Memorial Sloan Kettering Cancer Center


# Caring for The Long-Term Survivor of Pediatric Cancer: Dental and Oral Considerations

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# Greetings from MSKCC and New York City!

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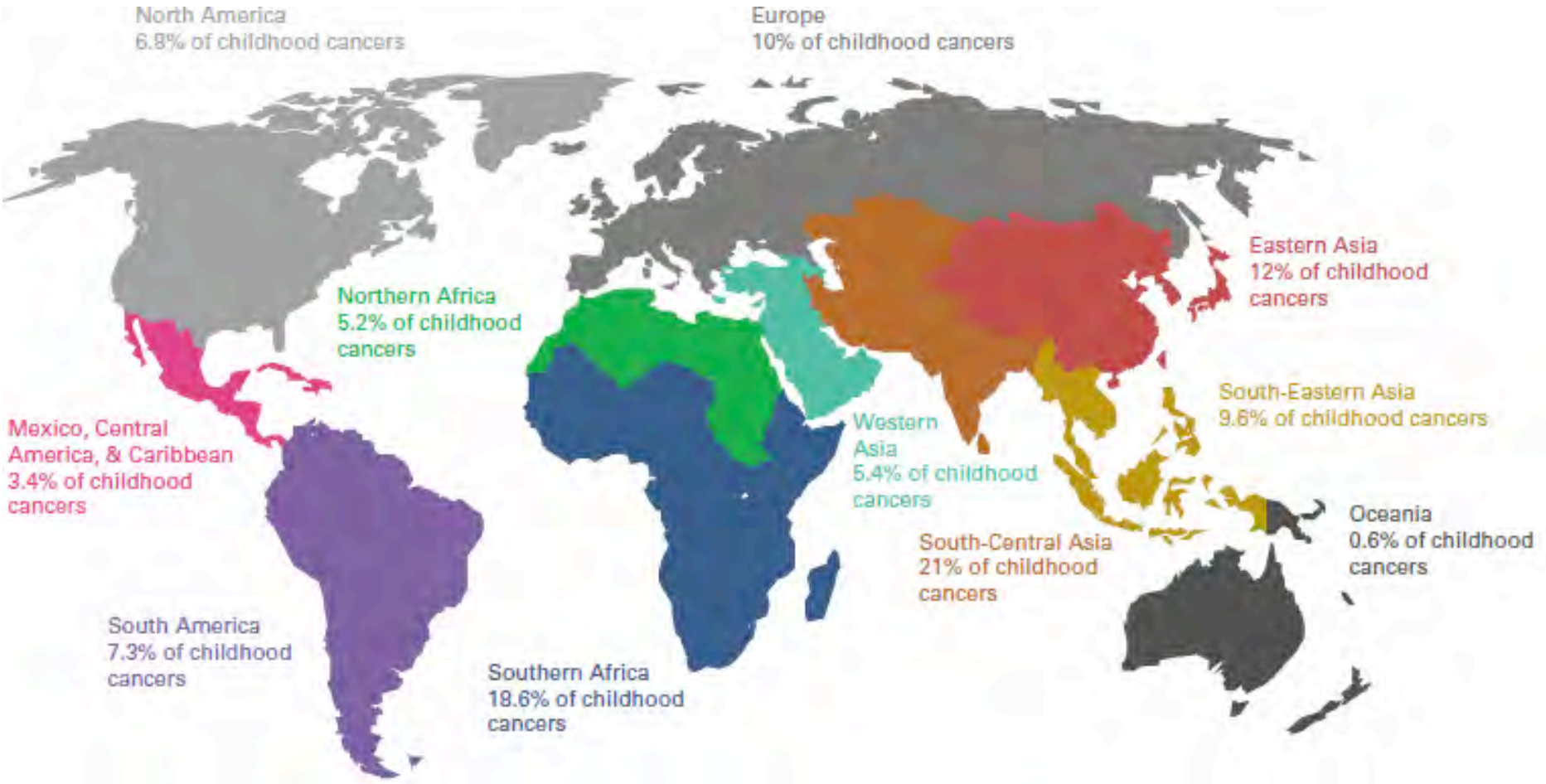
# Global Distribution of Childhood Cancer




- ~200,000 new cases/year < 15 years of age
  - 80% live in LMICs

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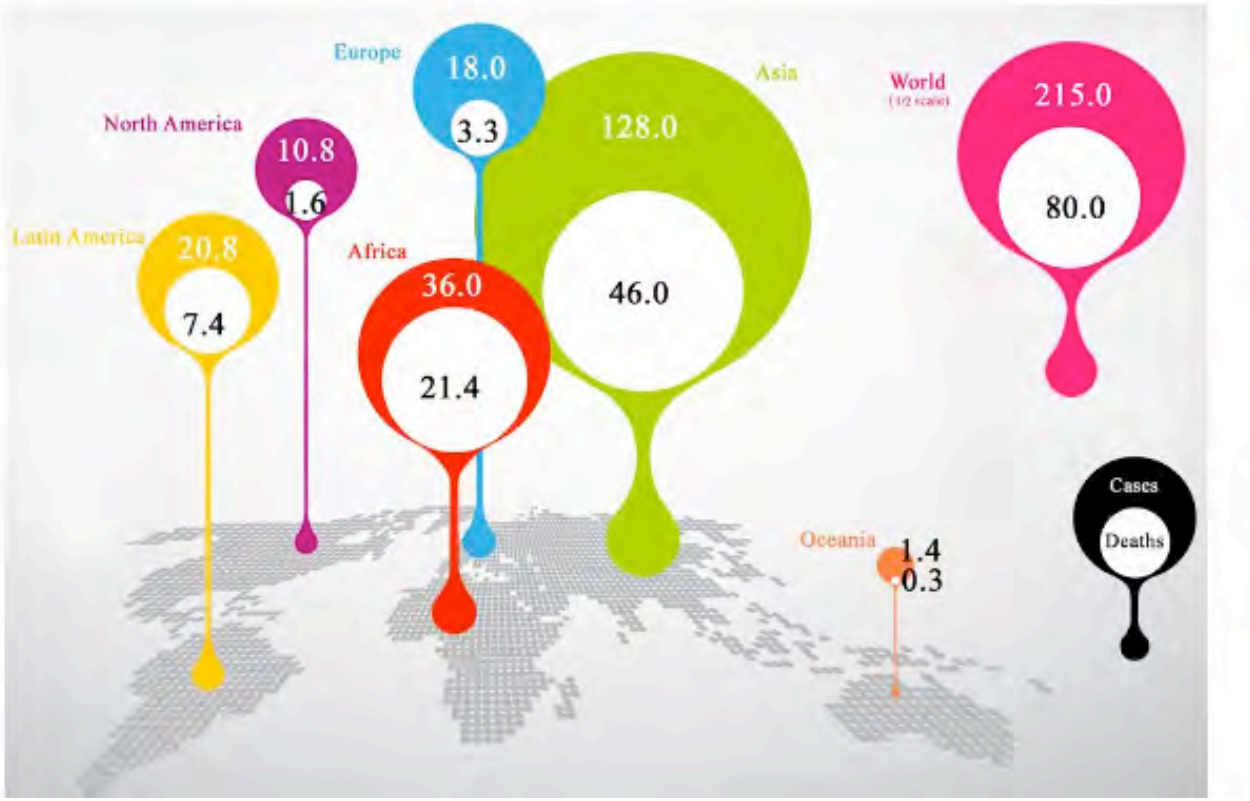
Source: World Bank Databank and GLOBOCAN 2012

# Worldwide Pediatric Cancer Statistics
# Estimated Number of Cases and Deaths (thousands)
# 0-14 years, 2010s




- ~90,000 deaths/year
- 80% cure rate in developed countries (much lower in LMICs)



International Agency for Research on Cancer (IARC), 2016

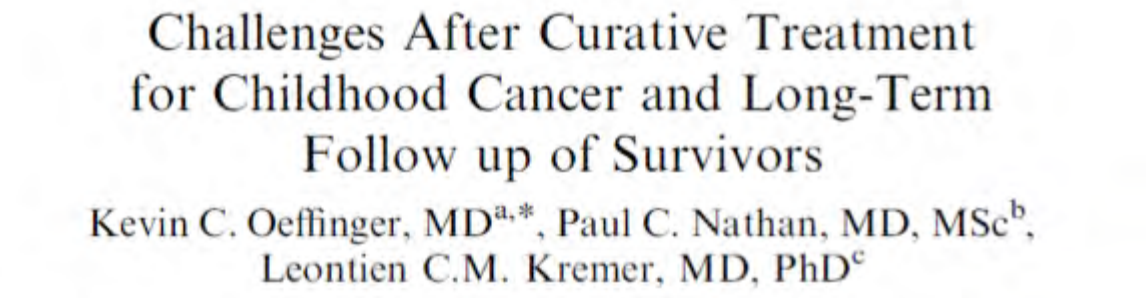
# Improved Survival in Childhood Cancer

- Nearly 80% of children diagnosed with cancer will survive into adulthood (high-income countries)
  - Much lower in low-resource settings
- There are ~ 379,000 survivors of childhood cancer in the U.S. (1 in every 500 young adults).
- Improvement in survival rates is due to advances in treatment.



Bleyer WA et al. CA 40: 1990.
Oeffinger KC et al. NEJM 355: 2006.
Effinger, KE et al Support Care Cancer 22: 2014.

# The Heavy Price of Cure



Challenges After Curative Treatment
for Childhood Cancer and Long-Term
Follow up of Survivors

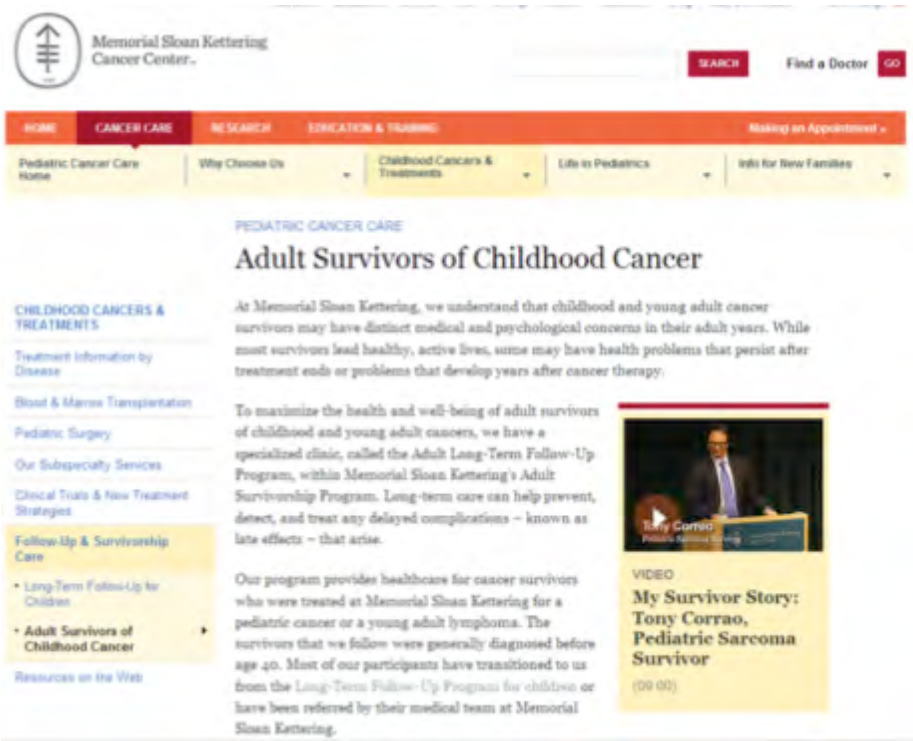
Kevin C. Oeffinger, MD[a,*], Paul C. Nathan, MD, MSc[b],
Leontien C.M. Kremer, MD, PhD[c]

- 2/3 of survivors have at least once chronic or late-occurring complications (late effects) of their cancer therapy.
- 1/3 have serious or life-threatening complications.
- Increased risk of developing second cancers
- Adverse health consequences may not manifest until years after completion of therapy.
- Highlights the importance of life-long care following treatment.



Oeffinger KC et al. Ped Clin N Am 55: 2008

# MSKCC's Program for Survivors of Pediatric Cancer

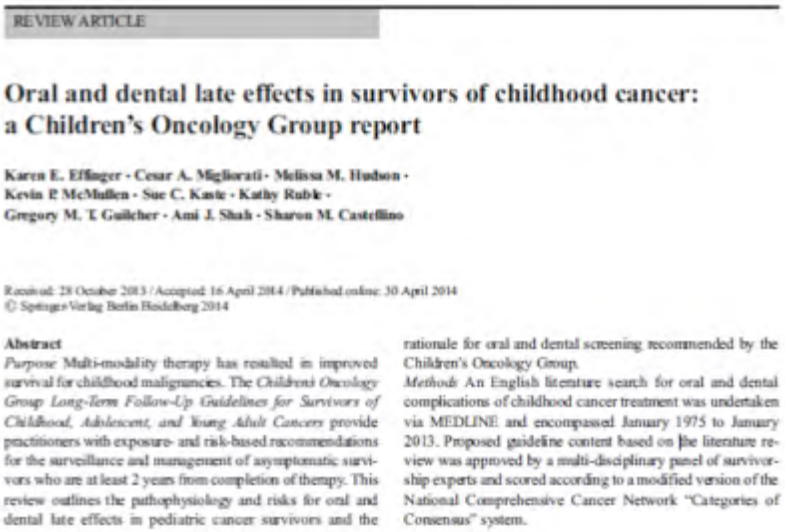



# Long-term Oral and Dental Effects of Pediatric Cancer Therapy

- Treatment-related dental/cranial abnormalities are common among long-term survivors (LTS)
- Often overlooked sources of morbidity and impaired health-related quality of life.
- LTS have higher prevalence of dental disease.
- LTS have worse overall dental health and higher risk of dental abnormality than their siblings.

Duggal MS et al. Oral Onc 33: 1997.
Effinger KE et al. Support Care Cancer 22: 2014.
Estilo CL et al. J Pediatr Hemat Onc 25: 2003.
Gawande PL et al. Pediatr Blood Cancer 61: 2014.
Hong C and daFonseca M. Dent Clin N Am 52: 2008.
Kaste SC et al. Cancer 115: 2009.

# Oral and Dental Effects: Literature Review



REVIEW ARTICLE

**Oral and dental late effects in survivors of childhood cancer: a Children's Oncology Group report**

Karen E. Effinger · Cesar A. Migliorati · Melissa M. Hudson · Kevin P. McMullen · Sue C. Kaste · Kathy Rubik · Gregory M. T. Guilcher · Ami J. Shah · Sharon M. Castellino

Received: 28 October 2013 / Accepted: 16 April 2014 / Published online: 30 April 2014


**Abstract**
*Purpose* Multi-modality therapy has resulted in improved survival for childhood malignancies. The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* provide practitioners with exposure- and risk-based recommendations for the surveillance and management of asymptomatic survivors who are at least 2 years from completion of therapy. This review outlines the pathophysiology and risks for oral and dental late effects in pediatric cancer survivors and the rationale for oral and dental screening recommended by the Children's Oncology Group.
*Methods* An English literature search for oral and dental complications of childhood cancer treatment was undertaken via MEDLINE and encompassed January 1975 to January 2013. Proposed guideline content based on the literature review was approved by a multi-disciplinary panel of survivorship experts and scored according to a modified version of the National Comprehensive Cancer Network "Categories of Consensus" system.

**REVIEW**

**A Systematic Review of Dental Late Effects in Survivors of Childhood Cancer**

Prasad L. Gawade, PhD,[1] Melissa M. Hudson, MD,[1,2] Sue C. Kaste, DO,[2,3,4] Joseph P. Neglia, MD, MPH,[5] Louis S. Constine, MD,[6] Leslie L. Robison, PhD,[1] and Kirsten K. Ness, PT, PhD[1]*

Survivors of childhood cancer are at risk for dental late effects. This systematic review summarizes associations between treatment exposures and dental late effects among survivors of childhood cancer. We included investigations with at least 20 study participants conducted for 2 or more years after completion of childhood, adolescent, or young adult cancer therapy. This review suggests both independent and additive effects of radiotherapy and chemotherapy on dental complications, and identifies vulnerable groups with specific host and treatment characteristics. This summary provides information that will assist clinicians to prevent, detect, and facilitate early intervention for dental late effects. Pediatr Blood Cancer 2014;61:407–416. © 2013 Wiley Periodicals, Inc.

**Key words:** chemotherapy; pediatrics; radiotherapy; tooth abnormalities



Effinger KE et al. Support Care Cancer 22: 2014.
Gawade PL et al. Pediatr Blood Cancer 61: 2014.

# Oral Sequelae/Complications of Head and Neck Radiation Therapy

## Short-term complications

- Oral mucositis
- Hyposalivation/xerostomia
- dysgeusia
- Intra-oral infection

## *Long-term sequelae/ complications*

- Bony hypoplasia; orofacial asymmetry; malocclusion
- Reduced salivary function
- Tooth agenesis; enamel hypoplasia; arrested root development
- Trismus (fibrosis in masticatory muscles)
- Osteoradionecrosis

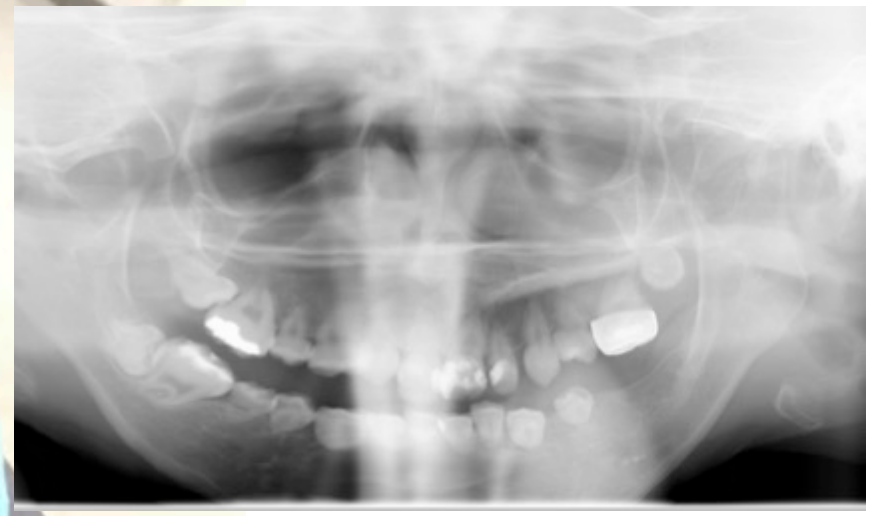
Effinger KE et al. Support Care Cancer 22: 2014.
Estilo CL et al. J Pediatr Hemat Oncol 25: 2003.
Gawande PL et al. Pediatr Blood Cancer 61: 2014
Maguire A and Welbury RR. Dental Update 1996.
Nasmn M et al. Pediatr Dent 16: 1994.
Paulino AC et al. Int J Radiat Oncol Biol Phys 48: 2000.

# RT-induced Craniofacial and Dental Abnormalities

- Threshold of RT damage
  - Threshold not fully known
  - TBI (1000 cGy) may increase risk for dental disturbance.
  - Craniofacial abnormalities can occur with 2400 cGy cranial RT
  - Most severe dental and craniofacial effects in head and neck soft tissue malignancy treated with chemotherapy and RT (~5000 cGy) at <6 years

- Multiple agents make it difficult to attribute defects to any single agent or treatment.

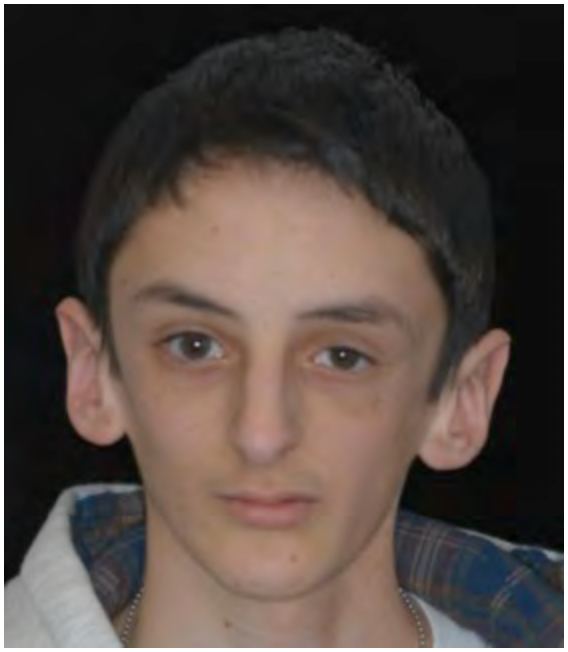
Effinger KE et al. Support Care Cancer 22: 2014.
Estilo CL et al. J Pediatr Hemat Oncol 25: 2003.
Maguire A and Welbury RR. Dental Update 1996.
Nasmn M et al. Pediatr Dent 16: 1994.
Paulino AC et al. Int J Radiat Oncol Biol Phys 48: 2000.

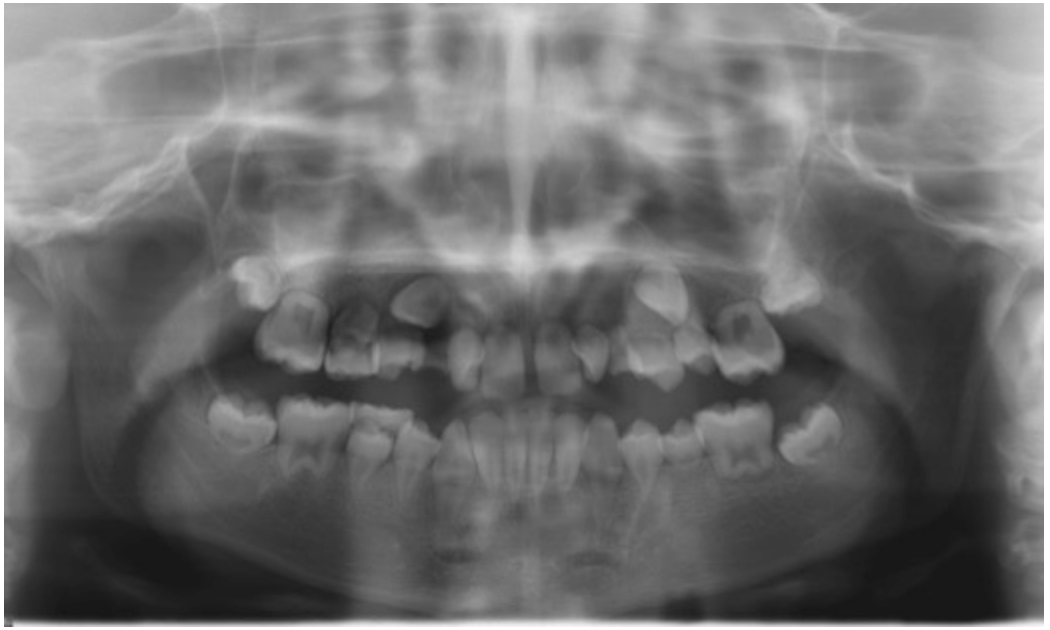


# Tooth/Root Agenesis and Shortened Roots Resulting from Radiation Therapy

RMS of the nasopharynx treated at age 3 years

# Bony Hypoplasia Following Head and Neck RT





# Manifestations of Craniofacial Defects Over Time
# Orbital RMS s/p chemoRT at 2 years old

6 years

13 years old

21 years old

# Craniofacial Defects in Those Treated with Chemotherapy and HNRT for HN RMS (@ <5 y.o.)

# Oral Sequelae/Complications of Chemotherapy

| Short-term complications | *Long-term sequelae/ complications* |
| --- | --- |
| • Cytotoxic: Oral mucositis<br>• Hemorrhagic: Thrombocytopenia<br>• Infectious: Neutropenia ( ↑ viral, bacterial and fungal infections)<br>• Nutritional: Nausea/anorexia, vomiting | • Tooth agenesis<br>• Microdontia<br>• Enamel hypoplasia<br>• Impaired root development: root agenesis; short/stunted/blunted roots |


Effinger KE et al. Support Care Cancer 22: 2014.
Maguire A and Welbury RR. Dental Update 1996.
Nasmn M et al. Pediatr Dent 16: 1994.
Rosenberg S. NCI Monogr 9: 1990.
Sonis AL et al. Cancer 66: 1990.

# Chemotherapy-induced Dental Abnormalities

- Younger age (<6 y.o.) at treatment and intensive chemotherapy increase the risk for long-term abnormalities.
- Damage is related to doses and repetition.
- Effect is systemic (vs. localized effects with RT)
- Both odontoblasts and ameloblasts appear to be affected.
- Putative agents:
  - Vinca alkaloids: vincristine and vinblastine
    - Enamel defects
  - Alkylating agents: cyclophosphamide
    - Root developmental defects

Gawade PL et al. Pediatr Blood Cancer 61: 2014.
Goho C. Ped Dent 15: 1993.
Maguire A and Welbury RR. Dental Update 1996.
Vahlsing HL et al. J Dent Res 56: 1977.
Stene T et al. Scand J Dent Res 84: 1976.

# Tooth/root Agenesis, Shortened Roots Resulting From Chemotherapy

No prior h/o chemoRT in childhood

13 y.o. male with h/o ALL diagnosed at 1 year old s/p chemotherapy and HSCT

# Enamel Hypoplasia

# Dental/Oral Considerations and Guidelines

- Dental and oral health should be optimized prior to commencement of treatment

- Routine (at least q6 months) periodic evaluation following treatment
  - Dental prophylaxis and preventive care
  - Consider use of silver diamine fluoride (SDF) to arrest caries in selected patients
  - Periodic panoramic radiograph to monitor development
    - Especially if treated <6 y.o. and/or HNRT

- Emphasis on importance of good oral hygiene practice
  - Consider Rx flouride toothpaste (5,000 ppm F-) in patients with high caries risk



Hong C and daFonseca M. Dent Clin N Am 52: 2008.
Oeffinger KE et al. Support Care Cancer 22: 2014.

# Dental/Oral Considerations and Guidelines

- Patients treated with HNRT (eg, HN RMS) and/or <6 yrs at initial treatment often require extensive dental rehabilitation
  - Participation of a multi-specialty team: radiation oncologist, pediatric oncologist, dental oncologist, local dental practitioners (pediatric dentist, oral surgeon, orthodontist)

- Trismus Management
  - Highest risk in patients treated for HN malignancy
  - Jaw stretching exercises
  - Trismus-release surgery
  - Use of jaw motion devices (Therabite®, Dynasplint®)
  - Botulinum toxin-A (Botox®) injection



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Estilo CL et al. J Pediatr Hemat Oncol 25: 2003.
Hong C and daFonseca M. Dent Clin N Am 52: 2008.

# Dental/Oral Considerations and Guidelines

- Orthodontic Treatment
  - Lack of evidence to guide clinicians
  - Based on expert opinion
  - Recommended modifications (Dahllof et al)
    - Appliances to minimize risk of root resorption
    - Weaker forces
    - Decreased treatment time
    - Selecting the simplest method
    - Avoid mandible
  - Survey to 2500 members of 2 orthodontic societies
    - Tendency for more experienced practitioners to have treated survivors of childhood cancer.
    - Orthodontic education regarding the treatment of these patients is limited.
    - Although most orthodontists reported having treated such patients, few had treated more than 10.



Neill CC et al.Am J Orthod Dentofac Orthop 148:2015
Dahllof G et al. Am J Orthod Dentofac Orthop 120: 2001.

# Dental/Oral Survivorship Care: Challenges

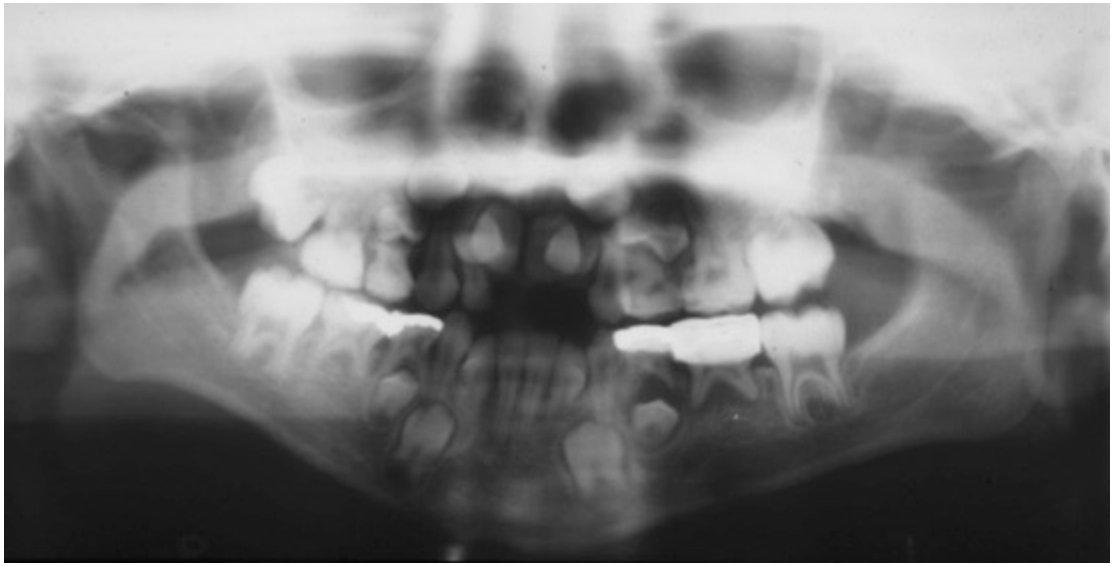
- LTS have worse overall dental health and higher risk of dental abnormality than their siblings.
- 28.3% of LTS had not visited the dentist and 32.6% had not received dental cleaning in the previous year.
- Lower rates of dental care reported in uninsured and publicly insured LTS.
- Those with insurance may have difficulty finding providers equipped to treat high-risk patients.
- PCPs play key roles in facilitating referrals.



Effinger KE et al. Support Care Cancer 22: 2014.
Kaste SC et al. Cancer 115: 2009.

# MSKCC Dept of Pediatrics Annual Prom

# YG: 8 y.o. Male with h/o Orbital RMS s/p Chemo-RT @ 2 yrs old



# YG at 13 Years Old

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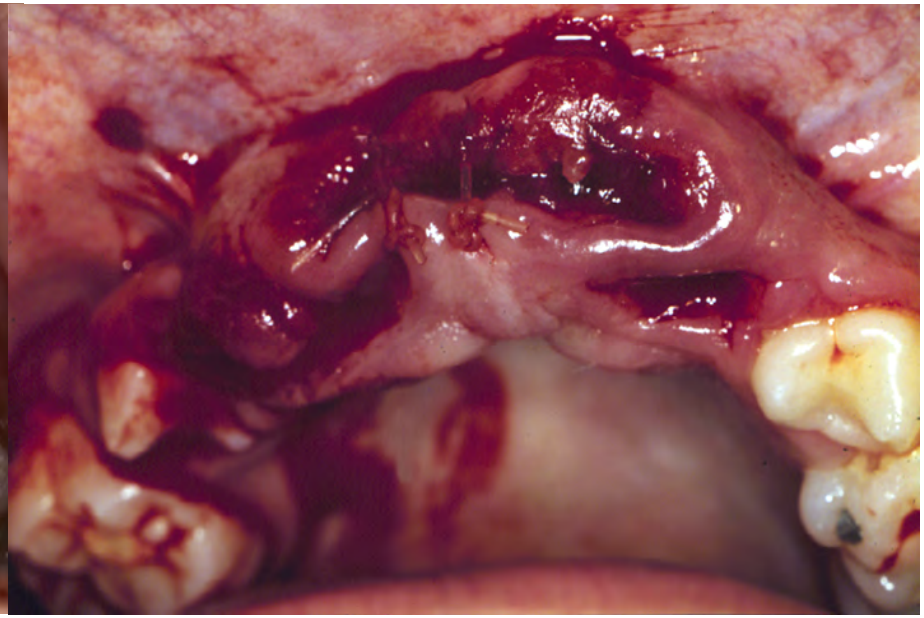

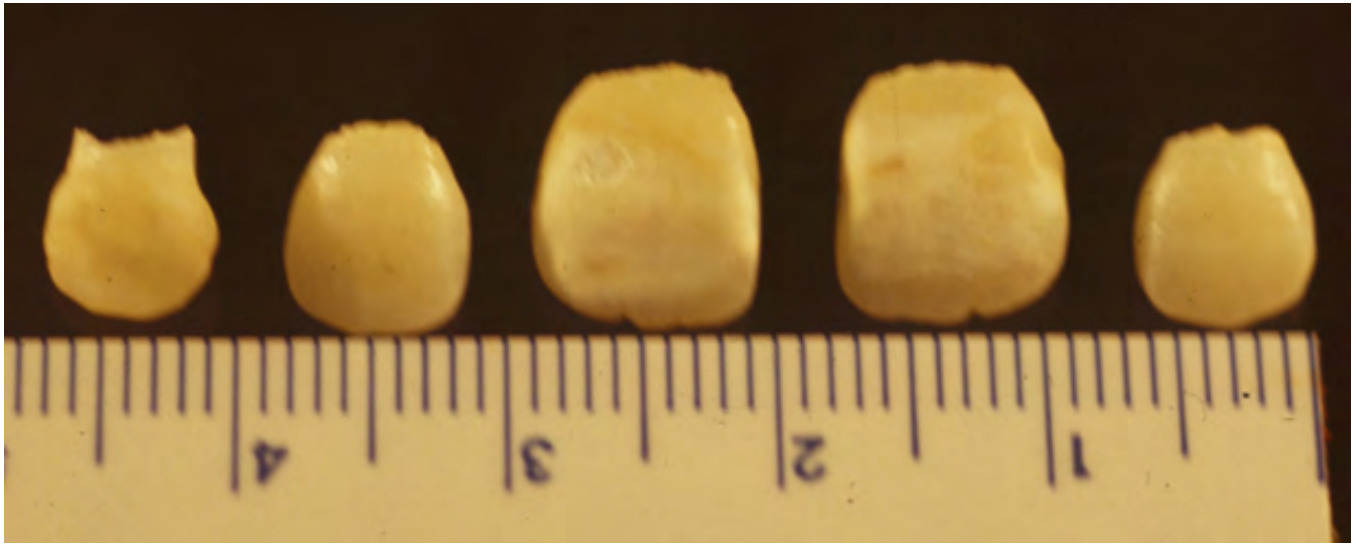
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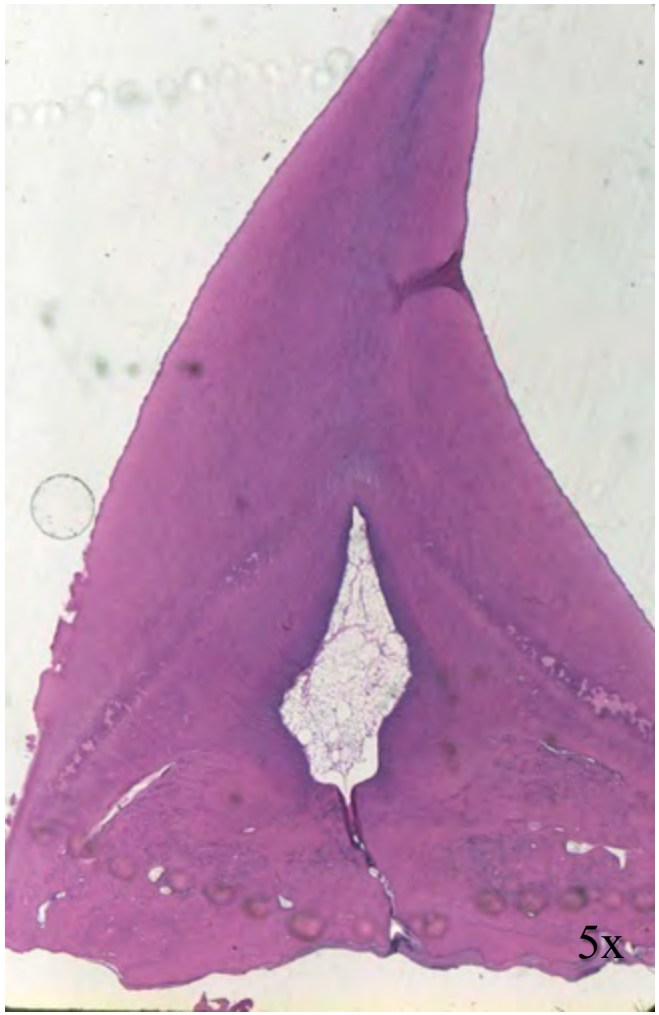
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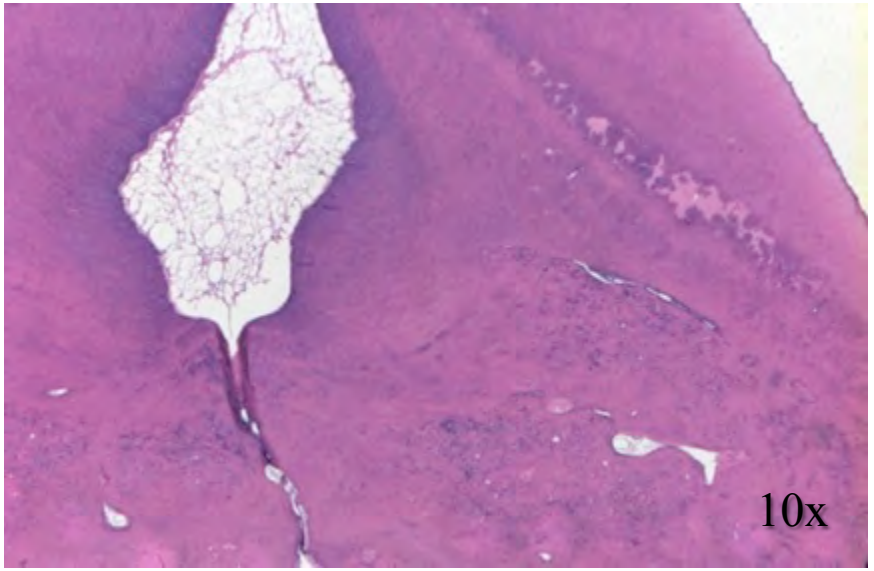
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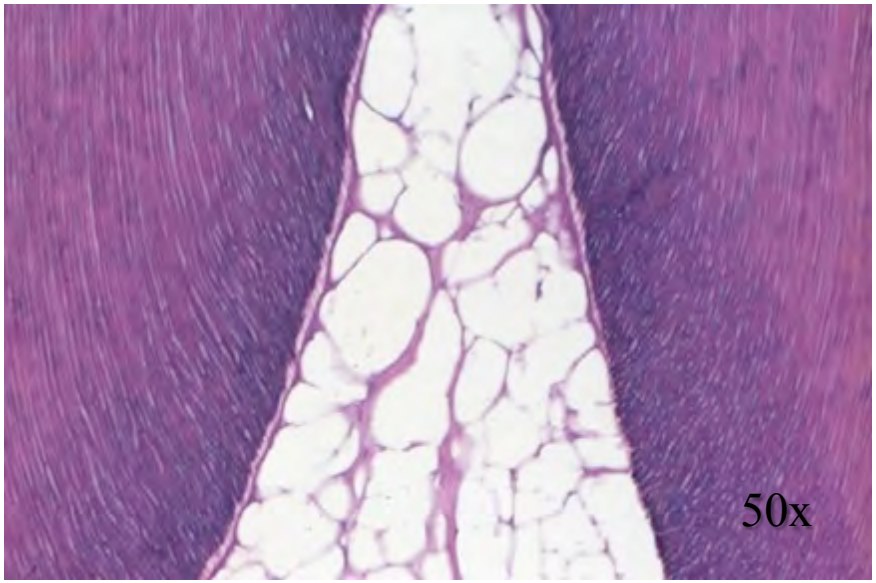
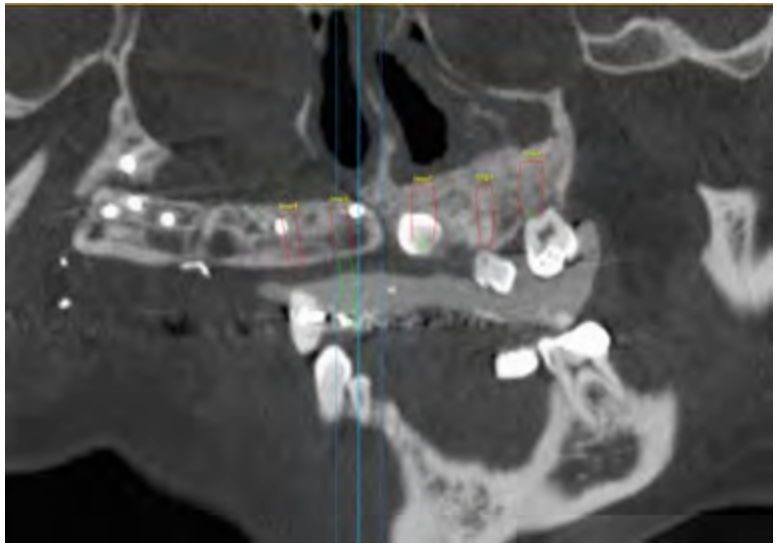
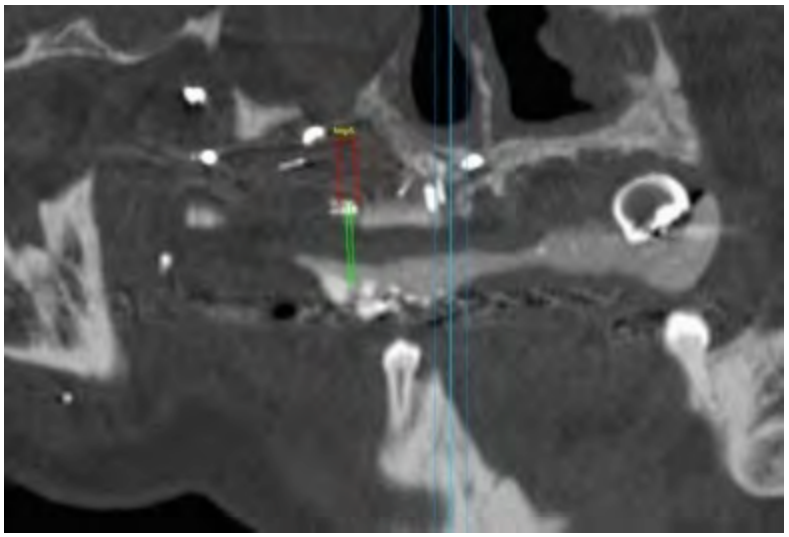

50x

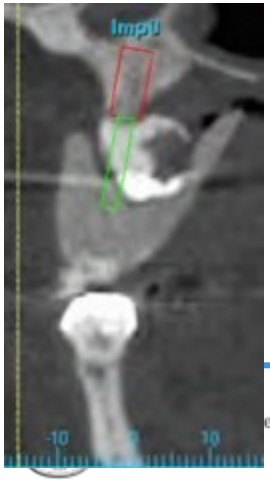
# YG at 21 Years Old

# s/p Fibula Free Flap Reconstruction

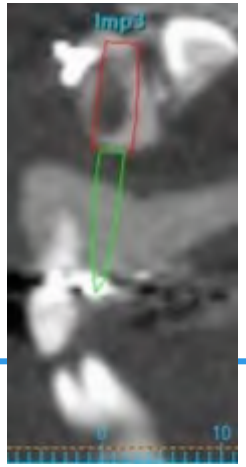
# Dental Implant Planning

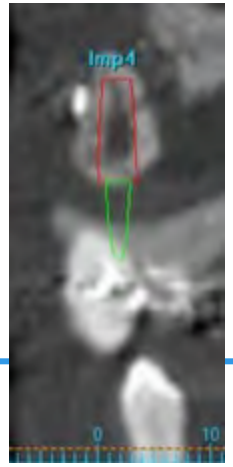


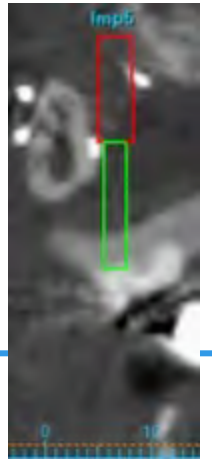






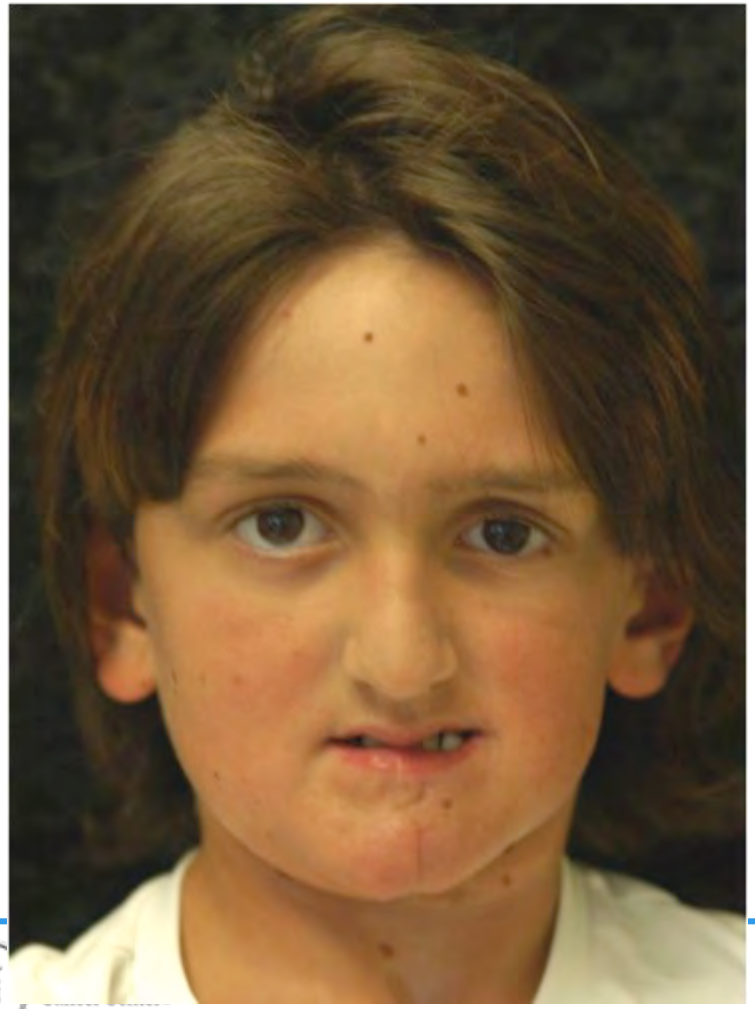



# Placement of Dental Implants

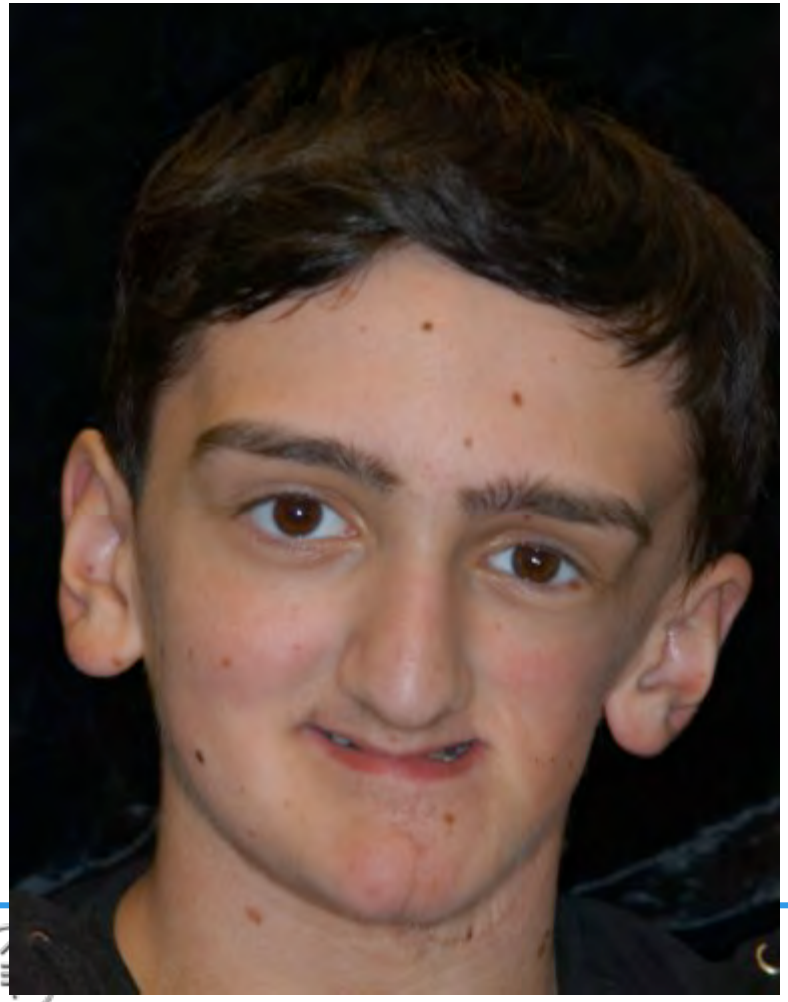
# Implant-Supported Prosthesis

# Development of Secondary Malignancy 27 years after Initial Treatment

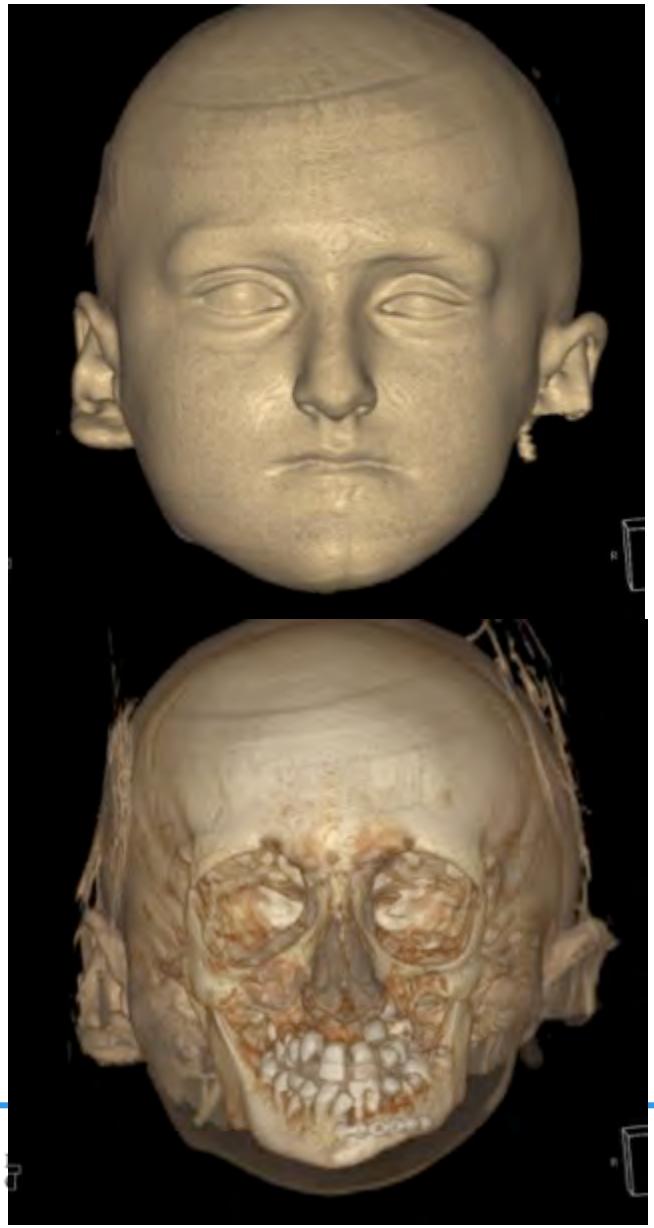
# MD: 11 y.o. Male with h/o Nasopharyngeal RMS s/p Chemo-RT @ 4 yrs old

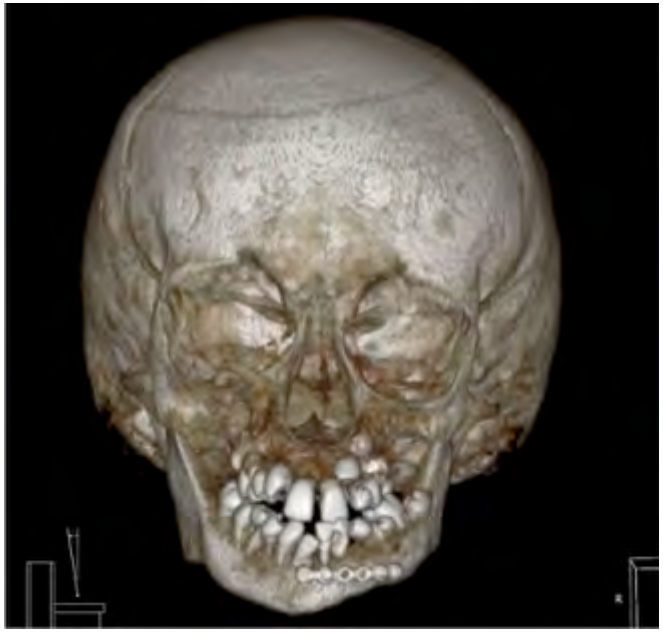


# MD at 13 y.o



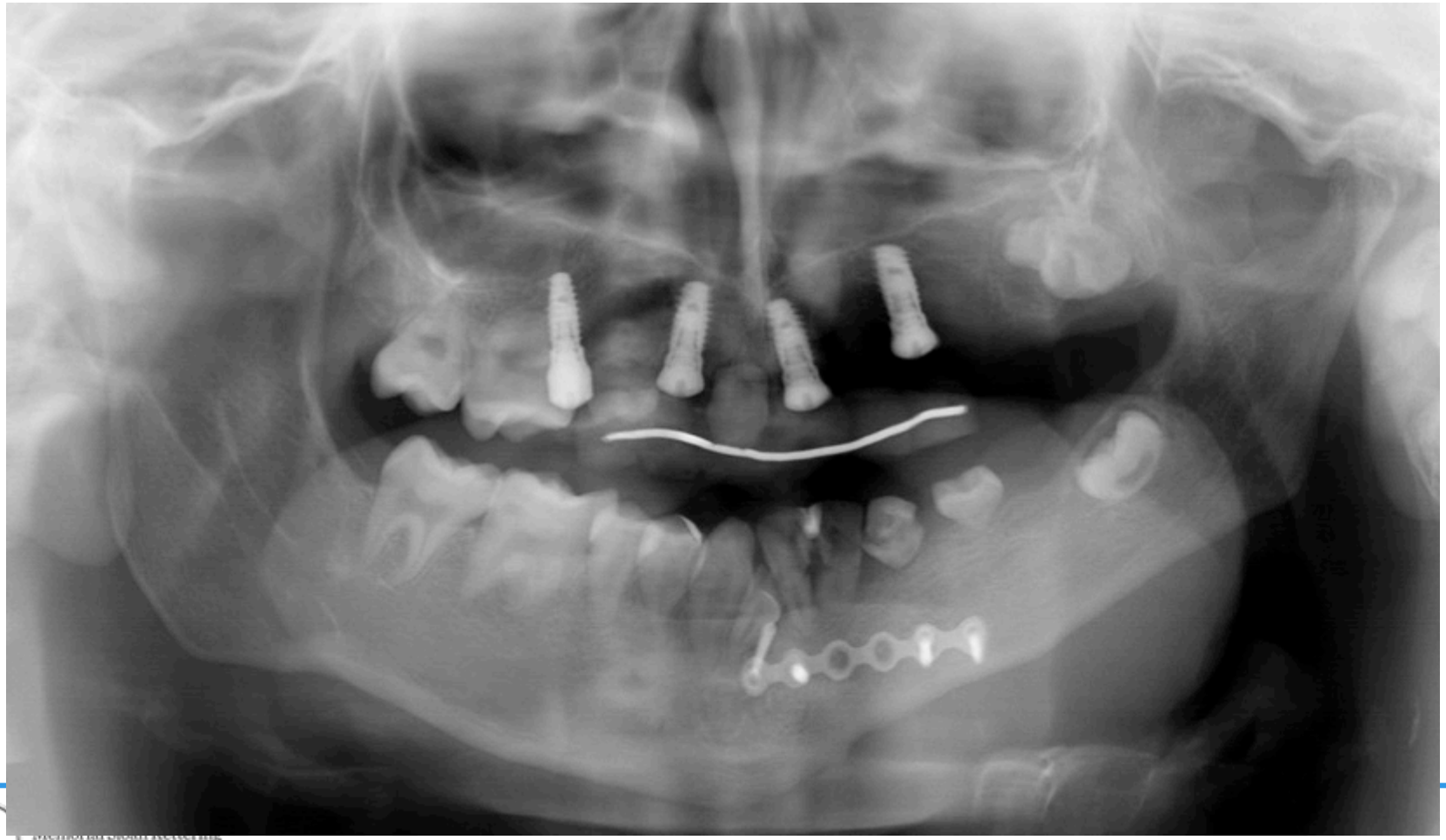
# Cone Beam CT/Stereolithography





# Tooth Preparation and Cementation of FPD (14 y.o.)

# Placement of 4 Dental Implants (15 y.o.)



# Placement of Custom Abutments

# Awaiting Definitive Restoration

# MD: Now 18 years old

# Final Thoughts

- Chemotherapy and head and neck RT can have profound long-term effects on dental and craniofacial growth.
  - Most severe in those treated with combined tx @ <6 years and/or RT for HN malignancy
- Awareness of oral and dental treatment-related sequelae/complications is important
  - Facilitate early detection and intervention
  - Optimize quality of life
- Long-term survivors (LTS) should be followed for life.
- The care of LTS requires a multidisciplinary team.
- Enhancing and maintaining QoL is paramount.

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# Thank You!

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www: mskcc.org