

Non-contrast MRI Surveillance of Craniopharyngiomas using a balanced steady state free precession (bSSFP) sequence

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ABSTRACT

BACKGROUND AND PURPOSE: Contrast-enhanced MRI (CEMRI) is a commonly used imaging modality for craniopharyngioma surveillance; however, it carries risks such as allergic reaction and gadolinium deposition. This study evaluates the efficacy of non-contrast enhanced MRI (NCMRI) with a balanced steady state free precession (bSSFP) sequence compared with CEMRI T1-weighted imaging for craniopharyngioma surveillance.

MATERIALS AND METHODS: 29 craniopharyngioma patients (16 female/13 male, mean age=21.5± 4.3 years) with CEMRIs including a bSSFP sequence were evaluated. For each patient, 2 blinded neuroradiologists compared the dimensions of residual craniopharyngioma on noncontrast and contrast-enhanced sequences. Tumor volume and solid/cystic component measurements were evaluated using paired t-tests. Diagnostic confidence levels for NC- and CE evaluations were measured using a 3-point scale (2=confident,1=adequate,0=unsure). Analyses of tumor involvement of cranial nerves and adjacent vasculature and diagnostic confidence were performed using Fisher's exact and chi-square tests.

RESULTS: No significant difference was observed between residual tumor volumes in both studies (18.86±21.67 cm³ vs 17.64±23.85 cm³, p=0.55) and measurements of dominant solid component volume, number of cystic components, and largest cystic component volume (2.71±3.47 cm³ vs 3.95±5.51 cm³, p=0.10; 2.5±1.5 vs 2.9±1.5, p=0.10; 7.61±13.41 vs 6.84±13.37 cm³, p=0.22, respectively). Tumoral involvement of cranial nerves II (p=0.64), III (p=0.42), and adjacent vasculature (p=0.05) showed no significant differences in detection. Diagnostic confidence was comparable evaluating cranial nerve II, vascular structures, and third ventricle (p>0.05) involvement. Higher levels of confidence were observed with bSSFP sequences for detection of cranial nerve III involvement (p=0.0001) and with ce-T1W for cavernous sinus involvement (p=0.02).

CONCLUSIONS: NCMRI techniques using a bSSFP sequence provides similar characterization of craniopharyngiomas as contrast enhanced techniques.

ABBREVIATIONS: 3D DRIVE, 3-dimensional driven equilibrium; ACA, anterior cerebral artery; bSSFP, balanced steady-state free precession; ce-T1W, contrast-enhanced T1-weighted imaging; CN, cranial nerve; GTR, gross total resection; STR, subtotal resection

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SUMMARY SECTION

PREVIOUS LITERATURE: Craniopharyngiomas are rare, benign brain tumors accounting for 1-3% of all brain neoplasms. CEMRI is the standard imaging protocol for detecting and monitoring the tumor. Post-treatment, patients undergo frequent ce-T1W imaging for tumor surveillance. Repeated exposure to gadolinium-based contrast can risk accumulation of free gadolinium in the brain parenchyma, which may have an impact on patients' neurological functions. The use of a bSSFP sequence has shown promise as an alternative to standard brain tumor surveillance. To date, our study is the first to evaluate the efficacy of bSSFP in craniopharyngioma surveillance in comparison to the conventional ce-T1W imaging.

KEY FINDINGS: Our study found that the bSSFP sequence performed comparably to ce-T1W for assessing the presence of residual craniopharyngioma and its involvement of surrounding structures. Similar diagnostic confidence was reported between the 2

sequences. bSSFP also provided higher diagnostic confidence for tumor involvement of cranial nerve III.

KNOWLEDGE ADVANCEMENT: Our study suggests that bSSFP can serve as an alternative for craniopharyngioma surveillance due to its high diagnostic accuracy, cost-effectiveness, and lack of gadolinium exposure. The sequence can be especially useful for monitoring craniopharyngioma in pediatric patients and patients with impaired renal function.

INTRODUCTION

Craniopharyngiomas are rare, benign brain neoplasms that account for approximately 1-3% of all brain tumors. [1] They originate from residual embryonic tissue within the squamous epithelium of the primitive pharynx and are typically found in the sella and suprasellar regions of the brain. [2] Contrast-enhanced MRI (CEMRI) is the standard protocol for imaging craniopharyngiomas at both baseline detection and for continued surveillance both during and after treatment. [3] As such, patients with craniopharyngiomas undergo frequent contrast-enhanced T1-weighted imaging (ce-T1W). The current protocol for imaging surveillance following the initiation of radiotherapy is a CEMRI every 3 months for the first year, followed by intervals of every 4-6 months up to 2 years, transitioning to annual scans, thereafter. [4]

Recent studies have shown that free gadolinium can accumulate in the brain parenchyma, raising concerns about the safety of recurrent contrast use. [5,6] These findings have prompted healthcare professionals to exercise increased caution when ordering contrasted studies, particularly since the long-term impact of gadolinium deposition remains unknown. This is especially relevant for pediatric patients who undergo repeated exposure to contrast for tumor surveillance. [7]

Magnetic resonance cisternographic imaging has emerged as an alternative approach for brain tumor surveillance. A balanced steady-state free precession (bSSFP) sequence (also known as CISS, FIESTA or 3D DRIVE) is a heavily fluid-weighted sequence with high spatial resolution that has been shown to be effective at evaluating cranial nerves and cisterns. [8,9] Previous work has demonstrated the effectiveness of bSSFP for evaluation and surveillance of various brain tumor types in comparison to conventional contrast-enhanced MRI. [9–11] A notable advantage of the bSSFP protocol is its independence from gadolinium-based contrast, thereby eliminating the risk of contrast deposition and making it more suitable for long-term surveillance.

In this study, we aimed to assess the diagnostic efficacy of a non-contrast enhanced MRI (NCMRI) protocol utilizing the bSSFP sequence for craniopharyngioma surveillance in comparison to conventional CEMRI exams.

MATERIALS AND METHODS

Patient Cohort

This was a retrospective study performed at a single institution that was approved by the Institutional Review Board and was compliant with the Health Insurance Portability and Accountability Act. A total of 29 patients under the age of 19 who had a pathology-proven sellar/suprasellar craniopharyngioma that underwent primary surgical resection between 2008 and 2018 were included in the study. Each patient underwent brain MRI examination with both bSSFP and conventional ce-T1W sequences between 3 to 6 months after surgery.

MRI Protocol

All patients underwent the same MRI protocol, consisting of axial T2-weighted imaging, axial FLAIR, axial susceptibility weighted imaging, axial DWI (including ADC reconstruction from the DWI images), pre-contrast T1-weighted imaging, ce-T1W, and bSSFP. All brain MR exams were performed on 3T scanners at our institution (MAGNETOM Prisma Fit and MAGNETOM Skyra, Siemens Healthineers, Erlangen, Germany).

The ce-T1W and bSSFP sequences were used for image evaluation. The parameters of these sequences are as follows: ce-T1W – TR 14.764 ms, TE 6.364 ms, flip angle 13°, NEX 1, FOV 260 x 260, matrix 0\260\260\0; bSSFP – TR 5.832 ms, TE 2.192 ms, flip angle 65°, NEX 4, FOV 180 x 180, matrix 0\448\256\0. The duration of bSSFP the sequence was 7:29 minutes.

Imaging Evaluation

Two board-certified neuroradiologists, blinded to all other imaging and clinical information, evaluated each patient's brain MRI exams in two rounds separated by greater than two weeks in time. For the first round of evaluation, only non-contrast MRI sequences including the bSSFP sequence were evaluated. The second round utilized post-contrast sequences excluding the bSSFP sequence. This technique of two rounds of imaging-based assessment is in line with techniques previously published in the literature. [9,10] The neuroradiologists evaluated the images together to reach consensus. The order of the patients was randomized for each evaluation session.

The axial, transverse, and craniocaudal dimensions of the residual craniopharyngioma were determined for both sequences. The neuroradiologists were asked to assess their diagnostic confidence for the tumoral involvement of the adjacent structures in each study using a 3-point scale (2=confident, 1=adequate, 0=unsure). This assessment was done for cranial nerve CN II, CN III, cavernous sinus, middle cerebral artery (MCA), anterior cerebral artery (ACA), basilar artery, internal carotid artery (ICA), and the third ventricle.

Statistical Analysis

Tumor volume as well as solid and cystic component measurements were evaluated using paired t-tests. The analysis of diagnostic confidence for tumoral involvement of the adjacent structures was performed using chi-square and Fisher's exact tests.

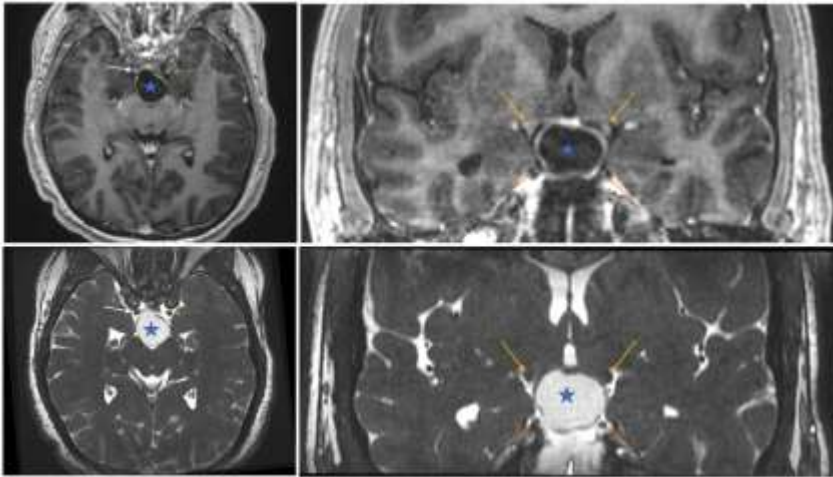


FIG 1. Axial post-contrast T1-weighted (top left) and bSSFP (bottom left) images demonstrate a suprasellar predominantly cystic craniopharyngioma (star). Both sequences demonstrate abutment of the right internal carotid artery by the craniopharyngioma (white arrows). The left internal carotid artery (green arrow) is spared. In the coronal view, both post-contrast T1-weighted (top right) and bSSFP (bottom right) images adequately show the relationship between the craniopharyngioma and the optic tract (orange arrows) and CN III (red arrows), which are not in direct contact.

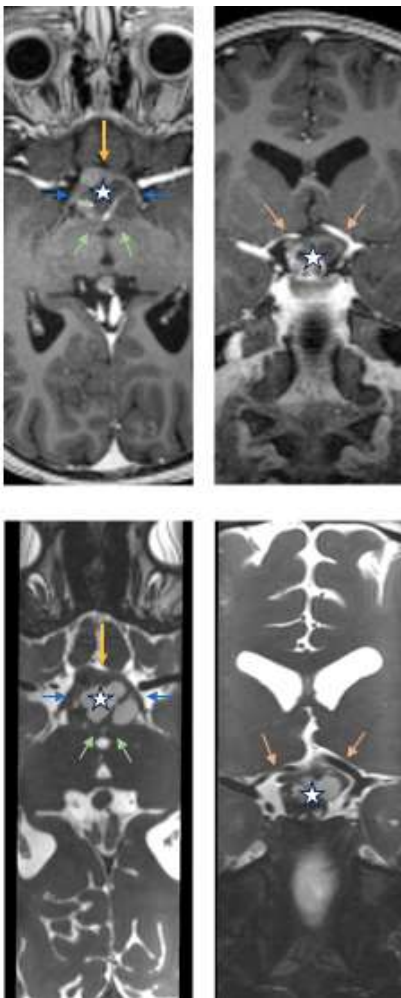


FIG 2. Axial post-contrast T1-weighted (top left) and bSSFP (bottom left) images demonstrate a suprasellar mixed cystic/solid craniopharyngioma (star). Both sequences demonstrate that the lesion abuts the optic chiasm anteriorly (yellow arrow), with splaying of the optic tracts (blue arrow) along the lateral aspects of the craniopharyngioma. Posteriorly, the craniopharyngioma abuts the mamillary bodies (green arrows). In the coronal view, both post-contrast T1-weighted (top right) and bSSFP images (bottom right) demonstrate how the craniopharyngioma is encroaching on, but not in direct contact, with the A1 segments of the anterior cerebral arteries (orange arrows).

RESULTS

Patient Demographics

A total of 29 patients were included in this study (**Table 1**) with 13 (44.8%) males and 16 (55.2%) females. The mean age was 21.5 ± 4.3 years. Approximately 21 (72.4%) patients exhibited the adamantinomatous type of craniopharyngioma, while the remaining 8 (27.6%) patients had an unspecified type. The majority of the patients (27, 93.1%) underwent subtotal resection (STR); meanwhile, gross total resection (GTR) was reported in 2 (6.9%) patients.

Evaluation of Tumoral Size and Involvement

No statistically significant difference was observed between residual tumor volume measured on bSSFP and ce-T1W sequences ($18.86 \pm 21.67 \text{ cm}^3$ vs $17.64 \pm 23.85 \text{ cm}^3$, $p=0.55$; **Table 2**). Similarly, measurements of the dominant solid component volume, the number of cystic components, and the largest cystic component volume demonstrated no significant differences between the two studies ($2.71 \pm 3.47 \text{ cm}^3$ vs $3.95 \pm 5.51 \text{ cm}^3$, $p=0.10$; 2.5 ± 1.5 vs 2.9 ± 1.5 , $P=0.10$; 7.61 ± 13.41 vs $6.84 \pm 13.37 \text{ cm}^3$, $p=0.22$, respectively). Furthermore, the tumoral involvement of CN II ($P=0.64$), CN III ($P=0.42$) and the adjacent vasculature ($P=0.05$) showed no significant differences. **Figures 1 and 2** show two representative craniopharyngioma cases where ce-T1W and bSSP sequences demonstrate similar evaluation of the tumor and its surrounding structures.

Interrater Reliability

The diagnostic confidence was comparable for evaluation of adjacent structures in both studies (**Table 3**). There was no statistically significant difference in the diagnostic confidence for tumor involvement of CN II, MCA, ACA, basilar artery, and the third ventricle between bSSFP and ce-T1W images (93.1 vs 96.6 , $p=0.55$; 100 vs 96.6 , $p=0.31$; 100 vs 96.6 , $p=0.31$; 100 vs 96.6 , $p=0.31$; 93.1 vs 89.7 ; $p=0.64$; 100 vs 93.1 ; $p=0.15$, respectively). Interestingly, a significantly higher level of confidence was observed when bSSFP was used to detect CN III involvement ($p=0.0001$) and ce-T1W images for cavernous sinus involvement ($p=0.02$).

DISCUSSION

Although the diagnostic utility of bSSFP sequences for evaluation and surveillance of skull base tumors has been well-established, its use in craniopharyngioma surveillance has yet to be described. The findings of our study suggest that bSSFP performs comparably to CEMRI for the assessment of craniopharyngiomas after treatment. Given its superior capability to distinguish between soft tissue and CSF within the basal cisterns and ventricular system, along with its high signal-to-noise ratio, bSSFP was able to effectively differentiate residual craniopharyngioma from the surrounding CSF, particularly in the suprasellar region where craniopharyngiomas are commonly found.

Additionally, a bSSFP sequence provides better diagnostic confidence in detecting involvement of CN III by residual craniopharyngioma. The improved confidence and accuracy in assessing tumor involvement can be important in optimizing treatment strategies and minimizing potential complications. [12]

Our observations align with the findings of a previous study that compared the diagnostic confidence in detecting residual germ cell tumors when bSSFP and ce-T1W sequences were used. [9] With its improved contrast and high spatial resolution, bSSFP was able to provide better detection of the tumor in the pineal and suprasellar regions where there is a high volume of CSF. [9] Moreover, this study indicated that the use of bSSFP can significantly improve diagnostic confidence when assessing the presence of residual tumor. [9] An improvement in interrater agreement was also reported with the use of bSSFP (0.872 with bSSFP and 0.128 without bSSFP). Interestingly, the study found that bSSFP can detect small tumor volumes that may be overlooked by ce-T1W imaging. [9] A bSSFP sequence has also been shown to have similar or increased effectiveness for surveillance of other types of brain tumors, such as for the detection of spinal drop metastases in pediatric patients. [10]

Cyst enlargement is a prevalent complication, which can present both during and after radiotherapy and surgical resection that may potentially result in obstructive hydrocephalus and visual deficits secondary to optic nerve compression. [13,14] Given the observed superiority of the bSSFP sequence in assessing the cystic component of tumors, bSSFP can facilitate the early recognition and detection of such complications, which allows proper and timely interventions that improve patient outcomes.

A bSSFP sequence offers additional advantages compared to traditional ce-T1W imaging. These include improved cost-effectiveness, feasibility, and a reduced risk of potential negative health outcomes due to gadolinium deposition. A bSSFP sequence can be considered more cost-effective since intravenous contrast administration is not used. Furthermore, prolonged use of gadolinium-based contrast may risk free gadolinium deposition in brain tissue and increase the risk of nephrogenic systemic fibrosis, especially in patients with reduced renal function or pediatric patients. [15] Additionally, bSSFP is considered more feasible for pediatric patients as obtaining intravenous access can be difficult.

Given the effectiveness and advantages of the bSSFP sequence with its superior spatial and contrast resolution, adopting a non-contrast protocol for craniopharyngioma surveillance is highly recommended, especially for pediatric patients and patients with impaired renal function. Because of the similar performance of bSSFP and ce-T1W for evaluating craniopharyngiomas, the use of both sequences may not be necessary for some patients. While some patients may benefit from the use of both imaging techniques for tumor surveillance, our results suggest that conducting only one of the two sequences can be sufficient for tumor surveillance.

This study's limitations include the small sample size, the lack of long-term follow up, and the retrospective nature of the study. Patients included in this study were 3-6 months post-surgery and thus, the follow-up window was relatively short. More information and a more detailed study are needed to fully investigate the use of the bSSFP sequence for long term follow-up of recurrent or residual tumors. Furthermore, some cases were excluded due to missing information. A prospective study should be conducted in the future to better compare post-treatment tumor surveillance between the two imaging techniques. However, our results provide valuable insight into the optimization of imaging protocols for craniopharyngioma surveillance. Further research with a larger cohort is warranted to validate the efficacy of bSSFP sequence in routine practice.

Table 1. Demographics

Characteristic	Value
Number of patients	29
Age	21.5± 4.3
Sex	
Male	13 (44.8%)
Female	16 (55.2%)
Tumor type	
Adamantinomatous	21 (72.4%)
Craniopharyngioma, Unspecified	8 (27.6%)
Type	
Resection type	
STR	27 (93.1%)
GTR	2 (6.9%)
Cyst Fenestration	7 (24.2%)
Shunt Placement	7 (24.2%)
Cyst Drainage	4 (13.8%)
Complication	
Panhypopituitarism	18 (62.1%)
Diabetes insipidus	9 (31.0%)

STR: subtotal resection; GTR: gross total resection

Table 2. Discrepancies in measurements between bSSFP and ceMRI

	bSSFP	ceMRI	p-value
Residual tumor volume	17.64 ± 23.85	18.86 ± 21.67 cm ³	0.55
Dominant solid component volume	3.95 ± 5.51 cm ³	2.71 ± 3.47 cm ³	0.10
Number of cystic components	2.9 ± 1.5	2.5 ± 1.5	0.10
Largest cystic components	6.84 ± 13.37 cm ³	7.61 ± 13.41 cm ³	0.22
CN II involvement			
Yes	26	27	0.64
No	3	2	
CN III involvement			
Yes	10	13	0.42
No	19	16	
Vascular involvement			
Yes	20	26	0.052
No	9	3	

bSSFP, balanced steady-state free precession; ceMRI, contrast-enhanced MRI

Table 3. Comparative assessment of diagnostic confidence for tumor involvement in adjacent structures

Location of tumor involvement	% diagnostic confidence		χ^2	p-value
	bSSFP	ceMRI		
CN II	93.1	96.6	0.35	0.55
CN III	100	55.2	15.74	0.0001*
Cavernous sinus	65.5	93.1	5.83	0.02*
MCA	100	96.6	1.02	0.31
ACA	100	96.6	1.02	0.31
Basilar	100	96.6	1.02	0.31
ICA	93.1	89.7	0.22	0.64
Third ventricle	100	93.1	2.07	0.15

CN, cranial nerve; MCA, middle cerebral artery; ACA, anterior cerebral artery; ICA, internal carotid artery; bSSFP, balanced steady-state free precession; ceMRI, contrast-enhanced MRI

CONCLUSIONS

This study suggests that non-contrast enhanced MRI using a bSSFP sequence is comparable to contrast-enhanced T1-weighted MRI for craniopharyngioma surveillance. The potential advantages include reduced contrast exposure and improved diagnostic confidence for cranial nerve III involvement.

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REFERENCES

1. Fouda MA, Day EL, Staffa SJ, Scott RM, Marcus KJ, Baird LC. Postoperative MR imaging surveillance of pediatric craniopharyngioma: new institutional guidelines. *Childs Nerv Syst.* 2021;37(3):853-861. doi:10.1007/s00381-020-04901-2
2. Bunin GR, Surawicz TS, Witman PA, Preston-Martin S, Davis F, Bruner JM. The descriptive epidemiology of craniopharyngioma. *J Neurosurg.* 1998;89(4):547-551. doi:10.3171/jns.1998.89.4.0547
3. Müller HL. The Diagnosis and Treatment of Craniopharyngioma. *Neuroendocrinology.* 2020;110(9-10):753-766. doi:10.1159/000504512
4. Lara-Velazquez M, Mehkri Y, Panther E, et al. Current Advances in the Management of Adult Craniopharyngiomas. *Curr Oncol.* 2022;29(3):1645-1671. doi:10.3390/curroncol29030138
5. Nakamura K, McGinley MP, Jones SE, et al. Gadolinium-based contrast agent exposures and physical and cognitive disability in multiple sclerosis. *J Neuroimaging.* 2023;33(1):85-93. doi:10.1111/jon.13057
6. Rasschaert M, Weller RO, Schroeder JA, Brochhausen C, Idée J. Retention of Gadolinium in Brain Parenchyma: Pathways for Speciation, Access, and Distribution. A Critical Review. *J Magn Reson Imaging.* 2020;52(5):1293-1305. doi:10.1002/jmri.27124
7. Buch K, Juliano A, Stankovic KM, Curtin HD, Cunnane MB. Noncontrast vestibular schwannoma surveillance imaging including an MR cisternographic sequence: is there a need for postcontrast imaging? *J Neurosurg.* 2018;131(2):549-554. doi:10.3171/2018.3.JNS1866
8. Cavallaro M, Coglitore A, Tessitore A, et al. Three-Dimensional Constructive Interference in Steady State (3D CISS) Imaging and Clinical Applications in Brain Pathology. *Biomedicines.* 2022;10(11):2997. doi:10.3390/biomedicines10112997
9. Mehan WA, Buch K, Brasz MF, et al. Balanced Steady-State Free Precession Techniques Improve Detection of Residual Germ Cell Tumor for Treatment Planning. *American Journal of Neuroradiology.* 2020;41(5):898-903. doi:10.3174/ajnr.A6540
10. Buch K, Caruso P, Ebb D, Rincon S. Balanced Steady-State Free Precession Sequence (CISS/FIESTA/3D Driven Equilibrium Radiofrequency Reset Pulse) Increases the Diagnostic Yield for Spinal Drop Metastases in Children with Brain Tumors. *AJNR Am J Neuroradiol.* 2018;39(7):1355-1361. doi:10.3174/ajnr.A5645
11. Ozgen B, Oguz B, Dolgun A. Diagnostic accuracy of the constructive interference in steady state sequence alone for follow-up imaging of vestibular schwannomas. *AJNR Am J Neuroradiol.* 2009;30(5):985-991. doi:10.3174/ajnr.A1472

12. Zacharia BE, Bruce SS, Goldstein H, Malone HR, Neugut AI, Bruce JN. Incidence, treatment and survival of patients with craniopharyngioma in the surveillance, epidemiology and end results program. *Neuro Oncol.* 2012;14(8):1070-1078. doi:10.1093/neuonc/nos142
13. Lamiman K, Wong KK, Tamrazi B, et al. A quantitative analysis of craniopharyngioma cyst expansion during and after radiation therapy and surgical implications. *Neurosurg Focus.* 2016;41(6):E15. doi:10.3171/2016.9.FOCUS16298
14. Winkfield KM, Linsenmeier C, Yock TI, et al. Surveillance of craniopharyngioma cyst growth in children treated with proton radiotherapy. *Int J Radiat Oncol Biol Phys.* 2009;73(3):716-721. doi:10.1016/j.ijrobp.2008.05.010
15. Holowka S, Shroff M, Chavhan GB. Use and Safety of Gadolinium Based Contrast Agents in Pediatric MR Imaging. *Indian J Pediatr.* 2019;86(10):961-966. doi:10.1007/s12098-019-02891-x