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Outcome and Prognostic Factors of low grade Astrocytoma in Patients in Namazi Hospital, Shiraz, Iran, 2006–2013

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ABSTRACT

Introduction: Primary brain tumors, although not among the most common site of tumors, are considered an important pathology, due to their high mortality rate. Astrocytoma is a glial brain tumor with a high mortality rate. The predictors of the patients' outcome is thus of great importance. In the present study, we investigated the results of 7–year follow–up of patients with astrocytoma in order to determine the prognostic factors associated with patients' survival.**Method:** In this cross–sectional study, 115 patients suffering from astrocytoma grade II, who referred to radio–oncology department of Nemazee hospital between 2006 and 2013, were included. The patients' overall survival (OS) and disease–free survival (DFS) were recorded and their difference according to demographic and clinical characteristics of patients, as well as the treatment used, was evaluated using SPSS v.25. **Results:** Mean age of patients was 35.34±15.17 years; most were younger than 40 years old (71%) and men (59%). Mean OS and DFS were 74.90±43.05 and 26.61±26.97 months, respectively. Patients younger than 40 had a significantly longer mean OS (84.04±37.93 vs. 53.04±47.41 months; P=0.004). Mean DFS was different according to chemotherapy and dose of radiotherapy (P=0.041 and 0.01, respectively), while OS was not (P>0.05). **Discussion:** Considering the difference in outcome of patients, specifically DFS, according to the performance of chemotherapy and the dose of radiotherapy, it is recommended to pay greater attention to appropriate choice of treatment strategy of patients with astrocytoma. Further randomized controlled studies are required to determine the predictors of patients' outcome.

Keywords: Brain Neoplasms; Astrocytoma; Radiotherapy; Chemotherapy

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INTRODUCTION

Primary brain tumors, which involve the intracranial structures, is a tumor of central nervous system (CNS) with an overall incidence of 10.82 per 100,000 person–years (1). Although brain is not among the most common site of tumor, accounting for less than 2% of all new cases of tumors, brain tumors are considered important, because of their high mortality rate (2). Accordingly, studies have focused on the factors associated with patients' prognosis. The unspecific clinical symptoms of brain tumors, including headache, nausea, vomiting, dizziness, seizure, and altered mental state, is one of the factors which makes diagnosis more difficult (3), while modern brain imaging techniques have taken a great step towards more accurate diagnosis (4). Additionally, the evolution of cancer treatment strategies have opened the door of hope to better prognosis (5); however, more studies are required for definite conclusion about the most appropriate treatment strategy for each type of brain tumor (6).

The world health organization (WHO) has classified primary brain tumors into tumors of meninges, neuroepithelial tissue, sellar region, cranial nerves and spine, lymphomas and hematopoet-

ic neoplasms, germ cell tumors and cysts, and unclassified (7, 8). Gliomas, a major subtype of neuroepithelial tissue tumors, refer to the tumors arising from glial or precursor cells, and the majority of gliomas (75.8%) are astrocytic tumors (9). According to WHO classification, patients' prognosis is significantly associated with astrocytoma grade, classified from I to IV: grade I (pilocytic astrocytoma) are mainly benign, grade II (diffuse astrocytoma [DA]) are diffusely infiltrative cells with cytological atypia, slow growth rate, and risk of malignancy, grade III includes tumors with anaplasia and mitotic activity (anaplastic astrocytoma), and grade IV are those with additional of microvascular proliferation and/or necrotic changes (7, 10).

Beside the tumor's grade, several factors have been identified to be associated with patient's prognosis. Prolonged prediagnostic symptomatic intervals and global delay interval has been identified as potential prognostic factors of survival of, especially high grade CNS tumors (11). Furthermore, appropriate treatment is an important predictor of patients' survival and several studies have shown the positive role of surgery, especially gross total resection (GTR), with improved survival in (high–grade) glioma (12-14). In this context, factors that influence the treatment choice, like the socioeconomic status, also affect the patients' outcome (12). In addition to surgery, additional treatments, such as chemotherapy and radiotherapy (RT), have been also identified as significant prognostic factors (15). Due to the significance of this issue and the different effects of different chemotherapy regimens and RT doses, it is important to report up–to–date information about the prognostic factors of survival in these patients. Therefore, the present study aimed to investigate the factors associated with overall and disease–free survival of patients with astrocytoma. As DA had the highest incidence rate among malignant tumors (after glioblastoma) (9) and poorer prognosis than other low–grade gliomas (LGG) (16), we have selected this subtype in the present study.

MATERIAL AND METHODS

Study design

In this cross–sectional retrospective study, all patients who referred to radio–oncology department of Namazi hospital between 2006 and 2013 and their diagnosis of DA was confirmed based on the pathologic or radiologic report, were included. All patients who had the inclusion criteria and gave consent for participation were enrolled by census method. The patients were assured that their participation choice does not affect their treatment strategies and/or medical care and no additional costs were imposed on the participants.

The patients' demographics, including age and sex, as well as the disease characteristics, including clinical symptoms, tumors' site, and the treatment strategies (RT dose and chemotherapy), were extracted from the medical records of the hospital information system and the missing information was completed by phone calls. Those who were reluctant to answer or did not answer to phone call were deleted from the study. Tumor's site was determined based on the results of magnetic resonance imaging. Surgery included GTR or subtotal resection (STR) of the tumor. For inoperable patients, treatment initiated without definite diagnosis (pathologic report); 54 Gy was considered as the optimal RT dose and the total RT dose was also recorded. All patients were going to have operation to obtain gross total resection .but it was not possible for all. Some were not operable due to location of tumor or patient refusal. For some, biopsy alone was done and for some others incomplete tumor resection was done. Chemotherapy was not routine at our center except in some cases according to discussion with patients.

The final outcome of patients, which included overall survival (OS) and disease–free survival (DFS), were also recorded. Survival analysis were done for those who completed the treatment Any patient with incomplete medical records, who declined to continue the study or could not be followed for any other reason, was excluded from the study.

Statistical analysis

Descriptive results of categorical variables were reported by frequency (percentage) and compared between groups using Chi square test. For numeric variables, descriptive analysis was presented by mean ± standard deviation (SD). The results of One–sample Kolmogorov–Smirnov test showed that the numeric variables did not have a normal distribution; therefore, comparison between two–group variables was performed or Mann–Whitney U test and among more than two–group variables using Kruskal Wallis test. Patients' age was categorized into below and above 40 years and subgroup analysis was performed considering this grouping, as well. For the statistical analysis, the statistical software IBM SPSS Statistics for Windows version 25.0 (IBM Corp. 2016. Armonk, NY: IBM Corp) was used. P values <0.05 were considered statistically significant.

RESULTS

A total of 115 patients completed the study and their data were analyzed. Mean age of patients was 35.34±15.17 years (minimum of 3 and maximum of 74 years) and 82(71%) patients were 40 years old and younger. Most patients (68 or 59%) were male and 47(41%) were female. Mean age of male and female patients were 32.29 ± 14.7 and 37.34±15.4 years.

A total of 36 patients were alive and 72 passed away. Mean OS and DFS were 74.91±43.05 and 26.16±26.96 months, respective-

Table 1. The comparison of mean overall survival, disease–free survival, and the frequency of dead or alive patients based on patients' demographics

			Overall survival	Disease–free survival
Variables	Categories	Number	Duration (months), mean±SD	Duration (months), mean±SD
Age categories	<40 years	50	84.08±37.94	28.92±27.59
	>40 years	21	53.05±47.41	20.96±24.93
	P–value	–	0.004*	0.125*
Total		71	74.90±43.05	26.61±26.97

* The results of Mann Whitney U test
† The result of chi square test

Table 2. The comparison of mean overall survival, disease–free survival, and the frequency of dead or alive patients based on the treatment strategies

		Overall survival		Disease–free survival
Variables	Categories	Number	Duration (months), mean±SD	Duration (months), mean±SD
Type of Surgery	Complete	36	79.22±45.02	26.92±28.48
	Subtotal	7	71.57±41.66	43.60±34.19
	Biopsy	27	68.78±41.84	24.24±24.16
	P–value*	–	0.639	0.339
Radiotherapy dose	5400/180	33	73.54±34.79	29.73±22.24
	<5400/200	29	73.97±50.83	22.51±27.83
	Other	8	81.25±50.46	35.45±35.83
	P–value*	–	0.874	0.041
Chemotherapy	Yes	18	70.89±40.21	37.68±27.84
	No	53	76.26±44.26	22.54±25.65
	P–value*	–	0.634†	0.010†
Total		71	74.90 ±43.05	26.61 ±26.96

* The results of Kruskal Wallis test

† The results of Mann Whitney U test

ly. Mean age of the alive patients was 29.68±14.15; while mean age of death patients was 37.77±15.59. Alive patients were significantly older than the dead (P=0.02). Mean OS and DFS in patients who were 40 or younger were 84.08± 37.93 and 28.92±27.59 months that is higher than older patients that were 53.04±47.41 and 20.96±24.92 months (P=0.004; table 1).

The results of comparing mean OS and DFS according to the type of treatment used for the patient are shown in table 2. As shown, mean OS was not different according to type of surgery, RT dose, and undergoing chemotherapy (P>0.05). But, mean DFS was different according to RT dose and chemotherapy (P=0.041 and 0.010, respectively). Chemotherapy in our study was procarbazine, CCNU and vincristine.

A few (6.1%) were asymptomatic and the rest had different symptoms, as presented in table 3. Mean OS was not different according to patients' symptoms, while mean DFS was (P=0.03; table 3). Also, the patients' tumor was located at different sites, while mean OS and DFS of patients were not significantly different accordingly (P>0.05; table 3).

DISCUSSION

The present study investigated the factors associated with survival of patients with definite diagnosis of DA and the results of seven–year follow–up of 115 patients recruited into the study by census method from a referral hospital in Shiraz, Iran, showed an overall OS of 74.90±43.05 months and DFS of 26.61±26.97 months. The results of the study by Tove and colleagues indicated a median OS of 70 months (17), which is close to that reported in the present study, while other studies have reported poorer prognosis. In the study by Tunthanathip and colleagues, 42–month follow–up of 64 patients with DA revealed the 1–, 2–, and 5–year survival rates at 85.9, 67.6, and 42.3%, respectively, with a median survival of 26 months (18). The OS of the present study is nearly three–

Table 3. The comparison of mean overall survival, disease–free survival, and the frequency of dead or alive patients based on the clinical symptoms and tumors' site

			Overall survival	Disease–free survival
	Categories	Number	Duration (months), mean±SD	Duration (months), mean±SD
Clinical symptoms	Headache	21	70.33±48.34	26.38±30.81
	Seizure	21	79.09±32.08	40.52±28.71
	Neurologic deficit	8	81.00±36.28	22.78±19.77
	Motor deficit	9	55.67±43.20	14.50±16.42
	Mental alteration	3	92.67±69.87	28.00±5.29
	Headache and nausea	1	96.00	10.00±4.24
	Nausea and vomiting	3	58.99±74.54	8.50±4.95
	P–value*	–	0.831	0.039
Tumor's site	Frontal lobe	16	76.31±37.42	37.42±39.14
	Parietal	13	63.07±31.24	30.11±24.94
	Temporal lobe	1	72.50±20.82	25.10±20.81
	Frontoparietal	8	70.87±42.97	38.75±36.26
	Frontotemporal	6	74.67±71.03	24.33±14.92
	Occipital	3	54.00±26.15	7.10±6.69
	Third ventricle	2	111.00±46.67	60.00
	Fourth ventricle	1	132.00	–
	Cerebellum	1	20.00	26.50±15.33
	Posterior fossa	3	116.00±18.33	12.67±8.45
	Thalamus	2	69.5±88.39	4.00±2.82
	Lateral ventricle	2	16.50±20.51	3.00±2.83
	Supracellar	2	120.00±67.88	16.33±16.26
	P–value*	–	0.524	0.656

* The results of Kruskal Wallis test

times longer than that reported by Tunthanathip and colleagues; although mean value was reported in the present study. In another study on 30 patients with DA, Spych and colleagues reported the mean OS at 36.2±28.6 and DFS at 33.6±27.6 (19). The mean OS reported in this study was longer than that reported by Tunthanathip and colleagues (although the median OS reported by Spych and colleagues was 26.9, which is close to that reported by Tunthanathip and colleagues); but is still lower than the present study. The dissimilarity in the OS rates reported by different studies can be attributed to several factors; firstly, the sample size of the above–mentioned studies was small, which reduces the reliability of the results. Secondly, there are several factors that can influence patients' prognosis, the variability of which among the study populations of different studies can cause divergent results in this context. In the following, we discuss some of the factors associated with OS and DFS of patients.

In the present study, the majority of patients (71%) were younger than 40 years and the results showed that this group of patients had

a significantly longer mean OS. In a retrospective study on 35 patients with DA, Kumthekar and partners reported the median OS of DA patients aged ≥50 years at 48 months (range: 30–138 months) (20), which is close to the mean OS of patients older than 40 years in the present study (53.05±47.41months). Our results are similar to that of previous studies, which considered age >40 as a negative predictor of OS in patients with DA (17) or LGG (17, 21), while other studies have rejected the role of age on prognosis of patients with LGG (22, 23). In addition to the fact that the prognosis of LGG subgroups is different according to the histologic type (16, 24), this difference in the results of studies, considering the role of age on OS, may be related to the effect of other factors associated with OS. Similar to age, the results of studies on the effect of gender is also dissimilar. In the present study, about 60% of our study population was men and gender did not influence OS or DFS of patients. Others have also shown no role for gender on patients' prognosis (20). However, some have considered gender as a significant predictor of OS in both uni– and multi–variate analysis (17). This controversy is also attributable to the effect of other factors associated with OS; meta–analysis of uniform studies can indicate more definite conclusions in this regard.

The effect of treatment strategy used for the patients on OS is investigated in several studies. The results of the present study showed that the type of surgery (GTR, STR, or biopsy) did not influence OS or DFS. The results of previous studies on the effect of surgical types on patients' survival is controversial. Kumthekar and colleagues showed no statistically significant difference in OS among the three types (total, subtotal, or biopsy), while resection showed improved progression–free survival over biopsy in patients with LGG (20). However, others have identified a poorer prognosis for biopsy rather than optimal resection (17, 23, 25). Vildan Kaya and colleagues have shown a better 10–year OS for LGG patients who were younger than 40 and had aggressive surgical resection (26). But, we did not observe any difference in OS and DFS of patients who underwent GTR, SRT, or biopsy. The results of a meta–analysis outlined the positive effect of GTR on survival of patients with gliomas, as it resulted in four–fold longer OS, compared to SRT (27). Another meta–analysis has also confirmed longer survival by more extensive surgical resection in patients with glioma (28). Nevertheless, these studies have considered gliomas in general, not DA, while the results of study on 4113 patients with DA during 1999–2010 showed that OS improved during the years, despite the constant clinical practice at the study center (29), which rejects the role of extent of surgical resection or RT dose on survival of patients with DA. The authors of this study have attributed this improvement of patients' OS to the use of Temozolomide and improved neuro–oncologic standard of care (29). Accordingly, it can be concluded that the diversity of the results of the studies about the effect of surgery on OS is related to the influence of other factors on this outcome.

The results of the present study also showed that chemotherapy and RT did not influence the OS of patients with DA, while mean DFS was different according to chemotherapy and RT dose. The results of the study by Tunthanathip and colleagues also showed that RT following surgery did not improve the prognosis of patients with DA (18), which is consistent with the results of the present study. Kumthekar and colleagues also showed no significant difference in OS of patients treated with adjuvant RT + chemotherapy, RT alone, or chemotherapy alone in older patients with LGG (20). Youland and colleagues have also reported that RT or chemotherapy after surgery had no effect on the OS of adult patients with nonpilocytic LGG (16). Although these results are consistent with that of the present study, considering no role for RT or chemotherapy on OS of patients with DA, each study has used a different regimen in this regard; therefore, the results of the studies cannot be easily compared. There is unfortunately great disagreements among neuro–oncologists considering the choice of RT and chemotherapy (alone or in combination) and appropriate amount and timing of it (adjuvant or at progression). In the study by Kashi and colleagues, RT at progression resulted in improved OS, compared to adjuvant RT, while adjuvant RT resulted in better DFS, compared to RT at progression (21). This difference in the results reported could also be related to the influence of other factors, as Spych and colleagues have also reported higher OS in patients treated with salvage chemotherapy due to disease progression after RT (19). These results suggest the usefulness of RT or chemotherapy for a specific subgroup of patients, while more extensive studies are required in this regard for definite conclusions (due to the heterogeneity of treatment strategies among studies).

One of the limitations of the present study included collection of samples from one medical center, which reduces the reproducibility of the results. Secondly, the results of this study was based on the data retrospectively collected from medical records and any bias in data collection could affect the results. We were also unable to suggest correlation between variables, due to the nature of the study. The last but not the least, there are several factors that can affect the study outcomes (OS and DFS), which could confound the results.

CONCLUSION

The preset study showed the OS and DFS rates of patients with DA and suggested the factors that can affect the patients' outcome. Considering the effect of performance of chemotherapy and RT dose on patients' outcome, specifically DFS, it is recommended to pay greater attention to appropriate choice of treatment strategy of patients with DA. Further randomized controlled studies are required to determine the significance of these treatment strategies on patients' outcome.

CONFLICT OF INTERESTS

The authors of the present study declare that there is no Conflict of interest

ABBREVIATIONS

OS; overall survival, DFS; disease–free survival, CNS; central nervous system, WHO; world health organization, DA; diffuse astrocytoma, GTR; gross total resection, RT; radiotherapy, LGG; low–grade gliomas; STR; subtotal resection, SD; standard deviation.

REFERENCES

1. de Robles P, Fiest KM, Frolkis AD, Pringsheim T, Atta C, St. Germaine-Smith C, et al. The worldwide incidence and prevalence of primary brain tumors: a systematic review and meta-analysis. Neuro-oncology. 2015;17(6):776-83.
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA: a cancer journal for clinicians. 2021;71(3):209-49.
3. Comelli I, Lippi G, Campana V, Servadei F, Cervellin G. Clinical presentation and epidemiology of brain tumors firstly diagnosed in adults in the Emergency Department: a 10-year, single center retrospective study. Annals of translational medicine. 2017;5(13).
4. Mabray MC, Barajas RF, Cha S. Modern brain tumor imaging. Brain tumor research and treatment. 2015;3(1):8-23.
5. Arruebo M, Vilaboa N, Sáez-Gutierrez B, Lambea J, Tres A, Valladares M, et al. Assessment of the evolution of cancer treatment therapies. Cancers. 2011;3(3):3279-330.
6. Aldape K, Brindle KM, Chesler L, Chopra R, Gajjar A, Gilbert MR, et al. Challenges to curing primary brain tumours. Nature reviews Clinical oncology. 2019;16(8):509-20.
7. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, et al. The 2007 WHO classification of tumours of the central nervous system. Acta neuropathologica. 2007;114(2):97-109.
8. Perkins A, Liu G. Primary brain tumors in adults: diagnosis and treatment. American family physician. 2016;93(3):211-7.
9. Ostrom QT, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2011–2015. Neuro-oncology. 2018;20(suppl_4):iv1-iv86.
10. Walker C, Baborie A, Crooks D, Wilkins S, Jenkinson M. Biology, genetics and imaging of glial cell tumours. The British journal of radiology. 2011;84(special_issue_2):S90-S106.
11. Barragán-Pérez EJ, Altamirano-Vergara CE, Alvarez-Amado DE, García-Beristain JC, Chico-Ponce-de-León F, González-Carranza V, et al. The Role of Time as a Prognostic Factor in Pediatric Brain Tumors: a Multivariate Survival Analysis. Pathology & Oncology Research. 2020;26(4):2693-701.
12. Deb S, Pendharkar AV, Schoen MK, Altekruse S, Ratliff J, Desai A. The effect of socioeconomic status on gross total resection, radiation therapy and overall survival in patients with gliomas. Journal of neuro-oncology. 2017;132(3):447-53.
13. Almenawer SA, Badhiwala JH, Alhazzani W, Greenspoon J, Farrokhyar F, Yarascavitch B, et al. Biopsy versus partial versus gross total resection in older patients with high-grade glioma: a systematic review and meta-analysis. Neuro-oncology. 2015;17(6):868-81.
14. Yang K, Nath S, Koziarz A, Badhiwala JH, Ghayur H, Sourour M, et al. Biopsy versus subtotal versus gross total resection in patients with low-grade glioma: a systematic review and meta-analysis. World neurosurgery. 2018;120:e762-e75.
15. Wegman-Ostrosky T, Reynoso-Noverón N, Mejía-Pérez SI, Sánchez-Correa TE, Alvarez-Gómez RM, Vidal-Millán S, et al. Clinical prognostic factors in adults with astrocytoma: Historic cohort. Clinical neurology and neurosurgery. 2016;146:116-22.
16. Youland RS, Brown PD, Giannini C, Parney IF, Uhm JH, Laack NN. Adult Low-grade Glioma 19-year Experience at a Single Institution. American journal of clinical oncology. 2013;36(6):612.
17. Tove L-L, Hanssøn HA, Stein S, Sverre H. Prognostic value of histological features in diffuse astrocytomas WHO grade II. International journal of clinical and experimental pathology. 2012;5(2):152.
18. Tunthanathip T, Ratanalert S, Sae-Heng S, Oearsakul T, Sakaruncchai I, Kaewborisutsakul A, et al. Prognostic factors and nomogram predicting survival in diffuse astrocytoma. Journal of neurosciences in rural practice. 2020;11(01):135-43.
19. Spych M, Gottwald L, Jesień-Lewandowicz E, Sztajer S, Fijuth J. Response to postoperative radiotherapy as a prognostic factor for patients with low-grade gliomas. Oncology letters. 2012;4(3):455-60.
20. Kumthekar P, Patel V, Bridge C, Rademaker A, Helenowski I, Mrugala MM, et al. Prognosis of older patients with low-grade glioma: a retrospective study. Integrative cancer science and therapeutics. 2017;4(5).
21. Kashi ASY, Rakhsha A, Houshyari M. Overall survival in adult patients with low-grade, supratentorial glioma: ten years' follow up at a single institution. Electronic physician. 2015;7(3):1114.
22. Mucha-Małecka A, Gliński B, Hetnał M, Jarosz M, Urbański J, Frączek-Błachut B, et al. Long-term follow-up in adult patients with low-grade glioma (WHO II) postoperatively irradiated. Analysis of prognostic factors. Reports of Practical Oncology and Radiotherapy. 2012;17(3):141-5.
23. Anvari K, Toussi MS, Shahidsales S, Motlagh F, Ehsaee MR, Afshari F. Treatment outcomes and prognostic factors in adult astrocytoma: In North East of Iran. Iranian journal of cancer prevention. 2016;9(4).
24. Daniels TB, Brown PD, Felten SJ, Wu W, Buckner JC, Arusell RM, et al. Validation of EORTC prognostic factors for adults with low-grade glioma: a report using intergroup 86-72-51. International Journal of Radiation Oncology* Biology* Physics. 2011;81(1):218-24.
25. Jakola AS, Unsgård G, Myrmel KS, Kloster R, Torp SH, Losvik OK, et al. Surgical strategy in grade II astrocytoma: a population-based analysis of survival and morbidity with a strategy of early resection as compared to watchful waiting. Acta neurochirurgica. 2013;155(12):2227-35.
26. Kaya V, Aksu MG, Korcum AF, Özdemir B, Çeçen Y, Sindir B, et al. Clinical prognostic factors of adjuvant radiation therapy for low-grade gliomas: results of 10 years survival. International journal of clinical and experimental medicine. 2014;7(5):1336.
27. Tang S, Liao J, Long Y. Comparative assessment of the efficacy of gross total versus subtotal total resection in patients with glioma: a meta-analysis. International Journal of Surgery. 2019;63:90-7.
28. Hardesty DA, Sanai N. The value of glioma extent of resection in the modern neurosurgical era. Frontiers in neurology. 2012;3:140.
29. Dong X, Noorbakhsh A, Hirshman BR, Zhou T, Tang JA, Chang DC, et al. Survival trends of grade I, II, and III astrocytoma patients and associated clinical practice patterns between 1999 and 2010: a SEER-based analysis. Neuro-oncology practice. 2016;3(1):29-38.

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