

Nephroblastoma: Does The Decrease In Tumour Volume Under Preoperative Chemotherapy Predict The Lymph Nodes Status At Surgery?

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for the SIOP Nephroblastoma Trial and Study Committee

conflict of interest disclosure for SIOP Boston 2010

there were no financial support for this study

Jan Godzinski

- who knows how to wake-up the anaesthesiologist ?



- SIOP ignores initial staging (but IV and V)
 - the treatment is based on the surgical/pathological status assessed at surgery after preop. ChT
 - marked decrease of tumor volume suggests that the tumour variant is chemosensitive and practically excludes anaplastic WT
 - Decrease of tumor volume induced by the preoperative ChT is observed in 82% of pts
 - Median Vol. decrease = 65%
 - High proportion of stage 1 patients (54%) and nearly 100% OS these pts
- less aggressive surgery in case of favorable location ?

1360 pts with unilateral, localized nephroblastoma and sufficient data from SIOP 9301

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Selected reports advocating feasibility and benefits of nephron sparing surgery in unilateral nephroblastoma (1989-2006)

- 1. Gentil Martins A, Espana M (1989) Partial nephrectomy for nephroblastoma – a plea for less radical surgery. *Med Pediatr Oncol* 17: 320**
- 2. Moorman-Voestermans CGM, Staalman CR, Delamarre JFM. Partial nephrectomy in unilateral Wilms' tumour is feasible without local recurrence. *Med. Pediatr Oncol* 23: 218, 1994**
- 3. Moorman-Voestermans CGM, Aronson DE.C. Staalman CR, Delamarre JFM., De Kraler J. Is partial nephrectomy appropriate treatment for unilateral Wilms' tumour? *J Ped Surg.*, 33: 165-170, 1998**
- 4. Cozzi DA, Schiavetti A, Morini F, Castello MA, Cozzi F. Nephron sparing surgery for unilateral primary renal tumor in children. *J Pediatr Surg*, 36, 2: 362-365, 2001**
- 5. Hoellwarth ME, Urban C, Linni K, Lackner H. Partial nephrectomy in patients with unilateral Wilms tumor. 3rd International Congress of Paediatric Surgery, Brussels, 6-8.05.1999, abstract book**
- 6. Cozzi F, Cozzi DA., Schiavetti A., Zani A., Spagnol L., Totonelli G., Nephron-sparing surgery in children with unilateral renal tumour: a systematic literature review. *Pediatric Blood & Cancer*; Vol. 47; 4, October 1, 2006; 360**
- 7. Cozzi DA, Zani A (2006) Nephron-sparing surgery in children with primary renal tumor: indications and results. *Semin Pediatr Surg.* 15: 3-9**

- nephron sparing surgery (NSS) is not associated with elevated risk of relapse in case of stage 1 int. and low risk WT (no relapses in 18 stage 1 pts, SIOP 2001)*

**Tuebingen 2007 and EUPSA 2008*

How to predict stage prior to surgery?

- good quality imaging may reliably suggest the staging.
- the LN status, however, remains obscure^{1, 2.}
(no evidence based data)

-
- Note 1: tumor positive LN's imply radiotherapy, which counteracts the functional benefits of NSS
 - Note 2: frozen-section of the LN's as the first step of surgery (before NSS is finally aproved) is considered not reliable enough

hypothesis

• NRP ignores initial staging (but IV and V)

- NSS is not associated with elevated risk of relapse in case of stage 1, int. and low

- the tr
asse
preop

marked decrease of tu volume under preop. ChT suggests that the tumour is chemosensitive (low or int risk), thus also LN's, even if initially invaded, shall be cleared of tumour cells.

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- if also imaging suggests stage 1, polar or peripheral tumour, without invasion of the collective system & renal vessels with $> \frac{1}{2}$ of the kidney free \rightarrow NSS is procedure of choice

g,
cure

or
the

- **The aim of this report**

is to verify whether marked decrease of tumour volume under preoperative chemotherapy, indicating chemosensitivity, also implies clearance of the regional LN

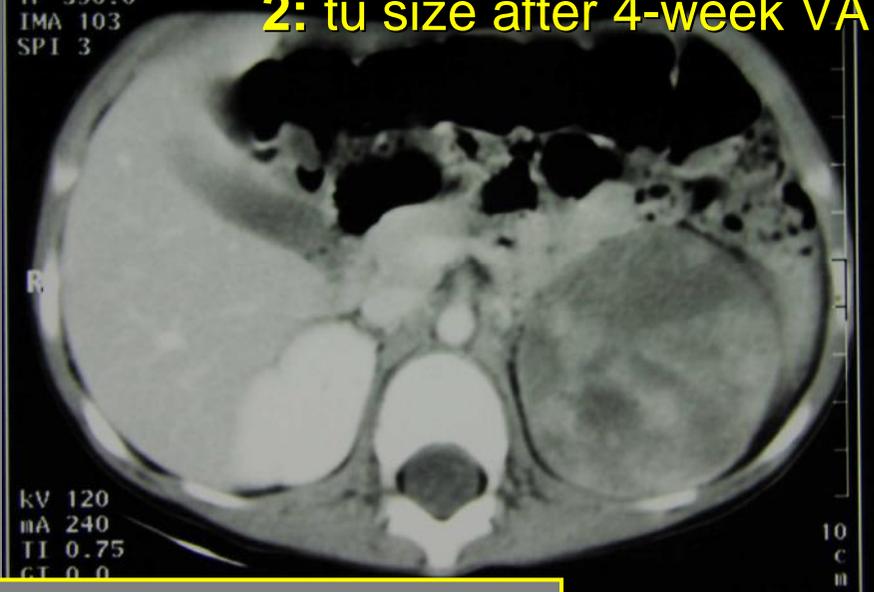
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1: tu size at dgn



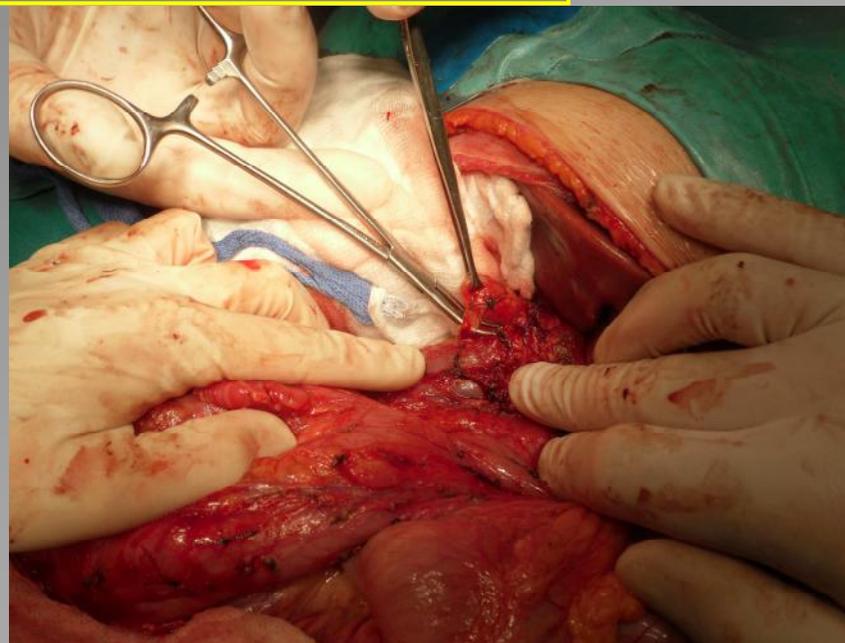
23-SEP-2002
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IMA 103
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2: tu size after 4-week VA



approx. 80% decrease in tumor volume

**3: sampling the LN's
at nephrectomy,
none of 6 sampled
nodes invaded**



Patients:

- SIOP 9301 (1993-2001):
 - 1450 localized WT
 - 1360 (93%) had sufficient data.
- Patients were divided in:
 - these with tumor positive LN (76 (5.5%)) at surgery
 - those with tumour negative LN (1284 (94.5%)) at surgery.

		LN- =1284	LN+ = 76	N=1360	p value
Gender	male	572 (45%)	35 (46%)	607 (45%)	chisq P=0.798
	female	712 (55%)	41 (54%)	753 (55%)	
Side	right	612 (48%)	25 (33%)	637 (47%)	chisq P=0.033
	left	626 (49%)	44 (58%)	670 (49%)	
	Missing	46 (4%)	7 (9%)	53 (4%)	
Stage	I	729 (57%)		730 (54%)	fisher P=<.001
	II	419 (33%)	5 (6%)	424 (31%)	
	III	136 (11%)	71 (93%)	207 (15%)	
Risk	low risk	72 (6%)	2 (3%)	74 (5%)	fisher P=0.195
	intermediate risk	1127 (88%)	65 (86%)	1192 (88%)	
	high risk	84 (7%)	9 (12%)	93 (7%)	
	nephrogenic rest	1 (0.1%)		1 (0.1%)	

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Continuous measures by LN status

	N-	N+	p
Vol at dgn (ml)	377 (200-622)	554 (318-772)	0.00091
Vol at surg (ml)	130 (44-294)	192 (63-458)	0.05553
Vol change (%)	62	67	0.04620
Vol increase (pts)	115	9	0.6199
Vol decrease (pts)	770	39	0.037

The variables have been tested within the different groups (multiple testing problem) the actual p-value of 0.05 can no longer be used as a threshold. Rather, p-values of <0.01 should be considered significant.

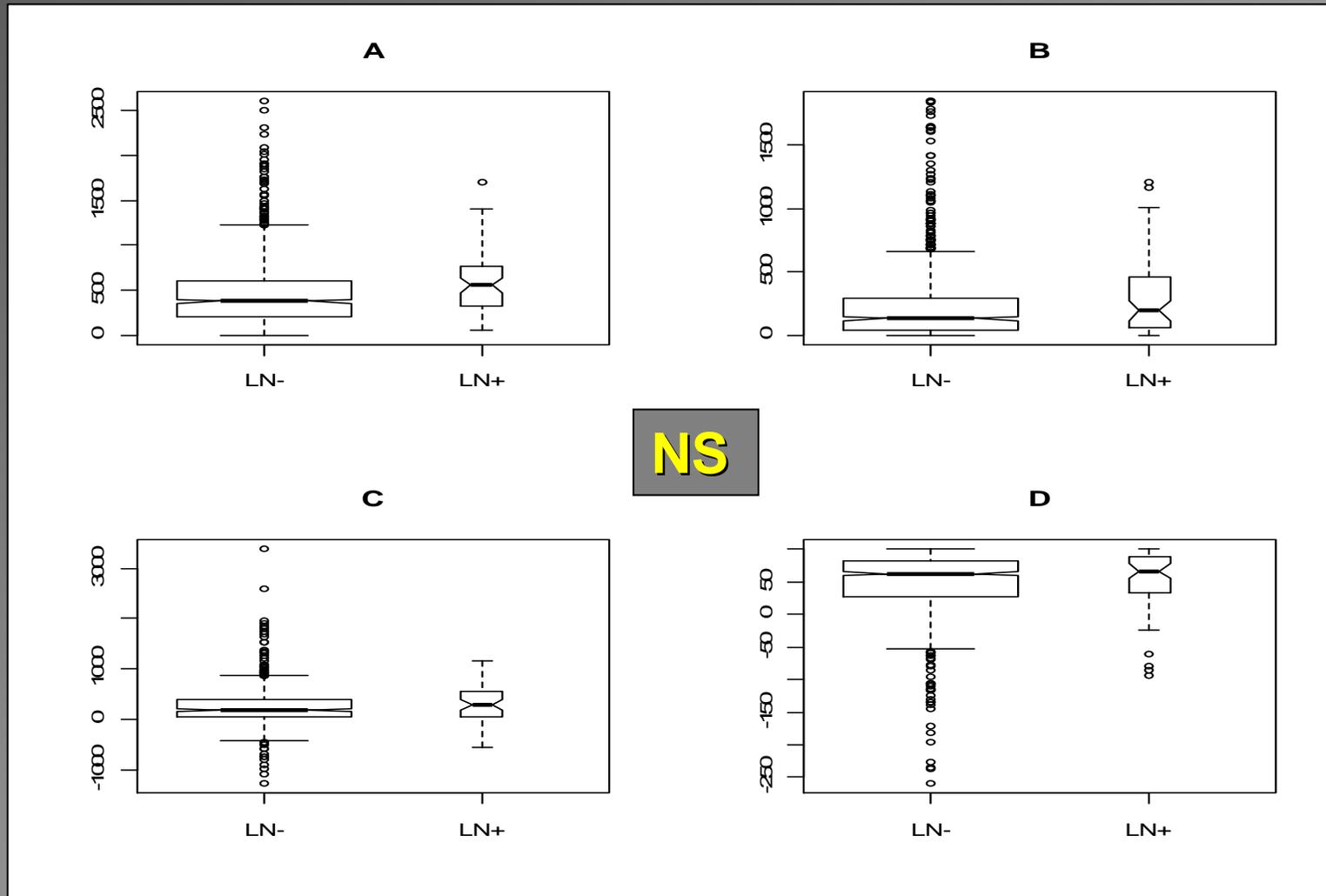
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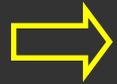
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Boxplot figures of (A) tu volume at dgn (Ultrasound), (B) tu vol. at surgery, (C) difference in tu vol. and (D) percentage change in volume.

All localized patients and pathological confirmed LN-status.





on what to build the guidelines?

- initial tumour volume was significantly larger in **LN(+)** patients; $p=0,00091$; Krusk.
(but not different (NS) at surgery)
- rate of **LN(+)** patients was low (5.5%)
- please note : not **a single case** of LN involvement if **initial volume < 318 ml**

Conclusions:

- Change in tumour volume under preoperative chemotherapy is not a predictor for LN status at surgery, although larger initial volume is associated with a higher risk of LN invasion after preoperative ChT.
- The decrease of tumour volume is not a good criterium for the safety of NSS.
- The low rate of positive LN (5.5%) in the whole group indicates that this risk should not be overestimated, especially if the patients with a small initial tumour volume are considered for NSS (not a single case of LN involvement if initial volume below 318 ml.)

Candidates for NSS according to SIOP 2001

Those who had no:

- pre-operative tumor rupture or biopsy
- infiltration of the extra renal structures
- intra-abdominal metastases or lymph nodes seen on pre-operative imaging
- thrombus in the renal vein or vena cava
- tumour involving more than 1/3 of the kidney
- multifocal or central tumour, involvement of calyces, haematuria
- little experience in partial nephrectomy.

- other low staged polar or peripheral tumours were potential candidates for NSS.

what is really required ?



1. WT with initial volume < 300 ml

2. Imaging prior to surgery:
 - polar or peripheral tumour
 - no extra renal invasion
 - collective system and renal vessels free

and no unfortunate events as ruptures, open biopsies etc

**all the „other” unilateral cases
are not candidates for NSS**

