# Medulloblastoma: Imaging pattern description using Magnetic Resonance Imaging

**A research paper submitted to the school of Graduate studies of Addis Ababa University, Department of Radiology, for partial fulfillment of the requirement for the subspecialty certificate in Neuroradiology**

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**Advisors:**

**Dr. Amal Saleh, Consultant Neuroradiologist**

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## Abbreviations

TASH- Tikur Anbessa Specialized Hospital

MB- Medulloblastoma

DN- Desmoplastic nodular

LC/A- Large cell/Anaplastic

MBEN- Medulloblastoma with extensive nodularity

CPA/CP- Cerebellopontine angle/ Cerebellar peduncle

CT- computed tomography

MRI- Magnetic resonance imaging

DWI/ADC-diffusion weighted image/ ADC mapping

CE- Contrast enhanced

## Abstract:

***Background**: Medulloblastoma is one of the most common pediatric brain tumors in children. It is a heterogeneous disease consisting of multiple histologic and molecular subgroups with distinctive origins, demographics, molecular alterations, and outcomes. Magnetic resonance imaging is the main imaging modality used for diagnosis and follow-up of patients with medulloblastoma.*

***Objective:** The objective of this study is to describe imaging patterns of medulloblastoma on conventional MRI and to correlate various imaging features with histopathologic subgroups.*

***Methodology:** Institution-based, cross-sectional, retrospective, descriptive study was done on 25 MRI images of histopathologically proven medulloblastoma cases, from Jan 2021- Dec 2023. Imaging features on conventional MRI were analyzed to describe imaging patterns and correlate findings with histopathologic subtypes.*

***Results**: 25 histopathologically confirmed medulloblastoma cases were included in the study. 13 were male and 12 were female. The mean age was 10 years ranging from 1-40 years, out of which four were adult patients. Out of the 10 cases that had available histopathologic subtype reports, 7 had classic histology, 2 were desmoplastic nodular and 1 was anaplastic. 40 % of tumors were located in the midline. Hemispheric location was commonly seen in adult medulloblastomas. Medulloblastoma had heterogenous T2W signal intensity with the presence of internal hemorrhage, calcification, cysts, cavities, and necrosis. Enhancement is variable ranging from weak, patchy to strong and solid. 32% of cases had evidence of leptomeningeal seeding at presentation. Leptomeningeal deposits can have a different appearance from the primary tumor in terms of diffusion restriction patterns. There was no statistically significant relation between MRI imaging features and histopathologic subtypes.*

***Conclusion**: The result of our study suggests hemispheric location is commonly seen in adult medulloblastomas. Leptomeningeal seeding is common and can show no diffusion restriction. Histopathologic subtypes are not uniformly reported in the pathology reports in our institution and should be a standard practice, considering differences in prognosis and treatment options among different subtypes. This study should serve as a preliminary report and prospective, multicentric cohort study should be done to further characterize imaging patterns of the different histopathologic and molecular subtypes as well as identify additional imaging biomarkers which can help predict subtypes.*

***Keywords- Medulloblastoma, Histopathologic subtypes, MRI, Imaging pattern***

# 1. Introduction

## 1.1- Background information

Central nervous system (CNS) cancers are the most common solid organ tumors in children[1]. Particularly in the first decade, the incidence of posterior fossa tumors is the highest. The majority of these tumors are medulloblastomas, ependymomas, and pilocytic astrocytomas [2]. A previous study done in Tikur Anbessa Specialized Hospital showed that the commonest brain tumor in the pediatric age group was medulloblastoma, followed by astrocytoma and craniopharyngioma. These children have a poor survival [3].

Medulloblastoma is a malignant, WHO grade IV embryonal tumor composed of densely packed, small round cells. These tumors can be classified into different histologic subtypes namely; Classic, desmoplastic nodular, Medulloblastoma with extensive nodularity, and large cell / anaplastic medulloblastoma. Additionally, they are classified into different subgroups defined by DNA methylation or transcriptome profiling, which include medulloblastoma, WNT-activated; medulloblastoma, SHH-activated and TP53 wild-type; medulloblastoma, SHH-activated and TP53-mutant; and medulloblastoma, non-WNT/non-SHH[4]. These subgroups have been shown to have distinct origins, demographics, molecular alterations, and clinical outcomes. The persistent mortality rates and serious side effects of non-targeted cytotoxic therapies indicate a need for more refined therapeutic approaches[5].

On imaging, medulloblastomas have variable features and prior studies have proposed that these phenotypic radiologic features may reflect underlying differences in tumor biology[6]. Distinctive MRI findings have been found to correlate with medulloblastoma subtypes[7]. This can be of benefit when genetic analysis is not available.

## 1.2 Statement of problem

To my knowledge, despite extensive research elsewhere in the world, the imaging patterns of medulloblastoma, the commonest pediatric posterior fossa mass, have not been studied in the Ethiopian population. In TASH genetic transcriptome profiling and immunohistochemistry are not available and the classification of medulloblastoma subtypes remains to be histopathology based. Hence, this study aims to describe imaging patterns of medulloblastoma in children and adults and to evaluate whether differentiation among histopathologic subtypes is possible based on imaging features.

# 2. Literature review and significance of the study

## 2.1- Literature review

Medulloblastomas are the most common malignant brain tumor in children constituting around 20% of all pediatric brain tumors. They are 10 times more likely to be diagnosed in children than adults, particularly in the ages 1-9 years [8]. They are WHO grade IV tumors grouped under the embryonal tumor category [4, 9].

The classification of medulloblastomas has come a long way since the first WHO Blue Book, continuously being modified to mirror new knowledge of their clinical and biological

heterogeneity. The histopathological classification of medulloblastoma, first recognized in the 2007 edition of the WHO Classification of Tumors of the Central Nervous System, comprised 4 morphologic types: classic, desmoplastic/nodular, medulloblastoma with extensive nodularity (MBEN), and Large cell/anaplastic. Later in 2016, molecular classification was introduced, which is more predictive of clinical behavior and outcome than either tumor histology or clinical staging system[6]. Nonetheless, the morphologic classification is not completely outdated. The current recommendation is reporting in a layered and integrated format, combining the histopathologic and molecular features, as these histologic and molecular subtypes have variable origins, demographics, molecular alterations, and clinical outcomes (9). There are 4 molecularly defined groups: WNT-activated, SHH-activated

(TP53-wildtype/mutant), Group 3 and Group 4 subtypes the latter two collectively called non-WNT/non-SHH subtypes. The histopathologic subgroups have now been combined into one section that describes them as morphologic patterns of an inclusive tumor type, Medulloblastoma, histologically defined. Furthermore, on the 2021 WHO brain tumor classification, through large-scale methylation and transcriptome profiling, new subgroups have emerged having: 4 subgroups of SHH and 8 subgroups of non-WNT/non-SHH medulloblastomas[4, 9].

Molecularly defined medulloblastomas demonstrate distinct associations with the morphologic patterns. For example, The vast majority of WNT-activated medulloblastomas have classic histology with occasional large cell/anaplastic histology[6, 7]. True desmoplastic/nodular medulloblastomas and MBENs align with the SHH molecular group [7, 9, 10]. Most of non-WNT/SHH medulloblastomas are large cell/ anaplastic and classic type variants [10]. The majority of G-3 medulloblastomas are classic histology, but a significant proportion of LCA histology is represented by the G-3 subtype. They are rarely of desmoplastic variant [6].

Among the histopathologically defined medulloblastoma subtypes, classic MB is the commonest in all age groups [7, 11-13], followed by desmoplastic nodular and Large cell/anaplastic [7]. These subtypes have variable origins, biologic behavior, and prognosis. Anaplastic MB has the poorest prognosis [12]. Desmoplastic nodular MB has a favorable prognosis and classic histology has an intermediate prognosis [14]. Molecular subtypes also predict outcome to an even greater extent. For instance, Childhood WNT MB shows a favorable prognosis.

Current treatment for MB consists of maximal safe resection, chemotherapy, and craniospinal radiation[15]. Traditionally, patients with medulloblastomas have been stratified into high or standard/average-risk groups to direct post-surgical adjuvant therapy. Categorization has been based on the extent of disease and resection and has not incorporated molecular subtyping. Standard risk MB should not have metastatic disease, histology should be non-anaplastic and the amount of post-surgery residual must be less than 1.5 $cm^2$ [16]. More recent classification also includes the absence of MYC or MYCN amplification on molecular analysis [15]. High-risk MB fulfills one of the following criteria; Metastatic disease, LC/A histology, and significant residual disease after surgery ( > 1.5$cm^2$) The presence of MYC or MYCN amplification also defines a high-risk MB in recent classifications [15]. Infant medulloblastomas constitute a separate category. The major difference in treatment between a standard and high-risk tumor is the

amount of craniospinal irradiation. The survival rate of average risk MB has been reported to be more than 80%[15]. Considering the long-term neurologic, cognitive, and endocrinologic sequelae of high-dose craniospinal irradiation, there are several ongoing efforts and trials to lower the treatment intensity of low-risk MB, particularly for the WNT subgroup, which has been shown to have a favorable prognosis with a 5-year survival rate of more than 90% despite histologic subtype and metastatic status [15].

MRI is a non-invasive and safe imaging modality and the imaging of choice for diagnosis, surgical guidance, and surveillance of medulloblastomas [17]. CT scan has been superseded by the higher characterization ability of MRI and its role is limited to assessment of hydrocephalus in emergency setup and as a complementary tool to assess attenuation of the tumor, which often appears hyper attenuating reflecting its high cellularity [18]. The appearance of medulloblastoma has been described to be more heterogeneous on MRI, presenting with variable T1 and T2 signal intensity, and heterogenous contrast enhancement owing to cyst formation, hemorrhage, and calcification[19].

Various studies explored conventional MRI features of medulloblastoma in order to identify potential cross-sectional biomarkers for specific histopathologic and molecular subtypes [11, 12, 14, 20-23]. Perreault et.al. were able to accurately predict specific subtypes of medulloblastoma in 66% of the cases using location and enhancement patterns [14].

There are conflicting results from literature, regarding the location of WNT-activated tumors. While Perreault et.al suggested that cerebellar peduncle/ cerebellopontine angle (CP/CPA) location was said to be almost 100% predictive for WNT-activated tumors[14], others argue that these tumors originate in the midline and may lateralize towards the CPA. In addition, they are often located caudally and frequently in contact with the brainstem [10, 24-26] This is in keeping with the hypothesis that they arise from neural progenitors in the dorsal brainstem nuclei, which are more predominantly expressed in the lower rhombic lip [27]. These tumors have also been shown to have smaller size at diagnosis, reflecting their indolent biology [20].

On the other hand, cerebellar hemispheric location is characteristic of SHH tumors. Particularly in adults, hemispheric location is very frequent [7, 14, 25, 28]. These tumors are thought to arise from granule neuron precursor cells in the external granular layer of the cerebellum and have distinct interface with the brainstem [7, 10]. Rostral location abutting the tentorium, multilocularity, and/ or synchronous multifocal tumor at presentation was found to be a specific feature for SHH medulloblastoma[21, 25, 29] The vast majority of G3 and G4 tumors are located in the midline, fourth ventricle [21, 25]. G-3 tumors, having the poorest prognosis, are usually small in size at diagnosis, tend to develop early metastasis, and hence are less commonly associated with hydrocephalus. Ill-defined tumor margin was also characteristic in G3 tumors [6, 7, 14].

Enhancement was one of the highly predictive features. G4 tumors typically show no or minimal enhancement despite prominent intra-tumoral vessels [14, 25], whereas, G3 tumors have extensive contrast enhancement (>75% of tumor volume enhancement)[7].

Dense intra-tumoral blood-degradation products and cysts with blood contents are frequently found and might help to differentiate wingless pathway medulloblastoma [24, 26], while other studies found no association between the presence of mineralization/ hemorrhage, cyst, peritumoral edema, necrosis [14]. Absence of hydrocephalus and macro metastasis has very predictive value for WNT medulloblastoma [20].

### 2.2- Significance of the study

According to a recent Worldometer survey, Ethiopia, one of Africa's largest countries, has a population of approximately 122 million people, the majority of whom are children and young adults. In Sub-Saharan Africa, infections continue to be the most common pathologies encountered in daily practice. However, the prevalence of non-communicable diseases, including neoplastic processes, has gradually increased over the last few decades. This could be due to the expansion of treatment facilities, increasing public awareness, and increased health-seeking behavior. Furthermore, various environmental and genetic factors may play a role, which remains to be investigated further in the future. Brain tumors are the second most common type of childhood cancer after hematologic malignancies.

The most recent WHO 2021 brain tumor classification is primarily focused on molecular brain tumor classifications, which have been proven to have a major impact on prognosis and therapy. Genetic/molecular studies are expensive and not widely available. Particularly in a resource-limited set up like ours, all efforts should be made to utilize imaging ( including brain MRI and spine MRI) as well as histopathologic information at hand, to be able to accurately stratify patients and choose appropriate treatment.

## 3. Objectives

### 3.1- General objectives

-To describe imaging patterns of medulloblastoma on MRI

### 3.2- Specific objectives

- To describe imaging patterns of medulloblastoma on MRI

- To correlate MRI imaging features of medulloblastoma with histopathologic subgroups

## 4. Methodology

### 4.1- Study setting

The study was conducted at Tikur Anbessa Specialized Hospital ( TASH), radiology department, Addis Ababa, Ethiopia. TASH is under the College of Health Sciences campus of AAU, which is one of the pioneer universities in the country. The hospital is a tertiary level referral and teaching hospital providing service to people from all corners of the country in its various departments such as internal medicine, surgery, gynecology and obstetrics, pediatrics, radiotherapy, adult oncology, pediatric oncology /hematology, nuclear medicine, psychiatry, laboratory, orthopedics, pharmacy, etc. It gives undergraduate, postgraduate, and several subspecialty training programs in medical and health sciences. The radiology department is equipped with a 128-slice GE CT scanner, 64 64-slice Philips Optima CT scanner, a 1.5T Philips Achieva MRI machine, 3 XRAY machines, and an adult and a pediatric ultrasound unit with 10 Ultrasound machines.

### 4.2- Study design

A hospital based cross sectional retrospective study was done at Tikur Anbessa specialized referral and teaching hospital, Radiology department.

### 4.3- Study duration

This took place from Jan 2023 – Dec 2023.

## 4.4-population

### 4.4.1 – Source Population

All patients who are diagnosed with medulloblastoma at TASH on histopathology basis.

### 4.4.2- Study Population

All patients who are diagnosed with medulloblastoma on histopathology and have pre-operative MRI during period of Jan 2021- Dec 2023

## 4.5- Eligibility criteria, inclusion criteria, exclusion criteria

### 4.5.1 - Eligibility criteria

All patients who are diagnosed with medulloblastoma on histopathology during period of Jan 2021- Dec 2023 with available pre-operative MRI.

### 4.5.2- Inclusion criteria

All patients who are diagnosed with medulloblastoma on histology during period of Jan 2021- Dec 2023 with available pre-operative MRI.

### 4.5.3- Exclusion criteria

Patients with no pre-operative MRI, poor image quality of pre -operative MRI due to poor image quality.

## 4.6- Sampling size and sampling technique

A consecutive sampling technique was used.

## 4.7- Data collection procedure

Patients with histopathologic diagnosis of medulloblastoma in the period of Jan 2021- Dec 2023 were identified from the pathology department registry ( MS Access). 43 patients had histopathology diagnosis of medulloblastoma at TASH, Pathology department. Pre-operative images of the patients were collected from neuroradiology fellows and neurosurgery archives. Demographic data was acquired from patient medical records and or imaging files. Pre-operative MRI image datasets were retrospectively analyzed by the investigator, blinded to histopathology subtypes. MRI features including location, T2 signal intensity, DWI/ADC appearance, degree and pattern of contrast enhancement, presence of cyst/cavities/necrosis, hemorrhage/calcification, tumor margin, leptomeningeal seeding, size of the mass, extension through foramen of Luschka or Magendie, hydrocephalus, and perilesional edema are recorded on a structured questionnaire and entered into SPSS Statistics 25.0. If head CT and spinal MRI images are available, it was also reviewed for additional information including attenuation, presence of calcification, and spinal seeding. Data on histopathologic subtypes into classic, desmoplastic/nodular, medulloblastoma with extensive nodularity, and large cell / anaplastic subtypes was retrieved from pathology reports, when available.

## 4.8- Study Variables:

- Gender
- Age
- Location [ Midline, Hemisphere ,CPA/CP]
- Foraminal extension [ foramen of Luschka and Magendie]
- Three dimensional size of tumor and volume

- Tumor Margin
- T2 signal homogeneity
- Pre dominant T2 signal of solid component.
- Presence of Cyst /cavity/necrosis
- Presence of hemorrhage/ calcification
- DWI/ADC appearance
- Pattern of enhancement [ homogenous, heterogenous]
- Degree of enhancement [ none, weak, strong]
- Extent of Enhancement [ none, patchy, solid]
- Leptomeningeal seeding [Supratentorial, Infratentorial, Spine]
- Presence of hydrocephalus
- Presence of edema
- CT attenuation
- Medulloblastoma histopathologic subtype

### 4.9- Data processing and analysis

Data was entered into IBM SPSS Statistics 25.0. Descriptive analysis including frequency, mean and median was performed. One-way ANOVA and Fischer's exact test were used to assess the relation of imaging patterns with histopathology subtypes. P-value of 0.05 was taken as a cut-off for statistical significance.

### 4.10- Dissemination of result

The results of this study will be published in a reputable journal. It will also be discussed during clinico-radiology-pathology interdepartmental joint session.

## 5- Ethical considerations

Data collection was commenced after ethical clearance was obtained from the ethical review committee of the Department of Radiology at TASH. On the data collection form, anonymity will be assured by omitting the names of patients. Information about patients will be kept confidential. The need for written consent is waived as the study was partially retrospective.

## 6. Results:

A total of 25 MRI brain imagings of histopathologically proven medulloblastomas were included in the study. Thirteen were Male and twelve were female patients [*Figure 1*].

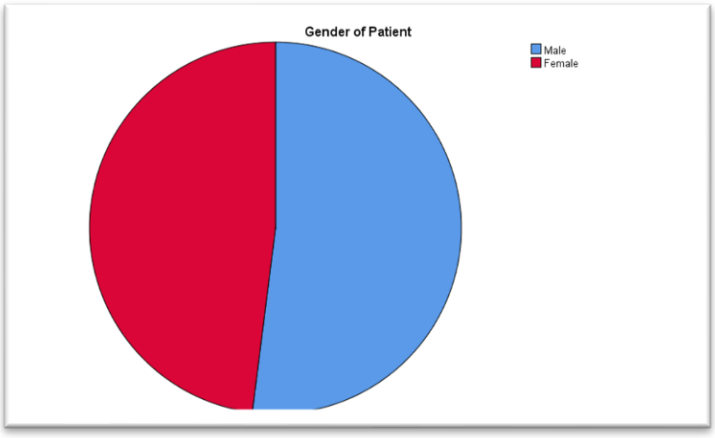


*Figure 1: Gender distribution*

The youngest patient was 1 year and the oldest patient was 40 years old, with a mean age of 10 and median age of 8. There were 4 adult patients. And the remaining were 14 years and younger [ *Figure 2*].

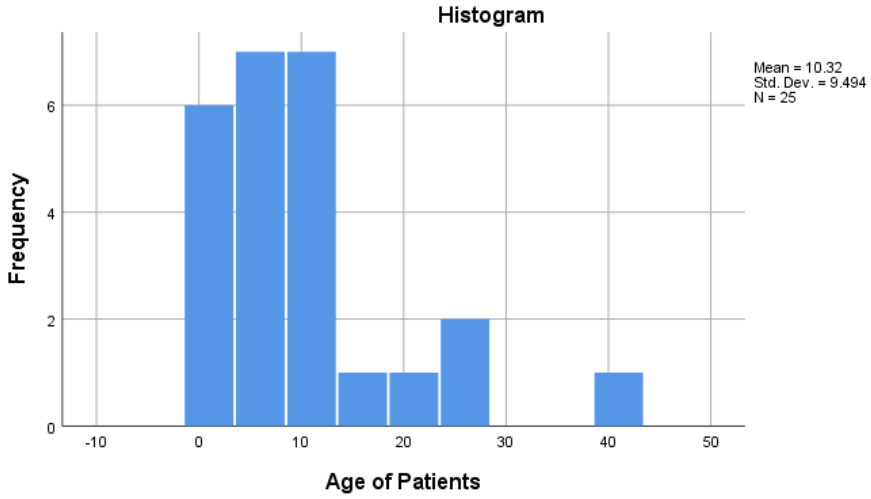


*Figure 2: Age distribution*

From the histopathologic reports, 15 had no subtype specified. 7 were diagnosed with Classic type MB, 2 were diagnosed with desmoplastic nodular MB and 1 had anaplastic histology. Out of 4 adult MB cases, 2 had classic histology and 1 was desmoplastic nodular type[ *Figure 3*].

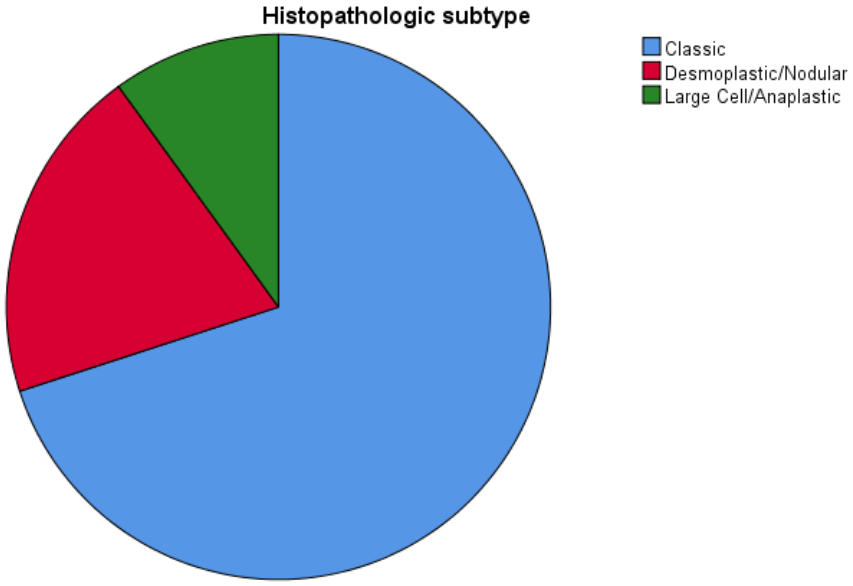


*Figure 3: Distribution of MB histopathologic subtypes among available subtype reports*

Mean AP, CC, and Transverse tumor dimensions were 4.8cm, 5.1cm, and 4.8cm. The maximum dimension of the largest tumor was 8cm and the mean tumor volume was 65 cm3.
20/25 ( 80%) of cases had tumor involving the midline vermis/ 4th ventricle, out of which 10( 40%) had purely midline tumor. The remaining 10 cases had extension to either the cerebellar hemisphere ( 6/10) or to the cerebellopontine cistern/ cerebellar peduncle ( 4/10). There was one case that had purely Cerebellopontine angle location[ *Table 1]*.

| Independent Variable | | N | % | Histopathology | | | | Fischer's exact test p-Value |
|---|---|---|---|---|---|---|---|---|
| | | | | Classic | DN | LC/ A | No subtype | |
| **Gender** | Male | 13 | 52 | 3 | 1 | 1 | 8 | 1.00 |
| | Female | 12 | 48 | 4 | 1 | 0 | 7 | |
| **Location** | Midline | 10 | 40 | 3 | 1 | 0 | 6 | 0.09 |
| | Hemisphere | 1 | 4 | 0 | 1 | 0 | 0 | |
| | CPA/ CP | 1 | 4 | 1 | 0 | 0 | 0 | |
| | Midline and Hemisphere | 4 | 16 | 3 | 0 | 0 | 1 | |
| | Midline and CPA/CP | 6 | 24 | 0 | 0 | 1 | 5 | |
| | Hemisphere and CPA/CP | 3 | 12 | 0 | 0 | 0 | 3 | |
| **Foraminal extension** | None | 11 | 44 | 5 | 1 | 0 | 5 | 0.129 |
| | Foramen of Luschka | 7 | 28 | 0 | 0 | 1 | 6 | |
| | Foramen of Magendie | 1 | 4 | 1 | 0 | 0 | 0 | |
| | Both | 6 | 24 | 1 | 1 | 0 | 4 | |
| **Tumor Margin** | Ill defined | 10 | 40 | 4 | 1 | 0 | 5 | 0.741 |
| | Well defined | 15 | 60 | 3 | 1 | 1 | 10 | |
| **T2W signal intensity** | Iso intense | 6 | 24 | 2 | 0 | 0 | 4 | 1.00 |
| | Hyper intense | 19 | 76 | 5 | 2 | 1 | 11 | |
| | Hypo intense | 0 | 0 | 0 | 0 | 0 | 0 | |
| **Cyst/Cavity/Necrosis** | None | 1 | 4 | 1 | 0 | 0 | 0 | 0.591 |
| | Minimal | 17 | 68 | 4 | 1 | 1 | 11 | |
| | Large | 7 | 28 | 2 | 1 | 0 | 4 | |
| **Hg/Ca++** | Yes | 14 | 56 | 4 | 1 | 0 | 9 | 0.562 |
| | No | 5 | 6 | 1 | 0 | 0 | 4 | |
| **Degree of enhancement** | None | 0 | 0 | 0 | 0 | 0 | 0 | 0.08 |
| | Weak | 2 | 8 | 1 | 1 | 0 | 0 | |
| | Strong | 23 | 92 | 6 | 1 | 1 | 15 | |
| **Extent of enhancement** | Patchy | 8 | 32 | 3 | 1 | 0 | 4 | 0.689 |
| | Solid | 17 | 68 | 4 | 1 | 1 | 11 | |
| **Perilesional edema** | None | 11 | 44 | 2 | 0 | 0 | 9 | 0.256 |
| | Minimal focal | 11 | 44 | 3 | 2 | 1 | 5 | |
| | Moderate to Marked | 3 | 12 | 2 | 0 | 0 | 1 | |
| **Leptomeningeal seeding** | Yes | 8 | 32 | 2 | 1 | 0 | 5 | 1.000 |
| | No | 17 | 68 | 5 | 1 | 1 | 9 | |

*Hg/Ca++ hemorrhage/ calcification*

*Table 1 : Summary of histologic subtypes of MB and MRI characteristics*

There was a statistically significant association between hemispheric location and age of patients with p value of 0.006. All four medulloblastomas in adults in our study were located laterally in the cerebellar hemisphere, whereas only 4/17 childhood medulloblastomas were located in the hemisphere [ *Table 2*].

| | | **Hemispheric Location** | | **Fischer's exact test p-Value** |
|---|---|---|---|---|
| | | **Yes** | **No** | **0.006*** ** |
| **Age** | **Child** | 4 | 17 | |
| | **Adult** | 4 | 0 | |

*Table 2 : Hemispheric Location in children vs adults*

56% ( 14/25) of cases had extension through either the foramen of Luschka or Magendie.
60% (15/25) of MB in our study had well-defined margin based on T2W images. 19 cases were predominantly hyper-intense on T2W images and 6 cases were iso-intense on T2W images, as compared to the cortex. All of them had heterogenous T2W signal intensity and heterogenous contrast enhancement pattern.
Contrast uptake was strong in 92% of cases, and solid enhancement ( > 90% enhancement of the tumor volume) was seen in 17/25 cases. 8/25 cases had only patchy enhancement.
There was evidence of diffusion restriction in all of the cases where optimal quality DWI/ADC images were available. There was one case where DWI images were not optimal enough for interpretation. ADC images were available but value measurement was not available for any of the cases.
Except for one case, all had internal cysts/ cavities/ necrosis. However, only 7/24 had large cystic components.
14/25 cases had susceptibility signal representing either hemorrhage or calcification. The presence of hemorrhage/ calcification could not be assessed in 6 cases, where T2* or SWI sequence was not included in the MRI sequence and CT was not available.
There was evidence of leptomeningeal seeding to either the supratentorial brain, infratentorial brain, or spine in 8/25 cases. Spine images were not available in 19 cases. Hydrocephalus was present in all cases. Minimal ( perifocal) edema was noted in 11/25 cases and only 3 had marked perilesional edema.
There were no statistically significant associations identified between the three histopathologic subtypes and gender, age, location, tumor margin, T2 signal intensity, presence of cyst/cavity/necrosis, presence of hemorrhage /calcification, degree and extent of enhancement, presence of perilesional edema and presence of leptomeningeal seeding.

## 7. Discussion

This study evaluated conventional MRI features of medulloblastoma in children and adult patients. They occur in childhood and adolescence with the incidence markedly decreasing in the second and third decades of life[30]. In this study, patient age ranged from 1 year to 40 years, with a mean age of 10.3 years, this was slightly higher than Hussein et.al, who found the mean age to be 8.97 years [12].This could be explained by the four adult patients included in this study. In the pediatric population, the mean age of classic medulloblastoma was 6.8 years which is comparable to prior studies[31]. Higher mean age ( 12.6years) was reported in other studies which included both adults and children[23]. The median was 8 years which was similar to multiple other cohorts [11, 14].

There was a nearly similar sex distribution with only a slight male predominance ( 1.08:1). Medulloblastomas are reportedly more common in male than in female patients with a male to female ratio of 1.5-2: 1[8, 12, 30, 31]. The smaller male to female ratio in our case is likely due to the small sample size.

Among the known histologic subtypes in this study, the majority were classic MB [ 7/10], similar to prior cohorts which reported 60-80% of medulloblastomas had classic histology [7, 11-13] . These tumors have been described to be typically midline/ fourth ventricular, well delineated, slightly T2 hyper intense tumors[18]. Interestingly, we found one case of classic medulloblastoma primarily located in the cerebellopontine angle, possibly extra axially [ *Figure 4* ]. There are multiple reports of CPA medulloblastoma and most ( 43%) have classic histology[32, 33]. It has been proposed that they may arise from residue in the external granular layer of the cerebellar hemisphere, specifically the flocculus facing the CPA. They can also emerge from the proliferation of the lateral medullary velum germinal residues, then protruding into the CPA[33].

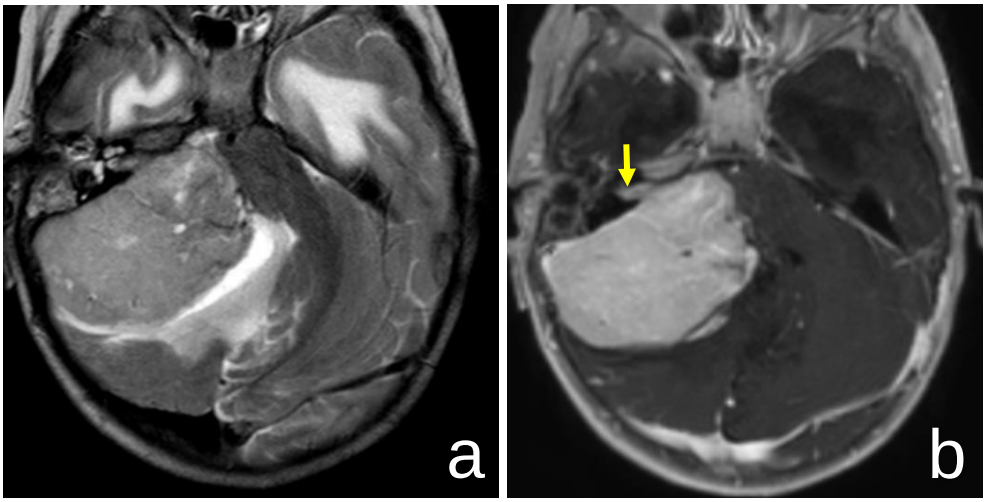


*Figure 4: T2W (a) and CE T1 axial (b) images of a 3 year old with classic medulloblastoma in the right cerebellopontine cistern. Note the extension in to the right intenral auditory canal ( arrow in b), an imaging feature previously described in vestibular schwannomas.*

In or study, 80% of MB were located in the midline, with or without lateral extension into the cerebral hemisphere and CPA. This was similar to previous studies which showed, that

medulloblastomas arise in the midline in 75-90% of cases, thought to arise from the posterior medullary velum, and grow from the inferior vermis into the fourth ventricle[18, 31], Although no single tumor feature should be used alone to determine tumor subtype or tailor treatment, we found a statistically significant relation between hemispheric location and adult medulloblastomas, with Fisher's exact test P-value of 0.006. Adults are more likely to have heterogeneous cerebellar hemisphere tumors[18], and this is thought to be related to the greater prevalence of desmoplastic tumors in adulthood[34]. In one study, one out of the two desmoplastic nodular medulloblastomas were located in the cerebellar hemispheres[31].In another series, out of 8 hemispherically located medulloblastomas, 7 were adults and all had desmoplastic nodular histology[23]. In our study, the oldest patient, a 40-year-old , had a hemispheric desmoplastic nodular medulloblastoma[ *Figure 5*].

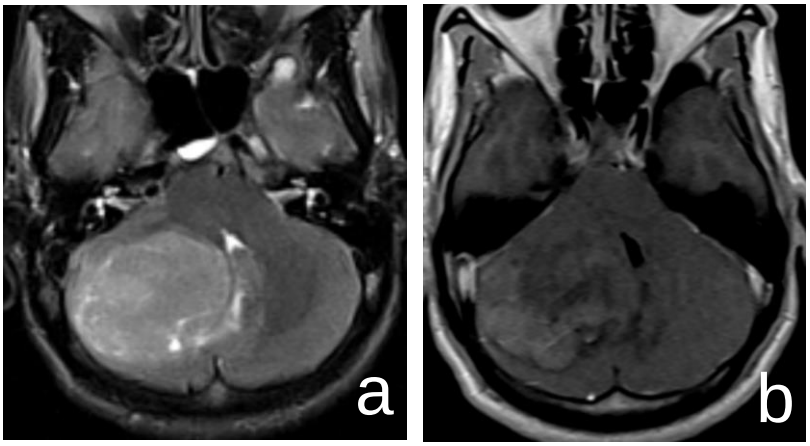


*Figure 5: T2W (a) and CE T1 axial images(b) of a 40 year old with desmoplastic nodular medulloblastoma: heterogenous,T2 hyper intense mass in the right cerebellar hemisphere having weak, patchy contrast enhancement.*

We observed that 56% of MB cases extend through either the foramen of Luschka or foramen magendie. Tumor extension through the fourth ventricle outflow foramina has been well described as an imaging feature suggestive of ependymomas[35]. However, MBs can also grow into and fill the fourth ventricle and may extend through the Magendie's and Lushka's foramina[12, 31]. This finding highlights the fact that foraminal extension is not a specific finding in ependymomas, and other posterior fossa masses, including medulloblastoma, can have similar growth if they attain large enough size [ *Figure 6*].

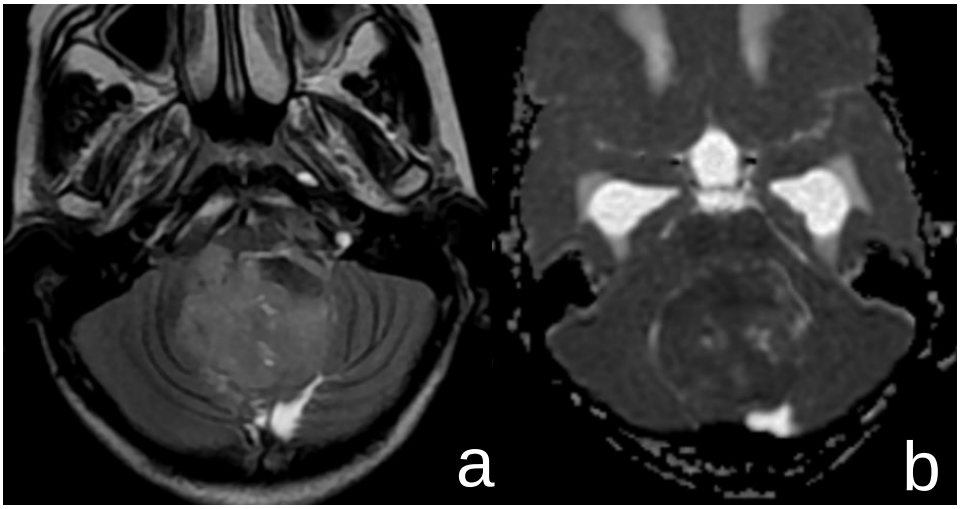

*Figure 6: T2W( a) and ADC ( b) images of 13 year old with medulloblastoma ( subtype not specified) shows a T2 hyper intense midline/ 4$^{th}$ ventricular mass extending through the right foramen of Luschka. Note the low ADC values characteristically seen in all cases in this series.*

32% of the cases had evidence of dissemination at initial diagnosis. Similar findings have been mentioned in previous studies. 20%-35% of patients with medulloblastoma present with metastatic disease at diagnosis [(25)]. However, the incidence of leptomeningeal seeding may have been underestimated in our study, as spinal imaging was not available in the majority of patients. Of the eight patients with imaging evidence of leptomeningeal seeding, 2 were classic MB, 1 was desmoplastic nodular MB, and 5 had no subtype specified. Prior reports concluded that leptomeningeal seeding is positively correlated with Large cell/anaplastic histology[(11)]. The only anaplastic medulloblastoma in our series did not have leptomeningeal seeding, at least intracranially. However, an initial spine MRI was not available for this case.

Intracranial leptomeningeal seeding patterns seen in this study include ependymal nodular enhancement, leptomeningeal linear and nodular enhancement as well as separate parenchymal nodules [ Figure 7]. All the metastatic lesions showed contrast enhancement. Despite all of the primary tumors in our study showing diffusion restriction, intracranial deposits in two of our cases did not show diffusion restriction [ Figure 8]. This finding parallels what has been described by Mata-Mbemba et. al . They found four cases with a ‘mismatch pattern of metastasis’, which is when the metastatic lesion showed diffusion restriction but no/minimal postcontrast enhancement. They also found four cases of leptomeningeal deposits showing contrast enhancement but no diffusion restriction, similar to ours. These findings were commonly seen in Group 4 MB [(25)], Our findings may still need further validation with ADC value measurements but highlight the importance of combining both contrast-enhanced images and DWI/ADC mapping for detection of seeding in medulloblastoma.

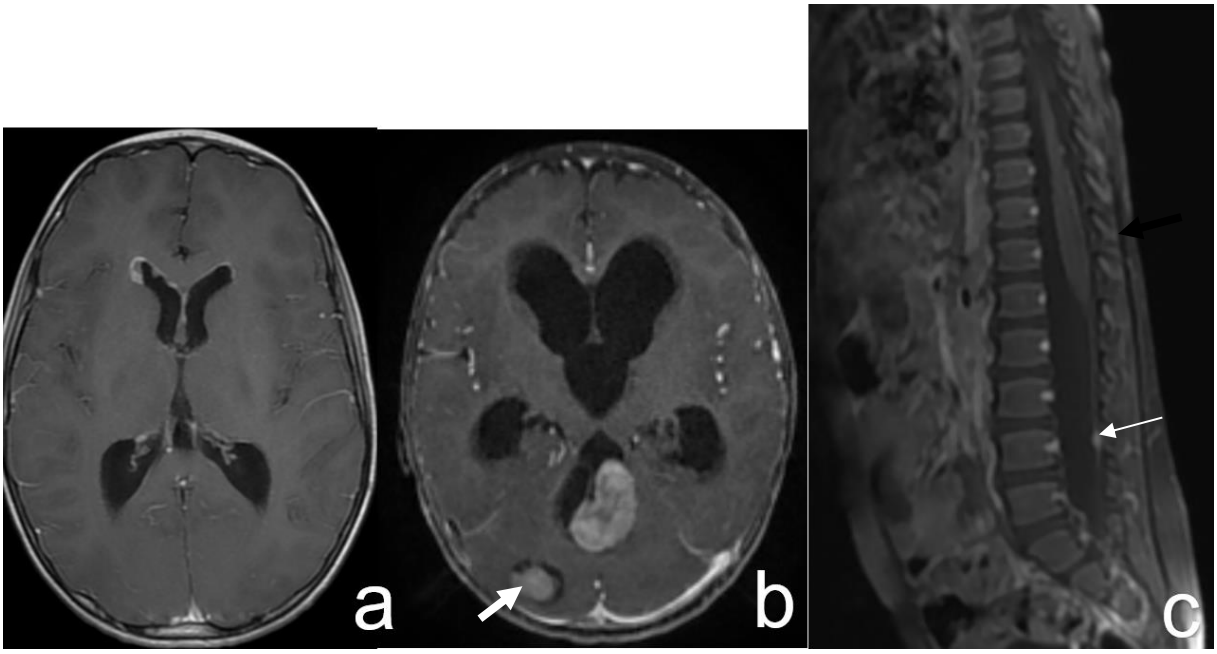


*Figure 7: different patterns of leptomeningeal seedng in medulloblastoma. CE T1 axial image of 9 year old with unknown subtype showing nodular ependymal deposits alog frontal horns of bilateral lateral ventricles (a), CE T1 axial image shows a separate parenchymal nodule ( white arrow) in addition to the larger primary midline mass(b), CE T1 sagittal image of the lumbar spine shows linear enhancement ( sugar coating) along the distal cord ( black arrow)and nodular deposit along the cauda nerve root ( thin white arrow) (c).*

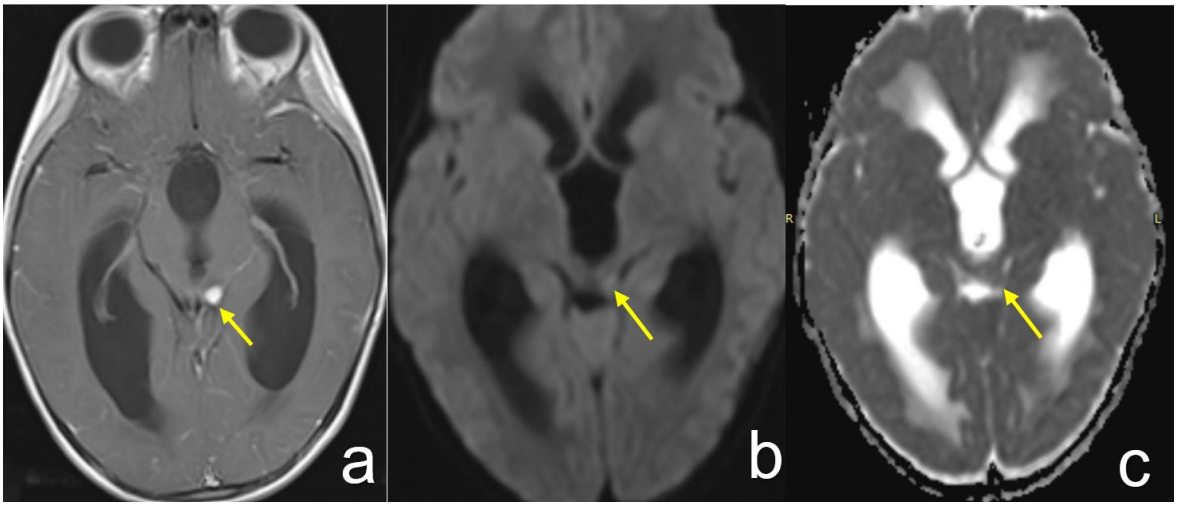


*Figure 8: Contrast enhanced T1 axial ( a) , DWI( b) and dADC (c) images of a 4 year old with medulloblastoma ( subtype unknown), showing an enhancing leptomeningeal nodular drop metastasis in the left ambient cistern, with slightly hyper intense signal on DWI but iso intense signal on ADC map ( arrows) suggesting absence of diffusion restriction on visual inspection. The primary mass showed diffusion restriction( not shown here).*

76% of the cases in our study had hyper-intense signal intensity on T2W images. 24% had iso-intense signal intensity and there was no T2 hypo intense MB in our series, consistent with

Fruehwald-Pallamar et. al.[31]. Iso intense signal on T2W image was previously described in relation to desmoplastic nodular and MB-EN, which was thought to represent higher cellularity. In our series, 2/6 cases having T2 iso intensity had classic histology however, the histologic subtype was not known in 4 cases.
MB are generally heterogenous tumors with internal calcification, hemorrhage, necrosis, and cystic components[11, 31]. 14/25 cases had susceptibility signal on T2* or SWI sequences representing either hemorrhage or calcification.

Hemorrhage/calcification, degree and extent of enhancement, perilesional edema and the presence of leptomeningeal seeding did not show any correlation with specific histopathologic subtypes. This may be due to the small sample size and unequal distributions between the number of each histologic type in this study and the unavailability of information on histopathologic subtype in 15/25 ( 60%) of the cases.

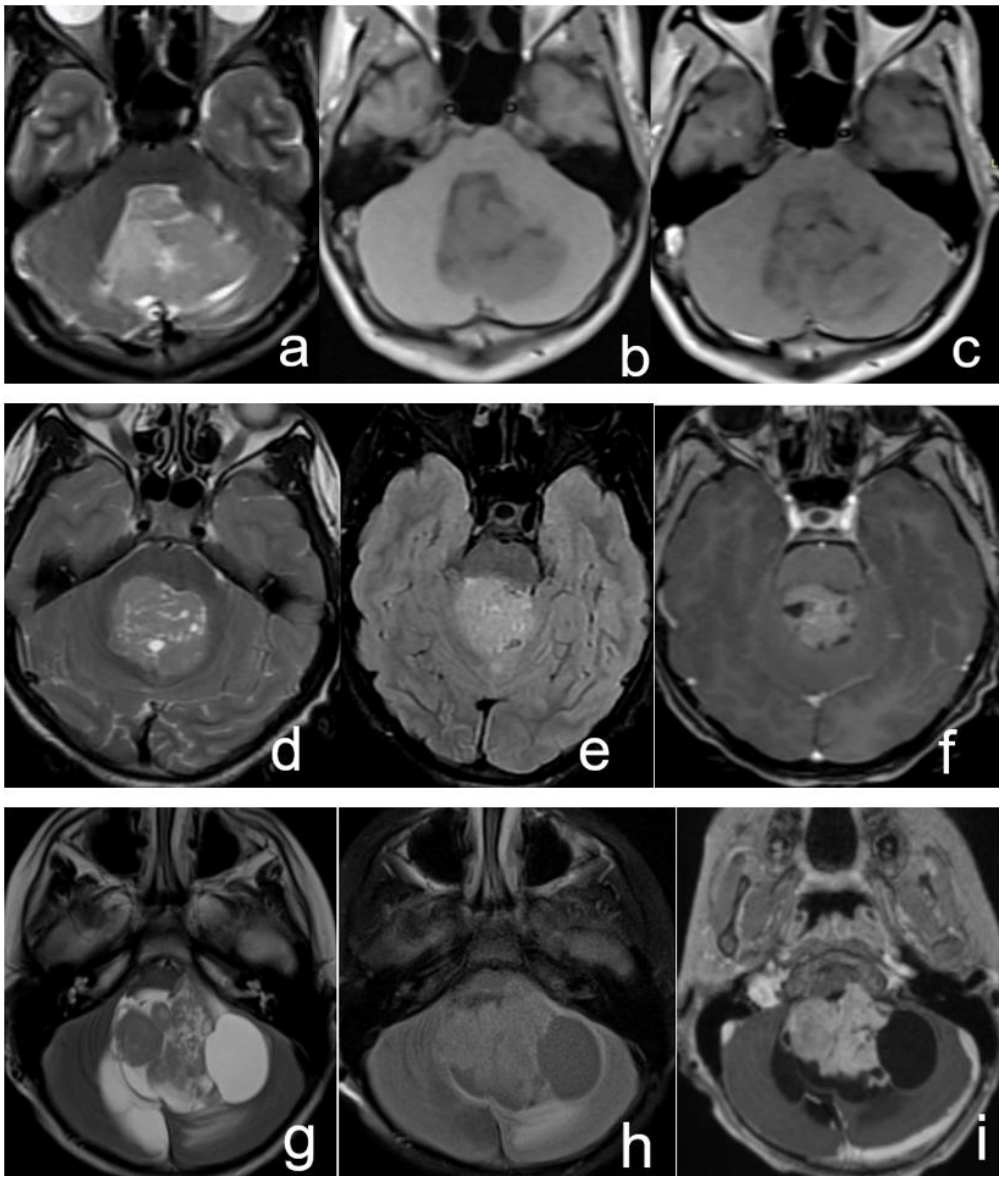

*Figure 8: Examples of MRI features of medulloblastomas:*
*(a,b,c )T2W, T1W, CE T1W axial images of a 22 year old with classic MB, showing a midline T2 hyper intense mass with ill-defined margins and weak contrast enhancement.*

*(d,e,f)T2W, FLAIR, CE T1W images of a 6 year old with MB (unspecified subtype) showing well defined T2 hyper intense midline mass with intense heterogenous contrast enhancement and multiple internal small cysts.*

*(g,h,i)T2W, FLAIR, CE T1W images of a 5 year old with classic MB showing a large, lobulated midline and hemispheric mass with large cysts and iso intense signal on T2 and intense heterogenous contrast enhancement*

This study was limited by its retrospective nature. We were unable to retrieve nearly half of the imaging studies of patients who were diagnosed with medulloblastoma, as most imagings are done at outside institutions due to the unavailability of MRI machines at TASH. In addition, pathology reports were not uniform, in that, most reports did not include histopathology subtypes. Spine image was not available for the majority of patients which might underestimate the incidence of leptomeningeal seeding at presentation. In addition, some heterogeneity in imaging protocols reduced the sample size for some components of our analysis, particularly diffusion-weighted sequences, and susceptibility/ T2* sequences.

## 8. Conclusion and Recommendation

Medulloblastomas have heterogeneous and variable imaging patterns. Hemispheric location is more commonly seen in adult medulloblastomas. One-third of patients have leptomeningeal seeding at presentation. Leptomeningeal deposits can have variable diffusion patterns which may differ from the primary mass. Contrast-enhanced images and DWI images should be used together to detect leptomeningeal deposits. Histopathologic subtypes are prognostically crucial in patient management, however, such data could not be obtained from pathology reports in the majority of the subjects. Pathology reporting should be standardized to at least uniformly include histopathologic subtypes. Efforts should be made to equip the institution with MRI so that all patients will get their imaging in one place. Pre-operative spine imaging should also be part of standard pre-operative protocol. This study shall serve as a preliminary report and further prospective multicentric cohort study should be done using a larger sample size in order to identify possible imaging biomarkers to predict histopathologic and molecular subtypes.

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