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ORIGINAL ARTICLE

Assessing fitness to drive in brain tumour patients: a grey matter of law, ethics, and medicine

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ABSTRACT

Background

Neurocognitive deficits from brain tumours may impair the ability to safely operate a motor vehicle. Although certain jurisdictions in Canada legally require that physicians report patients who are unfit to drive, criteria for determining fitness are not clearly defined for brain tumours.

Methods

Patients receiving brain radiotherapy at our institution from January to June 2009 were identified using the Oncology Patient Information System. In addition to descriptive statistics, details of driving assessment were reviewed retrospectively. The Fisher exact test was used to determine factors predictive of reporting a patient to the Ontario Ministry of Transportation (MTO) as unfit to drive. A logistic regression model was constructed to further determine factors predictive of reporting.

Results

Of the 158 patients available for analysis, 48 (30%) were reported to the MTO, and 64 (41%) were advised to stop driving. With respect to the 53 patients with seizures, a report was submitted to the MTO for 30 (57%), and a documented discussion about the implications of driving was held with 35 (66%). On univariate analysis, younger age, a central nervous system primary, higher brain radiotherapy dose, unifocal disease, and the presence of seizures were predictive of physician reporting ($p < 0.05$). On logistic regression modelling, the presence of seizures (odds ratio: 3.9) and a higher radiotherapy dose (odds ratio: 1.3) remained predictive of reporting.

Interpretation

Physicians frequently do not discuss the implications of driving with brain tumour patients or are not properly documenting such advice (or both). Clear and concise reporting guidelines need to be drafted given the legal, medical, and ethical concerns surrounding this public health issue.

KEY WORDS

Driving, brain tumours, Canadian heath care system, guidelines, radiation therapy

1. INTRODUCTION

The onus for determining medical fitness to drive in patients with neurocognitive deficits falls primarily on the physician, although few have been formally trained in the area[1]. Most provinces and all 3 territories in Canada have a legal requirement for physicians to report drivers who they feel are medically unfit to drive[2]. Guidelines to report medically unfit drivers were drafted by the Canadian Medical Association and are clear for selected conditions such as seizures, which are immediate grounds for cessation of driving[3]. For less clear-cut cases, physicians are faced with a dilemma that juxtaposes the need to advocate both for patient autonomy and for public safety. There is a paucity of published data to inform evidence-based recommendations on when to intervene for these patients.

The incidence of brain tumours is rising in Canada, with an estimated 10,000 new diagnoses of primary and metastatic disease annually[4]. Brain tumours may result in visual changes, motor deficits, delayed reflexes, headaches, and seizures—all of which can impair a patient's ability to drive safely. Our group previously reported a pilot study evaluating the

influence of provincial legislation on the likelihood that Canadian radiation oncologists would report a brain tumour patient as medically unfit to drive to the provincial ministry of transportation[4]. Other Canadian studies have explored the appropriateness of physician reporting and vehicle operation by patients in other disease sites[5–10]. Those studies collectively concluded that provincial laws are vague, physician responsibility is often unclear, and more tools are required to appropriately evaluate fitness to drive. However, like international studies, the foregoing studies were based solely on physician opinion rather than actual patterns of practice[11,12]. Thus, we report here on our institutional experience of rates of physician discussion of fitness to drive, submission of a report to the Ontario Ministry of Transportation (MTO), and time from either diagnosis or initial seizure to report submission in the context of brain tumours in a high-volume cancer centre in Southwestern Ontario.

2. METHODOLOGY

After obtaining institutional research ethics board approval, we used Cancer Care Ontario's Oncology Patient Information System to identify all patients diagnosed with primary or metastatic brain cancer and treated with brain radiotherapy between January and June 2009 at the London Regional Cancer Program. Records were cross-referenced with our institutional database to ensure accuracy of data. Three other regional cancer centres in Ontario were approached to participate in the study. All declined, with one centre citing legal concerns associated with the non-reporting of patients with seizures.

The records search at our institution identified 179 patients. Of those 179 patients, 21 were excluded from the analysis: 17 because they had received prophylactic cranial irradiation (12 for small-cell lung cancer, 5 for acute lymphoblastic leukemia), 2 because they were below the legal age to drive, and 2 because they died before discharge. Information pertaining to patient demographics (age, sex), diagnosis (date, site of origin, pathology), extent of disease (number of lesions), location of disease (anatomical lobe), presence of seizures, control of seizures (duration), previous treatment (surgery, chemotherapy, radiotherapy), potentially-unfit-to-drive report to the MTO (date, by whom), and license reinstitution (date, by whom) were abstracted from the charts.

Descriptive statistics were calculated for baseline patient, tumour, and treatment characteristics. Bivariate analysis was also performed for the same characteristics stratified by sex, seizures (yes or no), and MTO report (yes or no). Results of the bivariate analyses were compared using the chi-square test (or the Fisher exact test where appropriate) for categorical variables, and two-sample *t*-tests (or the Wilcoxon rank sum test, where appropriate) for continuous variables. Multivariate logistic regression modelling was performed to further determine factors associated with a MTO report submission. Variables associated with a dependent variable ($p < 0.15$) were entered into the model and removed stepwise, using backward elimination procedures. Only variables showing a moderate level of association ($p < 0.25$) were retained in the final model. Time-to-event outcomes were estimated using the Kaplan–Meier method. All statistical analyses were two-sided and were performed using the SAS software application (version 9.2: SAS Institute, Cary, NC, U.S.A.) with $p \leq 0.05$ indicative of statistical significance.

3. RESULTS

Table I summarizes patient, tumour, and treatment characteristics, and factors predictive of a report being submitted to the MTO. For the patient cohort, mean age was 62 years (range: 19–96 years), men predominated (58%), and the most common disease origins were metastasis from a lung primary (41%) and then a central nervous system primary (25%).

The overall rate of MTO reporting was low. Reports were submitted for 48 patients (30%), most commonly by neurologists (60%) and oncologists (29%). A documented discussion about safe driving was held with 64 patients (41%). With respect to the 53 patients with seizures, a report was submitted to the MTO for 30 (57%), and a documented discussion about the implications of driving was held with 35 (66%). A report was submitted to the MTO for 4 patients (3%) without documentation in their medical record of a discussion on driving, and for 90 patients, the medical record documented neither a discussion nor a report submitted (57%).

On univariate analysis, younger age, central nervous system primary, higher brain radiotherapy dose, unifocal disease, and the presence of seizures were predictive of a report being submitted to the MTO. On logistic regression analysis, the presence of seizures (odds ratio: 3.9) and a higher radiotherapy dose (odds ratio: 1.3) were the only predictive factors that remained statistically significant with respect to reporting (Table II).

Of the 53 patients with seizures, 15 (28%) were diagnosed with a brain tumour after their first seizure, 17 (32%) were diagnosed on the same day as their first seizure, and 21 (40%) were diagnosed before a seizure occurred. Of the 48 patients reported, 44 (92%) were diagnosed before the report (range: 1 day–37.3 months), and 4 (8%) were diagnosed after the report (at 5, 56, 84, and 207 days later). For reported patients, the mean time from diagnosis (that is, imaging showing an intracranial mass) to report was 2.3 months (range: –6.8 to 37.3 months); however, excluding the 4 patients who were diagnosed after the report, the mean increased to 2.8 months (range: 0.03–37.3 months; Figure 1). For the 30 patients having a documented seizure and a report submitted, the

TABLE I Baseline characteristics of the study patients

Characteristic	*Patients*			p *Value*	*Characteristic*	*Patients*			p *Value*
	All	*MTO report*				*All*	*MTO report*		
		No	*Yes*				*No*	*Yes*	
Patients (*n*)	158	110	48		EBRT dose (Gy)				
Age (years)[a]					Mean	32.93±13.59	28.78±11.61	42.45±13.08	<0.001
Mean	61.85±14.10	64.08±13.48	56.74±14.28	0.002	Median	30.00	30.00	40.00	
Median	63.41	65.29	57.02		Range	9.00–60.68	9.00–60.68	20.00–60.00	
Range	19.49–96.36	19.49–96.36	20.61–85.21		EBRT dose group [*n* (%)]				
Age groups [*n* (%)]					≤20 Gy	55 (34.8)	52 (47.3)	3 (6.3)	
≤55 Years	48 (30.4)	26 (23.6)	22 (45.8)		>20 to ≤30 Gy	50 (31.7)	36 (32.7)	14 (29.2)	
>55 to ≤65 Years	38 (24.1)	28 (25.5)	10 (20.8)		>30 to ≤40 Gy	18 (11.4)	9 (8.2)	9 (18.8)	
>65 to ≤75 Years	49 (31.0)	37 (33.6)	12 (25.0)		>40 to ≤50 Gy	8 (5.1)	3 (2.7)	5 (10.4)	
>75 Years	23 (14.6)	19 (17.3)	4 (8.3)		>50 Gy	27 (17.1)	10 (9.1)	17 (35.4)	
Age at diagnosis					Histology [*n* (%)]				
Mean	58.33±14.98	60.45±14.65	53.46±14.75	0.007	Non-small-cell lung cancer	41 (26.0)	33 (30.0)	8 (16.7)	<0.001
Median	60.00	61.89	53.93		High grade glioma	27 (17.1)	9 (8.2)	18 (37.5)	
Range	0.16–93.43	0.16–93.43	17.79–82.27		Adenocarcinoma	20 (12.7)	14 (12.7)	6 (12.5)	
Age at first seizure (*n*=53)					Small-cell lung cancer	17 (10.8)	13 (11.8)	4 (8.3)	
Mean	53.68±16.10	55.55±15.23	52.26±16.84	0.466	Melanoma	8 (5.1)	6 (5.5)	2 (4.2)	
Median	55.33	57.48	51.88		Renal carcinoma	8 (5.1)	7 (6.4)	1 (2.1)	
Range	17.78–82.28	19.94–77.63	17.78–82.28		Squamous carcinoma	8 (5.1)	8 (7.3)	—	
Age at report (*n*=28)					Low-grade glioma	6 (3.8)	—	6 (12.5)	
Mean	53.65±14.65	—	—		Other	23 (14.6)	20 (18.2)	(6.3)	
Median	54.24	—	—		Tumour location, *n*=153 [*n* (%)]				
Range	17.85–82.28	—	—		Multiple	98 (64.1)	73 (69.5)	25 (52.1)	0.138
Sex [n (%)]					Frontal	18 (11.8)	9 (8.6)	9 (18.8)	
Women	66 (41.8)	50 (45.5)	16 (33.3)	0.155	Temporal	13 (8.5)	10 (9.5)	3 (6.3)	
Men	92 (58.2)	60 (54.6)	32 (66.7)		Parietal	10 (6.5)	6 (5.7)	4 (8.3)	
CNS primary [*n* (%)]	40 (25.3)	14 (12.7)	26 (54.2)	<0.001	Occipital	7 (4.6)	3 (2.9)	4 (8.3)	
					Cerebellar	7 (4.6)	4 (3.8)	3 (6.3)	

TABLE I Continued

Characteristic	Patients			p Value
	All	MTO report		
		No	Yes	
Site of origin [*n* (%)]				
Lung	64 (40.5)	51 (46.4)	13 (27.1)	<0.001
Primary CNS	40 (25.3)	14 (12.7)	26 (54.2)	
Breast	15 (9.5)	14 (12.7)	1 (2.1)	
Genitourinary	9 (5.7)	8 (7.3)	1 (2.1)	
Skin	8 (5.1)	6 (5.5)	2 (4.2)	
Lymphoma	5 (3.2)	5 (4.6)	—	
Other[b]	17 (10.8)	12 (10.9)	5 (10.4)	

Characteristic	Patients			p Value
	All	MTO report		
		No	Yes	
Multifocal disease, *n*=153 [*n* (%)]	98 (64.1)	73 (69.5)	25 (52.1)	0.037
Seizures [*n* (%)]	53 (33.5)	23 (20.9)	30 (62.5)	<0.001
Seizure control [*n* (%)]	52 (32.9)	23 (20.9)	29 (60.4)	<0.001
Previous CNS surgery [*n* (%)]	45 (28.5)	21 (19.1)	24 (50.0)	<0.001
Previous chemotherapy [*n* (%)]	117 (74.1)	79 (71.8)	38 (19.2)	0.333
MTO report [*n* (%)]	48 (30.4)	—	—	—
Specialty of reporting physician, *n*=48 [*n* (%)]				
Neurology	29 (60.4)	—	—	—
Oncology	14 (29.2)	—	—	
Other	5 (10.4)	—	—	
Discussion [*n* (%)]	64 (40.5)	20 (18)	44 (92)	<0.001

[a] At December 31, 2011.
[b] Gastrointestinal, 4; gynecologic, 2; unknown, 3; leukemia, 2; prostate, 3; other, 3.
[c] Emergency room physician, 1; family physician, 1; ophthalmologist, 1; surgeon, 1; other, 1.
MTO = Ontario Ministry of Transportation; EBRT = external-beam radiation therapy; CNS = central nervous system.

TABLE II Logistic regression models examining relationships between predictors of Ontario Ministry of Transportation report submission (dependent variable)

Independent variable	Reference	Univariate			Multivariate		
		OR	95% CI	p Value	OR	95% CI	p Value
Radiation dose	Per 5-Gy increase	1.48	1.28 to 1.70	<0.001	1.27	1.03 to 1.58	0.029
CNS primary	Other primary	8.10	3.65 to 18.00	<0.001	2.20	0.64 to 7.57	0.211
Multifocal disease	Single focus	0.48	0.24 to 0.96	0.039	0.57	0.24 to 1.36	0.208
Seizures	No seizures	6.30	3.00 to 13.26	<0.001	3.94	1.70 to 9.16	0.001
Age	Per 10-unit increase	0.73	0.58 to 0.92	0.009	—	—	—
Male	Female	1.67	0.82 to 3.38	0.157	—	—	—
Previous CNS surgery	No surgery	4.24	2.02 to 8.87	<0.001	—	—	—

CNS = central nervous system.

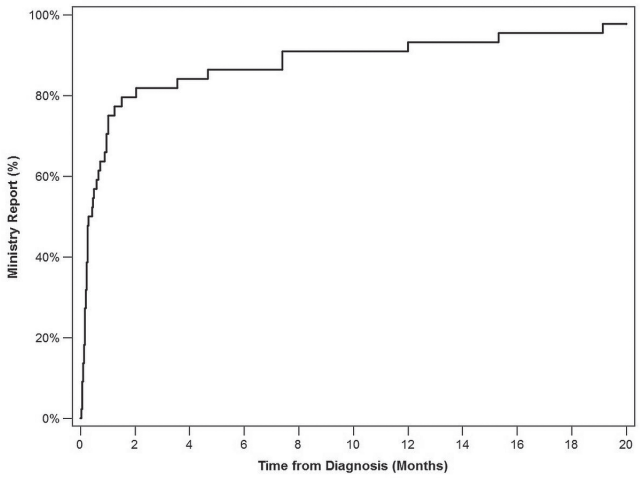

FIGURE 1 Time from diagnosis to Ontario Ministry of Transportation report.

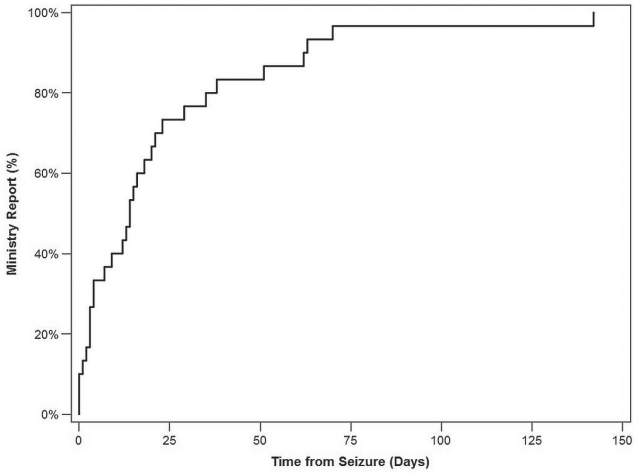

FIGURE 2 Time from first seizure to Ontario Ministry of Transportation report.

mean time from first seizure to report was 23 days (range: 0–142 days; Figure 2).

4. INTERPRETATION

Each year, an estimated 5000 people in the United States are killed in motor vehicle accidents by medically unfit drivers[13]. The relative risk of a motor vehicle accident attributable to various medical conditions has been estimated to range from 2 to almost 8 times that attributable to healthy drivers[14]. However, for many patients, the ability to drive is an essential means to maintain autonomy in social, professional, and familial obligations. Physicians in Canada are thus faced with the difficult medical, ethical, and (often) legal responsibility to determine whether their patients are medically fit to drive a motor vehicle.

The present study indicates that physicians frequently do not discuss the implications of driving or are not properly documenting such advice in medical records. We found that, although physicians were more commonly discussing the implications of driving for brain tumour patients with seizures, such patients were not routinely reported to the MTO as unfit to drive despite clear guidelines related to this disorder. Even for the patients who were reported, the mean time from first seizure to report was just over 3 weeks, and in patients not having seizures, it was almost 3 months.

It is clear that neurocognitive sequelae from brain tumours may impair ability to drive, but practice patterns in assessing and reporting fitness to drive are highly variable. In an Australian survey, 73% of physicians were unaware of national reporting guidelines, and accordingly, nearly half the respondents had difficulty making a decision when asked by patients about driving ability[11]. An American survey similarly demonstrated that only 31% of respondents addressed driving restrictions with every patient having a brain tumour[12]. In a survey of Canadian radiation oncologists, our research group found that roughly three quarters of respondents consider reporting brain tumour patients to the MTO, almost 90% feel that provincial laws are unclear about expectations, and nearly one quarter are unable to correctly identify their provincial legal requirement to report medically unfit drivers[4]. The only factor that significantly influenced inclination to report in 8 hypothetical brain tumour scenarios was the presence of provincial legislation in the respondent's jurisdiction of practice, suggesting that physicians may be practicing out of fear of litigation, rather than based on a medical assessment of risk.

The generalizability of our research might be challenged on the merits of it being performed retrospectively and within a single institution, but our findings do recapitulate previous survey studies that collectively concluded that physicians are uncertain in many cases about their duty in reporting medically unfit drivers. Another potential weakness of our study is that it examined only hospital records when, in fact, a driving assessment might have been performed or a report submitted by the family physician in the community. However, our research group previously conducted a multidisciplinary survey of specialists and family physicians caring for brain tumour patients and found that, compared with specialists, family doctors were even less comfortable with reporting, less likely to consider reporting, less likely to have patients inquire about driving, and less likely to engage in a discussion about safe driving[15]. Finally, given the retrospective nature of the present study, it was difficult to ascertain the driving status of patients at the time of disease presentation or whether other factors such as comorbidities or

medication use deterred a physician from discussing driving ability or submitting a report. Nonetheless, Ontario has some of the strictest reporting laws in North America, with section 203(1) of the *Highway Traffic Act* stating that "physicians shall report every person greater than 16 years of age who is suffering from a condition that may make it dangerous for the person to operate a motor vehicle"[2].

The utility of mandatory reporting laws for physicians caring for medically unfit drivers has been the subject of significant controversy, particularly for patients with seizure disorders[14]. A British study showed that only 72% of patients would inform their physician about breakthrough seizures in areas with mandatory reporting laws, compared with 96% of patients who would report breakthrough seizures if no mandatory reporting legislation was present[16]. Another British study similarly found that 75% of patients who experienced a seizure in the preceding year did not mention to their physician that they held a valid driving license[17]. Other confounding issues described in the literature include lengthy delays between reporting and license suspension[18], difficulty and delays in attempting to reinstate licences[19], and a sense of hostility or even a lack of compliance or hostility from patients after a report[20].

To allow a broad range of people to drive, a certain degree of risk must be tolerated, and that toleration involves striking a balance between the need for people to be licensed to drive and the safety of the public on the roads. In 2003, a multidisciplinary working group was assembled by the Canadian Cardiovascular Society Consensus Conference for the Assessment of the Cardiac Patient for Fitness to Drive and Fly, and it determined that a 1 in 20,000 annual risk of death or serious injury to other road users was considered acceptable[21]. This consensus panel also described the use of a risk-of-harm formula derivation to assess driving fitness after implantation of a left ventricular assist device. In that case, the risk of harm to other road users posed by the driver was thought to be directly proportional to the time spent behind the wheel or the distance driven in a given time; the type of vehicle driven; the risk of sudden cardiac incapacitation; and the probability that such an event would result in a fatal or injury-producing accident[5].

In the context of brain tumours, the United Kingdom recently created guidelines for driving restrictions designed according to perceived risk, based on histologic subtype and location of intracranial disease[22]. Similarly, the Cancer Institute of New South Wales Oncology Working Group for Neuro-Oncology assembled a multidisciplinary panel to create a brochure for clinicians that outlines a simple algorithm to provide informed advice and to guide decision-making on driving fitness[23]. A second pamphlet created by the same group is tailored for patients and their caregivers, outlining in lay terms why the patient should not be driving, what the responsibilities of the physician are, what the process is for returning to drive, and a list of alternatives to driving. At the present time, specific, clear, and concise guidelines for fitness to drive in brain tumour patients are lacking in Canada. Thus, we propose the formation of a multidisciplinary working group that would apply an evidence-based approach in devising Canadian standards to ensure that driving for patients with brain tumours is no longer a grey matter.

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6. CONFLICT OF INTEREST DISCLOSURES

There are no possible conflicts of interest, sources of financial support, corporate involvement, or patent holdings related to the present work.

7. REFERENCES

1. Yale SH, Hansotia P, Knapp D, Ehrfurth J. Neurologic conditions: assessing medical fitness to drive. *Clin Med Res* 2003;1:177–88.
2. Government of Ontario. *Highway Traffic Act,* R.S.O. 1990, c.H.8, s.203(1).
3. Canadian Medical Association (CMA). *Determining Medical Fitness to Operate Motor Vehicles: CMA Driver's Guide*. 7th ed. Ottawa, ON: CMA; 2006.
4. Louie AV, D'Souza DP, Palma DA, *et al.* Fitness to drive in patients with brain tumours: the influence of mandatory reporting legislation on radiation oncologists in Canada. *Curr Oncol* 2012;19:e117–22.
5. Sindwani R, Parnes LS. Reporting of vestibular patients who are unfit to drive: survey of Canadian otolaryngologists. *J Otolaryngol* 1997;26:104–11.
6. Baskett R, Crowell R, Freed D, Giannetti N, Simpson CS on behalf of the Canadian Cardiovascular Society. Canadian Cardiovascular Society focused position statement update on assessment of the cardiac patient for fitness to drive: fitness following left ventricular assist device implantation. *Can J Cardiol* 2012;28:137–40.
7. Jang RW, Man-Son-Hing M, Molnar FJ, *et al.* Family physicians' attitudes and practices regarding assessments of medical fitness to drive in older persons. *J Gen Intern Med* 2007;22:531–43.
8. Rapoport MJ, Herrmann N, Molnar FJ, *et al.* Sharing the responsibility for assessing the risk of the driver with dementia. *CMAJ* 2007;177:599–601.
9. Redelmeier DA, Vinkatesh V, Stanbrook MB. Mandatory reporting by physicians of patients potentially unfit to drive. *Open Med* 2008;2:e8–17.
10. McLachlan RS, Starreveld E, Lee MA. Impact of mandatory physician reporting on accident risk in epilepsy. *Epilepsia* 2007;48:1500–5.

11. Chin YS, Jayamohan J, Clouston P, Gebski V, Cakir B. Driving and patients with brain tumours: a postal survey of neurosurgeons, neurologists and radiation oncologists. *J Clin Neurosci* 2004;11:471–4.
12. Thomas S, Mehta MP, Kuo JS, Ian Robins H, Khuntia D. Current practices of driving restriction implementation for patients with brain tumors. *J Neurooncol* 2011;103:641–7.
13. Evans L. *Traffic Safety.* Bloomfield Hills, MI: Science Serving Society; 2004: 156.
14. Lee W, Wolfe T, Shreeve S. Reporting epileptic drivers to licensing authorities is unnecessary and counterproductive. *Ann Emerg Med* 2002;39:656–9.
15. Louie AV, Chan E, Hanna M, *et al.* Multidisciplinary assessment and reporting of fitness to drive in brain tumor patients: a gray matter [abstract 6130]. *J Clin Oncol* 2012;30:. [Available online at: http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=114&abstractID=101173; cited January 12, 2013]
16. Dalrymple J, Appleby J. Cross sectional study of reporting of epileptic seizures to general practitioners. *BMJ* 2000;320:94–7.
17. Salinsky MC, Wegener K, Sinnema F. Epilepsy, driving laws, and patient disclosure to physicians. *Epilepsia* 1992;33:469–72.
18. Simpson CS, Hoffmaster B, Mitchell LB, Klein GJ. Mandatory physician reporting of drivers with cardiac disease: ethical and practical considerations. *Can J Cardiol* 2004;20:1329–34.
19. Sindwani R, Parnes LS, Goebel JA, Cass SP. Approach to the vestibular patient and driving: a patient perspective. *Otolaryngol Head Neck Surg* 1999;121:13–17.
20. Coopersmith HG, Korner–Bitensky NA, Mayo NE. Determining medical fitness to drive: physicians' responsibilities in Canada. *CMAJ* 1989;140:375–8.
21. Simpson C, Dorian P, Gupta A, *et al.* Assessment of the cardiac patient for fitness to drive: drive subgroup executive summary. *Can J Cardiol* 2004;20:1314–20.
22. Cancer Research UK. Home > CancerHelp > Your cancer type > Brain tumours > Living with brain tumours > Brain tumours and driving [Web page]. London, UK: Cancer Research UK; 2012. [Available at: http://www.cancerhelp.org.uk/type/brain-tumour/living/brain-tumours-and-driving; cited November 21, 2011]
23. McDonald KL. Brain tumors and driving. *J Neurooncol* 2011;104:399–400.

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