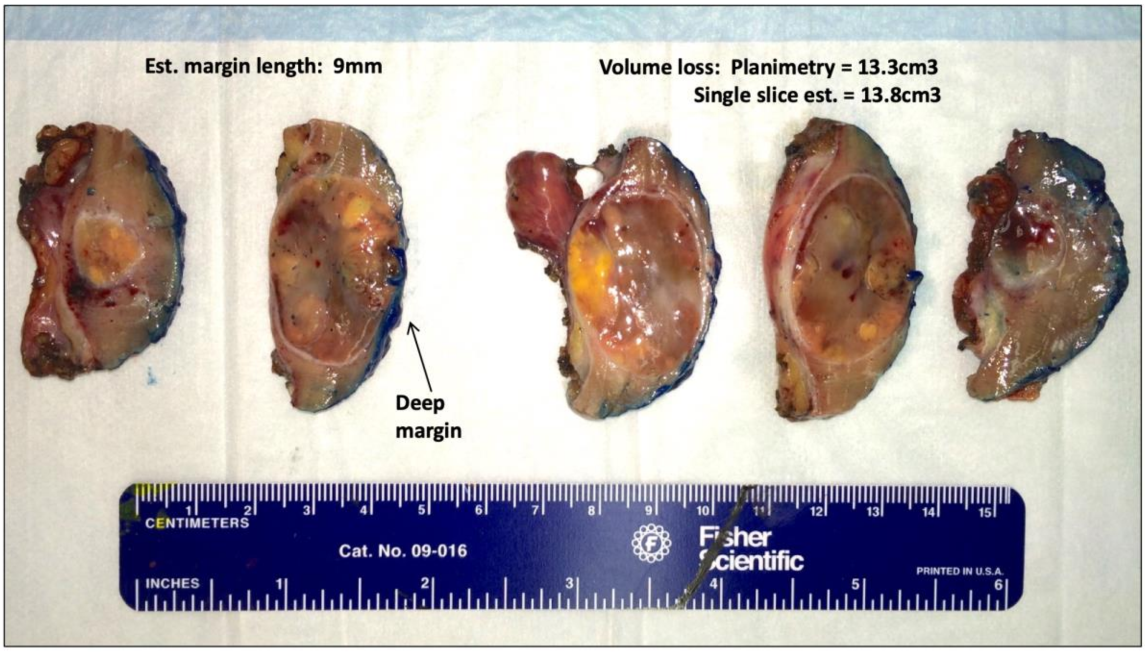
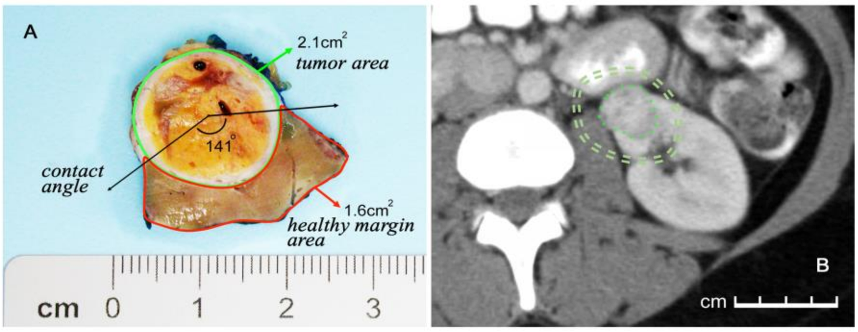
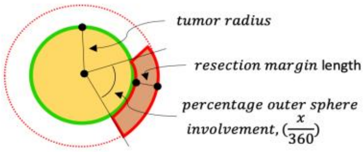


Figure 1. Planimetry calculation of resected margin volume. The healthy margin area was outlined in each slice using OsiriX Lite and multiplied by the slice thickness to get the volume removed in each slice. The slices are then summed to give the total volume excised.



C. Conceptual basis of formula (two concentric spheres):



Volume of healthy margin excised (cm^3)= ($Volume_{outer\ sphere}$ - $Volume_{inner\ sphere}$) * percent

D. Estimated volume of healthy margin excised (cm^3)=

$$\left[\frac{4}{3} * Pi * (tumor\ radius + margin\ length)^3 - \frac{4}{3} * Pi * (tumor\ radius)^3\right] * \%\ outer\ sphere$$

E. Estimated volume of healthy margin excised, used in this project (cm^3)=

$$\left[\frac{4}{3} * Pi * \sqrt{\frac{\left(healthy\ margin\ area * \frac{360}{contact\ angle}\right) + tumor\ area}{Pi}}^{\,3} - \frac{4}{3} * Pi * \sqrt{\frac{tumor\ area}{Pi}}^{\,3}\right] * \frac{contact\ angle}{360}$$

Figure 2. (A) The single-slice estimation equation used in this project requires 3 variables: contact angle, tumor area, and healthy margin area to estimate the volume of renal parenchyma resected with tumor. Figure 2.A. is reprinted with permission from JOURNAL OF ENDOUROLOGY, Volume 29, Issue 5, "Feasibility of Omitting Cortical Renorrhaphy.." by Bahler et al, published by Mary Ann Liebert, Inc., New Rochelle, NY" (B) preoperative imaging can be used to predict the volume loss by using the formula in (D). (C) The equation models two concentric spheres, subtracts the inner sphere from the outer, and multiplies by a percentage estimating the length of the healthy margin. (D) represents a form of the equation that could be used to quickly estimate volume loss based on the preoperative CT scan or bivalved specimen. (E) represents the equation used in this paper, which utilizes a software program (OsiriX lite) to measure areas in order to correct for irregularly shaped tumors or margins.

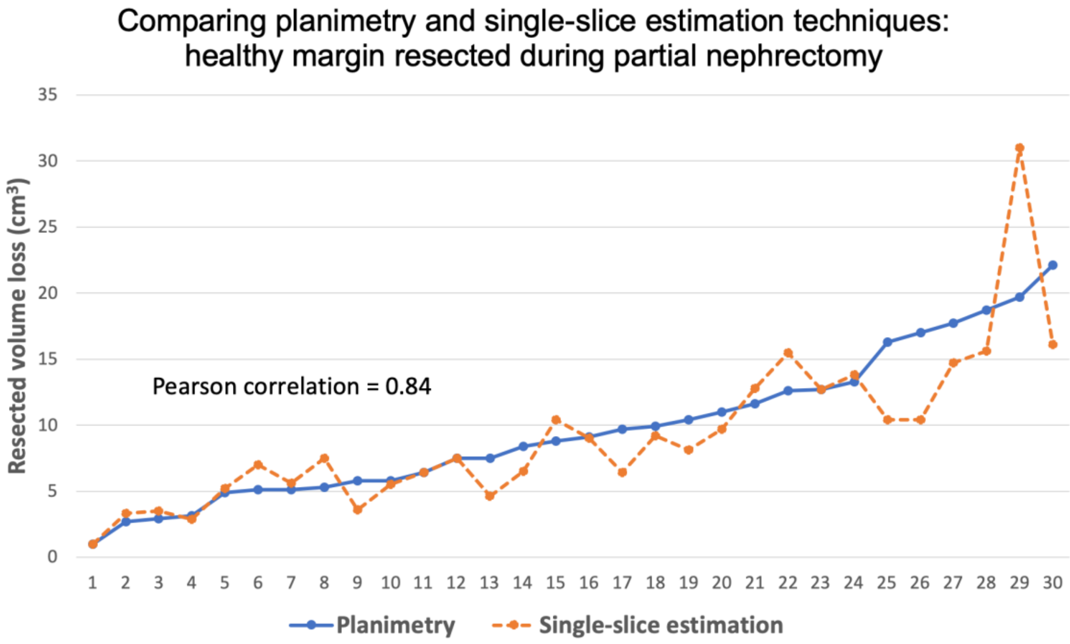


Figure 3. The single-slice equation was used to calculate volume loss and compared to planimetry (gold standard). Patient 29—the largest overestimation—had a large endophytic tumor.

A. Volume loss- Exophytic tumor (contact angle = 163°)

	Margin Length (cm)		
Tumor Diameter (cm)	0.2	0.5	1
2	1.4	4.5	13.3
2.5	2.1	6.5	17.9
3	2.9	8.8	23.2
3.5	3.9	11.4	29.3
4	5.0	14.5	36.0
4.5	6.3	17.8	43.5

B. Volume loss- Endophytic tumor (contact angle = 247°)

	Margin Length (cm)		
Tumor Diameter (cm)	0.2	0.5	1
2	2.1	6.8	20.1
2.5	3.1	9.8	27.1
3	4.4	13.3	35.2
3.5	5.9	17.3	44.4
4	7.6	21.9	54.6
4.5	9.5	27.0	65.9

Figure 4. Estimated healthy margin volume loss during partial nephrectomy using the single-slice equation for both a typical exophytic tumor (A) and a less common endophytic tumor (B). The healthy margin volume loss varies widely depending on 3 variables: exophytic/endophytic, tumor diameter, and resection margin.