The utility of routine surveillance screening with magnetic resonance imaging to detect tumour recurrence/progression in children with high-grade central nervous system tumours

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TABLE 1 Characteristics of included studies

Study (year) [ref] Location Years of study	Aim Study design	Population	Intervention	Outcomes reported
Korones et al (2001)[7] USA 1990 – 1999	To determine the frequency of detection of recurrent / progressive brain tumors in asymptomatic children are detected by surveillance MRI scans and to compare the survival of children with asymptomatic recurrence compared to those whose recurrences are detected by symptoms Retrospective case series study	Included: Patients with a brain tumor aged < 21 at diagnosis and for which neuro-imaging surveillance was performed exclusively by MRI. Excluded: Patients with spinal cord tumors or children followed by CT scans. Tumor type: both low and high-grade tumors, including 33 (72%) *recurrent* high-grade tumors including: - HGG (anaplastic astrocytoma, glioblastoma multiforme): n=10 (30%) - Brainstem glioma: n=7 (21%) - sPNET: n=5 (16%) - MB: n=4 (12%) - Epend: n=4 (12%) - CPC: n=1 (3%) - GCT: n=1 (3%) - AT/RT: n=1 (3%) N = 112 (although paper focuses exclusively on the 46 recurrent patients) Male: 45% Median age at diagnosis (n=46): 6.5 years (0.25 – 21) Median age at recurrence for 33 high grade patients: 6 years (0.25 – 21) Average follow-up: NR Tumor location: NR Previous treatment(s): - Surgery: n = NR	Surveillance MRI. Details: • MRI scanner: No details. • Image sequences taken: No details • Imaging schedule: 1 scan every 2.5 mths (range 1/1 mth to 1/ 6.7 mths). • Average number of MRI images per patient: NR for high-grade tumor patients only Surveillance MRI: "Scans done ≥1 month after surgery (or >1 month after the original diagnostic MRI if diagnosis was by MRI only) were considered surveillance scans. Immediate post-operative MRI scans were not considered surveillance scans."	• Recurrence by symptomatic status • Median time from diagnosis to recurrence by tumor grade • Median OS by symptomatic status for all patients • Median OS for symptomatic status for high grade tumor patients • Overall survival (n=46) • 2-year OS from time of recurrence by symptomatic status
Kornreich et al (2005)[8] Israel 1985 - 2001	To describe the MR findings of pontine tumors at diagnosis and during follow-up and correlate those with prognosis and to assess the value of MR imaging in	Included: Patients with a DIPG "according to the classification of Barkovich et al (center of the mass in the pons, involving >50% of the axial area) who underwent MR imaging at diagnosis and at least once during	Surveillance MRI Details: • MRI scanner: no details. • Image sequences taken: All patients underwent at least	• Progression rate • Medium time to progression • Median OS • Median PFS

Study (year) [ref] Location Years of study	Aim Study design	Population	Intervention	Outcomes reported
	patient management compared with clinical evaluation. Retrospective case series study	treatment." Excluded: NR Tumor grade: only pathologically confirmable in the 3 patients who underwent surgery at diagnosis: - glioblastoma multiforme (n=1) - astrocytoma grade II (n=1) - astrocytoma grade III (n=1) Tumor location: "center of the mass in the pons, involving >50% of the axial area" N = 15 Male: 73% Median age at diagnosis: 5.6 years (range 2–19) Average follow-up: - Median: 1.5 years[a] (range 0.17 to 9) - Mean: 2.17 years Previous treatment(s):- - Surgery (n=3 patients with a posterior cystic exophytic component underwent surgery at diagnosis)	T1-weighted (T1W) sagittal and T1W and T2W axial sequences, with contrast agent (gadopentate dimeglumine) used in all cases.	• Tumor response rates • Changes in patient treatment due to progression
Perreault et al (2014)[9] USA 2000 – 2011	To assess the benefits of surveillance MRI and more specifically spine MRI in a contemporary cohort. Retrospective case series study	Included: Patients "with at least one surveillance MRI following the diagnosis of MB, ATRT, PB, (s)PNET, (s)HGG (World Health Organization grade III–IV), CNS GCT or Epend." Excluded: Patients with "a malignant CNS tumor involving only the spine at diagnosis". N = 258 Male: 62% Median age at diagnosis: 8 years (range 0.3 – 21) Median follow-up (n=258): 3.12 years (range 0.13 to 11.8)	Surveillance MRI. Details: • No details of the MRI scanner used or the image sequences taken.	• Median follow-up; total and by tumor type • Median number of scans (range); total and by tumor type • Recurrence rate; total and by tumor type: first and subsequent recurrences • Symptomatic status at recurrence • Median time to recurrence; total and by tumor type; by symptomatic status at recurrence. • Median OS by symptomatic status at recurrence

Study (year) [ref] Location Years of study	Aim Study design	Population	Intervention	Outcomes reported
		Tumor type(s): Mixed: - MB: n=89 (35%) - AT/RT: n=10 (4%) - PB: n=9 (3%) - sPNET: n=25 (10%) - HGG: n=34 (13%) - GCT: n=39 (15%) - Ependymoma: n=52 (20%) Tumor grade: - HGG: WHO grade III–IV - GCT: WHO II and III - Epend: WHO II and III Tumor location: supratentorial (reported for PNET and HGG only) Previous treatment(s): NR		• Frequency of MRI-detected recurrence; total and by tumor type • Changes in patient treatment due to recurrence after first relapse

Key: AT/RT: Atypical Teratoid/Rhabdoid Tumor; CPC: Choroid Plexus Carcinoma; DIPG: Diffuse Pontine Glioma; Epend: Ependymoma; GCT: Germ Cell tumor; HGG: High Grade Glioma; MB: Medulloblastoma; MRI: Magnetic Resonance Imaging; mth(s): month(s); PB: Pineoblastoma; N: number of patients; N/A: not applicable; ND: not defined; NR: not reported; (s)HGG: (supratentorial) High Grade Glioma; (s)PNET: (supratentorial) Primitive Neuroectodermal Tumor; WHO: World Health Organization

[a]Not directly reported by the authors but calculated by the reviewer based on data reported in the publication.

TABLE 2 Summary of radiographic outcomes by tumor type for 33 high-grade tumor patients in Korones[7]

Tumor Type	N (Recurrent patients only)	Median frequency of imaging in months (range)	Patients with recurrent disease n (%)		Diagnostic yield of MRI[c] (%)	Median time to recurrence in years (range)	Median time to recurrence in years (range)	
			Asymp	Symp			Asymp	Symp
Total	33	1 scan / 2.5 (1/1 – 1/6.7)	17 (52)	16 (48)	4.4 (656 scans)	0.75 (0.17 – 6)	0.75 (0.17 – 4.33)	0.67 (0.17 – 6)
HGG	10	NR	4 (40)	6 (60)	6.3 (63 scans)	NR	NR	NR
DIPG	7	NR	3 (43)	4 (57)	15.3 (19 scans)	NR	NR	NR
sPNET[a]	5	NR	3 (60)	2 (40)	7.2 (42 scans)	NR	NR	NR
MB	4	NR	2 (50)	2 (50)	1.4 (147 scans)	NR	NR	NR
Epend	4	NR	3 (75)	1 (25)	3.5 (86 scans)	NR	NR	NR
Other[b]	3	NR	2 (67)	1 (33)	6.5 (31 scans)	NR	NR	NR

Key: Asymp, asymptomatic; DIPG, diffuse pontine glioma; Epend, ependymoma; GCT, germ cell tumor; HGG, high grade glioma; MB, medulloblastoma; N, number of patients; sPNET, supratentorial Primitive Neuroectodermal Tumor; Symp, symptomatic

a: As of 2016, the term PNET no longer appears in the current WHO classification of CNS tumors

b: "Other" includes choroid plexus carcinoma (n=1), germ cell tumor (n=1) and Atypical Teratoid / Rhabdoid Tumor (n=1)

c: Asymptomatic recurrence only

TABLE 3 Summary of radiographic outcomes by tumor type in Perreault[9]

Tumor type	N	Median Follow-up in years	Median no. of MRI scans per patient in years	First recurrence (n=113)			Subsequent recurrence (n=125)			Diagnostic yield of surveillance MRI (%)			Median time to recurrence in years (range)	Time to > 90% of recurrences in years
				Asymp N (%)	Symp N (%)	Unknown N (%)	Asympt N (%)	Sympt N (%)	Unknown N (%)	B	B/S	S		
Total	258	3.13	13	52 (46)	47 (42)	14 (12)	36 (29)	58 (46)	31 (25)	8.3	3.8	0.9	1.0 (0.03–11.4)	2.83
MB	89	4.33	18.5	17 (63)	6 (22)	4 (15)	6 (21)	12 (41)	11 (38)	5.2	2.5	0.7	1.3 (0.04–6.3)	2.17
Epend	52	3.96	11	12 (46)	7 (27)	7 (27)	10 (26)	15 (38)	14 (36)	11.3	4.3	1.1	1.3 (0.08–5.4)	3.0
GCT	39	4.25	15	5 (56)	4 (44)	0 (0)	1 (50)	1 (50)	0 (0)	2.1	2.4	1.6	3.17 (0.08–11.4)	8.1
HGG	34	1.25	6	7 (25)	19 (68)	2 (7)	5 (19)	19 (73)	2 (8)	21.6	11.4	2.8	0.88 (0.07-3.17)	2.25
sPNET[a]	25	3.75	17	5 (36)	8 (57)	1 (7)	11 (58)	6 (32)	2 (10)	10.5	1.6	0	0.96 (0.03-4.5)	2.42
AT/RT	10	0.54	7	4 (100)	0 (0)	0 (0)	2 (67)	1 (33)	0 (0)	10.9	13	0	0.46 (0.42-0.75)	0.75
PB	9	2.08	16	2 (40)	3 (60)	0 (0)	1 (14)	4 (57)	2(29)	9.3	19.7	4.9	1.67 (0.92-2.5)	2.5

Key: Asymp, asymptomatic; AT/RT, Atypical Teratoid / Rhabdoid Tumor; B, brain only; B/S, combined brain and spine; Epend, Ependymoma; GCT, Germ Cell Tumor; HGG, High Grade Glioma; MB, Medulloblastoma; N, number of patients; PB, Pineoblastoma; sPNET, supratentorial Primitive Neuroectodermal Tumor; s, spine only; symp, symptomatic.

[a]As of 2016, the term PNET no longer appears in the current WHO classification of CNS tumors