# Positive Surgical Margins in Robot-Assisted Partial Nephrectomy: A Multi-Institutional Analysis of Oncologic Outcomes (Leave No Tumor Behind)

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**Abbreviations and Acronyms**

NSM = negative surgical margin

PN = partial nephrectomy

PSM = positive surgical margin

RCC = renal cell carcinoma

RPN = robot-assisted laparoscopic PN

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**Purpose:** Expanding indications for robot-assisted partial nephrectomy raise major oncologic concerns for positive surgical margins. Previous reports showed no correlation between positive surgical margins and oncologic outcomes. We report a multi-institutional experience with the oncologic outcomes of positive surgical margins on robot-assisted partial nephrectomy.

**Materials and Methods:** Pathological and clinical followup data were reviewed from an institutional review board approved, prospectively maintained joint database from 5 institutions. Tumors with malignant pathology were isolated and statistically analyzed for demographics and oncologic followup. The log rank test was used to compare recurrence-free and metastasis-free survival between patients with positive and negative surgical margins. The proportional hazards method was used to assess the influence of multiple factors, including positive surgical margins, on recurrence and metastasis.

**Results:** A total of 943 robot-assisted partial nephrectomies for malignant tumors were successfully completed. Of the patients 21 (2.2%) had positive surgical margins on final pathological assessment, resulting in 2 groups, including the 21 with positive surgical margins and 922 with negative surgical margins. Positive surgical margin cases had higher recurrence and metastasis rates ($p < 0.001$). As projected by the Kaplan-Meier method in the population as a whole at followup out to 63.6 months, 5-year recurrence-free and metastasis-free survival was 94.8% and 97.5%, respectively. There was a statistically significant difference in recurrence-free and metastasis-free survival between patients with positive and negative surgical margins (log rank test $<0.001$), which favored negative surgical margins. Positive surgical margins showed an 18.4-fold higher HR for recurrence when adjusted for multiple tumors, tumor size, tumor growth pattern and pathological stage.

**Conclusions:** Positive surgical margins on final pathological evaluation increase the HR of recurrence and metastasis. In addition to pathological and molecular tumor characteristics, this should be considered to plan appropriate management.

**Key Words:** kidney; nephrectomy; robotics; carcinoma, renal cell; pathology



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NEPHRON sparing surgery has become the mainstay of treatment for single renal tumors.[1] Of available options for nephron sparing surgery PN is the most widely practiced and has proved to be as safe and efficient as radical nephrectomy.[2] In addition to sparing normal functional renal tissue, PN is the only approach that provides definite tumor excision. Ablative therapy cannot pathologically confirm complete ablation.[3,4] As in any other oncologic surgery, the surrogate of complete tumor resection during PN remains a NSM.

While nephron sparing surgery prevents the loss of renal functional mass, it carries the risk of incomplete tumor excision. As such, PSMs remain a worrisome issue. Early studies raised concern that PSMs in cases of tumors with high malignant potential are closely associated with a higher recurrence rate.[5] However, many subsequent reports contradicted those results. A number of larger series stated that PSMs have negligible or no impact on tumor recurrence or metastasis.[6]

The steep learning curve associated with laparoscopic PN requires extensive experience to master the approach.[7] The established benefits of the da Vinci® robot facilitate the ability to resect more challenging tumors while duplicating the steps of the open approach.[8] This has led to the wide adoption of RPN as the approach of choice for minimally invasive PN. We report the combined experience with PSMs in RPN cases at 5 major tertiary care institutions.

## PATIENTS AND METHODS

All RPNs performed at 5 institutions from May 2007 to October 2012 were included in study. Data from institutional review board approved, prospectively maintained databases at each center were collected and merged after proper de-identification and signing of sharing protocols among the institutions.

The surgical techniques of RPN at each institution were previously described.[9–12] After preparing the kidney, the surgeon scored tumor borders using a laparoscopic ultrasound probe controlled by the assistant or a decrease in the probe controlled by the console surgeon. As an essential step to avoid tumor violation, the surgeon took time to carefully score borders and observe tumor depth. The surgeon then proceeded to tumor excision. Using monopolar curved scissors with the curve aiming away from the tumor, cutting began from the scored borders. At times the surgeon reviewed computerized tomography images intraoperatively to reassess the excision depth at which to proceed. During tumor excision, close observation of cut tissue was critical to identify any gross tumor violation.

Pathological specimens were collected directly from the operation without bench manipulation or cutting by the surgical team. The orientation of the soft tissue and parenchymal margins, and the sinus fat location were examined and stained by the pathologist. This was intended to minimize the reporting of false-positive or false-negative margins.

PSMs were defined as malignant cells present at the inked parenchymal surgical margin of resection on the final pathology assessment. As such, normal parenchymal tissue around the resection margin, regardless of thickness, was considered a NSM. Surgeons did not methodically take frozen sections from the tumor bed resection.[13,14] Frozen sections were taken intraoperatively only in cases highly suspicious for incomplete tumor excision. If a PSM occurred, the tumor bed was resected again until a NSM was achieved. This was reported on the final pathological evaluation. When a NSM could not be achieved, the decision was made to convert to radical nephrectomy at surgeon discretion.

All operations converted to radical nephrectomy were excluded from the statistical analysis of oncologic outcomes. Benign and malignant tumors were included when calculating the disease recurrence rate. Only malignant tumors were considered in the analysis of cancer recurrence and metastasis.

Followup visits consisted of physical examination, chest x-ray and basic metabolic laboratory tests. Renal imaging was scheduled 6 and12 months postoperatively, and once annually thereafter for 5 years.

Local recurrence was defined as the detection of a new tumor in or abutting the excision bed. De novo tumors in different renal poles or in the contralateral kidney were not considered recurrence or metastasis but rather distant recurrence. The detection of RCC in distant organs or the peritoneal cavity was considered tumor metastasis. All metastatic tumors were confirmed to be RCC on percutaneous biopsy or cell cytology of peritoneal fluid aspirates.

Kaplan-Meier estimates were used to determine overall and cancer specific survival in the whole population. Recurrence-free and metastasis-free survival in patients with PSMs was compared to that in patients with NSMs using the log rank test. The fit proportional HR was determined to identify factors affecting recurrence and metastasis rates, including tumor size and growth pattern, pathological stage, Fuhrman grade, histological subtype, resection margin status and number of tumors excised at the same operation. Univariate and multivariate analyses were also done to identify factors that might predict the final surgical margin status. Among those factors was whether the surgeon was within or beyond the learning curve, which was considered 25 cases.[15]

## RESULTS

A total of 1,222 cases were performed at the 5 centers. The total number of positive surgical margins was 28 (2.3%), including benign and malignant tumors. In all study cases there were no grossly positive margins. PSMs on final pathological evaluation were reported as focally positive or a microscopic presence at the parenchymal resection margin.

Table 1 lists baseline clinical and demographic data on the whole population. As projected by the