



## Margin status and tumor recurrence after nephron-sparing surgery for bilateral Wilms tumor<sup>☆</sup>

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### Abstract

**Purpose:** Nephron-sparing surgery (NSS) has been advocated for patients with bilateral Wilms tumor (BWT). We sought to determine whether margin status impacted local tumor recurrence.

**Methods:** A retrospective review of patients undergoing NSS for BWT from November 1999 to March 2009 at our institution in which local recurrence rates based on margin status were compared.

**Results:** Of 21 patients, five (23.8%) had positive margins. These and 2 (9.5%) with focal anaplasia received flank XRT. Seven (33%) patients developed recurrent disease, a mean of 18.0 (range 1.3–39.9) months after NSS. Recurrence rates were similar in patients with positive and negative margins (1/5 [20%] vs 6/16 [37.5%];  $p=0.47$ ). Hypertension occurred more frequently in patients who received XRT (57.1% vs 28.6%). At a median follow-up of 28.6 months (range 5.2–142.3), 19 patients are alive, without evidence of disease; one patient (with a positive margin at initial NSS) died of metastatic anaplastic WT and another died of a brain tumor. One patient, with multiple risk factors, developed renal failure.

**Conclusions:** In our experience, local recurrence rates after NSS were not affected by surgical margin status although all patients with positive margins received XRT. These results support the aggressive use of NSS for patients with BWT.

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Wilms tumor (WT) is the most common renal tumor in children, affecting about 600 children annually in the United States [1]. Current therapy, consisting of unilateral nephrectomy, systemic chemotherapy and, in certain circumstances, ionizing radiation, has proven highly effective in improving both event-free and overall survival for patients with localized disease [2]. Because the contralateral kidney is typically normal in patients with unilateral WT, loss of a

single renal unit through nephrectomy is not routinely associated with an increased risk of renal insufficiency [3]. However, bilateral disease is an independent risk factor for the development of renal failure in children with WT [4]. The 5% of children with Wilms tumor who have bilateral disease (BWT) present the surgeon with the challenge of obtaining oncologic control while simultaneously optimizing renal function. In addition to the bilateral and often multifocal nature of BWT, children with BWT tend to develop tumors earlier than their counterparts with unilateral tumors and may be more likely to have syndromes which predispose them to abnormal renal function [3,5]. Chronic renal insufficiency adversely affects quality of life and overall health status at any age, but the impact is especially pronounced in young children owing to the deleterious effects on growth status as well as the challenges of dialysis administration in the pediatric population [6].

Nephron-sparing surgery (NSS) has enabled preservation of renal parenchyma and delayed the onset of renal failure in many children with BWT [7–9]. Because the renal unit is not removed in its entirety, care must be taken to excise all potentially neoplastic tissue without damaging adjacent normal renal parenchyma. The National Wilms Tumor Study has identified positive margins as an independent risk factor for local recurrence after nephrectomy [10]. However, data are still lacking on the prognostic value of positive margins on local recurrence following NSS for BWT; Horwitz et al. described a higher recurrence rate in patients with positive margins, but did not perform a formal statistical comparison because of the small number of patients involved [11]. We undertook this study to determine whether positive microscopic margins after NSS were associated with increased locoregional recurrence rates.

## 1. Methods

After obtaining Institutional Review Board approval, ICD-9 codes were utilized to identify all patients who had undergone NSS for BWT at St. Jude Children's Research Hospital between July 1999 and October 2008. Patients without at least 3 months of postsurgical follow-up were excluded, as were patients with diffuse anaplasia on histopathologic analysis. Data were collected on demographics, tumor characteristics, histopathologic findings including margin status, neoadjuvant and adjuvant therapy, locoregional and distant recurrence, and event-free and overall survival. Pathologic margins were considered positive if tumor microscopically extended to the inked border of a specimen. Demographic variables were described using measures of central tendency. Patients with or without positive margins were compared on the basis of locoregional recurrence and overall survival using t-tests for continuous variables and chi-square and Fisher's exact tests for categorical data. Analyses were performed using commer-

cially available statistical software (SAS; Cary, NC). However, because of the small number of patients in our series, multivariate statistical analyses comparing the demographics of these two groups were not performed. Because patients with positive margins routinely receive adjuvant radiotherapy, we also stratified patients on the basis of whether or not adjuvant radiotherapy was administered, and compared these groups with regard to rates of radiation-associated toxicity (e.g. radiation enteritis, hypertension). Patients were considered hypertensive if the medical record specifically noted a diagnosis of hypertension or if they were routinely taking antihypertensive medication.

## 2. Results

Twenty-one patients underwent NSS for favorable histology or focal anaplastic BWT at our institution over the study period. No patient underwent preoperative biopsy. The demographics of these patients are summarized in Table 1. Eighteen patients underwent bilateral NSS and three patients underwent unilateral nephrectomy with contralateral NSS. Of these latter three patients, two had been referred from other centers with contralateral disease after undergoing unilateral nephrectomy and a third did not have enough renal mass to spare after an intraoperative assessment of the feasibility of a nephron-sparing approach to a centrally-located tumor. All patients received both neoadjuvant and adjuvant chemotherapy per the contemporary Children's Oncology Group protocol for their pathologic stage. Each patient had between 1 and 10 separate specimens submitted from each renal unit for pathologic review. No patient had

**Table 1** Patient demographics.

Number of patients	21
Male/female	57.1%/42.9%
Race	
White	16 (76.2%)
Black	3 (14.3%)
Other	2 (9.5%)
Mean age at initial surgery	2.2 years (range: 0.5–5.6)
Surgery type	
Bilateral NSS	18 (85.7%)
Unilateral nephrectomy with contralateral NSS	3 (14.3%)
Positive margins	5 (23.8%)
Unilateral positive margin	2
Bilateral positive margin	3
Single positive margin/kidney	4
Multiple positive margins/kidney	1
Adjuvant flank radiotherapy	7 (33.3%)
Histology	
Favorable (%)	19 (90.5%)
Focal anaplasia (%)	2 (9.5%)

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