

# IMAGING OF PEDIATRIC CALVARIAL AND SKULL BASE TUMORS: A COG DIAGNOSTIC IMAGING COMMITTEE/SPR ONCOLOGY COMMITTEE/ASPNR WHITE PAPER

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## INTRODUCTION

The frequency of pediatric head and neck neoplasms ranges from approximately 2-15% of all pediatric cancers<sup>1</sup>. Skull base and calvarial neoplasms, including temporal bone and orbital masses are a subset of head and neck neoplasms occupying a number of neoplastic processes and categorically encompass several imaging patterns: singular dominant mass lesions with or without metastatic disease (e.g., rhabdomyosarcoma (RMS), chordoma), singular or multifocal metastatic disease (e.g., neuroblastoma), and multifocal disease due to systemic malignancy (e.g., leukemia, lymphoma, histiocytosis, etc.).

While pathologies certainly vary between pediatric and adult patients, there remains significant overlap. As such, imaging protocols for skull base and calvarial neoplasms are similar in their general construct. However, optimized pediatric-specific protocols remain a must, as a retrofitted adult head and neck protocol is often ill equipped to offer quality, efficient and safe imaging (e.g., limiting radiation exposure) of the size-variable infant and pediatric patient. Moreover, sedation or general anesthesia is often required in the pediatric population in order to minimize motion artifact. Thus, optimization of imaging acquisition time is a very important technical consideration because it may decrease the necessity and duration of sedation/anesthesia and their potential risks in this vulnerable population. Standardized protocols for anatomic sub sites of the head and neck offer significant benefit in individual patient follow up on a local scale, and, on a broader scale, allow for collaborative understanding of imaging pathologies and innovative or benchmarked standardized treatment response assessment across institutions.

In an effort to standardize protocols, this article offers minimum, pediatric specific anatomy-based initial and follow up imaging guidelines for pediatric malignancies of the orbits, calvarium, skull base and temporal

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## IMAGING RECOMMENDATION FOR THE ORBITS

Imaging of the orbit includes three sub anatomic locations; the ocular, the optic nerve sheath complex, and the orbital soft tissues are discussed here.

### *Imaging of Ocular Tumors*

Pediatric patients with ocular tumors can present with a wide variety of signs and symptoms, such as leukocoria, strabismus, limited eye movement, and decreased vision<sup>2</sup>. Many etiologies can cause leukocoria, including neoplastic (retinoblastoma being the most common, occurring in up to 1 in 15,000 births, with other ocular tumors exceedingly rare, e.g., intraocular medulloepithelioma) and non-neoplastic diseases, such as persistent fetal vasculature and Coats disease<sup>3</sup>. Imaging helps characterize ocular tumors and differentiate neoplastic from non-neoplastic entities. Imaging plays an important role in tumor detection, characterization, extent assessment and treatment planning.

### *Imaging in Ocular Tumor Staging*

Staging of retinoblastoma in the United States and other developed countries almost universally applies to intraocular retinoblastoma using the International Classification for Intraocular Retinoblastoma, a system that stratifies the chance of ocular sparing with current treatments. For extraocular retinoblastoma, several classification systems exist, including the International Retinoblastoma Staging System and the American Joint Committee on Cancer (AJCC) TNM Staging System, among others<sup>4</sup>. Choroidal invasion and early stages of optic nerve invasion remain challenging by imaging. As such, histopathologic evaluation remains the gold standard for such invasion assessment. Regardless, optimized, high resolution imaging of the orbit is critical in the preoperative assessment and characterization of tumor location and extent, including identifying extraocular invasion (e.g., optic nerve invasion) as it relates to these staging systems<sup>5</sup>.

### *Imaging Modalities for Ocular Tumors*

#### **MRI**

Besides dedicated MRI of the orbits, MRI of the entire brain should be performed concomitantly to assess for intracranial invasion and metastatic disease during initial diagnosis and follow up. Attention to details in the suprasellar and pineal regions is mandatory to assess for “trilateral” or “quadrilateral” retinoblastoma, respectively. For patients with extraocular retinoblastoma, imaging will also consist of a bone scan to assess for systemic metastatic disease, in addition to lumbar puncture and bone marrow aspiration. Routine MRI sequences of the orbits ought to be performed with dedicated thin-section, high resolution images of the orbits (< 3 mm slice thickness) using an optimal field of view (FOV). This includes at minimum: axial T1WI, axial and coronal fat suppressed (FS) gadolinium-enhanced T1WI, axial and coronal FS T2WI. High-resolution three-dimensional (3D) imaging of the orbits using a heavily T2-weighted 3D sequence and diffusion weighted imaging (DWI) are optional but recommended in the evaluation of retinoblastoma. Such ultrathin-slice images offer superior spatial resolution compared to conventional thin-sectional MRI and are particularly useful in the intraocular tumors and optic nerve sheath complex lesion to include perineural CSF space assessment<sup>6</sup>. It should be noted that thin-section high resolution imaging requires longer acquisition times and is more susceptible to motion degradation necessitating a fully cooperative or sedated patient. As noted, resolution DWI is often helpful. Retinoblastoma, for example, typically shows restricted diffusion (high signal) on DWI and exhibits low ADC values which is in contrast to high ADC values in the vitreous<sup>7</sup>. Furthermore, SWI is helpful in detecting and differentiating blood products from calcium.

#### **CT**

CT is a secondary imaging modality relative to MRI for the evaluation of an ocular mass lesion. CT only remains superior in documenting the presence of calcifications, which is an important imaging feature

of retinoblastoma. Such determination is however rarely needed as ophthalmologic and MRI features are typically diagnostic of retinoblastoma. The evaluation of optic nerve involvement and intracranial extension on CT is significantly limited compared to MRI.

## US

Ocular ultrasonography is useful in evaluation of an ocular tumor and commonly used as a first-line imaging technique for screening of ocular pathology in the pediatric population. It maintains an advantage in pediatric patients due to low cost, wide availability, lack of radiation exposure and can often be done without sedation. It is also sensitive for detection of calcification<sup>8</sup>. US can easily evaluate mass lesions of the globe. However, the visualization of deeper lesions, including retrobulbar lesions, is limited as the US wave cannot adequately penetrate to such deep structures. Furthermore, calcifications can obscure adjacent lesions and consequently limit assessment of the optic nerve. US alone is therefore not an adequate, complete diagnostic tool for definitive evaluation/ staging of ocular tumors such as retinoblastoma and medulloepithelioma.

### *Imaging of Optic Nerve Sheath Complex Tumors*

Common optic nerve sheath complex tumors in pediatric patients include optic pathway glioma and rarely optic sheath meningioma. Gliomas typically present with proptosis, vision loss, strabismus or nystagmus. Papilledema or optic nerve atrophy may be seen on ophthalmologic examination<sup>3</sup>.

### *Imaging Modalities for Optic Nerve Sheath Complex Tumors*

## MRI

Given its excellent soft tissue resolution, thin-section, high resolution multiplanar (i.e., axial, and coronal) MRI is the standard imaging modality for the evaluation of optic nerve and optic nerve sheath lesions with imaging protocols similar to those tailored for ocular tumors. Concomitant brain imaging with and without contrast is necessary.

## CT

CT is not an appropriate modality for such mass lesions.

### *Imaging of Orbital Tumors*

Rhabdomyosarcoma (RMS) is the most common extraocular malignant tumor in pediatric patients. Patients often present with a drooping eyelid with proptosis. A superonasal quadrant location is typical. Additional malignant masses including leukemia, lymphoma (especially Burkitt's lymphoma) and Langerhans cell histiocytosis (LCH) may similarly present with proptosis. Ocular involvement may occur especially with leukemia. An inflammatory presentation with a painful, edematous, erythematous mass lesion may occur with LCH. Infantile hemangiomas present within the first months of life. Lacrimal gland tumors are exceedingly rare in the pediatric population. Neuroblastoma is the most common metastatic tumor to the orbit in children<sup>3</sup>.

### *Imaging in Orbital Tumor Staging*

Staging of orbital RMS, like all other RMS in the head and neck, is via the Intergroup Rhabdomyosarcoma Study Group (IRSG)<sup>9</sup>. Imaging plays a critical role in clinical risk grouping of patients in the IRSG.

Staging of orbital RMS is recommended to occur via the IRSG staging system. (GRADE A, SOR 1.08, very strong recommendation)

## Imaging Modalities

## MRI

MRI is superior in characterizing soft tissue lesions due to its high soft tissue resolution. It can help characterize the soft tissue lesion and assess lesion extent including regional spatial invasion and intracranial extension via the skull base foramina and fissures. This includes evaluation of invasion into a parameningeal

location (nasopharynx, nasal cavity, parapharyngeal space, paranasal sinuses, infratemporal fossa, pterygopalatine fossa, tympanic and mastoid temporal bone)<sup>10</sup>. MRI is used for initial evaluation, staging, follow-up and treatment response evaluation of orbital tumors using a similar protocol as already described for ocular and optic nerve sheath lesions. DWI sequence is routinely included in MRI of the orbits because it can address potential histoarchitectural differences between various tumors and is therefore useful in lesion characterization alongside the use of gadolinium-based contrast. DWI may help differentiate benign from malignant tumors. For example, lymphoma has been shown to have low ADC values compared to benign tumors. This may help differentiate lymphoma from atypical lymphocytic infiltration or other inflammatory processes. Similarly, leukemia, RMS and LCH will typically demonstrate lower ADC values compared to benign tumors<sup>11</sup>. However, to date, no definite single ADC value threshold has been proposed as a cut-off value<sup>12</sup>. Single-shot echo-planar imaging DWI (EPI-DWI) is a commonly used technique. The newer multishot with readout-segmented echo-planar DWI and non-echo planar DWI may improve imaging quality, reduce distortion and susceptibility artifact from air-bone interfaces<sup>13</sup>. Furthermore, time resolved MR angiography (MRA) in which dynamic multiphase vascular imaging occurs during contrast injection is an optional but sometimes helpful technique in delineating vascular from nonvascular lesions and furthermore arterial from venous fed lesions.

## CT

CT offers superior bone resolution. It demonstrates bony destruction and/or remodeling and may offer complementary but not substitutive information to MRI for initial tumor evaluation and treatment response. It does not serve as an appropriate singular modality for initial diagnosis, on therapy follow up or off therapy surveillance unless MRI is contraindicated.

## PET CT

While PET CT can increase initial staging accuracy by identifying nodal metastasis and distant metastasis<sup>14</sup>, PET CT is not routinely performed in orbital RMS due to the rarity of metastatic disease.<sup>15</sup>

## Imaging at Diagnosis

MRI of the brain and orbits without and with contrast is recommended at diagnosis of an ocular, optic nerve sheath complex or orbital tumor. (GRADE C, SOR 1.00, very strong recommendation) CT is not a recommended modality at initial diagnosis. Contrast-enhanced CT may be performed if MRI is contraindicated.

## Imaging at Follow-up

MRI of the brain and orbits without and with contrast is recommended during on therapy follow up of an ocular, optic nerve sheath complex or orbital tumor. (GRADE C, SOR 1.00, very strong recommendation) CT is not a recommended modality for on therapy follow up. Contrast-enhanced CT may be performed if MRI is contraindicated.

## Imaging Off Therapy/Surveillance

MRI of the brain and orbits without and with contrast is recommended during off therapy surveillance of an ocular, optic nerve sheath complex or orbital tumor. (GRADE C, SOR 1.00, very strong recommendation) CT is not a recommended modality for off therapy surveillance. Contrast-enhanced CT may be performed if MRI is contraindicated.

## IMAGING RECOMMENDATION FOR CALVARIAL TUMORS

Calvarial neoplasms are rare among pediatric head and neck mass lesions. Primary pediatric calvarial lesions are often benign with dermoid and epidermoid cysts being the most common<sup>16</sup>. Very rare benign neoplasms of the calvarium include osteoma, osteoid osteoma, aneurysmal bone cyst, and osteoblastoma. Malignant calvarial tumors are mostly skeletal metastases, of which neuroblastoma is the most common<sup>17</sup>. Ewing sarcoma may also metastasize to the skull; primary calvarial Ewing sarcoma is rare. Multifocal or unifocal

disease in LCH is also a common diagnosis, accounting for up to 12% of calvarial mass lesions in pediatric patients<sup>18</sup>. Intraosseous meningiomas are exceedingly rare in children.

Calvarial mass lesions may present as a palpable mass, localized pain and swelling or be identified incidentally after identification at another site. For initial evaluation, imaging plays a role in lesion detection and determining the location and origin of lesion, whether it arises from the bone, soft tissue or extending from intracranially. Moreover, the imaging appearance can help characterize lesions, differentiating neoplastic versus non-neoplastic entities and benign versus malignant tumors. An additional goal of imaging is to provide detail regarding the extent of pathology and to determine the relationship between the lesion and the nearby structures such as brain and dura.

## **MRI**

MRI has superior soft tissue resolution and is a valuable imaging modality in the evaluation of a calvarial mass. MR imaging features are critical in characterizing the lesion as benign versus malignant neoplasm and non-neoplastic. MRI is necessary in evaluation of the lesion extent, especially for intracranial extension to include dural and parenchymal invasion.<sup>19</sup>. As discussed for orbital tumors, DWI is very helpful in characterizing the cellularity of the lesion and thereby honing benign and malignant differential considerations. The soft tissue component of the tumor in the scalp may be obscured by the subcutaneous fat, especially on the postcontrast T1WI with enhancing tumors displaying similar signal as the surrounding fat. Fat suppression (FS) is often performed to overcome this issue and allows better delineating of the lesion. The arterial and venous anatomy can be demonstrated on MRA and MR venography (MRV). MRA can display the arterial supply of the lesion. MRV is useful in assessment of the dural venous sinus involvement when the lesion is adjacent a dural venous sinus. MRA and MRV are considered optional.

## **CT**

Thin-slice (approximately 1 mm) axial CT images filtered in bone and soft tissue algorithms with multiplanar reconstructions is an adjunctive tool for the initial evaluation of a calvarial lesion. It serves as a primary modality to identify bone erosion or bony remodeling, and generally to identify the presence of a soft tissue component, evaluate the general spatiality and extent and potential multiplicity of the lesion. Contrast-enhanced CT is not typically necessary especially given that MRI will serve to otherwise fully characterize the mass, in particular the soft tissue component. CT venography (CTV), may be helpful for presurgical planning primarily in assessing for dural venous invasion. CT may be a helpful adjunctive tool that can be used for evaluation of treatment response due to its superiority in exhibiting bony lesions and expectant healing post treatment.

## **PET CT**

Owing to the rarity of calvarial based tumors, limited literature exists regarding the utility of PET CT in children with malignant calvarial tumors such as sarcoma. In general, use of PET CT at diagnosis, at follow-up, and during off therapy/ surveillance of calvarial sarcomas is typically as done for malignant skull base and temporal bone tumors as described below.

## **Imaging at Diagnosis**

MRI of the brain without and with contrast is recommended at diagnosis of a calvarial tumor. (GRADE C, SOR 1.08, very strong recommendation)

CT of the head without contrast is recommended at diagnosis of a calvarial tumor. (GRADE C, SOR 1.42, very strong recommendation) Contrast-enhanced CT is not recommended unless MRI is contraindicated.

## **Imaging at Follow-up**

MRI of the brain without and with contrast is recommended during on therapy follow up of a calvarial tumor. (GRADE C, SOR 1.00, very strong recommendation) CT of the head without contrast may provide complementary information at follow up especially as it relates to bony treatment response. CT however

does not serve as a primary method of follow up. Contrast-enhanced CT is not recommended for follow up unless MRI is contraindicated.

### **Imaging Off Therapy/Surveillance**

MRI of the brain without and with contrast is recommended during off therapy surveillance of a calvarial tumor. (GRADE C, SOR 1.00, very strong recommendation) CT of the head without contrast may provide complementary information during off therapy surveillance. CT however does not serve as a primary method of off therapy surveillance. Contrast-enhanced CT is not recommended for off therapy surveillance unless MRI is contraindicated.

## **IMAGING RECOMMENDATION FOR SKULL BASE AND TEMPORAL BONE TUMORS**

The skull base is a complex osseous structure that serves as a conduit between the intracranial and extracranial compartments. It contains several neural foramina and fissures with traversing neurovascular structures<sup>20</sup>. As in adults, there is a wide variety of benign and malignant skull base tumors that may occur in the pediatric population such as nerve sheath tumors, glomus tumors, RMS, Ewing sarcoma, olfactory neuroblastoma/esthesioneuroblastoma, chondrosarcoma and chordoma<sup>21-23</sup>. Systemic malignancies such as lymphoma, leukemia and especially LCH may involve the skull base.

Clinical presentation of children with skull base tumors varies with sub-location: anterior, middle versus posterior skull base. Children with anterior skull base mass lesions often present late and without distinction between neoplastic and non-neoplastic entities or between benign and malignant neoplasms. Nasal obstruction especially long term unilateral nasal obstruction, sinonasal pain, epistaxis, excessive lacrimation, anosmia and even visual changes may be presenting symptoms<sup>24</sup>. Tumors of the middle skull base may present with headache, hypothalamic-pituitary dysfunction, visual changes, facial dysesthesia and pain, deficits of CN III-XI, facial deformity and oropharyngeal obstruction. Finally, tumors of the posterior skull base present with headache, neck pain which may be from craniocervical instability, torticollis secondary to the craniocervical junction involvement, or cranial nerve dysfunction including visual abnormalities and dysphagia with involvement of the hypoglossal canal and jugular foramen<sup>25</sup>.

Temporal bone neoplasms in the pediatric population are exceedingly rare. These typically include RMS. Other sarcomas are rare. Systemic malignancies such as lymphoma, leukemia and especially LCH may involve the temporal bone. Patients typically present with signs and symptoms that mimic refractory and severe ear infection. Additionally, common presenting symptoms include hearing loss, otorrhea, otalgia, vertigo and headache. Facial weakness and diplopia may also occur. Extension of the mass to involve the orbital apex, cavernous sinus, hypoglossal canal and jugular foramina may produce additional cranial nerve dysfunction symptoms. Finally, with invasion of the dura, patients may present with CSF leakage and/or meningitis<sup>26</sup>.

### **Imaging in Skull Base and Temporal Bone Tumor Staging**

Both CT and MRI play complementary roles for evaluation of skull base and temporal bone tumors at both diagnosis and follow up<sup>27,28</sup>. Similar to head and neck tumors in other subsites, goals of imaging are to evaluate the origin and the extent of the lesion as well as to differentiate between neoplastic and non-neoplastic entities or between benign and malignant neoplasms. Following initial diagnosis, staging evaluation typically occurs via the AJCC TNM classification system for select sites. Esthesioneuroblastoma staging may occur via the Kadish or modified Kadish staging or Dulgerov systems which require imaging assessment of regional tumor invasion such as paranasal sinuses, orbits, skull base, dural and brain involvement, as well as evaluation of co-existing nodal and distant metastases<sup>29</sup>. Note that a universally agreed upon staging system does not exist for temporal bone tumors other than RMS.

Staging of skull base and temporal bone RMS, like all other RMS in the head and neck, is via the IRSG staging system<sup>9</sup>.

Staging of skull base and temporal bone RMS is recommended via the IRSG staging system. (GRADE A,

SOR 1.08, very strong recommendation)

## *Imaging Modalities*

### **MRI**

MRI has superior soft tissue contrast resolution with better assessment of soft tissue spatiality and extension and bone marrow involvement compared to CT<sup>27,28</sup>. MRI with post contrast T1WI with fat saturation is the imaging modality of choice for evaluation of perineural tumor spread although gross perineural spread may be seen with contrast-enhanced CT<sup>30,31</sup>. MRI sequences for skull base protocol should include T1WI and T2WI with FS and contrast-enhanced T1WI with FS in axial and coronal planes. Precontrast T1WI without FS allows for assessment of bone marrow replacement and abnormalities of adipose tissue within the extracranial spaces adjacent to skull base tumors as well as detection of intrinsic T1 hyperintensity if present. Intrinsic T1 hyperintensity within tumors may be secondary to intratumoral hemorrhage, fat, mineralization or melanin<sup>32</sup>. Images should be obtained with thin slices (slice thickness <3 mm). Sagittal images provide additional information regarding craniocaudal extension of the lesions. Detailed evaluation of cranial nerves is required for skull base and temporal bone tumors; dedicated MR sequences including high-resolution 3D T2WI, pre- and post-contrast 3D T1WI with multiplanar reformations of cranial nerves are recommended at the temporal bone and skull base<sup>33,34</sup>. Entire brain imaging is necessary to assess the integrity of the subjacent brain and dura. The role of advanced MRI techniques such as DWI, MR perfusion, or MR spectroscopy remains under investigation in research<sup>35</sup>. MRA and MRV (or CTA/CTV) are adjunctive radiological exams that can be used to assess vascular anatomy (compression, displacement, invasion)<sup>23</sup>.

### **CT**

In general, CT can provide better assessment of cortical bone such as cortical erosion or sclerosis as well as identification of intratumoral mineralization or calcified matrix which may prove helpful in differential considerations<sup>28</sup>. Spatiality of bony involvement of the tumor is best demonstrated by CT including expected healing changes post therapy.<sup>27,28,36,37</sup>. CT of the head to include the entire skull base should be acquired with multidetector CT using thin collimation (0.5 – 0.625 mm). Images should be reconstructed in axial, coronal and sagittal orthogonal planes in soft tissue and bone algorithms<sup>32</sup>. Contrast is not typically necessary when MRI is available. CTA and CTV (or MRA/MRV) are adjunct radiological exams that can be used to assess vascular anatomy<sup>23</sup>.

### **PET CT**

The use of PET CT in initial staging of skull base and temporal bone tumors should be tailored to individual patients and their specific type of tumor. Full body PET CT can be helpful in the preoperative staging of skull base and temporal bone RMS including at initial diagnosis, during on therapy follow up for patients with metastatic disease and during off therapy surveillance for patients with metastatic disease. Such evaluation is similarly true for the rare occurrence of other malignancies such as primary Ewing sarcoma in the skull base and temporal bone. For the assessment of metabolic response of rhabdomyosarcoma by FDG PET CT, it is still controversial whether FDG PET CT can predict treatment response<sup>38,39</sup>. Further studies are needed to determine the role of PET CT in predicting treatment response.

### **Imaging at Diagnosis**

MRI of the brain and skull base or temporal bones without and with contrast is recommended at initial diagnosis of a skull base or temporal bone tumor. (GRADE C, SOR 1.00, very strong recommendation)

CT of the temporal bones without contrast is recommended at initial diagnosis of a temporal bone tumor. (GRADE C, SOR 1.08, very strong recommendation) Contrast-enhanced CT is not recommended unless MRI is contraindicated.

CT of the head without contrast is recommended at initial diagnosis of a skull base tumor. (GRADE D, SOR 1.42, very strong recommendation) Contrast-enhanced CT is not recommended unless MRI is

contraindicated.

Full body PET CT is recommended at initial diagnosis/staging of a skull base or temporal bone sarcoma. (GRADE D, SOR 1.0, very strong recommendation) Standard chest CT is typically concomitantly performed.

### **Imaging at Follow-up**

MRI of the brain and skull base or temporal bones without and with contrast is recommended during on therapy follow up of a skull base or temporal bone tumor. (GRADE C, SOR 1.00, very strong recommendation) CT of the head without contrast for the skull base or CT temporal bone without contrast may provide complementary information at follow up, especially as it relates to bony treatment response. CT, however, does not serve as a primary method of follow up. Contrast-enhanced CT is not recommended for such follow up unless MRI is contraindicated.

Full body PET CT is recommended during on therapy follow up of a temporal bone or skull base sarcoma with metastatic disease at presentation. (GRADE C, SOR 1.00, very strong recommendation) Standard chest CT is typically concomitantly performed.

### **Imaging Off Therapy/Surveillance**

MRI of the brain and skull base or temporal bones without and with contrast is recommended during off therapy surveillance of a skull base or temporal bone tumor. (GRADE C, SOR 1.00, very strong recommendation) CT of the head without contrast for the skull base or CT temporal bone without contrast may provide complementary information during off therapy surveillance. CT, however, does not serve as a primary method of off therapy surveillance. Contrast-enhanced CT is not recommended for off therapy surveillance unless MRI is contraindicated.

Full body PET CT is recommended during off therapy surveillance of a skull base or sarcoma with metastatic disease at presentation. (GRADE C, SOR 1.0, very strong recommendation) Standard chest CT is typically concomitantly performed.

## **FUTURE TRENDS**

In the oncologic setting, CT and MRI play a pivotal role in not only providing the diagnosis and information on disease burden but also evaluating treatment response and imaging surveillance. However, conventional CT and MRI techniques occasionally have limitations in differentiating between different types of tumors that may occur in the same location or differentiating between treatment-related changes and viable tumor in the posttreatment setting. In addition, they do not provide detail regarding tumor histoarchitecture and physiology or imaging parameters that can be used for risk stratification. As a result, over past decades, there has been great effort in developing advanced imaging techniques that can address these formidable challenges<sup>35,40-42</sup>.

Dual-energy CT allows acquisition of images simultaneously at high- and low-energy spectra simultaneously with radiation doses that is equal to or less than the conventional single-energy CT. Virtual noncontrast images can be generated from dual-energy CT dataset reducing acquisition time and radiation<sup>43</sup>. Iodine concentration in the tumor can also be assessed qualitatively and quantitatively. This may help in tumor delineation and separation between residual viable tumor and treatment fibrosis<sup>44</sup>.

There are several advanced MRI techniques that are used for imaging of tumors in the skull base and head and neck region, such as high-resolution 3D MRI, DWI, MR perfusion, and MR spectroscopy. These techniques have demonstrated a wide range of potential utilities in diagnosis, tumor prognostication and posttreatment evaluation<sup>35,40,41</sup>. Moreover, newer MR technology such as fast MRI sequences can reduce the scan time which is particularly useful in pediatric population as it can minimize motion artifact and decrease sedation needs<sup>45</sup>. Furthermore, zero echo time (TE) sequences, so called black bone MRI, may show promise in bone evaluation due to its high soft tissue/ bone contrast reducing the need for CT<sup>46,47</sup>. More scientific data and research are needed to evaluate the efficacy of these advanced techniques in clinical practice.



Finally, with the advent of powerful processing capabilities, artificial intelligence in radiology (radiomics) will allow for extraction of quantifiable data from imaging furthering tumor and treatment imaging phenotype understanding. Combining radiomics and genomics, so called radiogenomics, may aid in tumor behavioral understanding and risk stratification and prognostication.

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## References

1. Arboleda LPA, de Mendonca RMH, Lopez EEM, et al. Global frequency and distribution of head and neck cancer in pediatrics, a systematic review. *Crit Rev Oncol Hematol* . Apr 2020;148:102892. doi:10.1016/j.critrevonc.2020.102892
2. Rao AA, Naheedy JH, Chen JY, Robbins SL, Ramkumar HL. A clinical update and radiologic review of pediatric orbital and ocular tumors. *J Oncol* . 2013;2013:975908. doi:10.1155/2013/975908
3. Castillo BV, Jr., Kaufman L. Pediatric tumors of the eye and orbit. *Pediatr Clin North Am* . Feb 2003;50(1):149-72. doi:10.1016/s0031-3955(02)00115-3
4. Chantada GL, Sampor C, Bosaleh A, Solernou V, Fandino A, de Davila MT. Comparison of staging systems for extraocular retinoblastoma: analysis of 533 patients. *JAMA Ophthalmol* . Sep 2013;131(9):1127-34. doi:10.1001/jamaophthalmol.2013.260
5. Silvera VM, Guerin JB, Brinjikji W, Dalvin LA. Retinoblastoma: What the Neuroradiologist Needs to Know. *AJNR Am J Neuroradiol* . Apr 2021;42(4):618-626. doi:10.3174/ajnr.A6949
6. McCaffery S, Simon EM, Fischbein NJ, et al. Three-dimensional high-resolution magnetic resonance imaging of ocular and orbital malignancies. *Arch Ophthalmol* . Jun 2002;120(6):747-54. doi:10.1001/archophth.120.6.747
7. Razek AA, Elkharmay S. MRI of retinoblastoma. *Br J Radiol* . Sep 2011;84(1005):775-84. doi:10.1259/bjr/32022497
8. Kendall CJ, Prager TC, Cheng H, Gombos D, Tang RA, Schiffman JS. Diagnostic Ophthalmic Ultrasound for Radiologists. *Neuroimaging Clin N Am* . Aug 2015;25(3):327-65. doi:10.1016/j.nic.2015.05.001
9. Raney RB, Maurer HM, Anderson JR, et al. The Intergroup Rhabdomyosarcoma Study Group (IRSG): Major Lessons From the IRS-I Through IRS-IV Studies as Background for the Current IRS-V Treatment Protocols. *Sarcoma* . 2001;5(1):9-15. doi:10.1080/13577140120048890
10. Freling NJ, Merks JH, Saeed P, et al. Imaging findings in craniofacial childhood rhabdomyosarcoma. *Pediatr Radiol* . Nov 2010;40(11):1723-38; quiz 1855. doi:10.1007/s00247-010-1787-3
11. Jaju A, Rychlik K, Ryan ME. MRI of Pediatric Orbital Masses: Role of Quantitative Diffusion-weighted Imaging in Differentiating Benign from Malignant Lesions. *Clin Neuroradiol* . Sep 2020;30(3):615-624. doi:10.1007/s00062-019-00790-4
12. Sepahdari AR, Politi LS, Aakalu VK, Kim HJ, Razek AA. Diffusion-weighted imaging of orbital masses: multi-institutional data support a 2-ADC threshold model to categorize lesions as benign, malignant, or indeterminate. *AJNR Am J Neuroradiol* . Jan 2014;35(1):170-5. doi:10.3174/ajnr.A3619
13. Yeom KW, Holdsworth SJ, Van AT, et al. Comparison of readout-segmented echo-planar imaging (EPI) and single-shot EPI in clinical application of diffusion-weighted imaging of the pediatric brain. *AJR Am J Roentgenol* . May 2013;200(5):W437-43. doi:10.2214/AJR.12.9854

14. Norman G, Fayter D, Lewis-Light K, et al. An emerging evidence base for PET-CT in the management of childhood rhabdomyosarcoma: systematic review. *BMJ Open* . Jan 8 2015;5(1):e006030. doi:10.1136/bmjopen-2014-006030
15. Weiss AR, Lyden ER, Anderson JR, et al. Histologic and clinical characteristics can guide staging evaluations for children and adolescents with rhabdomyosarcoma: a report from the Children's Oncology Group Soft Tissue Sarcoma Committee. *J Clin Oncol* . Sep 10 2013;31(26):3226-32. doi:10.1200/JCO.2012.44.6476
16. Gephart MGH, Colglazier E, Paulk KL, Vogel H, Guzman R, Edwards MSB. Primary Pediatric Skull Tumors. *Pediatr Neurosurg* . 2011;47(3):198-203. doi:10.1159/000330544
17. D'Ambrosio N, Lyo JK, Young RJ, Haque SS, Karimi S. Imaging of metastatic CNS neuroblastoma. *AJR Am J Roentgenol* . May 2010;194(5):1223-9. doi:10.2214/AJR.09.3203
18. Barnett RR, Piazza MG, Elton SW. Pediatric Neurosurgery in Primary Care: Masses of the Scalp and Skull in Children. *Pediatr Clin North Am* . Aug 2021;68(4):743-757. doi:10.1016/j.pcl.2021.04.003
19. Moron FE, Morriss MC, Jones JJ, Hunter JV. Lumps and bumps on the head in children: use of CT and MR imaging in solving the clinical diagnostic dilemma. *Radiographics* . Nov-Dec 2004;24(6):1655-74. doi:10.1148/rg.246045034
20. Policeni BA, Smoker WR. Imaging of the skull base: anatomy and pathology. *Radiol Clin North Am* . Jan 2015;53(1):1-14. doi:10.1016/j.rcl.2014.09.005
21. Hanbali F, Tabrizi P, Lang FF, DeMonte F. Tumors of the skull base in children and adolescents. *J Neurosurg* . Feb 2004;100(2 Suppl Pediatrics):169-78. doi:10.3171/ped.2004.100.2.0169
22. Mandonnet E, Kolb F, Tran Ba Huy P, George B. Spectrum of skull base tumors in children and adolescents: a series of 42 patients and review of the literature. *Childs Nerv Syst* . Jun 2008;24(6):699-706. doi:10.1007/s00381-008-0580-1
23. Riley CA, Soneru CP, Overdevest JB, Otten ML, Gudis DA. Pediatric sinonasal and skull base lesions. *World J Otorhinolaryngol Head Neck Surg* . Jun 2020;6(2):118-124. doi:10.1016/j.wjorl.2020.01.007
24. Oskouian RJ, Jr., Jane JA, Sr., Dumont AS, Sheehan JM, Laurent JJ, Levine PA. Esthesioneuroblastoma: clinical presentation, radiological, and pathological features, treatment, review of the literature, and the University of Virginia experience. *Neurosurg Focus* . May 15 2002;12(5):e4. doi:10.3171/foc.2002.12.5.5
25. Tsai EC, Santoreneos S, Rutka JT. Tumors of the skull base in children: review of tumor types and management strategies. *Neurosurg Focus* . May 15 2002;12(5):e1. doi:10.3171/foc.2002.12.5.2
26. Gluth MB. Rhabdomyosarcoma and other pediatric temporal bone malignancies. *Otolaryngol Clin North Am* . Apr 2015;48(2):375-90. doi:10.1016/j.otc.2014.12.010
27. Quirk B, Connor S. Skull base imaging, anatomy, pathology and protocols. *Pract Neurol* . Feb 2020;20(1):39-49. doi:10.1136/practneurol-2019-002383
28. Kelly HR, Curtin HD. Imaging of skull base lesions. *Handb Clin Neurol* . 2016;135:637-657. doi:10.1016/B978-0-444-53485-9.00030-1
29. Joshi RR, Husain Q, Roman BR, et al. Comparing Kadish, TNM, and the modified Dulguerov staging systems for esthesioneuroblastoma. *J Surg Oncol* . Jan 2019;119(1):130-142. doi:10.1002/jso.25293
30. Badger D, Aygun N. Imaging of Perineural Spread in Head and Neck Cancer. *Radiol Clin North Am* . Jan 2017;55(1):139-149. doi:10.1016/j.rcl.2016.08.006
31. Abdelaziz TT, Abdel Razek AAK. Magnetic Resonance Imaging of Perineural Spread of Head and Neck Cancer. *Magn Reson Imaging Clin N Am* . Feb 2022;30(1):95-108. doi:10.1016/j.mric.2021.06.017

32. Iida E, Anzai Y. Imaging of Paranasal Sinuses and Anterior Skull Base and Relevant Anatomic Variations. *Radiol Clin North Am* . Jan 2017;55(1):31-52. doi:10.1016/j.rcl.2016.08.009
33. Blitz AM, Aygun N, Herzka DA, Ishii M, Gallia GL. High Resolution Three-Dimensional MR Imaging of the Skull Base: Compartments, Boundaries, and Critical Structures. *Radiol Clin North Am* . Jan 2017;55(1):17-30. doi:10.1016/j.rcl.2016.08.011
34. Hwang JY, Yoon HK, Lee JH, et al. Cranial Nerve Disorders in Children: MR Imaging Findings. *Radiographics* . Jul-Aug 2016;36(4):1178-94. doi:10.1148/rg.2016150163
35. Touska P, Connor SEJ. New and Advanced Magnetic Resonance Imaging Diagnostic Imaging Techniques in the Evaluation of Cranial Nerves and the Skull Base. *Neuroimaging Clin N Am* . Nov 2021;31(4):665-684. doi:10.1016/j.nic.2021.06.006
36. Conley LM, Phillips CD. Imaging of the Central Skull Base. *Radiol Clin North Am* . Jan 2017;55(1):53-67. doi:10.1016/j.rcl.2016.08.007
37. Greenwood TJ, Lopez-Costa RI, Rhoades PD, et al. CT Dose Optimization in Pediatric Radiology: A Multiyear Effort to Preserve the Benefits of Imaging While Reducing the Risks. *Radiographics* . Sep-Oct 2015;35(5):1539-54. doi:10.1148/rg.2015140267
38. Casey DL, Wexler LH, Fox JJ, et al. Predicting outcome in patients with rhabdomyosarcoma: role of [(18)f]fluorodeoxyglucose positron emission tomography. *Int J Radiat Oncol Biol Phys* . Dec 1 2014;90(5):1136-42. doi:10.1016/j.ijrobp.2014.08.005
39. Harrison DJ, Chi YY, Tian J, et al. Metabolic response as assessed by (18) F-fluorodeoxyglucose positron emission tomography-computed tomography does not predict outcome in patients with intermediate- or high-risk rhabdomyosarcoma: A report from the Children's Oncology Group Soft Tissue Sarcoma Committee. *Cancer Med* . Feb 2021;10(3):857-866. doi:10.1002/cam4.3667
40. Dickerson E, Srinivasan A. Advanced Imaging Techniques of the Skull Base. *Radiol Clin North Am* . Jan 2017;55(1):189-200. doi:10.1016/j.rcl.2016.08.004
41. Kirsch CF, Ho ML. Advanced Magnetic Resonance Imaging of the Skull Base. *Semin Ultrasound CT MR* . Jun 2021;42(3):229-252. doi:10.1053/j.sult.2021.04.006
42. Prevedello LM. Advances in computed tomography evaluation of skull base diseases. *Int Arch Otorhinolaryngol* . Oct 2014;18(Suppl 2):S123-6. doi:10.1055/s-0034-1395269
43. McCollough CH, Leng S, Yu L, Fletcher JG. Dual- and Multi-Energy CT: Principles, Technical Approaches, and Clinical Applications. *Radiology* . Sep 2015;276(3):637-53. doi:10.1148/radiol.2015142631
44. Siegel MJ, Ramirez-Giraldo JC. Dual-Energy CT in Children: Imaging Algorithms and Clinical Applications. *Radiology* . May 2019;291(2):286-297. doi:10.1148/radiol.2019182289
45. Kozak BM, Jaimes C, Kirsch J, Gee MS. MRI Techniques to Decrease Imaging Times in Children. *Radiographics* . Mar-Apr 2020;40(2):485-502. doi:10.1148/rg.2020190112
46. Eley KA, McIntyre AG, Watt-Smith SR, Golding SJ. "Black bone" MRI: a partial flip angle technique for radiation reduction in craniofacial imaging. *Br J Radiol* . Mar 2012;85(1011):272-8. doi:10.1259/bjr/95110289
47. Kralik SF, Supakul N, Wu IC, et al. Black bone MRI with 3D reconstruction for the detection of skull fractures in children with suspected abusive head trauma. *Neuroradiology* . Jan 2019;61(1):81-87. doi:10.1007/s00234-018-2127-9

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