
Top 100 Most Cited Articles on Brain Tumors

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Abstract: Background: A large number of published articles exist regarding intracranial tumors. This article aims to present the 100 most-cited articles on brain tumors and to perform a bibliometric analysis. Methods: In May 2021, the authors performed a title- focused search using Clarivate's Web of Science database in order to identify the most cited articles centered on brain tumors. Results: Our search retrieved 99,652 articles on brain tumors. The top 100 most cited publications, published between 1979 and 2017, were identified by the number of times they were cited in other articles. The median number of citations for the top 100 articles was 726.5 citations. All of them combined have been cited 118,703 times, with an average citation per item of 24.84. The most cited article was from the European Organization for Research and Treatment of Cancer Brain Tumor and Radiotherapy groups in the New England Journal of Medicine, titled "Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma". Conclusion: The aim of this study was to present analysis of the top 100 most cited articles regarding any tumor type of the brain. All 100 articles in our dataset had over 400 citations each and can thus be considered citation classics, publications in the field that are highly cited. The citation analysis of the top 100 articles regarding brain tumors shows the current landscape of noteworthy publications in the field of study. Clinician scientists entering the field would benefit from understanding the most prominent citation classics. The findings of this study should also be of importance to all individuals entering the field of neuro-oncology.

Keywords: Bibliometrics, Brain Tumors, Most Cited

1. Introduction

In the past several decades, there has been a dramatic growth in brain tumor research, as genomic and metabolic studies become increasingly prevalent [1, 2], and as new chemo-radiotherapy modalities and surgical techniques emerge [3, 4]. A number of articles have significantly impacted the field of neuro-oncology, opening doors to new areas of investigation or providing evidence that define practice-changing guidelines in clinical management. However, owing to the exponential rise of publications on brain tumors, significant studies that may be foundational in our understanding of brain tumors or may pave the way for future research are often overlooked. It has become increasingly difficult to distinguish these

noteworthy studies, as journal databases such as PubMed often return many thousands of results for a given search.

Bibliometric citation analysis has emerged as a useful tool to identify the most frequently cited or high-impact articles within a given field, thus isolating landmark studies in the field. While bibliometric analysis has previously been done in other fields of oncology, no prior study to our knowledge has investigated all brain tumor subtypes in a combined analysis. This is important because in reviewing together these landmark studies, it is possible to gain insight into neuro-oncology as a whole, its development over time, and the various contributions of individual articles, researchers, institutions, and countries. This understanding may assist in

clinical decision-making at the bedside level, provide an efficient review of the field to clinician scientists, and highlight areas requiring further investigation. Thus, the purpose of this study was to use a bibliometric analysis to identify the 100 most cited articles in the brain tumor literature in order to identify the most influential contributions to the field.

2. Methods

Using Clarivate's Web of Science as prior studies have done [5–7], the following search strategy was run through Clarivate's Web of Science All Databases collection on May 17, 2021:

TS=("brain tumor" OR "brain neoplasm" OR "brain metastases" OR "brain metastasis" OR "brain cancer" OR "intracranial tumor" OR "intracranial neoplasm" OR "cerebral metastases" OR "cerebral metastasis").

No exclusion criteria, such as publication date restriction was applied. The results were sorted in descending order by the number of times cited. Authors reviewed the top 200 results, excluding articles that were not specific to brain tumor research. From the top 100 most cited articles, authors extracted the article's citation information, the country of origin, type of publication (eg. basic science, clinical outcome, review, case report, epidemiological study, neuroradiologic study), type of brain tumor, therapy investigated, publication date, years since publication, total times cited, citations per year, and citations per year (CY) rank. The CY rank was calculated as $CY = \text{total number of times cited} / \text{years since publication}$. 2019 two-year impact

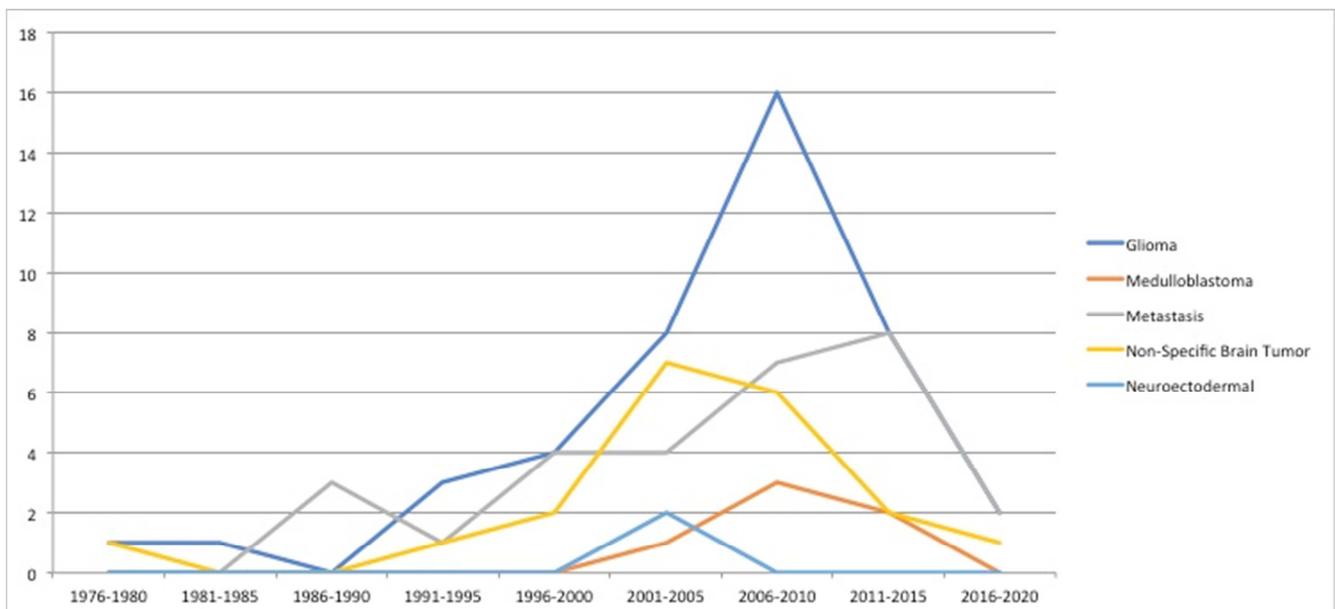
factor for journals were obtained from the Web of Science's Journal Citation Reports [8].

3. Results

The search retrieved 99,652 articles on brain tumors, and the top 100 most cited publications were identified by the number of times they were cited in other articles (Table 1). All 100 articles in our dataset had over 400 citations each and can thus be considered citation classics, publications in the field that are highly cited [9]. The median number of citations for the top 100 articles was 726.5 citations (628.5–1,119.75 IQR). Mean times cited were 1276.41 citations (1604.29 SD).

The top 100 articles were published between 1979 and 2017. Most publications were in the 2006–2010 5-year epoch ($n=32$). Over 38 years, noteworthy studies on gliomas, metastases, and non-specific brain tumors increased in frequency, peaking between 2000 and 2015. Noteworthy publications of basic studies or animal studies, clinical outcomes, or reviews also steadily increased and peaked between 2000 and 2015 (Figure 1).

Basic Science ($n=37$) was the most common type of paper (Table 2). Most basic science papers investigated gene expression or stem cells in glioma progression ($n=19$). Clinical outcome projects ($n=32$), including clinical trials, cohort studies, and case series, were the next most common type of paper. Most clinical outcome projects investigated radiotherapy or chemotherapy efficacy in treatment of brain metastases ($n=20$). Glioma ($n=43$) was the most commonly studied brain tumor subtype followed by brain metastasis ($n=29$).



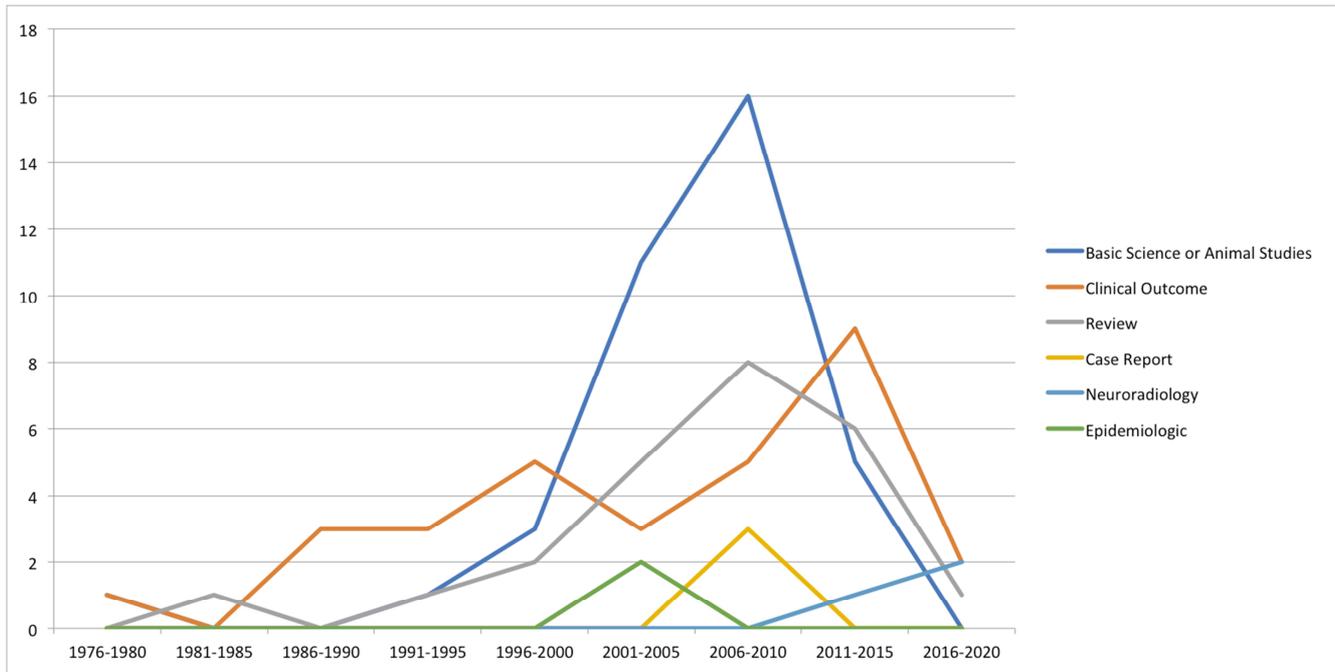


Figure 1. Temporal Trends: A) Frequency of publication by tumor type for each 5-year epoch in our top 100 cited articles. B) Frequency of publication by type of study conducted for each 5-year epoch in our top 100 cited articles.

The most cited article was from the European Organization for Research and Treatment of Cancer Brain Tumor and Radiotherapy groups in the New England Journal of Medicine, titled “Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma” and was cited 11,929 times [10] (Table 1). The article with the highest CY rank was authored by Dr. David N Louis *et al.* of Harvard Medical School in Acta Neuropathologica, titled “The 2016

World Health Organization Classification of Tumors of the Central Nervous System: a summary [11].” Most articles were published by first authors affiliated with institutions in the United States of America (n=68) (Table 3). The next most common country of publication was Germany (n=9). 14 total countries were represented. Over the 100 articles, 40 total journals were represented. The articles were most commonly published in the journal Nature (n=9, IF 42.779) (Table 4).

Table 1. Top 100 Articles. The top 100 most cited articles pertaining to brain tumors ranked by number of times cited. CY was calculated by total number of citations divided by number of years published. Top 100 articles were ranked by CY.

Article Citation	Total Times Cited	CY Rank
Stupp R, Mason WP, van den Bent MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005; 352 (10): 987-996. doi: 10.1056/NEJMoa043330	11,929	2
Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol. 2007; 114 (2): 97-109. doi: 10.1007/s00401-007-0243-4	7,279	3
Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol. 2016; 131 (6): 803-820. doi: 10.1007/s00401-016-1545-1	5,966	1
Singh SK, Hawkins C, Clarke ID, et al. Identification of human brain tumour initiating cells. Nature. 2004; 432 (7015): 396-401. doi: 10.1038/nature03128	5,530	5
Chin L, Meyerson M, Aldape K, et al. Comprehensive genomic characterization defines human glioblastoma genes and core pathways. Nature. 2008; 455 (7216): 1061-1068. doi: 10.1038/nature07385	4,857	4
Bao S, Wu Q, McLendon RE, et al. Glioma stem cells promote radioresistance by preferential activation of the DNA damage response. Nature. 2006; 444 (7120): 756-760. doi: 10.1038/nature05236	4,232	7
Singh SK, Clarke ID, Terasaki M, et al. Identification of a cancer stem cell in human brain tumors. Cancer Res. 2003; 63 (18): 5821-5828.	3,988	10
Parsons DW, Jones S, Zhang X, et al. An integrated genomic analysis of human glioblastoma Multiforme. Science (80-). 2008; 321 (5897): 1807-1812. doi: 10.1126/science.1164382	3,948	6
Dang L, White DW, Gross S, et al. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. Nature. 2009; 462 (7274): 739-U52. doi: 10.1038/nature08617	2,121	12
Chan JA, Krichevsky AM, Kosik KS. MicroRNA-21 is an antiapoptotic factor in human glioblastoma cells. Cancer Res. 2005; 65 (14): 6029-6033. doi: 10.1158/0008-5472.Can-05-0137	2,115	15
PATCHELL RA, Tibbs PA, Walsh JW, et al. A RANDOMIZED TRIAL OF SURGERY IN THE TREATMENT OF SINGLE METASTASES TO THE BRAIN. N Engl J Med. 1990; 322 (8): 494-500. doi: 10.1056/nejm19900223220802	2,080	44
Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012; 380 (9840): 499-505. doi: 10.1016/s0140-6736(12)60815-0	2,040	9

Article Citation	Total Times Cited	CY Rank
Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three radiation therapy oncology group (RTOG) brain metastases trials. <i>Int J Radiat Oncol Biol Phys.</i> 1997; 37 (4): 745-751. doi: 10.1016/s0360-3016(96)00619-0	1,751	39
Pomeroy SL, Tamayo P, Gaasenbeek M, et al. Prediction of central nervous system embryonal tumour outcome based on gene expression. <i>Nature.</i> 2002; 415 (6870): 436-442. doi: 10.1038/415436a	1,680	30
Andrews DW, Scott CB, Sperduto PW, et al. Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial. <i>Lancet.</i> 2004; 363 (9422): 1665-1672. doi: 10.1016/s0140-6736(04)16250-8	1,672	25
Calabrese C, Poppleton H, Kocak M, et al. A perivascular niche for brain tumor stem cells. <i>Cancer Cell.</i> 2007; 11 (1): 69-82. doi: 10.1016/j.ccr.2006.11.020	1,561	20
Chang EL, Wefel JS, Hess KR, et al. Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial. <i>Lancet Oncol.</i> 2009; 10 (11): 1037-1044. doi: 10.1016/s1470-2045(09)70263-3	1,448	17
Aoyama H, Shirato H, Tago M, et al. Stereotactic radiosurgery plus whole-brain radiation therapy vs stereotactic radiosurgery alone for treatment of brain metastases - A randomized controlled trial. <i>Jama-Journal Am Med Assoc.</i> 2006; 295 (21): 2483-2491. doi: 10.1001/jama.295.21.2483	1,446	26
Hemmati HD, Nakano I, Lazareff JA, et al. Cancerous stem cells can arise from pediatric brain tumors. <i>Proc Natl Acad Sci U S A.</i> 2003; 100 (25): 15178-15183. doi: 10.1073/pnas.2036535100	1,426	34
Liu G, Yuan X, Zeng Z, et al. Analysis of gene expression and chemoresistance of CD133 (+) cancer stem cells in glioblastoma. <i>Mol Cancer.</i> 2006; 5. doi: 10.1186/1476-4598-5-67	1,330	29
Menze BH, Jakab A, Bauer S, et al. The Multimodal Brain Tumor Image Segmentation Benchmark (BRATS). <i>IEEE Trans Med Imaging.</i> 2015; 34 (10): 1993-2024. doi: 10.1109/tmi.2014.2377694	1,271	11
DeAngelis LM. Medical progress: Brain tumors. <i>N Engl J Med.</i> 2001; 344 (2): 114-123. doi: 10.1056/nejm200101113440207	1,241	51
Patchell RA, Tibbs PA, Regine WF, et al. Postoperative radiotherapy in the treatment of single metastases to the brain - A randomized trial. <i>Jama-Journal Am Med Assoc.</i> 1998; 280 (17): 1485-1489. doi: 10.1001/jama.280.17.1485	1,209	60
Kocher M, Soffiotti R, Abacioglu U, et al. Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study. <i>J Clin Oncol.</i> 2011; 29 (2): 134-141. doi: 10.1200/jco.2010.30.1655	1,159	18
Omuro A, DeAngelis LM. Glioblastoma and Other Malignant Gliomas A Clinical Review. <i>Jama-Journal Am Med Assoc.</i> 2013; 310 (17): 1842-1850. doi: 10.1001/jama.2013.280319	1,134	14
Auperin A, Arriagada R, Pignon JP, et al. Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. <i>N Engl J Med.</i> 1999; 341 (7): 476-484. doi: 10.1056/nejm199908123410703	1,115	64
Bos PD, Zhang XHF, Nadal C, et al. Genes that mediate breast cancer metastasis to the brain. <i>Nature.</i> 2009; 459 (7249): 1005-U137. doi: 10.1038/nature08021	1,097	27
Vredenburgh JJ, Desjardins A, Herndon II JE, et al. Bevacizumab plus irinotecan in recurrent glioblastoma multiforme. <i>J Clin Oncol.</i> 2007; 25 (30): 4722-4729. doi: 10.1200/jco.2007.12.2440	1,080	37
Sturm D, Witt H, Hovestadt V, et al. Hotspot Mutations in H3F3A and IDH1 Define Distinct Epigenetic and Biological Subgroups of Glioblastoma. <i>Cancer Cell.</i> 2012; 22 (4): 425-437. doi: 10.1016/j.ccr.2012.08.024	1,013	19
Brem H, Piantadosi S, Burger PC, et al. PLACEBO-CONTROLLED TRIAL OF SAFETY AND EFFICACY OF INTRAOPERATIVE CONTROLLED DELIVERY BY BIODEGRADABLE POLYMERS OF CHEMOTHERAPY FOR RECURRENT GLIOMAS. <i>Lancet.</i> 1995; 345 (8956): 1008-1012. doi: 10.1016/s0140-6736(95)90755-6	1,009	76
Havaei M, Davy A, Warde-Farley D, et al. Brain tumor segmentation with Deep Neural Networks. <i>Med Image Anal.</i> 2017; 35: 18-31. doi: 10.1016/j.media.2016.05.004	996	8
Shaw E, Scott C, Souhami L, et al. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: Final report of RTOG protocol 90-05. <i>Int J Radiat Oncol Biol Phys.</i> 2000; 47 (2): 291-298. doi: 10.1016/s0360-3016(99)00507-6	975	70
Ohgaki H, Kleihues P. Genetic pathways to primary and secondary glioblastoma. <i>Am J Pathol.</i> 2007; 170 (5): 1445-1453. doi: 10.2353/ajpath.2007.070011	941	43
Van Meir EG, Hadjipanayis CG, Norden AD, Shu H-K, Wen PY, Olson JJ. Exciting New Advances in Neuro-Oncology The Avenue to a Cure for Malignant Glioma. <i>Ca-a Cancer J Clin.</i> 2010; 60 (3): 166-193. doi: 10.3322/caac.20069	925	32
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Jain RK, Di Tomaso E, Duda DG, Loeffler JS, Sorensen AG, Batchelor TT. Angiogenesis in brain tumours. <i>Nat Rev Neurosci.</i> 2007; 8 (8): 610-622. doi: 10.1038/nrn2175	909	47
Nakamizo A, Marini F, Amano T, et al. Human bone marrow-derived mesenchymal stem cells in the treatment of gliomas. <i>Cancer Res.</i> 2005; 65 (8): 3307-3318. doi: 10.1158/0008-5472.Can-04-1874	881	56
Barnholtz-Sloan JS, Sloan AE, Davis FG, Vigneau FD, Lai P, Sawaya RE. Incidence proportions of brain metastases in patients diagnosed (1973 to 2001) in the metropolitan Detroit cancer surveillance system. <i>J Clin Oncol.</i> 2004; 22 (14): 2865-2872. doi: 10.1200/jco.2004.12.149	875	61
Zhao S, Lin Y, Xu W, et al. Glioma-Derived Mutations in IDH1 Dominantly Inhibit IDH1 Catalytic Activity and Induce HIF-1 alpha. <i>Science (80-).</i> 2009; 324 (5924): 261-265. doi: 10.1126/science.1170944	838	42
Pereira S, Pinto A, Alves V, Silva CA. Brain Tumor Segmentation Using Convolutional Neural Networks in MRI Images. <i>IEEE Trans Med Imaging.</i> 2016; 35 (5): 1240-1251. doi: 10.1109/tmi.2016.2538465	823	13
Sperduto PW, Kased N, Roberge D, et al. Summary Report on the Graded Prognostic Assessment: An Accurate and Facile	794	31

Article Citation	Total Times Cited	CY Rank
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Carro MS, Lim WK, Alvarez MJ, et al. The transcriptional network for mesenchymal transformation of brain tumours. <i>Nature.</i> 2010; 463 (7279): 318-U68. doi: 10.1038/nature08712	788	41
Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults: a "state of the science" review. <i>Neuro Oncol.</i> 2014; 16 (7): 896-913. doi: 10.1093/neuonc/nou087	765	21
Rudin CM, Hann CL, Laterra J, et al. Brief Report: Treatment of Medulloblastoma with Hedgehog Pathway Inhibitor GDC-0449. <i>N Engl J Med.</i> 2009; 361 (12): 1173-1178. doi: 10.1056/NEJMoa0902903	762	49
Seoane J, Le H V, Shen LJ, Anderson SA, Massague J. Integration of Smad and Forkhead pathways in the control of neuroepithelial and glioblastoma cell proliferation. <i>Cell.</i> 2004; 117 (2): 211-223. doi: 10.1016/s0092-8674(04)00298-3	761	72
Vescovi AL, Galli R, Reynolds BA. Brain tumour stem cells. <i>Nat Rev Cancer.</i> 2006; 6 (6): 425-436. doi: 10.1038/nrc1889	755	65
Silber J, Lim DA, Petritsch C, et al. miR-124 and miR-137 inhibit proliferation of glioblastoma multiforme cells and induce differentiation of brain tumor stem cells. <i>Bmc Med.</i> 2008; 6. doi: 10.1186/1741-7015-6-14	746	52
Bals J, Meyer J, Mueller W, Korshunov A, Hartmann C, von Deimling A. Analysis of the IDH1 codon 132 mutation in brain tumors. <i>Acta Neuropathol.</i> 2008; 116 (6): 597-602. doi: 10.1007/s00401-008-0455-2	740	53
Fine HA, Dear KBG, Loeffler JS, Black PM, Canellos GP. METAANALYSIS OF RADIATION-THERAPY WITH AND WITHOUT ADJUVANT CHEMOTHERAPY FOR MALIGNANT GLIOMAS IN ADULTS. <i>Cancer.</i> 1993; 71 (8): 2585-2597. doi: 10.1002/1097-0142(19930415)71:8<2585::Aid-cnrc2820710825>3.0.Co; 2-s	727	90
Yung WKA, Albright RE, Olson J, et al. A phase II study of temozolomide vs. procarbazine in patients with glioblastoma multiforme at first relapse. <i>Br J Cancer.</i> 2000; 83 (5): 588-593. doi: 10.1054/bjoc.2000.1316	726	82
Kondziolka D, Patel A, Lunsford LD, Kassam A, Flickinger JC. Stereotactic radiosurgery plus whole brain radiotherapy versus radiotherapy alone for patients with multiple brain metastases. <i>Int J Radiat Oncol Biol Phys.</i> 1999; 45 (2): 427-434. doi: 10.1016/s0360-3016(99)00198-4	716	78
Ignatova TN, Kukekov VG, Laywell ED, Suslov ON, Vrionis FD, Steindler DA. Human cortical glial tumors contain neural stem-like cells expressing astroglial and neuronal markers in vitro. <i>Glia.</i> 2002; 39 (3): 193-206. doi: 10.1002/glia.10094	716	85
Vecht CJ, Haaxmareiche H, Noordijk EM, et al. TREATMENT OF SINGLE BRAIN METASTASIS - RADIOTHERAPY ALONE OR COMBINED WITH NEUROSURGERY. <i>Ann Neurol.</i> 1993; 33 (6): 583-590. doi: 10.1002/ana.410330605	715	91
Stommel JM, Kimmelman AC, Ying H, et al. Coactivation of receptor tyrosine kinases affects the response of tumor cells to targeted therapies. <i>Science (80-).</i> 2007; 318 (5848): 287-290. doi: 10.1126/science.1142946	712	63
Kircher MF, de la Zerda A, Jokerst J V, et al. A brain tumor molecular imaging strategy using a new triple-modality MRI-photoacoustic-Raman nanoparticle. <i>Nat Med.</i> 2012; 18 (5): 829-U235. doi: 10.1038/nm.2721	704	36
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Yuan XP, Curtin J, Xiong YZ, et al. Isolation of cancer stem cells from adult glioblastoma multiforme. <i>Oncogene.</i> 2004; 23 (58): 9392-9400. doi: 10.1038/sj.onc.1208311	645	48
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Loscher W, Potschka H. Drug resistance in brain diseases and the role of drug efflux transporters. <i>Nat Rev Neurosci.</i> 2005; 6 (8): 591-602. doi: 10.1038/nrn1728	636	74
Van den Bent MJ, Brandes AA, Taphoorn MJB, et al. Adjuvant Procarbazine, Lomustine, and Vincristine Chemotherapy in Newly	633	35

Article Citation	Total Times Cited	CY Rank
Diagnosed Anaplastic Oligodendroglioma: Long-Term Follow-Up of EORTC Brain Tumor Group Study 26951. <i>J Clin Oncol.</i> 2013; 31 (3): 344-350. doi: 10.1200/jco.2012.43.2229		
Yauch RL, Dijkgraaf GJP, Alicke B, et al. Smoothed Mutation Confers Resistance to a Hedgehog Pathway Inhibitor in Medulloblastoma. <i>Science</i> (80-). 2009; 326 (5952): 572-574. doi: 10.1126/science.1179386	632	59
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Article Citation	Total Times Cited	CY Rank
Rubin JB, Kung AL, Klein RS, et al. A small-molecule antagonist of CXCR4 inhibits intracranial growth of primary brain tumors. Proc Natl Acad Sci U S A. 2003; 100 (23): 13513-13518. doi: 10.1073/pnas.2235846100	530	87
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Table 2. Frequency of Publication. The top 100 most cited brain tumor articles by type of brain tumor studied and type of study conducted. Total for each category is represented in brackets.

	Basic Science (37)	Clinical Outcome (32)	Review (23)	Case Report (3)	Neuroradiology (3)	Epidemiologic (3)
Glioma (43)	19	9	11	2	2	0
Metastasis (29)	3	20	4	-	-	2
Non-Specific Brain Tumor [20]	10	3	6	-	1	-
Medulloblastoma (6)	3	-	2	1	-	-
Neuroectodermal (2)	2	-	-	-	-	-

Table 3. Countries of article origin. The top 100 most cited articles were categorized by first author institution's country.

Country	Number of Publications
United States of America	68
Germany	9
The Netherlands	5
France	4
Canada	3
Japan	3
Australia	1
China	1
Israel	1
Italy	1
Portugal	1
Sweden	1
Switzerland	1
United Kingdom	1

Table 4. Journals of Publication. The top 100 most cited articles were categorized by journal of publication. 2019 2-year Impact Factor for each journal was found in Web of Science's Journal Citation Reports. (8) "Other" includes journals that each published only one article.

Name of Journal	Count	2019 Impact Factor
Nature	9	42.779
International Journal Of Radiation Oncology, Biology, Physics	7	5.859
Journal Of Clinical Oncology	7	32.956
New England Journal Of Medicine	7	74.699
Lancet	6	60.390
Science	6	41.846
Acta Neuropathologica	5	14.256
Lancet Oncology	5	33.752
Cancer	4	5.772
Cancer Research	4	9.727
JAMA-Journal Of The American Medical Association	4	45.540
Proceedings Of The National Academy Of Sciences Of The United States Of America	3	9.412
Cancer Cell	2	26.602
IEEE Transactions On Medical Imaging	2	6.685
Nature Medicine	2	36.130
Nature Reviews Neuroscience	2	33.654
Other	25	N/A

4. Discussion

Bibliometric analysis plays an important role in understanding the current landscape of the literature in any field of study in order to appreciate the influence of various scientific articles and identify gaps in scientific inquiry. The frequency of citation can be used as surrogate for an article's academic success and impact on the field. Prior citation

studies have been completed in many fields of oncology including head and neck cancers [5], spinal oncology [6], and squamous cell carcinomas [7]. In neuro-oncology, prior citation analyses have been conducted regarding specific brain tumor subtypes, such as metastases, ependymomas, meningiomas, and astrocytomas [12–15]. Unlike these studies, the most cited articles in this study are fairly recent, with our oldest article published in 1979. To our knowledge, the present analysis is the first to analyze the most cited

articles regarding any tumor type of the brain and should be of importance to all individuals entering the field of neuro-oncology.

Elements like the impact factor of a journal or publications originating from the USA have traditionally been thought to influence the academic success of studies [16, 17]. Prior bibliometric analyses have found that most top 100 articles come from the USA [12–15]. Although most articles in the top 100 of our analysis were also published in the USA, of the top ten articles, only six were published in the USA. The most cited article was published in Switzerland [10], indicating that the country of publication may not be a major barrier to academic success of the article. As expected, journals with high two-year impact factors were more commonly represented in our dataset. The International Journal Of Radiation Oncology, Biology, Physics with a 2019 impact factor of 5.859 was tied for the second highest published journal in our dataset with seven articles of our top 100 list. Four of these articles were published prior to 2000, when the impact factor for the journal was 3.058 [8]. While all articles were published in journals with impressive impact factors, there is no clear correlation between size of impact factor and academic success in times cited.

Brain metastases and gliomas were the most commonly studied in our list with 72 publications of gliomas or brain metastases. This is not surprising, as brain metastases are the most common brain tumors, with varying reported incidence rate [18, 19] and gliomas are the most common malignant brain tumors, affecting 6.0 of 100,000 individuals [20]. Noteworthy publications on gliomas increased in frequency and peaked in 2006-2010, while publications on brain metastases increased in frequency and peaked in 2011-2015, suggesting that there have been many recent advances in the understanding of these brain tumor types. However, there remains a relative lack of research among other tumor subtypes, and in particular with neuroectodermal tumors.

19 of 43 articles on gliomas were basic science studies. As basic science research provides the foundation for the development of clinical therapies, we predict that a rise in future noteworthy studies on gliomas will be clinical outcome projects. 20 of 29 articles on brain metastases were clinical outcome projects, investigating the efficacy of radiotherapy, chemotherapy, radiosurgery, or a combination of these therapies. Our analysis suggests that the focus of research on gliomas is rooted in basic science discoveries that can lead to targeted therapies, while research on metastases is focused more on the application of clinical therapies based on experiences from other cancers.

As expected, the two most cited articles have had a tremendous impact on the clinical practice of neuro-oncology. The Stupp protocol for glioblastoma is now the standard treatment for the treatment of glioblastoma. The scientific article establishing this chemo-radiotherapy regimen, which received the most citations, was a clinical trial published in the New England Journal of Medicine that compared radiotherapy with radiotherapy and temozolomide combination therapy for the treatment of glioblastomas. In

this trial, patients were randomly assigned to either group and monitored for survival. The study found that the addition of temozolomide to radiotherapy improved overall rate of survival in patients with glioblastomas [10]. To this day, this combination continues to be standard therapy for glioblastomas [21].

The 2nd and 3rd most commonly cited articles were related to the World Health Organization Classification of Tumors of the Central Nervous System. This system revolutionized CNS tumor diagnoses and fundamentally combined both molecular features with histological analysis in classification schemes. The second and third most cited articles in the top 100 list are reviews of the fourth and fifth edition of the WHO Classification of CNS Tumors respectively [11, 22]. The fourth edition, published in 2007, detailed new tumor types including angiocentric gliomas, papillary glioneuronal tumours, rosette-forming glioneuronal tumors of the fourth ventricle, papillary tumors of the pineal region, pituicytomas and spindle cell oncocytomas of the adenohypophysis. Additionally, new histological variants were added and the WHO grading system was overhauled [22]. The fifth edition, published in 2016, updated the previous entry and was the article with the highest CY rank. This was the first WHO classification to include molecular parameters to classify tumors. Newly acknowledged neoplasms were added while others without diagnostic values were removed. The study has played a major role in guiding clinical and epidemiological studies to help improve patient care [11].

The citation analysis of the top 100 articles regarding brain tumors shows the current landscape of noteworthy publications in the field of study. Clinician scientists entering the field would benefit from understanding the most prominent citation classics. Limitations to our study include certain articles not being indexed in the Clarivate's Web of Science which may skew our times cited data points. However, we believe that the overall accuracy of our list remains.

5. Conclusion

In this study, the authors identified the top 100 most cited articles regarding supratentorial tumors of the brain. Most of the top 100 articles were published in the USA. Brain metastases and gliomas were the most commonly studied tumors. Basic science studies regarding gliomas were extremely prevalent, while clinical outcome projects regarding brain metastases were prevalent. The most cited article was the Stupp protocol that continues to be the standard therapy for glioblastoma treatment.

Abbreviations

Citations per year (CY).

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Authors have no conflicts of interest to disclose. All authors

contributed equally to the design and writing of this manuscript and take responsibility for the accuracy of our results.

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