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=total number of times cited/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).
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.

<table>
<thead>
<tr>
<th>Article Citation</th>
<th>Total Times Cited</th>
<th>CY Rank</th>
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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 a 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, pilapillary glioneuronal tumours, rosette-forming glioneuronal tumors of the fourth ventricle, pilapillary 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 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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[9] What is a Citation Classic? [Internet]. [cited 2021 Jun 9]. Available from: http://garfield.library.upenn.edu/classics.html


