






## PEDIATRIC THYROID SURGERY




A Multidisciplinary Approach  
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 Daniel Kwon MD  
 4/1/2020





Today




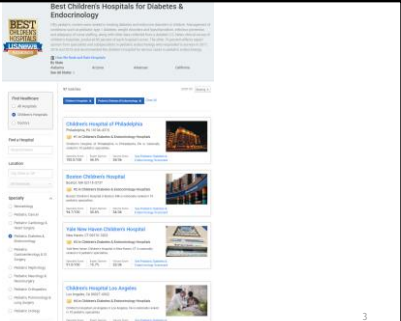
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It's Going to be Okay











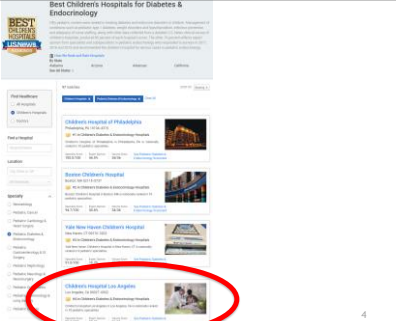






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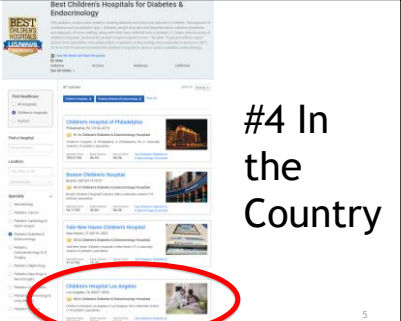




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# #1 On the West Coast



# #4 In the Country

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### CHLA Thyroid Team





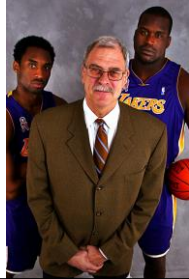
- Daniel Kwon, MD - H&N Surgery
- Juliana Austin, MD - Pediatric Endocrinology
- Gabriel Gomez, MD - Pediatric ENT

- Diagnostic Radiology/Interventional Radiology
- Medical Oncology
- Pathology/Cytopathology
- Nuclear Medicine
- Data scientists / Database

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### Team




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### Outline

- Background / Indications
  - Benign Disease
  - Endocrinopathy
  - Nodules/Malignancy
- Work-up of Thyroid Nodules
  - US and FNA
  - Pediatric considerations
- Thyroid Cancer
  - Nerve Monitoring, show how to modify ET tube for small kids
  - Calcium Mgmt
  - Neck Dissections
- Adjuvant therapy Radioactive Iodine
- Genetic Syndromes
- Case Presentation




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### Indications for Pediatric Thyroid Surgery

- Thyroid Cancer (~50%)
- Goiter (~20%)
- Graves/Toxic Nodules (20%)
- Other (~10%)
  - 4th branchial cleft cysts
  - Prophylactic
  - Intrathyroidal thymic tissue →
    - Surgery Not Needed

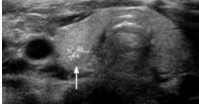
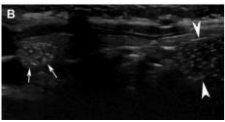


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### Intrathyroidal thymic tissue

- Can Mimic Malignancy
- In young Children
  - Version of Ectopic thymus
  - 3<sup>rd</sup>/4<sup>th</sup> Branchial Pouches
  - Inadequate descent embryologically

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### Intrathyroidal thymic tissue:

- Pathology/FNA: Lymphocytes and Hassall's Corpuscles
- Don't do unnecessary surgery
- It will regress





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### Graves' Disease



- Most Common Cause of Hyperthyroidism in Children
- Caused by antibodies to the thyrotropin receptor
- Presentation: **goiter**, **poor weight gain**, behavioral changes, restlessness, headaches, sleep disturbances, anxiety, and heat intolerance, **exophthalmos**
- ↓TSH, ↑Free T4, +TSH-Receptor Antibodies



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### Graves's Disease


- Treatment: Non-surgical
  - Beta-blockers
  - Anti-thyroidal Drugs: Methimazole, Propylthiouracil
    - May be poorly tolerated: autoimmune reactions, liver failure, leukopenia
    - Remission less common than in adults (<25%)
  - Radioactive Iodine Ablation
    - For Children >10 yo
- Endocrinologist →

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### Graves's Disease

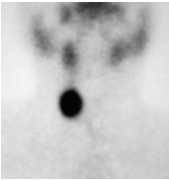
- Treatment: Surgical
  - Total or near-total thyroidectomy
  - Euthyroid state preferable
  - Beta-blockade (adrenergic symptoms)
  - Iodine pre-treatment (KI/SSKI/Lugol's) may be used
    - Decrease vascularity/intraoperative bleeding
    - Wolff-Chaikoff Effect : temporary effect



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### Toxic Nodules

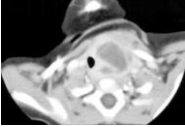
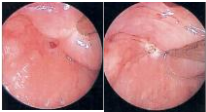
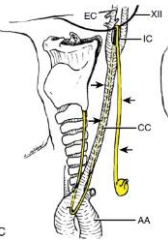
- Another Hyperthyroid State
  - Adults Often Treated with RAI
- Surgery usually recommended
  - RAI may be mutagenic for surrounding tissue
  - Some series described high rates of incidental malignancies



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### Fourth Branchial Cleft Cyst


- Not Thyroid Pathology...
- Fistula Course (often incomplete): Piriform Sinus → Pierce Cricothyroid Membrane → Deep to SLN and Superficial to RLN
- Left Thyroid Lobectomy maybe required for dissection

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### Prophylactic Thyroidectomy

- MEN2A
  - Before Age 5(yo) (ATA-H category)
  - Start Calcitonin Screen q6 months (ATA-MOD)
- MEN2B
  - Before Age 1(yo) (ATA-HST category)



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## PEDIATRIC THYROID NODULES

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### What is the Incidence of Thyroid Nodules in Children by Ultrasound?

- A. 0.5-5%
- B. 25-35%
- C. 55-65%
- D. >75%

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### What is the Incidence of Thyroid Nodules in Children by Ultrasound?

- A. 0.5-5%
- B. 25-35%
- C. 55-65% (upper limit of adult incidence)
- D. >75%

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### What is the Incidence of Cancer in Pediatric Thyroid Nodules?

- A. 5%
- B. 25%
- C. 50%
- D. 75%

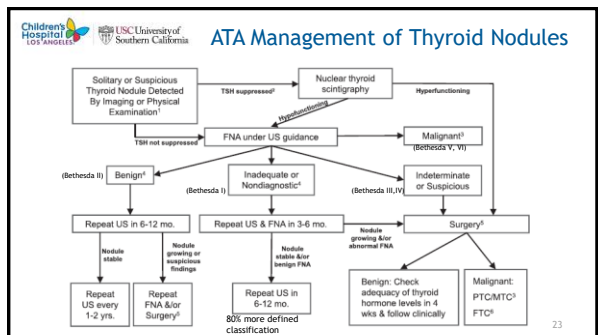
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### What is Incidence of Cancer in Pediatric Thyroid Nodules?

- A. 5% (adult)
- B. 25%
- C. 50%
- D. 75%

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### Thyroid Cancer

**Background:**

- <1% of all pediatric malignancies are thyroid cancer (2.5% in adults)
  - BUT: Adolescents: 8<sup>th</sup> most common cancer, 2<sup>nd</sup> for females
- Carcinoma 5x more likely in females (3x in adult women)
- 20-25% incidence in thyroid nodules (vs 5-10%)
- Increasing incidence in all Stages of pediatric thyroid cancer
  - SEER data

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### Thyroid Cancer

**Background:**

- Higher incidence of lymph node metastasis, pulmonary metastasis, extra-thyroidal extension
- Improved outcomes (Disease specific survival, Progression free survival)
- Different tumor genetic profiles:
  - Kids: RET/rearrangements
  - Adults: Point mutations BRAF
    - Pediatric PTC more RAI sensitive


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### Thyroid Cancer

**Risk Factors:**

- Radiation exposures
  - Younger children are particularly sensitive
  - Often survivors of other childhood cancers
- Iodine deficiency
- Family Hx
- Autoimmune thyroiditis



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### Thyroid Cancer

**Hereditary Tumor Syndromes:**

- APC Associated Polyposis (Familial Adenomatous Polyposis, Gardner and Turcot)
- DICER1 Syndrome
- PTEN hamartoma syndrome (Cowden Syndrome)
- Werner Syndrome
- Carney Complex
- ....

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### Thyroid Cancer: Adults vs Peds

**Guiding Differences in Evaluation and Management**

- Higher likelihood of malignancy
- Unique pathogenesis (gene rearrangements vs point mutations)
- More judicious use of RAI
- Relative lack of data**

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### Thyroid Cancer: Evaluation

- High Definition Ultrasound
  - US features rather than size

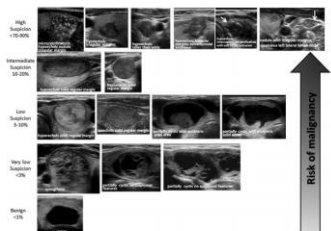


FIG. 2. ATA nodular ultrasonographic patterns and risk of malignancy.

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### Thyroid Cancer: Evaluation

- Adult TIRADS grading systems have mixed results
  - Lim-Dunham et al. *Am Jor Roentgenology*. 2019
  - Richman et al. *Radiology*. 2019
  - Martinez-Rios et al. *Pediatric Radiology*. 2018

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### Thyroid Cancer: Evaluation

- FNA
  - Should always be US guided
  - Anesthesia?
    - Moudgil Et al
      - 71/86, 83% required conscious sedation/general anesthesia
      - Avg age 14yo
  - This plays a factor on surveillance and prospect of repeat FNAs

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### Thyroid Cancer: Evaluation

- Cytopathology
  - Described using Bethesda system
  - Common Language
  - However different ROM rates have been shown

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### Thyroid Cancer: Evaluation

#### Bethesda Classification System (2017)

Diagnostic category	Risk of malignancy if NIFTP ≠ CA (%)	Risk of malignancy if NIFTP = CA (%)	Usual management <sup>a</sup>
Nondiagnostic or Unsatisfactory	5-10	5-10	Repeat FNA with ultrasound guidance
Benign	0-3	0-3	Clinical and sonographic follow-up
Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance	6-18	~10-30	Repeat FNA, molecular testing, or lobectomy
Follicular Neoplasm or Suspicious for a Follicular Neoplasm	10-40	25-40	Molecular testing, lobectomy
Suspicious for Malignancy	45-60	50-75	Near-total thyroidectomy or lobectomy
Malignant	94-96	97-99	Near-total thyroidectomy or lobectomy

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### Thyroid Cancer: Evaluation

- What is the Pediatric Rate of Malignancy in each category?

TABLE 4. CORRELATION OF FINAL CYTOLOGY WITH HISTOLOGICAL DIAGNOSIS IN PEDIATRIC AND ADULT THYROID NODULES

Final cytology	Pediatric (<19 years)				Adult (≥19 years)				Pediatric vs. adult malignancy rate		Bethesda implied rate <sup>a</sup>		
	Total n (%)	Resected n (%)	Malignant n (%)	% of resected	Total n (%)	Resected n (%)	Malignant n (%)	% of resected	% of total	% of total			
ND	53 (12)	20 (38)	6	30	11	835 (6)	192 (23)	34	18	4	0.23	0.03	5-10
Benign	275 (66)	26 (28)	9	3	13	1083 (21)	426 (14)	36	9	0.11	0.009	0-3	
AUS	32 (7)	26 (81)	14	54	44	90 (7)	530 (58)	199	38	23	0.10	0.004	10-30
SFN	14 (3)	14 (100)	10	71	71	69 (6)	681 (78)	248	36	24	0.007	0.001	25-40
SFN	24 (6)	24 (96)	19	79	72	660 (5)	620 (94)	252	41	26	0.52	0.07	50-75
Positive for malignancy	30 (7)	29 (97)	29	100	97	688 (5)	660 (96)	651	99	95	1	1	97-99
Total	430	190 (44)	80	43	19	11,412	3950 (29)	1671	42	12	1	0.0002	

From Chou and Ali (4).

Cherella et al. 34

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### Thyroid Cancer: Evaluation

- What is the Pediatric Rate of Malignancy in each category?

Bethesda Classification By Cytology	Pediatric Malignancy Rate	Adult Malignancy Rate
I (Non-Diagnostic)	11%	4%
II (Benign)	0.7%	1%
III (AUS)	44%	22%
IV (SFN)	71%	28%
V (suspicious)	73%	68%
VI (malignant)	97%	95%

Cherella et al. 35

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### Thyroid Cancer: Evaluation

- What is the Pediatric Rate of Malignancy in each category?

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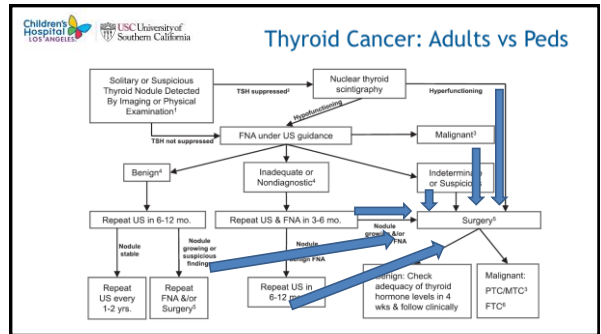
### Thyroid Cancer: Evaluation

- Molecular Testing
  - Shows promise as with adults
  - Unique genetic profiles
  - Need more data

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### Thyroid Cancer: Adults vs Peds

- Lower threshold for investigation
  - Any "suspicious nodule"
  - Diffuse enlargement
- Lower threshold for thyroidectomy
  - Toxic nodules
  - Indeterminate nodules
  - Growing nodules



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### Thyroid Cancer: Adults vs Peds

- More aggressive surgery
  - Total Thyroidectomy vs Lobectomy
    - Higher incidence of multifocal/bilateral disease
  - Central Neck Dissection
    - Higher incidence of metastasis
    - May help avoid RAI

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### Pediatric Surgical Management

- Surgeon Is Central to thyroid Disease
  - More Hemi thyroidectomies for any suspicious nodules
  - More Total thyroidectomies for any malignancy
  - More Neck Dissections

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## Thyroid Cancer: Adults vs Peds

- No validated staging system in children (AJCC, AMES, MACIS)
- ATA recommends 3-tier Pediatric Staging
  - Low risk: intrathyroidal tumor, "minimal" N1a or less
  - Intermediate risk: "extensive" N1a - N1b
  - High risk: "extensive" N1b, ETE, distant mets

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## THYROIDECTOMY

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## Surgery Video

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## Pediatric Thyroidectomy

- ATA Principles of Pediatric Thyroid Cancer
  1. Surgery outcome must beat Cancer outcome
    - <2% mortality
  2. Avoid Complications
    - Voice/Swallow
    - Hypoparathyroidism
    - Psycho-social
    - Secondary Malignancy

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## Pediatric Thyroidectomy

- Technique similar to adult
  - Para thyroids are even smaller
    - (higher rate of HypoPara)
  - Beware of Thymus in level 6 dissection
- Avoid drains or non-absorbable sutures
- Central Neck Dissection more commonly performed
- Remote Access Techniques not commonly used in children

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## Pediatric Thyroidectomy

- Rapid Frozen Analysis for Indeterminate Cytology
  - Not useful for follicular tumors
  - May help avoid secondary surgery

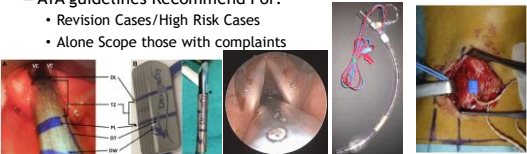
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### Pediatric Thyroidectomy

- **RLN Monitoring**
  - Medtronic NIM tube (Largest tube is 5.0 (7.8mm O.D) or 6.0)
  - Neurovision/Dragonfly surface electrodes wrapped ET tube
  - Use needle electrodes placed near vocal cords (sticker/hookwire)
  - ATA guidelines Recommend For:
    - Revision Cases/High Risk Cases
    - Alone Scope those with complaints



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### HypoParathyroidism

- Post-op HypoPTH, ~30% of patients
  - Numbers in literature range widely
  - % in cancer cases are higher
- Permanent HypoPTH - 1-3%
  - Calcium dependent
- CHLA Thyroid Cancer: ~80% / <1%
- Increased risk in young patients, concomitant neck dissection, graves

Yu et al 49

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### HypoParathyroidism

- Various post-op Calcium replacement regimens described
  - Standard dose vs PTH driven
- Unique Challenges in Children
  - Recurrent Lab Draws
  - High Dose Oral Supplementation
- CHLA
  - Standard routine postoperative calcium, calcitriol

Yu et al 50

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### Adjuvant Therapy

- Radioactive Iodine
  - Historically used routinely in all cases for thyroid remnant ablation
  - Clear indication for distant/pulmonary metastases
  - No consensus for intermediate risk cases

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### Adjuvant Therapy

Short Term	Long Term
Sialadenitis, xerostomia, dental caries, stomatitis, ocular dryness, nasolacrimal duct obstruction	Lifelong xerostomia, dental caries, salivary gland malignancy
Gonadal injury, transient amenorrhea, and menstrual irregularities	Increase in infertility, miscarriage, birth defects
Acute bone marrow suppression	Rare long-term bone marrow suppression
	Increased risk of secondary malignancy, increased mortality
	Pulmonary fibrosis

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### Adjuvant Therapy

- TSH Suppression
  - Based on risk profile
  - Generally normalized after long term remission
  - Poorly studied
- Principal: TSH stimulates both normal thyroid tissue and malignant thyroid tissue, so suppressing will reduce chance of recurrence

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### Adjuvant Therapy


- Tyrosine Kinase Inhibitors / Systemic Therapy
  - Reserved for iodine refractory progressive disease
  - Very rarely used
  - Poorly studied

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### CHLA Thyroid Team

- How we do it: The CHLA / USC Experience



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### CHLA Thyroid Team





- Daniel Kwon, MD – H&N Surgery
- Juliana Austin, MD – Pediatric Endocrinology
- Gabriel Gomez, MD – Pediatric ENT


- Diagnostic Radiology/Interventional Radiology
- Medical Oncology
- Pathology/Cytopathology
- Nuclear Medicine
- Data scientists / Database

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### CHLA Thyroid Team

- One of few high-volume interdisciplinary pediatric thyroid surgery centers
  - ~50-70 cases per year
  - Pediatric thyroidectomy database



**RECOMMENDATION 3**  
 Children with DTC should be cared for by teams of physicians experienced in the management of DTC in children. This will facilitate interdisciplinary decision regarding optimal therapy and will help to reduce the possibility that treatment and long-term follow-up will be either overly aggressive or inadequate.  
 Recommendation rating: C

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### CHLA Thyroid Team

Pre-op / Evaluation

- All referrals screened through Dr. Austin, the leader and “gate-keeper”
- All nodules/surgical cases have in-house high resolution US with concurrent US-FNA under GA
- All cases reviewed at multi-disciplinary thyroid conference / tumor board
- Consultation at multi-disciplinary TNC clinic

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### CHLA Thyroid Team

Surgery / Peri-operative

- 2-attending surgery (Peds ENT and Adult H&N ENT)
- Nerve monitoring with neuro-diagnostics staff
- Intra-operative rapid PTH
- If admitted, cared for by specialized Pediatric Hospitalist Team with ENT and Endocrine following

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### CHLA Thyroid Team

Post-op

- ~3 month post-operative staging (Tg, TgAb, scans)
- Re-presented at Thyroid Conference
- Initial surveillance at TNC clinic then Ped Endocrine clinic long-term

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### Importance of Thyroid Centers

- Tuggle et al. *Surgery*. 2008. Yale/Wisconsin

Outcome	High-volume	Pediatric	Other	P*
Complications (%)				
General	8.7	13.4	13.2	NS
Endocrine	5.6	11.0	9.5	NS
Duration of stay (days)	3.2	2.3	2.9	<.05
Cost (\$)	12,474	19,594	13,614	<.01

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### Importance of Thyroid Centers

Hauch et al. *Annals of Surgical Oncology*. 2014. Tulane/MEEI

Thyroidectomy	Low	Intermediate	High
Unilateral	11.8	9.9	7.6
Total/Bilateral	24.1	18.8	14.5

p=0.004, p<0.0001

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### Summary

- Thyroid disease (all comers) often treated with surgery
- Pediatric thyroid cancer often presents with greater burden of disease but with excellent prognosis
- Multi-disciplinary, high-volume care offer best outcomes
- More pediatric specific data is required
- Management guidelines will continue to evolve

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### GOAT

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### Dennis Maceri, MD

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### CHLA Thyroid Team



• Daniel Kwon, MD  
– H&N Surgery



• Juliana Austin, MD  
– Pediatric Endocrinology



• Gabriel Gomez, MD  
– Pediatric ENT

**Questions?**

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## RECENT CASE

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### 14 yo Hispanic Male

- Presented with lower neck swelling x 6 months
- What else do you want to know



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### 14yo Hispanic Male


- Slowly growing, Hyper/Hypothyroidism, Dysphagia/SOB, prior infections, Discharge, Constitutional symptoms, Trauma, prior Med/Surgical hx
- Extensive ROS
  - “Blurry vision sometimes”
- Famhx: Negative for any malignancies or tumors
- Allergies: None


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### 14yo Hispanic Male







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What do you do next?

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### 14yo Hispanic Male

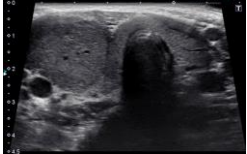
- Labs?
  - TSH, Free T4
  - Calcitonin
- Thyroid and Neck US
- CT Neck?

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### 14yo Hispanic Male

- Labs
  - TSH, Free T4: wnl
  - Calcitonin: **3287**
- Thyroid US :
  - Also shows bilateral lateral pathologic LAD

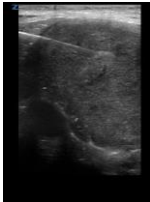


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### 14yo Hispanic Male

- FNA:
  - Results: Medullary Thyroid Carcinoma
- Refer to Heme Onc, Genetics, Ophthalmology, Endocrine
- Present at Multi Disciplinary Tumor Board



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### 14yo Hispanic Male

- Anything else needed prior to surgery?

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### 14yo Hispanic Male

- Rule out concomitant Pheochromocytoma/Metastatic Disease
  - Urine Methanephrines
  - PET CT
- If found, Pheochromocytoma
- Txt Total Thyroidectomy, Bilateral Central and Lateral Neck Dissections, Tongue Biopsy (confirmed neuromas)
  - Calcitonin : 3286→64

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- Nikiforov, Yuri, and Douglas R. Gnepp. "Pediatric thyroid cancer after the Chernobyl disaster. Pathomorphologic study of 84 cases (1991-1992) from the Republic of Belarus." *Cancer* 74, 2 (1994): 748-766.

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