Wilms Tumor

Update on current management

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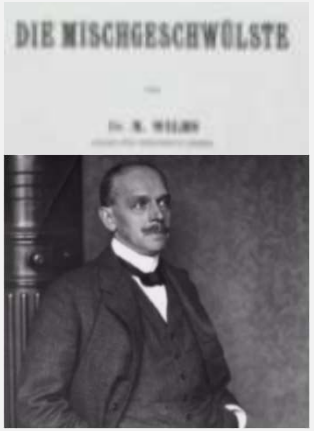
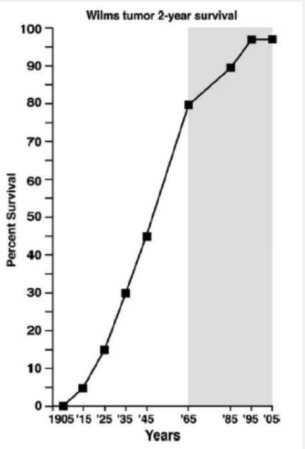
Basics

Background

- **1899, Carl Max Wilhelm Wilms:** Described the tumor
- Most common pediatric renal tumor (1:10,000)
- **Outcome significantly improved w**ith evolution of treatment
  - Multi-disciplinary, multi-institutional **study groups**
  - Move towards biology (markers) and **risk based therapy**
  - **Major changes** in treatment of stage 1, stage 4 and stage 5





The National Wilms Tumor Study: a 40 year perspective

Giulio J. D'Angio

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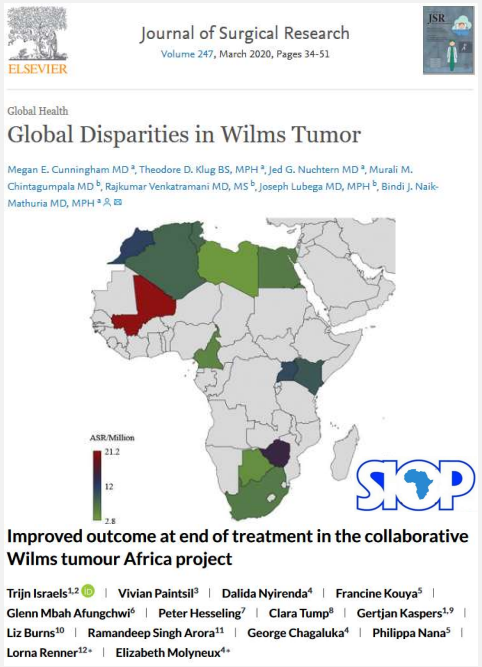
Lifetime Data Anal (2007) 13:463–470
https://doi.org/10.1007/s10985-007-9062-0

The situation in Africa

- Reported as the 2nd or 3rd most common malignancy in SSA
- **Poor survival** (reported rates 11% - 50%)
  - Access (physician per populace)
  - Late presentation (stage 4, malnourished)
  - Incomplete treatment (financial, chemo/radio availability)
- **SIOP Africa (2014)** collaborative project for SSA
  - in the first 4 years **improved outcome** (52% to 68%)



J Surg Res. 2020 March; 247:34-51
https://doi.org/10.1016/j.jss.2019.10.044

Pediatr Blood Cancer.2018;e26945
https://doi.org/10.1002/pbc.26945

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Histology

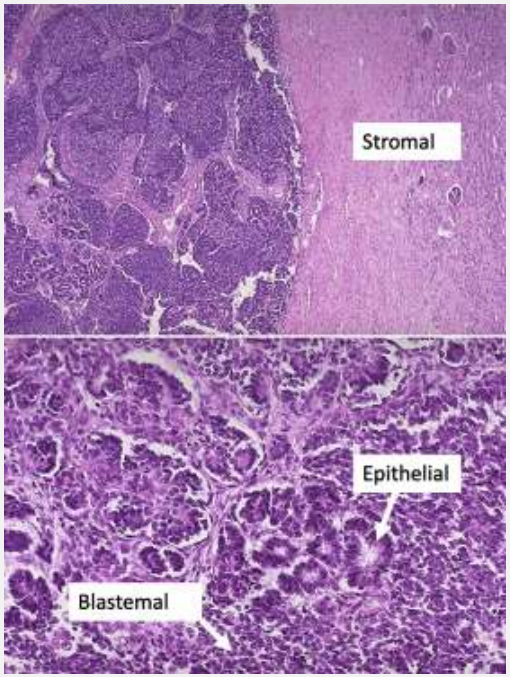
Immature renal elements (Nephroblastoma/renal embryoma)

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE
SIOP
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

- Low risk
  - Completely necrotic
- High Risk
  - Blastemal
  - Diffuse anaplasia

CHILDREN'S ONCOLOGY GROUP

- Favorable (90%)
  - triphasic (classic WT)
- Unfavorable
  - **Anaplastic** (focal/diffuse)



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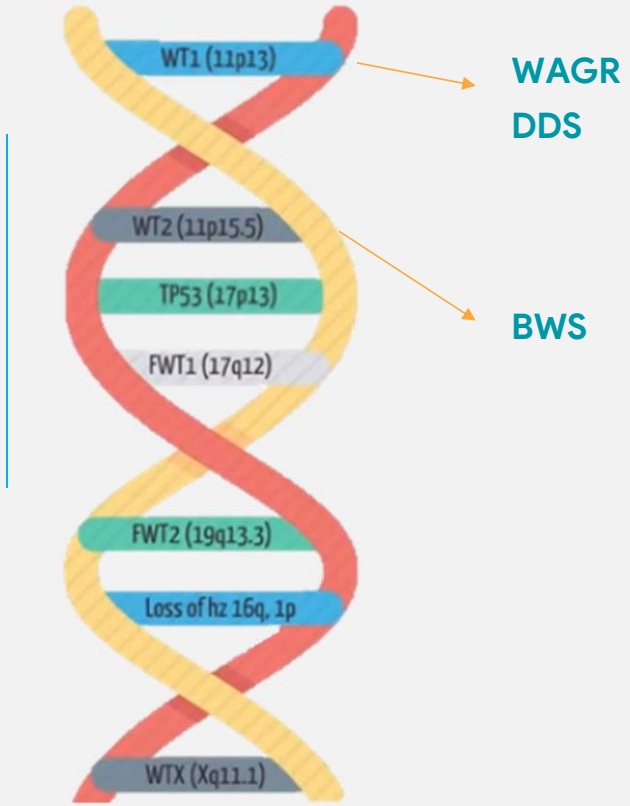
Genetics

- **Mutated Genes**
  - WTX (most common)
  - TP53 (anaplastic)
- **Loss/Gain of Genes**
  - LOH 1p/16q = poor prognosis
  - 1q Gain



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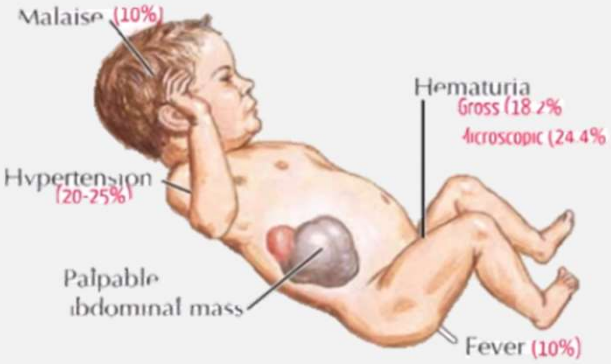
Clinical presentation

- 80% present **before 5 years** (6mo-10yr)
- Most are **asymptomatic** with palpable **abdominal mass**
- 20% **hematuria, hypertension**, flank pain
- 10% **coagulopathy, Lt varicocele**, [fever, anorexia, wt loss]
- Metastasis is common to lung or liver



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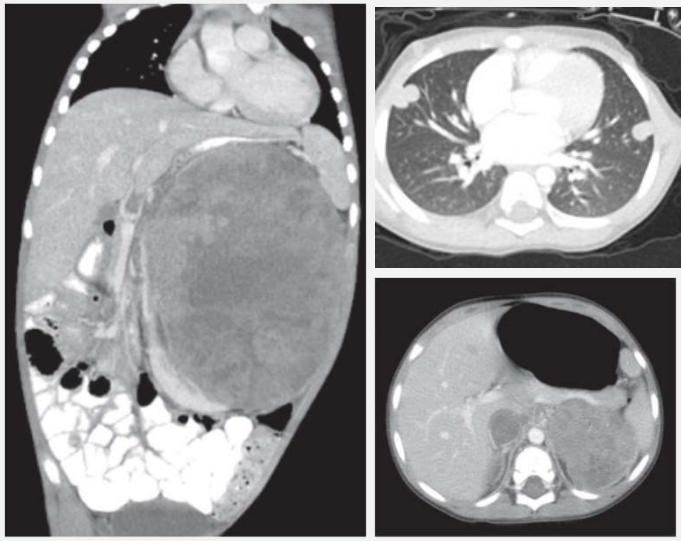
Diagnostic Evaluation

- **Abdominal imaging** (soft tissue mass from kidney)
  - **US :** screening, extension to veins or ureter
  - **CT** : renal origin and contralateral kidney
- **Chest imaging** (lung nodules)
  - **Chest CT** if there is any doubt on X-ray
- **Laboratory**
  - RFT, LFT
  - Serum calcium
  - Coagulation studies



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Principles of Treatment

	Neoadjuvant chemo	Primary resection
Approach	**Regimen**: 4wk dactinomycin & vincristine (localized) or 6wk + epirubucin (for mets)	**Exception:** Bilateral WT, predisposition syndromes, thrombus above hepatic vein
	Post-op **local RT** based on the local stage and **intensity of chemo** based on disease stage.	
Advantages	- **Decrease tumor volume** (easy resection, Significantly decrease rupture)	- **Early histologic diagnosis** (Avoid chemo for benign/other renal tumor)
Disadvantage	**Chemo without histologic diagnosis** -5% SIOP receive inappropriate chemo -Chemo changes tumor histology	**Tumor rupture** - SIOP reported 8% with significant decrease - COG reported 10% but definition is d/t
Arguments	Biopsy not needed (imaging diagnosis)	Rupture is over-defined by SIOP

Surgery

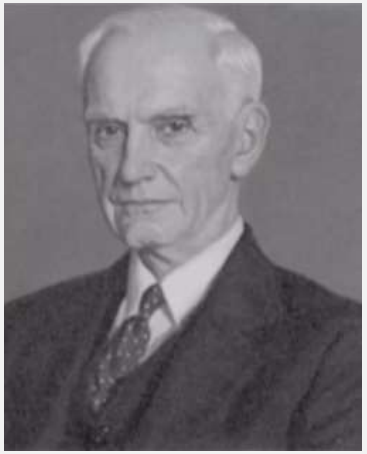
Activate Windows
Go to Settings to activate Windows.

Principles

- **1938, William Ladd:** principles of surgery for Wilms
  - **Trans-peritoneal exposure** (avoid rupture)
  - **Early ligation of vessels** (prior to tumor manipulation)
  - **Removal of perirenal fat** (resect LN)
- Survival with surgery alone improved (5% >> 32%)
- Resection remains the cornerstone of all therapies

EMBRYOMA OF THE KIDNEY (WILMS' TUMOR)

WILLIAM E. LADD, M.D.
BOSTON, MASS.



Ann Surg. 1938 Nov; 108(5): 885–902
https://doi.org/10.1097/00000658-193811000-00010

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Key Steps

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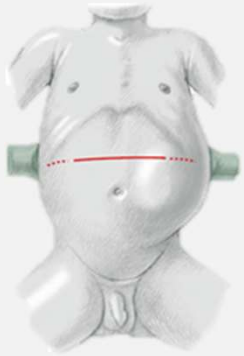

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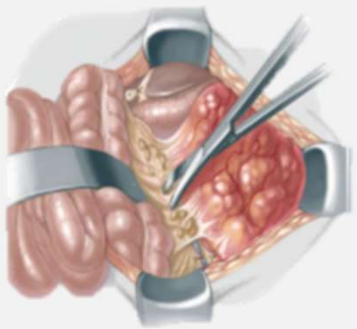

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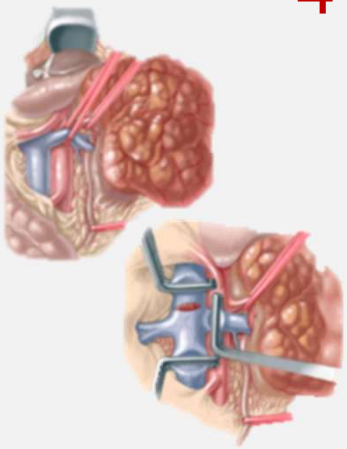

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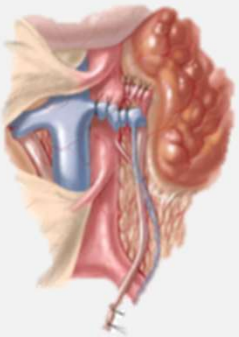

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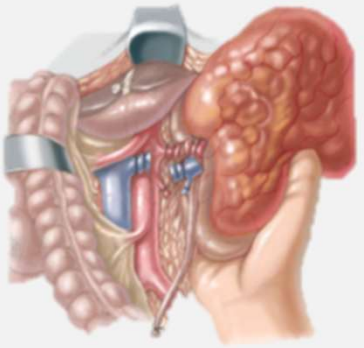


1. Incision & initial exploration

- **Exposure** – long transverse incision
- **Inspection** – intraabdominal cavity
  - Liver
  - Lymph nodes
  - Peritoneum, free fluid
  - **Blood (may be sign of rupture)

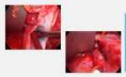
**Second surgery after initial biopsy

- **Care to prevent seeding the incision**
- remove previous incision down to the tumor (tract removed with kidney)

2. Entering the retroperitoneum

3-4. Ligating vessels & LN sampling

**Thrombus in renal vein/IVC



5. mobilize & remove kidney

**Partial nephrectomy

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Dr. Armando Lorenzo, Urology, Sick Kids
https://www.youtube.com/watch?v=KsRJQv4I9L4

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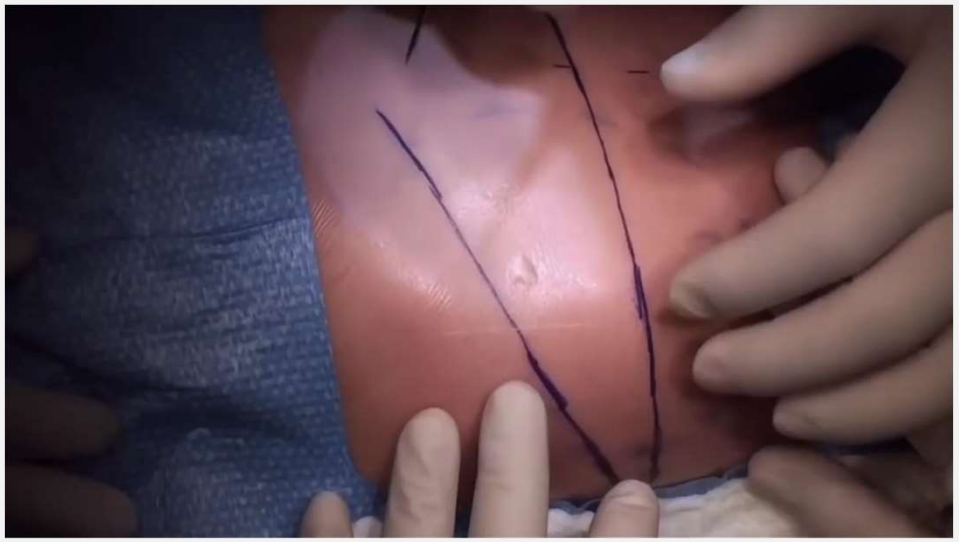

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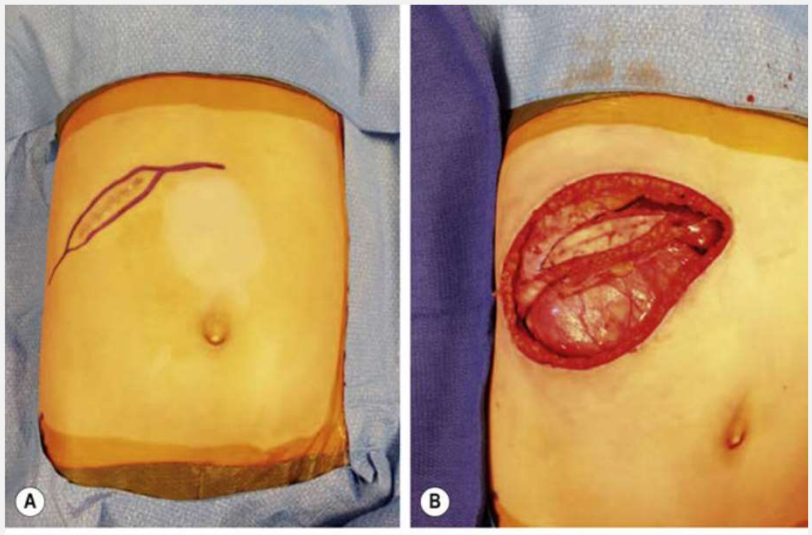

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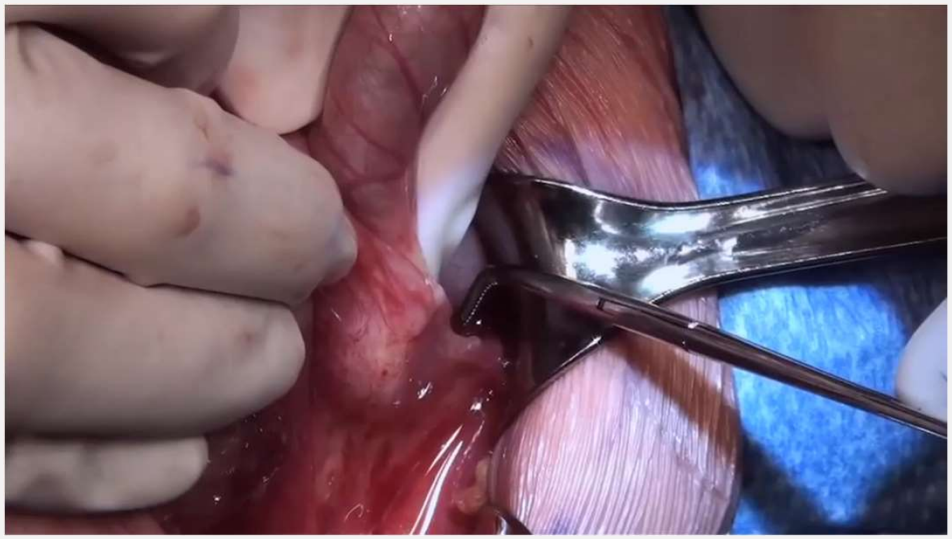
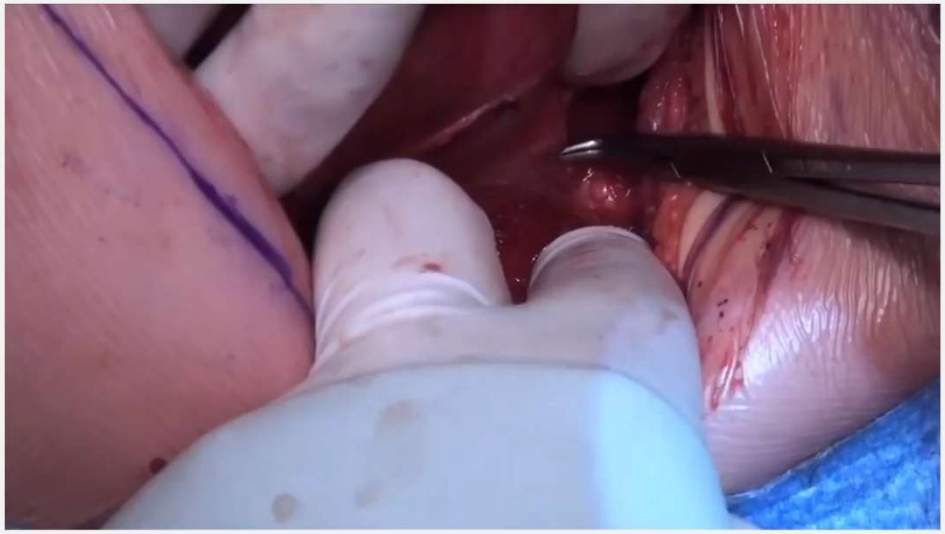


- **Open lateral peritoneum** and reflect colon/mesentery off anterior kidney
- WT is usually adherent (without invasion)
- **Invasion is considered inoperable** (biopsy+neoadjuvant) except
  - Adrenal
  - Diaphragm / psoas (small)
  - Mesentery (ligation avoiding resection)
  - pancreas (tip only)

3-4. Ligating vessels & LN sampling



- Aim for **early ligation unless difficult** (very large/cross midline, invasive, big LN in the way)
- Pass **sling** around vessels, **palpate** for thrombus
- **Ligate artery first** (avoid swelling, fragility and venous dissemination)
- **Obtain ≥ 5 Lymph Nodes** if possible
  - **Regional** (pericaval & para-aortic at renal artery origin, including contralateral)
  - **Extra-regional** (above/below regional)
  - **Hilar** (together with kidney)

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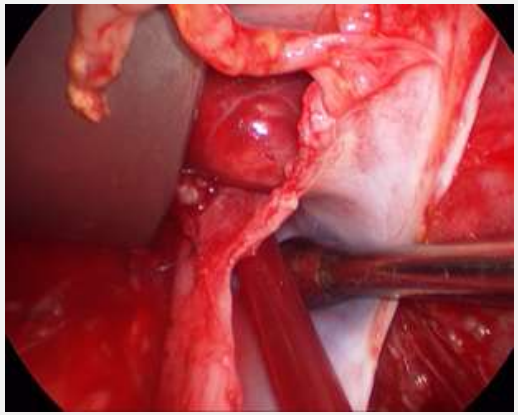
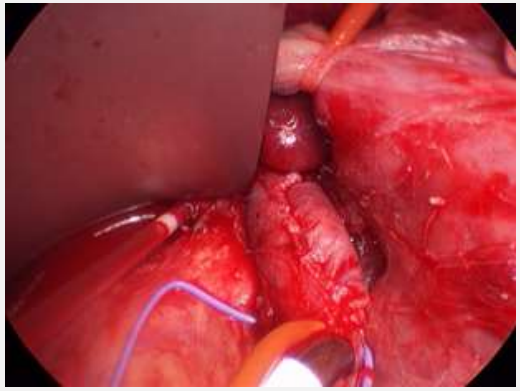
**Thrombus in renal vein/IVC





- **Aim for en-bloc removal with kidney** unless difficult (post chemo, IVC invasion)
- **Renal vein –** resect thrombus with vein
- **Free IVC thrombus -** pulled out with suction cannula or Fogarty balloon after venotomy
  - **Infra-hepatic -** proximal & distal control
  - **Supra-hepatic –** thoraco-abd. Incision, bypass
- **IVC wall invasion requires** resection and patching. (may not be completely removed)
- **Right atrium extension** is opened and pulled out the heart at same time with the abdomen

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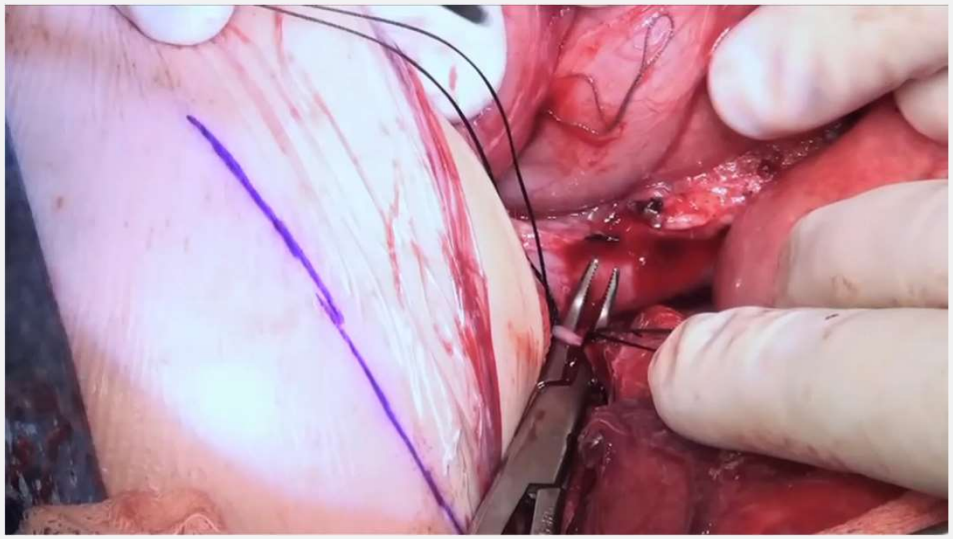
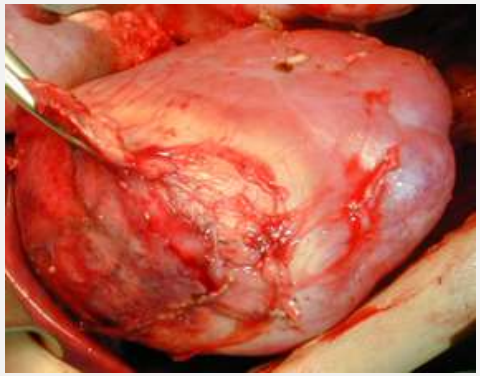
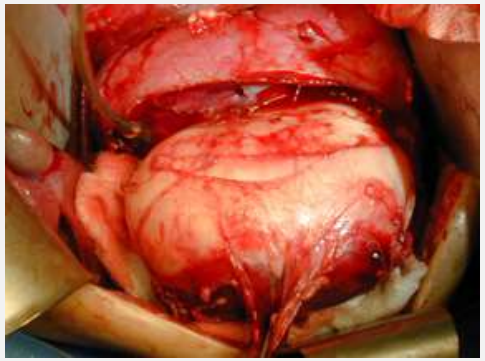
5. mobilize & remove kidney



- Plane is established **outside Gerota's fascia**
- Palpate **ureter** (thrombus) & resect distally
- Remove **adrenal** if tumor involves upper pole
- Remove segment of **diaphragm** if adherent
- **Titanium clips** to identify gross residual tumor
- **Hemostasis** (dry tumor bed at closure)

**Partial nephrectomy





- Plane is established **inside Gerota's fascia**
- Dissect off **perirenal fat** except around mass
- Control **renal vessel** ± hypothermia
- **Capsule** incised and peeled back to expose
- **Excise** with 0.5-1cm rim of parenchyma
  - **Enucleation** for centrally located tumor
  - **Additional surgery** for diffuse anaplasia and incomplete resection

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Staging

Stage		COG	SIOP
1	**Limited to kidney**	No penetration of capsule	Limited to pseudocapsule
2	**Outside kidney**	renal sinus vessel/capsule invasion	" + **biopsied**
3	**Incomplete resection**	**biopsied**, Inoperable, positive margin, spillage, rupture, transected thrombus, peritoneal surface involved, regional LN,	"
4	**Metastasis**	Hematogenous or LN outside abdomen	"
5	**Bilateral tumor**	Each kidney may have a local stage	"
			**Local staging is important even in metastatic (dictates radiotherapy)*

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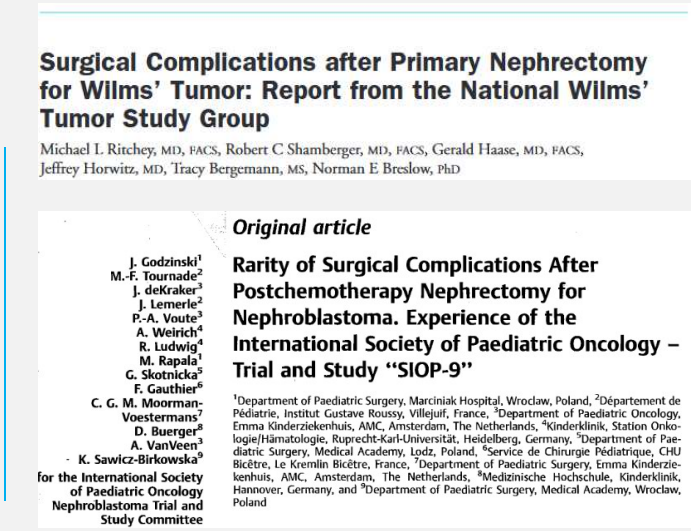
Compilations

- **2001, NWTS -** 13% complication
  - 5 % Intestinal obstruction
  - 2% extensive hemorrhage
  - 2% wound infection
  - 1.5% vascular injury
- **1998, SIOP** – 8% complication
  - 4% Small bowel obstruction
  - 3% tumor rupture



Surgical Complications after Primary Nephrectomy for Wilms' Tumor: Report from the National Wilms' Tumor Study Group

Michael I. Ritchey, MD, FACS, Robert C Shamberger, MD, FACS, Gerald Haase, MD, FACS, Jeffrey Horwitz, MD, Tracy Bergemann, MS, Norman E Breslow, PhD

Original article

Rarity of Surgical Complications After Postchemotherapy Nephrectomy for Nephroblastoma. Experience of the International Society of Paediatric Oncology – Trial and Study "SIOP-9"

J. Godzinski[1], M.-F. Tournade[2], J. deKraker[3], J. Lemerle[2], P.-A. Voute[3], A. Weirich[4], R. Ludwig[4], M. Rapala[1], G. Skotnicka[5], F. Gauthier[6], C. G. M. Moorman-Voestermans[7], D. Buerger[8], A. VanVeen[3], K. Sawicz-Birkowska[9] for the International Society of Paediatric Oncology Nephroblastoma Trial and Study Committee

[1]Department of Paediatric Surgery, Marciniak Hospital, Wroclaw, Poland, [2]Département de Pédiatrie, Institut Gustave Roussy, Villejuif, France, [3]Department of Paediatric Oncology, Emma Kinderziekenhuis, AMC, Amsterdam, The Netherlands, [4]Kinderklinik, Station Onkologie/Hämatologie, Ruprecht-Karl-Universität, Heidelberg, Germany, [5]Department of Paediatric Surgery, Medical Academy, Lodz, Poland, [6]Service de Chirurgie Pédiatrique, CHU Bicêtre, Le Kremlin Bicêtre, France, [7]Department of Paediatric Surgery, Emma Kinderziekenhuis, AMC, Amsterdam, The Netherlands, [8]Medizinische Hochschule, Kinderklinik, Hannover, Germany, and [9]Department of Paediatric Surgery, Medical Academy, Wroclaw, Poland

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Eur J Pediatr Surg. 1998 Apr;8(2):83-6
https://doi.org/10.1055/s-2008-1071127

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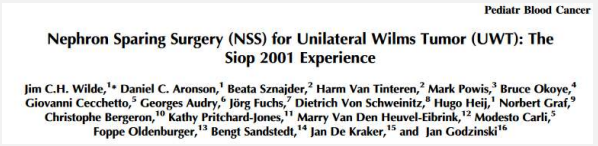
Update: Nephron sparing surgery for unilateral tumor

Not indicated in WT but being done for adults

- **Feasibility**: Ability of surgeon, not invading/abutting renal vessels, >1 cm margin while preserving 1/3 kidney
- **2013, COG:** Based on preop imaging only a small percentage are candidates (8%)
  - **Inclusion:** Very low risk tumor
- **2014 SIOP:** outcome of NSS comparable to RN but is feasible in only a small percentage (3%)
  - **Inclusion**: peripheral/polar tumors



J Urol. 2013 190 : 1546-1851
https://doi.org/10.1016/j.juro.2013.05.060

Pediatr Blood Cancer. 2014. 61:2175-2179
https://doi.org/10.1002/pbc.25185

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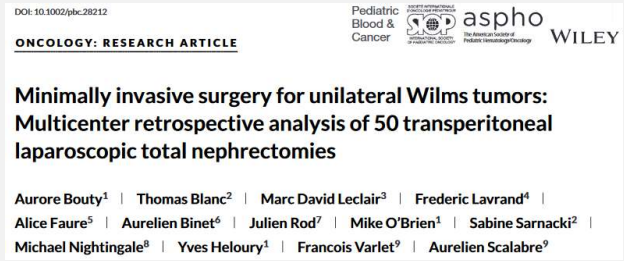
Update: Minimally invasive surgery

controversial (concerns about worse oncologic outcomes)

- **2020, SIOP:** MIS is feasible in 20% of WT with comparable outcome to open surgery
  - **Inclusion**: unilateral, total nephrectomy


DOI: 10.1002/pbc.28212

Pediatric Blood & Cancer

aspho

WILEY

ONCOLOGY: RESEARCH ARTICLE

Minimally invasive surgery for unilateral Wilms tumors: Multicenter retrospective analysis of 50 transperitoneal laparoscopic total nephrectomies

Aurore Bouty[1] | Thomas Blanc[2] | Marc David Leclair[3] | Frederic Lavrand[4] | Alice Faure[5] | Aurelien Binet[6] | Julien Rod[7] | Mike O'Brien[1] | Sabine Sarnacki[2] | Michael Nightingale[8] | Yves Heloury[1] | Francois Varlet[9] | Aurelien Scalabre[9]

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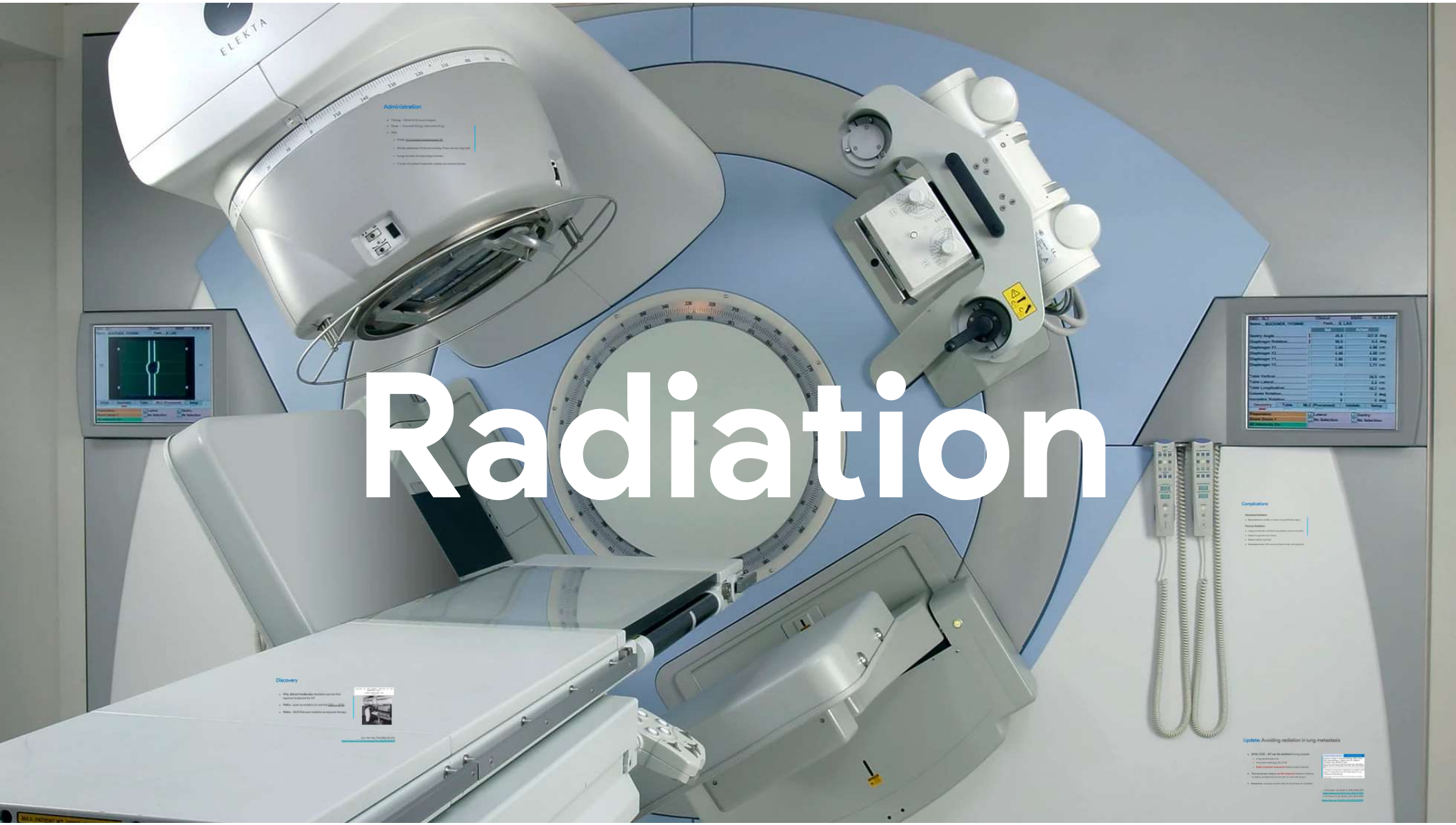
ELEKTA
Administration
Discovery
Complications
Update: Avoiding radiation in lung metastasis

Radiation

Discovery

- **1916, Alfred Friedlander**: Radiation was the first reported treatment for WT
- **1940s** – post op radiation inc survival (32% >> 47%)
- **1960s** – SIOP first used radiation as adjuvant therapy

SARCOMA OF THE KIDNEY TREATED BY THE ROENTGEN RAY *

ALFRED FRIEDLANDER, M.D.
CINCINNATI

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Am J Dis Child. 1916;XII(3):328-330.
https://doi.org/10.1001/archpedi.1916.04110150128009

Administration

- **Timing** - Within 10-14 days of surgery
- **Dose** - Favorable 10.8 gy, Unfavorable 20 gy
- **Site**
  - **Flank:** for all except favorable stage 1/2
  - **Whole abdomen:** Peritoneal seeding, Preop rupture, large spill
  - **Lung:** nodules not responding to chemo
  - **? Liver:** if localized/resectable, radiate only involved portion

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Complications

Abdominal Radiation

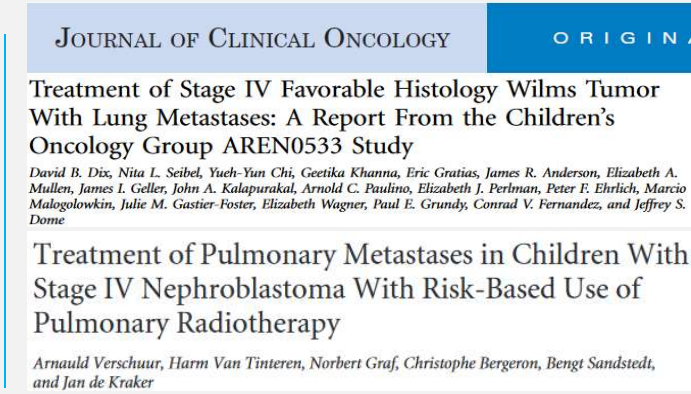
- **Renal failure:** In addition to chemo & hyperfiltration injury

Thoracic Radiation

- **Lung**: pneumonitis, restrictive lung disease, reduced capacity
- **Heart:** Congestive heart failure
- **Spine**; scoliosis, kyphosis,
- **Secondary tumor**: 15% breast ca (need earlier mammograph)

Update: Avoiding radiation in lung metastasis

- **2018, COG – RT can be omitted** in lung nodules
  - Lung metastasis only
  - Favorable histology, No LOH
  - Rapid complete responders (6wk postop chemo)
- **Thoracoscopic biopsy:** partial response (minimal residual, <4 lesion, peripheral) can be scar or necrotic tumor
- **Resection:** nodules remain after 12 wk chemo & radiation


JOURNAL OF CLINICAL ONCOLOGY ORIGINA

Treatment of Stage IV Favorable Histology Wilms Tumor With Lung Metastases: A Report From the Children's Oncology Group AREN0533 Study

David B. Dix, Nita L. Seibel, Yueh-Yun Chi, Geetika Khanna, Eric Gratias, James R. Anderson, Elizabeth A. Mullen, James I. Geller, John A. Kalapurakal, Arnold C. Paulino, Elizabeth J. Perlman, Peter F. Ehrlich, Marcio Malogolowkin, Julie M. Gastier-Foster, Elizabeth Wagner, Paul E. Grundy, Conrad V. Fernandez, and Jeffrey S. Dome

Treatment of Pulmonary Metastases in Children With Stage IV Nephroblastoma With Risk-Based Use of Pulmonary Radiotherapy

Arnauld Verschuur, Harm Van Tinteren, Norbert Graf, Christophe Bergeron, Bengt Sandstedt, and Jan de Kraker

J Clin Oncol. Vol 36, No 3. 2018: 3178-3179
https://doi.org/10.1200/JCO.2017.77.1931

J Clin Oncol Vol 30, No28, 2012: 3533-3539
https://doi.org/ 10.1200/JCO.2011.35.8747

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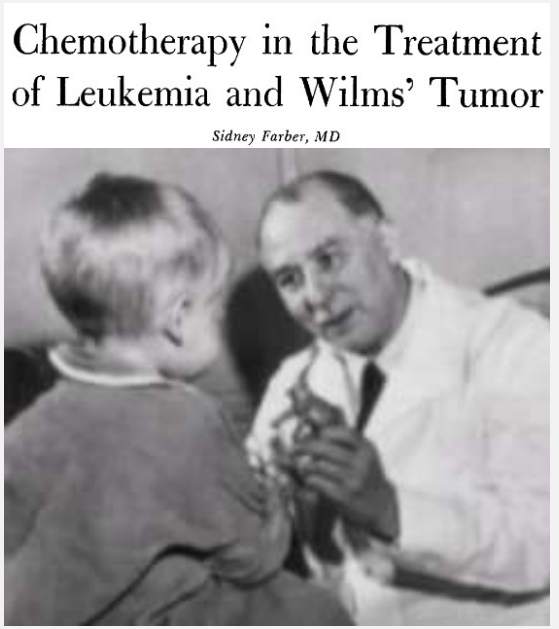
Chemotherapy

Discovery

- **1966, Sidney farber** – first adjuvant chemo
  - Used dactinomycin (first agent for WT)
  - 2 years later vincristine sulfate identified
- Outcome significantly improved (89% survival)
- With triple agent –92%


Chemotherapy in the Treatment of Leukemia and Wilms' Tumor

Sidney Farber, MD

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TIKUR ANBESSA

JAMA. 1966;198(8):826-836.
https://doi.org/10.1001/jama.1966.03110210076025

Regimen

SOCIÉTÉ INTERNATIONALE D'ONCOLOGIE PÉDIATRIQUE
SIOP
INTERNATIONAL SOCIETY OF PAEDIATRIC ONCOLOGY

(post-op regimen)

- **No chemo =** stage 1, low grade
- **Dactinomycin/Vincristine =** intermediate grade
- **+ Epirubicin** = Stage 2
- **+ Carboplatin, ifosfamide, VP16** = high grade

CHILDREN'S ONCOLOGY GROUP

- **Dactinomycin/Vincristine =** Favorable Stage 1/2
- **+ Doxorubicin** = Unfavorable/*LOH Stage 1/2, Favorable Stage 3/4, relapse
- **+ Cyclophosphamide/etoposide** = Unfavorable Stage 3/4.

*favorable stage 4 incomplete responders

- **Other agents** - Carboplatin, irinocetan

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Complications

- **Nephrotoxicity:** unilateral non-syndromic WT has very low risk
- **Secondary Malignancies (**leukemia)
- **Congestive heart failure** (doxorubicin 4%)

Update: Avoiding chemo in low risk

- **2017, COG – chemo can be avoided in very low risk**
  - Age < 2 year
  - Stage 1
  - Tumor wt <550g
  - No predisposition syndrome
  - Favorable histology
  - LN negative (after sampling)
- **Risk:** 10% relapse and more intensive therapy
- **Recommend** : Expanding surgery-only group

Clinical Outcome and Biological Predictors of Relapse After Nephrectomy Only for Very Low-risk Wilms Tumor:

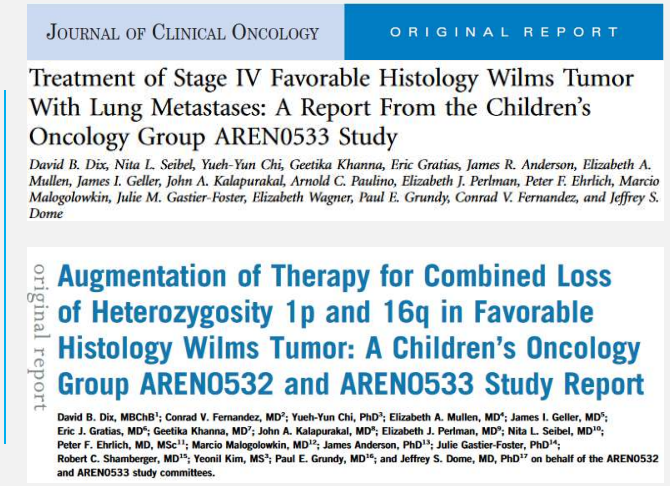
A Report From Children's Oncology Group AREN0532

Conrad V. Fernandez, MD, FRCPC*, Elizabeth J. Perlman, MD†, Elizabeth A. Mullen, MD‡, Yueh-Yun Chi, PhD§, Thomas E. Hamilton, MD¶, Kenneth W. Gow, MD‖, Fernando A. Ferrer, MD**, Douglas C. Barnhart, MD, MSPH††, Peter F. Ehrlich, MD, MSc‡‡, Geetika Khanna, MD§§, John A. Kalapurakal, MD, FACR¶¶, Tina Bocking, BN, RN*, Vicky Huff, PhD‖‖, Jing Tian, MS***, James I. Geller, MD†††, Paul E. Grundy, MD‡‡‡, James R. Anderson, PhD§§§, Jeffrey S. Dome, MD, PhD¶¶¶, and Robert C. Shamberger, MD¶

Ann Surg. 2017 April ; 265(4): 835–840
https://doi.org/ 10.1097/SLA.0000000000001716

Update: Intensive therapy for high risk

- **2018, COG:** better outcome of **incomplete responders** with Intensified chemo
- **2019, COG:** inc survival of **combined LOH** with intensified chemo



JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Treatment of Stage IV Favorable Histology Wilms Tumor With Lung Metastases: A Report From the Children's Oncology Group AREN0533 Study

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original report

Augmentation of Therapy for Combined Loss of Heterozygosity 1p and 16q in Favorable Histology Wilms Tumor: A Children's Oncology Group AREN0532 and AREN0533 Study Report

David B. Dix, MBChB[1]; Conrad V. Fernandez, MD[2]; Yueh-Yun Chi, PhD[3]; Elizabeth A. Mullen, MD[4]; James I. Geller, MD[5]; Eric J. Gratias, MD[6]; Geetika Khanna, MD[7]; John A. Kalapurakal, MD[8]; Elizabeth J. Perlman, MD[9]; Nita L. Seibel, MD[10]; Peter F. Ehrlich, MD, MSc[11]; Marcio Malogolowkin, MD[12]; James Anderson, PhD[13]; Julie Gastier-Foster, PhD[14]; Robert C. Shamberger, MD[15]; Yeonil Kim, MS[3]; Paul E. Grundy, MD[16]; and Jeffrey S. Dome, MD, PhD[17] on behalf of the AREN0532 and AREN0533 study committees.

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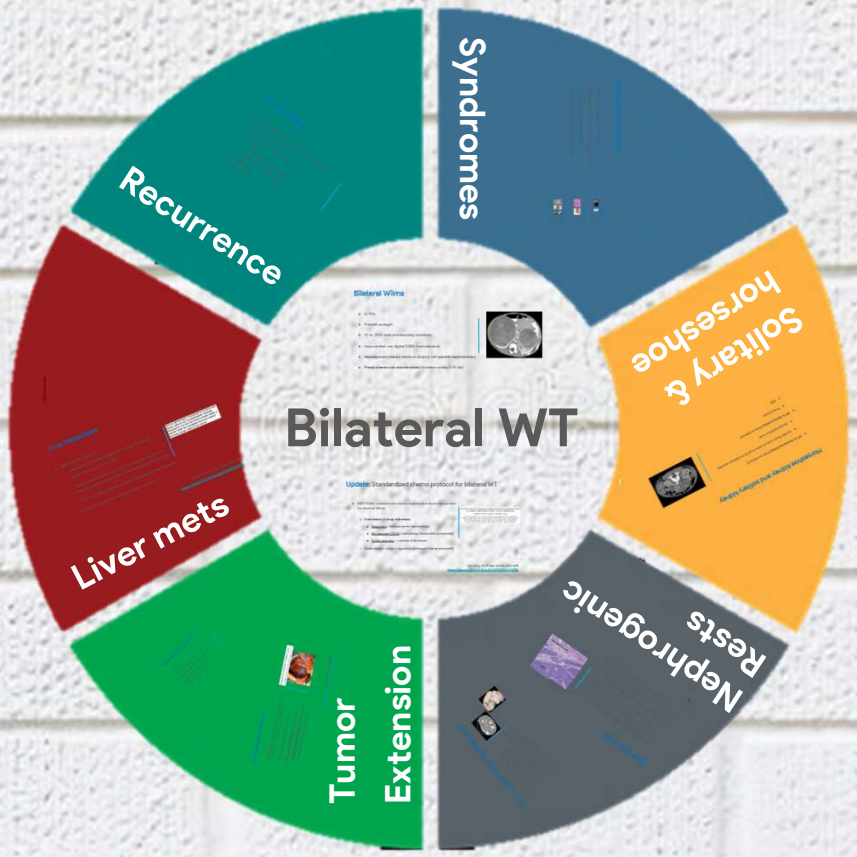
J Clin Oncol. 2019 Oct 20; 37(30): 2769–2777
https://doi.org/10.1200/JCO.18.01972

Special situations

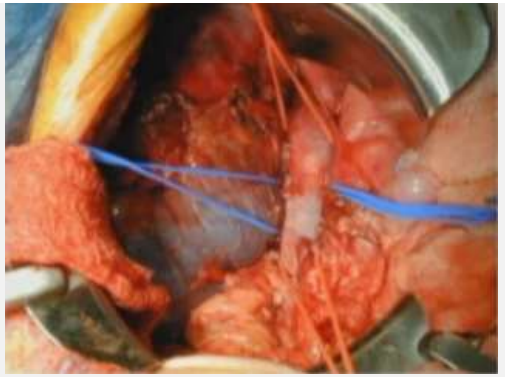


Intravascular extension

- **Incidence**: Renal vein (11%), IVC (5%). Can extend to right atrium causing dysfunction and PA embolus
- Historically managed with primary surgery
- **2001, Robert Shamberg**: key is hepatic vein
  - Preop chemo (above hepatic) dec comp. by 26%
  - Take biopsy first unless patient in heart failure

Intravascular Extension of Wilms Tumor

Robert C. Shamberger, MD,* Michael L. Ritchey, MD,† Gerald M. Haase, MD,‡ Tracy L. Bergemann, MS,§ Teri Loechelt-Yoshioka, AA,‖ Norman E. Breslow, PhD,§ and Daniel M. Green, MD¶



Ann Surg. 2001 Jul; 234(1): 116–121
https://doi.org/10.1097/00000658-200107000-00017

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Tumor extension into ureter

- Occurs in 2%
- Detected by imaging only in 30%
- Suspect in hematuria, hydronephrosis, urethral mass
- **Cystoscopy**, ureterogram if suspicious
- **Resect with clear margins**

Liver Metastases

- **2009, NWTS**: 3 findings
  - **Liver mets is not independent poor prognosis factor**
    (same outcome to pulmonary mets)
  - Primary resection inc survival but not statistically significant
    (improved outcome may be b/c better patients selected for resection)
  - **There is a role of hepatic resection for residual after adjuvant**
  - Issue of radiotherapy not settled (very few patients)

HEPATIC METASTASIS AT DIAGNOSIS IN PATIENTS WITH WILMS TUMOR IS NOT AN INDEPENDENT ADVERSE PROGNOSTIC FACTOR FOR STAGE IV WILMS TUMOR. A REPORT FROM THE CHILDRENS ONCOLOGY GROUP/ NATIONAL WILMS TUMOR STUDY GROUP

Ann Surg. 2009 Oct; 250(4): 642–648.
https://doi.org/10.1097/SLA.0b013e3181b76f20

Recurrent Wilms

- **Recurrence Rate:** 15% in favorable, 50% in anaplastic
- **Timing:** usually recur within 2 yr
- **Site:** usually lung ,tumor bed, liver
- **Treatment**
  - **Chemo:** avoid agents used primarily
  - **Resection:** tumor bed/metastasis
  - **Radiation**
- **Survival:** 48%

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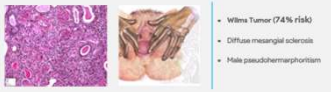
Predisposition syndromes

- Wilms tumor can be part of syndromes
- **Screening** if WT risk >5% (Renal ultrasound every 3 mo)
- **Renal sparing surgery** if develop WT
- prophylactic nephrectomy if renal failure (DDS)

WAGR Syndrome

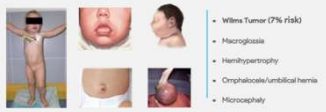
- Wilms Tumor (98% risk)
- Aniridia
- Genital abnormality
- mental Retardation

Denys Drash Syndrome



- Wilms Tumor (74% risk)
- Diffuse mesangial sclerosis
- Male pseudohermaphroditism

Beckiwth-Weideman Syndrome



- Wilms Tumor (7% risk)
- Macroglossia
- Hemihypertrophy
- Omphalocele/umbilical hernia
- Microcephaly
- visceromegaly

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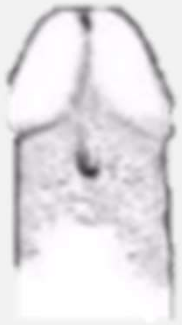
WAGR Syndrome



- **W**ilms Tumor (98% risk)
- **A**niridia
- **G**enital abnormality
- mental **R**etardation

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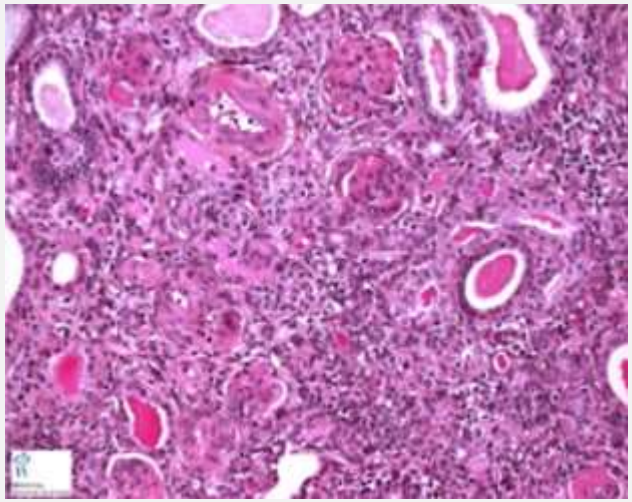
Denys Drash Syndrome



- **Wilms Tumor (74% risk)**
- Diffuse mesangial sclerosis
- Male pseudohermarphoritism

Beckiwth-Weideman Syndrome

- **Wilms Tumor (7% risk)**
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- visceromegaly

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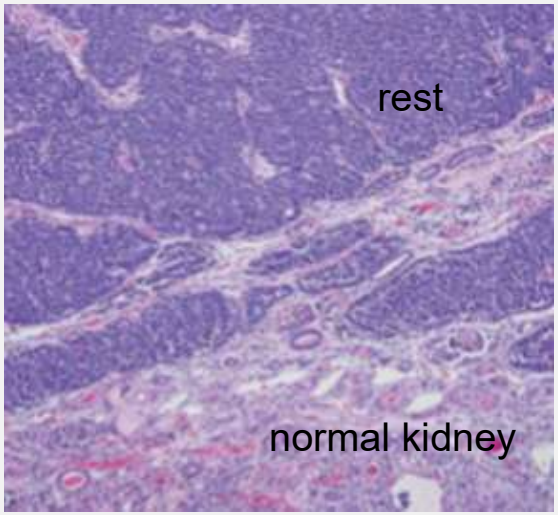
Horseshoe kidney and solitary kidney

- **WT in Horseshoe kidney** (treat as unilateral)
  - Identify blood supply & ureter to perform unilateral resection
  - Sample ipsilateral node
- **WT in Solitary kidney** (treat as bilateral)
  - Preop chemo
  - NSS

Nephrogenic rests

- Persistent metanephric tissue after 36 wk gestation
  - Most are **dormant/sclerosing** and resolve spontaneously
  - **Diffuse hyperplasia** (DPHLN) is considered premalignant
- Inside the rests can be focal areas of Wilms tumor
  - Occur with WT (41% of unilateral and 99% of bilateral WT)
  - WT + NR has **risk of metachronous tumor** (follow with US)



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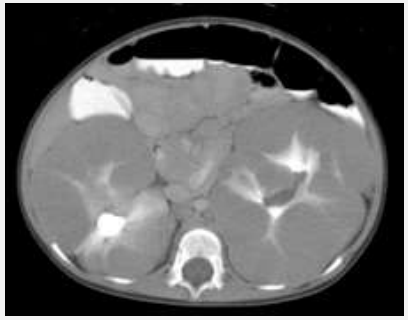
Diffuse Hyperplastic Perilobar Nephroblastomatosis

- Hyperplastic rests can confuse with Wilms tumor
  - **Imaging** difficult (normal renal configuration in NR)
  - **Core needle biopsy** cannot differentiate
  - **Open biopsy** must include normal tissue (capsule not found in NR)
- **Goal** : prevention of WT (DHPLN will progress if untreated)
  - **Start chemotherapy** with 2 drugs and reimage after 6 wk
  - **Continue chemo** 1yr (SIOP), 5mo (COG)
  - ? Surgery, ?Radiation



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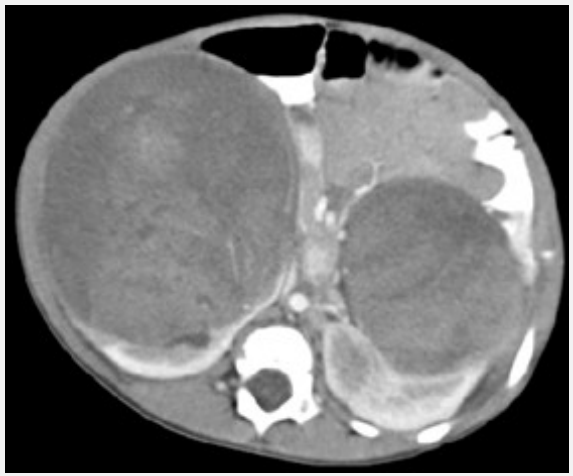
Bilateral Wilms

- 4-13%
- Present younger
- 10 to 20% have predisposing condition
- Less survival and higher ESRD than unilateral
- **Neoadjuvant chemo** (without biopsy) with **partial nephrectomy**
- **Preop chemo not standardized** (duration varies 3-27 wk)



Update: Standardized chemo protocol for bilateral WT

- **2017 COG –** standardize chemo regimen has improved survival for bilateral Wilms
  - **6 wk chemo (3 drug) and assess**
    - Resectable = bilateral partial nephrectomy
    - No response (<30%)= open biopsy (maturation vs anaplasia)
    - Partial response = + another 6 wk chemo
  - **12 wk chemo** = surgery regardless (prolonged chemo no benefit)

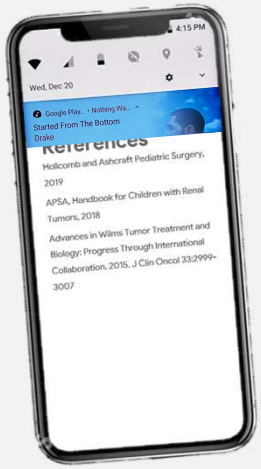
Results of the First Prospective Multi-institutional Treatment Study in Children With Bilateral Wilms Tumor (AREN0534)

A Report From the Children's Oncology Group

Peter Ehrlich, MD, MSC, Yuen Y. Chi, PhD,† Murali M. Chintagumpala, MD,‡ Fred A. Hoffer, MD,§ Elizabeth J. Perlman, MD,¶ John A. Kalapurakal, MD,|| Ann Warwick, MD,** Robert C. Shamberger, MD,†† Geetika Khanna, MD,‡‡ Tom E. Hamilton, MD,†† Ken W. Gow, MD,§§ Arnold C. Paulino, MD,¶¶ Eric J. Gratias, MD,|||| Elizabeth A. Mullen, MD,†† James I. Geller, MD,*** Paul E. Grundy, MD,††† Conrad V. Fernandez, MD,‡‡‡ Michael L. Ritchey, MD,§§§ and James S. Dome, MD, PhD¶¶¶*

Ann Surg. 2017 Sep; 266(3): 470–478
https://doi.org/10.1097/SLA.0000000000002356

Conclusion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Started From The Bottom
Drake
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APSA, Handbook for Children with Renal Tumors, 2018
Advances in Wilms Tumor Treatment and Biology: Progress Through International Collaboration. 2015. J Clin Oncol 33:2999-3007


Summary
Trials
Key findings


Thank you.

Summary

Trials	Key findings
SIOP 93-01 (1993-1999)	- Post chemo histology predicted relapse, with blastemal having worse outcome - lung radiation can be omitted in stage 4 WT with complete response
SIOP 2001 (2001-2012)	- Blastemal-type has better outcome with intensified chemotherapy - Stage IV with CT-only lung nodules had better survival rates than CXR–detectable
NWTS-5 (1995 - 2002)	-avoiding chemo (surgery only) had high recurrence leading to early study closure - Combined LOH at 1p and 16q predicted recurrence - Anaplastic WT had worse outcome , best survival using intensive chemo
COG AREN0321 (2006-2013)	-Vincristin/irinotecan produced high response rate for stage IV anaplastic WT
COG AREN0532 (2006-2013)	-Re-evaluation of surgery only for very low risk WT showed good outcome
COG AREN0533 (2007-2013)	- Lung radiation can be omitted if complete response, - Intensified chemo has better outcome for incomplete responders - Intensified chemo has better outcome for combined LOH
COG AREN0534 (2009-2015)	- Standardized chemo regimen for bilateral Wilms had better outcome