Photo by Vivid Eye Photography

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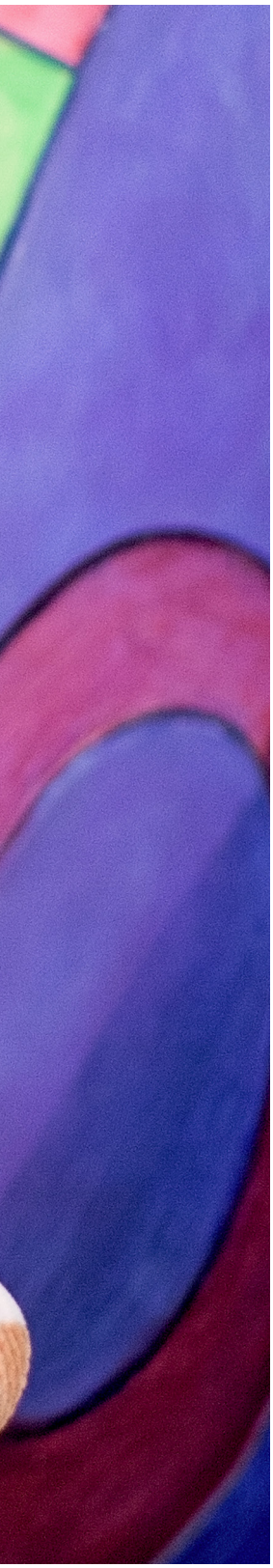

8

Central Nervous System Tumours

Executive Summary

Brain tumours are rare in children, with an overall cumulative age standardized incidence rate (ASIR) of 33.6 per million per year for children 14 years of age or younger in the Province of Ontario. This rate did not significantly change from 1990 to 2004. During this period, central nervous system (CNS) tumours were slightly more common in males than females (male:female ratio, 1.3:1). The age distribution remained fairly constant over the period (20.9% under 3 years of age at diagnosis, 45.2% aged 4–9 years, 33.8% aged 10–14 years). The most common histopathologic diagnosis was low grade astrocytoma (50.6%), followed by medulloblastoma (15.8%) and high grade glial tumours (14.7%). Ependymoma accounted for 6.6%, germ cell tumours for 2.5% and supratentorial primitive neuroectodermal tumours (PNETs) for 4.2%. Therapeutic modalities vary with age, with radiotherapy tending to be less commonly used in children 3 years of age and under. Though therapeutic options advanced over the study period, the 5 year survival rates remained relatively stable (69% in 1990; 73% by 2004). The only exceptions were for patients with the histologic diagnosis of medulloblastoma or germ cell tumours, for which there was a steady improvement in survival.

Introduction

Central nervous system tumours occur at all ages. They are more predominant in the posterior fossa (infratentorial) region.[1] The incidence is 49.7 per million person years for children aged less than 15 years in the United States.[2] An increase in the incidence rate was reported in the late 1970s and early 1980s.[3] Because the greatest increase occurred in the diagnosis of benign tumours, the increase was felt to be secondary to the availability of new investigational tools (i.e., cranial tomography and magnetic resonance imaging [MRI]).

Limitations in information obtained from cancer registries include incompleteness resulting from the surveillance techniques used.[4] This limitation may result in the populations included in the different registries not being comparable. The completeness of case ascertainment across reporting regions, provinces and countries may vary for several reasons. The registry may include cases for which the diagnosis was made at autopsy. Additionally, case definitions may vary. For example, only malignant tumours might be included and not benign tumours, resulting in an underestimate of persons at risk of developing a CNS tumour.

A second limitation is the histologic classification of the tumours at time of diagnosis. These tumours often demonstrate significant heterogeneity and different regions may show different characteristics. The histologic diagnosis can be limited by the amount of tissue available for analysis. This is particularly the case when only biopsy material is available: the smaller the sample size, the greater the risk of missing important changes that may be present within the tumour. These missed findings could lead to a misclassification (e.g., benign rather than malignant variant or combined tumour tissue types). Classification is often further complicated by a lack of universal agreement on the histologic criteria necessary for a given pathologic diagnosis and the changing of these criteria with time. Finally, multiple centres may be submitting cases to a central registry and patients may be seen in different centres at different times during treatment, resulting in duplicate case reporting in the registries.

Ontario has a unique medical system. Not only is universal medical and hospital care centrally funded by the provincial ministry of health, the care of children with CNS tumours is carried out in one of the 5 university affiliated hospitals. Thus all children under 14 years of age with a suspected CNS tumour are referred to one of these centres for diagnosis and treatment. The histologic classification system used in each of these centres is similar. All the centres are active participants in the Pediatric Oncology Group of Ontario Networked Information System (POGONIS), registering all newly diagnosed cases. This chapter provides a summary, based on the data from this registry, of CNS tumours occurring in children aged 14 years or less in Ontario between 1985 and 2004.

Discussion

The histology groupings used in this report are based on the International Classification of Childhood Cancer, third edition (ICCC-3), diagnostic group III, with exceptions. This chapter includes germ cell tumours, which are not included in the ICCC-3 categorization. CNS lymphoma is not included in this chapter because it is included in the chapter on lymphomas. Anaplastic gangliomas are included in the high grade glial tumour group. Desmoplastic neuroepithelial tumours and pituitary adenomas, if benign, are not included.

Incidence

EXHIBIT 8.1a: **Incidence of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**

		Period of diagnosis								
		All years			1985–1989			1990–1994		
Tumour type	Age (years)	Total N	%	Female (%)	Total N	%	Female (%)	Total N	%	Female (%)
All central nervous system tumours	Overall	**1448**	**100.00**	**43.16**	**274**	**100.00**	**41.61**	**394**	**100.00**	**47.21**
	0–3	303	20.93	45.54	70	25.55	48.57	83	21.07	50.60
	4–9	655	45.23	42.60	127	46.35	39.37	166	42.13	42.77
	10–14	490	33.84	42.45	77	28.10	38.96	145	36.80	50.34
Low grade glial tumours	Overall	**733**	**50.62**	**46.11**	**118**	**43.07**	**44.92**	**224**	**56.85**	**50.45**
	0–3	129	17.60	n/a	24	20.34	n/a	44	19.64	n/a
	4–9	330	45.02	n/a	57	48.31	n/a	95	42.41	n/a
	10–14	274	37.38	n/a	37	31.36	n/a	85	37.95	n/a
High grade glial tumours	Overall	**213**	**14.71**	**50.23**	**52**	**18.98**	**44.23**	**59**	**14.97**	**47.46**
	0–3	35	16.43	n/a	8	15.38	n/a	9	15.25	n/a
	4–9	110	51.64	n/a	28	53.85	n/a	27	45.76	n/a
	10–14	68	31.92	n/a	16	30.77	n/a	23	38.98	n/a
Ependymoma	Overall	**96**	**6.63**	**45.83**	**25**	**9.12**	**52.00**	**22**	**5.58**	**54.55**
	0–3	41	42.71	n/a	10	40.00	n/a	12	54.55	n/a
	4–9	28	29.17	n/a	10	40.00	n/a	4	18.18	n/a
	10–14	27	28.13	n/a	5	20.00	n/a	6	27.27	n/a
Medulloblastoma	Overall	**228**	**15.75**	**28.07**	**39**	**14.23**	**25.64**	**58**	**14.72**	**27.59**
	0–3	43	18.86	n/a	13	33.33	n/a	6	10.34	n/a
	4–9	120	52.63	n/a	18	46.15	n/a	31	53.45	n/a
	10–14	65	28.51	n/a	8	20.51	n/a	21	36.21	n/a
Supratentorial PNET	Overall	**61**	**4.21**	**45.90**	**12**	**4.38**	**58.33**	**9**	**2.28**	**55.56**
	0–3	24	39.34	n/a	5	41.67	n/a	4	44.44	n/a
	4–9	32	52.46	n/a	7	58.33	n/a	5	55.56	n/a
	10–14	5	8.20	n/a	0	0.00	n/a	0	0.00	n/a

PNET = primitive neuroectodermal tumour
n/a For privacy reasons percent female has been reported only overall and not by age group.

The terms used to describe the regions of the CNS are based on commonly used terms in neurologic anatomy. The supratentorial region includes the cerebral hemispheres (i.e., occipital, parietal, temporal and frontal lobes) and/or the midline axial structures (i.e., diencephalon, thalamus, basal ganglia, optic chiasm, optic nerves, pituitary fossa, olfactory nerves and tectal plate region). The infratentorial region includes the brain stem, cerebellum and/or the floor of the fourth ventricle. The meninges include the covering of the supratentorial region, the infratentorial region and/or the spinal cord.

1995–1999			2000–2004		
Total N	%	Female (%)	Total N	%	Female (%)
392	**100.00**	**41.33**	**388**	**100.00**	**42.01**
81	20.66	43.21	69	17.78	39.13
174	44.39	43.10	188	48.45	44.15
137	34.95	37.96	131	33.76	40.46
197	**50.26**	**43.15**	**194**	**50.00**	**44.85**
32	16.24	n/a	29	14.95	n/a
85	43.15	n/a	93	47.94	n/a
80	40.61	n/a	72	37.11	n/a
58	**14.80**	**56.90**	**44**	**11.34**	**52.27**
11	18.97	n/a	7	15.91	n/a
29	50.00	n/a	26	59.09	n/a
18	31.03	n/a	11	25.00	n/a
19	**4.85**	**52.63**	**30**	**7.73**	**30.00**
9	47.37	n/a	10	33.33	n/a
7	36.84	n/a	7	23.33	n/a
3	15.79	n/a	13	43.33	n/a
57	**14.54**	**24.56**	**74**	**19.07**	**32.43**
9	15.79	n/a	15	20.27	n/a
29	50.88	n/a	42	56.76	n/a
19	33.33	n/a	17	22.97	n/a
21	**5.36**	**28.57**	**19**	**4.90**	**52.63**
10	47.62	n/a	5	26.32	n/a
9	42.86	n/a	11	57.89	n/a
2	9.52	n/a	3	15.79	n/a

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EXHIBIT 8.1a: **Incidence of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**

		Period of diagnosis								
		All years			1985–1989			1990–1994		
Tumour type	Age (years)	Total N	%	Female (%)	Total N	%	Female (%)	Total N	%	Female (%)
Germ cell tumours	Overall	**36**	**2.49**	**25.00**	**10**	**3.65**	**20.00**	**4**	**1.02**	**50.00**
	0–3	2	5.56	n/a	1	10.00	n/a	0	0.00	n/a
	4–9	8	22.22	n/a	1	10.00	n/a	3	75.00	n/a
	10–14	26	72.22	n/a	8	80.00	n/a	1	25.00	n/a
Other central nervous system tumours	Overall	**81**	**5.59**	**43.21**	**18**	**6.57**	**33.33**	**18**	**4.57**	**55.56**
	0–3	29	35.80	n/a	9	50.00	n/a	8	44.44	n/a
	4–9	27	33.33	n/a	6	33.33	n/a	1	5.56	n/a
	10–14	25	30.86	n/a	3	16.67	n/a	9	50.00	n/a

PNET = primitive neuroectodermal tumour
n/a For privacy reasons percent female has been reported only overall and not by age group.

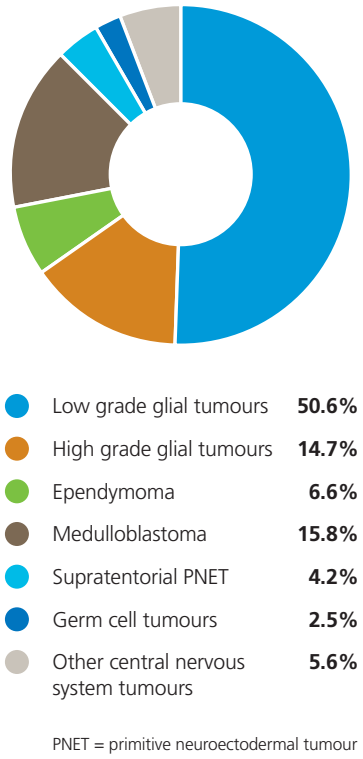
Exhibits 8.1a and 8.1b

During the period 1985–2004, a total of 1,448 cases of primary CNS tumours were reported in Ontario.

There was a male predominance (male:female ratio, 1.31:1). The commonest tumour histology was low grade glial, which accounted for 50.6% of tumours. Medulloblastoma and high grade glial tumours were almost equally distributed and together accounted for one-third of all tumours (medulloblastoma, 15.8%; high grade glial tumours, 14.7%), while ependymomas accounted for 6.6% of all tumours, supratentorial PNETs for 4.2% and germ cell tumours for 2.5%.

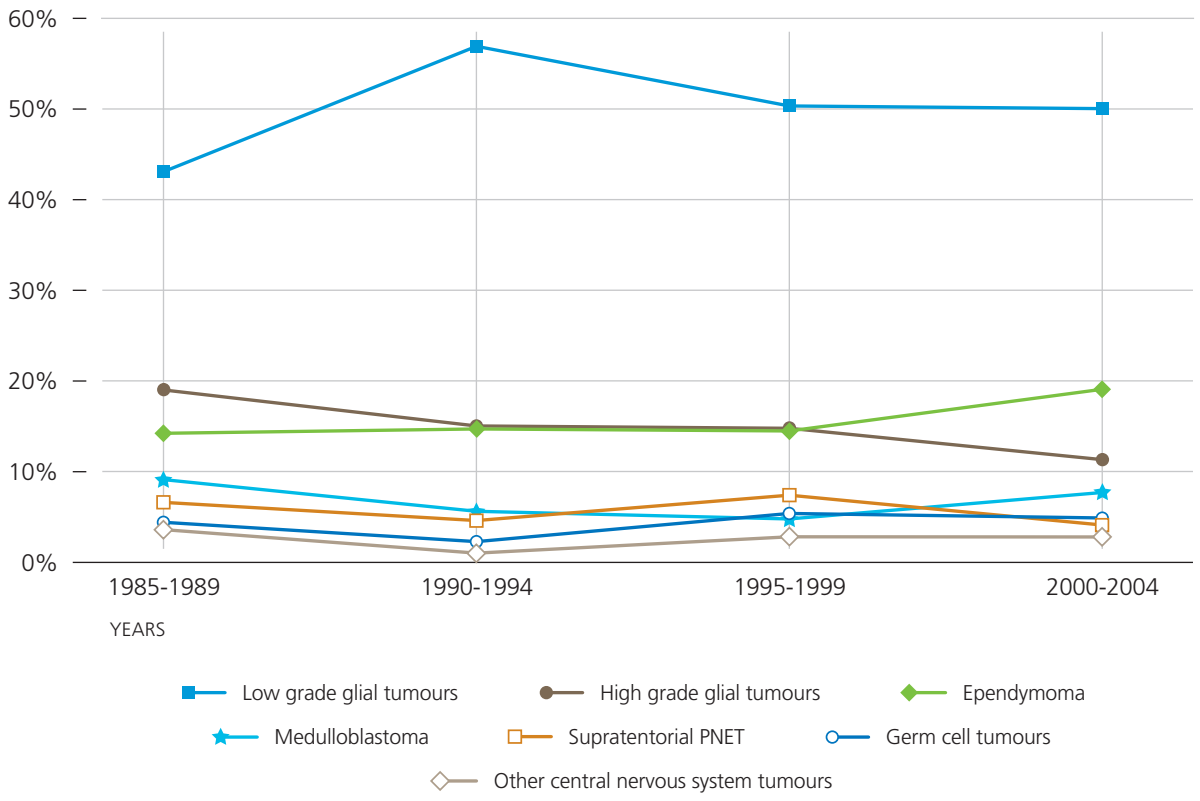
1995–1999			2000–2004		
Total N	%	Female (%)	Total N	%	Female (%)
11	**2.81**	**9.09**	**11**	**2.84**	**36.36**
0	0.00	n/a	1	9.09	n/a
4	36.36	n/a	0	0.00	n/a
7	63.64	n/a	10	90.91	n/a
29	**7.40**	**44.83**	**16**	**4.12**	**37.50**
10	34.48	n/a	2	12.50	n/a
11	37.93	n/a	9	56.25	n/a
8	27.59	n/a	5	31.25	n/a

EXHIBIT 8.1b: **Distribution of central nervous system tumours, by histology, age 0–14 years, in Ontario, 1985–2004**



PNET = primitive neuroectodermal tumour

EXHIBIT 8.2: **Distribution of CNS tumours by histology and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**



PNET = primitive neuroectodermal tumour

Exhibit 8.2

With the exception of the histologic diagnosis of medulloblastoma, the distribution of diagnoses remained relatively stable over the survey time periods. The proportion of total tumours with the histologic diagnosis of medulloblastoma increased from 14.2% in the 1985–1989 period to 19.1% in 2000–2004, with the increase being largely in the 4–9 year old group. There was an increase in the proportion of low grade glial tumours in 1990–1994, but this returned to baseline levels in subsequent study periods. However, the proportion of tumours diagnosed as high grade glial tumours decreased steadily from 19.0% in the 1985–1990 period to 11.3% in 2000–2004. The proportion of tumours diagnosed as PNET, ependymoma or germ cell was relatively constant over the different periods.

EXHIBIT 8.3: **Age-standardized incidence of primary central nervous system tumours by tumour type and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**

	Period of diagnosis										
	Total (1985–2004)		1985–1989		1990–1994		1995–1999		2000–2004		
Tumour type	ASIR/ million/ year	95% CI	ASIR/ million/ year	95% CI	ASIR/ million/ year	95% CI	ASIR/ million/ year	95% CI	ASIR/ million/ year	95% CI	Test for trend (p value)
All central nervous system tumours	**33.16**	**24.92-41.39**	**27.68**	**13.95-41.42**	**36.57**	**18.69-54.44**	**34.58**	**17.70-51.46**	**33.80**	**16.68-50.92**	**0.72**
Low grade glial tumours	16.78	12.45-21.11	11.94	5.84-18.05	20.81	10.45-31.17	17.48	8.66-26.29	16.90	8.11-25.69	0.50
High grade glial tumours	4.96	3.56-6.36	5.31	2.41-8.22	5.54	2.40-8.68	5.14	2.23-8.04	3.84	1.66-6.01	0.95
Ependymoma	2.18	1.51-2.84	2.51	1.00-4.01	1.96	0.78-3.14	1.62	0.54-2.71	2.61	1.11-4.11	0.96
Medulloblastoma	5.22	3.65-6.79	3.92	1.75-6.09	5.48	2.04-8.93	5.02	2.25-7.79	6.45	2.55-10.35	0.89
Supratentorial PNET	1.35	0.88-1.83	1.18	0.46-1.90	0.77	0.13-1.42	1.80	0.51-3.08	1.67	0.67-2.66	0.92
Germ cell tumours	0.84	0.48-1.21	1.05	0.22-1.89	0.39	0.01-0.77	1.00	0.17-1.83	0.94	0.18-1.70	0.95
Other central nervous system tumours	1.82	1.25-2.40	1.77	0.76-2.78	1.61	0.39-2.82	2.53	1.09-3.97	1.39	0.52-2.26	0.94

ASIR = age standardized incidence rate; PNET = primitive neuroectodermal tumour; CI = confidence interval

Exhibit 8.3

The overall cumulative ASIR of CNS tumours was 33.2 per million per year (95% confidence interval [CI], 24.92–41.39).

The age-standardized tumour incidence rates for the group as a whole, as well as when broken into histologic diagnoses, remained stable over the review period, with the exception of low grade glial tumours. The age-standardized tumour incidence rate for low grade glial tumours increased from 11.94 per million persons per year in 1985–1989 to 20.81 per million persons per year in 1990–1994. The incidence declined in the following 2 study periods (1995–1999 and 2000–2004) but did not return to the rate reported for 1985–1989.

Exhibit 8.4

At the time of diagnosis, 45.2% of the children were age 4–9 years, 33.8% were age 10–14 years and 20.9% were age 3 years or less. The diagnosis was rarely made in the first 60 days of life (1.5%, data not shown). The age at diagnosis based on histology followed a similar pattern except for ependymoma and germ cell tumours. Children with a diagnosis of ependymoma were more often age 3 years or younger (42.7%), whereas the majority of children diagnosed with a germ cell tumour were over age 10 years (72.2%) (Exhibit 8.1a).

EXHIBIT 8.4: **Distribution of CNS tumours by age at diagnosis, age 0–14 years, in Ontario, 1985–2004**

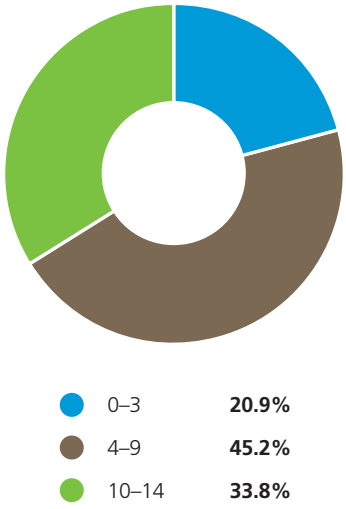


EXHIBIT 8.5: **Distribution of CNS tumours by age and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**

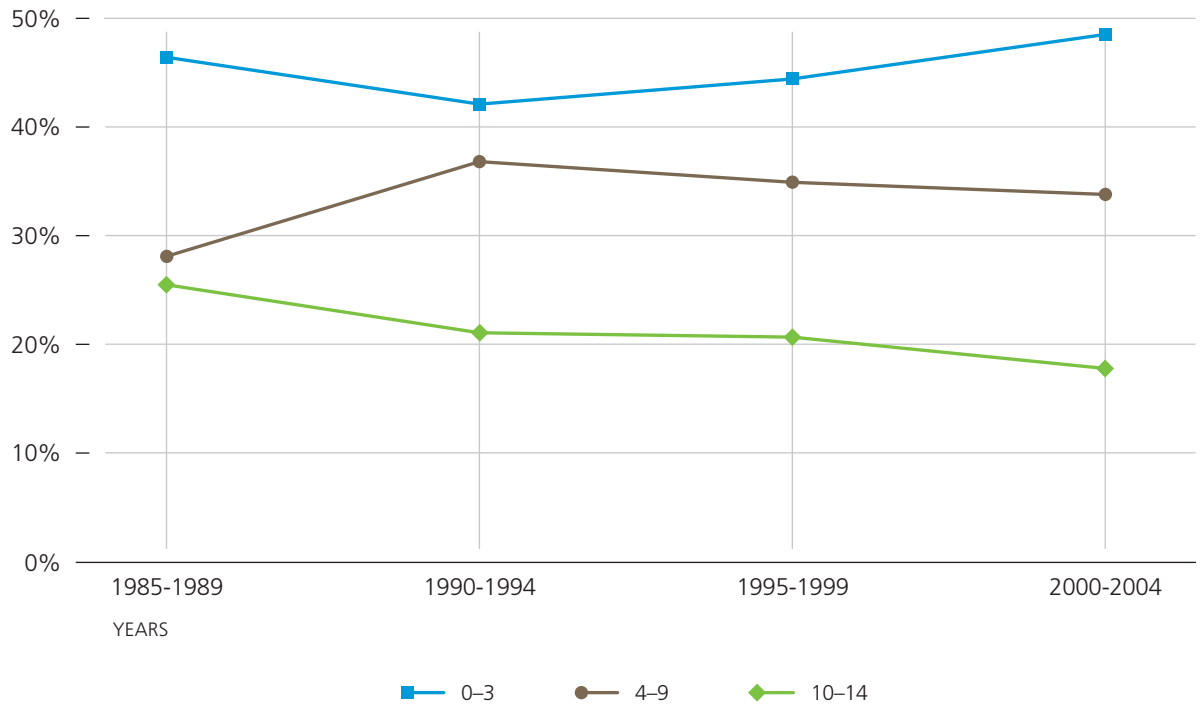
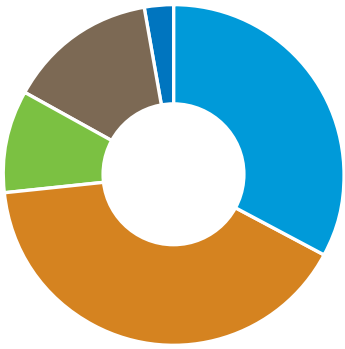


Exhibit 8.5

When the proportion of children diagnosed in each age group over the period 1985–2004 was examined, the proportion diagnosed at age 3 years or younger decreased from 25.6% in 1985–1989 to 17.8% in 2000–2004. For children aged 10–14 years, there was a small increase in the proportion from 1985–1989 (28.1%) to 1990–1994 (36.8%); however, after the 1990–1994 period, the proportion remained relatively constant (35.0–33.8%). For children aged 4–9 years, the proportion diagnosed remained relatively stable (46.4–48.5%) over the period 1985–2004.

EXHIBIT 8.6: **Distribution of central nervous system tumours, by location, age 0–14 years, in Ontario, 1985-2004**



Supratentorial	**43.0%**
Infratentorial	**52.6%**
Brain Stem	**12.8%**
Cerebellar	**18.4%**
Spinal Cord	**3.5%**

Footnote for Exhibit 8.6

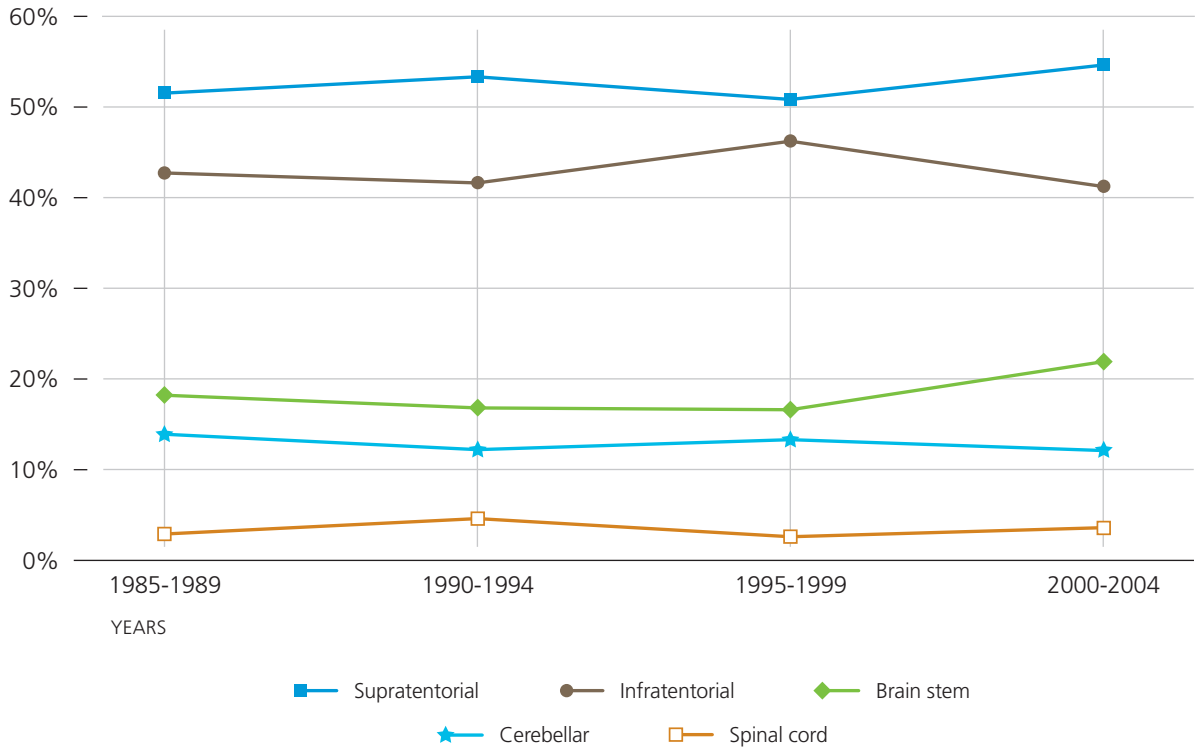
Locations as grouped are not mutually exclusive.

Supratentorial includes tumours in the hemispheric, midline axial, thalamic and 3rd ventricle regions.

Infratentorial includes tumours in the brain stem, cerebellum, 4th ventricle and posterior fossa (not otherwise specified) regions.

Cerebellar includes tumours in the 4th ventricle and posterior fossa (not otherwise specified) regions.

EXHIBIT 8.7: **Distribution of CNS tumours by location and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**



Exhibits 8.6 and 8.7

In terms of tumour location, there was a slight predominance of tumours in the infratentorial region (52.6%) over the supratentorial region (43.0%). The distribution of the supratentorial tumours was as follows: 41.0% involved principally the cerebral hemispheres, 51.0% involved mainly the midline axial structures and 8.0% arose from the third ventricle (data not shown). Tumours in the infratentorial region were mainly located in the cerebellum (75.7%), with only 24.3% involving primarily the brain stem region (data not shown).

Over successive 5 year intervals between 1985 and 2004, the proportion of tumours arising in the different anatomic regions (i.e., supratentorial, infratentorial, meninges and spinal cord) remained relatively stable.

Treatment

EXHIBIT 8.8a: First surgery for primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1995–2004

		Period of diagnosis					
		Total patients (1995–2004)		All years (1995–2004)			
Tumour type	Age (years)			No surgery		Biopsy or resection	
		Total N	%	No. of cases	%	No. of cases	%
All central nervous system tumours	**Overall**	**780**	**100.00**	**187**	**23.97**	**593**	**76.03**
	0–3	150	19.23	35	23.33	115	76.67
	4–9	362	46.41	97	26.80	265	73.20
	10–14	268	34.36	55	20.52	213	79.48
Low grade glial tumours	**Overall**	**391**	**100.00**	**96**	**24.55**	**295**	**75.45**
	0–3	61	15.60	24	39.34	37	60.66
	4–9	178	45.52	47	26.40	131	73.60
	10–14	152	38.87	25	16.45	127	83.55
High grade glial tumours	**Overall**	**102**	**100.00**	**59**	**57.84**	**43**	**42.16**
	0–3	18	17.65	6	33.33	12	66.67
	4–9	55	53.92	39	70.91	16	29.09
	10–14	29	28.43	14	48.28	15	51.72
Ependymoma	**Overall**	**49**	**100.00**	**1**	**2.04**	**48**	**97.96**
	0–3	19	38.78	0	0.00	19	100.00
	4–9	14	28.57	0	0.00	14	100.00
	10–14	16	32.65	1	6.25	15	93.75
Medulloblastoma	**Overall**	**131**	**100.00**	**8**	**6.11**	**123**	**93.89**
	0–3	24	18.32	1	4.17	23	95.83
	4–9	71	54.20	5	7.04	66	92.96
	10–14	36	27.48	2	5.56	34	94.44
Supratentorial PNET	**Overall**	**40**	**100.00**	**5**	**12.50**	**35**	**87.50**
	0–3	15	37.50	1	6.67	14	93.33
	4–9	20	50.00	2	10.00	18	90.00
	10–14	5	12.50	2	40.00	3	60.00
Germ cell tumours	**Overall**	**22**	**100.00**	**13**	**59.09**	**9**	**40.91**
	0–3	1	4.55	1	100.00	0	0.00
	4–9	4	18.18	2	50.00	2	50.00
	10–14	17	77.27	10	58.82	7	41.18
Other central nervous system tumours	**Overall**	**45**	**100.00**	**5**	**11.11**	**40**	**88.89**
	0–3	12	26.67	2	16.67	10	83.33
	4–9	20	44.44	2	10.00	18	90.00
	10–14	13	28.89	1	7.69	12	92.31

PNET = primitive neuroectodermal tumour

1995–1999				2000–2004			
No surgery		Biopsy or resection		No surgery		Biopsy or resection	
No. of cases	%	No. of cases	%	No. of cases	%	No. of cases	%
85	**21.68**	**307**	**78.32**	**102**	**26.29**	**286**	**73.71**
15	18.52	66	81.48	20	28.99	49	71.01
46	26.44	128	73.56	51	27.13	137	72.87
24	17.52	113	82.48	31	23.66	100	76.34
43	**21.83**	**154**	**78.17**	**53**	**27.32**	**141**	**72.68**
11	34.38	21	65.63	13	44.83	16	55.17
21	24.71	64	75.29	26	27.96	67	72.04
11	13.75	69	86.25	14	19.44	58	80.56
28	**48.28**	**30**	**51.72**	**31**	**70.45**	**13**	**29.55**
2	18.18	9	81.82	4	57.14	3	42.86
20	68.97	9	31.03	19	73.08	7	26.92
6	33.33	12	66.67	8	72.73	3	27.27
0	**0.00**	**19**	**100.00**	**1**	**3.33**	**29**	**96.67**
0	0.00	9	100.00	0	0.00	10	100.00
0	0.00	7	100.00	0	0.00	7	100.00
0	0.00	3	100.00	1	7.69	12	92.31
1	**1.75**	**56**	**98.25**	**7**	**9.46**	**67**	**90.54**
0	0.00	9	100.00	1	6.67	14	93.33
0	0.00	29	100.00	5	11.90	37	88.10
1	5.26	18	94.74	1	5.88	16	94.12
3	**14.29**	**18**	**85.71**	**2**	**10.53**	**17**	**89.47**
1	10.00	9	90.00	0	0.00	5	100.00
1	11.11	8	88.89	1	9.09	10	90.91
1	50.00	1	50.00	1	33.33	2	66.67
6	**54.55**	**5**	**45.45**	**7**	**63.64**	**4**	**36.36**
0	—	0	—	1	100.00	0	0.00
2	50.00	2	50.00	0	—	0	—
4	57.14	3	42.86	6	60.00	4	40.00
4	**13.79**	**25**	**86.21**	**1**	**6.25**	**15**	**93.75**
1	10.00	9	90.00	1	50.00	1	50.00
2	18.18	9	81.82	0	0.00	9	100.00
1	12.50	7	87.50	0	0.00	5	100.00

EXHIBIT 8.8b: **Treatment with chemotherapy of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1995–2004**

		Period of diagnosis								
		All years (1995–2004)			1995–1999			2000–2004		
Tumour type	Age (years)	Total	Chemotherapy		Total	Chemotherapy		Total	Chemotherapy	
		N	Yes (n)	%	N	Yes (n)	%	N	Yes (n)	%
All central nervous system tumours	Overall	**780**	**317**	**40.64**	**392**	**142**	**36.22**	**388**	**175**	**45.10**
	0–3	150	91	60.67	81	52	64.20	69	39	56.52
	4–9	362	147	40.61	174	57	32.76	188	90	47.87
	10–14	268	79	29.48	137	33	24.09	131	46	35.11
Low grade glial tumours	Overall	**391**	**74**	**18.93**	**197**	**28**	**14.21**	**194**	**46**	**23.71**
	0–3	61	27	44.26	32	15	46.88	29	12	41.38
	4–9	178	35	19.66	85	10	11.76	93	25	26.88
	10–14	152	12	7.89	80	3	3.75	72	9	12.50
High grade glial tumours	Overall	**102**	**45**	**44.12**	**58**	**21**	**36.21**	**44**	**24**	**54.55**
	0–3	18	9	50.00	11	5	45.45	7	4	57.14
	4–9	55	22	40.00	29	8	27.59	26	14	53.85
	10–14	29	14	48.28	18	8	44.44	11	6	54.55
Ependymoma	Overall	**49**	**24**	**48.98**	**19**	**13**	**68.42**	**30**	**11**	**36.67**
	0–3	19	14	73.68	9	9	100.00	10	5	50.00
	4–9	14	4	28.57	7	3	42.86	7	1	14.29
	10–14	16	6	37.50	3	1	33.33	13	5	38.46
Medulloblastoma	Overall	**131**	**114**	**87.02**	**57**	**45**	**78.95**	**74**	**69**	**93.24**
	0–3	24	23	95.83	9	9	100.00	15	14	93.33
	4–9	71	63	88.73	29	23	79.31	42	40	95.24
	10–14	36	28	77.78	19	13	68.42	17	15	88.24
Supratentorial PNET	Overall	**40**	**31**	**77.50**	**21**	**18**	**85.71**	**19**	**13**	**68.42**
	0–3	15	10	66.67	10	8	80.00	5	2	40.00
	4–9	20	16	80.00	9	8	88.89	11	8	72.73
	10–14	5	5	100.00	2	2	100.00	3	3	100.00
Germ cell tumours	Overall	**22**	**17**	**77.27**	**11**	**8**	**72.73**	**11**	**9**	**81.82**
	0–3	1	1	100.00	0	0	—	1	1	100.00
	4–9	4	2	50.00	4	2	50.00	0	0	—
	10–14	17	14	82.35	7	6	85.71	10	8	80.00
Other central nervous system tumours	Overall	**45**	**12**	**26.67**	**29**	**9**	**31.03**	**16**	**3**	**18.75**
	0–3	12	7	58.33	10	6	60.00	2	1	50.00
	4–9	20	5	25.00	11	3	27.27	9	2	22.22
	10–14	13	0	0.00	8	0	0.00	5	0	0.00

PNET = primitive neuroectodermal tumour

EXHIBIT 8.8c: **Treatment with radiotherapy of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1995–2004**

		Period of diagnosis										
		All years (1995–2004)										
Tumour type	Age (years)	Total	None		Received any		0–90 days		91–180 days		≥ 181 days	
		N	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%
All central nervous system tumours	Overall	**780**	**435**	**55.77**	**304**	**38.97**	**231**	**75.99**	**34**	**11.18**	**39**	**12.83**
	0–3	150	113	75.33	27	18.00	3	11.11	7	25.93	17	62.96
	4–9	362	175	48.34	160	44.20	145	90.63	6	3.75	9	5.63
	10–14	268	147	54.85	117	43.66	83	70.94	21	17.95	13	11.11
Low grade glial tumours	Overall	**391**	**312**	**79.80**	**41**	**10.49**	**18**	**43.90**	**6**	**14.63**	**17**	**41.46**
	0–3	61	48	78.69	3	4.92	0	0.00	1	33.33	2	66.67
	4–9	178	136	76.40	18	10.11	9	50.00	1	5.56	8	44.44
	10–14	152	128	84.21	20	13.16	9	45.00	4	20.00	7	35.00
High grade glial tumours	Overall	**102**	**30**	**29.41**	**69**	**67.65**	**63**	**91.30**	**2**	**2.90**	**4**	**5.80**
	0–3	18	14	77.78	4	22.22	1	25.00	1	25.00	2	50.00
	4–9	55	11	20.00	41	74.55	40	97.56	1	2.44	0	0.00
	10–14	29	5	17.24	24	82.76	22	91.67	0	0.00	2	8.33
Ependymoma	Overall	**49**	**13**	**26.53**	**36**	**73.47**	**22**	**61.11**	**6**	**16.67**	**8**	**22.22**
	0–3	19	10	52.63	9	47.37	1	11.11	2	22.22	6	66.67
	4–9	14	1	7.14	13	92.86	13	100.00	0	0.00	0	0.00
	10–14	16	2	12.50	14	87.50	8	57.14	4	28.57	2	14.29
Medulloblastoma	Overall	**131**	**21**	**16.03**	**110**	**83.97**	**104**	**94.55**	**1**	**0.91**	**5**	**4.55**
	0–3	24	19	79.17	5	20.83	1	20.00	0	0.00	4	80.00
	4–9	71	2	2.82	69	97.18	67	97.10	1	1.45	1	1.45
	10–14	36	0	0.00	36	100.00	36	100.00	0	0.00	0	0.00
Supratentorial PNET	Overall	**40**	**17**	**42.50**	**23**	**57.50**	**17**	**73.91**	**3**	**13.04**	**3**	**13.04**
	0–3	15	10	66.67	5	33.33	0	0.00	2	40.00	3	60.00
	4–9	20	5	25.00	15	75.00	14	93.33	1	6.67	0	0.00
	10–14	5	2	40.00	3	60.00	3	100.00	0	0.00	0	0.00
Germ cell tumours	Overall	**22**	**1**	**4.55**	**21**	**95.45**	**4**	**19.05**	**16**	**76.19**	**1**	**4.76**
	0–3	1	0	0.00	1	100.00	0	0.00	1	100.00	0	0.00
	4–9	4	1	25.00	3	75.00	1	33.33	2	66.67	0	0.00
	10–14	17	0	0.00	17	100.00	3	17.65	13	76.47	1	5.88
Other central nervous system tumours	Overall	**45**	**41**	**91.11**	**4**	**8.89**	**3**	**75.00**	**0**	**0.00**	**1**	**25.00**
	0–3	12	12	100.00	0	0.00	0	—	0	—	0	—
	4–9	20	19	95.00	1	5.00	1	100.00	0	0.00	0	0.00
	10–14	13	10	76.92	3	23.08	2	66.67	0	0.00	1	33.33

PNET = primitive neuroectodermal tumour

continued on following page

EXHIBIT 8.8c: **Treatment with radiotherapy of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1995–2004** (cont'd)

		Period of diagnosis										
		1995–1999										
Tumour type	Age (years)	Total	None		Received any		0–90 days		91–180 days		≥ 181 days	
		N	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%
All central nervous system tumours	Overall	**392**	**224**	**57.14**	**150**	**38.27**	**111**	**74.00**	**15**	**10.00**	**24**	**16.00**
	0–3	81	63	77.78	15	18.52	1	6.67	3	20.00	11	73.33
	4–9	174	84	48.28	76	43.68	66	86.84	4	5.26	6	7.89
	10–14	137	77	56.20	59	43.07	44	74.58	8	13.56	7	11.86
Low grade glial tumours	**Overall**	**197**	**157**	**79.70**	**23**	**11.68**	**10**	**43.48**	**2**	**8.70**	**11**	**47.83**
	0–3	32	27	84.38	2	6.25	0	0.00	0	0.00	2	100.00
	4–9	85	62	72.94	10	11.76	5	50.00	0	0.00	5	50.00
	10–14	80	68	85.00	11	13.75	5	45.45	2	18.18	4	36.36
High grade glial tumours	**Overall**	**58**	**18**	**31.03**	**39**	**67.24**	**34**	**87.18**	**2**	**5.13**	**3**	**7.69**
	0–3	11	8	72.73	3	27.27	1	33.33	1	33.33	1	33.33
	4–9	29	8	27.59	20	68.97	19	95.00	1	5.00	0	0.00
	10–14	18	2	11.11	16	88.89	14	87.50	0	0.00	2	12.50
Ependymoma	**Overall**	**19**	**6**	**31.58**	**13**	**68.42**	**7**	**53.85**	**2**	**15.38**	**4**	**30.77**
	0–3	9	4	44.44	5	55.56	0	0.00	1	20.00	4	80.00
	4–9	7	1	14.29	6	85.71	6	100.00	0	0.00	0	0.00
	10–14	3	1	33.33	2	66.67	1	50.00	1	50.00	0	0.00
Medulloblastoma	**Overall**	**57**	**8**	**14.04**	**49**	**85.96**	**47**	**95.92**	**0**	**0.00**	**2**	**4.08**
	0–3	9	8	88.89	1	11.11	0	0.00	0	0.00	1	100.00
	4–9	29	0	0.00	29	100.00	28	96.55	0	0.00	1	3.45
	10–14	19	0	0.00	19	100.00	19	100.00	0	0.00	0	0.00
Supratentorial PNET	**Overall**	**21**	**9**	**42.86**	**12**	**57.14**	**7**	**58.33**	**2**	**16.67**	**3**	**25.00**
	0–3	10	6	60.00	4	40.00	0	0.00	1	25.00	3	75.00
	4–9	9	2	22.22	7	77.78	6	85.71	1	14.29	0	0.00
	10–14	2	1	50.00	1	50.00	1	100.00	0	0.00	0	0.00
Germ cell tumours	**Overall**	**11**	**1**	**9.09**	**10**	**90.91**	**3**	**30.00**	**7**	**70.00**	**0**	**0.00**
	0–3	0	0	—	0	—	0	—	0	—	0	—
	4–9	4	1	25.00	3	75.00	1	33.33	2	66.67	0	0.00
	10–14	7	0	0.00	7	100.00	2	28.57	5	71.43	0	0.00
Other central nervous system tumours	**Overall**	**29**	**25**	**86.21**	**4**	**13.79**	**3**	**75.00**	**0**	**0.00**	**1**	**25.00**
	0–3	10	10	100.00	0	0.00	0	—	0	—	0	—
	4–9	11	10	90.91	1	9.09	1	100.00	0	0.00	0	0.00
	10–14	8	5	62.50	3	37.50	2	66.67	0	0.00	1	33.33

PNET = primitive neuroectodermal tumour

	2000–2004										
	Total	None		Received any		0–90 days		91–180 days		≥ 181 days	
	N	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%	Yes (n)	%
	388	**211**	**54.38**	**154**	**39.69**	**120**	**77.92**	**19**	**12.34**	**15**	**9.74**
	69	50	72.46	12	17.39	2	16.67	4	33.33	6	50.00
	188	91	48.40	84	44.68	79	94.05	2	2.38	3	3.57
	131	70	53.44	58	44.27	39	67.24	13	22.41	6	10.34
	194	**155**	**79.90**	**18**	**9.28**	**8**	**44.44**	**4**	**22.22**	**6**	**33.33**
	29	21	72.41	1	3.45	0	0.00	1	100.00	0	0.00
	93	74	79.57	8	8.60	4	50.00	1	12.50	3	37.50
	72	60	83.33	9	12.50	4	44.44	2	22.22	3	33.33
	44	**12**	**27.27**	**30**	**68.18**	**29**	**96.67**	**0**	**0.00**	**1**	**3.33**
	7	6	85.71	1	14.29	0	0.00	0	0.00	1	100.00
	26	3	11.54	21	80.77	21	100.00	0	0.00	0	0.00
	11	3	27.27	8	72.73	8	100.00	0	0.00	0	0.00
	30	**7**	**23.33**	**23**	**76.67**	**15**	**65.22**	**4**	**17.39**	**4**	**17.39**
	10	6	60.00	4	40.00	1	25.00	1	25.00	2	50.00
	7	0	0.00	7	100.00	7	100.00	0	0.00	0	0.00
	13	1	7.69	12	92.31	7	58.33	3	25.00	2	16.67
	74	**13**	**17.57**	**61**	**82.43**	**57**	**93.44**	**1**	**1.64**	**3**	**4.92**
	15	11	73.33	4	26.67	1	25.00	0	0.00	3	75.00
	42	2	4.76	40	95.24	39	97.50	1	2.50	0	0.00
	17	0	0.00	17	100.00	17	100.00	0	0.00	0	0.00
	19	**8**	**42.11**	**11**	**57.89**	**10**	**90.91**	**1**	**9.09**	**0**	**0.00**
	5	4	80.00	1	20.00	0	0.00	1	100.00	0	0.00
	11	3	27.27	8	72.73	8	100.00	0	0.00	0	0.00
	3	1	33.33	2	66.67	2	100.00	0	0.00	0	0.00
	11	**0**	**0.00**	**11**	**100.00**	**1**	**9.09**	**9**	**81.82**	**1**	**9.09**
	1	0	0.00	1	100.00	0	0.00	1	100.00	0	0.00
	0	0	—	0	—	0	—	0	—	0	—
	10	0	0.00	10	100.00	1	10.00	8	80.00	1	10.00
	16	**16**	**100.00**	**0**	**0.00**	**0**	**—**	**0**	**—**	**0**	**—**
	2	2	100.00	0	0.00	0	—	0	—	0	—
	9	9	100.00	0	0.00	0	—	0	—	0	—
	5	5	100.00	0	0.00	0	—	0	—	0	—

Exhibits 8.8a–8.8c

Complete information on treatment modalities employed was available for the period 1995–2004 only. Over this period treatment modalities evolved. These changes include advances in imaging technology (i.e., the availability of MRI) and surgical techniques, the availability of chemotherapeutic agents, differing combinations and dosages of chemotherapeutic agents, the changing knowledge of the effectiveness of therapeutic agents and an increased understanding of basic tumour biology. These factors make it difficult to provide an accurate overview of the treatment modalities used. Considering these limitations, Exhibits 8.8a-8.8c provide an overview of the different treatment modalities employed for the different age groups.

The number of children who did not undergo first look surgery did not vary greatly with age (0–3 years, 23.3%; 4–9 years, 26.8%; and 10–14 years, 20.5%). For low grade glioma, 24.6% did not undergo surgical intervention, suggesting that the diagnosis was based on radiologic findings or known predisposing circumstances (e.g., neurofibromatosis type 1). With respect to high grade glial tumours, the 57.8% who did not undergo surgery encompass a high proportion of diffuse intrinsic pontine glioma, which was treated nonsurgically (data not shown).

The relative frequency with which different modalities were used within treatment protocols has also changed with time. There has been an increase in the proportion of children who receive chemotherapy, both upfront and overall, as part of their initial treatment regimen. This increase is particularly evident in the 4–9 year and 10–14 year age groups and is true for all tumours except ependymoma. However, as Exhibit 8.8c demonstrates, the proportion of children who received upfront radiotherapy remained stable.

When the data were broken down into treatment by age group and examined over the same time periods, no significant changes were observed between the age groups.

The treatment protocols used are different for the different tumour types. As well, the components of the treatment protocol have changed over time. Between the 2 time periods (1995–1999 and 2000–2004), upfront surgical intervention was less frequently performed for germ cell tumours. Chemotherapy became more commonly used in the treatment of high grade glial tumours, medulloblastoma and germ cell tumours. There was a trend to decreased use of chemotherapy and increased use of radiotherapy in the treatment of children with ependymoma. In the low grade glioma group, the proportion of patients who received radiotherapy dropped from 11.7% to 9.3% from the early period to the later period. The drop is more dramatic in 0–3 and 4–9 year olds than in the 10–14 year age group (Exhibit 8.8c).

Survival

EXHIBIT 8.9: **5 year overall survival of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1985–2004**

		Period of diagnosis										
		All years (1985–2004)		1985–1989		1990–1994		1995–1999		2000–2004		
Tumour type	Age (years)	OSP	95% CI	OSP	95% CI	OSP	95% CI	OSP	95% CI	OSP	95% CI	Test for trend (p value)*
All central nervous system tumours	Overall	**0.69**	**0.66-0.72**	**0.51**	**0.40-0.62**	**0.68**	**0.63-0.73**	**0.71**	**0.66-0.75**	**0.73**	**0.68-0.77**	**0.00**
	0–3	0.57	0.50-0.62	0.32	0.09-0.59	0.68	0.57-0.77	0.59	0.48-0.68	0.46	0.35-0.57	0.21
	4–9	0.69	0.65-0.73	0.63	0.50-0.73	0.68	0.60-0.75	0.70	0.63-0.76	0.73	0.66-0.79	0.08
	10–14	0.76	0.72-0.80	0.66	0.51-0.77	0.68	0.58-0.76	0.77	0.70-0.83	0.86	0.79-0.91	0.00
Low grade glial tumours	Overall	**0.94**	**0.91-0.95**	**0.89**	**0.78-0.94**	**0.95**	**0.91-0.98**	**0.95**	**0.91-0.97**	**0.93**	**0.88-0.95**	**0.49**
	0–3	0.95	0.89-0.98	0.85	0.59-0.95	1.00	—	1.00	—	0.92	0.71-0.98	0.61
	4–9	0.94	0.90-0.96	0.91	0.75-0.97	0.96	0.90-0.99	0.96	0.88-0.99	0.91	0.83-0.96	0.59
	10–14	0.93	0.89-0.95	0.90	0.64-0.98	0.91	0.81-0.96	0.93	0.85-0.96	0.94	0.86-0.98	0.39
High grade glial tumours	Overall	**0.22**	**0.17-0.28**	**0.30**	**0.17-0.45**	**0.23**	**0.14-0.33**	**0.20**	**0.11-0.30**	**0.23**	**0.12-0.36**	**0.39**
	0–3†	0.45	0.28-0.60	—	—	0.55	0.21-0.80	0.50	0.23-0.73	0.29	0.04-0.62	—
	4–9†	0.19	0.12-0.27	—	—	0.23	0.11-0.38	0.14	0.06-0.27	0.17	0.04-0.39	—
	10–14	0.16	0.08-0.26	0.28	0.08-0.52	0.15	0.04-0.31	0.10	0.01-0.37	0.30	0.09-0.55	0.90
Ependymoma	Overall	**0.54**	**0.42-0.64**	**0.60**	**0.33-0.79**	**0.59**	**0.38-0.75**	**0.50**	**0.29-0.68**	**0.51**	**0.32-0.66**	**0.35**
	0–3†	0.33	0.18-0.48	—	—	0.50	0.23-0.72	0.15	0.03-0.36	0.19	0.06-0.39	—
	4–9	0.62	0.41-0.78	0.50	0.16-0.77	0.46	0.15-0.73	0.85	0.36-0.97	0.80	0.38-0.95	0.06
	10–14	0.84	0.59-0.94	1.00	—	1.00	—	0.72	0.23-0.93	0.69	0.29-0.90	0.07
Medulloblastoma	Overall	**0.58**	**0.51-0.65**	**0.20**	**0.00-0.69**	**0.48**	**0.34-0.60**	**0.59**	**0.46-0.69**	**0.68**	**0.56-0.78**	**0.00**
	0–3	0.36	0.21-0.50	0.12	0.00-0.51	0.36	0.09-0.65	0.38	0.12-0.64	0.44	0.18-0.68	0.11
	4–9†	0.61	0.51-0.70	—	—	0.51	0.33-0.67	0.60	0.42-0.74	0.69	0.52-0.81	—
	10–14†	0.67	0.52-0.78	—	—	0.41	0.13-0.68	0.67	0.43-0.83	0.85	0.61-0.95	—
Supratentorial PNET	Overall†	**0.20**	**0.11-0.32**	**—**	**—**	**0.25**	**0.08-0.47**	**0.00**	**0.00-0.00**	**0.19**	**0.07-0.35**	**—**
	0–3†	0.13	0.03-0.29	—	—	0.20	0.01-0.57	—	—	0.01	0.00-0.04	—
	4–9†	0.25	0.11-0.42	—	—	0.33	0.07-0.63	0.32	0.06-0.62	0.26	0.06-0.52	—
	10–14†	—	—	—	—	—	—	—	—	—	—	—
Germ cell tumours	Overall†	**0.85**	**0.68-0.93**	**0.60**	**0.22-0.84**	**1.00**	**—**	**0.89**	**0.52-0.98**	**0.92**	**0.56-0.99**	**0.05**
	0–3†	—	—	—	—	—	—	—	—	—	—	—
	4–9†	1.00	—	—	—	1.00	—	1.00	—	1.00	—	—
	10–14	0.87	0.66-0.95	0.71	0.25-0.92	1.00	—	0.82	0.30-0.97	1.00	—	0.12
Other central nervous system tumours	Overall	**0.62**	**0.49-0.72**	**0.28**	**0.04-0.61**	**0.37**	**0.15-0.60**	**0.82**	**0.62-0.92**	**0.82**	**0.58-0.93**	**0.00**
	0–3	0.28	0.13-0.45	0.41	0.10-0.71	0.17	0.02-0.43	0.47	0.16-0.74	0.36	0.05-0.71	0.68
	4–9†	0.87	0.62-0.96	—	—	0.75	0.05-0.97	1.00	—	1.00	—	—
	10–14†	0.82	0.55-0.94	—	—	0.21	0.02-0.53	1.00	—	1.00	—	—

OSP = overall survival proportion; PNET = primitive neuroectodermal tumour; CI = confidence interval
*Test for trend not calculated if any period specific OSP is missing.
†Owing to small sample sizes, rates are not provided for some time periods.

EXHIBIT 8.10: **5 year event free survival of primary central nervous system tumours, by tumour type, age at diagnosis and period of diagnosis, age 0–14 years, in Ontario, 1995–2004**

		Period of diagnosis					
		All years (1995–2004)		1995–1999		2000–2004	
Tumour type	Age (years)	EFSP	95% CI	EFSP	95% CI	EFSP	95% CI
All central nervous system tumours	Overall	**0.66**	**0.62-0.69**	**0.65**	**0.60-0.69**	**0.67**	**0.62-0.71**
	0–3	0.45	0.37-0.52	0.50	0.39-0.60	0.39	0.28-0.49
	4–9	0.66	0.61-0.71	0.64	0.57-0.71	0.67	0.60-0.74
	10–14	0.77	0.72-0.82	0.74	0.66-0.80	0.81	0.73-0.86
Low grade glial tumours	Overall	**0.89**	**0.85-0.91**	**0.90**	**0.86-0.94**	**0.87**	**0.81-0.91**
	0–3	0.85	0.74-0.92	0.86	0.71-0.93	0.84	0.63-0.93
	4–9	0.89	0.83-0.93	0.92	0.84-0.96	0.86	0.77-0.92
	10–14	0.90	0.84-0.93	0.90	0.82-0.95	0.89	0.80-0.94
High grade glial tumours	Overall	**0.18**	**0.12-0.26**	**0.19**	**0.11-0.30**	**0.18**	**0.08-0.31**
	0–3	0.35	0.16-0.55	0.50	0.22-0.73	0.08	0.00-0.39
	4–9	0.15	0.07-0.25	0.14	0.05-0.26	0.19	0.05-0.40
	10–14	0.12	0.04-0.25	0.10	0.01-0.37	0.23	0.05-0.48
Ependymoma	Overall	**0.44**	**0.30-0.57**	**0.48**	**0.28-0.66**	**0.42**	**0.24-0.58**
	0–3	0.17	0.06-0.33	0.18	0.04-0.40	0.18	0.04-0.40
	4–9	0.66	0.35-0.85	0.85	0.36-0.97	0.53	0.17-0.80
	10–14	0.64	0.36-0.82	0.72	0.23-0.93	0.61	0.28-0.82
Medulloblastoma	Overall	**0.54**	**0.45-0.62**	**0.50**	**0.37-0.60**	**0.58**	**0.46-0.69**
	0–3	0.24	0.09-0.43	0.27	0.05-0.55	0.21	0.05-0.45
	4–9	0.55	0.43-0.66	0.48	0.32-0.63	0.61	0.44-0.74
	10–14	0.70	0.53-0.82	0.61	0.38-0.77	0.81	0.56-0.93
Supratentorial PNET	Overall	**0.19**	**0.07-0.34**	**0.32**	**0.13-0.53**	**0.18**	**0.06-0.35**
	0–3*	0.07	0.00-0.27	—	—	0.01	0.00-0.06
	4–9	0.25	0.07-0.48	0.32	0.07-0.62	0.27	0.06-0.56
	10–14*	—	—	—	—	—	—
Germ cell tumours	Overall	**0.81**	**0.58-0.92**	**0.69**	**0.34-0.88**	**0.92**	**0.56-0.99**
	0–3*	—	—	—	—	—	—
	4–9*	0.65	0.20-0.89	0.45	0.07-0.78	1.00	—
	10–14*	0.94	0.66-0.99	0.82	0.35-0.96	1.00	—
Other central nervous system tumours	Overall	**0.71**	**0.55-0.82**	**0.60**	**0.37-0.78**	**0.82**	**0.58-0.93**
	0–3	0.31	0.10-0.56	0.37	0.10-0.65	0.36	0.05-0.71
	4–9*	0.93	0.59-0.99	0.86	0.26-0.98	1.00	—
	10–14*	0.85	0.50-0.96	0.72	0.26-0.92	1.00	—

EFSP = event free survival proportion; PNET = primitive neuroectodermal tumour; CI = confidence interval
*Owing to small sample sizes, rates are not provided for some time periods.

Exhibits 8.9 and 8.10

Survival information was available for 1,342 of the 1,448 cases contained in this registry.

The overall 5 year survival rate for all children diagnosed with a CNS tumour between 1985 and 2004 was 69% (95% CI, 66–72%). The survival rate varied with age. In children 3 years of age or less at initial diagnosis, the survival rate was 57% (95% CI, 50–62%), compared with 76% (95% CI, 72–80%) for children 10–14 years of age. Children 4–9 years of age at diagnosis had a 5 year survival rate between that of the other 2 age groups (i.e., 69% [95% CI, 65–73%]). The difference in survival rates based on age probably reflects the different distribution of tumour types by age and the treatment of the tumour based on the age of the child at diagnosis.

For the period 1990–2004, there was a progressive increase in the overall 5 year survival rate in each successive 5 year interval for all ages combined (from 68% to 73%). This improvement was most obvious in children over 10 years of age at the time of diagnosis (from 68% to 86%). It was also notable for children 4–9 years of age at the time of diagnosis (from 68% to 73%). However, overall survival for children aged 0–3 years at diagnosis declined (from 68% to 46%), although the confidence intervals are wide, reflecting the small sample size.

The reasons for the differences in 5 year survival rates between the different age groups are complex. They include differences in distribution by tumour type and thus therapy. Changes in treatment approaches may also have a role. The limitation of use of radiation therapy in the youngest age group may also have a significant impact.

As expected, children with a histologic diagnosis of low grade glial tumour did well (5 year survival rate of 94% [95% CI, 91–95%]), with no significant change in survival over the 20 year period. Children with a diagnosis of germ cell tumour had an 85% 5 year survival rate (95% CI, 68–93%), with appreciable improvement over successive time periods. Children with either medulloblastoma or ependymoma had similar 5 year survival rates: 58% (95% CI, 51–65%) and 54% (95% CI, 42–64%), respectively, with substantial improvement in overall survival for the former over successive periods and no change in survival for the latter. The poorest outcomes were seen in patients with either PNETs or high grade glial tumours (5 year survival of 20% [95% CI, 11–32%] and 22% [95% CI, 17–28%], respectively).

From 1990 to 2004, based on histologic diagnosis, 5 year survival rates remained constant, except for the medulloblastoma group. For this group of patients, the 5 year survival rate steadily increased, from 48% (95% CI, 34–60%) for 1990–1995 to 68% (95% CI, 56–78%) for 2000–2004. Similar improvements were seen in germ cell tumours, with survival rates increasing from 60% (95% CI, 22–84%) in the first 5 year period to 92% (95% CI, 56–99%) in the last.

For completeness, the event (progression) free survival rates for the subset diagnosed and treated between 1995 and 2004 are included in Exhibit 8.10; however, caution is needed in interpreting these data. At progression, a change in therapies being offered, including second look surgery, use of radiotherapy in children previously felt to be at risk of secondary cognitive impairment owing to age or change in chemotherapy regimen, may be the reason for this change in overall survival.

The proportion of children with different tumour histologies in this cohort varied with age. The number of children in each group was relatively small. Small shifts in outcome for a small number of children within a sub-group could affect the overall outcome. For similar reasons, a change in therapeutic strategies in 1 sub-group that resulted in increased 5 year survival rates for that tumour group could also affect the outcome for a certain age group if the proportion of the tumour type was great enough within that group.

Summary

Brain tumours are rare in children, with an annual incidence rate of 33.2 per million children 14 years of age or younger in the Province of Ontario. This rate did not change significantly over the study period. CNS tumours are slightly more common in males than females and in children over 3 years of age. Therapeutic modalities vary with age, with radiotherapy tending to be less commonly used in children 3 years of age or younger. Though therapeutic options advanced over the study period, the 5 year survival rates remained relatively stable, except for medulloblastoma and germ cell tumours, where there was a steady improvement in survival.

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